FluoRuGel: a versatile catalyst for aerobic alcohol oxidation in supercritical carbon dioxide

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FluoRuGel—a hybrid fluorinated silica glass doped with TPAP (tetra-*n*-propylammonium perruthenate)—is a versatile catalyst for the aerobic oxidation of different alcohols in dense phase CO_2 with marked stabilization and activity enhancement of perruthenate upon its confinement in the sol–gel fluorinated silica matrix. A brief competitive analysis shows large potential rewards.

Competitive advantage—and not benefits to the environment or to human health or safety—drives companies' choices in adopting new technologies, including any "greener" options designed to replace earlier methods.[1] For instance, the heterogeneously catalysed aerobic oxidation of alcohols in dense phase (or "supercritical")[2] carbon dioxide ($scCO_2$) is highly desirable as it would eliminate the need for both potentially polluting and toxic organic solvents[3] and stoichiometric Cr and Mn oxides employed in industrial oxidations.[4]

Remarkably, a number of highly selective heterogeneous catalytic reactions are carried out on an industrial scale in small, high-throughput reactors in which the CO_2 is recycled and eventually completely removed from the products by simply reducing the pressure.[5]

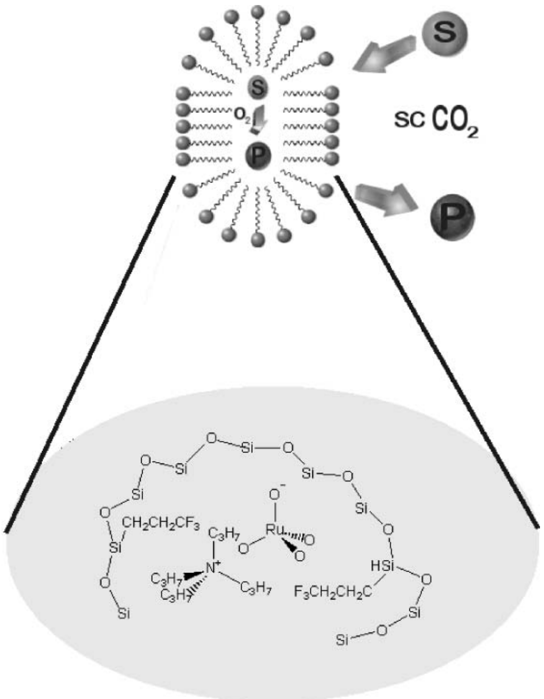
However, no oxidative conversions of alcohols are as yet conducted in this solvent[6] despite the fact that an efficient process in $scCO_2$ would afford a variety of carbonyls of high purity[7] meeting a key industry's requirement for commercial compounds which are widely used as precursors of drugs, vitamins, fragrances and other valuable fine chemicals.

The selective oxidation of alcohols to carbonyls in $scCO_2$ remained unexplored until the early 2000s when the aerial catalytic conversion of water-insoluble alcohols in supercritical CO_2 in a continuous fixed bed reactor over Pt–Pd–Bi/C was reported[8] to afford high yields of ketones and aromatic aldehydes, but *not* of primary aliphatic aldehydes, showing the same limitation in scope as noble metal-catalysed oxidation of alcohols in water.

A similar outcome was found using Pd/Al_2O_3 catalyst;[9] while higher selectivity to aldehydes was obtained using a Pt/C (teflon-coated) catalyst[10] in which the fluorinated surface, spilling off water molecules, prevented overoxidation to the acid. Finally, an interesting selectivity enhancement (compared to the process in liquid solvent) was recently reported for the aerobic oxidation of cyclohexanol to cyclohexanone in $scCO_2$ over a Cu-based catalyst.[11]

We recently introduced an efficient sol–gel solid catalyst (FluoRuGel) for the dehydrogenation of benzyl alcohol in $scCO_2$ with O_2 consisting of a fluorinated organic–inorganic silica glass doped with $[NPr_4]^+$ $[RuO_4]^-$.[12]

The oxoruthenate catalyst is entrapped in a porous sol–gel fluorinated matrix through which dense phase carbon dioxide dissolving both O_2 and the alcohol substrate, upon contact with the powdered CO_2-philic sol–gel material, rapidly spills the reactants into the cages where the oxidative dehydrogenation takes place, and then it extracts the benzaldehyde product (Scheme 1).



Scheme 1

Now we show how this results in another example of a molecule's reactivity change upon its sol–gel confinement, whereas the FluoRuGel–O_2–$scCO_2$ catalytic system selectively affords a variety of valuable carbonyl compounds (including those which are not obtained over supported noble metals) with the catalyst retaining its activity upon prolonged use.

Under the experimental conditions of Scheme 2, the aerobic oxidation of a variety of structurally different alcohols mediated by 10% mol of FluoRuGel-entrapped perruthenate proceeds to completion and no overoxidation of the alcohol to acid is observed (Table 1).

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Table 1 Oxidation of various alcohols (5×10^{-2} mmol) with O_2 (1 bar at 25 °C) catalysed by FluoRuGel (content of TPAP: 0.5×10^{-2} mmol per 100 mg) in $scCO_2$ at 75 °C and 22 MPa

Entry	Alcohol	$k \times 10^4/\text{mol}^{-1}\ \text{min}^{-1}$
1	Benzyl alcohol	49
2	Benzyl alcohol[a]	5.88 and 6.50[a]
3	2-Octanol	2.03
4	1-Octanol	5.02
5	1-Phenylethanol	6.46
6	*p*-MeO-benzyl alcohol	9.67 e 10.45
7	*m*-Cl-benzyl alcohol	8.27
8	*p*-Me-benzyl alcohol	8.27

[a] Upon washing the catalyst with CH_2Cl_2.

$$RR'\text{-CHOH} + 1/2\,O_2 \xrightarrow[\text{scCO}_2,\ 75^{\circ}\text{C, 220 bar}]{\textbf{FluoRuGel}\text{, 0.1 equiv.}} RR'\text{-CO} + H_2O$$

Scheme 2

The corresponding rate constants ($k_{cat.}$) were obtained from integrated pseudo first-order plots, *i.e.* ln(1-[aldehyde]$_{t=t}$/[aldehyde]$_{t=\infty}$) *vs.* time, which are linear up to 80–90% reaction as shown in Fig. 1 (the $k_{cat.}$ values are the slopes of these kinetic plots). The linearity of the plot shows that catalyst deactivation does *not* occur, at least in the time intervals examined.

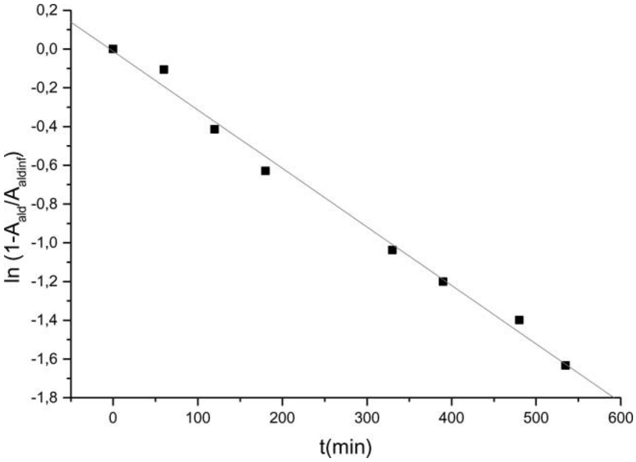

Fig. 1 Plot of log([aldehyde]$_{t=\infty}$ − ([aldehyde]$_{t=t}$) *vs.* time in the oxidation of benzyl alcohol (4.83×10^{-2} mmol) with oxygen (1 Pa at 25 °C) catalysed by FluoRuGel (TPAP content of 0.5×10^{-3} mmol) in $scCO_2$ at 22 MPa and 75 °C.

Carrying out the reaction at 75 °C, the pressure was set at 220 bar because $scCO_2$ at this pressure exhibits an optimal density of 0.67 g mL^{-1} which ensures complete solubilization of both the alcohol and the aldehyde in the homogeneous supercritical phase.

After recycling the catalyst upon washing with dichloromethane (DCM), the activity dropped to almost one tenth of its original value (entries 1 and 2 in Table 1). However, the same catalyst retained its activity in subsequent reaction runs with a variety of alcohol substrates with variations included in a factor of *ca.* 5 including the case of primary and secondary aliphatic substrates and showing the typical selectivity of TPAP for primary *vs.* secondary alcohols.

Washing the catalyst with DCM, as we originally attempted for recovering the product,[13] results in rapid evolution of gaseous Cl_2 bubbles with the significant reduction in the catalyst's original activity mentioned above (from 49 to 6×10^{-3} mol^{-1} min^{-1}). This shows first evidence that the sol–gel encapsulation of TPAP ion pairs indeed *changes* the reactivity of the entrapped dopant as TPAP alone readily dissolves in DCM which in fact is used as optimal solvent for perruthenate-mediated oxidations.[14]

We recently investigated this surprising outcome and found that rapid oxidation of DCM to Cl_2 does indeed take place; with a similar deactivation occurring also with a variety of other solvents, but deactivation occurred at the lowest pace with unreactive solvents such as *n*-hexane.[15] On the other hand, the use of dense phase CO_2 as the sole reaction and recovery solvent considerably improves catalyst stability and this, along with the sol–gel entrapment of the oxoruthenate, ensures stabilization of the material's reactivity. Ru-based oxidation catalysts generally lose their activity due to aggregation of the intermediate ruthenate species,[16] a phenomenon that is intrinsically prevented here by the encapsulation of perruthenate in the inner porosity of the sol–gel organosilica matrix.

We are currently investigating the nature (and the mechanism) of the entrapment of perruthenate in sol–gel glasses. XPS analysis of a similar ORMOSIL (organically modified silicate) doped with 1.7 wt% TPAP, for instance, is not capable of detecting the entrapped ruthenium even after two minutes' sputtering of the surface with Ar$^+$ ions accelerated at 4 keV to remove contaminants, showing how deep the encapsulation of Ru is in these catalysts.[17]

FluoRuGel consists of an agglomerate of organosilica particles whose regular surface geometry, upon large magnification, retains its morphology also on the nanometre scale (Fig. 2) which is that experienced by the approaching reactant molecules dissolved in $scCO_2$ (where the only diffusional barrier is that between the "supercritical" phase and the solid).[7]

In all cases, in fact, the oxidative dehydrogenation takes place *within* the sol–gel cages since no TPAP is leached from the catalyst during the reaction (in reaction samples withdrawn from the sc phase with a Ru detection limit <1 ppb).

Surprisingly, comparison between the reactivity of TPAP and TPAP encapsulated in FluoRuGel shows a different kinetic behaviour (Fig. 3).

While both homogeneous TPAP[14] and *also* ORMOSIL-entrapped TPAP[13] show typical perruthenate-mediated oxidation kinetics consisting of a fast initial stage up to 40–50% conversion, followed by a slower oxidation stage mediated by less reactive RuO_2, the reaction mediated by FluoRuGel shows an initial induction stage followed by a faster linear stage up to complete conversion of the substrate.

This points to improved catalysis by TPAP entrapped in the fluoroalkyl-modified silica matrix, *i.e.* a different chemistry of the entrapped dopant obtained by changing the properties of the entrapping silica sol–gel cage, similar to what happens when dopant molecules are co-entrapped in silica with a surfactant that modifies the sol–cage properties.[18]

We make the hypothesis that the partly positive carbon in highly dipolar $-CF_3$ groups[19] that concentrate at the cage surface[20] further attracts the entrapped RuO_4^- (Fig. 4) synergistically adding to the effect of the large $N(CH_2CH_2CH_3)_4^+$ cation whose use in combination with perruthenate was introduced to mitigate

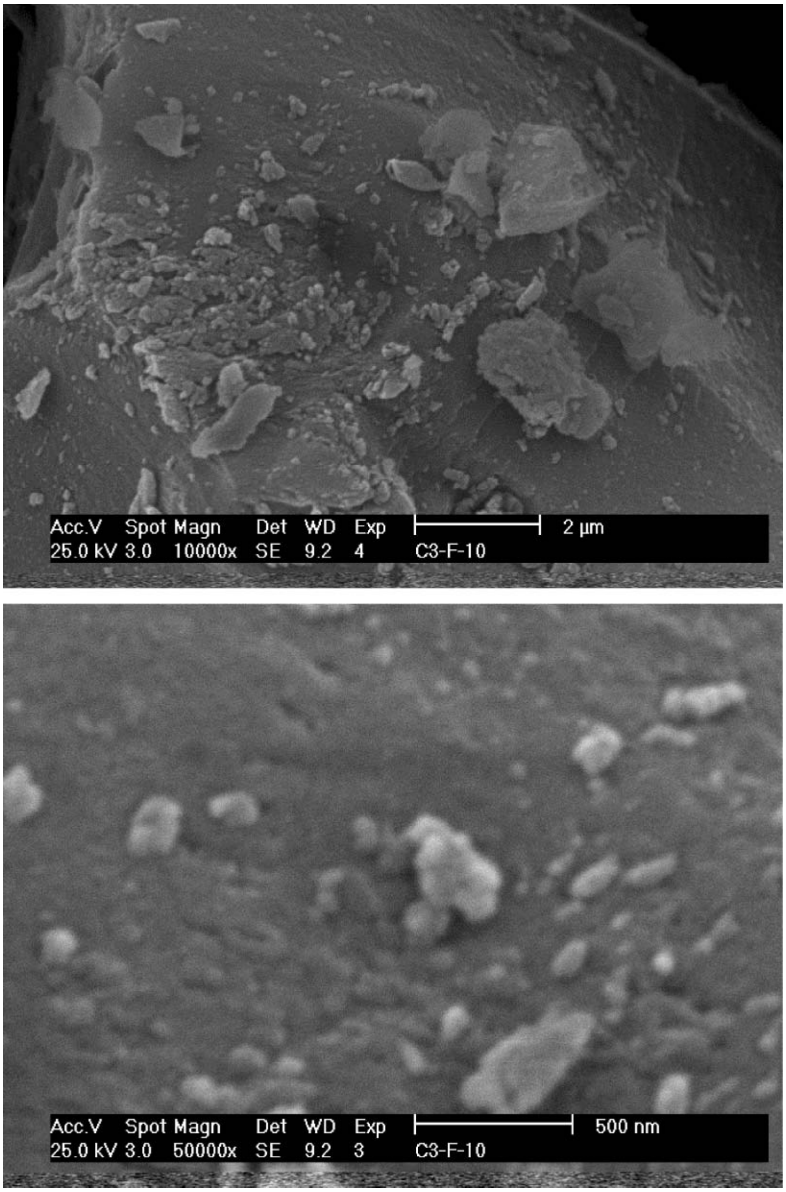

Fig. 2 FluoRuGel (shown here are SEM 100, 10 000 and 50 000x photographs) shows a regular, compact surface (*bottom*) which is experienced by the approaching reactant molecules.[25]

the strong oxidation power of RuO_4^- alone and thus promote selectivity.[21]

Eventually, this results in mutually isolated RuO_4^- anions entrapped in the inner porosity of the fluorinated gel where they mediate the oxidative dehydrogenation of the alcohol substrate according to a bi-electronic reaction mechanism that involves formation of the alcoholate,[15] but *without* formation of inactive RuO_2.[22]

In general, Ru-based aerobic catalysts[16] are highly selective and afford good yields of carbonyls but, in liquid-phase, they also show considerably lower activity compared to less selective carbon-supported Pt and Pd.[23] This is *not* the case in $scCO_2$. Hence, while Pt/C,[2] Pt–Pd–Bi/C[8] and Pd/Al_2O_3[9] afford the desired carbonyl in good yields with catalytic activity in the order of $10 \times {}^{-5}$ mol^{-1} min^{-1} (kinetic constant), FluoRugel is generally 100 times faster (Table 1) while retaining the pronounced selectivity typical of Ru catalysts even upon prolonged reaction time.

In general, the catalytic stability of all the catalytic materials mentioned above considerably improves in dense phase carbon dioxide with a concomitant enhanced activity with increasing lipophilicity of the catalyst support (*i.e.* Pt/teflon-coated carbon[10] > Pt/carbon[2] > Pt/charcoal > [8]Pt/SiO_2[2] and ORMOSIL > SiO_2.[13]

Only FluoRuGel, however, shows similar good activity in the oxidation of primary and secondary aliphatic alcohols such as 1- and 2-octanol (Table 1) whereas, for comparison, Pt/SiO_2 employed in $scCO_2$ is not capable of aerobically converting more than 20% of the secondary alcohol substrates.[2] FluoRuGel in fact is a mesoporous glass whose vast accessible porosity (0.53 cm^3 g^{-1}) narrowly distributed around 20 Å allows facile access of widely different alcohol molecules to the confined catalytic species.

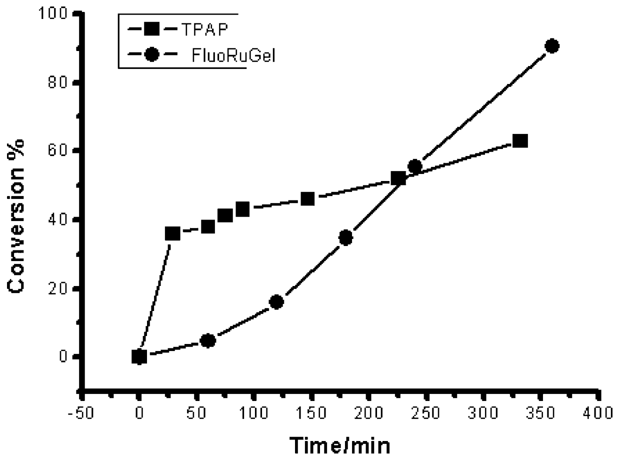

Fig. 3 Aerobic oxidation of benzyl alcohol to benzaldehyde in $scCO_2$ over sol–gel entrapped TPAP in FluoRuGel (*circles*) and TPAP alone (*squares*).

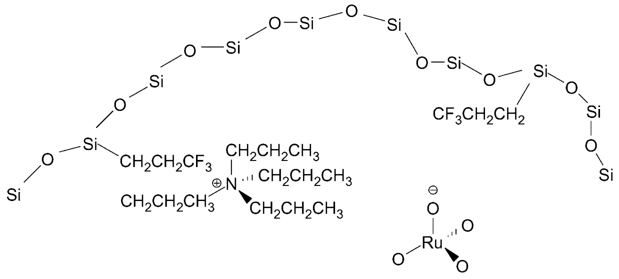

Fig. 4 Schematic representation of RuO_4^- and *n*-propylammonium relocation in the sol–gel entrapped microenvironment in response to fluorination of the cage.

Finally, along with performance, cost and feasibility of a new catalytic process are crucial in evaluating its practical introduction.[24] Based on the prices of its precursors from three chemical companies[25] (Table 2), one can see that the production cost of FluoRuGel is competitive with those of supported noble metals showing its potentially large rewards.[26]

Reactions in $scCO_2$ require a dedicated plant and a substantial amount of expensive electricity to compress the fluid at 100–250 bar typically applied for optimal conversions. Yet, as a leading industry practitioner puts it, they are "simple, safe, versatile, efficient, selective and clean. And therefore economic".[27] Production of carbonyls by oxidative dehydrogenation of alcohols in CO_2 over a similar fluorinated silica matrix will be convenient for all those products for which lack of heavy metals leaching and "solvent-free" conditions are required, such as in the case of the expensive carbonyls employed as aromes, fragrances, pharmaceuticals, nutritional and cosmetic products. Sol–gel catalysts can be obtained in practically any shape, and are thus easily adapted to the configuration of a continuous reactor. The route to oxidative dehydrogenations in $scCO_2$ is open.

Table 2 Price of FluoRuGel and commercial supported noble metals

Catalyst	Price (€/kg)	Amount/kg
FluoRuGel	230	>1000
FluoRuGel	630	<100
5% Pt/C	300	
4%Pd–1%Pt–5%Bi	500	

Experimental

Catalyst preparation

FluoRuGel was prepared by sol–gel processing the fluoro-alkyl containing monomer 3,3,3-trifluoropropyl-trimethoxysilane (TFPTMOS purchased from Fluka) with tetramethylorthosilicate (TMOS) in the presence of TPAP dissolved in methanol keeping the Si–MeOH–H_2O molar ratio at 1 : 8 : 4, *i.e.* using a stoichiometric amount of water (Si : H_2O = 1 : 4) and a high amount of co-solvent (Si–MeOH = 1 : 8), that was recently found to be crucial in promoting reactivity of analogous doped ORMOSILs in $scCO_2$.[13] Other chemicals including benzyl alcohol, *n*-decane, TMOS and TPAP were purchased from Sigma Aldrich and were used without further purification. Ultra pure water (Millipore Type 1) was used in all the preparations.

FluoRuGel, a 10% fluoro-propyl doped silica gel, was thus synthesised by adding TMOS (2.68 mL) and TFPTMOS (0.39 mL) to a solution of TPAP (24.5 mg) in MeOH (6.45 mL) cooled in an ice bath, followed by the addition of H_2O (1.44 mL). The mixture was stirred for 30 min when it gelled yielding a black alcogel which was sealed and left to age at room temperature for 24 h prior to drying at 50 °C (5 days). The grey xerogel thus obtained was powdered, washed under reflux ($CH_2Cl_2 \times 2$, 40 °C) and dried to 50 °C prior to use.

Oxidation procedure

A typical oxidation was carried out in the 10 mL modified Carlo Erba SFC 3000 reactor described elsewhere[13] at 75 °C and 22 MPa. Benzyl alcohol (5 μL, 0.5 mmol) and 0.1 equiv. of FluoRuGel (156 mg) were added to the reaction vessel with *n*-decane (5 μL, 1 mmol) as internal standard. After flowing the oxygen (1 bar), the reaction vessel was sealed, placed into a thermostated oven and liquid CO_2 was pumped into the autoclave using a cryogenic pump to bring the reactor pressure to 22 MPa. The reaction mixture was kept stirring at 400 rpm by means of an alternating magnetic field stirrer for the desired reaction time and reaction samples were withdrawn through a 6-way valve connected to a restrictor (kept at 90 °C) prior to GC analysis. When reaction was complete, the heating was stopped and the system was allowed to cool to ambient temperature. The reactor was then opened and the CO_2 gradually vented off in *n*-hexane allowing the total pressure inside the reactor to reach the atmospheric value, after which the product was extracted with a further amount of *n*-hexane and the catalyst recovered, dried and reused *as such* in a subsequent reaction run.

Analyses and reaction rates

The carbonyl products' content was determined by GC analysis on a Shimadzu chromatograph equipped with a Supelcowax 10 capillary column (30 m, 0.25 mm ID) using the internal standard method (with previously calculated response factors). The rate constants $k_{\text{cat.}}$ were assessed from the aldehyde formed integrating the pseudo first-order plots obtained from a quadratic equation in which one reactant (O_2 in this case) is in large excess, that is $\ln(1\text{-}[\text{ald.}]_t/[\text{ald.}]_{t=\infty}) = -k_{\text{cat}}[O_2]t$. The N_2–BET textural values were obtained with a Carlo Erba Instruments Sorptomatic 1900 powder analyzer, and ruthenium contents measured by ICP-MS on a HP 4500 spectrometer.

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