

Sol-Gel Entrapped TPAP: An Off-the-Shelf Catalyst Set for the Clean Oxidation of Alcohols

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Abstract: Whether in supercritical CO₂ or in organic solvent and using O₂ or aqueous H₂O₂ as primary oxidants, the series of sol-gel entrapped TPAP hybrid silica gels is a versatile class of oxidation catalysts suitable for the highly selective conversion of alcohols to carbonyls. These materials are generally more stable and active than traditional polymer-supported analogues. This report summarizes recent findings showing the large potential of this technology for synthetic chemistry.

1. INTRODUCTION

Ruthenium is an highly selective and versatile metal catalyst for the oxidation of alcohols [1]. In particular, the VII species tetra-*n*-propylammonium perruthenate (TPAP) either dissolved in solution or immobilized on polymer support is a very efficient and selective catalyst for the aerial oxidation of primary, secondary, benzyl and alkyl alcohols in non-aqueous media, including dense-phase carbon dioxide. Most functional groups such as carbon-carbon double bond, epoxy, indole, acetal, remain unaffected in the TPAP/O₂ conversion of alcohols which eventually are transformed into valued carbonyls [2]. However, after reaction the spent catalyst is isolated as a black colloidal suspension of RuO₂ which cannot be recycled. This limitates the commercial application of expensive TPAP-based catalysis only to those industrial processes where an extremely high degree of selectivity is needed such as in the pharmaceutical industry. In such cases, a solid heterogenized version of the catalyst is used to avoid product contamination and speed up product isolation from reactants [3]. In general, heterogenization of TPAP on commercial supports (Fig. 1) adds significant financial value [4].

For catalysis to achieve its full potential in the fine chemicals and pharmaceutical industries, where only about 10% of all productions currently use catalysis, heterogenous processes are to be developed in which reduction of waste, increased selectivity and shortened synthetic routes go along with process robustness and catalyst stability.

Remarkably, in the last few years a number of selective and clean catalytic processes for alcohols oxidations have been developed that are being increasingly adopted by industry [5]. Among these, the series of sol-gel entrapped TPAP catalysts are versatile mediators suitable for the selective oxidation of alcohols to carbonyls with oxygen or aqueous H₂O₂ as terminal oxidants. These materials and related ox-

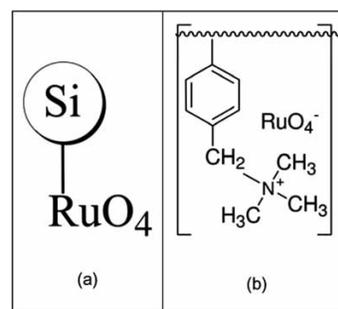


Fig. (1). Supported perruthenate commercial catalysts: silica-supported (a) and polymer-supported (b) such as in FibreCat.

idative processes are of urgent commercial interest to drugs, perfumery and fragrance manufacturers commercializing highly pure products (devoid of organic solvents and metals) to prevent drug contamination and alteration of olfactory test screenings. In general, the selectivity and the activity of entrapped TPAP materials are higher than for homogeneous perruthenate, i.e., the solid surface in these hybrid organic-inorganic catalysts participates actively in the reaction mechanism. Reactions can be carried out in conventional organic solvent with O₂ [6] or with H₂O₂ [7] or aerobically in dense phase carbon dioxide [8] affording in all cases high yields of aldehydes or ketones with pronounced selectivity.

We summarize here the achievements in each of these reaction media, and discuss how the versatility of the sol-gel entrapment process allows active site optimization affording a true off-the-shelf catalytic series suitable for application in diverse environments.

2. AEROBIC OXIDATION IN ORGANIC SOLVENT

Sol-gel nanohybrid silica particles organically modified and doped with TPAP are highly efficient catalysts for the selective oxidation of alcohols to carbonyls with O₂ at low pressure (1 bar) in toluene [6]. The materials are easily prepared by a one-step sol-gel process and their catalytic per-

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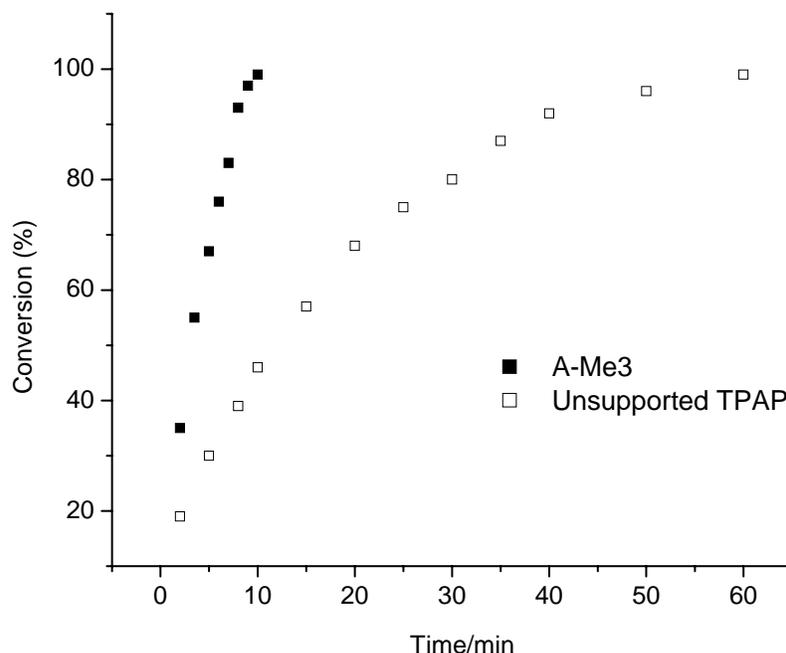


Fig. (2). Oxidation kinetics in the aerobic conversion of benzyl alcohol in toluene mediated by 10 mol% ORMOSIL-entrapped TPAP (A-Me3, ■) and unsupported (□). [Reproduced from Ref. 6, with permission].

formance can be optimised tailoring the conditions of their synthesis by hydrolytic co-polycondensation of tetramethoxysilane (TMOS) and alkyltrimethoxysilanes $R-Si(OMe)_3$ in the presence of TPAP. Eventually, leach-proof heterogeneous catalysts are obtained that are up to 6 times more active than unsupported perruthenate (Fig. 2).

The best performing catalysts require both an high degree of surface hydrophobicity as well as high amounts of water and co-solvent in the sol-gel polycondensation. The alcoholic oxidation is carried out by the oxygen in the coordination sphere of the metal center which leads to carbonyl products by an intramolecular hydride abstraction from the α -carbon (a primary KIE indicates that such abstraction is the rate determining step of the overall process) [9]. We invoked a ternary complex involving perruthenate, alcohol and oxygen which explains in a single mechanistic picture the overall kinetics. Indeed, high concentration of both oxygen and alcohol show a clear inhibitory effect resulting from a decrease in concentration of the catalytically effective 1:1:1 ternary complex.

3. AEROBIC OXIDATION IN $scCO_2$

Alkyl-modified silica gels doped with TPAP are good catalyst in the catalytic aerobic oxidation of alcohols in supercritical CO_2 [10]. The structure-activity relationship for these ORMOSILs shows that the best performing catalysts require both a high degree of surface hydrophobicity as well as high amounts of water in the sol-gel polycondensation process. Later on, the *FluoRuGel* series of hybrid fluorinated silica glasses doped with TPAP was introduced with marked stabilization and activity enhancement of perruthenate upon its confinement in the sol-gel fluorinated silica matrix [8].

The oxoruthenate catalyst is entrapped in a porous sol-gel fluorinated matrix. 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 reac-

tants into the cages where the oxidative dehydrogenation takes place, and then it extracts the carbonyl product.

In general, the activity and stability of these materials are subtly dictated by structure, depending on the degree of fluorination and on the length of the fluoroalkyl chain linked to the silica network of the matrix. While both homogeneous TPAP and also ORMOSIL-entrapped TPAP in $scCO_2$ show the typical perruthenate-mediated oxidation kinetics consisting of a fast initial stage up to 40-50% conversions, 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 (Fig. 3). This points to improved catalysis by TPAP entrapped in the fluoroalkyl-modified silica matrix: i.e., to a different chemistry of the entrapped dopant obtained by changing the properties of the sol-gel cage. We made the hypothesis that the partly positive carbon in highly dipolar $-CF_3$ groups that concentrate at the cage's surface further attracts the entrapped RuO_4^- adding to the effect of the large $N(CH_2CH_2CH_3)_4^+$ cation (whose use in combination with perruthenate was indeed introduced to promote selectivity by mitigation of the strong oxidation power of RuO_4^- alone) [11].

Finally, the general concept of supported ionic liquid catalysis in supercritical phase (*sc-Silic*) has been first successfully applied to the aerobic oxidation of alcohols by using perruthenate-based materials [12]. The methodology combines the advantages of ionic liquids as solvent booster; dense phase carbon dioxide as reaction (and extraction) solvent, and immobilized metal catalyst for easy product separation and catalyst recycle. The hybrid mesostructured silica gel co-encapsulating the ionic liquid imidazolium and the aerobic catalyst perruthenate prepared by co-polymerization of TEOS and imidazolium-modified organosilane, is the most active perruthenate-based catalyst in the oxidative dehydrogenation of alcohols in $scCO_2$. Its activity was substantially

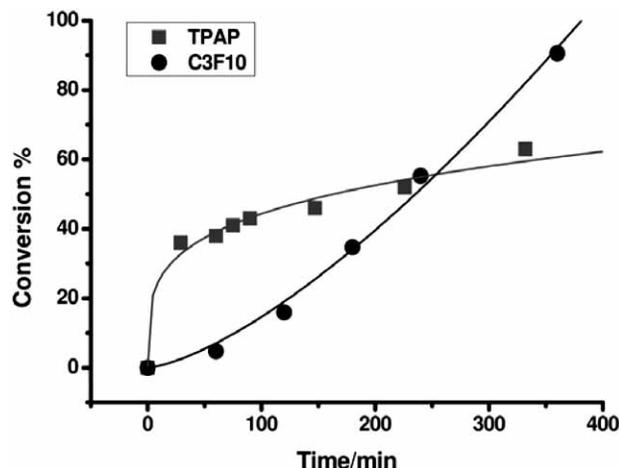


Fig. (3). Aerobic oxidation of benzyl alcohol to benzaldehyde in $scCO_2$ over sol-gel entrapped TPAP in FluoRuGel (circles) and TPAP (squares). [Reproduced from Ref. 8, with permission].

higher compared to a simple ORMOSIL-entrapped per-ruthenate, while site isolation of the entrapped Ru centers prevents catalyst degradation and renders these silica gels ideal candidates for practical use in commercial alcohols oxidation.

The system indeed meets industry requirement for heterogeneous conversions in $scCO_2$ (the catalyst is highly selective, stable, easily obtained with high catalytic loads and in any desired shape). Similarly, no conventional solvent is used to extract the product out of the IL, and the same leach-proof entrapped IL has broad application achieving what is required for practical use of ionic liquids.

4. OXIDATION WITH H_2O_2 IN ORGANIC SOLVENT

Even though molecular oxygen is the most environmentally and economically convenient primary oxidant, its use in association with TPAP suffers the disadvantage of requiring high reaction temperatures ($T > 70^\circ C$) in order to reoxidize the spent catalyst to the native species. Complementing thus the aerobic processes discussed above, unmodified SiO_2 gels doped with TPAP are effective catalysts for the oxidation of alcohols by hydrogen peroxide at room temperature, provided that the oxidant H_2O_2 solution is added slowly (Fig. 4) [7].

Two processes are involved: the oxidation of the alcohol and H_2O_2 decomposition. Hence, quick addition of the H_2O_2

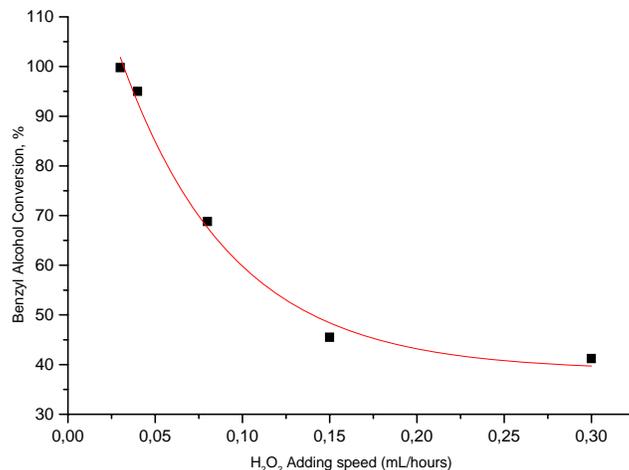


Fig. (4). Benzyl alcohol conversion in ether at $25^\circ C$ as function of the velocity of H_2O_2 (in ether) addition in the presence of silica-entrapped TPAP. [Reproduced from Ref. 7, with permission].

solution to the reaction mixture containing the substrate and the catalyst leads to very low alcohol conversion (3-4%), with peroxide decomposition being the main reaction. Conversely, when the H_2O_2 solution is added slowly by means of a syringe-pump, the alcohol conversion increases up to become almost quantitative. In other words, when the concentration of peroxide is kept low during the whole process the alcohol is smoothly oxidised and decomposition of H_2O_2 to water and O_2 is minimised.

Even the selectivity of the oxidative process is affected by the pace of hydrogen peroxide addition. Hence, when alcohol conversions are lower than 50%, benzaldehyde is the only product detected. At conversion higher than 50%, the alcohol overoxidation becomes significant and benzoic acid is detected along with benzaldehyde. However, the overoxidation can be completely eliminated by sequestering the water formed along with the aldehyde in the first oxidative step. Eventually, almost quantitative alcohol conversion and an excellent aldehyde selectivity are obtained.

The method is general and can be applied to widely different substrates (Table 1) because contrary to crystalline catalytic materials such as zeolites (including zeolite X [13] and MCM-41 [14] doped with perruthenate, which are shape selective), sol-gel silica glasses are amorphous materials showing a distribution of inner porosities which allows their application to the conversion of largely different substrates.

Table 1. Alcohol Conversions and Carbonyl Yields in the Oxidation at $25^\circ C$ of Various Substrates in Ether With Hydrogen Peroxide Added at the Velocity of 0.15 mL/h Catalysed by Silica-Entrapped TPAP in the Presence of 3Å Molecular Sieves

Substrate	Alcohol Conv. (%)	Carbonyl Yield (%)	Carboxylic Acid Yield (%)
Benzyl alcohol	94.3	94.3	0
(±)-1-Phenylethanol	63.3	63.0	0
1-octanol	71.6	41.7	29.9
(±)-2-octanol	58.9	58.9	0

[reproduced from Ref. 7, with permission]

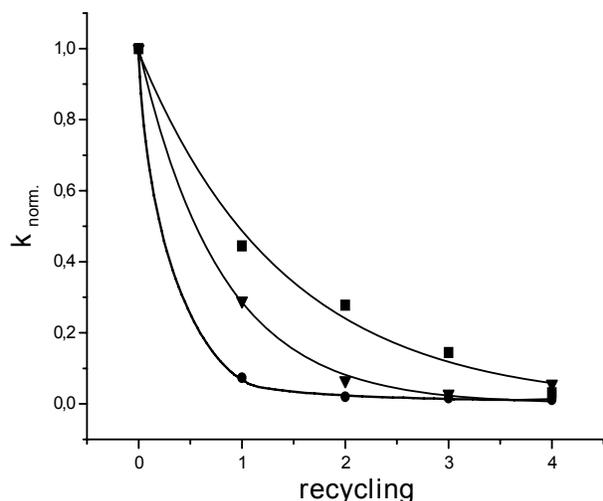


Fig. (5). Dependence of normalized rate constants for benzyl alcohol oxidation with O₂ (0.1 MPa at 25°C) catalyzed by ORMSOIL-entrapped TPAP in scCO₂ at 22 MPa and 75°C as a function of catalyst recycling (○ and washing solvent (Δ: ethyl ether; □: n-hexane; ○: dichloromethane). [Reproduced from Ref. 9, with permission].

5. STABILIZATION OF ENTRAPPED TPAP

Catalyst recycle experiments recovering the catalyst from scCO₂ medium and washing it with various organic solvents show (Fig. 5) that after only 10 TONs performed in the course of the first experiment, the catalyst retains only 10–40% of the initial efficiency in the second experiment (first recycle) [9].

Such efficiency decay continues with further recycling and after a total of five runs (four recycle) the catalyst becomes inactive. The rate of catalyst degradation depends on the nature of the solvent used for recovering and washing the material. In DCM, which is a good solvent for unsupported TPAP, the inactivation takes place very quickly and already after the first recycle the catalyst is almost inactive. On the other hand, in diethyl ether and even more in hexane, where unsupported TPAP does not dissolve at all, the efficiency decay is noticeably slower.

These observations corroborate the hypothesis of a TPAP inactivation caused by self-aggregation of Ru derivatives induced by the solvent. In fact, when the catalyst is recovered and washed with CH₂Cl₂, a fast development of chlorine gas bubbles occurs which is revealed by a pungent smell of chlorine during drying of the wet catalyst. To the contrary, use of chemically inert compressed carbon dioxide as unique reaction and washing solvent ensures excellent catalyst stability. Dense phase CO₂ indeed is easily vented off by a simple pressure release in the reaction system, leaving the unmodified solid catalyst physically ready for reuse.

6. OUTLOOK AND CONCLUSIONS

The catalysts of the sol-gel entrapped TPAP series are a true off-the-shelf class of powerful mediators for the selective oxidation of alcohols to carbonyls. Thus, a catalytic material can be chosen which is best suited for reaction in the desired medium with significant advantages in terms of reaction rate, stability and ease of separation over homogeneous perruthenate. Unmodified silica is suitable for oxidations

with H₂O₂ at room temperature; alkyl-modified organosilica works best in the aerobic oxidation in toluene; organofluorosilica or supported-ionic liquids are suited for oxidative dehydrogenation in scCO₂.

In general, sol-gel entrapment of TPAP in an organosilica matrix affords catalysts with enhanced activity and selectivity compared to homogeneous conditions. The sol-gel caging [15] of the Ru active centers within the inner surface of these highly porous oxides compared to few m²/g of external surface affords highly active catalytic glasses and ensures stability by preventing aggregation of the intermediate ruthenate species formed during the reaction. The main difference between a surface-heterogenized and a sol-gel entrapped perruthenate catalyst lies in that whereas in the first case the support limits its functions to being the physical carrier of the catalyst and promoting reactants solubility, in the entrapped catalyst the cage's surface of the entrapping matrix takes active part in the chemical reaction occurring at the interface by dictating the accessibility of the active center to the external reactants.

Fine chemicals companies in Europe and in the US have an expensive manufacturing base and the business is suffering from 25% excess capacity [16]. Moreover, all companies have very similar technology offerings whereas suppliers having specialized niche capabilities often report shortfalls in capacity. Production of active molecules over selective sol-gel catalysts would differentiate production and offer superior products capable to satisfy top market demand.

Indeed, a number of new heterogeneous silica-based sol-gel catalysts for the fine chemicals industry have been lately introduced ranging from Rhodia's immobilized Co(salen) cobalt catalyst [17] for hydrolytic kinetic resolution through Avecia's catalytic asymmetric cyanohydrin (CACHy) catalysts [18] and SiliCycle's SiliaCat TEMPO [19] for selective oxidations. Sol-gel entrapped catalysts are then not only prevented from becoming impurities but also lead to improved turnover numbers. Also, they can be easily adapted to continuous processes.

All these economic and technical drivers are likely to make the production of fine chemicals over sol-gel entrapped catalysts a central technology of the fine chemicals industry [20]. Entrapped perruthenate will be a most useful aerobic catalyst useful in the preparation of a large variety of important carbonyl compounds.

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REFERENCE

- [1] Pagliaro, M.; Camestrini, S.; Ciriminna, R. *Chem. Soc. Rev.*, **2005**, *34*, 837.
- [2] Hasan, M.; Musawir, M.; Davey, P.N.; Kozhevnikov, I.V. *J. Mol. Catal. A*, **2002**, *180*, 77.
- [3] For example, manufacturer Aldrich commercializes perruthenated supported on silica gel (572578), (polystyrene-supported (511587) and bound to polymeric FibreCat (590223). Codes are from the company's catalog accessible at: www.sigmaaldrich.com/catalog.
- [4] For instance, prices in Eur/g from above catalog of 100 g of supported perruthenate are: 1415 on silica; 2420 on resin; and 2900 on

- FibreCat. These materials generally have loadings in the range 0.2-0.4 mmol/g. Hence, 100 g contain up to 40 mmol of perruthenate which (as potassium salt) are commercialized at 930 Eur.
- [5] Roberts, S.M.; Whittall, J. (Editors), *Catalysts for Fine Chemical Synthesis, Volume 5, Regio- and Stereo-Controlled Oxidations and Reductions*, Wiley-VCH: Weinheim, **2007**.
- [6] Pagliaro, M.; Ciriminna, R. *Chem. Eur. J.*, **2003**, *9*, 5067.
- [7] Campestri, S.; Carraro, M.; Tonellato, U.; Pagliaro, M.; Ciriminna, R. *Tetrahedron Lett.*, **2004**, *45*, 7283.
- [8] Ciriminna, R.; Campestri, S.; Pagliaro, M. *Org. Biomol. Chem.*, **2006**, *4*, 2637.
- [9] Campestri, S.; Carraro, M.; Ciriminna, R.; Pagliaro, M. *Adv. Synth. Catal.*, **2005**, *347*, 825.
- [10] Ciriminna, R.; Campestri, S.; Pagliaro, M. *Adv. Synth. Catal.*, **2003**, *345*, 1261.
- [11] Ley, S.V.; Norman, J.; Griffith, W.P.; Marsden, S.P. *Synthesis*, **1994**, 639.
- [12] Ciriminna, R.; Hesemann, P.; Moreau, J.; Carraro, M.; Campestri, S.; Pagliaro, M. *Chem. Eur. J.*, **2006**, *12*, 5220.
- [13] Wu, D.L.; Wight, A.P.; Davis, M.E. *Chem. Commun.*, **2003**, 758.
- [14] Bleloch, B.F.; Johnson, G.; Ley, S.V.; Price, A.J.; Shephard, D.S.; Thomas, A.W. *Chem. Commun.*, **1999**, 1907.
- [15] Pagliaro, M.; Palmisano, G.; Ciriminna, R. *Chem. Soc. Rev.*, **2007**, *36*, 932.
- [16] Thayer, A. M. *Chem. Eng. News*, **2007**, *85* (07), 21. For a remarkable account on the fine chemicals industry, see also: P. Pollak, *Fine Chemicals. The Industry and the Business*, Wiley: Weinheim, **2007**.
- [17] Rouhi, A.M. *Chem. Eng. News*, **2002**, *80* (23), 43.
- [18] These sol-gel catalyst-immobilizing technologies originally developed by ICI Syntex (now Johnson Matthey after its purchase in **2002**).
- [19] Michaud, G.; Gingras, M.; Morin, F.; Béland, R.; Ciriminna, D.; Avnir, M.; Pagliaro, M. *Org. Proc. Res. Dev.*, **2007**, *11*, 766.
- [20] Ciriminna, R.; Pagliaro, M. *Org. Proc. Res. Dev.*, **2006**, *10*, 320.