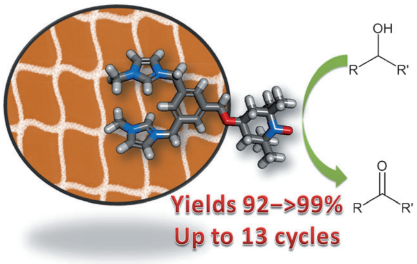
FULL PAPERS

Catch and release: Why spend money on covalent immobilization or ionic liquids with bulky cations? A bis(imidazolium)-modified 2,2,6,6-tetramethylpiperidine 1-oxyl catalyst can be adsorbed on an imidazolium-modified support, then released in the presence of a proper organic solvent and recaptured at the end of the reaction on removal of the solvent.



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Recyclable Catalyst Reservoir: Oxidation of Alcohols Mediated by Noncovalently Supported Bis(imidazolium)-Tagged 2,2,6,6-Tetramethylpiperidine 1-Oxyl

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Recyclable Catalyst Reservoir: Oxidation of Alcohols Mediated by Noncovalently Supported Bis(imidazolium)-Tagged 2,2,6,6-Tetramethylpiperidine 1-Oxyl

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Dedicated to Professor Maurizio Prato on the occasion of his 60th birthday

Bis(imidazolium)-tagged 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) catalysts were adsorbed on different supports such as silica gel, silica gel modified with highly cross-linked polymeric imidazolium networks, and highly cross-linked polymeric imidazolium networks entrapping magnetic particles. These systems provided a convenient tool for the oxidation of both primary and secondary alcohols working as recyclable reservoirs for the bis(imidazolium)-tagged TEMPO catalysts. By using EPR spectroscopy it was demonstrated that the catalyst was released as the corresponding oxoammonium salt in the solution during the recycling step, thus promoting the oxidative process in a homogeneous fashion. After solvent removal, the catalyst was readsorbed on the support allowing an easy recovery and recycle of the catalytic material up to 13 consecutive cycles with no loss in activity. The bis(imidazolium)-tagged TEMPO catalyst could be used in only 1 mol% both for the oxidation of benzylic and aliphatic alcohols. The catalytic material was highly recyclable if used on silica or imidazolium-modified silica gel in 10 mol% loading. Loading could be scaled down to 1 mol% and the catalyst proved to be recyclable up to 8 cycles only with imidazolium-modified silica gel. Such a "catalyst-sponge-like" system permits to combine the benefits of homogeneous and heterogeneous catalysis.

Introduction

Oxidation of primary and secondary alcohols into their corresponding carbonyl compounds is one of the most important processes both at laboratory and industrial level because of its strategic importance in organic synthesis.[1] Indeed this conversion, if performed in the absence of metal-based catalysts, may find application for the synthesis of fine chemicals such as fragrances or food additives.[2] In this light, the use of metal-free catalysts for selective oxidation of alcohols is very appealing, and to the date the most exploited compounds for this purpose are the 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) derivatives.[3] This family of stable nitroxyl radicals presents low toxicity along with an intriguing reversible redox behavior.[4] TEMPO may be used catalytically in combination with stoichiometric amounts of a co-oxidant that regenerates the active TEMPO species during the reaction. Among others, hypervalent iodine(III) reagent [bis(acetoxy)iodo]benzene (BAIB) has been found very useful for this purpose.[5] BAIB is a mild organic oxidant unable to oxidize TEMPO directly, but capable to regenerate TEMPO from TEMPOH species. Although BAIB is used in stoichiometric amounts, some procedures for its recovery and regeneration have been recently reported.[6] Nevertheless, whichever oxidant is used, separation of TEMPO from the products remains a key issue. In addition, TEMPO is considerably expensive and, consequently, its separation and reuse after the oxidation reaction is highly desirable. To this aim, several groups designed a number of different strategies in which TEMPO has been chemically anchored onto various supports such as silica,[6c,7] magnetic nanoparticles,[8] soluble[9] and insoluble organic polymers,[10] and also saponite[11] and nanotubes.[12] However, an inherent disadvantage of the covalent immobilization strategy relies in the generally decreased activity of the modified catalysts owing to the limited diffusion rates featuring the heterogeneous nature of the process.[13] On the other hand, as an alternative approach, the highly specialized TEMPO moiety has been functionalized with perfluoroalkyl groups[5d,14] (fluorous tags) or has been incorporated into task-specific ionic liquids[15] (IL tags) with the aim to be employed in homogeneous or biphasic systems. Unfortunately, their wider application is limited by the high costs of fluorinated systems and ionic liquid if used as solvents or for separation purposes, along with the problematic stemming from the high

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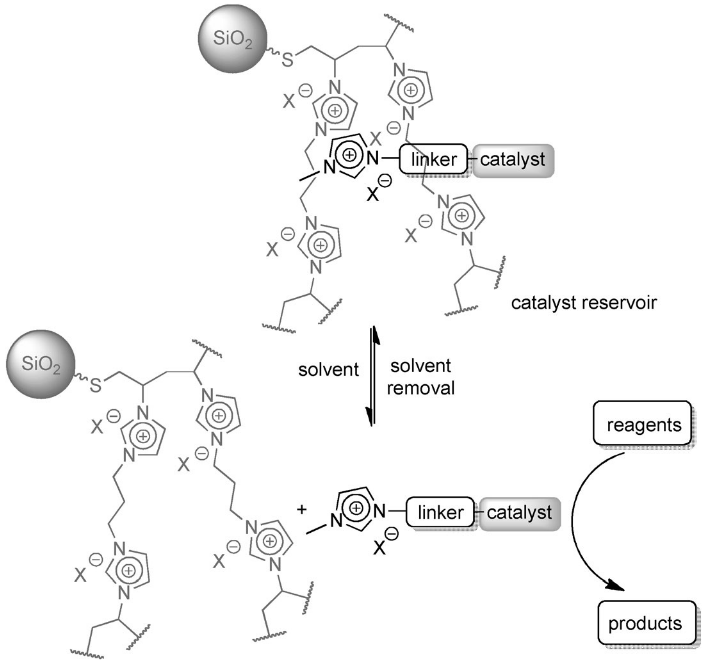
viscosity of IL that may lead both to mass- and heat-transfer limitations.

In the case of IL, to minimize the amount of utilized ionic liquids, the supported ionic liquid phase (SILP) approach has been developed.[16] This approach involves the presence of a support material that is modified with adsorbed layers of ionic liquid serving as the reaction phase in which the homogeneous catalyst is confined. An evolution of SILP involves the use of covalently attached ionic liquid moieties affording a supported ionic-liquid-like phase (SILLP).[17] In some cases, additional ionic liquid can be adsorbed on the SILLP giving rise to the formation of several layers of free ionic liquid on the support even if some leaching of the IL may occur. Recently we introduced a new approach in order to circumvent these problems and, in the meantime, to reduce the costs. Hence, a new class of multilayered covalently supported IL phase (mlc-SILP) materials have been reported by covalently linking and, at the meantime, polymerizing suitably functionalized bis-vinylimidazolium salts. A similar approach has been also applied for the preparation of magnetic particles entrapped into highly cross-linked imidazolium salts.[18] These novel materials displayed not only good catalytic activity in the cycloaddition of carbon dioxide to epoxides to yield cyclic carbonates,[18,19] but also excellent activity promoting the Suzuki coupling if Pd nanoparticles are immobilized in the polymerized imidazolium salt network.[20] Finally, mlc-SILP approach has been recently applied for the non-covalent immobilization of an IL-tagged organocatalyst.[21,22] This system has been successfully employed in the asymmetric aldol reaction for 15 cycles without loss of activity and selectivity. This approach is based on the desorption–adsorption route during the reaction and work-up steps. Initially, the catalyst is adsorbed on the surface of an imidazolium-modified silica gel support (Scheme 1).

In order to increase the affinity between the surface of modified silica gel and catalyst, the latter is modified with an imidazolium tag. During the reaction, the catalyst is dissolved in the reaction medium. If the reaction is complete, solvent is removed causing the readsorption of the catalyst, whereas the final product is extracted by using a proper solvent that does not dissolve the adsorbed catalyst. In this sense, the catalytic material (support + catalyst) acts as a catalyst reservoir. Herein we describe a similar approach for the oxidation of alcohols mediated by imidazolium-tagged TEMPO catalysts adsorbed on imidazolium-modified supports and unmodified silica gel.

The reversible immobilization of a soluble catalyst onto an insoluble support may provide the combination of the benefits of heterogeneous and homogeneous catalysis. In this regard, the easy separation of the catalyst from the reaction mixture and his reuse are associated to higher reaction rates, characteristic of homogeneous catalysis.[23,24]

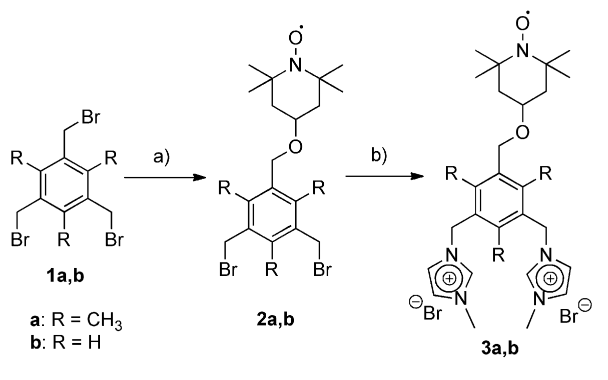


Scheme 1. Function of the IL-tagged catalyst adsorbed on the polymerized imidazolium network.

Results and Discussion

Catalyst preparation and catalytic activity

With the aim to increase the affinity of a nitroxide catalyst towards an imidazolium-modified silica gel, we introduced a bis-imidazolium tag in the 4-hydroxy-TEMPO moiety. Such modification has been achieved through a simple two-steps synthesis starting from the 1,3,5-tris(bromomethyl)benzene compounds **1 a**,**b** as reported in Scheme 2. As support, the imidazolium-modified silica gel **4**[21] and magnetic particles entrapped into highly cross-linked imidazolium salts (material **5**,[18] Figure 1) were used. In addition, unmodified silica gel was employed. As a first attempt we tested catalyst **3 a** or **3 b** in high catalytic amount (10 mol%)[15a,b] in the presence of BAIB (1.1 equiv.) in dichloromethane at room temperature for the oxidation of



Scheme 2. Reaction conditions: a) 4-Hydroxy-TEMPO, Bu_4NBr, toluene, 50% NaOH, 70 °C, 2 h, **2 a**: 60% yield, **2 b**: 63% yield; b) methylimidazole, $CHCl_3$, 60 °C, overnight, **3 a**: 89% yield; **3 b**: quantitative yield.

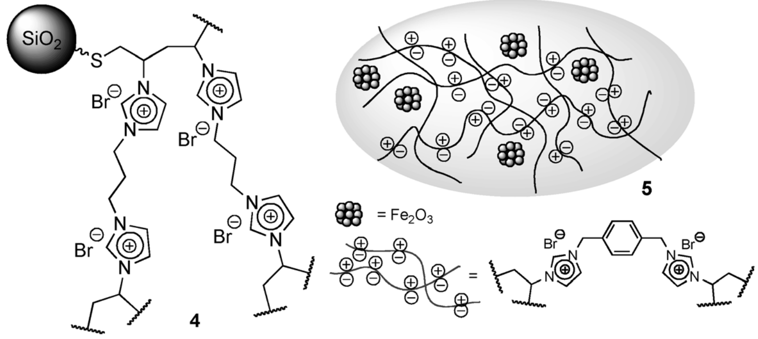
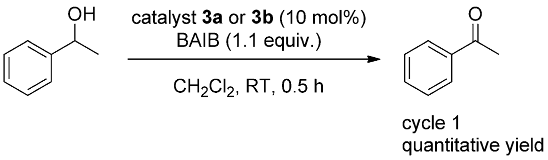


Figure 1. Imidazolium-modified supports used. Highly cross-linked imidazolium-modified silica gel **4** and highly cross-linked polymeric imidazolium networks entrapping magnetic particles **5**.

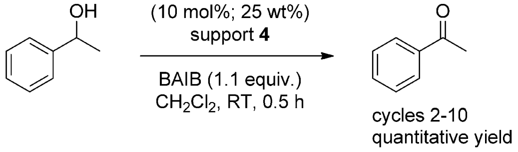
1-phenylethanol. Both catalysts gave a quantitative yield of the corresponding ketone (Scheme 3).



Scheme 3. Reaction conditions: Catalyst **3a** or **3b** (10 mol%), alcohol (0.82 mmol), BAIB (1.1 equiv.), CH_2Cl_2 (2 mL), RT, 0.5 h.

At the end of the reaction, support **4** was added and the solvent (CH_2Cl_2) removed under reduced pressure. The solid residue was washed with diethyl ether and filtered. The solid, which contained catalyst **3a** or **3b** adsorbed on support **4** (**3a**/**4** or **3b**/**4**, 25 wt% of **3a** or **3b** with respect to **4**) was employed for further 9 cycles. No loss in activity was observed (Scheme 4). In contrast, when catalyst **3a** or **3b** was recovered in the absence of the support, recovery was not quantitative and yield decreased after 3 cycles. Considering the good results obtained, the ratio **3**/**4** was not optimized.

Although catalysts appear to be highly recyclable, the possibility of reducing their loading has been considered. Then, 1-phenylethanol was oxidized by using 5, 2, and 1 mol% of catalyst **3a**. The ratio **3a**/**4** has been maintained (25 wt% of **3a** with respect to **4**). Up to four cycles were conducted in each case without loss in activity (yield > 95%). Very interestingly, the catalytic loading could be scaled down to 1 mol% without affecting the yield and the recyclability (Table 1, entry 1).

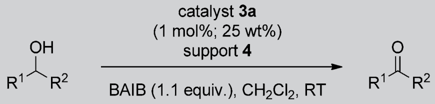


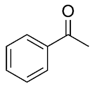
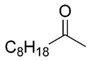
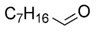
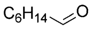
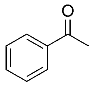
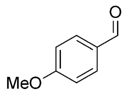
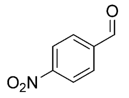
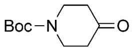
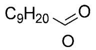
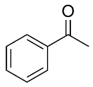
Scheme 4. Reaction conditions: Catalyst **3a** (10 mol%) + **4** (212 mg) or **3b** (10 mol%) + **4** (200 mg), alcohol (0.82 mmol), BAIB (1.1 equiv.), CH_2Cl_2 (2 mL), RT, 0.5 h.

Less reactive substrates were also tested, namely 2-decanol, 1-octanol, and 1-heptanol. The corresponding carbonyl compounds were obtained in high yields (Table 1, entries 2–4). Because of the interesting results obtained by employing only 1 mol% of catalyst **3a**, further cycles were conducted. 1-Phenylethanol was used in cycles 2–4 (entry 5) and primary benzylic alcohols, such as *p*-methoxy and *p*-nitrobenzylic alcohols were employed in the 5th and 6th cycle (entries 6–7). Excellent yields were observed. Then, less reactive substrates, such as aliphatic alcohols, were tested in the 7th and 8th cycle. 1-Boc-4-hydroxypiperidine was converted into the corresponding ketone in 53% yield in 2 h, whereas 1-decanol did not react after 6 h (entries 8–9). The recycling study was duplicated by using 1-phenylethanol in each cycle. Again the yield decreased after 8 cycles (entries 10–13).

The scope of this methodology was further explored by performing a complete recycling study in which different sub-

Table 1. Oxidation reactions with supported catalyst **3a**/**4** and recycling studies.[a]



Entry	Product	Cycle	*t* [h]	Yield[b] [%]
1		1	0.5	> 95
2		1	22	91
3		1	2	94
4		1	0.5	95
5		2–4	0.5	> 95
6		5	0.5	> 95
7		6	0.5	> 95
8		7	2	53
9		8	6	–
10		1–5	0.5	> 95
11		6	0.5	90
12		7	0.5	75
13		8	0.5	25

[a] Catalyst **3a** (1 mol%) and support **4** (loading 25 wt%, 21.2 mg); CH_2Cl_2 (2 mL); alcohol (0.82 mmol) and BAIB (1.1 equiv.). [b] By ^1H NMR spectroscopy.

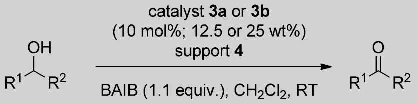
strates, benzylic primary and secondary alcohols, primary allylic and aliphatic alcohols, and cycloalkanols were oxidized by reusing the same catalyst sample recovered after each reaction. As both more reactive and less reactive alcohols were employed in consecutive cycles, we performed this investigation using catalysts **3a** or **3b** in 10 mol%.

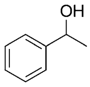
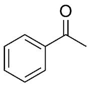
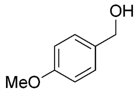
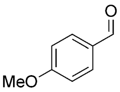
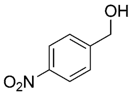
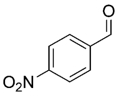
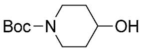
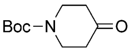
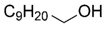
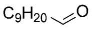
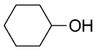
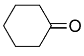
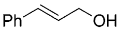
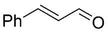
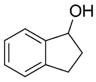
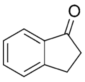
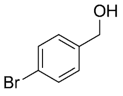
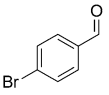
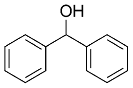
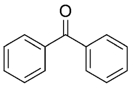
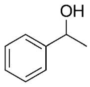
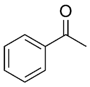
The results are reported in Table 2. To prove the high reusability of the catalytic systems in the 11th and 12th cycle, the same type of alcohol oxidized as in the 1st cycle, that is, 1-phenylethanol, was employed. Both catalytic systems, either bisimidazolium-derivative TEMPO **3a** or **3b** adsorbed on imidazolium-modified silica **4** were used. In all cases the carbonyl compounds were obtained in excellent yields. The high yields obtained up to ten cycles are a proof of the high reusability of the catalytic systems. This point is confirmed in the last two cycles, in which again 1-phenylethanol was used. Only a minor decrease in yield was observed.

To prove if catalysts are dissolved in the solvent under the reaction conditions adopted, the catalytic system **3b**/**4** was suspended in CH_2Cl_2 (by using the same concentration as employed in the reactions) and then filtered. After filtration, approximately 90% of catalyst **3b** was recovered, demonstrating that the catalyst was released during the oxidation reaction and readsorbed at the end of the reaction, if dichloromethane is removed under reduced pressure.

We also repeated the same reaction procedure with 1-phenylethanol by employing a solvent like diethyl ether, in which the nitroxide is completely insoluble. Under this condition the system should be considered as a truly heterogeneous system. Reaction time was longer (3 h) and conversion was not quantitative (87% yield, Scheme 5). It is known that the dielectric constant of the medium influences the yield,[25] however, in this case the increased reaction time and decreased yield can be ascribed also to the heterogeneous nature of the catalyst.

Table 2. Oxidation reactions with supported catalysts **3a**/**4** and **3b**/**4** and recycling studies.[a]



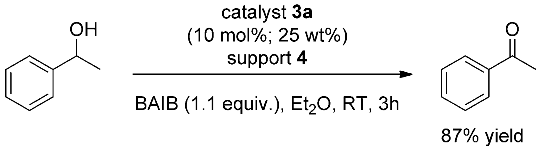
Entry	Substrate	Product	Cycle	Catalyst **3a**/**4** 25 wt%		Catalyst **3b**/**4** 25 wt%		Catalyst **3b**/**4** 12.5 wt%	
				t [h]	Yield[b] [%]	*t* [h]	Yield[b] [%]	*t* [h]	Yield[b] [%]
1			1	0.5	>95	0.5	>95	1	60
2			2	0.5	>95	0.5	>95	1	86
3			3	0.5	>95	0.5	>95	1	93
4			4	0.5	>95	0.5	>95	15	70
5			5	5	>95	5	>95	16	84
6			6	3	>95	3	>95	3	75
7			7	0.5	92	0.5	92	2	70
8			8	0.5	>95	0.5	>95	4	87
9			9	0.5	>95	0.5	>95	1	>95
10			10	0.5	>95	0.5	>95	15	90
11			11			0.5	92	3	84
12			12			0.5	92	3	87
13			13					1	68

[a] Catalyst **3a** or **3b** (10 mol%) and support **4** (loading 25 wt%: 212 mg for catalyst **3a**, 200 mg for catalyst **3b**; loading 12.5 wt%: 400 mg for catalyst **3b**); CH_2Cl_2 (2 mL); alcohol (0.82 mmol) and BAIB (1.1 equiv.). [b] By ^{1}H NMR spectroscopy.

Then, we tested the recycling properties of our catalytic system by employing a double amount of support **4** with respect to the previous systems in the presence of catalyst **3b** (12.5 wt% on **4**, Table 2, last two columns). A comparison with data previously discussed indicated that in the presence of a larger amount of support, longer reaction times and not quantitative conversions were obtained. These results are in agreement with the fact that the higher amount of support used imparts a more heterogeneous character to the system, in which catalyst **3b** is partitioned between the support and the solvent.

However, such a catalytic system still performs excellent recyclability, as indicated by the product yield in the 13th cycle, which was even slightly higher than in the first cycle.

To explore the nature of the support on the outcome of the reaction, we also employed magnetic particles entrapped into highly cross-linked imidazolium salts (material **5**, Figure 1).[18] The magnetic



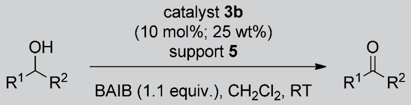
Scheme 5. Oxidation of 1-phenylethanol with **3a**/**4** in diethyl ether.

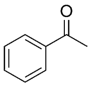
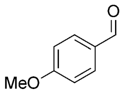
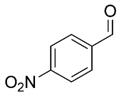
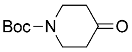
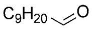
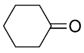
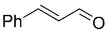
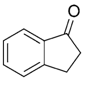
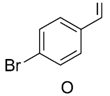
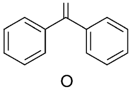
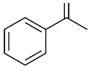
nature of such a support can be useful in the recovery procedure. Catalyst **3b** was adsorbed on support **5** and used in several oxidation cycles as reported in Table 3. In this case, after evaporation of CH_2Cl_2 and addition of diethyl ether the material was easily recovered by decantation after exposition to an external magnet.

Data reported in Table 3 show that in many cases yields were high or excellent, although slightly longer reaction times than in the **3b**/**4** system were needed (see Table 2). However, the **3b**/**5** system appeared less recyclable because lower yields were observed in the latter two cycles. Such behavior could be ascribed to the very low surface area of material **5**,[18] which may cause loss of catalyst **3b** upon recycling.

Finally, unmodified silica gel was used as the support. Catalyst **3a** was used in 1 or 10 mol% (Table 4). If catalyst **3a** was used in 1 mol%, yields of acetophenone dropped dramatically after only 3 cycles (Table 4, entries 1, 2). In this case, support **4** proved to be better than silica and the **3a**/**4** system was clearly more recyclable (see Table 1).

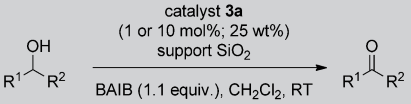
Table 3. Oxidation reactions with magnetic-particles-supported catalyst **3b**/**5** and recycling studies.

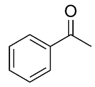
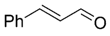
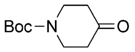
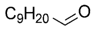


Entry	Product	Cycle	t [h]	Yield [%]
1		1	1	> 95
2		2	1	> 95
3		3	3	> 95
4		4	24	70
5		5	48	70
6		6	3	> 95
7		7	3	90
8		8	12	> 95
9		9	2	> 95
10		10	2	85
11		11	1	81
12		12	1	75

[a] Catalyst **3b** (10 mol%) and support **5** (loading 25 wt%: 200 mg); CH_2Cl_2 (2 mL); alcohol (0.82 mmol) and BAIB (1.1 equiv.). [b] By ^1H NMR spectroscopy.

Table 4. Oxidation reactions with supported catalyst **3a**/SiO_2 and recycling studies.[a]



Entry	Product	Loading [mol%]	Cycle	t [h]	Yield[b] [%]
1		1	1–2	0.5	> 95
2		1	3	0.5	< 10
3		10	1–5	0.5	> 95
4		10	6–7	0.5	94
5		10	8	3	> 95
6		10	9	3	95

[a] Catalyst **3a** (1 or 10 mol%) and support SiO_2 (loading 25 wt%: 21.2 mg or 212 mg); CH_2Cl_2 (2 mL); alcohol (0.82 mmol) and BAIB (1.1 equiv.). [b] By ^1H NMR spectroscopy.

On the other hand, **3a** in 10 mol% loading on silica worked very well for 9 cycles without loss in activity (Table 4, entries 3–6). High yields were observed even with a secondary and a primary aliphatic alcohol (Table 4, entries 5–6).

The results reported herein can be compared with those obtained by using similar IL–TEMPO catalysts and stoichiometric amounts of co-catalysts such as BAIB[15a] or nBuNHSO$_5$ in IL at 60 °C.[15b] However, in these cases, IL–TEMPO catalysts were used only in 10 mol% loading. Stoichiometric amount of co-catalyst may be avoided by using $CuCl_2$ and oxygen as the final oxidant. In these cases IL–TEMPO catalysts were used in 5 mol% at 40–100 °C and only benzylic alcohols were oxidized.[15c,g,j] The same catalyst loading (5 mol%) was used for the IL–TEMPO/$NaNO_2$/CO_2/H_2O at 100 °C, a method mainly developed for the oxidation of benzylic alcohols.[15e] However, no recycling studies were described. The amount of IL–TEMPO could be scaled down to 1 mol% if used with NaOCl/KBr system in IL/H_2O at 0 °C, but only 2 recycles were described.[15f]

Characterization

Support **4** had a surface area of 128 m^2g^{-1} and a cumulative pore volume of 0.2 cm^3g^{-1}. Catalytic materials, fresh and used, were characterized by SEM measurements and EPR analysis. In Figure 2, SEM images of support **4** are reported. From these

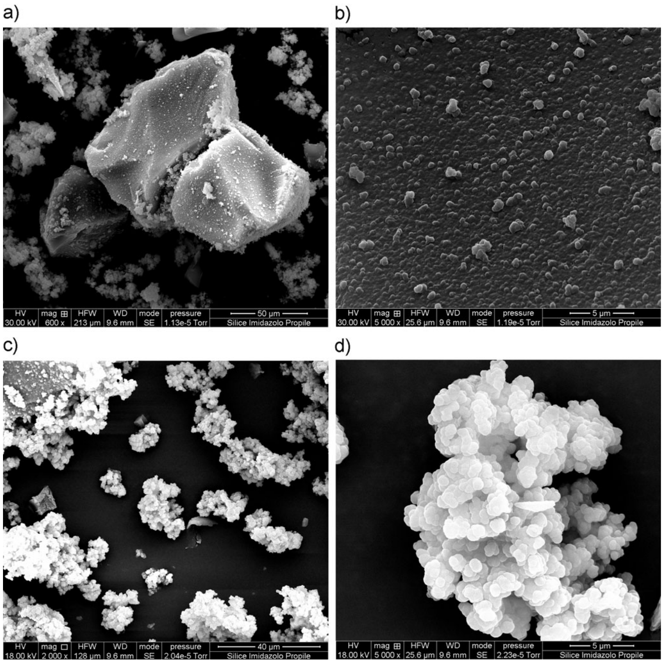


Figure 2. SEM images of support **4**. Pictures b) and d) are magnifications of a) and c), respectively. Scale bars: a) 50, b) 5, c) 40, and d) 5 um.

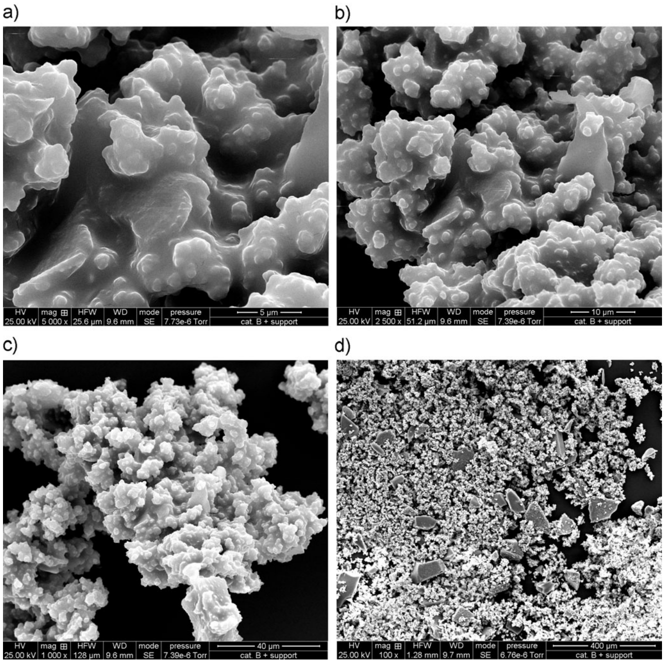


Figure 3. SEM images of freshly prepared **3a**/**4** at different magnifications. Scale bars: a) 5, b) 10, c) 40, and d) 400 μm.

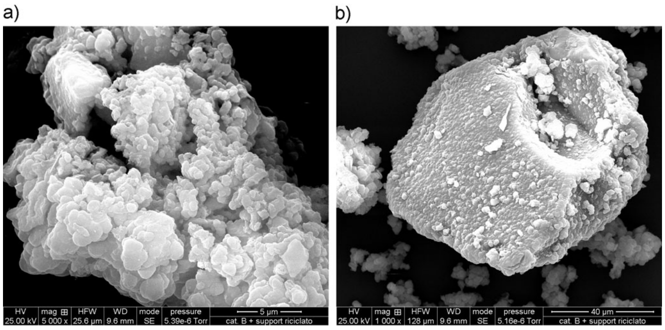


Figure 4. SEM images of **3a**/**4** after 12 cycles at different magnifications. Scale bars: a) 5 and b) 40 μm.

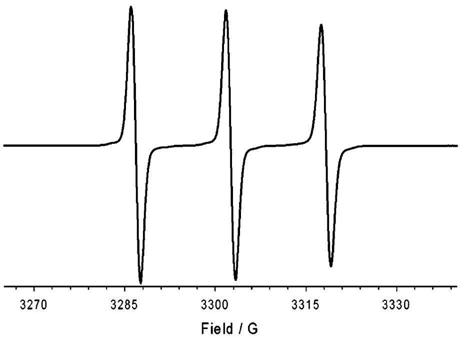


Figure 5. EPR spectrum of **3a** (0.1 mм) in CH_2Cl_2 at RT.

images it can be seen that such material is a physical mixture of silica-supported imidazolium salt and the polymer of the starting bis(vinylimidazolium) salt. After adsorption of the bis(imidazolium)-modified TEMPO catalyst, the surface of the support appeared as covered by a thin film (Figure 3). However, after 12 cycles the morphology of the material appeared to be similar to that of the starting material (Figure 4).

EPR measurements

The EPR spectrum of nitroxide **3a** (0.1 mм) in CH_2Cl_2 at room temperature is reported in Figure 5. The expected three-line spectrum was characterized by the coupling of the unpaired electron with a nitrogen nucleus with a hyperfine splitting constant, a_N, of 15.78 G ($g=2.0060$).

In Figure 6a the EPR spectrum of the powder catalytic system **3a**/**4** is reported instead. To see if in the reaction conditions catalysts were dissolved in the solvent, the catalytic system **3a**/**4** was suspended in CH_2Cl_2 (5 mg mL^{-1} corresponding to 1.25 mg mL^{-1} of nitroxide) and then filtered. After filtration, we recorded the EPR spectra of both the solid residue (Figure 6b) and the filtrate (Figure 6c). Quantitative analysis, performed by comparison of a doubly integrated spectrum to a spectrum of a solution of 2,2-diphenyl-1-picrylhydrazyl (DPPH) of known concentration by using the signal from a ruby crystal as internal standard, indicated that approximately 96% of catalyst **3a** was recovered in the solution. Only a negligible amount of the nitroxide ($<2\%$) was instead present in the solid residue after the extraction procedure. Similar results were obtained with **3b**/**4** system. These results confirmed that in the presence of CH_2Cl_2 both catalysts were released during the oxidation reaction and readsorbed at the end of the reaction, if dichloromethane was removed under reduced pressure.

We repeated the same EPR experiments on the catalytic systems **3a**/**4** or **3b**/**4** by using Et_2O as the solvent. In this case,

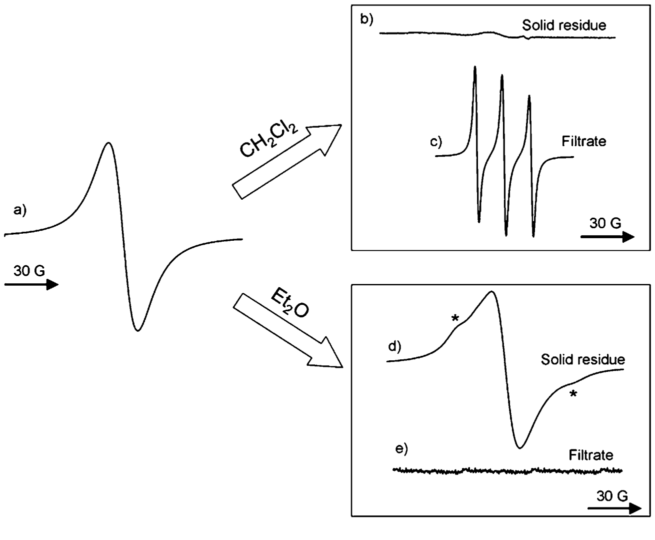


Figure 6. EPR spectra of **3a**/**4** (5 mg$\,$mL^{-1}) before (a) and after solvent extraction with CH_2Cl_2 (b, c) or Et_2O (d, e).

the solid residue exhibited a strong EPR signal at 298 K, the intensity of which was comparable to that of the starting sample indicating that the catalyst was recovered in a quantitative amount. On the other hand, no EPR signal was observed in the filtrate.

Notably, the EPR signal of the nitroxide in the solid residue was characterized by an additional broad signal (indicated by asterisks) besides the signal already present in the starting solid sample. We assigned the new broad signal to a new assembly of the catalyst in the support that resulted in a strong dipolar interaction between paramagnetic centers. Although it was impossible to obtain a clear picture of this aggregation, the new EPR spectrum shape observed after Et_2O removal was consistent with a significant interaction between the support and the catalyst. Actually, simple dissolution of the catalyst powder in Et_2O and removal of the solvent afforded an EPR spectrum that did not contain the spectral features observed in the presence of **4**.

To check the loss of catalyst during the oxidation process we recorded the EPR spectrum of the catalytic systems **3a**/**4** or **3b**/**4** after 12 cycles of activity in the powder form. Despite the good activity shown by the catalytic system after 12 cycles, the amount of nitroxide still present in the system was negligible in both cases.

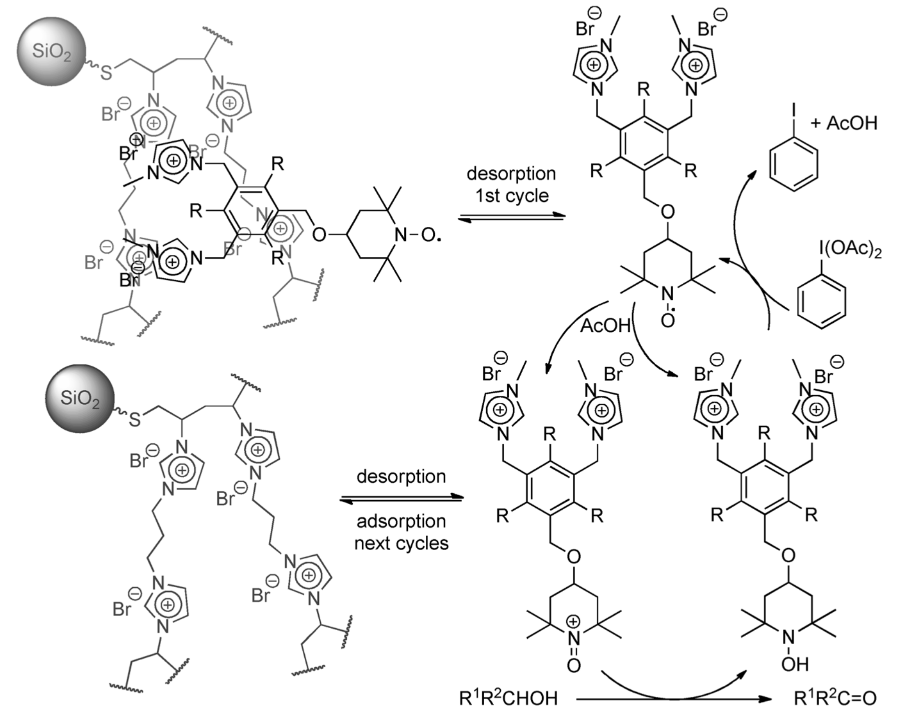
Previous investigations on the reaction mechanism[5a] suggest that the presence of AcOH, which can be generated by ligand exchange of $PhI(OAc)_2$ with the alcohol, results in the dismutation of TEMPO to an oxoammonium salt and hydroxylamine, the latter being oxidized to TEMPO by BAIB, resulting in the generation of AcOH (Scheme 6).

To check if the nitroxide was recovered in the oxoammonium form during the different catalytic cycles, we tried to reduce the oxoammonium salt electrochemically to the corresponding nitroxide by applying negative current to the EPR cell containing an acetonitrile (ACN) solution of the filtrate obtained after filtration of a suspension of the catalytic systems employed for 12 cycles (Figure 7).

Actually, an increase of the EPR signals attributable to the nitroxide with time was observed upon applying negative current to the EPR cell. In this case, the electron uptake led to the conversion of the oxoammonium salt to the corresponding nitroxide species. These evidences can be summarized in the mechanism proposed in Scheme 6, in which the fresh catalyst (1st cycle) is released in solution as a nitroxide species, whereas in the successive cycles the catalyst is adsorbed/released as an oxoammonium salt.

Conclusions

In conclusion, we have developed a recyclable catalytic reservoir for alcohol oxidation based on an imidazolium-tagged TEMPO catalyst adsorbed on an imidazolium-modified support or on unmodified silica gel. The imidazolium-tagged TEMPO catalysts were easily obtained with a simple two-steps synthesis. These systems, during the oxidation of alcohols, released in solution the imidazolium-tagged TEMPO catalyst thus promot-



Scheme 6. Proposed adsorption–desorption equilibrium and reaction mechanism.

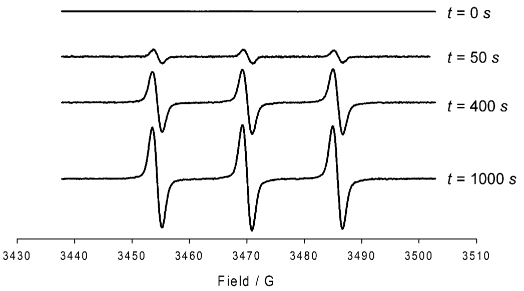


Figure 7. EPR spectra of **3a** recorded at different times in ACN, containing Bu_4NClO_4 (≈0.1 M) as supporting electrolyte, at a potential setting of −3.0 V. The starting solution was obtained after filtration of a suspension of the catalytic systems **3a**/**4** employed for 12 cycles in ACN.

ing the process in a homogeneous fashion. After solvent removal, the catalyst was readsorbed allowing an easy recovery and recycle of the catalytic material up to 13 consecutive cycles with no loss in activity. Such adsorption–desorption equilibrium has been unequivocally proven by EPR experiments, which further confirmed that the catalyst was in its oxoammonium salt form after the catalytic cycle.

The catalytic system could be employed in low catalytic amount (1 mol %), and resulted to be more recyclable if adsorbed on imidazolium-modified silica gel. Higher loading (10 mol %) both on silica gel or imidazolium-modified silica gel gave highly recyclable materials. Thanks to the high recyclability of the system, the use of such high amounts does not represent, in our opinion, a limitation of the method.

In summary, our system appears to be more recyclable with respect to other IL–TEMPO catalysts reported in the literature, although improvements are desirable. Further studies are in progress to avoid the use of stoichiometric amounts of the co-oxidant.

Experimental Section

General

Chemicals and solvents were purchased from commercial suppliers or purified by standard techniques. For thin-layer chromatography (TLC), silica gel plates (Merck 60 F254) were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of $KMnO_4$. Flash chromatography was performed by using Macherey–Nagel silica gel (0.04–0.063 mm). Light petroleum refers to the fraction with the boiling range 40–60 °C. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker 300 MHz spectrometer. SEM images were recorded by using an instrument with 20 kV operating voltage. Support **4** was prepared as described in the literature.[21] Silica gel used as a support has a surface area of 750 $m^2 g^{-1}$ and a cumulative pore volume of 0.68 $cm^3 g^{-1}$ and is commercially available (Aldrich).

EPR experiments

EPR spectra were recorded at RT using an ELEXYS E500 spectrometer equipped with an NMR gaussmeter for the calibration of the magnetic field and a frequency counter for the determination of g factors that were corrected against that of the perylene radical cation in concentrated sulfuric acid ($g=2.002583$). Nitroxide concentrations were measured with respect to a solution of DPPH of known concentration by using the signal from a ruby crystal as an internal standard.[25] The electrochemical cell was home-made and consisted of an EPR flat cell (Wilmad WG-810) equipped with a 25×5×0.2 mm platinum gauze (cathode) and a platinum wire (anode). The current was supplied and controlled by an AMEL 2051 general-purpose potentiostat. In a typical experiment, the cell was filled with an acetonitrile solution obtained after filtration of a suspension of the catalytic systems employed for 12 cycles in ACN (5 mg mL^{-1}) containing tetrabutylammonium perchlorate (≈0.1 M) as supporting electrolyte. After thoroughly purging the solution with N_2, spectra were recorded at a potential settings of −3.0 V.[26]

Synthesis of TEMPO derivatives 2a and 2b

To a solution of 4-hydroxy-TEMPO (2.32 mmol, 400 mg) in toluene (4 mL), Bu_4NBr (0.124 mmol, 40 mg) was added followed by 1,3,5-tri(bromomethyl)mesitylene **1a** (4.64 mmol, 1.85 g) and NaOH 50 % (8 mL). The mixture was heated at 70 °C for 2 h. After cooling at RT, toluene and water were added. The aqueous layer was separated and extracted with ethyl acetate (3×), then organic layers were mixed and evaporated. The residue was purified by column chromatography by using dichloromethane/petroleum ether 7:3 to recover the unreacted tribromo compound **1a**, whereas the desired compound **2a** was eluted with dichloromethane (60 % yield).[27]

Compound **2b** was prepared by following the same procedure (63 % yield).

Synthesis of catalysts 3a and 3b

A solution of compound **2a** (1.13 mmol, 0.55 g) and methylimidazole (2.49 mmol, 0.197 mL) in $CHCl_3$ (13 mL) was heated at 60 °C overnight. After cooling at RT, the solvent was removed and the solid residue was carefully washed with hot diethyl ether and filtered to give compound **3a** as a light orange solid (89 % yield). TEMPO catalyst **3b** was obtained as reddish viscous oil (99 % yield).

Alcohol oxidation

General procedure: Catalyst **3a** or **3b** (10 mol %) were dissolved in methanol (4 mL) in a round-bottom flask and support **4** (loading 25 wt %: 212 mg for catalyst **3a**, 200 mg for catalyst **3b**; loading 12.5 wt %: 424 mg for catalyst **3a**, 400 mg for catalyst **3b**) was added. The solvent was removed under reduced pressure and a powder **3a**/**4** or **3b**/**4** was obtained. Then, dichloromethane (2 mL) was added and, to this suspension, the appropriate alcohol (0.82 mmol) and BAIB (1.1 equiv.) were added. The mixture was stirred at RT for the time indicated in the tables, then the solvent was removed under reduced pressure and the residue washed with diethyl ether and filtered. The catalytic material was dried for a few minutes and then reused for the next cycle.

Acknowledgements

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Keywords: alcohols · aldehydes · EPR spectroscopy · ketones · oxidation · supported catalysts

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