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TEMPO radical polymer grafted silicas as solid state catalysts for the oxidation of alcohols†

Cite this: DOI: 10.1039/c3ra41823e

Received 5th November 2012,
Accepted 29th April 2013

DOI: 10.1039/c3ra41823e

www.rsc.org/advances

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TEMPO polymer-grafted silicas were synthesized by ''grafting from'' and ''grafting to'' methods using RAFT polymerization, and their catalytic activities as a new class of solid state catalyst for oxidation reactions with alcohols demonstrated.

One of the most important *desiderata* in the field of green and sustainable technological processes is improvement in catalyst performance.[1] Although heterogeneous catalysts are favoured for many chemical reactions within industrial settings, the ability to recycle the catalyst often remains a challenge after the chemical reaction is completed, or when improvements to the overall economic efficiency of the process have to be realised.[2] One of the most significant tasks in organic synthesis is the oxidation of alcohols.[3] However, such oxidation reactions have frequently been performed with stoichiometric amounts of inorganic oxidants, many of which are extremely hazardous to use or toxic.[4] The availability of easy-to-handle heterogeneous catalysts, which can easily recycled after use in liquid phase oxidation reactions, and which have low toxicity, good stability and high efficiency is thus an essential requirement.

The compound 2,2,6,6-tetramethylpiperidinyloxyl (TEMPO) is known to be a stable organic radical that can be stored for long periods of time without decomposition. A wide variety of derivatives and analogues of this type of stable free organic radical has been reported.[5] Since TEMPO can work as a redox reagent, it has been used in oxidation reactions under a variety of conditions‡.[6] Several TEMPO functionalized solid catalysts, prepared by immobilising individual TEMPO molecules onto solid support materials as a covalently anchored mono-molecular layer, have been previously studied for their potential in oxidation reactions.[7] However, these reactions usually require more than stoichiometric amounts of these mono-molecular layer solid state catalysts to achieve acceptable product yields due to the low loading of TEMPO molecules onto the solid support. To overcome this constraint, attention has turned to the generation of TEMPO functionalized polymers allowing the introduction of higher densities of TEMPO. For example, our group has reported the preparation of TEMPO functionalized polyvinyl polymers for use as new materials in organic batteries, which can be charged in seconds *via* the oxidation of the nitroxide radical and reduction of the corresponding oxoammonium moiety of the TEMPO molecule.[8] However, polymeric TEMPO functionalized solid state catalysts based on multiply-displayed TEMPO units introduced into a polymeric backbone, which has been concomitantly immobilized onto a carrier surface, have not been previously reported for use in oxidation reactions.

Based on the hypothesis that a multiply-displayed TEMPO polymer grafted solid state catalyst of high radical density would lead to recyclable heterogeneous catalysts with improved catalytic activity and efficiency due to the increased number and accessibility of the active sites of the catalyst to the substrate, we describe herein methods to prepare a new type of TEMPO polymer grafted silica materials and describe their application as novel solid state catalysts for oxidation reactions. The intent of this study was to evaluate the catalytic performance of this new class of oxidative heterogeneous catalyst when used *in loco* multiple times, thus circumventing the constraints found with single cycle heterogeneous catalysts.

To this end, a series of multiply-displayed TEMPO polymer grafted silicas has been synthesized by grafting poly(2,2,6,6-tetramethylpiperidinyl-oxy methacrylate) (PTMA)[9] onto silica. In initial experiments, a ''grafting from'' method was employed using the RAFT chain transfer agent, *S*-methoxycarbonyl-phenyl-methyl

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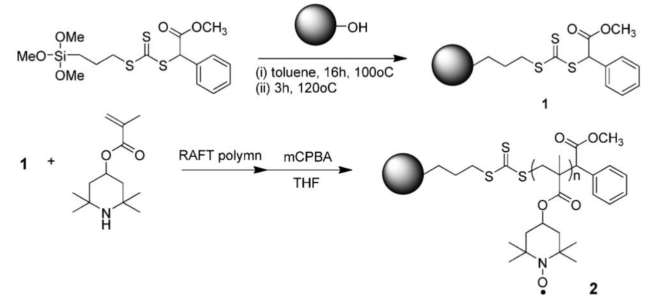
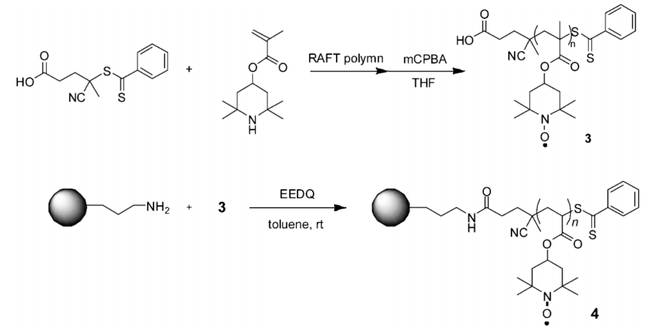
† Electronic supplementary information (ESI) available. See DOI: 10.1039/c3ra41823e

‡ **Typical conditions for the oxidation of alcohols**: The alcohol (4 mmol) was mixed with the catalyst (0.02 mmol) in 10 mL of CH_2Cl_2 at 5 °C. An aqueous solution of KBr (0.5 M, 0.8 mL) and NaOCl (0.35 M, 14.3 mL with the pH adjusted to pH 9 by $NaHCO_3$) was added to the reaction mixture, which was then stirred for 10 min at 5 °C. After this time, the catalyst was removed by filtration, the organic layer recovered and the CH_2Cl_2 removed by gentle rotary evaporation to yield the product. Analogous procedures were employed with water and the other solvent systems. The oxidation reaction of benzylalchol was carried out in a large scale and the product conversion of the reaction was calculated by isolated yield.



Scheme 1 TEMPO polymer grafted silica synthesis by ''grafting from'' method.



Scheme 2 Synthesis of the TEMPO polymer grafted silica by the ''grafting to'' method.

S′-trimethoxysilylpropyltrithiocarbonate, introduced onto the silica surface to form a silica-supported chain transfer agent, **1**.[10] Then, 2,2,6,6-tetramethylpiperidine methacrylate was graft polymerized using **1** by RAFT polymerization and the so-formed precursor, poly(2,2,6,6-tetra-methylpiperidine methacrylate) grafted silica treated with 3-chloroperoxybenzoic acid to yield the TEMPO polymer grafted silica **2** (Scheme 1).

The product, **2**, was characterized by IR, elemental analysis, and thermogravimetric analysis (TGA). The polymer graft ratio present for **2** was 57 wt% as calculated from the weight loss observed by TGA from 200 °C to 600 °C due to the decomposition and removal of TEMPO polymer from the surface of the silica. Depending on the polymerization conditions, immobilized densities of the TEMPO units on **2**, determined from the graft ratio, up to 1.6 mmolg^{-1} could be achieved. This density level is considerably higher than that of commercially available silicas partially functionalized with a mono-layer of TEMPO molecules (*e.g.* mono-TEMPO-Si, 0.6 mmol g^{-1}).[11] The molecular weight of the optimally grafted TEMPO polymer was determined by cleaving the polymer from **2** using an aminolysis reaction.[12] The molecular weight of the cleaved TEMPO polymer was measured by gel permeation chromatography (GPC) and found to be $M_n = 1.9 \times 10^4$, $M_w/M_n = 2.6$. This value is close to the theoretical value ($M_n = 2.3 \times 10^4$) calculated from the monomer and chain transfer agent concentration, indicating that the molecular weight of the grafted polymer can be controlled by the RAFT polymerization conditions. The most important value, the number of radical groups introduced onto the silica surface, was estimated by superconducting quantum interference device (SQUID) measurements. The amount of radical groups on **2** was found to be only *ca.* 45% of the theoretical value. This result suggests that under the ''grafting to'' conditions, treatment of the TEMPO precursor molecule of **2** with 3-chloroperoxybenzoic acid to form the radical grafted polymer species was mainly associated with surface modification, with the intra-porous regions of **2** not readily accessed due to steric restriction.

Based on these results, the synthesis of a series of TEMPO polymer grafted silicas with a radical densities approaching 100% of the theoretical value, was undertaken using a ''grafting to'' method. 2,2,6,6-Tetramethylpiperidine methacrylate was RAFT polymerized with the chain transfer agent, (4-cyano-4-[(phenyl-thioxomethyl)thio]-1-(2-carboxyethyl)-1-cyanoethylbenzodithio-ate),[13] and treated with 3-chloroperoxybenzoic acid to form poly(PTMA), **3**. By tuning the amount of the chain transfer agent present, different **3**′s of various molecular weights were synthesized. The molecular weights of these polymers were again measured by GPC. The number of radical groups introduced onto the poly(PTMA) was measured by SQUID, demonstrating that all of these polymers had very high radical concentrations, typically above 90% of the theoretical value.

The prepared **3**′s were then grafted onto synthesized amino-functionalized silica (*ca.* 2.0 mmol g^{-1}) of particle size of *ca.* 10 nm using a condensation agent to yield a series of different TEMPO polymer grafted silicas, **4**′s (Scheme 2). *N*-ethoxy-carbonyl-2-ethoxy-1,2-dihydroquinoline (EEDQ) was used as the condensation agent. EEDQ was selected for this condensation reaction since this reagent is readily available at low cost and allows the coupling in high yield in a single one-pot operation.[14] The molecular weights of the poly(PMTA)s and the other characterization data of the different **4**′s are summarised in Table 1. All samples showed a high level of TEMPO immobilization (up to 2.1 mmol g^{-1}) and a radical concentration greater than 90% of the theoretical value The physical form and size of the derived TEMPO immobilization particles was consistent with the presence of an extensively grafted layer.

Illustrative of these results, the morphology of the synthetic material **4-2** (entry 2, in Table 1) was determined by scanning electron microscope (SEM) and dynamic light scattering (DLS). A SEM image of **4-2** (Fig. 1) demonstrated the presence of largely spherical objects in the size range of 80–110 nm. The presence of a small percentage of particles of *ca.* 10 nm average diameter can be attributed to the un-reacted fumed silica material. The average size of **4-2** was 108 nm from DLS which supported the result from SEM. The size of **4-2** was significantly higher than the size of the original amino functionalized silica support, which had an average particle size of 9 nm. As noted above, the size difference between the synthesized **4-2** and amino functionalized silica confirms the existence of an extensively grafted TMEPO polymer layer on the surface of the silica.

Table 1 TEMPO polymer grafted silica **4** synthesis by grafting to method

	3				
entry	M_n (x 10^4)	M_w/M_n	graft ratio[a] (wt%)	immobilized TEMPO[a] (mmol g^{-1})	radical conc.[b] (%)
1 (**4-1**)	1.0	1.2	54	1.56	92
2 (**4-2**)	1.7	1.2	64	1.71	91
3 (**4-3**)	3.0	1.1	66	1.76	90
4 (**4-4**)	7.4	1.2	91	2.11	99

[a] Calculated by TGA. [b] Estimated by SQUID.

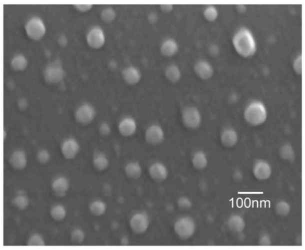


Fig. 1 SEM image of TEMPO Catalyst **4-2**.

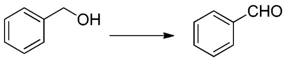
As an initial evaluation of the catalytic performances of the TEMPO polymer grafted silicas **4-1**, **4-2**, **4-3**, and **4-4** (entry 1–4 in Table 1, respectively), the oxidation of benzyl alcohol as the substrate was examined (Table 2). The efficiency of the TEMPO polymer grafted silica was also compared to a commercially available mono-TEMPO Si. The reactions can be carried out in water or in a CH_2Cl_2/water bi-phasic system. As evident from the results, **4-2** showed the highest product conversion and reaction rate constant compared to the other synthetic materials. In addition, the conversion and the reaction rate constant of **4-2** (>95%, 1.01×10^{-2} L mol^{-1} s^{-1}) was much higher than that of the mono-TEMPO Si (58%, 0.23×10^{-2} L mol^{-1} s^{-1}). No evidence for the oxidative modification of the aromatic ring was obtained as has previously been noted[15] with other types of TEMPO-mediated oxidation reactions. The need to use a co-catalyst, such as transition metal or nitric oxide derivatives,[16,17] or to employ surface coating with an ionic liquid,[18] is also circumvented with this new class of immobilised polyTEMPO silica-based catalysts. Moreover, the above results indicate that TEMPO polymer grafted silicas have a greatly enhanced capability as oxidation catalysts compared to monomer TEMPO functionalized silicas due to the higher radical density that can be achieved by the grafted TEMPO polymerisation procedure.

Interestingly, the oxidative capacity of the catalysts, **4**, appeared to follow a parabolic dependency on the molecular weight of the grafted TEMPO polymer. For example, the catalytic performance of **4** initially increased with polymer molecular weight (**4-1** → **4-2**). This can be explained by the number of immobilized TEMPO units on the catalyst increasing along with the molecular weight of the grafted TEMPO polymer. However, above a certain value, the catalytic performance of **4** decreased with the molecular weight of the grafted polymer (**4-2** → **4-4**) with **4-4**, which corresponded to the highest molecular weight grafted TEMPO polymer (M_n = 7.4×10^4), yielding the lowest conversion and rate constant of the four different types of **4**. Although dispersion of the catalyst, and thus its efficiency, will be affected by the molecular weight of the grafted polymer, an alternative explanation for the decrease in catalytic performance of the catalyst containing the highest molecular weight polymer species would be steric crowding of the TEMPO moieties and lower solvation propensity of the larger polymeric chains.

In order to establish the reusability of the catalyst, the catalyst was recovered by filtration and reutilised in subsequent cycles (Fig. 2). The catalyst was found to retain its activity for at least five cycles of reuse. The performance of the catalyst remained almost constant above 90% for all of these recycle experiments.

These oxidation reactions with **4** were extended to various other alcohols. The oxidation of 1-octanol and 1-decanol yielded the corresponding aldehydes in high yield (*ca.* 98–

Table 2 Product conversion and reaction rate constant of the oxidation benzyl alcohol to benzaldehyde with TEMPO catalysts[a]



Catalyst	**4-1**	**4-2**	**4-3**	**4-4**	mono-TEMPO-Si
conversion (%)[b]	90	95	89	80	58
rate constant k_1 ($\times 10^{-2}$ $Lmol^{-1}$ s^{-1})	0.91	1.01	0.62	0.45	0.23

[a] Reaction time: 10 min, reaction temp: 5 °C, catalyst/alcohol: 0.5 mol%, solvent CH_2Cl_2/water. [b] Conversions were determined by NMR and GC.

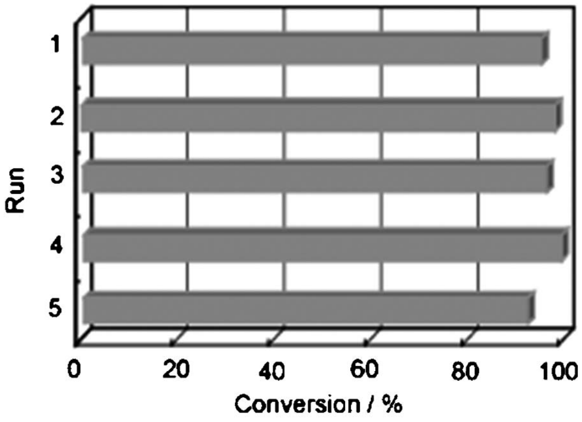


Fig. 2 Recycling of the catalyst **4-2** in the oxidation of benzyl alcohol (reaction time: 10 min, reaction temp: 5 °C, catalyst/alcohol: 0.5 mol%, solvent $CHCl_3$/water).

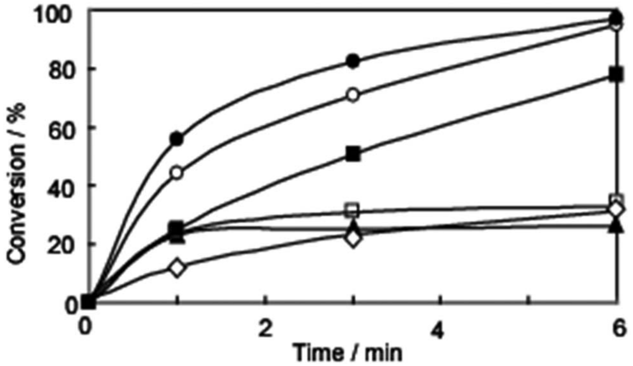
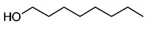
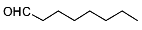
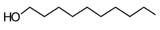
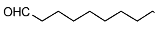
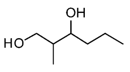
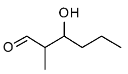
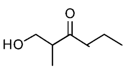


Fig. 3 Time *vs.* conversion of the oxidation of benzyl alcohol with **4-2** (• = CH_2Cl_2/water, ○ = ethyl acetate/water, ■ = toluene/water, □ = *N*,*N*-dimethylformamide/water, ▲= MeTHF/water, ◇ = CPME/water).

99%). The reaction with 1-undecanol, 1-dodecanol, and 4-hydroxy-methylbiphenyl also gave similar results (*ca.* 99%, 97%, 84%, respectively). In contrast, the reaction with secondly alcohols, *e.g.* 2-octanol and 2-decanol, only gave trace amounts of the corresponding aldehydes (*ca.* 4% and 2%, respectively) which suggesting a high level of substrate specificity of the catalyst. The catalyst was also evaluated for the oxidation of the diol. 2-methyl-1,3-hexanediol. The reaction yielded 54% (rate constant $k_1 = 1.1 \times 10^{-2}$ Lmol^{-1} s^{-1}) of the corresponding 1-hydroxy-2-methyl-3-ketohexane and a trace amount of the 2-methyl-3-hydroxyhexanaldehyde from the reaction (Table 3). Compared to conventional alternatives, the conversion was much higher than that of, for example, mono-TEMPO Si (product conversion = 5%, rate constant k_1 = 0.45×10^{-2} L mol^{-1} s^{-1}). The oxidation of another diol, 2,2,4-trimethyl-1,3-pentanediol, did not proceed with either **4** or the mono-TEMPO-Si and this observation can be explained by the steric effect of access to the alcohol sites. Moreover, the formation of carboxylic acids was not detected by ^{1}H NMR or ^{13}C NMR in the products from these reactions. These results suggest that these new types of polyTEMPO grafted catalysts have potential as effective and selective solid oxidation catalysts for both primary and secondary alcohols.

Table 3 Conversion (%) of alcohols to aldehydes with TEMPO catalyst[a]

			conversion (%)[c]	
Entry	Substrate	product	**4**[b]	mono-TEMPO-Si
1			98	51
2			99	34
3			53	5
			0.1	0.3

[a] Reaction time: 10 min, reaction temp: 5 °C, catalyst/alcohol: 0.5 mol%, solvent CH_2Cl_2/water. [b] **4-3** for entry 1 and 2, **4-2** for entry 3. [c] Conversions were determined by NMR and GC.

As noted above, these reactions can be carried out using a CH_2Cl_2/water solvent biphasic condition. In order to replace CH_2Cl_2/water (Fig. 3) with a greener solvent for the reaction, ethyl acetate/water, 2-methyltetrahydrofuran (MeTHF)/water, cyclopentyl methyl ether (CPME)/water were examined as alternatives for the oxidation reaction of benzyl alcohols. As a result, ethyl acetate/water resulted in comparable yields as CH_2Cl_2/water, and would thus be a preferred option for these oxidative reactions including those for the more hydrophobic alcohols.

Conclusions

This study documents the synthesis and properties of multiply-displayed TEMPO polymer grafted silicas prepared by the "grafting to" method. The route that was followed involved the synthesis of several TEMPO polymers by the RAFT polymerization of PMTA and then immobilising these precursors onto the carrier silica. The derived TEMPO polymer silicas have been found to be very effective as a heterogeneous catalyst for the oxidation of various alcohols. In this study, aqueous sodium hypochlorite was used as the terminal oxidant for the regeneration of these polyTEMPO polymer-grafted solid state catalysts. Although these conditions lead to a reduction in atom efficiencies vis-a-vis the use of molecular oxygen within a single cycle, the described reactions can nevertheless be readily and efficiently employed in a recycling mode as facile, transition metal free liquid phase oxidations. In comparison to alternative procedures based on the use of free or mono-functionalised TEMPO materials with molecular oxygen for the aerobic oxidation reactions of a variety of compound classes,[19] although superficially of higher atom efficiency, these alternative conditions are based on the use of (i) highly flammable solvents such as α,α,α-trifluorotoluene,[20] known also to be very toxic towards aquatic organisms; (ii) high mole percentages of TEMPO, typically[21] in excess of 10 mole%; or (iii) the need for various organometallic complexes, *e.g.* Fe(III) or oxamide Cu(II) co-catalysts,[19,22] in the presence of ionic liquids such as [bmim]PF_6. As a consequence, assessment of the "green-ness" of a particular chemical reaction should take into account considerations that extend beyond just the atom efficiency of the reactants themselves, but also incorporate the "whole-of-reaction" attributes of the various other chemicals and materials that are employed as part of the synthetic protocol. As such, oxidative reactions carried out with these new multiply-displayed TEMPO solid state heterogeneous catalysts provide a useful addition to the green chemical panel of catalysts. Moreover, these alternative conditions do not capture the advantages of densely immobilised TEMPO polymers as solid state catalysts with very high radical concentrations for the rapid high yield oxidation of alcohols as described in this investigation. This study thus documents useful routes to the preparation and application of a new class of solid phase oxidation catalysts for use in synthetic reactions based on more benign and green chemical procedures.

Acknowledgements

This work was partially supported by the Global COE program "Practical Chemical Wisdom" at Waseda University from MEXT, Japan and the Australian Research Council.

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