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# Aerobic oxidation of alcohols to carbonyl compounds mediated by poly(ethylene glycol)-supported TEMPO radicals

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**Abstract**—Two poly(ethylene glycol)-supported TEMPO (PEG-TEMPO) has been successfully applied as soluble, recyclable catalysts in the chemoselective oxidation of primary and benzylic alcohols with molecular oxygen in the presence of  $Co(NO_3)_2$  and  $Mn(NO_3)_2$  as co-catalysts (Minisci's conditions). Under those conditions, secondary alcohols are also oxidized to ketones, although usually in lower yields. The insertion of a spacer between the PEG moiety and TEMPO has beneficial effects on both the activity and ease of recovery of the supported catalyst.

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#### 1. Introduction

Catalytic oxidation using the stable nitroxyl radical 2,2,6,6tetramethylpiperidine-1-oxyl (TEMPO) in combination with safe and easy to handle primary oxidants has become one of the most promising procedures to convert primary and secondary alcohols into the corresponding carbonyl compounds.<sup>1–4</sup> Indeed, efficient traditional methods for this functional group transformation involve the use of stoichiometric amounts of either inorganic oxidants (e.g., chromium (VI) salts) or organic oxidants (e.g., activated DMSO).<sup>5–7</sup> These methods hardly satisfy the current demand for non-polluting chemical processes of high atom efficiency, thus rendering new selective procedures, which do not generate large amounts of by-products highly desirable.<sup>8,9</sup>

Several organic and inorganic oxidants react with TEMPO generating the corresponding oxoammonium salt. The latter is a much stronger oxidant than the nitroxyl radical and cleanly reacts with alcohols to give aldehydes or ketones.<sup>10</sup> Based on this, several catalytic systems in which the oxoammonium salt is (re)generated in situ from substoichiometric amounts of TEMPO have been developed. Early examples of TEMPO-mediated reactions included the oxidation of secondary alcohols to ketones with *m*-chloroperbenzoic acid,<sup>11</sup> and the oxidation of primary, secondary and benzylic alcohols in an electrochemical

process.<sup>12</sup> A more versatile and efficient catalytic procedure in which buffered bleach acts as the terminal oxidant was introduced in 1987 by Montanari and co-workers.<sup>13</sup> The oxidation reaction proceeds under mild conditions and both primary and secondary alcohols are converted to carbonyl compounds in high yields, even in large scale operations. In addition, the oxidation of primary alcohols can be driven to give carboxylic acids by adding a phase-transfer catalyst to the biphasic aqueous/organic system.<sup>14</sup> Many other organic and inorganic terminal oxidants (e.g., [bis(acetoxy)iodo]benzene (BAIB),<sup>15</sup> trichloroisocyanuric acid (TCCA),<sup>16</sup> oxone,<sup>17</sup> or iodine<sup>18</sup>) have been subsequently introduced with the aim of further expanding the already wide applicability of Montanari's procedure.

A different approach, pioneered by Semmelhack and co-workers,<sup>19</sup> consists of the use of oxygen as the primary oxidant in conjunction with a TEMPO/metal catalyst combination. The use of oxygen would be preferred over that of the above-mentioned oxidants from both an economic and an environmental standpoint and Semmelhack actually demonstrated the aerobic oxidation of allylic and benzylic alcohols to aldehydes by TEMPO/CuCl in DMF. Unfortunately, this method is ineffective with aliphatic and alicyclic alcohols and its applicability is therefore, limited.<sup>†</sup> Better results were obtained by Sheldon

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<sup>&</sup>lt;sup>†</sup> According to Semmelhack, an oxoammonium salt generated by oxidation of TEMPO by Cu(II) is the actual oxidant, but, as pointed out by Sheldon, the lack of reactivity of aliphatic alcohols is not consistent with this hypothesis. For an exhaustive discussion and more plausible reaction mechanisms see Ref. 4.

and co-workers who achieved the aerobic oxidation of a broad range of alcohols using a combination of RuCl<sub>2</sub>-(PPh<sub>3</sub>)<sub>3</sub> and TEMPO in chlorobenzene, toluene or even in the absence of a solvent.<sup>8,20,21</sup> Besides requiring an expensive transition-metal complex, the method operates at a relatively high temperature (100 °C) and, in the case of secondary alcohols, high oxygen pressure (up to 10 bar). These drawbacks are partly avoided by using a combination of TEMPO and the polyoxometalate H<sub>5</sub>[PV<sub>2</sub>Mo<sub>10</sub>O<sub>4</sub>].<sup>22</sup> More recently, the aerobic oxidation of alcohols under fluorous biphasic conditions and atmospheric pressure in the presence of TEMPO and synthetically demanding fluorous Cu(I) complexes has been independently described by two groups.<sup>23,24</sup> A mixture of CuBr<sub>2</sub>, 2,2,'-bipyridine and t-BuOK was shown to catalyze the aerobic oxidation of primary and benzylic alcohols in the presence of TEMPO in CH<sub>3</sub>CN/H<sub>2</sub>O 1:1 as a solvent under mild conditions.<sup>25,26</sup> Another uncomplicated and cheap catalytic system comprised of TEMPO in combination with tiny amounts of  $Mn(NO_3)_2$  and  $Co(NO_3)_2$  in CH<sub>3</sub>COOH was reported by Minisci and co-workers.<sup>27,28</sup> This combination is particularly effective for the oxidation of primary and benzylic alcohols, but good results are also obtained with less reactive secondary alcohols. In order to avoid the use of metal salts, Hu and co-workers developed two aerobic processes in which TEMPO is used in combination with Br<sub>2</sub>/NaNO<sub>2</sub> or 1,3-dibromo-5,5'-dimethylidantoin/NaNO<sub>2</sub> TEMPO, respectively.<sup>29,30</sup> Teflon-lined apparatus, operating pressures up to 9 bar and relatively high amounts of TEMPO and co-catalysts (up to 10 mol% in the case of the oxidation of secondary alcohols in the presence of 1,3-dibromo-5,5'-dimethylidantoin/NaNO<sub>2</sub>) were required.

Recovery and recycling of TEMPO by immobilization on either inorganic or organic supports has been actively investigated. Indeed, whichever oxidant is used, separation of the products from TEMPO could require lengthy workup procedures, especially when reactions are run on large scale. Moreover, TEMPO is quite expensive, so it is desirable to be able to separate the catalyst after the oxidation reaction and to reuse it. Electrochemical processes were readily adapted to meet these goals and several examples of graphite felt electrodes and glassy carbon electrodes coated with TEMPO and related radicals have been used for the electrochemical oxidation of alcohols.<sup>31,32</sup> In 1985, Miyazawa and Endo reported the synthesis of soluble and insoluble polystyrene-type polymers featuring TEMPO residues, which were used as catalysts for the oxidation of benzyl alcohol to benzaldehyde with K<sub>3</sub>Fe(CN)<sub>6</sub> or CuCl<sub>2</sub>/ Cu(OH)<sub>2</sub> as the terminal oxidants.<sup>33,34</sup> While no mention of recovery and recycling of these catalysts was provided, the same group later reported that 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl (4-OH-TEMPO) immobilized onto silica or ferrite (previously functionalized by the reaction of their surface hydroxyl groups with 4-trimethoxysilyl-1,2,5,6-tetrahydrophthalic anhydride) could be recycled up to 45 times in the benzyl alcohol oxidation promoted by CuCl<sub>2</sub>/Cu(OH)<sub>2</sub>.<sup>35</sup> Silica-supported TEMPO radicals and their use in alcohol oxidations were subsequently reported by several groups. Both silica gel and ordered mesoporous silica (e.g., MCM-41) were used,<sup>36-39</sup> the best results being obtained by Bolm and co-workers who attached 4-oxo-2,2,6,6-tetramethylpiperidine-1-oxyl to a commercially available aminopropylfunctionalized silica and an aminopropyl-functionalized porous glass. These catalysts were employed in combination with bleach under Montanari's conditions affording high yields and selectivities. Ten subsequent reaction runs were demonstrated, although partial degradation of the supported TEMPO catalysts was observed.<sup>38,40</sup> Silica matrices doped with TEMPO prepared under mild conditions by the sol-gel approach were also found to be selective and recyclable heterogeneous catalysts for the oxidation of alcohols with bleach.<sup>41,42</sup> A polymer immobilized nitroxyl radical derived from a commercially available oligomeric 2,2,6,6-tetramethylpiperidine (Chimassorb 994) was developed by Sheldon and co-workers.<sup>43</sup> Analogously to TEMPO, this catalyst allowed the smooth conversion of benzylic, primary and secondary alcohols to carbonyl compounds with bleach as the terminal oxidant. In addition, when using methyl-tertbutylether or no solvent, the catalyst proved to be heterogeneous and could be recycled.<sup>44</sup> Very recently, Toy and co-workers have shown that TEMPO attached to a swellable resin and polystyrene-supported diacetoxyiodosobenzene can be used simultaneously for the selective oxidation of a variety of alcohols.<sup>45</sup> The polymeric oxidant in excess and the supported TEMPO catalyst can be recovered by simple filtration and reused.

As a result of the increasing interest in recoverable soluble reagents and catalysts,<sup>46</sup> in the last few years immobilization of TEMPO onto soluble polymers has started to emerge as an alternative to the above-mentioned heterogeneous supports. Soluble polymer-supported TEMPO radicals have been prepared by ring-opening methatesis of norbornene derivatives.<sup>47</sup> Preliminary tests revealed that the activity of these catalysts was consistently lower than that of TEMPO in the oxidation of alcohols under Montanari's conditions. Promising results have been obtained in the oxidation of alcohols with various primary oxidants (including bleach) catalyzed by a TEMPO derivative tethered onto a modified commercially available poly-(ethylene glycol) (PEG) monomethyl ether of molecular weight of about 5000 Da.48 The catalyst was easily recovered by selective precipitation from Et<sub>2</sub>O and its recyclability was studied using the oxidation of 1-octanol with the mild oxidant BAIB as a model reaction. The results of independent studies on the catalytic performance and recyclability of a series of PEG-supported TEMPO derivatives in the oxidation of alcohols under Montanari's conditions has been also disclosed.<sup>49,50</sup> Even more recently, it has been shown that recoverable soluble TEMPO catalysts can be designed without recourse to polymeric supports. Fluorous TEMPO derivatives have been used as selective catalysts for the oxidation of alcohols under mild, homogeneous conditions.<sup>51</sup> The peculiar solubility properties ensured by the presence of highly fluorinated domains allowed the easy recovery of some of these catalysts by liquid-liquid or solid-phase extraction of the reaction mixture. Gao and co-workers reported the synthesis of a TEMPO radical attached to an imidazolium cation and investigated its catalytic activity for the oxidation of alcohols with bleach in a biphasic system ionic liquid/ water. The catalytic activity of this system was similar to that observed with TEMPO and the ionic liquid phase containing the catalyst was recycled up to three times.<sup>52</sup>

Despite the obvious advantages of using of oxygen as terminal oxidant, examples of aerobic oxidation of alcohols in the presence of recoverable and recyclable nitroxyl radicals are limited. A few solid polymer-supported TEMPO derivatives have been tested as catalysts for the aerobic oxidation of benzylic alcohols under Semmelhack's conditions (CuCl/DMF).<sup>39,44</sup> A tetranitroxyl radical poorly soluble in most organic solvents, developed by Ciba chemists, gave good results in the aerobic oxidation of a wider range of substrates under slightly modified Minisci's conditions and was recycled for four times.<sup>53</sup> Analogously, a new polymer-supported TEMPO prepared by reaction between 4-OH-TEMPO and a carboxylic acid functionalized fiber was used as an heterogeneous catalyst under Minisci's conditions showing high activity and selectivity for the oxidation of primary alcohols to aldehydes.<sup>54</sup>

We here show that PEG-supported TEMPO derivatives can be conveniently employed as homogeneous, recoverable and recyclable catalysts for the aerobic oxidation of alcohols under Minisci's conditions, combining the advantages typical of heterogenized TEMPO with those of the soluble parent compound.



#### 2. Results and discussion

Poly(ethylene glycol)s (PEGs) of  $M_w$  greater than 2000 Da are readily functionalized, inexpensive polymers that exhibit excellent solubility in many organic solvents, including CH<sub>2</sub>Cl<sub>2</sub> and CH<sub>3</sub>COOH. PEG precipitation as a semicrystalline solid can be then induced by dilution of the solution with an incompatible solvent, such as Et<sub>2</sub>O. This behavior and the ease of functionalization make PEG a popular soluble polymeric support for homogeneous catalysts.<sup>55</sup> Indeed, the choice of proper solvent combinations makes it possible to run a reaction under homogeneous catalysis conditions (where the PEG-supported catalyst is expected to perform at its best) and then to recover the catalyst by precipitation/filtration as if it were bound to an insoluble matrix.

In a recent communication, we described the synthesis of the PEG-supported nitroxyl radical **1** (PEG-TEMPO **1**, Fig. 1) in which a TEMPO moiety is connected to the polymeric backbone  $(M_w = 5000)^{\ddagger}$  by a benzylic ether linker (Scheme 1).<sup>48</sup> As shown by Ferreira et al., the same TEMPO residue can be attached directly to the PEG chain terminus via an ether linkage.<sup>49</sup> A slight modification of their original method (Scheme 2) allowed us to prepare PEG-TEMPO **2** in 80% yield from 4-OH-TEMPO and the known PEG mesylate derivative **3**.<sup>56</sup>

Both PEG-supported TEMPO derivatives were found to be completely soluble in CH<sub>3</sub>COOH, the solvent of choice for the oxidation of alcohols under the conditions developed by Minisci, which are the most convenient among those







Scheme 1. Synthesis of PEG-TEMPO 1.

<sup>&</sup>lt;sup>‡</sup> Commercially available PEGs possess very narrow polydispersity indices.  $M_{\rm w}$  of the PEG used actually ranges from 4500 to 5500 Da.

proposed for the aerobic oxidation of alcohols catalyzed by TEMPO.<sup>27,28</sup> Thus, the oxidation of the model compound 4-bromobenzyl alcohol was studied using a combination of  $Mn(NO_3)_2 \cdot H_2O$  (2 mol%),  $Co(NO_3)_2 \cdot H_2O$  (2 mol%) and PEG-TEMPO (1 or 2) in acetic acid (Scheme 3). We were pleased to observe that using  $5 \mod \%$  of either 1 or 2, 4-bromobenzaldehyde was formed quantitatively at room temperature under atmospheric pressure of oxygen in less than 3 h (Table 1, entries 1 and 2). It should be noted that under similar conditions, but in the presence of TEMPO, the aerobic oxidation of para-substituted benzyl alcohols proceeds much slower, requiring up to 6 h and 10 mol% of nitroxyl radical to go to completion.<sup>27</sup> When the amount of PEG-TEMPO was reduced to 2 mol%, the oxidation still went to completion smoothly in 4 h in the case of 1, whereas only 92% conversion was attained using the linker-less radical 2 (entries 3 and 4). The higher activity of 1 was further evidenced by experiments carried out using 1 mol% of PEG-TEMPO (entries 5 and 6).

Attempts to recover and recycle the two PEG-TEMPO radicals also gave good results (Table 2). The post-reaction work-up was particularly straightforward in the case of 1, which was precipitated out from the acetic acid solution by adding ice-cold Et<sub>2</sub>O. The radical was recovered by filtration, dried under vacuum and re-used without any further treatment. Fresh  $Mn(NO_3)_2 \cdot H_2O$  and  $Co(NO_3)_2 \cdot$ H<sub>2</sub>O were added to each successive run. No decrease in the rate and in the selectivity of oxidation was observed in the first three runs. However, the activity of the catalytic system progressively decreased in the fourth and fifth run and conversion of 4-bromobenzyl alcohol to 4-bromobenzaldehyde was as low as 74% after a reaction time of 3 h in the sixth run. These results compare well with those reported in the case of a soluble tetranitroxyl radical, which has been used as catalyst in the oxidation of benzyl alcohol with a ratio substrate/radical=41 (corresponding to a concentration = 10 mol% of nitroxyl radical) and recycled for four times affording benzaldehyde in 95% yield in the fourth run.53

$$\begin{array}{c} OH \\ R \\ R \\ R \\ \end{array} \xrightarrow{O_2, \text{ Catalyst}} \\ CH_3CO_2H \\ \end{array} \xrightarrow{O} \\ R \\ R \\ R \\ \end{array}$$

R = Alk, Ar, Bn, H; R' = Alk, H

Catalyst = 1 or  $2 + Mn(NO_3)_2 + Co(NO_3)_2$ 

**Scheme 3.** Aerobic oxidation of alcohols under Minisci's conditions catalyzed by PEG-TEMPO.

 Table 2. Aerobic oxidation of 4-bromobenzyl alcohol

Run	PEG-TEMPO	Conversion (%)	Selectivity (%)
1	1	>99	>99
2		>99	>99
3		>99	>99
4		91	>99
5		83	>99
6		74	>99
1	2	>99	>99
2		98	>99
3		96	>99
4		92	>99
5		84	>99
6		80	>99

Recycling of PEG-TEMPO radicals. T=25 °C;  $O_2=1$  atm; PEG-TEM-PO=5 mol%; Mn(NO<sub>3</sub>)<sub>2</sub>=2 mol%; Co(NO<sub>3</sub>)<sub>2</sub>=2 mol%; reaction time = 3 h; conversion and selectivity determined by GC (see Section 4 for details).

Recovery and recycling of PEG-TEMPO 2 was also demonstrated, but in that case direct precipitation of the radical was not viable. Indeed, a slurry formed upon addition of ice-cold  $Et_2O$  to the reaction solution and a sensible loss of 2 was observed after filtration. A procedure similar to that employed for the recovery of the abovementioned tetranitroxyl radical, proved to be more effective. Acetic acid was first evaporated, followed by addition of ice-cold  $Et_2O$  to dissolve the reaction product leaving the insoluble PEG-TEMPO 2 as a solid residue. Six subsequent runs using 4-bromobenzyl alcohol as a substrate were thus carried out, with results very close to those obtained in the case of PEG-TEMPO 1.

The aerobic oxidation of a variety of alcohols catalyzed by PEG-TEMPO radicals under Minisci's conditions was next examined (Table 3). Benzylic alcohols were readily oxidized with high conversion and high selectivity to the corresponding aldehydes both in the presence of PEG-TEMPO 1 and PEG-TEMPO 2 (catalyst loading = 5 mol%, entries 1-3). Analogously to what was observed with TEMPO,<sup>27</sup> the oxidation of primary alcohol was best performed at 40 °C in the presence of either 5 or 10 mol% of PEG-TEMPO 1 depending on the substrate (entries 4, 7 and 9). Besides aldehydes, small amounts of carboxylic acids (<5% of the starting alcohol) were detected. The difficult conversion of unreactive aliphatic primary alcohols using oxygen as terminal oxidant proceeded more slowly in the presence of PEG-TEMPO 2. For instance, with a catalyst loading of 5 mol% conversion of 1-octanol attained 65% in 4 h (entry 5) against 97% attained in the reaction catalyzed by PEG-TEMPO 1 (entry 4). The reaction did not go to completion even in the presence of 10 mol% of PEG-

Table 1. Aerobic oxidation of 4-bromobenzyl alcohol to aldehyde, catalyzed by PEG-TEMPO radicals in combination with Mn(II) and Co(II) nitrates<sup>a</sup>

Entry	Radical	Mol%	Time (h)	Conversion (%)	Selectivity (%)
1	1	5	3	>99	>99
2	2	5	3	>99	>99
3	1	2	4	>99	>99
4	2	2	4	92	>99
5	1	1	5	90	>99
6	2	1	5	72	>99
7 <sup>b</sup>	TEMPO	10	6	>99	>99

<sup>a</sup> T=25 °C;  $O_2=1$  atm; Mn(NO<sub>3</sub>)<sub>2</sub>=2 mol%; Co(NO<sub>3</sub>)<sub>2</sub>=2 mol%; conversion and selectivity determined by GC (see Section 4 for details). <sup>b</sup> Literature data (Ref. 27). Substrate=4-methylbenzyl alcohol. T=20 °C.

Table 3. Aerobic oxidation of alcohols to carbon	l compounds, catalyzed l	by PEG-TEMPO radicals in combination v	with Mn(II) and Co(II) nitrates <sup>a</sup>

Entry	PEG-TEMPO	Alcohol	<i>T</i> (°C)	Time (h)	Conversion (%)	Selectivity (%)
1	1	Benzyl alcohol	25	3	>99	>99
2	2	Benzyl alcohol	25	3	>99	>99
3	1	4-Nitrobenzyl alcohol	25	3	>99	>99
4	1	1-Octanol	40	4	97	95
5	2	1-Octanol	40	4	65	94
6	<b>2</b> <sup>b</sup>	1-Octanol	40	4	75	94
7	1	1-Undecanol	40	4	>99	96
8	$2^{\mathrm{b}}$	1-Undecanol	40	4	78	96
9	<b>1</b> <sup>b</sup>	Cinnamyl alcohol	40	6	>99	>99
10	1	1-Phenylethanol	25	5	96	>99
11	<b>1</b> <sup>b</sup>	Cyclooctanol	40	4	>99	>99
12	<b>2</b> <sup>b</sup>	Cyclooctanol	40	4	68	>99
13	<b>1</b> <sup>b</sup>	2-Octanol	40	24	51	>99
14	<b>2</b> <sup>b</sup>	2-Octanol	40	24	43	>99
15	1 <sup>b</sup>	2-Undecanol	40	24	52	>99

<sup>a</sup>  $O_2 = 1$  atm; PEG-TEMPO=5 mol%; Mn(NO<sub>3</sub>)<sub>2</sub>=2 mol%; Co(NO<sub>3</sub>)<sub>2</sub>=2 mol%; conversion and selectivity determined by GC (see Section 4 for details). <sup>b</sup> PEG-TEMPO=10 mol%.

TEMPO 2 (entry 6). Secondary alcohols were also oxidized to ketones (entries 10-15) at 40 °C, reaction rates depending on the steric hindrance of the substrate as found in the case of other primary oxidants.<sup>48</sup> Thus, in the presence of PEG-TEMPO 1, 1-phenylethanol and cyclooctanol were readily oxidized in high yield to acetophenone and cyclooctanone, respectively, (entries 10 and 11), whereas conversion of 2-octanol and 2-undecanol slightly exceeded 50% after 24 h (entries 13 and 15). The lower activity of PEG-TEMPO 2 with respect to PEG-TEMPO 1 was demonstrated again in the oxidation of 2-octanol and cyclooctanol (entries 12 and14). Seen as a whole, these results clearly show that the insertion of a spacer separating the PEG chain from the TEMPO moiety has a beneficial effect on the catalytic activity of these supported systems. The presence of a spacer possibly prevents that partial hindrance of the active site within the polymeric structure as a result of coiling of the PEG polymeric backbone, which was suggested to be the cause of the reduced catalytic activity of certain linkerless PEG-TEMPO.<sup>49</sup>

#### **3.** Conclusions

Two poly(ethylene glycol)-supported TEMPO (PEG-TEMPO) prepared from readily available precursors proved to be efficient catalysts in the chemoselective oxidation of alcohols with molecular oxygen under mild conditions. Catalytic activities and selectivities of these soluble TEMPO derivatives are similar to those exhibited by the parent compound, and even higher in the case of PEG-TEMPO 1. In addition, both PEG-TEMPO offer the advantages of simplified workup procedure and easy recycling, which are usually associated with the use of heterogenized TEMPO.

#### 4. Experimental

#### 4.1. General

Solvents were purified by standard methods and dried if necessary. Commercially available reagents were used as received. PEG-TEMPO 1 and PEG mesylate 3 was prepared as previously described.<sup>48,56</sup> GC analyses were performed on an Agilent 6850 instrument (column: HP-1 100% dimethylpolysiloxane 30 m×320 µm×0.25 µm). Carrier=He (constant flow, 2.2 mL/min); mode=split (split ratio=80:1); injector T=250 °C; detector (FID) t=280 °C. The products of the oxidation reactions were determined by comparison with the commercially available carbonyl compounds and carboxylic acids.

#### **4.2. PEG-TEMPO 2**

To a suspension of 60% NaH in mineral oil (25 mg, 0.63 mmol) in dry DMF (4 mL) was added 4-hydroxy-TEMPO (108 mg, 0.63 mmol) and the resulting slurry was stirred at room temperature for 1 h under nitrogen. A solution of PEG-mesylate **3** (800 mg, 0.16 mmol), previously dried under vacuum at 100 °C for 1 h, in dry DMF (4 mL) was then added and the mixture was stirred for 70 h at 70 °C. After cooling to room temperature, the suspension was filtered and the filtrate evaporated to dryness under reduced pressure. The residue was taken up in CH<sub>2</sub>Cl<sub>2</sub> (2 mL) and added to Et<sub>2</sub>O (70 mL). The precipitate was collected by filtration, washed with Et<sub>2</sub>O (3×30 mL) and dried under vacuum. PEG-TEMPO **1** (650 mg, 80%) was obtained as a pale orange solid (physical data in agreement with those reported in the literature).<sup>50</sup>

### **4.3.** General procedure for the aerobic oxidation of alcohols

Reactions were carried out in a jacketed 20 mL Schlenk tube thermostated by circulating water (Haake F3 Cryostat) and fitted with a stirring bar. The reactor was charged with (a) a freshly prepared solution of alcohol (1 mmol) and *n*-decane (71.1 mg, 0.5 mmol, internal standard for GC) in acetic acid (1 mL); (b) a freshly prepared solution of  $Mn(NO_3)_2 \cdot H_2O$  (5.0 mg, 0.02 mmol) and  $Co(NO_3)_2 \cdot H_2O$  (5.8 mg, 0.02 mmol) in acetic acid (1 mL). The combined solutions were stirred 5 min, then PEG-TEMPO (0.05–0.1 mmol) was added. The Schlenk tube was attached to a gas burette filled with oxygen and the solution was stirred for the time indicated in Tables 1–3. A 20 µL sample of the solution was diluted with 0.2 mL ice-cold Et<sub>2</sub>O.

The precipitated catalyst was eliminated by filtration on PTFE septum and the liquid layer was analyzed by GC.

## 4.4. Oxidation of 4-bromobenzyl alcohol: catalyst recycling

The jacketed reactor thermostated at 25 °C was charged with (a) a freshly prepared solution of 4-bromobenzyl alcohol (374.1 mg, 2 mmol) and n-decane (142.2 mg, 1 mmol, internal standard for GC) in acetic acid (2 mL); (b) a freshly prepared solution of  $Mn(NO_3)_2 \cdot H_2O$  (10.0 mg, 0.04 mmol) and  $Co(NO_3)_2 \cdot H_2O$  (11.6 mg, 0.04 mmol) in acetic acid (1 mL). The combined solutions were stirred 5 min, then PEG-TEMPO 1 (550 mg, 0.1 mmol) was added and the solution was stirred for 3 h under an atmosphere of molecular oxygen. Ice-cold Et<sub>2</sub>O (10 mL) was added and the precipitated PEG-TEMPO 1 was filtered on a sintered glass funnel and washed with cold  $Et_2O$  (3×3 mL). The combined organic phase was analyzed by GC, whereas the recovered PEG-TEMPO 1 was dried under vacuum and used for the subsequent run. When PEG-TEMPO 2 (510 mg, 0.1 mmol) was used, acetic acid was evaporated under reduced pressure prior to the addition of Et<sub>2</sub>O. Results are reported in Table 2.

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#### **References and notes**

- De Nooy, A. E. J.; Besemer, A. C.; van Bekkum, H. Synthesis 1996, 1153–1174.
- Adam, W.; Saha-Möller, C. R.; Ganeshpure, P. A. Chem. Rev. 2001, 101, 3499–3548.
- Bragd, P. L.; van Bekkum, H.; Besemer, A. C. Top. Catal. 2004, 27, 49–66.
- 4. Sheldon, R. A.; Arends, I. W. C. E. Adv. Synth. Catal. 2004, 346, 1051–1071.
- 5. Hudlicky, M. Oxidations in Organic Synthesis; American Chemical Society: Washington, DC, 1990; pp 114–149.
- 6. Tidwell, T. T. Synthesis 1990, 857-870 and references therein.
- Luzzio, F. A. In The Oxidation of Alcohols by Modified Oxochromium (VI)-Amine Reagents; Paquette, L.A. Ed.; Organic Reactions, John Wiley: New York, 1998; Vol. 53, pp 1–221.
- Sheldon, R. A.; Arends, I. W. C. E.; ten Brink, G.-J.; Dicksmann, A. Acc. Chem. Res. 2002, 35, 774–781.
- Sheldon, R. A.; Arends, I. W. C. E. In *Modern Oxidation of Alcohols Using Environmentally Benign Oxidants*; Bäckvall, J.-E., Ed.; Modern oxidation methods; Wiley-VCH: Weinheim, 2004; pp 83–118.
- Merbouh, N.; Bobbitt, J. M.; Brueckner, C. Org. Prep. Proced. Int. 2004, 36, 3–31 and references therein.
- Cella, J. A.; Kelley, J. A.; Kenehan, E. F. J. Org. Chem. 1975, 40, 1860–1862.
- Semmelhack, M. F.; Chou, C. S.; Cortés, D. A. J. Am. Chem. Soc. 1983, 105, 4492–4494.

- Anelli, P. L.; Biffi, C.; Montanari, F.; Quici, S. J. Org. Chem. 1987, 52, 2559–2562.
- Anelli, P. L.; Banfi, S.; Montanari, F.; Quici, S. J. Org. Chem. 1989, 54, 2970–2972.
- De Mico, A.; Margarita, R.; Parlanti, L.; Vescovi, A.; Piancatelli, G. J. Org. Chem. 1997, 62, 6974–6977.
- De Luca, L.; Giacomelli, G.; Porcheddu, A. Org. Lett. 2001, 3, 3041–3043.
- 17. Bolm, C.; Magnus, A. S.; Hildebrand, J. P. Org. Lett. 2000, 2, 1173–1175.
- 18. Miller, R. A.; Hoerrner, R. S. Org. Lett. 2003, 5, 285-287.
- Semmelhack, M. F.; Schmid, C. R.; Cortés, D. A.; Chou, C. S. J. Am. Chem. Soc. 1984, 106, 3374–3376.
- Dijksman, A.; Arends, I. W. C. E.; Sheldon, R. A. Chem. Commun. 1999, 1591–1592.
- Dijksman, A.; Marino-Gonzales, A.; Mairata y Payeras, I.W.C. E.; Sheldon, R. A. J. Am. Chem. Soc. 2001, 123, 6826–6833.
- 22. Ben-Daniel, R.; Alsters, P.; Neumann, R. J. Org. Chem. 2001, 66, 8650–8653.
- Betzemeier, B.; Cavazzini, M.; Quici, S.; Knochel, P. Tetrahedron Lett. 2000, 41, 4343–4346.
- Contel, M.; Izuel, C.; Laguna, M.; Villuendas, P. R.; Alonso, P. J.; Fish, R. H. *Chem. Eur. J.* **2003**, *9*, 4168–4178.
- 25. Gamez, P.; Arends, I. W. C. E.; Reedijk, J.; Sheldon, R. A. *Chem. Commun.* **2003**, 2414–2415.
- Gamez, P.; Arends, I. W. C. E.; Sheldon, R. A.; Reedijk, J. Adv. Synth. Catal. 2004, 346, 805–811.
- 27. Cecchetto, A.; Fontana, F.; Minisci, F.; Recupero, F. *Tetrahedron Lett.* **2001**, *42*, 6651–6653.
- Minisci, F.; Recupero, F.; Cecchetto, A.; Gambarotti, C.; Punta, C.; Faletti, R.; Paganelli, R.; Pedulli, G. F. *Eur. J. Org. Chem.* 2004, 109–119.
- 29. Liu, R.; Liang, X.; Dong, C.; Hu, X. J. Am. Chem. Soc. 2004, 126, 4112–4113.
- Liu, R.; Dong, C.; Liang, X.; Wang, X.; Hu, X. J. Org. Chem. 2005, 70, 729–731.
- Deronzier, A.; Limosin, D.; Moutet, J.-C. *Electrochim. Acta* 1987, 32, 1643–1647.
- 32. Kishioka, S.; Ohki, S.; Ohsaka, T.; Tokuda, K. J. Electroanal. Chem. **1998**, 452, 179–186 and references therein.
- 33. Miyazawa, T.; Endo, T. J. Polym. Sci. Chem. Ed. 1985, 23, 2487–2494.
- 34. Miyazawa, T.; Endo, T. J. Mol. Catal. 1988, 49, L31-L34.
- Tsubokawa, N.; Kimoto, T.; Endo, T. J. Mol. Catal. A 1995, 101, 45–50.
- Heeres, A.; van Doren, H. A.; Gotlieb, K. F.; Bleeker, I. P. Carbohydr. Res. 1997, 299, 221–227.
- Brunel, D.; Lentz, P.; Sutra, P.; Deroide, B.; Fajula, F.; Nagy, J. B. Stud. Surf. Sci. Catal. 1999, 125, 237–244.
- Verhoef, M. J.; Peters, J. A.; van Bekkum, H. Stud. Surf. Sci. Catal. 1999, 125, 465–472. Bolm, C.; Fey, T. Chem. Commun. 1999, 1795–1796.
- Brunel, D.; Fajula, F.; Nagy, J. B.; Deroide, B.; Verhoef, M. J.; Veum, L.; Peters, J. A.; van Bekkum, H. *Appl. Catal., A* 2001, *213*, 73–82.
- Fey, T.; Fischer, H.; Bachmann, S.; Albert, K.; Bolm, C. J. Org. Chem. 2001, 66, 8154–8159.
- 41. Ciriminna, R.; Blum, J.; Avnir, D.; Pagliaro, M. Chem. Commun. 2000, 1441–1442.
- 42. Ciriminna, R.; Bolm, C.; Fey, T.; Pagliaro, M. Adv. Synth. Catal. 2002, 344, 159–163.

- 43. Dijksman, A.; Arends, I. W. C. E.; Sheldon, R. A. *Chem. Commun.* **2000**, 271–272.
- 44. Dijksman, A.; Arends, I. W. C. E.; Sheldon, R. A. Synlett **2001**, 102–104.
- 45. But, T. Y. S.; Tashino, Y.; Togo, H.; Toy, P. H. Org. Biomol. Chem. 2005, 3, 970–971.
- 46. Gladysz, J. A. *Chem. Rev.* **2002**, *102*, 3215–3216. The whole issue is devoted to recoverable catalysts and reagents.
- 47. Tanyeli, C.; Gümü, A. Tetrahedron Lett. 2003, 44, 1639–1642.
- 48. Pozzi, G.; Cavazzini, M.; Quici, S.; Benaglia, M.; Dell'Anna, G. *Org. Lett.* **2004**, *6*, 441–443.
- 49. Ferreira, P.; Hayes, W.; Phillips, E.; Rippon, D.; Tsang, S. C. *Green Chem.* **2004**, *6*, 310–312.

- Ferreira, P.; Phillips, E.; Rippon, D.; Tsang, S. C.; Hayes, W. J. Org. Chem. 2004, 69, 6851–6859.
- 51. Holczknecht, O.; Cavazzini, M.; Quici, S.; Shepperson, I.; Pozzi, G. Adv. Synth. Catal. 2005, 347, 677–688.
- 52. Wu, X.-E.; Ma, L.; Ding, M.-X.; Gao, L.-X. Synlett 2005, 607–610.
- 53. Minisci, F.; Recupero, F.; Rodinò, M.; Sala, M.; Schneider, A. *Org. Process Res. Dev.* **2003**, *7*, 794–798.
- 54. Gilhespy, M.; Lok, M.; Baucherel, X. Chem. Commun. 2005, 1085–1086.
- 55. Dickerson, T. J.; Reed, N. N.; Janda, K. D. Chem. Rev. 2002, 102, 3325–3344.
- Annunziata, R.; Benaglia, M.; Cinquini, M. Chem. Eur. J. 2000, 6, 133–138.