

# Polymer immobilised TEMPO (PIPO): an efficient catalyst for the chlorinated hydrocarbon solvent-free and bromide-free oxidation of alcohols with hypochlorite

Arné Dijkman, Isabel W. C. E. Arends and Roger A. Sheldon\*

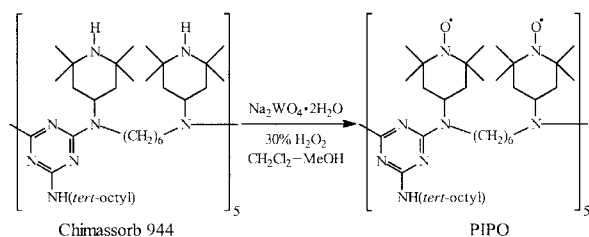
Laboratory for Organic Chemistry and Catalysis, Department of Biotechnology, Delft University of Technology, Julianalaan 136, 2628 BL Delft, The Netherlands. E-mail: secretariat-ock@stm.tudelft.nl

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**PIPO, a readily prepared polymer immobilised TEMPO, can be employed as an efficient recyclable heterogeneous catalyst for the chlorinated hydrocarbon solvent-free and bromide-free bleach oxidation of a variety of alcohols and polyols.**

The use of stable nitroxyl radicals, such as TEMPO, as catalysts for the oxidation of alcohols to aldehydes, ketones and carboxylic acids is well documented.<sup>1</sup> Typically, these transformations employ 1 mol% of the nitroxyl radical and a stoichiometric amount of a terminal oxidant, e.g. sodium hypochlorite,<sup>2</sup> MCPBA (*m*-chloroperbenzoic acid),<sup>3</sup> sodium bromite,<sup>4</sup> trichloroisocyanuric acid<sup>5</sup> and oxygen in combination with CuCl<sup>6</sup> or RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>.<sup>7</sup> In particular, the TEMPO-bleach protocol using bromide as co-catalyst introduced by Anelli *et al.*<sup>2</sup> is finding wide application in organic synthesis. Although only a small amount of catalyst is used, recyclability is an issue and several heterogeneous TEMPO systems have been reported.<sup>8</sup> For example, MCM-41<sup>8g</sup> and silica-supported TEMPO<sup>8h,i</sup> have been applied in oxidation reactions using hypochlorite as the oxidant. The preparation of these catalysts involves initial functionalisation of the support followed by covalent attachment of a 4-substituted TEMPO.

Here, we report the use of a readily prepared polymer immobilised TEMPO as a catalyst for alcohol oxidations. It was derived from a commercially available oligomeric, sterically hindered amine, poly[[6-[(1,1,3,3-tetramethylbutyl)amino]-1,3,5-triazine-2,4-diyl][2,2,6,6-tetramethyl-4-piperidinyl-imino]-1,6-hexanediyl][(2,2,6,6-tetramethyl-4-piperidinyl-imino)], better known as Chimassorb 944 (MW ≈ 3000; see Scheme 1 for structure). This compound is used as an antioxidant and a light stabiliser for plastics. It contributes significantly to the long term heat stability of polyolefins and has broad approval for use in polyolefin food packaging.<sup>9</sup>



Scheme 1 Synthesis of PIPO.

Nitroxyl radicals are normally prepared by treating the analogous secondary amine with Na<sub>2</sub>WO<sub>4</sub>·2H<sub>2</sub>O and hydrogen peroxide.<sup>10</sup> In the case of Chimassorb 944, the same procedure was applied resulting in the formation of an oligomeric TEMPO (Scheme 1). Probe-MS data revealed that the mass of each segment increased by 30 owing to transformation of two secondary amine moieties into the corresponding nitroxyl radicals. This new polymer immobilised TEMPO, further referred to as PIPO (polyamine immobilised piperidinyl oxyl),

proved to be an effective catalyst for oxidations of alcohols with hypochlorite using the Anelli protocol.<sup>2†</sup>

Primary and secondary aliphatic and benzylic alcohols were smoothly converted to the corresponding aldehydes and ketones in CH<sub>2</sub>Cl<sub>2</sub> (Table 1). Under these conditions the system was homogeneous as PIPO is soluble in dichloromethane. In contrast, in the absence of solvent (entry 3) PIPO was an active heterogeneous catalyst. The heterogeneous nature of the catalyst was confirmed in a filtration experiment, in which the reaction mixture was filtered after 10 min. The filtrate showed no activity at all during 1 h after filtration. The residue, however, could be reused at least twice as a catalyst. The minor loss of activity (< 5%) observed is probably due to mechanical losses occurring during filtration of the small amount of catalyst.

Table 1 PIPO-catalysed oxidation of alcohols with bromide/hypochlorite<sup>a</sup>

Entry	Substrate	Product	t/min	Conv.(%) <sup>b</sup>	Sel.(%) <sup>b</sup>
1	Octan-1-ol	Octanal	20	>99	>99
2	Octan-2-ol	Octan-2-one	20	>99	>99
3 <sup>c</sup>			45	95	>99
4	Benzyl alcohol	Benzaldehyde	20	>99	>99
5	1-Phenylethanol	Acetophenone	20	>99	>99

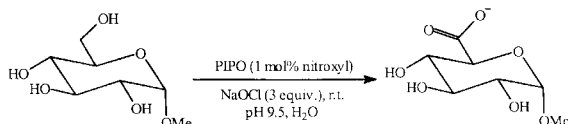
Further investigation revealed that the use of bromide was not necessary. Thus, in contrast to the conventional TEMPO-bleach oxidations, which use dichloromethane as solvent and bromide as a co-catalyst,<sup>2</sup> PIPO catalyses the oxidation of a variety of alcohols in the absence of organic solvent and using only a hypochlorite solution (0.35 M, pH 9.1) as the oxidant (Table 2). However, under these conditions primary aliphatic alcohols such as octan-1-ol, gave low selectivities to aldehydes owing to over-oxidation of octanal to octanoic acid (entry 1). This problem was circumvented by using MTBE as the organic solvent, in which PIPO is not soluble, affording an increase in selectivity to 94% (entry 2). Here again, filtration experiments confirmed that this system was heterogeneous, analogous to the solvent-free conditions.

In addition to primary and secondary aliphatic alcohols (entries 2–7), benzylic alcohols were also efficiently oxidised (entries 9 and 10), complete conversion being observed within 30 min. In competition experiments, the catalyst showed a marked preference for primary alcohols (entries 8 and 11). This is analogous to the already reported homogeneous<sup>2</sup> and heterogeneous<sup>8h</sup> TEMPO systems. Chirality on the α-position is not affected during oxidation as shown by the selective oxidation of (*S*)-2-methylbutan-1-ol to (*S*)-2-methylbutanal (entry 12).<sup>11</sup>

**Table 2** PIPO-catalysed oxidation of alcohols with hypochlorite<sup>a</sup>

Entry	Substrate	Product	t/min	Conv. (%) <sup>b</sup>	Sel. (%) <sup>b</sup>
1	Octan-1-ol	Octanal	45	90	50 <sup>d</sup>
2 <sup>c</sup>	Octan-1-ol	Octanal	45	80	94
3 <sup>c</sup>	Hexan-1-ol	Hexanal	45	89	95
4	Octan-2-ol	Octan-2-one	45	99	>99
5	Hexan-2-ol	Hexan-2-one	45	99	>99
6	Octan-3-ol	Octan-3-one	45	70	>99
7	Cyclooctanol	Cyclooctanone	45	100	>99
8 <sup>c</sup>	Octan-1-ol/ octan-2-ol	Octanal/ octan-2-one	45	86/<1	96
9	Benzyl alcohol	Benzaldehyde	30	100	>99
10	1-Phenylethanol	Acetophenone	30	100	>99
11	Benzyl alcohol/ 1-Phenylethanol	Benzaldehyde/ acetophenone	30	95/4	>99
12	(S)-2-Methyl- butan-1-ol	(S)-2-Methyl- butanal	45	90	>99

<sup>a</sup> 0.8 mmol substrate, 2.5 mg PIPO (1 mol% nitroxyl), 0.14 g KHCO<sub>3</sub>, 2.86 ml 0.35 M hypochlorite solution (1.25 equiv.), 0 °C. <sup>b</sup> Conversion and selectivity determined by GC using *n*-hexadecane as internal standard. <sup>c</sup> 2 ml MTBE as solvent. <sup>d</sup> Octanoic acid and octyl octanoate as side products.

**Scheme 2** Oxidation of methyl  $\alpha$ -D-glucopyranoside using PIPO/NaOCl.

Carbohydrates are also oxidised by the PIPO/NaOCl system analogous to TEMPO/NaOCl.<sup>12</sup> For example, methyl  $\alpha$ -D-glucopyranoside afforded methyl  $\alpha$ -D-glucopyranosiduronate in 70% yield (Scheme 2).<sup>‡</sup> As in the case of the oxidation of simple alcohols, filtration experiments confirmed that the catalyst is truly heterogeneous. Further investigation in the field of carbohydrate oxidations using PIPO/NaOCl is in progress and will be reported on in due course.

Besides hypochlorite, oxygen can also be used as oxidant.<sup>6,7</sup> Unfortunately, in contrast to homogeneous TEMPO the combination of PIPO and RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> in chlorobenzene<sup>7</sup> is not able to catalyse the aerobic oxidation of octan-2-ol, probably owing to coordination of ruthenium to the polyamine. On the other hand, in combination with CuCl/O<sub>2</sub> in DMF,<sup>6</sup> it is capable of completely oxidising benzyl alcohol to benzaldehyde within 2 h. This system, however, is limited to benzylic and allylic alcohols as for homogeneous TEMPO.

In summary we have developed a recyclable heterogeneous catalyst for the bleach oxidation of alcohols and polyols. In contrast to previously reported systems, neither a chlorinated hydrocarbon solvent nor a bromide is necessary to achieve good activity. A further advantage of our system is that the catalyst is readily prepared from inexpensive and commercially available raw materials. We believe that it will find wide application in organic synthesis.

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## Notes and references

<sup>†</sup> *General procedure* for the oxidation of alcohols with PIPO as catalyst: in a glass reaction vessel was placed 2.5 mg of PIPO (8  $\mu$ mol based on complete functionalisation; degree of functionalisation = 3.2 mmol g<sup>-1</sup>). Then a CH<sub>2</sub>Cl<sub>2</sub> solution (2 ml) of the alcohol (0.4 M) and *n*-hexadecane (0.12 M; as internal standard) was added followed by an aqueous solution (0.16 ml) of KBr (0.5 M). After the cooling of the reaction mixture to 0 °C, 2.86 ml of aqueous NaOCl (0.35 M and buffered by the addition of 0.14 g KHCO<sub>3</sub> to pH 9.1) was added. Then, the reaction mixture was vigorously shaken for 45 min. After destroying the excess of hypochlorite with Na<sub>2</sub>SO<sub>3</sub>, the reaction mixture was extracted with diethyl ether, dried over Na<sub>2</sub>SO<sub>4</sub> and analysed on GC (Chrompack CP-WAX 52 CB column; 50 m  $\times$  0.53 mm).

<sup>‡</sup> *Procedure* for the oxidation of methyl  $\alpha$ -D-glucopyranoside with PIPO as catalyst: in a glass reaction vessel was placed 15.7 mg of PIPO (50  $\mu$ mol based on complete functionalisation; degree of functionalisation = 3.2 mmol g<sup>-1</sup>) and 200 mg methyl  $\alpha$ -D-glucopyranoside (1.03 mmol). Then, 8 ml of aqueous NaOCl (0.56 M and brought to pH 9.5 with an aqueous 1 M hydrochloride solution) was added. During the reaction the pH was kept constant at 9.5 by automatic titration with a 0.1 M KOH solution. When the hydroxide consumption stopped (1.3 equiv. of hydroxide were consumed), Na<sub>2</sub>SO<sub>3</sub> was added to destroy the excess of hypochlorite. The crude mixture was analysed using HPLC.

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