TEMPO oxidations with a silica-supported catalyst

Carsten Bolm* and Thomas Fey

Institut für Organische Chemie der RWTH Aachen, Professor-Pirlet-Straße 1, D-52056 Aachen, Germany.
E-mail: carsten.bolm@oc.rwth-aachen.de

Received (in Cambridge, UK) 14th July 1999, Accepted 29th July 1999

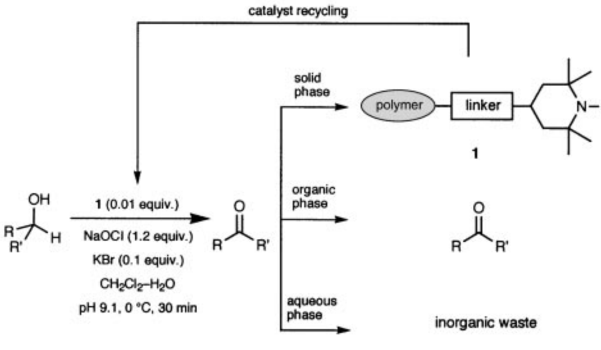
Silica-supported 1-hydroxy-2,2,6,6-tetramethylpiperidine (SG-TMP-OH) was successfully applied as a recyclable catalyst in the oxidation of various alcohols.

Aminoxyl† radicals are well-established catalysts for the oxidation of alcohols.[1] Typically, such oxidations are carried out in the presence of 1 mol% of catalyst and a stoichiometric amount of a terminal oxidant such as bleach,[2] sodium chlorite,[3] sodium bromite,[4] *tert*-butyl hypochlorite,[5] *N*-chlorosuccinimide,[6] MCPBA,[7] [bis(acetoxy)iodo]benzene,[8] or oxygen in combination with a high-valent metal salt.[9] Furthermore, electrochemical reoxidation of the catalyst is possible.[10]

Especially for large scale oxidations, the TEMPO–bleach protocol introduced by Anelli *et al.*[2] appears most useful.[11] Although usually a small quantity of the catalyst is sufficient for an efficient transformation, it is still desirable to develop improved work-up conditions which allow simple product isolation as well as catalyst separation and recycling.[12] We envisaged that both requirements could be realised by using a polymer-supported aminoxyl radical. Usually TEMPO-catalysed reactions afford the desired carbonyl compounds in high yields without the formation of significant amounts of by-product, and thus catalyst separation and product isolation could easily be accomplished by simple filtration and phase separation followed by evaporation of the organic solvent (Scheme 1).

Although several polymer-bound aminoxyl radicals have already been synthesised,[13] only a very few of them were applied as oxidation catalysts.[13*a–d*] To the best of our knowledge, none of them has been studied under the conditions mentioned above. Due to several publications concerning the application of polymer-supported oxidation reagents and catalysts,[14] and based on our own expertise in the use of heterogenised alkaloids in the Sharpless dihydroxylation reaction,[14*g*,15] we focused our attention on the attachment of the TEMPO precursor 1-hydroxy-4-oxo-2,2,6,6-tetramethylpiperidine (**2**)[16] onto silica. The synthesis of **3** (SG-TMP-OH) was accomplished by reductive amination of **2** with commercially available aminopropyl-functionalised support (Scheme 2).[17]‡ The resulting solid was carefully washed with hot MeOH using a Soxhlet extractor for several days in order to ensure complete removal of non-chemically bounded hydroxypiperidine derivatives from the surface.

SG-TMP-OH **3** was then applied as catalyst in the oxidation of various alcohols according to the Anelli protocol (Table 1).[2*a*]§ As shown by quantitative GC analysis, aldehydes and ketones were formed in high yields from the corresponding primary and secondary alcohols, respectively. Both benzylic and aliphatic substrates react equally well.

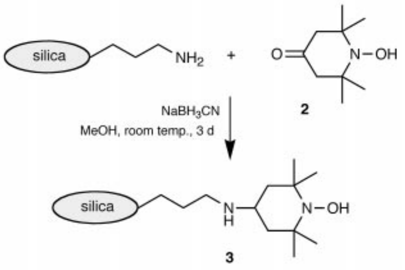


Scheme 1

In order to study the selectivity profile in the oxidation of primary and secondary alcohols, we performed competition experiments using equimolar mixtures of both. Entries 8 and 9 of Table 1 show a high selectivity towards the oxidation of the primary alcohols, which resembles the known behaviour of the unsupported TEMPO catalyst.[19] Thus, the corresponding aldehydes of nonan-1-ol and benzyl alcohol were formed in 96 and 92% yield, respectively, whereas the oxidation of the secondary alcohols nonan-2-ol and 1-phenylethanol occured in low yield only (1 and 3%, respectively). In addition, as in catalysed oxidations with TEMPO itself,[2*c*] no racemisation of optically active compounds occured (entry 10).

We finally investigated the possibility of recycling the catalyst. Therefore, the silica-bound TEMPO derivative was recovered by filtration after the reaction and reapplied in a sequence of oxidations using nonan-1-ol as substrate. The results illustrated in Fig. 1 show that even after 10 subsequent runs the catalyst activity remained high. In both substrate conversion and product yield only a minor decrease was observed, proving the high efficiency of the catalyst recovery.

In conclusion, we have demonstrated that silica-supported TEMPO is an excellent catalyst for the oxidation of alcohols, affording the corresponding carbonyl derivatives in high yields. Primary alcohols are selectively oxidised in the presence of



Scheme 2

Table 1 TEMPO oxidation of various alcohols to the corresponding aldehydes and ketones with silica-supported catalyst **3**[a]

Entry	Substrate	Yield (%)[b]
1	Benzyl alcohol	92 (75)
2	Heptan-1-ol	90
3	Octan-1-ol	88
4	Nonan-1-ol	90 (85)
5	Dodecan-1-ol	81
6	Nonan-2-ol	65
7	1-Phenylethanol	91
8	Nonan-1-ol/nonan-2-ol	96/1
9	Benzyl alcohol/1-phenylethanol	92/3
10	*(S)*-2-Methylbutan-1-ol[c]	60

[a] Oxidation experiments conducted following the protocol in note §. [b] Yields were determined by quantitative GC analysis using decane or dodecane as internal standard. Values in parentheses are isolated yields. [c] The ee of 95% remained unchanged (ref. 18).

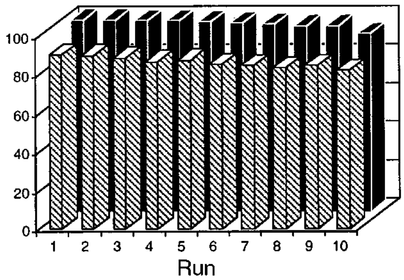


Fig. 1 Yields [hatched (%)] and conversions [black (%)] in consecutive oxidation reactions of nonan-1-ol when using silica-supported catalyst **3**.

secondary substrates. Optically active starting materials can be used without racemisation. Finally, the catalyst was shown to be stable under the reaction conditions, thus allowing it to be recycled without significant loss of activity.

This research was supported by the Katalyseverbund NRW and the Fonds der Chemischen Industrie.

Notes and references

† CAS nomenclature = nitroxyl.

‡ Aminopropyl-functionalised silica was purchased from Aldrich. According to the distributor's information the degree of functionalisation is approximately 1.0 mmol g^{-1}.

§ *General procedure* for the oxidation of alcohols with SG-TMP-OH **3** as catalyst: The reaction was performed in a glass tube with a cooling mantle. The bottom of the tube was equipped with a ceramic filter plate and a stopcock allowing easy separation of the supported catalyst from the reaction mixture by filtration. In this vessel was placed 9.2 mg of SG-TMP-OH **3** (8 μmol based on complete functionalisation; degree of functionalisation = 0.87 mmol g^{-1}). Then a CH_2Cl_2 solution (2 ml) of the alcohol (0.4 M) and decane or dodecane (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, 2.7 ml of aq. NaOCl (diluted to a final concentration of 0.37 M and buffered by the addition of $NaHCO_3$ to a pH of 9.1) was added. Then, the reaction mixture was vigorously shaken for 30 min. After filtration, the organic phase was separated, dried over $MgSO_4$, and the product composition was analysed by means of GC [ultra-2-column (Hewlett Packard)]. The filtered solid was washed five times with water, MeOH and CH_2Cl_2 (2 ml each), air-dried, and reused as such. Preparative runs were carried out on a five-fold scale, and the reaction time was extended to 1 h. After filtration the organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 once. The combined organic phases were dried over $MgSO_4$, the solvent was removed *in vacuo*, and the crude product purified by column chromatography on silica gel with CH_2Cl_2 as eluent.

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Communication 9/05683A