Tetra-*n*-propylammonium perruthenate (TPAP)-catalysed oxidations of alcohols using molecular oxygen as a co-oxidant

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Tetra-*n*-propylammonium perruthenate (TPAP) has been used as an efficient catalyst for the conversion of primary and secondary alcohols to the corresponding aldehydes and ketones under very mild aerobic conditions.

The growing importance of combinatorial chemistry has led to an increasing demand in clean technology processes, *i.e.* reactions that use environmentally friendly reagents and avoid the need for time-consuming purification steps. A particularly important reaction in this context is the aerobic oxidation of alcohols to the corresponding carbonyl compounds in the presence of a transition metal catalyst, since the use of molecular oxygen as a co-oxidant results in the formation of water as the only by-product. Although a variety of different catalytic systems for this reaction has been developed,[1–11] their application is often restricted to reactive substrates or they suffer from long reaction times and relatively harsh conditions.

Since we introduced tetra-*n*-propylammonium perruthenate (TPAP) as a mild, catalytic oxidant,[12,13] this reagent has become increasingly popular for the conversion of primary and secondary alcohols to aldehydes and ketones especially when used together with *N*-methyl-morpholine-*N*-oxide (NMO) as a co-oxidant. In this communication we wish to report our prelimin-
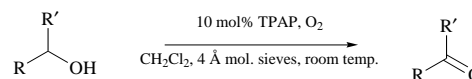
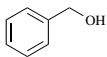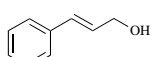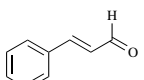R = alkyl, allyl, aryl
R′ = alkyl, H

Scheme 1
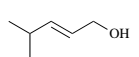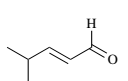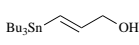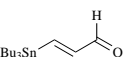
ary results on the use of *molecular oxygen* as a stoichiometric oxidant in TPAP-catalysed oxidation reactions of alcohols to carbonyl compounds.

The oxidation reactions were carried out following the standard TPAP protocol[13] with the modification of using 10 mol% of catalyst and molecular oxygen as co-oxidant (Scheme 1).†

The results of this study are summarised in Table 1. Benzylic

† General experimental procedure: the alcohol was dissolved in CH$_2$Cl$_2$ (4 ml per mmol substrate) and activated powdered 4 Å molecular sieves (200 mg per mmol) and TPAP (10 mol%) were added. The reac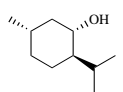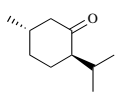tion mixture was then stirred at room temperature under an oxygen atmosphere (O$_2$-balloon). After 30 min the suspension was filtered through a small plug of silica gel and the residue washed with CH$_2$Cl$_2$ or EtOAc. Evaporation of the solvent *in vacuo* afforded the desired product.

Table 1 Oxidations of alcohols to carbonyl compounds using TPAP–O$_2$ [a]

entry	alcohol	product	reaction time	GLC yield	isolated yield	purity[b]
1			30 min	>99%	98%	>95%
2			30 min	>99%	97%	>95%
3			40 min	>99%		
4			30 min		83%	90%
5			1 h	80%[c]		
6			20 min	92%[d]		
7			30 min	99%	90%	>95%

[a] Reaction conditions: 10 mol% TPAP, O$_2$-atmosphere, 4 Å mol. sieves, CH$_2$Cl$_2$, room temp. [b] As judged by NMR analysis of the crude product. [c] 16% of starting material left, longer reaction times led to acid formation. [d] 5 mol% of catalyst used.

or allylic alcohols were very cleanly transformed into the corresponding aldehydes in less than 40 min (entries 1—3). No other products could be detected by GLC analysis. The oxidation of a non-activated primary alcohol however proceeded somewhat less efficiently (entry 5). After 1 hour, 80% of aldehyde was formed, the only by-product being unreacted alcohol. Prolonged reaction times did not improve the yield but led to the slow formation of the corresponding carboxylic acid (7% after 2 h). Conversely, oxidations of secondary alcohols, such as cyclohexanol or the sterically hindered (+)-menthol, resulted in high yields of the corresponding ketones (entries 6 and 7). In the former case, where only 5 mol% of catalyst was used, the product was obtained in 92% yield as determined by GLC analysis with the sole by-product being unreacted starting material. Upon extending the reaction time to 3 h no further conversion to cyclohexanone could be observed. This observation led to a reinvestigation of the described oxidation reactions using smaller amounts of TPAP (2–5 mol%). This study revealed that in all cases the reactions stopped after about 30 min and 10 catalytic cycles (non-activated primary alcohol) or 15–20 catalytic cycles (activated primary and secondary alcohols), respectively. The precise reasons for the deactivation of the catalyst have not yet been found, although unpublished studies of Markó and co-workers[14] using the same catalytic system suggest that this deactivation is solvent dependent with toluene giving the best results. Since the limited number of catalyst turnovers can be overcome by using 10 mol% of TPAP, the described oxidation protocol is very efficient in the rapid and clean transformation of alcohols into carbonyl compounds. A further advantage is the very simple procedure used to isolate some of the products. The only purification step consisted of a filtration through a very short column of silica gel followed by removal of the solvent *in vacuo* leading to the products in excellent yields and purities (entries 1, 2 and 7). Even the isolation of a very lipophilic organotin derivative (entry 4), which is difficult and tedious to purify under standard conditions, was possible in good yield and acceptable purity.

Further investigations on the application of the TPAP–O_2 system and our polymer supported perruthenate reagent (PSP)[15] in clean organic syntheses are underway.

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