Preparation and Use of Tetra-n-butylammonium Per-ruthenate (TBAP reagent) and Tetra-n-propylammonium Per-ruthenate (TPAP reagent)† as New Catalytic Oxidants for Alcohols

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Tetra-n-butylammonium per-ruthenate $(Bu^n{}_4N)(RuO_4)$ and tetra-n-propylammonium per-ruthenate $(Pr^n{}_4N)(RuO_4)$, with *N*-methylmorpholine *N*-oxide, function as mild catalytic oxidants for the high yield conversion of alcohols to aldehydes and ketones and are competitive with more conventional reagents.

One of the most common transformations in organic synthesis is the oxidation of the hydroxy group and although certain procedures remain popular there is a constant need to develop new systems. Swern oxidants[1] are excellent but there are problems with obnoxious side products and difficulties of large-scale operation. Likewise the chromium oxidants[2,3] can cause problems during work-up of the products and disposal of the toxic residues. Catalytic alternatives to these well tried methods are therefore attractive, but must demonstrate clear advantages over these systems, be reliable and easy to use, and be applicable to a wide range of substrates.

Our previously reported ruthenium based oxidation catalyst, $[RuO_4]^{2-}/(S_2O_8)^{2-}$, functioned only in strong aqueous base and was therefore unsuitable for a number of oxidations.[4]

We report here the new catalytic oxidants tetra-n-butylammonium per-ruthenate (TBAP) and tetra-n-propyl ammonium per-ruthenate (TPAP) using *N*-methyl morpholine *N*-oxide (NMO) as co-oxidant. We have earlier reported the use of TBAP as a stoicheiometric oxidant.[5] These reagents function in organic solvents, are easy to prepare, and are selective. TBAP was obtained by dissolution of $K[RuO_4]$[6] (2.0 g, 9.8 mmol) in water (200 cm^3) at 5—10 °C followed by immediate addition of tetra-n-butylammonium hydroxide (50 cm^3 of a 40% aqueous solution). The resulting green precipitate of TBAP (3.61 g, 91%) must be filtered rapidly, washed with cold water (3 × 10 cm^3), and dried *in vacuo.* TPAP was more conveniently prepared. Hydrated ruthenium trichloride (1.5 g, 6.2 mmol) and sodium periodate (5.5 g, 0.026 mol) were stirred overnight in water (50 cm^3). The RuO_4 formed was transferred in an oxygen atmosphere into a solution of tetra-n-propylammonium hydroxide (5 cm^3 of 1 M aqueous solution), 10 cm^3 of water and 1 M sodium hydroxide

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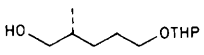
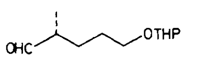
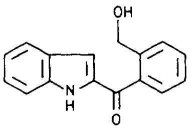
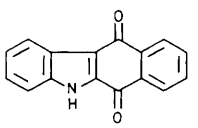
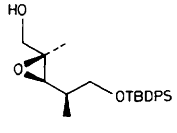
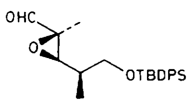
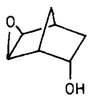
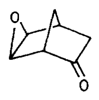
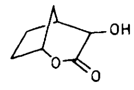
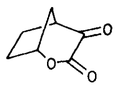
† Systematic names tetra-n-butylammonium tetra-oxoruthenate(VII) and tetra-n-propylammonium tetra-oxoruthenate(VII).

Table 1. Oxidation of alcohols using TBAP and TPAP.

		TBAP		TPAP	
Alcohol	Product	% Yield	*t*/h	% Yield	*t*/h
n-Butanol	n-Butanal	94^{c}	0.8	95^{c}	1
Undec-10-en-1-ol	Undec-10-en-1-al	70^{a}	3		
Citronellol	Citronellal	75^{a}	5		
E-Cinnamyl alcohol	*E*-Cinnamaldehyde	91^{a}	3	75^{a}	5
Chrysanthemyl alcohol	Chrysanthemaldehyde	90^{a}	5	76^{a}	0.5
Benzyl alcohol	Benzaldehyde	80^{b}	2	71^{a}	0.5
o-Chlorobenzyl alcohol	*o*-Chlorobenzaldehyde	81^{b}	4		
4-Methoxybenzyl alcohol	4-Methoxybenzaldehyde			68^{a}	12
3,4-Dimethoxybenzyl alcohol	3,4-Dimethoxybenzaldehyde	98^{b}	1.5		
Piperonyl alcohol	Piperonaldehyde	89^{b}	3	70^{a}	1
Cyclobutanol	Cyclobutanone	95^{c}	1.1		
(±)-Menthol	(±)-Menthone	85^{a}	1.0		
endo-Norborneol	Bicyclo[2.2.1]heptan-2-one	73^{a}	0.3		
5α-Androstan-17β-ol-3-one	5α-Androstan-3,17-dione	96^{a}	6	99^{a}	1.5
Lanost-8-en-3β-ol	Lanost-8-en-3-one	86^{a}	6	81^{a}	1.5
		71^{a}	0.7		
		85^{a}	5		
				70^{a}	1
		73^{a}	0.5		
		80^{a}	1.5		

[a] Isolated yield. [b] 2,4-Dinitrophenylhydrazone derivative. [c] G.l.c. yield.

(40 cm^3) at 0—5 °C. The green product (1.53 g, 87%) was removed by filtration every 20 min, washed with ice-cold water (2 × 2 cm^3), and dried *in vacuo*.

In the oxidation experiments (Table 1) primary alcohols give aldehydes and secondary alcohols afford ketones, while labile functional groups such as epoxides, tetrahydropyranyl ethers, silyl ethers, esters, double bonds, indoles *etc.* remain intact. Importantly, oxidation of alcohols containing adjacent chiral centres gives products without any detectable racemisation. Typically the oxidations proceed rapidly (0.2—6 h) at room temperature in dichloromethane using less than 0.5 mole % of catalyst. We also find that addition of 4 Å molecular sieves to be beneficial since they remove both the water formed during reaction, and the water of crystallisation of the NMO.

Although we have not tested the ultimate limits of turnover and scale of reaction, these oxidations can be performed on a reasonable scale without any noticeable problems. Thus 4-methoxybenzyl alcohol (26.6 g, 0.19 mol) and piperonyl alcohol (10 g, 0.066 mol) are catalytically oxidised by TPAP to the corresponding aldehyde in 12 h, with 70 and 68% yields respectively, corresponding to catalytic turnovers of 215 and 210. During the oxidations on a >5 g scale it was useful to pre-dry the NMO by first treating the dichloromethane solution with anhydrous $MgSO_4$.

In a typical oxidation experiment the alcohol (0.5 mmol) was dissolved in CH_2Cl_2 (5 cm^3) containing both the 4 Å sieves and NMO (0.1 g, 0.75 mmol). After stirring the mixture for 10 min, TBAP (or TPAP, 0.025 mmol) was added and the reaction followed by t.l.c. until complete. The initial green mixture darkened as the reaction proceeded. When complete, the mixture was diluted with CH_2Cl_2 (50 cm^3) and then washed with sodium sulphite solution (10 cm^3), brine (10 cm^3) and finally saturated copper(II) sulphate solution (10 cm^3). The organic layer was dried ($MgSO_4$), filtered, and worked up in the usual way to give the product.

Although in most of the experiments we have reported the use of TBAP, the convenience of preparation of TPAP makes this the superior reagent which we would recommend for future applications.

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