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New Version of the TEMPO-based Catalytic System for the Oxidation of Alcohols to Aldehydes

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A new chemoselective catalytic system for the title oxidation was developed using methyltrioxorhenium (3 mol%), KBr (10 mol%) and TEMPO (3 mol%) as co-catalysts and Oxone® as a terminal oxidant.

Key words: catalytic oxidation, TEMPO, methyltrioxorhenium, aldehydes

The catalytic conversion of alcohols into the corresponding carbonyl derivatives enjoys much interest in synthetic organic chemistry [1]. Chemoselectivity is a primary goal of the research directed towards new catalytic oxidizing systems. There are many reagents suitable for the oxidation of secondary alcohols, but quite few oxidants are available for the selective preparation of aldehydes by oxidation of primary hydroxyls, leaving unchanged secondary hydroxy groups. Among others, we [2] have reported a successful application in such selective reaction of the Anelli catalyst system (TEMPO/KBr/NaOCl) [3] based on the use of *in situ* generated 2,2,6,6-tetra- methylpiperidinyl-1-oxoammonium salt [4]. Nonetheless, in some cases, the system using aqueous sodium hypochlorite led to the unwanted side reactions, *e.g.* ring chlorination in the case of 2-phenoxyethanol. Afterward, many different stoichio- metric oxidants were studied with TEMPO [4]. Recently, Herrmann *et al.* reported oxidation of benzyl alcohol using TEMPO/HBr/H_2O_2 in acetic acid, with methyl- trioxorhenium (MTO) added as a co-catalyst [5]. Also recently, Bolm described an efficient oxidation of primary and secondary benzylic-type alcohols using TEMPO/Bu_4NBr/$KHSO_5$ (Oxone®) in CH_2Cl_2 or toluene, but the aliphatic alcohols were oxidized with much less yields [6]. Moreover, it was observed that the secondary alcohols were more reactive with this catalytic system than the primary ones [6]. The last effect is usually ascribed to the acidic reaction medium [7]. Being aware of all these new findings, we studied an applicability of the peroxide-based TEMPO catalytic systems for the chemoselective conversion of primary aliphatic alcohols into corresponding aldehydes.

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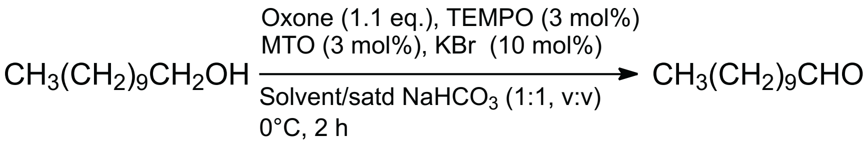
RESULTS AND DISCUSSION

Thus, we examined application of the proposed stoichiometric oxidants in the TEMPO-catalyzed oxidation of primary aliphatic alcohol, using undecanol as a model substrate. Since it is known that the oxidation of primary alcohols by 1-oxoammonium salt (an active oxidant) is fast and efficient at 0°C [4,7], we run the reaction in a two-phase system (organic solvent/buffered aqueous soln) at this temperature. Under these conditions there was only a slight oxidation of undecanol (8% of undecanal) with TEMPO/KBr/Oxone® in methylene dichloride/water. This outcome did not change much (9%), when Bu_4NBr, used previously by Bolm [6], was applied instead of KBr. Similarly, 30% aqueous H_2O_2 or urea-hydrogen peroxide complex (UHP) with TEMPO/KBr (0°C, 2 h), even in the presence of MTO, led to a complete recovery of substrate. However, when to the Oxone®-based system MTO (3 mol%) was added, undecanol reacted, but the outcomes were highly dependent on the organic solvent used. The results collected in Table 1 show that acetonitrile and acetone were the most appropriate solvents. Additionally, for the oxidation run in acetonitrile in the absence of MTO, the replacement of KBr by Bu_4NBr resulted in the significant formation of undecanal (50%). Unexpectedly, also tributyl amine was obtained there in amount corresponding to the ammonium salt added.

Scheme 1



$$CH_3(CH_2)_9CH_2OH \xrightarrow[\text{Solvent/satd } NaHCO_3 \text{ (1:1, v:v)}\; 0°C,\ 2\text{ h}]{\text{Oxone (1.1 eq.), TEMPO (3 mol\%)}\; \text{MTO (3 mol\%), KBr (10 mol\%)}} CH_3(CH_2)_9CHO$$

Table 1. Organic solvents and terminal oxidants effects in the catalytic oxidation of undecanol [a].

Run	Solvent	Yield (%)	Recovered substrate (%)
1	CH_2Cl_2	8.0	91
2	$(CH_3)_2C{=}O$	72	20
3	CH_3CN	89	–
4		97[b]	–
5		1.0[c]	98
6		0.0[d]	100
7	THF	66	6.0
8	$CH_3CO_2CH_3$	6.0	84

[a] As in Scheme 1, stoichiometric oxidant OXONE® added during 45 min, reaction time 2 h. [b] Reaction time 5 h, OXONE® added during 120 min. [c] Stoichiometric oxidant H_2O_2. [d] Stoichiometric oxidant UHP.

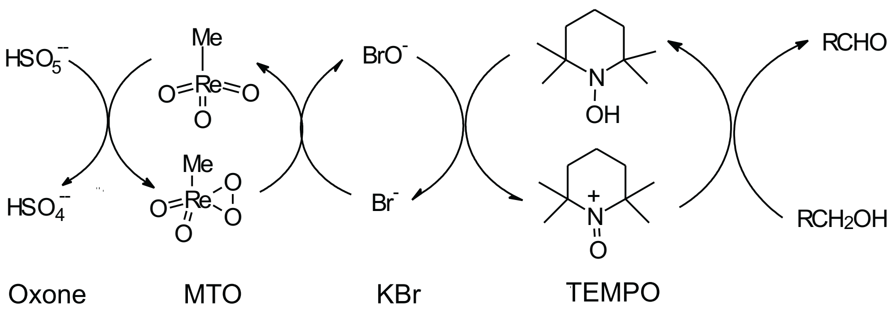
Thus, the experiments designed to test the components of the catalytic system (Table 2) confirm the necessity of each co-catalyst, as it is demonstrated on Scheme 2. Since it has been known that caroate anion (HSO_5^-) is a fast oxidant turning bromide into hypobromite [8], one could expect a catalytic cycle excluding MTO. However, if it was withdrawn, the reaction stopped earlier, leaving some unreacted substrate along with carboxylic acid, the product of concurrent aldehyde oxidation with the unused caroate (Table 2, entries 1–4). Similarly, in the oxidation of 2-phenylethanol in the absence of MTO the respective acid was formed (26%) along with phenylacetaldehyde (18%), while with MTO the aldehyde was the main product (Table 3, entry 8). In the reactions without MTO we also observed the oxidative destruction of TEMPO by caroate [9], and this explains why the alcohol oxidation was halted.

Table 2. Influence of components of the catalytic system on the Oxone® oxidation of undecanol (5 h, 0°C).

Run	MTO (%mol)	KBr (%mol)	TEMPO (%mol)	Yield (%)	Recovered substrate/other products (%)
1	0.0	10	3.0	35	29/20[a)]
2	1.0	10	3.0	72	0.0/20[a)]
3	2.0	10	3.0	70	0.0/20[a)]
4	3.0	10	3.0	97	0.0/0.0
5	3.0	3.0	3.0	43	51/5[a)]
6	3.0	10	0	0	100

[a)] Undecanoic acid.

Scheme 2



It seems that the presence of MTO speeds up the re-oxidation of both hydroxylamine derivative and bromide, thus, leading to the effective concentration of oxoammonium salt. A concept that this kind of oxidizing species is responsible for the reaction with alcohol in both cases is supported by a very similar selectivity (albeit different yields) of both reactions. The oxidation of equimolar mixture of 1- and 5-undecanol with MTO gave 88% excess of aldehyde in the carbonyl products, and 80% excess without MTO, respectively. As it was proved earlier for the other

TEMPO-based catalytic systems, also in this case, bromide played a key role and its concentration decrease reduced the oxidant efficiency (Table 2, entry 5). To exclude any doubt about the role played by TEMPO, we checked the oxidation in its absence. There was no reaction. Moreover, when 4-MeO-TEMPO/MTO was used instead of TEMPO/MTO, undecanal (44%), undecanoic acid (15%) and the recovered substrate (30%) were obtained, compared to undecanal (97%) as the sole product for the second catalyst system. The observed lack of oxidation of 2-phenoxyethanol (Table 3) was corroborated when the reaction was run under basic conditions (excess of Na_2CO_3). It is noteworthy that, in our hands, the Anelli system allowed for this oxidation giving 54% of phenoxyacetaldehyde, but also led to the ring-chlorinated products [10].

Thus, several aliphatic alcohols were oxidized under the conditions optimized for undecanol and the results are shown in Table 3. The oxidizing system is suitable for the conversion of the long chain substrates of this type into the corresponding carbonyl compounds. The primary hydroxy groups reacted faster than the secondary ones. Unfortunately, due to the limited stability of the catalytic oxidant in this system, less reactive, sterically hindered alcohols, which were oxidized using TEMPO/KBr/NaOCl, namely oleic alcohol (54%) [10] and 2-hexyl-1,3-butanediol (98%) [2], here were recovered unchanged.

Table 3. Oxidation of alcohols using Oxone®/TEMPO, MTO, KBr.

Substrate	Yield (%)	
	Aldehyde	Substrate/Other
$CH_3(CH_2)_8CH_2OH$	78	6/6 [b)]
$CH_3(CH_2)_9CH_2OH$	97	–
$CH_3(CH_2)_{10}CH_2OH$	53	38/6 [b)]
$CH_3(CH_2)_3CH(OH)(CH_2)_5CH_3$	76 [c)]	23/–
$CH_3(CH_2)_9CH_2OH + CH_3(CH_2)_3CH(OH)(CH_2)_5CH_3$ [a)]	85 + 5 [c)]	3 + 95
$CH_3(CH_2)_4CH(CH_2CH_3)CH_2OH$	54	27/1.5 [b)]
$CH_3[CH(CH_3)(CH_2)_3]_3CH(CH_3)(CH_2)_2OH$	56	35
$PhCH_2CH_2OH$	55	0.0/10 [d)]
$PhOCH_2CH_2OH$	3.5	80/3 [e)]

[a)] Equimolar mixture of alcohols was oxidized with 1.7 eq of Oxone®. [b)] Yield of corresponding acid. [c)] Yield of ketone. [d)]Benzaldehyde. [e)]Ring bromination product.

Concluding, TEMPO/KBr/MTO/Oxone® system used under buffering conditions can be considered as a tool for the chemoselective conversion of primary aliphatic alcohols, the substrates that are rather difficult to oxidize to the corresponding aldehydes. Thus, the present catalyst combination supplements the earlier used TEMPO/Bu_4NBr/Oxone and TEMPO/KBr/MTO/H_2O_2 systems and broaden the scope of this oxidation method.

EXPERIMENTAL

Procedure. To the stirred mixture of a solution of the alcohol (2 mmol), TEMPO (9.4 mg, 3 mol%) in acetonitrile (2 ml) and a satd solution of $NaHCO_3$ (2 ml) containing KBr (23.8 mg, 10 mol%) and MTO (14.9 mg, 3 mol%) solid Oxone (676 mg, 2.2 mmol) was added portionwise over 2 h at 0°C. Then, in order to prevent gelation, the mixture was diluted with acetonitrile (1 ml) and satd aq. $NaHCO_3$ (1 ml). After 2 h additional stirring at this temperature, the mixture was extracted with CH_2Cl_2 (3×2 ml). The organic extract was washed with brine and dried over Na_2SO_4. The solvent was evaporated *in vacuo* and the weighted residues were analyzed by GC/MS. The respective yields were calculated accordingly. GC/MS spectra were determined on a Hewlett-Packard 5890 II gas chromatograph (25 m capillary column) with a Hewlett-Packard mass spectrometer 5971A operating on the electron impact mode (70 eV).

All the obtained products are known compounds. Their identity were additionally confirmed by comparison of their MS spectra with that of original samples. The unreported MS spectrum for the known 3,7,11,15-tetramethylhexadecanal [11]: m/z (%): 296 (M^+, <0.5%), 278 (M^+-H_2O, 2), 252 (M^+-CH_2CHOH^+·15%), 123 (57%), 111 (21%), 97 (38%), 81 (47%), 71 (93%), 69 (50%), 57 (75%), 55 (79%), 43 (100%).

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