

N°403 / OC

TOPIC(s) : Homogenous, heterogenous and biocatalysis / Alternative solvents

## Selective TEMPO-oxidation of alcohols to aldehydes in alternative solvents

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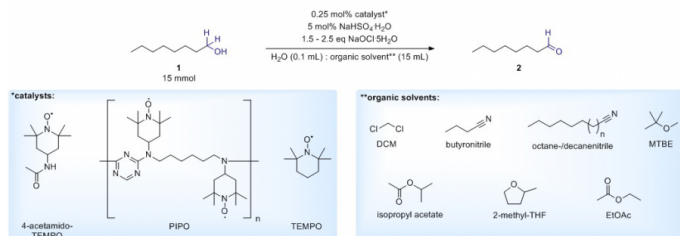
## PURPOSE OF THE ABSTRACT

Selective oxidation of alcohols to the corresponding aldehydes is a pivotal reaction in organic synthesis, however, this reaction still remains challenging.[1] Especially only a few green oxidation methods are known, which do not require toxic oxidation agents such as potassium dichromate, are applicable in industrial scale and do not require immoderate reaction conditions.[2] Among others, the oxidation catalyst 2,2,6,6-tetramethylpiperidine-1-oxyl radical (TEMPO) by using sodium hypochlorite as oxidation agent is designated as a green oxidation method, since TEMPO is easily accessible from acetone and as oxidation reagent the multi-tons chemical bleach is used.[3] However, only a very few examples are known in which dichloromethane as organic solvent in the required two-phase reaction system can be exchanged by a greener alternative.[4]

We intensively studied the oxidation of aliphatic alcohols to the corresponding aldehydes using TEMPO, 4-acetamido-TEMPO and polyamine-immobilized piperidinyloxyl radical (PIPO) in different solvent systems. First, optimal oxidation conditions in terms of substrate concentration, amount of sodium hypochlorite pentahydrate and phase transfer catalyst of 1-octanol (1) to octanal (2) were screened using TEMPO as catalyst.[5] High substrate concentrations of 1 M, 5 mol% sodium hydrogensulfate as phase transfer catalyst and low catalyst concentrations of 0.25 mol% TEMPO were found to be optimal conditions for this alcohol oxidation. Afterwards we investigated alternative catalysts (4-acetamido-TEMPO and PIPO) and alternative organic solvents to dichloromethane (DCM).[6] Green solvents like methyl-tert-butyl ether (MTBE), ethyl acetate (EtOAc), 2-methyl tetrahydrofuran (2-methyl-THF) and isopropyl acetate were tested. Beside these well-known and often used solvents we were interested in aliphatic nitriles, such as butyronitrile, octanenitrile and decanenitrile, as green organic solvents for the oxidation reaction. These nitrile solvents were, best of our knowledge, never tested as organic solvents for TEMPO-oxidation (except for acetonitrile). Nitrile solvents are used in special applications, for example for extreme temperature operations,[7] and were recently found as beneficial ingredients in electrolyte compositions for rechargeable lithium ion batteries. [8] A green access towards nitriles is recently investigated by our group using aldoxime dehydratases as biocatalyst, which dehydrate aldoximes to nitriles.[9] Nitrile degrading microorganisms are known for years, thus a biodegradability of many nitrile compounds is already known.[10]

We found, that using aliphatic nitriles as organic solvent for TEMPO-oxidation, alcohols can selectively be oxidized by TEMPO and TEMPO-derivatives to the corresponding aldehydes. Especially the combination of PIPO as catalyst and butyronitrile, octane- or decanenitrile as solvents reached full conversion of the alcohol 1 with selectivities of higher than 97 %. Currently, the substrate scope of the TEMPO-oxidation of alcohols to the corresponding aldehydes in nitriles as organic solvents is under investigation. The oxidation of 1,8-octandiol (3) was already tested using PIPO as catalyst, butyronitrile as solvent and sodium hypochlorite as oxidation agent. After only a few minutes reaction time full conversion was reached with selectivity towards the dialdehyde of 90 %. The oxidation of cinnamyl alcohol (4) towards the aldehyde using the same condition resulted in >99 % conversion and a selectivity of 95 %. Similar results were obtained for 4-nitrobenzyl alcohol (5) oxidation towards the aldehyde, indicating that this oxidation method is also applicable for aromatic alcohols. Further alcohol oxidations to broaden the substrate scope is under investigation.

## FIGURES



**FIGURE 1**

Optimized oxidation conditions of 1-octanol to octanal  
Oxidation of 1-octanol to octanal using sodium hypochlorite under optimized conditions in different organic solvents and using different nitroxylradical catalysts.

#	Catalyst	Solvent	Conversion* /%	Selectivity** /%
1	TEMPO	DCM	87	96.5
2	TEMPO	EtOAc	0	--
3	TEMPO	MTBE	8	>99
4	TEMPO	2-methyl-THF	4	75
5	TEMPO	neat	57	88
6	TEMPO	butyronitrile	96	92
7	TEMPO	isopropyl acetate	99	72
8	TEMPO	octanenitrile	99	>99
9	4-acetamido-TEMPO	DCM	93	95
10	4-acetamido-TEMPO	butyronitrile	82	89
11	PIPO	butyronitrile	99	97.5
12	PIPO	octanenitrile	99	98
13***	PIPO	decanenitrile	99	98

\* Conversion (consumption of alcohol) determined by GC-analytcs.  
\*\* Selectivity (amount of product(aldehyde)/amount of product (aldehyde) and by-products) determined by GC.  
\*\*\* Reaction performed with 1-decanol as substrate.

**FIGURE 2**

Results of 1-octanol oxidation to octanal  
Results of 1-octanol oxidation screening using TEMPO (-derivatives) in different organic solvents.

## KEYWORDS

Alcohol oxidation | TEMPO | Green solvents | Aldehydes

## BIBLIOGRAPHY

- [1] M. Hudlicky, *Oxidations in Organic Chemistry*; American Chemical Society: Washington, DC, 1990.
- [2] a.) G. Cainelli, G. Cardillo, *Chromium Oxidations in Organic Chemistry*; Springer: Berlin, 1984; b.) M. Besson, P. Gallezot, *Catalysis Today* 2000, 57, 127; c.) T. Mallat and A. Baiker, *Chemical Reviews* 2004, 104, 3037; d.) R. A. Sheldon, I. Arends, G. J. Ten Brink and A. Dijkman, *Accounts of Chemical Research* 2002, 35, e.) S. E. Davis, M. S. Ide, R. J. Davis, *Green Chemistry* 2013, 15, 17. 774.
- [3] R. Ciriminna, M. Pagliaro, *Organic Process Research & Development* 2010, 14, 1, 245–251.
- [4] M. H. A. Janssen, J. F. Chesa Castellana, H. Jackman, P. J. Dunn, R. A. Sheldon, *Green Chemistry* 2011, 13, 905.
- [5] J. Busch, Master Thesis 2018.
- [6] a.) S. Glinski, Bachelor Thesis 2018. b.) A. Hinzmann, unpublished results 2018.
- [7] V. Ruiz, T. Huynh, S. R. Sivakkumar, A. G. Pandolfo, *RSC Advances* 2012, 2, 5591–5598.
- [8] Z. Zhang, X. Hu, J. Zhang, WO2016095116A1, 2016.
- [9] a.) T. Betke, J. Higuchi, P. Rommelmann, K. Oike, T. Nomura, Y. Kato, Y. Asano, H. Gröger, *ChemBioChem* 2018, 19(8): 768-779; b.) A. Hinzmann, H. Gröger, Manuscript in preparation 2018.
- [10] W. B. Betts, *Biodegradation: Natural and Synthetic Materials*; Springer: Berlin, 1991.