SYNLETT
Spotlight 153

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

New Achievements in TEMPO-Mediated Oxidations

Compiled by Félix Calderón

Félix Calderón was born in 1976 in Madrid, Spain. He studied chemistry at the Autonoma University of Madrid where he obtained his B.Sc. and M.Sc. degrees. His pre-doctoral experience includes collaborations at the Department of Applied Organic Chemistry of the University of Turin (Italy), the Drug Discovery Department of GlaxoSmithKline (Tres Cantos, Madrid) and the Medicinal Chemistry Institute of CSIC (Madrid). In 2002 he joined the research group of Dr. Alfonso Fernández-Mayoralas at the Organic Chemistry Institute of CSIC (Madrid) to pursue his Ph.D. His primary interests include asymmetric organocatalysis, green chemistry, medicinal chemistry and molecular modeling.

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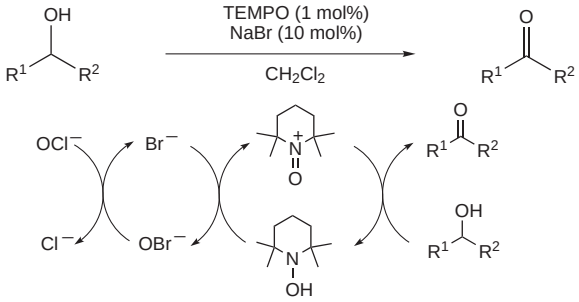
Introduction

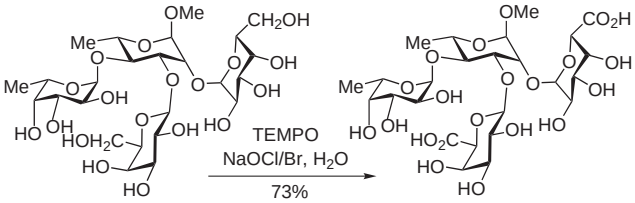
TEMPO (2,2,6,6-Tetramethyl-1-piperidinyloxy radical), as an oxidizing reagent, is the most representative member of the generally called nitroxyl radical oxidant family. They are characterized as weak oxidants that are stable, and soluble in both polar and apolar solvents. However, the radical can be oxidized to form the corresponding oxoammonium salt that is capable of oxidizing many organic functional groups. This oxidized species (Scheme 1) can be generated separately from the reaction mixture or, more interestingly, in situ, allowing a catalytic cycle.

Some reviews can be found in the literature,[1] but due to the increasing interest for this family of oxidants, new applications have been published. This Spotlight compiles novel oxidations catalyzed by TEMPO-oxoammonium salt from 2004 to present.

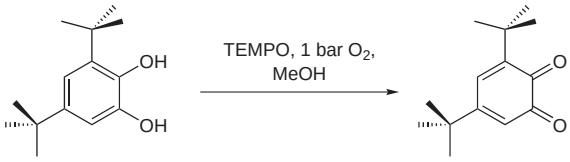


Abstracts

(A) Due to the high regioselectivity observed in polyalcohol systems towards primary alcohols in TEMPO-catalyzed oxidations, this reagent has been widely used in carbohydrate chemistry. An extensive review dealing with the application of TEMPO in the oxidation of polysacchararides has been published,[2] showing the efficiency of TEMPO and derivatives in this field. More recently new applications have been reported:[3] i) synthesis of galactopyranosyluronic acids (shown here);[3a] ii) oxidation of sucrose and isomaltulose;[3b] iii) synthesis of iduronic acids;[3c] and iv) preparation of uronates.[3d]



(B) Oxidation of catechol compounds can be achieved by TEMPO-initiated reactions at room temperature in MeOH under 1 bar of O_2.[4]



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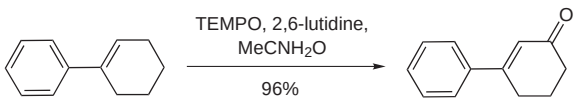
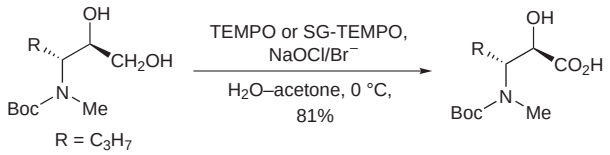
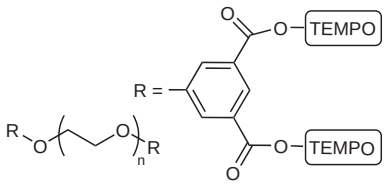
(C) TEMPO, in the presence of water and lutidine is able to convert activated alkenes and dienes to their corresponding alkenone[5] in excellent yields. In all cases studied, no traces of alkenol were detected.



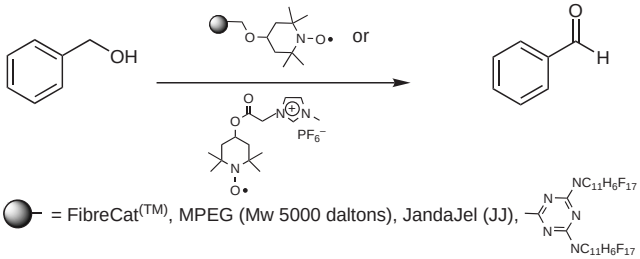
(D) The classical catalytic TEMPO/NaOCl/Br⁻ oxidation protocol can be applied to the oxidation of amino diols to aminohydroxy acids in homogeneous phase or entrapped in a sol-gel (SG) matrix.[6]



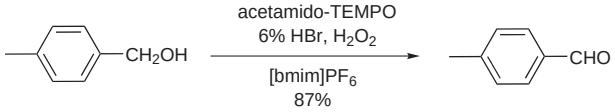
(E) Due to TEMPO being a rather expensive chemical agent, different efficient recycling methodologies have been studied.[7] (i) Notable are the results published by Hayes et al.[7a] where they present a branched catalyst obtained by attaching four nitroxyl radicals onto a functionalized PEG support. Results show an enhancement in the catalytic activities up to five times greater than the 4-methoxy-TEMPO analogue. Recycling experiments showed that the supported catalyst can be reused up to three times with no loss of catalytic activity. (ii) Baucherel et al.[7b] supported the catalyst onto FibreCat™, a carboxylic acid functionalized polymer. Other supports used: (iii) methylpoly(ethylene glycol) (MPEG),[7c] (iv) JandaJel (JJ),[7d] (v) perfluoroalkyl derivatives,[7e] and (vi) ionic liquids.[7f]



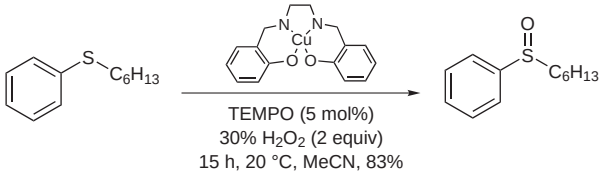
substrate	time	yield
1-undecanol	1	>99
trans-geraniol	0.8	82.7
benzyl alcohol	1.5	91.6



(F) Ionic liquids have been also used as solvents in TEMPO oxidations. Ragauskas et al.[8] published a three-component catalytic system (TEMPO/HBr/H_2O_2, using [bmim]PF_6 as solvent) where electron-deficient and electron-neutral benzylic alcohols were easily oxidized. The use of the (diethyl ether)-insoluble acetamide-TEMPO allows reuse of the ionic liquid and the catalyst.



(G) The addition of a catalytic amount of TEMPO to a mixture of copper(II) complex in a 30% aqueous H_2O_2 solution enhances the oxidation of sulfides to sulfoxides in selectivity and yield, providing a new environmentally friendly method to obtain these interesting compounds.[9]



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