

SYNLETT Spotlight 28

2,2,6,6-Tetramethylpiperidin-1-oxyl (TEMPO)

Compiled by Susana Barriga

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

Dpto. de Química Orgánica Universidad de Extremadura. Avda. de la Universidad s/n, E-10071 Cáceres, Spain.

Susana Barriga studied chemistry at the University of Extremadura where she received her diploma in 1997. Currently she is working on her Ph. D. thesis under the supervision of Prof. Tomás Torroba and Dr. Carlos F. Marcos at the University of Extremadura.



Nitroxyl radicals (**1**) contain the *N*, *N*-disubstituted NO group with one unpaired electron delocalised over the nitrogen-oxygen bond. One of the most popular nitroxyl radicals is 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO, **2**), a remarkably stable radical, that has found many applications in organic synthesis since it was first synthesised by Lebelev and Kazarnovskii in 1960.¹

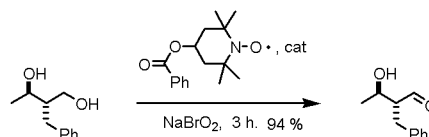
TEMPO is normally prepared by oxidation of the corresponding tetramethylpiperidine or tetramethylpiperidine hydroxide, but it is also commercially available from several sources. Many analogues have also been prepared, mainly

from their common precursor 2,2,6,6-tetramethyl-4-piperidone.²

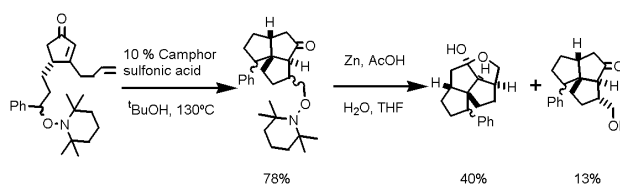
Due to its inert nature, TEMPO is widely used in electron spin resonance spectroscopy as a probe for biological systems, and also as a radical trap.³ Optically active nitroxyl radicals have been stereoselectively coupled with transient prochiral carbon radicals.⁴ One of the most important synthetic applications of TEMPO is its use in the oxidation of several organic substrates, such as amines, phosphines, phenols, anilines, and particularly primary and secondary alcohols.⁵

Abstracts

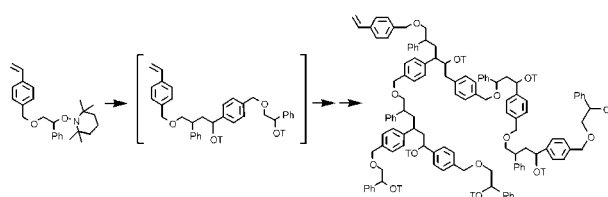
(A) TEMPO and some 4-derivatives are widely used in the oxidation of alcohols to aldehydes, ketones, or carboxylic acids, in moderate to excellent yields. They are used in stoichiometric amounts or, most commonly, as catalysts in combination with a second oxidant such as sodium hypochlorite.⁶ Remarkably, primary alcohols are selectively oxidised in presence of secondary alcohols or other oxidisable moieties.



(B) Alkyl halides react photochemically with TEMPO to give alkoxyamines, which can be isolated in excellent yields.⁷ These alkoxyamines have weak C-O bonds, which are homolytically cleaved upon heating. This can be used in radical cascade reactions, in which TEMPO traps the end radical formed in the process. Final N-O cleavage liberates the product as an alcohol. Studer used this methodology for the synthesis of an angular triquinane.⁸



(C) TEMPO is involved in radical polymerisation, being of special interest its use in “living” free radical polymerisation, in which, after relatively fast initiation, chains only propagate and the contribution of chain breaking reactions, such as transfer and termination, is negligible. This is used in the preparation of well defined polymers, unavailable by other synthetic techniques, allowing the synthesis of unique macromolecular architectures, such as linear block copolymers and hyperbranched and dendritic structures.⁹



References and Notes

- Lebelev, O. L.; Kazarnovskii, S. N. *Zhur. Obshch. Khim.* **1960**, *30*, 1631.
- a) Rozantsev, E. G.; Sholle, V. D. *Synthesis* **1971**, 401.
b) Couet, W. R. *Tetrahedron* **1985**, *41*, 1165. c) Sen, V. D.; Golubev, V. A.; Efremova, N. N. *Bull. Acad. Sci. USSR Div. Chem. Sci. (Engl. Transl.)* **1982**, *31*, 53.
- Naik, N.; Braslau, R. *Tetrahedron* **1998**, *54*, 667.
- Braslau, R.; Burril II, L. C.; Mahal, L. K.; Wedeking, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 237.
- de Nooy, A. E. J.; Besemer, A. C.; van Bekkum, H. *Synthesis* **1996**, 1153.
- Bolm, C.; Fey, T. *Chem. Commun.* **1999**, 1795 and references therein.
- Gilbert, B. C.; Kalz, W.; Lindsay, C. I.; McGrail, P. T.; Parsons, A. F.; Whittaker, D. T. E. *Tetrahedron Lett.* **1999**, *40*, 6095.
- Studer, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 1108.
- Hawker, C. J. *Acc. Chem. Res.* **1997**, *30*, 373.

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