

# SYNLETT Spotlight 70

## 2,2,6,6-Tetramethylpiperidine-Based Oxoammonium Salts

Compiled by Nabyl Merbouh



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

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### Introduction

Oxoammonium salts are derived from nitroxide free radicals by a one-electron oxidation (Figure 1). Their discovery in 1965 by Golubev et al.<sup>1</sup> has led to the synthesis of a series of oxidizing agents with diverse properties. The parent nitroxides have been the subject of numerous oxidation studies,<sup>2</sup> which involve the in situ synthesis of oxoammonium salt by a secondary oxidant, thus making the nitroxide a catalyst. These catalytic reactions and many stoichiometric reactions of oxoammonium salts have been reviewed.<sup>2,3</sup> Oxoammonium salts used for stoichiometric oxidations can be obtained by the oxidation of nitroxides with halides or by the acid catalyzed disproportionation of nitroxides. Oxoammonium salts are stable and highly specific oxidants. When the counter anion is bromide or chloride, the salts are usually quite hygroscopic, however the tetrafluoroborates are not. The perchlorates are well known, but due to their latent ability to detonate their use cannot be recommended.

Oxoammonium salts, generated in situ, by the oxidation of a catalytic amount of nitroxide with a stoichiometric amount of a secondary oxidant have found extensive use in the oxidation of alcohols to aldehydes, ketones and, under special circumstances, to carboxylic acids. The secondary oxidant can be bleach,<sup>4</sup> oxone,<sup>5</sup> bromine or chlorine,<sup>6</sup> iodine,<sup>7</sup> MCPBA,<sup>8</sup> sodium bromite and chlorite,<sup>9</sup> and many other oxidants. Oxoammonium salts can also be generated in situ electrochemically.<sup>10,11</sup>

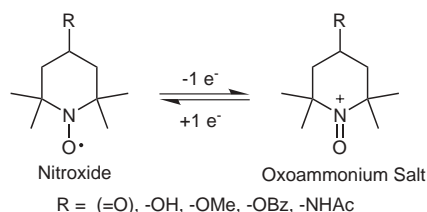
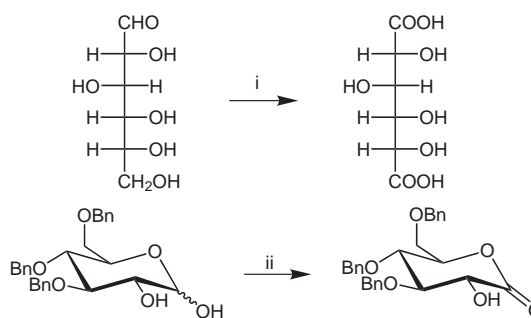


Figure 1

### Abstracts

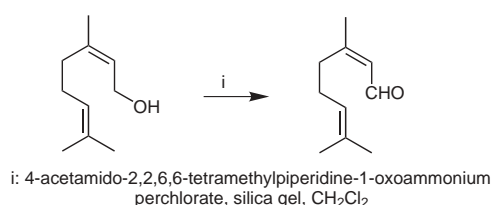
(A) In carbohydrate chemistry, oxoammonium salts, generated in situ, are selective oxidants. For instance, primary alcohols or hemiacetals can be oxidized in the presence of secondary alcohols, thus making them useful for the oxidation of many sugar derivatives. These oxidations are pH and temperature dependent.<sup>12</sup> Under basic conditions, the selective oxidation of hemiacetals to the corresponding lactones/esters can be achieved in the presence of unprotected secondary alcohols.<sup>13</sup>



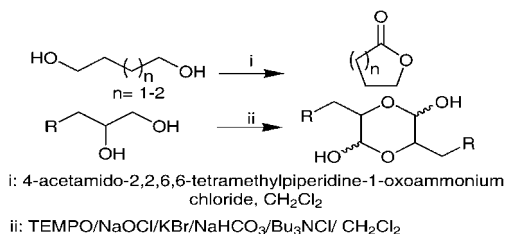
i: TEMPO/NaOCl/KBr, H<sub>2</sub>O, pH 11.5

ii: 4-acetamido-2,2,6,6-tetramethylpiperidine-1-oxoammonium tetrafluoroborate, pyridine, CH<sub>2</sub>Cl<sub>2</sub>

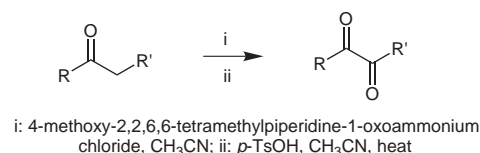
(B) As stoichiometric reagents, oxoammonium salts represent a family of non-heavy metal-based oxidation reagents. Since they are colored, many reactions can be interpreted colorimetrically. The oxidants tend to be highly functional group specific. The reactions show counter-ion-dependent rates and specificities. These oxidants do not induce isomerization of allylic alcohols, and phenolic benzyl alcohols can be oxidized without phenol protection. The reactions do not take place when the alcohol carries a  $\beta$ -oxygen or a  $\beta$ -electron-withdrawing group. Benzyl and allyl alcohols are rapidly oxidized, secondary aliphatic alcohols are less so, and primary aliphatic alcohols require silica gel catalysis.<sup>14</sup>



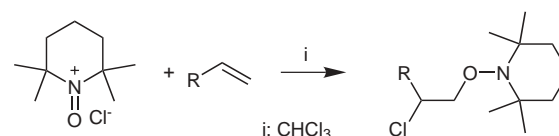
(C) Using a stoichiometric amount of oxidant, oxidation of diols with 4 or 5 carbons generates cyclic lactones. 1,2-diols or 1,3-diols dimerize to generate cyclic acetals.<sup>15</sup> However, under catalytic conditions, the oxidation of 1,2-diols leads to the synthesis of cyclic hemiacetals.<sup>16</sup>



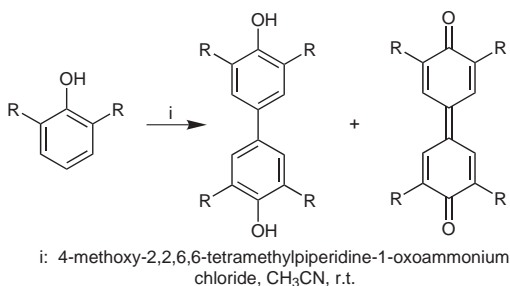
(D) Selective oxyfunctionalization of enolizable ketones with oxoammonium salts can be achieved in high yields, thus making them reagents of choice for the synthesis of vicinal-diketones.<sup>17</sup>



(E) 1,2-Addition of oxoammonium salts to electron rich olefins such as vinyl ethers, enamines and trialkylalkenes takes place in high yields.<sup>18</sup>



(F) Oxoammonium salts will induce oxidative phenol couplings. The phenol or quinone coupling products are obtained in good yields.<sup>19,20</sup>



## References

- Golubev, V. A.; Rozantsev, E. G.; Neiman, M. B. *Bull. Acad. Sci. USSR Div. Chem. Sci.* **1965**, 1898.
- de Nooy, A. E. J.; Besemer, A. C.; van Bekkum, H. *Synthesis* **1996**, 1153.
- Bobbitt, J. M.; Flores, C. L. *Heterocycles* **1988**, 27, 509.
- de Nooy, A. E. J.; Besemer, A. C.; van Bekkum, H. *Tetrahedron* **1995**, 51, 8023.
- Bolm, C.; Magnus, A. S.; Hildebrand, J. P. *Chem. Lett.* **2000**, 2, 1173.
- Merbouh, N.; Bobbitt, J. M.; Brückner, C. *J. Carbohydr. Chem.* **2002**, 21, 65.
- Miller, R. A.; Hoerner, R. S. *Org. Lett.* **2003**, 5, 285.
- Rychnovsky, S. D.; Vaidyanathan, R. *J. Org. Chem.* **1999**, 64, 310.
- Zhao, M.; Li, J.; Mano, E.; Song, Z.; Tsahen, D. M.; Grabowski, E. J. J.; Reider, P. *J. Org. Chem.* **1999**, 64, 2564.
- Semmelhack, M. F.; Chou, C. S.; Cortes, D. A. *J. Am. Chem. Soc.* **1983**, 105, 4492.
- Kishioka, S.; Ohki, S.; Ohsaka, T.; Tokuda, K. *J. Electroanal. Chem.* **1998**, 452, 179.
- Thaburet, J. F.; Merbouh, N.; Ibert, M.; Marsais, F.; Queguiner, G. *Carbohydr. Res.* **2001**, 21, 330.
- Merbouh, N.; Bobbitt, J. M.; Brückner, C. *Tetrahedron Lett.* **2001**, 42, 8793.
- Bobbitt, J. M. *J. Org. Chem.* **1998**, 63, 9367.
- Miyazawa, T.; Endo, T. *J. Org. Chem.* **1985**, 50, 3930.
- Siedlecka, R.; Skarzewski, J.; Mlochowski, J. *Tetrahedron Lett.* **1990**, 31, 2177.
- Ren, T.; Liu, Y. C.; Guo, Q. X. *Bull. Chem. Soc. Jpn.* **1996**, 69, 2935.
- Takata, T.; Tsujino, Y.; Nakanishi, S.; Nakamura, K.; Yoshida, E.; Endo, T. *Chem. Lett.* **1999**, 937.
- Bobbitt, J. M.; Ma, Z. *Heterocycles* **1992**, 33, 641.
- Liu, Y. C.; Wang, L. W.; Guo, Q. X. *Chin. Chem. Lett.* **1996**, 7, 790.