

# Green Oxidation of Organic Compounds: Manganese Sulphate/Oxone®/Water

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**Abstract:** We present a methodology for the oxidation of aromatic organic compounds based on manganese sulphate, Oxone® and water. The proposed method, which involves mild reaction conditions, was shown to produce various functional groups of interest in good yield, when applied to amines, alcohols and benzylic groups. This method has several advantageous characteristics, including low-cost reagents, aqueous reaction conditions, moderate temperatures, and short reaction times.

**Key words:** Green oxidation, aromatic compounds, manganese sulphate, oxone, amines, alcohols, benzylic groups.

**Resumen:** Presentamos una nueva metodología para la oxidación de compuestos aromáticos basada en sulfato de manganeso, Oxone® y agua. El método propuesto, el cual involucra condiciones de reacción suaves, produce distintos grupos funcionales de interés en buenos rendimientos, cuando se aplica a aminas, alcoholes y metilos benzoílicos. Este método tiene varias ventajas, incluyendo bajo costo de reactivos, medio acuoso, temperaturas moderadas y tiempos cortos de reacción.

**Palabras clave:** Oxidación verde, compuestos aromáticos, sulfato de manganeso, oxone, aminas, alcoholes, grupos benzoílicos.

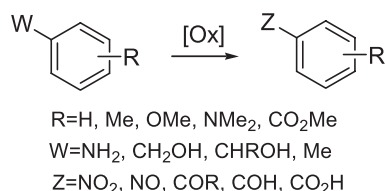
## Introduction

Oxidation reactions are of great importance in organic chemistry for the transformation of functional groups. Numerous methods and reagents have been developed for performing such reactions [1]. However, many existing methods have serious drawbacks. These include extremely reactive oxidant mixtures [2,3b], and, as a consequence, weak chemoselectivity, highly toxic products [3], complex methodologies and expensive reagents [4].

Here we present a new methodology of green chemistry that has several advantages over previous methods: inexpensive reagents, the use of H<sub>2</sub>O as the sole solvent, reactions at room temperature or no higher than 90 °C and short reaction times.

The oxidizing power of manganese salts on organic substrates is well known [5]. The manganese acts as a Lewis acid to facilitate cleavage of the O-O bond [5e]. Moreover Mn<sup>3+</sup> salts in non-aqueous systems are excellent catalysts for oxidation of benzyl groups to the corresponding aldehydes via electrochemical methods [6]. Oxidation reactions promoted by Oxone® [7] have also been reported, but under drastic conditions with the assistance either of patented catalysts or compounds whose structure is extremely complex [8].

In a general way we can describe the oxidation reaction (MnSO<sub>4</sub>/Oxone®/Water) described here as follows: (Scheme 1)



Scheme 1

The tests were performed on the following aromatic functional groups (Table 1): amines, alcohols and benzylic methyl groups. Good to excellent results were obtained in all cases.

## Results

### Discussion and Conclusions



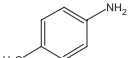
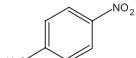
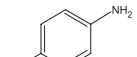
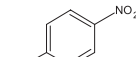
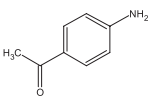
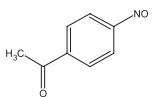
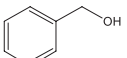
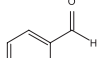
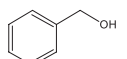
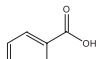
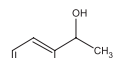
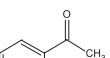
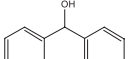
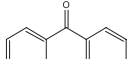
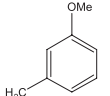
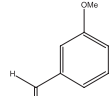
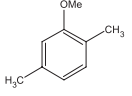
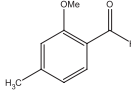
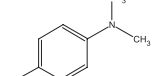
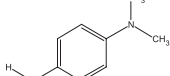
Using the method here described, aromatic rings without substituent or electron-rich groups (CH<sub>3</sub>, OCH<sub>3</sub> and N(CH<sub>3</sub>)<sub>2</sub>), exhibited high yields and short reaction times, possibly because these groups stabilize the intermediates produced along the reaction pathway for the incorporation of oxygen into the molecule. This hypothesis is reinforced by our results for the oxidation reactions of anilines. For these compounds, the electron-rich group was directly oxidized, and thus the appropriate reaction occurs immediately and with excellent yield.

For compounds with rings containing electron-attracting groups or groups at positions not favored by stabilizing charge resonance effects (i.e., *meta* position), by contrast, the yields are lower and the reaction times longer. These findings provide further support for the hypothesis that the efficacy of the oxidation reaction relies on the stabilization of intermediates by electronic resonance effects.

In both cases, it is important to control the stoichiometric amounts of reagents to ensure complete oxidation. In general, the best results were obtained using an excess of the oxidizing agent (MnSO<sub>4</sub>/Oxone®/Water), although this was not the case for oxidation reactions requiring chemoselectivity such as those of primary alcohols.

In the oxidation reactions of primary alcohols, chemoselectivity could be achieved if an appropriate quantity

Table 1

Entry	Substrate	Product	Time	Yield (%)
a <sup>9a,b,c, 4c</sup>			30 sec.	92
b <sup>9b,c,d,e</sup>			30 sec.	94
c <sup>9b,c, 4c, 11c</sup>			30 sec.	95
d <sup>10a,b</sup>			1h	64
e <sup>8a, 11a,b</sup>			30 min	53
f <sup>8d,e,f</sup>			45 min	95
g <sup>8a,c,11a,b</sup>			40 min	98
h <sup>8a,11a,b</sup>			45 min	98
i <sup>12a,b</sup>			1h	68
j <sup>13a,b,c</sup>			30 min	82
k <sup>14a,b,c</sup>			30 min	80

of oxidizing agent was used, and the corresponding acid was obtained in excellent yield when an excess of oxidizing agent was present.

The method described here provides a new alternative for the oxidation of various functional groups. Notably, the proposed method uses low-cost reagents, a simple experimental procedure friendly to the environment and byproducts whose waste treatment is simple. This method also achieves excellent yields, and involves mild reaction conditions and short reaction times, following green chemistry protocols.

## Experimental

General Remarks: Thin layer and flash column chromatography were performed on silica gel using hexane, ethyl acetate as eluent. GC analyses were performed on a Hewlett Packard 5890-SERIE II equipped with a HP-5MS column (95%

dimethylpolysiloxane), mobile phase (Helium). The infrared spectra were recorded on Perkin Elmer 1600 FT spectrometer. NMR spectra were acquired in CDCl<sub>3</sub>, at 300 and 400 MHz for <sup>1</sup>H. Chemical shifts are reported in δ from tetramethylsilane as the internal standard. <sup>13</sup>C NMR (75 and 100 MHz) spectra were recorded on a Oxford NMR 300 spectrometer. Mass spectra were measured at 70 eV (EI) on JEOL SX-102.

All of the oxidation reactions of activated anilines were conducted using the following procedure:

### Preparation of Nitrobenzene (a) [9].

In a flask of 50 mL, aniline (250 mg, 2.68 mmol, 1 eq) was placed with a magnetic stirrer. In a 100 mL beaker, oxone (4.2 g, 6.72 mmol, 2.5 eq.) and MnSO<sub>4</sub>·H<sub>2</sub>O (0.65 g, 4 mmol, 1.5 eq) were placed. H<sub>2</sub>O (7 mL) was then added and the mixture was stirred for 3-5 min. The resulting mixture was then added to the flask containing the aniline, with continuous stirring.

The reaction mixture immediately changed color and a dark precipitate formed. The mixture was stirred for a further 30 sec, and then it was extracted with ethyl ether (5 mL × 4). The organic phase was collected and washed with 5% NaHCO<sub>3</sub> (5 mL × 1) and with saturated NaCl solution (5 mL × 2). The organic phase was separated and dried on anhydrous Na<sub>2</sub>SO<sub>4</sub>. The extract was concentrated under vacuum and the crude oil was purified by column chromatography to afford 0.30 g of Nitrobenzene (a) (92%).

In the case of *p*-aminoacetophenone (d) and all other substrates (e-k), the following operation was performed: after adding the mix down, Oxone®/MnSO<sub>4</sub>·H<sub>2</sub>O the mixture is warmed to 90°C in a reflux system during the time specified in each case. After this time, the mixture was left cool to room temp for 15 min and then the procedure continued as described above.

In the case of benzaldehyde (e), 1.2 eq. of Oxone® and 0.5 eq. of MnSO<sub>4</sub>·H<sub>2</sub>O were placed to keep the chemoselectivity.

- (a) Nitrobenzene: <sup>1</sup>H-NMR δ: 8.18 (m, 2H), 7.5 (m, 2H), 7.71 (m, 1H). Lit. [16a]; mp 5-8°C. lit. [17], 6°C
- (b) *p*-Nitrotoluene: <sup>1</sup>H-NMR δ: 8.15 (m, 2H), 7.85 (m, 2H), 2.48(s, 3H). Lit. [15]; MS: *m/z*: 137 (100%); mp 53-55°C, lit. [17] 53-54°C
- (c) *p*-Nitroanisole: <sup>1</sup>H-NMR δ: 8.25 (m, 2H), 6.99 (m, 2H), 3.93(s, 3H). Agree lit. [4c] MS: *m/z*: 153 (100%) mp 52-54°C, lit. [17]; 54°C
- (d) *p*-nitrosoacetophenone: <sup>1</sup>H-NMR δ: 8.21 (m, 2H), 7.95 (m, 2H), 2.42(s, 3H). Lit. [10b]; MS: *m/z*: 149 (100%)
- (e) Benzaldehyde: <sup>1</sup>H-NMR δ: 10.05 (s, 1H), 7.88 (m, 2H), 7.48(s, 2H), 7.54(m,1H). Lit. [16b].
- (f) Benzoic acid: <sup>1</sup>H-NMR δ: 11.58 (s, 1H, D<sub>2</sub>O disappears), 8.10 (m, 2H), 7.46(s, 2H), 7.54(m,1H). Lit. [16d]; mp 118-120°C, lit. [17]; 122°C
- (g) Acetophenone: <sup>1</sup>H-NMR δ: 7.96 (m, 2H), 7.57(s, 1H), 7.47(m, 2H), 2.61 (s, 3H). Lit. [16c]; mp 20-22°C, lit. [17]; 20.5 °C
- (h) Benzophenone: <sup>1</sup>H-NMR δ: 7.96 (m, 2H), 7.57(s, 1H), 7.47(m, 2H), 2.61 (s, 3H). Lit. [16c]; mp 46-48°C, lit. [17]; 48.5 °C
- (i) *m*-Anisaldehyde: <sup>1</sup>H-NMR δ: 9.96 (s, 1H), 7.42(m, 2H), 7.25(m, 1H), 7.11 (m, 1H), 3.78 (s, 3H) Lit. [15].
- (j) 2-Methoxy-4-methyl-Benzaldehyde: <sup>1</sup>H-NMR δ: 10.39 (s, 1H), 7.74(d, 1H, J 7Hz), 6.84(d, 1H, J 7Hz), 6.78 (s, 1H), 3.91 (s, 3H), 2.41 (s, 3H). Lit. [13b]; mp 40-43°C, lit. [13b]; 42-43°C
- (k) *p*-*N,N*-dimethylaminobenzaldehyde: <sup>1</sup>H-NMR δ: 9.70 (s, 1H), 7.71(m, 2H), 6.69(m, 2H), 3.01 (s, 6H). Lit. [15]; mp 71-73°C, lit. [17] 74°C

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## References

1. a) Richardson, W. H., in: Oxidation in Organic Chemistry, K.B. Wiberg, Ed. Part A, Academic Press, New York-London, **1965**, Ch. IV. b) W.A. Watters, W. A. *Trans. Faraday Soc.* **1946**, *42*, 184-189. c) Wan, P.; Yates, K. *Can. J. Chem.* **1986**, *64*, 2076-2086. d) Langley, W. D. *Org. Synth. Coll.* Vol. 3; Horning, E. C., Ed. Wiley & Sons, New York, **1955**, 334-336. e) Das, B. C.; Iqbal, J. *Tetrahedron Lett.* **1997**, *38*, (7), 1235-1238.
2. a) Jefford, C. W.; Wang, Y. *J. Chem. Soc., Chem. Commun.* **1988**, 634-635. b) Oyster, L.; Adkins, H. *J. Am. Chem. Soc.* **1921**, *43*, 208-210. c) Schaeffer, J. R.; Snoddy, A. O. *Organic Syntheses*. **1963**. Coll. Vol. 4, 19-21.
3. a) Ho, T. L. *Synthesis* **1973**, 347-353. b) Bowden, K.; Heilbron, I. M.; Jones, E. R. H.; Weedon, B. C. L. *J. Chem. Soc.* **1946**, 39-45. c) Hayakawa, Y.; Uchiyama, M.; Noyori, R. *Tetrahedron Lett.* **1986**, *27*, 4195-4196. d) Postowsky, J.; Lugowkin, B. P. *Chem. Ber.* **1935**, *68*, 852-856.
4. a) Carmelli, M.; Rozen, S. *J. Org. Chem.* **2006**, *71*, 4585-4589. b) Jain, S. L.; Sain, B. *Angew. Chem. Int.* **2003**, *42*, 1265-1267. c) Suresh, S.; Joshep, R.; Jayachandran, B. *Tetrahedron* **1995**, *51*, 11305-11318.
5. a) Fatiadi, A. J. *Synthesis* **1976**, 65-104. b) Fatiadi, A. J. *Synthesis* **1976**, 133-167. c) Gritter, R. J.; Wallace, T. J. *J. Org. Chem.* **1959**, *24*, 1051-1056. d) Sondheimer, F.; Amendolla, C.; Rosenkraz, E. *J. Am. Chem. Soc.* **1953**, *75*, 5932-5935. e) Lane, B. S.; Vogt, M.; DeRose, V. J.; Burgess, K. *J. Am. Chem. Soc.* **2002**, *124*, 11946-11954.
6. Tallec, A. *Electrochimie Organique. Synthèses et Mecanismes*. **1985**, 95-97. Ed Masson. Paris.
7. a) Webb, K. S.; Ruzskay, S. J. *Tetrahedron* **1998**, *54*, 401-410. b) Varma, R. S.; Dahiya, R. K. *Molecules* **1998**, 282-285. c) Curini, M.; Epifanio, F.; Marcotullio, M. C.; Rosati, O. *Synlett* **1999**, *6*, 777-779. d) He, W. *Synlett* **2006**, *20*, 3548-3549.
8. a) Haijipur, A. R.; Mallakpour, S. E.; Adibi, H. *Chem. Lett.* **2000**, *5*, 460-461. b) Deasi, U. V.; Pore, D.M.; Tamhankar, B. V.; Jaghav, S. A.; Wadgaonkar, P. P. *Tetrahedron Lett.* **2006**, *47*, 8559-8561. c) Adams, J. *Am. Chem. Soc.* **1924**, *46*, 1889-1896. d) Vogel, A. I.; *Practical Organic Chemistry*. **1959** (Longmans, London, 3<sup>o</sup> ed.), 755-757.
9. a) Suresh, S.; Joshep, R.; Jayachandran, B. *Tetrahedron* **1995**, *51*, 11305-11318. b) Sharma, V. B.; Jain, S. L.; B. Sain. *Tetrahedron Lett.* **2003**, *44*, 3235-3237. e) Clarke, H. T.; Taylor, E. R. *Organic Syntheses* **1923**, *3*, 91-92.
10. a) A. Defoin, A. *Synthesis* **2004**, *5*, 706-710. b) Siraki, A. G.; Chan, T. S.; Galati, G.; Teng, S.; O'Brien, P. *Drug Metabolism Reviews* **2002**, *34*, 549 - 564 c) Eyer, P.; Gallemann, D. *The Chemistry of Amino, Nitroso, Nitro and Related Groups* **2003**. John Wiley & Sons, Ltd. Israel. 999-1039.
11. a) Pratt, E. F.; Van de Castle, J. F. *J. Org. Chem.* **1961**, *26*, 2973-2975. b) Haijipur, A. R.; Rafiee, F. *Synth. Commun.* **2006**, *36*, 2563-2568. c) Zabrowski, D. L.; Moorman, A. E.; Beck, K. R. *Tetrahedron Lett.* **1988**, *29*, 4501-4504.
12. a) Niedzielski, N. *J. Am. Chem. Soc.* **1941**, *63*, 1462-1463. b) Sisti, A.; Burgmaster, J.; Fudim, M. *J. Org. Chem.* **1962**, *27*, 279-281.
13. a) Loitz, C.; Looper, R.; Peterson, E. *Tetrahedron Lett.* **1981**, *22*, 2605-2608. b) Harmata, M.; Hong, X.; Barnes, C. *Synthesis* **1987**, *8*, 723-724. c) Kimachi, T.; Takemoto, Y. *Tetrahedron Lett.* **2004**, *45*, 5109- 5112.
14. a) Campaigne, E.; Archer, W. L. *Organic Syntheses* **1963** Coll. Vol. 4, 331-333. b) Vilsmeier, A.; Haack, A. *Chem. Ber.* **1927**, *60*,

- 119-122. c) Adams, R.; Coleman, G. H. *Org. Syntheses* **1941** Coll. Vol. 1, 214-217.
15. [http://riodb01.ibase.aist.go.jp/sdbs/cgi-bin/cre\\_index.cgi?lang=eng](http://riodb01.ibase.aist.go.jp/sdbs/cgi-bin/cre_index.cgi?lang=eng), accessed in June, 2007.
16. a) Prestch, E.; Bühlmann, P.; Affolter, C.; Herrera, A.; Martínez, R. *Determinación Estructural de Compuestos Orgánicos* **2005**. Ed. Masson. España.
17. The Merck Index. Whitehouse Station, New Jearsy. USA. **2001**.