Rhenium-Catalyzed Highly Efficient Oxidations of Tertiary Nitrogen Compounds to *N*-Oxides Using Sodium Percarbonate as Oxygen Source

Suman L. Jain, Jomy K. Joseph, Bir Sain*
Chemical and Biotechnology Division, Indian Institute of Petroleum, Dehradun 248005, India
Fax +91(135)2660202; E-mail: birsain@iip.res.in

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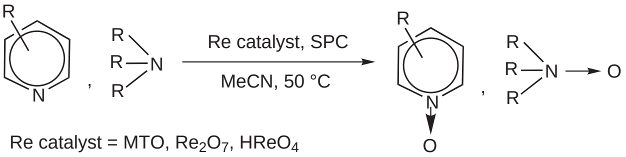
Abstract: Sodium percarbonate was found to be an ideal and efficient oxygen source for the oxidation of tertiary nitrogen compounds to *N*-oxides in excellent yields in presence of various rhenium-based catalysts under mild reaction conditions.

Key words: rhenium, solid oxidants, sodium percarbonate, oxidation, *N*-oxides

The development of metal-catalyzed green and environmentally benign synthetic methodologies using hydrogen peroxide and molecular oxygen as oxidants is an area of tremendous importance.[1] Rhenium-based systems, owing to their unique properties such as higher oxidation ability, versatility and non-productive decomposition of hydrogen peroxide have attracted particular attention in recent years in various oxidation reactions. Methyltrioxorhenium (MTO) first reported by Herrmann et al.[2] due to its ease of synthesis, commercial availability and stability in air has proven to be an exceptionally versatile oxygen transfer catalyst for various oxygenation reactions with aqueous hydrogen peroxide in both organic and aqueous solvents. The major drawback of this efficient system is the limited stability of MTO due to its decomposition in water. Solid peroxy compounds such as sodium perborate (SPB) and sodium percarbonate (SPC) owing to their ease of synthesis, safe handling and storage stability have proven to be safe alternatives of dangerous anhydrous hydrogen peroxide.[3] However, potential of these solid oxidants in MTO-catalyzed oxidation reactions has remained largely unexplored and to the best of our knowledge there is only one literature report on the use of sodium percarbonate as oxygen source for the epoxidation of alkenes using MTO as catalyst.[4] In continuation to our studies on the development of green synthetic methods[5] herein we wish to report an efficient and simple methodology for the oxidation of tertiary nitrogen compounds using sodium percarbonate as solid oxidant[6] in presence of various rhenium-based catalysts such as MTO, Re_2O_7 and $HReO_4$ under very mild reaction conditions (Scheme 1).



Scheme 1

To evaluate the efficiency of various rhenium-based catalysts we carried out the oxidation of 4-picoline (10 mmol) with sodium percarbonate (20 mmol) in the presence of acetic acid (20 mol%) and Re catalyst (1 mol%) at 50 °C. The results are summarized in Table 1. Among the various catalysts studied, methyltrioxorhenium was found to be the most competent for this transformation. To evaluate the effect of catalyst, blank oxidation of 4-picoline with sodium percarbonate was also carried out under similar reaction conditions in the absence of catalyst. The reaction was found to be very slow and afforded a poor yield of the corresponding *N*-oxide (Table 1, entry 1). In order to compare the effectiveness of this solid oxidant, we also studied the oxidation of 4-picoline using aqueous hydrogen peroxide as oxidant in place of SPC in the presence of various Re catalysts under similar reaction conditions as shown in Table 1 (entries 2–4). All the reactions were found to be slow and afforded poor yields of the *N*-oxide, confirming the deactivation of Re catalyst due to the presence of water

To generalize the method, a variety of tertiary nitrogen compounds was subjected to the oxidation using substrate (10 mmol) with a catalytic amount of methyltrioxorhenium (1 mol%) and sodium percarbonate (20 mmol) in the presence of acetic acid (20 mol%) in acetonitrile at 50 °C

Table 1 Comparison of Results of Rhenium-Catalyzed Oxidation of 4-Picoline with Sodium Percarbonate/Hydrogen Peroxide Oxidants[a]

Entry	Catalyst	Sodium percarbonate		30% H_2O_2	
		Reaction time (h)	Yield (%)[b]	Reaction time (h)	Yield (%)[b]
1[c]	–	8	30	8	Trace
2	MTO	1.5	92	3.5	90
3	Re_2O_7	2.5	85	4.5	30
4	$HReO_4$	2.0	90	5.0	50

[a] Reaction conditions: 4-picoline (10 mmol), oxidant (20 mmol), AcOH (20 mol%), catalyst (1 mol%), MeCN (3 mL) at 50 °C.
[b] Isolated yields.
[c] Experiment carried out in the absence of Re catalyst.

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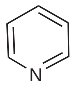
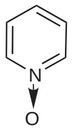
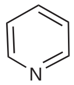
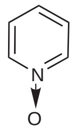
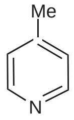
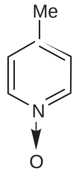
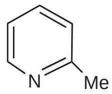
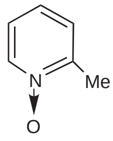
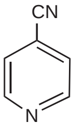
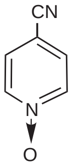
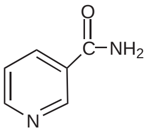
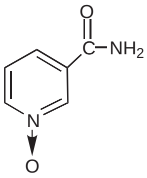
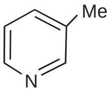
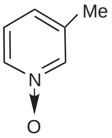
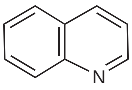
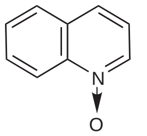
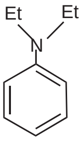
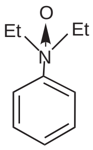
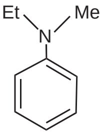
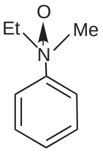
under nitrogen atmosphere.[7] All the substrates were selectively converted into the corresponding *N*-oxides and the results are presented in Table 2. In general triethylamine and substituted anilines were found to be most reactive (Table 2, entry 9–11) while among the various pyridines studied, those substituted with electron-donating groups were found to be more reactive and required shorter reaction times for their oxidation (Table 2, entry 3, 4 and 7). The presence of acetic acid was found to be essential for these reactions and in its absence reactions were found to be very slow and gave very poor yields of the oxidized products, probably due to the fact that presence of acid may help in releasing the hydrogen peroxide from both sodium percarbonate and sodium perborate reagents. The use of triflouroacetic acid in place of acetic acid also yielded comparable results while the use of inorganic acids such as hydrochloric acid and sulfuric acid gave no oxidation. It was also observed that the addition of acetic acid in one portion gave poor yields of the products while its dropwise addition gave better yields of the oxidized products. The reaction mixture of substrate, MTO and sodium percarbonate in acetonitrile upon addition of acetic acid gave vibrant yellow color indicating the formation of activated peroxo species during the reaction, while the disappearance of the yellow color indicates the completion of the reaction. To compare the efficiency of both solid oxidants, we carried out the oxidation of pyridine with SPB instead of SPC in presence of catalytic amount of MTO under similar reaction conditions. Neither the yellow color of the reaction mixture upon addition of acetic acid nor the oxidation was observed as shown in Table 2 (entry 2).

Table 2 Methyltrioxorhenium-Catalyzed Oxidation of Tertiary Nitrogen Compounds Using SPC as Oxygen Source[a]

Entry	Substrate	Product	Time (h)	Yield (%)[b,c]
1			2.5	90
2[d]			8.0	–
3			1.5	92
4			2.5	89
5			4.0	75
6			6.5	70
7			2.75	90
8			8.5	55
9			1.25	92
10			1.0	94
11	Et_3N	$Et_3N \rightarrow O$	1.0	95

[a] Reaction conditions: substrate (10 mmol), MTO (1 mol%), SPC (20 mmol), AcOH (20 mol%), acetonitrile (3 mL), at 50 °C under nitrogen atmosphere.

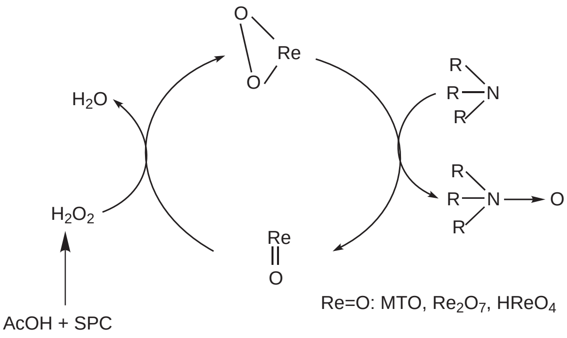
[b] Isolated yields; purity >99% as determined by GC.

[c] All the products were characterized via their physical (mp) and spectral (IR and ^{1}H NMR) data.[8]

[d] Experiment carried out using SPB as oxidant in place of SPC.

The effect of various solvents was studied by carrying out the oxidation of 4-picoline under similar reaction conditions using different solvents such as acetonitrile, dichloroethane, toluene and ethanol. Among the various solvents studied acetonitrile and dichloroethane were found to be the good solvents for this transformation.

A plausible mechanism of these reactions may involve the formation of active peroxo species of rhenium by the reaction with sodium percarbonate in the presence of acetic acid as shown in the Scheme 2. The subsequent oxygen transfer from these reactive peroxo species to tertiary nitrogen compound yields the corresponding *N*-oxide.



Scheme 2

In summary sodium percarbonate was found to be an efficient and versatile oxygen source for the oxidation of tertiary nitrogen compounds to *N*-oxides using various rhenium-based compounds as catalysts under mild reaction conditions. The safe and ease of handling of the SPC in place of anhydrous hydrogen peroxide, controlled release of the hydrogen peroxide, easy workup and better yields of the products makes this a facile and valuable protocol for the oxidation of tertiary amines.

Acknowledgment

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Reference and Notes

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(7) **Typical Experimental Procedure**: To a stirred solution of 4-picoline (10 mmol, 0.93 g), in MeCN (3 mL) were added SPC (3.12 g, 20 mmol) and MTO (25 mg, 1 mol%) and the mixture was heated to 50 °C under nitrogen atmosphere. AcOH (20 mol%) was added dropwise over a period of 15 min at 50 °C to this vigorously stirred solution. A vibrant yellow color appeared in the reaction mixture upon addition of AcOH. The progress of the reaction was monitored by TLC (SiO_2). After completion, the solvent was evaporated and the residue was dissolved in CH_2Cl_2. The organic layer was washed with water (2 ×) and dried over anhyd Na_2SO_4. The solvent was evaporated under reduced pressure and the residue thus obtained was purified by passing through a short silica gel column using EtOAc–hexane (4:6) as eluent. Evaporation of the solvent under reduced pressure yielded pure 4-picoline *N*-oxide (1.02 g, 92%); mp 180–181 °C (Lit.[9] 182 °C). IR: 3033, 1470, 1250, 1176 cm^{-1}. ^1H NMR: $\delta = 2.39$ (s, 3 H), 7.10–7.22 (d, 2 H), 8.09–8.20 (d, 2 H).

(8) **Product Characterization Data.**

Pyridine *N*-Oxide (Table 2, entry 1): mp 60–61 °C (Lit.[9] 62–63 °C). IR: 3076, 1388, 1265, 1176 cm^{-1}. ^1H NMR: $\delta =$ 7.42–7.45 (m, 3 H), 8.25–8.40 (m, 2 H).

2-Picoline *N*-Oxide (Table 2, entry 4): Hygroscopic oil. IR: 3030, 1482, 1252, 1190 cm^{-1}. ^1H NMR: $\delta = 2.42$ (s, 3 H), 7.10–7.19 (m, 3 H), 8.10–8.23 (m, 1 H).

4-Cyanopyridine *N*-Oxide (Table 2, entry 5): mp 180–182 °C (Lit.[9] 182–183 °C). IR: 3076, 2247, 1492, 1282, 1176 cm^{-1}. ^1H NMR: $\delta =$ 7.89–8.00 (d, 2 H), 8.42–8.46 (d, 2 H).

Nicotinamide *N*-Oxide (Table 2, entry 6): mp 289–290 °C (decomp.). IR: 3350, 3060, 1694, 1450, 1140 cm^{-1}. ^1H NMR: $\delta =$ 7.37–7.45 (m, 2 H), 8.27–8.40 (m, 2 H).

3-Picoline *N*-Oxide (Table 2, entry 7): Hygroscopic oil. IR: 3030, 1470, 1252, 1162 cm^{-1}. ^1H NMR: $\delta = 2.35$ (s, 3 H), 7.11–7.21 (m, 2 H), 8.18–8.20 (m, 2 H).

Quinoline *N*-Oxide (Table 2, entry 8): mp 50–52 °C (Lit.[9] 52–53 °C). IR: 3030, 1484, 1298, 1176 cm^{-1}. ^1H NMR: $\delta =$ 7.21–7.35 (m, 4 H), 8.10–8.19 (m, 2 H), 8.40 (m, 1 H).

***N,N*-Diethylaniline *N*-Oxide** (Table 2, entry 9): Hygroscopic solid. IR: 3013, 2941, 1369, 1219, 1190 cm^{-1}. ^1H NMR: $\delta = 1.2$ (t, 6 H), 3.3 (q, 2 H), 6.9 (m, 3 H), 7.3 (m, 2 H).

***N,N*-Dimethylaniline *N*-Oxide** (Table 2, entry 10): Hygroscopic solid. IR: 3010, 2941, 1367, 1219, 1175 cm^{-1}. ^1H NMR: $\delta = 3.32$ (s, 6 H), 7.22–7.28 (m, 3 H), 7.49–7.55 (m, 2 H).

Triethylamine *N*-Oxide (Table 2, entry 11): Hygroscopic solid. IR: 2940, 2870, 1470, 1250 cm^{-1}. ^1H NMR: $\delta = 1.12$ (t, 9 H), 3.30 (q, 6 H).

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