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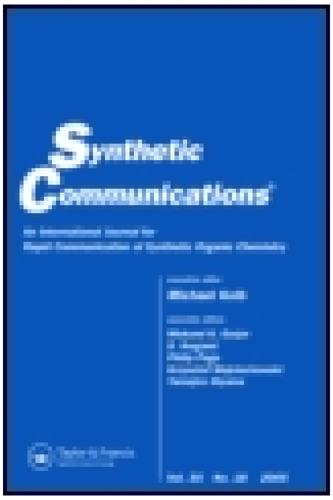

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OXIDATION OF TERTIARY NITROGEN COMPOUNDS TO N-OXIDES BY MOLECULAR OXYGEN-ALDEHYDE SYSTEM IN THE ABSENCE OF METAL CATALYST

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OXIDATION OF TERTIARY NITROGEN COMPOUNDS TO N-OXIDES BY MOLECULAR OXYGEN-ALDEHYDE SYSTEM IN THE ABSENCE OF METAL CATALYST

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ABSTRACT

A variety of tertiary nitrogen compounds have been oxidized to corresponding N-oxides in near quantitative yields by molecular oxygen/2-methylpropanal system in the absence of metal catalyst.

Oxidation of tertiary nitrogen compounds is an important synthetic transformation as the N-oxides find wider application as oxidants (1–7), offer functional group manipulation, structural modification possibilities (8–10), and can activate the nitrogen-containing ring towards both electrophilic and nucleophilic attack (11). A variety of oxidants—*m*-chloroperoxybenzoic acid (MCPBA) (12), acetic acid and hydrogen peroxide (12–15), magnesium monoperphthalate (MMPP) (16), dioxiranes (17,18), Caro's acid (H_2SO_5) (19), 2-sulfonyloxaziridines (20), ∝-azohydroperoxides (21), and peroxytrifluroacetic acid (22)—have been used for carrying out this transformation.

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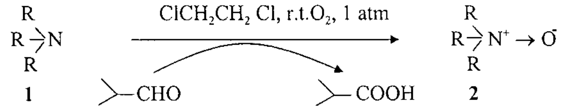


Scheme 1.

Recently the oxidation of tertiary nitrogen compounds with hydrogen peroxide using methyltrioxorhenium (MTO) (23), manganese porphyrin (24), and flavin (25) as catalysts has been reported in pursuit of the development of eco-friendly synthetic methodologies. Molecular oxygen is an attractive oxidant from both an environmental and an economic point of view, and there has been great interest in the development of oxidation methodologies using molecular oxygen-aldehyde system with or without transition metal complexes as catalysts (26). The molecular oxygen-aldehyde system without any catalyst has been reported to be a most effective oxidant for epoxidation of olefins (27), Baeyer-Villiger oxidation of ketones (28), oxidation of secondary alcohols (29), and sulphides (30).

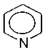
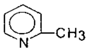
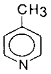
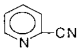
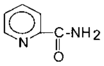
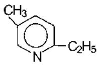
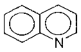
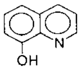
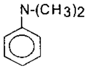
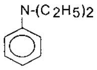
In continuation of our studies with molecular oxygen as a primary oxidant (30–33), herein we report for the first time, a simple and convenient method for the oxidation of tertiary-nitrogen compounds (**1**) to N-oxides (**2**) in near quantitative yields with molecular oxygen/2-methylpropanal system in the absence of metal catalyst (Scheme 1).

A wide variety of tertiary nitrogen compounds (pyridines and tertiary amines) was oxidized to N-oxides in near quantitative yields (Table 1).

The protocol developed consists of simply bubbling molecular oxygen in a solution of 2-methylporpanal in 1,2-dichloroethane for 1 h, followed by the addition of tertiary nitrogen compound, and further bubbling oxygen until completion of the reaction (via TLC). It was observed that 3.5 mmoles of 2-methylpropanal per mmole of tertiary nitrogen compound are required for the oxidation to N-oxide in a reasonable time of 10–24 h. Pyridines, in general, were found to be less reactive than tertiary amines.

In the oxidation with molecular oxygen-aldehyde system without any catalyst, while alphatic aldehydes like isobutyraldehyde, cyclohexanecarboxaldehyde showed high reactivities for epoxidation of olefins (27) and oxidation of sulphides (30), aromatic aldehydes like benzaldehyde proved to be more effective for the Baeyar-Villiger oxidation of ketones (28) and secondary alcohols oxidation (29). With a view to determine the relative efficiency of various aldehydes, we studied the oxidation of pyridine with a series of aldehydes (alphatic, aromatic, and heterocyclic). These results are presented in Table 2 and clearly show that the aliphatic aldehydes isobutyraldehyde and cyclohexanecarboxaldehyde are most effective among those studied for oxidation of pyridine to the pyridine N-oxides under these conditions.

Table 1. Oxidation of Tertiary Nitrogen Compounds to N-Oxides

Entry	Tertiary Nitrogen Compound	Reaction Time (h)	N-Oxide Yield[a] (%)
1		20	76
2		17	85
3		17	92
4		24	76
5		18	84
6		15	87
7		24	88
8		22	84
9		10	87
10		12	90

[a] Isolated yield.
[b] Aldehyde/tertiary nitrogen compound mole ratio = 3.5.

In conclusion, 2-methylpropanal-molecular oxygen provides a simple, efficient, convenient, and eco-friendly system for the oxidation of tertiary nitrogen compounds to N-oxides under mild conditions. This methodology avoids the direct use of hazardous peracids, which are difficult to handle and transport.

EXPERIMENTAL

A typical procedure for the oxidation of tertiary nitrogen compound to N-oxide is as follows: Molecular oxygen was bubbled into the solution of 2-methylpropanal (3.18 mL, 35 mmol) in 1,2-dichloroethane (30 mL) in a 50-mL, two-necked, round-bottom flask for 1 h at ambient temperature (30°C). The flask was fitted with well-cooled (10°C) condensor to minimize the aldehyde losses. Pyridine (0.81 mL, 10 mmol) was then added while oxygen was kept bubbling and the reaction mixture stirred with a magnetic stirrer. The reaction was monitored

Table 2. Efficiency of Different Aldehydes in the Oxidation of Pyridine by Molecular Oxygen Aldehyde System (Aldehyde/Pyridine Mole Ratio = 3.5)

Aldehyde	Reaction Time (h)	Conversion to Pyridine N-Oxide (%)[†]
Isobutyraldehyde	20	100
n-Butyraldehyde	22	100
n-Heptaldehyde	24	75
Cyclohexanecarboxaldehyde	21	100
Benzaldehyde	24	10
m-Anisaldehyde	24	4
p-Tolualdehyde	24	8
p-Nitrobenzaldehyde	24	—
2-Furaldehyde	24	5

[†] Conversion was determined by HPLC using C_{18} Bondapack reverse phase column (4.6 mm × 250 mm, 10μ), methanol as eluant (0.5 mL/min).

by TLC (SiO_2 gel). At the end of the reaction (20 h), the reaction mixture was washed successively with aqueous sodium metabisulphite, 5% aqueous sodium carbonate and brine, dried (Na_2SO_4), followed by removal of the solvent under reduced pressure. The residue thus obtained was purified by passing it through a basic alumina column using chloroform, methanol (3:1) as eluent and recrystallized from acetone, hexane (1:1) to obtain pyridine N-oxide as light yellow crystals (0.72 g, 76%). Similarly, other N-oxides were prepared, and their reaction time and yields obtained are shown in Table 2. The products were identified by comparing their physical and spectral data with those of authentic compounds reported in the literature.

For comparing the efficiency of various aldehydes, experiments were similarly conducted for a maximum of 24 h and the residue obtained after passing through the basic alumina column was analyzed by HPLC using C_{18} Bandapack reverse phase column (4.6 mm × 250 mm, 10μ) methanol (0.5 mL/min) as eluent.

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REFERENCES

1. Van Rheenen, V.; Cha, D.Y.; Hartley, W.M. Org. Synth. Coll. Vol. **1988**, *6*, 342.
2. Schroder, M. Chem. Rev. **1980**, *80*, 87.
3. Ahrgren, L.; Sutin, L. Org. Proc. Res. Dev. **1997**, *1*, 425.
4. Ley, S.V.; Norman, J.; Griffith, W.P., Marsden, S.P. Synthesis **1994**, 639.
5. Franzen, V.; Otto, S. Chem. Ber. **1961**, *94*, 1360.
6. Suzuki, S.; Onishi, T.; Fujita, Y.; Misawa, H.; Otera, J. Bull. Chem. Soc. Jpn. **1986**, *59*, 3287.
7. Godfrey, A.G.; Ganem, B. Tetrahedr. Lett. **1990**, *31*, 4825.
8. Cope, A.C.; Ciganek, E. Org. Synth. Coll. Vol. **1963**, *4*, 612.
9. Cope, A.C.; Trumbull, E.R. Org. React **1960**, *11*, 317.
10. *Ullmann's Encyclopedia of Industrial Chemistry*, 5th Ed; VCH: Germany; **1993**, *A22*, 399.
11. Katritzky A.R.; Lagowski, X. *Chemistry of the Heterocyclic N-oxides*; Academic Press: New York, **1971**.
12. Albini, P. *Heterocyclic N-Oxides*; CRC Press: Boca Raton, FL, **1991**, 31–41.
13. Boekelheide, V.; Linn, W.J. J. Am. Chem. Soc. **1954**, *76*, 1286.
14. Taylor, E.C., Jr.; Crovetti, A.J. Org. Synth. Coll. Vol. **1963**, *4*, 704.
15. Mosher, H.S.; Turner, L.; Carlsmith, A. Org. Synth. Coll. Vol. **1963**, *4*, 828.
16. Brougham, P.; Cooper, M.S.; Cummerson, D.A.; Heaney, H.; Thompson, N. Synthesis **1987**, 1015.
17. Murray, R.W.; Jeyaraman, R. J. Org. Chem. **1985**, *50*, 2847.
18. Ferrer, M.; Sanchez-Baeza, F.; Messeguer, A. Tetrahedron **1997**, *53*, 15877.
19. Robke, J.G.; Behrman, E.J. J. Chem. Res (s) **1993**, 412.
20. Zajac, W.W., Jr.; Walters, T.R., Darcy, M.G. J. Org. Chem. **1988**, *53*, 5856.
21. Baumstark, A.L.; Dotrong, M.; Vasquez, P.C. Tetrahedr. Lett. **1987**, *29*, 1963.
22. Chivers, G.E.; Suschitzky, H. J. Chem. Soc., Chem. Commun. **1971**, 28.
23. Coperet, C.; Adolfsson, H.; Khuong, Tinh-Alfredo, V.; Yudin, A.K.; Sharpless, K.B. J. Org. Chem. **1998**, *63*, 1740.
24. Thellend, A.; Battioni, P.; Sanderson, W.; Mansuy, D. Synthesis **1997**, 1387.
25. Bergstad, K.; Backvall, Jan-E. J. Org. Chem. **1998**, *63*, 6650.
26. For a review on oxidations using molecular oxygen-aldehyde system, see Mukaiyama, T.; Yamada, T. Bull. Chem. Soc. Jpn. **1995**, *68*, 17.
27. Kaneda, K.; Haruna, S.; Imanaka, T.; Hamamoto, M.; Nishiyama, Y.; Ishii, Y. Tetrahedr. Lett. **1992**, *33*, 6827.
28. Kaneda, K.; Ueno, S.; Imanaka, T.; Shimotsuma, E.; Nishiyama, Y.; Ishii, Y. J. Org. Chem. **1994**, *59*, 2915.
29. Choudary, B.M.; Sudha, Y. Synth. Commun. **1996**, *26*, 1651.
30. Venkateshwar Rao, T.; Sain, B.; Kumar, K.; Murthy, P.S.; Prasada Rao, T.S.R.; Joshi, G.C. Synth. Commun. **1998**, *28*, 319.

31. Sain, B.; Murthy, P.S.; Venkateshwar Rao, T.; Prasada Rao, T.S.R.; Joshi, G.C. Tetrahedr. Lett. **1994**, *35*, 5083.
32. Venkateshwar Rao, T.; Sain, B.; Murthy, P.S.; Prasada Rao, T.S.R.; Jain, A.K.; Joshi, G.C. J. Chem. Res (s) **1997**, 300.
33. Venkateshwar Rao, T.; Sain, B.; Murthy, P.S.N.; Joshi, G.C.; Prasada Rao, T.S.R. Stud. Surf. Sci. Catal. **1998**, *113*, 921.

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