Selective Oxidation of *N*-Alkyl Imines to Oxaziridines using UHP/Maleic Anhydride system

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Abstract: Several structurally differentiated N-alkyl imines were oxidized to their corresponding oxaziridines using UHP/maleic anhydride system. Oxidation reaction was performed under mild conditions and oxaziridines were obtained in good to excellent yields.

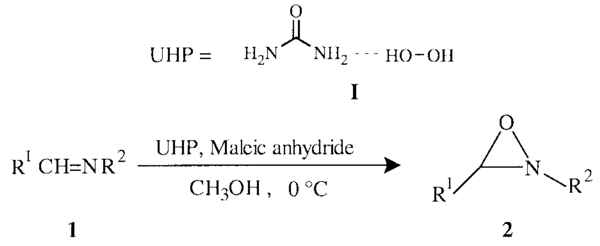
Key words: UHP, *N*-alkyl imines, oxaziridines

Oxaziridines are useful aprotic oxidizing reagents for a large variety of substrates. The aprotic nature of these reagents has made possible the facile synthesis of extremely acid-sensitive species such as α-siloxy epoxides[1] and sulfenic acids.[2] In recent years, the asymmetric oxidation of prochiral centers to the desired optically active products by using chiral oxaziridines have received considerable attention.[3]

Several methods have been employed for the oxidation of imines into the corresponding oxaziridines. The most general reagent is *m*-chloroperbenzoic acid.[4,5] Other oxidizing agents such as buffered oxone® ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$)[6], in situ generation of sulfonic or carboxylic peracids,[7] and molecular oxygen in the presence of transition-metal complexes[8] have been also used.

Although a variety of reagents are capable of affecting these oxidations,[1–8] as far as we know this transformation is not so easy and is a tricky step because these compounds are very sensitive to the oxidizing agents and reaction conditions. However, most of the reported reagents produce by-products, which either destroy, or are difficult to remove from the sensitive oxaziridines. For example, *m*-chloroperbenzoic acid is expensive and large-scale oxidations are sometimes contaminated with bis-(*m*-chloroperbenzoyl) peroxide, which complicates product purification. Meanwhile, we also know that imines are susceptible to hydrolysis in aqueous media.[1–8] For these reasons an oxidizing reagent that would avoid these difficulties was sought. Therefore, we were interested in finding a new reagent or reagent system to overcome the above limitations and we have investigated a number of different reaction conditions based upon the in situ generation of H_2O_2. In continuing our studies on the application of oxone® ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$)[9–11] and H_2O_2 we found that UHP[12] [**I** an addition compound of hydrogen peroxide and urea] is the best candidate for this purpose. A survey of the literature revealed that UHP **I** is an inexpensive, stable, and easy to handle source of pure H_2O_2.[13] In the last few years, several reports appeared on the use of UHP in the oxidations, namely for the conversion of amines to nitroalkane,[14] Baeyer–Villiger oxidations of ketones to lactones,[15] oxidations of sulfides to sulfones,[16] oxidation of aromatic aldehydes,[17] aromatization of 1,4-dihydropyridines,[18] selective oxidation of uracil and adenine derivatives,[19] epoxidation of alkenes,[20] and conversion of pyridines to pyridine *N*-oxides under different conditions.[21,22] Thus, in this article we wish to report a simple, cheap and convenient method for the effective conversion of *N*-alkyl imines **1** to their corresponding oxaziridines **2** under mild conditions (Scheme).

A good range of N-alkyl imines **1** were subjected to the oxidation reaction in the presence of UHP **I**, and maleic anhydride in methanol. The oxidation reactions were performed under mild conditions at 0 °C with good to excellent yields (Scheme). The reactions were completed after 40–50 min. Highly pure oxaziridines **2** were finally obtained after removing of solvent.[23,24]



1, 2	R^1	R^2	1, 2	R^1	R^2
a	Ph	CH_2Ph	**d**	2-Furyl	*n*-Bu
b	4-$CH_3C_6H_4$	CH_2Ph	**e**	*n*-Pr	*n*-Bu
c	4-$CH_3C_6H_4$	*n*-Bu	**f**	*n*-Bu	*iso*-Pr

Scheme

Unlike *N*-alkyl imines **1a**–**f**. (Table, entries 1–6) *N*-aryl imines (Table, entries 7 and 8) were converted to the corresponding nitrones. The remaining of conjugation in N-aryl imines may be the main reason why nitrones are formed instead of oxaziridines. We hope that the described method due to the its non-toxicity makes the UHP/

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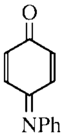
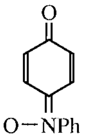
Table Oxidation of N-Alkyl Imines **1** to the Corresponding Oxaziridines **2** and of N-Aryl Imines to the Corresponding Nitrones with a Combination of UHP I and Maleic Anhydride in Methanol at 0 °C

Entry	Substrate	Product	Time (min)	Yield[a] (%)
1	**1a**	**2a**	40	95
2	**1b**	**2b**	40	95
3	**1c**	**2c**	45	93
4	**1d**	**2d**	50	90
5	**1e**	**2e**	50	80
6	**1f**	**2f**	50	80
7	PhCH=NPh	 $\mathrm{PhCH{=}\overset{O}{\overset{\vert}{N}}Ph}$	40	85
8			40	95

[a] Isolated yields.

maleic anhydride system a reagent of choice for replacing transition metals-based oxidants.[25–27]

In conclusion, practical and efficient oxidation of *N*-alkyl imines was achieved using the present methodology. The UHP, with easy preparation and handling can act as a safe, stable and efficient reagent for this transformation under mild conditions. We believe that the present methodology is an important addition to existing methodologies.

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References

(1) Davis, F. A.; Sheppard, A. C. *J. Org. Chem.* **1987**, *52*, 954.
(2) Davis, F. A.; Billmers, R. H. *J. Am. Chem. Soc.* **1981**, *103*, 7016.
(3) (a) Davis, F. A.; Jenkines, R. H. Jr. *Asymmetric Synthesis: Synthesis and Utilization of Compounds with Chiral Nitrogen Centers*; Academic Press, INC.: New York, **1985**, Chap. 4, 313–345. (b) Davis, F. A.; Sheppard, A. C. *Tetrahedron* **1989**, *45*, 5703.
(4) Kidwai, M.; Dave, B.; Kohli, S. *Indian J. Chem.* **1999**, *38B*, 728.
(5) Davis, F. A.; Stringer, O. D. *J. Org. Chem.* **1982**, *47*, 1774.
(6) Davis, F. A.; Chattopadhyay, S.; Towson, J. C.; Lal, S.; Reddy, T. R. *J. Org. Chem.* **1988**, *53*, 2087.
(7) (a) Kluge, R.; Schulz, M.; Liebsch, S. *Tetrahedron* **1996**, *52*, 5773. (b) Schirmann, J. P.; Weiss, E. F. *Tetrahedron Lett.* **1972**, 633.
(8) (a) Martiny, L.; Jorgensen, K. A. *J. Chem. Soc. Perkin Trans. 1* **1995**, 699. (b) Auret, B. J.; Boyd, D. R.; Coulter, P. B. *J. Chem. Soc., Chem. Commun.* **1984**, 463.
(9) Zolfigol, M. A.; Bagherzadeh, M.; Madrakian, E.; Ghaemi, E.; Taqian-nasab, A. *J. Chem. Res. (S)* **2001**, 140.
(10) Zolfigol, M. A.; Bagherzadeh, M.; Chehardoli, G.; Mallakpour, S. E. *Synth. Commun.* **2001**, *31*, 1149.
(11) Zolfigol, M. A.; Bagherzadeh, M.; Ghorbani Choghamarani, A.; Keypour, H.; Salehzadeh, S. *Synth. Commun.* **2001**, *31*, 1661.
(12) Zolfigol, M. A.; Bagherzadeh, M.; Chehardoli, G.; Mallakpour, S. E.; Mamaghani, M. *J. Chem. Res. (S)* **2001**, 390.
(13) Cooper, M. S.; Heaney, H.; Newbold, A. J.; Sanderson, W. R. *Synlett* **1990**, 533.
(14) Ballini, R.; Marcantoni, E.; Petrini, M. *Tetrahedron Lett.* **1992**, *33*, 4835.
(15) (a) Astodillo, L.; Galindo, A.; Gonzalez, A. G.; Mansilla, H. *Heterocycles* **1993**, *36*, 1075. (b) Uchida, T.; Katsuki, T. *Tetrahedron Lett.* **2001**, *42*, 6911.
(16) Balicki, R. *Synth. Commun.* **1999**, *29*, 2235.
(17) Heaney, H.; Newbold, A. J. *Tetrahedron Lett.* **2001**, *42*, 6607.
(18) Perez, J. M.; Lopez-Alvardo, P.; Pascual-Alfonso, E.; Avendano, C.; Menendez, J. C. *Tetrahedron* **2000**, *56*, 4575.
(19) Salandino, R.; Carlucci, P.; Danti, M. C.; Crestini, C.; Mincione, E. *Tetrahedron* **2000**, *56*, 10031.
(20) (a) Pietikainen, P. *J. Mol. Cat. A: Chem.* **2001**, *165*, 73. (b) Kureshy, R. I.; Khan, N. H.; Abdi, S. H. R.; Patel, S. T.; Jasra, R. V. *Tetrahedron: Asymmetry* **2001**, *12*, 433.
(21) Varma, R. S.; Naicker, K. P. *Org. Lett.* **1999**, *1*, 189.
(22) Caron, S.; Do, N. M.; Sieser, J. E. *Tetrahedron Lett.* **2000**, *41*, 2299.
(23) Yields refer to isolated pure products. The oxidation products were characterized by comparison of their spectral (IR, ^{1}H NMR, and ^{13}C NMR) and physical data with the authentic samples.
(24) Oxidation of *N*-benzylphenyl imine(**1a**) to 2-benzyl-3-phenyl oxaziridine(**2a**) with UHP/maleic anhydride system. A typical procedure: A suspension of compound **1a** (0.390 g, 2 mmol), **I** (0.188 g, 2 mmol), maleic anhydride (0.176 g, 2 mmol) in methanol (8 mL) was stirred at 0 °C. The progress of the reaction was monitored by TLC (eluent, EtOAc–*n*-hexane, 1:5). The reaction was completed after 40 min. The reaction mixture was filtered and the filtrate was passed through a short pad of silica gel. Methanol was removed under reduced pressure. Highly pure oxaziridine(**2a**) was obtained in 95% yield (0.354 g). (FT-NMR 500 MHz) $CDCl_3$: δ_{ppm} 4.03–4.22 (dd, 2 H), 4.8 (s, 1 H), 7.45–7.6 (m, 10 H).[7a]
(25) Cicchi, S.; Marradi, M.; Goti, A.; Brandi, A. *Tetrahedron Lett.* **2001**, *42*, 6503.
(26) Nakama, K.; Seki, S.; Kanemasa, S. *Tetrahedron Lett.* **2001**, *42*, 6719.
(27) Long, A.; Baldwin, S. W. *Tetrahedron Lett.* **2001**, *42*, 5343.