Oxidation of sulfides to sulfoxides with 3-aryl-2-*tert*-butyloxaziridines under high pressure

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3-Phenyl-2-*tert*-butyloxaziridine has been shown to behave as an oxidant under 800 MPa at 100 °C to oxidize sulfides to sulfoxides, in spite of having been reported to be inactive as an oxidant and to undergo thermal rearrangement to *N-tert*-butyl-α-phenylnitrone at atmospheric pressure. It has been shown that under thermal and high-pressure conditions the ability of the oxaziridine to react changes dramatically. The mechanism for the high-pressure reaction is also discussed.

High pressure sometimes accelerates organic reactions which are difficult or slow at atmospheric pressure to give high yields of the desired products; this phenomenon arises from the close packing of the molecules under such conditions. High-pressure effects were particularly noticeable in the reactions of sterically crowded molecules such as 2,6-disubstituted pyridines where *N*-alkylation was accelerated under such conditions.[1]

Although some oxaziridines, which are unique three-membered heterocycles having a carbon-, nitrogen- and oxygen-containing ring,[2] are oxidants,[3] 2-*tert*-butyl-3-phenyloxaziridine **1a** has little such ability[4] and acts in this capacity only with trisubstituted phosphines[5] and halides[6] to give phosphine oxides and halogens, respectively. The lower reactivity of **1a** is the result of steric hindrance around active sites which obstructs attack by substrates. Since we expected that high pressure would effectively counter such steric hindrance, we attempted to oxidize sulfides to sulfoxides with 3-aryl substituted 2-*tert*-butyloxaziridines. The oxaziridine **1a** was packed and sealed in a Teflon tube with an excess of methyl phenyl sulfide **2a**, and then subjected to 800 MPa at 100 °C. After 20 h, the reaction products were analyzed by GLC and the yields calculated on the basis of the amount of starting oxaziridine consumed. The sulfide **2a** was successfully oxidized to methyl phenyl sulfoxide **3a** (64%) and *N-tert*-butylbenzaldimine **4a**, *N-tert*-butyl-α-phenylnitrone **5a** and benzaldehyde **6a** were also identified in the reaction mixture. The imine **4a** was produced as the result of oxygen transfer from the oxaziridine ring to the sulfide while the nitrone **5a** was formed by thermal rearrangement of the oxaziridine ring. This oxidation was repeated under a variety of conditions, and the results are summarized in Table 1. The product distribution was dramatically changed between 400 (entry 2) and 800 MPa (entry 4), the highest yield of **2a** being obtained for a reaction at 800 MPa and 100 °C.
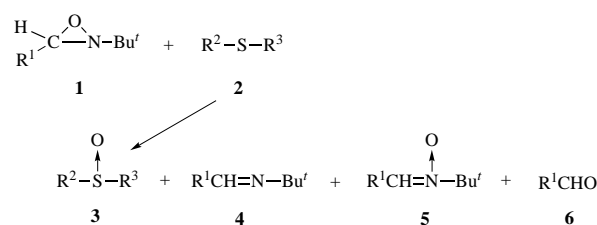
The sulfide **2a** was oxidized under high pressure with other oxaziridines, higher product yields being obtained for compounds having electron-withdrawing substituents (Entries 7, 10 and 12) compared with those having electron-donating substituents (Entries 8, 9 and 11). This result agrees with those reported by Tamagaki *et al.* for the oxidation of triphosphine with oxaziridines.[5]

The effect of the high pressure in this oxidation is explained as follows. Because their ring size is small, oxaziridines are always subject to structural strain. When a mixture of **1a** and **2a** was heated under atmospheric pressure, the bulky substituent on the nitrogen atom of **1a** prevented approach of **2a** to the adjacent oxygen atom of the oxaziridine ring; in other words, the oxidation centre and substrate were insufficiently close to

Table 1 Oxidation of the sulfides **2** with oxaziridines **1** under high pressure[a]

Entry	Oxaziridine 1	Sulfide 2	Yield[b] (%)			
			3	4	5	6
1[c]	1a	2a	2	8	54	18
2[d]	1a	2a	3	6	81	12
3[e]	1a	2a	7	22	6	22
4	1a	2a	64	62	18	6
5	1a	2b	25	53	36	8
6	1a	2c	3	5	38	20
7	1b	2a	42	62	18	—
8	1c	2a	6	6	58	—
9	1d	2a	8	7	63	15
10	1e	2a	37	66	8	—
11	1f	2a	18	36	23	8
12	1g	2a	39	51	13	—

[a] Reaction conditions, **1** (1 mmol) and **2** (5 mmol), 800 MPa, 100 °C, 20 h. [b] Calculated based on **1**. [c] Under atmospheric pressure. [d] 400 MPa. [e] 40 °C.

1, 4, 5, 6	R¹
a	Ph
b	$p\text{-}O_2NC_6H_4$
c	$p\text{-}MeC_6H_4$
d	$p\text{-}MeOC_6H_4$
e	2-Pyridyl
f	3-Pyridyl
g	4-Pyridyl

2, 3	R²	R³
a	Ph	Me
b	Me	Me
c	Ph	Ph

Scheme 1 *Reaction conditions*: 800 MPa, 100 °C, 20 h

react. Addition of thermal energy to the oxaziridine, however, reduced the ring strain, the result being rearrangement of the oxaziridine ring to the thermally stable nitrone compound then becoming the main reaction (Entry 1). Having lost its oxidation activity,[6] the rearrangement nitrone **5a** was unable to oxidize the sulfide **2a** even at 800 MPa and 100 °C, and was recovered unchanged after 20 h. In contrast, under high pressure condi-

tions, the reaction system brought **1a** and **2a** into close contact with the result that the oxaziridine-ring strain was reduced by oxygen atom transfer to the substrate, and the imine compound **4a** and the sulfoxide **3a** were formed. The reaction was, in effect, a competitive one between oxaziridine-ring rearrangement and sulfide oxidation. Therefore, in the oxidation of diphenyl sulfide **2b**, which has bulkier substituents than methyl phenyl sulfide, the yield of diphenyl sulfoxide **3c** was very low and the ring rearrangement became the main reaction (Entry 6).

In conclusion, 3-aryl-2-*tert*-butyloxaziridines have been shown to behave as oxidants under high pressure, even with a compound such as thioanisole which has been reported to be resistant to oxidation. These results can be explained in steric terms as high pressure overcomes the hindrance engendered by the bulkiness of the oxaziridine substituents and brings the oxaziridine and sulfides sufficiently close to reaction.

Experimental

Mps determined on a Yanagimoto micro-melting point apparatus are uncorrected. ^{1}H NMR spectra were obtained with a Hitachi R-40 High-Resolution Spectrometer (90 MHz) and Varian Gemini 300 BB (300 MHz) with tetramethylsilane as an internal standard; J values given in Hz. IR spectra were recorded on a JASCO FTIR-7000 Fourier transfer infrared spectrophotometer. Gas chromatographic analyses were performed on a Shimadzu GC-14A chromatograph fitted with a Neutrabond-1 column (OV-1 equivalent).

Oxaziridines were prepared by reported methods.[7,8] Compounds **1a**,[7] **1b**[6] and **1c**–**e**,**g**[9] were found to have spectral characteristics and physical properties identical with those reported. 2-*tert*-Butyl-3-(3-pyridyl)oxaziridine **1f**, mp 32–33 °C (pentane) (Found: C, 67.7; H, 7.8; N, 15.5. $C_{10}H_{14}N_2O$ requires C, 67.4; H, 7.9; N, 15.7%); ν_{max}(neat)/cm^{-1} 2976, 1599, 1580, 1479, 1435, 1390, 1365, 1328, 1267, 1205, 1027, 863, 806 and 710; δ_H(300 MHz; CDCl$_3$) 1.19 (9H, s, Bu^t), 4.73 (1H, s, C-3), 7.32 (1H, dd, J 5, 8). 7.73 (1H, dt, J 8, 2), 8.64 (1H, br, d, J 4) and 8.71 (1H, br, s).

Sulfoxides were identified by comparison with commercially available authentic samples (concordant retention times on GLC).

Nitrones obtained by high pressure oxidation were isolated from the reaction mixtures with column chromatography on silica gel with dichloromethane–acetone–methanol (100:10:2 or 100:40:8) as eluent. *N-tert*-Butyl-α-phenylnitrone **5a**, mp 71–72 °C (hexane) (lit.,[6] 75–76 °C). *N-tert*-Butyl-α-(*p*-nitrophenyl)-nitrone **5b**, mp 130–131 °C (lit.,[6] 134–135 °C). *N-tert*-Butyl-α-(*p*-methylphenyl)nitrone **5c**, mp 69–70 °C (hexane) (lit.,[10] 72–74 °C). *N-tert*-Butyl-α-(*p*-methoxyphenyl)nitrone **5d**, bp 202 °C/270 Pa. (Found: C, 68.7; H, 8.2; N, 6.65. $C_{12}H_{17}$-NO$_2$·0.1H$_2$O requires C, 68.9; H, 8.2; N, 6.7%); ν_{max}(neat)/cm^{-1} 2978, 1605, 1363, 1261, 1172, 1125, 1033 and 843; δ_H(90 MHz; CDCl$_3$) 1.57 (9H, s, Bu^t), 3.81 (3H, s, CH$_3$O), 6.92 (2H, d, J 10), 7.47 (1H, s, CH=) and 8.29 (2H, d, J 10). *N-tert*-Butyl-α-(2-

pyridyl)nitrone **5e**, mp 62–63 °C (Found: C, 67.6; H, 7.9; N, 15.7. $C_{10}H_{14}N_2O$ requires C, 67.4; H, 7.9; N, 15.7%); ν_{max}(neat)/cm^{-1} 2980, 1560, 1437, 1400, 1197, 1123, 911, 816 and 733; δ_H(300 MHz; CDCl$_3$) 1.64 (9H, s, Bu^t), 7.26–7.30 (1H, m), 7.79 (1H, td, J 8, 2), 7.90 (1H, s, CH=), 8.64 (1H, dd, J 2, 5) and 9.22 (1H, d, J 8). *N-tert*-Butyl-α-(3-pyridyl)nitrone **5f**, mp 81–82 °C (hexane) (Found: C, 67.6; H, 8.0; N, 15.6. $C_{10}H_{14}N_2O$ requires C, 67.4; H, 7.9; N, 15.7%); ν_{max}(neat)/cm^{-1} 2990, 1560, 1417, 1361, 1199, 1131, 909, 832 and 710; δ_H(300 MHz; CDCl$_3$) 1.64 (9H, s, Bu^t), 7.36 (1H, dd, J 5, 8), 7.61 (1H, s, CH=), 8.59 (1H, br, d, J 4), 8.98 (1H, br, s) and 9.11 (1H, dt, J 2, 8). *N-tert*-Butyl-α-(4-pyridyl)nitrone **5g**, mp 84–86 °C (hexane) (lit.,[11] 99–101 °C) (Found: C, 67.3; H, 8.05; N, 15.7. $C_{10}H_{14}N_2O$ requires C, 67.4; H, 7.9; N, 15.7%); ν_{max}(neat)/cm^{-1} 2980, 1644, 1568, 1417, 1365, 1137, 990, 843, 669 and 530; δ_H(300 MHz; CDCl$_3$) 1.63 (9H, s, Bu^t), 7.58 (1H, s, CH=), 8.07 (2H, d, J 6) and 8.69 (2H, br, s).

General oxidation procedure

A homogeneous mixture of the oxaziridine (100 mg) and the sulfide (300 mg) in a sealed Teflon tube was compressed to 800 MPa and heated at 100 °C for 20 h in high-pressure equipment.[12] After the reaction, the reaction mixture was cooled to room temperature and the products were analyzed with GLC with naphthalene as a standard.

References

1 W. J. le Noble and Y. Ogo, *Tetrahedron*, 1970, **26**, 4119.
2 Reviews: E. Schmitz, *Adv. Heterocycl. Chem.*, 1963, **2**, 83; 1979, **24**, 63; J. P. Freeman, in *The Chemistry of Heterocyclic Compounds*, eds., A. Weissberger and E. C. Taylor, Part 3, Wiley, New York, 1985, p. 283; F. A. Davis and A. C. Sheppard, *Tetrahedron*, 1989, **45**, 5703.
3 Y. Hata and M. Watanabe, *J. Org. Chem.*, 1981, **46**, 610; L. C. Vishwakarma, O. D. Stringer and F. A. Davis, *Org. Synth.*, 1987, **66**, 203; V. A. Petrov and G. Resnati, *Chem. Rev.*, 1996, **96**, 1809.
4 F. A. Davis, R. Jenkins Jr. and S. G. Yocklovich, *Tetrahedron Lett.*, 1978, 517.
5 S. Tamagaki, K. Sakaki and S. Oae, *Bull. Chem. Soc. Jpn.*, 1972, **45**, 3179.
6 W. D. Emmons, *J. Am. Chem. Soc.*, 1957, **79**, 5739.
7 W. D. Emmons and A. S. Pagano, *Org. Synth.*, *Coll.* vol. 5, p. 191.
8 F. A. Davis, S. Chattopadhyay, J. C. Towson, S. Lal and T. Reddy, *J. Org. Chem.*, 1988, **53**, 2087.
9 K. Kloc, E. Kubicz, J. Młochowski and L. Syper, *Synthesis*, 1987, 1084.
10 D. R. Boyd, P. B. Coulter, M. R. McGuckin, N. D. Sherma, W. B. Jennings and V. E. Wilson, *J. Chem. Soc.*, *Perkin Trans. 1*, 1990, 301.
11 E. G. Janzen, R. L. Dudley and R. V. Shetty, *J. Am. Chem. Soc.*, 1979, **101**, 243.
12 M. Kurabayashi, K. Yanagiya and M. Yasumoto, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 3414.