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Facile Conversion of Sulfilimines into Sulfoximines Using Dioxiranes†

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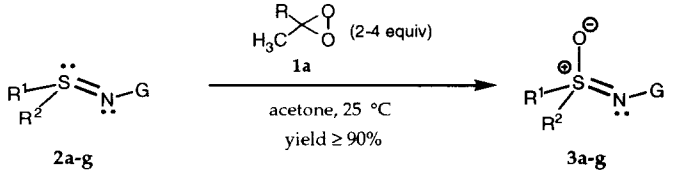
Abstract: Employing dimethyldioxirane, the direct conversion of several *N*-(*p*-tolylsulfonyl)sulfilimines and of one *N*-(acetyl)sulfilimine into the corresponding sulfoximines was achieved in high yield under mild conditions. Optically active *S*-(*p*-tolyl)-*S*-methyl-*N*-(*p*-tolylsulfonyl)sulfilimine could be transformed into its sulfoximine in high enantiomeric excess with retention of configuration. The effect of substituents indicates that the oxidation involves electrophilic *O*-transfer from the dioxirane to the sulfilimine sulfur.

Keywords: *Dioxiranes; sulfilimines; oxidation; sulfoximines*

Sulfoximines,[1] and especially the *N*-(arylsulfonyl)sulfoximines and their anions,[1a] are valuable in organic synthesis; for instance, as alkylidene transfer reagents they provide easy access to oxiranes starting with aldehydes or ketones.[1] A straightforward route to these synthons involves the oxidation of the parent sulfilimines, since the latter represent readily available starting materials.[2] However, it appears that just a few reagents are satisfactory in achieving this transformation; among these is the use of the sodium *m*-chloroperoxybenzoate[3] or of alkaline hydrogen peroxide.[4] It appears that the success of these *nucleophilic* oxidants is due to the markedly electrophilic character of the sulfilimine sulfur.

Dioxiranes nowadays represent a popular class of powerful oxidants.[5] Employing dimethyldioxirane (**1a**: R = CH_3)[6] or methyl(trifluoromethyl)dioxirane (**1b**: R = CF_3),[7] a variety of synthetic transformations has been achieved involving selective *electrophilic O*-transfer to a number of substrates.[5-7]

We report herein our finding that representative sulfilimines **2a-g** are readily oxidized in high yield to sulfoximines using dimethyldioxirane (eq 1). The results are summarized in Table 1.



(1)

The sulfilimine starting materials were synthesized upon reaction of the parent sulfides with chloramine-T by following literature procedures.[2] To these, dioxirane **1a** was applied in the isolated form as acetone solutions;[5] the latter were obtained according to described protocols.[6,7]

† Dedicated to Prof. Waldemar Adam (University of Würzburg, Germany) on the occasion of his 60th birthday.

Table 1. Oxidation of Sulfilimines to Sulfoximines with Excess Dimethyldioxirane (4 equiv) in Acetone at 25 °C.

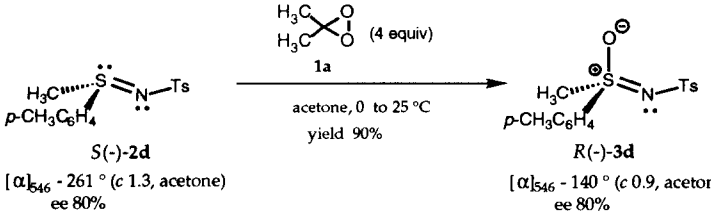
Entry	R^1	R^2	G	Substrate	Reaction time (h)	Conv. (%)[a]	Sulfoximine	Yield (%)[b]	Lit.
1	Ph	Ph	Ts	**2a**	6	70	$Ph_2S(:O)$=NTs (**3a**)	92	1c,1d
2	p-ClC_6H_4	Me	Ts	**2b**	6	54	p-ClC_6H_4(Me)S(:O)=NTs (**3b**)[c]	90	1c
3	Ph	Me	Ts	**2c**	6	80	Ph(Me)S(:O)=NTs (**3c**)[d]	90	1c
4	p-MeC_6H_4	Me	Ts	**2d**	6	85	p-MeC_6H_4(Me)S(:O)=NTs (**3d**)	90	1c,1d
5	p-$MeOC_6H_4$	Me	Ts	**2e**	6	90	p-$MeOC_6H_4$(Me)S(:O)=NTs (**3e**)[e]	95	1c
6	Et	Me	Ts	**2f**	4	95	Et(Me)S(:O)=NTs (**3f**)[f]	91	1e
7	Et	Me	Ac	**2g**[g]	2	95	Et(Me)S(:O)=NAc (**3g**)[h]	90	-

[a] As determined by HPLC monitoring (Perkin-Elmer mod. LC250, UV detector LC290; Licrospher 100-RP18, 12.5 cm × 0.4 cm ID.; 30% MeCN/70% water, 1 mL/min) of the reaction mixture. [b] Isolated yield. [c] ^1H NMR (300 MHz, $CDCl_3$): δ 2.4 (s, 3 H), 3.3 (s, 3 H), 7.05-8.0 (m, 8 H). [d] ^1H NMR (300 MHz, $CDCl_3$): δ 2.4 (s, 3 H), 3.3 (s,3 H), 7.0-8.0 (m, 9 H). [e] ^1H NMR (300 MHz, $CDCl_3$): δ 2.4 (s, 3 H), 3.4 (s, 3 H), 3.8 (s, 3 H) ,6.95-8.0 (m, 8 H). [f] ^1H NMR (300 MHz, $CDCl_3$): δ 1.4 (t, J = 7.0 Hz, 3 H), 2.4 (s, 3 H), 3.3 (s, 3 H), 3.5 (q, J = 7.0 Hz, 2 H), 7.2-7.8 (m, 4 H). [g] A dioxirane excess of 2 equiv was employed. [h] Ref. 8.

The simple general procedure merely entails the addition of a cold (ca. 0 °C) 0.08 M dimethyldioxirane solution in acetone (8 mL, 0.64 mmol), in two equal aliquots during 10-15 min, to 0.15 mmol of the sulfilimine in acetone (5 mL). The reaction mixture is left to stand at 25 °C, and monitored periodically by TLC and/or HPLC. Solvent removal under reduced pressure and column chromatography (silicagel, Et_2O/MeOH 95:5) affords the sulfoximine.

Examples in Table 1 suggest that dimethyldioxirane (**1a**) should be the oxidant of choice to carry out the transformation of sulfilimines into sulfoximines in consistently high (>90%) yield. It has been reported previously that the oxidation of *S,S*-dimethyl-*N*-4-(4-chlorophenyl)furazan sulfilimine with excess **1a** yields the corresponding sulfoximine in 63% yield, accompanied by 3-(4-chlorophenyl)-4-nitrofurazan (yield 37%) derived from the *oxidative cleavage* of the substrate.[9]

The method appears suitable for the synthesis of chiral sulfoximines in high enantiomeric excess. For instance, we were able to achieve the oxidation of optically active *S*-(*p*-tolyl)-*S*-methyl-*N*-(*p*-tolylsulfonyl)sulfilimine[10] to the corresponding sulfoximine[11] with no loss of enantiomeric excess and with retention of configuration under the conditions given in eq 2.



(2)

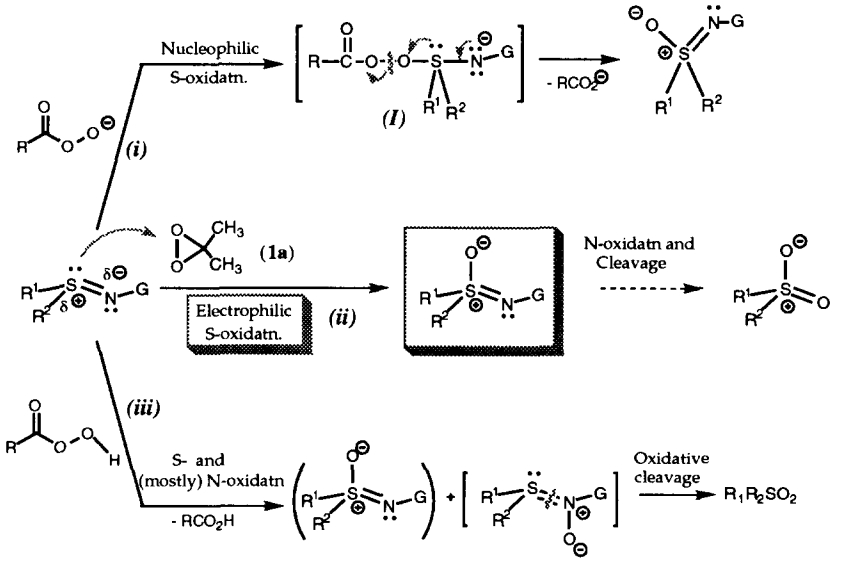
Inspection of data in Table 1 leaves no doubt that the oxidation involves *electrophilic O*-transfer from the dioxirane to the lone electron-pair at the substrate sulfonium sulfur. For instance, for a series of substituted

sulfilimines **2b-e** under identical conditions, electron-donating substituents enhance the oxidation rate, while an electron-withdrawing *p*-Cl substituent has the opposite effect (Table 1, entry 2 to 5).

Also, the oxidation of *S,S*-dialkyl sulfilimines **2f** and **2g** (entry 6 and 7) occurs distinctly faster than that of either the *S*-phenyl-*S*-methyl sulfilimines **2b-e** or *S,S*-diphenyl sulfilimine **2a**; this suggests that the oxidation is facilitated as the sulfonium reaction center becomes more *nucleophilic*.

On the basis of existing literature[3,4,9,10b,12] and of the findings herein, it is useful to compare the pathways available for sulfilimine oxidation with peracids and with dimethyldioxirane; these are sketched in Scheme 1.

Scheme 1



It would appear that the limited success normally encountered with electrophilic peracid oxidation (path *iii)* is due to competing *S*- and *N*-oxidation; typically, mixtures of sulfilimine, sulfone (major) and sulfoxide (minor) are formed.[9,12] Ensuing oxidative scission of the sulfilimine, the rôle of the nitrogen-containing moiety seems to be that of forming initially nitroso compounds, which then suffer further rapid oxidation. The greater success met using alkaline peracid RCO_3^- (path *i*),[3,10b] as well as other oxoanions such as HOO^- and ClO^-,[1c,4,13] should be ascribed to the ease of attack by these α-nucleophiles[14a] at the sulfonium sulfur, i.e. the electrophilic site of the sulfilimine S=N dipole. Then, the sulfoximine would be formed via the adduct ***I*** by the addition-elimination mechanism shown in Scheme 1, akin to the mechanism of alkaline oxidation of sulfoxides to sulfones by peracids; the latter was first established by us some time ago.[14b,c]

In view of the facts above, the finding that the *electrophilic S*-oxidation becomes feasible for sulfilimines using dioxiranes is quite telling; in fact, the high reactivity of these powerful oxidants allows *O*-transfer to the sulfonium sulfur (path *ii*, Scheme 1) in spite of the scarce electron density at this reaction center. In view of the distinctly lower nucleophilicity of the sulfilimine sulfur, it is perhaps not surprising that the electrophilic oxidation of sulfilimines with dioxiranes is much slower than the parent sulfoxides.[5a]

With dimethyldioxirane, *electrophilic S*-oxidation of sulfilimines competes favorably with *N*-oxidation. In fact, control experiments revealed that — under the conditions adopted — consecutive *N*-oxidation in the sulfoximine product (hence its oxidative fragmentation) is negligible. The more powerful methyl(trifluoromethyl)dioxirane (**1b**) is seemingly less selective than **1a** since, along with the sulfoximine, sizeable amounts of sulfoxide and sulfone are also obtained.

Aside from the mechanistic details, we believe that the data reported herein indicate that the clean, direct oxidation of sulfilimines should be considered a new entry to sulfoximines.

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8. ***S*-Ethyl-*S*-methyl-*N*-(acetyl)sulfoximine** (**3g**): oil, b.p. 57-58 °C/21 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$):δ 1.4 (t, *J* = 7.0 Hz, 3 H), 2.4 (s, 3 H), 3.3 (s, 3 H), 3.5 (q, *J* = 7.0 Hz, 2 H), 7.2-7.8 (m, 4 H); Anal. Calcd for $C_5H_{11}NO_2S$: C, 40.25; H, 7.43; N, 9.39. Found: C, 40.01; H, 7.33; N, 9.46.
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10. (a) **S(-)-*S*-(*p*-tolyl)-*S*-methyl-*N*-(*p*-tolylsulfonyl)sulfilimine** was obtained by a literature procedure (ref. 10b) upon reaction of (+)-methyl *p*-tolyl sulfoxide ($[\alpha]_D$ +124°; *c* 1.5, acetone; ee 85%) with *p*-toluenesulfonamide in the presence of P_2O_5 and Et_3N: m.p. 123-125 °C; ($[\alpha]_{546}$ -261°; *c* 1.3, acetone); ^{1}H NMR identical with that of racemic **2d**. (b) Cram, D. J.; Day, J.; Rayner, D. R.; von Schriltz, D. M.; Duchamp, D. J.; Garwood, D. C. *J. Am. Chem Soc.* **1970**, *92*, 7369.
11. **R(-)-*S*-(*p*-tolyl)-*S*-methyl-*N*-(*p*-tolylsulfonyl)sulfoximine** : m.p. 158-161 °C; ($[\alpha]_{546}$ -140°; c 0.9, acetone); ^{1}H NMR identical with that of racemic **2d** (cf., ref. 10b reporting the characteristics of optically pure material); its enantiomeric excess was determined as 80% by HPLC of the reaction mixture, employing a chiral stationary phase (DAICEL Chiralcel OD, 25 cm × 0.46 cm ID.; 30% EtOH /70% n-hexane, 1 mL/min).
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