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Asymmetric Oxidation of Sulfides to Sulfoxides by Organic Hydroperoxides with Optically Active Schiff Base-Oxovanadium(IV) Catalysts

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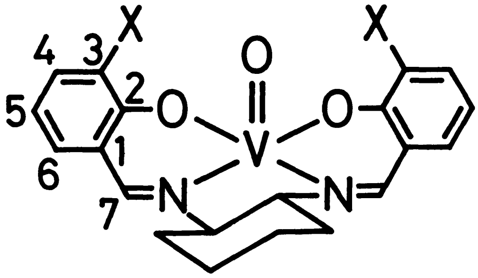
The asymmetric oxidation of sulfides into the corresponding sulfoxides was achieved with organic hydroperoxides in the presence of a catalytic amount of optically active Schiff base-oxovanadium(IV) complexes; in most cases the optical yields (e.e.) ranged between 20 and 40%.

The usefulness of optically active sulfoxides in asymmetric synthesis of organic compounds has received attention.1) An efficient asymmetric oxidation of prochiral organic sulfides into optically active sulfoxides has been reported, using a modified Sharpless reagent ($Ti(OPr^i)_4$/diethyl (R,R)-tartrate/Bu^tOOH) for asymmetric epoxidation.2,3) However, a stoichiometric amount of the complex was required because of the inhibition effect of sulfoxides, and the reaction was carried out under nitrogen.2) We found that a similar asymmetric oxidation of sulfides proceeded by a catalytic amount of optically active Schiff base-oxovanadium(IV) complexes in air. Although optical yields (e.e.) obtained in this study were 40% at best, the value is the highest reported so far in similar studies with a catalytic amount of complex catalysts.3) In the present reaction system, the kinds of Schiff bases, metals, and organic hydroperoxides are readily varied; an appropriate combination of these parameters may lead to better results.



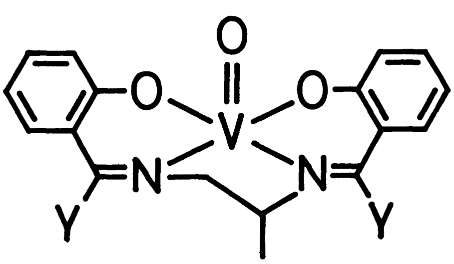
1

VO(sal-(RR)-chxn): X=H

VO(3-MeOsal-(RR)-chxn): $X=OCH_3$

VO(3-EtOsal-(RR)-chxn): $X=OC_2H_5$

VO(3-Bu^tsal-(RR)-chxn): $X=C(CH_3)_3$



2

VO(sal-(R)-pn): Y=H

VO(7-Mesal-(R)-pn): $Y=CH_3$

Table 1. Asymmetric oxidation of sulfides to the sulfoxides[a)]

$$R^1\text{-S-}R^2 \xrightarrow[CH_2Cl_2]{\text{ROOH/VO(Schiff base)}} R^1\text{-S(O)-}R^2$$

Entry	Complex Catalyst[b)]	Sulfide R^1	R^2	Peroxide[c)]	Reaction conditions Temp/ °C	Time/h	Yield/%[d)]	e.e./%[e)] (config.)
1	VO(3-MeOsal-(RR)-chxn)*	Ph	Me	CHP	-20	720	79	40 (S)
2	VO(3-MeOsal-(RR)-chxn)	Ph	Me	CHP	0	120	96	40 (S)
3	VO(3-MeOsal-(RR)-chxn)	Ph	Me	CHP	20	37	94	31 (S)
4	VO(3-MeOsal-(RR)-chxn)	Ph	Me	CHP	40	15	75	26 (S)
5	VO(3-MeOsal-(RR)-chxn)	Ph	Me	TBHP	0	120	90	16 (S)
6	VO(3-MeOsal-(RR)-chxn)	Ph	Me	TMHP	0	120	92	7 (S)
7	VO(3-EtOsal-(RR)-chxn)*	Ph	Me	CHP	0	120	81	40 (S)
8	VO(sal-(RR)-chxn)	Ph	Me	CHP	0	120	77	21 (S)
9	VO(3-Bu^tsal-(RR)-chxn)*	Ph	Me	CHP	0	156	70	10 (S)
10	VO(sal-(R)-pn)	Ph	Me	CHP	0	120	74	ca. 0
11	VO(7-Mesal-(R)-pn)	Ph	Me	CHP	0	120	89	17 (R)
12	VO(3-MeOsal-(RR)-chxn)	p-Tol	Me	CHP	0	144	71	35 (S)
13	VO(3-MeOsal-(RR)-chxn)	2-Naphthyl	Me	CHP	0	120	76	30
14	VO(3-MeOsal-(RR)-chxn)	p-Tol	Bu^n	CHP	0	120	70	10 (S)
15	VO(3-MeOsal-(RR)-chxn)	2-Pyridyl	Me	CHP	0	120	82	32

a) All reactions were performed as described in detail in the text. Molar ratio of complex catalyst:organic hydroperoxide:sulfide=0.1:1:1, in CH_2Cl_2. b) The complexes with asterisk are new complexes. All complexes were characterized by elemental analysis, and IR, UV, CD, and ESR spectroscopy. c) Peroxide: CHP, cumene hydroperoxide; TBHP, t-butyl hydroperoxide; TMHP, 1,1,3,3-tetramethylbutyl hydroperoxide. d) Isolated yields, based on the sulfide. e) Based on the optical rotation of the pure enantiomer reported in Refs 2, 6, and 7.

Stereochemistry of optically active Schiff base complexes has been studied extensively, which is also advantageous to study reaction mechanisms.

A typical run was performed as follows. VO(3-MeOsal-(RR)-chxn)·1/3CH_2Cl_2 (34.5 mg, 7.25 x 10^{-5} mol) prepared from $VOCl_2$ and H_2(3-MeOsal-(RR)-chxn)[4)] was stirred in dichloromethane (10 cm^3) with 73% cumene hydroperoxide (151 mg, 7.25 x 10^{-4} mol) at room temperature. The resulting dark green solution was cooled to 0 °C, and allowed to react with methyl phenyl sulfide (90 mg, 7.25 x 10^{-4} mol) at that temperature for 120 h. The solvent was removed by blowing a stream of N_2 over the surface of the reaction mixture. The residue was extracted with diethyl ether, which was evaporated under reduced pressure. From the resulting oil, methyl phenyl sulfoxide was isolated and purified by column chromatography on silica gel (eluent: cyclohexane-ethyl acetate (1:1 v/v)). Yield: 98 mg (96%). The enantiomeric excess (e.e.) was determined on the basis of the reported optical rotation of the pure enantiomer;6) $[\alpha]^{20}_{589}$ (c 0.76, acetone) -59.3°; e.e. 40%. In the absence of complex catalyst, the oxidation of the sulfide proceeds very slowly.

Several optically active Schiff base-oxovanadium(IV) catalysts and peroxides were used for the asymmetric oxidation of sulfides and the results are given in Table 1. The complex catalysts containing an (RR)-chxn moiety give an (S)-sulfoxide, while those containing an (R)-pn moiety an (R)-sulfoxide (entry 11) or a racemic one (entry 10). The results can be understood if we assume that a catalytically active species has conformational chirality similar to that of the added complex. VO(sal-(RR)-chxn) and VO(7-Mesal-(R)-pn) give circular dichroism (CD) spectra almost mirror image of each other despite the fact that both parent diamines have the same absolute configuration. In VO(sal-(RR)-chxn), the central chelate ring is locked in a λ gauche conformation (see **1**), while VO(7-Mesal-(R)-pn) has been suggested to take a δ gauche conformation to reduce the steric interaction between the methyl substituent on the azomethine carbon atom and the pn methyl group (see **2**).8) Such a difference in conformational chirality between the complexes should be responsible for the enantioselectivity. In the oxidation with VO(sal-(R)-pn) essentially no asymmetric induction was observed (entry 10),

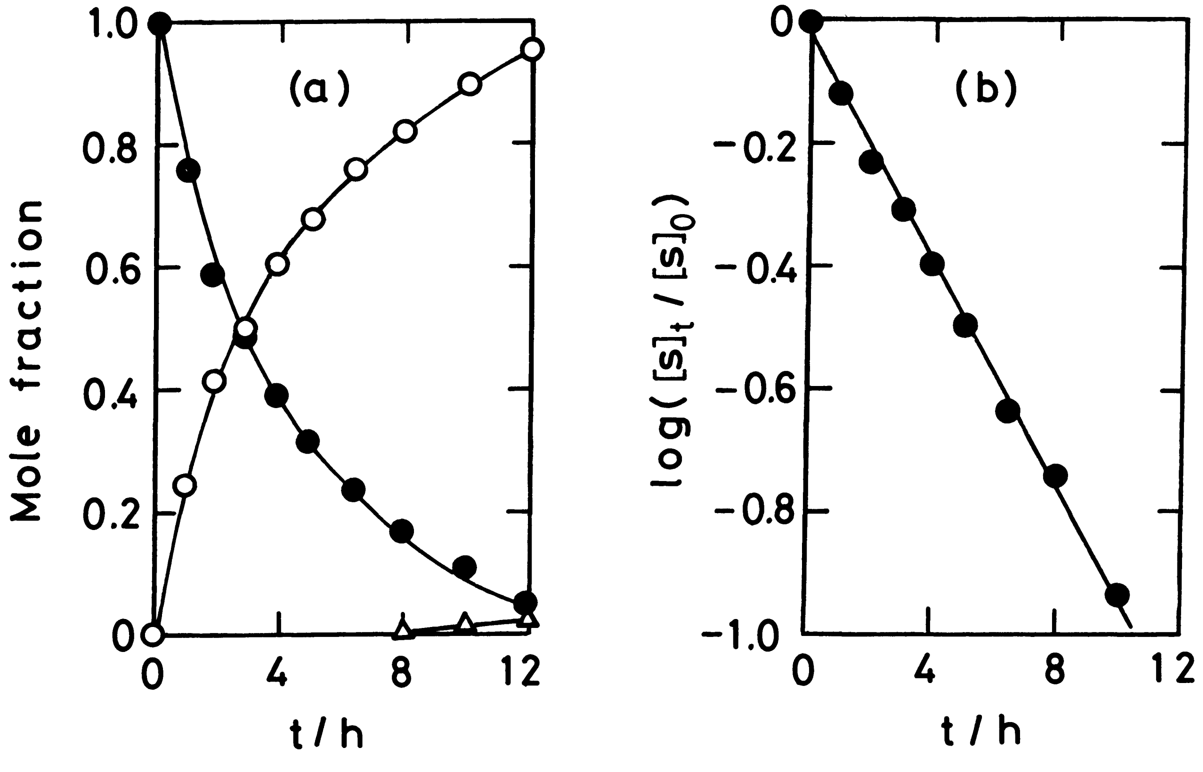


Fig. 1. Oxidation of methyl phenyl sulfide (45.1 mg, 3.63×10^{-4} mol) by t-butyl hydroperoxide (80%, 61.3 mg, 5.45×10^{-4} mol) with the VO(3-MeOsal-(RR)-chxn)· $1/3CH_2Cl_2$ (17.3 mg, 3.63×10^{-5} mol) catalyst in CH_2Cl_2 (10 cm^3) at 20 °C. (a) Reaction profile: ●, sulfide; ○, sulfoxide; △, sulfone, and (b) the plot of $\log([s]_t/[s]_0)$ vs. reaction time. [s]=sulfide concentration.

and the result also seems to be related to the conformation of the complex. The CD spectral pattern of VO(sal-(R)-pn) is similar to that of VO(7-Mesal-(R)-pn), however, the strength is very small compared with the latter; probably the former complex in solution is in an equilibrium mixture of the conformational isomers (δ and λ) with a small preference of the δ form.

Figure 1(a) shows the reaction profile for the oxidation of methyl phenyl sulfide with t-butyl hydroperoxide in dichloromethane catalyzed by VO(3-MeOsal-(RR)-chxn)$\cdot$1/3CH_2Cl_2. The reaction products were analyzed by high-performance liquid chromatography on JASCO Fine pack SIL $C_{18}S$ (eluent: CH_3CN-H_2O (9:1 v/v)). The oxidation of the sulfide is first order in the sulfide concentration; the plot of $\log([s]_t/[s]_0)$ vs. time gave a straight line for at least three half-lives (Fig. 1(b), [s] represents the concentration of the sulfide at the subscripted time), although the complex catalyst decomposed by ca. 40% in 10 h. These results suggest that the concentration of catalytically active species is constant in the course of the oxidation reaction. The rate of conversion of vanadium(IV) to vanadium(V) indicated by ESR spectroscopy was slow compared with that of the sulfoxide formation, and thus the active species is suggested to be vanadium(IV).

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References

1) For example, G. Solladié, Synthesis, 1981, 185.
2) P. Pitchen and H. B. Kagan, Tetrahedron Lett., 1984, 1049; P. Pitchen, E. Duñach, M. N. Deshmukh, and K. B. Kagan, J. Am. Chem. Soc., 106, 8188 (1984).
3) F. Di Furia, G. Modena, and R. Seraglia, Synthesis, 1984, 325.
4) $H_2$3-MeOsal-(RR)-chxn was prepared from 3-methoxysalicylaldehyde and (R,R)-1,2-cyclohexanediamine by a method similar to that for H_2sal-(RR)-chxn.$^{5)}$
5) M. Gulotti, A. Pasini, P. Fantucci, R. Ugo, and R. D. Gillard, Gazz. Chim. Ital., 102, 855 (1972).
6) J. Jacobus and K. Mislow, J. Am. Chem. Soc., 89, 5228 (1967).
7) K. Mislow, M. M. Green, P. Laur, J. T. Melilo, T. Simmons, and A. L. Ternay, Jr., J. Am. Chem. Soc., 87, 1958 (1965).
8) R. L. Farmer and F. L. Urbach, Inorg. Chem., 9, 2562 (1970).

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