

REDUCTION OF SULFOXIDES AND SULFILIMINES CATALYZED BY METALLOPORPHINS

Toshiyuki Nagata, Toshiaki Yoshimura, Ken Fujimori and Shigeru Oae* 1)

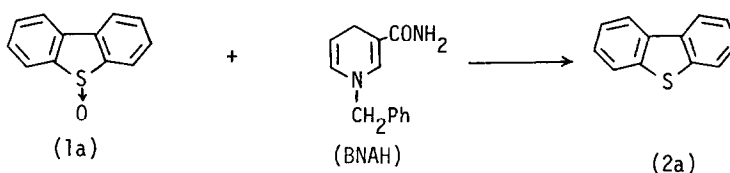
Department of Chemistry, The University of Tsukuba, Sakura, Ibaraki, 305, Japan

Summary : Reduction of sulfoxides and sulfilimines to the corresponding sulfides by both BNAH and NaBH₄ have been found to proceed in the presence of a catalytic amount of metallo-meso-tetraphenylporphins.

Reduction of sulfoxides is known to proceed generally either by nucleophilic substitution on the sulfur atom as in the reduction with HI²⁾ or thiols,³⁾ or nucleophilic attack at oxygen terminal as in the case with phosphins.⁴⁾ Meanwhile, occurrence of sulfoxides in nature has been recognized and their metabolic reactions have also been reported.⁵⁾ Actually, sulfoxides are reduced enzymatically to the corresponding sulfide. The reduction of methionine sulfoxide to methionine with NADPH is known to be catalyzed by an enzyme isolated from yeast.⁶⁾

Recently an interesting one-electron transfer mechanism has been proposed by Ohno *et. al.* for the reduction of thioketones⁶⁾ or carbonyl compounds⁷⁾ with N-alkyl-1,4-dihydronicotinamide. This work has been initiated with an anticipation that the reduction of sulfoxide would proceed by treatment with NAD(P)H model through a similar electron transfer process in the successful reduction of N,N-dimethylanilin N-oxide with 1-benzyl-1,4-dihydronicotinamide(BNAH).⁹⁾

However, dibenzothiophene oxide(1a) was found to be completely inert to BNAH alone in benzene or CH₃CN in argon atmosphere at 80° in the dark, and even in the presence of Mg²⁺ which is an effective catalyst for the reduction of carbonyl compounds by NAD(P)H model compounds.¹⁰⁾ However, in the presence of a catalytic amount of metalloporphins, (1a) was converted to dibenzothiophene(2a) by BNAH quantitatively. A typical run is as follows. A mixture of the



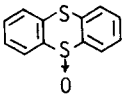
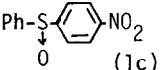
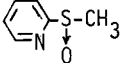
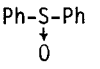
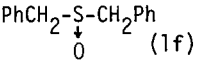
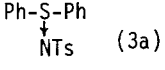
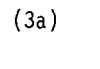
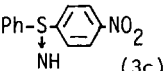
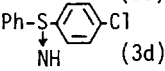
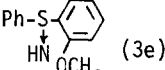
sulfoxide(1a, 1.0 mmol), BNAH(1.1 mmol) and *meso*-tetraphenylporphinato iron(III) chloride (TPPFeCl, 0.05 mmol) were added into 5ml of benzene in a flask equipped with an argon balloon, and the mixture was kept at 80° for 2 hr in the dark. Then the mixture was concentrated *in vacuo* and the residue was column-chromatographed through silica-gel with hexane. From the hexane solution the pure sulfide was obtained quantitatively. The sulfide(2a) was identified by comparison of its IR spectra with that of the authentic sample and also by the mixed melting point with the authentic sample. The results are summarized in Table 1 which shows that the presence of metalloporphins is essential in the reduction of (1a) to (2a), while the porphin without metal does not catalyze the reduction. The catalytic ability of metalloporphin decreases of its reduction potential. The electrochemical data shown in Table 1 suggest that the reducing ability of the metalloporphin decreases in the following order : $\text{TPPCu(I)}^- > \text{TPPCo(I)}^- > \text{TPPFe(II)}$. However, the actual data reveal that the catalytic ability of metalloporphin in the reduction of sulfoxide with BNAH increases in the order of $\text{TPPCu(II)} < \text{TPPCo(II)} < \text{TPPFe(III)}^+$, suggesting that the rate of electron transfer from BNAH to metalloporphin decreases with the decrease of the reduction potential of the catalyst. Namely, the rate of the metalloporphin-catalyzed reduction of sulfoxide with BNAH is associated

Table 1. Reduction of (1a) with BNAH in the presence of catalyst at 80° in Ar atmosphere

BNAH(eq.)	catalyst ^{a)}	solvent	time(hr)	sulfide(2a, %) ^{b)}	reduction potential of metalloporphin c)
5.0	none	C ₆ H ₆	24	0 ^{d)}	
5.0	Mg(ClO ₄) ₂	CH ₃ CN	12	0 ^{d)}	
5.0	FeCl ₃	CH ₃ CN	12	10	
1.1	TPPFeCl	C ₆ H ₆	2	96	-0.19
e)	TPPFeCl	C ₆ H ₆ -EtOH	3	99	
1.5	(TPPFe) ₂ O	C ₆ H ₆	4	98	-
1.5	TPPCo	C ₆ H ₆	10	98	-0.82
2.0	TPPCu	C ₆ H ₆	12	12	-1.17
2.5	TPPH ₂	C ₆ H ₆	12	0 ^{d)}	-1.07

a) Mg(ClO₄)₂ and FeCl₃ were employed twice molar amounts of (1a), porphins were used 5 mol% of (1a). b) isolated yield c) E_{1/2} vs. SCE in DMF d) (1a) was recovered quantitatively. e) NaBH₄ was used as a reducing agent at room temperature.

Table 2. Reduction of sulfoxides and sulfilimines by TPPFeCl/BNAH system in benzene^{a)}

compound	BNAH(eq.)	temp.(°C)	time(hr)	sulfide(%) ^{b)}
 (1b)	1.5	80	15	65
 (1c)	1.5	80	18	75
 (1d)	2.0	80	15	43
 (1e)	3.0	80	40	38
 (1f)	3.0	80	40	12
 (3a)	2.0	80	1	96 ^{c)}
(3a)	d)	r.t.	1.5	94 ^{c)}
 (3b)	5.0	r.t	12	trace ^{e)}
(3b)	1.1	r.t	70 min	88
(3b)	d)	r.t	5 min	98
 (3c)	1.05	r.t.	5 min	98
 (3d)	1.1	r.t	15 min	95
 (3e)	1.5	r.t	90 min	92

a) TPPFeCl was employed 5 mol% of substrate.

b) isolated yield c) TsNH₂ was also obtained.

d) NaBH₄ was used as reducing agent in C₆H₆-EtOH.

e) without TPPFeCl and (3a) was recovered.

at least partly with the rate of electron transfer from BNAH to the catalyst.

Actually, TPPFeCl catalyzed reduction of sulfoxides and sulfilimines with NaBH₄ which is better reducing agent of TPPFeCl than BNAH appeared to proceed much faster than that with BNAH as shown in Tables 1 and 2.

Since TPPFeCl appeared to be the best catalyst, the reaction of several sulfoxides and sulfilimines with TPPFeCl/BNAH system has been examined. The results are shown in Table 2. The data in Table 2 reveal that electron withdrawing substituents on diphenyl sulfoxide accelerate the reaction, while dialkyl sulfoxide such as (1f) is much less reactive than the aromatic ones, suggesting that an electron

transfer process from the catalyst to the sulfoxide also reflects on the rate of reaction.

Nitro group was not found to be affected under the same condition to reduce aromatic sulfoxides.

Diphenyl-N-*p*-toluenesulfonylsulfilimine was also reduced to diphenyl sulfide and *p*-toluenesulfonamide quantitatively in this system. The reaction of N-unsubstituted sulfilimines were found to proceed much more readily than the corresponding sulfoxides or N-*p*-toluenesulfonyl-

sulfilimine, the reaction completing within 1.5 hr at room temperature. Thus, the rate of the reduction with TPPFeCl/BNAH system decreases in the order of N,N-dimethylaniline N-oxide > N-*p*-toluenesulfonylsulfilimine > N-unsubstituted sulfilimine > diarylsulfoxide. This order of reactivity is consistent with the coordinating abilities to the ferric catalyst.^{9,11)} In other words, the extent of polarities of these semi-polar bonds decreases in the order of $\geq N \rightarrow O > > S \rightarrow NH > > S \rightarrow NTs > > S \rightarrow O$, and the energies of the particular semi-polar bond which is cleaved reductively increases in the order of $\geq N \rightarrow O < > S \rightarrow NH < > S \rightarrow NTs < > S \rightarrow O$. Thus, both the initial coordination of the substrate to the catalyst and the subsequent bond cleavage processes seem to be quite important in the reductive cleavage of these semi-polar bond with TPPFeCl/BNAH system.

References and Footnotes

- 1) Present address : Okayama University of Science, Ridai-cho, Okayama, 700, Japan.
- 2) S. Tamagaki, M. Mizuno, H. Yoshida, H. Hirota and S. Oae, Bull. Chem. Soc. Jpn., 44, 2456 (1976).
- 3) T. J. Wallace and J. J. Mahon, J. Am. Chem. Soc., 86, 4099(1964). T. Numata, H. Togo and S. Oae, Chem. Lett., 329(1979). See also J. Drabowicz, T. Numata and S. Oae, Org. Prep. Proced. Int., 9(2), 63(1977).
- 4) H. H. Szmant and O. Cox, J. Org. Chem., 31, 1596(1966).
- 5) D. C. Wood and S. W. Jacob, Quart. Repts. on Sulfur Chem., 3, 159(1968), and references cited therein.
- 6) S. Black, E. M. Harte, B. Hudson and L. Wartofsky, J. Biol. Chem., 235, 2910(1960).
- 7) A. Ohno and N. Kito, Chem. Lett., 369(1972). S. Yasui, K. Nakamura, A. Ohno and S. Oka Bull. Chem. Soc. Jpn., 55, 196(1982).
- 8) A. Ohno, H. Yamamoto and S. Oka, J. Am. Chem. Soc., 103, 2041(1981).
- 9) K. Fujimori, T. Takata, S. Fujiwara and S. Oae, to be published.
- 10) Y. Ohnishi, M. Kagami and A. Ohno, J. Am. Chem. Soc., 97, 4766(1975).
- 11) Spectroscopic analysis showed that N-unsubstituted sulfilimines have much weaker coordination abilities to TPPFeCl than N,N-dimethylaniline N-oxide, while diaryl sulfoxides and N-*p*-toluenesulfonylsulfilimine have so weak coordinating abilities that the addition of the sulfoxides and the N-*p*-toluenesulfonylsulfilimine to the solution of TPPFeCl did not cause any spectral change at visible region. However, dimethyl sulfoxide has been found to coordinate to iron(III) porphyrins based on the electrochemical studies: L. A. Constant and D. G. Davis, Anal. Chem., 47, 2253(1975).

(Received in Japan 18 October 1983)