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THE REACTION OF 3-METHYLBENZOTHIAZOLIUM SALTS WITH SUPEROXIDE

Takashi Itoh, Kazuhiro Nagata, Mamiko Okada, and Akio Ohsawa*

School of Pharmaceutical Sciences, Showa University, 1-5-8 Hatanodai
Shinagawa-ku, Tokyo 142, Japan

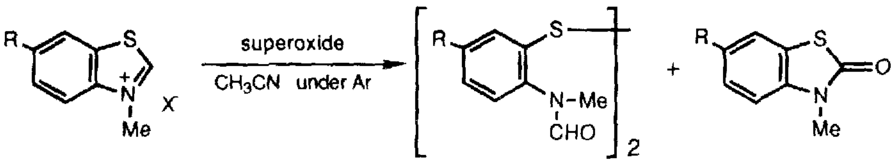
Abstract: 3-Methylbenzothiazolium salts reacted with superoxide to afford dimeric bis[*o*-(*N*-formyl-*N*-methylamino)phenyl]disulfides and 3-methyl-2-benzothiazolones. The reaction was entirely specific for superoxide, and is of interest from the biological and mechanistic viewpoint.

Thiazolium cations,[1)] which are active moieties of thiamine, have received considerable attentions. Especially, the reactivities of C-2 acidic protons and the intermediates formed by the proton elimination have been the controversial matters up to now.[2)]

In the course of our studies of electron-deficient heteroaromatics with superoxide,[3)] it was revealed that 3-methyl benzothiazolium salts **1** reacted with superoxide to afford bis[*o*-(*N*-formyl-*N*-methylamino)phenyl]disulfides **2** as major products, which we wish to report in this paper.

It was shown that in aprotic medium triethylamine deprotonated 3-alkylbenzothiazolium salts **1** at their 2-positions to afford a carbene-like intermediate, which dimerized to form bi(3-alkylbenzothiazolinylidenes) in good yields.[2,4)] In fact, when 3-methylbenzothiazolium iodide **1a** was allowed to react with finely powdered KOH and 18-crown-6 in acetonitrile,[5)] corresponding dimer was obtained as was mentioned above, along with the small amount of 3-methylbenzothiazolone **3a**.

However, when **1a** reacted with 2.0 eq. of potassium superoxide in the presence of 0.1 eq. of 18-crown-6 in acetonitrile(Table, method B), bis[*o*-(*N*-formyl-*N*-methylamino)phenyl]disulfide **2a**[6)] was obtained in 71% yield accompanied by 13% yield of **3a** (scheme 1 and Table). In the entries **7** and **8**, the yields were low because of the production of dimers formed by base. The same reaction proceeded more readily when electrolytically generated superoxide[7)] was employed instead of KO_2 (method A). These facts suggest that the reaction which gave **2** was specific for superoxide, and not the base catalyzed one. The reaction of 2,3-dimethylbenzothiazolium iodide with electrogenerated superoxide gave the similar product, bis[*o*-(*N*-acetyl-*N*-methylamino)phenyl]disulfide in 41% yield. The fact also indicated that the C-2 proton elimination was not essential for the reaction.



1 **2** **3**

scheme 1

Table Reaction of 3-Methylbenzothiazolium Salts **1** with Superoxide

entry	substrate	R	X	method	yield of 2	yield of 3
1	**1a**	H	I	A	89%	3%
2	**1b**	NO_2	OSO_3Me		95%	0
3	**1c**	OMe	I		84%	7%
4	**1d**	Me	I		87%	9%
5	**1a**	H	I	B	71%	13%
6	**1b**	NO_2	OSO_3Me		33%	41%
7	**1c**	OMe	I		23%	19%
8	**1d**	Me	I		11%	13%

A) In 0.1M tetraethylammonium perchlorate solution of acetonitrile, oxygen gas was bubbled into the cathode chamber of a H cell and electroreduced at -0.87 V until 0.375 mF of electric current was consumed. Then the current was stopped and **1** (0.15mmol) was added and allowed to stand at room temperature under an argon atmosphere for 2h.

B) Compound 1 (0.3mmol) and potassium superoxide (0.6mmol) were allowed to react in the presence of 18-crown-6 (0.03mmol) in acetonitrile at room temperature for 2h.

Superoxide is known to have a variety of reactivities, and one of the most noteworthy radical species from the viewpoint of oxygen toxicity.8) However, chemical reactivity of superoxide itself is considered to be low9) without the activator.10) In addition, the reactions of superoxide which were available for organic chemistry mostly can proceed when superoxide is substituted for hydroxide anion.11) Thus, our reaction system is specific in next two points. First, thiazolium cation 1, which is ubiquitous in living system, reacted readily with superoxide to afford unique dimeric disulfides, and secondly, the reaction of 1 with hydroxide anion gave entirely different compounds. The reaction mechanism is under investigation.

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5. The compound **1a** and powdered KOH (1.2 eq.) were allowed to react in the presence of 18-crown-6 (0.1 eq.) in abs. CH_3CN under oxygen atmosphere for 3h.
6. This kind of products were obtained by the reaction of 3-substituted 2-nitrosoimino-2,3-dihydrobenzothiazoles with $LiAlH_4$. See, Akiba, K.; Kawamura, T.; Ochiumi, M.; Inamoto, N. *Heterocycles*, **1973**, *1*, 35.
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