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THE REACTION OF 3,3'-DIMETHYL-2,2'-BITHIAZOLINIUM SALTS WITH SUPEROXIDE

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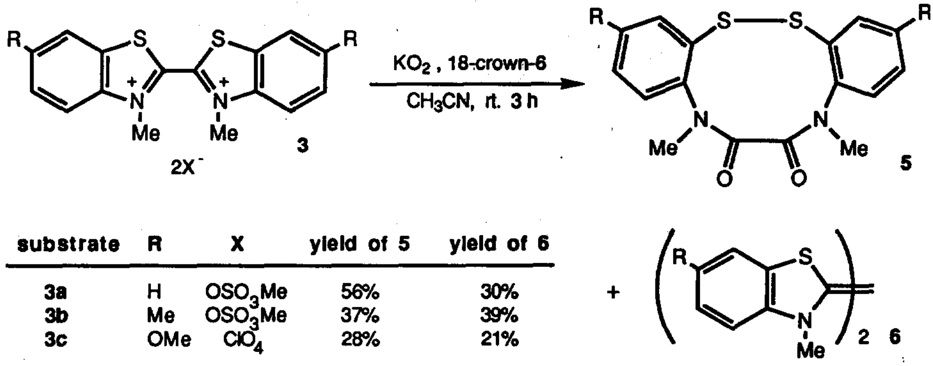
Abstract: The reaction of 3,3'-dimethyl-2,2'-bithiazolium salts with potassium superoxide afforded new ten-membered ring compounds 1,2,5,8-dithiadiazecine-6,7-diones in moderate yields. Since these compounds were not obtained from the reaction of KOH-O_2 or KOH-H_2O_2, the reaction is revealed to be specific for superoxide.

Active oxygen species1) have attracted considerable attention with respect to biological oxygen damage,2) and it is a matter of importance to research real active oxygen concerning various biological phenomena.3) Superoxide4) is one of the most noteworthy active oxygens, and its reactivities have been investigated from both biological and chemical viewpoints. In the course of our study of electron deficient heteroaromatics with superoxide,5) it was revealed that benzothiazolium salts afforded novel disulfide compounds by the reaction with superoxide.6) The results prompted us to the application of the reaction to another systems and it was found that 3,3'-dimethyl-2,2'-bithiazolium salts were treated with superoxide to give new ten-membered ring compounds 1,2,5,8-dithiadiazecine-6,7-diones, which we wish to report in this paper.



3

5

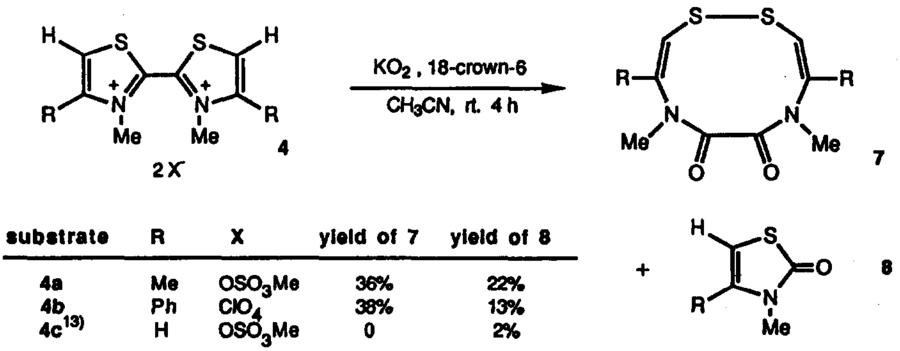
substrate	R	X	yield of 5	yield of 6
3a	H	OSO_3Me	56%	30%
3b	Me	OSO_3Me	37%	39%
3c	OMe	ClO_4	28%	21%

6

scheme 1

2,2'-Bibenzothiazoles 1[7] and 2,2,'-bithiazoles 2[8,9] were synthesized according to the reported methods. They were treated with dimethyl sulfate to form 3 and 4.[10] When 3 was allowed to react with 2 eq. of potassium superoxide in the presence of 18-crown-6, dibenzo-1,2,5,8-dithiadiazecine-6,7-dione 5 was obtained accompanied by bi(3-methylbenzothiazolinylidene) 6 (scheme 1). When 3a was treated with KOH-O_2 or KOH-H_2O_2[11] in acetonitrile, only 6 was obtained in 86% or 90% yield, respectively, without trace amount of 5a. Thus the formation of 5 is proved to be entirely specific reaction for superoxide.

Next, bithiazolium salt 4 was subjected to the reaction with potassium superoxide to give 1,2,5,8-dithiadiazecine-6,7-dione 7 and 2-thiazolone 8 (scheme 2). In these cases, the use of KOH-O_2 or KOH-H_2O_2[12] instead of KO_2 resulted in the sole formation of 8. The facts also suggested that dithiadiazecinediones were derived specifically from the reaction with superoxide.



4

7

8

substrate	R	X	yield of 7	yield of 8
4a	Me	OSO_3Me	36%	22%
4b	Ph	ClO_4	38%	13%
4c[13]	H	OSO_3Me	0	2%

scheme 2

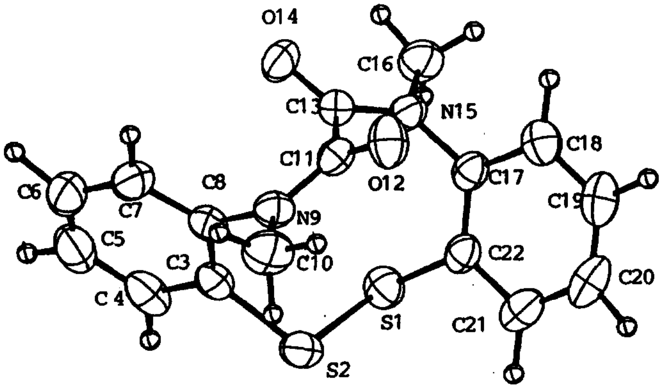
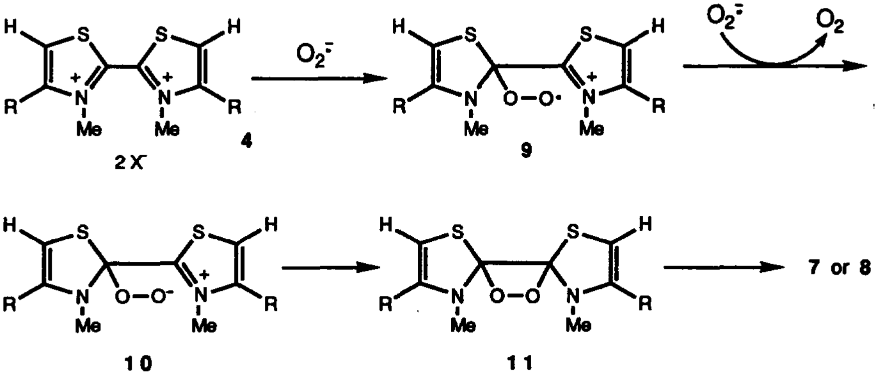


Figure 1 The ORTEP drawing of dibenzo[*c,i*]5,8-dimethyl-1,2,5,8-dithiadiazecine-6,7-dione.[14]

The compounds **5** and **7** prohibited sufficient spectral data, and the final structural elucidation was carried out using X-ray crystallographic analysis. Figure 1 shows the ORTEP drawing of dibenzo[*c,i*]5,8-dimethyl-1,2,5,8-dithiadiazecine-6,7-dione **5a**.[15]

Since the above reactions were not subject to the influence of aerobic or anaerobic conditions, reaction mechanism was assumed as shown in scheme 3. No influence of the reaction atmosphere suggested that superoxide attacked directly bisthiazolium salt to form peroxy radical **9**. The radical **9** was reduced by next superoxide to give peroxy anion **10**, which was cyclized intramolecularly to afford the dioxetane **11**. The dioxetane **11** was supposed to be cleaved at O-O bond, and simultaneous S-S bond formation[16] afforded **7**, while normal dioxetane-type cleavage afforded thiazolone **8**.[17] If C2-C2' bond doesn't exist, the mechanism will claim that bis[2-(*N*-formyl-*N*-methylamino)ethenyl]disulfide will be formed. Our previous report[6] supported the assumption, thus this reaction mechanism was thought to be reasonable. Meanwhile, compounds **6** might be formed by electron transfer from two moles of superoxide.[18]



scheme 3

In this paper, we described the formation of novel dithiadiazecinediones **5** and **7** by the reaction of bithiazolium salts with superoxide. The reaction is unique in next two points. First, the formation of **5** or **7** is specific for superoxide, and other reagents such as KOH-O_2 or KOH-H_2O_2 gave other products. Secondly, this reaction is the first example that superoxide gave the new compounds which have never been synthesized by other methods. The application of the reaction to biological system is now under investigation.

ACKNOWLEDGMENT

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10. Since it was difficult to crystallize the compound **3c** and **4b** as methosulfate salts, it was treated with$NaClO_4$ to afford corresponding perchlorate salts.
11. Treatment of the compound **3** with 30% H_2O_2 in acetonitrile resulted in the recovery of the starting material.
12. No reaction also proceeded with only H_2O_2.
13. The compound **4c** was almost insoluble in acetonitrile, and the starting material was recovered even after 7 h's reaction.
14. Monoclinic $P2_1/n$, $a=27.229(3)$, $b=7.6493(8)$, $c=7.358(4)$Å, $\beta=90.82(2)°$, $V=1532.5(7)$Å^3, $R=0.049$. Detailed crystallographic analysis will be published elsewhere.
15. The compound **5a** was reported in a communication, which showed only melting point (205-206°C) as the datum. See, Baldwin, J. E.; Walker, J. A. *J. Am. Chem. Soc.*, **1974**, *96*, 596. All other **5** and **7** are new compounds.
16. Similar rearrangement of dioxetane to large membered ring instead of diketone was observed in the reaction of 2-(1,3-dithia-2-cyclohexylidenyl)-1,3-dithiane with singlet oxygen. See, Adam, W.; Liu, J-C. *J. Am. Chem. Soc.*, **1972**, *94*, 1206.
17. The formation of **8** by the reaction of **4** with hydroxide ion might be rationalized by the autooxidation of a diol intermediate which was formed by **4** and two moles of hydroxide ion.
18. Bibenzothiazolium salts **3** have higher redox potentials than those of bithiazolium salts **4**, therefore reduction by superoxide might readily proceed in the case of **3** as substrates.

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