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Deprotection of 1,3-Dithianes by 2,3-Dichloro-5,6-dicyano-p-benzoquinone (DDQ)

Kiyoshi TANEMURA,* Hiroshi DOHYA,† Masanori IMAMURA,†
Tsuneo SUZUKI, and Takaaki HORAGUCHI†
School of Dentistry at Niigata, The Nippon Dental University,
Hamaura-cho 1-8, Niigata 951
†Department of Chemistry, Faculty of Science, Niigata University,
Ikarashi, Niigata 950-21

A variety of 1,3-dithianes were converted to the corresponding carbonyl compounds in good yields by treatment with 1.5 equiv. of 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) in MeCN-H_2O (9:1).

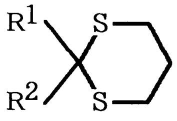
1,3-Dithianes are useful protecting groups for carbonyl functions in synthetic organic chemistry.1) The deprotection of 1,3-dithianes is performed by mercury (II) salts-induced, halogenative, and oxidative hydrolysis.1) However, it is necessary to develop an efficient new method because mercury salts are highly toxic and some oxidative methods require inconvenient procedures.

In the connection with our synthetic study using DDQ, we became interested in the deprotection of 1,3-dithianes by DDQ, since acetals were easily deprotected by a catalytic amount of DDQ.2,3) In this paper, we report that 1,3-dithianes are hydrolyzed to the corresponding carbonyl compounds in good yields in aqueous MeCN at room temperature by 1.5 equiv. of DDQ.4)

First, 2-(p-chlorophenyl)-1,3-dithiane (1a) (R^1 = p-ClC_6H_4, R^2 = H) was treated with various amounts of DDQ in MeCN-H_2O (9:1) under nitrogen at room temperature. When 1.0, 1.2, and 1.5 equiv. of DDQ were employed, p-chlorobenzaldehyde (2a) was isolated in 64, 69, and 87% yields, respectively. In the absence of water, most of dithiane 1a was recovered.

Next, the solvent effect was examined using 1.5 equiv. of DDQ. The results are summarized in Table 1. In polar solvents such as MeCN-H_2O (9:1) or MeOH-H_2O (9:1), dithiane 1a was hydrolyzed to give aldehyde 2a (Entries 1 and 2). In less polar solvents such as C_6H_6-H_2O (9:1) or CH_2Cl_2-H_2O (9:1), thioester 3a (R^1 = p-ClC_6H_4) was produced exclusively

(Entries 5 and 6).



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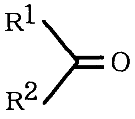

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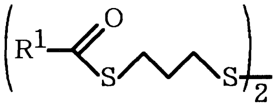

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Table 1. The reaction of dithiane 1a with DDQ

Entry	Solvent	Time/h	Conv./%	Yield/%[a)] 2a	Yield/%[a)] 3a
1	MeCN-H_2O (9:1)	2	100	87	0
2	MeOH-H_2O (9:1)	6	61	32	0
3	THF-H_2O (9:1)	2	27	9	0
4	Et_2O-H_2O (9:1)	3	56	31	22
5	C_6H_6-H_2O (9:1)	4	62	0	39
6	CH_2Cl_2-H_2O (9:1)[b)]	5	100	0	93

a) Isolated yields. b) 14 ml of the solvent was used.

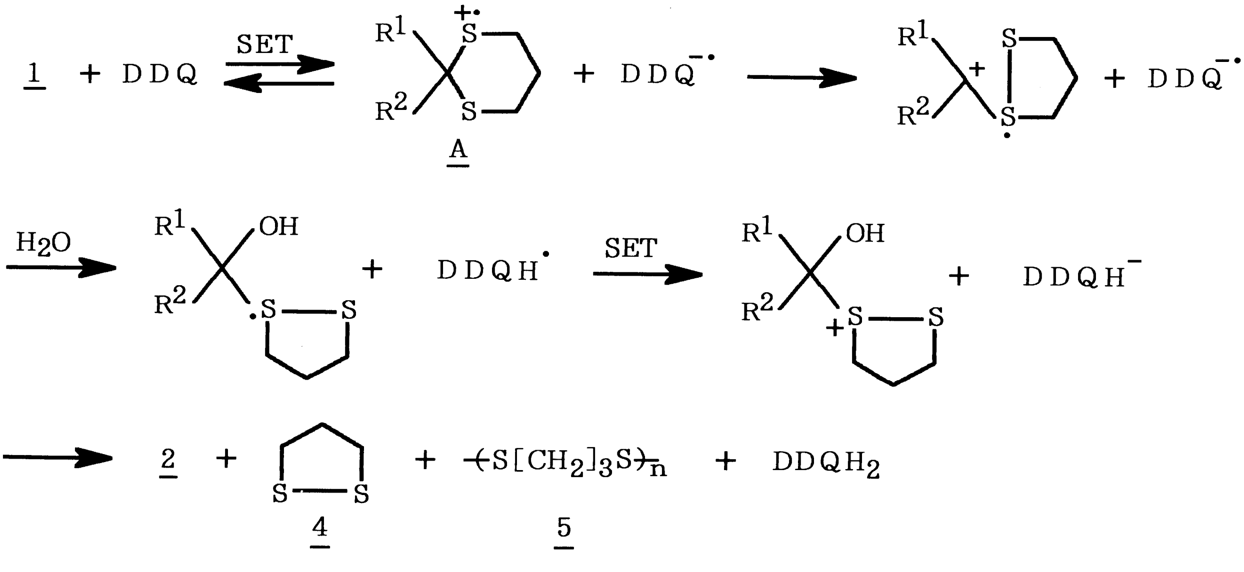
Finally, hydrolysis of various dithianes was examined (Table 2). In most cases, the reaction proceeds smoothly to give the corresponding aldehydes or ketones in good yields. Dithianes 1b and 1c possessing an electron-withdrawing group such as nitro and cyano groups on the benzene ring required longer reaction time (Entries 1 and 2). Dithianes 1e and 1f bearing electron-donative groups on the benzene ring afforded thioesters 3e and 3f as well as aldehydes 2e and 2f (Entries 5 and 6).

As shown in Scheme 1, we suppose that deprotection of dithianes occurs via a single electron transfer (SET) mechanism,[5,6)] although the details are not clear at this moment.[7)] The first step is a SET process from dithiane 1 to DDQ. Subsequent reaction of the resulting cation radical A, which involves carbon-sulfur bond cleavage, the attack by water and the second SET process, leads to aldehyde 2. 1,2-Dithiolane 4[8)] (2%), polymeric organosulfur compound 5[8)] (42%) and $DDQH_2$ (1.0 equiv.) were isolated from the reaction of 1a with DDQ. Addition of 1,2,4,5-tetramethoxybenzene (TMB) (1.5 equiv.), which is a SET quencher, suppressed the formation of 2i (2%), while 1,4-dimethoxybenzene (DMB) did not.[9)] These results suggest that SET processes are involved in the reaction. On the other hand, a possible mechanism for the formation of thioester 3 is shown in Scheme 2. Proton transfer from cation radical A to DDQ anion radical would lead to a geminate radical pair. The second SET process would produce a geminate ion pair and cation 6 is hydrolyzed to give 7. Compound 7 is further oxidized to 3 by DDQ. Under these reaction conditions employed, thiols such as 1-dodecanethiol were oxidized to disulfides rapidly by DDQ. Oxidation of p-methoxybenzilidene acetals to the corresponding esters by DDQ is known and explained by the similar mechanism.

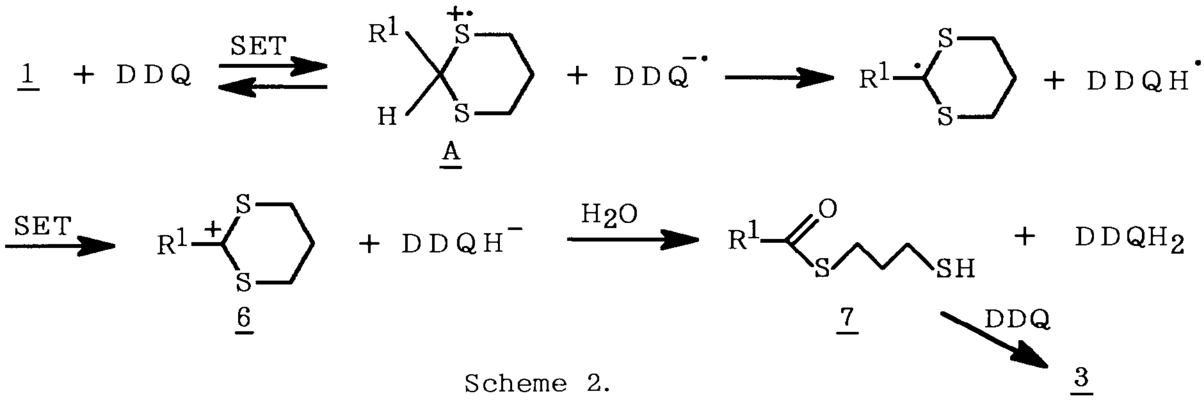
Table 2. The reaction of dithianes 1a-l with DDQ in aqueous MeCN

Entry	Dithiane	R^1	R^2	Time/h	Conv./%	Yield/%a)
1	1b	p-$O_2NC_6H_4$	H	6	66	30
2	1c	p-NCC_6H_4	H	6	76	61
3	1a	p-ClC_6H_4	H	2	100	87
4	1d	Ph	H	1	100	70b)
5	1e	p-MeC_6H_4	H	3	100	88c)
6	1f	p-$MeOC_6H_4$	H	2	100	43d)
7	1g	$PhCH_2CH_2$	H	2	91	70
8	1h	n-$C_{11}H_{23}$	H	1	95	71
9	1i	Ph	Me	0.5	100	75
10	1j	Ph	Ph	2	87	82
11	1k	$-(CH_2)_2CH(t\text{-}Bu)(CH_2)_2-$		1.5	97	81
12	1l	n-C_9H_{19}	Me	1	100	87

a) Isolated yields of 2. b) Determined by ^{1}H NMR spectroscopy. c) Thioester 3e was obtained in 8% yield. d) Thioester 3f was obtained in 41% yield.



Scheme 1.



Scheme 2.

A typical experimental procedure is as follows: To a solution of 1a (1.0 mmol) in MeCN-H_2O (9:1) (3.5 ml), was added a solution of DDQ (1.5 mmol) in MeCN-H_2O (9:1) (3.5 ml) under nitrogen. After stirring for 2 h at room temperature, the mixture was quenched with saturated $NaHCO_3$ (50 ml) and extracted with ether. The extracts were washed with water, dried and evaporated and the residue was chromatographed (benzene) on silica gel to give 2a in 87% yield.

References

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