

CLEAVAGE OF 2-METHOXY-1,3-DITHIOLES BY ACIDS

by Daniela BUZA and Wanda GRADOWSKA

Department of Organic Chemistry, Polytechnical University, 00664 Warszawa

Badano reakcję 2-metoksy-1,3-ditioli (1) z kwasami, w której wyniku otrzymuje się sole 1,3-ditioliowe (2) lub 2,2'-bi(1,3-ditiolilideny) (3), lub też ich mieszaninę. Stwierdzono, że czynnikami wyznaczającymi kierunek tej reakcji są moc użytego kwasu oraz jego względna ilość. Zaproponowano i przedyskutowano mechanizm reakcji.

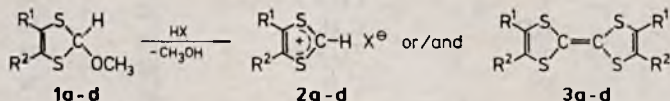
The reaction of 2-methoxy-1,3-dithioles (1) with acids, yielding 1,3-dithiolium salts (2) or 2,2'-bi(1,3-dithiolyliidenes) (3) or both, was studied. It was found that the direction of this reaction was determined by the strength and the proportion of the acid used. The proposed mechanism of reaction has been discussed.

The cleavage of 2-methoxy-1,3-dithioles (1) by acids has been the principal method of generation of 1,3-dithiolium carbenes (4) used in our studies on reactivity of these carbenes¹). Therefore we were interested in the more detailed knowledge of the course of the reaction of compounds 1 with acids. The literature data on this subject are scarce and mostly they contain only information of general character²⁻⁴). Moreover, some of reported results were not fully confirmed by us. Therefore, we submitted several differently substituted 2-methoxy-1,3-dithioles 1a-d to treatment with mineral and organic acids (HClO₄, CCl₃COOH, CH₃COOH) or with several 1,3-dithiolium salts. In this paper we wish to present the results of these experiments and compare them with the literature data. We would like, moreover, to discuss the course of the cleavage of 2-methoxy-1,3-dithioles by acidic reagents.

RESULTS

The experiments presented in this paper were performed on: 2-methoxy-4,5-dimethyl-1,3-dithiole (1a), 2-methoxy-4,5-diphenyl-1,3-dithiole (1b), 2-methoxy-4-phenyl-1,3-dithiole (1c) and 2-methoxybenzo-1,3-dithiole (1d). These compounds were treated with the following acids: perchloric acid, trichloroacetic acid and acetic acid.

Scheme 1



X = ClO₄, CCl₃COO, CH₃COO
 a: R¹=R²=CH₃, b: R¹=R²=C₆H₅, c: R¹=C₆H₅, R²=H,
 d: R¹R²=-CH=CH-CH=CH-

We have noticed that the conversion of compounds **1a—d** into corresponding 1,3-dithiolium⁺perchlorates **2a—d** ($X = ClO_4$) does not require an excess of strong acid as has been suggested previously for various 2-alkoxy-1,3-dithioles²⁻⁴). Treatment with an equimolar quantity of $HClO_4$ causes a complete transformation of compounds **1a—d** into perchlorates **2a—d**. On the other hand, in the reaction with smaller than equimolar quantity of $HClO_4$, compounds **1** are partly transformed into 2,2'-bi(dithiolylidenes) **3*** and partly into perchlorates **2**, the quantity of the perchlorate formed being exactly equivalent to that of the acid used; the latter experiments were performed only with 4,5-diphenyl derivative **1b**. Results of reactions with perchloric acid are presented in Table 1.

Table 1

Results of reactions of 2-methoxy-1,3-dithioles **1a—d** with perchloric acid 70% in CH_3CN

2-Methoxy-1,3-dithiole	Moles of $HClO_4$ per 1 mole of 1	Yields of products			
		1,3-dithiolium perchlorate	%	dimer	%
1a	1	2a	ca. 100	—	
1b	1	2b	97	—	
1b	0.5	2b	42	3b	51
1b	ca. 0.1	2b	12	3b	79
1c	1	2c	91	—	
1d	1	2d	91	—	

Thus, our results do not confirm the experiments reported by Pazdro and Polaczkowa⁸) who examined similar reactions with 2-methoxy-4,5-diphenyl-1,3-dithiole (**1b**), finding that this compound was transformed

Table 2

Results of reactions of 2-methoxy-1,3-dithioles **1a—d** with trichloroacetic acid

2-Methoxy-1,3-dithiole	Moles of acid per 1 mole of 1	Solvent	Time of reaction hrs.	Yields of product	
				dimer	%
1a	1	CH_3CN	1	3a	49
1a	0.1	C_6H_6	1	3a	95
1b	1	CH_3CN	1	3b	44
1b	1	CH_3CN	2	3b	55
1b	0.1	CH_3CN	1	3b	34
1b	0.1	CH_3CN	1	3b	62
1b	0.1	CH_3CN	5	3b	90
1b	0.1	C_6H_6	1	3b	6
1c	1	CH_3CN	1	3c	36
1c	0.1	C_6H_6	1	3c	ca. 1
1d	1	CH_3CN	1	3d	6
1d	0.1	C_6H_6	1	3d	

* Compounds of this type are commonly defined as dimers of 1,3-dithiolium carbenes **4**.

into dimer **4b** with the theoretical yield, on treatment with an equimolar quantity of HClO_4 .

The results of our experiments concerning the treatment of 2-methoxy-1,3-dithioles **1a—d** with trichloroacetic acid, presented in Table 2, do not differ essentially from the literature data³⁾: the products obtained in these reactions are dimers **3a—d**, respectively. As can be seen from data in Table 2, the transformation of compounds **1** into dimers **3** occurs more readily in benzene than in an acetonitrile solution. Furthermore, it appeared that the reaction was distinctly influenced by substituents in the 1,3-dithiole ring of compound **1**: it is evident that dimethyl derivative **1a** is the more reactive and benzo derivative **1d** is the less reactive one. Compounds **1a** and **1b** are quantitatively converted into dimers **3a** or **3b** by refluxing for 1 hr in benzene solution with a catalytic quantity of trichloroacetic acid.

Our next experiments have confirmed previous suggestions³⁾ that acetic acid may also transform 2-methoxy-1,3-dithioles **1a—d** into dimers **3a—d** (Table 3). However, each of these compounds reacts with acetic acid considerably more slowly than with trichloroacetic acid.

Table 3
Results of reactions of 2-methoxy-1,3-dithioles **1a—d** with acetic acid

2-Methoxy-1,3-dithiole	Moles of acid per 1 mole of 1	Time of reaction hrs	Yields of product	
			dimer	%
1a	1	1	3a	19
1b	1	1	3b	18
1b	1	2	3b	26
1b	0.1	3	3b	TLC
1c	1	1	3c	9
1d	1	1	—	—

We have also shown that 2-methoxy-1,3-dithioles **1a—d** can be transformed into respective dimers **3a—d** by treatment with 1,3-dithiolium perchlorates **2a—d**; the results of these experiments are presented in Table 4.

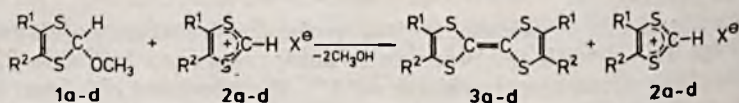
Table 4
Results of reactions of 2-methoxy-1,3-dithioles **1a—d** with 1,3-dithiolium perchlorates **2a—d** ($\text{X} = \text{ClO}_4$)

Substrates		Moles of salt 2 per 1 mole of 1	Time of reaction hrs	Yield of dimer 3 %*	Salt 2 recovered %
2-Methoxy-1,3-dithiole	1,3-Dithiolium perchlorate				
1a	2a	1	1	97	79
1b	2b	1	1	98	94
1b	2b	1	0.25	98	83
1b	2b	0.1	1	98	97
1b	2b	10	1	71	98
1c	2c	1	1	91	79
1d	2d	1	1	39**	96

* In relation to compound **1** used.

** Unchanged **1d** was shown by TLC and $^1\text{H NMR}$.

Scheme 2



The salts **2** are, seemingly, not consumed during this reaction and they are quantitatively recovered from the reaction products. For the compound **1b** additional tests were performed in which the following molar proportions of reagents **1b** and **2b** were used: 10:1, and 1:10. No evident effect on the degree of conversion of compound **1b** into dimer **3b** was observed.

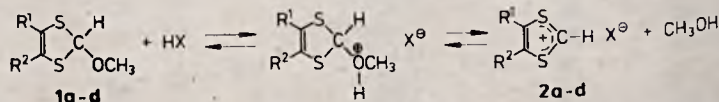
The following ¹H NMR spectra of 2-methoxy-1,3-dithioles **1a-d** in acetonitrile-D₃ solutions were recorded: (a) **1a-d** with HClO₄ in equimolar proportion, (b) **1b** with CCl₃COOH in equimolar proportion, (c) **1b** with a tenfold molar excess of CH₃COOH; results of this measurements are reported in Table 5. The spectra with perchloric acid (Nos 1-4, Table 5) have confirmed that compounds **1a-d** react immediately with this acid yielding 1,3-dithiolium perchlorates **2a-d** as the sole reaction products. Spectrum No 5 (Table 5) demonstrates that compound **1b** is partly converted into 1,3-dithiolium salt (**2b**, X = CCl₃COO) by trichloroacetic acid. The second product, formed together with this salt, is the dimer **3b**; it is, however, precipitated from the solution during measurement of the spectrum and for this reason it does not contain the signals derived from dimer **3b**. Similarly, precipitation of dimer **3b** has been observed during the measurement of spectrum of **1b** with acetic acid (spectrum No 6, Table 5). This spectrum contains only signals derived from **1b**, while none of signals corresponding to 4,5-diphenyl-1,3-dithiolium cation is observed. One may assume that in this case the salt **2b** (X = CH₃COO) is also formed, but its concentration is too low to be detectable by ¹H NMR spectrum measurement.

DISCUSSION

We think that the results of the foregoing experiments justify the advancement of the following two-stage course for the cleavage of 2-methoxy-1,3-dithioles **1** by acids.

The first stage of this cleavage involves protonation of methoxy group of compounds **1** by an acid and an instantaneous elimination of methanol molecule with formation of 1,3-dithiolium salts **2** (Scheme 3). This reaction

Scheme 3



is reversible and the position of equilibrium state is primarily determined by the strength of the acid used. Such a strong acid as HClO₄ reacts instantaneously with the whole quantity of compounds **1** to form perchlorates **2**. Thus, in presence of an equimolar quantity of HClO₄, the

Table 5

Results of measurements of ¹H NMR spectra of 2-methoxy-1,3-dithioles 1a-d in CD₃CN solution with acids (HX) added

No of spectrum	Compound 1	HX	Moles of HX per 1 mole of 1	Signals of protons in spectrum (δ, ppm)						
				derived from salt 2		derived from compound 1				
				H-C-2	others	H _{arom}	H-C-2	OCH ₃		
1	1a	HClO ₄ *	1	10.85	2.73	CH ₃				
2	1b	HClO ₄ *	1	11.18	7.44	H _{arom}				
3	1c	HClO ₄ *	1	11.19	9.22	H-C-5				
4	1d	HClO ₄ *	1	11.50	7.53-7.89	H _{arom}				
5**	1b	CCl ₃ CO ₂ H	1	11.15	7.06-7.45	H _{arom}		7.17	6.68	3.37
6**	1b	CH ₃ CO ₂ H	10		7.44	H _{arom}		7.18	6.69	3.37

* 70% HClO₄.

** Precipitation of dimer 3 was observed during measurements of spectra Nos 5 and 6.

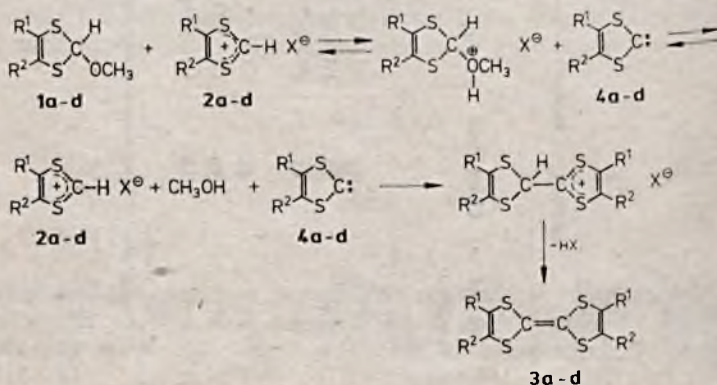
cleavage of 2-methoxy-1,3-dithioles stops at the stage, as demonstrated by ^1H NMR spectra (Table 5) as well as by isolation of perchlorates **2a-d** (Table 1).

Acids of moderate strength (CCl_3COOH) or relatively weak acids (CH_3COOH), on the other hand, react only partially with compounds **1** and a certain equilibrium is established. In such a case 2-methoxy-1,3-dithioles **1** and 1,3-ditholium salts **2** exist in the reaction mixture in proportion arising from the equilibrium position, i.e. depending upon the strength of HX, as demonstrated by ^1H NMR measurements (Table 5). Then, the second stage of cleavage of compounds **1** may be realized; it begins by the reaction between compounds **1** and **2** (Scheme 4). We believe that the 1,3-ditholium carbenes **4** are generated during this second stage of the reaction, which probably involves the following sequence of steps. First, the protonation of compounds **1** by salts **2** leads to formation of carbenes **4** and protonated compounds **1**, which eliminates a methanol molecule to form salts **2**. Next, the nucleophilic attack of carbenes **4** on salts **2**, followed by elimination of HX molecule, leads to formation of the final products, i.e. dimers **3**.

The validity of the above pathway of cleavage of 2-methoxy-1,3-dithioles **1** by acids HX, particularly of the second stage of this reaction, is confirmed by experiments resulting in the conversion of compounds **1** into dimers **3** by treatment with salts **2** (Table 4). In those reactions the salts used are nearly quantitatively recovered, probably owing to the fact that perchloric acid eliminated in the last step of the reaction leading to dimers **3** (cf. Scheme 4), as a very strong acid, reacts immediately with compounds **1** to yield perchlorates **2** (cf. Scheme 3). In consequence, despite continuous consumption of perchlorate **2**, the concentration of this salt in the reacting mixture remains constant during the reaction, due to its permanent and very fast regeneration.

The transformation of compounds **1** in presence of less than molar equivalent of perchloric acid used (Table 1) should be considered as fully analogous to the reaction of these compounds with perchlorates **2**. It is obvious that HClO_4 , as a very strong acid, reacts instantaneously with an equivalent quantity of compounds **1** to form salts **2** (Scheme 3), whereafter the reaction proceeds according to Scheme 4.

Scheme 4



Evidently, 2-methoxy-1,3-dithioles undergo fairly complex transformations in presence of acids, involving undoubtedly formation of salts 2 as well as that of carbenes 4. The generation of carbenes 4 takes place when protonation of compounds 1 by 1,3-dithiolium salts is possible at least at the same degree as protonation by acid HX used to initiate the cleavage of compounds 1. Thus the acid used should not be so strong as perchloric acid, since in this case a certain quantity of the dithiole substrate is transformed into 1,3-dithiolium perchlorate, but also not so weak as acetic acid because then the reaction runs very slowly. Trichloroacetic acid seems to be a suitable catalyst of the cleavage of compounds 1.

EXPERIMENTAL

¹H NMR spectra were determined on a Jeol JNM MN 100 spectrometer, using TMS ($\delta = 0$ ppm) as internal standard. Acetonitrile used was refluxed over and distilled from P₂O₅ and stored over molecular sieves.

Starting materials and standard samples

2-Methoxy-1,3-dithioles 1a-c were prepared by modification of the procedure described in³⁾.

A solution of 0.01 mole of 2-piperidine-4,5-dimethyl-1,3-dithiole⁵⁾ (or 2-piperidine-4,5-diphenyl-1,3-dithiole⁶⁾ or 2-piperidine-4-phenyl-1,3-dithiole⁶⁾) in 20 ccm of methanol, 10 ccm of acetic acid and 30 ccm of benzene was stirred and heated to 40°C for 3 hrs. Acetic acid was neutralized with triethylamine. After dilution with ca. 30 ccm of benzene the reaction mixture was washed with water several times and dried over MgSO₄. The solvent was evaporated in vacuum. The crude 2-methoxy-4,5-dimethyl-1,3-dithiole (1a) and purified by distillation under reduced pressure to yield 1.3 g (81%) of colorless oil, b.p. 70°C/1 mm Hg. ¹H NMR (CCl₄), δ : 1.91 (s, 6H), 3.10 (s, 3H), 6.45 (s, 1H).

Analysis:

For C₆H₁₀S₂O — Calcd.: 44.4% C, 6.2% H, 39.5% S;
found: 44.3% C, 6.1% H, 38.6% S.

The crude 2-methoxy-4,5-diphenyl-1,3-dithiole (1b) and 2-methoxy-4-phenyl-1,3-dithiole (1c) were crystallized from hexane to afford 2.3 g (80%) of colorless crystals, m.p. 75–76°C (Lit.³⁾: m.p. 78°C) and 1.8 g (87%) of yellow crystals, m.p. 60–61°C (Lit.²⁾: m.p. 61°C), respectively.

2-Methoxybenzo-1,3-dithiole (1d). A solution of 6.3 g (0.025 mole) of benzo-1,3-dithiolium perchlorate (2d, X = ClO₄) in 80 ccm of methanol was stirred at room temperature for 1 hr. Then 0.025 mole of triethylamine and a little of charcoal were added to the reaction mixture. After filtration, the solution was slowly added dropwise to ca. 200 ccm of ice water. The mixture was left standing in a refrigerator for 1 hr. The precipitate was filtered off, washed with ice water and dried over P₂O₅. The crude product was purified by crystallization from hexane to yield 4 g (86%) of colorless crystals, m.p. 37–38°C (Lit.⁴⁾: colorless oil solidified in a refrigerator, b.p. 80°C/0.5 mm Hg).

4,5-Dimethyl-1,3-dithiolium perchlorate (2a, X = ClO₄) was prepared as described in⁵⁾; m.p. 119–120°C.

4,5-Diphenyl-1,3-dithiolium perchlorate (2b, X = ClO₄, m.p. 186–187°C (decomp.), Lit.⁶⁾: m.p. 181°C) and 4-phenyl-1,3-dithiolium perchlorate (2c, X = ClO₄, m.p. 182–183°C (decomp.), Lit.⁶⁾: m.p. 179–180°C (decomp.)) were prepared by a modified procedure described in⁶⁾.

Benzo-1,3-dithiolium perchlorate (2d, X = ClO₄, m.p. 186–187°C (decomp.), Lit.⁷⁾: m.p. 185°C (decomp.)) was prepared by analogy to⁶⁾.

Standard samples of dimers 3a-d were prepared by treatment of respective 1,3-dithiolium perchlorate with triethylamine in acetonitrile solution: 2,2'-bi(4,5-dimethyl-1,3-dithiolydene) (3a), m.p. 240–243°C (Lit.⁸⁾: m.p. 244–245°C); 2,2'-bi(4,5-

-diphenyl-1,3-dithiolyldene) (3b), m.p. 262—263°C (Lit.¹⁰): m.p. 262—263°C); 2,2'-bi(4-phenyl-1,3-dithiolyldene) (3c), m.p. 196—198°C (Lit.¹¹): m.p. 202—206°C); 2,2'-bi(benzo-1,3-dithiolyldene) (3d), m.p. 236—238°C (Lit.⁷): m.p. 236—240°C).

Reactions of 2-methoxy-1,3-dithioles 1a—d

(a) With perchloric acid. A solution of 1 mmole of compound 1 in 10 ccm of acetonitrile with a definite quantity (Table 1) of 70% HClO₄ was refluxed for 1 hr. In the reactions of 1b with 0.5 mmole and 0.1 mmole of HClO₄ crystals of dimer 3b were precipitated. After cooling to room temperature, the solid was filtered off and washed with acetonitrile. The filtrate, or the reaction mixture, was concentrated to half its volume under reduced pressure and diluted with ca. 100 ccm of anhydrous diethyl ether. The precipitated perchlorates 2a—d (X = ClO₄) were filtered off and washed with diethyl ether. The obtained dimer 3b and perchlorates 2a—d (X = ClO₄) were identified by comparison with standard samples. Yields of products are listed in Table 1.

(b) With trichloroacetic acid. A solution of 1 mmole of compound 1 in 10 ccm of suitable solvent and a definite quantity of trichloroacetic acid was refluxed. Other experimental data are collected in Table 2. The reaction mixture was concentrated to half its volume under reduced pressure. Precipitated crystals of dimer 3 were filtered off and washed with acetonitrile. The filtrate was diluted with benzene, washed with water several times and dried over MgSO₄. After evaporation of solvent, to the residue 2 ccm of acetonitrile was added. The next portion of dimer 3 was filtered off. The filtrate was analyzed by TLC and ¹H NMR. In the reaction mixtures of compounds 1a and 1b with 0.1 mmole of CCl₃COOH in benzene unchanged substrates 1 were not observed. In other reactions compounds 1 were stated, but not isolated. The obtained dimers 3 were identified by comparison with standard samples (m.p. and TLC). Yields of dimers 3 are listed in Table 2.

(c) With acetic acid. Compounds 1a—d were treated with acetic acid in the same manner as above. Detailed experimental data are listed in Table 3.

(d) With 1,3-dithiolium perchlorates 2a—d (X = ClO₄). A solution of 1 mmole of compound 1 and 1,3-dithiolium perchlorate 2 (X = ClO₄) in 10 ccm of acetonitrile was refluxed (other experimental details are listed in Table 4). The reaction mixture was concentrated to half its volume under reduced pressure. The solid of dimer 3 was filtered off and washed with acetonitrile. The filtrate was diluted with anhydrous diethyl ether to precipitate perchlorate 2. The solid was filtered off, washed with diethyl ether. After evaporation of solvent, the residue was tested by TLC and ¹H NMR. Only in the reaction of 1d with 2d unchanged substrate 1d was stated. Moreover in all cases traces of dimers 3a—d were observed. The obtained dimers 3 and recovered salts 2 were identified by comparing them with standard samples (m.p. and TLC). Yield of products are listed in Table 4.

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