# Niobium(V) Chloride Catalyzed Oxidation of Dithioacetals with 30% Hydrogen Peroxide: A Concise Preparation of Bissulfonylmethylene Compounds

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# The oxidation of dithioacetals with 16eq of 30% hydrogen peroxide in the presence of 10 mol% niobium(V) chloride at room temperature provides bissulfonylmethylenes in high yields.

Key words niobium(V) chloride; hydrogen peroxide; oxidation; dithioacetal; bissulfonylmethylene

The bissulfonylmethylene compounds (1) can act as active methylene compounds, therefore, they are important building blocks in organic synthesis.<sup>1–4)</sup> Moreover, some of them (sulfonal, trional, and tetronal) are classical sedative-hypnotics<sup>5)</sup> (Fig. 1).

One of the representative methods for preparing **1** is the oxidation of dithioacetals (**2**, bissulfinylmethylenes) using potassium permanganate  $(\text{KMnO}_4)$ ,<sup>6)</sup> peracids  $(\text{RCO}_3\text{H})$ ,<sup>7,8)</sup> or dimethyldioxorane  $(\text{DMDO})^{9)}$  (Chart 1). These reactions have some drawbacks, such as producing large amounts of waste (for KMnO<sub>4</sub>), low chemoselectivity (for KMnO<sub>4</sub> and RCO<sub>3</sub>H), using explosive reagents (for RCO<sub>3</sub>H), and the need to prepare the reagent by troublesome methods prior to the reaction (DMDO).

We have been working on the oxidations of organosulfur compounds using hydrogen peroxide as the oxidant, and reported that the reaction of sulfides with 30% hydrogen peroxide in the presence of catalytic amounts of Nb(V),<sup>10)</sup> Ta(V),<sup>10,11)</sup> or niobium carbide (NbC)<sup>12)</sup> in methanol provided the corresponding sulfones in high yields (Chart 2).

We also found that the reaction of **2** with 30% hydrogen peroxide catalyzed by Nb(V)-NaI or Ta(V)-NaI in ethyl acetate effectively afforded the corresponding carbonyl compounds<sup>13,14</sup> (Chart 3). The use of iodide ion ( $\Gamma$ ) as the catalyst is essential to obtain the carbonyl compounds. Actually,



Fig. 1. Structures of Bissulfonylmethylene Compounds



Chart 1. Representative Methods for Preparing Bissulfonylmethanes

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the reaction of a dithioacetal with 30% hydrogen peroxide in the presence of only a catalytic amount of tantalum(V) chloride (without NaI) in aqueous acetonitrile did not proceed at all within 20 h.

During the further study of the reaction of 2 with 30% hydrogen peroxide catalyzed by Nb(V), Ta(V), or NbC, we found that 1 can be efficiently prepared from the reaction of 2 with 30% hydrogen peroxide in the presence of a catalytic amount of niobium(V) chloride in methanol (Chart 4).

### **Results and Discussion**

As we noted in the introduction, we found that methanol is the good solvent for the synthesis of sulfones from the oxidation of sulfides with 30% hydrogen peroxide catalyzed by Nb(V),<sup>10)</sup> Ta(V),<sup>10,11)</sup> or NbC.<sup>12)</sup> Therefore, the reactions of 2-methyl-2-(2-naphthyl)-1,3-dithiane (**2a**) with 16 eq of 30% hydrogen peroxide in methanol were examined in the presence of 0.1 eq of niobium or tantalum compounds (Table 1).

The desired compound (1a) was obtained in all cases accompanied by small amounts of the ketone (3a) (runs 1–6). Conversely, in the absence of catalysts, the reaction proceeded very slow and afforded complex mixtures (run 7). Among the



Chart 2. Oxidation of Sulfides with  $H_2O_2$  Catalyzed by Nb or Ta Compounds

$$\begin{array}{c} \overbrace{\substack{S\\S\\R^{1}\\2}}^{0.02 \text{ eq. NbCl}_{5} \text{ or } 0.1 \text{ eq. TaCl}_{5}, \\ 0.1 \text{ eq. Nal, 4 eq. 30\% H}_{2}O_{2} \\ \hline \\ EtOAc -H_{2}O, \text{ rt} \end{array} \xrightarrow{O}_{R^{1}} R^{2}$$

Chart 3. Deprotection of Dithioacetals with 30%  $\rm H_2O_2$  Catalyzed by NbCl\_5 (or TaCl\_5) and NaI



Chart 4. NbCl<sub>5</sub> Catalyzed Oxidation of Dithioacetals with 30% H<sub>2</sub>O<sub>2</sub>

#### Table 1. Examination of Niobium or Tantalum Catalysts



Run	Catalyst	Time –	<sup>1</sup> H-NMR ratio (%)	
			1a	3a
1	Nb(OEt) <sub>5</sub>	1 h 30 min	>99	Trace
2	Ta(OE) <sub>5</sub>	2 h 40 min	>99	Trace
3	NbCl <sub>5</sub>	2 h	93	7
4	TaCl <sub>5</sub>	19h	>99	Trace
5	NbC	25 h	98	2
6	TaC	94h 40 min	>99	Trace
7	—	192 h	Complex mixture	

Table 2. Examination of Solvents



Run	Solvent	Time —	<sup>1</sup> H-NMR ratio (%)	
			<b>1</b> a	3a
1	MeOH	2 h	93	7
2	MeCN	5h 15min	84	16
3	EtOAc	67 h	60	40
4	$CH_2Cl_2$	78 h	62	38
5	Toluene	143 h	63	37

Table 3. Examination of Amounts of 30% H<sub>2</sub>O<sub>2</sub>



Run	30% H <sub>2</sub> O <sub>2</sub> (eq)	Time (h) –	Isolated yield (%)	
			<b>1</b> a	3a
1	16	2	95	5
2	8	3	79	10
3	4	5	68	5

catalysts, niobium(V) ethoxide (run 1) and niobium(V) chloride (run 3) exhibited a strong catalytic activity. Niobium(V) chloride was chosen as the catalyst for the hydrogen peroxide oxidation of  $\mathbf{2}$ , and further reaction conditions were examined, because it is less expensive than niobium(V) ethoxide.

The oxidations of 2a with 30% hydrogen peroxide using niobium(V) chloride as a catalyst were examined in several solvents in order to evaluate the solvents effect. In solvents other than methanol, the reactions proceeded more slowly and afforded 1a in lower yields and accompanied by notable amounts of 3a (Table 2).

The amount of 30% hydrogen peroxide required to prepare the bissulfonylmethylene (1a) was further examined (Table 3). The reaction rates and the isolated yields decreased in the cases of 8 and 4 eq of 30% hydrogen peroxide.

Several dithioacetals were treated with 30% hydrogen peroxide in the presence of 10 mol% niobium(V) chloride in methanol to produce the desired bissulfonylmethylene compounds including sulfonal (sedative-hypnotic) in high yields (Table 4).

Although the reaction mechanism has not been totally clarified, the niobium(V) peroxide species might play important roles as in the cases of the niobium(V) catalyzed oxidation of sulfides with 30% hydrogen peroxide. The plausible reaction mechanism is depicted in Chart 5.

Niobium(V) chloride immediately reacts with water to form niobium(V) hydroxides. The resulting hydroxides react with hydrogen peroxide or methyl hydroperoxides (derived from the reaction of hydrogen peroxide with methanol) to produce niobium(V) peroxides. Because the niobium(V) compounds Table 4. Oxidation of Several Dithioacetals with 30%  $\rm H_2O_2$  Catalyzed by  $\rm NbCl_s$ 

	R' R" NbCl <sub>5</sub> 0.1 eq. 30% H <sub>2</sub> O <sub>2</sub> 16 eq MeOH, r.t.	$ \xrightarrow{O_{R}^{R}} \xrightarrow{P_{R}^{R}} \xrightarrow{O_{R}^{S}} \xrightarrow{S_{R}^{S}} O_{R'}^{S} \xrightarrow{S_{R''}^{S}} O $	
Entry	Product	Time	Yield (%)
1		2 h	95
2	$\overset{O}{\underset{CH_3}{\overset{C_2H_5}}{\overset{C_2H_5}{\overset{C_2H_5}}{\overset{C_2H_5}}{\overset{C_2H_5}}{\overset{C_2H_5}}{\overset{C_2H_5}}{\overset{C_2H_5}}{\overset{C_2H_5}}{\overset{C_2H_5}}{\overset{C_2H_5}}{\overset{C_2H_5}}{\overset{C_2H_5}}{\overset{C_2H_5}}{\overset{C_2H_5}}{\overset{C_2H_5}}}{\overset{C_2H_5}}}{\overset{C_2H_5}}{\overset{C_2H_5}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}$	9h 30min	86
3	$\begin{array}{c} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ CH_3 \\ CH_3 \\ \end{array} \begin{array}{c} C_2H_5 \\ 0 \\ S \\ CH_3 \\ CH_3 \\ \end{array} \begin{array}{c} 0 \\ S \\ S \\ CH_3 \\ \end{array} \begin{array}{c} 0 \\ S \\ S \\ CH_3 \\ CH_3$	3 h	72
4	$\overset{C_2H_5}{\overset{I_2H_5}{\overset{C_2}{\overset{C_2H_5}{\overset{C_2}{\overset{C_2H_5}{\overset{C_2}{\overset{C_2}{\overset{C_2}{\overset{C_2H_5}{\overset{C_2}}{\overset{C_2}{\overset{C_2}{\overset{C_2}}{\overset{C_2}{\overset{C_2}}{\overset{C_2}{\overset{C_2}}{\overset{C_2}{\overset{C_2}}{\overset{C_2}{\overset{C_2}}{\overset{C_2}{\overset{C_2}}{\overset{C_2}}{\overset{C_2}{\overset{C_2}}{\overset{C_2}}{\overset{C_2}{\overset{C_2}}{\overset{C_2}}{\overset{C_2}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}$	1 h 10 min	98
5	O B H H H H	2h 15min	85



Chart 5. Plausible Reaction Mechanism

act as a Lewis acid,<sup>10,11)</sup> the methanol coordinates with the metal peroxides to produce niobium(V) peroxide complexes. These peroxide complexes oxidize dithioacetals and revert back to the niobium(V) hydroxides (or a complex with the solvent). The resulting niobium(V) hydroxides then react with peroxide to reform the niobium(V) peroxide complexes.

#### Conclusion

The bissulfonylmethylene compounds (1) can be prepared by the oxidation of thioacetals with 30% hydrogen peroxide in the presence of a catalytic amount of niobium(V) chloride in methanol.

## Experimental

All reagents were commercially obtained from Nacalai Tesque, Inc., Wako Pure Chemical Industries, Ltd., Kanto Chemical Co., Inc., Kishida Chemical, Co., Ltd., Tokyo Chemical Industry, Co., Ltd. and Sigma-Aldrich Corp., and used without further purification. Melting points were measured using a Yanaco micromelting point apparatus (MP-J3) and are uncorrected. The <sup>1</sup>H- and <sup>13</sup>C-NMR spectra were recorded by a JEOL (JNM-EX400) spectrometer as solutions in CDCl<sub>3</sub> using tetramethylsilane (TMS) or the residual CHCl<sub>3</sub> peak as the internal standard. The IR spectra were recorded

using a Jasco IR-8300 FT-IR spectrophotometer. The mass spectra were recorded on a Shimadzu GCMS-QP1100EX spectrometer.

Oxidation of Dithioacetals to Bissulfonylmethylenes; General Procedure To a stirred solution of a dithioacetal (1 mmol) in methanol (6 mL) was added niobium(V) chloride (27 mg, 0.1 mmol) and 30% hydrogen peroxide (1.6 mL, 16.0 mmol), then the mixture was stirred at r.t. The reaction was monitored by TLC. After the dithioacetal disappeared from the TLC, sat. aq. sodium thiosulfate (20 mL) was added, and the resulting mixture was extracted with dichloromethane (20 mL×2). The extract was dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel column chromatography (hexane–EtOAc) to afford the 1,3-bissulfonylmethylenes.

**2-Methyl-2-naphthalen-2-yl-[1,3]dithiane 1,1,3,3-Tetraoxide** Colorless crystals; mp 182–183°C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 2.25 (3H, s), 2.31–2.42 (1H, m), 2.51–2.57 (1H, m), 3.20–3.28 (2H, m), 3.57–3.62 (1H, m), 3.76–3.84 (1H, m), 7.56–7.62 (2H, m), 7.95–7.98 (1H, m), 8.01–8.05 (3H, m), 8.40 (1H, s). <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$ : 10.71, 16.93, 46.35, 46.41, 82.38, 126.62, 127.03, 127.20, 127.45, 127.48, 127.83, 128.65, 131.25, 132.99, 133.56. IR (KBr) cm<sup>-1</sup>: 1559, 1314, 1136, 1056. MS (*m/z*): 324 (M<sup>+</sup>). HR-MS Calcd for C<sub>15</sub>H<sub>17</sub>O<sub>4</sub>S<sub>2</sub> (M<sup>+</sup>+H): 325.0568. Found: 325.0559.

**2,2-Bis(ethanesulfonyl)propane** (Sulfonal)<sup>6)</sup> Colorless crystals; mp 126–128°C (lit.<sup>6)</sup> 124–125°C). <sup>1</sup>H-NMR (acetone- $d_6$ )  $\delta$ : 1.37 (6H, t, J=7.5Hz), 1.76 (6H, s), 3.47 (4H, q, J=7.5Hz). <sup>13-</sup>C-NMR (acetone- $d_6$ )  $\delta$ : 4.44, 16.22, 43.91, 81.16. IR (neat) cm<sup>-1</sup>: 3425, 1633, 1304, 1107. MS (m/z): 228 (M<sup>+</sup>), 135, 95, 77, 59.

**1,1-Bis(ethanesulfonyl)ethane**<sup>6)</sup> Colorless crystals; mp 75–76°C (lit.<sup>6)</sup> 74–75°C). <sup>1</sup>H-NMR (acetone- $d_6$ )  $\delta$ : 1.37 (6H, t, J=7.3 Hz), 1.77 (3H, d, J=7.3 Hz), 3.37–3.52 (4H, m), 4.84 (1H, q, J=7.3 Hz). <sup>13-</sup>C-NMR (acetone- $d_6$ )  $\delta$ : 4.85, 8.21, 46.28, 73.50. IR (neat) cm<sup>-1</sup>: 1313, 1127. MS (m/z): 214 (M<sup>+</sup>), 122, 94, 66.

**1,1-Bis(ethanesulfonyl)methane**<sup>6)</sup> Colorless crystals; mp 101–103°C (lit.<sup>6)</sup> 100–101.5°C). <sup>1</sup>H-NMR (acetone- $d_6$ )  $\delta$ : 1.38 (6H, t, J=7.6Hz), 3.44 (4H, q, J=7.6Hz), 4.98 (2H, s). <sup>13</sup>C-NMR (acetone- $d_6$ )  $\delta$ : 5.31, 48.26, 66.63. IR (neat) cm<sup>-1</sup>: 3452, 1635, 1316, 1129, 1050. MS (m/z): 200 (M<sup>+</sup>), 108, 80.

**Bis(benzenesulfonyl)methane**<sup>6)</sup> Colorless crystals; mp 121–122°C (lit.<sup>6)</sup> 117–119°C). <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 5.38 (2H, s), 7.64 (4H, t, *J*=7.5 Hz), 7.77 (2H, t, *J*=7.5 Hz), 7.96 (4H, d, t, *J*=7.5 Hz). <sup>13</sup>C-NMR (acetone-*d*<sub>6</sub>)  $\delta$ : 73.11, 128.82, 129.23, 134.50, 139.41. IR (neat) cm<sup>-1</sup>: 3616, 3235, 1642, 1328, 1152. MS (*m/z*): 142 (M<sup>+</sup>–2×C<sub>6</sub>H<sub>5</sub>–H), 107, 91, 77.

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