

## Pyrylium Salt Sensitized Photochemical Deprotections of Dithioacetals and Ketals

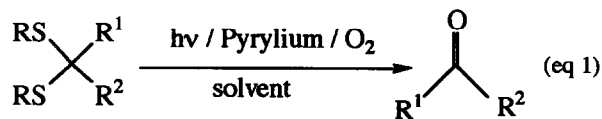
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**Abstract:** Photoreactions of various dithioacetals and ketals using tris(*p*-chlorophenyl)pyrylium perchlorate as a sensitizer were studied. Irradiation ( $\lambda > 360$  nm) of dichloromethane solutions containing dithioacetals or ketals and pyrylium salt afforded the corresponding carbonyl compounds in good to excellent yields in the presence of molecular oxygen.

### INTRODUCTION

Protection and deprotection are essential requirements for multistep organic synthesis.<sup>1</sup> Since dithioacetals and ketals are often used as masked carbonyls, several methods for the deprotection of these compounds have been developed.<sup>2</sup> Among those is an electrochemical oxidation which is promoted by the sequence of electron transfer and carbon-sulfur bond cleavage followed by hydrolysis.<sup>3</sup> Based on the results from the electrochemical studies and those from the studies on photoinduced electron transfer (PET) reactions of organosulfur compounds,<sup>4</sup> we expected that PET process could be useful for the deprotections of dithioacetals and ketals. Our expectation has been proved to be correct by the studies conducted by others<sup>5</sup> and ourselves.<sup>6</sup> Our preliminary mechanistic study on the 2,4,6-triphenylpyrylium salt sensitized photoreactions of aromatic dithianes and dithiolanes demonstrated that the key step of this oxidative deprotection is the trapping of intermediate carbon radicals by molecular oxygen.<sup>6a</sup> Now, we would like to report the synthetic generality and limitation of the pyrylium salt sensitized photochemical deprotections of dithioacetals and ketals (eq 1).



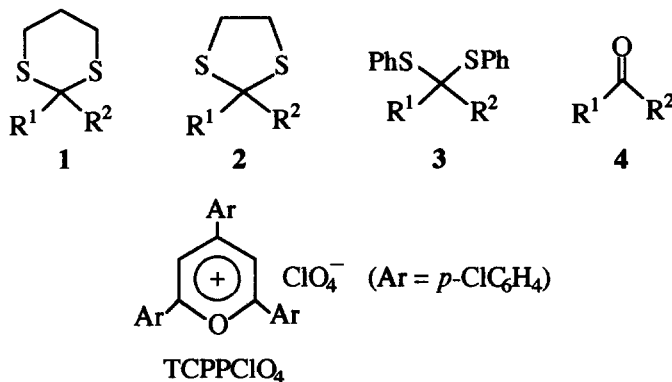


Figure 1

## RESULTS AND DISCUSSION

### Photochemical Deprotections

We chose 2,4,6-tris(*p*-chlorophenyl)pyrylium perchlorate (TCPPClO<sub>4</sub>) as a photosensitizer whose absorption band reaches visible region ( $\lambda_{\text{max}} = 370$  and  $416$ ,  $\epsilon = 25100$  and  $34400$  in CH<sub>3</sub>CN, respectively).<sup>7</sup> Substrates studied here, aromatic and aliphatic dithianes, dithiolanes, and diphenyldithioacetals, have the oxidation potentials typically between 1.0~1.6 V (vs. SCE). Therefore, single electron transfer from these compounds to the excited singlet state of TCPPClO<sub>4</sub> is considered to be highly exothermic.<sup>8</sup> In a typical experiment, irradiation ( $\lambda > 360$  nm) of an oxygen purged CH<sub>2</sub>Cl<sub>2</sub> solution of TCPPClO<sub>4</sub> and dithiane **1a** for 2 h resulted in the formation of the ketone **4a** in 95%. In the absence of light, no **4a** was obtained after 24 h. On the other hand, only small amounts of **4a** (1~3%) were isolated under the nitrogen purged conditions. Interestingly, addition of water into the solution did not increase the yields of **4a** (1~4%), which was a remarkable contrast to the other PET reactions.<sup>5</sup> Photoreaction in CH<sub>3</sub>CN similarly gave **4a** (2h, 96%), which was accelerated by addition of Mg(ClO<sub>4</sub>)<sub>2</sub> (1h, 96% of **4a**). However, we found that the photoreaction time in CH<sub>2</sub>Cl<sub>2</sub> was usually shorter than that in CH<sub>3</sub>CN.

In order to determine the generality and limitation of this method, we subjected various dithianes **1** and dithiolanes **2** to TCPPClO<sub>4</sub> sensitized photooxygenation reactions in CH<sub>2</sub>Cl<sub>2</sub>. As shown in Table 1, both dithianes and dithiolanes of ketones (**1a**~**1h**, **2a**, **2b**, and **2d**) were converted to the corresponding carbonyl compounds in good to excellent yields. On the other hand, the yields of aldehydes obtained from deprotections of dithianes and dithiolanes (**1i**~**1l**, **2i**~**2l**) were relatively low under the similar conditions. Particularly, photoreactions of dithianes of aliphatic nonconjugated aldehydes such as **1j** and **1k** required longer irradiation time and gave complicated product mixtures which contained less than 15% of desired carbonyl compounds. This observation is not due to the efficiency of the PET process between the dithianes and the excited TCPPClO<sub>4</sub> since there is no marked difference of the oxidation potentials among **1j**, **1k** and

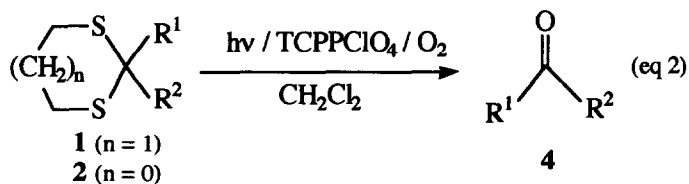


Table 1. TCPPClO<sub>4</sub> Sensitized Photo-deprotections of Dithianes **1** and Dithiolanes **2** in Dichloromethane.

Substrate	R <sup>1</sup>	R <sup>2</sup>	E <sub>p</sub> <sup>ox</sup> /V vs SCE	Time/min	Yield of <b>4</b> /%
<b>1a</b>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	1.14	120	95
<b>1b</b>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	Me	1.08	100	72
<b>1c</b>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Me	1.12	240	59
<b>1d</b>	PhCH <sub>2</sub> CH <sub>2</sub>	Me	1.07	180	75
<b>1e</b>	<i>n</i> -C <sub>13</sub> H <sub>27</sub>	Me	1.03	240	64
<b>1f</b>	-(CH <sub>2</sub> ) <sub>2</sub> CHPh(CH <sub>2</sub> ) <sub>2</sub> -		1.06	420	63
<b>1g</b>	PhCOCH <sub>2</sub>	Me	1.06	180	88
<b>1h</b>	PhCH=CH	Me	1.15	90	50
<b>1i</b>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	H	1.05	90	68
<b>1j</b>	PhCH <sub>2</sub> CH <sub>2</sub>	H	1.08	360	13
<b>1k</b>	<i>n</i> -C <sub>11</sub> H <sub>23</sub>	H	1.10	300	14
<b>1l</b>	PhCH=CH	H	1.05	90	74
<b>2a</b>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	1.55	30	90
<b>2b</b>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	Me	1.57	60	50
<b>2d</b>	PhCH <sub>2</sub> CH <sub>2</sub>	Me	1.49	120	66
<b>2i</b>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	H	1.48	18	39
<b>2j</b>	PhCH <sub>2</sub> CH <sub>2</sub>	H	1.64	90	35
<b>2l</b>	PhCH=CH	H	1.64	60	41

other dithianes. Instead, subsequent bond cleavage processes of dithiane cation radicals would be more important to govern the overall reaction progress. We were also interested in knowing the possibility if the substrates undergo undesired photoreactions competing with deprotections when they possess both dithioacetal parts and the other photo-labile parts. Aryl substituted C-C double bond is known to be a reactive structure to PET oxygenation.<sup>7a</sup> However, styryl substituted dithianes **1h**, **1l** and dithiolane **2l** did not seriously decompose and were converted to the corresponding carbonyl compounds in moderate yields.

Finally, diphenyldithioacetals **3** were found to be more reactive than **1** and **2** as indicated by shorter reaction time and higher yields of carbonyl compounds (Table 2). In these reactions, substantial amount of diphenyldisulfide (59-74%) were also isolated. Better reactivity of **3** is probably attributed to the ease of C-S bond cleavage in its cation radical.<sup>9</sup> Particularly, the yield of **4j** has been much improved by the use of dithiophenyl protecting group instead of dithioalkyl protecting groups (compare **3j** in Table 2 with **1j** and **2j** in Table 1). Another notable observation is that the reaction of **3a** proceeded at some extent even under the deoxygenated conditions (1 h, 22% of **4a** at 44% conversion of **3a**). We suspected that the moisture in the reaction solution is an oxygen source for the formation of **4a**. Indeed, addition of water (1 ml) to the solution increased both the conversion of **3a** (100%) and the yield of **4a** (44%). This result clearly suggests the generation of benzylic cation intermediate which reacts with water in the reactions of **3**.<sup>5</sup>

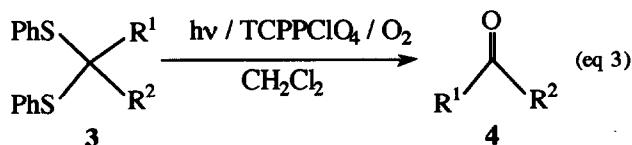
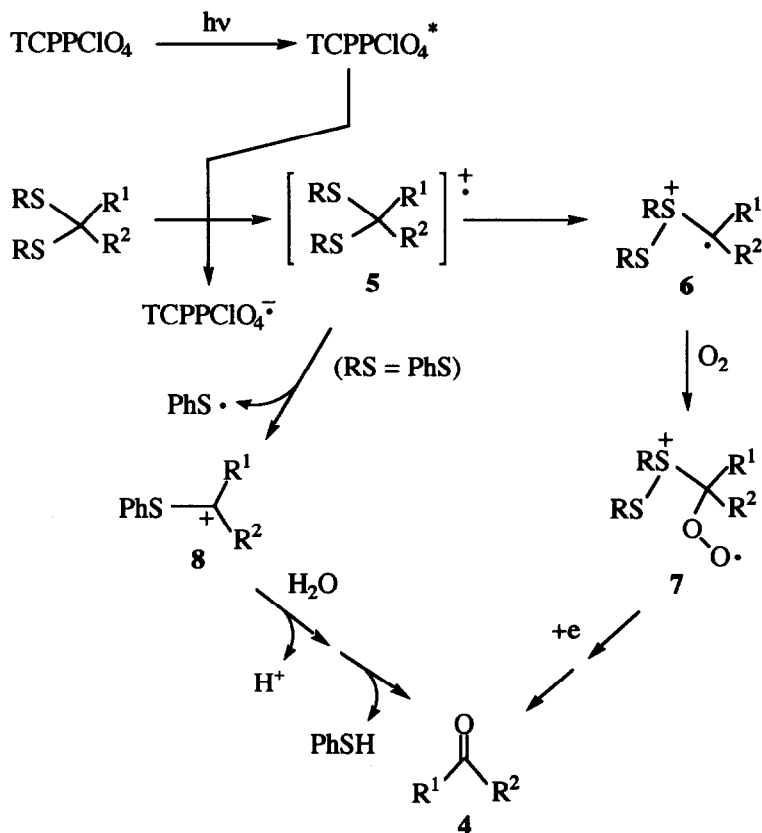


Table 2. TCPPClO<sub>4</sub> Sensitized Photo-deprotections of Diphenyldithioacetals **3** in Dichloromethane.

Substrate	R <sup>1</sup>	R <sup>2</sup>	E <sub>p</sub> <sup>ox</sup> /V vs SCE	Time/min	Yield of <b>4</b> /%
<b>3a</b>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	1.47	18	96
<b>3d</b>	PhCH <sub>2</sub> CH <sub>2</sub>	Me	1.59	12	74
<b>3i</b>	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	H	1.48	12	83
<b>3j</b>	PhCH <sub>2</sub> CH <sub>2</sub>	H	1.48	24	83
<b>3l</b>	PhCH=CH	H	1.45	12	73

### Mechanism

On the basis of the results obtained in this and related studies,<sup>6</sup> the reaction mechanism in Scheme 1 is proposed. Single electron transfer from the substrate to the excited state of TCPPClO<sub>4</sub> gives the cation



radical intermediate **5**. Acceleration of the reaction by the addition of  $\text{MgClO}_4$  is attributed to the efficient formation of **5** through the suppression of the back electron transfer from **5** to pyryl radical.<sup>10</sup> The formed cation radical **5** undergoes carbon-sulfur bond cleavage in dual fashion depending on the structure of **5**. Usually, bond cleavage of **5** gives a sulfonium part and a carbon radical part as shown in **6**. The radical part of **6** is captured by molecular oxygen to give the peroxy radical **7** which rearranges to the carbonyl compound **4** through another electron transfer step. In the case of **3**, it is also probable that the cation radical **5** can release phenylthio radical to form the carbocation **8**. The formed cation **8** is attacked by water and finally converted to the carbonyl compound **4**. Although both dimerization of phenylthio radical and fragmentation of **7** can produce diphenyldisulfide, the latter process would be more probable under the photooxygenation conditions without water.

## CONCLUSION

We have found that triarylpyrylium salt is an efficient photosensitizer for the deprotection reactions of dithioacetals and ketals. Photosensitized conditions described above must be synthetically attractive since, i) a catalytic amount of oxidant is sufficient, ii) visible light which is safe for most of organic compounds is used, iii) triarylpyrylium salt is easily prepared and its redox ability can be controlled by proper substitution. A mechanistically important issue associated with this chemistry is the selectivity of carbon-sulfur bond cleavage in the cation radical intermediates (carbon radical or carbocation formation). Further studies in this area will hopefully provide a chance to understand mechanistic details of sulfur containing cation radicals and to develop synthetically useful PET reactions of organosulfur compounds.

## EXPERIMENTAL

*General.* The dithioacetals and ketals **1**, **2**, and **3** were prepared from the corresponding carbonyl compound and the thiol by using FeCl<sub>3</sub>-silica gel in dichloromethane according to the procedure reported by Patney.<sup>11</sup> Typical experiment is described below. Diphenyldithioacetal **3a** was prepared by the modified procedure of the reported methods<sup>12,5d</sup> using BF<sub>3</sub>-etherate in benzene (see below). Purifications of these compounds were accomplished either by column chromatography on silica gel (Wako gel C-300) or recrystallization from ethanol. The photoproducts were identified by direct comparison of their spectroscopic data with those of authentic samples. Acetonitrile was distilled twice from phosphorous pentoxide and then from calcium hydride. Dichloromethane was washed with sulfuric acid and water, and distilled from calcium hydride. Redox potentials were measured for an acetonitrile solution containing tetraethylammonium perchlorate (0.1 M) at a scan rate of 100 mV/s on a BAS CV-1B using SCE as a reference electrode.

*Synthesis of 1a.* A mixture of anhydrous iron (III) chloride (1.62g)-silica gel (8.38g) was added to an ice cooled solution of 4,4'-dimethylbenzophenon (4.21 g, 20 mmol) and ethandithiol (3.25 g, 30 mmol) in dry dichloromethane (50 ml). The reaction mixture was stirred for 3 h at room temperature and then filtered through Celite. The filtrate was washed with 2% aqueous NaOH (30 ml x 3), water (30 ml x 3), and then dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the crude product was purified by column chromatography on silica gel to give **1a** (5.48 g, 92%) as colorless prisms (mp. 135°C).

*Synthesis of 3a.* BF<sub>3</sub>-etherate (15 ml, 118 mmol) was added to a solution of 4,4'-dimethylbenzophenon (4.21 g, 20 mmol) and benzenethiol (10.69 g, 97 mmol) in dry benzene (70 ml) over a period of 5 min. The reaction mixture was stirred for 24 h at room temperature and then hydrolyzed with aqueous NaHCO<sub>3</sub>. The resulting mixture was extracted with ether (50 ml x 3). The extracts were washed with water and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the crude product was purified by column chromatography on silica gel to give **3a** (6.972 g, 78%) as colorless prisms (mp. 115°C).

**Modified Synthetic Procedure for 2,4,6-Tris(*p*-chlorophenyl)pyrylium perchlorate:**<sup>13</sup> A mixture of 8.63 g (0.02 mol) of 1,3,5-tris(*p*-chlorophenyl)pentane-1,5-dione,<sup>14</sup> 4.16 g (0.02 mol) of chalcone, and 7.0 g of 60% perchloric acid was heated at reflux for 1 h. After cooling to 50°C, the mixture was diluted with 50 ml of ethanol and chilled. The precipitates were collected by filtration and recrystallized from acetonitrile to give 3.41 g (33 % yield) of TCPPClO<sub>4</sub> as yellow-orange prisms: mp 336°C (dec.); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) δ 7.88 (m, 6H), 8.63 (m, 6H), 9.20 (s, 2H). IR (KBr) 3107, 3077, 1620, 1584, 1508 cm<sup>-1</sup>. Anal. Calcd for C<sub>23</sub>H<sub>14</sub>Cl<sub>4</sub>O<sub>5</sub>: C, 53.93; H, 2.75. Found: C, 54.10; H, 2.64. E<sub>1/2</sub><sup>red</sup> = -0.27 V.

**Photochemical Deprotections.** A dichloromethane (50 ml) solution of the dithioacetal or the ketal (1.0 mmol) and TCPPClO<sub>4</sub> (0.05 mmol) was irradiated in a Pyrex tube immersed in a water bath with a 2 kW xenon lamp through a Toshiba glass cut filter (λ>360 nm). The solution was bubbled with oxygen before and during irradiation. The reaction progress was monitored by silica gel TLC. Concentration of the photolysate followed by silica gel TLC using CH<sub>2</sub>Cl<sub>2</sub>-*n*-hexane (1:1 ~ 1:3 v/v) as eluent afforded the carbonyl compounds.

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8. The estimated reduction potential of the excited TCPPClO<sub>4</sub> is 2.6 V (vs SCE).
  9. a) Bond dissociation energies for alkylphenylsulfides are known to be about 10 kcal/mol lower than those for dialkylsulfides: 66.4 kcal/mol for Et-SPh; 76.4 kcal/mol for Et-SMe.<sup>9b</sup> b) Wayner, D. D. M.; Griller, D. In *Advances in Free Radical Chemistry*; Tanner, D.D. Ed.; JAI Press Inc.: Greenwich, 1990; Vol. 1; pp. 159-192.
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