

## An Efficient and Mild Oxidation of Thiols to Disulfides with Tributylammonium Chlorochromate

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Various kinds of aliphatic and aromatic thiols are converted into the corresponding disulfides by tributyl ammonium chlorochromate in excellent yields under different reaction conditions.

**Key Words:** Tributyl ammonium chlorochromate, Thiol, Oxidation, Disulfide, Microwave.

### INTRODUCTION

There is continued interest in the development of new chromium(VI) reagents for the effective and selective oxidation of organic substrates, in particular thiols, under mild conditions. Disulfides are one of the most important organic sulfur compounds possessing an exclusive chemistry both in biochemistry<sup>1</sup> and in synthetic area<sup>2</sup>. Disulfides are also key intermediates in a wide variety of organic synthetic routes<sup>3-5</sup>. Sweetening of catalyst poisons thiols to low volatile disulfides in oil industries<sup>6,7</sup> and also industrial applications of disulfides in vulcanization of rubbers and elastomers led us to investigate the introduction and applications of new member of chromium reagents in oxidation of thiols to the corresponding disulfides. In this respect, we wish to report that tributylammonium chlorochromate (TriBACC) able to oxidize thiols to their disulfides efficiently under different reaction conditions.

### EXPERIMENTAL

#### Preparation of tributylammonium chlorochromate (TriBACC)

Chromium(VI) oxide (10.0 g, 0.10 mol) was dissolved in water in a beaker and hydrochloric acid (2.51 mL, 0.15 mol) was added with stirring at 0°C. To the resultant clear orange solution, tributylamine (23.5 mL, 0.10 mol) was added dropwise with stirring to this solution over a period of 0.5 h and stirring was continued for 0.5 h at 0-4°C. The precipitated orange solid was isolated by filtration, washed with anhydrous ether (3 × 60 mL) and dried in vacuum for 2 h at room temperature. Yield: 22.82 g (71%); m.p. 126°C. C<sub>12</sub>H<sub>28</sub>CrNO<sub>3</sub>Cl: Calcd. (%): C 44.79, H 8.70, N 4.35. Found

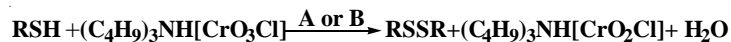
(%): C 44.59, H 8.81, N, 4.38. IR (KBr,  $\text{cm}^{-1}$ ): 898  $\nu_1(\text{A}_1)$  or  $\nu(\text{CrO}_3)$ , 436  $\nu_2(\text{A}_1)$  or  $\nu(\text{Cr-Cl})$ , 940  $\nu_4(\text{E})$  or  $\nu(\text{CrO}_3)$ . UV/visible,  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR were all consistent with the TriBACC structure. The above procedure can be scaled up to larger quantities, if desired. The pH of 0.01 M solution of TriBACC in water was 2.9.

### General procedure for oxidative coupling of thiols

To a stirred suspension of tributylammonium chlorochromate (1 mmol) in dichloromethane (*ca.* 5 mL), a solution of the substrate in the minimum amount of dichloromethane was added dropwise, the molar ratio of substrate to the oxidant being 1:2. (The mixture was irradiated for the time indicated in the table by microwave radiation). The completion of the reaction is followed by UV/Visible and TLC using ether/petroleum ether (60/40) as eluant. The mixture was diluted with ether (1:1 v/v) and filtered through a short column of silica gel to give a clear solution. The solution was evaporated and the residual product purified by distillation, recrystallization or column chromatography. The filtrate was washed with water ( $3 \times 10$  mL) and dried. On evaporation the corresponding disulfide is obtained. The progress of the reactions was also monitored and checked by UV/visible spectrophotometry. The amount of the oxidant during the reaction was measured spectrophotometrically at 356 nm. A very small magnetic stirrer was designed at the cell (10 mm quartz cell) compartment just in the bottom of sample cell in the spectrophotometer to stir up the solution under study in cell. The reaction mixtures remained homogenous in the solvent system used.

## RESULTS AND DISCUSSION

Among several methods of preparing disulfides, most methods involve oxidation of thiols. Oxidation of thiols to disulfides is an important process in organic chemistry and biochemistry, which has been extensively investigated over the years. TriBACC is an easily prepared reagent, but there is no examples of its applications in organic synthesis recorded. The oxidative coupling of thiols with this reagent was investigated in dichloromethane at room temperature and in dichloromethane solution under microwave radiation. A series of aliphatic and aromatic thiols were reacted with 0.5 molar equivalent of the reagent to afford the corresponding disulfides in excellent yields (Table-1). This oxidation was also performed under microwave radiation with 0.5 molar equivalent of the reagent. The results show that under microwave radiation, the reaction times are shorter. This advantage makes this procedure as a valuable method of preparation of disulfides (**Scheme-I**).



**A: Dichloromethane, Room Temperature**

**B: Dichloromethane, Room Temperature, Microwave**

### Scheme-I

TABLE-1  
OXIDATIVE COUPLING OF THIOLS WITH TriBACC IN SOLUTION AND  
MICROWAVE CONDITIONS

Substrate	Time (min)	Product	Yield (%)	Solution under microwave	
				Time (min)	Yield (%)
	150		91	15	90
$n\text{-C}_5\text{H}_{11}\text{-SH}$	120	$\text{C}_5\text{H}_{11}\text{-S-S-C}_5\text{H}_{11}$	87	12	89
$n\text{-C}_8\text{H}_{17}\text{-SH}$	80	$\text{C}_8\text{H}_{17}\text{-S-S-C}_8\text{H}_{17}$	91	8	94
	152		89	18	87
$\text{HOOC-CH}_2\text{-SH}$	212	$\text{HOOC-CH}_2\text{-S-S-CH}_2\text{-COOH}$	85	23	86
	38		92	5	93
	34		89	4	90
	50		92	10	87

In conclusion, the TriBACC acts as a simple, efficient and fast oxidizing reagent for coupling thiols. The easy procedure, simple work-up, the easy preparation of the reagent, short reaction times and excellent yields of the products will make this reagent a useful addition to available oxidant. It should also be emphasized that the reactions could be performed cleanly and controlled to stop at the disulfide stage. Over-oxidation has not been observed, even when the reactions were carried out in different conditions.

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