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## Fast and highly efficient oxidative coupling of thiols by *o*-xylylene bis (triphenylphosphonium) dichromate under solvent-free conditions

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### ABSTRACT

A fast and efficient solid state method for the chemoselective room temperature oxidative coupling of thiols to afford their corresponding disulfides using *o*-xylylene bis (triphenylphosphonium) dichromate as reagent is described. The reaction was applicable to a variety of thiols for giving high yields after short reaction times. Comparison of time/yield ratios of this method with some of those reported in the literature shows the superiority of this reagent over others under these conditions.

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### KEYWORDS

Solid state reaction;

Oxidation;

*o*-XBTPPDC;

Thiols;

Disulfides.

### INTRODUCTION

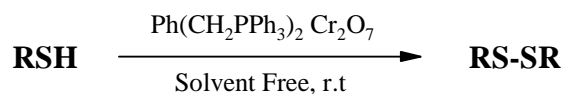
The selective oxidation of thiols to disulfides is of biological and synthetic interest<sup>[1]</sup>. Thiols can be readily overoxidised so that many studies have been carried out for their controlled oxidation<sup>[2]</sup>. Thus, a number of oxidising agents such as oxygen<sup>[3]</sup>, barium permanganate<sup>[4]</sup>, iodine–hydrogen iodide<sup>[5]</sup>, aqueous HIO<sub>3</sub><sup>[6]</sup>, (NO<sub>3</sub>)<sub>3</sub>CeBrO<sub>3</sub><sup>[7]</sup>, sodium perborate<sup>[8]</sup>, pyridinium chlorochromate<sup>[9]</sup>, MnO<sub>2</sub>–HCl<sup>[10]</sup>, Caro's acid supported on silica gel<sup>[11]</sup>, and CuNO<sub>3</sub>·3H<sub>2</sub>O<sub>12</sub> have been used to oxidise thiols to disulfides. However some of the reported methods suffer from disadvantages such as prolonged reaction time, toxicity or high cost of the required reagent(s), unfavorable conditions for preparing the reagent(s), over-oxidation, unpleasant work-ups or the need to use halogenated or other environmen-

tally unfriendly solvents.

Therefore, the discovery of clean procedures and the use of green and eco-friendly reagent with high selective oxidation of thiols and short reaction times for the production of disulfides have gained considerable attention.

### RESULTS AND DISCUSSION

In continuation with the search for the selective oxidation in organic synthesis using halogenating agents silica chloride<sup>[12-17]</sup>, herein we report interested in using *o*-xylylene bis(triphenylphosphonium)dichromate



Scheme 1

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for the oxidation of thiols to disulfides under solvent free for high yields of products in short reaction times. (Scheme 1)

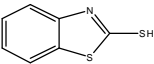
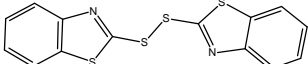
During our investigation, at first, we chose benzenethiol, under thermal condition as model reactants and examined the effect of the amount of *o*-XBTPPDC (Scheme 2, TABLE 1). According to this data, the optimum amount of reagent 1:2 molar ratio of *o*-XBTPPDC to thiol was established as other ratios led to incomplete reactions or extended reaction times. Further increasing the amount of catalyst did not improve the yield and the reaction time. In order to evaluate the effect of solvent, we examined different solvents

and solvent free under room temperature for the above model reaction (TABLE 1).

**TABLE 1 : The effect of amount of *o*-XBTPPDC/thiol and solvent different for oxidative of benzenethiol**

Entry	Reagent/ Substrate (g)	Solvent	Time (s)	Yield <sup>s</sup> (%)
1	1:1	free	5	95
2	1:1	CH <sub>2</sub> Cl <sub>2</sub>	5	89
3	1:1.5	free	10	93
4	1:1.5	CH <sub>2</sub> Cl <sub>2</sub>	10	80
5	1:2	free	50	94
6	1:2	CH <sub>2</sub> Cl <sub>2</sub>	50	84
7	0:1	CH <sub>2</sub> Cl <sub>2</sub>	100	0

**TABLE 2 : The oxidation of thiols to the corresponding disulfides with *o*-XBTPPDC under solvent- free conditions at room temperature.**

Entry	Substrate	Time (s)	Product <sup>a</sup>	Yield <sup>b</sup> (%)	M.p., °C (Lit.) <sup>c</sup>
1	C <sub>6</sub> H <sub>5</sub> SH	5	C <sub>6</sub> H <sub>5</sub> S-SC <sub>6</sub> H <sub>5</sub>	95	61-62 [63]
2	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub> SH	immediately	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub> S-SC <sub>6</sub> H <sub>4</sub> Me- <i>p</i>	97	43-44 [42]
3	<i>p</i> -CH <sub>3</sub> SC <sub>6</sub> H <sub>4</sub> SH	immediately	<i>p</i> -CH <sub>3</sub> SC <sub>6</sub> H <sub>4</sub> S-SC <sub>6</sub> H <sub>4</sub> SCH <sub>3</sub> - <i>p</i>	98	40-43 [40]
4	<i>p</i> -FC <sub>6</sub> H <sub>4</sub> SH	immediately	<i>p</i> -FC <sub>6</sub> H <sub>4</sub> S-SC <sub>6</sub> H <sub>4</sub> F- <i>p</i>	99	Oil [Oil]
5	<i>p</i> -BrC <sub>6</sub> H <sub>4</sub> SH	immediately	<i>p</i> -BrC <sub>6</sub> H <sub>4</sub> S-SC <sub>6</sub> H <sub>4</sub> Br- <i>p</i>	99	90-92 [94]
6	<i>o</i> -NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> SH	immediately	<i>o</i> -NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> S-SC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> - <i>o</i>	97	89-91 [90]
7	<i>p</i> -NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> SH	immediately	<i>p</i> -NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> S-SC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> - <i>p</i>	99	77 [77]
8	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> SH	immediately	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> S-SC <sub>6</sub> H <sub>4</sub> Cl- <i>p</i>	99	70-73 [70]
9	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub> SH	immediately	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub> S-SC <sub>6</sub> H <sub>4</sub> MeO- <i>p</i>	92	76-80 [78]
10	<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> SH	30	<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> S-SC <sub>6</sub> H <sub>4</sub> NO <sub>2</sub> - <i>p</i>	89	184-186 [183]
11	PhCH <sub>2</sub> SH	10	PhCH <sub>2</sub> S-SCH <sub>2</sub> Ph	95	68-70 [69]
12	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> CH <sub>2</sub> SH	60	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub> CH <sub>2</sub> S-SCH <sub>2</sub> (CH <sub>2</sub> ) <sub>2</sub> CH <sub>3</sub>	96	Oil [Oil]
13	cyclo-C <sub>6</sub> H <sub>11</sub> SH	80	cyclo-C <sub>6</sub> H <sub>11</sub> S-SC <sub>6</sub> H <sub>11</sub> -cyclo	90	Oil [Oil]
14	HOCH <sub>2</sub> CH <sub>2</sub> SH	72	HOCH <sub>2</sub> CH <sub>2</sub> S-SCH <sub>2</sub> CH <sub>2</sub> OH	95	Oil [Oil]
15	HOOCCH <sub>2</sub> CH <sub>2</sub> SH	120	HOOCCH <sub>2</sub> CH <sub>2</sub> S-SCH <sub>2</sub> CH <sub>2</sub> COOH	98	157-159 [156]
16	<i>o</i> -HOCC <sub>6</sub> H <sub>4</sub> SH	23	<i>o</i> -HOCC <sub>6</sub> H <sub>4</sub> S-SC <sub>6</sub> H <sub>4</sub> COOH- <i>o</i>	91	286 [284]
17		130 (min)		82	178-179 [178]

<sup>a</sup>) Isolated yields. <sup>b</sup>) All the products are known, characterized by IR, NMR spectral analysis and compared with the authentic samples. <sup>c</sup>) Melting points of compounds are consistent with reported values<sup>[4-12]</sup>.

A series of disulfides were prepared in high to excellent yields in short reaction times under solvent free. (TABLE 2)

As shown in TABLE 2, the method offers a simple, mild, and efficient solid state route for the oxidation of a variety of thiols to the corresponding disulfides. Notably, disulfides did not undergo further oxidation to their corresponding disulfide S-oxides (thiolsulfonates), disulfide S-dioxides (thiolsulfonates), and/or sulfonic ac-

ids under the reaction conditions. It must also be noted that no severe exothermal or other safety problems were observed during the mixing of the starting materials and the reactions themselves.

The advantages or the characteristic aspects of the method described in this paper in comparison with other previously reported ones are the following: non-toxicity, reagent availability, higher yields, shorter reaction times, milder conditions and easy work up at

room temperature.

## EXPERIMENTAL SECTION

### General

All chemical materials were purchased from Merck, Fluka and Aldrich and used without further purification. The products were characterized by a comparison of their physical (melting point) and spectral data with those reported in the literature [5-26]. All yields refer to isolated products. <sup>1</sup>H-NMR spectra were recorded on a Bruker 500 MHz in CDCl<sub>3</sub>, CD<sub>3</sub>OD or DMSO-d<sub>6</sub> relative to TMS as an internal standard. IR spectra were run on a FTIR-8400S SHIMADZU spectrophotometer. All of the reactions were carried out in the solid state conditions in mortar under fume hood with strong ventilation at room temperature.

### Typical procedure for the solid state oxidation of benzenethiol

*O*-XBTPPDC (1 mmol, 0.845 g) was added to thiophenol (2 mmol, 0.220 g) placed in a mortar. The reaction mixture was ground by pestle at room temperature under solvent-free condition for 5 seconds. After the disappearance of starting material as monitored by TLC, the mixture was washed twice with diethylether (2 × 8 mL) and filtered. The filtrate was evaporated under reduced pressure and the resulting crude material was purified by column chromatography on SiO<sub>2</sub> using a mixture of ethyl acetate and hexane as eluent (20:80) to afford diphenyl disulfide (95%); m.p = 60°C; <sup>1</sup>HNMR (CDCl<sub>3</sub>): δ 7.47-7.24 (m, 10H) ppm. The other substrates were treated similarly.

## CONCLUSIONS

We have presented application of *o*-XBTPPDC as an effective reagent for the solid state oxidation of the thiols that offers potential green chemistry advantages. It is important to note that most of the previously reported methods for the oxidation of thiols use toxic reagents and/or suffer from other disadvantages such as long reaction times and low yields, but this method uses a readily synthesizable reagent and additionally offers the advantages of high yields, very short reaction times (0.1-2 min.), no side reactions, mild reaction condi-

tions, a solid state reaction and simple isolation of the products. Consequently, this methodology should represent a good addition to list of methods already available for this purpose.

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