SHORT PAPER

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Benzyltriphenylphosphonium dichromate as a mild reagent for oxidation of thiols and sulfides†

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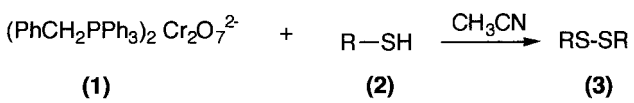
Oxidation of thiols and sulfides under non-aqueous and aprotic conditions uses benzyltriphenylphosphonium dichromate (**1**, $PhCH_2PPh_3)_2\ Cr_2O_7$) which is very easily prepared by mixing an aqueous solution of benzyltriphenylphosphonium chloride with CrO_3 in 3N HCl at room temperature. This reagent, a stable orange powder which may be stored for a month without loss of activity, is soluble in acetonitrile, chloroform and dichloromethane and slightly soluble in carbon tetrachloride, ether and hexane.

The conversion of mercaptans to disulfides is a useful transformation and is of importance both from a biological and practical point of view.[1]

The reported reagents known to convert thiol to disulfide include, iodine–hydrogen iodide,[2] thallium (III) acetate,[3] bromine/aqueous potassium hydrogen carbonate,[4] barium permanganate,[5] zinc bismuthate,[6] and lead tetraacetate.[7] These reagents suffer from either one or more of the following drawback such as availability of the reagent, cumbersome work-up procedure, toxic or high cost of the reagent and oxidation of other functional groups in the presence of thiol group.

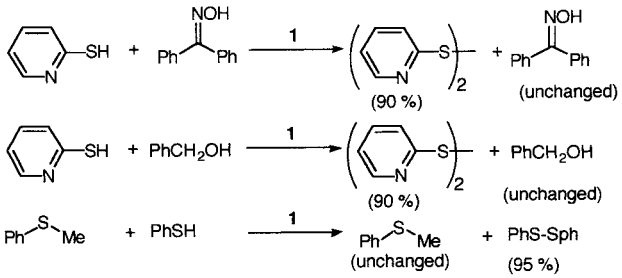
Sulfoxide find wide application in organic synthesis, particulary in carbon–carbon bond forming process.[8] These compounds are almost invariably prepared by oxidation of the corresponding sulfides, and several ways of achieving this transformation have been reported.[9] Unfortunately, many of these processes suffer major drawbacks, for example, where hazardous organic peracids are used, or in use of mixed phase reactions which lead to problems during work-up and also further oxidation of intermediate sulfoxides to the corresponding sulfones.[10]

As part of ongoing synthetic project we required an efficient and rapid method for the synthesis of a number of disulfides and sulfoxides from the corresponding thiols and sulfides respectively. We have found that reaction of benzyltriphenylphosphonium dichromate (**1**, $PhCH_2PPh_3)_2\ Cr_2O_7$), which is very easily prepared by mixing an aqueous solution of benzyltriphenylphosphonium chloride with CrO_3 in 3N HCl at room temperature, with thiols gave disulfides **(2)**. The reagent (**1**) was examined on a wide array of substrates such as aliphatic, aromatic and heterocyclic thiols (Scheme 1, Table 1), and we observed that the corresponding disulfides (**2**) were obtained in excellent yield (90–98%), and in highly diminished reaction time (10–25 min). Another advantage of this method is that the over oxidation of sulfide to sulfone will not occur at all during the reaction.



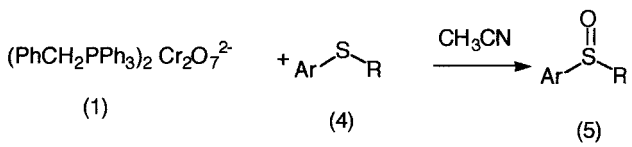
Scheme 1

Another noteworthy feature of the reagent lies in the exclusive formation of the disulfides irrespective of the presence of other oxidisable function (oximes, sulfide and alcohol). In order to evaluate the selectivity of reagent **(1)**, the competitive reactions shown in Scheme 2 were carried out. We took an equimolar amount of benzophenoneoxime in the presence of 2-mercaptopyridine; only 2-mercaptopyridine was selectively oxidised. Treatment of a mixture of benzyl alcohol and 2-mercaptopyridine with the reagent **(1)**, resulted exclusively in the oxidation of 2-mercaptopyridine. Eventually, treatment with reagent **(1)** on thioanisol in the presence of thiopenol, showed that only thiophenol was oxidised.



Scheme 2

We have also found that by oxidation of sulfides **(4)** with **(1)** to the corresponding sulfoxides **(5)** (Scheme 3), the oxidation is rapid (10–30 min), and almost quantitative from TLC and ^{1}H NMR analysis. In all cases, the yield of crude product was judged to be >95% from ^{1}H NMR and TLC analysis. It is clear from Scheme 3 that a variety of functional groups are unaffected and the corresponding sulfones do not form in these reactions.



Scheme 3

In conclusion, we report herein an inexpensive oxidant which is very easily prepared by mixing an aqueous solution of benzyltriphenylphosphonium chloride with CrO_3 in 3N HCl at room temperature. This reagent, a stable orange powder which may be stored for month without loss of activity. This oxidant is able to oxidise thiols and sulfides to the corresponding disulfides and sulfoxides. This methodology is rapid and inexpensive and is superior to previously reported methods in terms of selectivity, yield and purity of products and also rapid and easy to work-up.

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1. Oxidation of thiols **(2)** to disulfides **(3)**.

Entry		Reaction time (min)	Yield (%)[a,b]	mp °C or bp °C/torr[ref]
1	phenyl	10	98	58–60 (58–60)[5,6]
2	4-nitrophenyl	35	87	184–186 (184–186)[5,6]
3	2-pyridyl	25	92	56–58 (56-58)[5, 6]
4	2-benzimidazoyl	15	86	144–145 (142–145)[5,6]
5	2-furyl	12	95	118–120/0.8 (112–115/0.5)[5,6]
6	benzyl	10	98	69–72 (68–72)[5,6]
7	*n*-butyl	10	95	224–226/760 (226)[5,6]
8	*t*-butyl	20	90	197–200/760 (198–200)[5,6]
9	2-benzimdazoyl	20	95	200–201 (198)[11]
10	2-benzthiazoyl	18	97	180–182 (182–183)[12]
11	2-naphthyl	15	98	145 (143–144)[13]
12	*p*-tolyl	10	99	48 (45–56)[4]
13	*o*-aminophenyl	15	96	80 (79–80)[14]
14	*o*-carboxyl phenyl	15	86	286 (289–290)[12]

[a]Confirmed by comparison with authentic sample (IR, TLC and NMR). [b]Yield of isolated pure product.

Experimental

All yields refer to isolated products after purification. All the products were Confirmed by comparison with authentic sample (IR, TLC and NMR)[5-8]. All mpts were taken on a Gallenkamp melting apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Varian EM-390 NMR Spectrometer operating at 90 MHz. The spectra were measured in $CDCl_3$ unless otherwise stated, relative to TMS (0.00 ppm).

*Preparation of benzyltriphenylphosphonium dichromate (***1***):* To an aqueous solution of benzyltriphenylphosphonium chloride (8.55 g, 22 mmol, 75 ml H^2O), was added a solution of chromium (VI) oxide (11 g, 11 mmol) in HCl 3 N (220 ml). The reaction mixture was stirred at room temperature for 15 min. The resulting orange solid products was collected, washed with water (20 ml) and dried in a desiccator under vacuum over calcium chloride, yield 9.43 g (10.34 mmol, 94 %) of **(1)**, mpt 210–212 °C. ^{1}H NMR: δ 7.93–6.87 (m, 20 H), 4.7 (d, *J*=25.6 Hz, C$\underline{H}^2$-P). ^{13}C NMR: δ 133.50, 133.20, 130.20, 129.60, 129.40, 128.10, 127.70, 127.2, 117.30 (d, *J*=85.5 Hz, P-$\underline{C}H^2$). IR (KBr): 1298, 1269, 1098, 1060, 700, 658, 590, 546 cm^{-1}. Found: C, 69.60; H, 50.20; Cr, 11.90 %. Calcd for $C^{50}H^{44}Cr^2O^7$: C, 69.70; H, 5.15; Cr, 12.08 %.

General procedure: oxidation of **2** *to* **3** *or* **4** *to* **5***:* A mortar was charged with alcohol **(2)**, sulfide **(6)** or sulfoxide **(8)** (1 mmol) and a supported oxidant **(1)** on silica gel (prepared from 1 mmol, 0.91 g of oxidant and 0.3 g silica gel). The mixture was grinding with a pestle until TLC showed complete disappearance of starting material. The mixture was then extracted with acetone (2 × 10 ml). Evaporation of the solvent gave the products.

Conversion of **4** *or* **5** *to* **3***: General procedure:* The thiol **(2)** or sulfide **(4)** (1 mmol) was added to a stirred solution of the oxidant **(1)** (1 mmol, 0.92 g) in acetonitrile (10 ml). The mixture was heated at reflux until TLC showed complete disappearance of starting material, which required 10–30 min depending on substrate (Tables 1 and 2). The mixture was cooled and 2 g of silica gel was added to the reaction mixture. It was stirred for 5 min. The solid was then separated by suction filtration through Celite and washed with acetonitrile (2 × 10 ml). Evaporation of the solvent gave disulfide (3) or sulfoxide (5). The products were purified by column chromatography on silica gel using a mixture of ethyl acetate and hexane as eluent (90:10).

Competitive oxidation typical procedure: A mixture of benzyl alcohol (1 mmol) and 2-mercaptopyridine (1 mmol) was added to a stirred solution of the oxidant (1) (1 mmol, 0.92 g) in acetonitrile (20 mL). The mixture was heated at reflux until TLC showed complete disappearance of 2-mercaptopyridine (15 min). The other competitive reactions for Scheme 2 are the same as above.

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Table 2. Oxidation of sulfides **(4)** to sulfoxides **(5)**.

Entry	Ar	R	Reaction time (min)	Yield (%)[a,b]	mp °C or bp °C/torr (refs. [6, 8, 15, 16])
1	benzyl	benzyl	15	93	134–136 (133–135)
2	phenyl	benzyl	20	97	120–122 (122–124)
3	4-nitrophenyl	phenyl	15	90	107–108 (107–108)
4	benzyl	n-butyl	20	96	63–64 (62-63)
5	phenyl	methyl	20	93	124–126/0.8 (139–141/14)
6	phenyl	*n*-butyl	20	92	103–105 (102–104)
7	phenyl	phenylCOCH^2	25	94	70–71 (70–71)
8	phenyl	3,4-dimethoxyphenylCOCH$_2$	25	92	88–89 (88–89)
9	tolyl	phenyl	20	95	84–85 (84–85)
10	tolyl	3,4-dimethoxyphenylCOCH$_2$	25	90	96–98 (96–98)
11	tolyl	cyclohexanone	20	93	102–103 (100–101.5)
12	tolyl	phenylCOCH$_2$	20	95	83–84 (83–84)
13	tolyl	HOCOCH$_2$	15	94	100–101 (97.5–99)

[a]Confirmed by comparison with authentic sample (IR, TLC and NMR). [b]Yield of isolated pure product.