

O-Xylylenebis (Triphenylphosphonium) Dibromochromate: A Selective and Efficient Reagent for Oxidation of Alcohols, Trimethylsilyl Ethers and Thiols

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Abstract: Alcohols, trimethylsilyl ethers and thiols were efficiently converted to their corresponding carbonyl and disulfides compounds using *o*-xylylenebis (triphenylphosphonium) dibromochromate (XTPPDBC). This reagent can selectively oxidize thiols to disulfides in the presence of alcohols and trimethylsilyl ethers in acetonitrile at room temperature.

Key words: O-Xylylenebis (triphenylphosphonium) dibromochromate • Alcohols • Trimethylsilyl ethers • Thiols • Disulfides

INTRODUCTION

The oxidation of organic compounds under mild conditions has found valuable applications in modern organic synthesis. The oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones is a fundamental area that is encountered at all levels of organic synthesis. Disulfides are one of the most important classes of organic sulfur compounds, possessing noteworthy reactivity in biochemistry and as key intermediates in wide variety of organic synthetic routes. In recent years significant improvements have been achieved by the use of new oxidizing agents, examples being: silica-supported 1,1,3,3-tetramethylguanidine/Br₂ complex [1], melamine hydrogen peroxide (MHP) [2], K₂S₂O₈ [3], bis-(2,4,6-trimethylpyridinium) dichromate (BTMPDC) [4], (PhCH₂PPh₃)⁺Br⁻ [5], TEMPO-linked metalloporphyrins [6], NaIO₄/TEMPO/NaBr [7]. Unfortunately, many of the reagents mentioned in the literature suffer from at least one of the following disadvantages: cost of preparation, hygroscopicity, photosensitivity, instability, lack of selectivity and tedious work-up procedure [5-8].

In connection with our ongoing work on the application of selective oxidation of organic compounds [9-21], we report here the oxidation of structurally different alcohols, trimethylsilyl ethers and thiols using *o*-xylylenebis (triphenylphosphonium) dibromochromate in acetonitrile at reflux conditions. *o*-xylylenebis(triphenylphosphonium) dibromochromate

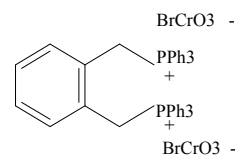


Fig. 1: O-xylylenebis(triphenylphosphonium) dibromochromate

(XTPPDBC, Figure 1) as an oxidant can overcome most of the above-mentioned disadvantages for the oxidation of organic compounds.

Experimental: All the alcohols were purchased from Fluka and Merck. The reactions were monitored by TLC using silica gel plates. The products were purified by flash column chromatography on silica gel (Merck; 230-400 mesh) and were identified by comparison of their IR and ¹H NMR spectra and physical data with those of authentic samples. ¹H NMR spectra were measured at 90 MHz with a JEOL JNM-EX 90 spectrometer with tetramethylsilane as an internal reference and DMSO-d₆ as solvent. IR spectra were recorded with a Pye-unicam SP 1100 spectrophotometer. Elemental analyses were performed on a LECO 250 instrument.

Preparation of O-xylylenebis(triphenylphosphonium) Dibromochromate (XTPPDBC): To a solution of *o*-xylylenebis (triphenylphosphonium bromide) (5 mmol, 3.49 g) in water (25 ml) was added a solution of CrO₃ (10 mmol, 0.99 g) in HCl 6 N (15 ml) under stirring at room

temperature until an orange precipitate was formed. After 30 min stirring, the mixture was filtered, washed with water (2 × 15 ml) and dried at room temperature (4.27 g, 95% Yield). m.p: 185°C to a light brown material; ¹H NMR (DMSO): δ 4.5 (d, 4H, CH₂), 6.85-7.98 (m, 34H, arom. H). IR (KBr) $\tilde{\nu}$ (cm⁻¹): 3053, 2096, 1900, 1586, 1495, 1484, 1437, 1115, 954, 937, 787, 746, 696; Elemental analysis: Calculated C, 62.56; H, 4.53, Found: C, 62.50; H, 4.48.

General Procedure for Oxidation of Alcohols and Trimethylsilyl Ethers and Coupling of Thiols: In a round-bottomed flask (25 ml), equipped with a reflux condenser and a magnetic stirrer, a solution of substrate (1 mmol) and *o*-xylylenebis (triphenylphosphonium) dibromochromate (0.5 mmol, 0.44 g for thiols and 1 mmol, 0.89 g for alcohols and trimethylsilyl ethers) in acetonitrile was added and stirred for 2-80 min at refluxed temperature (7-15 min at room temperature for thiols). The reaction was monitored by TLC (EtOAc/*n*-Hexane 10:90). The reaction mixture was cooled to room temperature and the solid was then separated through a short pad of silica gel and washed with acetonitrile (5 ml). The solvent was evaporated to afford pure corresponding product. If necessary, the crude product was purified by column chromatography on silica gel using a mixture of ethyl acetate and *n*-hexane as eluent (10:90).

RESULTS AND DISCUSSION

O-Xylylenebis (triphenylphosphonium) dibromochromate was readily prepared in high yield by adding a solution of CrO₃ in HCl (6 N) into a stirring solution of *o*-xylylenebis (triphenylphosphonium bromide) in water and continued to stir for 30 min at room temperature. Filtration and drying the precipitate produced an orange powder (Scheme 1). The chromium content of the reagent was determined by atomic absorption. Elemental analyses (C, H, N) were also performed and the experimental and calculated results were in very good agreement with the proposed structure.

This compound is non-hygroscopic and can be stored in a polyethylene bag for long periods without decomposition. It is soluble in polar solvents such as acetonitrile and *N,N* dimethylformamide and slightly soluble in THF, chloroform and dichloromethane and insoluble in benzene, *n*-hexane and carbon tetrachloride.

The effect of solvent on the oxidation reaction was evaluated by carrying out the oxidation in different solvents. Oxidation of benzyl alcohol with *o*-xylylenebis (triphenylphosphonium) dibromochromate was carried out in acetonitrile, chloroform, dichloromethane, *n*-hexane and tetrahydrofuran at reflux temperature. The results are presented in Table 1.

As indicated in Table 1, a 1:1 molar ratio of benzyl alcohol and *o*-xylylenebis (triphenylphosphonium) dibromochromate in acetonitrile gave excellent yield of benzaldehyde (entry 1). The effect of temperature on this reaction was also studied by carrying out the oxidation of benzyl alcohol at lower temperatures, but, much longer reaction time was necessary to achieve complete conversion to benzaldehyde.

In order to evaluate the general applicability of this method we have treated benzylic, allylic and aliphatic alcohols, trimethylsilyl ethers and thiols with *o*-xylylenebis(triphenylphosphonium) dibromochromate in refluxing acetonitrile (room temperature for thiols) and results are shown in Table 2.

It is evident from Table 2, that aromatic substrates, including benzylic alcohols as well as, trimethylsilyl ethers and thiols were rapidly converted to the corresponding carbonyl compounds and disulfides in excellent yields under the reaction conditions, whereas aliphatic compounds needed longer reaction time.

It is noteworthy that, unlike other oxidative hydrolytic methods, the major drawback of over oxidation of the resulting aldehydes is not observed under the reaction conditions. α,β -Unsaturated derivatives are oxidized very efficiently without affecting the olefinic bond and the reaction is essentially chemoselective (Table 2, entries 15, 26). Furthermore, functional groups such as methoxy, nitro and alkyl groups were also inert to this reagent and no byproduct formation was observed (Table 2).

Aliphatic and aromatic thiols are easily oxidized to their corresponding disulfides with XTPPDBC at room temperature in excellent yield (Table 2, entries 32-44).

It is interesting to mention that XTPPDBC can selectively oxidize thiols to disulfides in the presence of alcohols or trimethylsilyl ethers in acetonitrile at room temperature (Scheme 2). When an equimolar mixture of thiol and alcohol or trimethylsilyl ether was treated with XTPPDBC, only the thiol was oxidized, while the alcohol or trimethylsilyl ether remained unaffected (Table 3).


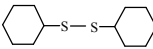

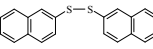

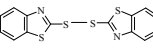

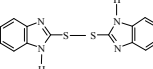

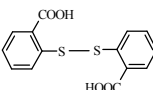
Table 1: Oxidation of benzylalcohol in different solvents with XTPPDBC ^a

Entry	Solvent	Time (min)	Yield (%)
1	CH ₃ CN	17	96
2	CHCl ₃	65	75
3	CH ₂ Cl ₂	60	55
4	<i>n</i> -C ₆ H ₁₄	70	40
5	THF	60	55

^aReactions were carried out at reflux condition using substrate/oxidant molar ratio (1:1).^bYields refer to isolated products.Table 2: Oxidation of Alcohols and Trimethylsilyl Ethers to Carbonyl Compounds and Conversion of thiols to disulfides with XTPPDBC ^a

Entry	Substrate	Product	Time (min)	Yield (%) ^b
1	C ₆ H ₅ CH ₂ OH	C ₆ H ₅ CHO	9	97
2	<i>m</i> -MeOC ₆ H ₄ CH ₂ OH	<i>m</i> -MeOC ₆ H ₄ CHO	15	95
3	<i>p</i> -MeOC ₆ H ₄ CH ₂ OH	<i>p</i> -MeOC ₆ H ₄ CHO	12	85
4	<i>o</i> -MeC ₆ H ₄ CH ₂ OH	<i>o</i> -MeC ₆ H ₄ CHO	15	90
5	<i>o</i> -ClC ₆ H ₄ CH ₂ OH	<i>o</i> -ClC ₆ H ₄ CHO	8	95
6	<i>p</i> -ClC ₆ H ₄ CH ₂ OH	<i>p</i> -ClC ₆ H ₄ CHO	18	98
7	<i>o</i> -BrC ₆ H ₄ CH ₂ OH	<i>o</i> -BrC ₆ H ₄ CHO	10	90
8	<i>p</i> -BrC ₆ H ₄ CH ₂ OH	<i>p</i> -BrC ₆ H ₄ CHO	25	92
9	<i>o</i> -NO ₂ C ₆ H ₄ CH ₂ OH	<i>o</i> -NO ₂ C ₆ H ₄ CHO	37	85
10	<i>m</i> -NO ₂ C ₆ H ₄ CH ₂ OH	<i>m</i> -NO ₂ C ₆ H ₄ CHO	25	84
11	C ₆ H ₅ CH(OH)CH ₃	C ₆ H ₅ COCH ₃	7	95
12	C ₆ H ₅ CH(OH)CH ₂ CH ₃	C ₆ H ₅ COCH ₂ CH ₃	7	97
13	C ₆ H ₅ CH(OH)COC ₆ H ₅	C ₆ H ₅ COCOC ₆ H ₅	34	90
14	(C ₆ H ₅) ₂ CHOH	(C ₆ H ₅) ₂ CO	9	89
15	C ₆ H ₅ CH=CHCH ₂ OH	C ₆ H ₅ CH=CHCHO	40	85
16	C ₆ H ₅ CH ₂ CH ₂ OH	C ₆ H ₅ CH ₂ CHO	68	82
17	CH ₃ (CH ₂) ₅ CH ₂ OH	CH ₃ (CH ₂) ₅ CHO	80	75
18	CH ₃ (CH ₂) ₆ CH ₂ OH	CH ₃ (CH ₂) ₆ CHO	80	80
19	Cyclohexanol	Cyclohexanone	68	83
20	C ₆ H ₅ CH ₂ OSiMe ₃	C ₆ H ₅ CHO	5	90
21	(C ₆ H ₅) ₂ CHOSiMe ₃	(C ₆ H ₅) ₂ CO	8	85
22	<i>p</i> -ClC ₆ H ₄ CH ₂ OSiMe ₃	<i>p</i> -ClC ₆ H ₄ CHO	7	80
23	<i>o</i> -ClC ₆ H ₄ CH ₂ OSiMe ₃	<i>o</i> -ClC ₆ H ₄ CHO	7	80
24	<i>p</i> -BrC ₆ H ₄ CH ₂ OSiMe ₃	<i>p</i> -BrC ₆ H ₄ CHO	8	83
25	<i>p</i> -NO ₂ C ₆ H ₄ CH ₂ OSiMe ₃	<i>p</i> -NO ₂ C ₆ H ₄ CHO	95	65
26	C ₆ H ₅ CH=CHCH ₂ OSiMe ₃	C ₆ H ₅ CH=CHCHO	25	80
27	C ₆ H ₅ CH(OSiMe ₃)COC ₆ H ₅	C ₆ H ₅ COCOC ₆ H ₅	12	85
28	C ₆ H ₅ CH ₂ CH ₂ OSiMe ₃	C ₆ H ₅ CH ₂ CHO	40	70
29	CH ₃ (CH ₂) ₅ CH ₂ OSiMe ₃	CH ₃ (CH ₂) ₅ CHO	60	80
30	CH ₃ (CH ₂) ₆ CH ₂ OSiMe ₃	CH ₃ (CH ₂) ₆ CHO	45	78
31	C ₆ H ₅ SH	C ₆ H ₅ SSC ₆ H ₅	12	85
32	<i>p</i> -MeC ₆ H ₄ SH	<i>p</i> -MeC ₆ H ₄ SSC ₆ H ₄ Me- <i>p</i>	13	90
33	<i>p</i> -ClC ₆ H ₄ SH	<i>p</i> -ClC ₆ H ₄ SSC ₆ H ₄ Cl- <i>p</i>	12	92
34	<i>p</i> -BrC ₆ H ₄ SH	<i>p</i> -BrC ₆ H ₄ SSC ₆ H ₄ Br- <i>p</i>	14	84
35	C ₆ H ₅ CH ₂ SH	C ₆ H ₅ CH ₂ SSC ₆ H ₅	12	89
36	CH ₃ (CH ₂) ₃ CH ₂ SH	CH ₃ (CH ₂) ₃ CH ₂ SSCH ₂ (CH ₂) ₃ CH ₃	15	85
37	CH ₃ (CH ₂) ₆ CH ₂ SH	CH ₃ (CH ₂) ₆ CH ₂ SSCH ₂ (CH ₂) ₆ CH ₃	15	85

Table 2: Continue

Entry	Substrate	Product	Time (min)	Yield (%) ^b
38	HOOCCH ₂ SH	HOOCCH ₂ SSCH ₂ COOH	14	76
39	HOCH ₂ CH ₂ SH	HOCH ₂ CH ₂ SSCH ₂ CH ₂ OH	12	86
40			13	78
41			12	80
42			18	35
43			15	87
44			15	75

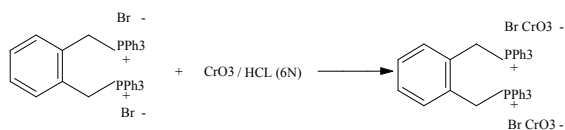
^aReactions were carried out in acetonitrile (at reflux temperature for alcohol and trimethylsilyl ethers and at room temperature for thiols). Substrates/oxidant molar ratio for alcohol and trimethylsilyl ethers (1:1), for thiols (1:0.5). ^bYields refer to pure isolated products.

Table 3: The selective coupling of thiols to disulfides in the presence of alcohols or trimethylsilyl ethers in acetonitrile at room temperature

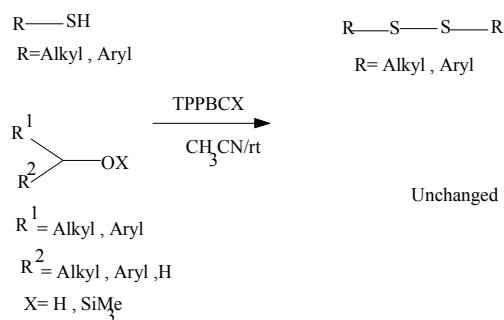
Entry	Substrates	Products	Time (min)	Yield (%) ^a
1	<i>p</i> -ClC ₆ H ₄ SH Cyclohexanol	<i>p</i> -ClC ₆ H ₄ SSC ₆ H ₄ Cl- <i>p</i> Cyclohexanone	12	85 -
2	C ₆ H ₅ CH ₂ SH C ₆ H ₅ CH ₂ OH	C ₆ H ₅ CH ₂ SSCH ₂ C ₆ H ₅ C ₆ H ₅ CHO	10	90 -
3	CH ₃ (CH ₂) ₆ CH ₂ SH <i>p</i> -ClC ₆ H ₄ CH ₂ OH	CH ₃ (CH ₂) ₆ CH ₂ SSCH ₂ (CH ₂) ₆ CH ₃ <i>p</i> -ClC ₆ H ₄ CHO	17	84 -
4	<i>p</i> -ClC ₆ H ₄ SH (C ₆ H ₅) ₂ CHOSiMe ₃	<i>p</i> -ClC ₆ H ₄ SSC ₆ H ₄ Cl- <i>p</i> (C ₆ H ₅) ₂ CO	12	89 -
5	C ₆ H ₅ CH ₂ SH C ₆ H ₅ CH ₂ OSiMe ₃	C ₆ H ₅ CH ₂ SSCH ₂ C ₆ H ₅ C ₆ H ₅ CHO	12	75 -
6	CH ₃ (CH ₂) ₆ CH ₂ SH CH ₃ (CH ₂) ₅ CH ₂ OSiMe ₃	CH ₃ (CH ₂) ₆ CH ₂ SSCH ₂ (CH ₂) ₆ CH ₃ CH ₃ (CH ₂) ₅ CHO	15	87 -

^aYield refers to pure isolated products or GC.

Scheme 1



Scheme 2



CONCLUSION

In summery, we have developed a convenient and efficient method for oxidation of structurally different alcohols and trimethylsilyl ethers to the corresponding carbonyl compounds and coupling of thiols to disulfids. Our new method has significant advantages such as selective procedure, high yields and mild reaction conditions.

ACKNOWLEDGMENTS

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