

## H<sub>2</sub>O<sub>2</sub> as green and environmentally benign reagent for the oxidation of TMS ethers, THP ethers, and alcohols in the presence of {[K.18-Crown-6]Br<sub>3</sub>}<sub>n</sub>

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To cite this article: Mohsen Rasouli, Mohammad Ali Zolfigol, Mohammad Hossein Moslemin & Gholamabbas Chehardoli (2017) H<sub>2</sub>O<sub>2</sub> as green and environmentally benign reagent for the oxidation of TMS ethers, THP ethers, and alcohols in the presence of {[K.18-Crown-6]Br<sub>3</sub>}<sub>n</sub>, Green Chemistry Letters and Reviews, 10:2, 117-120, DOI: [10.1080/17518253.2017.1306614](https://doi.org/10.1080/17518253.2017.1306614)

To link to this article: <https://doi.org/10.1080/17518253.2017.1306614>



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Published online: 03 Apr 2017.



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## H<sub>2</sub>O<sub>2</sub> as green and environmentally benign reagent for the oxidation of TMS ethers, THP ethers, and alcohols in the presence of {[K.18-Crown-6]Br<sub>3</sub>}<sub>n</sub>

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### ABSTRACT

In the presence of {[K.18-Crown-6]Br<sub>3</sub>}<sub>n</sub>, a unique tribromide reagent, trimethylsilyl (TMS) ethers, tetrahydropyranyl (THP) ethers, and alcohols were oxidized to their corresponding aldehydes and ketones in H<sub>2</sub>O<sub>2</sub>. One-pot deprotection and oxidation of TMS ethers/THP ethers were performed directly and the conversion was complete. Avoiding the isolation of the corresponding alcohol as an intermediate step, the direct transformation of such substrates to carbonyls is the main aim of this work. {[K.18-Crown-6]Br<sub>3</sub>}<sub>n</sub> regeneration was performed via the addition of Br<sub>2</sub> to the residue of the reaction and recrystallization in acetonitrile.

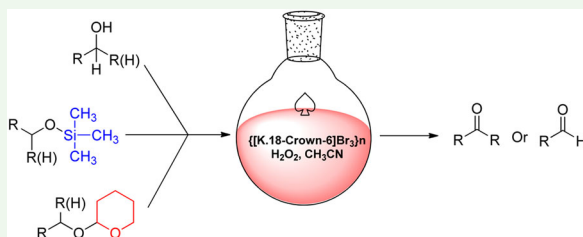
### ARTICLE HISTORY

Received 2 January 2017

Accepted 10 March 2017

### KEYWORDS

H<sub>2</sub>O<sub>2</sub>; TMS ethers; THP ethers; {[K.18-Crown-6]Br<sub>3</sub>}<sub>n</sub>; alcohols



### Introduction

Owing to the importance of aldehydes and ketones as precursors and/or intermediates for numerous drugs, vitamins, and fragrances, the oxidation of alcohols to their corresponding carbonyl groups is of great importance compared to some other organic reactions (1). Most oxidation reactions require stoichiometric amounts of toxic reagent. Removal of the trace reagent from the reaction mixture is often costly and difficult. Therefore, in environment-friendly methods, oxidation reactions using cheap green oxidants, such as oxygen and hydrogen peroxide, have become increasingly popular (2).


Tetrahydropyranyl (THP) and trimethylsilyl (TMS) ethers are widely utilized in organic synthesis (3), and are the most versatile protective groups for alcohols due to their reasonable stability in nonacidic media. One of the attractive advantages of these protective groups is their ability to convert into carbonyl groups. Deprotective oxidation of THP and TMS ethers to their aldehydes or ketones is an important transformation in organic chemistry (4, 5).

Organic tribromides (OTBs) as reagents/catalysts are preferable to molecular bromine because of the high toxicity of elemental bromine. Some of these reagents include hexamethonium bis(tribromide) (6), poly(4-vinylpyridinium tribromide) (7), and tribromide ion immobilized on magnetic nanoparticle (8).

We reported {[K.18-crown-6]Br<sub>3</sub>}<sub>n</sub> as a particular tribromide type and columnar nanotube-like structure (I, Figure 1) in 2007. We have applied this compound to the bromination of aromatic rings, conversion of thiols to disulfides (9), and protection of amines and alcohols (10).

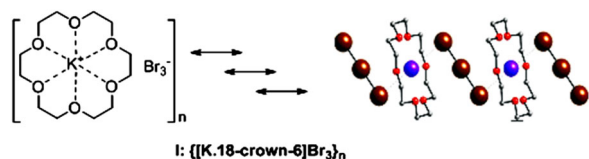
Previously, we have studied the oxidation of organic functional groups (11), especially oxidation of alcohols (12), using H<sub>2</sub>O<sub>2</sub> derivatives, such as urea hydrogen peroxide (13), melamine-H<sub>2</sub>O<sub>2</sub> (14), and polyvinylpyrrolidone-H<sub>2</sub>O<sub>2</sub> (15), in various organic transformations. Consequently, the aim of this study was to evaluate the effect of {[K.18-crown-6]Br<sub>3</sub>}<sub>n</sub> as a unique tribromide reagent for oxidation of alcohols, TMS ethers, and THP ethers in the presence of H<sub>2</sub>O<sub>2</sub>.

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 Supplemental data for this article can be accessed at [doi:10.1080/17518253.2017.1306614](https://doi.org/10.1080/17518253.2017.1306614).

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**Figure 1.** The structure of {[K.18-crown-6]Br<sub>3</sub>}<sub>n</sub>.

## Experimental section

Chemicals were purchased from Merck. Products were characterized by comparison of their spectral (IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR) with those of known samples. Preparation of {[K.18-crown-6]Br<sub>3</sub>}<sub>n</sub> and its recycling were performed according to our previously reported procedure (9).

## General procedure for the oxidation of alcohols to aldehydes/ketones

To a solution of alcohols (1 mmol)/[K.18-crown-6]Br<sub>3</sub> (2 mmol) in CH<sub>3</sub>CN (8 mL) was added H<sub>2</sub>O<sub>2</sub> 30% (1.1 mmol). The solution was stirred at reflux for the appropriate time (Table 1). The progress of the reaction was monitored by thin layer chromatography (TLC). After the completion of reaction, CH<sub>3</sub>CN was removed by water-bath distillation. Column chromatography on short pad of silica gel with CH<sub>3</sub>CN afforded pure products in good-to-excellent yields. {[K.18-Crown-6]Br<sub>3</sub>}<sub>n</sub> can regenerate (70%) via adding the Br<sub>2</sub> to the residue of the reaction and recrystallization in acetonitrile.

**Table 1.** Oxidation of alcohols, TMS ethers, and THP ethers to aldehydes/ketones using H<sub>2</sub>O<sub>2</sub> in the presence of {[K.18-Crown-6]Br<sub>3</sub>}<sub>n</sub>.

Entry	Substrate (X=H, TMS, THP)	Time (min)			Isolated yields (%)		
		H <sup>a</sup>	TMS	THP	H	TMS	THP
1		30	37	42	85	89	92
2		28	36	42	87	92	78
3		30	32	35	81	82	90
4		41	45	47	82	87	84
5		23	29	32	91	83	86
6		33	37	37	95	90	87
7		22	29	32	81	92	78
8		27	36	39	82	84	89
9		25	35	35	93	85	65
10		26	35	39	88	87	89
11		21	40	45	94	78	63
12		31	38	44	88	93	79
13		37	44	52	90	79	70
14		32	36	45	93	76	79

<sup>a</sup>Under the reflux of CH<sub>3</sub>CN.

## General procedure for the deprotective oxidation of TMS ethers and THP ethers to aldehydes/ketones

H<sub>2</sub>O<sub>2</sub> 30% (1.1 mmol) was added to the solution of TMS ethers or THP ethers (1 mmol)/[K.18-crown-6]Br<sub>3</sub> (2 mmol) in CH<sub>3</sub>CN (5 mL). The solution was stirred at reflux for the appropriate time (Table 1). The progress of the reaction was monitored by TLC. After completion of the reaction, CH<sub>3</sub>CN was removed by water-bath distillation. Column chromatography on short pad of silica gel with CH<sub>3</sub>CN afforded pure products in good-to-excellent yields.

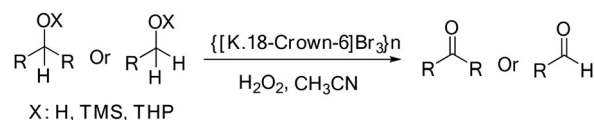
## Results and discussion

In this study, we report that {[K.18-crown-6]Br<sub>3</sub>}<sub>n</sub> acts as an efficient reagent for the oxidation of alcohols, and direct conversion of TMS ethers and THP ethers to aldehydes/ketones. Control experiments were done to optimize the reaction conditions. First, oxidation of benzyl alcohol was used as a model reaction. This reaction was carried out in the presence of different amounts of {[K.18-crown-6]Br<sub>3</sub>}<sub>n</sub>, H<sub>2</sub>O<sub>2</sub>, and different solvents. The optimized reaction conditions were 2 mmol of {[K.18-crown-6]Br<sub>3</sub>}<sub>n</sub>, 1.1 mmol H<sub>2</sub>O<sub>2</sub>, and CH<sub>3</sub>CN as the best solvent (Table 2).

Second, we converted a range of TMS ethers, THP ethers, and alcohols to their corresponding carbonyl groups under the optimized reaction conditions without any isolation of alcohols as intermediate (Scheme 1 and Table 1).

As seen in Table 1, a wide range of aliphatic and aromatic alcohols, TMS ethers and THP ethers could be converted to their corresponding aldehydes or ketones in high-to-excellent yields, and no over-oxidation products were observed under the reaction conditions.

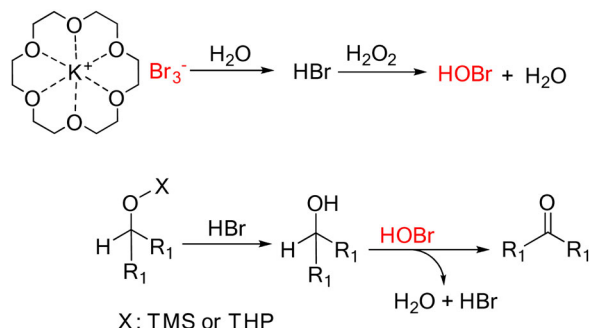
According to the previous reported paper (16) and our obtained results, we propose that the mechanism for the oxidation of alcohols, TMS ethers and THP ethers to aldehydes/ketones using H<sub>2</sub>O<sub>2</sub> in the presence of {[K.18-Crown-6]Br<sub>3</sub>}<sub>n</sub> proceeds by the generation of HOBr that allows oxidation of alcohols and one-pot deprotective oxidation of TMS ethers and THP ethers (Scheme 2).



**Scheme 1.** Oxidation of alcohols, TMS ethers, and THP ethers to aldehydes/ketones.

**Table 2.** Optimization of the reaction condition for the oxidation of benzyl alcohol in the presence of {[K.18-crown-6]Br<sub>3</sub>}<sub>n</sub>, H<sub>2</sub>O<sub>2</sub> and diversity of solvents.

Entry	{[K.18-crown-6]Br <sub>3</sub> } <sub>n</sub> (mmol)	H <sub>2</sub> O <sub>2</sub> (mmol)	Solvent (8 mL)	Temperature (°C)	Time (min.)	Isolated yield (%)
1	2	–	–	25	30	Sluggish
2	2	–	CH <sub>3</sub> CN	Reflux	50	Sluggish
3	1	1.1	CH <sub>3</sub> CN	25	30	45
4	1.5	1.1	CH <sub>3</sub> CN	Reflux	30	60
5	2	1	CH <sub>3</sub> CN	Reflux	30	65
6	2	1.1	CH <sub>3</sub> CN	Reflux	30	81
7	2	1.1	CHCl <sub>3</sub>	Reflux	45	55
8	2	1.1	EtOAc	Reflux	45	67
9	2	1.1	THF	Reflux	45	71
10	2	1.1	<i>m</i> -hexane	Reflux	45	44

**Scheme 2.** Suggested mechanism for oxidation of alcohols and deprotective oxidation of TMS ethers and THP ethers to aldehydes/ketones using H<sub>2</sub>O<sub>2</sub> in the presence of {[K.18-Crown-6]Br<sub>3</sub>}<sub>n</sub>.

## Conclusions

In this research, we explain the oxidation of alcohols, and deprotective oxidation of TMS ethers and THP ethers to aldehydes/ketones using H<sub>2</sub>O<sub>2</sub> in the presence of {[K.18-Crown-6]Br<sub>3</sub>}<sub>n</sub>. Avoiding the isolation of the corresponding alcohol as an intermediate step, the direct transformation of such substrates to carbonyls is the main aim of this work. {[K.18-Crown-6]Br<sub>3</sub>}<sub>n</sub> can be regenerated via adding the Br<sub>2</sub> to the residue of the reaction and recrystallized it in acetonitrile. The reaction is carried out at reflux conditions and yields of products are good to excellent. We believe that this procedure will be a useful addition to existing methods for the oxidation of alcohols, TMS ethers, and THP ethers.

## Disclosure statement

No potential conflict of interest was reported by the authors.

## Funding

The authors acknowledge partial support for this work from the research affairs of Hamadan University of Medical Sciences, Hamadan, I.R. Iran.

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