

## Oxidative Transformations in Aqueous Medium by Cerium Based Phase-Transfer Oxidant Impregnated on Fumed Silica

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A simple, convenient, inexpensive and environmentally benign oxidative transformation of alcohol and oxime in aqueous medium to their corresponding carbonyl compounds by cerium based phase-transfer oxidants impregnated on fumed silica is presented.

**Key Words:** Oxidative transformation, Aqueous medium, Phase-transfer oxidant, Ceric ammonium nitrate.

### INTRODUCTION

An oxidative transformation like oxidation of alcohols to carbonyl compound is an important reaction in organic synthesis<sup>1</sup>. In particular, controlled oxidation of primary alcohol to aldehyde without forming the over-oxidized product proved to be a challenging task for the synthetic chemists. As a result much research efforts were made in the past for the development of oxidizing agents for this purpose. The present day emphasis is on the development of either new oxidizing agents or the modification of the existing ones to work in an environmentally benign, milder reaction conditions. In this respect, Ce(IV) complexes are of considerable importance as they are unlike the traditionally used oxidizing agents based on chromium and manganese, which are toxic in nature. Among the Ce(IV) complexes, Ce(IV) ammonium nitrate (CAN) is the commonly used reagent, which is soluble in water and to some extent in acetic acid. However, the reported oxidation of alcohols with CAN is beset with problems such as use of acetic acid as solvent<sup>2</sup>, low yields, cyclic ether formation in case of primary alcohol<sup>3</sup> and oxidative cleavages. In an effort to modify CAN, the hydrogens of ammonium were replaced by organic groups. This has several advantages like solubility in a wider range of solvents and possibility to induce selectivity by manipulating the size of the organic groups. We have used two variants of modified CAN *viz.*, cetyldimethylbenzyl ammonium cerium nitrate (CDBACN) and cetyltrimethylammonium cerium nitrate (CTACN) impregnated on fumed silica to oxidize alcohols to carbonyl compounds. The reactions were carried out in a predominantly aqueous medium. The same reagents were also used to regenerate carbonyl compounds from their oximes, which is another important reaction, because

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oxime serves as an efficient protecting group<sup>4</sup>. It can also be used as intermediates for the preparation of nitriles<sup>5</sup>, amides and to activate the carbonyl groups<sup>6</sup>. They are also used for the isolation, purification and characterization of the parent carbonyl compounds<sup>7,8</sup>. Moreover, the oximes can be prepared from non-carbonyl compounds and hence the formation of carbonyl compounds from oximes represents a potential route for the synthesis of aldehydes and ketones<sup>9</sup>. These oxidative transformations will have additional advantage if these reactions could be carried out in aqueous medium with only a small percentage of organic solvent.

## EXPERIMENTAL

Alcohols and the other chemicals were purchased from Merck, Loba Cheme and Aldrich. The two phase-transfer oxidants CTACN<sup>8</sup> and CDBACN<sup>10</sup> were synthesized as described elsewhere. The melting points of all compounds were recorded in an apparatus from scientific device, Indian, Type MP-D in open capillary. FTIR spectra were recorded in a Perkin-Elmer RX 1 FTIR spectrometer and <sup>1</sup>H NMR spectra were recorded at 400 M Hz and 200 M Hz in CDCl<sub>3</sub>. The results were verified by comparison with those of authentic samples.

### **Preparation of cerium based phase-transfer oxidant impregnated on silica:**

A mixture of 2 mmol of appropriate phase-transfer oxidant and 0.05 g fumed silica were mixed in a mortar until a homogeneous mixture was formed.

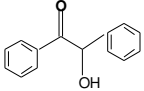
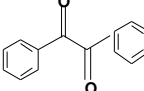
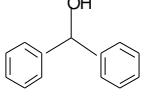
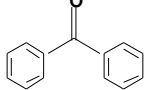
**General procedure for oxidative transformation:** 1 mmol of the substrate was dissolved in 16 mL of water and dioxane in the ratio 15:1 as a solvent. To this solution 2 mmol of cerium based phase-transfer oxidant impregnated on silica and 0.3 mmol H<sub>2</sub>SO<sub>4</sub> were added. The reaction mixture was refluxed for varying duration and progress of the reaction was monitored by TLC in prepared silica gel plates. After completion of the reaction, the reaction mixture was cooled and filtered through celite pad. The solvent was then removed in a rotary evaporator (Buchi). Product was recovered by extraction with diethyl ether and purified by column chromatography.

## RESULTS AND DISCUSSION

The two phase-transfer oxidant CDBACN and CTACN have been used for the oxidation of alcohol and deoxygenation of oximes in organic solvents under reflux<sup>10,11</sup>. However when these reagents were impregnated on various forms of silica they could oxidize alcohols and oximes to the carbonyl compounds in aqueous medium also. We investigated the effectiveness of CDBACN and CTACN impregnated on various forms of silica like, colloidal silica, silica used for column chromatography and fumed silica. Table-1 represents the effectiveness of CDBACN impregnated on different types of silica as an oxidizing agent in the oxidation of benzoin to benzil and benzhydrol to benzophenone.

These reactions were carried out in a solvent system of water and dioxane in the ratio 15:1. Of the three forms of silica used as solid supports, fumed silica was found to be most efficient with maximum yield and lowest reaction time. Further to

TABLE-1  
OXIDATION REACTION BY CDBACN IN PRESENCE OF  
DIFFERENT FORMS OF SILICA AS SOLID SUPPORT

Entry	Substrate	Product	Silica gel for column chromatography		Colloidal silica		Fumed silica	
			Time (h)	Yield (%)	Time (h)	Yield (%)	Time (h)	Yield (%)
1			26	65	4	70	1.00	90
2			28	60	5	70	0.75	85

optimize the reaction conditions a series of reactions were carried out by varying the substrate to oxidant molar ratio as well as reaction time (Tables 2 and 3). It was found that a molar ratio 1:2 (substrate:oxidant) gives maximum yield in shortest reaction time. So all oxidation reactions (Table-4, **Scheme-I**) and deoxygenation reactions (Table-5, **Scheme-II**) were carried out with fumed silica as the solid support maintaining a substrate to oxidant molar ratio of 1:2.

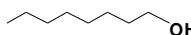
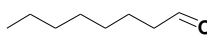
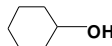

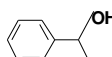
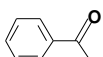
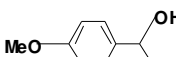
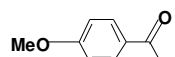
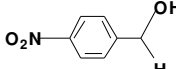
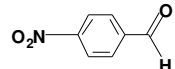
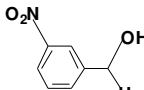
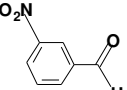
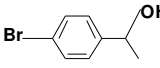
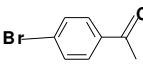
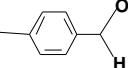
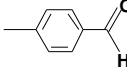
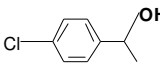
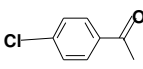
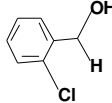
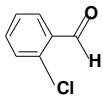
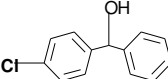
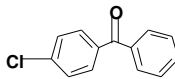
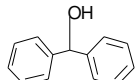
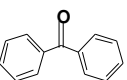
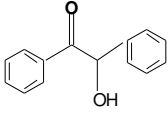
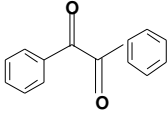
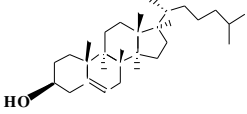
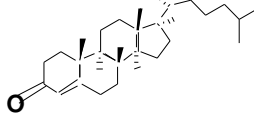
TABLE-2  
EFFECT OF VARIATION OF SUBSTRATE TO OXIDANT MOLAR RATIO ON  
THE YIELD OF OXIDATION OF BENZOIN TO BENZIL

Entry	Substrate (Benzoin)	Oxidizing agent (CDBACN)	Time (h)	Yield (%)
1	1	0.5	2	20
2	1	1.0	2	50
3	1	1.5	2	75
4	1	2.0	1	90
5	1	3.0	1	90

TABLE-3  
EFFECT OF VARIATION OF SUBSTRATE TO OXIDANT MOLAR RATIO ON  
THE YIELD OF OXIDATION OF *p*-NITROBENZALDEHYDE OXIME TO  
*p*-NITROBENZALDEHYDE

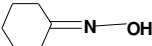
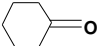
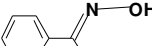
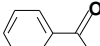
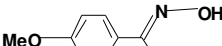
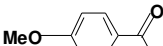
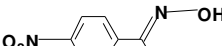
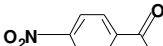
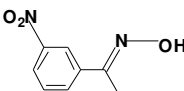
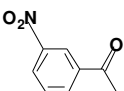
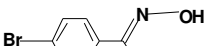
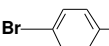
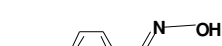
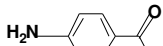
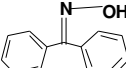
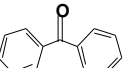
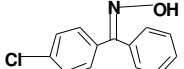
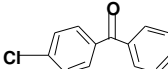
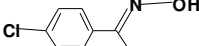
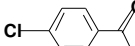
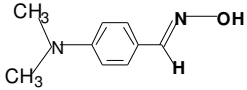
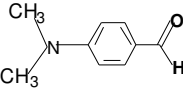
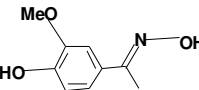
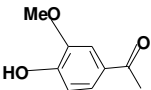
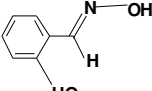
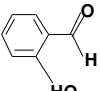


Entry	Substrate ( <i>p</i> -nitrobenzaldehyde oxime)	Oxidizing agent (CDBACN)	Time (h)	Yield (%)
1	1	0.5	2.0	10
2	1	1.0	2.0	45
3	1	1.5	2.0	70
4	1	2.0	1.5	85
5	1	3.0	1.5	85

TABLE-4  
 OXIDATION REACTION USING CERIUM BASED OXIDANTS  
 IMPREGNATED ON FUMED SILICA IN AQUEOUS MEDIUM

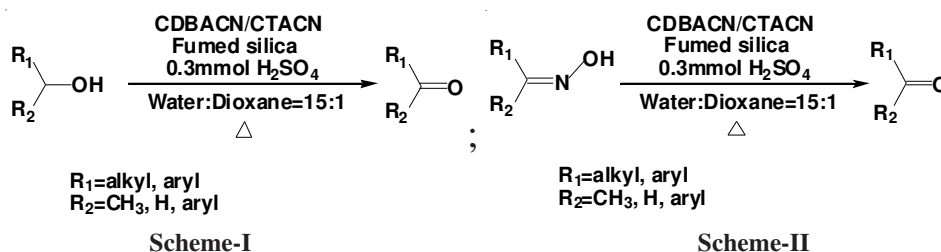
Entry	Substrate	Product	m.p. (°C)	CTACN		CDBACN	
				Time (h)	Yield (%)	Time (h)	Yield (%)
1			105 (106) <sup>a</sup>	3	75	No reaction	
2			160 (162) <sup>a</sup>	2	75	3	70
3			104 (105) <sup>b</sup>	2	80	3	75
4			38 (39)	2	75	3	65
5			105 (106)	1	80	3	20
6			59 (58)	45 min	85	3	30
7			50 (51)	2	75	3	25
8			111 (112) <sup>b</sup>	50 min	80	1	80
9			45 (47)	3	60	No reaction	
10			85 (86)	3	70	No reaction	
11			77 (78)	3	60	No reaction	
12			50 (51)	25 min	85	45 min	85
13			94 (95)	30 min	90	1	90
14			79 (79-80)	2	70	No reaction	

<sup>a</sup>m.p. of 2,4-dinitrophenyl hydrozone (DNP) derivative; <sup>b</sup>m.p. of phenyl hydrozone derivative.

TABLE-5  
DEOXIMATION REACTION USING CERIUM BASED OXIDANTS  
IMPREGNATED ON FUMED SILICA IN AQUEOUS MEDIUM

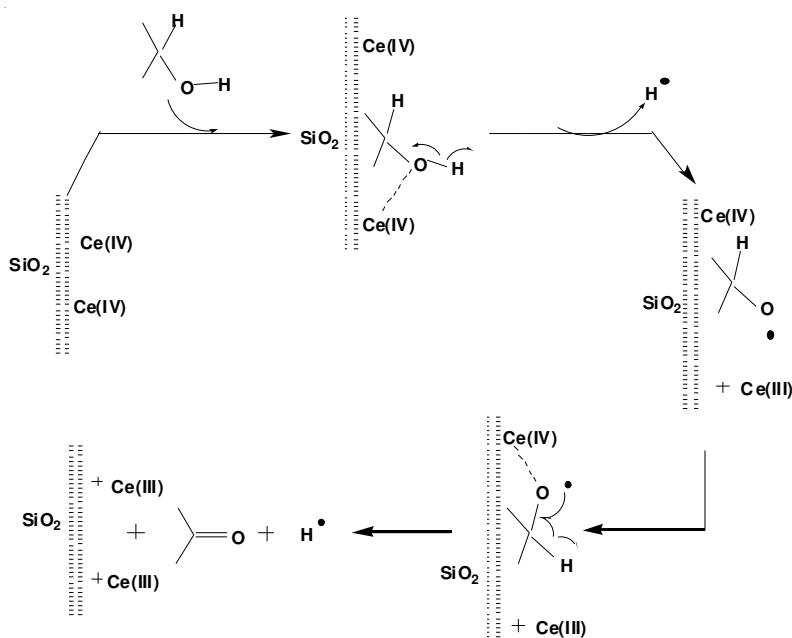
Entry	Substrate	Product	m.p. (°C)	CTACN		CDBACN	
				Time (min)	Yield (%)	Time (min)	Yield (%)
1			160 (162) <sup>a</sup>	30	85	45	80
2			104 (105) <sup>b</sup>	40	80	60	80
3			38 (39)	10	90	15	90
4			105 (106)	50	90	90	85
5			59 (58)	20	90	30	85
6			50 (51)	5	90	10	90
7			107 (106)	25	80	30	65
8			50 (51)	1	95	1	90
9			77 (78)	5	90	10	90
10			46 (47)	10	90	15	90
11			71 (72-74)	20	85	30	80
12			79 (81)	10	85	15	85
13			142 (143) <sup>b</sup>	30	85	45	80
14			105 (106) <sup>a</sup>	60	50	60	30

<sup>a</sup>m.p. of 2,4-dinitrophenyl hydrozone (DNP) derivative; <sup>b</sup>m.p. of phenyl hydrozone derivative.

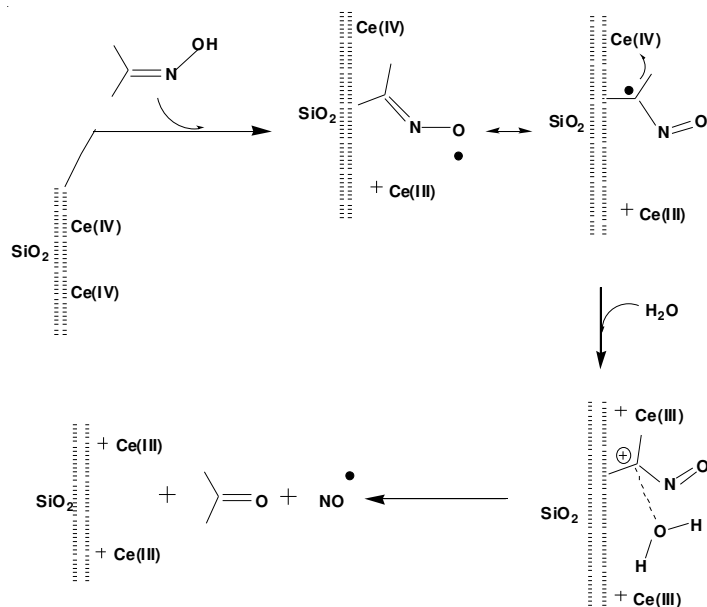


The phase-transfer oxidant impregnated on silica could bring the substrate and the reactant into close proximity<sup>12,13</sup> which facilitates the electron transfer process between Ce(IV) and the substrate. This enhances the reaction rate<sup>14-16</sup>. Use of silica as support could also increase the effective surface area and constrain both substrate and the reactant in pores for decreasing the entropy of activation for electron transfer<sup>12,13</sup>.

Of these two cerium based phase-transfer oxidants investigated CTACN was found to be more efficient than CDBACN. In case of oxidation of alcohol (Table-4) it was found that CDBACN is more selective. It cannot oxidize aliphatic alcohol and alcohols having electron withdrawing group in benzene ring. The probable mechanisms for the reactions are shown in **Schemes III** and **IV**. Two observations *viz.*, the requirements of substrate and oxidant in the molar ratio 1:2 to give the highest yield as well as the free radical nature of the reaction, indicated by their inhibition by hydroquinone are in conformity with the proposed mechanisms.



**Scheme-III:** Probable mechanism of oxidation of alcohol



**Scheme-IV:** Probable mechanism of deoxygenation of oxime

The selectivity of present reagents have also been investigated. A mixture of acetophenone oxime and cyclohexene was used as the substrate and acetophenone was found to be the sole oxidation product, with cyclohexene remaining unchanged. This showed the selective nature of the reagent as well.

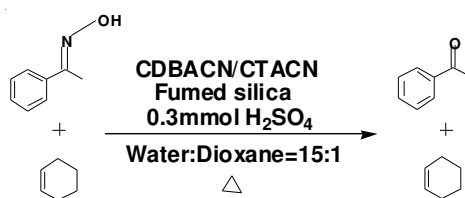


Fig. 1.

## Conclusion

In summary, we have reported two cerium based phase transfer oxidants CDBACN and CTACN impregnated on fumed silica which effectively oxidizes alcohol to carbonyl compounds and regenerates carbonyl compounds from their oximes, in a predominantly aqueous medium. Further, CDBACN was effective against only secondary alcohols, which provides an opportunity for selective oxidation of secondary alcohols in presence of both primary and secondary alcoholic groups. Moreover, a major drawback of over oxidation to acid was also not observed. In conclusion, we have developed a simple method of oxidation of alcohol and regeneration of carbonyl compounds from their oximes in aqueous medium, with high yields and involving easy workup procedures.

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