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Pseudohalide assisted aerobic oxidation of alcohols in the presence of visible-light

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ABSTRACT

Pseudohalides are well known to do similar chemistry like halides. Thiocyanate, a pseudohalide acts like halides in many ways. Thiocyanate radicals ('SCN) are generated from readily available thiocyanate salts using Rose Bengal through single electron transfer (SET) in the presence of visible light. Thiocyanate radicals abstract hydrogen like other halide radicals, so this aspect of chemistry was used for the oxidation of alcohols to their corresponding aldehydes using oxygen as the terminal oxidant. This method shows a broad scope and well tolerance towards various functional groups.

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Visible light assisted organic reactions have emerged as one of the most promised pathways in green synthesis. However, most common organic molecules do not absorb light in the visible wavelength region (400–800 nm), that accounts for approximately 43% of the incoming solar spectrum.¹ This limits the usage of visible light for carrying out various organic reactions. To overcome the above limitation, researchers have started developing catalytic systems which can utilize visible light to promote organic transformations.²

In the last few decades, Ru and Ir polypyridyl complexes have been widely exploited as a visible light photocatalyst to carry out photochemical reactions such cycloaddition.^{3a} as decarboxylation,^{3b} dehalogenation,^{3c} C-H functionalization.^{3d} On the other hand, organic dyes such as eosin Y and rhodamine-6G have been utilized as an active visible light photocatalyst for reactions like direct C-H bond arylation of heteroarenes with aryl diazonium salt,^{4a} reduction of aryl halides^{4b} and hydrogen evolution.^{4c} Further, inorganic semiconductors have also been sensitized by organic dye molecules to achieve longer lifetimes of the excited states via electron transfer.⁵ Herein, the organic dye molecule is excited on exposure to visible light rather than the semiconductor. The excited dye molecules then inject electrons into the conduction band of the semiconductor particles, which does not create holes in the valence band of the semiconductor.

* Corresponding author. *E-mail address:* ndpradeep@chem.iitkgp.ernet.in (N.D. Pradeep Singh). Thus resulting longer excited state life time, as noted in the case of dye-sensitized TiO_2 solar cell.⁶

The selective oxidation of alcohols to their corresponding carbonyl compounds is known to be one of the most fundamental transformations in both laboratory and industrial synthetic chemistry, as carbonyl compounds serve as important and versatile intermediates for the synthesis of fine chemicals, drugs, vitamins, and fragrances.⁷ Generally, the oxidation of benzyl alcohols are carried out using rather toxic and expensive reagents such as chromate, permanganate and noble metal catalysts including Pt, Pd, Au.^{8,9}

To date, several photocatalytic methods have been developed for the oxidation of benzyl alcohols.¹⁰ In 1984 Cano-Yelo and Deronzier reported that the ruthenium(II) photocatalyst oxidizes benzylic alcohols to the corresponding aldehydes using aryldiazonium salts as a sacrificial oxidant.¹¹ There are numerous report on photocatalysis using TiO₂.TiO₂ photocatalyst is a clean catalytic system for oxidation of organic compounds under UV irradiation, but ineffective under visible light.¹² Recently, Zhao and co-workers synthesized dye/TiO₂photoredox catalyst coupled with TEMPO (2266-tetramethylpiperidinyloxyl) for selective oxidation of alcohols in the presence of molecular oxygen under visible light.¹³ On the other hand, Flavin photocatalysts are also shown to oxidize benzyl alcohols to their corresponding aldehydes under visible light. However, these Flavin photocatalysts are found to be more effective for the oxidation of electron-rich benzyl alcohols rather than electron-poor benzyl alcohols. Moreover, the photooxidation ability of Flavin analogs can be enhanced by the simple addition







of Lewis acids (such as $Mg^{2+}, Zn^{2+}, Yb^{3+}$ and Sc^{3+} ions).¹⁴ Further, Su et al. showed mesoporous carbon nitride (mpg-C₃N₄) polymer can act as a photocatalyst to activate molecular oxygen for the selective oxidation of benzyl alcohols under visible light irradiation.¹⁵

Though several methods have been developed for the oxidation of benzyl alcohols, they suffer certain drawbacks to some extent such as the use of expensive and toxic metals, low selectivity, and limited substrate scope. Hence there is a need to develop a simple method for the oxidation of benzyl alcohols which can surpass the above limitations.

Recently, pseudohalide, thiocyanate ions (SCN⁻) have gained considerable importance mainly in the areas like modulation of catalytic activity,^{16a} shape-controlled synthesis of metal nanostructures^{16b} and as a dopant in photovoltaic applications.^{16c} Pseudohalides, viz. cyanide, thiocyanate and azide anions, show chemical properties analogous to single halogen atoms.¹⁷

It is well known that halide radicals are potential candidates for hydrogen abstraction.^{18–20} This motivates us to reason that, like halide radicals pseudohalide radicals can show similar property of abstracting hydrogen.

In the literature we have found Pixu Li's research group and others showed the generation of thiocyanate radicals from thiocyanate anion on exposure to visible light in the presence of organic dyes.²¹ Their studies prompted us to explore, for the first time, thiocyanate radical for the oxidation of benzyl alcohols. We hypothesize that thiocyanate radical can abstract hydrogen, like the halide radicals, from the benzylic position of the alcohols, which will then subsequently convert to their corresponding aldehydes in the presence of molecular oxygen. Based on the above assumptions, we designed a metal free, non-toxic and cheap method for the photooxidation of aromatic alcohols under visible light. In this method, we have used a very cheap organic dye, Rose Bengal (RB), as the photocatalyst, thiocyanate radical as the hydrogen abstractor and air as the oxidant (Scheme 1).

Results and discussion

Initially, we investigated the photooxidation of 4-Chlorobenzyl alcohol. The reaction was performed using 4-Chlorobenzyl alcohol (0.1 mmol), Rose Bengal (1 mol%), NH₄SCN (1 eq.), acetonitrile as the solvent in presence of air under the irradiation of a CFL light. After 60 min of irradiation, we have detected 4-Chlorobenzalde-hyde (**2a**). Further, increasing the irradiation time up to 20 h, we noted that 4-Chlorobenzyl alcohol (**1a**) was oxidized to 4-Chlorobenzaldehyde (**2a**) with a moderate yield (23%) and high selectivity (100%) (Table S1, Supporting information). This method is highly selective towards the conversion of the alcohols to their corresponding aldehydes over other products (such as carboxylic acid). We have calculated the selectivity according to the reported equation (Supporting Information – page 3).



Scheme 1. Photooxidation of benzyl alcohols to their corresponding benzaldehydes under different conditions.

This result encouraged us to optimize our reaction conditions.

First, we were interested to find out the optimum amount of the photocatalyst, Rose Bengal, required for the photooxidation. For this purpose, we have carried out the photooxidation of 1a with varying amount of Rose Bengal. The result showed that as we increase the concentration of Rose Bengal the yields improves significantly. It is worthy to note that Rose Bengal (5 mol%) in acetonitrile gives the maximum product (76%) with high selectivity (100%) (Table 1, Entry 2). The photooxidation of 1a was completely inhibited in the absence of Rose Bengal (Table 1, Entry 13). On the other hand, when we have used Eosin Y (Table 1, Entry 3) or Fluorescein (Table 1, Entry 4) as the organic photocatalyst in place of Rose Bengal, the photooxidations produced similar yield. The above experiment confirms the need of organic photocatalyst. Second, we investigated the optimum amount of NH₄SCN required for the photooxidation of 4-Chlorobenzvl alcohol. It was found that 3 equivalent of NH₄SCN in acetonitrile vielded 4-Chlorobenzaldehvde (2a) in maximum yield (76%) (Table 1, Entry 2).

In addition, to check the importance of pseudohalide precursor NH₄SCN, we performed the photooxidation of **1a** using KSCN in place of NH₄SCN (Table 1, Entry 11). We found that photooxidation was not effective like in the case of NH₄SCN, and there was no photoproduct formation in the absence of NH₄SCN (Table 1, Entry 10). Third, we noted that irradiation time has great influence on the yield of photooxidised product. Increasing the irradiation time significantly improve the yield of 2a. Maximum yield of 2a was obtained after 20 h of irradiation. Finally, to understand the significance of solvent on the photooxidation, we have carried out the photooxidation of 4-Chlorobenzyl alcohol in different solvents such as acetonitrile (CH₃CN), chloroform (CHCl₃) and tetrahydrofuran (THF). In CH₃CN, we noted **1a** produces 76% of 4-Chlorobenzaldehyde (Table 1, Entry 2). However, when THF was used as a solvent the oxidation of **1a** produced **2a** with 38% in yield (Table 1, Entry 5). In CHCl₃, this method oxidizes **1a** only in trace quantities, this might be due to the insolubility of thiocyanate salts in CHCl₃ (Table 1, Entry 6). Further, we also showed that **1a** can be oxidized to 2a in CH₃CN/H₂O (1:1) solvent system, proving that our method can be useful in the presence of water.

It is of significance that there is no photooxidation of alcohol in absence of O_2 (Table 1, Entry 9) and visible-light irradiation (Table 1, Entry 14). After optimization of the reaction conditions, we carried out the photooxidation of **1a** in large scale, we noted our method produced **2a** in good yield with high selectivity (Table 1, Entry 16). These results suggest that visible light, photocatalyst, oxygen and thiocyanate play their unique roles for the successful oxidation of various alcohols.

The only limitation of our method is that it requires an excess amount of thiocyanate anion for the oxidation of alcohol. This is because of the thiocyanate radicals produced from thiocyanate anion combines with each other to form an inorganic polymer known to be polythiocyanogen (or parathiocyanogen) with the empirical formula (SCN)x as a yellow solid after completion of the reaction. The polymer was characterized by UV/Vis, FT-IR, and MALDI-TOF mass spectroscopy. UV/Vis spectrum shows a λ_{max} at 450 nm (Supporting information, Fig. S1). For (SCN)x, the MALDI-TOF mass spectroscopy showed a parent ion at 1030 and a series of peaks with $(SCN)_2$ repeat units (116 m/z); this result implies that (SCN)₂ may be the monomer unit of the polymer (Supporting information, Fig. S2). Further, IR spectrum shows a peak with the maximum at 1145 cm⁻¹ (Supporting information, Fig. S3). The observed data suggest that the polymer may be consists of 1,2,4-dithiazole rings linked by nitrogen atoms.²

The parathiocyanogen itself is photoactive,²³ so we hypothesized that this polymer may contribute to the reaction to improve the yield. When we replaced Rose Bengal with parathiocyanogen, the oxidation of **1a** produced **2a** (Table 1, entry 15). Hence, this

Table 1

Optimization of the photooxidation of 4-Chlorobenzyl alcohol.^a



Entry	Catalyst	Solvent	Yield [%] ^b	Sel. [%] ^c
1 ^d	Rose Bengal	CH ₃ CN	66	100
2	Rose Bengal	CH ₃ CN	76	100
3	Eosin Y	CH ₃ CN	70	100
4	Fluorescein	CH ₃ CN	65	100
5	Rose Bengal	THF	38	100
6	Rose Bengal	CHCl ₃	Trace	-
7	Rose Bengal	CH ₃ CN/H ₂ O	9	100
8 ^e	Rose Bengal	CH ₃ CN	40	100
9 ^f	Rose Bengal	CH ₃ CN	0	0
10 ^g	Rose Bengal	CH ₃ CN	0	0
11 ^h	Rose Bengal	CH ₃ CN	42	100
12 ⁱ	Rose Bengal	CH₃CN	Trace	-
13	-	CH₃CN	0	0
14 ^j	Rose Bengal	CH ₃ CN	0	0
15	Parathiocyanogen	CH ₃ CN	7	100
16 ^k	Rose Bengal	CH ₃ CN	45	100
17 ^L	Rose Bengal	CH ₃ CN	71	100

Reaction condition: alcohol (0.1 mmol), NH4SCN (3 eq.), catalyst (5 mol%), solvent (2 ml), O2 bubbling for 15 min, irradiation under a 23 W CFL lamp for 20 h at room temperature.

^{b,c} calculated from the isolated product.

^d 2 eq. of NH₄SCN.

In presence of air.

In presence of N2.

In absence of NH₄SCN.

In presence of KSCN.

In presence of TEMPO.

In absence of light.

Scaled-up reaction: alcohol (1 mmol). 1

In presence of green LEDs.

method involves a synergistic effect of both 'SCN and in-situ generated parathiocyanogen to oxidize alcohols efficiently with excellent yield.

After establishing optimal conditions, we then sought to explore the substrate scope of our photocatalytic system for a broad range of alcohols (Table 2). Electron-rich aromatic alcohols namely, p-methoxybenzyl alcohol was oxidized to p-methoxybenzaldehyde with high conversion (100%) and selectivity (100%) (Table 2, Entry 4a). Interestingly, Electron-poor aromatic alcohols having electron withdrawing groups such as Cl, Br and NO₂ were also converted to their corresponding aldehydes with high selectivity (100%) (Table 2, Entries 7a-11a, 21a). Aromatic alcohols having substituents at ortho, meta, or para positions were successfully oxidized to their corresponding aldehydes with comparable yield and high selectivity (100%) (Table 2, Entries 17a-19a). In particular, secondary alcohols such as 1-phenyl ethanol were oxidized to their corresponding ketone with high selectivity (Table 2, Entries 12a-14a). Cinnamyl alcohol was oxidized with 60% in yield to cinnamaldehyde (Table 2, Entry 24a). Finally, heteroaromatic alcohols were also oxidized using our photocatalytic system to their corresponding aldehydes in moderate yields (Table 2, Entries 15a, 16a, 22a, 23a).

Further, we explored our method for aliphatic alcohols. We noted that only secondary and allylic aliphatic alcohols were oxidized to their corresponding aldehydes with poor yield (Table S2, Entries 13,678).

The oxidation of primary alcohols yielded aldehydes only in trace quantities (Table S2, Entry 2,4,5). The present method is inefficient for the oxidation of aliphatic alcohols.

After successful oxidation of alcohols in millimolar scale, we thus interested to scale up our method. The gram scale oxidation of alcohols namely p-methoxybenzyl alcohol and 4-chlorobenzyl alcohol were performed. The results showed that the mentioned alcohols were oxidized to their corresponding aldehydes with moderate yields (Scheme 2).

In order to understand the mechanism of this reaction, we performed the oxidation of **1a** in the presence of a radical quencher. The oxidation was quenched in presence of TEMPO (Table 1, Entry 12), which indicates a radical mechanism was involved in the reaction.

On the basis of our observations and literature reports, a plausible mechanism is proposed (Scheme 3).^{21,24} Under visible-light irradiation, Rose Bengal (RB) gets to the excited state, RB*. A single electron transfer between -SCN anion ($E_{SCN/SCN}^{-} = +0.61 \text{ V}$) and RB* ($E_{*RB/RB}^{-}$ = +0.99 V) affords 'SCN radical and RB⁻ radical anion. Further, RB^{•-} return to the ground state RB by oxidizing the molecular oxygen, and thus the photoredox cycle is complete. Then, the *SCN radical abstracts a hydrogen from the benzylic position of the alcohol to produce Ar(CH) OH and thiocyanic acid (HSCN). The Ar(CH) OH reacts with O_2 to afford the corresponding aldehyde. (SCN)x polymer was found to be the by-product, which is believed to be formed by the combination of *SCN radicals.25

To support the involvement of 'SCN radical in the photooxidation of alcohols, we performed the oxidation of alcohol in the presence of various radical scavenger such as 1,1-Diphenylethylene and N-tert-Butyl- α -phenylnitrone (PBN) (Supporting information, Scheme S1). In presence of 6 equivalent of 1,1-Diphenylethylene

Table 2

Products of the aerobic oxidation of various aromatic alcohols with the NH₄SCN/RB catalyst system under visible-light irradiation.^a



^a Reaction condition: alcohol (0.1 mmol), NH₄SCN (3 eq.), catalyst (5 mol%), solvent (2 ml), O₂ bubbling for 15 min, irradiation under a 23 W CFL lamp for 20 hrs at room temperature. ^b Yield of isolated product.

^c Selectivity of isolated product.

^d Calculated from GC instrument.



Scheme 2. Gram scale level oxidation of alcohols.

2a was detected only in trace quantities. The alcohol conversion was completely ceased in presence of excess N-tert-Butyl- α phenylnitrone (PBN) (Supporting information, Scheme S1). So,

the involvement of thiocyanate radical is inevitable. Further to rule out the possibility of oxidation of SCN⁻ by ¹O₂, we performed the photooxidation using photocatalyst fluorescein, since fluorescein does not generate ${}^{1}O_{2}$. Interestingly, we noted **2a** was formed in 65% yield (Table 1, entry 4). Moreover, to check any possibilities of hydrogen abstraction by superoxide radicals, we have carried out the oxidation in presence of various electron donors such as triethylamine, diisopropylethylamine, and thiols, the oxidation of benzyl alcohols was not satisfactory, this excludes the possibility of abstraction of benzylic hydrogen by the superoxide radical. In addition, We have carried out the reaction in the presence of BrCCl₃, which is a non hydrogen donating oxidant. We have obtained the oxidation product, which suggests the O₂ acts as an oxidant here (Supporting information).



Scheme 3. The proposed visible-light-induced alcohol oxidation in the SCN/RB system.

Thus, thiocyanate acts as an electron donor as well as hydrogen abstractor. The formation of thiocyanic acid was further confirmed by using FeCl₃ solution (Supporting information).

In conclusion, a simple and clean method was achieved for the selective oxidation of alcohols under visible-light irradiation in a system containing an inexpensive and readily available organic dye, Rose Bengal, as the photocatalyst, thiocyanate as the hydrogen abstractor and air as the terminal oxidant. This photocatalytic system does not require any transition-metal ions or deleterious oxidants such as Br₂ and chromate. Generally, the reaction is high-yielding, efficient, and scalable. Moreover, no heavy-metal waste was generated during the process. This straightforward method may find usefulness in the synthesis of fine chemicals.

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A. Supplementary data

Supplementary material for the detail synthesis, characterization, and other experimental data of this article is available and provided as a separate electronic file. That file can then be transformed into PDF format and submitted along with the manuscript and graphic files to the appropriate editorial office.

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.tetlet.2017.12.018.

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