

Expeditious oxidation of alcohols to carbonyl compounds using iron(III) nitrate[☆]

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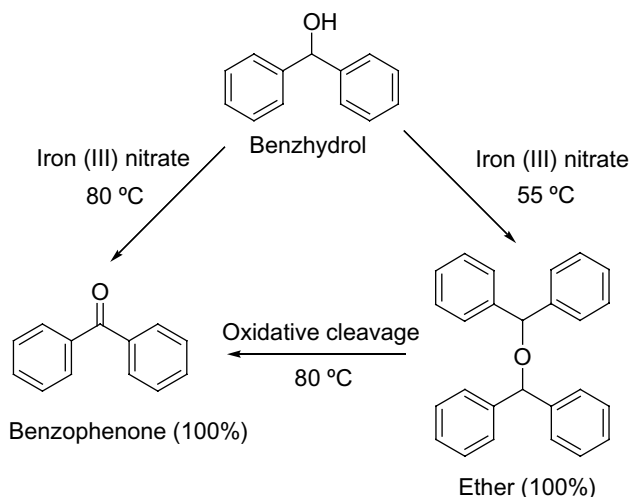
Abstract—An efficient and solvent-free protocol for the oxidation of alcohols to corresponding carbonyl compounds using iron(III) nitrate nonahydrate has been developed.
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The oxidation of alcohols to the corresponding carbonyl compounds is one of the most important transformations in organic synthesis. There are numerous methods available in the literature¹ and the development of new selective oxidative protocols is still considered a challenge.² This void was filled, in part, by using a set of clay-supported metal nitrate salts such as iron(III) nitrate supported on clay, clayfen,^{3,4} and on zeolites, zeofen,⁵ which are known for various applications including oxidation of alcohols. The main drawbacks of clayfen and other related solid supported metal nitrate salts in oxidative transformations are the use of large excess of solvents, reflux reaction conditions, longer reaction times, high ratio of reagent to substrate, and the generation of solid waste (40–50 g/mol). Varma and Dahiya were able to eliminate solvents from these oxidations by employing microwave heating which also helped to reduce the reaction time from hours to seconds.^{2b}

In our continued quest for the development of environmentally friendly alternatives,⁶ we sought to develop an improved methodology which minimizes the use of any solvent or support and requires a low catalyst/substrate ratio. Herein, we describe this facile approach for the

oxidation of secondary aliphatic, alicyclic, and benzylic alcohols (Scheme 1).

Numerous reports have been described for the enhanced oxidative potential of metal nitrates on various mineral oxide supports.^{3–5} We decided to investigate the proper control reactions in the absence of any solvent or support. In order to render these oxidations economically more viable and simpler, we focused our attention on iron(III) nitrate nonahydrate which is abundant, cheap, and relatively nontoxic.³ Benzyl alcohol was used as a model compound to evaluate the oxidative potential of



Scheme 1. Iron(III) nitrate catalyzed oxidation of alcohol under solvent-free condition.

Keywords: Iron(III) nitrate; Oxidation; Solvent-free reaction; Alcohols; Carbonyl compounds.

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Table 1. Reactivity trend of nitrate salts in the oxidation of benzyl alcohol

| Entry | Nitrate (1 mmol) | Time (min) | Temperature (°C) | GC conversion (isolated yield) (%) |
|-------|------------------|------------|------------------|------------------------------------|
| 1 | Fe | 15 | 80 | 100 (97) |
| 2 | Cu | 25 | 90 | 88 (91) |
| 3 | Zn | 60 | 90 | <20 |
| 4 | NH ₄ | 240 | 90 | <5 |

various nitrate salts and for optimizing the reaction conditions (Table 1).

Iron nitrate nonahydrate showed better reactivity than copper nitrate at lower temperature and was selected for the detailed investigations. The melting point of iron nitrate nonahydrate is only 48 °C and it is miscible with the benzyl alcohol at this temperature. This makes the oxidation a homogeneous catalytic reaction and the formation of benzaldehyde can be visibly seen as a separate layer that forms during the course of the reaction. Copper nitrate was also equally effective but its higher melting point requires an elevated reaction temperature and relatively longer reaction time when compared to iron nitrate. The oxidative protocol involves the liberation of brown fumes of nitrogen dioxide which ceases upon completion of the oxidation.^{3b}

Since the iron nitrate and copper nitrate impregnated on solid support are effective as oxidants, we questioned the theory based on the premise that the oxidation rate enhancements are due to their impregnation on the solid supports.³ The earlier control experiments may have the following drawback: a large excess of non-polar solvent pentane was used as the reaction medium in which iron nitrate is completely insoluble thus reducing the probability of interaction with the substrate. Undoubtedly, the impregnation of iron nitrate on solid support helped to disperse the oxidant and presumably polar alcohols got trapped on the support to facilitate the reaction.

The amount of iron nitrate required for the complete conversion is shown in Table 2, which indicates that ~0.66 mmol of iron nitrate was adequate for the safe conversion of benzyl alcohol to benzaldehyde and is in agreement with the earlier proposed mechanism that requires at least two nitrate groups for the completion of oxidation.^{3c}

The reaction rate was slow at room temperature and increased with the rise in temperature and the oxidation

Table 2. Optimization of amount of iron nitrate for the oxidation of benzyl alcohol to benzaldehyde^a

| Entry | Benzyl alcohol (mmol) | Iron nitrate (mmol) | GC conversion (%) | Isolated yield (%) |
|----------------|-----------------------|---------------------|-------------------|--------------------|
| 1 | 1 | 1.5 | 100 | 96 |
| 2 | 1 | 1 | 100 | 96 |
| 3 | 1 | 0.66 | 100 | 96 |
| 4 | 1 | 0.33 | 76 | 72 |
| 5 ^b | 1 | 1 | 0 | 0 |

^a The reaction was carried out at 60 °C for 30 min.

^b 1 mL of water as reaction medium.

Table 3. Effect of temperature on the benzyl alcohol oxidation with iron nitrate^a

| Entry | Temperature (°C) | Time (min) | GC conversion (%) | Isolated yield (%) |
|-------|------------------|------------|-------------------|--------------------|
| 1 | 30 | 240 | <60 | 52 |
| 2 | 50 | 30 | >90 | 95 |
| 3 | 60 | 15 | >90 | 96 |
| 4 | 70 | 10 | >90 | 96 |
| 5 | 80 | 5 | >90 | 96 |

^a 0.66 mmol of Fe(NO₃)₃ per mmol of alcohol was used.

rate became relatively faster above the melting point of iron nitrate nonahydrate due to increased homogeneity of the reactant (Table 3).

Effect of oxygen atmosphere on the benzyl alcohol oxidation showed that under oxygen pressure iron nitrate can be used in less quantity than the stoichiometric amount (Table 4).

Using these optimized reaction conditions,⁷ the efficiency of this approach was studied for the oxidation of various benzylic alcohols and the results are summarized in Table 5. All benzylic alcohols gave excellent conversion, but chloro-, fluoro-, and bromo-substituted benzylic alcohols were less reactive than the corresponding benzyl alcohol with the reactivity order, Cl < Br < F (entries 1–5). Oxidation of 1,4-benzenedimethanol delivered exclusively the corresponding 1,4-phthalaldehyde while 1,2-benzenedimethanol gave 65% of aldehyde and 35% isobenzofuranone (entry 8).

On close analysis of the reaction, we found that trace amount of dibenzyl ether was formed during the oxidation of benzyl alcohol. The amount of the benzyl ether was higher at lower temperature indicating that the reaction mechanism may involve the formation of ether as an intermediate. A control experiment of the oxidation of benzyl ether with iron nitrate was conducted at 60 °C for 15 min that resulted in benzaldehyde. Similarly, the oxidation of benzhydrol at 50 °C led to the quantitative formation of a white solid; the ¹³C and ¹H NMR spectra and CHN analysis confirmed that the intermediate was the ether of benzhydrol. This benzhydrol ether also underwent oxidative cleavage to benzophenone above 65 °C. The rate of oxidation was increased with temperature and a complete conversion was obtained at 80 °C. Direct heating of benzhydrol at 80 °C for 30 min also gave complete conversion to benzo-

Table 4. Effect of oxygen atmosphere in the oxidation of benzyl alcohol

| Alcohol (mmol) | Fe(NO ₃) ₃ (mmol) | Temperature (°C) | Pressure (bar) | Time (h) | GC yield (%) |
|----------------|--|------------------|----------------|----------|-----------------|
| 5 | 1.00 | 80 | 1 | 1 | >95 |
| 10 | 1.00 | 80 | 1 | 1 | 55 |
| 50 | 1.00 | 50 | 20 | 5 | 23 |
| 50 | 1.00 | 60 | 20 | 5 | 36 |
| 50 | 1.00 | 80 | 20 | 5 | 56 |
| 50 | 1.00 | 60 | 20 | 5 | 10 ^a |

^a 2 ml water was added to check the effect of water.

Table 5. Iron nitrate catalyzed oxidation of substituted benzyl alcohols

| Entry | Alcohol | Fe(NO ₃) ₃ (mmol) | Temperature (°C) | Time (min) | GC yield (isolated) (%) |
|-------|------------------------|--|------------------|------------|---------------------------|
| 1 | 4-F-benzyl alcohol | 0.66 | 60 | 15 | 76 (70) |
| 2 | 4-F-benzyl alcohol | 0.66 | 60 | 30 | 100 (94) |
| 3 | 4-Cl-benzyl alcohol | 0.66 | 60 | 15 | 60 (57) |
| 4 | 4-Br-benzyl alcohol | 0.66 | 60 | 15 | 70 (65) |
| 5 | 4-Cl-benzyl alcohol | 0.66 | 60 | 30 | 100 (95) |
| 6 | 1,4-benzenedimethanol | 1.32 | 60 | 15 | 100 (96) |
| 7 | Naphthalene 2-methanol | 1.00 | 60 | 30 | 100 (96) |
| 8 | 1,2-Benzenedimethanol | 1.32 | 60 | 15 | 100 (65, 35) ^a |
| 9 | Benzylether | 0.66 | 60 | 15 | 100 (95) |
| 10 | Benzhydrol | 1.00 | 80 | 30 | 100 (95) |
| 11 | Benzhydrol | 1.00 | 50 | 15 | 100 ^b (98) |

^a 35% of the product is isobenzofuranone.

^b Complete conversion to ether of benzhydrol.

Table 6. Oxidation of alcohols using iron(III) nitrate

| Entry | Alcohol (1 mmol) | Fe(NO ₃) ₃ (mmol) | Temperature (°C) | Time (min) | GC yield (%) |
|-------|--------------------------------|--|------------------|------------|-----------------|
| 1 | Norborneol | 1.00 | 80 | 30 | 69 |
| 2 | <i>tert</i> -Butylcyclohexanol | 1.00 | 80 | 30 | 60 |
| 3 | Isoborneol | 1.00 | 80 | 30 | 85 |
| 4 | 1-Phenylethanol | 1.00 | 60 | 30 | 52 ^a |
| 5 | Benzoin | 1.00 | 60 | 30 | 95 |
| 6 | Pinacol | 0.66 | 80 | 5 | 53 |
| 7 | Pent-2-ol | 0.66 | 60 | 30 | 54 |
| 8 | Hexan-1-ol | 0.66 | 60 | 30 | 60 |

^a 32% is the ether of 1-phenylethanol.

phenone. These observations reveal that the formation of ether via dehydration is the first step in the oxidation of alcohols prior to the conversion to the corresponding aldehyde/ketone. This may be a reason that the clayfen-based method gave only about 78% benzaldehyde from benzyl alcohol in which the proximity of the alcohol molecules to form ether is rather limited.

The thermogravimetric analysis of iron nitrate showed that it is stable up to 120 °C and then starts decomposing.⁸ Under our mild reaction conditions with moderate temperature the iron nitrate was stable enough and did not produce completely anhydrous condition that minimizes the possibility of explosion. The oxidations of other alcohols were studied at different reaction conditions and the results are summarized in Table 6. Primary aliphatic alcohols, however, gave a mixture of products which is in agreement with the earlier observations.³

The literature reports also show that supported reagents such as clayfen may induce alkylation reactions in competition with the oxidation reactions.⁹ In contrast, the present method using only iron nitrate selectively oxidized benzyl alcohols to benzaldehydes.

Conclusion

Relatively inexpensive iron nitrate nonahydrate was used in the oxidation of benzyl alcohols and various secondary alcohols to generate the carbonyl compounds. The reaction occurred simply by warming the alcohol with the iron nitrate in the absence of any solvents or

support and delivered excellent yields without over oxidation, and with minimum generation of waste. This oxidative protocol can also be used to nitrate phenol, toluene, and styrene and for the selective oxidation of styrene to benzaldehyde.¹⁰

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