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Combination of $NH_2OH{\cdot}HCl$ and $NaIO_4$: a new and mild oxidizing agent for selective oxidation of alcohols to carbonyl compounds

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ABSTRACT

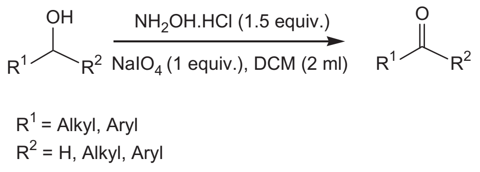
A new method for oxidation of alcohols to carbonyl compounds has been developed using $NH_2OH{\cdot}HCl$ and $NaIO_4$ under mild reaction conditions at room temperature. Application of the method for the synthesis of diiodo compound from α,β-unsaturated carbonyl compound is also described.

The search of a new reagent in organic chemistry is of prime interest to chemists. Oxidation of various organic compounds is an important methodology for both academic and industrial purposes. Thus finding a new oxidizing agent is always interesting. Traditionally oxidation is carried out using transition metal compounds, peracids, and hypervalent halogen compounds. Generally in each of the cases stoichiometrically excess amount of oxidizing agent is used. In particular, chromium(VI) is established as a versatile oxidizing agent for effective and selective oxidation of alcohols to the corresponding carbonyl compounds under mild conditions. In recent times significant improvements were achieved by the development of new oxidizing agents such as pyridinium chlorochromate (PCC),[1,2] pyridinium dichromate (PDC),[3] pyridinium fluorochromate (PFC),[4] pyridinium bromochromate (PBC),[5] quinolinium chlorochromate (QCC),[6] quinolinium fluorochromate (QFC),[7] prolinium chlorochromate,[8] caffeinilium chlorochromate[9] and other reagents such as H_2O_2,[10] NBS,[11] TEMPO,[12] etc. Hypervalent halogen compounds are the other class of oxidizing agents such as IBX,[13] $NaBrO_2$,[14] $NaBrO_3$,[15,16] etc. Most of the previous methods suffer from at least one of the following general disadvantages such as low to moderate yields, long reaction time, harsh reaction conditions, and use of toxic metals and hazardous solvents.

Thus there is still scope for the search of new oxidizing agent. It is well known that use of hypervalent iodine reagents such as IBX, $PhICl_2{\cdot}Py$,[17] and iodic acid[18] has increased the interest in oxidation during last few years because they are rather selective and mild oxidizing agents.

In continuation of our ongoing research for developing newer methodologies,[19] we have investigated the oxidizing ability of $NaIO_4$. In the literature it is found that $NaIO_4$ itself acts as an oxidizing agent in the presence of RuO_2[20] or in the presence of Mn(III) porphyrins[21] and wet silica.[22] Herein we wish to report that the combination of $NaIO_4$ and $NH_2OH{\cdot}HCl$ as a good, selective, and mild oxidizing agent for the oxidation of alcohols to the corresponding carbonyl compounds at room temperature (Scheme 1).

The experimental procedure is very simple.[23] The reaction was carried out using 1 equiv of $NaIO_4$ and 1.5 equiv $NH_2OH{\cdot}HCl$ in dichloromethane solvent at room temperature. The reaction is very fast. We have examined the generality of the present reaction conditions to a variety of alcohols. The results are summarized in Table 1. A wide range of alcohols undergoes oxidation to give the corresponding carbonyl compounds. Aliphatic, benzylic, and heteroaryl substituted alcohols reacted to produce the corresponding carbonyl compounds in good yields. It was also observed that primary alcohols were oxidized to corresponding aldehydes only without any noticeable further oxidation to acids. The reaction condition is mild



Scheme 1. Oxidation of alcohols.

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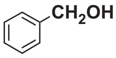
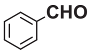
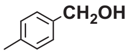
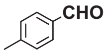
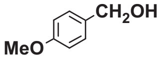
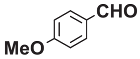
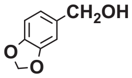
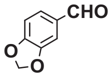
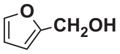
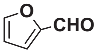
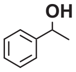
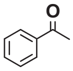
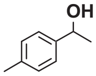
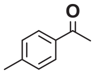
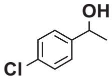
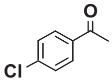
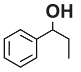
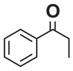
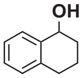
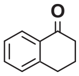
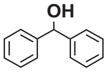
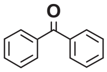
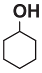
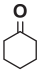
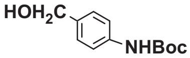
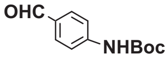
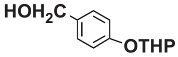
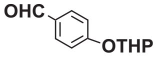
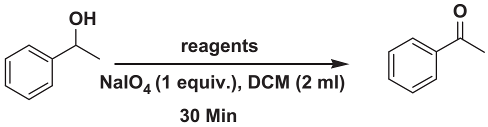
Table 1
Oxidation of alcohols.

Entry	Substrate	Product	Yield[a] (%)	Ref.
1			80	18
2			85	18
3			82	13d
4			80	28
5			77	18
6			85	13d
7			85	24
8			80	24
9			80	25
10			86	24
11			90	18
12			82	13d
13	Isobutanol	Isobutyraldehyde	80	26
14	Isoamyl alcohol	Isovaluraldehyde	82	27
15			78	–
16			74	–

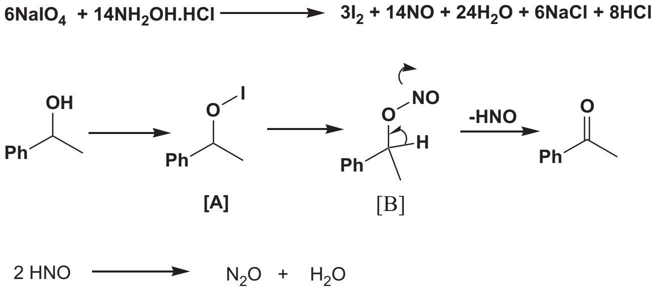
[a] Isolated yields.

Table 2
Oxidation of alcohol in different conditions



Entry	Reagents	Yield[a] (%)
1	$NH_2NH_2{\cdot}H_2O$	0
2	$PhNHNH_2{\cdot}HCl$	0
3	$PhNH_2$	0
4	$PhNH_2{\cdot}HCl$	0
5	1 ml 0.1 N HCl	0
6	L(+) Alanine	0

[a] 100% Starting material recovered.



Scheme 2. The plausible reaction mechanism.

enough as evidenced by the oxidation of piperonol (entry 4, Table 1) to piperonal where the acetal functionality is at risk for cleavage in acidic condition. Protecting groups like NHBoc (entry 15, Table 1) and OTHP (entry 16, Table 1) remain unaffected under the present technique of oxidation. Hydrobenzoin on oxidation gives benzoin as the sole product. By increasing the stoichiometry of the reagents, only a trace of benzil has been found in the crude mixture. The process is equally effective for compound containing electron withdrawing group (entry 8, Table 1) as well as electron donating group (entry 3, Table 1).

To investigate the role of $NH_2OH{\cdot}HCl$, and the plausible reaction mechanism of the present method we have carried out several experiments as shown in Table 2. From the following experiments it is proved that $NH_2OH{\cdot}HCl$ plays a vital role in oxidation of the alcohols. The oxidation does not take place in combination of $NaIO_3$ and $NH_2OH{\cdot}HCl$ instead of $NaIO_4$. We also did the experiments in the presence of different bases such as NaOAc (1 equiv), NaOH (1 equiv), and excess NaOH under the present reaction conditions. It shows that oxidation does not take place in the presence of excess NaOH but the reaction proceeds in the presence of 1 equiv of either NaOAc or NaOH.

The plausible reaction mechanism is shown in Scheme 2. We assumed from the literature (29 **a**–**e**) in the presence of iodine, alcohol forms an intermediate [**A**] which on reaction with NO (generated in situ by the reaction of $NH_2OH{\cdot}HCl$ and $NaIO_4$) forms a nitrosated intermediate [**B**][29e] which is responsible for oxidation of alcohols to aldehydes.

In addition, to support our hypothesis we carried out the oxidation of 1-phenyl ethanol in the presence of chalcone using different molar ratios of $NaIO_4$ (Scheme 3). It was observed that in the presence of 2 equiv of $NaIO_4$ and 3 equiv of $NH_2OH{\cdot}HCl$ only iodination of double bond occurs to form α,β-diiodo carbonyl compound without oxidizing the alcohol. However, both iodination of chalcone and oxidation of alcohol occurred in the presence of 4 equiv of $NaIO_4$ and 6 equiv of $NH_2OH{\cdot}HCl$. The iodination of double bond is not only limited for chalcone, that is α,β-unsaturated carbonyl compound but also equally effective for simple unsaturated systems and systematic observation is on under process.

In summary, we have developed a simple and mild oxidizing agent for oxidation of alcohols to carbonyl compounds. The notable superiorities of this procedure are: (a) simple operation; (b) high yields; (c) fast reaction; (d) neutral reaction conditions and (e) above all, transition metal-free protocol. We believe that the present methodology of oxidation will be very much useful for both academic and industrial purposes.

Acknowledgments

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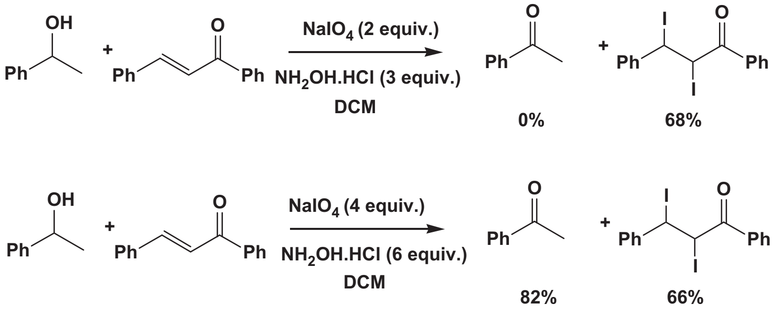

Scheme 3.

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23. ***Typical experimental procedure for the synthesis of Piperonal:*** (entry 4, Table 1**)** In a typical experimental procedure a mixture of benzo[*d*][1,3]dioxol-5-ylmethanol (1 mmol, 152 mg), $NaIO_4$ (1 mmol, 213 mg) in 2 ml of DCM was taken in an open round bottomed flask at room temperature and then $NH_2OH{\cdot}HCl$ (1.5 mmol, 105 mg) was added by portion for 5 min. After completion (TLC), the reaction mixture was diluted with a 1:1 mixture of water/DCM (10 mL) and washed with 10% (w/v) $Na_2S_2O_3$ (3×5 ml). Then the combined organic layer was dried over anhydrous Na_2SO_4. Evaporation of solvent furnished the crude product which was subjected to column chromatography using ethyl acetate-petroleum ether (1:10) to obtain the analytically pure product as a white solid (122 mg, 80%). mp. 36–38 °C; IR (KBr) cm^{-1} 2966, 1676, 1598, 1481, 1440 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.41 (dd, J = 1.5, 1.5 Hz, 1H), 7.33 (d, J = 1.2 Hz, 1H), 6.93 (d, J = 8.1 Hz, 1H), 6.09 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.2, 152.9, 148.6, 131.7, 128.5, 108.2, 106.7, 102.0. *Tert-butyl 4-formylphenylcarbamate* (entry 15, Table 1): Light yellow liquid. IR (KBr) 3311, 2976, 1714, 1683, 1589 cm^{-1}.^1H NMR (300 MHz, $CDCl_3$): δ 9.80 (s, 1H), 7.33 (d, J = 4.8 Hz, 2H), 7.25 (d, J = 4.2 Hz, 2H), 6.62 (br, 1H), 1.51 (s, 9H). *4-(Tetrahydro-2H-pyran-2-yloxy)benzaldehyde* (entry 16, Table 1): Colourless liquid. IR (KBr) 2935, 1685, 1595, 1508 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 9.86 (s, 1H), 7.79 (d, J = 5.1 Hz, 2H), 7.13 (d, J = 5.4 Hz, 2H), 5.52–5.51 (m, 1H), 3.53–3.50 (m, 2H), 1.73–1.67 (m, 2H), 1.61–1.47 (m, 4H).
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