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Solvent-Free Oxidation of Organic Compounds with $Fe(NO_3)_3.9H_2O$ Catalyzed by $NaHSO_4.H_2O$

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The oxidation of alcohols, methoxymethyl ethers, acetals and ketals to their corresponding carbonyl compounds with $Fe(NO_3)_3.9H_2O$ is efficiently promoted in the presence of $NaHSO_4.H_2O$. All reactions were performed in the absence of solvent in good to high yields. Availability, stability and non-toxicity of the reagents, mild reaction conditions, absence of solvent, relatively short reaction times, good to high yields of the products, and easy work-up are advantages of the proposed method.

Keywords: Alcohols, Methoxymethyl ethers, Acetals and ketals, Solvent free reactions, $Fe(NO_3)_3.9H_2O$, $NaHSO_4.H_2O$

INTRODUCTION

Because of the wide-ranging utility of aldehydes and ketones as an important synthetic intermediates, especially for the construction of carbon-skeletones [1,2] and preparation of many drugs, vitamins and fragnances [3], many methods are reported for the preparation of these type of compounds.

Oxidation of alcohols, as a method of the preparation of aldehydes and ketones, is so important that a large number of methods and reagents have been reported for this purpose [4-8]. However, the development of newer methods and methodologies is currently gaining much attention due to the significance of these oxidation reactions [9].

In recent years, $Fe(NO_3)_3.9H_2O$, as a cheap, non-toxic and commercially available reagent has been used for the oxidation processes, either as supported on silica-gel and K10-clay [10], or mixed with HZSM-5 zeolite [11], tungstophosphoric acid [12], and molibdatop-hosphoric acid [13].

In continuation of our ongoing research program directed toward the development of the applications of hydrogen sulfate salts in organic reactions [14-17], herein we wish to report that $NaHSO_4.H_2O$ is efficiently able to promote the oxidation of alcohols with $Fe(NO_3)_3.9H_2O$. All reactions were performed in the absence of solvent in good to high yields (Scheme 1).

$$R^1R^2CHOH \xrightarrow[\text{Solvent-free, Oil bath (90 } ^{o}\text{C)}]{Fe(NO_3)_3.9H_2O\ /\ NaHSO_4.H_2O} R^1R^2CO$$

Scheme 1

EXPERIMENTAL

Chemicals were purchased from Fluka, Merck and Aldrich Chemical Companies. Yields refer to isolated products. Products were characterized by comparing their physical constants with authentic samples and IR and NMR spectroscopy. The purity determination of the substrates and reaction monitoring were accompanied by TLC on silica gel polygram SILG/ UV 254 plates.

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Table 1. Oxidation of Alcohols in the Absence of Solvent[a]

Entry	Substrate	Product	Time (min)	Yield (%)[b]
1	$PhCH_2OH$	PhCHO	5	95
2	$4\text{-}ClC_6H_4CH_2OH$	$4\text{-}ClC_6H_4CHO$	5	95
3	$2\text{-}BrC_6H_4CH_2OH$	$2\text{-}BrC_6H_4CHO$	18	92
4	$3\text{-}NO_2C_6H_4CH_2OH$	$3\text{-}NO_2C_6H_4CHO$	90	70
5	$4\text{-}NO_2C_6H_4CH_2OH$	$4\text{-} NO_2C_6H_4CHO$	8	92
6	$2\text{-}MeC_6H_4CH_2OH$	$2\text{-}MeC_6H_4CHO$	7	95
7	$4\text{-}Me_3CC_6H_4CH_2OH$	$4\text{-}Me_3CC_6H_4CHO$	6	92
8	$4\text{-}Me_2CHC_6H_4CH_2OH$	$4\text{-}Me_2CHC_6H_4CHO$	15	90
9	$4\text{-}MeOC_6H_4CH_2OH$	$4\text{-}MeOC_6H_4CHO$	6	95
10	$PhCH(OH)CH_3$	$PhCOCH_3$	25	95
11	PhCH(OH)Ph	PhCOPh	8	92
12	PhCH(OH)COPh	PhCOCOPh	70	95
13	$PhCH_2CH_2OH$	$PhCH_2CHO$	35	75
14	$PhCH_2CH_2CH_2OH$	$PhCH_2CH_2CHO$	80	80
15	Cyclohexanol	Cyclohexanone	185	90
16	2-Adamantanol	2-Adamantanone	60	92
17	$PhCH=CHCH_2OH$	PhCH=CHCHO	25	-[c]
18	$PhCH_2OH$	PhCHO	30	0[d]

[a]Reaction conditions: $Fe(NO_3)_3.9H_2O$ (0.5 mmol, 0.202 g), $NaHSO_4.H_2O$ (0.25 mmol, 0.035 g), Oil bath = 90 ºC. [b]Isolated Yields. [c]Mixture of products. [d]Reaction was performed in the absece of $NaHSO_4.H_2O$.

General Procedure

A thoroughly mixed mixture of the substrate (1 mmol), $Fe(NO_3)_3.9H_2O$ (0.5-1 mmol, 0.202-0.404 g) and $NaHSO_4.H_2O$ (0.25-1 mmol, 0.035-0.139 g) was heated in an oil bath (90-95 ºC) for the specified time (Tables 1 and 2). The progress of the reaction was monitored by TLC. The reaction mixture was triturated with CH_2Cl_2 (5 ml) and filtered, and the solid residue was washed with CH_2Cl_2 (2 × 3 ml). The combined organic solution were washed with aqeous solution of $NaHCO_3$ (2 × 5 ml) and dried over $MgSO_4$. Evaporation of the solvent followed by column chromatography on silica gel gave the corresponding carbonyl compounds in good to high yields.

Oxidation of Benzyl Alcohol as a Typical Procedure

A thoroughly mixed mixture of benzyl alcohol (1 mmol, 0.108 g), $Fe(NO_3)_3.9H_2O$ (0.5 mmol, 0.202 g) and $NaHSO_4.H_2O$ (0.25 mmol, 0.035 g) was heated in an oil bath (90 ºC) for 5 min. The progress of the reaction was monitored by TLC. The reaction mixture was triturated with CH_2Cl_2 (5 ml) and filtered, and the solid residue was washed with CH_2Cl_2 (2 × 3 ml). The combined organic solution were washed with aqeous solution of $NaHCO_3$ (2 × 5 ml) and then dried over $MgSO_4$ and concentrated in vacuum. The residue was purified by column chromatography on silica gel to give benzaldehyde as a colourless liquid in 95% yields. IR (neat): $\upsilon = 1700\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 7.48\text{-}7.52$ (m, 2H), 7.60-7.65 (m, 1H), 7.85-7.90 (m, 2H), 9.95 (s, 1H).

Oxidation of 2-(4-Chlorophenyl)-1,3-dioxolane as a Typical Procedure

A thoroughly mixed mixture of 2-(4-Chlorophenyl)-1,3-dioxolane (1 mmol, 0.185 g), $Fe(NO_3)_3.9H_2O$ (1 mmol, 0.404 g) and $NaHSO_4.H_2O$ (1 mmol, 0.139 g) was heated in an oil bath (90 ºC) for 10 min. The progress of the reaction was monitored by TLC. The reaction mixture was triturated with CH_2Cl_2 (5 ml) and filtered, and the solid residue was washed with CH_2Cl_2 (2 × 3 ml). The combined organic solution were washed with aqeous solution of $NaHCO_3$ (2 × 5 ml) and then dried over $MgSO_4$ and concentrated in vacuum. The residue was purified by column chromatography on silica gel to give 4-chlorobenzaldehyde as a white solid in 95% yields. m.p.: 45-46 °C; IR (KBr): IR (neat): $\upsilon = 1703\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$, ppm): $\delta = 7.55$ (d, $J = 7.8$ Hz, 2H), 7.85 (d, $J = 7.8$ Hz, 2H), 9.95 (s, 1H).

RESULTS AND DISSCUTION

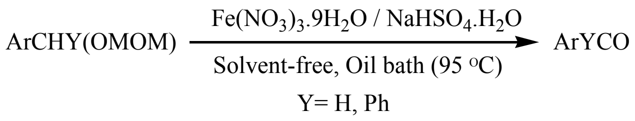
As, shown in Table 1, benzylic alcohols are efficiently converted to their corresponding carbonyl compounds in high yields under optimized reaction conditions. It was noticed that the substitution of electron-donating and electron- withdrawing groups on aromatic ring do not affect the yields of the reactions. This method is also very effective for the oxidation of primary and secondary aliphatic alcohols (Table 1, entries 13-16). Over-oxidation of the products was not observed using this method. However, the method is not suitable for the oxidation of allylic alcohols (Table 1, entry 17).

We have noticed that, in the absence of $NaHSO_4.H_2O$, the oxidation of benzyl alcohol to benzaldehyde does not progress at all and, after 30 min, the starting material remained unchanged (Table 1, entry 18) [12].

The methoxymethylation is used for the protection of alcoholic hydroxyl groups. Although a number of methods are available for deprotection of methoxymethyl ethers to the parent alcohols [18,19], to the best of our knowledge, there is no any report for the direct oxidation of these ethers to the corresponding carbonyl compounds. $NaHSO_4.H_2O$ is a suitable catalyst for efficient oxidation of benzylic methoxymethyl ethers to the carbonyl compounds (Scheme 2, Table 2, entries 1-10). The method is not recommended for the oxidation of aliphatic methoxymethyl ethers which produces a mixture of different products (Table 2, entries 11, 12).

Direct oxidative deprotection of acetals and ketals to carbonyl compounds can also be done with $Fe(NO_3)_3.9H_2O/NaHSO_4.H_2O$ reagent system in the absence of solvent in good to high yields (Scheme 3, Table 2, entries 13-18).

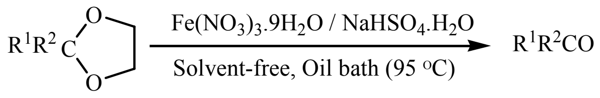
To illustrate the efficiency of the proposed method, we have compared some of the results with some of those reported in the literature (Table 3) [5,20,21].



$$ArCHY(OMOM) \xrightarrow[\text{Solvent-free, Oil bath (95 °C)}]{Fe(NO_3)_3.9H_2O\ /\ NaHSO_4.H_2O} ArYCO$$

Y= H, Ph

Scheme 2



Scheme 3

In conclusion, a very simple and convenient protocol for the oxidation of alcohols, acetals, ketals and benzylic methoxymethyl ethers using $Fe(NO_3)_3.9H_2O/NaHSO_4.H_2O$ reagent system in the absence of solvent was demonstrated. Availability, stability and non-toxicity of the reagents, mild reaction conditions, absence of solvent, relatively short reaction times, good to high yields of the products, and easy work-up are advantages which make this methodology as an important addition to existing methodologies.

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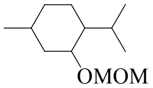
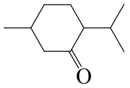
Table 2. Oxidation of Methoxymethyl Ethers, Acetals and Ketals in the Absence of Solvent[a]

Entry	Substrate	Product	Time (min)	Yield (%)[b]
1	$PhCH_2OMOM$	$PhCHO$	40	90
2	$2\text{-}ClC_6H_4CH_2OMOM$	$2\text{-}ClC_6H_4CHO$	20	92
3	$4\text{-}ClC_6H_4CH_2OMOM$	$4\text{-}ClC_6H_4CHO$	30	88
4	$2\text{-}BrC_6H_4CH_2OMOM$	$2\text{-}BrC_6H_4CHO$	30	95
5	$4\text{-}BrC_6H_4CH_2OMOM$	$4\text{-}BrC_6H_4CHO$	15	90
6	$3\text{-}NO_2C_6H_4CH_2OMOM$	$3\text{-}NO_2C_6H_4CHO$	30	90
7	$4\text{-}NO_2C_6H_4CH_2OMOM$	$4\text{-}NO_2C_6H_4CHO$	45	85
8	$2\text{-}MeC_6H_4CH_2OMOM$	$2\text{-}MeC_6H_4CHO$	35	90
9	$3\text{-}MeOC_6H_4CH_2OMOM$	$3\text{-}MeOC_6H_4CHO$	45	90
10	$Ph_2CH(OMOM)$	Ph_2CHO	90	90
11	$PhCH_2CH_2OMOM$	$PhCH_2CHO$	20	-[c]
12			20	-[c]
13	$4\text{-}ClC_6H_4CH(OCH_2CH_2O)$	$4\text{-}ClC_6H_4CHO$	10	95
14	$2,4\text{-}Cl_2C_6H_3CH(OCH_2CH_2O)$	$2,4\text{-}Cl_2C_6H_3CHO$	10	90
15	$3\text{-}NO_2C_6H_4CH(OCH_2CH_2O)$	$3\text{-}NO_2C_6H_4CHO$	20	95
16	$PhCH(Me)CH(OCH_2CH_2O)$	$PhCH(Me)CHO$	60	95
17	$4\text{-}ClC_6H_4C(Me)(OCH_2CH_2O)$	$4\text{-}ClC_6H_4COMe$	15	90
18	$PhCH_2C(Me)(OCH_2CH_2O)$	$PhCH_2COMe$	20	90

[a] Reaction conditions: $Fe(NO_3)_3.9H_2O$ (1 mmol, 0.404 g), $NaHSO_4.H_2O$ (1 mmol, 0.139 g), Oil bath = 90 ºC. [b] Isolated Yields. [c] Mixture of products.

Table 3. Comparison of Some of the Results Obtained by the Proposed Method, with the Corresponding Results Reported by PhIO in the Presence of Phen-Ru-Phen Complex [5], $NaIO_4$/TEMPO/NaBr System [20], and Potassium Dodecatangestocobaltate Trihydrate [21]

Entry	Substrate	Time (h)/Yield (%)			
		This work	Ref. [5]	Ref. [20]	Ref. [21]
1	$4\text{-}MeOC_6H_4CH_2OH$	6 (min)/95	4/100	15/93	-
2	$PhCH_2CH_2OH$	0.6/75	8/10	20/95	-
3	Cyclohexanol	3/90	8/73	28/95	-
4	$3\text{-}NO_2C_6H_4CH(OCH_2CH_2O)$	0.3/95	-	-	5/85
5	$4\text{-}ClC_6H_4C(Me)(OCH_2CH_2O)$	0.25/90	-	-	1/97

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