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Facile Oximation of Carbonyl Compounds with Titanyl Acetylacetonate/NH_2OH System

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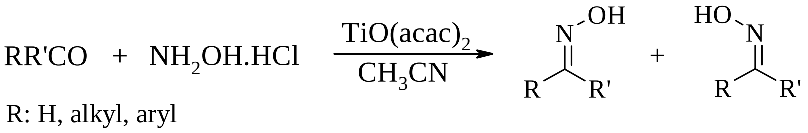
Structurally different aldehydes and ketones were efficiently converted to their corresponding oximes by $TiO(acac)_2/NH_2OH \cdot HCl$ system. The reactions were carried out in refluxing CH_3CN to give the products in high to excellent yields.

Key Words: Titanyl acetylacetonate, Carbonyl compounds, Oxime.

INTRODUCTION

Conversion of a carbonyl group into oxime is an important synthetic transformation in organic chemistry. Oximes are not only useful for protection, purification and characterization of carbonyl compounds, but also they can serve as intermediates for conversion into nitro compounds[1], amides[2], nitriles[3], nitrones[4], amines[5] and isoxazolines[6]. Conventionally, oximes are prepared in refluxing alcoholic solution of carbonyl compounds with hydroxylamine hydrochloride in the presence of acids or bases such as formic acid[7], sulfuric acid[8], pyridine[9], sodium hydroxide or sodium acetate[10]. However, low yields, long reaction times and limitation to use acid or base sensitive functionalities in aldehyde or ketone compounds are the major limitations of the classical methods. The literature review shows that many improvements have been carried out for the preparation of oximes. Ammoximation with ammonia/oxidant/catalyst systems[11], microwave irradiation in the presence of wet basic Al_2O_3[12] or NH_2OH supported on silica gel[13] and in the absence of any catalyst[14], using TiO_2/SO_4^{2-} solid superacid[15], CaO at solvent-free condition[16], ethylenediamine/oxone in water[17], ultrasound irradiation in the presence or absence of Na_2SO_4[18], using aqueous $NH_2OH \cdot HCl$ in ionic liquids[19], using heterogeneous polyoxometalate at solvent-free condition[20], phase transfer catalysis[21] and using ion-exchange amberlyst A-21[22] are some of the protocols which have been reported for the transformation of carbonyl compounds to oximes.

The challenge in chemistry to develop efficient processes, reaction media, conditions and utility of materials based on the idea of green chemistry is one of the most important issues in the scientific community. In this context and continuation of our earlier works on the application of titanyl acetylacetonate, $TiO(acac)_2$, in organic synthesis[23,24], herein we wish to report this Ti(IV) reagent efficiently promotes the conversion of structurally different aldehydes and ketones to the corresponding oximes with hydroxyl amine hydrochloride in refluxing CH_3CN (**Scheme-I**).



Scheme-I

EXPERIMENTAL

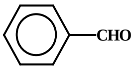
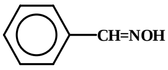
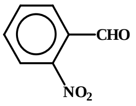
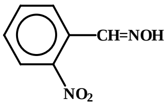
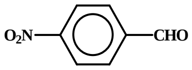
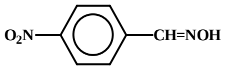
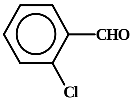
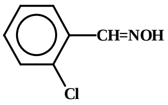
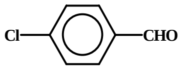
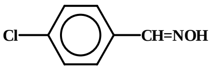
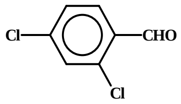
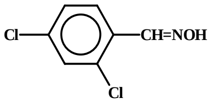
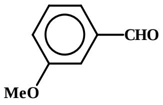
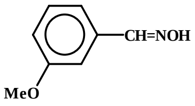
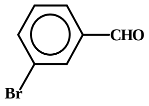
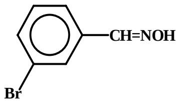
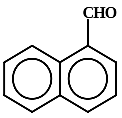
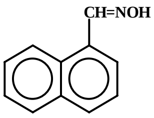
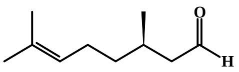
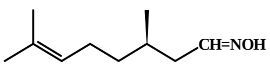
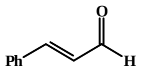
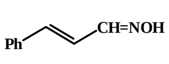
All substrates were purchased from Merck and Fluka companies with the best quality and were used without further purification. IR and ^1H NMR spectra were recorded on Thermo Nicolet Nexus 670 FT-IR and 300 MHz Bruker spectrometers, respectively. The products were characterized by their $^1H/^{13}C$ NMR or IR spectra. All yields refer to isolated pure products. TLC was applied for the purity determination of substrates, products and reaction monitoring over silica gel 60 F_{254} aluminum sheet.

A typical procedure for oximation of carbonyl compounds with $TiO(acac)_2$/NH_2OH system: In a round-bottomed flask (10 mL), equipped with a magnetic stirrer and condenser, a solution of 4-chlorobenzaldehyde (0.141 g, 1 mmol) in CH_3CN (2 mL) was prepared. $NH_2OH\cdot HCl$ (0.139 g, 2 mmol) and $TiO(acac)_2$ (0.131, 0.5 mmol) was added and the reaction mixture was stirred under reflux condition for 25 min. TLC monitored the progress of the reaction (eluent, CCl_4/Et_2O: 5/2). After completion of the reaction, distilled water (5 mL) was added and the reaction mixture was continued to stirring for 5 min. The mixture was extracted with Et_2O (3 × 7 mL) and then dried over anhydrous Na_2SO_4. Evaporation of the solvent affords the pure white crystalline 4-chlorobenzaldoxime (0.153 g, 98 % yield, Table-1).

RESULTS AND DISCUSSION

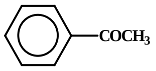
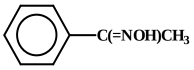
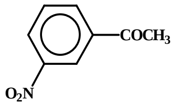
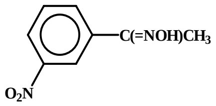
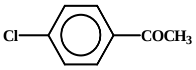
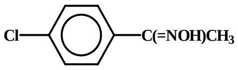
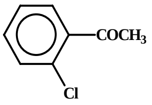
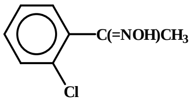
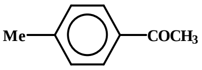
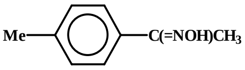
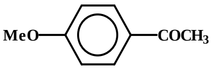
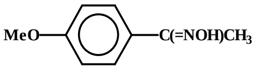
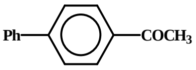
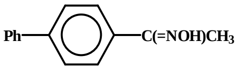
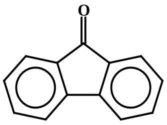
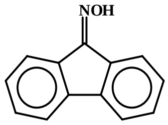
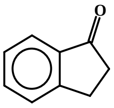
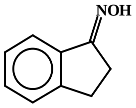
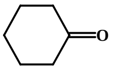
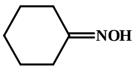
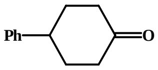
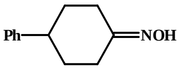
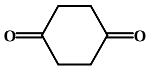
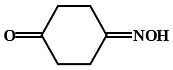
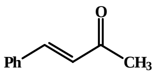
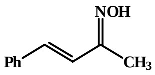
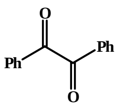
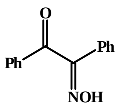
The ability of titanyl acetylacetonate in oxime formation was demonstrated by the reaction of various aliphatic/aromatic aldehydes and ketones with hydroxylamine hydrochloride in the absence of any acid or base promoter. The reactions were carried out in refluxing CH_3CN for appropriate time. The results of this investigation are summarized in Tables 1 and 2. Depending to the reactivity of aldehydes, $NH_2OH\cdot HCl$ (1-2 mmol) and $TiO(acac)_2$ (0.5 mmol) was used per 1 mmol of the substrate. Selectivity in oximation of aldehydes with titanyl acetylacetonate is a perfect and the corresponding E isomer of aldoximes were obtained in high to excellent yields (Table-1). The oximation of ketones was also performed well with titanyl acetylacetonate/$NH_2OH\cdot HCl$ system. However, due to inherent less reactivity of ketones, the oximation procedure takes excess amounts of $NH_2OH\cdot HCl$ in longer reaction times (Table-2). Ketoximes were also obtained in high to excellent yields with a perfect selectivity of E isomer. Oximation of 9-fluorenone was not completed in one step more than 50-60 % conversion within 3 h. However, isolation of unreacted starting material and the corresponding oxime from the reaction mixture and then

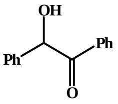
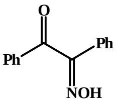
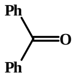
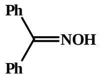
TABLE-1
OXIMATION OF ALDEHYDES WITH $TiO(acac)_2/NH_2OH\cdot HCl$ SYSTEM[a]

Entry	Substrate	Product	Molar ratio Subs./ NH_2OH/ Ti(IV)	Time (min)	E:Z ratio	Yield (%)[b]
1			1:2:0.5	30	100:0	96
2			1:1:0.5	30	100:0	93
3			1:1:0.5	30	100:0	94
4			1:1:0.5	30	100:0	95
5			1:1:0.5	25	100:0	98
6			1:2:0.5	30	100:0	98
7			1:2:0.5	45	100:0	97
8			1:2:0.5	30	100:0	94
9			1:2:0.5	30	100:0	95
10			1:2:0.5	40	100:0	92
11			1:2:0.5	43	100:0	93

[a] All reactions were carried out in CH_3CN (2 mL) under reflux conditions.
[b] Yield refer to isolated pure products.

TABLE-2
OXIMATION OF KETONES WITH $TiO(acac)_2/NH_2OH{\cdot}HCl$ SYSTEM[a]

Entry	Substrate	Product	Molar ratio Subs./ NH_2OH/ Ti(IV)	Time (h)	E:Z ratio	Yield (%)[b]
1			1:3:1	2.0	95:5	85
2			1:2:0.5	1.0	100:0	97
3			1:3:0.7	2.5	100:0	95
4			1:3:1	3.0	96:4	94
5			1:3:0.5	2.0	100:0	95
6			1:3:1	2.5	87:13	96
7			1:3:0.5	2.0	100:0	98
8			1:3:0.5	3+2	–	96
9			1:3:0.7	2.0	100:0	95
10			1:2:0.5	1.0	–	96
11			1:2:0.5	0.8	–	97
12			1:2:0.5	1.0	–	95
13			1:3:0.5	2.5	100:0	92
14			1:2:0.5	3.0	100:0	97

Entry	Substrate	Product	Molar ratio Subs./ NH_2OH/ Ti(IV)	Time (h)	E:Z ratio	Yield (%)[b]
15			1:2:0.5	3.0	100:0	98
16			1:3:1	3.0	–	0

[a] All reactions were carried out in CH_3CN (2 mL) under reflux conditions.
[b] Yield refer to isolated pure products.

repeating the oximation procedure gave 9-fluorenone oxime in 96 % yield within 2 h (Entry 8). α,β-Unsaturated aldehydes/ketones were also converted to their corresponding oximes with $TiO(acac)_2/NH_2OH\cdot HCl$ system in high yields. It is also observed that the oximation procedure in compounds with two carbonyl functionalities was selective and even in excess amounts of the reagents and longer reaction times proceeded only on one carbonyl group (Entries 12,14). In the case of benzoin, both oxidation and oximation reactions were occurred to give the corresponding product in 98 % yield (Entry 15). Benzophenone under the experimental conditions did not show any reactivity for oximation (Entry 16).

Conclusion

In this paper, the oximation of varieties of carbonyl compounds was carried out efficiently with $TiO(acac)_2/NH_2OH\cdot HCl$ system. The reactions were performed in refluxing CH_3CN to give E isomers of oximes in a perfect selectively. Oximation of compounds with two carbonyl groups was carried out selectively on one carbonyl moiety. Therefore, in view points of the applicability of this method to wide range of aldehydes and ketonts, high to excellent yields of the products, neutral and eco-friendly nature of titanyl acetylacetonate as well as the easy workup procedure, it is suggested that the present protocol could be considered a useful addition to the existing methodologies.

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