A Simple Protocol for Oxidative Decarboxylation of Phenyl Acetic Acid using Oxone and Iodobenzene

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Abstract

A facile and novel protocol for the oxidative decarboxylation of phenyl acetic acid and α-substituted phenyl acetic acid by active hypervalent (III) Iodine species generated in situ, from Iodobenzene and Oxone, as a highly active reaction system was developed. The generated species exhibited remarkable activity and also used in oxidative decarboxylation of α-substituted phenyl acetic acid to obtainable product in good yield, the protocol was applicable for a variety functionalized phenyl acetic acid and afforded the desired benzaldehydes, ketones as products in good to excellent yield. Advantages of this system are short reaction time, easy work-up and good yields

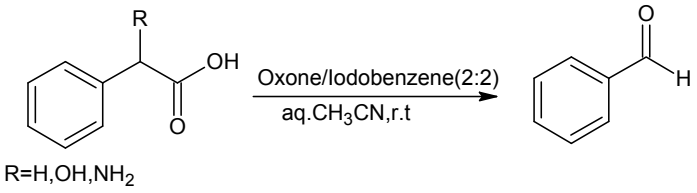
Keywords: Oxidative decarboxylation, Oxone, Hypervalent iodine reagents.

Introduction:

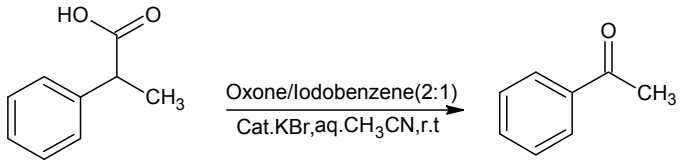
Oxidative decarboxylation of carboxylic acids is a ‘‘classical” procedure in synthetic organic chemistry which is well known in scope and mechanism. It is one of the most significant protocols for synthesis of benzaldehydes, ketones and Nitriles rendering their applications in organic synthesis, biological systems, natural products and perfumery industry. Hypervalent iodine reagents have become increasingly popular for affecting a variety of synthetic transformations. [1,2] as well as have wide application as versatile and environmentally benign oxidizing reagents in organic chemistry.[3] The object of our present study is to investigate the possibility of oxidative decarboxylation by hypervalent iodine species generated in situ from Iodobenzene and a low-priced commercial oxone ($2KHSO_5•KHSO_4•K2SO_4$). Viktor V. Zhdankin et al found that active iodine (III) species [i.e. (hydroxy (phenyl) iodonium ion,)] [4] can be inventively generated in solution by treatment of Iodobenzene with oxone in aqueous acetonitrile at room temperature. There are several methods reported for oxidative decarboxylation of phenyl acetic acid to benzaldehyde and ketones by using oxidizing agents such as in recent years, transition-metal-catalysts are emerged. Generally, Mn (III) and Fe (III) Schiff base complexes, [5] Iron and Manganese Porphyrin Periodate Systems, [6] n-Bu4NIO4) and imidazole (ImH) manganese(III), [7] polystyrene-bound Mn (III) catalyst complexes and Fe (III) complexes, [8] are widely used for the oxidative decarboxylation of phenyl acetic acid. FSM-16/hυ, [9] pyridine N-Oxide, [10] Further Akichika ITOH et al.use strategy of oxidative photodecarboxylation with the help of messoporous silicas. [11] In addition, Saeid Farhadi et al. also represented the applicability of their protocol for oxidative decarboxylation using HgF_2, [12] Yong Hae Kim et al. were explore the scope of 2-nilrobenzenesulfonyl chloride with potassium superoxide, [13] In case of α-hydroxyl phenyl acetic acid, bismuth-catalyzed oxidation system based on Bi0/DMSO/O2, [14] chromic acid, [15] MJJHYU9OKJO[Mnickel peroxide, [16] sodium bismuthate, [17] periodate, lead tetra acetate, N-iodosuccinamide, [18] hypochlorite induced

decarboxylation have been used as oxidizing reagents. However, very few reports can be found in case of oxidative degradation of α-amino acids by using coenzyme PQQ/cetyltrimethyammonium bromide. [19] Drawback of above all reactions is that it requires longer reaction time, use of Heavy metals and complexes, lower yield. Many of these reports on the oxidative decarboxylation of α- amino acid have drawbacks like low amount of yield, mostly aliphatic acids under goes this transformation longer reaction time and lower substrate compatibility, which limits their applications. To the best of our knowledge till date, the (hydroxy(phenyl)iodonium ion, which can be efficiently generated in solution by simple treatment of Iodobenzene with Oxone in aqueous acetonitrile at room temperature are not yet explored for the present methodology and no report exist in which single reaction system, which can effectively use for oxidative decarboxylation reactions of variety of phenyl acetic acid, α-hydroxy phenyl acetic acid, α-amino phenyl acetic acids for the formation of benzaldehydes and ketones.

Therefore, there is need to develop a one single reaction system which can be truly useful, active and mild protocol for the oxidative decarboxylation of phenyl acetic acids and α-substituted phenyl acetic acids, which can operate under milder reaction conditions. As part of our interest in oxidative decarboxylation reaction, [20] we herein report a facile protocol for the oxidative decarboxylation of phenyl acetic acid and α- substituted phenyl acetic acid with (hydroxy (phenyl) iodonium ion Hence, in continuation with our previous work on oxidative decarboxylation herein, we firstly report the (hydroxy (phenyl) iodonium ion applicable for oxidative decarboxylation of phenyl acetic acid. The wide range of phenyl acetic acids like α-alkyl or aryl phenyl acetic acid, α-hydroxy and α-amino phenyl acetic acid reacted well with reaction system providing the corresponding products benzaldehydes, and ketones in a single step synthesis (Scheme 1). Good yield of preferred products were obtained by using only 2 mmol of Oxone and 2 mmol of Iodobenzene in aq.acetonitrile at r.t reaction condition.



Scheme1: Oxidative decarboxylation of phenyl acetic acid to benzaldehyde using Oxone and Iodobenzene in aq. acetonitrile.



Scheme 2: Oxidative decarboxylation of α- methyl acetic acid to Acetophenone Using Oxone, Iodobenzene, and catalytic KBr in aq. Acetonitrile

Experimental

General: ^{1}H NMR spectra were recorded on Brukar (AVANCE-II) NMR operating at 300 MHz internal STD CDCL3 as solvent using TMS as internal reference, IR spectra were recorded on FTIRRX1 Perkin-Elmer Instrument. Melting points were determined with Veego melting point apparatus having stirred paraffin bath. Silica gel 60-120 was used for column chromatography and Thin Layer Chromatography (TLC) was performed using Merck Silica gel 60 F254 Plates.

Typical procedure for decarboxylation of phenyl acetic acid (Table 1, entry 1):

Mixture of Oxone (614 mg, 2 mmol) and Iodobenzene (408 mg, 2 mmol) in aqueous acetonitrile stirred at room temperature for 10 min, followed by addition of phenyl acetic acid (136mg, 1 mmol) under stirring at room temperature. The resultant reaction mixture was stirred at room temperature until the starting material was completely consumed (TLC). The reaction mixture was diluted with CH_2Cl_2 and washed successively with 10% sodium bicarbonate (2 x15 mL), followed by water (2 x20 mL). The organic layer was dried over anhydrous sodium sulphate and concentrated under reduced pressure to obtained crude product. The pure product was obtained after silica gel column chromatography (10% EtOAc–Hexane).

Typical procedure for decarboxylation of α-substituted Phenyl acetic acid (Table 1, entry 8):

Mixture of Oxone (614 mg, 2 mmol) and Iodobenzene (204 mg, 1mmol) in aqueous acetonitrile stirred at room temperature for 10 min, followed by addition of α-methyl phenyl acetic acid (150 mg, 1mmol) and catalytic amount of KBr (59 mg) under stirring at room temperature. Isolation and purification of the product was carried out by following above procedure. (Table 2, Entry 8) Solid, MP 306 .IR (KBr): 2925, 2867, 2854,1668,1401,1365,940,700 cm-^{1} ^{1}H NMR (300 MHz, $CDCl_3$) δ=7.8(2H, d, J=6.9Hz) 7.79-7.44(8H, m)

Results and Discussion

To develop a suitable protocol for oxidative decarboxylation reactions, initially the reaction of phenyl acetic acid with Oxone (2 mmol) and Iodobenzene (2 mmol) in the acetonitrile water solvent system was chosen as a model reaction (Scheme 1) and influence of various reaction parameters, such as time, and reagent concentration were examined In the case, this reaction systems the amount of reagents employed proves to be an important feature, and considering such efforts were made to determine the optimum concentration of the reagents (Table 1, entries 1–5). Various mole ratio of reagent were used from (0.5 mmol to 2 mmol).

Initially, the reaction was carried out by using 0.5 mmol of oxone, which provided desired product in 40%yields. An increase in the oxone concentration up to 2 mmol resulted in an increase in the yield of 86% (Table 1, Entry 4). Further increase in the amount of oxone had no profound effect on the yield of the desired product (Table 1, entry 5). Also, the reaction was carried out at different Iodobenzene concentration ranging from 0.5 mmol 2 mmol (Table 1, entries 5-9). It was observed that when Iodobenzene concentration is 0.5mmol then the yield of the product was very low(Table 1,entry,5), and with an increase up to 2 mmol, the yield of product increased to 86%(Table1,Entry,8) However, a further increase in concentration did not show any significant enhancement in the yield (Table 1, entry 9). The influence of time on the reaction outcome was also studied.

Table1: Effect of reaction parameters on the oxidative decarboxylation of phenyl acetic acid

Sr. No.	Oxone (2mmol)	Iodobenzene (2mmol)	Yield (%)
Effect of Oxone Concentration			
1	0.5	2	40
2	1	2	55
3	1.5	2	78
4	**2**	**2**	**86**
5	2.5	2	86
Effect of Iodobenzene Concentration			
6	2	0.5	38
7	2	1	68
8	2	1.5	74
9	**2**	**2**	**86**
10	2	2.5	86

To expand the scope of our reaction system α-hydroxyl and α-amino phenyl acetic acid subjected to oxidative decarboxylation, in both cases we were found to respond smoothly providing highest yield of benzaldehyde as preferred product. It is noteworthy to mention that no benzonitrile product in case of phenyl glycine was obtained. We also checked the role catalytic amount of KBr in Our reaction System. In the presence of catalytic KBr the yield of the desired product doesn't increase.

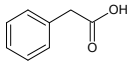
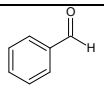
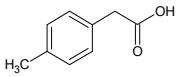
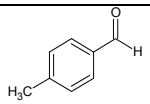
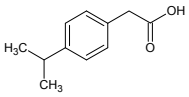
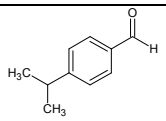
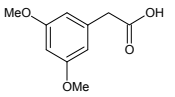
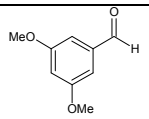
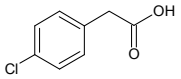
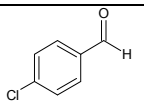
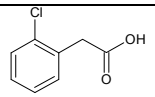
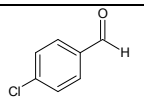
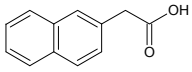
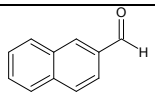
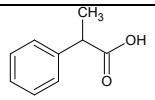
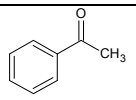
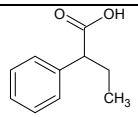
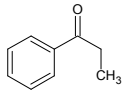
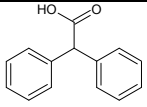
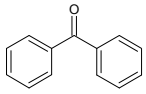
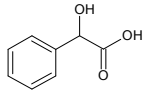
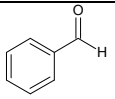
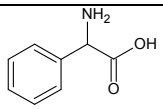
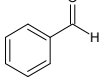
To explore the simplification and applicability of the protocol, we turned our attention towards the oxidative decarboxylation of α-alkyl phenyl acetic and α-aryl phenyl acetic acid with oxone (2mmol) and Iodobenzene (0.5mmol) (Table 2, Entry 1) The reaction gave 45% yield of ketones under the optimized reaction conditions, further increase in Iodobenzene concentration up to 2 mmol providing the product in fair yields (Table 2, Entry 4). We also checked the role Catalytic KBr in Our reaction System In the presence of catalytic KBr, the yield of the desired product was finest, that is, 82% however, in the absence of KBr, the yield obtained fair .Thus, the developed protocol proved to be general for the oxidative decarboxylation of α-alkyl or α-phenyl acetic acid with Oxone (2mmol), Iodobenzene (1mmol) and Catalytic KBr providing good to excellent yields of the desired product .We think that the presence of KBr plays the role of catalyst, which is to be in agreement with the observation made by Hideo Togo and co-workers[21] the effect of various solvents on oxidative decarboxylation was studied to find out the Acetonitrile: water solvent system provides good yields. During optimization of the reaction parameters, we observed that in case of phenyl acetic acid, mendalic acid and phenyl glycine if the mmol ratio of oxone and Iodobenzene is (2:2) acetonitrile: water solvent system at r.t. then product formed with good yield.

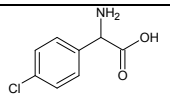
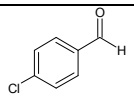
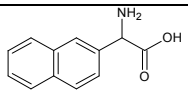
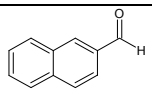
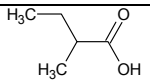
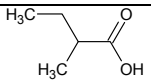
In case of α-alkyl or aryl phenyl acetic acid desired product obtained with good yield using oxone (2 mmol) and Iodobenzene(1 mmol) and cat. KBr in acetonitrile: water reaction system at r.t. the reaction of α- aryl or alkyl phenyl acetic acid with Oxone and Iodobenzene in the presence cat. KBr was selected as a model reaction (Scheme 2)

In order to study the promising and general applicability of the developed methodology, various phenyl acetic acids containing different functional groups were subjected to this transformation (Table2). We observed that electron donating as well as electron withdrawing groups provided significant yield of

products. A variety of functional groups including methoxy, methyl, chloro, isopropyl group, were well tolerated and gave good yield (Table 2, entry 2-6) In order to study the α-alkyl or aryl phenyl acetic acid under these reaction conditions, we treated α-methyl phenyl acetic acid with Oxone and Iodobenzene which was resulted in the formation of poor yield of ketones. So, by increasing Iodobenzene concentration and use of catalytic KBr Improving reaction conditions good yields were achieved (Table 2, entry 8, 9, 10).

Table 2: Oxidative decarboxylation of aryl carboxylic acid using Oxone and Iodobenzene in aq. Acetonitrile

Sr. No.	Substrate	Product	Time (Min)	Yield%[c]
1			40	85
2			45	85
3			45	85
4			45	80
5			45	75
6			50	75
7			60	80
8[b]			130	82
9			125	80
10			135	82
11			40	85
12			45	90

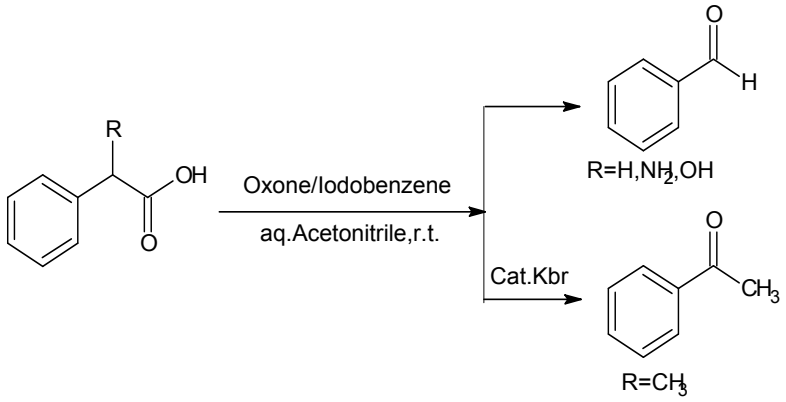
13			45	80
14			50	85
15			24h	[d]NR

[a] Reaction conditions: substrate (1 equiv), Oxone (2 equiv), Iodobenzene (2 equiv) in aqueous acetonitrile, room temperature. [b] Oxone (2mmol), Iodobenzene (1mmol) and Catalytic KBr required (entry 8-10).
[c] Isolated yields by column chromatography and structures were confirmed by comparison of IR and ^{1}H NMR with authentic materials.
[d] NR: no reaction.

To expand the scope of our reaction system α-hydroxyl and α-amino phenyl acetic acid subjected to oxidative decarboxylation in both cases we were found to respond smoothly providing highest yield of products benzaldehyde as preferred product (Table 2, entries 10-11) it is noteworthy to mention that no Benzonitrile product in case of phenyl glycine was obtained. However, no reaction was observed when aliphatic acids were subjected under this reaction conditions (Table 2, entries 15-16).

Conclusion

In summary, we developed a new protocol for oxidative decarboxylation of phenyl acetic acid and α-alkyl or aryl phenyl acetic acid to obtained benzaldehydes and ketones as products which is as shown in below figure



Where all types of phenyl acetic acid, α-alkyl or aryl phenyl acetic acid and Mendalic acid as well as phenyl glycine under goes oxidative decarboxylation to achieve an excellent yield of desired products. Lower reaction time adds an additional credit to the present study. In general, all kinds of functional groups were very well tolerated giving higher yields. The reaction was optimized with respect to various reaction parameters and enabled oxidative decarboxylation of various electron-rich, electron-deficient phenyl acetic acid and α-substituted phenyl acetic acid, affording excellent yields of the desired products, thus illustrating the broad applicability of the methodology. The developed protocol might prove a hopeful alternative for oxidative decarboxylation for benzaldehydes and ketones synthesis.

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Synthesis of benzimidazole Derivatives using Silica as catalyst –Green Approach

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Abstract

Synthesis of benzimidazole derivatives using under microwave using catalyst like silica from Arabian Sea near Mumbai area. This reaction is between orthophenyl diamines and aromatic aldehyde using silica as catalyst .synthesized products are confirmed by physical methods, and Spectral analysis. This method is green and gives better yield.

Key words: Benzimidazole, aromatic aldehyde, silica.

Introduction

Benzimidazoles are important chemical and biological derivaties.this exhibit wide range of biological activities such as antihistaminic [2], antiprotozoal [1], ant allergic [3] and anti-diabetic [4]. Several compounds from this class have been used as inhibitors of hepatitis C virus NS5B polymerase [5].They also act as thrombopoietin receptor agonists [6], good and selective inhibitors of 1KK-ε kinase [7] and non-steroidal anti-androgen [8].Mostly these Compounds are synthesized by the condensation reaction of OPDA with the aromatic aldehydes. For this synthesis and oxidative cyclo-dehydrogenation of o-phenylenediamine or o-aminothiophenol with aldehydes.[9-11] Various oxidative reagents such as DDQ,[12] NaHSO3(aq),[13] nitrobenzene,[14] MnO2,[15]1,4benzoquinone,[16]benzofuroxan,[17]tetracyanoethylene, [18] $Pb(OAc)_4$ [19] and Oxone[20] have been employed for the synthesis of benzimidazoles and Benzothiazole. However, a number of these methods have some drawbacks such as low yields, long reaction times, drastic reaction conditions, tedious work-up procedures, and co-occurrence of several side reactions. Recently several reports on MW technology in solid-phase synthesis. Recently, several reports [20-21] that have applied are microwave and sonication methods .in this current study we use novel catalyst and microwave method.

Experimental

Melting points were measured in capillary tube method using paraffin's. The IR spectra were recorded FTIR Spectrophotometer using on a Shimadzu instrument. 1H NMR spectra were recorded on a Brucker 300 spectrometer. All products were known and characterized by comparison of their physical and spectroscopic data with those already reported [14-17].

General procedure for the synthesis of benzimidazoles

Freshly distilled aromatic aldehyde (10 mmol), o-phenylenediamine (10 mmol) and 1.1 g of catalyst were mixed thoroughly in a 100 cm3 beaker with glass rod and then irradiated in the MW oven for about 10 min at power level 800 W with 30 sec pause after every one min. Upon completion of the reaction (TLC), the reaction mixture was cooled at room temperature, ethyl acetate (20 cm3) was added, and stirred well followed by filtration through celite under suction. The organic layer was washed with water (2 × 30

cm3) and brine (20 cm3). After drying over anhydrous Na2SO4, the solvent was evaporated under reduced pressure and the residue upon column chromatography affords the pure product.

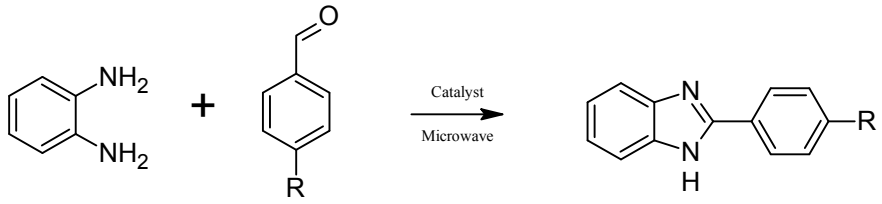

Table 1 Reaction under Microwave Irradiation

Entry I	Aldehyde	Time sec.	Yields	M.P. ^{o}C
1	Benzaldehyde	120	60	287
2	Anisaldehyde	130	75	230
3	4-methyl benzaldehyde	130	80	228
4	4-chlorobezaldehyde	100	88	290
5	4-flurobenzaldehyde	100	90	248
6	3-bromobenzaldehyde	120	90	267
7	Furan-2carbaldehyde	120	90	288
8	Cinnamaldehyde	130	85	199-200
9	3-nitrobanzaldehyde	100	90	309-310

Conclusion

We have reported work using the silica the synthesis of various benzimidazoles by using substituted OPDA and a series of aldehydes in microwave oven. This method is quite simple and selective one. The catalyst gave high isolated yield of the derivatives of benzimidazoles in a shorter reaction time and can be recycled 4-5 times catalyst gives better yield of benzimidazole and its derivatives and create the good platform for the commercialization of the process by replacing the existing homogenous catalysts which suffered from various drawbacks such as corrosion, toxicity, waste production and high cost

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