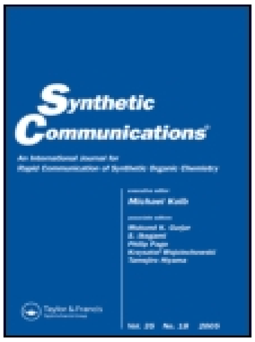

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IRON(III)-ETHYLENEDIAMINETETRAACETIC ACID MEDIATED AEROBIC OXIDATION OF α-HYDROXYKETONES: A SIMPLE AND CONVENIENT SYNTHESIS OF α-DIKETONES

T. Venkateshwar Rao, Rajendra S. Dongre,
Suman L. Jain, and Bir Sain*

Chemical and Biosciences Division, Indian Institute of
Petroleum, Dehradun-248 005, India

ABSTRACT

Iron(III)-ethylenediaminetetraacetic acid in aqueous methanol offers a simple, environmentally acceptable synthetic tool to oxidize α-hydroxyketones α-diketones with molecular oxygen, in excellent yields and under mild conditions and without any side reactions.

Key Words: α-Hydroxyketone; α-Diketone; Molecular oxygen; Iron(III)-ethylenediaminetetraacetic acid

α-Diketones are synthetically important building blocks[1] and have been used for benzylic acid rearrangement[2] and synthesis of heterocyclic compounds.[3–7] The oxidation of α-hydroxyketones is a simple and direct route for the synthesis of α-diketones and many stoichiometric reagents such

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*Corresponding author. E-mail: birsain@iip.res.in

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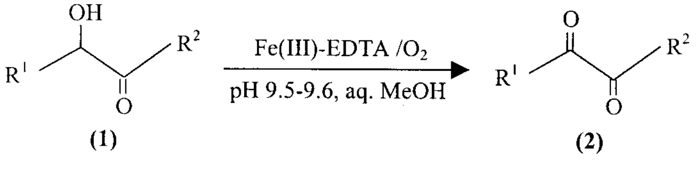
as cupric salts,[8,9] ammonium nitrate,[10] bismuth oxide,[11] thallium nitrate,[12] have been reported to be effective oxidants for this transformation. The increasing environmental concerns surrounding the use of toxic and dangerous oxidants have impelled organic chemists to develop catalytic oxidation methodologies using molecular oxygen as primary oxidant.[13–16]

In this context Nobile et al. [17] reported the oxidation of α-hydroxyketones to α-diketones with molecular oxygen using Co(II) and Fe(II) complexes as catalysts and excess of aldehyde or aldoacetal as sacrificial agent. This method suffers from the drawback that 3.6 mmol of isobutyraldehyde or 6.0 mmol of propionaldehyde dimethyl acetal per mmol of α-hydroxyketone are required as sacrificial agent. Recently, Kirihara et al. [18] reported the aerobic oxidation of a variety of α-hydroxyketones to α-diketones using $VOCl_3$ as catalyst without the use of sacrificial aldehyde or aldoacetal. However, $VOCl_3$ is moisture sensitive, hazardous material and is not easy to use in practice.[19] Among the transition metals iron has been singled out as nontoxic and in the recent years, increasing emphasis, is being given on the development of iron-based oxidants.[20–22]

Earlier we reported iron(III)-ethylenediaminetetraacetic acid catalyzed aerobic oxidation of 2,6 di-*tert*-butylphenol, substituted hydroquinones and thiols.[23,24] Herein, we report for the first time Iron(III)-ethylenediaminetetraacetic acid [Fe(III)-EDTA][25–27] mediated oxidation of α-hydroxyketones (**1**) to α-diketones (**2**) using molecular oxygen as the sole oxidant (Scheme 1).

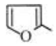
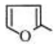
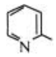
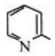
Oxidation of a variety of α-hydroxyketones with molecular oxygen in presence of catalytic amount of Fe(III)-EDTA yielded α-diketones in excellent yields, without any evidence for the formation of any byproduct which could arise due to cleavage of carbon–carbon bond of α-diketones[28,29] (Table 1). Benzoins containing electron withdrawing groups were found to be more reactive and required lesser reaction time for their oxidation.

To determine the effect of pH, we studied the Fe(III)-EDTA catalyzed oxidation of benzoin at different pH. The reaction was found to be highly dependent upon pH of the system. While oxidation of benzoin to benzil at



Scheme 1.

Table 1. Iron(III)-ethylenediaminetetraacetic Acid Catalyzed Oxidation of α-Hydroxyketones (1) to α-Diketones (2) with Molecular Oxygen

Entry	R^1	R^2	pH	Reaction Time (h)	α-Diketone Yield (%)[a]
1	C_6H_5	C_6H_5	9.50	3.50	98
2	C_6H_5	C_6H_5	8.00	12.0	96
3			9.60	7.0	90
4			9.59	5.0	89
5	$4\text{-}ClC_6H_4$	$4\text{-}ClC_6H_4$	9.58	4.5	96
6	$4\text{-}CH_3C_6H_4$	$4\text{-}CH_3C_6H_4$	9.60	15.5	93
7	$4\text{-}CH_3OC_6H_4$	$4\text{-}CH_3OC_6H_4$	9.61	22.5	94
8	C_6H_5	$4\text{-}CH_3OC_6H_4$	9.60	14.0	92
9	C_6H_5	$4\text{-}(CH_3)_2NC_6H_4$	9.61	12.0	91
10	$4\text{-}ClC_6H_4$	$4\text{-}(CH_3)_2NC_6H_4$	9.60	10.5	94
11	$4\text{-}CH_3C_6H_4$	$4\text{-}CH_3OC_6H_4$	9.60	20.0	95

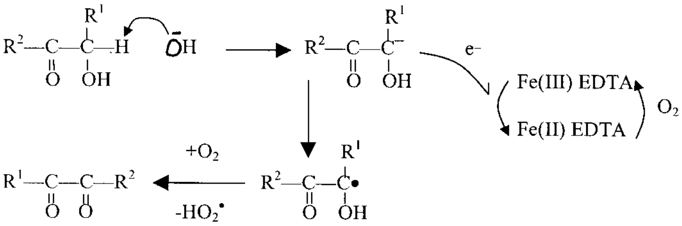
[a] Isolated yield.

pH 9.5 could be completed in 3.5 h (Entry 1), at pH 8.0 the observed reaction time remained 12 h (Entry 2) (Table 1).

To evaluate the catalytic effect of Fe(III)-EDTA, blank, experiment was carried out with benzoin, under similar conditions but without catalyst and it was observed that even after 48 h the reaction did not complete.

Although mechanism of this reaction is not clear at this stage, probably the reaction proceeds through removal of proton from carbon attached to hydroxyl group of α-hydroxyketone by hydroxide ion leading to the formation of carbanion and subsequent transfer of one electron of Fe(III)-EDTA. The radical thus generated is oxidized to α-diketones and Fe(II)-EDTA formed is reoxidized to Fe(III)-EDTA by molecular oxygen (Scheme 2). This type of mechanism has been conceived by Smith et al.,[30] for oxidation of substituted benzyl alcohols with ferrate (VI) ion. Our observations that the reaction rate is increased with the increase in pH and that the presence of electron donating substituents in the benzene ring of α-hydroxyketones decreases the rate of reaction, support this mechanism of reaction. Further studies concerning the mechanistic aspects of this reaction are currently underway.

In conclusion, simplicity of the system, excellent yields, wide applicability and reasonable reaction time make Fe(III)-EDTA catalyzed oxidation with molecular oxygen, an attractive and environmentally acceptable synthetic tool for the oxidation of α-hydroxyketones to α-diketones.



Scheme 2.

EXPERIMENTAL

Fe(III)-EDTA (0.1 M) solution was prepared by adding ethylenediaminetetraacetic acid (EDTA) disodium salt solution to the ammonium ferric sulphate solution and raising the pH of the mixture to 8.00 by adding aqueous sodium carbonate solution. A typical experimental procedure is as follows: α-hydroxyketone (1 mmol), Fe(III)-EDTA (0.1 mmol, 1 mL of 0.1 M solution) and methanol (10 mL) were taken in 50 mL double necked round bottomed flask fitted with gas inlet tube and reflux condenser. The solution was brought to the desired pH (9.5–9.6) by adding 5% aqueous sodium carbonate solution. The mixture was then stirred and refluxed with oxygen gas bubbled into at slow rate. The reaction progress was monitored by TLC (SiO_2 gel) and after completion methanol was removed under reduced pressure. The residual mixture was then taken in toluene (20 mL) and toluene layer was washed three times with distilled water (3 × 20 mL) followed by drying (anhydrous Na_2SO_4) and passing through a small column of silica gel. Evaporation of toluene yielded pure α-diketone.

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