

Synthesis of Methyl Phenyl Glyoxylate via Clean Oxidation of Methyl Mandelate over a Nanocatalyst Based on Heteropolyacid Supported on Clay

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Abstract:

Oxidation is an important class of reaction from both industrial and academic points of view. In recent years, a large number of oxidizing agents have been used for a variety of industrial reactions, but many of them are polluting, giving poor yields. Mandelates have played an important role in organic synthesis and are used in artificial flavoring and perfumes. Methyl phenyl glyoxylate, which contains two carbonyl groups, is an important intermediate used in fine chemical industry. Oxidation of methyl mandelate was carried out to prepare methyl phenyl glyoxylate, with 85% selectivity, by using hydrogen peroxide in the presence of a novel catalyst, namely, 20% w/w $\text{Cs}_{2.5}\text{H}_{0.5}\text{PW}_{12}\text{O}_{40}$ /K-10 catalyst, which is partly substituted dodecatungstophosphoric acid supported on clay. The catalyst is a nano material and reusable. The workup is easy.

Introduction

Carbonyl compounds are a prominent class in synthetic organic chemistry having several applications as solvents and precursors to several products such as alcohols, acids, and heterocyclic compounds.^{1–3} Methyl phenyl glyoxylate, which contains two carbonyl groups, is an important intermediate used in fine chemical industry. α -Dicarbonyl compounds are obtained by the oxidation of α -hydroxylcarbonyl precursors. Due to the sensitivity of the α -dicarbonyl compounds, special reagents and reaction conditions are required to prevent side reactions during the oxidation of α -hydroxycarbonyls.¹ Although a number of methods have been developed to achieve this transformation, most of them suffer from the use of corrosive acids or toxic metallic compounds that generate undesirable waste materials. There are several methods available in the literature on the oxidation of α -hydroxyl compounds by oxidizing agents such as *N*-bromosuccinimide,⁴ *N*-bromoacetamide,⁵ trichloroisocyanuric acid,⁶ *N*-bromobenzene sulphonamide,⁷ *N*-chlorobenzene

sulphonamide,⁸ 1-chlorobenzotriazole,⁹ *N*-bromosaccharin,¹⁰ bromate,¹¹ and *N*-bromophthalimide.¹² In the past few years, the oxidation of α -hydroxyl compounds has been reported by using catalytic amounts of chromium oxide in conjunction with *tert*-butylhydroperoxide^{13,14} or hydrogen peroxide.^{14,15} Oxidation is also reported with the catalytic amounts of VOCl_3 in acetonitrile under an oxygen atmosphere.¹³ Phenyl glyoxylic acid esters were prepared by treating a Grignard reagent phenylmagnesium bromide with diethyl oxalate.¹⁶ Oxidation of phenylacetylene derivatives can also be utilized for the synthesis of α -keto ester.¹⁷ Methyl phenylglyoxylate was synthesized via ozonolysis of 1-bromophenylacetylene followed by reaction with potassium iodide,¹⁸ whereas the oxidation was improved¹⁹ by treatment of trimethylsilyl phenylacetylenes with osmium tetroxide and *tert*-butyl hydroperoxide in methanol to get methyl phenyl glyoxylate. It is also reported that ammonium chlorochromate adsorbed on alumina was used for the preparation of phenyl glyoxylic esters.¹⁷ The use of heterogeneous catalysts with a clean oxidizing agent is necessary for the synthesis of methyl phenyl glyoxylate, and this work is concerned with that aspect.

Heteropolyacids are a very important class of acid and redox catalysts. The novelty of clay-supported heteropolyacids as reusable benign catalysts was reported by us²⁰ for the first time, and a series of commercially important reactions were studied.^{21–27} We have also developed a novel nanocatalyst by using partially substituted dodecatungstophosphoric acid (DTP) with cesium and supporting it on acid-activated clay. Thus, nanoparticles of 20% w/w $\text{Cs}_{2.5}\text{H}_{0.5}\text{PW}_{12}\text{O}_{40}$ were created in the pore network of acid treated

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K-10 clay (designated as Cs-DTP/K-10) and used for a number of acid-catalyzed reactions.^{28–31} This novel catalyst was reusable and more active and selective than several others. It was therefore thought desirable to make use of Cs-DTP/K-10 in the clean synthesis of methyl phenyl glyoxylate by the oxidation of methyl mandelate with hydrogen peroxide.

Experimental Section

Chemicals and Catalysts. All chemicals and catalysts were procured from firms of repute and used without further purification: Methyl mandelate, acetonitrile, 50% w/v hydrogen peroxide, cesium chloride, and dodecatungstophosphoric acid (AR grade; s.d. Fine Chem. Ltd, Mumbai, India); K-10 clay (Aldrich, USA).

Preparation of 20% w/w Cs_{2.5}H_{0.5}PW₁₂O₄₀/K-10 Catalyst. The catalyst was prepared by a well developed incipient wetness technique in our laboratory.^{28–31} K-10 clay was dried at 120 °C in an oven for 1 h. A cesium chloride quantity of 0.2808 g (1.67×10^{-3} mol) was weighed, dissolved in 10 mL of methanol, and added to 8.0 g of K-10 clay. The volume of solvent used was approximately equal to the pore volume of clay support. The slurry was stirred vigorously and air-dried. The resulting material was then dried at 120 °C for 2 h. The solid material was further subjected to impregnation by an alcoholic solution of 2.0 g (6.688×10^{-4} mol) of dodecatungstophosphoric acid (DTP) in 10 mL of methanol. The slurry was once again mixed thoroughly and air-dried. It was further dried at 120 °C for 2 h and calcined at 300 °C for 3 h. The catalyst so formed was found to possess the highest activity when calcined at the above-mentioned temperature in our previous studies.^{28–31}

Reaction Procedure. The reactor consisted of a flat-bottomed cylindrical glass vessel of 70 mL capacity equipped with four baffles, a pitched-turbine stirrer, and a condenser. The assembly was kept in a thermostatic oil bath at a known temperature and mechanically agitated with an electric motor. In a typical experiment, 0.0036 mol of methyl mandelate was dissolved in 50 mL of acetonitrile, 0.026 g/cm³ catalyst was charged, and 0.037 mol of hydrogen peroxide was added dropwise at 50 °C. Then agitation was started at 1000 rpm and continued for 2 h. Samples were withdrawn periodically and analyzed.

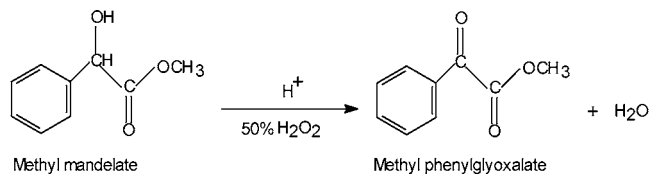
Method of Analysis. Analysis of the reaction mixture was performed by HPLC (A Knauer, model K-501: 63614) with the UV detector (A Knauer, model K-2501: 62964) by using acetonitrile/water (60:40) as mobile phase with a flow rate 1 mL/min at a λ_{\max} of 261 nm. Mandelic acid, benzaldehyde, and benzoic acid were detected as byproducts of the oxidation of methyl mandelate. The quantification data were done by standard calibration method.

Isolation and Identification of the Product. For isolation of the product, the catalyst was filtered and the solvent acetonitrile evaporated in a rotary evaporator. The residue

left in the round-bottom flask was cooled. The unreacted methyl mandelate and trace amounts of mandelic acid were solidified. The yellow colored oil of methyl phenyl glyoxylate was separated by filtration. The filtrate contained a trace amount of benzaldehyde which was volatilized by passing steam through the oil. The confirmation of the product was done by IR.

Results and Discussions

Mechanism. Scheme 1 depicts the reaction mechanism. Hydrogen peroxide is an excellent nucleophile containing –O–O–H structure. Thus it is also an excellent reactant for the preparation of hydroxyperoxide, in the presence of a catalytic quantity of an acid such as Cs-DTP/K-10 which is used as a source of hydrogen ion to undergo S_N¹ displacement involving a carbonium ion intermediate. Further, the C–H bond is ruptured with the loss of hydrogen as a proton to form the methyl phenyl glyoxylate, thus supporting the mechanism suggested by Kwart and Francis³² for the oxidation of secondary alcohols involving C–H bond rupture.



It is already reported in the literature that mandelic acid³³ reacts about six times faster than its methyl ester. The slower oxidation of the ester vis-à-vis mandelic acid can be explained as the –COOH group is known to have a stronger –I effect than –COOMe. The oxidation for the ester is slower because groups with an –I effect assist C–H bond rupture in the rate determining step in which hydrogen is removed as a proton.³⁴ The formation of mandelic acid may be because the ester–acid balance is sensitive to the amount of water present in the reaction at any time and the esters can hydrolyze to acid. This mandelic acid further undergoes degradation to form benzaldehyde and decarbonised with the loss of hydrogen ion, as given in Scheme 1. H⁺ represents the Cs-DTP/K-10 catalyst.

Effect of Speed of Agitation. External mass-transfer resistances created by insufficient mixing can limit the overall methyl mandelate conversion rate, if the difference between the methyl mandelate conversion in bulk solution and the methyl mandelate concentration at the particle outer surface is large. The reaction was studied at 500, 1000, 1500, and 2000 rpm (Figure 1). The conversions are 500 rpm which were a little lower than those at 1000 rpm. Then the conversions remained practically the same at all speeds studied beyond 1000 rpm, thereby indicating the absence of external mass-transfer resistance. Thus a speed of 1000 rpm was sufficient to be used in all further experiments.

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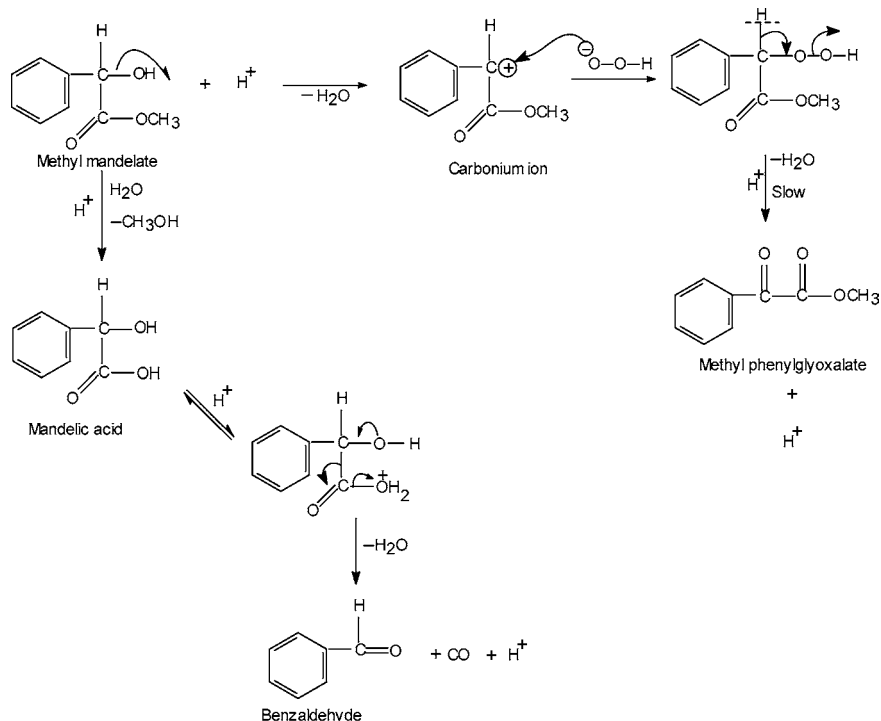
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Scheme 1. Reaction mechanism involving H₂O₂ and Cs-DTP/K10



Effect of Catalyst Quantity. The effect of catalyst quantity was studied in the range 0.4–5.4 g keeping all other conditions the same (Figure 2). It was observed that as the catalyst quantity was increased, the conversion also increased but byproduct formation increased at higher catalyst quantity and the isolated yields suffered (Table 1). The best results were obtained with 1.4 g of catalyst quantity. Therefore, further reactions were carried out by using this quantity of the catalyst.

Effect of Mole Ratio. The effect of mole ratio of methyl mandelate to hydrogen peroxide was studied in the range 1:4.2, 1:8.3, 1:16.6, 1:24.5 (Figure 3, Table 2). It should be noted that the peroxide was added continuously, and hence the mole ratio relates to the total amount added. The

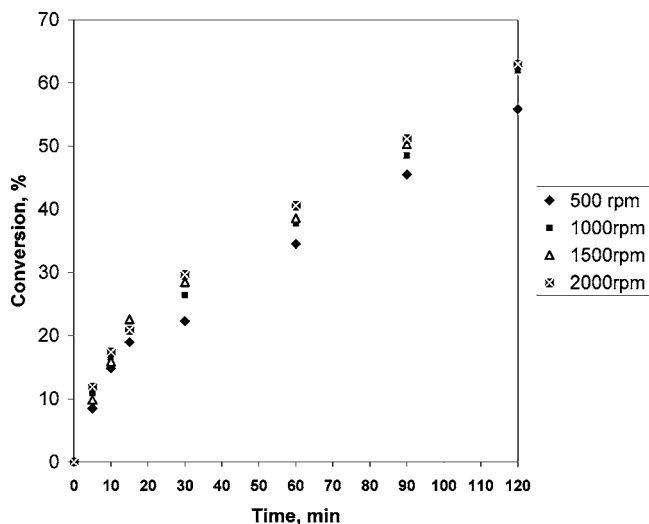


Figure 1. Effect of speed of agitation on conversion of methyl mandelate. Methyl mandelate, 0.0036 mol; acetonitrile, 50 mL; catalyst loading, 0.026 g/cm³; 50% hydrogen peroxide, 0.037 mol; temperature, 50 °C.

Table 1. Selectivity and yield of methyl phenyl glyoxalate at different catalyst quantities after 2 h^a

catalyst quantity (g)	selectivity (%)	isolated yield %
0.4	55.3	12.8
1.4	86.4	50.2
3.4	65.5	42.0
5.4	67.3	47.0

^a Methyl mandelate, 0.0036 mol; acetonitrile, 50 mL; 50% hydrogen peroxide, 0.037 mol; temperature, 50 °C; speed of agitation, 1000 rpm; time, 2 h.

selectivity observed towards the desired product methyl phenylglyoxalate was maximum at a mole ratio of 1:8.3. Therefore, further reactions were carried out with a mole ratio of 1:8.3.

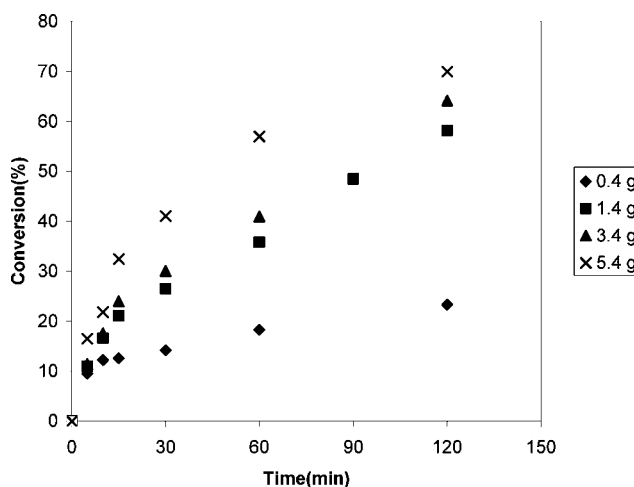


Figure 2. Effect of total catalyst quantity (g) on conversion of methyl mandelate. Methyl mandelate, 0.0036 mol; acetonitrile, 50 mL; 50% hydrogen peroxide, 0.037 mol; temperature, 50 °C; speed of agitation, 1000 rpm.

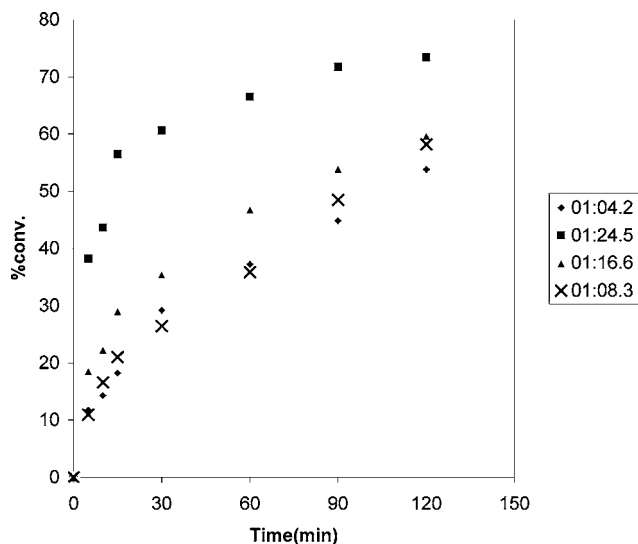


Figure 3. Effect of mole ratio of hydrogen peroxide to methyl mandelate on conversion of methyl mandelate. Acetonitrile, 50 mL; catalyst quantity (20% w/w Cs-DTP/K-10), 0.026 g/cm³; temperature, 50 °C; time, 2 h; speed of agitation, 1000 rpm.

Table 2. Selectivity and yield of methyl phenyl glyoxylate at different mole ratios after 2 h^a

mole ratio	selectivity (%)	isolated yield %
1:4.2	84.9	45.6
1:8.3	86.4	51.6
1:16.6	63.8	46.8
1:24.5	56.3	32.7

^a Acetonitrile, 50 mL; catalyst quantity (20% w/w Cs-DTP/K-10), 0.026 g/cm³; temperature, 50 °C; time, 2 h; speed of agitation, 1000 rpm.

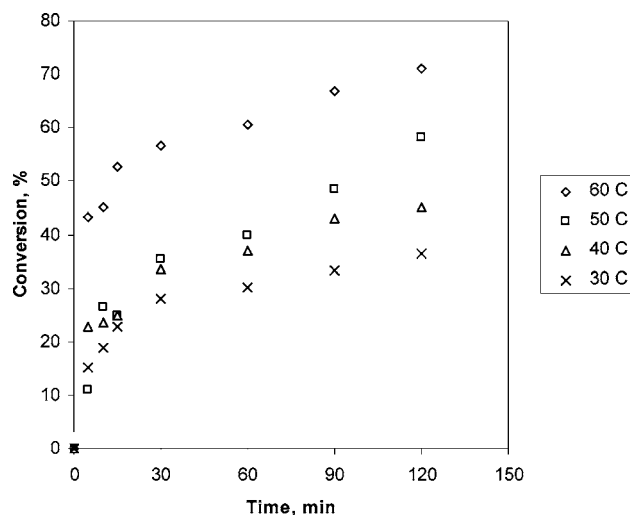


Figure 4. Effect of temperature on conversion of methyl mandelate. Methyl mandelate, 0.0036 mol; acetonitrile, 50 mL; catalyst quantity (20% w/w Cs-DTP/K-10), 0.026 g/cm³; 50% hydrogen peroxide, 0.037 mol; speed of agitation, 1000 rpm.

Effect of Temperature. The reaction was studied in the range 30–60 °C, under otherwise similar conditions (Figure 4). It was observed that, with an increase in temperature, the conversion increased. The selectivity decreased due to predominance of side reactions (Table 3).

Effect of Catalyst Reusability. The reusability of the catalyst was tested by employing it thrice. After each run

Table 3. Effect of temperature on selectivity and yield of methyl phenyl glyoxylate after 2 h^a

temperature, °C	selectivity (%)	isolated yield %
30	95.0	34.5
40	92.5	41.6
50	86.4	51.6
60	61.5	46.8

^a Methyl mandelate, 0.0036 mol; acetonitrile, 50 mL; catalyst quantity (20% w/w Cs-DTP/K-10), 0.026 g/cm³; 50% hydrogen peroxide, 0.037 mol; speed of agitation, 1000 rpm.

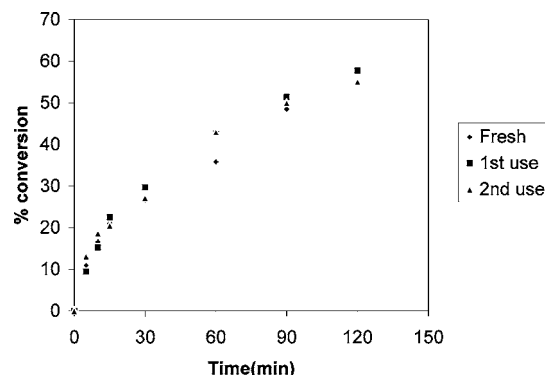


Figure 5. Effect of catalyst reusability on conversion of methyl mandelate. Methyl mandelate, 0.0036 mol; acetonitrile, 50 mL; catalyst loading (20% w/w Cs-DTP/K-10), 0.026 g/cm³; 50% hydrogen peroxide, 0.037 mol; temperature, 50 °C; speed of agitation, 1000 rpm.

the catalyst was filtered and washed with methanol in order to remove the adsorbed organic substances from the active sites. But washing was insufficient to remove all the adsorbed organic substance from the active sites, and therefore the catalyst was refluxed with methanol for 5 h. The marginal decrease in the conversion of methyl mandelate was observed. In the second and third reuse, makeup catalyst was added to match the losses during filtration to find if the catalyst is reusable, which is the case. The selectivity in all these cases practically remained the same (Figure 5).

Conclusions

Methyl phenyl glyoxylate is an important intermediate used in fine chemical industry. The normal routes of its synthesis are highly polluting. In the current work, a clean oxidation process was developed by which methyl phenyl glyoxylate was prepared with 85% selectivity, from methyl mandelate with hydrogen peroxide and 20% w/w Cs_{2.5}H_{0.5}-PW₁₂O₄₀/K-10 catalyst at 50 °C. This catalyst contains nanoparticles of the heteropolyacid trapped in cages of acid-treated clay and is reusable. The workup was simple, and the product can be easily separated. The procedure is better than others so far reported.

Acknowledgment

Research grant under NMITLI programme of CSIR, New Delhi and Darbari Seth Professorship endowment to G.D.Y. is gratefully acknowledged.

Received for review August 2, 2004.

OP049858P