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Selective oxidation of methyl mandelate to methyl phenyl glyoxylate using liquid–liquid–liquid phase transfer catalysis

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ABSTRACT

The conversion of the traditional liquid–liquid (L–L) phase transfer catalysis (PTC) into liquid–liquid–liquid (L–L–L) PTC offers several advantages. L–L–L PTC is a novel strategy which offers catalyst recovery, waste reduction including better selectivity and improving profitability. The middle catalyst-rich phase formed between the other two phases is the locale of main reaction and it intensifies the rates of reaction by order of magnitude. In the current work, oxidation of methyl mandelate to methyl phenyl glyoxylate has been studied by using L–L–L PTC with tetra-butyl ammonium bromide as a catalyst at 45 °C. It leads to 100% selectivity towards methyl phenyl glyoxylate within very short reaction time. The method offers several advantages including catalyst separation and reusability. The effects of different parameters were studied in detail. A mathematical model is developed and validated with the observed reaction data.

1. Introduction

Phase transfer catalysis (PTC) is one of the most widely used synthetic techniques and it finds more than 700 industrial applications [1,2]. Major advantages of PTC are its simplicity, use of inexpensive reagents under mild conditions, high reaction rates, and high selectivity to the desired product [3]. A large number of industrially important reactions have been reported by using liquid–liquid (L–L) phase transfer catalysis wherein recovery and reuse of the catalyst is not usually practised. Also, L–L PTC is not preferred for systems in which the presence of water leads to side reactions such as hydrolysis. It would be possible to achieve the same objective most economically by converting a biphasic reaction into a triphasic system such as liquid–liquid–solid (L–L–S) and liquid–liquid–liquid (L–L–L) PTC. In L–L–S PTC, the expensive catalyst is bound to a solid support like polymeric resin [4–5] or inorganic oxides [6] or polymeric capsule membrane (CM) [7–9]. In L–L–L PTC, the third-liquid phase (catalyst-rich phase) is an immiscible middle-liquid phase which is the locale of reaction. The rates are very high, thereby reducing the reaction times and reactor volumes. The advantages of L–L–L PTC over forms of PTC include enhanced reaction rates, absence of intra-particle diffusion resistance prevalent in L–L–S PTC, milder reaction conditions, ease of catalyst recovery and reuse, suppression of by-product formation, high selectivity with respect to the desired product [9–22]. L–L–L PTC requires more amount of catalyst but the catalyst-rich phase is recovered and reused. Hence it is an excellent way of waste reduction from the Green Chemistry point of view.

Oxidation is an important class of reaction from both industrial and academic perspectives. Several oxidizing agents have been employed for a variety of industrial reactions, but many of them are polluting and result into poor yields. PTC offers many excellent opportunities for conducting oxidation reactions by using inexpensive primary oxididizing agents such as oxygen, sodium hypochlorite and hydrogen peroxide [23–25]. Aqueous hypochlorites such as NaOCl and $Ca(OCl)_2$ are mild and used for the oxidation of various organic substrates at 20–40 °C by using PTC [26].

This paper deals with an insight into the selective oxidation of methyl mandelate to methyl phenyl glyoxylate by using sodium hypochlorite under L–L–L PTC and delineates kinetics and mechanism of the reaction. 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 [27–35].

2. Experimental

2.1. Materials

Methyl mandelate and aqueous sodium hypochlorite (4%, w/w) were obtained from M/s Merck India ltd. and used without further

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Nomenclature

A	methyl mandelate
C_A^{org}	concentration of methyl mandelate in the organic phase (mol/cm^3 of organic phase)
C_A^{th}	concentration of methyl mandelate in the third phase (mol/cm^3 of third phase)
$C_{\text{QClO}}^{\text{aq}}$	concentration of QClO in aqueous phase (mol/cm^3 aqueous phase)
$C_{\text{QX}}^{\text{aq}}$	concentration of QX in aqueous phase (mol/cm^3 aqueous phase)
$C_{\text{QClO}}^{\text{th}}$	Concentration of QClO in third phase (mol/cm^3 third phase)
$C_{\text{QX}}^{\text{th}}$	concentration of QX in third phase (mol/cm^3 third phase)
$C_{\text{QClO}}^{\text{org}}$	concentration of QClO in organic phase (mol/cm^3 organic phase)
$C_{\text{QX}}^{\text{org}}$	concentration of QX in organic phase (mol/cm^3 organic phase)
K_i	distribution constants, as given as follows: $K_1 = \frac{C_{\text{QX}}^{\text{th}}}{C_{\text{QX}}^{\text{aq}}}, K_2 = \frac{C_{\text{QClO}}^{\text{th}}}{C_{\text{QClO}}^{\text{aq}}}, K_3 = \frac{C_{\text{ClONa}}^{\text{th}}}{C_{\text{ClONa}}^{\text{aq}}}, K_4 = \frac{C_{\text{NaX}}^{\text{aq}}}{C_{\text{NaX}}^{\text{th}}},$ $K_5 = \frac{C_{\text{QClO}}^{\text{org}}}{C_{\text{QClO}}^{\text{th}}},\ K_6 = \frac{C_{\text{QX}}^{\text{org}}}{C_{\text{QX}}^{\text{th}}},\ K_7 = \frac{C_{\text{R(OH)R}'}^{\text{th}}}{C_{\text{R(OH)R}'}^{\text{org}}},\ K_8 = \frac{C_{\text{ROR}'}^{\text{th}}}{C_{\text{ROR}'}^{\text{org}}},$ $K_9 = \frac{C_{\text{H}_2\text{O}}^{\text{th}}}{C_{\text{H}_2\text{O}}^{\text{org}}}, K_9 = \frac{C_{\text{H}_2\text{O}}^{\text{aq}}}{C_{\text{H}_2\text{O}}^{\text{th}}}, K_{r1-\text{aq}} = \frac{k_{r1-\text{aq}}}{k'_{r1-\text{aq}}},$ $K_{r1-\text{th}} = \frac{k_{r1-\text{th}}}{k'_{r1-\text{th}}}$
k_{app}	apparent first order rate constant, cm^3/(mol of catalyst s)
k_{org}	organic phase reaction rate constant, cm^3/(mol of catalyst s)
$k_{r1-\text{aq}}$	rate of exchange in the aqueous phase, cm^3/(mol of catalyst s)
$k_{r1\text{-th}}$	rate of exchange reaction in the third phase, cm^3/(mol of catalyst s)
$k_{r2\text{-th}}$	rate of main reaction in the third phase, cm^3/(mol of catalyst s)
$k_{r1\text{-org}}$	rate of reaction in the organic phase, cm^3/(mol of catalyst s)
N_{Qtot}	total moles of catalyst added to the system (mol)
N_A^{th}	moles of A in third phase (mol)
N_A^{org}	moles of A in organic phase (mol)
$N_{\text{QClO}}^{\text{th}}$	moles of QClO in third phase (mol)
QX	quaternary salt
R(OH)R′	methyl mandelate
NaClO	sodium hypochlorite
ROR′	methyl phenyl glyoxylate (or benzyl formate)
t	time of reaction (s)
V^{aq}	volume of aqueous phase (cm^3)
V^{org}	volume of organic phase (cm^3)
V^{th}	volume of the third phase (cm^3)
	$X_A = \frac{N_{A0} - N_A}{N_{A0}}$, fractional conversion
$\alpha = \frac{V^{\text{th}}}{V^{\text{aq}}}$	ratio of third to aqueous phase volumes
$\beta = \frac{V^{\text{th}}}{V^{\text{org}}}$	ratio of third to organic phase volumes
$\eta = \frac{C_{\text{QClO}}^{\text{th}}}{C_{\text{QClO}}^{\text{th}} + C_{\text{QX}}^{\text{th}}}$	molar ratio of Q$^+$ in the form of QClO at any time in the third phase.

purification. Tetra-butyl ammonium bromide (TBAB) was obtained as a gift sample from Dishman Pharmaceuticals and Chemicals Ltd., Ahmadabad, India. All other chemicals were procured from M/s S.D. Fine Chemicals, Mumbai, India and were analytical grade reagents.

2.2. *Procedure*

The reaction was studied in a 5 cm internal diameter, fully baffled mechanically agitated glass reactor of 100 cm^3 total capacity. It was equipped with a 6 bladed-turbine impeller and equi-spaced baffles. The reactor was kept in an isothermal oil bath whose temperature could be maintained at a desired value. The reaction mixture was agitated mechanically with the help of an electric motor.

A typical three phase reaction mixture contained 0.03 mol methyl mandelate in toluene (made up to 10 cm^3), 0.03 mol 4% sodium hypochlorite in aqueous phase, 0.0046 mol TBAB and 0.0375 mol NaCl in aqueous phase (made up to 10 cm^3) at 45 °C. Upon mixing these two mixtures, the third phase would appear and its volume was 1.3 cm^3 with a density of 0.84 g/cm^3. The experiments were repeated and an average of three data points was taken in each case.

2.3. *Method of analysis*

The samples were periodically withdrawn at regular time intervals. The stirring was stopped momentarily and the phases were allowed to separate. The samples of a predetermined quantity were collected from the respective phases and then analyzed. The volume of third phase does not change as the aqueous phase is saturated with sodium chloride. The volume of third phase practically remains the same till the reaction goes to completion. This has been brought out in different systems involving tri-liquid PTC [36–40]. Analysis of the reaction mixture was performed by HPLC (A Knauer, model K-501: 63614) with a UV detector (Knauer, model K-501: 62964) by using acetonitrile/water (60: 40) as a mobile phase with a flow rate of 1 ml/min at $\lambda_{\max}$ of 261 nm. The quantification of the data was done by a standard calibration method.

The composition of the third phase was analyzed on GC (Chemito model 8510) by using a 4 m × 3.8 mm stainless steel column packed with 10% OV 17 on Chromosorb WHP, coupled with a thermal conductivity detector. The injector and detector temperatures were kept at 300 °C. Synthetic mixtures of the reactant and internal standard were used to calibrate the chromatograms and quantify the data.

The amount of the water present in the third phase was analyzed by Karl-Fisher apparatus.

2.4. *Determination of third phase composition*

The formation and stability of the third phase was verified independently at the reaction temperature by a trial and error procedure. In a typical experiment, the composition of the third phase was analyzed by gas chromatography. The third phase volume was 1.3 cm^3 with a density of 0.84 g/cm^3 containing 31.13% toluene, 51.37% TBAB, 0.04% methyl mandelate, 2.38% methyl phenyl glyoxylate and 15.08% water by weight.

2.5. *Reaction mechanism*

The overall reaction is represented in Scheme 1 and the mechanism is depicted in Scheme 2, which is as follows:

- Firstly the quaternary ammonium salt reacts with sodium hypochlorite to form the quaternary ammonium hypochlorite