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Modeling of microwave irradiated liquid–liquid–liquid (MILLL) phase transfer catalyzed green synthesis of benzyl thiocyanate

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ABSTRACT

Intensification of multiphase reactions with 100% selectivity to the desired product is a cherished goal in fine chemical industry. In this regard, converting bi-liquid phase transfer catalysis (L–L PTC) into a tri-liquid PTC can dramatically intensify the reaction rates and give 100% selectivity. The novelty of liquid–liquid–liquid phase transfer catalysis (L–L–L PTC) is that the catalyst forms a third middle liquid phase, that can be repeatedly reused. Additionally the aqueous phase can also be reused. Microwave technology is a novel approach towards clean and green chemistry and is relatively a very convenient, safe and rapid method. In the current work, synergistic combination of low energy microwave irradiated liquid–liquid–liquid (MILLL) PTC reaction has been brought out in intensification of reaction rates and selectivity towards benzylthiocyanate in nucleophilic substitution reaction of benzyl chloride. Tetra-*n*-butylammonium bromide (TBAB), ethyl triphenyl phosponium bromide (ETPB) and Cyphose 163 were evaluated as phase transfer catalysts. ETPB was the BEST catalyst. Effects of various parameters were studied. A mechanism of the reaction is proposed and the kinetics is established and validated against experimental data. Waste minimization was achieved in two ways in this process, namely, the aqueous and the catalyst rich middle phases were reused several times which reduces the waste. There is 100% selectivity to benzyl thiocyanate due to the creation of the third phase. The creation of third phase allows minimization of waste with complete selectivity, thereby improving profitability and environmental benefits.

1. Introduction

Phase transfer catalysis (PTC) is a versatile and powerful technique for conducting multiphase reactions and it has been applied to over 700 processes in several industries such as intermediates, dyestuffs, agrochemicals, perfumes, flavors, pharmaceuticals and polymers [1,2]. A majority of PTC reactions are conducted under liquid–liquid (L–L) conditions, and the catalyst is normally not recovered and reused. The conversion of an L–L PTC process into Liquid–Liquid–Liquid PTC (L–L–L PTC) leads to several benefits. The novelty of L–L–L PTC is that the middle liquid phase is the catalyst rich phase that can be repeatedly reused. Besides, the aqueous phase can be reused to reduce waste. This third phase becomes the main reaction phase to intensify the rates of reaction and to improve the selectivity of the desired product, apart from the economical and environmental benefits [3]. The major advantages of L–L–L PTC over normal PTC are (i) increased rate of reaction; (ii) easier catalyst recovery and reuse; (iii) high yields, purity, and selectivity towards desired products; (iv) low investment cost; (v) low energy consumption; (vi) minimization of industrial wastes; and (vii) the catalyst does not need to be bound to a solid support [4]. Several industrially useful reaction have been reported by our group [2–13] among others [4–25].

Microwave technology is a novel approach towards clean and green chemistry and it is relatively a very convenient, safe and rapid methodology [26]. In microwave heating, microwave is coupled directly with the molecules in reaction mixture leading to rapid rise in temperature, whereas conductive heating results in long equilibrium time and absolute control over the reaction becomes difficult. The fundamental mechanism for transferring energy from microwave to the reaction mass being heated is by dipole rotation or ionic conduction. Microwave will transfer energy in 10^{-9}s with each cycle of electromagnetic energy [27]. The conductivity mechanism is much stronger interaction than the dipole mechanism with regard to heat generating capacity [28]. Absorption of microwave photons cannot induce any chemical bond breaking [29]. Employing a focused energy input when using mono-mode microwave radiation for chemical reactions is advantageous when compared to using multimode radiation. In a mono-mode microwave device the reactor is directly inserted into the wave guide. The wave guide

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Nomenclature

A	benzyl chloride
B	potassium thiocyanate
CH	conventional heating
C_A^{org}	concentration of benzyl chloride in the organic phase, mol/cm^3 of organic phase
C_A^{th}	concentration of benzyl chloride in the third phase, mol/cm^3 of third phase
C_B^{aq}	concentration of potassium thiocyanate in the aqueous phase, mol/cm^3 of aqueous phase
C_B^{th}	concentration of potassium thiocyanate in the third phase, mol/cm^3 of third phase
C_Q^{th}	concentration of catalyst in the third phase, mol/cm^3 of the third phase
ETPB	ethyl triphenyl phosphonium bromide
K_1–K_8	equilibrium constants
K_e^{th}, K_e^{aq}	equilibrium constants
k^{org}	rate constant for the formation of benzyl thiocyanate in the organic phase (cm^3/(mol min))
kth	rate constant for the formation of benzyl thiocyanate in the third phase (cm^3/(mol min))
L–L–L PTC	liquid–liquid–liquid phase transfer catalysis
M	N_{Bo}/N_{Ao}
MW	microwave
N_A	moles of A
N_{Qtot}	total moles of catalyst added (mol)
QX	ethyl triphenyl phosphonium bromide
RSCN	benzyl thiocyanate
RX	benzyl chloride
t	time of reaction (min)
TBAB	tetra butyl ammonium bromide
V^{aq}	volume of aqueous phase (cm^3)
V^{org}	volume of organic phase (cm^3)
V^{th}	volume of third phase (cm^3)
X_A	fractional conversion

Greek letters

$\alpha = V^{th}/V^{aq}$	ratio of third to aqueous phase volumes
$\beta = V^{th}/V^{org}$	ratio of third to organic phase volumes
$\eta = C_{QX}^{th}/C_Q^{th}$	molar ratio of Q$^+$ in the form of QX at any time in the third phase

is designed in such a way that the empty wave guide microwaves are reflected in phase [30]. Microwave irradiation has been applied in PTC reactions in recent years [26,31–38].

Benzyl thiocyanate has wide applications as insecticide, biocides, etc. [39]. It is used in the preparation of 2, 6-dimethyl-4-aryl pyridine-3, 5-dicarbonitrile for its antibacterial activity as nifedipine analogue, and as intermediate in thrombin inhibition [40]. The various synthetic methods by which benzyl thiocyanate is synthesized include starting materials such as: benzyl alcohol [41–43], benzyl bromide using ionic liquid [44], benzyl chloride in the presence of ion exchange resins [45], using polymer supported reagents [46–48], ethers with triphenyl phosphine [43,49], and benzyl bromide by in situ formation of tetrabutyl ammonium thiocyanate [50]. Under drastic temperature conditions benzyl thiocyanate is known to isomerise to benzyl isothiocyanate. However, this reaction does not take place under mild conditions [51]. Many of these routes are fraught with problems of low yields and long reaction times. Polymer supported reagents lead to very poor reaction rates. During the nucleophilic substitution reaction of benzyl chloride, the formation of the isomer benzylisothiocyanate can be suppressed or reduced to a very low level by conducting the reaction using L–L–L PTC, and the selectivity can be further tuned by using microwave irradiation. There is no study reported in published literature.

The current work deals with the process intensification and enhancement of selectivity towards benzyl thiocyanate in reaction of benzyl chloride using L–L–L PTC. This reaction is carried out by conventional heating and by microwave irradiation. Reaction under microwave irradiation has shown much better enhancement in reaction rate as well as selectivity. This paper covers the determination of optimum process parameters, mechanism and kinetics of the reaction.

2. Experimental

2.1. Materials

Benzyl chloride, toluene, dodecane, potassium thiocyanate, sodium chloride all of analytical reagent (A.R.) grade were obtained from M/s s.d. Fine Chem. Ltd., Mumbai, India. Ethyl triphenyl phosphonium bromide (ETPB) was obtained as a gift sample from M/s Dishman Pharmaceuticals and Chemicals Ltd., Ahmedabad, India. Tetrabutylphosphonium bromide (CYPHOS IL 163), an ionic liquid, was obtained from Cytec Technologies, Canada as a gift sample.

2.2. Procedure

2.2.1. Conventionally heated reactor

The reaction was studied in a 4 cm internal diameter, fully baffled mechanically agitated glass reactor of 100 cm^3 total capacity. The reactor was equipped with a standard 6 blade-pitched turbine impeller and a reflux condenser. The reactor was kept in an isothermal water bath whose temperature could be maintained at a desired value by using a PID controller. The reaction mixture was agitated mechanically with the help of an electric motor.

The control experiment was conducted at conditions of: 50 °C, speed of agitation of 1000 rpm, 0.02 mol benzyl chloride, 0.005 mol dodecane as internal standard dissolved in toluene to make the volume of organic phase to 20 cm^3, 0.02 mol potassium thiocyanate and 0.128 mol sodium chloride dissolved in water to make up volume of aqueous phase to 20 cm^3, 0.009 mol ETPB as the catalyst. The amounts of ETPB and sodium chloride determine the formation of third liquid phase. The said composition of the reaction mixture created three distinct and stable phases at the operating conditions. This composition was arrived at by conducting several blank experiments.

2.2.2. Microwave reactor

The microwave experiments were conducted in commercially available “Discover” system of CEM Corporation, USA (Model CEM-SP 1245), with proper temperature and pressure feedback systems for complete control of the reaction conditions. It is a mono-mode microwave system. The frequency of microwave generated in the magnetron is 2455 MHz.

The reactor was of 4.5 cm internal diameter, fully baffled mechanically agitated vessel of 120 cm^3 capacity. The reactor was equipped with four equi-spaced standard baffles and a six-bladed pitched-turbine standard impeller and a reflux condenser. However, the actual reactor volume exposed to the microwave irradiation was 45 cm^3 with 5.5 cm height.

The organic and aqueous phases comprised of the same composition as mentioned above for the conventional heating system. The said composition of the reaction mixture created three distinct and stable phases at the operating conditions (Fig. 1). The reaction was allowed to reach the desired temperature and then the organic reactant benzyl chloride was added and initial/zero time sample was collected. Typically runs were conducted at 50 °C and