

Regioselective bromination of toluene by electrochemical method

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Abstract

A simple, regioselective, environmentally cleaner and economical method for the electrochemical preparation of benzyl bromide from toluene by two-phase electrolysis is reported. Electrochemical bromination of toluene is carried out in an undivided cell at 0 °C and the process parameters are studied and optimized. In this method 94% yield and 98% conversion is achieved.

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Keywords: Regioselective; Electrochemical bromination; Undivided cell; Two-phase electrolysis; α -Bromination

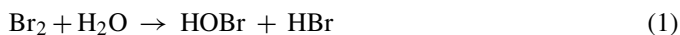
1. Introduction

Aromatic halogenated compounds have been used over a century as important chemical or to prepare various key synthetic intermediates for pharmaceuticals, dyestuffs, polymers, etc. in organic synthesis. Radical bromination on benzylic position has been achieved using bromine [1–3] and *N*-bromosuccinimide [4,5]. In addition, the bromine complex of the styrene vinylpyridine co-polymer [6], bromotrichloroethane [7,8] and copper(II) bromide [9] have been reported to be effective for benzylic bromination. The majority of brominating agents require the presence of peroxide or another radical initiator. Side-chain bromination using sodium bromate and bromotrimethylsilane has also been reported [10] but in only low yields. Using electrochemical technology, it is possible to get the same products by two-phase electrolysis resulting in high yield and selectivity.

Electrochemical bromination has been investigated in different solvents [11–19] and most of the work deals with ring brominated products. Side-chain bromination has not been much explored. Although dibromine monoxide's generation and its properties were reported in literature [20,21] its use in synthetic chemistry has not been reported. In our earlier work, in situ generation of Br_2O from aqueous HOBr and its use in the bromination of alkyl aromatic compounds have been reported [22]. Although two-phase electrolytic chlorination is reported in literature [23,24] to get selective product, no report is available

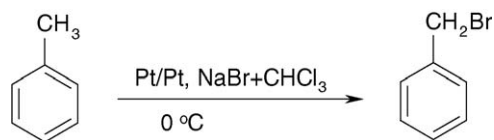
about the two-phase bromination. In homogenous electrochemical bromination, mixture of products are obtained [17,19]. In continuation of our work on electrochemical halogenation of aromatic compounds, we studied the process parameters on the α -bromination of toluene to benzyl bromide by two-phase electrolysis using an aqueous 60% NaBr solution as the supporting electrolyte containing a catalytic amount of HBr (5%) at 0 °C in a single compartment cell as shown in Scheme 1. We observed smooth bromination at the α -position of the side-chain without formation of any poly-brominated product. The reaction proceeds under mild conditions in an efficient way in the presence of a less hazardous brominating agent than Br_2 , *N*-bromosuccinimide and pyridinium tribromide.

Side-chain bromination of toluene follows a free radical mechanism and the brominating species is dibromine monoxide (Br_2O), which is formed by two-phase electrolysis Eqs. (1) and (2). In the first step, electrochemically generated bromine is combined with water giving hypobromous acid and hydrogen bromide. In presence of an acid (HBr), one molecule of water is removed from two molecules of hypobromous acid as a hydronium ion resulting in the formation of Br_2O as the brominating species, which is extracted by the organic phase where the selective bromination occurs:



As the reactive species Br_2O is unstable, it is cleaved homolitically into Br^\bullet and $^\bullet\text{OBr}$. The more reactive $^\bullet\text{OBr}$ abstract a

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Scheme 1. Electrochemical bromination of toluene by two-phase electrolysis.

benzylic hydrogen to form HOBr. Subsequently bromine radical attack benzyl radical and benzyl bromide is formed as product. If HOBr alone present as brominating agent in absence of HBr, then the product obtained from toluene is a mixture of side-chain brominated (53%) and nuclear brominated products (mixture of 22% *ortho*- and 25% *para*-isomers). The product formation was confirmed by chemically generating HOBr as per Eq. (3) [25] and toluene was brominated by as usual method:



Further, dibromine monoxide was prepared chemically in CCl_4 solvent as per Eq. (4) and toluene was brominated. The product obtained was benzyl bromide as a sole product:



2. Experimental

2.1. Electrochemical bromination of toluene

Deionised water was used for preparing sodium bromide solution. An Aplab power source was used as the direct current source for the electrolysis. A beaker type glass cell (120 ml capacity) equipped with a magnetic stirrer was used for the electrolysis and two platinum sheets of 10-cm^2 area were used as the anode and the cathode. Fifty milliliters of 60% sodium bromide solution containing a catalytic amount of hydrobromic acid (5%) was used as the electrolyte and the bromine source. The reaction was monitored by HPLC using a Shimpack ODS-18 column ($125\text{ mm} \times 4.5\text{ mm}$) as the stationary phase. The eluent consisted of methanol/water (70:30) at a flow rate of 1 ml/min. Samples were analysed at a wavelength of 254 nm with a UV detector. Authentic samples of benzyl bromide, *p*-bromobenzyl bromide, *p*-bromotoluene were used to calculate the peak areas of all the experimental products for yield calculation.

A solution of toluene (1.74 g, 19 mmol) in chloroform (25 ml) was taken in a single compartment electrolytic cell. To the above solution, 50 ml of 60% NaBr containing 5% HBr was added. The aqueous upper phase acted as the supporting electrolyte and also as the bromine source. Two platinum electrodes were placed in the aqueous phase without touching the organic phase but very close to the interphase. The organic phase alone was stirred with a magnetic stirrer at a rate of 40 rpm in such a way that the organic layer does not touch the electrodes. The temperature of the electrochemical cell content was monitored at $0\text{--}2^\circ\text{C}$ throughout the electrolysis. The electrolysis was conducted galvanostatically at a current density of 50 mA/cm^2 until the quantity of the current indicated in Table 1 was passed. An aliquot was drawn periodically from the organic phase and analysed by HPLC. After

Table 1
Experimental conditions for bromination

S. no.	Parameters	Value
1	Temperature ($^\circ\text{C}$)	0
2	Stirring rate (rpm)	40
3	Current density (mA/cm^2)	50
4	Substrate	Toluene 19 mmol (1.7 g)
5	Pressure	Atmospheric pressure
6	Current rate (mA)	500
7	Anode	Platinum (10 cm^2)
8	Cathode	Platinum (10 cm^2)
9	Electrolyte	50 ml of 60% NaBr + HBr 5 ml
10	Charge passed (F mol^{-1})	4

the completion of the electrolysis, the lower organic phase was separated, washed with water ($2 \times 25\text{ ml}$), dried over anhydrous Na_2SO_4 and the solvent was removed by distillation. HPLC analysis of the residue indicated the presence of 94% benzyl bromide and 4% nuclear brominated toluene along with 2% unconverted toluene.

2.2. Bromination of toluene with chemically generated Br_2O

Br_2O was produced by the reaction of Br_2 with HgO in CCl_4 solvent. Bromine (1.6 g, 10 mmol), toluene (0.46 g, 5 mmol) were taken in 25 ml CCl_4 solvent. The above solution was cooled to 0°C and HgO (1.1 g, 5 mmol) was added little by little for an half-an-hour with stirring the reaction mixture. The same temperature was maintained for another 30 min. The reaction mixture was filtered to remove solid HgBr_2 , then the organic phase was washed with water and analysed by HPLC. The spectrum showed the presence of benzyl bromide (86%) and toluene (14%) without any bye product formation.

2.3. Bromination of toluene with chemically generated HOBr and HBr

To a solution of bromine (1.6 g, 10 mmol) in 25 ml chloroform, toluene (0.46 g, 5 mmol) and 5 ml of 40% HBr solution were added. The reaction mixture was cooled to 0°C and HgO (1 g, 5 mmol) was added in portions over a period of 30 min. After completion of addition, stirring was continued further for 30 min. Then the reaction mixture was washed with water and analysed by HPLC. The spectrum showed the presence of benzyl bromide (82%) without any bye products (i.e. benzal bromide and *o*- and *p*-bromotoluene).

2.4. Bromination of toluene with chemically generated HOBr

The aqueous solution of hypobromous acid can be generated by treating bromine water with mercuric oxide [23]. The above-mentioned experiment (Section 2.3) was conducted in the absence of HBr and the product obtained was a mixture of benzyl bromide (53%) and *o*- and *p*-bromo toluenes (47%). From this experiment it is observed that in the absence of

Table 2
Effect of current density

S. no.	Current density (mA/cm ²)	Toluene (mmol)	Benzyl bromide (mmol)	Yield (%)	Current efficiency (%)
1	20	19	17.5	92	48
2	30	19	18.0	94	50
3	50	19	17.7	94	48
4	80	19	12.0	63	36
5	100	19	10.7	56	30

HBr, electrochemically formed HOBr molecule attack toluene without control giving non-selective products. In the presence of HBr, Br₂O is formed and gives selective product.

3. Result and discussion

3.1. Electrochemical bromination of toluene

Two-phase electrolysis is one where the electrolyte and the substrate are present in different phases. Two-phase electrolysis is advantageous than the homogenous electrolysis because in the homogenous system less selectivity is observed due to substrate gets oxidised on the surface of the electrode giving mixture of nuclear and side-chain brominated products. When electrolysis occurs, electrolytically generated species travels from aqueous phase to organic phase and attacks the substrate (Fig. 1). The products obtained in two-phase electrolysis will not be the same as in the homogenous electrolysis. In the homogenous electrolysis the products are non-selective. If the two phases are made into emulsion by vigorous stirring, then this type of electrolysis is called emulsion electrolysis.

In the electrochemical bromination of toluene, the following process parameters were studied and the results are reported:

- current density;
- temperature;
- electrolyte concentration;
- solvent;
- anode material.

3.2. Effect of current density

Electrochemical bromination reactions were carried out in an undivided cell at a current density from 10 to 80 mA/cm². Table 2 shows the effect of current density on product yield

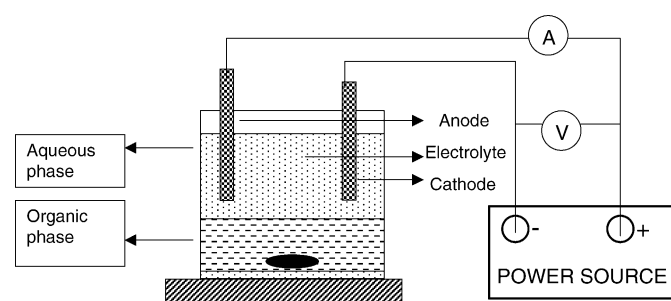


Fig. 1. Electrochemical bromination reaction set-up.

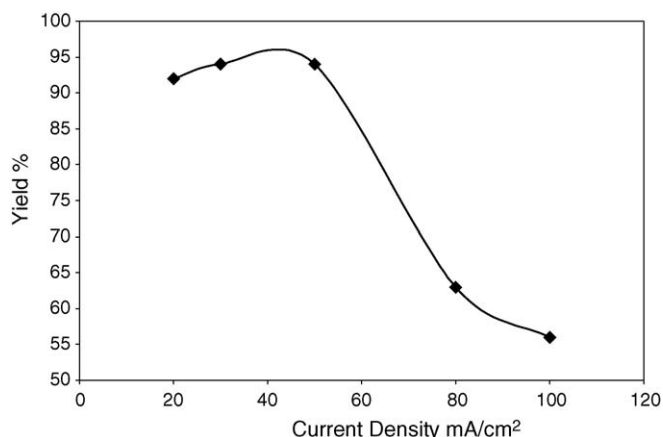


Fig. 2. Effect of current density on benzyl bromide yield.

and current efficiency. The yield of benzyl bromide is increased with increase of current density from 10 to 50 mA/cm² and further increase in current density did not make any improvement (Fig. 2). Hence, the optimum current density for the electrochemical bromination of toluene is 50 mA/cm².

3.3. Effect of temperature

Electrochemical bromination of toluene was carried out at a temperature range of 0–30 °C. The rate of formation of benzyl bromide varies at different reaction temperature (Fig. 3). The reaction temperature plays a crucial role in the bromination reaction as the Br₂O decomposes at higher temperature. Table 3 shows the effect of temperature on the bromination of toluene.

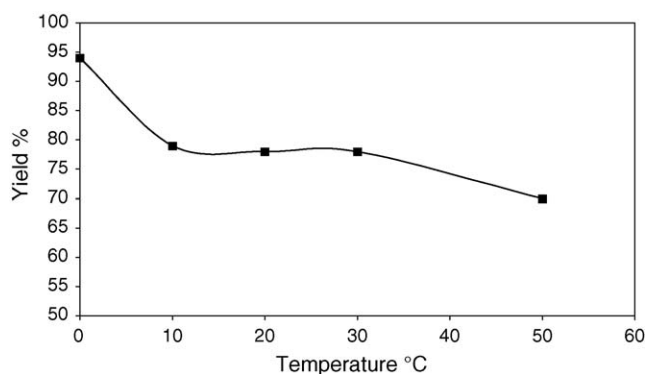


Fig. 3. Effect of temperature on benzyl bromide yield.

Table 3
Effect of temperature

S. no.	Temperature (°C)	Toluene (mmol)	Benzyl bromide (mmol)	Yield (%)	Current efficiency (%)
1	0	19	18	94	49
2	10	19	15	79	40
3	20	19	14	78	39
4	30	19	14	76	38
5	50	19	13.4	70	34

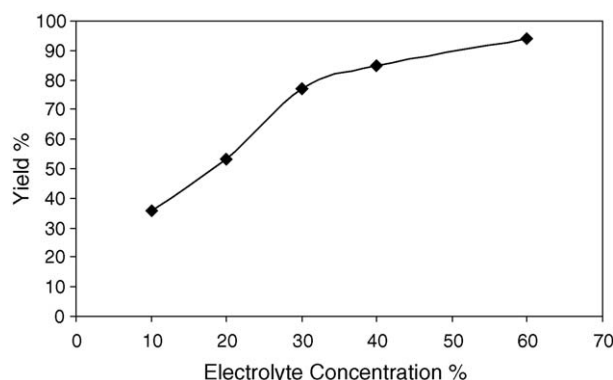


Fig. 4. Effect of electrolyte concentration on benzyl bromide yield.

Table 4
Effect of electrolyte concentration

S. no.	NaBr		Toluene (mmol)	Benzyl bromide (mmol)	Yield (%)	Current efficiency (%)
	(g)	(%)				
1	5	10	19	7	36	20
2	10	20	19	10	53	22
3	15	30	19	14	77	39
4	20	40	19	16	85	43
5	30	60	19	18	94	48

3.4. Effect of electrolyte concentration

Sodium bromide was used as electrolyte for the electrochemical bromination of toluene in an undivided electrochemical cell at a temperature of 0 °C. The yield of benzyl bromide varies with the electrolyte concentration (Fig. 4). The optimum electrolyte concentration favours the formation of brominating species and passing into organic phase for selective bromination. The electrolyte concentration was prepared from 10% to 60% and the electrochemical bromination of toluene was carried out at an optimum current density, temperature and stirring rate. Table 4 shows the effect of electrolyte concentration on bromination

Table 5
Effect of solvent study

S. no.	Solvent	Toluene (mmol)	Benzyl bromide (mmol)	Yield (%)	Current efficiency (%)
1	Chloroform	19	18	94	48
2	Dichloro methane	19	14	77	39
3	Acetonitrile	19	8	42	21

Table 6
Selection of anode

S. no.	Anode	% of product formed based on charge passed		
		2 F	3 F	4 F
1	Platinum	40	82	94
2	Platinised titanium	40	80	91
3	Dimensionally stable anode (DSA)	67	75	80
4	Graphite	30	72	79

of toluene. The bromination occurs smoothly at 60% NaBr solution.

3.5. Effect of solvent study

In two-phase electrolysis system, the substrate is taken in an organic solvent like chloroform, having higher density than 60% aqueous sodium bromide solution. After completion of electrolysis, the lower organic layer is separated and processed further. The selection of suitable solvent is necessary in two-phase electrolysis. Chloroform, methylene dichloride and acetonitrile were used as solvent. When chloroform was used as a solvent it acted as lower phase and electrochemically generated dibromine monoxide migrate from the upper aqueous phase into organic phase and the selective product formed in very good yield. Since acetonitrile is miscible with water it forms a homogenous phase with electrolyte, leading to direct attack of substrate on the electrode surface and gives non-selective products (i.e. 40% benzyl bromide, 37% *p*-bromo benzyl bromide along with 8% *o*- and *p*-bromo toluenes). Alternatively we have conducted the two-phase electrolysis, where the dichloromethane acted as upper phase. As the density of the dichloromethane is very close to the density of 60% NaBr solution it forms an emulsion while stirring the reaction mixture during electrolysis. As the organic solvent interferes with the aqueous phase, the Br₂O formation from HOBr is delayed and hence the reaction rate of bromination is slow. During this process, it is also observed that the cell voltage is raised to two-fold leading to higher energy consumption. Therefore, chloroform is an ideal solvent for the two-phase electrolysis. Table 5 shows the effect of solvent on bromination of toluene.

3.6. Selection of anode materials

The behaviour of various anode materials on the electrochemical bromination of toluene was studied using platinum, platinised titanium, graphite and dimensionally stable anode (DSA) as anode while keeping the platinum as cathode. Among

them, except DSA anode all the electrodes provide 86–94% yield of benzyl bromide. In the case of DSA 80% benzyl bromide is obtained along with 14% *p*-bromo benzal bromide as a by product after passing 4 F mol⁻¹ charge. Table 6 shows the behaviour of anodes on bromination of toluene.

4. Conclusion

Electrochemical bromination of toluene to benzyl bromide can be carried out in an undivided cell with good yield and conversion by two-phase electrolysis. In electrochemical bromination reaction, selective bromination occurs on the side-chain of toluene and the reaction can be controlled easily and avoids the formation of di/tri-bromomethyl compounds and other impurities like nuclear brominated compounds. This electrochemical bromination process is an alternate process for the synthesis of benzyl bromide and other substituted benzyl bromides. The advantages of electrochemical bromination are:

- high current efficiency;
- high yield and conversion;
- selective product formation.;
- avoids handling of bromine;
- in situ generation of bromine;
- reaction can be controlled easily;
- no by products formation.

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