

Chloromethylation of Meta Xylene by Phase Transfer Catalysis

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Abstract: The chloromethylation of *m*-xylene has been improved by using quaternary ammonium salts as phase transfer catalyst (PTC).

The results obtained during chloromethylation by using quaternary ammonium salts have been optimized to give optimal values of $[CH_2O]/[m\text{-xylene}] = 2$ at 90 min and 80 °C.

This optimization gives relatively high yields of mono and di *m*-xylene. All the reaction products have been characterized by IR and Mass spectroscopy coupled to gas chromatography. The best catalyst was found to be $C_6H_3(CH_3)_2[CH_2N^+(CH_3)_3]Cl$ with an optimal concentration of 0.07 mol.

Keywords: Chloromethylation, *m*-xylene, Phase transfer catalysis, Quaternary ammonium salt.

I. Introduction

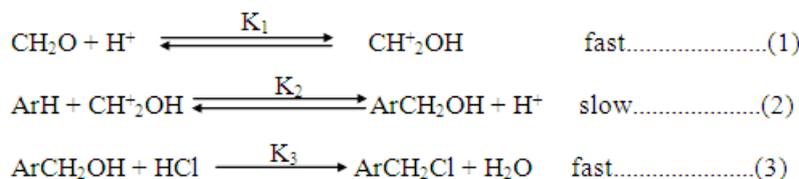
Aromatic molecules are actively used as raw materials in the petrochemical industry. The insertion of chloromethyl (-CH₂Cl) group on the aromatic nucleus of xylenes allows a substitution of many functions. Up to now, the chloromethylated groups were introduced by the Friedel Craft alkylation with mono chloro methyl ether (MCME). This compound has been found to be highly carcinogenic whereas di chloro methyl ether (DCME) is dangerous by inhalation owing to its high vapour pressure [1].

Since the discovery of the chloromethylation reaction by Grassi-Cristaldi and Maselli, the research focused on the role of formaldehyde. It is generally accepted that the electrophilic reagent in the chloromethylations in aqueous and polar solvents (such as glacial acetic acid) is the hydroxycarbenium ion (protonated formaldehyde (CH₂⁺=OH) [2]. Interestingly, in recent work [2] protonated chloromethyl alcohols, ClCH₂O⁺H₂ were obtained as stable specie, thus indicating its possible significance in the chloromethylations. In addition, the chloromethylation shows high substrate and positional selectivity [3]. In most cases, it is assumed that molecules of two or more carbon atoms split to give a fragment containing a single carbon atom which reacts with the aromatic nucleus, introducing a chloromethyl group. Formalin in acid medium has been used with a protonated acid as catalyst [4].

Blanc reaction or chloromethylation is one of the most fundamental reactions in organic chemistry [5]. It has been widely applied in the synthesis of fine chemicals, like Pharmaceuticals, agrochemicals and polymers, in which chloromethyl can be easily changed to CH₂OH, CHO, CH₂CN, CH₂NH₂, CH₃, CH₂R, etc. Blanc reaction is normally performed in polar solvents and is usually carried in heterogeneous medium in presence of Lewis acid, e.g. ZnCl₂ or SnCl₄ to activate formaldehyde [6]. The technology of phase-transfer catalysis (PTC) was originally developed in the mid-1960s to enhance chemical reactions catalysed by quaternary ammonium salts in which the reactants are in two separate phases [7]. By now, PTC is now considered to be one of the most effective tools for organic synthesis from two or more immiscible solutions [8]. The methodology involves a reactant (organic-soluble compound) and an anionic reactant (often an aqueous-soluble nucleophile). The organic-soluble reactant and the water-soluble anion are then brought together by a catalyst, which transports the anion into the organic phase where reaction takes place with the organic reactant. Quaternary ammonium and phosphonium salts with their capability to dissolve in both aqueous and organic liquids are the catalysts of choice for PTC applications[9]. Further advantage of PTC lies in the elimination of organic solvents and dangerous or expensive bases, together with simplicity of the procedure, its high yields and the purity of the products. PTC has been considered as a fascinating area of current research interest. It is a versatile technique applicable to a number of organic mixed phase reactions. The significant applications of PTC include the preparation of compounds from an unreactive starting material, dramatic enhancement in yields and product selectivity. The first soluble single-site phase transfer catalyst has come during 1960s[10] and then a variety of quaternary ammonium[11] have been reported and used to carry out reactions particularly O-alkylation, C-alkylation, N-alkylation, dichlorocarbene addition to olefinic double bonds, oxidation, reduction[12], etc. The primary advantage of PTC is to elevate the reaction rate and increase the selectivity in mild conditions. Jarrouse found that quaternary ammonium salt is an effective catalyst for enhancing the two-phase reaction[13], many chemists have investigated PTC in numerous reactions, such as substitution, condensation, electro-oxidation, etc.[14]. The principle of PTC is based on the ability of certain "phase-transfer agents" to facilitate the transport of one reagent from one phase into another (immiscible) wherein the other reagent exists. Thus, reaction is made possible by bringing together the reagents which are originally in different phases. However, it is also necessary that the transferred species are in an active state for effective PT catalytic action, and that it is regenerated

during the organic reaction. Primary applications are in nucleophilic substitution reactions and in reactions in the presence of bases involving the deprotonation of moderately and weakly acidic organic compounds. Careful choice of chloromethylation conditions leads to higher selectivity and reactivity simultaneously.

On a technological scale the use of PTC allows to improve the synthesis of chloromethyl m-xylene with the privilege to use a simple and convenient installation with a low energetic consumption and inexpensive solvents. The novelty resides in the fact that PTC is a quaternary ammonium salt which permits to obtain substituted compounds namely mono, di and trichloromethyl m-xylenes. It has been demonstrated that the rate of transformation of paraformaldehyde is proportional to the concentrations of both reactants and products. The following mechanism has been proposed by Brown and Nelson[14].



It has been shown elsewhere that the reaction is speeded up in polar solvents such as o-dichlorobenzene or methylene chloride[15]. The process described by Menger[16] has been adopted by most authors and symmetrical quaternary ammonium salts (in two centres) are found to be more efficient than non-symmetrical ones[17]. The aim of this work is to use quaternary ammonium salts as a phase transfer catalyst for chloromethylation of m-xylene and to find the optimum reaction time and temperature for the optimal values of $[\text{CH}_2\text{O}]/[\text{m-xylene}]$.

II. Materials And Methods

2.1. Synthesis of chloromethyl m-xylene (phase transfer catalyst PTC)

The m-xylene chloromethylation was performed as follows: concentrated H_2SO_4 was added to the paraformaldehyde /m-xylene mixture (molar ratio= 2) and NaCl (0.26 moles) with PTC (quaternary ammonium salt catalyst). The mixture was kept at 80 °C in an oil bath under intense agitation for 2 h. The organic phase was extracted with ether and dried in presence of CaCl_2 , the products were analysed by gas chromatography.

2.2. Analysis

Separation and quantitative analysis of the chloromethyl groups was performed using an HP 5890 gas chromatograph (GC) (Hewlett Packard, GMI, Ramsey, Minnesota, USA) (FID) and equipped with a capillary fused silica 25 m long, 0.25 mm internal diameter and 0.25 micron thick film. The column temperature was programmed from 50 to 240°C at 5°C/min. The injector temperature was set at 220°C and the detector (FID) at 250°C. The flow of carrier gas (nitrogen) was set at 1 ml/min. The respective part of each compound was deduced from the peak areas. The retention times were 19.81, 37.64 and 51.65 s for mono-, di- and trichloromethyl, respectively.

The identification of the components was carried out by gas chromatography (Hewlett-Packard 5890 Series II) coupled to a mass spectrometer Hewlett-Packard 5989A (Py-GC/MS), at 70 eV recording. The gradient temperature of the column (identical to that used for GC) is programmed from 60 °C to 200 °C at 3 °C/min rate. The temperature of the injector was set at 250 °C, the pressure of the carrier gas (helium) was set at 20 psi and the injected volume was 1 µl of 1 % diluted solution of chloromethyl meta-xylene in hexane.

Information dealing with molecular weight of products was expressed in units of mass per elementary charge (m/z), and including chloromethyl products as well as the likelihood of the chloromethyl fragments, leading to the molecular weight of the target molecular compound.

An infrared spectrometer Perkin-Elmer 1310 (Waltham, Massachusetts, USA) was used and analysis was performed using the routine KBr (approximate amount 0.5% in mass of product).

UV-Visible spectra (Perkin Elmer spectrophotometer Lambda 45, were performed after proper dilutions, down to 10^{-6} M. Samples were placed in quartz cells of 1 cm optical path.

III. Results And Discussion

The proposed reaction mechanism for aromatic chloromethylation of formaldehyde in acidic medium has been accepted for long time to explain the kinetic in presence of other hydrocarbons as well as the role of hydrochloric acid [18]. From chloromethylation various xylenes by paraformaldehyde in presence of a Lewis acid (catalyst) and acetic acid (solvent) were prepared and the method has succeeded in industrial applications. The synthesis reaction can be presented as follows:

.....(4)

Monochloromethyl m-xylene

.....(5)

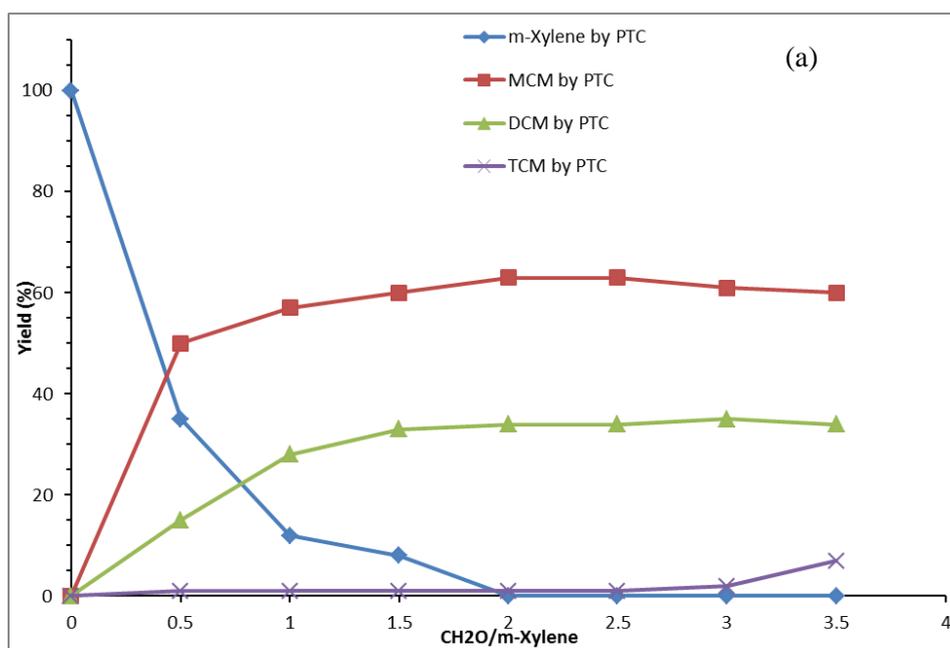
Dichloromethyl m-xylene

.....(6)

Trichloromethyl m-xylene

3.1. Optimization of reaction parameters:

To optimize the chloromethylation reaction, the influence of the operational parameters namely the molar ratio [CH₂O/m-xylene], the reaction time, the temperature and the nature of the catalyst on the reaction yields for PTC methods were presented in Table 1 and Fig. [1(a,b,c),2,3]. The optimum values of these results shows concentration of the ratio = 2 at the time of 90 min. at the temperature of 80 °C. The products were identified by gas chromatography. The products were mono, di and trichloromethyl m-xylenes.



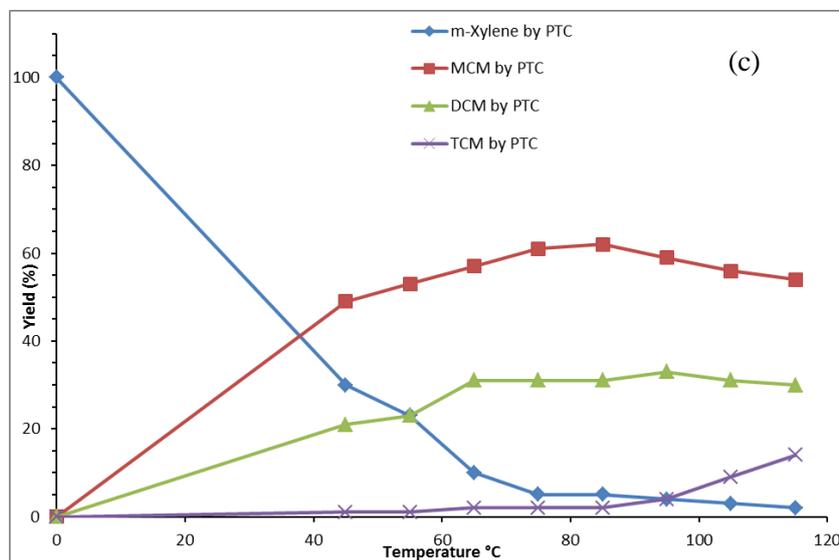
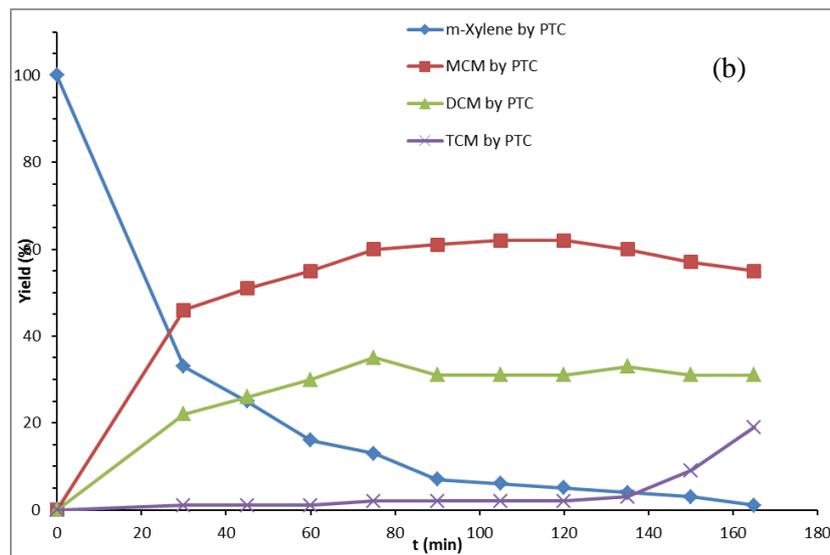


Figure (1): Influence of (a) molar ratio [CH₂O/m-xylene], (b) reaction time and (c) temperature on the chloromethylation.

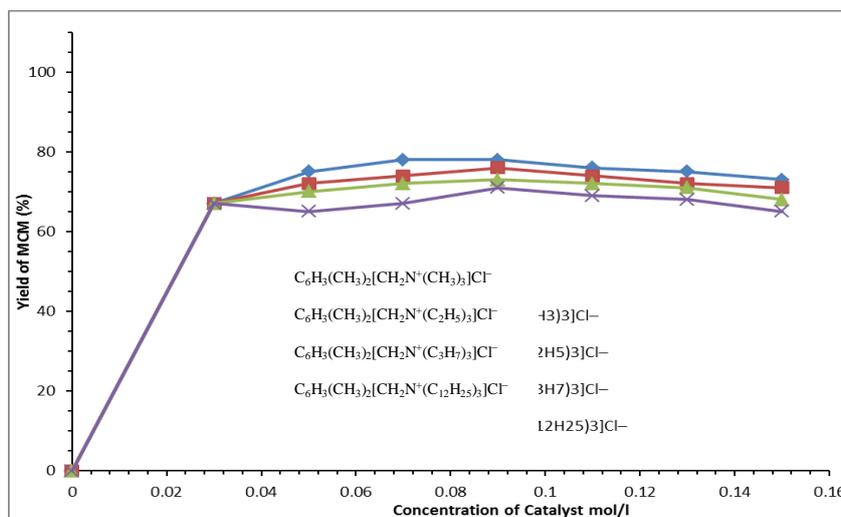


Figure (2): Yield of MCM as a function of different PTC catalysts and their concentrations

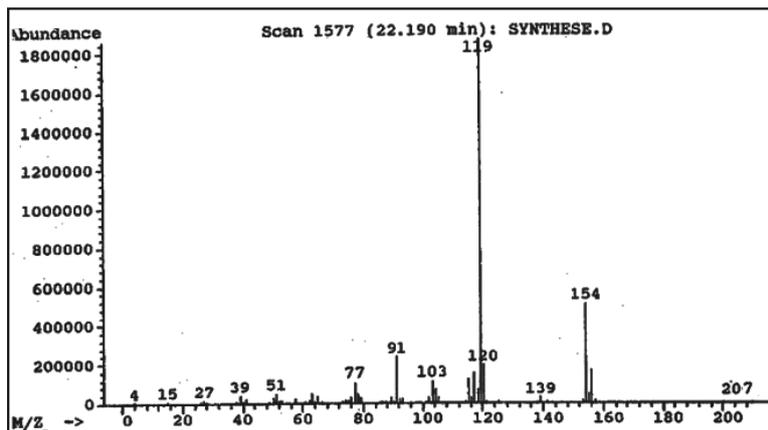


Figure (5): Mass spectrum of Monochloromethyl m-xylene.

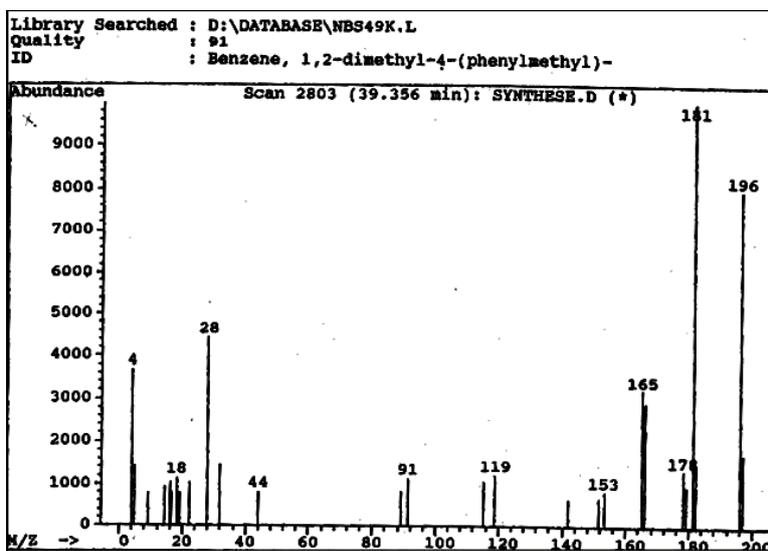


Figure (6): Mass spectrum of DCM m-xylene

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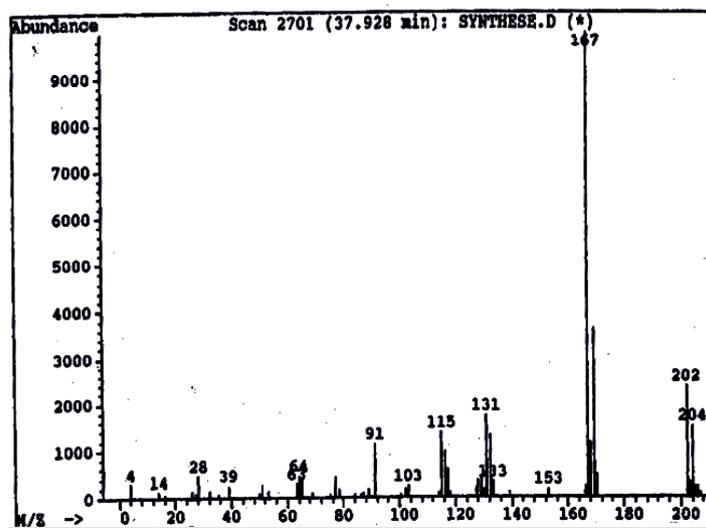


Figure (7): Mass spectrum of TCM m-xylene

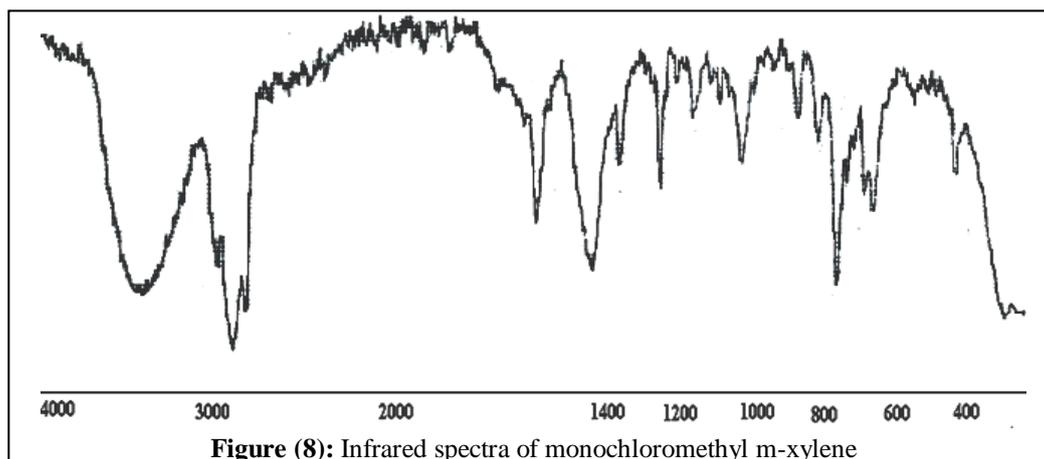


Figure (8): Infrared spectra of monochloromethyl m-xylene

IV. Conclusion

The chloromethylation of m-xylene was improved on a technological level by the use of phase transfer catalyst. The reaction gives high yield of mono and di m-xylene. This method has the privilege to use a simple and convenient installation, low cost reagents and low energy consumption compared to the classical techniques. Among several quaternary ammonium salts phase transfer catalysts, the best catalyst was found to be $C_6H_3(CH_3)_2[CH_2N^+(CH_3)_3]Cl^-$ with an optimum concentration of 0.07 mol. The optimum yields was obtained at molar ratio of $[CH_2O]/[m\text{-xylene}] = 2$ and reaction time and temperature of 90 min and 80 °C respectively.

The quaternary ammonium salts of mono, di, and tri chloromethyl m-xylene are recommended to be used in waste water treatment to remove some heavy metals such as Zn, Cu, Ni, Fe, Cr, Cd and Hg.

Table (1): Optimal values for the molar ratio $[CH_2O]/[m\text{-xylene}]$, the reaction time, the temperature and the nature of the catalyst recorded by the phase transfer catalysis (PTC).

Parameters	Results
$[CH_2O/ meta\ xylene]$	2
Reaction time (min)	90
Reaction temperature (°C)	80
Catalyst concentration	0.07 mol/L
Best catalyst	$C_6H_3(CH_3)_2[CH_2N^+(CH_3)_3]Cl^-$
m- xylene yield (%)	0.017
MCM meta xylene yield (%)	76.37
DCM meta xylene yield (%)	20.80
TCM meta xylene yield (%)	2.82

Abbreviations

MCME	Monochloromethyl ether
DCME	dichloromethyl ether
DMF	dimethyl formamide
DCME	dichloromethyl ether
PTC	phase transfer catalysis
MCM.	Monochloromethy metaxylene
DCM.	dichloromethy metaxylene
TCM.	Trichloromethy metaxylene
t	Time
T	Temperature

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