

APPLICATIONS OF POLYSTYRENE SUPPORTED BROMODERIVATIVES OF 2-PYRROLIDONE IN MICROWAVE ASSISTED ORGANIC SYNTHESIS

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ABSTRACT

Polymer supported catalysts and reagents have become popular in organic synthesis over the past decades. The use of polymer supported reagents can combine the benefits of solid – phase chemistry with the advantages of solution – phase synthesis. But the poor diffusion of the reactants through the polymeric network resulting in slow reaction rate limits its synthetic application compared to the conventional solution phase. This drawback can be minimized by performing polymer supported reactions under microwave conditions. Microwave activation as a means of non-conventional energy source is becoming a very popular and useful technique in organic chemistry. Microwave irradiation often leads to shorter reaction times, increased yields, easier workup and matches with the green chemistry protocols. In the present work a novel, efficient and recyclable polymeric reagent, Polystyrene supported Bromoderivatives of 2-Pyrrolidone was prepared and characterized. 3% crosslinked Polystyrene was prepared by free radical aqueous suspension polymerization technique using Tetra Ethylene Glycol Diacrylate (TTEGDA) as the crosslinking agent and the resulting beads were functionalized by chloromethylation followed by reaction with 2-pyrrolidone. Then it is functionalized with bromine by treating with Br₂ in CCl₄. The synthesized bromo resin was found to be a versatile oxidizing reagent for microwave-assisted organic synthesis. This reagent could be easily recycled several times. A Comparative study of microwave assisted synthesis with conventional techniques was also carried out in order to study the oxidizing efficiency under both conditions.

KEYWORDS: Microwave Assisted Organic Synthesis, 2-Pyrrolidone, and Bromo Resin

In the past few years, heating and driving chemical reactions by Micro Wave (MW) energy has been an increasingly popular theme with the scientific community, as demonstrated by the rapidly growing number of annual publications on microwave assisted organic synthesis (J.J. Shah and Krishnapriya Mohanraj; 2014, Alex C. Bissember and Martin G. Banwell; 2009). This nonclassical heating technique is slowly moving from a laboratory curiosity to an established technique, and is heavily used in both academia and industry (Frecentese F et.al; 2016). Apart from applications in the area of standard solution-phase organic synthesis (SPOS), there are a growing number of publications that report the use of MW heating for SPOS or in conjunction with polymer supported reagents and catalysts, using a variety of different polymeric materials as insoluble supports (Abu Taher et.al 2015). The combination of solvent free reaction conditions and microwave irradiation leads to a remarkable reduction in reaction time, enhancement in conversion and selectivity with several advantages of the eco-friendly approach, termed green chemistry (Lidstrom P. et.al;2001). The impressive speed combined with the unmatched control over reaction parameters justifies the growing interest in this application of microwave heating.

In polymer-supported reactions the inherent chemical reactivity of a supported species may be

modified by the chemical and structural characteristics of the support (Takemoto et.al; 1987). The efficiency of a supported reaction mainly depends upon the accessibility of the immobilized functional groups to low molecular weight soluble substrate and solvent molecules. Thus, the compatibility of the supports with substrates and solvents is a decisive factor for the success of supported reaction. Use of supports that can be employed in both polar and nonpolar medium can increase the efficiency of supported reactions. One important strategy to achieve this is by copolymerization with appropriate monomers and by using different types of crosslinking agents.

In the present study we synthesized and characterized a novel, efficient and recyclable polymeric reagent, TTEGDA crosslinked Polystyrene supported Bromoderivatives of 2-Pyrrolidone. Facile oxidation of alcohols to corresponding carbonyl compound was carried out using the prepared polymer supported reagent under microwave condition. In order to compare thermal heating with microwave heating, each reaction was also carried out under conventional heating conditions.

MATERIALS AND METHODS

Styrene, TTEGDA (Tetra Ethylene Glycol Diacrylate) and 2-Pyrrolidone were purchased from Sigma Aldrich Germany. Chloromethyl methyl ether (CMME)

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was prepared using literature procedure (Marvel C S and Porter P K; 1967). All other solvents and reagents used were of general reagent grade. The reactions were monitored by thin layer chromatography (TLC) with Merck precoated silica plates. All microwave experiments were performed using an Onida Powersolo 20 microwave oven. IR spectra were recorded on a Perkin Elmer Spectrum Version 10.4. The size and morphology of the synthesized resin was investigated by SEM JEOL (JSM6100). In addition; the presence of Nitrogen and bromine in the sample were confirmed by EDX spectroscopic analysis.

1. Preparation of chloromethylated TTEGDA- Polystyrene (TTEGDA-PS) support (P1)

3% TTEGDA crosslinked polystyrene was prepared by free radical suspension polymerization (M. Renil, V. N. Rajasekharan Pillai; 1994) followed by functionalization with Chloromethyl group (Jashmin P.Patel et.al; 2013). Chlorine capacity of the resultant resin was estimated by pyridine fusion method

2. Preparation of polystyrene supported of 2-Pyrrolidone resin (P2).

P1 (1g) were dispersed in DCM and allowed to swell for 2 hours. To the swollen bead 2g 2-pyrrolidone was added and refluxed for 24hours at 120°C in presence of pyridine (4ml). The resulting resin was washed with methanol and acetone and dried at 80°C and designated as P2.

3. Preparation of Bromo derivatives of polystyrene supported of 2-Pyrrolidone resin (P3).

1g P2 is stirred with 2ml bromine in 25 ml CCl₄ solution for 4 hours at room temperature. The resultant dark orange reagent was filtered, washed with CCl₄, dried and was designated as P3. The yield of the newly synthesised resin was 1.6g.

4. Estimation of Bromine capacity and Microwave stability of the bromo resin (P3).

The bromine capacity of P3 was determined by iodometric titration. To a suspension of 100mg of polymer in 20ml DMF (0°C), 1g KI was added and kept in dark with occasional shaking. The liberated iodine was titrated against std. (0.05N) Na₂S₂O₃. From the titer value the bromine capacity was calculated. In order to study the stability of bromo polymer to microwave irradiation, the reagent was subjected to irradiation for different time interval (2, 4, 6, 8 and 10mts). After each time interval a definite amount of the reagent was taken out and

determines its bromine capacity. Microwave power of 350W is used for this study.

5. Microwave assisted oxidation reactions using polystyrene supported Bromo derivatives of 2-Pyrrolidone resin (P3).

A fivefold molar excess of P3 (2.5g) was impregnated with a solution of organic substrate (0.5g) in DCM. The solvent was evaporated and the polymeric reagent with the adsorbed substrate was MW irradiated for 10minutes at a power of 350W. Impregnation of the polymeric reagent with low molecular weight substrate was repeated after every two minutes of microwave irradiation, by adding dichloromethane followed by evaporation of the solvent. The reactions were monitored by thin layer chromatography (TLC). After the complete conversion, the insoluble spent reagent was filtered and washed with more solvent. The combined filtrate and washings was dried over anhydrous sodium sulphate and the solvent evaporated to afford the product. The products were characterized by physical and spectral characteristics with authentic specimens.

6. Oxidation reactions using Bromo resin (P3) under conventional method.

In conventional method the reactions were carried out by heating a solution of the substrate in cyclohexane with fivefold molar excess of the reagent under refluxing temperature. Continuous stirring of the reaction mixture was done during the course of the reaction. The rate of the reaction was followed by TLC.

7. Regeneration of the spent reagent.

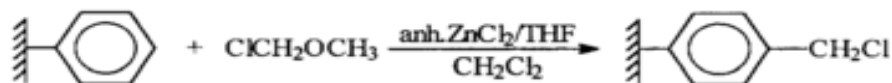
The spent reagent obtained from different reactions were collected together and washed several times with dichloromethane to remove any trace of the organic substrate or product. Then the bromo group is introduced in to the polymer by following the original procedure.

RESULTS AND DISCUSSION

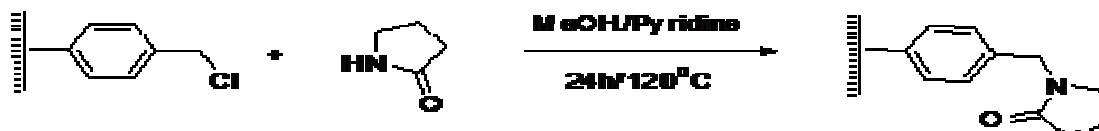
The polymer supported bromo resin P3 was prepared in three steps. As shown in scheme 1, the beads of polystyrene (3% TTEGDA crosslinked, 200 mesh size) were treated with chloromethylmethylether (CMME) in the presence of ZnCl₂/THF (zinc chloride in Tetrahydrofuran), to produce chloromethylated TTEGDA-PS support (P1). Chlorine capacity of the resultant resin was 3.2mmol/g as estimated by pyridine fusion method. 2-Pyrrolidone was then grafted on to P1 in methanol under reflux in the presence of pyridine for 24 hours at 120°C to yield TTEGDA crosslinked polystyrene supported 2-

pyrrolidone, P2(scheme-2). Functionalization of P2 with bromine was achieved by treating with bromine in carbon tetra chloride. The bromine capacity of P3 was found to be 1.4984mmol/g and remains almost the same even after

10mts of irradiation at a microwave power of 350W. The resin is found to be stable for about 15mts and charring occurred after 15mts.



Scheme 1: Chloromethylation of TTEGDSA crosslinked Polystyrene.



Scheme 2: Synthetic pathway for the synthesis of Polystyrene supported 2-pyrrolidone (P2)

P1 and P2 were characterized by IR spectroscopy. The FTIR spectra of P1 shows a band at 1729cm^{-1} corresponds to ester carbonyls and a band at 1151cm^{-1} corresponds to ether linkages of the cross linking agent. In addition to these spectral features the spectra also shows a band at 746cm^{-1} corresponds to $\text{C}-\text{Cl}_{\text{str}}$. The chemical modification of P1 with 2-pyrrolidone has been confirmed by the splitting of the peak at 1723.5cm^{-1} in the IR spectrum of P2 due to merging of amide carbonyl from the pyrrolidone unit with ester carbonyl from the crosslinking agent. Fig.1 and Fig-2.

The scanning electron micrograph of P2 shows that the particles are spherical, micro porous and almost uniform in size. Fig.3

Energy dispersive X-ray spectroscopy (EDX) elucidates the chemical nature of the synthesized bromo resin P3. The EDX profile displayed strong peaks at the energy of 1.4 keV, 0.2 keV and 2.6 keV for bromine, carbon and chlorine respectively. Some weak peaks for N and O were also observed which strongly indicates the presence of all these elements in the synthesized bromoresin. Fig.4.

P3 was also characterized by Thermo gravimetric (TG) analysis. TGA shows that the bromo resin was stable up to 300°C . Fig.5

The synthesized bromo resin P3 was found to be an efficient oxidizing agent under microwave condition. The various alcohols oxidized by the reagent, time taken, products and conditions of oxidation are given in Table-1. In the case of primary alcohols no over oxidation to acids was observed. The products were characterized by comparison of the physical and spectral characteristics with authentic specimens. Under conventional heating complete conversion was not achieved even after 30 mts. Table- 1. The results revealed that the rate of the reaction drastically increased under microwave heating than conventional method. Under microwave condition the reactions were completed within few minutes due to direct coupling of microwave with molecules in the reaction mixture where as in conventional method there is wall effect, the heat given to the reaction mixture first passes through the wall of the vessel before it reaches the molecules of the reaction mixture. Moreover the damage caused to the polymeric reagent due to mechanical stirring can be avoided.

One of the important advantages of polymeric reagent is that they can be recycled and reused many times without much loss of stability and activity. By washing with dichloromethane followed by reaction with bromine in carbon tetrachloride the spent reagent can be regenerated.

Table 1: Oxidation of alcohols using Polystyrene supported Bromo derivatives of 2-Pyrrolidone.

Entry	Substrate	Product	Time taken for complete conversion (minutes)	
			MW ^a	Δ^b
1.	Benzoin	Benzil	8	Complete conversion is not achieved even after 30 minutes.
2.	Benzyl alcohol	Benzaldehyde	6	
3.	Cyclohexanol	Cyclohexanone	8	
4.	4-Chlorobenzyl alcohol	4-Chloro benzaldehyde	10	
5.	3-Nitrobenzyl alcohol	3-Nitro benzaldehyde	8	

a- All microwave reactions were carried out at 350 W for 10 minutes in cycles of 2 minutes.

b- All thermal reactions were performed at refluxing temperature in cyclohexane.

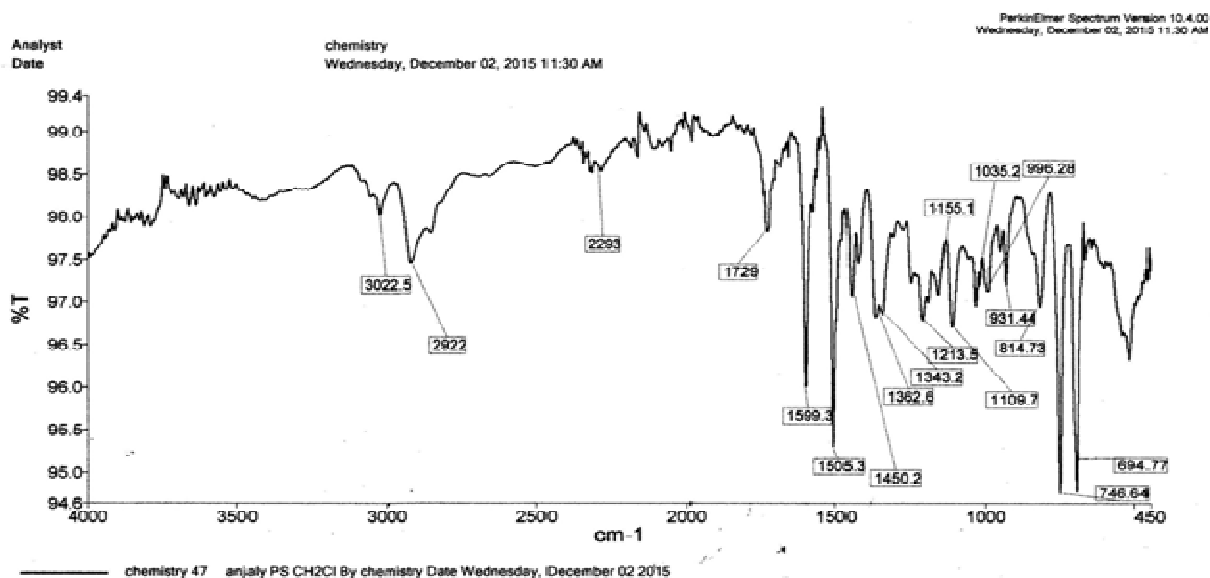


Figure 1: FTIR spectra of chloromethylated TTEGDA crosslinked polystyrene -P1

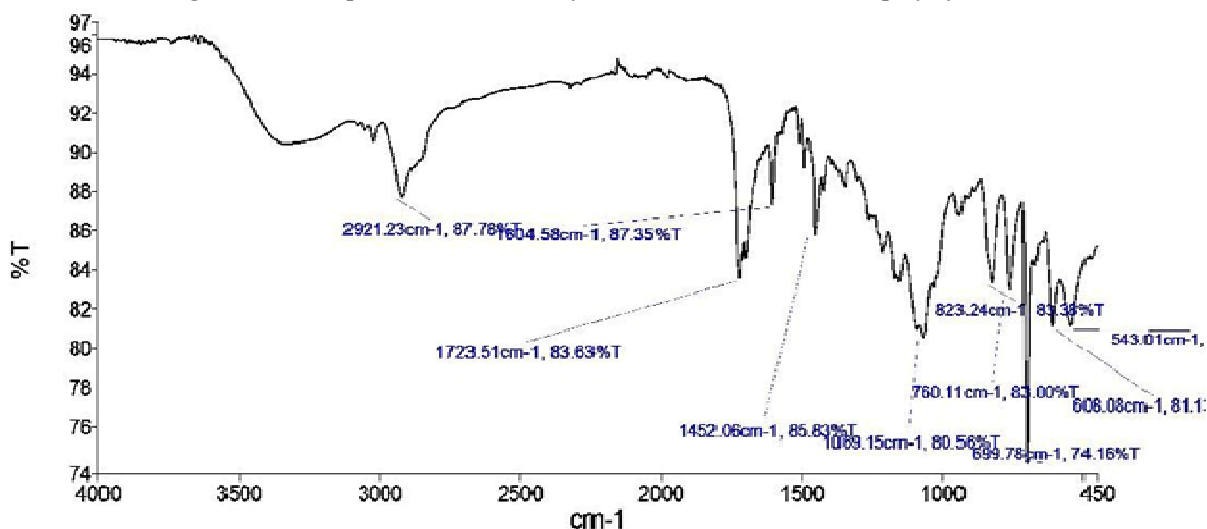


Figure 2: FTIR spectra of Polystyrene supported 2-pyrrolidone P2

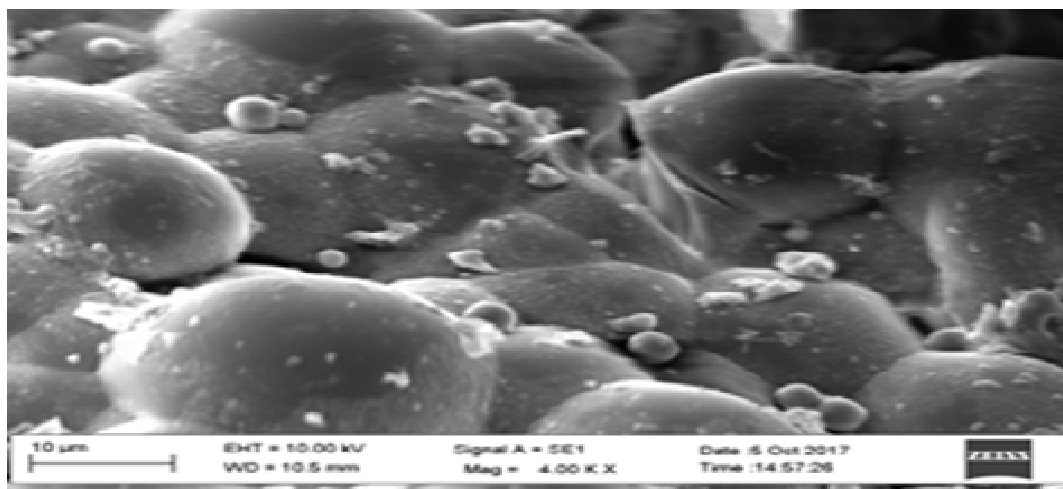
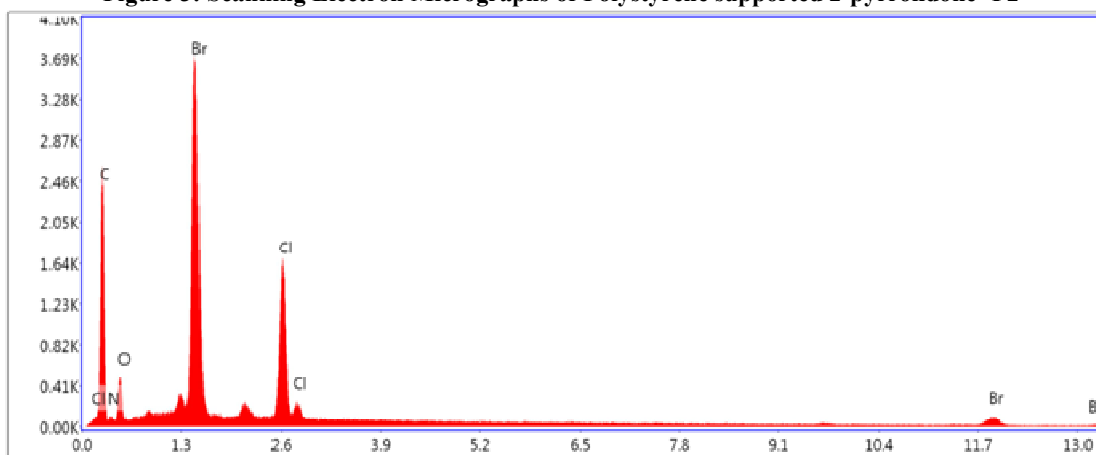


Figure 3: Scanning Electron Micrographs of Polystyrene supported 2-pyrrolidone -P2



Lsec: 23.0 0 Cnts 0.000 keV Det: Octane Plus Det

Figure 4: EDX Spectrum of Polystyrene supported Bromo derivatives of 2-Pyrrolidone -P3

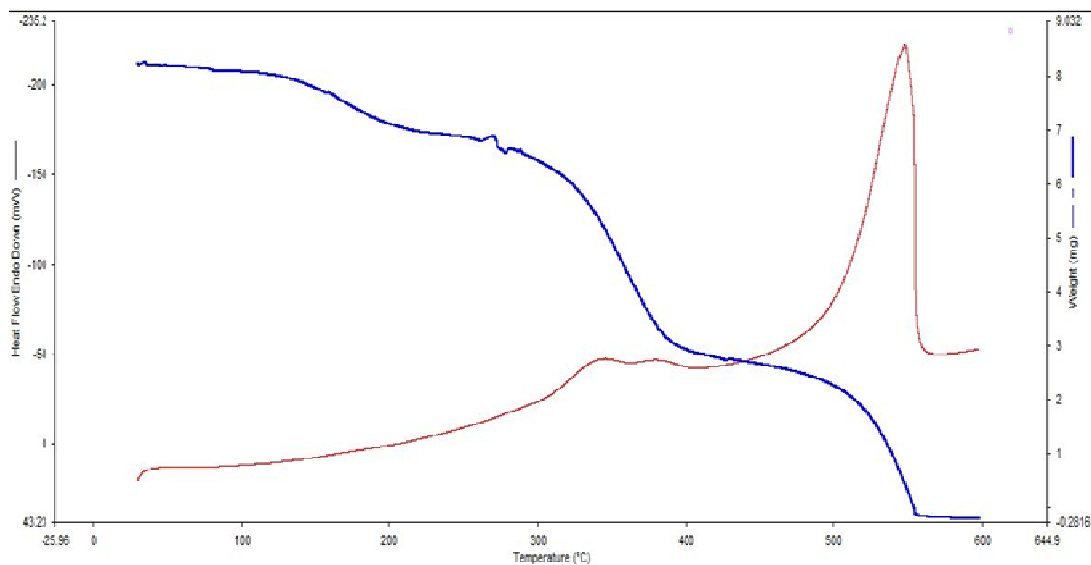


Figure 5: TGA of Polystyrene supported Bromo derivatives of 2-Pyrrolidone -P3

CONCLUSION

TTEGDA-PS was prepared by free radical aqueous suspension polymerization technique and the resulting beads were functionalized by chloromethylation followed by reaction with 2-pyrrolidone. The bromo derivatives of the 2-pyrrolidone supported resin was synthesized by using Br₂ in CCl₄ and found to be stable under microwave irradiation. This polymeric reagent is found to be capable of oxidizing primary and secondary alcohols to the corresponding carbonyl compounds under microwave condition. This bromoresin is stable under ordinary laboratory condition and can be stored for a long time without any appreciable loss of activity. This work can be extended by optimizing the reaction conditions for the oxidation of different organic compounds and further investigations are in progress.

ACKNOWLEDGEMENT

The authors would like to thank the UGC, New Delhi, India for financially supporting the research in the form of minor research project and also to the authorities of 27th Swadeshi Science Congress.

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