

Microwave-Assisted Synthesis of Room-Temperature Ionic Liquid Precursor in Closed Vessel[†]

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Abstract:

We report here the synthesis of various alkylpyridinium and 1-alkyl-3-methylimidazolium halides on a large scale under microwave irradiation, in a closed vessel. The reaction time was drastically reduced as compared to conventional methods, and good yields were obtained.

Introduction

Room-temperature ionic liquid (RTIL) is no more a new word to the scientific community today. The rising number of publications is indicative of the potential of RTILs as “neoteric solvents” for various chemical reactions. These include Friedel–Crafts reactions,^{1–3} enzyme-catalyzed reactions,^{4,5} hydrogenations,^{6,7} benzylation,⁸ Heck reaction,⁹ Fischer indole synthesis,¹⁰ and so forth. RTILs are being looked upon as future commercial¹¹ solvents. The acidic ionic liquids can act both as catalyst and as solvent. This dual property of RTIL has turned out to be a boon in itself to carry out a variety of chemical transformations and is aptly given the name “designer solvent”. Most RTILs¹² known today consist of alkylpyridinium or dialkylimidazolium salts which may be complexed with a Lewis acid for example, AlCl_3 .

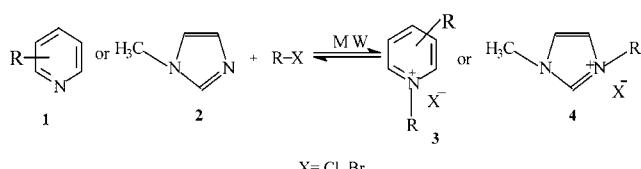
The preparation of some of these salts, for example, 1-butylpyridinium and 1-butyl-3-methylimidazolium chlo-

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[†] This work has been presented at the 5th International Electronic Conference on Synthetic Organic Chemistry ECSOC-5, a symposium on MW-assisted chemistry as poster; <http://www.mdpi.net/ecsoc-5/>.

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Scheme 1



rides, required for the widely used RTILs is quite time-consuming. Conventionally it requires as long as 72 h of reflux.^{13,14} Our aim was to reduce the overall time of preparation of the ionic liquids and to synthesize the precursor salts on a large scale in a shorter time period. While we had been working on microwave-assisted synthesis of these salts, we recently came across a report¹⁵ on the preparation of alkyl-3-methylimidazolium salts under microwave irradiation. However, there are some major drawbacks to this method. It is carried out in an open test tube. The hygroscopic nature of salts may not permit a large-scale preparation by this method. Also the irritant volatile alkyl halides as well as the corrosive and hygroscopic 1-methylimidazole are released inside the microwave cavity and wasted. Heating volatile materials in an open vessel in a microwave oven can be hazardous.

We report here the simple and quick method of preparation of alkylpyridinium and 1-alkyl-3-methylimidazolium salts on a large scale in a closed vessel under microwave irradiation in a CEM microwave digester, MARS 5.

Results and Discussion

The quaternization (see Scheme 1) of some alkyl halides such as BuBr and PrBr with 1-methylimidazole took place under reflux conditions in a domestic microwave oven. However, alkyl halides such as BuCl gave only a trace amount of product formation, whereas 2-phenylethyl chloride, bromohexane, and 2,6-lutidine did not react under reflux conditions under microwave irradiation at normal pressure. When we carried out the reaction in a closed vessel in a

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Table 1. Optimized results of quaternary salts prepared in closed vessel

entry	amine	R-X	^b irradiation time/min		temp °C	pressure ^c psi	yield %
			x	y			
1	1-methylimidazole	1-chlorobutane	2	22	150	57	91
2	1-methylimidazole	1-bromobutane ^a	2.5		105		99
3	1-methylimidazole	1-bromopropane ^a	1.6		85		90
4	pyridine	1-chlorobutane ^d	5	30	180	181	
			+1	24	200	271	66
5	pyridine	1-bromopropane	1	2	120	29	86
6	pyridine	1-chloropropane	5	85	150	79	56
7	pyridine	1-bromobutane ^d	2	13	120	10	
			+2	3	150	32	97
8	pyridine	2-phenethyl chloride	5	55	200	56	98
9	pyridine	1-bromohexane	2	28	120	5	90
10	2,6-lutidine	1-bromobutane	5	55	200	180	58
11	2,6-lutidine	1-chlorobutane ^d	5	55	200	180	
			+5	25	230	191	10
12	2,6-lutidine	1-bromopropane	5	55	200	329	83

^a Reactions were carried out under reflux in a modified domestic microwave oven (Kenstar model) at 750 W, 30% power, irradiated for the time and the MW end temp noted. ^b x represents the time set to reach the given temp, and y, the hold time to continue irradiation at the given temp. ^c Represents maximum pressure reached in the reaction. ^d For BuBr and BuCl, irradiation was done by programming in two steps.

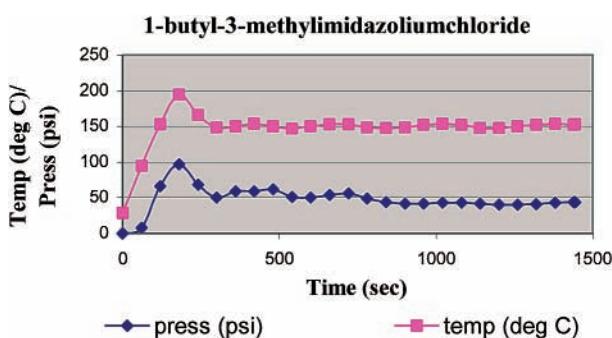


Figure 1. Thermal profile of the microwave irradiation of 1-methylimidazole and 1-BuCl.

microwave digester, an excellent yield of the product was obtained. The microwave digester used for the reaction has a provision for recording temperature and pressure during irradiation. To investigate the effect of a change in temperature on the reaction, we carried out the reaction of 1-butyl chloride with pyridine and 1-methylimidazole at three different temperatures: 100, 150, and 200 °C. It was observed that in both cases at 100 °C and under pressure no product was formed; at 150 °C maximum conversion of 1-butyl-3-methylimidazoliumchloride salt was obtained, whereas 1-butylpyridiniumchloride was formed only in trace amount. It was only at 200 °C that the 1-butylpyridiniumchloride salt was formed in quantitative yield; however, the product obtained was partially tarnished, which was probably due to the direct heating of the reactants to such a high temperature. Hence, to improve the quality and the yield of the salt, we irradiated the reaction mixture in two stages which resulted in better quality of the salt. The reaction times were reduced drastically from 72 to 1 h and from 22 h to 24 min in case of 1-butylpyridinium and 1-butyl-3-methylimidazolium chlorides, respectively. This also shows that 1-methylimidazole reacts faster compared to pyridine. The thermal profile of the reaction during microwave irradiation is shown in Figures 1 and 2. In Figure 2 we observe the rise in pressure, this is due to the unreacted reactants which are

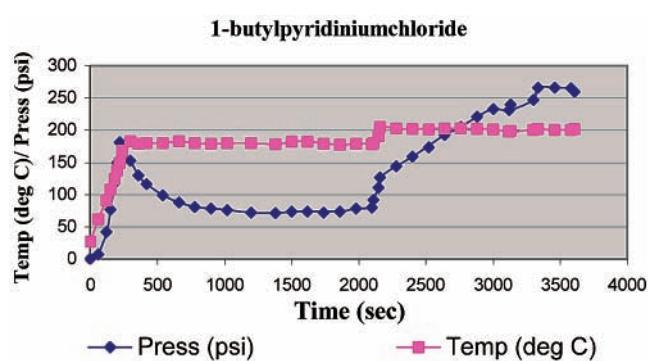


Figure 2. Thermal profile of the microwave irradiation of pyridine and 1-BuCl.

not consumed and are in the vapor phase since the boiling points of the reactants are less than the reaction temperature. The results of quaternization are presented in Table 1.

Chemicals and Materials

Pyridine (S.d. Fine-Chem Ltd., Mumbai, India) and 1-methylimidazole (Merck-India) were dried, distilled, and stored over KOH, and ethyl acetate was dried over CaH_2 . The alkyl halides (commercial grade) were used without further purification. A MARS 5 microwave oven digester supplied by CEM Corporation was used.

Experimental Section

(1) Preparation of 1-Butyl-3-methylimidazoliumchloride (BMIMC). 1-Methylimidazole (155 mmol, 12.5 g) and 1-BuCl (155 mmol, 14.5 g) were mixed in the microwave reactor and irradiated in the microwave oven (model-CEM-MARS 5) at 300 W power, programmed to 150 °C for 2 min, and the irradiation continued at this temperature for 22 min. The resulting viscous liquid on refrigeration gave a white solid. It was washed with dry EtOAc twice, filtered, and dried under *vacuo*. The yield obtained was 91%. The products were characterized by ^1H and ^{13}C NMR spectroscopy.

¹H NMR (500 MHz, DMSO-*d*₆): δ = 0.86 (t, 3H, *J* = 7.37 Hz, CH₃), 1.23 (m, 2 H, CH₂), 1.77 (m, 2 H, CH₂), 3.9 (s, 3 H, NCH₃), 4.22 (t, 2 H, *J* = 7.1 Hz, NCH₂), 7.88 (s, 1 H_{arom}), 7.96 (s, 1 H_{arom}), 9.71 (s, 1 H_{arom})

¹³C NMR (125 MHz, DMSO-*d*₆): δ = 13.55, 19.04, 31.78, 35.98, 48.6, 122.64, 123.83, 137.15.

(2) Preparation of 1-Butylpyridiniumchloride (BPC).

Pyridine (300 mmol, 24 g) and 1-BuCl (300 mmol, 28 g) were irradiated at 300 W in the microwave digester in two stages: in the 1st stage it was programmed to 180 °C for 5 min, irradiation continued at this temperature for 30 min, and in the second stage the temperature was set to 200 °C for 1 min and was continued for another 24 min. The workup was done similar to that for the above compound. Yield: 66%.

¹H NMR (300 MHz, DMSO-*d*₆): δ = 0.9 (t, 3 H, *J* = 7.2 Hz, CH₃), 1.3 (m, 2 H, CH₂), 1.94 (m, 2 H, CH₂), 4.69 (t, 2 H, *J* = 7.2 Hz), 8.1 (t, 1 H_{arom}), 8.6 (t, 1 H_{arom}), 9.23 (d, H_{arom}).

¹³C NMR (300 MHz, DMSO-*d*₆): δ = 13.22, 18.6, 32.68, 60.1, 127.94, 144.86, 145.39.

Conclusions

We have developed a very efficient, quick, and practical method for the preparation of alkylpyridinium and 1-alkyl-3-methylimidazolium salts. The pressure reactor used for the

reaction is very easy to handle and to set up. The time required to synthesize the salts is reduced by the factor of 72 and 60 in case of BPC and BMIMC, respectively, when compared to conventional method. The reaction in the digester could be scaled up to 50-g scale, the capacity of the digester being 100 cm³.

The use of a closed vessel allows for stoichiometric amounts of alkyl halides to be reacted instead of excess, with no apparent loss of yield. This highlights the “green” aspect of this improved procedure. It also provides a greener and safer synthesis of the ionic liquid precursors, the quaternary salts. In the reported method, reaction is carried out in an open test tube. This poses serious problems of hazards and also results in wastage of the reactants. Our method overcomes all these problems and is far safer.

Acknowledgment

We are thankful to B.R.N.S, Dept of Atomic Energy, Government of India; A.I.C.T.E. for financial assistance, and G. D. Gokhale Trust for awarding a fellowship to one of the authors.

Received for review May 20, 2002.

OP025551J