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The reusable couple "PTSA/1-alkyl-3-methylimidazolium ionic liquids": excellent reagents–catalysts for halogenation of fatty diols

Hoang-Phuong Nguyen*, Plamen Kirilov, Hubert Matondo, Michel Baboulène

Laboratoire des Interactions Moléculaires et Réactivité Chimique et Photochimique, Université Paul Sabatier, 118 route de Narbonne, F-31062 Toulouse Cedex, France

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Abstract

The conversion of 1,ω-dialcohols (C_6–C_{16}) to dihalides—dibromides and diiodides—was successfully obtained in the couple "PTSA/1-alkyl-3-methylimidazolium ionic liquids" (OMIM/X, BMIM/X; *i*-PMIM/X) for 2 h at 110 °C. The dihalogenation was improved by the use of microwaves irradiation. The "PTSA-ionic liquid"-couple was regenerated and reused. The kinetics of halogenation of fatty dialcohols confirmed the A2 (or SN2c) mechanism in which monohalogenation was four-fold faster than dihalogenation.

Keywords: Dihalogenation; Microwaves; Ionic liquids; PTSA; Fatty alcohols; Brønsted acid catalysis

1. Introduction

Recently, environmental awareness received new impetus in chemical research with the introduction of ionic liquids (IL). Salts that are in the molten state below 100 °C, they are a class of solvent that are renewable owing to their remarkable properties: ionic character, stable at temperatures above 200 °C, often chemically inert particularly in acid media, non-volatile and hence easy to recover. It is well known that the micro-environment created by a solvent can modify the outcome of a reaction in terms of equilibria and rates [1]. The exact nature of the anion and the cation that make up the ionic structure of the IL is therefore an important parameter which appears to be at the origin of the diversity of the results obtained in IL-based applications [2].

In an attempt to progress in the understanding of these effects, we decided to study a simple, well-known reaction namely a halogenation in the presence of an IL of the type 1-methylimidazolium. This reaction involves protonation of the alcohol and therefore requires a strong acid. Currently, a few groups [3–5] and our laboratory [6] have reported halogenation and esterification reactions in the presence of IL. Two distinct approaches have been adopted. The first, working with the esterification reaction, recommends the use of an IL that acts as a Brønsted acid. 1-Alkyl-3-methylimidazolium hydrogenosulfates [3] proved to be efficient in ester synthesis when the reaction mixture was heated to 80 °C for several hours—the duration depending on the type of alcohol involved. With 1-methylimidazolium tetrafluoroborate [4], which is a weak acid, the reaction only occurs above 110 °C. The second approach associates an IL to a Brønsted acid and has been used for the halogenation of alcohols at room temperature [5]. We proposed a major improvement by the use of paratoluene sulfonic acid (PTSA) in the preparation of long-chain alkane bromides and iodides [6] from the corresponding alcohols where H_2SO_4 cannot produce the conversion at high temperature or under microwave in good yields. The use of this acid often leads to the formation of by-products and the modification of the IL structure and hence its properties. The superiority of PTSA over HBr was also recognized in the conversion of octanol into its bromated derivative under microwave irradiation [7]. Moreover, PTSA, a strong acid, non-volatile solid, is easy to manipulate. Exploring the synthetic possibilities of the use and the recovery of an IL associated to PTSA, we report here the role played by the couple IL-PTSA as "reagent–catalyst" using the example of halogenation of long-chain 1,ω-alkanediols.

* Corresponding author. Tel.: +33-5-61556272; fax: +33-5-61558155.
E-mail address: nguyen@chimie.ups-tlse.fr (H.-P. Nguyen).

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2. Experimental

2.1. Instruments and reagents

Microwaves irradiation was carried out in a domestic microwave oven with selectable power and operator selectable time (Moulinex Micro-Chef FM 1515—750 W). Reaction progress and halogenation kinetics were monitored using a Varian CP-3800 chromatograph equipped with an apolar capillary column BPX 5 (5% phenyl(equiv)-polysilylphenylene-siloxane) and by TLC on precoated plates of silica gel 60 F_{254} in hexane-AcOEt:1/1. ^{1}H NMR spectra were obtained with a Bruker AC 200 spectrometer.

Fatty diols and PTSA·H_2O were commercially available and used without further purification. The IL: 1-alkyl-3-methylimidazolium bromides (*iso*-propyl: *i*-PMIM, butyl: BMIM and octyl: OMIM) were synthesised by quaternisation of 1-methylimidazole with alkyl bromides according to [8]. The structure was determined by ^{1}H NMR in D_2O by comparing characteristic signals intensities (δ(ppm): imidazolium$\underline{C(2)H}$: 9.55 (s,1H),$\underline{CH_3}$: 3.80 (s, 3H); alkyl chain-$\underline{CH_3}$: 0.75 (t, 3H)). The singlet of imidazolium C(2)H was reduced with time and disappeared after 2 days at room temperature in D_2O (exchange H–D). This phenomenon did not occur in DMSO-d_6.

The iodated IL were prepared from bromides by exchange in using two-fold excess of NaI source in acetone [6]. For example, to NaI (3000 mg, 20 mmol) in acetone (2 mL), was added dropwise at room temperature a solution of OMIM/Br (2750 mg, 10 mmol) in acetone (2 mL). The mixture was stirred for 12 h. The solid (NaBr) was filtered off, the solvent was removed, the residue was extracted in acetonitrile (5 mL). The solvent was removed under vacuum, 1-octyl-3-methylimidazolium iodide (3000 mg, 93%) was obtained as an yellow oil which gave a yellow solid that tested positive with $AgNO_3$. Mass spectrometry (Waters mass spectrometer) confirmed the absence of OMIM/Br.

2.1.1. Dihalogenation

2.1.1.1. By heating. A typical procedure for the dihalogenation of fatty diols using the PTSA/IL couple: a mixture of 1,10-decanediol (871 mg, 5 mmol), PTSA·H_2O (1900 mg, 10 mmol) and OMIM/Br (2750 mg, 10 mmol) was stirred (oil bath at 110 °C) for 2 h. The mixture was extracted by hexane (3 mL × 2 mL). The combined hexane phase, treated with silica gel 60 then evaporated to dryness, afforded 1,10-dibromodecane (85%). The structure was confirmed by IR and ^{1}H NMR spectra and by comparison of these data with those of authentic sample.

2.1.1.2. Under microwaves. The same mixture was submitted to 10 cycles of irradiation by microwaves: 5 s (75 W) followed by mechanical stirring for 20 s (final temperature <100 °C). 1,10-Dibromodecane was isolated and characterised as before.

1,ω-Diiodoalkanes were also obtained in same process by using IL iodides. Darkened mixtures were dried in vacuum at 50 °C then extracted in hexane. 1,ω-Diiodoalkanes were isolated and characterised as previously.

2.1.2. Kinetic studies

2.1.2.1. Monohalogenation. Kinetic solutions were prepared as follows: IL/PTSA·H_2O/1-dodecanol (equimolar proportions: 5 mmol) were dissolved in acetonitrile (10 mL). The solution was divided into10 portions (1 mL each). The solvent was evaporated to dryness in vacuo at room temperature and the portions were heated in an oil bath at fixed temperatures. At known times, each fraction was analysed by GC and ^{1}H NMR.

2.1.2.2. Dihalogenation. The same procedure was applied for a mixture of IL (10 mmol), PTSA·$H_2$0 (10 mmol) and 1,10-decanediol (5 mmol).

2.1.3. IL recycling

The residue (IL(PTS) ∼10 mmol) obtained after extraction with hexane, was treated with 1.5 equivalents of NaBr dissolved in water. The mixture was evaporated to dryness in vacuo and taken up in acetonitrile (2 mL). The solution was maintained under mechanical stirring for 12 h at room temperature, the filtrate evaporated to dryness, a liquid ($AgNO_3$ positive test) was obtained for reuse in the next cycle.

The same procedure was used for recycling IL iodides with NaI as iodide source.

3. Results and discussion

The excellent results obtained with the halogenation of fatty alcohols [6], initially directed us towards the use of the couple "1-octyl-3-methylimidazolium bromide (OMIM/Br)–PTSA" with heating to 110 °C.

$$\text{R–OH} \xrightarrow{\text{PTSA,OMIM/Br}} \text{R–Br}$$

In these conditions, we used GC to follow the kinetics of 1,ω-decanediol consumption with respect to the appearance of the mono- and dibrominated compounds with time (Fig. 1).

It can be seen that the conversion into 1,ω-dibromoalkane is complete in less than 2 h, while in the first 20 min, about 95% of the diol is consumed yielding 50% of the ω-bromodecanol. If the reaction is carried out at 90 °C, there is a considerable decrease in the yield without changing the general pattern of the curves. So, using these results, we subjected various diols to the IL/PTSA couple in order to reach the corresponding 1,ω-dihalogenoalkanes (Table 1).

It can be noted that the 1,ω-dibromoalkane yields were good or even excellent especially for long-chain diols. It can be considered that the difficulty to extract dibromoalkanes

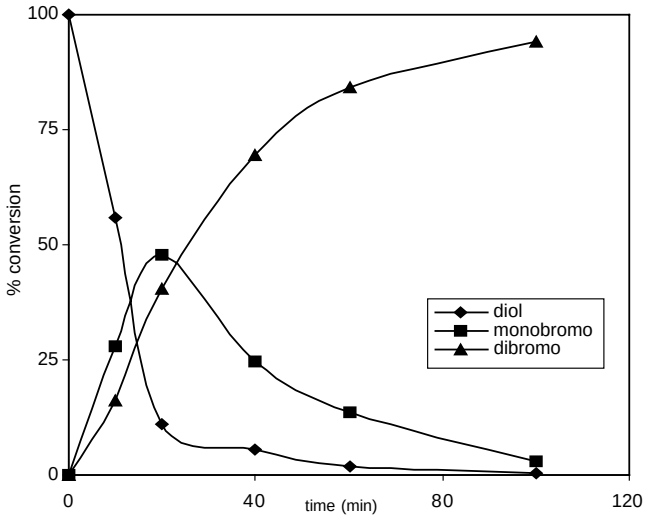

Fig. 1. Bromation of 1,ω-decanediol at 110 °C, molar ratio of OMIM(Br)/PTSA/diol = 2:2:1.

produced from light diols ($n = 3$–5) is what causes the lower yields for the smaller molecules. During the iodation with 1-alkyl-3-methylimidazolium iodide, degradation by oxidation was sometimes observed by formation of a darkened mixture, in spite of the inert conditions used (nitrogen flow).

It had been hoped that the miscibility of the diols and the insolubility of the 1,ω-dibromoalkanes in the reaction mixture would favour the conversion. To our surprise, and unlike in our previous results on the halogenation of monoalcohols [6], a negligible influence was seen on changing the lipophilic character of the IL as reported (Table 2). It is our opinion that the formation of the monobromoalcohol disturbs the characteristics of the reaction media. This difference could be explained by the fact that in a less lipophilic IL, e.g. *i*-PMIM/X, the polar diols are more soluble favouring halogenation. But, as soon as the first alcohol function is converted, the monohalogenated derivative becomes more lipophilic and thus less soluble in the reaction mixture, making the second step much slower. When the IL is more lipophilic, for instance OMIM/X, the second step is faster, while the first is slow. As any given IL only enhances one of the two steps, the overall rates remain the same.

Table 1
Conversion of fatty diols into dihalogenated derivatives

Chain length (n)	Percentage of conversion[a] (X = Br)	Percentage of conversion[a] (X = I)
3	45	65
5	60	73
6	87	82
8	90 (85)[b]	89 (79)[b]
10	95 (87)[b]	95 (85)[b]
16	95 (90)[b]	95 (95)[b]

Diol–OMIM/X–PTSA: 1/2/2 at 110 °C, 2 h.
[a] Determined by GC, decane as internal reference.
[b] Percentage of product actually isolated.

Table 2
Influence of IL on conversion of fatty diols at 110 °C

IL cation	Percentage of conversion[a]		
	OMIM	BMIM	*i*-PMIM
Dibromation			
C_8	90	98	96
C_{10}	95	95	92
Diiodation			
C_8	89	71	87
C_{10}	95	71	91

[a] Conversion estimated by GC and ^{1}H NMR (200 MHz, in $CDCl_3$, TMS as internal reference) after 2 h.

However, in spite of the relatively short reaction times (∼2 h), the process could be improved by using the properties of microwave irradiation. This was confirmed, as seen in Table 3. Irradiation was carried out in a domestic microwave oven in mild conditions: using cycles of 25 s:5 s irradiation at 75 W, 20 s stirring. This process enabled us to maintain the temperature of the reaction mixture under 100 °C. The reactions were carried out in two IL: OMIM/X and BMIM/X with three diols: C_8, C_{10}, C_{16}. Conversion yields were quasi-quantitative with extremely short irradiation reaction times from 45 to 90 s.

Considering the overall results, access to ω-bromoalcohols is an added advantage to the use of the IL/PTSA couple. With this aim, we determined the kinetic parameters of the reactions. From the two-step mechanism proposed (Scheme 1), we plotted the curves of 1/[dodecanol] versus time when the reagents were in equimolar proportions. Obtaining straight lines confirms that the reaction is second-order and provides the possibility of calculating the halogenation rate constants at the various temperatures (Table 4). These results indicate that bromide ion is more nucleophilic than iodide ion in IL-environment contrary to their known behaviour in classic polar solvents.

Eyring's equation is then used to deduce the activation thermodynamic parameters (Table 5). The activation enthalpies are of the same order of intensity for bromation

Table 3
Conversion of 1,ω-diols under microwaves[a]

	Dibromation			Diiodation	
	Irradiation time (s)	%[b]		Irradiation time (s)	%[b]
OMIM/Br			OMIM/I		
C_8	80	95	C_8	75	97
C_{10}	50	100	C_{10}	50	98
C_{16}	50	98	C_{16}	50	98
BMIM/Br			BMIM/I		
C_8	90	96	C_8	95	95
C_{10}	60	99	C_{10}	70	98
C_{16}	50	100	C_{16}	50	98

[a] See Section 2.
[b] Conversion estimated by GC and ^{1}H NMR (200 MHz, in $CDCl_3$, TMS as internal reference).

Rapid step

$$CH_3(CH_2)_{11}\text{-}OH + PTSA \rightleftharpoons CH_3\text{-}(CH_2)_{11}\text{-}OH_2^+ + PTS^-$$

Rate limited step

$$CH_3\text{-}(CH_2)_{11}\text{-}OH_2^+ + PTS^- + OMIM/X \longrightarrow CH_3\text{-}(CH_2)_{11}\text{-}X + OMIM/PTS + H_2O$$

Scheme 1. The two-step halogenation mechanism.

Halogenation of monoalcohol

$$CH_3\text{-}(CH_2)_n\text{-}OH \xrightarrow{k_{obs1}} CH_3\text{-}(CH_2)_n\text{-}Br$$

Halogenation of diol

$$HO\text{-}(CH_2)_n\text{-}OH \xrightarrow{k_{obs2}} HO\text{-}(CH_2)_n\text{-}Br \xrightarrow{k_{obs3}} Br\text{-}(CH_2)_n\text{-}Br$$

Scheme 2.

Table 4
k_{obs1} ($M^{-1}\,s^{-1}$) of 1-dodecanol halogenation

T (°C)	$k_{obs1} \times 10^5$	
	Bromation	Iodation
90	0.8	0.4
100	2.4	1.8
110	3.3	2.7

and for iodation, indicating that the rates of these two reactions are extremely close. The negative activation entropies confirm the nucleophilic substitution mechanism of the A2 type (or SNc2) in which the alcohol leaving group is protonated beforehand.

Considering that in the same experimental conditions, the presence of a bromine substituent in the ω-position of a long-chain alcohol ($n > 10$) only has a slight influence on the bromination kinetics, it can be considered that the observed rate constants for the bromination of a long-chain alcohol and of a long-chain ω-bromoalcohol are quite similar: $k_{obs1} \cong k_{obs3}$ (Scheme 2).

Using the results reported in Table 4, we have k_{obs3}:

$$k_{obs3} \cong k_{obs1} = 6 \times 10^{-5}\,M^{-1}\,s^{-1} \text{ at } 110\,°C$$

Moreover, the curves in Fig. 1 allow the calculation of the ratio $k_{obs2}/k_{obs3} = 4$ considering that at 20 min the ω-bromoalcohol concentration reaches its maximum. Rate constant k_{obs2} can then be calculated at $24 \times 10^{-5}\,M^{-1}\,s^{-1}$. These results indicate that the step of ω-bromoalcohol formation is four-fold faster than the transformation of ω-bromoalcohol into the 1,ω-dibromoalkane, suggesting that it could be possible to gain access to ω-bromoalcohols using this procedure. It is very likely that the use of excess diol with respect to the PTSA in less lipophilic IL then using selective extraction with an apolar solvent will enhance the synthesis of the ω-bromoalcohols. Investigations along these lines are in progress.

Table 5
Thermodynamic parameters of 1-dodecanol halogenation

	Bromation	Iodation
$\Delta H^{\#}$	+83	+110
$\Delta S^{\#}$	−14	−42
$\Delta G_{298}{}^{\#}$	+87	+122

$\Delta H^{\#}$, $\Delta G_{298}{}^{\#}$ (kJ mol^{-1}); $\Delta S^{\#}$ (J mol^{-1} K^{-1}).

The IL were regenerated by simple ion exchange of the PTS ion against bromide or iodide ions using NaBr and NaI as halide sources as described [6] which were then reused. After about five cycles, a slight drop in yields by about 10–15% was found with the recycled IL after activation by heating. It is feasible that this decrease in activity could be due either to partial decomposition of the IL during the reaction at high temperature [9] and/or to incomplete exchange of the PTS anions during the regeneration stage. In order to avoid IL recycling process, we investigated the action of an aqueous HBr solution (∼30%) as bromide source on the residue IL/PTS. But dialcohols conversion into dihaloalkanes was not observed. The insolubility of aqueous HBr in fatty alcohol or the water excess which would reduce or cancel the IL media effect on the charge separation in the transition state, is probably the cause for this unsuccessful reaction. However, HBF_4 or HPF_6 led the dibromation even at room temperature; but for unknown reasons, the halogenation was not complete.

4. Conclusion

We have developed simple and efficient methods for the synthesis of dihalogenated derivatives with a long alkyl chain, from diols using the "halogenated ionic liquids-PTSA" couple as halogenation "reagent–catalyst" with classic heating and microwaves irradiation. Conversion is extremely rapid under microwaves. This method improves

fatty dihalogenoalkanes synthesis in the laboratory. The use of bromide- and iodide-based IL as halogenation agents is therefore very advantageous with respect to the usual methods. In addition, the IL is readily regenerated and successfully reused, presenting considerable advantages with respect to standard halogenation reagents which cause more pollution to the environment. Moreover, the kinetics results open a new synthesis route for ω-bromoalcohols.

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