Bromination of Alkynes in Ionic Liquids − A Kinetic Investigation

Cinzia Chiappe,*[a] Valeria Conte,[b] and Daniela Pieraccini[a]

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The kinetic behaviour and the product distributions of brominations of several arylalkynes with Br_2 in the room-temperature ionic liquids (ILs) 1-butyl-3-methylimidazolium hexafluorophosphate [bmim][PF_6] and 1-butyl-3-methylimidazolium bromide [bmim]Br, have been investigated at different temperatures. In [bmim]Br, alkynes stereospecifically gave the *anti* addition products, the reactions following a second-order rate law. In [bmim][PF_6], mixtures of *syn* and *anti* addition products were obtained, and the reactions followed a second- or third-order rate law, depending on the structure of the alkyne and the concentration of Br_2. The data obtained for the reactions in [bmim]Br are interpreted on the basis of a mechanism involving a product- and a rate-determining nucleophilic attack by bromide on the alkyne–Br_2 π complex. The data relating to the electrophilic addition in [bmim][PF_6] are explained in terms of the initial formation of a 1:1 alkyne–Br_2 π complex, the ionisation of which, probably catalysed either by a second halogen molecule or by the imidazolium cation, gives a bromirenium (or β-bromovinyl cation) Br^- or $[Br_3]^-$ intermediate. Such intermediates then collapse to give the corresponding dibromo adduct(s). The kinetic constants and the activation parameters for the reaction in [bmim]Br are compared with those relating to the second-order reaction of the same alkynes with tetrabutylammonium tribromide ([NBu_4][Br_3]) in 1,2-dichloroethane (DCE). On the basis of the kinetic data, a significant role for solvent viscosity in determining the reaction rate may be envisaged.

Introduction

Current interest in ionic liquids[1−4] (ILs) arises primarily from awareness of the potential applications for ILs in green chemistry and the associated emphasis on clean manufacturing processes. The past few years have witnessed growing interest in room-temperature ILs that are air- and moisture-stable, even hydrophobic in some cases, and certainly much easier to handle than the chloroaluminate melts first described.[1−4] *N*-Alkylpyridinium and *N*,*N*′-dialkylimidazolium cations, with a variety of substituents and paired with a larger variety of anions, have been reported to be suitable solvents for several organic reactions and catalytic processes. In this context, we have recently investigated some ILs as clean, environmentally benign alternatives to chlorinated solvents for the stereoselective halogenation of alkenes and alkynes.[5]

Electrophilic bromination of double and triple bonds is a fundamental reaction in organic chemistry,[6] providing products that are key intermediates in organic synthesis and in analytical chemistry.[7] The mechanistic and synthetic aspects of bromination in molecular solvents have been very thoroughly studied over the years, and important features have been identified through kinetic and product distribution studies. The chemo-, regio-, and stereoselectivities of this reaction, as well as the kinetic behaviour, are deeply influenced by the solvent,[6] and the role of molecular solvents on the rate and reaction course has been widely investigated.[8] Extensive investigations[9] of the effects of molecular solvents in several organic reactions have allowed correlation of the reaction course to some solvent properties such as, inter alia, polarity, nucleophilicity, and coordination ability. In contrast, the limited number of systematic investigations concerning some properties of ILs, such as polarity,[10−12] and the absence of kinetic investigations in these solvents, drastically reduce the possibility of correlating the outcome of a chemical process with specific or nonspecific features of these reaction media. On the other hand, research in this field is important for the establishment of efficient criteria to determine the right ionic liquid candidate for a given solvent application. The physical and chemical properties of ILs, often defined as “designer solvents”,[1b,13] can indeed be varied over a wide range by the selection of suitable cations and anions. However, solvent polarity and solvation strength, which imply specific solute−solvent interactions, are not easy to evaluate, even for molecular solvents. The polarity of a solvent is usually determined[9] in a purely empirical fashion by the use of solvatochromic dyes or fluorescence probes; both have in fact been applied to determine the polarity of a small number of ILs.[10−12] However, as has recently been stressed,[14] taking into account the vertical nature of the UV transition

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[a] Dipartimento di Chimica Bioorganica e Biofarmacia,
Via Bonanno 33, 56126 Pisa, Italy
Fax: (internat.) + 39-050/43321
E-mail: cinziac@farm.unipi.it
[b] Dipartimento Scienze e Tecnologie Chimiche,
Via Della Ricerca Scientifica, 00133 Roma, Italy

(Franck−Condon principle), the physical meaning of the change in UV wavelength of a dye when the solvent is in a nonequilibrium distribution about the excited state is not clear. This question may be particularly important for ILs, due to the viscosity of these media, a property which is influenced by the temperature.[15,16b]

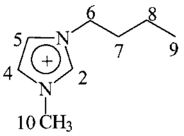
Therefore, in order to obtain more information about how ILs may affect reactivity, we have further investigated the kinetic and stereochemical course of the bromine addition reaction to aryl-alkyl-substituted alkynes in 1-butyl-3-methylimidazolium hexafluorophosphate [bmim][PF_6] and 1-butyl-3-methylimidazolium bromide [bmim]Br. The kinetic and product distribution data are compared with those obtained in electrophilic bromination of the same compounds with Br_2 and tribromide ions (tetrabutylammonium tribromide, [Bu_4N][Br_3]) in chlorinated solvents. The mechanistic aspects are discussed, highlighting the properties of these ILs in comparison with molecular solvents.

Results and Discussion

Brominating Species

Addition of appropriate amounts of Br_2 to 1-butyl-3-methylimidazolium hexafluorophosphate [bmim][PF_6] and 1-butyl-3-methylimidazolium bromide [bmim]Br gave coloured solutions that could be stored at room temperature in the dark for several hours with no significant changes in their respective electronic absorption spectra. The electronic absorption spectra of Br_2 solutions in [bmim]Br were characterised by a strong UV/Vis absorption band, with its maximum at a wavelength below 300 nm, which could be attributed to the formation of the tribromide ion $[Br_3]^-$. The values of λ_{max} and ε_{max} could not be evaluated, as the UV cut-off point of the ionic liquid occurs in this region. In contrast, Br_2 solutions in [bmim][PF_6] showed an absorption band between 380 and 500 nm. The absorption maximum ($\lambda_{max} \approx 400$ nm) and the band intensity ($\varepsilon_{max} \approx 200\ \mathrm{M}^{-1}\cdot\mathrm{cm}^{-1}$) were very similar to those recorded for Br_2 solutions in chlorinated solvents (in 1,2-dichloroethane: $\varepsilon_{max} = 211\ \mathrm{M}^{-1}\cdot\mathrm{cm}^{-1}$, $\lambda_{max} = 410$ nm).[17] The band shape, however, was different from those observed in chlorinated solvents; in particular, the lower wavelengths (below 380 nm) were characterised by a stronger absorption. This may be attributed to the formation of a charge-transfer complex between bromine and the solvent[18] with the corresponding charge-transfer band in this region, although the possibility that at least a part of this absorption may be due to the presence of another species also with an absorption band in this region − possibly $[Br_2Cl]^-$ anion − cannot be excluded. These latter species could indeed arise from reaction between Br_2 and traces of Cl^- present in the solvent as impurities (evaluated by titration in several lots of solvents at around 0.001 $\mathrm{mol\cdot kg^{-1}}$, 0.03% w/w). It is noteworthy that $[Br_2X]^-$ salts have very strong absorptions in this region and that therefore even very small amounts, unable to affect the product distribution and the kinetic behaviour, can be detected. On the basis of the electronic absorption data, we can thus infer that two different brominating reagents were formed in the two solvents: free Br_2 in [bmim][PF_6], and $[Br_3]^-$ in [bmim]Br. To support this hypothesis, we also analysed our solutions by ^1H NMR. It is known that the chemical shifts of the imidazolium core show a counter-anion dependency, which may be a useful tool for determining whether $[Br_3]^-$ formation accompanies bromine dissolution in these solvents. Since it has been shown[16] that the chemical shifts of the imidazolium protons are anion- and concentration-dependent, and that these two factors may exert opposite effects, the NMR spectra were recorded on the pure ionic liquids, with [D_6]acetone as external lock, to avoid the concentration-dependence factors. The spectra were recorded at 17 °C in the absence and in the presence of increasing amounts of Br_2. No formation of ring-bromination products was ever observed. The chemical shift values of [bmim]Br showed an appreciable dependence on the Br_2 concentration. Table 1 collects the chemical shifts of the proton signals of the two solvents in the presence of an amount of bromine corresponding to

Table 1. Proton chemical shifts for [bmim]Br and [bmim][PF_6] in the absence and in the presence of equimolar amounts of Br_2 at 17 °C



Imidazolium protons	[bmim]Br Pure solvent δ	+ Br_2 δ	Δδ	[bmim][PF_6] Pure solvent δ	+ Br_2 δ	Δδ
2-H	8.78	7.17	1.61	7.26	7.15	0.11
4-H	7.01	5.99	1.02	6.22	6.12	0.10
5-H	7.11	5.99	1.12	6.26	6.15	0.11
6-H	3.19	2.73	0.46	2.99	2.90	0.09
10-H	2.89	2.48	0.41	2.72	2.63	0.09
7-H	0.54	0.38	0.16	0.66	0.59	0.07
8-H	−0.11	−0.16	0.05	0.11	0.06	0.05
9-H	−0.54	−0.62	0.08	−0.32	−0.36	0.04

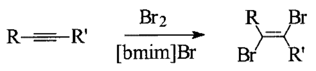
the molarity of the solvent giving the greatest variation in chemical shifts. Addition of higher concentrations of Br_2 did not produce further significant modification in the ^1H NMR spectra.

It appears from the data reported in Table 1 that, while the addition of Br_2 to [bmim][PF_6] had a very small effect, if any, the addition of an "equimolar" amount of the halogen to [bmim]Br gave rise to considerable variation of the chemical shift of the imidazolium ring protons, in particular on 2-H, which may be attributable to a change in the nature of the counter-anion. Aliphatic protons were only moderately affected, and the effect decreased with increasing distance from the aromatic ring. Since in general the chemical shifts of the ring protons move downfield with increasing anion basicity, and thus hydrogen-bonding capability, these experimental data were indicative of a decrease in the anion basicity after addition of Br_2 to [bmim]Br, corroborating a change of the counter-anion from Br^- to $[Br_3]^-$. It is worth noting that the conversion was not necessarily quantitative even when an equimolar or a moderate excess of Br_2 was added to the solvent. In addition, in the presence of an excess of Br_2, the species $[Br_5]^-$ may also be formed. However, although the stability constant of $[Br_3]^-$ species in this medium has not been determined, it seems highly probable that under the reaction conditions (high excess of Br^-) only $[Br_3]^-$ is present as counter-anion.

Electrophilic Bromination

a. Product Distributions

We recently reported[5] that addition of Br_2 to alkynes and alkenes in [bmim]Br was *anti*-stereospecific, independently of the nature of the substituents at the double or triple bond, while Br_2 addition in [bmim][PF_6] gave mixtures of *syn* and *anti* adducts.

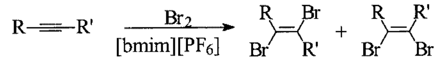


1 2

R	C_6H_5	C_6H_5	C_6H_5	C_6H_5	pCF$_3$-C_6H_4
R'	H	CH_3	C_2H_5	n-C_3H_7	n-C_5H_{11}
1	**a**	**b**	**c**	**d**	**e**

The stereochemical behaviour observed in the reaction of alkynes in [bmim]Br was therefore in agreement with the presence in solution of $[Br_3]^-$ as electrophile. This species is known to add to alkenes[19] and alkynes[20] in molecular solvents by a mechanism that does not involve ionic intermediates and occurs through a product- and rate-determining attack by bromide on the olefin$-Br_2$ π complex (Scheme 1).

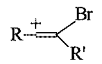
In contrast, the formation of both diastereoisomers in Br_2 addition to alkynes **1a−d** in [bmim][PF_6] indicated[5] that open vinyl cations (*a*) had been formed as intermediates, similarly to what has been observed[21] in 1,2-dichloroethane (DCE).



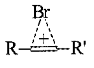
1 2 3

R	C_6H_5	C_6H_5	C_6H_5	C_6H_5	pCF$_3$-C_6H_4
R'	H	CH_3	C_2H_5	n-C_3H_7	n-C_5H_{11}
1	**a**	**b**	**c**	**d**	**e**

The stereoselective formation of the *anti* addition product in the reaction of **1e** instead suggested the involvement of a bridged bromirenium ion (*b*).



a



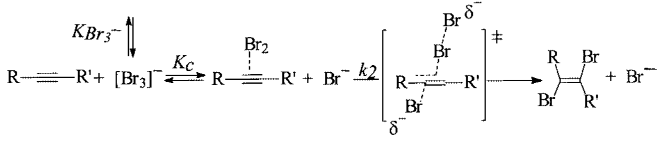
b

Although the stereochemical behaviour of the reactions of **1b** and **1c** was similar to that observed[21] in addition of Br_2 to the same alkynes in chlorinated solvents (Table 2), that of **1a** and **1d** was significantly different.

Table 2. Product distributions for bromination of **1a−d** with Br_2 in [bmim][PF_6] and DCE

	Solvent	Products **2**	 **3**
1a	[bmim][PF_6]	88	12
	DCE	57	43
1b	[bmim][PF_6]	77	23
	DCE	78	22
1c	[bmim][PF_6]	75	25
	DCE	70	30
1d	[bmim][PF_6]	75	25
	DCE	66	34
1e	[bmim][PF_6]	99	1
	DCE	99	1

In particular, the reaction of **1a** was characterised by a higher *anti* stereoselectivity. Both a more bridged nature of the cationic moiety of the intermediate in the ionic solvent, and a more favourable translocation process of the nucleophile prior to the attack, may play a role in determining



Scheme 1

such behaviour. In the cases of **1b** and **1c** the presence of the alkyl substituent probably obstructed a stronger increase in the (*E*)/(*Z*) ratio.

b. Bromination Rates

In [bmim]Br

To obtain further information on the mechanism of Br_2 addition in ILs, and to compare these solvents with molecular ones, we undertook a kinetic investigation. The rates of bromination of alkynes **1a−d** in [bmim]Br were measured spectrophotometrically, under *pseudo*-first-order conditions (in the presence of a large excess of alkyne) by monitoring the disappearance of the perhalide $[Br_3]^-$. All reactions obeyed the second-order rate law of Equation (1).

$$-d[Br_3^-]/dt = k_{Br_3^-}\cdot[Br_3^-]\cdot[\text{alkyne}] \qquad (1)$$

Table 3. Second-order rate constants for the bromination of **1a−d** by $[Br_3]^-$ in [bmim]Br and DCE

Alkyne	*T* [°C]	[bmim]Br *k* [$M^{-1}\cdot s^{-1}$][a]	DCE *k* [$M^{-1}\cdot s^{-1}$][a]
1a	10	n. d.	$1.67\cdot10^{-5}$
	25	$1.25\cdot10^{-3}$	$5.60\cdot10^{-5}$
	40	$1.60\cdot10^{-3}$	$2.50\cdot10^{-4}$
	55	$2.80\cdot10^{-3}$	$8.76\cdot10^{-4}$
1b	10	n. d.	$6.70\cdot10^{-5}$
	25	$2.57\cdot10^{-4}$	$2.65\cdot10^{-4}$
	40	$1.42\cdot10^{-3}$	$7.10\cdot10^{-4}$
	55	$5.92\cdot10^{-3}$	$2.05\cdot10^{-3}$
1c	10	n. d.	$9.60\cdot10^{-5}$
	25	$5.02\cdot10^{-4}$	$3.57\cdot10^{-4}$
	40	n. d.	$8.26\cdot10^{-4}$
1d	25	$1.04\cdot10^{-4}$	$2.01\cdot10^{-4}$

[a] Error limits within ±10% of quoted number, n. d. = not determined.

The values of $k_{Br_3^-}$ are reported in Table 3 together with the second-order kinetic constants for $[Br_3]^-$ addition in DCE. In this latter solvent, tetrabutylammonium tribromide ($[Bu_4N][Br_3]$) was used as the Br_3^- source.

The values of the activation parameters for the reaction behaviour of **1a**, **1b**, and **1c**, obtained from fittings of the kinetic constants to the Arrhenius equation, are reported in Table 4.

Table 4. Apparent activation parameters for the second-order reaction of **1a** and **1b**

	Solvent	$E_{a,obsd}$ [$kJ\cdot mol^{-1}$]	$\Delta H^{\neq}$ [$kJ\cdot mol^{-1}$]	$\Delta S^{\neq}$ [$J\cdot mol^{-1}\cdot K^{-1}$]
1a	[bmim]Br	21.5 (4)	19.0 (4)	−236 (6)
1a	DCE	67.8 (4)	65.3 (4)	−104 (4)
1b	[bmim]Br	85.0 (4)	82.5 (4)	−34.4 (4)
1b	DCE	57.7 (2)	55.2 (2)	−128 (4)
1c	DCE	53.1 (6)	50.6 (6)	−145 (4)

The rate constants measured in DCE showed that the introduction of an alkyl group only moderately accelerated the bromination reaction. Since the presence of an alkyl group should inductively stabilize a neighbouring cationic centre, the measured effect, smaller than one order of magnitude, was in agreement only with very small, if any, positive charge development at the acetylenic carbon atom C-2. The behaviour of alkynes **1a−d** in [bmim]Br, however, was quite different; in the ionic solvent, the presence of the alkyl group at C-2 always decreased the reaction rate. Furthermore, while the rate constants for alkynes **1b−d** in this solvent were of the same magnitude as in DCE, the reaction behaviour of **1a** showed an acceleration by a factor of 20 relative to the same reaction in DCE.

The ionic solvent had therefore affected the kinetic behaviour of the reaction, although an explanation is surely complicated by the fact that polarity, viscosity and hydrogen-bonding capability of [bmim]Br may affect the rate-determining step of reaction (k_2) and/or the equilibrium constant (K_c).

If we assume that the reaction in [bmim]Br occurs through the mechanism generally accepted for the reaction in molecular solvents,[19,21] shown in Scheme 1, the process should involve as the first step an equilibrium between two complexes of Br_2: $[Br_3]^-$ and 1:1 alkyne−Br_2 π complex.

The equilibrium constant K_c is given by the ratio of the formation constants of the two species: $K_c = K_{\pi\ \text{complex}}/K_{Br_3^-}$. This step is followed by the rate-determining nucleophilic attack by the bromide, either detached from Br_2 after the formation of a 1:1 alkyne−Br_2 π complex or present in solution, while the Br−Br bond is being broken and a new bromide ion is formed.

The concentration of Br^- in [bmim]Br is higher than that attainable with $[Bu_4N][Br_3]$ in DCE. However, the accelerating effect on the rate of nucleophilic attack due to the higher concentration of Br^- in the ionic solvent may very probably be balanced by a reduction in the concentration of alkyne−Br_2 π complex. Generally, at least in molecular solvents,[19] the bromination rate is not affected by added bromide salts, except for a small negative salt effect on a transition state (TS) with more charge delocalisation than the initial state.

In molecular solvents, this latter feature of the TS dictates a decrease in reaction rates with increasing solvent polarity. Nevertheless, reaction rates in these solvents are markedly affected by the ability of the medium to enter into hydrogen bonding.

As shown by NMR measurements, electrophilic solvation of $[Br_3]^-$ by the ionic liquid is relatively unimportant, while the Br^- ion is hydrogen-bonded to the solvent. This would reduce its nucleophilicity and produce a reduction in k_2. On the other hand, hydrogen bonding to the leaving bromide ion formed by breaking of the Br−Br bond may well balance or overbalance this retarding effect. In molecular solvents, the electrophilic solvation of the leaving group is possibly more important than that of the attacking bromide; this has been attributed[22] to the proximity of the ammonium cation to the latter anion, but not to the former. The kinetic constant for bromination of **1c** with $[Bu_4N][Br_3]$ measured in $CHCl_3$ at 25 °C was indeed $8.7(0.5)\ \times10^{-2}$ $M^{-1}\cdot s^{-1}$. In [bmim]Br, however, the situation was different;

the solvent able to enter into hydrogen bonding was also the counteranion of Br^-. The anion is always coordinated to the cation, and consequently both bond formation and bond breaking are affected by electrophilic solvation. In ILs, hydrogen bonding may therefore be less important, in particular if bond formation and bond breaking in the TS are synchronous.

Finally, it can be pointed out that viscosity, several tens to hundreds of times that of water for ILs at room temperature, may affect the rate constant, although the effect of solvent viscosity on reactivity is a question that chemists seldom consider. Of course, at high viscosity "encounter control" reigns, and diffusion-controlled reactions are slower, with an inverse relationship existing between the diffusion coefficient D and the solvent viscosity η. However, activation-controlled reactions may also be affected by solvent viscosity. Rate constants in viscous media can be treated by the approach introduced by Kramers,[23] who studied the effects of solvent frictional forces on the rate of single-step reactions, of the type $S \rightarrow X^{\neq} \rightarrow P$, by modelling the reaction motion as the passage of the solute over a potential barrier. Kramers' theory predicts that for a large solvent viscosity η the rate constants should scale down with η [Equation (2)], while at low η the rate should increase [Equation (3)].

$$k \propto \eta^{-1} \cdot e^{-E^*/RT} \tag{2}$$

$$k \propto \eta \cdot e^{-E^*/RT} \tag{3}$$

The viscosity of a solvent depends on the temperature, and so the dependence of the rate constant on the viscosity can be translated into a temperature dependence by the recognition that viscosity is generally a decreasing function of increasing temperature, Equation (4). Thus, at lower temperatures (high η) one would have Equation (5), while at high temperatures (low η) Equation (6) holds.

$$\eta = A \cdot e^{E_\eta/RT} \tag{4}$$

$$k \propto \eta^{-1} \cdot e^{-E^*/RT} \approx e^{(-E^* - E_\eta)/RT} \tag{5}$$

$$k \propto \eta \cdot e^{-E^*/RT} \approx e^{(E_\eta - E^*)/RT} \tag{6}$$

On the basis of Equations (5) and (6), the temperature dependence of a single-step reaction in a viscous solvent originates from two sources: (i) from the true activation energy E^*, and (ii) from the dependence of solvent viscosity on temperature E_η.

For a reaction that obeys Kramers' relationship, the apparent activation energy E_a at low temperatures, as derived from an Arrhenius plot [Equation (7)], is thus larger than the true activation energy by a factor E_η [Equation (8)], while at high temperatures it is lower by the same factor.

$$k = A \cdot e^{-E_a/RT} \tag{7}$$

$$E^* = E_a - E_\eta \tag{8}$$

Kramers' theory has, however, been questioned[24] in a number of investigations. Recently it has in fact been reported[25] that solvent viscosity increases the rates of bimolecular reactions. In particular, it has been stated on the basis of the vibration-activation theory[25] that reactions involving implicit bond formation in the TS occur more efficiently as viscosity is progressively increased. If this is the case, Equation (6) alone should account for the temperature dependence.

The activation parameters for the reactions of **1a** and **1b** in [bmim]Br obtained from a fitting of the kinetic constants to the Arrhenius equation and given in Table 4 are really apparent activation parameters, $k_{Br_3^-}$ being the product of two constants: K_c and k_2. It is worth noting that the activation parameters determined for the reactions in [bmim]Br are significantly different from those obtained for the reaction of $[Bu_4N][Br_3]$ in DCE. In particular, the reaction of **1b** in [bmim]Br was characterised by a higher activation energy and a less negative activation entropy with respect to the reaction in DCE, while that of **1a** showed a much lower activation energy and a more negative activation entropy. Brominations by $[Br_3]^-$ in molecular solvents able to form hydrogen bonds, such as chloroform, are generally characterised[19] by much lower apparent activation energies and more negative activation entropies, with respect to the reactions in DCE. The activation parameter found for **1a** in [bmim]Br may therefore be explained in terms of a hydrogen-bonding effect of the solvent. This explanation, however, is not able to account for the behaviour of **1b**, which shows an opposite trend. An explanation may be found by considering that bromination with $[Br_3]^-$ occurs through a TS characterised by a nonsynchronous formation of a C−Br bond and breaking of a Br−Br bond. If bond formation is advanced with respect to bond breaking, viscosity may have an accelerating effect while hydrogen bonding should have an inverse role. If, on the other hand, bond breaking prevails, opposite effects may be observed. The different reactivities of **1a** and **1b**, as shown by the different activation parameters, may be attributable to a shift of the TS towards bond breaking or bond formation as a consequence of the introduction of the alkyl group. Considering that alkyl substituent should reduce bond formation and favour bond breaking due to steric and inductive effects, the reaction of **1a** should occur through a TS involving more bond formation and that of **1b** through one involving more bond breaking. In other words, activation parameters suggest that solvent viscosity is more important than hydrogen bonding in determining the reactivity of alkynes in $[Br_3]^-$ addition reaction.

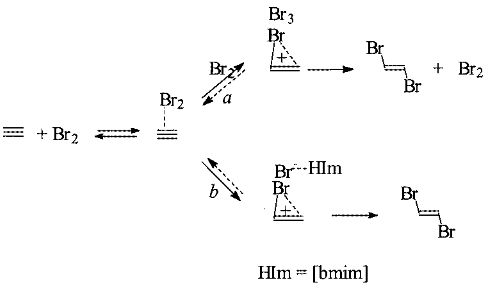
In [bmim][PF_6]

The rates of bromination of alkynes **1a**, **1d**, and **1e** in [bmim][PF_6] were measured spectrophotometrically, under *pseudo*-first/second-order conditions (in the presence of a large excess of alkyne) by monitoring the disappearance of the halogen, Br_2. At 25 °C, when the Br_2 concentration was relatively low ($< 3 \cdot 10^{-2}$ M), the reactions of **1a** and **1d** were characterised by the immediate loss of part of the absorbance, followed by an at least apparently slower disappearance of the halogen. This latter process obeyed the second-order rate law of Equation (9), while the values of k_2 are given in Table 5.

Table 5. Second- and third-order rate constants for the bromination of **1a**−**d** by Br_2 in [bmim][PF_6] at 25 °C

Alkyne	k_2 [$\text{M}^{-1}\cdot\text{s}^{-1}$][a]	k_3 [$\text{M}^{-2}\cdot\text{s}^{-1}$][a]
1a	$1.7\cdot10^{-3}$	
1d	$7.2\cdot10^{-3}$	
1e		$5.50\cdot10^{-1}$

[a] Error limits within ±10% of quoted number.



Scheme 2

$$-d[Br_2]/dt = k_2\cdot[Br_2]\cdot[\text{alkyne}] \tag{9}$$

Unfortunately, the initial rapid disappearance of Br_2 could not be monitored by stopped-flow techniques, due to the high viscosity of the solvent, which allowed the formation of very small air bubbles during the mixing phase, preventing correct determination of absorbance. It should be remarked that the values of k_2 found for **1a** and **1d** showed that the effect of increased alkyl substitution, which would be expected to stabilize a neighbouring cationic centre inductively, was of the same order of magnitude as observed in DCE, suggesting that the nature of the cationic moiety is not affected by the solvent. The higher *anti* stereoselectivity observed in the reaction of **1a** in [bmim][PF_6] with respect to that in DCE cannot be attributed to a different nature of the intermediate.

Unlike those of **1a** and **1d**, the reaction of **1e** was sufficiently slow for analysis by conventional spectrophotometry. At 25° C, for Br_2 concentrations $\geq 6\cdot10^{-2}$ M, bromine disappearance follows the third-order rate law reported in Equation (10) for two half lives, and the value of k_3 is given in Table 5.

$$-d[Br_2]/dt = k_3\cdot[Br_2]^2\cdot[\text{alkyne}] \tag{10}$$

In molecular solvents unable to enter into in hydrogen bonding, bromine addition to alkynes follows the third-order rate law of Equation (10),[21] while in solvents such as acetic acid, the rate law depends upon the reaction conditions.[26] At low bromine concentrations only the first term of Equation (11) makes a significant contribution to the observed rate. Both the k_2 and k_3 terms contribute to the overall rate equation at bromine concentrations of approximately 10^{-2} M.

$$-d[Br_2]/dt = k_2\cdot[Br_2]\cdot[\text{alkyne}] + k_3\cdot[Br_2]^2\cdot[\text{alkyne}] \tag{11}$$

In [bmim][PF_6], both terms of Equation (11) seem to contribute to the observed rate. This behaviour could be due to the ability of [bmim]$^+$ to enter into hydrogen bonding. However, since the brominations of **1a**, **1d**, and **1e** were carried out at similar bromine concentrations, the nature of the intermediate, bromirenium ion or β-bromovinyl cation, should presumably play a role in determining the kinetic order.

On the basis of the kinetic and product distribution data, a mechanism of the type shown in Scheme 2, characterised by the competition of two pathways, may therefore be proposed for Br_2 addition to alkynes in [bmim][PF_6].

By analogy with the situation in molecular solvents, the initial formation of a π complex has been hypothesised, although no evidence for the formation of this intermediate has been obtained in this work. The ionisation of this complex, catalysed by a second molecule of Br_2, gives a bromirenium (or bromovinyl cation) tribromide intermediate, depending on the ability of the substituents on the triple bond to stabilise the positive charge. This then collapses to give the dibromo adduct. For simplicity, the ionic intermediate is represented in Scheme 2 as a partially bridged intermediate. This pathway (path *a*) involves a second-order dependence of the rate on Br_2. In pathway *b* an imidazolium-assisted bromine−bromine bond breaking occurs in the 1:1 π complex to give a bromirenium (or bromovinyl cation) bromide intermediate and the reaction is of first order in Br_2.

Comparison of the kinetic constant k_3 found for **1e** with the reported value[21] in DCE (k_3 = 0.046 at 25 °C) and of kinetic constants k_2 for **1a** and **1d** with those relating[26] to bromination of **1a**−**c** in acetic acid, which ranged from $2.4\cdot10^{-3}$ to $6.3\cdot10^{-3}$ $\text{M}^{-1}\cdot\text{s}^{-1}$, shows that the ionic solvent produces only a moderate increase of the rate constant for the third-order process. In this reaction, involving ionic intermediates, the reaction rate should instead be markedly affected by the polarity of the medium. Through the use of solvatochromic dyes and fluorescence probes, a polarity similar to that of short-chain primary alcohols (ethanol, butanol), and higher than that of DCE and acetic acid, has been estimated[10−12] for [bmim][PF_6]. The kinetic results therefore show that, at least for this kind of reaction, the polarity parameter alone is not sufficient to account for the medium effect on rate. It is possible that the viscosity is also able to affect the reaction rate in this case, increasing the activation energy for bond breaking in the TS affording the ionic intermediate. On the other hand, the accelerating effect on the nucleophilic step (bond formation) could reduce the lifetime of the intermediate and make possible reversion of the intermediates to reagents less important.

In conclusion, the kinetic data determined in this work for bromination of alkynes, and comparison with data relating to molecular solvents, strongly suggest that not only polarity but also hydrogen-bonding capability and viscosity can affect the reaction pathway and the reactivity of organic compounds in these solvents.

Experimental Section

General Remarks: ^1H and ^{13}C NMR spectra were recorded with a Bruker AC 200 instrument, using [D$_6$]acetone as external lock solvent, contained in a capillary. Kinetic measurements were performed with a Cary 2200 spectrophotometer. Bromine (1 mL in sealed ampoules, > 99.5%), tetrabutylammonium tribromide ([Bu$_4$N][Br$_3$], puriss. p.a.), and 1,2-dichloroethane (DCE, > 99.5%) were used as supplied. Compounds **1a−e** were synthesised as previously reported;[21] [bmim]Br and [bmim][PF$_6$] were prepared by the reported procedures.[27] In the case of [bmim]Br, attention was paid to the cooling process, to avoid solidification.

UV and NMR Measurements: Appropriate quantities of Br_2 were weighed into known volumes of [bmim]Br or [bmim][PF$_6$] to prepare stock solutions, which were stored in the dark. The UV/Vis spectra of these solutions were recorded at 25±0.1 °C in the 300−500 nm range. Aliquots of these solutions were analysed by NMR using a co-axial tube, and data are given in Table 1.

Bromination Procedure and Product Analyses: The ionic liquid (2 mL) and Br_2 (96 mg, 0.6 mmol) were placed in a round-bottomed flask, equipped with a magnetic stirrer bar. To the Br_2 solution, maintained in the dark at room temperature, an equimolar amount of alkyne was then added whilst stirring. A water bath was used in order to avoid any temperature increase during the addition. Products were then extracted at the end of the reaction by three subsequent processes of addition of Et_2O (2 mL), followed by decantation of the ethereal solution of the products. The combined extracts were concentrated in a rotary evaporator and the products were analysed by NMR spectroscopy and identified on the basis of the reported spectra.[21]

Kinetic Measurements: Solutions of Br_2 in [bmim]Br or in [bmim][PF$_6$] were prepared by weighing the halogen into known amounts of solvents. Analogously, solutions of [Bu$_4$N][Br$_3$] were prepared by weighing the reagent into known volumes of DCE. In this case concentrations were also checked by UV measurements. All these solutions were prepared shortly before use, were protected from daylight, and were adjusted to twice the desired initial concentrations in the kinetic runs. Aliquots of these pre-thermostatted solutions were mixed with equal volumes of pre-thermostatted solutions of alkynes **1a−e** of suitable concentrations.

The reactions of **1a−d** with Br_2 in [bmim]Br, or with [Bu$_4$N][Br$_3$] in DCE, were carried out at halogen concentrations ranging from $1\cdot10^{-2}$ to $1\cdot10^{-1}$ M, in the presence of at least a tenfold excess of olefin, following the disappearance of the halogens at 420 or 440 nm. The experiments were repeated at least in triplicate and accepted on condition of a 5% maximum difference of the respective absorption/time curves. The second-order rate constants, $k_{Br_3^-}$, obtained by fitting the absorption/time data to the appropriate integrated rate equation, are reported in Table 3. The apparent activation parameters, reported in Table 4, were obtained from Arrhenius plots. The rate constants for the bromination of alkynes **1a**, **1b**, and **1e** with Br_2 in [bmim][PF$_6$], were measured at 25±0.1 °C, the disappearance of halogen being monitored by a conventional spectrophotometer. *Pseudo*-first-order kinetics were obtained by mixing Br_2 (ca. $2-3\times10^{-2}$ M) with at least a tenfold excess of **1a** or **1b**, while *pseudo*-second-order kinetics were recorded on treatment of Br_2 (ca. $6-8\times10^{-2}$ M) with a tenfold excess of **1e**. All reactions were carried out in triplicate. The kinetic constants k_2 and k_3 are given in Table 5.

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[1] [1a] J. D Holbrey, K. R. Seddon, *Clean Prod. Processes* **1999**, *1*, 223−236. [1b] M. J. Earle, K. R. Seddon, *Pure Appl. Chem.* **2000**, *72*, 1391−1398.

[2] T. Welton, *Chem. Rev.* **1999**, *99*, 2071−2083.

[3] P. Wasserscheid, W. Keim, *Angew. Chem. Int. Ed.* **2000**, *39*, 3773−3789.

[4] R. Sheldon, *Chem. Commun.* **2001**, 2399−2407.

[5] C. Chiappe, D. Capraro, V. Conte, D. Pieraccini, *Org. Lett.* **2001**, *3*, 1061−1063.

[6] [6a] G. H. Schmid, *The Chemistry of Double-Bonded Functional groups* (Ed.: S. Patai), Wiley, New York, **1989**, suppl. A, vol. 2, part 1, p. 699. [6b] M. F. Ruasse, *Adv. Phys. Org. Chem.* **1993**, *28*, 207−291. [6c] R. S. Brown, *Acc. Chem. Res.* **1997**, *30*, 131−137. [6d] G. Melloni, G. Modena, U. Tonellato, *Acc. Chem. Res.* **1981**, *14*, 227−231.

[7] N. R. Hardas, R. Adam, P. C. Uden, *J. Chromatogr. A* **1999**, *844*, 249−258.

[8] M. F. Ruasse, G. Lo Moro, B. Galland, R. Bianchini, C. Chiappe, G. Bellucci, *J. Am. Chem. Soc.* **1997**, *119*, 12492−12502.

[9] C. Reichard, *Solvents and Solvent Effects in Organic Chemistry*, 2nd ed., VCH, Weinheim, **1988**.

[10] A. J. Carmichael, K. R. Seddon, *J. Phys. Org. Chem.* **2000**, *13*, 591−595.

[11] S. N. V. K. Aki, J. F. Brennecke, A. Samanta, *Chem. Commun.* **2001**, 413−414.

[12] M. J. Muldoon, C. M. Gordon, I. R. Dunkin, *J. Chem. Soc., Perkin Trans. 2* **2001**, 433−435.

[13] M. Freemantle, *Chem. Eng. News* **1998**, *76*, 32−37 (March, 30).

[14] J. J. Gajewski, *J. Am. Chem. Soc.* **2001**, *123*, 10877−10883.

[15] D. Behar, C. Gonzalez, P. Neta, *J. Phys. Chem. A* **2001**, *105*, 7607−7614.

[16] [16a] A. G. Avent, P. A. Chaloner, M. P. Day, K. R. Seddon, T. Welton, *J. Chem. Soc., Dalton Trans.* **1994**, 3405−3413. [16b] P. Bonhôte, A. P. Dias, N. Papageorgiou, K. Klyanasundraram, M. Gratzel, *Inorg. Chem.* **1996**, *35*, 1168−1178.

[17] G. Bellucci, R. Bianchini, C. Chiappe, R. Ambrosetti, *J. Am. Chem. Soc.* **1989**, *111*, 199−202.

[18] Gmelin Handbook of Inorganic Chemistry, "Bromine", 8th ed., Springer-Verlag, **1985**.

[19] G. Bellucci, C. Chiappe, G. Lo Moro, *J. Org. Chem.* **1997**, *62*, 3176−3182.

[20] J. Berthelot, M. Fournier, *Can. J. Chem.* **1986**, *64*, 603−607.

[21] R. Bianchini, C. Chiappe, G. Lo Moro, D. Lenoir, P. Lemmen, N. Goldberg, *Chem. Eur. J.* **1999**, *5*, 1570−1580.

[22] G. Bellucci, R. Bianchini, R. Ambrosetti, G. Ingrosso, *J. Org. Chem.* **1985**, *50*, 3313−3318.

[23] Kramers, *Physica (Leipzig)* **1940**, *7*, 284−304.

[24] M. D. Ediger, *Annu. Rev. Phys. Chem.* **1991**, *42*, 225−250.

[25] K. A. Swiss, R. A. Firestone, *J. Phys. Chem. A.* **1999**, *103*, 5369−5372.

[26] G. H. Schmid, A. Modro, K. Yates, *J. Org. Chem.* **1980**, *45*, 665−667.

[27] V. P. W. Böhm, W. A. Herrmann, *Chem. Eur. J.* **2000**, *6*, 1017−1025. J. Fuller, R. T. Carlin, H. C. De Long, D. Haworth, *J. Chem. Soc., Chem. Commun.* **1994**, 299−300.

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