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An alternative oxidising and brominating method converting alcohols to aldehydes and β-bromoethyl esters using ionic liquid [Bmim][Br_3]

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[Bmim][Br_3] is an oxidising reagent which converts alcohols into aldehydes and ketones in mild conditions and good yields; the use of the ionic liquid (IL) as both an oxidising and a brominating reagent in the one-pot synthesis of β-bromoethyl esters from benzyl alcohols and diols has also been studied.

Keywords: [Bmim][Br_3], alcohols, aldehydes, β-bromoethyl esters

The transformation of alcohols to aldehydes is a key reaction in synthetic organic chemistry. It is not surprising, therefore, that a large number of procedures[1] have been introduced to generate this functionality from the oxidation of alcohols. Most notably the Oppenauer and Swern oxidations and reactions utilising high-valent metal compounds such as MnO_2, ammonium perruthenates and pyridinium chlorochromate[2] have been reported. Benzaldehydes can be obtained from benzyl alcohols with $RuCl_2(PPh_3)_3$[3] and $ZrO(OAc)_2$ using PhIO or *t*-butyl hydroperoxide,[4] and also with SeO_2–bis (4-anisyl)selenoxide[5] as oxidants. A valuable alternative is the [NBu_4][RuO_4]–*N*-methylmorpholine oxide system.[6] However, almost all of the systems require stoichiometric or catalytic amounts of metal compounds which may lead to concomitant environmental problems. So the introduction of a metal-free effective oxidising reagent which could be easily synthesised has drawn our attention.

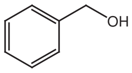
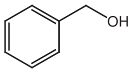
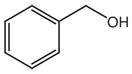
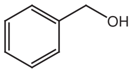
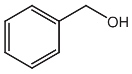
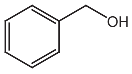
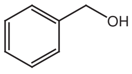
Ionic liquids (ILs) have been known for long as an environmentally benign excellent solvent for a large number of organic reactions, due to properties such as a widely accessible temperature range, lack of vapor pressure and flammability, as well as ease of reuse.[7,8] Many different task-specific ionic liquids have been synthesised to achieve the anticipated benefits.[9-21] Our group has used [Bmim][Br_3] /[Bmim]Br in the bromination reaction of α,β-unsaturated carboxylic acids.[22] During the course of our further investigation on the synthetic use of [Bmim][Br_3], we find it has also shown its effectiveness in oxidation. Liquid bromine is a classical oxidising reagent and it usually oxidises alcohols to carboxylic acids completely. However, we find that when it is mixed with [Bmim]Br to form the [Bmim][Br_3] IL, its oxidising ability is heavily reduced and the IL converts alcohols only into aldehydes and ketones rapidly under mild conditions. So, it is suggested that [Bmim][Br_3] could be used as an excellent selective oxidising reagent. Here we report the procedure using the ionic liquid [Bmim][Br_3] as the solvent and the oxidising reagent for the synthesis of aldehydes and ketones from alcohols.

The ionic liquid [Bmim][Br_3] could easily be prepared by dropping liquid bromine into [Bmim]Br in a round-bottomed flask and stirring for 0.5 h at room temperature. Then the alcohol was dropped in and reacted under heating.

In the first several runnings to find the best conditions, we found a little of the benzyl bromide was also produced as a by-product. So a base should be added into the oxidising system to neutralise the HBr produced in the oxidation and inhibit the formation of benzyl bromide. Several bases and

Scheme 1 Typical oxidative reaction of alcohols.

Table 1 Different reaction conditions[a]

Entry	Substrates(2 mmol)	React temperature/°C	Bases(3 mmol)	Time/h	Yields/%
1		60	No Base	0.5	70[b]
2		60	NaOAc	0.5	85[c]
3		60	NaOAc(water existed in IL)	2	45[d]
4		60	K_2CO_3	1	60[e]
5		60	NaOH	1	67[e]
6		Room temperature	NaOAc	2	66[e]
7		40	NaOAc	1.5	75[e]

[a] Reaction conditions: BmimBr (4 mmol) was mixed with liquid bromine (4 mmol) and base (6 mmol). After stirring at room temperature for 0.5 h, benzyl alcohol (2 mmol) was added and the reaction began. The progress of the reaction was monitored by TLC; [b] Completely converted, but benzyl bromide was found; [c] Completely converted; [d] Incomplete conversion, benzyl bromide was found; [e] Incomplete conversion, no benzyl bromide was found.

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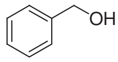
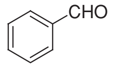
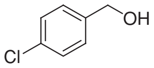
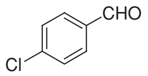
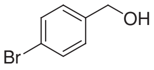
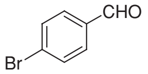
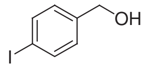
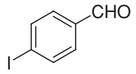
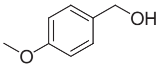
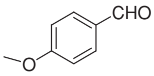
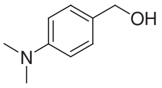
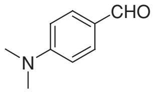
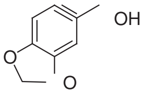
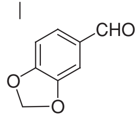
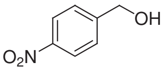
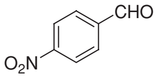
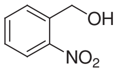
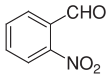
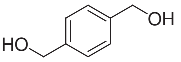
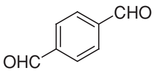
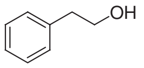
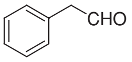
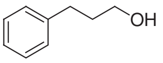
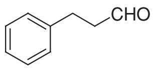
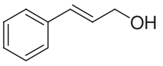
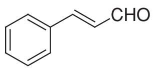
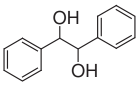
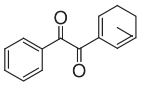
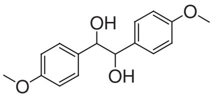
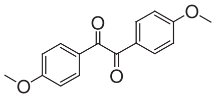
Table 2 Different aldehydes and ketones products and yields

Entry	Substrates	Products	Time/h	Yields[a]/%	m.p(Lit.)/b.p (Lit.)/°C/mmHg
1			0.75	85	65–67/10(62/10)[23]
2			1.5	84	44–46(47)[24]
3			1.25	85.5	60–62(59–60)[24]
4			0.75	87	75–77(77–78)[24]
5			1	83.5	190–191(191)[25]
6			4	36[b]	75–77(74)[24]
7			1.5	77.5	35–38(37)[23]
8			2	82[c]	104–107(104–105)[26]
9			3	61.5[c]	44–46(43–44)[24]
10			2.5	75	116–118(116)[24]
11			4	47.5[d]	33–35(33–34)[24]
12			4	40[d]	46–48(45–47)[27]
13			4	N.R[e]	
14			1.5	81.5	95–97(95)[28]
15			1	85.5	133–135(132–134)[29]

[a] Isolated yields after chromatographic purification; [b] The substrates reacted at a temperature of 80 °C; [c] The ratio of IL and bromine to benzyl alcohols was 4:1, and at a temperature of 80 °C; [d] No base was added and reaction temperature of 80 °C; [e] No new spot of product was found on TLC after reaction at 80 °C for 4 h.

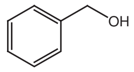
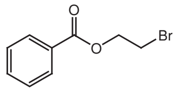
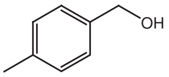
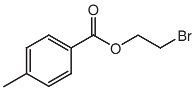
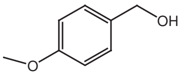
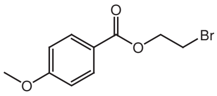
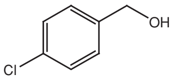
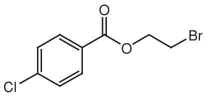
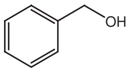
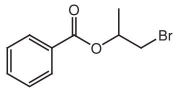
temperature conditions were tested. Eventually, NaOAc was found to be best base and the reaction was best conducted at 60 °C. The results are shown in Table 1.

Under these conditions, different aldehydes and ketones were synthesised, as shown in Table 2.

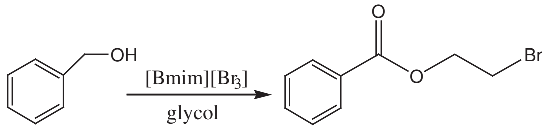
From the results we could see that this oxidising system applied to the benzyl alcohols much better than to other alcohols. Phenylethanol and phenylpropanol with the site of elecron density further removed from the reaction site had similar properties to aliphatic alcohols, and gave rather bad yields after reaction for a long time. Aliphatic alcohols did not show good results either. We could also see from Table 2 that the electron density determined the yields and reaction conditions. For instance, for the three halosubstituted benzyl alcohols, *p*-Cl-, *p*-Br-and *p*-I-benzyl alcohol, the most electron-rich one *p*-I-benzyl alcohol reacted fastest and in the best yield. In the comparison of *p*-NO_2-benzyl alcohol and *o*-NO_2-benzyl alcohol, the former one with slightly higher electron density reacted more rapidly and had a much higher yield than the latter one. For hydroxy-substituted substrates such as salicyl alcohol, we got bad results. Maybe the phenol under the basic conditions of the reaction was transformed to the phenoxide anion and the benzene ring of the anion was much more active than the usual benzyl alcohol, so that the bromosubstitution or oxidation of benzene ring would happen prior to the oxidation of the benzyl alcohol. For cinnamic alcohol, the bromo-addition reaction on the unsaturated bond occurred prior to the oxidation of the hydroxyl group.

Because in the course of oxidation HBr was produced as the by-product we thought it could just be used as the acid catalyst in the synthesis of β-bromoethyl esters from benzylaldehydes and diols; so a one-pot method for the synthesis of β-bromoethyl esters was also carried out, and rather good yields were obtained. The results are shown in Table 3.

Table 3 One-pot reactions between alcohols and diols

Entry	Substrates	Diols	Products	Yields^a/%	b.p(Lit.)/°C/mmHg
1		Glycol		75	110–113/10(102–105/1)[31]
2		Glycol		78	141–144/10(128–130/1)[31]
3		Glycol		82	169–171/10(156–158/1)[32]
4		Glycol		70	176–180/10(309.9/760)[33]
5		Propane-1,2-diol		75 ^{b}	121–123/10(112–114/1)[31]

^{a}Isolated yields after chromatographic purification; ^{b}The ratio of product to isomer byproduct was 5:1.



Scheme 2 One-pot synthesis of β-bromoethyl esters from benzyl alcohols.

In this reaction, [Bmim][Br$_3$] was used as a trifunctional reagent, solvent, oxidising and brominating reagent in one, which converted benzyl alcohols into β-bromoethyl esters.

In contrast with the literature which used PHPB as the brominating reagent and aldehyde as starting material,[30] our procedure took the advantage of tandem reactions and had similar good results, but in the absence of catalyst triethoxymethane.

In conclusion, the easily obtained IL, [Bmim][Br$_3$], had shown its utility both as an oxidising and a brominating reagent. Two useful molecular building blocks, aldehydes and β-bromoethyl esters were synthesised in good to excellent yields under rather mild conditions. Further studies of properties and uses of this IL will be pursued.

Experimental

Reactions were carried out in a 25 ml flask equipped with a magnetic stirrer bar with no special precautions in a fume cupboard. All the compounds were characterised by ^{1}H NMR. Melting points and boiling points were in good agreement with the literature.

Typical procedure for the oxidation of alcohols using [Bmim][Br$_3$]
[Bmim]Br (4 mmol) was mixed with liquid bromine (4 mmol). After stirring at room temperature for 0.5 h, NaOAc (6 mmol) was added followed by the benzyl alcohol (2 mmol) and then the reaction temperature was raised to 60 °C. Once the reaction had finished, the reaction complex was extracted 3 times by 5 ml portions of diethyl ether. The combined extract was concentrated and then separated by column chromatography to get the pure product.

Typical procedure for the synthesis of β-bromoethyl esters using [Bmim][Br$_3$]
[Bmim]Br (4 mmol) was mixed with liquid bromine (4 mmol). After stirring at room temperature for 0.5 h, their benzyl alcohol (2 mmol) and the diol (8 mmol) were dropped in. The reaction temperature was held at 80 °C for 8 h. After the finish of the reaction three 15 ml portions of diethyl ether were dropped into the reaction mixture in the ether extract being separated each time to extract the product. The combined extract was concentrated and then separated by column chromatography to get the pure product.

Representative data
p-Methoxybenzyl aldehyde: M.p: 190–191 °C(191 °C)[27] ; ^{1}H NMR (400 MHz) CDCl$_3$/TMS: δ = 3.81(s, 3H), 6.92–6.95 (m, J^* = 9 Hz, 2H), 7.75–7.78(m, J^* = 9 Hz, 2H), 9.81(s, 1H); IR: 2850, 2750, 1700, 1610, 1510, 1255 cm^{-1}. ($J^* = J_{2,3} + J_{2,5}$)

β-Bromoethyl benzoate: b.p: 110–113 °C/10 mmHg(102–105 °C/1 mmHg)[31]; ^{1}H NMR (400 MHz) CDCl$_3$/TMS: δ = 3.64(t, J = 6 Hz, 2H), 4.62(t, J = 6 Hz, 2H), 7.43–7.47(m, 2H), 7.50–7.59(m, 2H), 8.05–8.08(m, 2H). IR: 3030, 1725, 1525, 1150, 600 cm^{-1}.

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