Non-acid catalytic acetalisation of aldehydes with diols in ionic liquids

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The acetalisation of aldehydes with diols to corresponding 1,3-dioxolanes has been accomplished using ionic liquids as catalyst and reaction media. In the reaction process the removal of water produced and other catalysts were not necessary. High conversion and good selectivity were obtained when using $HMImBF_4$, which could be easily recycled and reused.

Keywords: ionic liquid, acetalisation, aldehyde, diol, 1,3-dioxolane

Ionic liquids (ILs) have emerged as a set of green solvents with unique properties such as solvating ability, tunable polarity, wide liquid range, high thermal stability, negligible vapour pressure and ease of recycling. The use of ILs as novel reaction media offers a convenient solution to both the solvent emission and the catalyst-recycling problem. It has made significant advancement in the development of clean chemical processes in organic synthesis.[1-2]

The protection of carbonyl groups with diols *via* acetalisation reactions plays an important role in organic, medicinal, carbohydrate and fragrance-material chemistry. In general, this method requires protonic or Lewis acids as catalysts, such as zinc (II) or iron (III) chlorides, or *p*-toluensulfonic acid. The most important shortcomings of the acid-induced method are the long reaction time, the substrate selectivity of Lewis-catalysts and the side reactions induced by the rather harsh acids. Moreover, environmentally harmful toxic solvents, such as benzene and toluene are often used in such acetalisations as dehydrators to remove the water produced in the reaction.[3-7] Therefore, the development of clean, good selective process for acetalisation reactions is highly desired.

Some acetalisations in ILs were reported in earlier paper.[8] In that paper, chloroaluminate ionic liquids were used. As these ILs are reactive toward air and water, they were not stable in the acetalisation reaction and were disadvantageous for recycle use. In this paper, we wish to report the use of air- and water-stable ILs as novel and recyclable reaction media and as catalysts for the acetalisation of aldehydes to 1,3-dioxolanes (Scheme 1). The ionic liquids used were: $BMImBF_4$ (BMIm=1-*n*-butyl-3-methyl imidazolium), $HMImBF_4$, $HMImPF_6$, HMImBr (HMIm=1-*n*-hexyl-3-methyl imidazolium), $OMImBF_4$ (OMIm=1-*n*-octyl-3-methyl imidazolium), $BDMImBF_4$ (BDMIm= 1-*n*-butyl-2,3-dimethyl imidazolium), and $BPyBF_4$ (BPy=1-*n*-butyl pyridinium), which were synthesised according to the procedures described in the literature.[9-12]

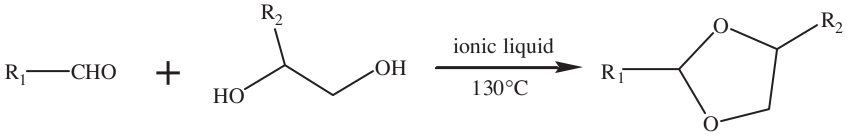
Initially acetalisation of phenylacetaldehyde with ethylene glycol was carried out in several different ionic liquids (Table 1). As shown in Table 1, the best result was obtained with good aldehyde conversion and dioxolane selectivity when using $HMImBF_4$ as the reaction medium (entry 2), while only the aldol condensation product was obtained when using $HMImPF_6$ and HMImBr (entries 7 and 8). This showed that both the cation and the anion had an impact on the conversion and selectivity, and the activity of ILs was not noticably decreased after reuse for the third time (entry 3). Based on the results obtained, the ionic liquid $HMImBF_4$ was selected as the reaction media and catalyst in the following acetalisation reaction.

Table 1 Acetalisation of phenylacetaldehyde with ethylene glycol in different ILs[a]

Entry	ILs	Conversion of aldehyde/%	Selectivity to dioxolane/%	Selectivity to aldol product/%
1	$BMImBF_4$	60	8	92
2	$HMImBF_4$	95	81	19
3[b]	$HMImBF_4$	95	80	20
4	$OMImBF_4$	96	60	40
5	$BDMImBF_4$	84	52	48
6	$BPyBF_4$	82	48	52
7	$HMImPF_6$	82	~0	~100
8	HMImBr	86	~0	~100

[a]The acetalisation was performed at 130°C for 3h with the ratio of aldehyde to diol = 1 : 2.
[b]The IL was reused for the third time.

Then the acetalisations of different aldehydes with diols were carried out in $HMImBF_4$. The results were listed in Table 2. Medium to excellent performances were obtained, showing some dependence on the structures of aldehyde and diol. The acetalisation of the aliphatic aldehydes isopentaldehyde and ligustral was very satisfactory, both high conversion and perfect selectivity to dioxolane were obtained and no aldol condensation product was found (entries 1–4). The aldol condensation product was only detected in the acetalisation of phenylacetaldehyde among all the aliphatic aldehydes (entries 1–6). This may be due to the active α-H on the benzyl group. Excellent selectivity to dioxolane was obtained for aromatic aldehydes, since these aldehydes do not contain an α-H and it is impossible for them to perform the aldol reaction. As acetalisation is a nucleophilic addition reaction, the group R_1 that can withdraw the electron of the carbonyl group is advantageous to the acetalisation. Since the electron withdrawing ability of the *p*-substituting group on the phenyl is in the sequence $–NO_2>–Cl>–OCH_3$, as shown in the results, the conversion was entry 9>entry 11>entry 7>entry 13. The reactivity of the nucleophilic reagent also impacted



Scheme 1

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Table 2 Acetalisations of aldehydes with diols in $HMImBF_4$[a, b]

Entry	R_1	R_2	Conversion of aldehyde/%	Selectivity to dioxolane/%	Stereoselectivity ($trans/cis$)[c]/%
1[d]	$(CH_3)_2CHCH_2$	H	96	100	–
2[d]	$(CH_3)_2CHCH_2$	CH_3	98	100	77/23
3	ligustral[e]	H	91	100	–
4	ligustral[e]	CH_3	97	100	65/35
5	$C_6H_5CH_2$	H	95	81	–
6	$C_6H_5CH_2$	CH_3	97	86	58/42
7	C_6H_5	H	61(76[f])	100	–
8	C_6H_5	CH_3	88	100	56/44
9	p-$NO_2C_6H_4$	H	94	100	–
10	p-$NO_2C_6H_4$	CH_3	95	100	69/31
11	p-ClC_6H_4	H	71	100	–
12	p-ClC_6H_4	CH_3	86	100	57/43
13	p-$CH_3OC_6H_4$	H	51(64[f])	100	–
14	p-$CH_3OC_6H_4$	CH_3	65	100	61/39

[a] The acetalisation was performed at 130°C for 3h with the ratio of aldehyde to diol = 1 : 2.

[b] ^1H NMR, IR and MS characterised all the products, which were consistent with the literature data .

[c] The stereoselectiyity of isomers detected by GC–MS.

[d] The reaction was carried out at 75°C.

[e] Ligustral is 2,4-dimethyl-3-cyclohexenecarboxaldehyde. [f] The conversion for 5h.

on the acetalisation. In general, 1,2-propanediol is superior to ethylene glycol, as the methyl group adds to the nucleophilicity of propanediol, as shown by the results in Table 2 that the acetalisation conversion of the latter was higher than those of the former for every aldehyde. When R_2 was the methyl group, the obtained dioxolanes had *cis*- and *trans*-isomers.

In summary, this paper describes a novel method for the conversion of aldehydes to 1,3-dioxolanes using air- and water-stable ionic liquids $HMImBF_4$ as recyclable reaction media and catalysts. The method has several advantages: (1) avoiding using protonic or Lewis acids and volatile organic solvents; (2) elimination of an additional process required in the traditional method to remove the water during the reaction; and (3) the ionic liquid could be easily recycled and directly reused after removal of water. These facts may open new opportunities and alternatives of great interest for acetalisation reactions.

Experimental

^1H NMR spectra were determined on a Bruker AC-400 (TMS as internal standard). IR spectra were obtained on Bruker Equinox 55 (KBr pellets). GC/MS spectra were recorded on an Agilent 6890N/5973N.

Typical procedure for synthesis of 2-benzyl-1,3-dioxolane: $HMImBF_4$ (2 ml), phenylacetaldehyde (0.3 g, 2.5 mmol) and ethylene glycol (0.31 g, 5 mmol) were introduced into a 20 ml flask. The mixture was stirred at 130°C for 3h. Reaction progress was monitored by GC-MS. After reaction, the mixture was extracted with diethyl ether (3×10 ml). After the ether was removed from the combined extracts, the 2-benzyl-1,3-dioxolane was separated from the excessive ethylene glycol automatically and could be further purified by preparative TLC (Silica gel 254) with ethyl acetate/hexane (2: 8) as eluent. The rest of the ionic liquid was dried at 80°C under reduced pressure (0.01torr) for 1h to retain its activity in subsequent runs.

Representative spectroscopic data (*2-benzyl-1,3-dioxolane*): ^1H NMR (400MHz, δppm): 7.21–7.36 (5H, m), 5.07 (1H, t, J=4.4Hz), 3.96-3.85 (4H, m), 2.97 (2H, d, J=4.4Hz); IR (KBr, cm^{-1}): 700, 755,1031, 1042, 1137, 1400, 1467, 1497, 2888, 2928, 2955; MS (m/e): 164 (M^+), 91 (29.8), 73 (100).

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