Ionic liquids: a convenient solvent for environmentally friendly allylation reactions with tetraallylstannane

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Ionic liquids based on the 1-butyl-3-methylimidazolium cation have been used as solvents for the preparation in good yield of homoallylic alcohols from tetraallylstannane and a range of aldehydes.

In recent years chemists have striven to develop new synthetic methodologies and techniques which are more environmentally benign, work generally referred to under the title of 'clean technology'. Organostannanes are extremely useful reagents in organic synthesis, but are also notoriously environmentally unfriendly due to the presence of toxic tin residues. There have been a number of attempts to develop cleaner organostannane reagents and reaction conditions. Examples include the development of polymer supported organostannanes,[1] the use of water as solvent,[2] and water-soluble reagents.[3]

Room temperature ionic liquids are attracting increasing interest as environmentally benign reaction media for organic and organometallic synthetic chemistry, for example Friedel–Crafts[4] and hydrogenation reactions.[5] These solvents possess a number of interesting properties, notably their lack of vapour pressure, ease of reuse, lack of flammability, and large accessible temperature range. Furthermore, by alteration of the cation and anion it is possible to adjust the solubility properties of an ionic liquid, for example making it immiscible with water or certain organic solvents. Recent studies on Diels–Alder reactions in ionic liquids based on the 1-alkyl-3-methylimidazolium cation in conjunction with a variety of anions (*e.g.* PF_6^- and BF_4^-) have suggested reactivity patterns similar to those observed in alcoholic solvents.[6,7] Herein we report for the first time the combination of organostannane chemistry and ionic liquid methodology.

The allylation of aldehydes to produce homoallylic alcohols is a useful organic transformation, which has attracted considerable attention in recent years.[8] The most common method is the use of metal–allyl complexes, and one of us (AM) has recently reported the use of tetraallylstannane (**1**) for allylation under very mild conditions (Table 1).[9]

The reaction was found to be most efficient when carried out in MeOH solution. **1** has a number of advantages as a reagent compared with the allyltrialkylstannanes traditionally used for such reactions. In particular, all of the allyl ligands are transferred, leaving the tin by-product in the form of inorganic salt which is much more easily separated from the reaction mixture than organostannane residues resulting from allyltrialkylstannane reactions. Most importantly from a clean chemistry standpoint, as each molecule of **1** will react with four separate aldehyde molecules the reaction is extremely 'atom efficient', since the only reagent atom not incorporated into the product is tin.

The reaction of a range of aromatic and aliphatic aldehydes with **1** was investigated. In a typical experiment, the chosen aldehyde was stirred at room temperature for 16 h with 0.25 equiv. of **1** dissolved in 2 ml of the chosen ionic liquid. The ionic liquids employed were 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF$_4$]) and hexafluorophosphate ([bmim][PF$_6$]), which were prepared by literature methods.[10] On completion of the allylation reaction the ionic liquid was observed to be cloudy. Work-up was achieved simply by extraction of the reaction mixture with Et$_2$O followed by removal of the solvent.† This approach generally allowed isolation of products of excellent purity, unreacted starting material being the only contaminant in some cases, as discussed below. The cloudy residue was assumed to be the tin by-product, and this did not transfer into the Et$_2$O extracts. The yields obtained are listed in Table 1. Product characterisation was carried out using ^{1}H and ^{13}C NMR spectroscopy.

As can be seen in Table 1, excluding entry 5 the yields varied from 66–93% depending on the nature of the aldehyde employed. Such values are in good agreement with those previously reported for the equivalent reaction in MeOH solution.[9] Reactions were judged to have gone to completion if the ^{1}H and ^{13}C NMR spectra showed no signals for the aldehyde group. It should be noted that the small scale on which the reactions were carried out meant that mechanical losses were proportionally quite large, so larger scale preparations would be expected to give higher yields. The allylation of benzaldehyde in [bmim][PF$_6$] was investigated on a larger scale to confirm this. When 2.50 g of **1** (8.87 mmol) was reacted with 3.765 g of benzaldehyde (35.46 mmol) in 10 ml of ionic liquid, an isolated yield of 5.17 g (96%) of the homoallylic alcohol was obtained.

The reaction was observed to proceed to completion with simple aromatic aldehydes like benzaldehyde (entry 1). Similar behaviour was observed when electron-withdrawing substituents were present (*e.g.* *p*-Cl, entry 2), and the presence of weakly electron-donating substituents did not appear to hinder the reaction significantly. Thus good yields were obtained in the reactions of tolualdehyde (entry 3) and anisaldehyde (entry 4).

Table 1 Yields of homoallylic alcohol using [bmim][BF$_4$] and [bmim][PF$_6$] ionic liquids

Entry	R	Yield (%) [bmim][BF$_4$]	[bmim][PF$_6$]
1	Ph	79[a]	82[a]
2	*p*-ClC$_6$H$_4$	93[a]	82[a]
3	*p*-MeC$_6$H$_4$	80[b]	72[b]
4	*p*-MeOC$_6$H$_4$	84[a]	76[b]
5	*p*-Me$_2$NC$_6$H$_4$	0	0
6	Pr	70[b]	70[b]
7	C$_5$H$_{12}$	72[b]	74[b]
8	*trans*-PhC=CMe	69[b]	66[b]
9	(S)-Me$_2$C=CH(CH$_2$)$_2$CHMeCH$_2$	73[b]	78[b]

[a] Isolated yield. [b] NMR yields.

Table 2 Results obtained using recycled ionic liquids

Entry	R	Cycle	Yield (%) [bmim][BF$_4$]	[bmim][PF$_6$]
1	Ph	1	79[a]	82[a]
2	Ph	2	82[a]	81[a]
3	Ph	3	78[a]	83[a]

[a] Isolated yield.

When a strongly electron-donating substituent such as Me$_2$N was present, however, only starting materials were obtained on work-up (entry 5). The greatly reduced reaction rate with electron-donating substituents was also observed in the reactions carried out in MeOH solution.[9]

The presence of significant amounts of unreacted **1** in the organic extracts from the reactions involving simple aliphatic aldehydes suggested that these did not go to completion (entries 6 and 7). No traces of unreacted aldehyde were observed in these cases, but these are probably sufficiently volatile to be lost during work-up. Traces of **1** were also found in the reaction products of *trans*-2-methylcinnamaldehyde (entry 8), suggesting that here too the reaction was incomplete. Yields obtained in all three cases were reasonable despite this.

The product of the (*S*)-(−)-citronellal reaction (entry 9) can contain both *threo*- and *erythro*-isomers. The NMR spectra suggested that any selectivity was modest at best, with peaks corresponding to each isomer being of almost identical intensity. This is perhaps not surprising given the combination of the small size of the methyl group and its distance from the reactive site. Similarly small degrees of selectivity have been reported in the crotylstannanation of citronellal carried out in aqueous solution using (*E/Z*)-Bu$_2$(MeCH=CHCH$_2$)SnCl.[11]

In general it was found that there was no contamination of the products with tin by-products when the reaction proceeded to completion. This was confirmed by recording ^{119}Sn NMR spectra of the organic products, which indicated that no tin was present in any form. In cases where partial conversion was observed, however, some **1** was found in the organic extracts. No contamination of the products with ionic liquid was observed, however. The reaction between **1** and benzaldehyde was monitored using ^{119}Sn NMR spectroscopy to attempt to determine the fate of the tin residues. A signal corresponding to **1** was observed at −45.8 ppm before addition of the benzaldehyde. This disappeared rapidly when the reagents were mixed, but no further ^{119}Sn signals were observed in either the ionic liquid or the organic product. The reaction was accompanied by the formation of an insoluble white residue, more noticeable than in the preparative experiments due to the lower volume of ionic liquid employed. Attempts were made to identify this species, but it proved to be relatively insoluble in all solvents investigated, and no signals were seen in the ^{119}Sn spectrum. It should be noted that these results contrast strongly with ^{119}Sn investigations carried out on the reaction in MeOH solution, where no insoluble product was observed, and signals were seen in the region −600 to −640 ppm which were assigned to polymeric tin(IV) methoxide species.[9c]

Little difference was found in the yields obtained using the two different solvents. Recycling of the ionic liquid was carried out for the reaction of benzaldehyde following an extremely straightforward protocol.‡ The results gained are shown in Table 2. It can be seen that no decrease in yield was observed in runs carried out using 'old' ionic liquid, and furthermore the products obtained were of the same purity as in the first run. In the case of the recycled [PF$_6$]$^-$ salt the purification removed all of the cloudy residue, while some cloudiness was observed in the recycled [BF$_4$]$^-$ salt, but this did not seem to impair the performance of the liquid.

At present the mechanism of the reaction is not clear. Previous studies on the reaction in MeOH have suggested the presence of an eight-membered ring transition state involving both reactants and the solvent.[9] The results presented here do not give any direct clue as to the role of the ionic liquid in this reaction. Further mechanistic investigations are currently in progress.

In conclusion, ionic liquids appear to be excellent solvents in which to carry out allylation reactions using tetraallylstannane. The reaction proceeds most readily with aromatic aldehydes, provided that no strongly electron donating substituent is present. The reaction is less rapid in aliphatic aldehydes, but it should be stressed that all of the investigations reported here were carried out at 15 °C. Allylation of an aldehyde containing a chiral centre gave little evidence for stereoselectivity in the reaction, although the example chosen was relatively unfavourable. Separation of the products from the ionic liquid is very straightforward, as is recycling of the liquid. The latter will be an important concern if ionic liquids are truly to be considered environmentally friendly solvents. Future work will address the reaction of a wider range of substrates, and a mechanistic investigation will be attempted, part of which will be an attempt to identify the insoluble tin by-product of the reaction.

Notes and references

† *Typical procedure for the allylation of alkanals by tetraallylstannane in ionic liquids.* Benzaldehyde (106 mg, 1 mmol) was placed in a 5 ml reaction vial with a spin vane. To this was added 2 ml of [bmim][BF$_4$] followed by tetraallylstannane (70.7 mg, 0.25 mmol), the septum cap was replaced, and the mixture stirred vigorously at room temperature (typically 15 °C) for 16 h. After this time the mixture was extracted with Et$_2$O (3 × 10 ml), the organic extracts were combined and dried over anhydrous MgSO$_4$. The Et$_2$O was removed *in vacuo* to yield a pale oil, 117 mg (79%).

‡ *Recycling of ionic liquids.* After complete reaction and work-up as described above, the ionic liquid could be used with no further treatment. Since this would result in the build-up of tin residues over a period of time, however, the procedure generally employed was to dissolve the ionic liquid in EtOAc (10 ml), and wash with water (2 × 5 ml) and brine (5 ml). Addition of Et$_2$O (20 ml) caused two layers to form, the lower being essentially pure ionic liquid.

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