Wittig reactions in the ionic solvent [bmim][BF_4]

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The ionic salt [bmim][BF_4] is an attractive solvent for Wittig reactions, allowing both easier separation of alkenes from Ph_3PO together with efficient reuse of the solvent.

Ionic liquids are a new class of solvents which have attracted growing interest over the past few years due to their unique physical and chemical properties.[1] They usually consist of poorly coordinating ion pairs, and a classical example is the readily accessible 1-butyl-3-methylimidazolium tetrafluoroborate [bmim][BF_4], which is a colourless mobile but non-volatile liquid with no smell (Fig. 1).[2] Since such solvents easily dissolve metal salts and transition metal catalysts interesting developments have recently appeared in synthesis using organometallic reagents.[3] Some applications of these solvents in organic chemistry have also been reported, for instance in alkylations,[4] benzoin condensation,[5] and Diels–Alder[6] and Friedel–Crafts[7] type reactions. Furthermore, their possible use for selective extraction of organic compounds has been noted recently.[8]

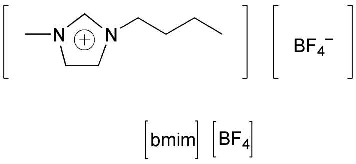
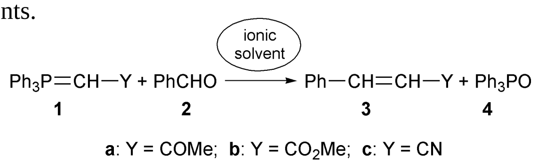


Fig. 1

The Wittig reaction is amongst the most popular methods for C=C bond formation, giving in most cases good to excellent stereocontrol.[9] The separation of the alkene from the by-product (Ph_3PO) is a classical problem: it is usually done by crystallisation and/or chromatography. In this communication we demonstrate the usefulness of the ionic solvent [bmim] [BF_4] as a medium to perform Wittig reactions using stabilized ylides allowing both easier separation of alkenes from Ph_3PO and also the recycling of the solvent. Phosphorane **1a** and benzaldehyde were selected as first models (Scheme 1) to develop this method and study the selectivity in the extraction by appropriate solvents.



Scheme 1

The reaction was complete in 2.5 h at 60 °C and the results obtained with different solvents are reported in Table 1.† Extraction of the reaction mixture with Et_2O gave **3a**‡ (79% isolated yield after filtration on a short SiO_2 pad) and Ph_3PO (21%). Further extraction with toluene removed almost completely the residual Ph_3PO and phosphorane.

Table 1 Recovery of **3a** in three different combinations of solvents

	Exp. 1		Exp. 2		Exp. 3	
	Ether[a]	Tol[b]	tBuOMe[a]	Tol[b]	Hexane[a]	Tol[b]
3a yield (%)	79	—	87	—	49	41
Ph_3PO yield (%)	21	72	11	78	1	54

[a] First solvent of extraction. [b] Second solvent of extraction.

Careful ^1H and ^{13}C NMR analysis of the ionic solvent after these successive extractions gave no evidence for residual PhCHO and **3a** (less than 2% for both compounds). Only residual **1a** and a small amount ($\approx 5\%$) of Ph_3PO could be detected. Slightly better results were obtained with tBuOMe as the first solvent (87% of **3a** with only 11% of Ph_3PO). Extraction with hexane was not convenient, even though very little Ph_3PO was obtained in that case.

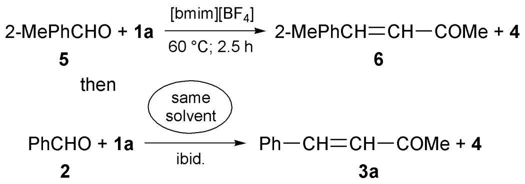
One of the advantages of ionic solvents is ease of recycling. As indicated in Table 2, such is indeed the case for this Wittig reaction since excellent yields of **3a** were obtained, even after 6 consecutive runs.

Table 2 Reuse of [bmim]BF_4] in the reaction of **1a** + **2**

Run	1	2	3	4	5	6
3a Yield (%)[a]	82	83	86	82	90	91
3a Yield (%)[b]	86	88	93	92	88	92

[a] Extraction with Et_2O. [b] Extraction with tBuOMe.

A more difficult challenge was to reuse the solvent, *but for two different Wittig reactions*. This was established in the following way (Scheme 2): the reaction of **1a** with *o*-tolualdehyde gave **6** in excellent yield (95%). Then, the *same* ionic solvent was used for the reaction of **1a** with benzaldehyde: careful ^1H and ^{13}C NMR analysis of the product isolated in the latter reaction indicated that **3a** was obtained, with no trace ($\leqslant 2\%$) of **6**.



Scheme 2

Other stabilized ylides can also be used the obtain alkenes **3** in good yields (Table 3).

Finally, this method could also be extended to other aldehydes (Table 4). Various aromatic and aliphatic aldehydes,

Table 3 Reaction of phosphorus ylides **1** with **2** in [bmim][BF_4]

Y	**3** Yield (%)	*E*/*Z*[a]
COMe	82	97/3
CO_2Me	90	96/4
CN	79	50/50
CN[b]	66	77/23

[a] Established using ^1H NMR. [b] For comparison, reaction in toluene (60 °C, 2.5 h) was also performed.

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Table 4 Reaction of ylide **1a** with different aldehydes in [bmin][BF_4] at 60 °C

RCHO + **1a**		RCH=CHCOMe + Ph_3PO	
R	Time/h	Yield olefin (%)	*E*/*Z*[a]
4-Cl-Ph-	2.5	86	97/3
4-NO_2-Ph	2.5	44[b]	98/2
4-MeO-Ph-	72	82	96/4
2-Me-Ph-	4	95	96/4
Cyclohexyl-	4	80	85/15
C_5H_{11}	12	82	98/2
i-Butyl-	4	84	98/2
(*E*) Ph-CH=CH-	12	86	90/10
(*E*) Me-CH=CH-	12	88	95/5

[a] Established using ^1H NMR. [b] Low solubility of this olefin in either.

as well as enals react with **1a** to give corresponding alkenes in good yield and selectivity. In the case of the *para*-nitro derivative however athough the Wittig reaction was complete, the corresponding alkene was isolated in lower yield due to the low solubility of the product in ether. For these stabilized ylides, the *E*-stereoselectivity in the ionic solvent appears at least equivalent, if not better, than the reactions performed in the usual organic solvents.[9] The only exception was **1c** which is a little less selective (see Table 3).

In conclusion, Wittig reactions of stabilized ylides with aldehydes are easily performed in the ionic solvent [bmim][BF_4]. This method offers attractive possibilities for selective extraction of alkenes and Ph_3PO. Furthermore it is possible to efficiently reuse the ionic solvent.

Notes and references

† Representative procedure, preparation of **3a**: a solution of benzaldehyde **2** (0.2 mL, 2 mmol) and phosphorane **1a** (0.689 g, 2.16 mmol) in the [bmim][BF_4] salt (2 mL) was heated at 60 °C, under magnetic stirring, for 2.5 h. The reaction mixture was extracted first with tBuOMe (3 × 3mL) and then with toluene (3 × 3 mL). The extracts were evaporated *in vacuo*. Filtration of the tBuOMe extract on a short SiO_2 pad gave **3a** (0.254 g, 87% yield) and then Ph_3PO (0.061 g, 11% yield). Similarly, the toluene extract yielded Ph_3PO (0.434 g, 78% yield).

‡ All isolated compounds gave spectra (^1H and ^{13}C NMR) consistent with indicated structures and in agreement with literature data. For the alkenes, isolated yields refer to the (*E* + *Z*) mixtures.

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