Palladium catalysed allylation reactions in ionic liquids

Weiping Chen, Lijin Xu, Craig Chatterton and Jianliang Xiao*

Leverhulme Centre for Innovative Catalysis, Department of Chemistry, University of Liverpool, Liverpool, UK L69 7ZD. E-mail: j.xiao@liv.ac.uk

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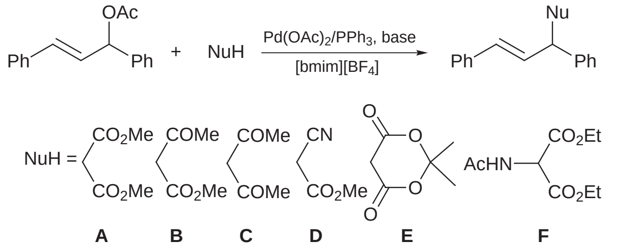
Palladium catalysed allylic alkylation and amination reactions have been demonstrated to proceed readily in the room temperature ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF$_4$]) with easy catalyst/solvent recycling and no need to generate separately the carbanion nucleophiles.

Room temperature ionic liquids consisting of 1,3-dialkylimidazolium cations and their counter ions have attracted growing interest in the last few years.[1–8] These ionic liquids offer an attractive alternative to conventional organic liquids for clean synthesis, as they are easy to recycle and possess no effective vapor pressure. As with water and perfluoro solvents, they also offer the potential for easy catalyst/product separation, owing to their limited miscibility with many common organic liquids. A few types of catalytic reactions have been carried out in these and related ionic liquids; recent examples include Friedel–Crafts reactions,[1,4] Diels–Alder reactions,[2] alkylations,[3] olefin dimerisation and oligomerisation,[5–7,9] hydrogenation,[8] Heck reaction[10] and hydroformylation.[11] We report herein the first examples of palladium catalysed allylic alkylation and amination reactions in the ionic liquid [bmim][BF$_4$]. [bmim][BF$_4$] has a liquid range down to −81 °C. It is miscible with polar compounds such as lower alcohols but immiscible with less polar compounds such as toluene and Et$_2$O. Many organometallic compounds have been found to display good solubility in this liquid.

Palladium(0) catalysed allylic alkylations of soft carbon nucleophiles represent a very useful tool for organic synthesis.[12] As summarised by Hegedus, the alkylation reactions are usually conducted by mixing stabilised carbanions with a substrate-catalyst mixture in THF and then heating the resultant mixture at reflux.[13] The carbanions are generated separately using bases such as NaH in dipolar solvents like THF. Catalyst and solvent recycling, which will undoubtedly be difficult with conventional solvents, has rarely been addressed for these reactions.[14] Prompted by Seddon's recent report on *in situ* generation of anions in the alkylaton of indole and 2-naphthol in [bmim][PF$_6$],[3] we examind the room temperature, one-pot alkylation of the active methylene compounds **A**–**F** by 1,3-diphenylallyl acetate in [bmim][BF$_4$] (Scheme 1). The results are presented below.

The alkylation of dimethyl malonate **A** by 3-acetoxy-1,3-diphenylprop-1-ene was investigated first. The catalyst or catalyst precursor was formed by heating Pd(OAc)$_2$ (2 mol%, based on the acetate) with PPh$_3$ (8 mol%) in [bmim][BF$_4$] at 80 °C for 20 min. The ionic liquid was then cooled to ambient temperature, and the reaction started by adding the substrates and K$_2$CO$_3$. ^{1}H NMR monitoring showed that the alkylation was complete after 5 h reaction time at ambient temperature. The initial rate was slightly lower, due perhaps to the dissolution of the substrates and base or to the formation of active Pd^0 species at the beginning of the reaction. A few variables have been identified to be important for the success of the alkylation in [bmim][BF$_4$] (Table 1). (i) As with allylic alkylations in molecular solvents,[13] no reaction takes place in the ionic liquid without PPh$_3$. (ii) The reaction rate decreases markedly when the molar ratio of PPh$_3$: Pd(OAc)$_2$ is less than 4 : 1. Thus, with 3 equiv. (relative to palladium acetate) of PPh$_3$, the conversion of the acetate was only 50% after 15 h reaction time and, with 1 equiv. of PPh$_3$, a much lower conversion of 13% was observed. (iii) The reaction is slower without initial heating of Pd(OAc)$_2$ and PPh$_3$ in [bmim][BF$_4$]. Thus, heating of Pd(OAc)$_2$ and PPh$_3$ with the substrates in the absence of [bmim][BF$_4$] followed by reaction in the ionic liquid at ambient temperature for 15 h afforded only a 68% conversion. As a base, K$_2$CO$_3$ and DBU are equally effective but, in the case of the latter, the reaction mixture is homogeneous. K$_2$CO$_3$ only partly dissolves in [bmim][BF$_4$] under the reaction conditions. The quantity of palladium used can be lowered to 0.2 mol% without affecting the 100% conversion for reactions carried out overnight.



Scheme 1

Using the procedures developed for dimethyl malonate, the alkylation was extended to the active methylene compounds **B**–**F**. The results are summarised in Table 2. All the reactions were completed with 100% conversion within the time indicated when using DBU as the base. The lower yield obtained with the acetylacetone **C** was partly due to double alkylation. Alkylation of the amido malonate **F** was sluggish at room temperature, but the reaction proceeded smoothly at 50 °C to give the product with 86% isolated yield. For the reactions involving methyl acetoacetate **B** and methyl cyanoacetate **D**, the product was a 1:1 mixture of two diastereomers. Replacing DBU with K$_2$CO$_3$ resulted in lower conversions for the substrates **B**–**F** under identical conditions; the reason is not immediately clear.

Using similar procedures, we also tested the amination of 1,3-diphenylallyl acetate. The amination by pyrrolidine pro-

Table 1 Palladium catalysed allylic alkylations in [bmim][BF$_4$] under various conditions[a]

PPh$_3$/Pd(OAc)$_2$	t/h	Conversion (%)
0	48	0
1	15	13
2	15	36
3	15	50
4	5	100
4	15	68[b]
4	15	100[c]

[a] General reaction conditions: 1.0 mmol of 3-acetoxy-1,3-diphenylprop-1-ene, 2 mol% Pd(OAc)$_2$, 1.5 mmol of dimethyl malonate and 2.0 mmol of K$_2$CO$_3$ in 1 ml of [bmim][BF$_4$] at ambient temperature. Before starting the reaction, Pd(OAc)$_2$ and PPh$_3$ were heated at 80 °C for 20 min in the ionic liquid. [b] Pd(OAc)$_2$, PPh$_3$ and the substrates were heated at 80 °C before introducing the base and ionic liquid at ambient temperature. [c] 0.2 mol% Pd(OAc)$_2$.

Table 2 Palladium catalysed allylations in [bmim][BF_4] with various nucleophiles[a]

NuH	Base	t/h	Yield (%)[b]
A	K_2CO_3	5	91
B	DBU	15	87[c]
C	DBU	15	54
D	DBU	14	88[c]
E	DBU	15	79
F	DBU	12	86[d]

[a] The reaction conditions were the same as the general reaction conditions given in Table 1, unless otherwise indicated. All the reactions completed with 100% conversion. [b] Isolated yield. [c] The product was a 1:1 mixture of two diastereomers. [d] Reaction was carried out at 50 °C.

ceeded readily to give the corresponding 1,3-diphenylallylamine with 100% conversion. Unlike the alkylations, no additional base is required in this transformation.

Catalyst separation/recycling appears to be difficult under the conditions established above, because the organic compounds and the ionic liquids form a homogeneous mixture and so catalyst separation *via* phase separation is not feasible. Further, extraction of the products with solvents of various polarity resulted in significant leaching of palladium species out of the ionic liquid. However, replacing PPh_3 with the hydrophilic phosphine $P(m\text{-}C_6H_4SO_3Na)_3$ led to effective recycling of the catalyst-containing ionic liquid phase; the catalyst along with the ionic liquid was reused three times without losing activity in the alkylation of dimethyl malonate. The product was extracted with toluene after each cycle of the reaction.

In summary, we have demonstrated that allylic alkylation and amination can effectively be performed in the room temperature ionic liquid [bmim][BF_4] with the additional benefit of easy catalyst/solvent recycling. Ionic liquids like this provide an ideal environment where ionic intermediates may be generated *in situ* and stabilised therein. Reactions in such media offer an attractive ‘greener’ alternative to the conventional processes where volatile organic solvents are frequently employed and catalyst reuse is difficult to implement.

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Notes and references

1 A. Stark, B. L. MacLean and R. D. Singer, *J. Chem. Soc., Dalton Trans.*, 1999, 63.
2 T. Fischer, A. Sethi, T. Welton and J. Woolf, *Tetrahedron Lett.*, 1999, **40**, 793.
3 M. J. Earle, P. B. McCormac and K. R. Seddon, *Chem. Commun.*, 1998, 2245.
4 C. J. Adams, M. J. Earle, G. Roberts and K. R. Seddon, *Chem. Commun.*, 1998,2097.
5 L. C. Simon, J. Dupont and R. F. de Souza, *Appl. Catal. A: Gen.*, 1998, **175**, 215.
6 J. E. L. Dullius, P. A. Z. Suarez, S. Einloft, R. F. de Souza, J. Dupont, J. Fischer and A. DeCian, *Organometallics*, 1998, **17**, 815.
7 Y. Chauvin, H. Olivier, C. N. Wyrvalski, L. C. Simon and R. F. de Souza, *J. Catal.*, 1997, **165**, 275.
8 A. L. Monteiro, F. K. Zinn, R. F. de Souza and J. Dupont, *Tetrahedron*: *Asymmetry*, 1997, **8**, 177.
9 B. Ellis, W. Keim and P. Wasserscheid, *Chem. Commun.*, 1999, 337.
10 W. A. Herrmann and V. P. W. Bohm, *J. Organomet. Chem.*, 1999, **572**, 141.
11 N. Karodia, S. Guise, C. Newlands and J.-A. Andersen, *Chem. Commun.*, 1998, 2341.
12 G. Giambastiani and G. Poli, *J. Org. Chem.*, 1998, **63**, 9608 and references therein.
13 L. S. Hegedus, in *Organometallics in Synthesis*, ed. M. Schlosser, Wiley, Chichester, 1994.
14 R. Kling, D. Sinou, G. Pozzi, A. Choplin, F. Quignard, S. Busch, S. Kainz, D. Koch and W. Leitner, *Tetrahedron Lett.*, 1998, **39**, 9439.

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