

Moisture Stable Ambient Temperature Ionic Liquids: Solvents for the New Millennium. 1. The Heck Reaction

Joshua Howarth* and Andrea Dallas

MOLTEK, School of Chemical Sciences, Dublin City University, Glasnevin, Dublin 9, Ireland
Tel.: +353 1 7045312, Fax: +353 1 7045503, E-mail: howarthj@ccmail.dcu.ie

Received: 24 January 1999; revised form: 8 March 2000 / Accepted: 29 May 2000 / Published: 9 June 2000

Abstract: In this paper we report examples of the Heck reaction in the new moisture stable ambient temperature ionic liquid 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim]PF₆). We have found that the yield of product is comparable with Heck reactions carried out in DMF, the conventional solvent for this reaction, and that the ionic liquid/catalyst mixture can be recycled several times.

Keywords: Ionic liquids; Heck reaction; [bmim]PF₆; [bmim]BF₄.

Introduction

In the early 1970s both Mizoroki [1] and Heck [2] reported the palladium-catalysed arylation of alkenes using aryl bromides and iodides. Since then the reaction has been studied in depth [3] and has been refined to create a useful synthetic method.

The ionic liquids [emim]PF₆ and [emim]BF₄, where [emim]⁺ is the 1-ethyl-3-methyl-imidazolium cation, were first discovered in 1994 and 1992 respectively [4]. The analogous [bmim]PF₆ and [bmim]BF₄ ionic liquids followed shortly after [5]. These liquids have several very interesting properties: they can solvate a wide range of organic and inorganic materials, they are highly polar yet non-coordinating, they are immiscible with a wide range of organic solvents, and they have a nonvolatile nature. It is also possible to vary their immiscibility with water by varying the counter ion, allowing for the possibility of biphasic reactions. Thus, for example, [bmim]PF₆ is water immiscible and [bmim]BF₄ is water miscible.

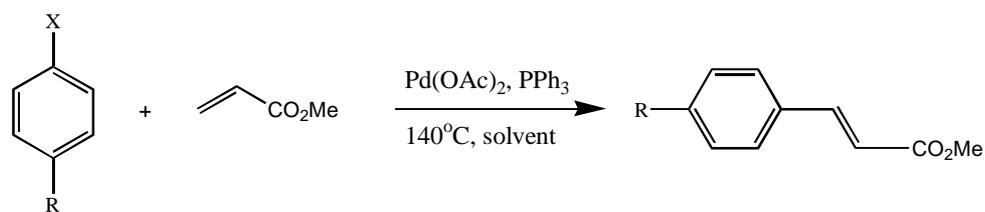
One of the prime concerns of industry and academia is the search for replacements to the environmentally damaging solvents used on a large scale, especially those that are volatile and difficult to contain. Moisture stable ionic liquids, with their unique properties, provide the promise of a credible alternative. As such a rapid growth in the investigation of the [bmim]PF₆ and [bmim]BF₄ type ionic liquids as substitutes for classical solvents is underway.

To date the reactions that have been carried out and investigated in [bmim]PF₆ and [bmim]BF₄ are a simple Diels-Alder reaction between cyclopentadiene and methyl methacrylate [6], *N*-alkylation of indole and *O*-alkylation of 2-naphthol [7], hydrogenations [8], hydroformylation [9], and dimerization of olefins [10]. The Heck reaction has been carried out in tetraalkylammonium and phosphonium bromide molten salts [11] with good yields, and with the catalyst being used again for at least two more runs. However the use of this type of molten salt as a replacement for common solvents is unlikely to come about. We report here the results of the first [12] Heck reactions to be carried out in the new and versatile solvent [bmim]PF₆, a further example of the general application of this type of solvent.

Results and Discussion

We have investigated the simple Heck reaction, Scheme 1 (R = OMe, NO₂, CHO or Cl, X = Br or I), between a number of aryl halides and methyl acrylate, using Pd(OAc)₂/PPh₃ as the catalyst and NaOAc as the base, entries 1-5 in Table 1. We have carried out a comparative study of the reactions in the classical solvent DMF, and the new ionic liquid [bmim]PF₆ at 140°C for 17h. The results for these reactions after addition of water and extraction of the products with diethyl ether from the solvent/water layers are given in Table 1. The products formed in these reactions were exclusively the *E*-isomers. The factors controlling the stereochemistry of the Heck reaction have been previously discussed [13,14]. The reaction did not proceed in the ionic liquid if the temperature was not greater than 130°C.

We found that for entries 1, 2, 3, and 5 we could distill the products under high vacuum directly from the reaction mixture, when [bmim]PF₆ was used as the solvent, and after it had been separated from the aqueous layer. This negates the use of an extraction solvent. Yields for the direct distillation of products are given in brackets, Table 1. Each of the reactions, entries 1-5, involving [bmim]PF₆ were repeated six times using the same ionic liquid/catalyst. We observed that the yield of product for each of these subsequent reactions only varied by a maximum of 4% loss compared to the first run. The yield of product produced in a given reaction when [bmim]PF₆ is used as the solvent tends to be less than when DMF is used. This could be because the reaction conditions have not been optimised, or that the product is reasonable soluble in [bmim]PF₆. There appeared to be negligible leaching of the catalyst from the ionic liquid into the diethyl ether. This was tested by extracting the catalyst containing [bmim]PF₆ six times, after addition of water, with diethyl ether. The six extractions were combined and dried. No evidence for the leaching of the catalyst was found after removal of the solvent. The six aqueous layers were also combined and again no evidence for leaching of the catalyst was found after removal of the water.



Scheme 1.

Table 1.

Entry	Aryl	Product	Solvent	Yield
1			DMF [bmim]PF ₆	35 29 (26)
2			DMF [bmim]PF ₆	76 61 (57)
3			DMF [bmim]PF ₆	95 83 (71)
4			DMF [bmim]PF ₆	70 62
5			DMF [bmim]PF ₆	70 95 (92)

Conclusion

We have shown that the new solvent [bmim]PF₆ can replace DMF in the Heck coupling reaction shown in Scheme 1. Not only are the yields for the reaction in [bmim]PF₆ comparable, but the solvent and catalyst are reusable several times. This has positive environmental and cost implications.

Experimental

General

¹H and ¹³C NMR spectra were obtained using a Bruker Avance 400 NMR and were recorded at 400 and 100 MHz respectively. All reagents and chemicals were obtained from Aldrich Chemical Company (UK) and were used as received unless otherwise noted. The Heck reactions in DMF were carried out in accordance with the procedure laid out by Spencer [15], and the ionic liquid [bmim]PF₆ was synthesised as in reference [5]. The ionic liquid [bmim]PF₆ was dried under high vacuum at 40°C for 48h, and degassed with dry nitrogen for 1h.

General experimental procedure for the Heck reaction in [bmim]PF₆; 4-bromoanisole (Table 1, entry 1)

To a solution of palladium acetate (0.05 mmol, 0.011g, 0.10%) and triphenylphosphine (0.10 mmol, 0.026g, 0.20%) dissolved in anhydrous and degassed [bmim]PF₆ (20 mL), 4-bromoanisole (5 mmol, 0.990g), methyl acrylate (5 mmol, 0.431g), and sodium acetate (6.25 mmol, 0.450g) were added with stirring under argon. The reaction mixture was heated to 140°C for 17h to ensure that the reaction had gone to completion. It was then cooled and poured into water (50 mL). The mixture was (1) extracted with diethyl ether (3 x 70 mL), the combined extracts were dried (MgSO₄), filtered and the solvent was removed *in vacuo*, to yield the crude product. After flash chromatography (R_f 0.6, silica, CH₂Cl₂) the product (entry 1) was obtained; or (2) the water and ionic liquid were separated and the ionic liquid was heated under vacuum (0.8 mmHg) and the product was distilled at 46-48°C.

Distillation of Heck reaction products directly from the ionic liquid was observed for entry 2 at 0.05 mmHg, 52-54°C; for entry 3 at 0.06 mmHg, 65-67°C and for entry 5, at 0.05 mmHg, 70-72°C.

Spectral Data

All spectral data for the compounds synthesised in DMF or [bmim]PF₆ was in agreement with that given in reference [15].

References and Notes

1. Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Japan.* **1971**, *44*, 581.
2. Heck, R. F.; Nolley, J. P. *J. Org. Chem.* **1972**, *37*, 2320.

3. Heck, R. F. *Organic Reactions*; John Wiley and Sons: New York, 1982; Vol. 27, p 345.
4. (a) Wilkes, J. S.; Zaworotko, M. J. *J. Chem. Soc., Chem. Commun.* **1990**, 965; (b) Fuller, J.; Carlin, R. T.; De Long, H. C.; Haworth, D. *J. Chem. Soc., Chem. Commun.* **1994**, 299.
5. (a) Wilkes, J. S.; Levisky, J. A.; Wilson, R. A.; Hussey, C. L. *Inorg. Chem.* **1982**, 21, 1263; (b) Huddleston, J. G.; Willauer, H. D.; Swatloski, R. P.; Visser, A E.; Rogers, R. D. *J. Chem. Soc., Chem. Commun.* **1998**, 1765.
6. Fischer, T.; Sethi, A.; Woolf, J. *Tetrahedron Lett.* **1999**, 40, 793.
7. Earle, M. J.; McCormac, P. B.; Seddon, K. R. *J. Chem. Soc., Chem. Commun.* **1998**, 2245.
8. (a) Chauvin, Y.; Olivier, H. *CHEMTECH* **1995**, 26; (b) Chauvin, Y.; Einloft, S.; Olivier, H. *Ind. Eng. Chem. Res.* **1995**, 34, 1149; (c) Suarez, P. A. Z.; Dullius, J. E. L.; Einloft, S.; De Souza, R. F.; Dupont, J. *Polyhedron* **1996**, 15, 1217; (d) Simon, L. C.; Dupont, J.; De Souza, R.F. *Applied Catalysis A: General* **1998**, 175, 215.
9. Chauvin, Y.; Mussmann, L.; Olivier, H. *Angew. Chem. Int. Ed. Eng.* **1995**, 34, 2698.
10. (a) Kobryanskii, V. M.; Arnautov, S. A. *J. Chem. Soc., Chem. Commun.* **1992**, 727; (b) Arnautov, S. A. *Synth. Metals* **1997**, 84, 295; (c) Goldenberg, L. M.; Osteryoung, R.A. *Synth. Metals* **1994**, 64, 63.
11. Kaufmann, D. E.; Nouroozian, M.; Henze, H. *Synlett* **1996**, 1091.
12. After submission and during revision of this paper the authors became aware of similar work recently published by Carmichael, A. J.; Earle, M. J.; Holbrey, J. D.; McCormac, P. B.; Seddon, K. R. *Org. Lett.* **1999**, 1, 997.
13. Dieck, H. A.; Heck, R. F. *J. Am. Chem. Soc.* **1974**, 96, 1133.
14. Spencer, A. *J. Organomet. Chem.* **1982**, 240, 209.
15. (a) Spencer, A. *J. Organomet. Chem.* **1983**, 258, 101; (b) Newsoroff, G. P.; Sternhell, S. *Aust. J. Chem.* **1968**, 21, 747; (c) De La Mare, P. B. D. *J. Chem. Soc., Perkin Trans., 2* **1973**, 1480; (d) Benhaoua, H.; Piet, J-C.; Danion-Bougot, R.; Toupet, L.; Carrie, R. *Bull. Soc. Chim. Fr.* **1987**, 325; (e) Castells, J. *J. Chem. Soc., Perkin Trans., 1* **1979**, 1; (f) Hanessian, S.; Bennan, Y.; Leblanc, Y. *Heterocycles* **1993**, 35, 1411.

Samples Availability: Not available.