CHEMCOMM
Communication
www.rsc.org/chemcomm

Ultrasound promoted C–C bond formation: Heck reaction at ambient conditions in room temperature ionic liquids

Ravindra R. Deshmukh, R. Rajagopal and K. V. Srinivasan*

Organic Chemistry, Technology Division, National Chemical Laboratory, Pune - 411 008, India.
E-mail: kvsri@dalton.ncl.res.in

Received (in Cambridge, UK) 22nd May 2001, Accepted 27th June 2001
First published as an Advance Article on the web 1st August 2001

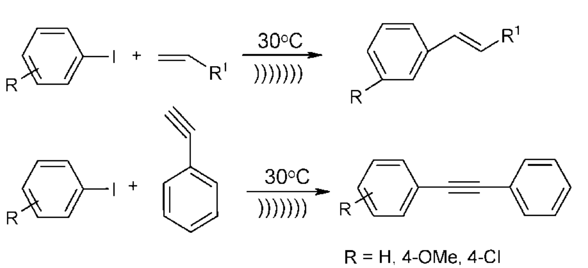
Heck reaction proceeds at ambient temperature (30 °C) with considerably enhanced reaction rate (1.5–3 h) through the formation of Pd–biscarbene complexes and stabilized clusters of zero-valent Pd nanoparticles in ionic liquids under ultrasonic irradiation.

The palladium catalyzed Heck reaction involving the coupling of alkenes/alkynes with aryl and vinyl halides is one of the most powerful tools in synthetic organic chemistry.[1] The reactions which are carried out in polar solvents such as DMF and NMP generally involve long reaction times (8–72 h) at temperatures ranging from 80–140 °C.[2] In recent times, ionic liquids have gained prominence as attractive alternatives to volatile organic solvents for catalytic reactions and separation processes.[3] Heck reaction in ionic liquids, in particular those involving dialkylimidazolium salts, have been reported very recently.[4] However, even in such media, wherein the ionic liquid anion and cation can exert a marked effect on the rate of the reaction, the reaction times involved are 24–72 h at temperatures ranging from 80–100 °C. This communication reports for the first time an ultrasound promoted Heck reaction in ionic liquids at ambient temperature (30 °C) with considerably enhanced reaction rates (reaction times 1.5–3 h) than those reported so far.

The sonochemical reactions were carried out in a thermostated ultrasonic cleaning bath of frequency 50 KHz (Branson 5200). Iodobenzene and substituted iodobenzenes were reacted with various alkenes/phenylacetylene in ionic liquids 1,3-di-*n*-butylimidazolium bromide [$(bbim)^+Br^-$] and 1,3-di-*n*-butylimidazolium tetrafluoroborate [$(bbim)^+BF_4^-$][5] using $Pd(OAc)_2$ as well as $PdCl_2$ as catalyst and sodium acetate as base under ultrasonic irradiation as shown in Fig. 1.

The products could be easily separated from the catalyst by extraction with 10% ethyl acetate in petroleum ether leaving behind the palladium catalyst in the dissolved state in the immiscible ionic liquid. The catalyst thus recovered as a solution in the ionic liquid could be reused at least three times without any loss of activity. Pure products were isolated by column chromatography.

The results are summarized in Table 1. As is evident, the ultrasound assisted Heck reaction of the iodobenzenes with alkenes/alkynes proceeded smoothly at ambient temperature (30 °C) with complete conversion of iodobenzenes in just 1.5–3 h to afford the *trans* products in excellent isolated yields (73–87%). No reaction under similar sonication conditions was observed when the ionic liquid was replaced by molecular solvents such as DMF and NMP even in the presence of a ligand such as PPh_3. The reaction also did not proceed with the less reactive aryl chlorides (chlorobenzene, *p*-nitrochlorobenzene and 2,4-dinitrochlorobenzene) and aryl bromides (bromobenzene) under the sonochemical conditions of the present work. Obviously, no reaction even in traces could be observed under ambient conditions in the absence of ultrasound.



R = H, 4-OMe, 4-Cl
R^1 = COOMe, COOEt, Ph

Fig. 1

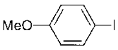
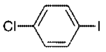
Phosphine ligands, ammonium and phosphonium halides and quarternary ammonium salts have been found to stabilize the Pd-catalysts probably *via* formation of zero-valent Pd species and accelerate the olefination reaction.[6,7] In particular, Pd–carbene complexes with alkylimidazol-2-ylidenes have been reported very recently to be active in the Heck reaction.[4b] In the present work, the formation of such a complex was studied by subjecting a mixture of $Pd(OAc)_2$ or $PdCl_2$ and NaOAc in [bbim] + Br^- and [bbim] + BF_4^- respectively to ultrasound irradiation for 1 h. The complex was extracted into chloroform from the ionic liquid, the chloroform evaporated and the resulting crude product purified by column chromatography [petroleum ether–EtOAc, 1:1]. Indeed, the formation of the complex A was established and characterized by ^{1}H-NMR by the appearance of N–CH vinylic protons at δ 6.85 as a multiplet in the complex similar to the value reported by Xiao *et al.*[4b] and by the conspicuous absence of the N_2CH protons which appears as a singlet at δ 8.82 in the parent ionic liquid. The complexes were also characterized by MS which showed the respective molecular ion peaks. It is highly probable that complex A could be the immediate precursor for the likely active catalyst which could lead to a zero-valent Pd-species whose *in situ* generation by reduction of the divalent Pd–carbene complex is accelerated by electron transfer reactions under the sonochemical conditions primarily through the phenomenon of cavitation. It is well known that sonochemical processes proceed through SET mechanistic pathway by means of formation and adiabatic collapse of transient cavitation bubbles.[8,9] It is also highly probable that the Pd complexes formed *in situ* will experience secondary reactions in the liquid phase after the bubble collapses. Moreover, such Pd carbene complexes have been shown to be the precursors for active catalysts for the Heck and related C–C bond forming reactions in both molecular solvents and ionic liquids.[10–12] Detailed investigation of the mechanistic pathways as regards the formation/decomposition of the Pd–carbene complex under the sonochemical conditions is in progress and will form part of a full paper.

It has long been known that chemical or electrochemical reduction of transition metal salts in the presence of ammonium salts leads to $R_4N^+X^-$ stabilized colloids.[13] A recent study points to the involvement of intermediary colloidal Pd-nanoparticles generated under thermolytic conditions for the catalysis of the Heck reaction.[14] The formation of such Pd-nanoparticles was investigated in the present work by subjecting the reaction mixture, after successful Heck reaction of iodobenzene with ethyl acrylate in $[bbim]^+BF_4^-$ under sonochemical conditions, for '*in situ*' TEM analysis.

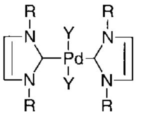
TEM analysis was carried out in Transmission Electron Microscope Model JEOL-1200 EX operated at 100 kV with a magnification of 200 K. The sample after appropriate dilution with isopropyl alcohol was directly deposited on carbon film

DOI: 10.1039/b104532f

Table 1 Heck reaction of iodobenzenes with activated alkenes/alkyne under sonication in $[bbim]^+ Br^-/[bbim]^+ BF_4$[a]

No.	Aryl halide	Olefin/alkyne	Time/h	Product	% Yield[b] (Isolated)
1.		Methyl acrylate	2.0	Methyl cinnamate	81
		Ethyl acrylate	1.5	Ethyl cinnamate	87
		Styrene	1.5	Stilbene	82
		Phenylacetylene	2.0	Diphenylacetylene	78
2.		Methyl acrylate	3.0	4-Methoxymethyl cinnamate	82
		Ethyl acrylate	3.0	4-Methoxyethyl cinnamate	79
		Styrene	3.0	4-Methoxystilbene	80
		Phenylacetylene	2.0	(4-Methoxyphenyl)phenylacetylene	77
3.		Methyl acrylate	1.5	4-Chloromethyl cinnamate	79
		Ethyl acrylate	1.5	4-Chloroethyl cinnamate	77
		Styrene	1.5	4-Chlorostilbene	73
		Phenylacetylene	2.0	(4-Chlorophenyl)phenyl acetylene	78

[a] *Reaction conditions*: a mixture of iodoarene (2 mmol), alkene/alkyne (2.1 mmol), sodium acetate (0.2 g), $Pd(OAc)_2$ (0.02 mmol) and ionic liquid (1.5 ml) sonicated in an atmosphere of argon. [b] Yields are based on iodobenzenes. All the products were *trans* and fully characterized by ^1H-NMR, IR, MS and elementary analysis.



A

R = n-butyl
Y = Br, BF_4

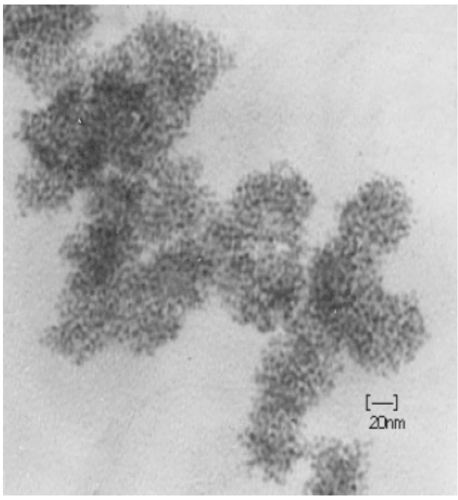


Fig. 2 TEM image of palladium clusters formed in the sonolytic Heck reaction.

coated TEM grids forming a thin film of colloidon. The TEM image (Fig. 2) shows the presence of monodispersed grains nearly spherical in shape. The average size of the grains obtained from the TEM picture is about 20 nm. The porous grains show that they are composed of dispersed particles of approximately 1 nm size. The clusters of Pd^0 nanoparticles in ionic liquids were found to be stable even after storage for a week since no change in the TEM picture was observed after this period, the ionic liquid obviously contributing to the stability. Further work is in progress in investigating the structural details of the nano-assembly of metallic palladium and its dispersion in ionic liquids under sonolytic conditions.

In conclusion, the Heck reaction has been performed at ambient temperature with considerably enhanced reaction rates by the combined use of ultrasonic irradiation and ionic liquids as solvent. Under the sonochemical conditions, the formation of Pd–biscarbene complex as a precursor and its subsequent sonolytic conversion to a highly stabilized cluster of zero-valent Pd nanoparticles has been established by NMR/MS and *in situ* TEM analyses respectively. Further work is in progress to elaborate these findings to other C–C bond formations such as Suzuki and Stille coupling reactions.[6]

R. R. D. and R. R. thank CSIR, New Delhi for the award of a Senior Research Fellowship. We thank Dr M. Bhadbhade and Dr Rajesh Gonnade for help in TEM analysis.

Notes and references

1 (*a*) H. A. Dieck and R. F. Heck, *J. Org. Chem.*, 1975, **40**, 1083; (*b*) T. Jeffery, *J. Chem. Soc., Chem. Commun.*, 1984, 1287.
2 (*a*) J. I. i. Kim, B. A. Patil and R. F. Heck, *J. Org. Chem.*, 1981, **46**, 1067; (*b*) D. D. Bender, I. G. Stakem and R. F. Heck, *J. Org. Chem.*, 1982, **47**, 1278.
3 (*a*) T. Welton, *Chem. Rev.*, 1999, **99**, 2071; (*b*) P. Wasserschied and W. Keim, *Angew. Chem., Int. Ed.*, 2000, **39**, 3772.
4 (*a*) A. J. Carmichael, M. J. Earle, J. D. Holbrey, P. B. McCormac and K. R. Seddon, *Org. Lett.*, 1999, **1**, 997; (*b*) L. Xu, W. Chem and J. Xiao, *Organometallics*, 2000, **19**, 1123.
5 $[bbim]^+ Br^-$ was prepared by heating 1-butylimidazole with 1-bromobutane at 70 °C for 2 h and distilling off excess 1-bromobutane under high vacuum to afford a thick brownish yellow liquid having density, 1.228 g cm^{-3}. $[bbim]^+ BF_4^-$ was obtained by the metathesis of $[bbim]^+ Br^-$ with $NaBF_4$ in water to give a pale yellow free flowing liquid having density, 1.152 g cm^{-3}. Both the ionic liquids were well characterized by IR, ^1H and ^{13}C NMR, and elemental analysis.
6 (*a*) S. Brase and A. de Meijere, *Metal catalyzed cross coupling reactions*, ed. F. Diederich and P. J. Stang, Wiley-VCH, Chichester, 1998; (*b*) J. Tsuji, *Palladium Reagents and Catalyst-Innovations in Organic Synthesis*, Wiley, Chichester, 1995.
7 (*a*) T. Jeffery, *Tetrahedron Lett.*, 1985, **26**, 2267; (*b*) C. Amatore, M. Azzahi and A. J. Juand, *J. Am. Chem. Soc.*, 1991, **113**, 8375.
8 J. L. Luche, *Ultrasonics*, 1992, **30**, 156.
9 A. Henglein, *Advances in Sonochemistry*, ed. T. J. Mason, JAI Press, London and Greenwich, 1993, vol. 3, pp. 17–83.
10 W. A. Herrmann and C. Kocher, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2163.
11 W. A. Herrmann, V. P. W. Bohm and C. J. Reisinger, *J. Organomet. Chem.*, 1999, **576**, 23.
12 C. Zhang, J. Huang, M. L. Trudell and S. P. Nolan, *J. Org. Chem.*, 1999, **64**, 3804.
13 (*a*) H. Bonnemann, W. Brijoux, R. Brinkmann, E. Dinjus, T. Joussen and B. Korall, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 1312; (*b*) M. T. Reetz and S. A. Quaiser, *Angew. Chem., Int. Ed.*, 1995, **34**, 2240.
14 M. T. Reetz and E. Westermann, *Angew. Chem., Int. Ed.*, 2000, **39**, 165.