Contents lists available at SciVerse ScienceDirect







journal homepage: www.elsevier.com/locate/apcata

Effect of chiral ionic liquids on palladium-catalyzed Heck arylation of 2,3-dihydrofuran

Rafał Roszak^{a,b}, Anna M. Trzeciak^{a,*}, Juliusz Pernak^c, Nina Borucka^c

^a University of Wrocław, Faculty of Chemistry, 14 F. Joliot-Curie St., 50-383 Wrocław, Poland

^b Wrocław University of Technology, Institute of Physical and Theoretical Chemistry, Wybrzeże Wyspiańskiego 27, 50-370 Wrocław, Poland

^c Poznań University of Technology, Department of Chemical Tehnology, pl. M. Skłodowskiej-Curie 2, 60-965 Poznań, Poland

ARTICLE INFO

Article history: Received 30 July 2011 Received in revised form 25 September 2011 Accepted 29 September 2011 Available online 6 October 2011

Keywords: Homogeneous catalysis Palladium Heck reaction Asymmetric catalysis Ionic liquids

1. Introduction

The Heck coupling is one of the most important C–C bond forming reactions [1] with many applications such as the synthesis of heterocyclic compounds [2] or total synthesis of natural products [3]. Typically, this reaction involves monosubstituted olefin and aryl halide in the presence of a base and a palladium compound as a catalyst precursor. In the case of olefins bearing electron-withdrawing substituents (EWG, e.g. –COOR, –CN), reaction selectivity is controlled by two factors: electronic, which causes arylation in the β -position to the EWG, and steric, which facilitates the formation of the trans product. Consequently, the formation of 1,2-trans-disubstituted olefin is preferred. The arylation of an electron-reach olefin, such as an olefin with the –OR group, can produce 1,2-trans or 1,1-branched products. In the latter case, selectivity can be controlled by the solvent or other factors [4].

The Heck coupling involving an olefin bearing a hydrogen atom in the allylic position can be accompanied by migration of the carbon–carbon double bond leading to the formation of a product with a chiral carbon atom. Reactions of this type have been intensively investigated in four variants with respect to the kind of substrate used: (i) arylation of allylic alcohols where double bond

ABSTRACT

It is demonstrated that a relatively small amount of IL (IL = ionic liquid) can dramatically affect conversion in the Heck arylation of 2,3-dihydrofuran with iodobenzene, catalyzed by $Pd(OAc)_2$ in DMF as a solvent. In all reactions, 2-phenyl-2,3-dihydrofuran (**3**) was obtained as the main product, and conversion increased even up to 10 times when pyridinium salts with 1-butyl-4-methylpyridinium cation were applied. In a 1:1 mixture of DMF and H₂O as solvent, the addition of ILs led to a remarkable deactivation of the catalyst, and this effect was most visible in the presence of imidazolium salts containing a 1-butyl-3methylimidazolium cation. The influence of the anionic part of ILs on the reaction course was tested using a series of morpholinium salts and, depending on the anion, conversion varied from 0.4% to even 100%. When morpholinium salts with chiral anions were used, e.e. values of up to 10% were obtained, which is the highest value for the Heck reaction involving IL as a chirality source.

© 2011 Elsevier B.V. All rights reserved.

migration resulted in the formation of carbonyl products [5]; (ii) arylation of other linear olefins [6]; (iii) arylation of cyclic olefins including ring-closing Heck coupling [7]; (iv) arylation of heterocyclic olefins.

As a model Heck reaction of cyclic olefin containing a heteroatom, primarily 2,3-dihydrofuran (DHF) was tested. Arylation of DHF occurred exclusively at the C2 position (Fig. 1); however, due to carbon–carbon double bond migration, three products, namely **2**, **3** and **4**, can be formed. Arylation of DHF performed in the presence of a palladium catalyst containing a phosphorous ligand can lead selectively to 2-aryl-2,5-dihydrofuran (**2**) or 2-aryl-2,3-dihydrofuran (**3**), depending on the kind of ligand used. Monodentate phosphorous ligands [8] and bidentate ligands with P–N [9], P–As [10], P–S [11], or P–O [12] donor atoms gave predominantly product **2**. In contrast, when palladium complexes with bidentate P–P ligands [13] were used, **3** was formed as the main reaction product [14]. However reversed selectivity was also noted [14].

Compounds **2** and **3** possess chiral centers on tertiary carbon atoms, and, consequently, they can be obtained as nonracemic mixtures. The stereoselective version of the Heck reaction was intensively tested with various phosphorous ligands [15].

Due to economical and environmental factors, P-free catalytic systems have been attracting increasing interest. Several P-free catalysts for the Heck reaction of DHF have been reported [16], and the most promising one was the application of "Jeffery conditions"

^{*} Corresponding author. Tel.: +48 71 3757253; fax: +48 71 3282348. *E-mail address*: anna.trzeciak@chem.uni.wroc.pl (A.M. Trzeciak).

⁰⁹²⁶⁻⁸⁶⁰X/\$ - see front matter © 2011 Elsevier B.V. All rights reserved. doi:10.1016/j.apcata.2011.09.038

which made it possible to selectively obtain product **2** or **3**. When performed in the presence of $[Bu_4N]OAc$, the reaction led mainly to **2** with the ratio of **3** to **2** amounting to up to 3:97, whereas when $[Bu_4N]Cl$ was applied, product **3** dominated with the ratio of **3** to **2** amounting to up to 92:8 [16d].

To the best of our knowledge only one example of a Heck reaction of DHF designed to obtain chiral products under P-free conditions has been reported [17]. In that reaction, involving a chiral 2-[4-alkyl-4,5-dihydro-1,3-oxazol-2-yl]pyridine bidentate ligand, a mixture of both products **2** and **3** was obtained, (the ratio of **3** to **2** was in the range 0.76–2.56) with e.e. up to 29% for compound **2** and up to 60% for product **3**.

Another approach to performing the Heck coupling in a stereoselective fashion involves the application of chiral ionic liquids (CIL). A recent review [18] surveys the latest most representative developments and the progress concerning ILs from their fundamental properties to applications in catalytic processes.

Chiral ionic liquids represent one of the most interesting groups of ionic liquids, and the number of publications dealing with CILs has been growing rapidly [19–23]. Recently, the synthesis of CILs directly from a natural (1R,2S,5R)-(–)-menthol-based chiral pool has been described [24].

The source of chirality can be provided either on the anion or on the cation or on both the anion and the cation. However, the most common chiral anions used are natural aminoacids [25,26]. CILs can be applied in asymmetric catalysis (e.g. aldol reaction, Baylis–Hillman reaction or the Michael addition reaction) [27]. In a case of metal mediated catalysis, CILs are used mainly in double bond addition reactions as a chirality source [28] or as a "chiral booster" for classic chiral ligands [29].

There are only three reports about application of CILs in the Heck coupling. Gayet et al. [30] reported the arylation of DHF with iodobenzene catalyzed by a chiral pyridinium IL with $[PdCl_4]^{2-}$ as a counterion in $[BMIM]PF_6$ medium; however, no enantiomeric excess was observed. Two other examples of Heck-type arylation involving CILs are the oxyarylation of 7-benzyloxy-2H-chromene [31], which gave a desirable product with 5% e.e., and the arylation of aza-endocyclic acrylate [32] in various imidazolium and pyridinium CILs, which produce only racemic mixtures.

In this paper, we present the first stereoselective Heck coupling performed in the presence of CILs with stereogenic centers present in the anionic part of the CIL. In particular, morpholinium based CILs were studied. The increasing interest in studies of ILs containing morpholinium cations is related to their characteristic structure and, especially, the presence of nitrogen and oxygen atoms, which are responsible for their unique properties. Morpholinium ILs have found application as electrolytes [33] and gel electrolytes [34], ionic liquid crystals (ILC), a class of liquid-crystalline compounds [35], and reaction medium [36]. In particular, ILs based on the morpholinium cation are favored because of their electrochemical stability [37]. Morpholinium ILs are, in fact, less toxic than commonly used imidazolium-, pyridinium-, or tetraalkylammonium-based ILs [38].

2. Results and discussion

The arylation of DHF with iodobenzene was performed with $Pd(OAc)_2$ as a catalyst precursor, and first the effect of the solvent and the base on the reaction course was studied. The preliminary results showed that DMF and a DMF/H₂O mixture (1:1) were the most suitable for our system, and the highest conversions were obtained using cesium and potassium carbonates as bases. Next, the effect of ILs was investigated, and imidazolium and pyridinium ILs used in these studies are presented in Fig. 2.



Fig. 1. Heck cross-coupling of 2,3-dihydrofuran with iodobenzene.

Imidazolium IL (5)			R1 N $R3$ $R2$ $R3$		
IL	R1	R2	R3	Х	
5a	Bu	Н	Me	BF ₄	
5b	Bu	Η	Me	PF_6	
5c	Bu	Η	Me	Cl	
5d	Bu	Η	Me	Br	
5e	Et	Н	Me	EtSO ₃	
5 f	Et	Η	Me	Me(OEt) ₂ OSO ₃	
5g	octyl	Н	Me	BF_4	
5h	Me	Me	C_2H_4OH	Cl	
Pyridinium IL (6)			Me	eBu X-	
6a				BF ₄	
6b				PF ₆	
6c				Cl	
6d				Br	

Fig. 2. Imidazolium and pyridinium ILs.

In a reference reaction performed in a DMF/H_2O mixture without an IL, 27% of cross-coupling products were obtained.

The effect of the IL amount on the course of the Heck arylation in this solvent was tested with two imidazolium ILs, namely 1butyl-3-methylimidazolium salts, **5a** and **5c**, with different anions (Fig. 3). It could be expected that **5c**, which contained a coordinating Cl⁻ counterion, could easily form a Pd-carbene complex, whereas **5a** could exhibit a much weaker tendency to form a Pd-carbene complex [39]. However, actually both of the imidazolium salts acted



Fig. 3. Effect of the IL/Pd ratio on conversion in the Heck cross-coupling of DHF with PhI.

Selectivity 3/(2+4)

Table 1 Heck arylation of DHF in DMF/H2O with various ILs.			
IL	Conversion (%)		
_	27.0		

-	27.0	5.4
5a	34.0	5.0
5b	21.4	5.3
5c	25.1	4.7
5d	22.5	7.7
5e	8.0	1.9
5h	27.2	4.1
5f	2.5	0.9
5g	10.7	3.5
6d	12.8	6.5
6a	20.4	4.1
6b	18.4	3.9
6c	19.5	4.6
71	21.2	3.8
7f	30.1	4.6

Reaction conditions: 8 mg Pd(OAc)₂; 0.4 mL PhI; 0.7 mL DHF; 0.6 g K₂CO₃; 2 h; 60 °C; IL/Pd = 20, solvent: DMF:H₂O 3 mL: 3 mL; 0.15 mL mesitylene (GC standard).

very similarly; namely, in both cases the addition of a small amount of an IL slightly increased reaction conversion compared with the reaction performed without an IL. However, further increase of the IL amount, up to IL-to-Pd of *ca.* 30, caused a dramatic deactivation of the system (Fig. 3). As the highest conversion was obtained with **5a** at an IL/Pd ratio of 20, we tested a broad range of different ILs under these conditions, and the results are presented in Table 1 (Table 1).

In the best case, conversion of up to 34% was achieved, and the highest selectivity was 7.7. In most cases, the conversion to cross-coupling products was lower than in the absence of ILs.

To obtain more information about the kinetics of the reactions studied, additional experiments were carried out for two selected systems containing **5a** and **5d**, respectively. As can be concluded from the data presented in Fig. 4, a reaction started without any induction period with the highest rate noted in the first 30 min.

Interestingly, extension of the reaction time to 4 h made it possible to obtain higher conversions, 31% and 40% in the presence of **5d** and **5a**, respectively. At the same time, regioselectivity expressed as [3/(2+4)] ratio, decreased in reaction with **5a** and increased only slightly in reaction with **5d** (Fig. 5).

In further studies, DMF was used as solvent instead of a DMF/H₂O mixture. Under these conditions, the conversion of DHF in the absence of an IL was only 23.5%. The effect of imidazolium **(5)**, pyridinium **(6)**, and morpholinium **(7)** salts on the Heck arylation of DHF shown in Fig. 6 is much more pronounced than in DMF/H₂O. Thus, a remarkable increase in conversion, up to 83%, was obtained when pyridinium salts **(6)** were used. In contrast, imidazolium salts



Fig. 4. Heck reaction over time.



Fig. 5. Regioselectivity [(3/(2+4)] of the Heck reaction over time.

(5) caused catalyst deactivation. It can also be concluded that the effect of the anion seems to be less important in this case.

It is worth to note that in the Heck reaction performed in DMF/H₂O only a very small effect of ILs on the DHF conversion was observed, in contrast to reactions performed in pure DMF. Conversion of DHF in DMF/H2O remainded on the level of 30%, similarly as in the absence of ILs (Table 1). Most probably, the presence of water facilitated deactivation of the catalyst with formation of inactive "palladium black". Reduction of Pd(II) to Pd(0) is generally expected under basic conditions [40]. There is an important step of the catalytic reaction, however in the absence of efficient stabilization "palladium black" can be formed easily. In the absence of water, DMF, strong donor solvent, stabilizes better a coordinatively unsaturated Pd(0) species preventing their agglomeration. The higher activity of palladium in the presence of pyridinium salts can be related to the formation of more active ionic species of the type $Pd(0)L_2(OAc)^-$ [43b], while imidazolium salts can form Pd-carbene complexes, less active under these conditions.



Fig. 6. Effect of the IL/Pd ratio on conversion in the Heck cross-coupling of DHF with PhI.



Fig. 7. Effect of the 6a/Pd ratio on conversion in the Heck cross-coupling of DHF with PhI.

Therefore, we chose **6a** for further studies of the influence of IL concentration on the Heck arylation (Fig. 7). Conversion to the Heck product with 1 mol% of Pd(OAc)₂ in DMF increased from 23.5% (without an IL) to 91% at IL/Pd = 80 which corresponded to a concentration of **6a** equal to 0.39 mol/dm³. The effect of the IL amount is even more visible at lower catalyst loading, and in reactions performed with 0.1 mol% of Pd, conversion increased from 6% (reaction without an IL) to 73% at IL/Pd = 800 (reaction with **6a** concentration of 0.39 mol/dm³). A reverse tendency, namely a decrease in conversion with increasing [**6a**]:[Pd] ratio, was observed in DMF/H₂O. This shows again that DMF/H₂O is not an appropriate solvent for the Heck reaction with imidazolium and pyridinium ILs. However, when pure **6a**, without DMF, was used as solvent, conversion was only 30% (for 1 mol% of Pd).

It has been suspected [41] that the anionic part of the IL can play an important role in the Heck arylation, so to study such an effect, a series of morpholinium salts was prepared (Fig. 8).

As shown in Table 2, thermal stability of morpholinium ILs depends on chiral anion. The most stable CILs contained anion **7k** and **7j** and their decomposition started about 200 °C. The less stable was compound with anion **7f** decomposed at 104 °C. For four morpholinium CILs the second step of decomposition was observed, for **7g** at 232 °C (39% mass loss), **7h** at 238 °C (43.4% mass loss), **7i** at 239 °C (41.9% mass loss) and for **7l** at 214 °C (31.2% mass loss). A

Table 2

4-Benzyl-4-methylmorpholinium ILs ([Bmorf][A]), thermal stability and phase transition.

A =	T_{g}^{a} (°C)	$T_{\text{onset}(5\%)}^{\text{b}}$ (°C)	$T_{\text{onset}}^{c}(^{\circ}C)$	$T_1^{\mathbf{d}} (^{\circ} \mathbf{C})$
7f	-31.42	104	210	-
7g	-27.85	170	249	232(39)
7ĥ	-40.53	132	250	238(43.4)
7i	-38.20	142	268	239(41.9)
7j	-25.50	196	272	
7k	-24.77	200	276	-
71	-17.73	114	274	214(31.2)
7m	-	156	232	
7n	-40.43	107	250	-

^a Glass transition temp determined by DSC.

^b Decomposition temp determined from onset to 5 wt% mass loss.

^c Decomposition temp determined from onset to 50% mass loss.

^d Second step decomposition (in parenthesis decomposition in percent).

 Table 3

 Heck arylation of DHF in DMF with various [Bmorf][A] salts.

<i>A</i> =	Conversion [%]	Selectivity $[3/(2+4)]$	e.e. of 3 (%)	e.e. of 2 (%)
7a	19.6	5.7	-	-
7b	20.4	4.2	-	-
7c	29.2	5.7	-	-
7d	35.8	5.1	-	-
7e	35.6	4.1	-	-
7n	0.4	-	<4.0	<4.0
7m	16.3	6.0	9.9	<4.0
7h	63.2	3.3	5.8	<4.0
7i	67.3	3.1	<4.0	<4.0
7k	70.8	3.7	6.0	<4.0
7 o	71.7	2.7	<4.0	<4.0
71	99.3	1.9	<4.0	<4.0
7f	100.0	2.4	4.0	4.2
80	80.2	2.7	<4.0	17.3

Reaction conditions: 8 mg Pd(OAc)₂; 0.4 mL PhI; 0.15 mL mesitylene; 0.7 mL DHF; 0.6 g K₂CO₃; 2 h; 70 °C; IL/Pd = 20, solvent: DMF 6 mL; **80** – dimethyldidodecylammonium (*S*)-lactate.

glass transition was found almost for all compounds, with the only exception of **7m**. For all studied CILs any phase transitions (crystallization temperature and melting point) were noticed, however a wide liquid range (difference between glass transition $-T_g$ and thermal degradation $-T_{onset(5\%)}$) was observed, even 300 °C or more as for CILs **7j** and **7i**, respectively.

The yield of the Heck reaction performed in DMF with morpholinium salts containing inorganic anions varied from 19.6% for the Cl⁻ anion (**7a**) to 35.8% for the BF_4^- anion (**7d**), whereas selectivity ranged from 4.2 (for 7b) to 5.7 (for 7a and 7c) (Table 3). In the case of morpholinium ILs with organic anions, the anion effect was even more clearly seen. When 4-hydroxyproline anion, **7n**, was applied, only traces of the product were obtained, whereas with benzyloxypropionate, 7l, or methylnitromethyloxocyclopentaneacetate, 7f, anion conversion was almost quantitative. In reaction with **7m** (morpholinium quinate), the products were obtained with significantly lower yields than in reactions with inorganic morpholinium salts, whereas all other ILs with organic anions gave products with yields that were approximately three times higher. The selectivity of reactions with morpholinium salts containing organic anions, equal to 1.9-3.7, was generally lower than with those containing inorganic anions. However, exceptionally, the reaction proceeding with **7m** gave product **3** with higher selectivity than all the other morpholinium ILs tested.

The stereoselective Heck coupling of DHF with iodobenzene has to the best of our knowledge not been reported in the literature. In the typical procedure applied for the Heck arylation of DHF, phenyl triflate was used. However, the main disadvantage of this procedure is the easy hydrolysis of triflate, limiting its application in the presence of water. Thus, iodobenzene is a cheaper and more easily available substrate. Table 3 summarizes the data, illustrating the effect of anions present in morpholinium salts on the yield and selectivity of the coupling reaction. The obtained e.e. values were up to 9.9% for 7m; lower e.e. values were obtained for 7h and 7k (nearly 6.0%), whereas for 7f, e.e. was equal 4.0%. For all other CILs, e.e. values below 4.0% were noted. These values are lower compared with results obtained with phosphorus ligands; however, they are higher than those obtained in reactions proceeding in CILs with chiral cations. Interestingly, the highest e.e. value, 17.3, for side-product 2, was obtained with the application of tetraalkylammonium salt **80** with a (S)-lactate anion. It is worth noting the influence of the type of cation on reaction stereoselectivity, which is clearly seen when the results obtained with 70 and **80** are compared.

The proposed mechanism of the Heck reaction, inspired by the literature [42], is presented in Fig. 9. After the oxidative addition of aryl halidate to palladium, there are two possible routes, starting



Fig. 8. Morpholinium ILs used in the Heck reaction.

from the **B1** or the **B2** intermediate respectively. The anionic part of ILs can play an important role in the **B1–B2** equilibrium and, in particular, carboxylate anions can compete with halide X^- (originating from ArX or from IL) for a place in the coordination sphere of palladium. Consequently, a halide-free pathway can be considered, as shown in the left cycle in Fig. 9.

The reactivity of **B**-type intermediates depends on the type of ligand rather than on the charge of the complex, and the relative activity of these complexes, as described by Amatore [43], decreased in the order ArPdL₂OAc > ArPdL₂⁺ > ArPdL₂I. Therefore, promotion of the halide-free pathway should cause higher conversion.



Fig. 9. The proposed mechanism of Heck reaction.

In fact, the yields of reactions involving morpholinium salts with carboxylate anions were around twice as high as those with noncoordinating BF_4 or PF_6 anions. An exceptionally low yield was observed for **7m** and **7n** containing a carboxylic group directly linked to a bulky substituent. In this case, the ability of the anion to coordinate to palladium can be limited by the steric hindrance.

In the case of phosphorus-free Heck arylation, as in the system under study, the mechanism involving Pd(0) nanoparticles is commonly accepted [44]. Consequently, the role of the IL as a stabilizing agent for nanoparticles preventing their agglomeration should be considered. The surface of palladium(0) nanoparticles can be negatively charged [45], and therefore the cationic part of the IL can play a decisive role in electrostatic interaction. Accordingly, a strong influence of the cation on the reaction course was observed in a series of imidazolium, pyridinium, and morpholinium salts.

3. Conclusions

The Heck cross-coupling reaction of iodobenzene with 2,3dihydrofuran, catalyzed by $Pd(OAc)_2$ in the absence of ionic liquids, gives the highest conversion in DMF/water mixture as a solvent. The addition of a small amount of ILs leads to a significant increase in conversion, but only in absence of water.

ILs have a very strong effect on the catalytic reaction conversion, depending on their composition. The strongest promoting effect was observed when pyridinium salts were applied, whereas imidazolium salts caused deactivation of the catalyst. The effect of the anionic part of ILs on the reaction conversion seems to be even more significant. We suggest that reaction pathway leading to the higher DHF conversion proceeds according to the left part of the scheme presented on Fig. 9, with participation of Pd-carboxylate intermediates. With only two exceptions, namely **7n** and **7m**, in the presence of ILs containing carboxylate functionalized anion, the DHF conversion was higher than with non-carboxylate type anions. An important effect of anions on the reactivity of anionic Pd(0) complexes in Heck reaction was also demonstrated by Amatore et al. [43,46].

In order to explain an observed effect of the cations on the reaction course we propose to consider interactions of the *in situ* formed Pd(0) nanoparticles with cationic part of IL, according to the model described in the literature [45]. Important role of such interactions in the formation of new palladium species on the surface of Pd(0) nanoparticles was also discussed in [47]. Alternatively, the formation of discrete supramolecular species of the type $[(cation)_x(X)_{x-n}]^{n+}$ [$(cation)_{x-n}(X)_x$]^{*n*-} on the surface of Pd(0) nanoparticles can be considered [48]. Most probably, both forms, namely monomolecular palladium complexes and palladium nanoparticles, participate in the catalytic process; however, details of the mechanism are not clear yet

Reactions with morpholinium salts containing chiral anions exhibited asymmetric induction, which confirmed an efficient interaction of the anionic part of CILs with palladium intermediate. The obtained e.e. values are up to 10% which is the highest value for Heck arylation in CILs. On the basis of the obtained results, we believe that tuning the anionic part of the CIL, in contrast to tuning the cationic part, is a much more efficient way to receive a chiral product in Heck arylation.

4. Experimental

4.1. Materials

4-Methylmorpholine, benzyl chloride, potassium hydroxide, ((1*S*-(1 β ,2 α ,3 β)-(+)-3-methyl-2-(nitromethyl)-5-oxocyclopentaneacetic acid, (*S*)-(+)-mandelic acid, (*R*)-(-)-mandelic acid, (*R*)-(-)-3-chloromandelic acid, (*S*)-(-)-2-bromo-3-methylbutyric acid, (*R*)-(-)-quinic acid were obtained from Aldrich and used without further purification. (R)-(+)-2-(Benzyloxy)propionic acid and (2S, 4R)-4-hydroxypyrrolidine-2-carboxylic acid were obtained from Fluka. All solvents were used as obtained without further purification.

Synthesis of 4-benzyl-4-methylmorpholinium nitrate(V), tetrafluoroborate and hexafluorophosphate have been recently described [49].

4.2. Synthesis of 4-benzyl-4-methylmorpholinium ionic liquids

4-Benzyl-4-methylmorpholinium chloride was synthesized by treating 4-methylmorpholine with benzyl chloride. Morpholinium ionic liquids with anions 7f - 7l were synthesized by adding appropriate chiral carboxylic acid (0.015 mol) to portion of 4-benzyl-4-methylmorpholinium chloride (0.015 mol) and a stoichiometric amount of potassium hydroxide dissolved in methanol. The solution was stirred at room temperature for 1 h and then filtrated to remove the precipitated potassium chloride. After evaporation of methanol, the product was dissolved in acetone and the rest of inorganic salt was removed. The final product was dried in vacuum at 45 °C for 2 h.

Two ILs, with anions **7m** and **7n**, were obtained in the similar procedure, only after evaporation of methanol the product was dissolved in acetone and methanol (1:1) mixture and the rest of inorganic salt was removed. The final product was dried in vacuum at 45 °C for 2 h.

¹H NMR spectra were recorded on the Mercury Gemini 300 spectrometer operating at 300 MHz with TMS as the internal standard. ¹³C NMR spectra were obtained with the same instrument at 75 MHz. CHN elemental analyses were performed at the Adam Mickiewicz University, Poznan (Poland).

4-Benzyl-4-methylmorpholinium $((1S-(1\beta,2\alpha,3\beta)-(+)-3-methyl-2-(nitromethyl)-5-oxocyclopentaneacetate,$

[BMmorf][**7f**] ¹H NMR (DMSO- d_6) δ ppm 1.03 (d, J=3.11 Hz, 3H); 2.00 (m, 3H); 2.35 (m, 2H); 2.61 (d, J=7.88 Hz, 2H); 3.10 (s, 3H); 3.39 (t, J=4.21 Hz, 2H); 3.55 (qw, J=4.94 Hz, 2H); 3.97 (t,J=1.59 Hz, 4H); 4.71 (d, J=8.42 Hz, 2H); 4.79 (s, 2H); 7.52 (m, 3H); 7.61 (m, 2H); ¹³C NMR (DMSO- d_6) δ ppm 18.1; 33.1; 36.6; 44.8; 45.8; 46.5; 50.4; 58.4; 59.9; 67.5; 78.1; 127.4; 128.8; 130.3; 133.4; 172.9; 216.8.

Elemental analysis calc. (%) for C₂₁H₃₀N₂O₆ (406.47): C 62.05, H 7.44, N 6.89. Found: C 62.55, H 7.79, N 6.11.

4-Benzyl-4-methylmorpholinium (*S*)-(+)-mandelate, [BMmorf][**7g**], ¹H NMR (DMSO- d_6) δ ppm 3.02 (s, 3H); 3.30 (t, *J*=4.29 Hz, 2H); 3.51 (qw, *J*=5.02 Hz, 2H); 3.93 (t, *J*=2.57 Hz, 4H); 4.10 (s, 1H); 4.46 (s, 1H); 4.70 (s, 2H); 7.20 (m, 3H); 7.35 (m, 2H); 7.51 (m, 3H); 7.54 (m, 2H); ¹³C NMR (DMSO- d_6) δ ppm 44.7; 58.4; 59.8; 67.5; 73.6; 125.8; 126.2; 127.22; 127.25 128.8; 130.3; 133.3; 144.3; 173.6.

Elemental analysis calc. (%) for C₂₀H₂₅NO₄ (343.41): C 69.95, H 7.34, N 4.08. Found: C 70.46, H 6.78, N 4.64.

4-Benzyl-4-methylmorpholinium (*R*)-(-)-mandelate, [BMmorf][**7h**], ¹H NMR (DMSO- d_6) δ ppm 2.07 (s, 1H); 3.02 (s, 3H); 3.31 (t, *J*=4.27 Hz, 2H); 3.51 (qw, *J*=5.05 Hz, 2H); 3.93 (t, *J*=1.71 Hz, 4H); 4.54 (s, 1H); 4.70 (s, 2H); 7.22 (m, 3H); 7.37 (m, 2H); 7.52 (m, 3H); 7.55 (m, 2H); ¹³C NMR (DMSO- d_6) δ ppm 44.8; 58.4; 59.9; 67.6; 73.5; 126.0; 126.3; 127.2; 127.3; 128.9; 130.3; 133.3; 143.9; 173.9.

Elemental analysis calc. (%) for C₂₀H₂₅NO₄ (343.41): C 69.95, H 7.34, N 4.08. Found: C 69.51, H 7.84, N 3.69.

4-Benzyl-4-methylmorpholinium (*R*)-(–)-**3-chloromandelate**, [BMmorf][**7i**], ¹H NMR (DMSO- d_6) δ ppm 3.05 (s, 3H); 3.33 (t, *J* = 4.27 Hz, 2H); 3.53 (qw, *J* = 5.13 Hz, 2H); 3.95 (t, *J* = 1.77 Hz, 4H); 4.51 (s, 2H); 4.72 (s, 2H); 7.20 (t, *J* = 1.16 Hz, 1H); 7.25 (s, 1H) 7.34 (d, *J* = 0.64 Hz, 1H); 7.40 (d, *J* = 0.82 Hz, 1H); 7.52 (m, 3H); 7.55 (m, 2H); ¹³C NMR (DMSO- d_6) δ ppm 44.7; 58.4; 59.8; 67.5; 72.8; 124.8; 125.7; 125.8; 127.2; 128.9; 129.1; 130.3; 132.1; 133.2; 146.6; 172.8.

Elemental analysis calc. (%) for C₂₀H₂₄ClNO₄ (377.86): C 63.57, H 6.40, N 3.71. Found: C 63.93, H 6.02, N 3.99.

4-Benzyl-4-methylmorpholinium (*S*)-(–)-2-bromo-3methylbutyrate, [BMmorf][**7**]], ¹H NMR (DMSO- d_6) δ ppm 1.02 (d, *J* = 1.28 Hz, 6H); 2.19 (m, 1H); 3.13 (s, 3H); 3.40 (t, *J* = 4.21 Hz, 2H); 3.59 (qw, *J* = 5.20 Hz, 2H); 4.00 (t, *J* = 1.65 Hz, 4H); 4.68 (d, *J* = 1.92 Hz, 1H); 4.85 (s, 2H); 7.54 (m, 3H); 7.62 (m, 2H); ¹³C NMR (DMSO- d_6) δ ppm 19.0; 31.7; 44.9; 55.4; 58.4; 59.8; 67.2; 127.3; 128.8; 130.3; 133.2; 170.2.

Elemental analysis calc. (%) for C₁₇H₂₆BrNO₃ (372.29): C 54.84, H 7.06, N 3.76. Found: C 54.33, H 6.75, N 4.18.

4-Benzyl-4-methylmorpholinium (*R*)-(+)-2-bromo-3methylbutyrate, [BMmorf][7k] ¹H NMR (DMSO- d_6) δ ppm 1.02 (d, *J* = 1.10 Hz, 6H); 2.19 (m, 1H); 3.14 (s, 3H); 3.40 (t, *J* = 4.27 Hz, 2H); 3.60 (qw, *J* = 5.20 Hz, 2H); 4.00 (t, *J* = 1.71 Hz, 4H); 4.65 (d, *J* = 1.83 Hz, 1H); 4.86 (s, 2H); 7.54 (m, 3H); 7.63 (m, 2H); ¹³C NMR (DMSO- d_6) δ ppm 19.2; 31.7; 44.8; 55.7; 58.4; 59.8; 67.2; 127.3; 128.8; 130.3; 133.2; 170.3.

Elemental analysis calc. (%) for C₁₇H₂₆BrNO₃ (372.29): C 54.84, H 7.04, N 3.76. Found: C 55.27, H 7.52, N 3.07.

4-Benzyl-4-methylmorpholinium (*R*)-(+)-2-(benzyloxy)propionate, [BMmorf][7I] ¹H NMR (DMSO- d_6) δ ppm 1.21 (d, *J*=3.39 Hz, 3H); 3.11 (s, 3H); 3.39 (t, *J*=4.27 Hz, 2H); 3.59 (qw, *J*=5.24 Hz, 2H); 3.65 (kw, *J*=5.04 Hz, 1H); 3.96 (t, *J*=1.65 Hz, 4H); 4.61 (s, 2H); 4.82 (s, 2H); 7.31 (m, 5H); 7.52 (m, 3H); 7.61 (m, 2H); ¹³C NMR (DMSO- d_6) δ ppm 19.5; 44.7; 58.3; 59.9; 67.4; 69.8; 76.6; 126.8; 127.3; 127.4; 128.0; 128.8; 130.2; 133.3; 139.7; 174.8.

Elemental analysis calc. (%) for C₂₂H₂₉NO₄ (371.47): C 71.13, H 7.87, N 3.77. Found: C 70.75, H 8.27, N 3.23.

4-Benzyl-4-methylmorpholinium (*D*)-(–)-quinate, [BMmorf][**7m**] ¹H NMR (DMSO- d_6) δ ppm 1.45 (d, *J*=1.83 Hz, 1H); 1.49 (d, *J*=2.01 Hz, 1H); 1.62 (d, *J*=5.58 Hz, 1H); 1.71 (d, *J*=2.20 Hz, 1H); 3.09 (s, 3H); 3.37 (t, *J*=7.14 Hz, 2H); 3.44 (m, 3H); 3.57 (m, 3H); 3.98 (t, *J*=2. 62 Hz, 4H); 4.35 (m, 2H); 4.77 (s, 2H); 4.89 (m, 1H); 7.54 (m, 3H); 7.59 (m, 2H); ¹³C NMR (DMSO- d_6) δ ppm 44.9; 58.5; 59.9; 66.2; 67.5; 69.0; 73.2; 73.5; 127.2; 128.9; 130.3; 133.3; 179.3.

Elemental analysis calc. (%) for C₁₉H₂₉NO₇ (383.43): C 59.52, H 7.62, N 3.65. Found: C 59.94, H 8.08, N 3.01.

4-Benzyl-4-methylmorpholinium(2S,4R)-4-hydroxypyrrolidine-2-carboxylate,[BMmorf][7n]¹HNMR(DMSO- d_6) δ ppm 1.71 (t, 2H); 3.03 (m, 2H); 3.11 (s, 3H); 3.39 (t,J=4.27 Hz, 2H); 3.58 (qw, J=3.77 Hz, 2H); 3.97 (t, J=2.56 Hz, 4H);4.02 (t, J=3.36 Hz, 1H); 4.81 (s, 2H); 7.26 (m, 1H); 7.53 (m, 3H);7.60 (m, 2H); ¹³C NMR (DMSO- d_6) δ ppm 40.3; 44.8; 48.5; 55.0;58.4; 59.9; 66.0; 67.4; 127.4; 128.8; 130.3; 133.3; 176.2.

Elemental analysis calc. (%) for $C_{17}H_{26}N_2O_4$ (322.40): C 63.33, H 8.13, N 8.69. Found: C 62.75, H 8.57, N 9.03.

4.3. Thermal analysis

Melting points and other thermal transitions of the CILs were determined (DSC), Mettler Toledo DSC Instruments model cooled with an intracooler. The calorimeter was calibrated for temperature and cell constants using indium (melting point 156.61 °C, ΔH 28.71 J g⁻¹). Data were collected at constant atmospheric pressure, using samples between 10 and 40 mg in aluminum sample pans. Experiments were performed heating at the rate 10 °C min⁻¹. An empty sample pan was used as reference.

Thermal decomposition temperatures were measured in the dynamic heating regime using a TGA (TA Instruments 2950) under air atmosphere. Samples between 2 and 10 mg were heated from 40 to $500 \,^{\circ}$ C under constant heating at $10 \,^{\circ}$ C min⁻¹. Decomposition

temperatures ($T_{\text{onset5\%}}$ and T_{onset}) were determined from onset 5 mass loss and 50% mass loss respectively, under nitrogen.

4.4. Heck reaction

The Heck arylation of DHF with PhI was carried out under N₂ atmosphere using standard Schlenk technique. Reagents were introduced to the Schlenk tube in a following order: Pd(OAc)₂ (8.0 mg, 0.0356 mmol, 1 mol.%), solvent DMF (6 mL) or DMF/H₂O (3 mL + 3 mL), IL (appropriate amount), K₂CO₃ (0.6 g, 4.34 mmol), PhI (0.4 mL, 3.57 mmol) mesitylene (internal standard, 0.15 mL) and DHF (0.7 mL, 8.59 mmol). If not mentioned otherwise the reaction was carried out at 70 °C for 2 h. Afterwards, reaction mixture performed in DMF was quenched with H₂O (3 mL) and organic products were separated by extraction with diethyl ether (3 times: 10 mL, 7 mL and 7 mL). Products were analysed by GC-FID (Hewlett Packard 8454A). Products **2**, **3**, **4** were identified by comparison of MS spectra and retention times with literature data. Products of reactions proceeding in DMF:H₂O mixture were extracted as mentioned above but without quenching.

Enantiomeric excess (e.e.) values were determined by GC-FID (Hewlett Packard 8454A) with chiral β -cyclodextrine column.

References

- (a) R.F. Heck, Acc. Chem. Res. 12 (1979) 146–151;
 (b) A.M. Trzeciak, J.J. Ziółkowski, Coord. Chem. Rev. 249 (2005) 2308–2322;
 (c) I.P. Beletskaya, A.V. Cherpakov, Chem. Rev. 100 (2000) 3009–3066;
 (d) N.J. Whitcombe, K.K. Hii, S.E. Gibson, Tetrahedron 57 (2001) 7449–7476;
 (e) I. Tsuji, Palladium Reagents and Catalysts. New Perspectives for the 21 st Century, John Wiley & Sons, Ltd., 2004;
 (f) R.B. Bedford, C.S.J. Cazin, D. Holder, Coord. Chem. Rev. 248 (2004) 2283–2321.
- [2] M.M. Heravi, A. Fazeli, Heterocycles 81 (2010) 1979–2026.
- [3] A. Steven, L.E. Overman, Angew. Chem. Int. Ed. 46 (2007) 5488-5508.
- [4] Z. Hyder, J. Ruan, J. Xiao, Chem. Eur. J. 14 (2008) 5555–5566, and references cited there.
- [5] V. Calò, A. Nacci, A. Monopoli, V. Ferola, J. Org. Chem. 72 (2007) 2596–2601.
- [6] D. Pan, N. Jiao, Synlett 11 (2010) 1577–1588.
- [7] (a) F. Ozawa, A. Kubo, Y. Matsumoto, T. Hayashi, Organometallics 12 (1993) 4188;
 - (b) T. Hayashi, A. Kubo, F. Ozawa, Pure Appl. Chem. 64 (1992) 421-427;
 - (c) F. Ozawa, Y. Kobatake, T. Hayashi, Tetrahedron Lett. 34 (1993) 2505–2508; (d) F. Mieczyńska, A.M. Trzeciak, Molecules 15 (2010) 2166–2177.
- [8] S. Hillers, S. Sartori, O. Reiser, J. Am. Chem. Soc. 118 (1996) 2087–2088.
- [9] J. Mazuela, O. Pàmies, M. Diéguez, Chem. Eur. J. 16 (2010) 3434–3440, and references cited there.
- [10] S.Y. Cho, M. Shibasaki, Tetrahedron Lett. 39 (1998) 1773–1776.
- [11] (a) J. Kang, J.H. Lee, K.S. Im, J. Mol. Catal. A: Chem. 196 (2003) 55-63;
- (b) G.A. Molander, J.P. Burke, P.J. Carroll, J. Org. Chem. 69 (2004) 8062-8069.
- [12] W.-M. Dai, K.K.Y. Yeung, Y. Wang, Tetrahedron 60 (2004) 4425–4430.
- [13] D.A. Rankic, D. Lucciola, B.A. Keay, Tetrahedron Lett. 51 (2010) 5724–5727.
- [14] (a) L.F. Tietze, K. Thede, Chem. Commun. (1999) 1811–1812;
- (b) T. Tu, W.-P. Deng, X.-L. Hou, L.-X. Dai, X.-C. Dong, Chem. Eur. J. 9 (2003) 3073–3081.
- [15] For review of stereoselective Heck coupling see M. Shibasaki, E.M. Vogl, T. Ohshima, Adv. Synth. Catal. 346 (2004) 1533–1552.
- [16] (a) A.A. Sabino, A.H.L. Machado, C.R.D. Correia, M.N. Eberlin, Angew. Chem. Int. Ed. 43 (2004) 2514–2518;
 - (b) S.-K. Kang, S.-C. Choi, H.-C. Ryu, T. Yamaguchi, J. Org. Chem. 63 (1998) 5748–5749;
 - (c) M. Rosol, A. Moyano, J. Organomet. Chem. 690 (2005) 2291-2296;
 - (d) T. Jeffery, M. David, Tetrahedron Lett. 39 (1998) 5751-5754;
 - (e) A.H.L. Machado, M.A. de Sousa, D.C.S. Patto, L.F.S. Azevedo, F.I. Bombonato, C.R.D. Correia, Tetrahedron Lett, 50 (2009) 1222–1225.
- [17] D.W. Dodd, H.E. Toews, F.d.S. Carneiro, M.C. Jennings, N.D. Jones, Inorg. Chim. Acta 359 (2006) 2850–2858.
- [18] (a) H. Olivier-Bourbigou, L. Magna, D. Morvan, Appl. Catal. A: Gen. 373 (2010) 1-56:
 - (b) F. Bellina, C. Chiappe, Molecules 15 (2010) 2211-2245.
- [19] A. Winkel, P. Vasu Govardhana Reddy, R. Wilhelm, Synthesis 7 (2008) 999–1016.
- [20] K. Bica, P. Gaertner, Eur. J. Org. Chem. 19 (2008) 3235-3250.
- [21] S. Garre, E. Parker, B. Ni, A.D. Headley, Org. Biomol. Chem. 6 (2008) 3041-3043.
- [22] V. Jurcik, M. Gilani, R. Wilhelm, Eur. J. Org. Chem. (2006) 5103-5109.
- [23] Z. Wang, Q. Wang, Y. Zhang, W. Bao, Tetrahedron Lett. 46 (2005) 4657-4660.
 - [24] (a) J. Pernak, J. Feder-Kubis, Chem. Eur. J. 11 (2005) 4441–4449;
 (b) J. Pernak, J. Feder-Kubis, Tetrahedron: Asymmetry 17 (2006) 1728–1737;

(c) J. Feder-Kubis, M. Kubicki, J. Pernak, Tetrahedron: Asymmetry 21 (2010) 2709–2718.

- [25] Ch. Baudequin, D. Brégeon, J. Levillain, F. Guillen, J.-Ch. Plaquevent, A.-C. Gaumont, Tetrahedron: Asymmetry 16 (2005) 3921–3945.
- [26] X. Chen, X. Li, A. Hu, F. Wang, Tetrahedron: Asymmetry 19 (2008) 1–14.
- [27] (a) A. Paczal, A. Kotschy, Monatsch. Chem. 138 (2007) 1115–1123;
 (b) M.H.G. Prechtl, J.D. Scholten, B.A.D. Neto, J. Dupont, Curr. Org. Chem. 13 (2009) 1259–1277.
- [28] S.V. Malhotra, Y. Wang, Tetrahedron: Asymmetry 17 (2006) 1032-1035.
- (a) D. Cheng, M. Schmitkamp, G. Franciò, J. Klankermayer, W. Leitner, Angew. Chem. Int. Ed. 47 (2008) 7339–7341;
 (b) D. M. Michael, Chem. Commun. 0 (2008) 40, 44
- (b) D.K. Mukherjee, N. Ghosh, Catal. Commun. 9 (2008) 40-44.
- [30] F. Gayet, J.-D. Marty, N. Lauth-de Viguerie, ARKIVOC xvii (2008) 61-76.
- [31] L. Kiss, T. Kurtán, S. Antus, H. Brunner, ARKIVOC v (2003) 69–76.
- [32] J.C. Pastre, Y. Génisson, N. Saffon, J. Dandurand, C.R.D. Correia, J. Braz. Chem. Soc. 21 (2010) 821–836.
- [33] C. Brigouleix, M. Anouti, J. Jacquemin, M. Caillon-Caravanier, H. Galiano, D. Lemordant, J. Phys. Chem. B 114 (2010) 1757–1766.
- [34] K. Hanabusa, H. Fukui, M. Suzuki, H. Shirai, Langmuir 21 (2005) 10383-10390.
- [35] (a) W. Yu, H. Peng, H. Zhang, X. Zhou, Chin. J. Chem. 27 (2009) 1471–1475;
- (b) K. Lava, K. Binnemans, T. Cardinaels, J. Phys. Chem. B 113 (2009) 9506–9511.
 [36] (a) G. Xiao, H. Zhang, X. Hong, G. Zhang, X. Zhou, B. Xia, J. Appl. Polym. Sci. 108 (2008) 3683–3689;
- (b) C. Yue, Q. Liu, T. Yi, Y. Chen, Monatsh. Chem. 141 (2010) 975–978.
- [37] (a) T.-Y. Wu, S.-G. Su, S.-T. Gung, M.-W. Lin, Y.-Ch. Lin, Ch.-A. Lai, I.-W. Sun, Electrochim. Acta 55 (2010) 4475–4482;
 - (b) S. Kim, S.-M. Park, W.-K. Kang, K.-S. Kim, J. Kor, Phys. Soc. 6 (2010) 1639–1643.

- [38] C. Pretti, C. Chiappe, I. Baldetti, S. Brunini, G. Monni, L. Intorre, Ecotoxic. Environ. Safety 72 (2009) 1170–1176.
- [39] L. Xu, W. Chen, J. Xiao, Organometallics 19 (2000) 1123-1127.
- [40] A.M. Trzeciak, Z. Ciunik, J.J. Ziółkowski, Organometallics 21 (2002) 132–137.
- [41] (a) J. McNulty, J.J. Nair, A. Robertson, Org. Lett. 9 (2007) 4575–4578;
 (b) J. McNulty, S. Cheekoori, T.P. Bender, J.A. Coggan, Eur. J. Org. Chem. (2007) 1423–1428.
- [42] (a) J.P. Knowles, A. Whiting, Org. Biomol. Chem. 5 (2007) 31-44;
- (b) B.M.M. Wheatley, B.A. Keay, J. Org. Chem. 72 (2007) 7253-7259.
- [43] (a) C. Amatore, E. Carré, A. Jutand, M.A. M'Barki, G. Meyer, Organometallics 14 (1995) 5605–5614;
 (b) C. Amatore, A. Jutand, Acc. Chem. Res. 33 (2000) 314–321.
- [44] N.T.S. Phan, M. Van Der Sluys, C.W. Jones, Adv. Synth. Catal. 348 (2006)609–679, and references cited there.
- [45] (a) H. Böhnemann, R. Brinkmann, P. Neiteler, Appl. Organomet. Chem. 8 (1994) 361–378;
 (b) H. Böhnemann, W. Brijoux, R. Brinkmann, E. Dinjus, T. Joußen, B. Korall, Angew. Chem. Int. Ed. Engl. 30 (1991) 1312–1314;
 (c) M. Reetz, S.A. Quaiser, Angew. Chem. Int. Ed. Engl. 34 (1995) 2240–2241;
 (d) N. Cioffi, L. Torsi, I. Losito, L. Sabbatini, P.G. Zambonin, T. Bleve-Zacheo,
 - Electrochim. Acta 46 (2001) 4205–4211.
- [46] C. Amatore, A. Jutand, J. Organomet. Chem. 576 (1999) 254-278.
- [47] L. Starkey Ott, M.L. Cline, M. Deetlefs, K.R. Seddon, R.G. Finke, J. Am. Chem. Soc. 127 (2005) 5758–5759.
- [48] P. Migowski, J. Dupont, Chem. Eur. J. 13 (2007) 32–39.
- [49] N. Borucka, B. Markiewicz, J. Pernak, Przem. Chem. 89/11 (2010) 1397-1401.