Kinetic resolution of pent-4-ene-1,3-diol by Pd(II)-catalysed oxycarbonylation in ionic liquids

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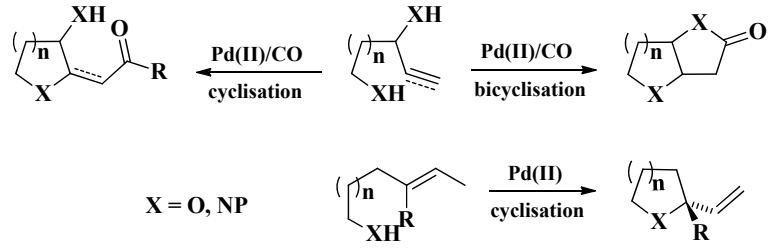
Abstract: The first example of the use of ionic liquids as reaction media in the asymmetric Pd(II)-catalysed oxycarbonylation was investigated. Based on a ligand screening, the chiral box-type ligands were successfully used in the Pd(II)-promoted bicyclisation of pent-4-ene-1,3 diol (±)-**1**. The kinetic resolution of (±)-**1** in the presence of chiral catalyst, *p*-benzoquinone and acetic acid in ionic liquids under carbon monoxide atmosphere afforded enantioenriched 2,6-dioxabicyclo[3.3.0]octane-3-ones (*S*,*S*)-2 (80% ee) and (*R*,*R*)-2 (57% ee), respectively.

Keywords: Kinetic resolution, oxycarbonylation, chiral ligand, asymmetric catalysis, ionic liquids.

Introduction

Catalytic carbonylation chemistry is widely used in organic synthesis and represents a useful method for bisfunctionalisation of the unsaturated carbon-carbon bonds.[1] Transition metals and their complexes functioning as catalysts for carbonylation reactions usually promote the introduction of a carbonyl moiety into an organic molecule. Among the most interesting and synthetically useful carbonylation reactions are the Pd-catalysed cyclisations of unsaturated alcohols and amines accompanied by the insertion of carbon monoxide.[2] These reactions provide a convenient and effective one-step access to oxygen and nitrogen-containing heterocyclic compounds[3] (Scheme 1). Along with the different carbonylation reactions, the intramolecular Pd-catalysed oxycarbonylative bicyclisations are also attracting raising attention within the last

decades.[4] They allow for the direct incorporation of CO, the most inexpensive and readily available C1-source, into parent molecules. The resulting bicyclic lactones can be easily refined further on. Such a transformation of optically pure substrates provides chirons which have found numerous applications in the total syntheses of natural products and relevant bioactive compounds.[5] Conversely, there is a significant deficiency of the effective asymmetric version of this synthetically valuable domino process. In contrast with the impressive evolution of asymmetric reactions with palladium(0) catalyst, palladium(II)-catalysed asymmetric Wacker-type oxidations have received scant attention. The first asymmetric variant of a Pd-catalysed alkoxylation-methoxycarbonylation reported by Kato, Akita *et al*.[6] accomplishing desymmetrisation of cyclic *meso*-2-methyl-2-propargyl-1,3-cyclohexane-diols[6a,c] and -1,3-diones[6b,d] using Pd(II)-complex bearing chiral bis(oxazoline) ligands. An enantioselective intramolecular amino-carbonylation of alkenyl amine derivatives was achieved by Sasai[7] with Pd(II)-spiro bis(isoxazoline) catalyst.



Scheme 1: Intramolecular Pd(II)-catalysed (bi)cyclisations.

Chiral bis(oxazolines) based on binaphtyl (Boxaxs[8]) or biphenyl backbone[9] were also successfully applied in the asymmetric Pd(II)-catalysed cyclisation of allylphenols[10] and allylanilines.[11] Sasai and co-workers[12] disclosed asymmetric cyclisation of alkenyl alcohols,[12a,b] aminoalkenes[12c] and alkenoic acids[12d] with spiro bis(isoxazolines) (SPRIXs[12e,f]). Kóóš *et al*. have recently reported the asymmetric intramolecular alkoxy- and amidolactonisation of alkene-1,3-diols[13] and amino alcohols[14] using $Pd(OAc)_2$-{(*R*,*S*)-indabox} and $Pd(OAc)_2$-{2,2'-methylenebis[(4*R*,5*S*)-4,5-diphenyl-2-oxazoline]} respectively.

Ionic liquids (ILs), or room temperature molten salts, have attracted considerable attention thanks to their ability to serve as effective reaction media for a wide range of organic reactions and other applications in chemistry.[15] By modifying the structure of cations or anions of ionic liquids, it has been shown that their properties can be altered in order to influence the outcomes of reactions. Many applications of ILs as a clean media for green catalytic transformations were

described in literature.[16] However, no asymmetric Pd-catalysed oxycarbonylation using ILs has been reported so far.

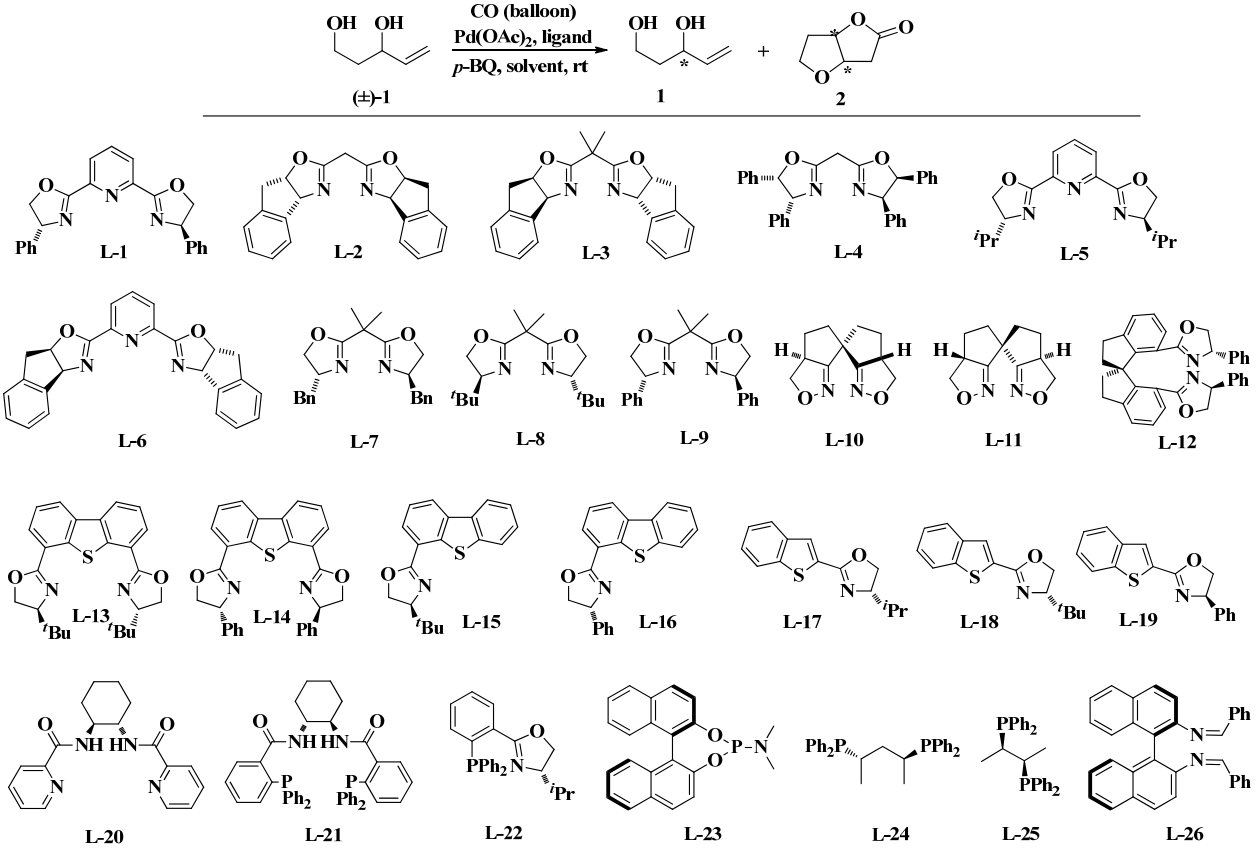
In connection with our studies on ionic liquids and our ongoing project on the asymmetric catalysis, we report herein the screening of several types of chiral ligands and the ionic liquids effect under microwaves activation on the Pd(II)-catalysed oxycarbonylation of alkene diols.

Results and discussion.

Screening of ligands.

The kinetic resolution of pent-4-ene-1,3-diol (±)-**1** was chosen as a model reaction to explore the catalytic behaviour of complexes. The complex formation conditions were described in details in the experimentation section.

We have initiated our investigation by screening the chiral ligands effects on this model reaction. The standard catalytic trials were carried out with different chiral PdX_2-(L*) complexes, p-benzoquinone in acetic acid under carbon monoxide atmosphere (balloon). In accordance with the kinetic resolution process, the 50% conversion was maintained by use of 0.5 equivalent of reoxidant (*p*-benzoquinone). The reaction conversion was monitored by GC with methyl benzoate as an internal standard. The bicyclic product **2** and the remaining diol **1** were separated by flash chromatography. The enantiomeric excesses of lactone **2** and diol **1** (as its 1-acetyl derivative Ac-**1**[17]) were determined by chiral GC analysis using Chiraldex B-PM capilary column. The absolute configuration of (*R*,*R*)-**2** was assigned by comparison of the specific rotation value with the literature data ($[\alpha]_D^{20}$ = +62 (c 0.9, $CHCl_3$) for (*R*,*R*)-**2** prepared from D-glucose;[18] $[\alpha]_D^{20}$ = -67 (c 0.639, $CHCl_3$) for (S,S)-**2** prepared by microbial regiodivergent Baeyer-Villiger oxidation with 99% ee[19]).



Scheme 2: Kinetic resolution of pent-4-ene-1,3-diol (±)-**1** in Pd(II)-catalysed oxycarbonylation.

Table 1 summarizes the results of a ligand screening. Generally, palladium(II)-complexes with C_2-symmetric bis(oxazolines) (box) ligands **L-1**–**L-5**, **L-7**-**L-9**, **L-12** (Scheme 2) were proven to be the most suitable catalysts for studied kinetic resolution process (entries 15-19, 2, 4, 20-22). The catalysts with sulphur-containing ligands like dibenzothiophene bis(oxazolines) (DBT-box[20]) **L-13**, **L-14**, dibenzothiophene oxazolines (DBT-mox) **L-15**, **L-16** and benzothiophene oxazolines (BT-mox[20]) **L-17**–**L-19** showed moderate to good catalytic activity without chemo- and enantiocontrolling ability (entries 7, 8, 23-27). Similarly, Pd(II) salts with (*S*,*S*)-DACH-pyridyl Trost ligand **L-20**[21] (entry 9) and binaphtyl derived bis(imine) **L-26** (entry 28) catalysed oxycarbonylation but with no selectivity. Bidentate phosphorus-containing ligands, such as (*R*,*R*)-DACH-phenyl Trost **L-21**[21] (entry 10), oxazoline **L-22** (entry 11), phosphoramidite **L-23** (entry 12), or bisphosphines **L-24**, **L-25** (entries 13, 14), significantly misbehaved in this

catalytic system. As we can observe, in this set of experiments (entries 1-14), the best enantioselectivity was obtained by using the ligand **L-1**.

Table 1. Kinetic resolution of pent-4-ene-1,3-diol (±)-**1** in Pd(II)-catalysed oxycarbonylation.

Entry	Ligand (mol %)	Catalyst, additives and reaction conditions	Conv. (%)	Lactone **2**			Diol **1**	
				Yield[a] (%) GC	Yield[b] (%)	Ee[c] (%) Config.	Yield[b] (%)	Ee[d] (%) Config.
1	**L-1 (12)**	**$Pd(OAc)_2$ (4 mol %), BQ (0.5 equiv), AcOH, rt, 3 d**	**50**	**-**	**22**	**49 (*S*,*S*)**	**46**	**27 (*R*)**
2	**L-5** (12)	$Pd(OAc)_2$ (4 mol %), BQ (0.5 equiv), AcOH, rt, 4 d	33	24	22	6 (*S*,*S*)	55	1 (*R*)
3	**L-6** (12)	$Pd(OAc)_2$ (4 mol %), BQ (0.5 equiv), AcOH, rt, 5 d	29	13	-	0	-	-
4	**L-7** (12)	$Pd(OAc)_2$ (4 mol %), BQ (0.5 equiv), AcOH, rt, 4 d	50	40	27	9 (*R*,*R*)	36	3 (*S*)
5	**L-10** (7.5)	$Pd(OAc)_2$ (2.5 mol %), BQ (0.5 equiv), AcOH, rt, 90 min	53	25	-	9 (*R*,*R*)[e]	-	-
6	**L-11** (7.5)	$Pd(OAc)_2$ (2.5 mol %), BQ (0.5 equiv), AcOH, rt, 50 min	52	23	-	5 (*S*,*S*)[e]	-	-
7	**L-13** (9)	$[Pd(\pi\text{-allyl})Cl]_2$ (3 mol %), BQ (0.5 equiv), AcOH, rt, 5 d	50	11	-	5 (*S*,*S*)[e]	-	-
8	**L-14**(9)	$Pd(OAc)_2$ (3 mol %), BQ (0.5 equiv), AcOH, rt, 2 d	54	14	-	5 (*R*,*R*)[e]	-	-
9	**L-20** (6)	$Pd(PhCN)_2Cl_2$ (5 mol %), BQ (0.5 equiv), AcOH, rt, 3 d	45	35	32	2 (*S*,*S*)	-	-
10	**L-21** (6)	$Pd(PhCN)_2Cl_2$ (5 mol %), BQ (0.5 equiv), AcOH, rt, 24 h	2	-	-	-	-	-
11	**L-22** (6)	$Pd(PhCN)_2Cl_2$ (5 mol %), BQ (0.5 equiv), AcOH, rt, 2 d	5	-	-	-	-	-
12	**L-23** (12)	$Pd(CH_3CN)_2Cl_2$ (6 mol %), BQ (0.5 equiv), AcOH, rt, 3 d	10	-	-	-	-	-
13	**L-24** (6)	$Pd(PhCN)_2Cl_2$ (5 mol %), BQ (0.5 equiv), AcOH, rt, 3 d	10	-	-	-	-	-
14	**L-25** (6)	$Pd(PhCN)_2Cl_2$ (5 mol %), BQ (0.5 equiv), AcOH, rt, 5 d	22	20	-	4 (*S*,*S*)[e]	-	-
15	**L-1** (12)	$Pd(OAc)_2$ (4 mol %), BQ (0.75 equiv), AcOH, rt, 29 h	42	28	19	43 (*S*,*S*)	40	26 (*R*)
16	**L-2** (12)	$Pd(OAc)_2$ (4 mol %), BQ (0.75 equiv), AcOH, rt, 24 h	42	27	26	57 (*R*,*R*)	57	21 (*S*)
17[f]	**L-2** (12)	$Pd(OAc)_2$ (4 mol %), BQ (0.75 equiv), AcOH, rt, 24h	56	36	28	57 (*R*,*R*)	44	27 (*S*)
18	**L-3 (12)**	**$Pd(OAc)_2$ (4 mol %), BQ (0.75 equiv), AcOH, rt, 27 h**	**36**	**32**	**22**	**61 (*S*,*S*)**	**61**	**26 (*R*)**
19	**L-4** (12)	$Pd(OAc)_2$ (4 mol %), BQ (0.75 equiv), AcOH, rt, 55 h	46	23	21	37 (*R*,*R*)	54	14 (*S*)
20	**L-8** (12)	$Pd(OAc)_2$ (4 mol %), BQ (0.75 equiv), AcOH, rt, 48 h	37	12	12	10 (*S*,*S*)	54	4 (*R*)
21	**L-9** (12)	$Pd(OAc)_2$ (4 mol %), BQ (0.75 equiv), AcOH, rt, 21 h	61	45	39	18 (*R*,*R*)	37	10 (*S*)
22	**L-12** (12)	$Pd(OAc)_2$ (4 mol %), BQ (0.75 equiv), AcOH, rt, 20 h	56	24	13	41 (*S*,*S*)	42	12 (*R*)
23	**L-15** (24)	$Pd(OAc)_2$ (8 mol %), BQ (1 equiv), AcOH, rt, 2 d	55	16	-	12 (*S*,*S*)[e]	-	-
24	**L-16** (24)	$Pd(OAc)_2$ (8 mol %), BQ (1 equiv), AcOH, rt, 2 d	63	26	-	12 (*R*,*R*)[e]	-	-
25	**L-17** (24)	$Pd(OAc)_2$ (8 mol %), BQ (1 equiv), AcOH, rt, 2 d	50	8	-	4 (*R*,*R*)[e]	-	-
26	**L-18** (24)	$Pd(OAc)_2$ (8 mol %), BQ (1 equiv), AcOH, rt, 2 d	26	7	-	2 (*R*,*R*)[e]	-	-
27	**L-19** (24)	$Pd(OAc)_2$ (8 mol %), BQ (1 equiv), AcOH, rt, 2 d	56	11	-	4 (*S*,*S*)[e]	-	-
28	**L-26** (12)	$Pd(OAc)_2$ (4 mol %), BQ (1.5 equiv), AcOH, rt, 15 h	33	8	-	2 (*S*,*S*)[e]	-	-

[a] Yield of **2** determined by GC with methyl benzoate as an internal standard.

[b] Isolated yield after flash column chromatography.

[c] Enantiomeric excess of isolated lactone **2** determined by chiral GC analysis using chiraldex-B-PM column.

[d] Enantiomeric excess of 1-monoacetylated diol Ac-**1** determined by chiral GC analysis using chiraldex-B-PM column.

[e] Enantiomeric excess of **2** determined from the crude reaction

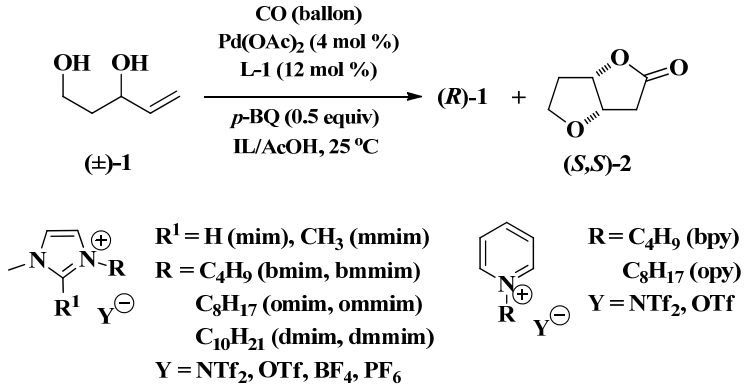
In order to further improve the enantioselectivity of the reaction, we explored spiro bis(isoxazoline) ligands **L-10** (*M*,*S*,*S*-H-SPRIX[12e,f]), **L-11** (*P*,*R*,*R*-H-SPRIX[12e,f]), which were

successfully applied in an asymmetric Pd-catalysed Wacker-type cyclisations.[12] It is notable that the use of Pd-SPRIX complexes efficiently promote the reaction. The 50% conversion of the racemic diol (±)-**1** was reached with both enantiomers **L-10** and **L-11** in 90 min (entry 5) and 50 min (entry 6), respectively, albeit with low enantioselectivity. Next, we examined the relative stoichiometry of reagents used in the reaction and we found that catalytic system containing $Pd(OAc)_2$ (4 mol %), ligand (12 mol %) and *p*-BQ (0.75 equiv), with respect to substrate (±)-**1**, accelerated reaction and increased the yield of product (entries 15-22). Thus, kinetic resolution of (±)-**1** in this reaction conditions using $Pd(OAc)_2$-{(*S*,*R*)-indabox (**L-3**)} provided enantioenriched lactone (*S*,*S*)-**2** (22% yield, 61% *ee*, entry 18) and with $Pd(OAc)_2$-{(*R*,*S*)-indabox (**L-2**)} formation of (*R*,*R*)-**2** (26% yield, 57% *ee*, entry 16) was preferred.

Influence of ionic liquids.

As reported in literature, ionic liquids could be used as green solvents and catalysts for organic synthesis as well as for catalytic transformations. At present, many applications of ILs as reaction media for asymmetric catalysis processes have been described.[16] However, no asymmetric Pd-catalysed oxycarbonylation using ILs has been reported so far.

Thus, in order to improve kinetic resolution of diol (±)-**1** by asymmetric Pd(II)-L* catalysed oxycarbonylation, we decided to evaluate the ionic liquids effect on the transformation. For this purpose, a set of imidazolium and pyridinium-based ILs[22] were chosen (Scheme 3). The experiments were carried out with $Pd(OAc)_2$ (4 mol %), 2,6-bis[(*R*)-4-phenyloxazolin-2-yl]pyridine (pybox) **L-1** (12 mol %) and *p*-benzoquinone (0.5 equiv) under carbon monoxide at 25 °C in the presence of ILs. The selected results are given in Table 2.



Scheme 3. Kinetic resolution of pent-4-ene-1,3-diol (±)-**1** by Pd(II)-catalysed oxycarbonylation in ILs.

Table 2. Kinetic resolution of pent-4-ene-1,3-diol (±)-**1** by Pd(II)-catalysed oxycarbonylation in ionic liquids.

Entry	Ionic liquid (equiv)	Ligand	AcOH (equiv)	Reaction time (d)	Conversion (%)	Lactone **2**		Diol **1**
						Yield[a] (%)	Ee[c] (%) Configuration	Ee[c] (%) Configuration
1	[bmim][NTf_2] (3)	**L-1**	3	4	55	14	68 (*S*,*S*)	55 (*R*)
2	[bmim][NTf_2] (10)	**L-1**	3	9	26	-	78 (*S*,*S*)[d]	-
3	[bmim][NTf_2] (10)	L-1	10	7	49	14	80 (*S*,*S*)	49 (*R*)
4	[bmim][NTf_2] (3)	**L-1**	-	3	<5	-	-	-
5	[omim][NTf_2] (3)	**L-1**	3	6	10	-	28 (*S*,*S*)[d]	-
6	[dmim][NTf_2] (3)	**L-1**	3	3	47	18	68 (*S*,*S*)	42 (*R*)
7	[bpy][NTf_2] (3)	**L-1**	3	3	48	20	71 (*S*,*S*)	43 (*R*)
8	[opy][NTf_2] (3)	**L-1**	3	3	30	10	46 (*S*,*S*)	-
9	[bmim][BF_4] (3)	**L-1**	3	3	38	15	77 (*S*,*S*)	38 (*R*)
10	[omim][BF_4] (3)	**L-1**	3	3	42	17	71 (*S*,*S*)	39 (*R*)
11	[bmim][OTf] (3)	**L-1**	3	6	<5	-	-	-
12	[omim][OTf] (3)	**L-1**	3	3	<5	-	-	-
13	**[omim][PF_6] (3)**	**L-1**	**3**	**3**	**55**	**20**	**79 (*S*,*S*)**	**60 (*R*)**
14	[ommim][NTf_2] (3)	**L-1**	3	7	<10	-	32 (*S*,*S*)[d]	-
15	[ommim][BF_4] (3)	**L-1**	3	7	<5	-	24 (*S*,*S*)[d]	-
16	[ommim][PF_6] (3)	**L-1**	3	7	<5	-	26 (*S*,*S*)[d]	-
17	[bmim][NTf_2] (3)	**L-4**	-	3	<5	2	23 (*R*,*R*)	-
18	[bmim][BF_4] (3)	**L-4**	-	7	<5	4	36 (*R*,*R*)	-
19	-	**L-1**	solvent	3	50	22	49 (*S*,*S*)	27 (*R*)

[a] Isolated yield after flash column chromatography.

[b] Enantiomeric excess of isolated lactone **2** determined by chiral GC analysis using chiraldex-B-PM column.

[c] Enantiomeric excess of 1-monoacetylated diol Ac-**1** determined by chiral GC analysis using chiraldex-B-PM column..

[d] Enantiomeric excess of **2** determined from the crude reaction mixture by chiral GC analysis using chiraldex-B-PM column.

As illustrated in Table 2, experiments performed in pure ionic liquids afforded only traces of lactone **2** (entries 4, 17, 18). Fortunately, the addition of acetic acid to the reaction mixture initiated bicyclisation affording enantioenriched lactone **2** (entries 1-3, 6-10, 13). Apparently, the presence of AcOH seems to be important for accomplishment of this domino process (entries 4, 17-18). Next, a series of different alkyl chain lengths (R = C_4H_9, C_8H_{17}, $C_{10}H_{21}$) was tested on this model reaction. However, no relationship between alkyl substituent (R) and the enantioselectivity was observed. On the other hand, no reaction occurred when hydrogen at C-2 (R^1) was substituted by a methyl group (entries 14-16), showing the loss of catalytic activity due to the complete absence of mobile hydrogen on the imidazolium nucleus. No hydrogen bonding could be formed between the hydroxyl function of the substrate and the imidazolium cation in this case. We then studied the influence of anion nature on this transformation. To that end, some

common anions were tested under similar reaction conditions. The obtained results showed a crucial effect of anion nature on the catalytic activity, for example, when anion OTf^- was used instead of NTf_2^- or BF_4^- (entries 11, 12 vs. 1-3, 5-10), a notable retardation of the reaction was observed. No interpretation of these obtained results was suggested, but this may be due to the interaction of acetic acid with ionic liquid anion. In-depth studies should be carried out for better understanding of the use of ILs in this reaction. Nevertheless, the enantioselectivity of the studied reaction was generally increased by the use of ILs. The best result (80 % *ee*, 20% isolated yield, 3h reaction time, entry 13) was noted with $Pd(OAc)_2$–pybox (**L-1**) in the mixture of 1-octyl-3-methylimidazolium hexafluorophosphate ([omim][PF_6]) and acetic acid in the ratio 1:1. It should be noted that ionic liquids could be recycled while their efficiency is preserved.

These results confirmed that not only may ILs be used as solvent but they also play the role of catalyst in the asymmetric Pd-catalysed oxycarbonylation of alkene diol. The key to effective asymmetric induction enhancement is the existence of strong intermolecular interactions, like electrostatic attraction and hydrogen bonding, between ionic solvents and intermediates or transition states of the diastereoselective reaction step. This observation was made by our group[16d] and further confirmed by Leitner and co-workers.[16o]

As we can observe, in almost all the cases of our studies, long reaction time was required for obtaining moderate to good reaction conversions, even in the presence of ILs. Thus, we turned our attention to the use of microwave activation (MW). This technique was widely developed in our laboratory and in other research groups.[23, 24] As shown in Table 3, microwave irradiation of the reaction mixture exhibited expected influence on rate enhancement especially in the presence of ILs (entries 4, 5) by untouched enantioselectivity.

Table 3. Kinetic resolution of pent-4-ene-1,3-diol (±)-**1** by Pd(II)-catalysed oxycarbonylation under microwave irradiation.

Entry	Ligand (mol %)	Catalyst, additives and reaction conditions	Conv. (%)	Time	Lactone **2**		
					Yield[a] (%) GC	Yield[b] (%)	Ee[c] (%) Config.
1	**L-1** (12)	$Pd(OAc)_2$ (4 mol %), BQ (0.5 equiv), [bmim][NTf_2] (3 equiv.), AcOH (3 equiv.), rt	55	4 days	27	14	68 (*S*,*S*)
2	**L-1** (12)	$Pd(OAc)_2$ (4 mol %), BQ (0.5 equiv), [bmim][NTf_2] (3 equiv.), AcOH (3 equiv.), 80 °C, 10W, cooling	39	4 h	13	11	77 (*S*,*S*)
3	**L-1** (12)	$Pd(OAc)_2$ (4 mol %), BQ (0.5 equiv), [bmim][NTf_2] (3 equiv.), AcOH (3 equiv.), 100 °C, 12W, cooling	50	2 h	-	16	73 (*S*,*S*)

[a] Yield of **2** determined by GC with methyl benzoate as an internal standard.

[b] Isolated yield after flash column chromatography.

[c] Enantiomeric excess of isolated lactone **2** determined by chiral GC analysis using chiraldex-B-PM column.

Conclusion

In summary, we have developed the enantioselective oxycarbonylative bicyclisation of alkenols catalysed by chiral palladium(II) complexes. Based on a ligand screening, the box-type *N*,*N*-bidentate ligands 2,6-bis[(*R*)-4-phenyloxazolin-2-yl]pyridine **L-1**, {(3a*R*,8a*S*)-bis(8,8a-dihydro-3a*H*-indeno[1,2-*d*]oxazol-2-yl)}methane **L-2** and {(3a*S*,8a*R*)-bis(8,8a-dihydro-3a*H*-indeno[1,2-*d*]oxazol-2-yl)}isopropane **L-3** have been identified as the most suitable ligands for Pd-catalysed oxidative lactonisation of unsaturated diols. Sulphur and/or phosphorus-containing ligands have been proven to be incompatible with the oxidative catalytic system. The kinetic resolution of pent-4-ene-diol (±)-**1** using Pd(II)-[(*R*,*S*)-indabox] (**L-2**) and Pd(II)-[(*S*,*R*)-indabox] (**L-3**) provided both enantiomerically enriched lactones (*R*,*R*)-**2** (26 % yield, 57 % *ee*) and (*S*,*S*)-**2** (22% yield, 61% *ee*), respectively.

Moreover, we have presented a kinetic resolution process of racemic diol catalysed by $Pd(OAc)_2$-[(*R*)-pybox] using ionic liquids and/or microwave activation. Noticeable propitious enhancements in both reaction rate and enantiomeric excess (up to 80 % *ee*) were observed using ILs as reaction media and MW-assisted conditions. This is the first report on the Wacker-type carbonylation taking advantage of the use of ionic liquids and microwave activation. Based on these results, further studies to improve the performance of asymmetric catalysts using ionic liquids are now under way. The use of chiral ionic liquids as chiral reaction media for this transformation will be also studied.

Experimental

General information

Commercial reagents were used without further purification. Flash column liquid chromatography (FLC) was performed on silica gel Kieselgel 60 (40-63 μm, 230-400 mesh) using Buchi Sepacore® preparative MPLC system. Optical rotations were measured with a JASCO P-2000 polarimeter and are given in units of 10^{-1} deg·cm^2·g^{-1}. Chiral gas chromatography analyses were performed on a Fisons Instruments GC 8000 Series Top chromatograph using Chiraldex B-PM capilary column with 2,3,6-tri-*O*-methyl-β-cyclodextrin stationary phase (50 m, id 0.25 mm, film thickness 0.12 μm) or on a Carlo Erba Fractovap chromatograph using β-DEX 225 capilary column with 25% 2,3-di-*O*-acetyl-6-*O*-TBDMS-β-cyclodextrin stationary phase (30 m, id 0.25 mm, film thickness 0.25μm), using hydrogen as a carrier gas. Microwave experiments were conducted on a CEM Discover or a CEM Discover S-Class microwave reactor operating in single mode at 2.45 GHz. The monitoring was performed using a Synergy software operating under Windows OS. The temperature was measured by optical fiber and maintained at a constant value by power modulation (0-200 W).

*A typical procedure for asymmetric oxycarbonylation of pent-4-ene-1,3-diol (±)-**1** with Pd-L* in acetic acid*

A mixture of chiral ligand (0.09-0.12 equiv) and Pd(II)-salt (0.03-0.04 equiv) was stirred in dichloromethane (0.5 mL) under Ar atmosphere for 15 min to give a clear solution. After removal of solvent *in vacuo* resulting chiral Pd-complex was dissolved in glacial AcOH (1 mL), substrate (±)-**1** (0.5 mmol), methyl benzoate (internal standard, 0.5 equiv) and *p*-benzoquinone (0.5-0.75 equiv) in AcOH (1 mL) were added. The Schlenk tube was purged with CO from balloon and the reaction mixture was vigorously stirred at room temperature until approx. 50% conversion of (±)-**1** as judged by GC. The reaction mixture was filtered through a short celite column and concentrated *in vacuo*. Both, enantiomerically enriched lactone **2** and diol **1** were separated by flash column chromatography.

*(R,R)-Dioxabicyclo[3.3.0]octan-3-one {(R,R)-**2**}*

Following a typical procedure; $Pd(OAc)_2$ (3.4 mg, 0.015 mmol), {(3a*R*,8a*S*)-bis(8,8a-dihydro-3a*H*-indeno[1,2-*d*]oxazol-2-yl)}methane **L-2** (14.9 mg, 0.045 mmol), methyl benzoate (34.0 mg, 0.250 mmol), *p*-benzoquinone (40.5 mg, 0.375 mmol), diol (±)-**1** (51.1 mg, 0.500 mmol) in AcOH (0.5 mL) were stirred at rt for 24 h (42% conversion by GC). The reaction mixture was filtered through a short celite column, concentrated and purified by flash chromatography (3.8 g of silica gel, ethyl acetate/cyclohexane 1:3). Yield 16.5 mg (26%),

colorless liquid, R_f = 0.50 (AcOEt/cyclohexane 3:1), 57% *ee* (GC), $[\alpha]_D^{25}$ = +20 (c 0.098, $CHCl_3$) at 45% *ee*, [lit.[13a] $[\alpha]_D^{20}$ = +20 (c 0.40, $CHCl_3$), 45% *ee*).

*Asymmetric oxycarbonylation of (±)-**1** with $Pd(OAc)_2$ – pybox (**L-1**) in ionic liquids*

A mixture of 2,6-bis[(4*R*)-4-phenyl-2-oxazolinyl]pyridine **L-1** (0.12 equiv) and $Pd(OAc)_2$ (0.04 equiv) was stirred in dichloromethane (0.5 mL) under Ar atmosphere for 15 min. The solvent was removed *in vacuo* and the mixture of (±)-**1** (1 equiv), methyl benzoate (0.5 equiv), ionic liquid (3 equiv), *p*-benzoquinone (0.5 equiv) and AcOH (3 equiv.) was added to the solid Pd-complex. The Schlenk tube was purged with CO from balloon and the reaction mixture was vigorously stirred at rt until approx. 50% conversion of (±)-**1** as judged by GC. The reaction mixture was extracted with Et_2O (3 x 3 mL) and combined extracts were concentrated *in vacuo*. Lactone **2** and diol **1** were separated by flash column chromatography.

Microwave irradiation experiments

The reaction mixture of chiral palladium complex (0.04 equiv, prepared as above), substrate (±)-**1** (1 equiv), methyl benzoate (0.5 equiv), *p*-benzoquinone (0.5-0.75 equiv), ionic liquid (3 equiv) and glacial AcOH (3 equiv) was transferred into a special MW vessel which was purged with CO (balloon). The mixture was irradiated under corresponding microwave conditions (the temperature was measured by optical fiber and maintained at a constant value by power modulation 0-200 W) until approx. 50% conversion of (±)-**1** (GC control). The reaction mixture was extracted with Et_2O (3 x 3 mL) and combined extracts were concentrated *in vacuo*. Lactone **2** and diol **1** were separated by flash column chromatography.

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