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Towards DES Compatible Metallic Catalysts: Cationic Pyridiniophosphine Ligands in Palladium Catalyzed Cross-Coupling Reactions

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Abstract: Cationic pyridiniophosphine ligands have been synthesized in an attempt to develop a Deep Eutectic Solvents (DESs) compatible catalytic systems. These ligands, in combination with PdCl₂, have been successfully applied to different palladium-catalyzed cross coupling reactions, such as Suzuki-Miyaura, Sonogashira or Heck couplings. While traditional palladium ligands failed to reproduce in DES medium the results obtained in VOC solvents, these cationic phosphines improved the catalytic activity of palladium as no other traditional ligand could in such polar medium. In addition, the recyclability of these processes was studied, allowing us to reuse both, catalyst and solvent up to 5 times in Suzuki and Sonogashira reactions without a significant drop in the catalytic activity. Regarding the structure of the Pd catalysts, titration, NMR, and DFT studies have clearly demonstrated the coordination properties of the DES-compatible cationic phosphine ligands.

Nowadays, C-C bond formation is one of the reaction type that most interest attracts among organic chemists. Thus, it has become an essential tool in organic synthesis that provides access to compounds of great value for different areas; such as materials, pharmaceuticals or fine chemicals. This kind of reactions can be performed under catalytic conditions employing transition-metals, as for Suzuki-Miyaura,¹ Heck,² Negishi,³ Stille,⁴ Kumada,⁵ Hiyama,⁶ and Sonogashira reactions.⁷ All these approaches are typically performed in volatile organic solvents (VOC), which nowadays are trying to be replaced by greener media. A medium can be considered green when its components satisfy different criteria such as non-toxicity, recyclability, low price, availability, biodegradability and renewability, among others. Some DESs (Deep Eutectic Solvents) could be considered as an alternative to hazardous VOC solvents. DESs are systems formed by simple mixing Lewis or Brønsted acids and bases.⁸ As a result of the strong hydrogen bond interactions, the melting or phase transition point became much lower than that of each individual component.⁹ Nevertheless, the use of DES as reaction media in Organic Synthesis is in its childhood,¹⁰ with very few reports of the related metal-catalyzed process.¹¹

Only, very recently, palladium chemistry has started to be tested in DES media. More specifically, Suzuki reaction has

been carried out using Pd(OAc)₂ (10 mol%) in a ternary mixture of mannitol, dimethyl urea and ammonium chloride as DES combination.¹² Regarding Sonogashira coupling, the synthesis of only two products have been published in DES medium (D-mannose/DMU), while the Heck cross-coupling reaction has been performed in D-mannose-dimethyl urea (DMU) as reaction media.¹³ Other published palladium-catalyzed reactions performed in DES media include Tsuji-Trost allylation of amines in methylated β-cyclodextrine-DMU,¹⁴ synthesis of thiophenes in ChCl-glycerol,¹⁵ as well as the Stille reaction in lactose-DMU-NH₄Cl.¹⁶ This latest example is especially interesting, because is one of the few examples in which a ligand was added to the DES media: triphenylarsine, in combination with palladium, permitted the coupling of 4-bromoanisole and tetraphenylstannane in 87 % yield. However, when the reaction was carried out using CyJohnPhos (a Hartwig-Buchwald-type ligand), only a modest 61 % yield was obtained. These facts clearly demonstrate the importance of appropriate design of the ligand in order to get good results in this new media.

With all this precedents, we aimed to develop DES compatible phosphine ligands, since the best traditional palladium ligands for cross-coupling reactions seemed not to be so effective in this kind of solvents. We thought in cationic pyridiniophosphine structures¹⁷ as general strategy for ligands in the palladium-catalyzed cross-coupling reactions.

We started by the synthesis of a cationic pyridiniophosphine ligand with a chloride as counter ion (Scheme 1). In order to do this, we started by the *N*-alkylation of 2-hydroxypyridine, followed by chlorination which afford salts **2**. Then, the dicyclohexylphosphine was inserted in order to obtain the final ligand.

Scheme 1. Ligand preparation. a) CuI (10 mol%), K₂CO₃ (2.1 eq), DMSO; b) oxalyl chloride (2 eq), 1,2-dichloroethane, 60°C; c) HPCy₂ (2 eq), MeCN (dry) reflux.

Once we prepared these ligands we started to test them in different cross-coupling reactions, starting by the Suzuki-Miyaura reaction (Figure 1, Table 1). Optimization studies were performed in order to determine the best catalyst. The reaction worked poorly with only 0.1 mol% of a palladium(II) salt alone (Table 1, entries 1-2), but when a pyridiniophosphine ligand was added, the yield after 2 h raised up to 49 % (entry 3). The fine tuning of electronic properties of *N*-substitution showed that neutral phenyl substituent gave a better result than electron-poor 2-pyridyl or electron-rich 2-thienyl moieties (entries 3-5).

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Table 1. Optimization of the catalyst.

Entry	Pd source (mol%)	Ligand (mol%)	Yield (%) ^a
1	PdCl ₂ (0.1)	-	12
2	Pd(OAc) ₂	-	10
3	PdCl ₂ (0.1)	3a (0.3)	49
4	PdCl ₂ (0.1)	3b (0.3)	37
5	PdCl ₂ (0.1)	3c (0.3)	40
6	PdCl ₂ (0.1)	PCy ₃ (0.3)	5
7	PdCl ₂ (0.1)	P(Fu) ₃ (0.3) ^b	25
8	PdCl ₂ (0.1)	3d (0.3) ^c	9
9	PdCl ₂ (0.5)	3a (1.5)	64
10	PdCl ₂ (1.0)	3a (3.0)	88

^aIsolated yields after column chromatography. ^bP(Fu)₃ stands for tri(furan-2-yl)phosphine. ^c**3d** stands for [1,1'-biphenyl]-2-ylidicyclohexylphosphine.

Fig 1. Effects of ligand in Suzuki coupling in DES.

Other traditional phosphine ligands were also tested, showing only a slight increase in the yield in relation to the uncomplexed palladium salt, or no effect at all (entries 6-8). Surprisingly, CyJohnPhos (**3d**), which only differs from ligand **3a** by the cationic nature, gave the same result as in absence of ligand. Since the best results were obtained with cationic pyridiniophosphines, it has been proven that, in a system as polar as DES, these ligands are more suitable. Finally, the reaction was repeated increasing the catalyst loading, showing a good yield with just 1 mol% of palladium source and 3 mol% of ligand (entry 10), amounts inferior to those previously reported, what makes evident that the adequate design of ligand is mandatory.

Table 2. Optimization of the reaction conditions

Entry	T (°C)	Base	Solvent	Yield
1	25	K ₂ CO ₃	ChCl:Urea (1:2)	24
2	80	K ₂ CO ₃	ChCl:Urea (1:2)	82
3	100	K ₂ CO ₃	ChCl:Urea (1:2)	88
4	120	K ₂ CO ₃	ChCl:Urea (1:2)	82
5	150	K ₂ CO ₃	ChCl:Urea (1:2)	56
6	100 ^a	K ₂ CO ₃	ChCl:Urea (1:2)	44
7	100	Cs ₂ CO ₃	ChCl:Urea (1:2)	86
8	100	Et ₃ N	ChCl:Urea (1:2)	38
9	100	NaOH	ChCl:Urea (1:2)	44
10	100	^t BuOK	ChCl:Urea (1:2)	56
11	100	TABOH	ChCl:Urea (1:2)	72
12	100	K ₂ CO ₃	ChCl:Ethylene glycol (1:2)	97
13	100	K ₂ CO ₃	ChCl:Resorcinol (1:1)	43
14	100	K ₂ CO ₃	ChCl:Glycerol (1:2)	92
15	100	K ₂ CO ₃	ChCl:Trifluoroacetamide (1:2)	34
16	100	K ₂ CO ₃	Ph ₃ PMeBr:Glycerol (1:2)	75

[a] Reaction carried out under microwave irradiation.

With the best palladium salt and ligand established, a study to find the best reaction condition was performed (Table 2). Firstly, different temperatures were tested, obtaining the best results at 100 °C under conventional heating (entries 1-6). Then we tried a sort of bases (entries 7-11), founding out that both, potassium and cesium carbonates provided the best yields. We decided to follow the study with the more available K₂CO₃. Finally, different eutectic mixtures were tested as solvent (entries 12-22). Best results were obtained with choline chloride:ethylene glycol followed closely by choline chloride:glycerol. Since the latest is a more environmental-friendly system and the difference in the obtained yield was minimal, it was the chosen solvent for carrying out the study of the scope.

With the optimized conditions, the scope of the Suzuki reaction was evaluated. Thus, different activated and deactivated aryl iodides and bromides were cross-coupled with phenylboronic acid (Table 3). In general, very good isolated yields (80-98%) were obtained for biaryls **6** regardless of the electronic nature of the employed aryl iodide or bromide (Table 1, entries 1-4 and 6-13). However, the catalytic system showed moderate activity when an activated aryl chloride such as 1-

chloro-4-nitrobenzene reacted with phenylboronic acid affording 4-nitro-1,1'-biphenyl (**6b**) in a 46% yield after 10 h (Table 3, entry 5). Interestingly, we did not observe in any of the tested experiments the formation of palladium black which points to a possible stabilization of the cationic Pd-complex by the DES.

Table 3. Scope of the Suzuki-Miyaura reaction

Entry	R	Hal	x	Product	Yield (%) ^[a]
1	MeCO	I	0.1	6a	98
2	MeCO	Br	1	6a	95
3	NO ₂	I	0.1	6b	97
4	NO ₂	Br	1	6b	98
5	NO ₂	Cl	1	6b	46 ^[b]
6	H	I	0.1	6c	94
7	H	Br	1	6c	93
8	<i>t</i> -Bu	I	0.1	6d	89
9	<i>t</i> -Bu	Br	1	6d	90
10	CH ₂ OPh	I	0.1	6e	95
11	CH ₂ OPh	Br	1	6e	96
12	MeO	I	0.1	6f	81
13	MeO	Br	1	6f	80

[a] Isolated yield after flash chromatography. [b] Reaction time: 10 h.

The Sonogashira reaction was also evaluated. Preliminary attempts to perform this reaction pointed out Ph₃PMeBr:glycerol (1:2) as the optimal DES. Because of that, reaction between 4'-iodoacetophenone (**4a**) and phenylacetylene (**7**) was evaluated in the aforementioned DES as reaction medium (Table 4). Despite that the reaction worked well with just one equivalent of **7** (entry 1), using 2 equivalents raised the obtained yield to 95 % (entry 3), while using 1.2 equivalents did not affect to the reaction yield (entry 2). When the reaction was carried out employing Pd(OAc)₂ instead of PdCl₂ as palladium source, the obtained yield was slightly lower (entry 4). Different bases were also tested (entries 5-8), obtaining better results with organic bases. Specifically, the best result was obtained with ⁱPr₂NH. With the best base chosen, its amount was decreased, obtaining similar results with just 2 equivalents (entry 9), but observing a significant drop in the yield when only one equivalent was employed (entry 10). Surprisingly, when the catalyst amount was decreased to 0.1 mol%, the yield was practically kept in the same range (entry 11), avoiding the formation of minor by-products. The optimal temperature was also determined. Decreasing the reaction temperature to 50 °C produced a drop in the yield to 52 % (entry 12) while when it was decreased to 80 °C the yield was maintained (entry 13). Finally, other DES were

tested with this optimized conditions (entries 15-17), but poorer results were obtained. It should be pointed out that no copper source was needed.

Table 4. Optimization of the reaction conditions

Entry	[Pd] (mol%)	3a (mol%)	T (°C)	7 (eq)	Base	Yield (%) ^a
1	1.0	3.0	100	1	ⁱ Pr ₂ NH (3 eq)	89
2	1.0	3.0	100	1.2	ⁱ Pr ₂ NH (3 eq)	88
3	1.0	3.0	100	2	ⁱ Pr ₂ NH (3 eq)	95
4	1.0	3.0	100	2	ⁱ Pr ₂ NH (3 eq)	90 ^b
5	1.0	3.0	100	2	K ₂ CO ₃ (3 eq)	81
6	1.0	3.0	100	2	NaOAc (3 eq)	74
7	1.0	3.0	100	2	^t BuOK (3 eq)	22
8	1.0	3.0	100	2	Et ₃ N (3 eq)	89
9	1.0	3.0	100	2	ⁱ Pr ₂ NH (2 eq)	94
10	1.0	3.0	100	2	ⁱ Pr ₂ NH (1 eq)	80
11	0.1	0.3	100	2	ⁱ Pr ₂ NH (3 eq)	>99
12	0.1	0.3	50	2	ⁱ Pr ₂ NH (2 eq)	52
13	0.1	0.3	80	2	ⁱ Pr ₂ NH (2 eq)	>99
14	0.1	0.3	120	2	ⁱ Pr ₂ NH (2 eq)	>99
15	0.1	0.3	80	2	ⁱ Pr ₂ NH (2 eq)	70 ^c
16	0.1	0.3	80	2	ⁱ Pr ₂ NH (2 eq)	71 ^d
17	0.1	0.3	80	2	ⁱ Pr ₂ NH (2 eq)	62 ^e

[a] Yield determined by GC using tridecane as internal standard. [b] Reaction carried out employing Pd(OAc)₂ instead of PdCl₂. [c] Reaction carried out in ChCl:ethyleneglycol (1:2) [d] Reaction carried out in ChCl:urea (1:2) [e] Reaction carried out in ChCl:glycerol (1:2).

The scope of the Sonogashira coupling employing this methodology was evaluated (Table 5). Good to excellent yields were obtained using aryl iodides bearing electron-withdrawing groups (entries 1 and 4), and electron-donating groups (entries 5 and 7). Steric hindrance seems to be an issue for this reaction as it can be seen in entry 9. Heteroaryl iodides were also tested with good results (entries 11 and 14). When the reaction was performed with aryl bromides using this approach, only 15 % yield was obtained (entry 2) and we decided to increase the catalyst amount to 1.0 mol%. With this amount, the reaction worked fine only with electron-poor systems (entries 3, 8, 12). 2-chloropyridine was also tested (entry 13), proving that the reaction could take place with electron-poor heteroaryl chlorides.

The Heck cross-coupling reaction was tested as well. At first, reaction between 1-iodo-4-nitrobenzene and methyl acrylate was evaluated (Table 6). When only 0.1 mol% of PdCl_2 was employed the reaction did not take place (entry 1). Then the catalyst loading was increased until 0.5 mol%, and the reaction yield was still poor (entry 2). Other DESs were tested without increasing the catalyst loading anymore, obtaining good yields with CHCl_3 :glycerol (1:2) and Ph_3PMeBr :glycerol (1:2) as solvents (entries 3, 5).

Then, the scope of the reaction was evaluated, using methyl acrylate and different substituted aryl iodides (Table 7). The reaction took place with moderate to good yields with aryl iodides bearing electron-withdrawing and electron-donating groups. Reaction worked worse with 2-substituted aryl iodides, probably owing to the steric hindrance.

On the other hand, the recyclability of the DES and catalyst was evaluated. Once the reaction finished, cyclopentyl methyl ether, a potential green alternative solvent,¹⁸ was added to the reaction mixture in order to perform an extraction.

Table 5. Scope of Sonogashira reaction.

$\text{Ar-X} + \text{Ph} \equiv \text{H} \xrightarrow[\text{PdCl}_2 (0.1 \text{ mol}\%), \text{ 3a} (0.3 \text{ mol}\%), 80^\circ\text{C}, 5 \text{ h}]{\text{Pr}_2\text{NH} (2 \text{ eq}), \text{ Ph}_3\text{PMeBr:glycerol} (1:2), 2 \text{ ml}} \text{Ar} \equiv \text{Ph}$					
Entry	Ar (R)	X	Product	Yield (%) ^a	
1		COMe	I	8a	99
2		COMe	Br	8a	15
3		COMe	Br	8a	75 ^b
4		CF ₃	I	8b	79
5		Me	I	8c	80
6		Me	Br	8c	9 ^b
7		NO ₂	I	8d	98
8		NO ₂	Br	8d	89 ^b
9		Me	I	8e	49
10		Me	Br	8e	20 ^b
11			I	8f	75
12			Br	8f	99 ^b
13			Cl	8f	36 ^b
14			I	8g	97
15			Br	8g	67 ^b

[a] Isolated yield after flash chromatography. [b] Reaction carried out with 1.0 mol% of PdCl_2 and 3 mol% of **3a**.

Table 6. Optimization of the reaction conditions.

$\text{4fa} + \text{9} \xrightarrow[\text{NaOAc} (1.5 \text{ mmol}), \text{ DES (molar ratio, 2 mL), } 100^\circ\text{C}, 3 \text{ h}]{\text{PdCl}_2 (\text{mol}\%), \text{ 3a} (\text{mol}\%)}$			
Entry	Catalyst (mol%)	Solvent	Yield (%) ^a
1	PdCl_2 (0.1) + 3a (0.3)	CHCl_3 :urea (1:2)	0
2	PdCl_2 (0.5) + 3a (1.5)	CHCl_3 :urea (1:2)	29
3	PdCl_2 (0.5) + 3a (1.5)	CHCl_3 :glycerol (1:2)	76
4	PdCl_2 (0.5) + 3a (1.5)	CHCl_3 :F ₃ C CONH_2 (1:2)	10
5	PdCl_2 (0.5) + 3a (1.5)	Ph_3PMeBr :glycerol (1:2)	89
6	PdCl_2 (0.5) + 3a (1.5)	Betaine:oxalic acid (1:2)	11

[a] Yield determined by GC using tridecane as internal standard

All organic compounds were removed and the mixture of DES and catalyst, lower phase in the decantation, was reused under the same reaction conditions. This study was repeated for the three studied cross-coupling reactions, obtaining excellent yields even after the five cycle for the Suzuki and Sonogashira couplings (Figure 2).

We next turned to DFT studies (M06/6-311G** (SDD) (IEFPCM-CH₃CN)) to shed some light into the structures and energies of the Pd complexes with the different ligands **3a**, **3b** and **3c** (Figure 3). We were especially interested in the stoichiometry and the coordination modes of the complexes. For comparison purposes, we also included the ligand **3d**, a neutral counterpart of ligand **3a**, which could provide information about the similarities or differences of our ionic complexes with the well-known $\text{PdCl}_2(\text{PR}_3)_2$ type of ligands. For the sake of accuracy, we used the complete ligands, without any structural simplification, at the expense of a significant computation time.

Table 7. Scope of Heck reaction.^a

$\text{R} \text{---} \text{C}_6\text{H}_4 \text{---} \text{I} + \text{O}=\text{C}(\text{OMe})\text{CH}=\text{CH}_2 \xrightarrow[\text{NaOAc} (1.5 \text{ mmol}), \text{ ChCl:glycerol} (1:2), 2 \text{ ml}, 100^\circ\text{C}, 3 \text{ h}]{\text{PdCl}_2 (0.5 \text{ mol}\%), \text{ 3a} (1 \text{ mol}\%)}$		
4	9	10
1.0 mmol	1.2 mmol	
10a	10b	10c
78%	53%	44%
10d	10e	10f
38%	49%	99%

[a] Isolated yield after flash chromatography

Fig 2. Recyclability experiments.

First, ligand **3a** can operate only as a monodentate ligand, and we found computationally that the most stable complex corresponds to the *trans* dicoordinated square-planar *trans*-[PdCl₂(**3a**)₂] (*G* = 0 kcal/mol, Scheme 2). The Free Gibbs (*G*) energy of the *cis* isomer is 18.5 kcal/mol higher than the *trans*, and the sum of monocoordinated complex PdCl₂(**3a**) and one more equivalent of the free ligand **3a** is even less favorable (+23.7 kcal/mol). This preference is consistently repeated regardless the number of chlorine atoms introduced in the computed structures, like in the forms of PdCl₂(**3a**)₂²⁺ 2Cl[−], PdCl₂(**3a**)₂²⁺, or Pd(**3a**)₂⁴⁺ (See SI for further details). The same trend was observed for the neutral ligand **3d**, as the *trans*-PdCl₂L₂ complex is the most stable one, over the *cis* (+14.4 kcal/mol) and the monocoordinated species (+37.1 kcal/mol). This finding indicates that the ionic or neutral nature of the ligands (**3a** vs **3d**) is not affecting significantly the structure and coordination mode of the complexes, and that pyridinium chloride based ligands like **3a** can act as ionic surrogates of the well known triphenyl or tricyclohexyl phosphine substrates.

Fig 3. Phosphine ligands **3a-d** used in the computational study.

Scheme 2. Computed structures and Free Gibbs energies for the complexes of ligands **3a** and **3d** at M06/6-311G** (iefpcm, solvent=MeCN) level of theory.

On the other hand, the complexes formed by ligands **3b** and **3c** were computed (Scheme 3). Due to their bidentate nature, we hypothesized that their geometrical requirements could in principle be different to the previous ligand **3a**. However the complexation energies showed that for **3b**, the *trans* dicoordinated complex Pd(**3b**)₂²⁺ 2Cl[−] renders again the most stable situation, with a narrower energy gap (5.5 kcal/mol) with its *cis*-Pd(**3b**)₂²⁺ 2Cl[−] counterpart.

Scheme 3. Computed structures and Free Gibbs energies for the complexes of ligands **3b** and **3c** at M06/6-311G** (iefpcm, solvent=MeCN) level of theory.

The monocoordination as in Pd(**3b**)³⁺ is again heavily penalized probably due to the poor coordination ability of the pyridine ring in **3b**. Remarkably, the thiophene containing ligand **3c** shows a divergent behavior, and the coordination of a single equivalent (like in Pd(**3c**)²⁺ Cl[−]), is preferred over than any of the dicoordinated *cis* or *trans* isomers of Pd(**3c**)₂²⁺ 2Cl[−] in 10.9 and 19.5 kcal/mol respectively.

Experimental UV-VIS studies were in agreement with the DFT findings for the coordination of ligands **3**. Thus, the spectrophotometric titrations (see SI) of acetonitrile solutions (5.0 × 10^{−5} M) of ligands **3a** (λ = 269 and 300 nm),¹⁹ **3b** (λ = 233 and 271 nm) and **3c** (λ = 243 nm) with increasing amounts of an acetonitrile solution of Pd(OAc)₂ (2.5 × 10^{−5} M) confirmed the formation of a 1:2 metal:ligand complex. A similar study with the thiophene-derived ligand **3c** (λ = 273 nm) also confirmed the formation of a 1:1 metal:ligand complex, as anticipated by the DFT calculations. Representative spectra for the UV-VIS studies are shown in Figure 4.

Fig 4. Representative UV-VIS studies for the Pd complexes of ligands **3a-d**.

Finally, $^{31}\text{P}\{^1\text{H}\}$ NMR studies were performed in order to confirm the coordination of the phosphine to palladium. Thus, a 2/1 mixture of **3a**/PdCl₂ was analyzed by $^{31}\text{P}\{^1\text{H}\}$ NMR (DMSO-d₆, 121 MHz) and compared with the results obtained for the free ligand **3a** (Figure 5). The $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of free ligand **3a** showed a broad singlet at -2.25 ppm,²⁰ absorption frequency which hardly appeared in the spectrum of the *in situ* prepared palladium complex together with a broad singlet at 43.15 ppm, resonance frequency corresponding to the phosphine ligand coordinated to the metal.

Fig 5. a) ^{31}P (green) and $^{31}\text{P}\{^1\text{H}\}$ (blue) NMR spectra (DMSO-d₆, 121 Mz) of ligand **3a**. b) $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum (DMSO-d₆, 121 Mz) of PdCl₂(**3a**)₂.

Conclusion

In conclusion, we have demonstrated that small modifications of typical ligand structures, as the change from phosphines to cationic pyridiniophosphines, seems to be enough to keep the excellent results obtained in classical organic solvents in the new DES medium, with this new approach being possible to be used in the design of other type of ligands. The possibilities of classical organometallic catalysis can be maintained, while avoiding the environmental problem occasioned by typical hazardous volatile solvents by the use of these cationic phosphine ligands and eutectic mixtures as reaction medium. The aforementioned ligands, in association with PdCl₂ have been successfully applied to some of the most important cross-coupling reactions such as Suzuki-Miyaura, Sonogashira and Heck reactions, showing the general applicability of them.

Experimental Section

Melting points were obtained with a Reichert Thermovar apparatus. NMR spectra were recorded on a Bruker AC-300 or a Bruker AC-400 (300/400 MHz for ^1H , 100/75 MHz for ^{13}C , and 162/121 MHz for ^{31}P) using CDCl₃ or DMSO-d₆ as solvents. TMS was used as internal standard for ^1H and ^{13}C NMR spectra, while H₃PO₄ for ^{31}P NMR analyses. Chemical shifts are given in δ (parts per million) and coupling constants (J) in Hertz. FT-IR spectra were obtained on a JASCO 4100LE (Pike Miracle ATR) spectrophotometer. Mass spectra (EI) were obtained at 70 eV on a Himadzu QP-5000 spectrometer, giving fragment ions in m/z with relative intensities (%) in parentheses. The chromatographic analyses (GLC) were determined with a Hewlett Packard HP-5890 instrument equipped with a flame ionization detector and 12 m HP-1 capillary column (0.2 mm diam, 0.33 mm film thickness, OV-1 stationary phase), using nitrogen (2 mL/min) as a carrier gas, $T_{\text{injector}} = 275^\circ\text{C}$, $T_{\text{detector}} = 300^\circ\text{C}$, $T_{\text{column}} = 60^\circ\text{C}$ (3 min) and $60\text{--}270^\circ\text{C}$ (15 $^\circ\text{C}/\text{min}$), $P = 40$ kPa. DIP analyses were performed using an Agilent mass spectrometer, model Network 5973 Mass Selective with direct sample introduction to the ion source through the SIS (Scientific Instrument Services) probe Direct Insertion Probe (73DIP-1). Thin layer chromatography (TLC) was carried out on Schleicher&Schuell F1400/LS 254 plates coated with a 0.2 mm layer of silica gel; detection by UV₂₅₄ light. Column chromatography was performed using silica gel 60 of 40-63 mesh. All reagents were commercially available (Acros, Aldrich, Fluorochem) and were used as received.

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Keywords: Cross-coupling • Green Chemistry • Palladium-Phosphane Ligands • Solvent effects

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- [19] A 1:2 metal/ligand ratio was also obtained by titration of ligand **3a** ($\lambda = 244, 271, \text{ and } 313 \text{ nm}$) with $\text{Pd}(\text{MeCN})_2\text{Cl}_2$. See SI.
- [20] ^{31}P NMR spectrum ($\text{DMSO}-d_6$, 121 MHz) of **3a** showed a sharp singlet at -2.25 ppm.

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COMMUNICATION

Cationic pyridiniophosphine ligands have been synthesized as a general Deep Eutectic Solvents (DESS) compatible catalytic system. These ligands, in combination with PdCl_2 , have been successfully applied to different cross coupling reactions. These cationic phosphines improved the catalytic activity of palladium as no other traditional ligand could in such polar media. The catalyst and solvent could be recycled up to 5 times without depletion of yields.

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