Synthesis of Novel Room Temperature Chiral Ionic Liquids. Application as Reaction Media for the Heck Arylation of Aza-endocyclic Acrylates

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Novos líquidos iônicos aquirais e quirais foram preparados utilizando-se rotas sintéticas inéditas e/ou otimizadas. Estas séries de líquidos iônicos do tipo imidazolínico, imidazólico e piridínico foram totalmente caracterizadas, incluindo-se análises por calorimetria diferencial de varredura (DSC). O desempenho desses líquidos iônicos (LIs) foi demonstrado empregando-se a arilação de Heck de aza-acrilato endocíclicos com sais de arenodiazônio ou iodetos de arila. As arilações de Heck realizadas na presença destas entidades iônicas quirais, seja como um solvente ou um aditivo, foram eficazes levando à completa conversão do substrato, em bons a excelentes rendimentos do aduto de Heck na maioria dos casos, apesar de não ser observada indução assimétrica em nenhum dos casos estudados. Dois novos complexos quirais de paládio do tipo carbeno *N*-heterocíclico foram preparados em bons rendimentos a partir de um sal imidazólico quiral e suas estruturas caracterizadas por difração de raios-X. De modo geral, a arilação de Heck empregando tetrafluoroboratos de arenodiazônio em líquidos iônicos demonstrou ser mais eficiente do que os protocolos tradicionais em termos de reatividade e rendimentos de reação.

New achiral and chiral RTILs were prepared using novel and/or optimized synthetic routes. These new series of imidazolinium, imidazolium, pyridinium and nicotine-derived ionic liquids were fully characterized including differential scanning calorimetry (DSC) analysis. The performance of these achiral and chiral room temperature ionic liquids (RTILs) was demonstrated by means of the Heck arylation of endocyclic acrylates employing arenediazonium salts and aryl iodides. The Heck arylations performed in the presence of these ionic entities, either as a solvent or as an additive, were effective leading to complete conversion of the substrate and good to excellent yield of the Heck adduct. In spite of the good performances, no asymmetric induction was observed in any of the cases studied. Two new diastereoisomeric NHC-palladium complexes were prepared in good yields from a chiral imidazolium salt and their structure characterized by X-ray diffraction. Overall, the Heck arylations employing arenediazonium tetrafluoroborates in RTILs were more effective than the traditional protocols employing aryl iodides in terms of reactivity and yields.

Keywords: ionic liquids, chiral ionic liquids, Heck arylation, arenediazonium salts, aryl iodides

Introduction

Room temperature ionic liquids (RTILs) have been proposed as a safer and more eco-friendly alternative to classical organic solvents.[1] In addition, they can offer unique opportunities to modulate the course of a reaction, which combined with their highly adaptable structure opens up almost unlimited prospects in synthesis.[2] In the context of homogenous catalysis, in particular with Pd(0), RTILs have also proven to be

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highly beneficial, contributing to catalyst stabilization, immobilization and recovery.[3]

Among the Pd(0)-catalyzed C-C coupling reactions employed in multi-step synthesis, the Heck reaction plays a preponderant role. However, Heck arylations employing arenediazonium salts as electrophiles have received relatively less attention in comparison to the more traditional aryl halide- or triflate-based arylation protocols.[4] Yet, arenediazonium salts offer several economical, environmental and practical advantages over aryl halides. Arenediazonium salts are easily prepared, are often less expensive than the aryl halides, provide faster palladium-catalyzed arylation reactions, are used under phosphine-free conditions and allow more user-friendly open-air experimental conditions. Surprisingly, the Heck arylation employing arenediazonium salts have been scarcely studied in RTILs.[5]

In view of the increasing importance of RTILs as reaction media in organic synthesis, several groups have recently focused on the synthesis of chiral ionic liquids (CILs), particularly for their potential applications to chiral discrimination and to optical resolution of racemates.[6]

Main advantages of using water-immiscible CILs as solvents include the following: (*i*) the CILs are inexpensively, easily made, and can be recycled; (*ii*) enantiomers of the ionic liquids can be synthesized; (*iii*) they are easily removed from the reaction mixture, and as a result the analyses are usually simpler and more accurate. Additionally, because of their high degree of organization and ionic properties there is also a potential for a more effective solvent-solute interaction and ion-paring formation. The impact of the latter effect on chirality transfer has been illustrated by Wasserscheid and co-workers[7] who reported the asymmetric hydrogenation of a prochiral imidazolium salt embedding a chiral camphorsulfonate anion with the enantioselectivity reaching 94%.

However, despite the large variety of CILs reported so far, their use as reaction media in asymmetric transformations has met with limited success in term of chiral induction.[8] For example, Armstrong *et al.*[9] reported on an enantioselective photoisomerisation induced by a chiral ionic liquid (12% *ee*), and Vo-Thanh and co-workers[10] demonstrated that asymmetric inductions of up to 44% *ee* could be achieved using CILs as reaction media for the Baylis-Hillman reaction. More recently, Afonso *et al.*[11] disclosed the application of CILs as an asymmetric inducing agent in the catalytic Rh(II) carbenoid C-H insertion (27% *ee*) and in the Sharpless dihydroxylation (85% *ee*). Finally, the highest level of induced enantioselectivity reported to date by a solvent as the only source of chirality in an asymmetric reaction was described by Leitner and co-workers.[12] Using a specifically designed ionic liquid with a chiral anion, enantioselectivities of up to 84% *ee* were obtained in the aza-Baylis-Hillman reaction. These results are comparable with the values obtained with the best catalysts for the enantioselective aza-Baylis-Hillman reaction in conventional solvents (94% *ee*,[13] 83% *ee*[14]).

These results indicate that the key to effective chirality transfer lies in strong intermolecular interactions such as electrostatic attraction and hydrogen bonding between the solvent molecules and the intermediates or the transition states of the enantioselective reaction step.

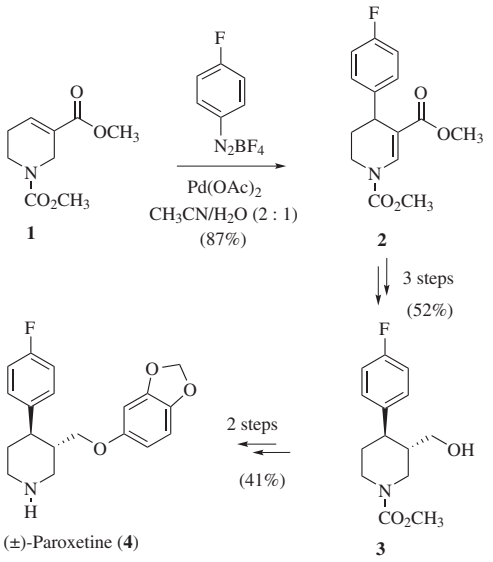
In view of their intrinsic structural flexibility, RTILs also offer wide prospects for potential chirality transfer in organometallic catalysis. This includes *in situ* generation of the active catalyst through carbene palladium complexes. Indeed, the participation of 1,3-dialkylimidazolium-type ionic liquids in the stabilization of catalytic Pd species, related to the so-called "non-innocent" nature of these cations, has been proposed in several cases.[15] In particular, in the course of Heck arylation[16] and Suzuki cross-coupling,[17] 1,2-diaminocarbenes formed *in situ* from an imidazolium-based ionic liquid have been suggested to be involved as Pd ligands.

However, examples of asymmetric versions of this approach based on the use of chiral ionic reaction medium remain scarce. Kiss *et al.*[18] have notably studied the influence of a 1-((S)-2-methylbutyl)imidazolium hexafluorophosphate on the stereochemical course of a Heck oxyarylation reaction. Although the enantioselectivities observed were very modest (4-5% *ee*), this interesting precedent validated the concept.

The eventuality of creating a stereogenic center in a stereocontrolled manner in the course of the Heck reaction would certainly contribute to strengthen its synthetic potential. In line with our continuous efforts to widen the scope and demonstrate the potential of the Heck arylation with arenediazonium in multi-step synthesis of bioactive compounds,[19] we recently reported a new synthesis of the antidepressant drug (±)-paroxetine (**4**) (Scheme 1).[20]

Our synthetic route was based on a fast, clean and simple palladium-catalyzed arylation of a substituted acrylate in CH_3CN/H_2O (2:1) with $Pd(OAc)_2$ as catalyst. Application of this protocol to the aza-endocyclic acrylate **1** afforded an efficient access to an arylated tetrahydropyridine **2**.

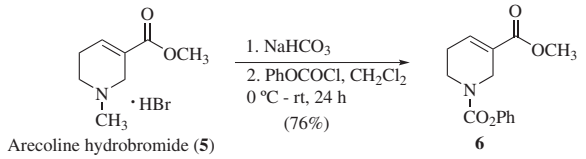
We wish to report herein the synthesis of several chiral ionic liquids, as well as our initial results concerning the performance of these new ionic species as reaction media and additive for the Heck arylation of aza-endocyclic acrylates employing either arenediazonium salts or aryl iodides as electrophiles.



Scheme 1. The Heck arylation with an arenediazonium salt as a key step of the synthesis of (±)-paroxetine (**4**).[7]

Results and Discussion

The aza-endocyclic acrylate **1** was employed in our previous total synthesis of (±)-paroxetine (**4**). However, in the context of the present study, it was found more advantageous to employ the *N*-phenoxycarbonyl starting tetrahydropyridine **6**, since it can be prepared in one step from arecoline hydrobromide (**5**), in 76% yield (Scheme 2).



Scheme 2. Preparation of the tetrahydropyridine precursor.

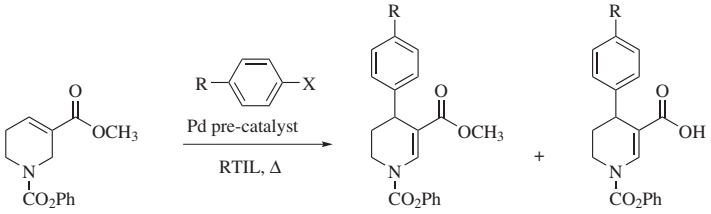
Use of achiral ionic media for the key Heck arylation

We first screened a series of 1-*n*-butyl-3-methylimidazolium (BMIM) salts as a reaction media for the Heck arylation reaction (Table 1). A standard protocol was established as follows: the arenediazonium salt and the $Pd(OAc)_2$ were simultaneously added to a solution of the olefin in the RTIL and the reaction mixture was rapidly heated to 65-70 °C. Alternatively, complete solubilization of the palladium acetate could be first ensured by a brief sonication before addition of the arenediazonium salt, giving essentially the same results. The expected Heck product was accompanied by a side product which revealed to be the carboxylic acid derivative generated by acidic hydrolysis of the α,β-unsaturated methyl ester. The feasibility of the palladium catalyzed process was found to be highly dependent on the nature of the imidazolium counter-ion.[21] These observations paralleled Kabalka's study.[5] Heck arylations were sluggish in [BMIM][Br] and [BMIM][BF_4], providing low conversion and decomposition under forced conditions (Table 1, entries 1 and 2). On the other hand, the reaction proceeded smoothly in the hydrophobic RTILs embedding an hexafluorophosphate (PF_6^-) as well as a bis(trifluoromethanesulfonyl)imide (NTf_2^-) anion.[22] Complete and clean conversions were observed after only one hour at 65 °C, thus allowing isolation of the expected adduct in good yields (Table 1, entries 3 to 5). Interestingly, the reaction worked equally well in [BDIM][NTf_2] (1-*n*-butyl-2,3-dimethylimidazolium bis(trifluoromethanesulfonyl) imide) where the critical C-2 position of the imidazolium cation is substituted with a methyl group (Table 1, entries 5 and 6). The use of $Pd(OAc)_2$ or $Pd_2(dba)_3$ as pre-catalyst gave comparable results (compare entries 3 and 4 or entries 6 and 7). Several bases were also tested in [BMIM][NTf_2] in order to neutralize the HBF_4 produced in the course of the reaction. Remarkably, the presence of 2 equivalents of either DIPEA, K_2CO_3 or NaOAc totally precluded the reaction. The same trend has previously been observed in protic solvents and might be imputed to the relative instability of the arenediazonium salt in basic media.

In order to better evaluate the performance of arenediazonium salts in RTILs, the reactivity of other electrophiles was also assessed. A first set of experiments was run at 100 °C. Phenyl triflate revealed ineffective in the presence of NaOAc in [BMIM][NTf_2] (Table 1, entry 8) and the same outcome was observed using iodobenzene with NaOAc in [BMIM][Br] (Table 1, entry 9). An encouraging result was obtained with the iodobenzene thanks to the use of Ag_2CO_3 in [BMIM][NTf_2] (Table 1, entry 10). Since a comparable result was obtained with 1-fluoro-4-iodobenzene (Table 1, entry 11) we briefly optimized these conditions (Table 1, entries 12 to 15). Running the reaction at 120 °C for 5 h with $Pd(OAc)_2$ in [BDIM][NTf_2] gave rise to a reasonably efficient process (Table 1, entries 14) while the use of $Pd_2(dba)_3$ proved much less efficient. Altogether, these observations confirmed the higher reactivity of arenediazonium salts as compared to other electrophilic reagents, even in ionic media.

With the feasibility of the key Heck arylation step of our synthesis of paroxetine in RTILs ensured, we then turned our attention toward the use of chiral media. A chiral environment surrounding the metal might indeed lead to some asymmetric induction in the course of the migratory insertion step during which the stereogenic center is created. Ordinary asymmetric induction in the course of the Heck coupling with arenediazonium salts is a challenging task

Table 1. The key Heck arylation reaction in various RTILs



6 **7a**, R = F; **7b**, R = H **8a**, R = F; **8b**, R = H

Entry	R[a]	X	RTIL	Pre-catalyst[b]	Base	T (°C)	t (h)	Conv. (%)[c]	Yield (%)[d] ester/acid
1	F	N_2BF_4	[BMIM][Br]	$Pd(OAc)_2$	/	70	48	11	59/11
2	F	N_2BF_4	[BMIM][BF_4]	$Pd(OAc)_2$	/	65	72	66	35/12
3	F	N_2BF_4	[BMIM][PF_6]	$Pd(OAc)_2$	/	65	1	100	75/16
4	F	N_2BF_4	[BMIM][PF_6]	$Pd_2(dba)_3$	/	65	1	100	77/5
5	F	N_2BF_4	[BMIM][NTf_2]	$Pd(OAc)_2$	/	65	1	100	71/18
6	F	N_2BF_4	[BDIM][NTf_2][e]	$Pd(OAc)_2$	/	65	1	100	72/17
7	F	N_2BF_4	[BDIM][NTf_2][e]	$Pd_2(dba)_3$	/	65	1	100	70/18
8	H	OTf[f]	[BMIM][NTf_2]	$Pd(OAc)_2$	NaOAc[g]	100	24	0	/
9	H	I[f]	[BMIM][Br]	$Pd(OAc)_2$	NaOAc[g]	100	24	0	/
10	H	I[f]	[BMIM][NTf_2]	$Pd(OAc)_2$	Ag_2CO_3[h]	100	24	46	56/0
11	F	I[i]	[BMIM][NTf_2]	$Pd(OAc)_2$	Ag_2CO_3[h]	100	22	45	30/0
12	F	I[i]	[BMIM][NTf_2]	$Pd(OAc)_2$	Ag_2CO_3[h]	120	5	55	82/0
13	F	I[i]	[BMIM][NTf_2]	$Pd_2(dba)_3$	Ag_2CO_3[h]	120	24	45	9/0
14	F	I[i]	[BDIM][NTf_2][e]	$Pd(OAc)_2$	Ag_2CO_3[h]	120	5	100	68/0
15	F	I[i]	[BDIM][NTf_2][e]	$Pd_2(dba)_3$	Ag_2CO_3[h]	120	24	63	35/0

[a] Unless otherwise stated, 1.5 equiv. of electrophile were used; [b] $Pd(OAc)_2$ 10 mol%; $Pd_2(dba)_3$ 5 mol%; [c] Conversion calculated on the basis of the recovered starting material; [d] Isolated yields, based on starting material recovering, when appropriate; [e] [BDIM] = 1-*n*-butyl-2,3-dimethylimidazolium; [f] 2.0 equiv. of halide were used; [g] 1.5 equiv. of base were used; [h] 1.1 equiv. of base were used; [i] 3.0 equiv. of halide were used.

though, partly because of the arenediazonium instability in the presence of the phosphine ligands. Moreover, the use of chiral RTILs as medium for the more traditional Heck reactions employing aryl halides and aryl triflates as arylating agents were also evaluated.

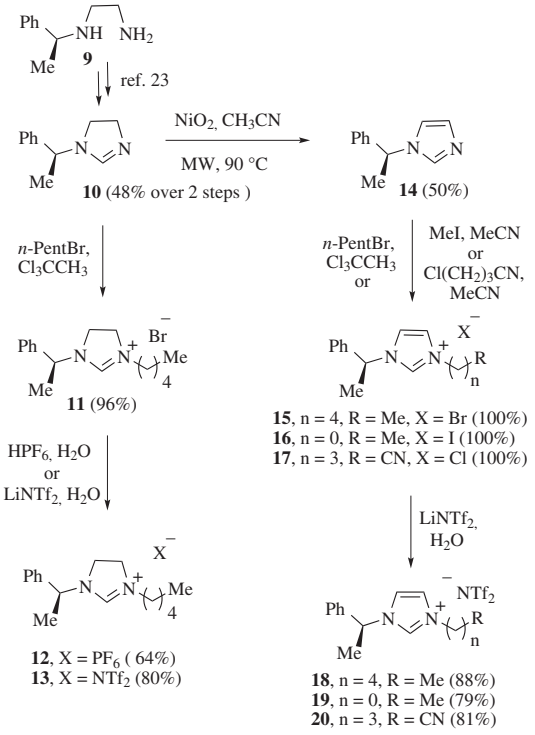
Use of C-2 unsubstituted imidazolinium and imidazolium chiral ionic liquid

In the first part of this study we focused on the possible interaction between the palladium-based catalytic species and the chiral imidazolium cation of the ionic liquid through the C-2 position, bearing in mind the opportunities for the *in situ* formation of imidazol-2-ylidene metal complexes.

Preparation of the chiral ionic liquids

Access to C-2 unsubstituted chiral imidazolinium/imidazolium salts was envisioned from the corresponding imidazoline/imidazole through a straightforward quaternarisation/anion metathesis sequence (Scheme 3).

The imidazolinic precursors were prepared according to our previously described route based on the condensation between an orthoester and the chiral diamine **9**.[23] Preparation of the latter was carefully optimized: slow addition (2 mL h^{-1}) of a concentrated (5.4 mol L^{-1}) aqueous solution of 2-chloroethylamine to neat chiral amine (2 equiv.) at 80 °C provided, after workup, a crude mixture from which the excess of chiral amine was distilled off (40-50 °C/3 × 10^{-2} mbar). A bulb to bulb distillation (90-100 °C/3 × 10^{-2} mbar) allowed isolation of the pure chiral diamine **9** in 60% yield. The use of triethylorthoformate as the orthoester gave access to C-2 unsubstituted imidazoline **10**. Aromatising dehydrogenation then produced the corresponding imidazole **14**.[23] We found that this transformation can be accomplished in a few minutes by the use of the commercially available NiO_2 (8 equiv.) in acetonitrile under microwave activation (200W irradiation while cooling with compressed air so as to maintain the temperature at 90 °C). The imidazole **14** was thus obtained in 50% yield after a simple filtration over grade III alumina. Alternatively, this compound can be prepared by means of a cyclocondensation reaction[24]



Scheme 3. Preparation of the imidazolinium and imidazolium chiral RTILs.

from glyceraldehyde, α-methylbenzylamine, formaldehyde and ammonium acetate using the Saigo's procedure (70% yield).[25] Prolonged reflux of the imidazoline **10** or imidazole **14** in 1,1,1-trichloroethane in the presence of an excess of 1-bromopentane furnished the expected 3-pentyl derivatives **11** and **15**, respectively. Treatment of the imidazole **14** with methyl iodide at room temperature in acetonitrile smoothly delivered the 3-methylimidazolium **16**. In order to enhance chances of interactions between the catalytic palladium species and the imidazolium nucleus of the ionic solvent we also prepared the imidazolium salt **17** in which the alkyl chain bears a coordinating nitrile functionality.[26] Indeed, mechanistic studies from our laboratories have shown the role of the solvent acetonitrile in stabilizing catalytic species generated from $Pd_2(dba)_3$ in the course of the Heck arylation with arenediazonium salts.[27]

At this stage, it appeared critical to control the enantiomeric purity of our derivatives. This was realized by ^{1}H NMR analysis of the representative imidazolium bromide **15**. The chiral shift reagent tris[3-trifluoromethylhydroxymethylene)-D-camphorato] europium III allowed splitting ($\Delta\delta = 0.1$ ppm) of the H-2 signal of the racemate at 12.78 ppm in $CDCl_3$. Analysis of the enantiopure material under the same conditions clearly demonstrated the absence of any detectable racemization. This high degree of enantiomeric purity was independent of the procedure used to prepare the chiral imidazole precursor.

The preparation of the targeted ionic liquids required a final anion metathesis step, which was performed using known procedures (Scheme 3). The imidazolinium hexafluorophosphate salt **12** was prepared from the corresponding acid (64% yield) as a solid melting at 86-87 °C. The bis(trifluoromethanesulfonyl)imide was introduced by mean of the corresponding lithium salt yielding imidazolinium **13** (80% yield), and imidazolium **18-20** (79-88% yield). Interestingly, ^{1}H NMR analysis of the imidazolium **20** revealed that the H-2 proton had become highly exchangeable with deuterium, thus indicating an increased acidity.

All these salts are liquid at room temperature and differential scanning calorimetry (DSC) analyses were recorded in order to characterize the thermal behaviour of these new chiral ionic liquids. In sharp contrast with its hexafluorophosphate counterpart (mp 86-87 °C), the imidazolinium bis(trifluoromethanesulfonyl)imide **13** displayed glass transition (Tg) at –59 °C. A comparable Tg of –57 °C was found for the corresponding *n*-pentyl imidazolium salt **18**. This behaviour parallels, yet to a lesser extent, what we previously observed in the C-2-substituted series in which the aromatic imidazolium salts displayed Tg values 7 to 11 °C higher than the corresponding imidazolinium derivatives. Overall, the lack of substituent at C-2 lowered the Tg values which were of –55 °C and –48 °C for the corresponding 2-ethyl derivatives. Finally the side chain was also found to exert a certain influence on the thermal behaviour of these salts since a slightly higher Tg of –50 °C was observed for the methyl imidazolium bis(trifluoromethanesulfonyl)imide **19**, whereas the nitrile substituted derivative **20** displayed a glass transition at –46 °C.

Evaluation of the chiral ionic liquids

In order to evaluate the asymmetric induction effectively, analytical conditions were sought for the key arylated product. The enantiomers of **7a** were readily resolved by HPLC using a Chiralcel OD column (Hexane/*i*-PrOH 70:30 (v:v), Rt = 6.6 min and 11.5 min). Separation was sufficient to allow isolation of an enantiomerically pure sample of each enantiomers on a semi-preparative column. Characterization of the arylated compound **7a** in an enantiopure form allowed assessment of its configurational stability. Importantly, no racemisation was observed, as judged by chiral HPLC analysis, after prolonged heating of **7a** in basic media (Ag_2CO_3, [BMIM][NTf_2], 120 °C, 24 h).

On a strictly chemical standpoint, the nature of the RTIL was found to have a certain influence on the course of the reaction. In the imidazolinium series the

bis(trifluoromethanesulfonyl)imide salt **13** revealed less favourable, even under more vigourous conditions, than the hexafluorophosphate salt **12** which allowed smooth and clean conversion of the starting acrylate (Table 2, entries 1, 2 and 3). As far as the imidazolium salts were concerned, the 3-pentyl derivative **18** gave the best result. Unexpectedly, the reaction proved rather sluggish when the less hindered 3-methyl imidazolium salt **19** was used, which might be correlated to an increase in viscosity (Table 2, entry 6). A complete conversion was achieved with the nitrile-functionalized salt **20** after prolonged heating with $Pd_2(dba)_3$ as a pre-catalyst which presented a marked contrast with $Pd(OAc)_2$ (Table 2, entries 7 and 8).

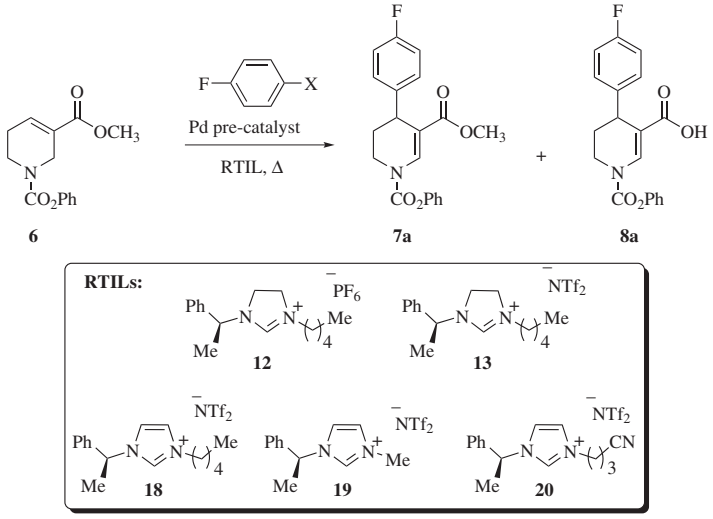
Several of these chiral RTILs gave rise to an efficient transformation, although the enantiomeric excess of the isolated product was found negligible, independently of the chiral ionic liquid used. In order to ensure that this behavior was not due to a mechanistic particularity of the Heck arylation employing arenediazonium salts, we performed the Heck arylation with the corresponding aryl iodide. When the olefin **6** was treated with 1-fluoro-4-iodobenzene in the chiral imidazolium **18** a satisfactory transformation was obtained (Table 2, entry 5), but unfortunately no asymmetric induction was evidenced in the Heck adduct.

Preparation and use of imidazolium-derived diaminocarbene Pd complexes

Aiming at increasing the interaction between the imidazolium nucleus of the RTIL and the palladium catalyst, we also studied the use of imidazolium-derived pre-formed diaminocarbene palladium complexes.[28]

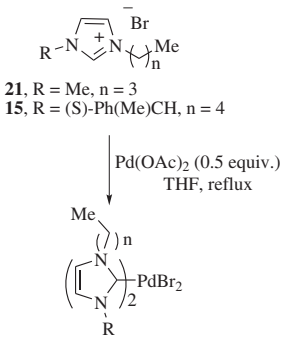
Thus, we first prepared the 1-*n*-butyl-3-methylimidazolium bromide-derived *N*-heterocyclic carbene palladium complex **22** described by Xiao (Scheme 4).[16] The latter was generated from $Pd(OAc)_2$ in refluxing THF in 77% isolated yield as the sole *trans* isomer (*anti*/*syn,* 1:1). When evaluated in our model reaction of **6** with 4-fluorobenzenediazonium tetrafluoroborate, this entity proved poorly active in [BMIM][Br] (20 mol%, 80 °C, 48 h, 9% yield bsmr at 60% of conversion) and totally inefficient in [BMIM][PF_6] (20 mol%, 65 °C, 24 h).

Table 2. The Heck arylation in various imidazolinium and imidazolium chiral RTILs



Entry [a]	X	RTIL	Pre-catalyst [b]	T (°C)	t (h)	Conv. (%) [c]	Yield (%) [d] ester/acid
1	N_2BF_4	**12**	$Pd(OAc)_2$	90	6	100	72/0
2	N_2BF_4	**13**	$Pd(OAc)_2$	65	27	26	50/0
3	N_2BF_4	**13**	$Pd(OAc)_2$	90	7	39	53/0
4	N_2BF_4	**18**	$Pd(OAc)_2$	65	6	100	66/24
5[e]	I[f]	**18**	$Pd(OAc)_2$	90	4	50	74/0
6	N_2BF_4	**19**	$Pd(OAc)_2$	65	11	23	47/0
7	N_2BF_4	**20**	$Pd(OAc)_2$	65	5	27	79/0
8	N_2BF_4	**20**	$Pd_2(dba)_3$	65	24	100	53/10

[a] 1.5 equiv. of the arenediazonium salt was used; [b] $Pd(OAc)_2$ 10 mol%; $Pd_2(dba)_3$ 5 mol%; [c] Conversion calculated on the basis of the recovered starting material; [d] Isolated yields, based on starting material recovering; [e] 1.1 equiv. of the base Ag_2CO_3 were used; [f] 2.0 equiv. of iodide were used.



21, R = Me, n = 3
15, R = (S)-Ph(Me)CH, n = 4

22, R = Me, n = 3 (*trans-syn/trans-anti* 1:1) (77%)
23, R = (S)-Ph(Me)CH, n = 4 (*cis-syn/trans-anti* 1:1) (54%)

Scheme 4. Preparation of palladium complexes from imidazolium salts.

In parallel, the behaviour of our chiral imidazolium cation in the presence of $Pd(OAc)_2$ was also explored by means of the reaction of the bromide **15** with 0.5 equiv. of the palladium salt in refluxing THF (Scheme 3). A smooth transformation occurred after heating **15** with $Pd(OAc)_2$ for 6 h, allowing isolation of the expected palladium complex **23** in 54% yield as a 1:1 mixture of isomers according to ^1H and ^{13}C NMR. Assignment of the stereochemical identity of these diaminocarbenes complexes was not trivial. Gratifyingly, a single crystal suitable for X-ray diffraction analysis could be obtained for each isomer thus allowing to identify the two products as the *trans-anti* isomer **23a** along with the quite unexpected *cis-syn* derivative **23b** (Figure 1).[29] A π-stacking interaction between the phenyl groups of each diaminocarbene moieties might account for the formation of this strained isomer.

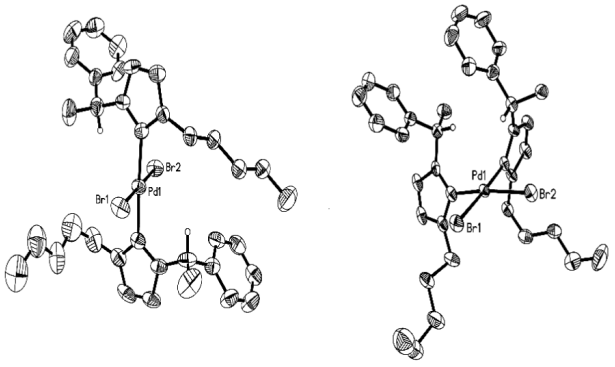


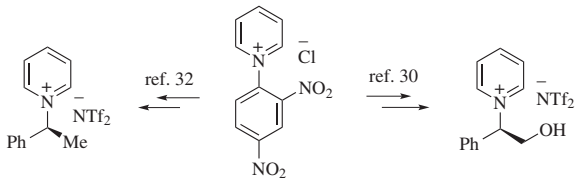
Figure 1. X-ray structure of the *trans-anti* **23a** (left) and *cis-syn* **23b** (right) diaminocarbene Pd complexes obtained from the chiral imidazolium **15** and $Pd(OAc)_2$.[19]

The mixture of isomers **23a, b** was evaluated in our key Heck arylation with 4-fluorobenzenediazonium tetrafluoroborate. However, the use of 10-20 mol% of these complexes in either THF (reflux, 24 h), CH_3CN (reflux, 24 h), or [BMIM][PF_6] (100 °C, 24 h) failed to induce any transformation. The same behavior was observed when 1-fluoro-4-iodobenzene was used (3.0 equiv. Ag_2CO_3, DMF, 130 °C, 24 h). The intrinsic stability of these bis-diaminocarbene palladium complexes might be responsible for their lack of catalytic activity.

Use of an hydroxylated chiral ionic liquid

In the course of the development of our synthetic methodology we found out that the key Heck reaction could be run efficiently in MeOH. The beneficial effect of protic solvents prompted us to explore the influence of hydroxyl-containing chiral ionic liquids for this transformation.

We took advantage here of the preparation of the phenylglycinol derivative **26** we reported recently.[30] This ionic liquid was synthesized from pyridinium **25** employing a route previously described by us based on the use of the Zincke reaction (Scheme 5).[31] The bis(trifluoromethanesulfonyl)imide anion was selected on the basis of previous studies.[32] To our satisfaction, it was found that this hydroxylated derivative displayed a Tg of –45 °C measured by DSC analysis as compared to –30 °C for the its non-hydroxylated counterpart **24**.[32] The latter was also considered for the matter of comparison.

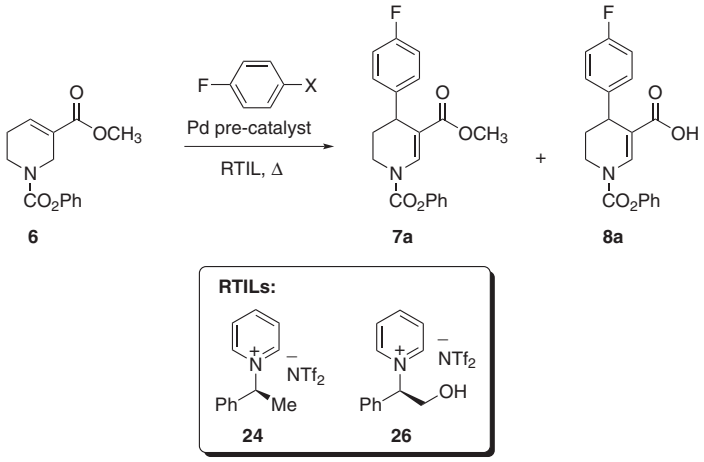


24 (74%) **25** **26** (61%)

Scheme 5. Preparation of the pyridinium chiral RTILs.

The unsubstituted α-methylbenzylamine-derived salt **24** gave rise to a smooth transformation with 4-fluorobenzenediazonium tetrafluoroborate (Table 3, entry 1). Despite the high tolerance of the key Heck coupling for alcoholic media, the reaction in the hydroxylated derivative **26** proved much less efficient, irrespectively to the pre-catalyst (Table 3, entries 2 and 3). The conversions were not altered, but the yields were strongly affected. For the sake of comparison, the iodide was also evaluated as under the reaction conditions determined previously (Table 3, entries 4 and 5). As observed before, $Pd(OAc)_2$ was more efficient than $Pd_2(dba)_3$. Notably, in this case the halide gave rise to a better transformation than the corresponding arenediazonium salt. Unfortunately, no enantiomeric excess was detected from the analysis of the isolated products.

Table 3. The Heck arylation in hydroxylated and non-hydroxylated chiral pyridinium RTILs



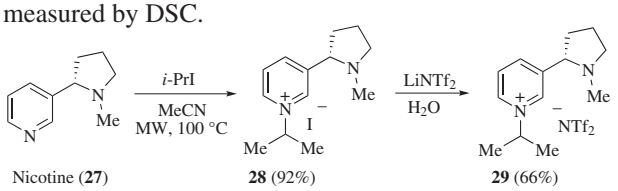
Entry	X [a]	RTIL	Catalyst [b]	T (°C)	t (h)	Conv. (%) [c]	Yield (%) [d] ester/acid
1	N_2BF_4	**24**	$Pd(OAc)_2$	65	1	100	53/18
2	N_2BF_4	**26**	$Pd(OAc)_2$	65	1.5	100	34/4
3	N_2BF_4	**26**	$Pd_2(dba)_3$	65	1.5	100	21/3
4 [e]	I	**26**	$Pd(OAc)_2$	120	1	100	80/0
5 [e]	I	**26**	$Pd_2(dba)_3$	120	2	100	51/0

[a] 1.5 equiv. of arenediazonium salt and 3.0 equiv. of iodide were used; [b] $Pd(OAc)_2$ 10 mol%; $Pd_2(dba)_3$ 5 mol%; [c] Conversion calculated on the basis of the recovered starting material; [d] Isolated yields, based on starting material recovering; [e] 1.1 equiv. of the base Ag_2CO_3 was used.

The use of chiral ionic liquid bearing a basic functionality as a potential coordination site

In the last part of this study we adopted an alternative strategy. In order to drive the interaction between the ionic liquid and the catalytic species we opted for the use of chiral ionic entities bearing a *N*-heterocycle susceptible to coordination to the metal centre. Indeed, several studies by Shreeve and co-workers[33] have recently described catalytically active entities based on the complex between a palladium salt and an ionic liquid bearing a basic functionality. To the best of our knowledge, no examples of chiral derivative of that kind were reported so far. We reasoned that such electron-rich entities might interact significantly with the cationic palladium species involved in the catalytic cycle operating in the case of arenediazonium salts.

We first focused on the readily accessible nicotine derivative. Albrecht has recently used such a pyridinium halide as a carbene precursor to prepare a catalytically active palladium complex.[34] The quaternarization of nicotine had already been described earlier by Shibagaki *et al.*[35] who showed that it was possible to chemoselectively *N*-alkylate the pyridine nucleus versus the pyrrolidine ring on the basis of steric considerations. However, as the yields and conversion reported were not satisfactory we first optimized the access to the required pyridinium salt. In this regard, the use of microwave activation proved highly efficient. Indeed, treatment of the nicotine (**27**) with *i*-propyl iodide in CH_3CN at 100 °C under microwave irradiation led to the clean and efficient formation of the expected pyridinium iodide **28** in only 2 h (Scheme 6). Anion metathesis proceeded uneventfully for this iodide salt to afford the desired chiral pyridinium bis(trifluoromethanesulfonyl) imide **29**. The latter displayed a glass transition at –56 °C measured by DSC.



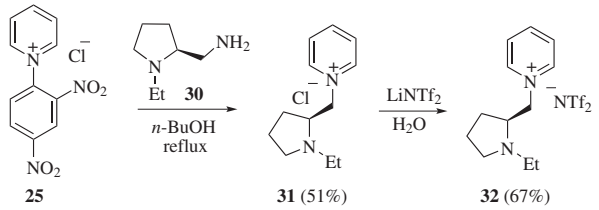
Scheme 6. Preparation of the nicotine-derived chiral RTIL **29**.

We then evaluated the influence of this chiral pyridinium as an additive in the course of our model arylation (Table 4). Since HBF_4 is formed during the transformation, 1.2 equiv. of the basic ionic liquid were used. On the other hand, the C-2 methyl derivative [BDIM][NTf_2] was selected as a potentially "innocent" ionic media, although carbene formation at C-4 and C-5 of the imdazolium ring has also been reported.[36] The presence of the additive strongly changed the conversion in

the case of 4-fluorobenzenediazonium tetrafluoroborate and of the aryl iodide counterpart. In spite of lower conversions, yields were higher using the aryl halide (Table 4, entries 3 and 4). This observation might be related with some decomposition of the arenediazonium salt in the reaction media.

Another pyridinium ionic liquid bearing a chiral pyrrolidine moiety was prepared by the Zincke reaction (Scheme 7). Thus, treatment of the so-called Zincke salt by the commercially available chiral primary amine **30** afforded the desired pyridinium chloride **31**, which upon anion metathesis provided the bis(trifluoromethanesulfonyl) imide salt **32** in 35% overall yield. A Tg of –52 °C was measured by DSC for this chiral ionic liquid.

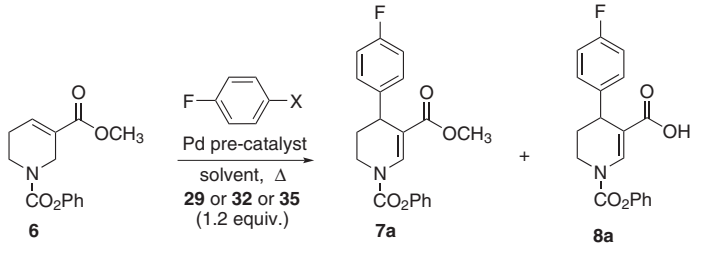
The impact of the chiral pyridinium ionic liquid **32** on the outcome of the Heck reaction is similar that observed previously for the ionic liquid **29** (Table 4). The basic nature of the additive seems to hamper the transformation, although to a lesser extent than that observed with the nicotine-

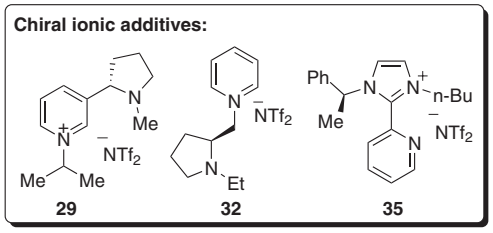


25 31 (51%) 32 (67%)

Scheme 7. Synthesis of the chiral pyridinium RTIL **33** by means of the Zincke reaction.

Table 4. The Heck arylation in an achiral ionic media in the presence of different chiral ionic additives



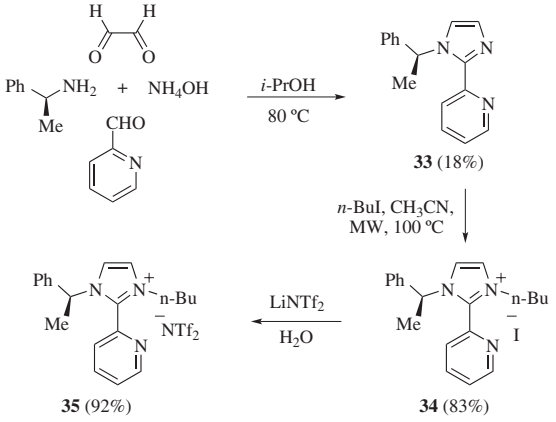


Entry	Additive	X [a]	Solvent	Pre-catalyst [b]	T (°C)	t (h)	Conv. (%) [c]	Yield (%) [d] ester/acid
1	**29**	N_2BF_4	[BDMIM][NTf_2]	$Pd(OAc)_2$	65	24	31	47/0
2	**29**	N_2BF_4	[BDMIM][NTf_2]	$Pd_2(dba)_3$	65	24	23	52/0
3[e]	**29**	I	[BDMIM][NTf_2]	$Pd(OAc)_2$	120	24	9	80/0
4[e]	**29**	I	[BDMIM][NTf_2]	$Pd_2(dba)_3$	120	24	12	92/0
5	**32**	N_2BF_4	[BDIM][NTf_2]	$Pd(OAc)_2$	65	24	47	57/0
6	**32**	N_2BF_4	[BDIM][NTf_2]	$Pd_2(dba)_3$	65	24	32	47/0
7	**32**	N_2BF_4	THF	$Pd(OAc)_2$	65	24	19	100/0
8	**32**	N_2BF_4	THF	$Pd_2(dba)_3$	65	24	11	31/0
9 [e]	**32**	I	[BDIM][NTf_2]	$Pd(OAc)_2$	120	24	29	91/0
10 [e]	**32**	I	[BDIM][NTf_2]	$Pd_2(dba)_3$	120	24	14	70/0
11	**35**	N_2BF_4	[BDIM][NTf_2]	$Pd(OAc)_2$	65	24	100	90/0
12	**35**	N_2BF_4	[BDIM][NTf_2]	$Pd_2(dba)_3$	65	24	100	96/0
13	**35**	N_2BF_4	THF	$Pd(OAc)_2$	65	3	54	84/0
14	**35**	N_2BF_4	THF	$Pd_2(dba)_3$	65	3	31	86/0
15 [e]	**35**	I	[BDIM][NTf_2]	$Pd(OAc)_2$	120	7	100	58/0
16 [e]	**35**	I	[BDIM][NTf_2]	$Pd_2(dba)_3$	120	24	45	55/0

[a] 1.5 equiv. of arenediazonium salt and 3.0 equiv. of iodide were used; [b] $Pd(OAc)_2$ 10 mol%; $Pd_2(dba)_3$ 5 mol%; [c] Conversion calculated on the basis of the recovered starting material; [d] Isolated yields, based on starting material recovering; [e] 1.1 equiv. of the base Ag_2CO_3 was used.

derived pyridinium salt. For comparison, the reaction with the 4-fluorobenzenediazonium tetrafluoroborate was also carried out in THF instead of [BDIM][NTf_2] and the conversions were even lower in this molecular solvent (Table 4, entries 7 and 8).

Finally, in an attempt to reduce the basicity of the chiral additive, we turned our attention to the possibility of introducing a heteroaromatic appendage into the structure of the ionic liquid. Shreeve has described a series of achiral 2-imidazolyl or 2-pyridylimidazolium salt useful for the preparation of palladium complexes.[33] In line with this work we envisioned the synthesis of such compounds from a chiral primary amine by means of a one-pot multi-component reaction. Although application of this route to the preparation of chiral 2,2'-bisimidazole did not appear viable,[37] we succeeded in preparing a 2-pyrydylimidazole. Indeed, after careful optimization it was found that treatment of α-methylbenzylamine with glyoxal, ammonium hydroxide and pyridine-2-carboxaldehyde furnished imidazole **33** in 18% yield (Scheme 8).



Scheme 8. Preparation of the chiral imidazolium ionic liquid **35**.

Quaternarization of the more basic imidazole nucleus was then carried out in a highly convenient and efficient manner. Microwave activation and anion metathesis step provided the expected chiral ionic liquid **35** in 76% overall yield (Scheme 8). Despite the presence of the aromatic substituent at C-2, this bis(trifluoromethanesulfonyl)imide salt displayed a Tg of –40 °C as measured by DSC.

The less basic additive **35** was found to be fully compatible with the use of 4-fluorobenzenediazonium tetrafluoroborate in our key palladium-catalyzed arylation (Table 4). The expected product was isolated in high yield, although the transformation appeared to be slower in [BDIM][NTf_2] (Table 4, entries 11 and 12). Remarkably, in this particular case the pre-catalyst $Pd_2(dba)_3$ gave a better result than $Pd(OAc)_2$. A sluggish, yet clean, reaction was also observed in THF (Table 4, entries 13 and 14). The aryl iodide also gave a reasonably efficient reaction thanks to the use of $Pd(OAc)_2$ (Table 4, entries 15 and 16).

Conclusions

Eight new chiral RTILs were prepared using novel and/or carefully optimized synthetic routes. This series of imidazolinium, imidazolium and pyridinium ionic liquids were fully characterized, including differential scanning calorimetry (DSC) analysis. The Heck reaction of substituted aza-endocyclic acrylates using arenediazonium tetrafluoroborates and aryl iodides as electrophiles were investigated in these new RTILs. A strong influence of the counter-ion was observed, with the lipophilic RTILs providing the best results. The Heck arylations performed in these chiral ionic entities, either as a solvent or an additive, were effective leading to complete conversion of the substrate and good to excellent yield of the Heck adduct. In spite of the overall performance of the Heck arylations in all the cases studied no asymmetric induction was detected. Two new diastereoisomeric NHC-palladium complexes were prepared in moderate yields and their structure characterized by X-ray diffraction analysis thus allowing the identification of the unusual *cis-syn* stereoisomer **23b**. Overall, the Heck arylations employing arenediazonium tetrafluoroborates in RTILs were more effective than the traditional protocols employing aryl iodides in terms of reactivity and yields. Applications of the new chiral RTILs described herein to other synthetic transformations are in progress and the results concerning these studies will be reported in due course.

Experimental

General

Reagents and solvents are commercial grade and were used as supplied, except when specified in the experimental procedure. CH_2Cl_2 was distilled from calcium hydride and THF was distilled from Na. Reactions were monitored by TLC analysis using Merck Silica Gel 60 F-254 thin layer plates. Flash column chromatography was performed on Acros silica gel 60, 0.040-0.063 mm. ^{1}H NMR and ^{13}C NMR data were recorded on a Varian Gemini 2000 (300 MHz for ^{1}H and 75 MHz for ^{13}C NMR), Varian Inova (500 MHz for ^{1}H and 125 MHz for ^{13}C NMR) or Bruker Avance (250 MHz for ^{1}H and 63 MHz for ^{13}C NMR or 300 MHz for ^{1}H and 75 MHz for ^{13}C NMR) spectrometer using as internal standard the residual nondeuterated solvent ($CHCl_3$, CH_3OH, acetone or DMSO) or TMS (^{1}H NMR). Data are reported as follows: chemical shift

in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signal), coupling constant (Hz), integration. High-resolution mass spectra (HRMS) were measured on a VG Auto-spec-Micromass spectrometer (EI) or in a Waters Q-Tof Ultima API (ESI). Infrared spectra (IR) were obtained on a Thermo-Nicolet IR-200 spectrometer and absorptions are reported in reciprocal centimeters. Melting points were recorded on an Electrothermal 9100 melting point apparatus and are uncorrected. Differential scanning calorimetry (DSC) analyses were recorded on a DSC Diamond Perkin Elmer.

General procedures for the quaternarization

A solution of imidazoline **10** or imidazole **14** (1 equiv.) and alkyl halide (3.0-5.0 equiv.) in 1,1,1-trichloroethane or acetonitrile (0.6 mL $mmol^{-1}$) was refluxed until TLC monitoring showed complete consumption of the starting material (2-3 days). For the reaction in 1,1,1-trichloroethane, the insoluble oily material was separated by decantation and washed several times with 1,1,1-trichloroethane to give the expected halide salt. For the reaction in acetonitrile, the mixture was concentrated to dryness and partitioned between Et_2O and water. After two additional extractions with Et_2O, the aqueous phase was concentrated to dryness to give the expected halide salt.

General procedure for the anion metathesis with lithium bis(trifluoromethanesulfonyl)imide

A solution of halide salt (1.0 equiv.) in water (6.5 mL $mmol^{-1}$) containing lithium bis(trifluoromethanesulfonyl)imide (1.1 equiv.) was heated with stirring at 70 °C for 2 h and allowed to stand at room temperature overnight. The insoluble oily material was extracted with dichloromethane and the organic layer was separated and washed with water and brine, dried over Na_2SO_4, filtered and concentrated to dryness to give the expected bis(trifluoromethanesulfonyl)imide salt.

General procedure for the Heck coupling with arenediazonium salts in ionic liquids

To a solution of olefin **6** (1 equiv., typically 0.25 mmol) in ionic liquid (4.0 mL $mmol^{-1}$) was added, at once, a mixture of the 4-fluorobenzenediazonium tetrafluoroborate (1.5 equiv.) and Pd pre-catalyst (5-10 mol%). The reaction mixture was immersed in an oil bath and heated under stirring (see tables for the temperature and reaction time). After cooling, the mixture was extracted (6 × 40 mL $mmol^{-1}$) with Et_2O and with 1,1,1-trichloroethane (3 × 40 mL $mmol^{-1}$). The combined organic layers were then concentrated to dryness and purified by flash column chromatography over silica gel (petroleum ether/ethyl acetate, 4:1) to furnish the desired Heck adduct **7a** and, in some cases, the corresponding acid **8a**.

General procedure for the Heck coupling with aryl iodides in ionic liquids

To a solution of olefin **6** (1 equiv., 0.25 mmol) in ionic liquid (4.0 mL $mmol^{-1}$) was added the aryl iodide (3 equiv.), Ag_2CO_3 (1.1 equiv.) and Pd pre-catalyst (5-10 mol%). The reaction mixture was immersed in an oil bath and heated under stirring (see tables for the temperature and reaction time). After cooling, the mixture was extracted with Et_2O (6 × 10 mL) and with 1,1,1-trichloroethane (3 × 10 mL). The combined organic layers were then concentrated to dryness and purified by flash column chromatography over silica gel (petroleum ether/ethyl acetate, 4:1) to furnish the arylated product **7a,b**.

Specific procedures and compounds data

*3-Pentyl-1-((1S)-1-phenylethyl)-4,5-dihydro-1H-imidazolium bromide (**11**)*

Prepared from imidazoline **10** (1.0 g, 5.75 mmol) according to the general procedure for quaternarization in 1,1,1-trichloroethane. Bromide **11** (1.80 g, 96%) was obtained as light brown liquid. $[\alpha]^{25}_D$ –6.8 (*c* 1.20, $CHCl_3$); IR ν_{max}/cm^{-1}: 2933, 2872, 1646, 1495, 1455, 1382, 1255, 1201, 1142, 703 (thin film); ^1H NMR (300 MHz, $CDCl_3$) δ 9.76 (s, 1H), 7.28-7.42 (m, 5H), 5.06 (q, *J* 7.0 Hz, 1H), 3.95-3.84 (m, 2H), 3.79-3.64 (m, 4H), 1.79 (d, *J* 7.0 Hz, 3H), 1.71-1.60 (m, 2H), 1.35-1.23 (m, 4H), 0.87 (t, *J* 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.6 (CH), 137.3 (C_0), 129.0 (CH), 128.6 (CH), 126.7 (CH), 57.6 (CH), 48.2 (CH_2), 48.0 (CH_2), 46.3 (CH_2), 28.1 (CH_2), 26.8 (CH_2), 21.9 (CH_2), 19.5 (CH_3), 13.6 (CH_3); MS (ESI +) *m/z*: 245 [M^+]; MS (ESI–) *m/z*: 79, 81 [Br^-]; HRMS (ESI +) *m/z*: Calcd for $C_{16}H_{25}N_2$ [M^+] 245.2018, Found 245.2021.

*3-Pentyl-1-((1S)-1-phenylethyl)-4,5-dihydro-1H-imidazolium hexafluorophosphate (**12**)*

To a stirred solution of imidazolinium bromide **11** (1.97 g, 6.04 mmol) in water (12 mL) at 0 °C was added hexafluorophosphoric acid (1.16 mL of a 60% solution in H_2O, 7.85 mmol, 1.3 equiv.). The stirring was continued at 0 °C for 2 h and the solution was allowed to stand at room temperature overnight. The reaction mixture was then extracted with CH_2Cl_2 and the combined organic layers were washed with water, dried over Na_2SO_4, filtered and concentrated to dryness to give **12** (1.52 g, 64%), obtained as a light yellow solid. $[\alpha]^{25}_D$ –4.0 (*c* 1.50, $CHCl_3$); mp 86-87 °C; IR ν_{max}/cm^{-1}: 2935, 1659, 1451, 1383, 1344, 1297, 1258, 1200, 1144, 827, 764,

705 (thin film); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.46-7.26 (m, 5H), 4.76 (q, *J* 6.8 Hz, 1H), 3.96-3.81 (m, 2H), 3.80-3.68 (m, 2H), 3.50 (t, *J* 7.6 Hz, 2H), 1.72 (d, *J* 6.9 Hz, 3H), 1.69-1.59 (m, 2H), 1.40-1.21 (m, 4H), 0.89 (t, *J* 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2 (CH), 137.4 (C_0), 129.3 (CH), 128.9 (CH), 126.7 (CH), 58.2 (CH), 48.5 (CH_2), 47.9 (CH_2), 46.8 (CH_2), 28.3 (CH_2), 26.7 (CH_2), 22.0 (CH_2), 19.1 (CH_3), 13.7 (CH_3); MS (ESI +) *m/z*: 245 [M^+]; MS (ESI –) *m/z*: 145 [PF_6^-]; HRMS (ESI +) *m/z*: Calcd for $C_{16}H_{25}N_2$ [M^+] 245.2018, found 245.2028; HRMS (ESI +) *m/z*: Calcd for PF_6 [PF_6^-] 144.9642, found 144.9635.

*3-Pentyl-1-((1S)-1-phenylethyl)-4,5-dihydro-1H-imidazolium bis(trifluoromethanesulfonyl)imide (**13**)*

Prepared from imidazolinium bromide **11** (1.80 g, 5.54 mmol) according to the general procedure for the anion metathesis with lithium bis(trifluoromethanesulfonyl)imide. Salt **13** (2.32 g, 80%) was obtained as a light yellow liquid. $[\alpha]^{25}_D$ –2.7 (*c* 1.49, $CHCl_3$); Tg –59 °C; IR ν_{max}/cm^{-1}: 2961, 1649, 1456, 1350, 1186, 1136, 1056, 788, 739, 703 (thin film); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.46-7.34 (m, 3H), 7.32-7.27 (m, 2H), 4.80 (q, *J* 7.0 Hz, 1H), 3.96-3.84 (m, 2H), 3.82-3.70 (m, 2H), 3.48 (t, *J* 7.6 Hz, 2H), 1.71 (d, *J* 6.9 Hz, 3H), 1.68-1.58 (m, 2H), 1.39-1.20 (m, 4H), 0.89 (t, *J* 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3 (CH), 137.1 (C_0), 129.4 (CH), 129.1 (CH), 126.7 (CH), 119.8 (q, $J_{C\text{-}F}$ 321.3 Hz, SO_2CF_3), 58.2 (CH_3), 48.6 (CH_2), 48.0 (CH_2), 46.7 (CH_2), 28.3 (CH_2), 26.8 (CH_2), 22.0 (CH_2), 19.1 (CH_3), 13.7 (CH_3); MS ESI +) *m/z*: 245 [M^+]; MS (ESI –) *m/z*: 280 [NTf_2^-]; HRMS (ESI +) *m/z*: Calcd for $C_{16}H_{25}N_2$ 245.2018 [M^+], found 245.2029; HRMS (ESI –) *m/z*: Calcd for $C_2NO_4F_6S_2$ 279.9173 [NTf_2^-], found 279.9190.

*3-Pentyl-1-((1S)-1-phenylethyl)-1H-imidazolium bromide (**15**)*

Prepared from imidazole **14** (284 mg, 1.65 mmol) according to the general procedure for quaternarization in 1,1,1-trichloroethane. Imidazolium **15** (530 mg, quant.) was obtained as light brown liquid. $[\alpha]^{25}_D$ –13.2 (*c* 1.80, $CHCl_3$); IR ν_{max}/cm^{-1}: 3056, 2957, 2871, 1672, 1561, 1456, 1382, 1162, 732(thin film); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.77 (s, 1H), 7.47-7.41 (m, 2H), 7.40-7.32 (m, 4H), 7.28-7.25 (m, 1H), 5.99 (q, *J* 7.0 Hz, 1H), 4.35 (t, *J* 7.4 Hz, 2H), 2.00 (d, *J* 7.4 Hz, 3H), 1.92 (quintet, *J* 7.4 Hz, 2H), 1.37-1.24 (m, 4H), 0.85 (t, *J* 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.5 (CH), 135.1 (C_0), 128.5 (CH), 128.4 (CH), 126.2 (CH), 121.9 (CH), 120.4 (CH), 58.9 (CH), 49.2 (CH_2), 29.2 (CH_2), 27.5 (CH_2), 21.3 (CH_2), 20.5 (CH_3), 13.1 (CH_3); MS (ESI +) *m/z*: 243 [M^+]; MS (ESI –) *m/z*: 79, 81 [Br^-]; HRMS (ESI +) *m/z*: Calcd for $C_{16}H_{23}N_2$ [M^+] 243.1861, found 243.1865.

*3-Methyl-1-((1S)-1-phenylethyl)-1H-imidazolium iodide (**16**)*

A solution of imidazole **14** (166 mg, 0.96 mmol) and iodomethane (120 µL, 1.30 mmol, 1.35 equiv.) in acetonitrile (2.0 mL) was stirred at room temperature for 20 h. The solution was concentrated to dryness to give **16** (300 mg, quant.) as a light yellow oil. $[\alpha]^{25}_D$ +4.3 (*c* 5.3, $CHCl_3$); IR ν_{max}/cm^{-1}: 3120, 2934, 1604, 1572, 1496, 1330, 1156, 721 (thin film); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.19 (s, 1H), 7.57 (t, *J* 1.7 Hz, 1H), 7.51-7.37 (m, 5H), 7.34 (t, *J* 1.8 Hz, 1H), 5.89 (q, *J* 7.0 Hz, 1H), 4.14 (s, 3H), 2.06 (d, *J* 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.5 (CH), 135.9 (C_0), 129.3 (CH), 126.9 (CH), 123.8 (CH), 120.8 (CH), 59.9 (CH), 37.1 (CH_3), 21.4 (CH_3); MS (ESI +) *m/z*: 187 [M^+]; MS (ESI –) *m/z*: 127 [I^-]; HRMS (ESI +) *m/z*: Calcd for $C_{12}H_{15}N_2$ [M^+] 187.1235, found 187.1237.

*3-(3-cyanopropyl)-1-((1S)-1-phenylethyl)-1H-imidazolium chloride (**17**)*

Prepared from imidazole **14** (1.04 g, 6.03 mmol) according to the general procedure for quaternarization in acetonitrile. Chloride **17** (1.66 g, quant.) was obtained as light yellow oil. $[\alpha]^{25}_D$ –1.2 (*c* 1.07, $CHCl_3$); IR ν_{max}/cm^{-1}: 3057, 2938, 2467, 2247, 1558, 1496, 1456, 1258, 1158, 1014, 878, 853, 753, 706, 660 (thin film); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.68 (s, 1H), 7.82 (s, 1H), 7.27-7.21 (m, 5H), 7.15 (s, 1H), 5.68 (q, *J* 6.9 Hz, 1H), 4.57 (t, *J* 6.7 Hz, 2H), 2.58 (t, *J* 6.9 Hz, 2H), 2.28 (quintet, *J* 6.7 Hz, 2H), 1.89 (d, *J* 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.7 (CH), 129.3 (CH), 126.7 (CH), 123.0 (CH), 120.7 (CH), 118.6 (C_0), 60.0 (CH), 48.3 (CH_2), 26.1 (CH_2), 21.1 (CH_3), 14.4 (CH_2); MS (ESI +) *m/z*: 240 [M^+]; HRMS (ESI +) *m/z*: Calcd for $C_{15}H_{18}N_3$ [M^+] 240.1501, found 240.1481.

*3-Pentyl-1-((1S)-1-phenylethyl)-1H-imidazolium bis(trifluoromethanesulfonyl)imide (**18**)*

Prepared from imidazolium bromide **15** (909 mg, 2.81 mmol) according to the general procedure for the anion metathesis with lithium bis(trifluoromethanesulfonyl)imide. Salt **18** (1.30 g, 88%) was obtained as a light yellow liquid. $[\alpha]^{25}_D$ –8.1 (*c* 1.73, $CHCl_3$); Tg –57 °C; IR ν_{max}/cm^{-1}: 3146, 2962, 1557, 1557, 1457, 1349, 1186, 1136, 1055, 789, 704 (thin film); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.87 (s, 1H), 7.46-7.37 (m, 3H), 7.36-7.32 (m, 2H), 7.31-7.28 (m, 1H), 7.25-7.22 (m, 1H), 5.67 (q, *J* 7.0 Hz, 1H), 4.18 (t, *J* 7.5 Hz, 2H), 1.95 (d, *J* 7.0 Hz, 3H), 1.86 (quintet, *J* 7.5 Hz, 2H), 1.42-1.22 (m, 4H), 0.88 (t, *J* 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.5 (CH), 134.3 (C_0), 129.5 (CH), 126.7 (CH), 122.5 (CH), 121.0 (CH), 119.8 (q, $J_{C\text{-}F}$ 321.4 Hz, SO_2CF_3), 60.1 (CH), 50.2 (CH_2), 29.7 (CH_2), 28.0 (CH_2), 21.8 (CH_2), 20.6 (CH_3), 13.6 (CH_3); MS (ESI +) *m/z*: 243 [M^+]; MS (ESI –) *m/z*: 280 [NTf_2^-]; HRMS (ESI +) *m/z*: Calcd for $C_{16}H_{23}N_2$ [M^+] 243.1861, found 243.1865; HRMS (ESI –) *m/z*: Calcd for $C_2NO_4F_6S_2$ [NTf_2^-] 279.9173, found 279.9170.

*3-Methyl-1-((1S)-1-phenylethyl)-1H-imidazolium bis(trifluoromethanesulfonyl)imide (**19**)*

Prepared from imidazolium iodide **16** (300 mg, 0.95 mmol) according to the general procedure for the anion metathesis with lithium bis(trifluoromethanesulfonyl)imide. Salt **19** (350 mg, 79%) was obtained as a light yellow liquid. $[\alpha]^{25}_{D}$ –4.3 (*c* 2.8, $CHCl_3$); Tg –50 °C; IR ν_{max}/cm^{-1}: 3154, 2989, 1621, 1572, 1457, 1345, 1194, 1137, 1055, 707 (thin film); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.45-7.36 (m, 3H), 7.35-7.30 (m, 2H), 7.28 (t, *J* 1.8 Hz, 1H), 7.21 (t, *J* 1.8 Hz, 1H), 5.60 (q, *J* 7.0 Hz, 1H), 3.91 (s, 3H), 1.93 (d, *J* 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.3 (CH), 135.0 (C_0), 129.6 (CH), 129.5 (CH), 126.7 (CH), 123.8 (CH), 121.0 (CH), 119.8 (q, $J_{C\text{-}F}$ 318.7 Hz, SO_2CF_3), 60.2 (CH), 36.4 (CH_3), 20.6 (CH_3); MS (ESI +) *m/z*: 187 [M^+]; MS (ESI –) *m/z*: 280 [NTf_2^-]; HRMS (ESI +) *m/z*: Calcd for $C_{12}H_{15}N_2$ [M^+] 187.1235, found 187.1235; HRMS (ESI –) *m/z*: Calcd for $C_2NO_4F_6S_2$ [NTf_2^-] 279.9173, found 279.9164.

*3-(3-cyanopropyl)-1-((1S)-1-phenylethyl)-1H-imidazolium bis(trifluoromethanesulfonyl)imide (**20**)*

Prepared from imidazolium chloride **17** (1.66 g, 6.03 mmol) according to the general procedure for the anion metathesis with lithium bis(trifluoromethanesulfonyl)imide. Salt **20** (2.54 g, 81%) was obtained as a light yellow liquid. $[\alpha]^{25}_{D}$ –4.5 (*c* 1.78, CH_3OH); Tg –46 °C; IR ν_{max}/cm^{-1}: 3153, 2251, 1561, 1457, 1351, 1180, 1141, 1054, 740, 704, 614, 570 (thin film); ^{1}H NMR (300 MHz, acetone-d_6) δ 9.23 (t, *J* 1.6 Hz, 1H), 7.82 (t, *J* 1.9 Hz, 1H), 7.76 (t, *J* 1.9 Hz, 1H), 7.44-7.34 (m, 5H), 5.84 (q, *J* 7.0 Hz, 1H), 4.48 (t, *J* 7.1 Hz, 2H), 2.59 (t, *J* 7.4 Hz, 2H), 2.32 (quintet, *J* 7.2 Hz, 2H), 1.96 (d, *J* 7.0 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 140.0 (CH), 130.5 (CH), 130.3 (CH), 127.9 (CH), 124.1 (CH), 123.1 (CH), 121.2 (q, J_{CF} 320.5 Hz, SO_2CF_3), 119.8 (C_0), 61.4 (CH), 49.7 (CH_2), 26.8 (CH_2), 21.2 (CH_3), 14.7 (CH_2); MS (ESI +) *m/z*: 240 [M^+]; MS (ESI –) *m/z*: 280 [NTf_2^-]; HRMS (ESI +) *m/z*: Calcd for $C_{15}H_{18}N_3$ [M^+] 240.1501, found 240.1481.

*Diaminocarbene palladium complexes **23a,b***

$Pd(OAc)_2$ (47 mg, 0.21 mmol) and 3-pentyl-1-[(1*S*)-1-phenylethyl]-1*H*-imidazolium bromide **15** (135 mg, 0.42 mmol) were dissolved in 7.0 mL of dry THF. After refluxing for 6 h under argon and cooling to room temperature, the mixture was filtered through a pad of silica gel. The solvent was removed under vacuum and the crude product was purified by flash column chromatography (petroleum ether/ethyl acetate, 4:1) to furnish a 1:1 mixture of compound **23a,b** (85 mg, 54%), obtained as a pale yellow amorphous solid. $[\alpha]^{25}_{D}$ –190.0 (*c* 1.17, $CHCl_3$); mp: 114-116 °C; IR ν_{max}/cm^{-1}: 3156, 3124, 3094, 3060, 2957, 2929, 2867, 1602, 1560, 1497, 1453, 1425, 1378, 1216, 1184, 770, 734, 703 (thin film); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, *J* 7.1 Hz, 2H), 7.57 (d, *J* 6.8 Hz, 2H), 7.43-7.28 (m, 6H), 6.86 (q, *J* 7.2 Hz, 1H), 6.80 (d, *J* 1.8 Hz, 1H), 6.78 (d, *J* 1.8 Hz, 1H), 6.76 (q, *J* 7.2 Hz, 1H), 6.57 (apparent d, *J* 7.1 Hz, 1H), 6.55 (apparent d, *J* 1.9 Hz, 1H), 4.61-4.35 (m, 4H), 2.19-2.04 (m, 4H), 2.01 (d, *J* 7.1 Hz, 3H), 1.89 (d, *J* 7.1 Hz, 3H), 1.50-1.40 (m, 4H), 1.37-1.27 (m, 4H), 0.96 (apparent t, *J* 6.9 Hz, 3H), 0.80 (apparent t, *J* 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.9 (C_0), 168.8 (C_0), 140.2 (C_0), 139.9 (C_0), 128.6 (CH), 128.6 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 58.3 (2 CH), 51.2 (CH_2), 51.1 (CH_2), 30.6 (CH_2), 30.5 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 22.4 (CH_2), 22.3 (CH_2), 20.3 (CH_3), 20.2 (CH_3), 14.0 (CH_3), 13.9 (CH_3); MS (ESI +) *m/z*: 671 [M-Br] (most abundant isotopic distribution); HRMS (ESI +) *m/z*: Calc. for $C_{32}H_{44}N_4BrPd$ [M-Br] 671.1783, found 671.1818 (most abundant isotopic distribution).

*1-isopropyl-3-((S)-1-methylpyrrolidin-2-yl)pyridinium iodide (**28**)*

A solution of (–)-nicotine (**27**) (406 mg, 2.50 mmol) and 2-iodopropane (250 µL, 2.55 mmol) in acetonitrile (2.5 mL) was heated at 100 °C in a sealed tube under microwave irradiation (150 W) for 2 h. Next, the volatiles were removed under reduced pressure and the residue obtained was dissolved in water (50 mL). The resulting solution was extracted with diethyl ether (2 × 60 mL) and the aqueous layer was concentrated to dryness under reduced pressure to give the desired pyridinium iodide **28** (1.49 g, 92%), obtained as a dark red viscous oil. $[\alpha]^{25}_{D}$ –65.3 (*c* 1.68, CH_3OH); IR ν_{max}/cm^{-1}: 3023, 2971, 2789, 1497, 1462, 1269, 1149, 731, 691 (thin film); ^{1}H NMR (300 MHz, CD_3OD) δ 9.18 (s, 1H), 9.07 (d, *J* 6.1 Hz, 1H), 8.67 (d, *J* 8.0 Hz, 1H), 8.14 (apparent t, *J* 7.4 Hz, 1H), 5.12 (septet, *J* 6.7 Hz, 1H), 4.00-3.75 (m, 1H), 3.42 (apparent t, *J* 9.6 Hz, 1H), 2.67 (apparent q, *J* 8.6 Hz, 1H), 2.58-2.30 (superposed multiplet, 1H and a singlet centered at 2.40, 3H), 2.19-1.85 (m, 3H), 1.75 (d, *J* 6.7 Hz, 6H); ^{13}C NMR (75 MHz, CD_3OD) δ 146.2 (CH), 145.2 (C_0), 143.5 (CH), 143.1 (CH), 129.7 (CH), 68.8 (CH), 66.7 (CH), 57.8 (CH_2), 40.6 (CH), 35.5 (CH_2), 23.8 (CH_2), 23.3 (CH_3), 23.2 (CH_3); MS (ESI +) *m/z*: 205 [M^+]; HRMS (ESI +) *m/z*: Calcd for $C_{13}H_{21}N_2$ [M^+] 205.1705, found 205.1713.

*1-isopropyl-3-((S)-1-methylpyrrolidin-2-yl)pyridinium bis(trifluoromethanesulfonyl)imide (**29**)*

Prepared from pyridinium iodide **28** (1.07 g, 3.23 mmol) according to the general procedure for the anion metathesis with lithium bis(trifluoromethanesulfonyl)imide. Pyridinium **29** (1.04 g, 66%) was obtained as a light brown oil. $[\alpha]^{25}_{D}$ –69.2 (*c* 1.59, $CHCl_3$); Tg –56 °C; IR ν_{max}/cm^{-1}: 3073, 2977, 2948, 2791, 1499, 1465, 1352, 1268, 1196, 1138, 1059, 739 (thin film); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.79-8.76 (m, 2H),

8.46 (apparent d, *J* 8.0 Hz, 1H), 8.02 (dd, *J* 6.2 and 7.9 Hz, 2H), 5.02 (septet, *J* 6.7 Hz, 1H), 3.55 (t, *J* 8.1 Hz, 1H), 3.27 (ddd, *J* 2.8, 7.2 and 9.6 Hz, 3H), 2.48 (q, *J* 8.3 Hz, 1H), 2.41 (tdd, *J* 6.5, 8.8 and 12.9 Hz, 1H), 2.24 (s, 3H), 2.03-1.82 (m, 2H), 1.80-1.59 (doublet centered at 1.71, *J* 6.7 Hz, 6H, and a superposed multiplet, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.2 (C_0), 144.6 (CH), 141.1 (CH), 140.7 (CH), 128.7 (CH), 119.8 (q, $J_{C\text{-}F}$ 319.5 Hz, SO_2CF_3), 67.0 (CH), 65.5 (CH), 56.6 (CH_2), 40.2 (CH), 35.7 (CH_2), 23.1 (CH_2), 23.1 (CH_3), 23.0 (CH_3); MS (ESI +) *m/z*: 205 [M^+]; MS (ESI –) *m/z*: 280 [NTf_2^-]; HRMS (ESI +) *m/z*: calcd for $C_{13}H_{21}N_2$ [M^+] 205.1705, found 205.1710.

*(S)-1-((1-ethylpyrrolidin-2-yl)methyl)pyridinium chloride (**31**)*

To a suspension of 1-(2,4-dinitrophenyl)pyridinium chloride (**25**) (2.30 g, 8.17 mmol) in *n*-butanol (80.0 mL) was added (*S*)-2-(aminomethyl)-1-ethylpyrrolidine (1.01 g, 7.96 mmol) and the resulting mixture was refluxed for 20 h. After cooling to room temperature, the solvent was removed under reduced pressure and water (60.0 mL) was added to the residue obtained. The aqueous solution was washed with dichloromethane (3 × 80 mL) and concentrated to dryness under reduced pressure. The brown oil obtained was purified by flash column chromatography (dichloromethane/methanol, 9:1 to 1:1 + 3 drops of NH_4OH/10 mL of eluent) to furnish the pyridinium chloride **31** (1.88 g, 51%), obtained as a light yellow viscous oil. $[\alpha]^{25}_D$ +1.3 (*c* 1.17, CH_3OH); IR ν_{max}/cm^{-1}: 3044, 2974, 2612, 2505, 1581, 1490, 1455, 1187, 1055, 777, 729 (thin film); ^{1}H NMR (300 MHz, CD_3OD) δ 9.30 (d, *J* 5.8 Hz, 2H), 8.74 (apparent t, *J* 7.9 Hz, 1H), 8.24 (dd, *J* 6.8 and 7.4 Hz, 2H), 5.27 (AB of an ABX, $\Delta\delta$ = 0.36, *J* 5.6, 8.7 and 13.7 Hz, 2H), 4.26 (quintet, *J* 7.3 Hz, 1H), 3.90-3.82 (m, 1H), 3.53-3.19 (m, 3H), 2.31-1.99 (m, 4H), 1.40 (t, *J* 7.2 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 148.5 (CH), 146.9 (CH), 130.1 (CH), 67.6 (CH), 61.0 (CH_2), 55.2 (CH_2), 51.5 (CH_2), 29.3 (CH_2), 22.8 (CH_2), 11.1 (CH_3); MS (ESI +) *m/z*: 191 [M^+]; HRMS (ESI +) *m/z*: Calcd for $C_{12}H_{19}N_2$ [M^+] 191.1548, found 191.1562.

*(S)-1-((1-ethylpyrrolidin-2-yl)methyl)pyridinium bis(trifluoromethanesulfonyl)imide (**32**)*

Prepared from pyridinium chloride **31** (1.66 g, 5.90 mmol) according to the general procedure for the anion metathesis with lithium bis(trifluoromethanesulfonyl)imide. Pyridinium **32** (1.85 g, 67%) was obtained as a light brown viscous oil. $[\alpha]^{25}_D$ +5.6 (*c* 1.05, CH_3OH); Tg –52 °C; IR ν_{max}/cm^{-1}: 3138, 3095, 3072, 2976, 2872, 2812, 1490, 1456, 1353, 1196, 1137, 1059, 790, 740 (thin film); ^{1}H NMR (300 MHz, CD_3OD) δ 8.98 (apparent d, *J* 5.6 Hz, 2H), 8.65 (apparent t, *J* 7.9 Hz, 1H), 8.14 (apparent t , *J* 7.4 Hz, 2H), 4.79-4.66 (m, 2H), 3.58-3.44 (m, 1H), 3.42-3.29 (m superposed with the solvent peak, 1H), 3.00-2.58 (m, 3H), 2.18-2.01 (m, 1H), 2.00-1.82 (m, 1H), 1.81-1.56 (m, 2H), 1.14 (t, *J* 7.2 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 147.6 (CH), 146.8 (CH), 129.2 (CH), 121.2 (q, $J_{C\text{-}F}$ 320.3 Hz, SO_2CF_3), 65.6 (CH), 63.7 (CH_2), 54.6 (CH_2), 50.7 (CH_2), 28.9 (CH_2), 23.9 (CH_2), 13.0 (CH_3); MS (ESI +) *m/z*: 191 [M^+]; MS (ESI –) *m/z*: 280 [NTf_2^-]; HRMS (ESI +) *m/z*: Calcd for $C_{12}H_{19}N_2$ [M^+] 191.1548, found 191.1582.

*(S)-2-(1-(1-phenylethyl)-1H-imidazol-2-yl)pyridine (**33**)*

To a solution of (*S*)-α-methylbenzylamine (2.25 g, 18.6 mmol) and aqueous ammonia (2.0 mL, 37.2 mmol) in propan-1-ol (10.0 mL) at 0 °C was added dropwise a solution of glyoxal (2.34 mL, 20 mmol) and 2-pyridinecarboxaldehyde (1.9 mL, 20 mmol) in propan-1-ol (20 mL). After 1 h at 0 °C, the solution was heated to 80 °C and left stirring for 4 h. It was then cooled to room temperature and water was added. Subsequently, the mixture was extracted with dichloromethane (3 × 100 mL) and the combined extracts were washed with water (2 × 100 mL), dried over anhydrous Na_2SO_4, filtered and the dichloromethane removed under reduced pressure. The brown oil obtained was purified by flash column chromatography (petroleum ether/ethyl acetate, 1:1) to furnish imidazole **33** (0.84 g, 18%), obtained as a light brown oil. $[\alpha]^{25}_D$ –244.4 (*c* 1.00, $CHCl_3$); IR ν_{max}/cm^{-1}: 3108, 3046, 2981, 2936, 1589, 1566, 1484, 1451, 1404, 1265, 1149, 1093, 1023, 792, 738, 700 (thin film); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (dt, *J* 0.8 and 4.8 Hz, 1H), 8.19 (dd, *J* 0.5 and 8.0 Hz, 2H), 7.75 (tdd, *J* 0.5, 1.8 and 8.0 Hz, 1H), 7.36-7.16 (m, 7H and a superposed bs centered at 7.18, 1H), 7.10 (bs, 1H), 1.88 (d, *J* 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.0 (C_0), 148.1 (CH), 144.6 (C_0), 142.2 (C_0), 136.5 (CH), 128.6 (CH), 128.4 (CH), 127.3 (CH), 126.4 (CH), 123.2 (CH), 122.4 (CH), 119.7 (CH), 54.8 (CH), 21.6 (CH_3); MS (ESI +) *m/z*: 250 [M+H^+]; HRMS (ESI +) *m/z*: Calcd for $C_{16}H_{16}N_3$ [M+H^+] 250.1344, found 250.1346.

*(S)-3-butyl-1-(1-phenylethyl)-2-(pyridin-2-yl)-1H-imidazol-3-ium iodide (**34**)*

A solution of imidazole **33** (500 mg, 2.00 mmol) and 1-iodobutane (1.14 mL, 10.0 mmol) in acetonitrile (4.0 mL) was heated at 100 °C in a sealed tube under microwave irradiation (150 W) for 2 h. Next, the volatiles were removed under reduced pressure, and the residue obtained was dissolved in water (70.0 mL). A saturated NaCl solution (30.0 mL) was added and the resulting solution was extracted with diethyl ether (2 × 80 mL) and dichloromethane (3 × 90 mL). The combined dichloromethane extracts were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give the desired imidazolium iodide **34** (0.72 g, 83%), obtained as a light yellow oil. $[\alpha]^{25}_D$ –109.4 (*c* 1.56, $CHCl_3$); IR ν_{max}/cm^{-1}: 3089, 3054, 2960, 2934, 2873, 2190, 1594, 1571,

1499, 1455, 1427, 1221, 1190, 920, 800, 727, 702 (thin film); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.82 (ddd, *J* 1.0 , 1.7 and 4.8 Hz, 1H), 8.32-8.19 (m, 1H), 8.07 (apparent td, *J* 1.7 and 7.8 Hz, 1H), 7.95 (s, 1H), 7.66-7.60 (m, 2H), 7,33-7,24 (m, 3H), 7.21-7.12 (m, 2H), 5.70 (q, *J* 6.9 Hz, 1H), 4.23 (quintet of d, *J* 2.4 and 7.4 Hz, 2H), 1.96 (d, *J* 7.7 Hz, 3H), 1.76 (quintet, *J* 7.5 Hz, 2H), 1.24 (quintet, *J* 7.4 Hz, 2H), 0.80 (t, *J* 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.9 (CH), 142.0 (C_0), 141.1 (C_0), 138.3 (CH), 137.5 (C_0), 129.1 (CH), 128.9 (CH), 128.3 (CH), 126.8 (CH), 126.4 (CH), 123.0 (CH), 119.9 (CH), 58.4 (CH), 49.4 (CH_2), 31.6 (CH_2), 21.1 (CH_3), 19.3 (CH_2), 13.2 (CH_3); MS (ESI +) *m/z*: 306 [M^+]; MS (ESI –) *m/z*: 127 [I^-]; HRMS (ESI+) *m/z*: Calcd for $C_{20}H_{24}N_3$ [M^+] 306.1970, found 306.2000.

*(S)-3-butyl-1-(1-phenylethyl)-2-(pyridin-2-yl)-1H-imidazol-3-ium bis(trifluoromethanesulfonyl)imide (**35**)*

Prepared from imidazolium iodide **34** (274 mg, 0.63 mmol) according to the general procedure for the anion metathesis with lithium bis(trifluoromethanesulfonyl)imide. Imidazolium **35** (339 mg, 92%) was obtained as a light brown oil. $[\alpha]^{25}_D$ –97.6 (*c* 1.36, $CHCl_3$); Tg –40 °C; IR ν_{max}/cm^{-1}: 3142, 3067, 2966, 2939, 2878, 1595, 1573, 1499, 1455, 1353, 1332, 1226, 1195, 1138, 1058, 790, 617, 570, 513 (thin film); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.84 (ddd, *J* 0.9, 1.7 and 4.8 Hz, 1H), 8.03 (td, *J* 1.8 and 7.8 Hz, 1H), 7.83 (dt, *J* 1.0 and 7.9 Hz, 1H), 7.62 (ddd, *J* 1.2, 4.8 and 7.8 Hz, 1H), 7.54 (d, *J* 2.1 Hz, 1H), 7.43 (d, *J* 2.1 Hz, 1H), 7.35-7.29 (m, 3H), 7.11 (ddd, *J* 0.5, 2.2 and 5.2 Hz, 1H), 5.63 (q, *J* 7.0 Hz, 1H), 4.09 (t, *J* 7.6 Hz, 2H), 1.89 (d, *J* 7.0 Hz, 3H), 1.72 (apparent quintet, *J* 7.5 Hz, 2H), 1.22 (septet, *J* 7.5 Hz, 2H), 0.81 (t, *J* 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.1 (CH), 142.2 (C_0), 141.2 (C_0), 138.4 (CH), 137.4 (C_0), 129.3 (CH), 129.2 (CH), 127.5 (CH), 126.9 (CH), 126.4 (CH), 122.6 (CH), 119.9 (q, $J_{C\text{-}F}$ 321.5 Hz, SO_2CF_3), 119.7 (CH), 58.6 (CH), 49.2 (CH_2), 31.7 (CH_2), 20.6 (CH_3), 19.3 (CH_2), 13.1 (CH_3); MS (ESI +) *m/z*: 306 [M^+]; MS (ESI –) *m/z*: 280 [NTf_2^-]; HRMS (ESI +) *m/z*: Calcd for $C_{20}H_{24}N_3$ [M^+] 306.1970, found 306.1982.

Supplementary Information

^{1}H and ^{13}C NMR spectra of compounds **11**, **12**, **13**, **15**, **16**, **17**, **18**, **19**, **20**, **23**, **28**, **29**, **31**, **32**, **33**, **34** and **35**, and selected crystallographic data for compounds **23a** and **23b** are available free of charge at http://jbcs.sbq.org.br, as PDF file.

Acknowledgments

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29. See Supporting Information for selected crystallographic data for **23a,b**. CCDC 724261 (**23a**) and CCDC 724262 (**23b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).
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37. Despite extensive experimentation, attempts to prepare a chiral 2,2'-bisimidazole from α-methylbenzylamine, a source of ammonia (either ammonium hydroxide or ammonium chloride) and 2 equivalents of glyoxal invariably led to the known C-2 unsubstituted imidazole **15** through an unexpected decarbonylative process.

Synthesis of Novel Room Temperature Chiral Ionic Liquids. Application as Reaction Media for the Heck Arylation of Aza-endocyclic Acrylates

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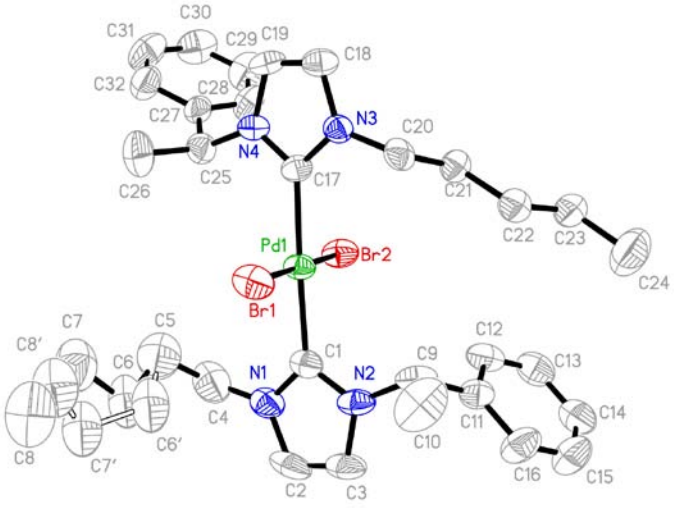
Crystal Structure Determination

The structures of two compounds were determined. The selected crystals were mounted on a glass fibber using perfluoropolyether oil and cooled rapidly in a stream of cold N_2. For all the structures data collection were collected at low temperature (213 K for compounds **23a** and 173 K for compounds 23b) and using a graphite-monochromated MoKα radiation (λ = 0.71073Å). The structure were solved by direct methods (SHELXS-97, G. M. Sheldrick, *Acta Crystallogr.* **1990**, *A46*, 467-473) and all non hydrogen atoms were refined anisotropically using the least-squares method on F^2 (SHELXL-97, Program for Crystal Structure Refinement, G. M. Sheldrick, University of Göttingen **1997**). CCDC 724261 (**23a**) and CCDC 724262 (**23b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

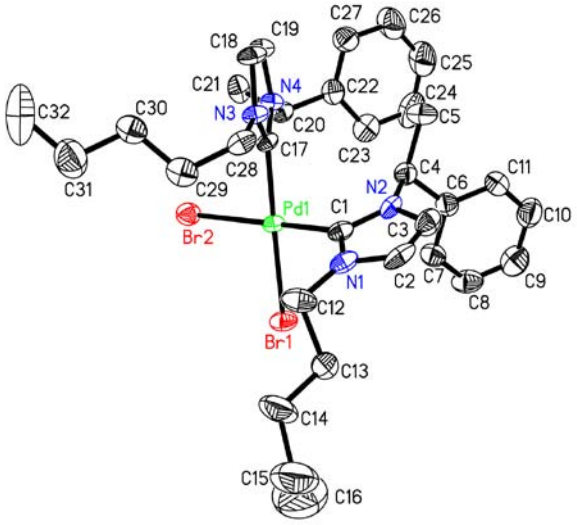
*Selected crystallographic data for compound **23a***



*e-mail: genisson@chimie.ups-tlse.fr; roque@iqm.unicamp.br

Selected data for trans-*anti* Pd complex **23a**: $C_{32}H_{44}Br_2N_4Pd$, M = 750.93, orthorhombic, space group *P2(1)2(1)2(1)*, a = 8.7609(2) Å, b = 12.0766(3) Å, c = 31.6211(9) Å, $\alpha = \beta = \gamma = 90°$, V =3345.57(15) Å^3, Z = 4, crystal size 0.35 x 0.15 x 0.05 mm^3, 32050 reflections collected (6787 independent, R_{int} = 0.0821), 383 parameters, $R1$ [I>2σ(I)] = 0.0423, $wR2$ [all data] = 0.0804, largest diff. peak and hole: 0.422 and –0.392 eÅ^{-3}.

Selected crystallographic data for compound ***23b***



Selected data for cis-*syn* Pd complex **23b**: $C_{33}H_{46}Br_2C_{12}N_4Pd$, M = 835.86, orthorhombic, space group *P2(1)2(1)2(1)*, a = 7.7314(8) Å, b = 17.6948(17) Å, c = 27.018(3) Å, $\alpha = \beta = \gamma = 90°$, V = 3696.3(6) Å^3, Z = 4, crystal size 0.40 x 0.20 x 0.05 mm^3, 33902 reflections collected (9117 independent, R_{int} = 0.0759), 447 parameters, $R1$ [I>2σ(I)] = 0.0544, $wR2$ [all data] = 0.1145, largest diff. peak and hole: 0.624 and –0.727 eÅ^{-3}.

^{1}H NMR and ^{13}C NMR spectra for compounds ***11***, ***12***, ***13***, ***15***, ***16***, ***17***, ***18***, ***19***, ***20***, ***23***, ***28***, ***29***, ***31***, ***32***, ***33***, ***34*** *and* **35**

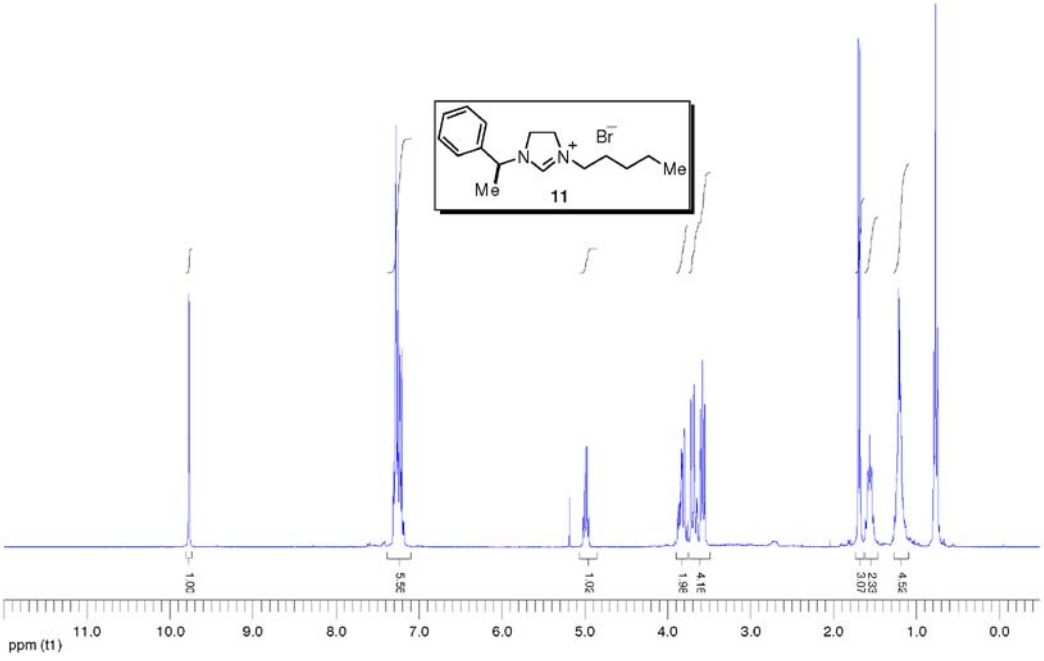


Figura S1. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **11**.

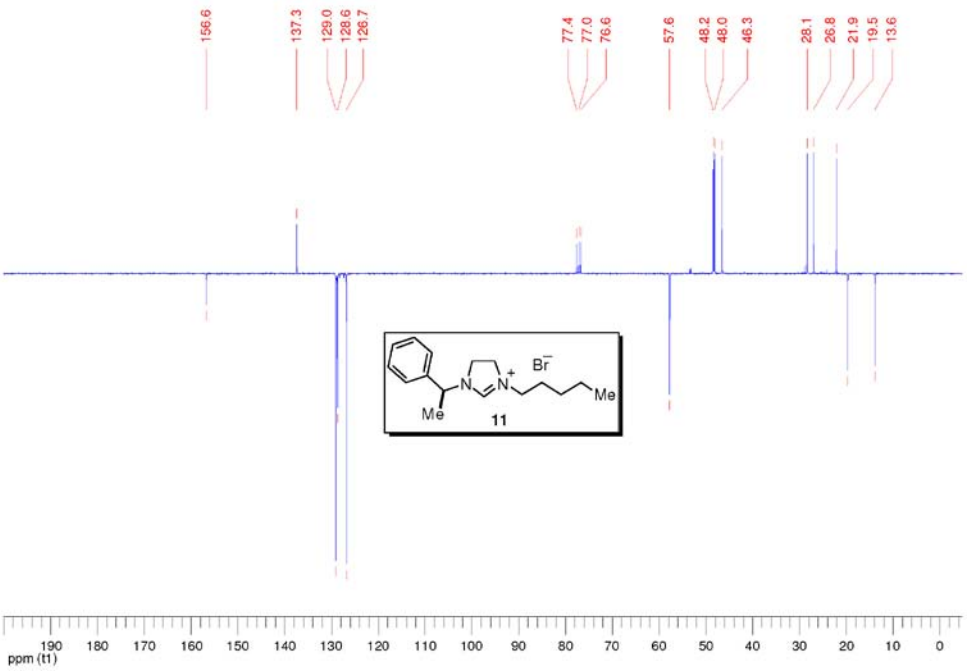


Figura S2. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **11**.

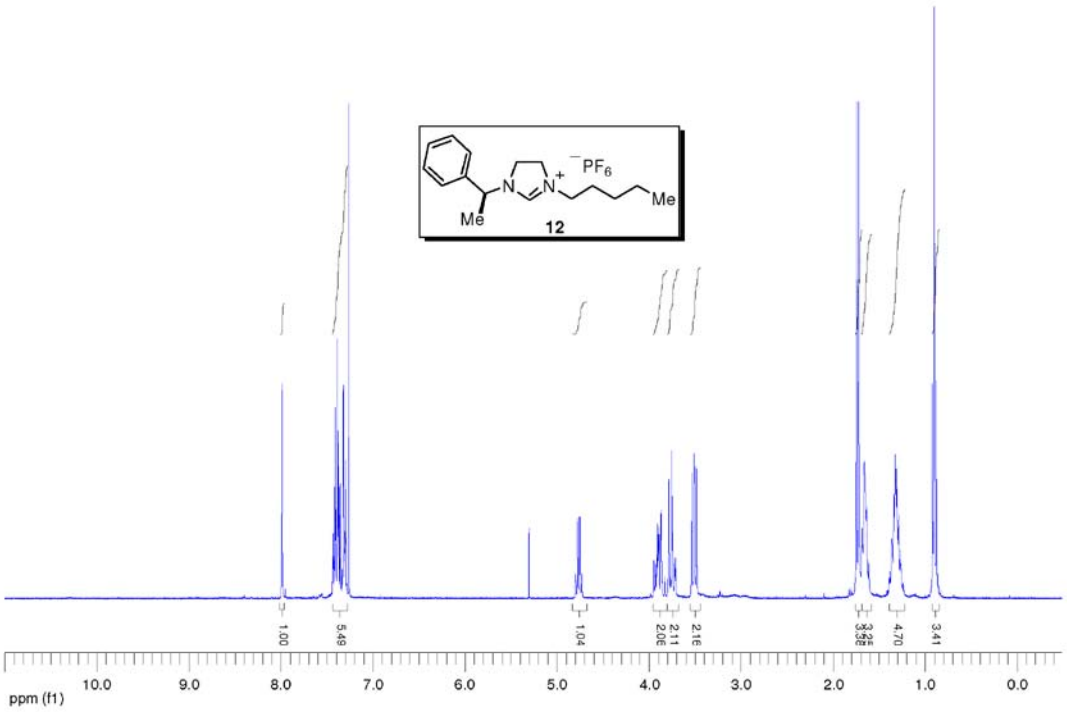


Figura S3. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **12**.

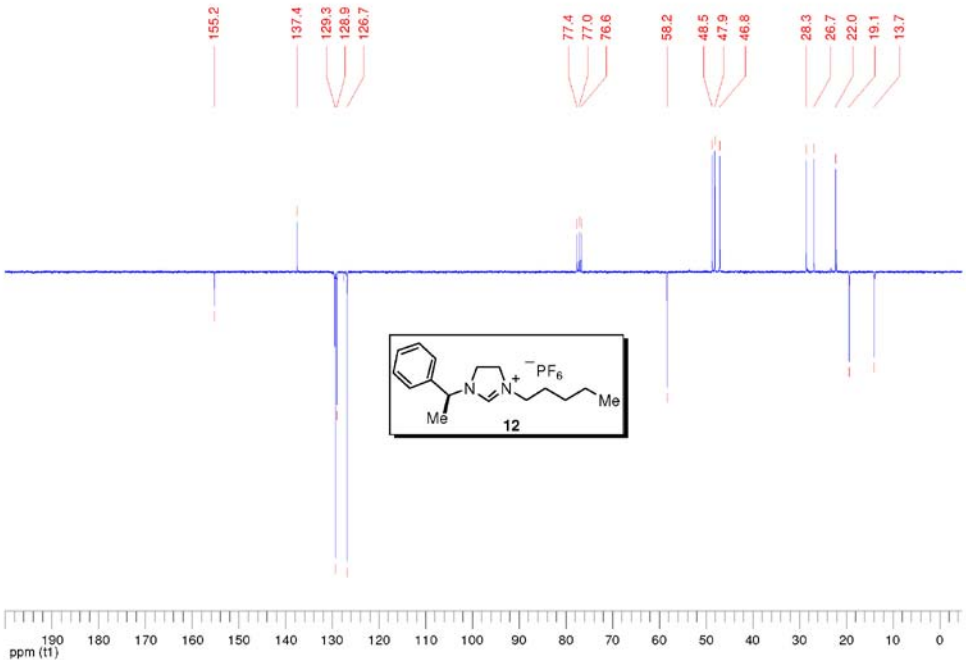


Figura S4. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **12**.

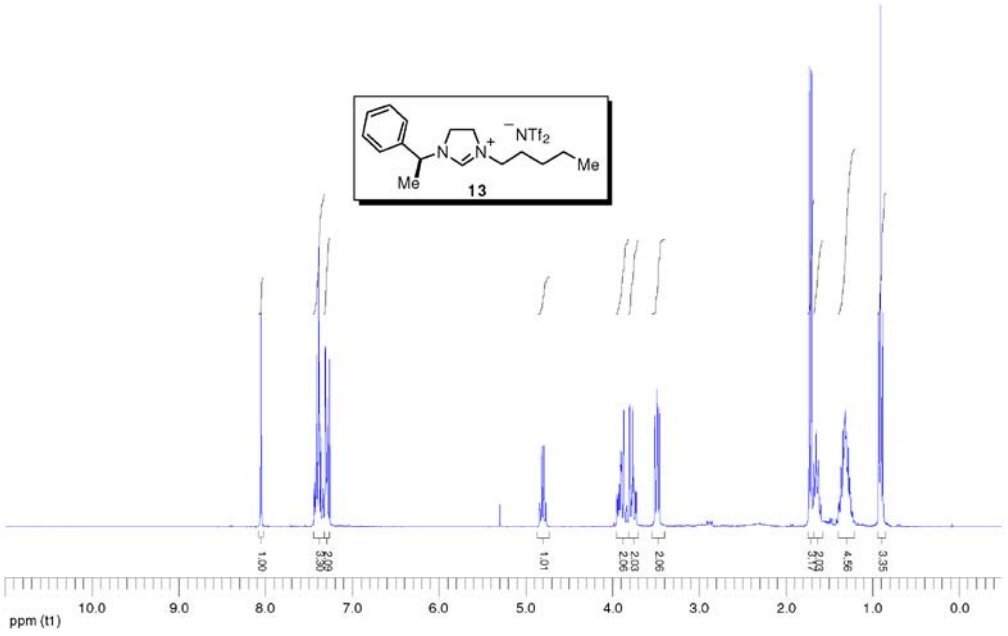


Figura S5. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **13**.

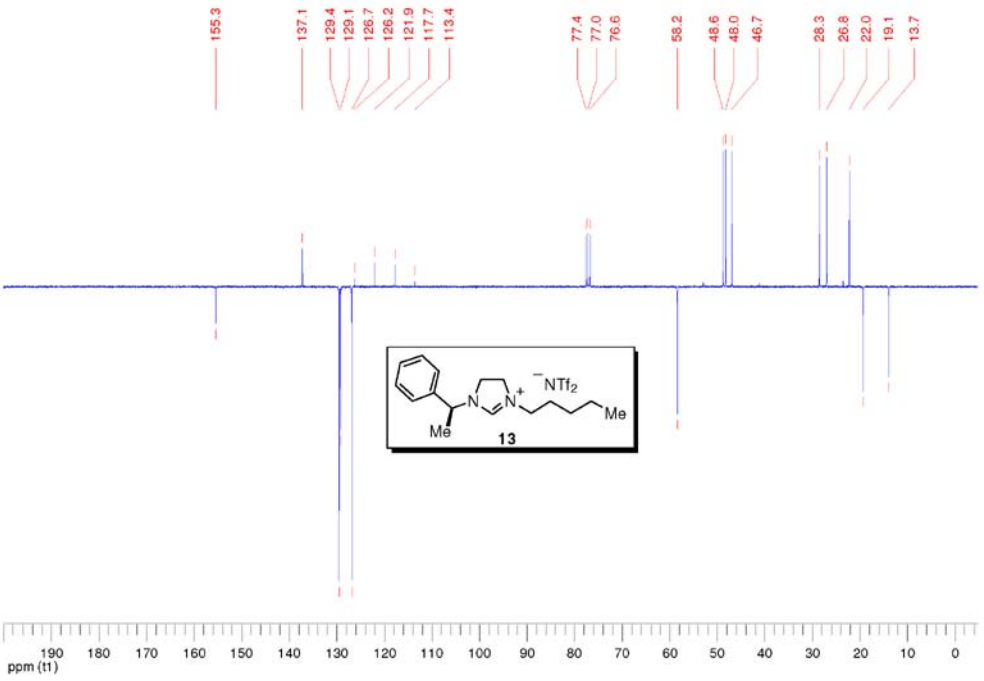


Figura S6. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **13**.

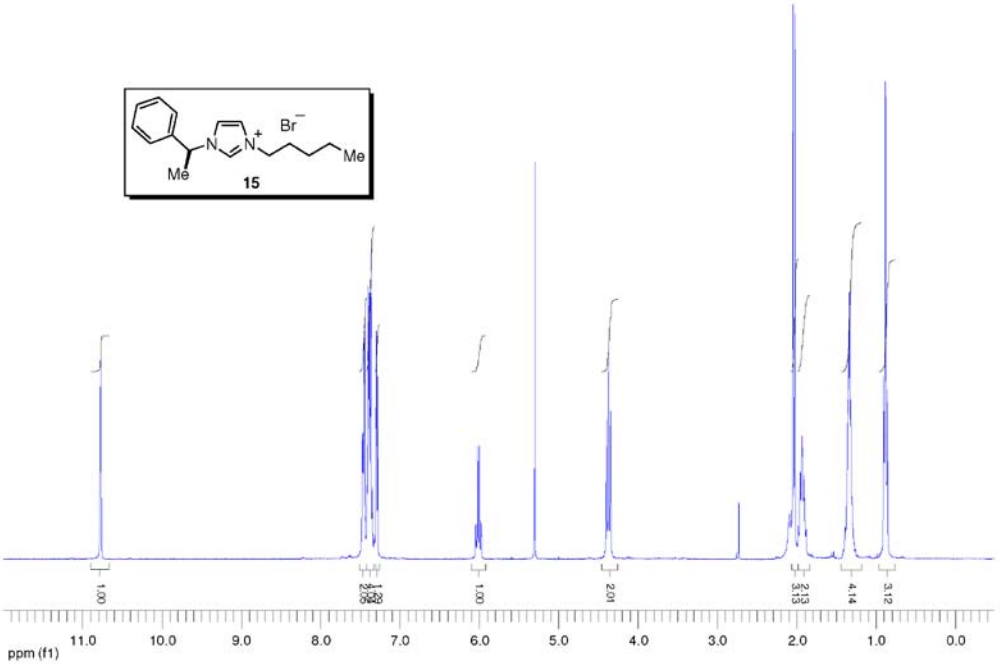


Figura S7. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **15**.

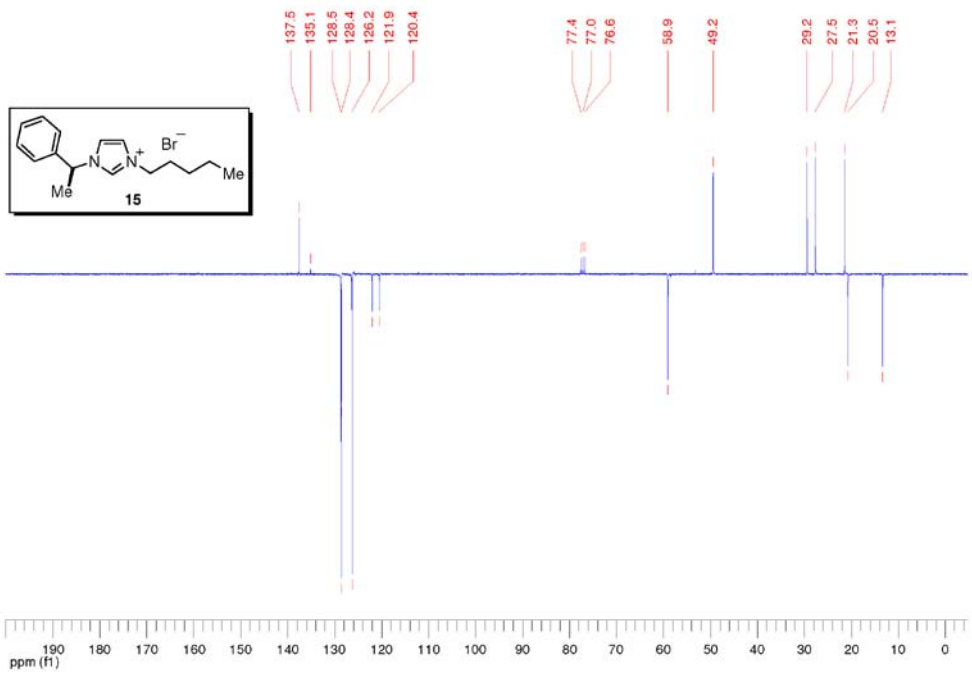


Figura S8. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **15**.

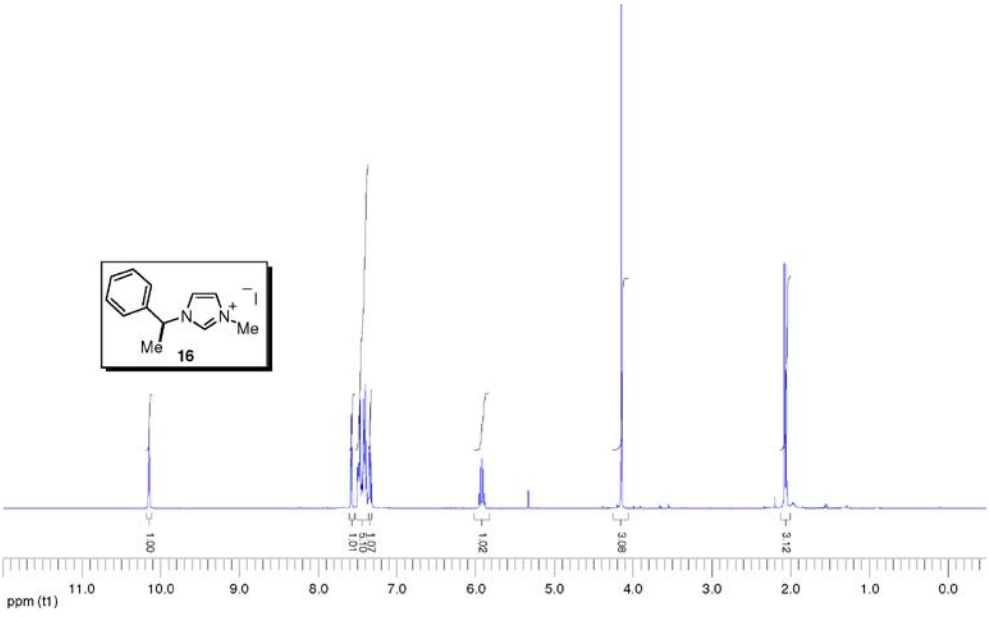


Figura S9. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **16**.

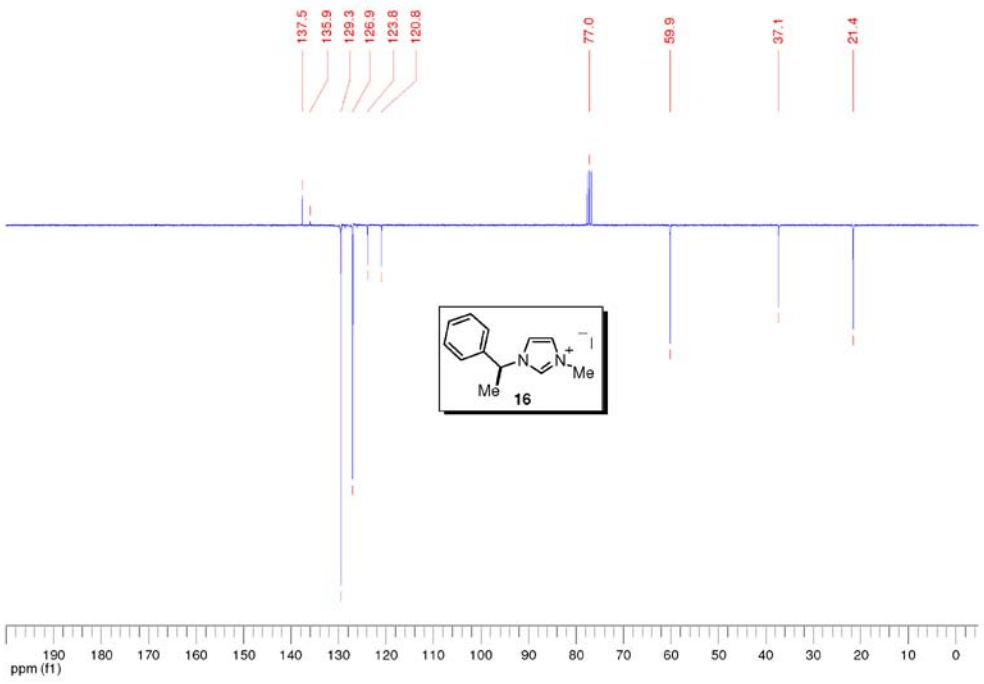


Figura S10. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **16**.

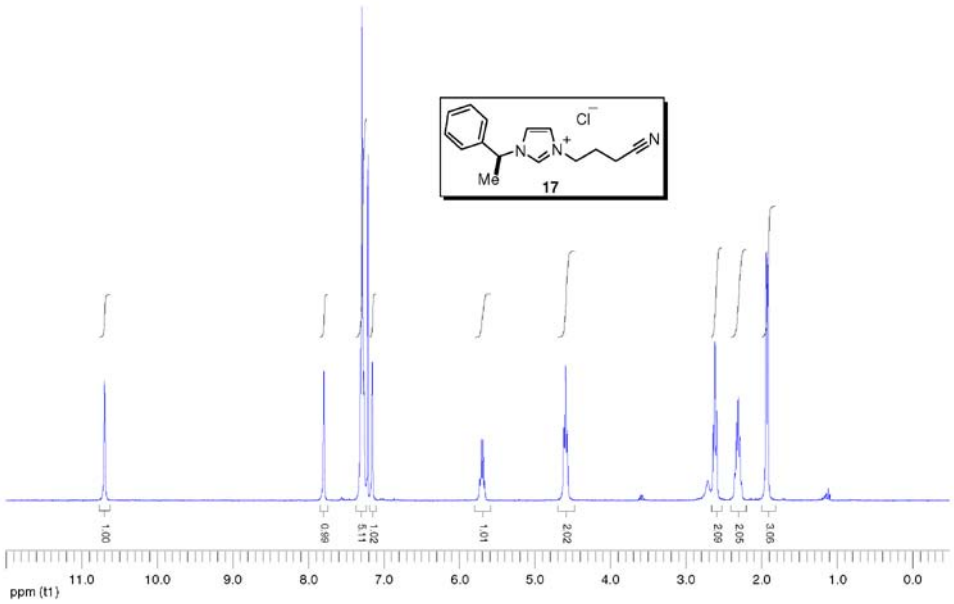


Figura S11. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **17**.

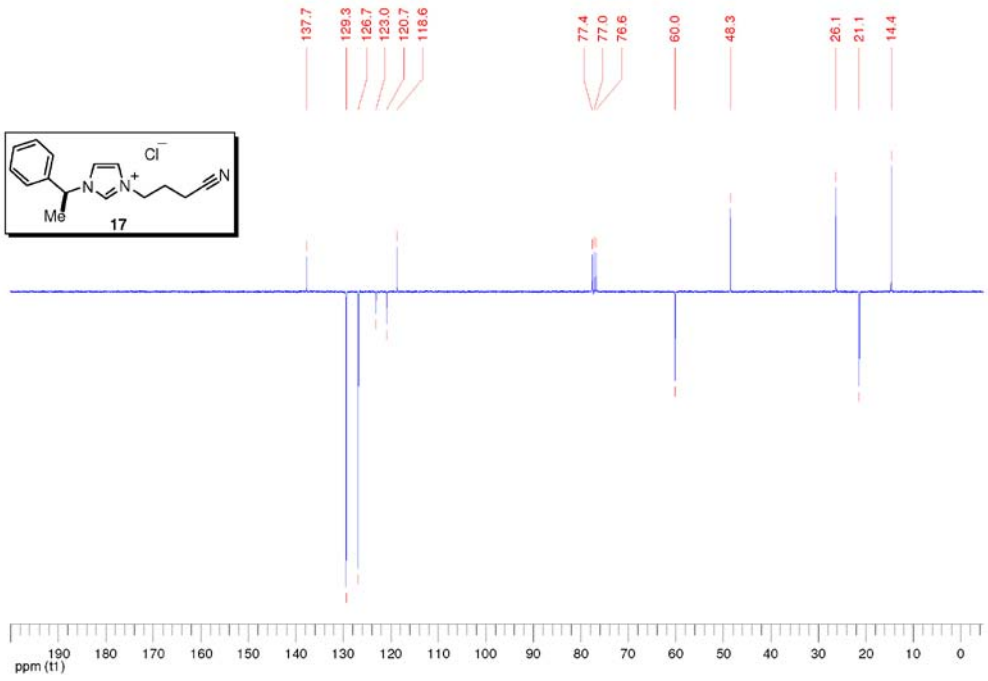


Figura S12. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **17**.

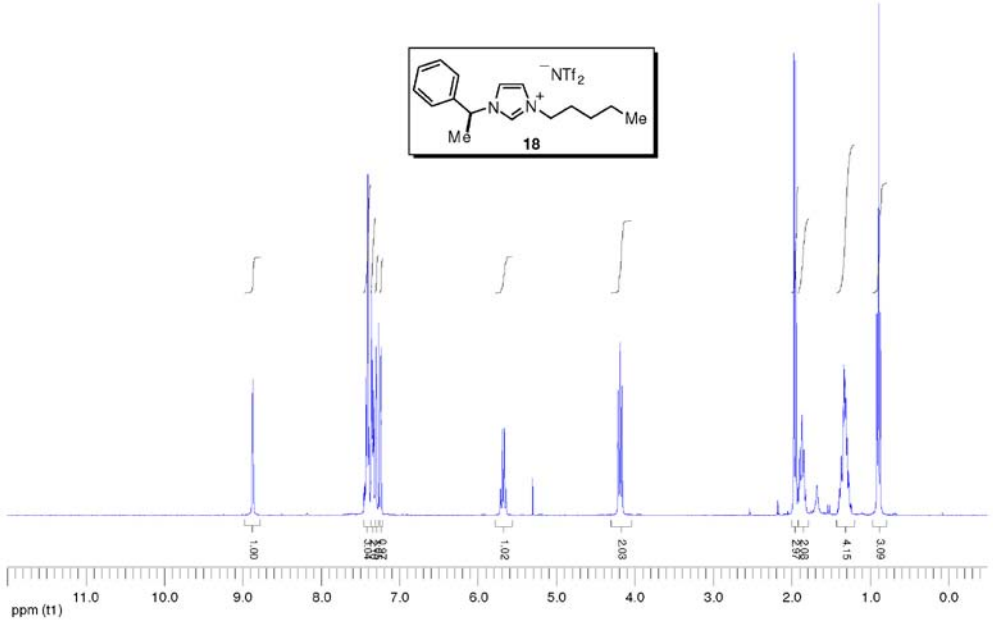


Figura S13. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **18**.

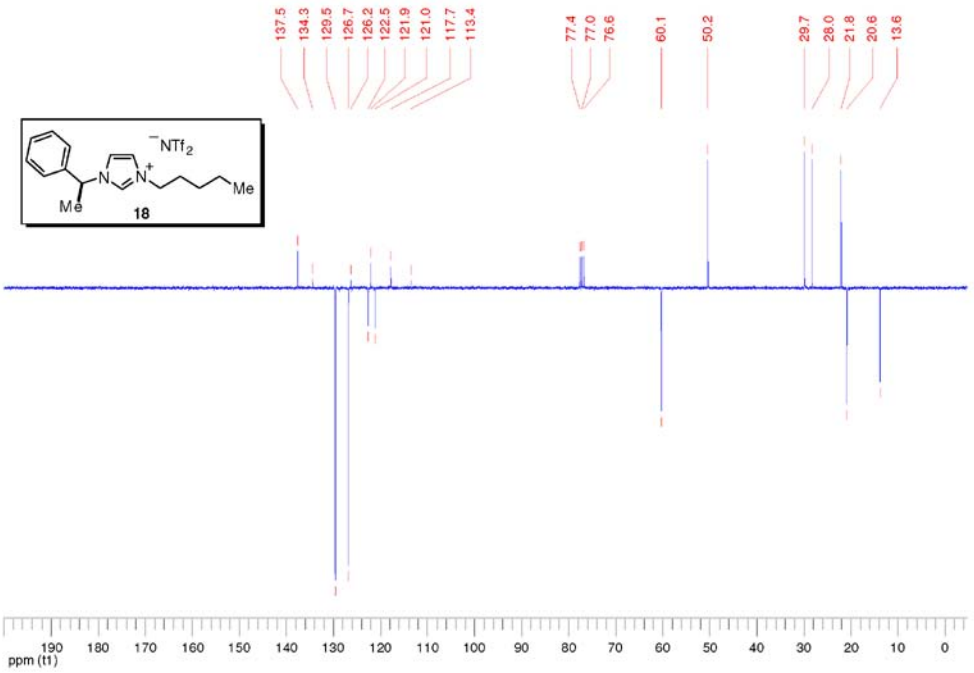


Figura S14. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **18**.

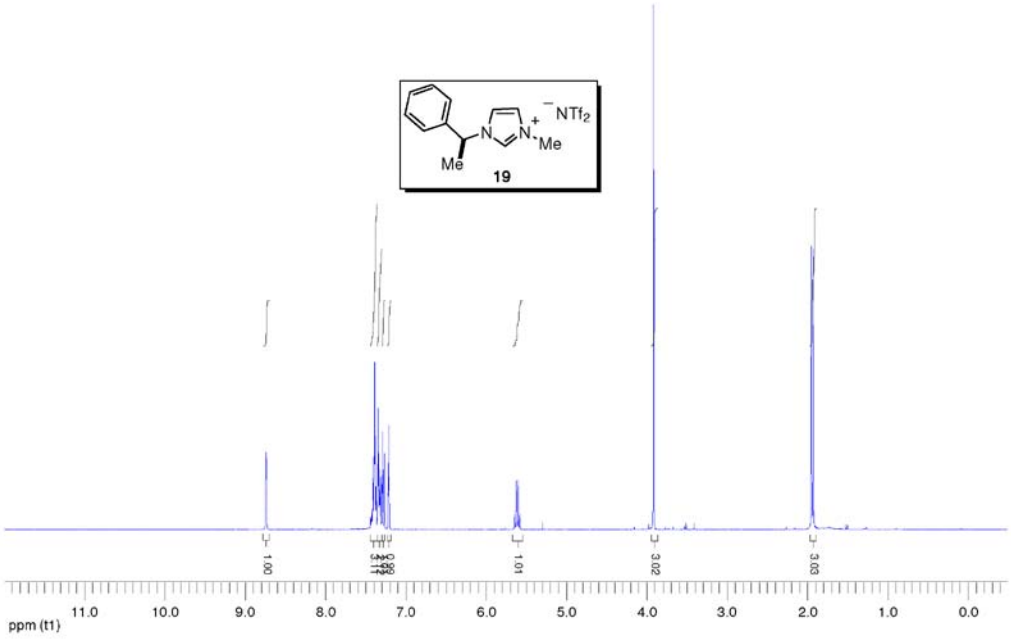


Figura S15. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **19**.

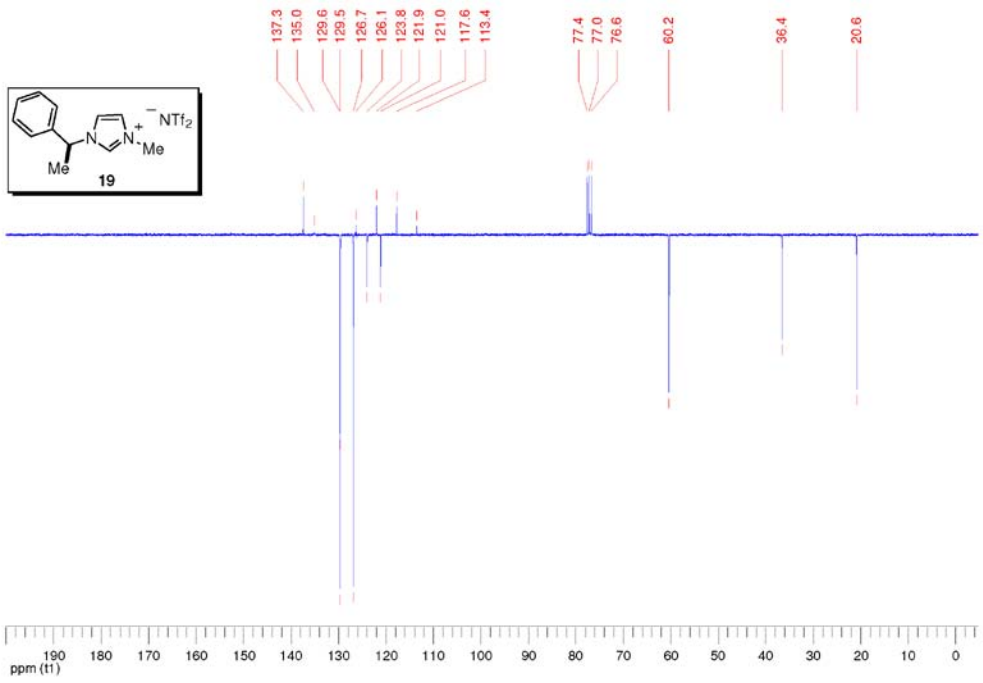


Figura S16. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **19**.

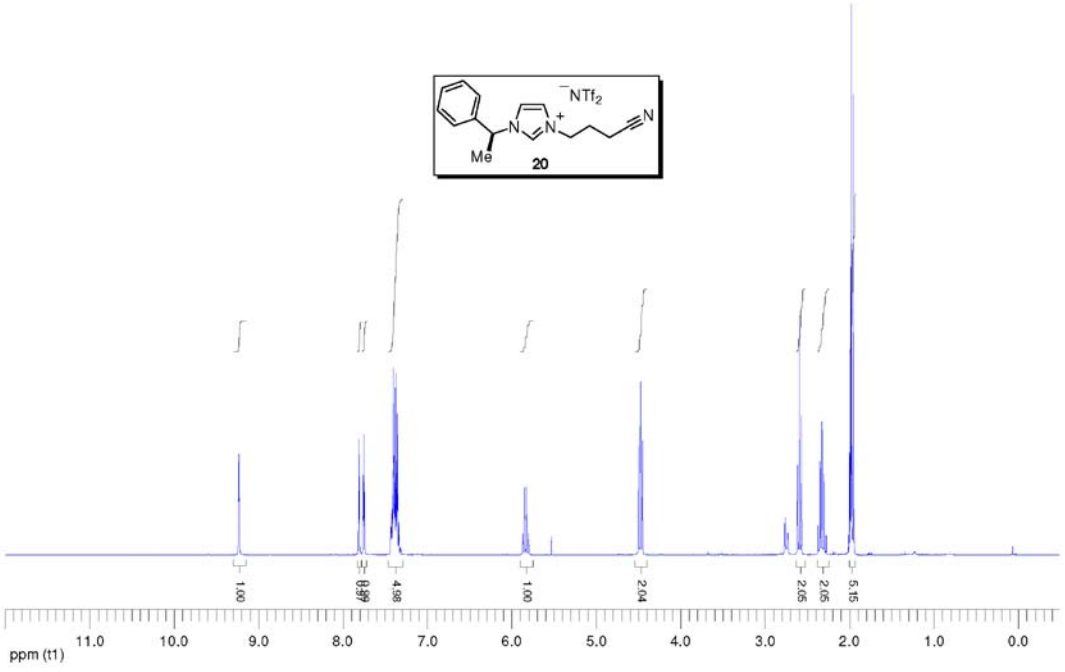


Figura S17. ^{1}H NMR spectrum (300 MHz, acetone-d_6) of compound **20**.

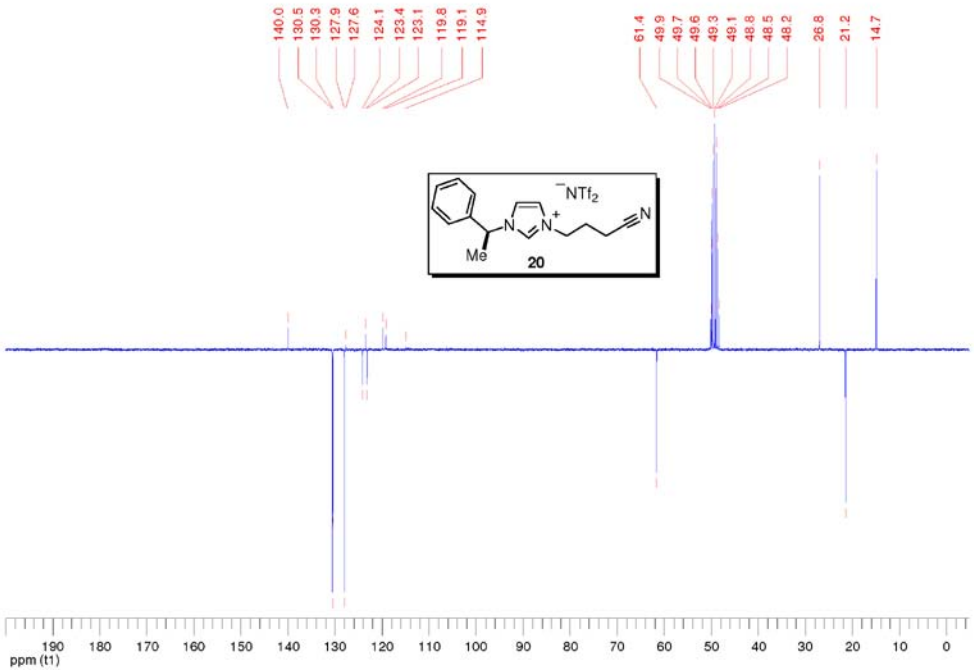


Figura S18. ^{13}C NMR spectrum (75 MHz, CD_3OD) of compound **20**.

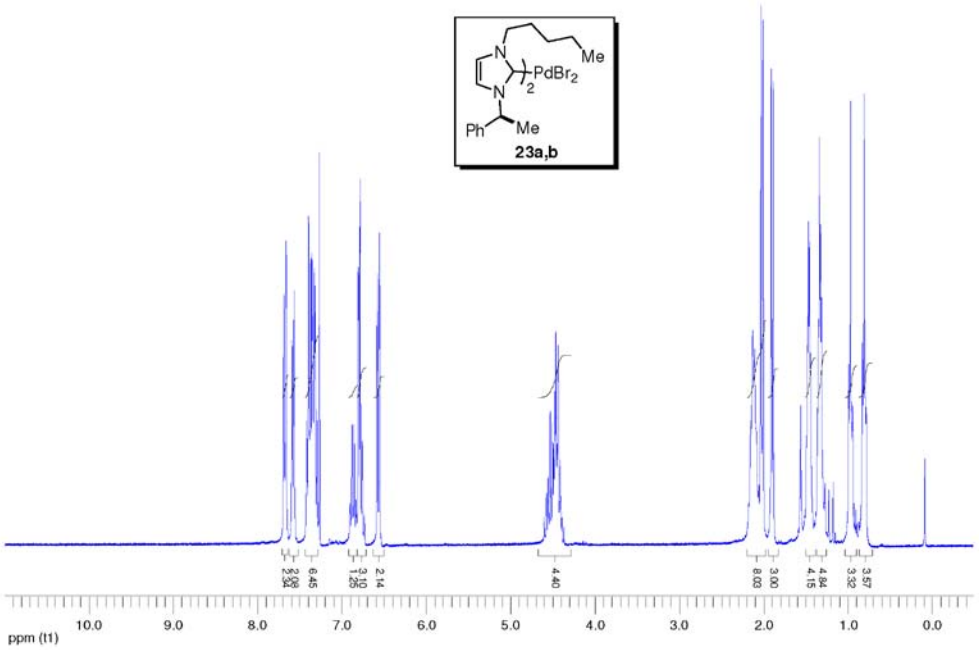


Figura S19. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **23a,b**.

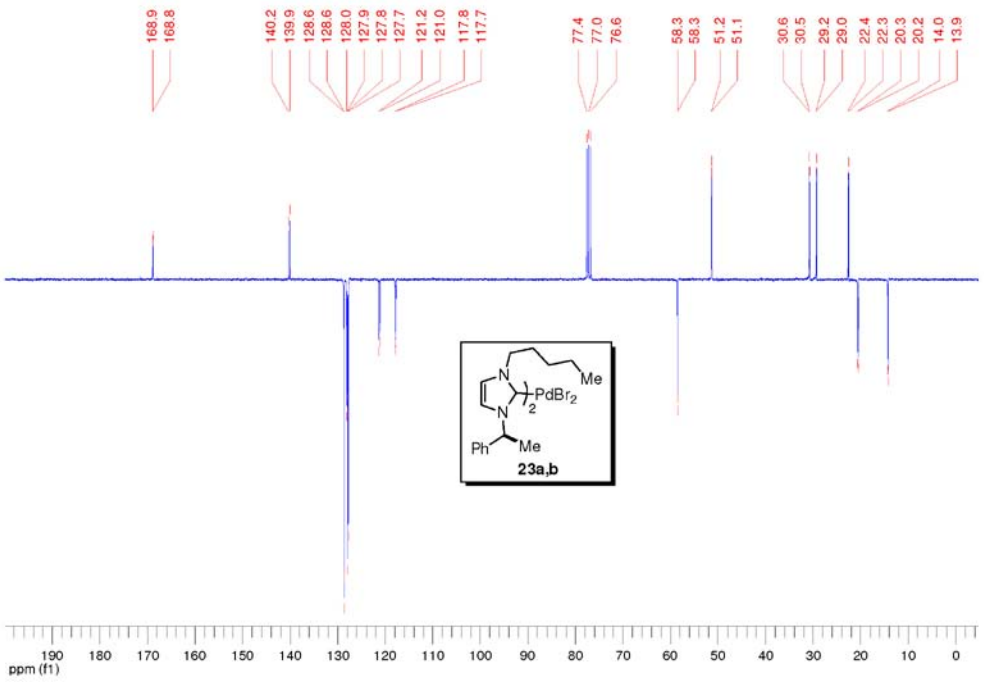


Figura S20. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **23a,b**.

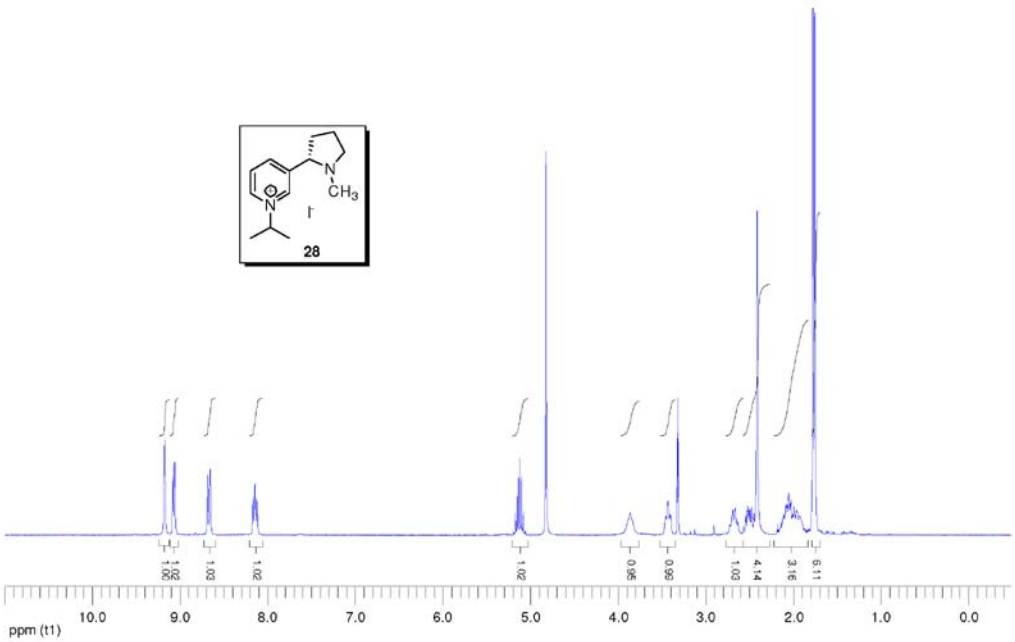


Figura S21. ^{1}H NMR spectrum (300 MHz, CD_3OD) of compound **28**.

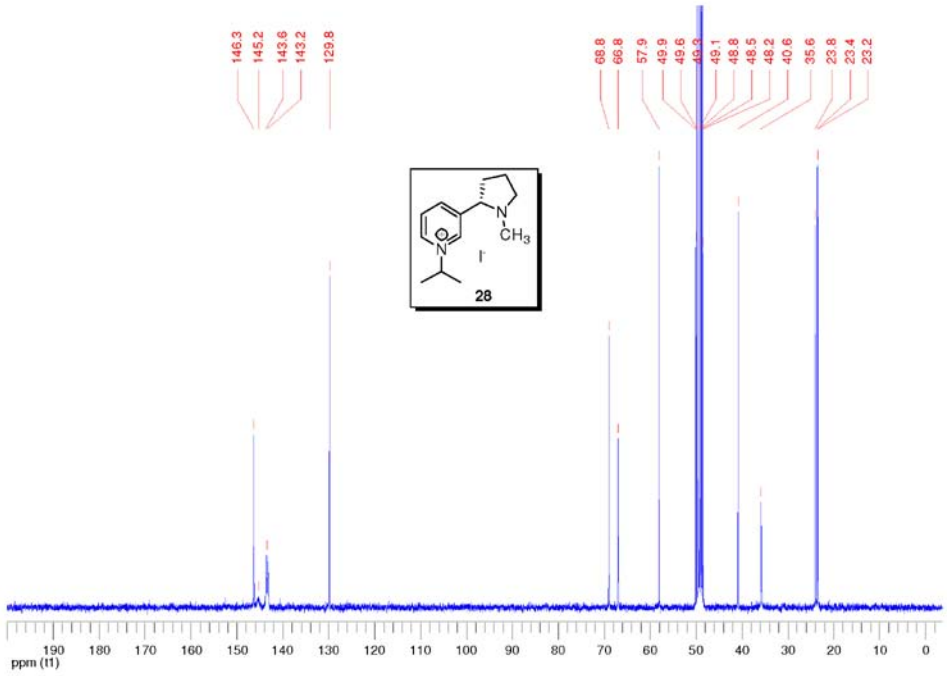


Figura S22. ^{13}C NMR spectrum (75 MHz, CD_3OD) of compound **28**.

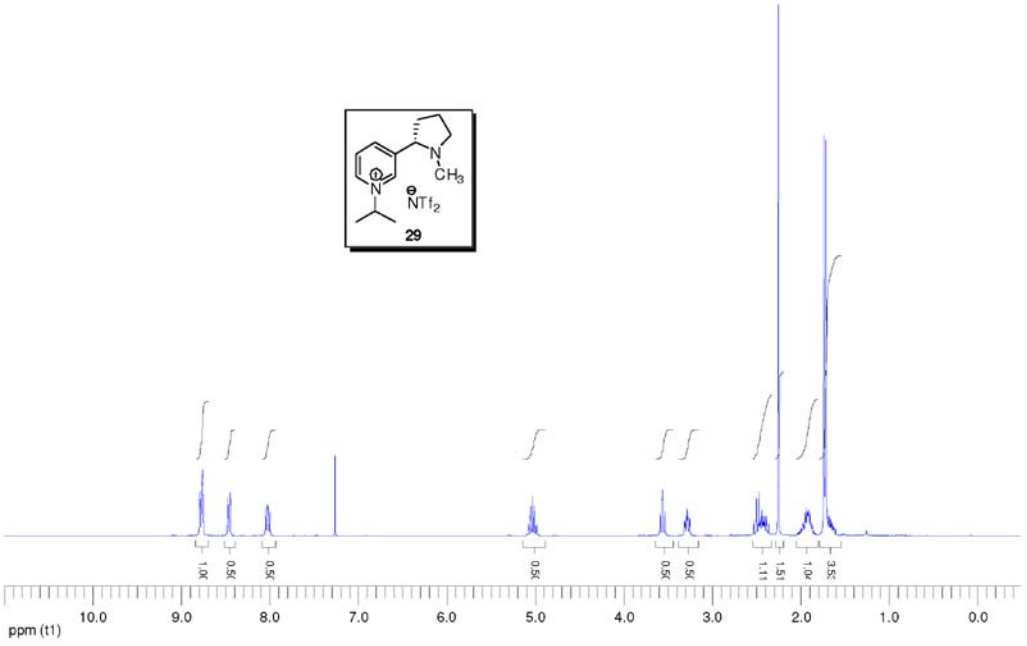


Figura S23. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **29**.

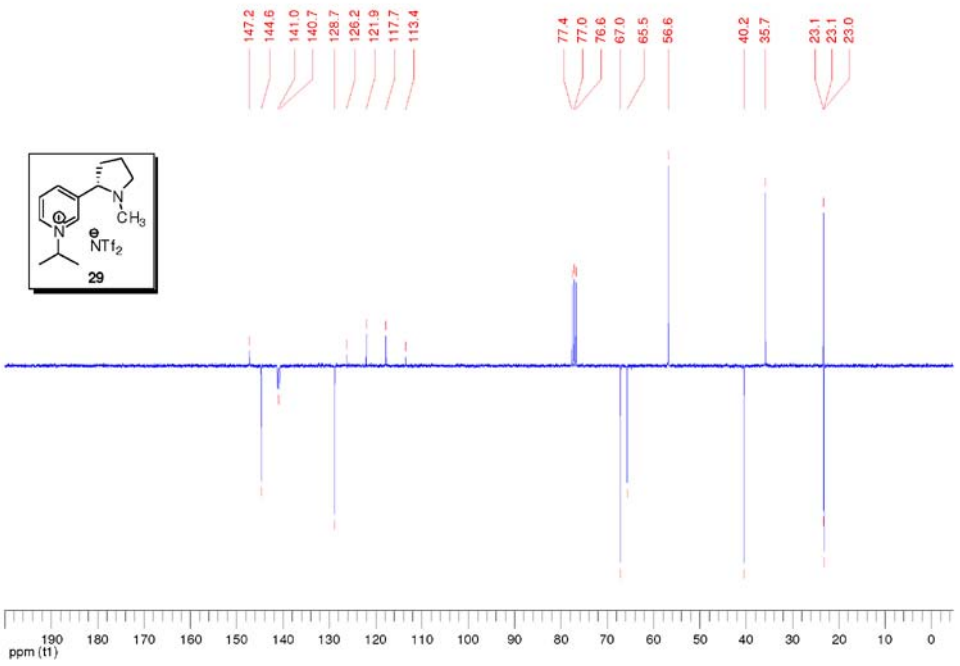


Figura S24. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **29**.

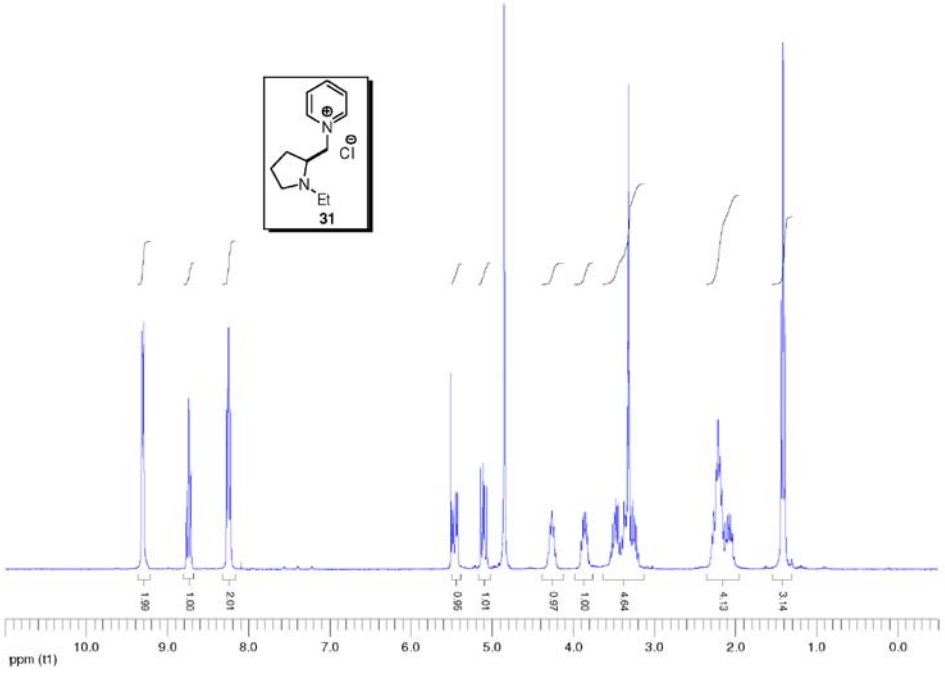


Figura S25. ^{1}H NMR spectrum (300 MHz, CD_3OD) of compound **31**.

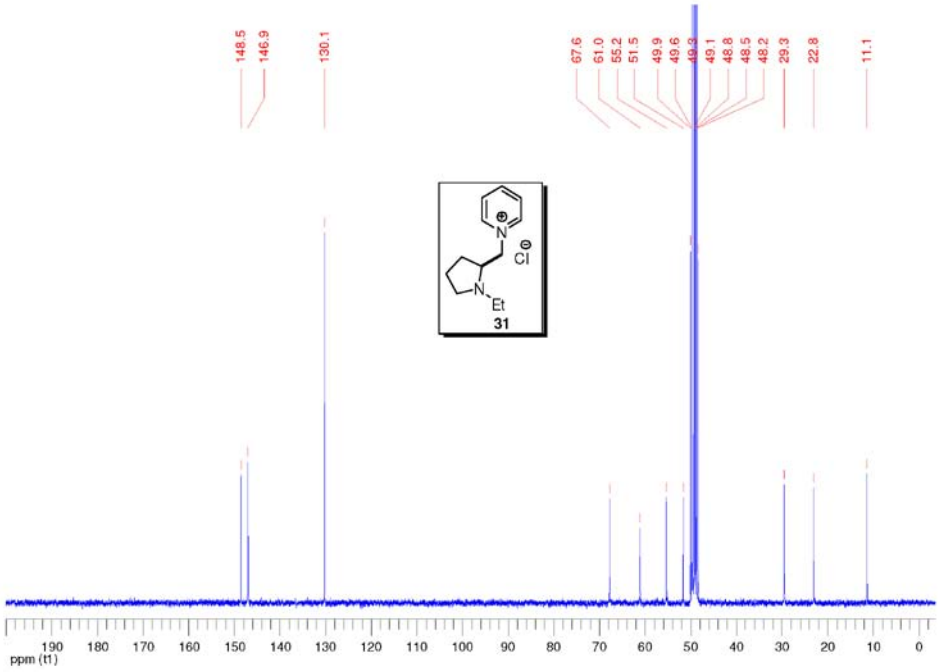


Figura S26. ^{13}C NMR spectrum (75 MHz, CD_3OD) of compound **31**.

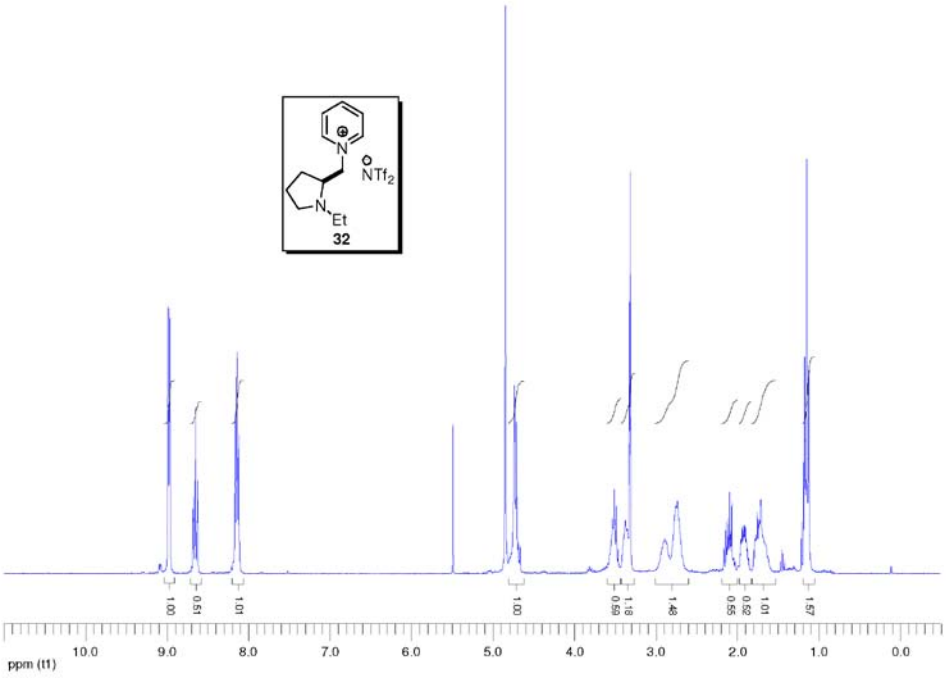


Figura S27. ^{1}H NMR spectrum (300 MHz, CD_3OD) of compound **32**.

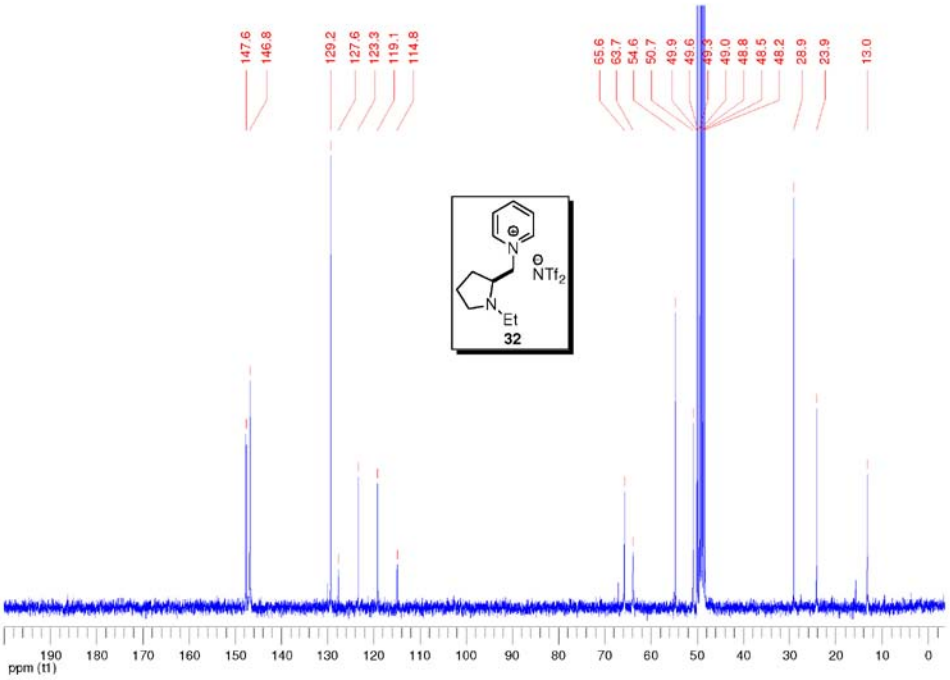


Figura S28. ^{13}C NMR spectrum (75 MHz, CD_3OD) of compound **32**.

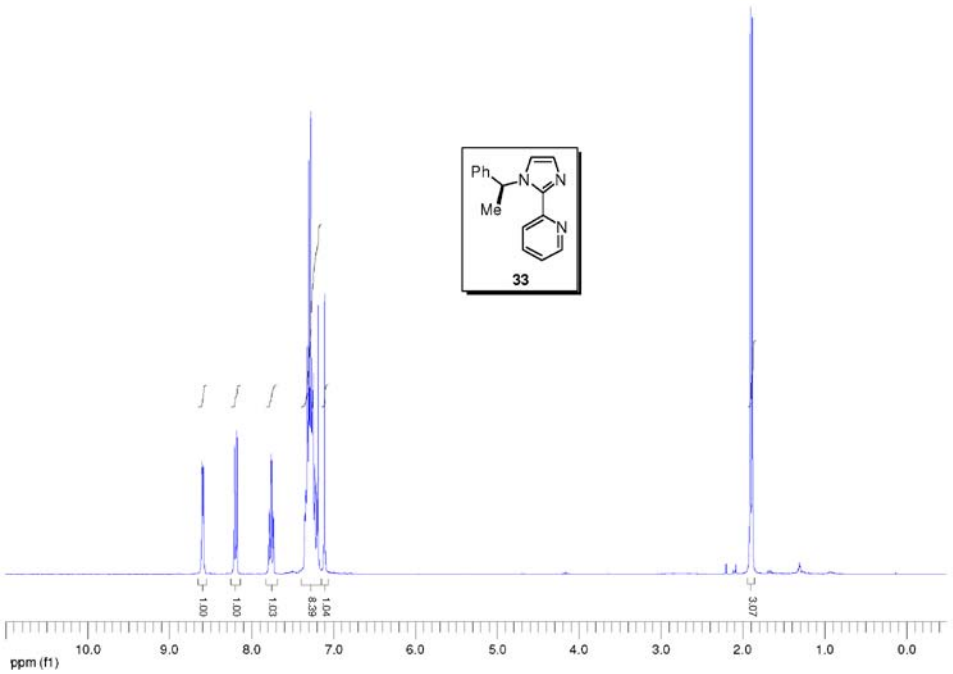


Figura S29. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **33**.

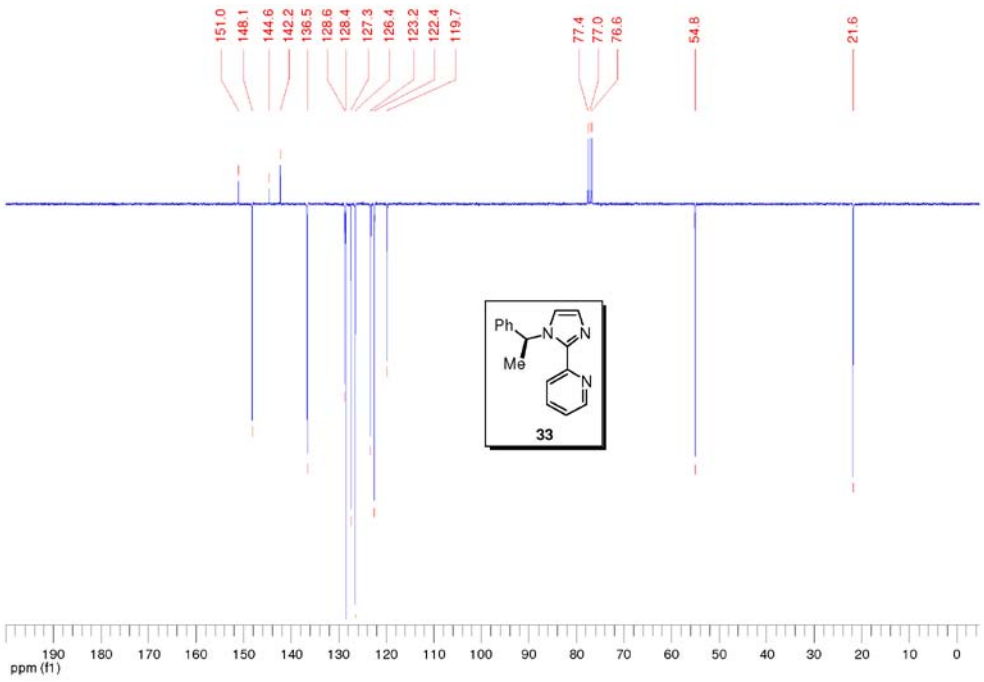


Figura S30. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **33**.

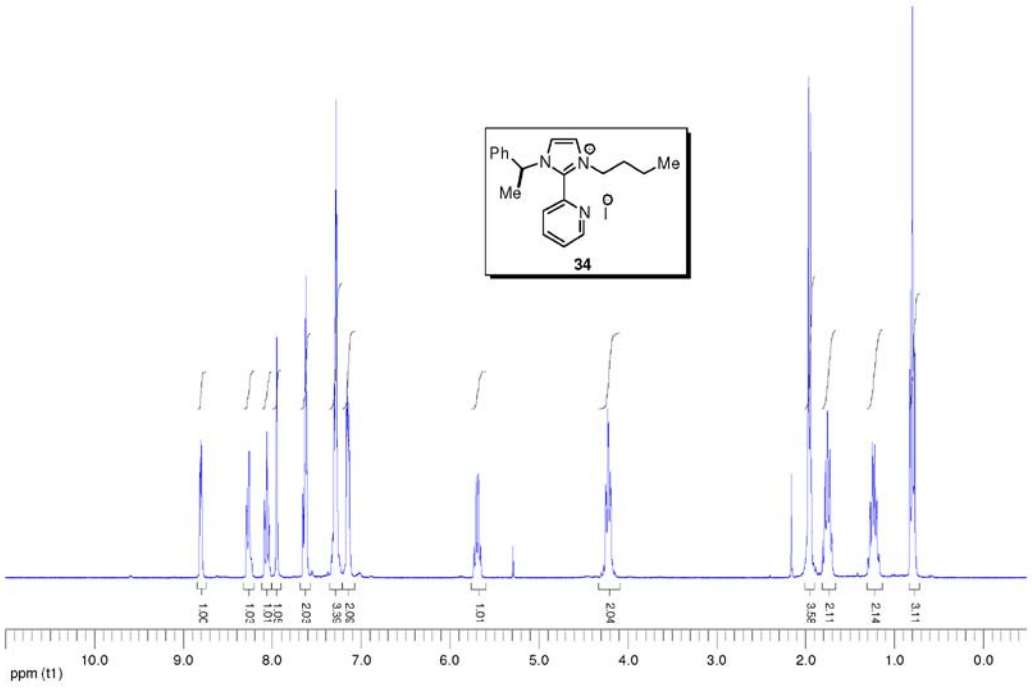


Figura S31. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **34**.

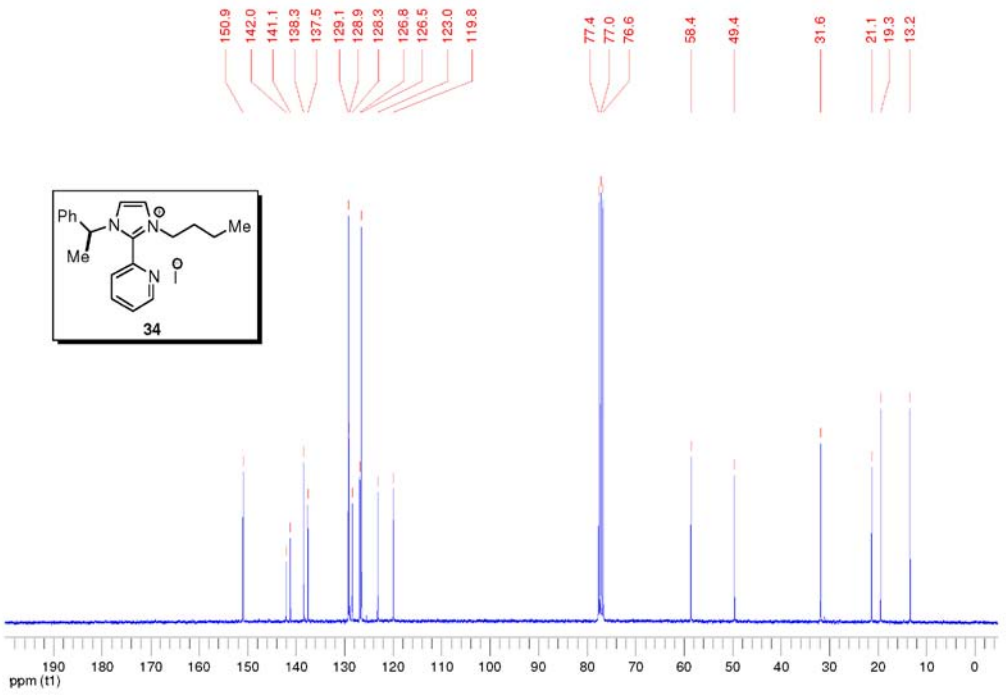


Figura S32. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **34**.

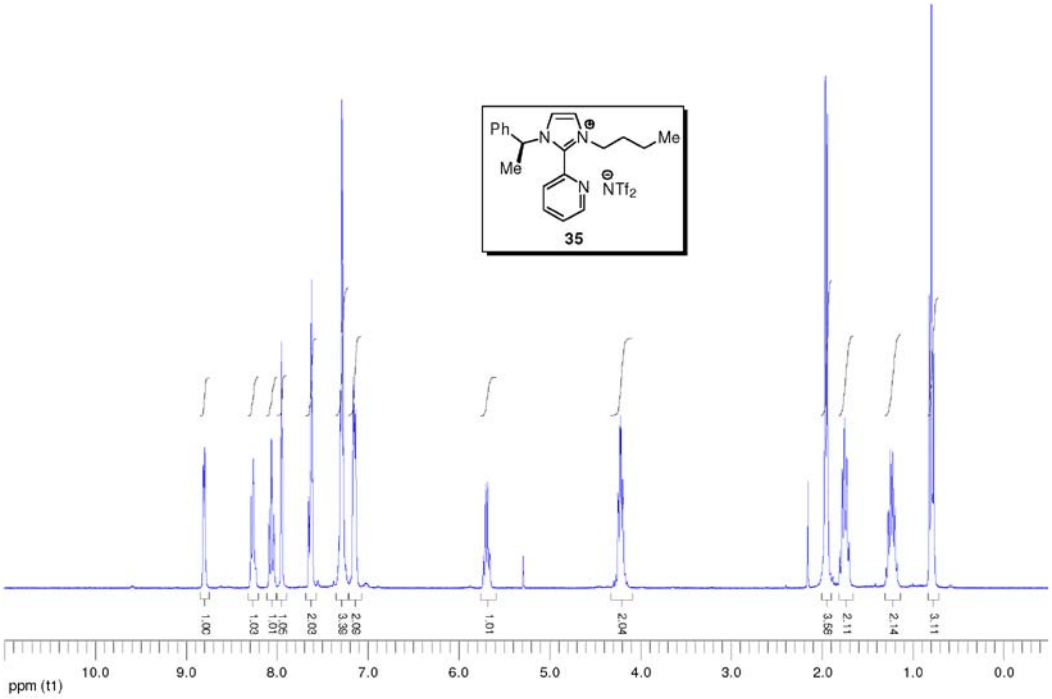


Figura S33. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound **35**.

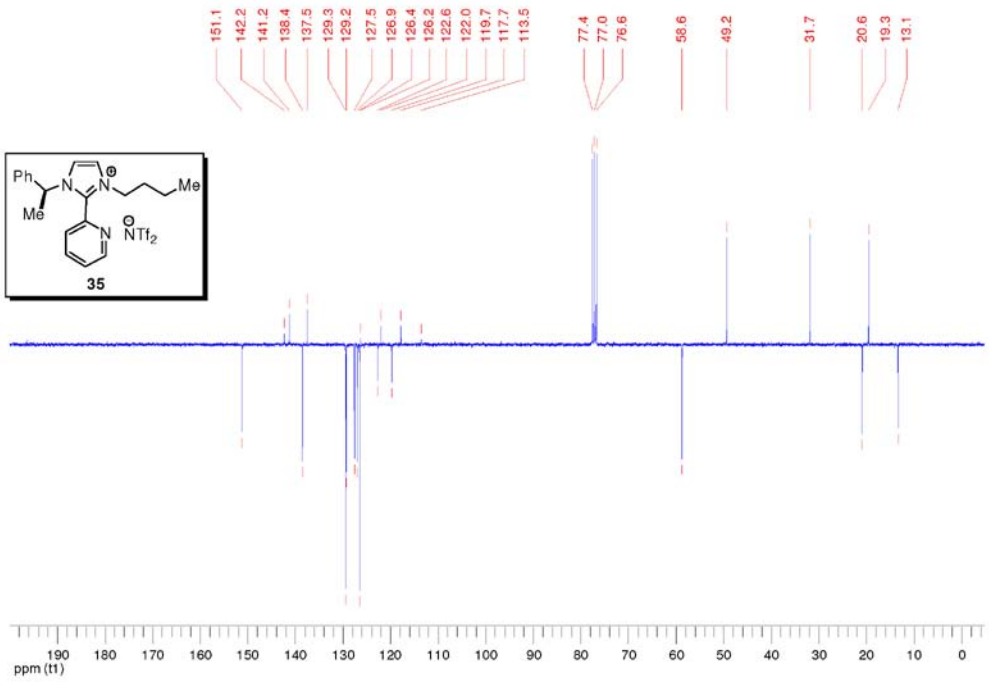


Figura S34. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound **35**.