# Grignard Reagents in Ionic Solvents: ET Reactions and Evidence for Facile Br/Mg Exchange

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## General Procedure

An MBraun UL-99-245 dry box and standard Schlenk techniques on a double manifold vacuum line were used in the manipulation of air and moisture sensitive compounds. NMR spectra were recorded on a Varian AS 500 MHz spectrometer or a Bruker AMX 400 MHz spectrometer in five millimeter quartz tubes. $^1$H and $^{13}$C{$^1$H} chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane (TMS), $^{31}$P{$^1$H} chemical shifts are reported with respect to 85% phosphoric acid (0 ppm). Infrared spectra were obtained using a Bomem MB spectrometer with the % transmittance values reported versus cm$^{-1}$. Gas Chromatography Mass Spectrometry (GC-MS) were carried out on the extracts using a Gas Chromatography Electron Ionisation G 1800A GCD system. Tetradecyl(trihexyl)phosphonium decanoate (PIL-$C_9H_{19}$COO$^-$) and tetradecyl(trihexyl)phosphonium phosphinate were donated by Cytec and purified as described below. All other reagents and solvents were purchased from Aldrich and used without further purification except *p*-benzoquinone which was purified by sublimation. EPR spectra were collected on a Bruker ECS-106 X-band spectrometer. Measurements were made at room temperature with samples contained in flame-sealed Pasteur pipettes sealed with a rubber septum. All the samples were made and sealed under inert atmosphere. The samples in phosphonium ionic liquids were diluted with toluene to reduce viscosity. The EPR spectra were simulated using Bruker's WINEPR SimFonia software.

## Purification of phosphonium ionic liquids

We have chosen to study PIL-$C_9H_{19}$COO (CYPHOS® IL 103) for this particular work, however the same procedure is used to purify other phosphonium-based ionic liquids. We have found that commercially produced phosphonium ionic liquids (PILs) contain traces of residual phosphines (observed through NMR studies), HCl and water (4.87 ppm). Recognizing the sensitivity of organometallic reagents to these aforementioned species we designed a method to purify the PILs. The excess HCl in the PILs is neutralized by aqueous sodium hydrogen carbonate. Care should be taken since there can be excessive foaming in this step. The ionic liquid layer is then washed vigorously with water and extracted using hexanes. The PILs can be dried by azeotropic distillation with toluene. They can also be further dried at this stage with a small amount of solid potassium, but we have found that this is not generally required. $^1$H NMR and $^{31}$P NMR and subsequent reactivity studies confirmed the absence of any other impurities. Only one $^{31}$P peak consistent with PIL-$C_9H_{19}$COO was observed at 33.5 ppm.[1]

## Synthetic Procedures and Characterization of Compounds

### Reaction of *p*-benzoquinone with phenylmagnesium bromide in tetrahydrofuran

Phenylmagnesium bromide (5.0 ml, 5.0 mmol) was added dropwise to a solution of *p*-benzoquinone (BQ) (0.54 g, 5.0 mmol) in 30 ml of THF. The solution underwent a spontaneous colour change from yellow to dark blue with concomitant formation of a blue precipitate. EPR measurements of a solution of the blue filtrate in THF showed a 9-line spectrum. As shown in Figure S1, the line pattern is consistent with 4-hydroxy-4-phenyl-cyclohexa-2,5-dienone radical. GC-MS studies on the blue precipitate gave *m/z* peak at 187.1 anticipated for 4-hydroxy-4-phenyl-cyclohexa-2,5-dienone. The blue mixture (the supernatent and the solution) was quenched with saturated ammonium chloride and extracted using dichloromethane to give 4-hydroxy-4-phenyl-cyclohexa-2,5-dienone (94%), dihydroxybenzene (3%) and benzene (3%).

The same procedure was performed using 2,4,6-trimethylphenylmagnesium bromide or ethylmagnesium bromide as shown in Scheme S1 with all yields as indicated.
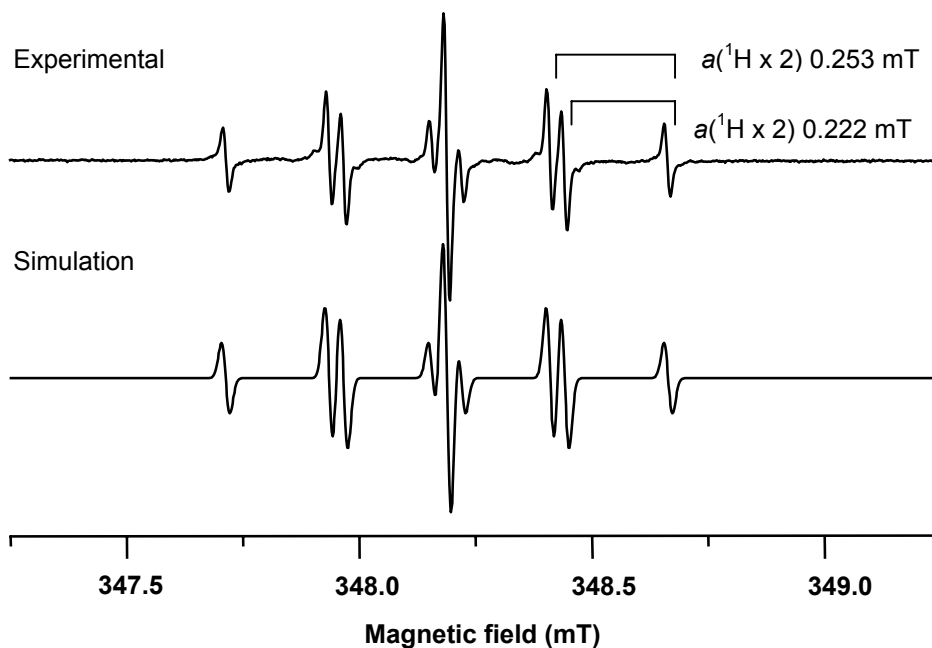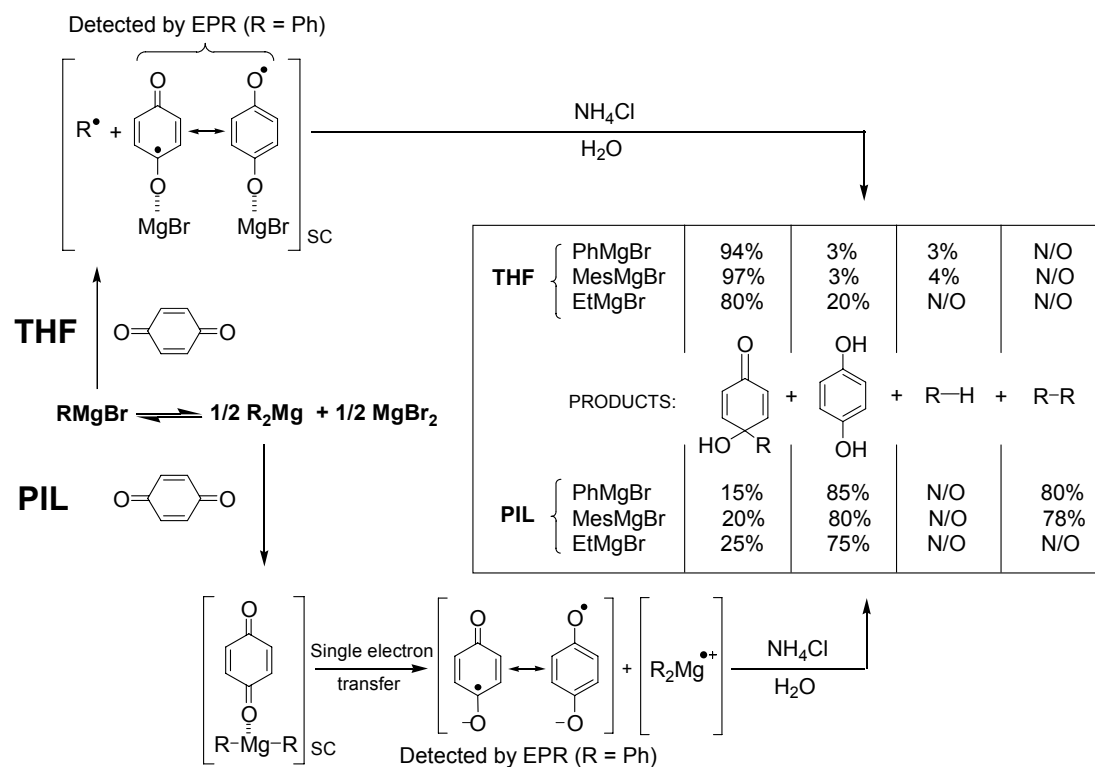
**Figure S1**: EPR spectrum of the filtrate of PhMgBr with BQ in THF. *Experimental Conditions*: Modulation amplitude: 0.05 mT, MW freq. = 9.84 GHz, scan time = 671 s, time constant = 327.7 ms, microwave power = 0.64 mW. *Simulation Parameters*: $a(^1H \times 2) = 0.253$ mT, $a(^1H \times 2) = 0.222$ mT, Linewidth = 0.018 mT.



**Scheme S1**: Reaction of *p*-benzoquinone with PhMgBr in molecular solvent and $PIL-C_9H_{19}COO$ where Ph = phenyl, Mes = 2,4,6-trimethylphenyl and Et = ethyl. N/O = not observed.

We have probed the reaction system to account for benzene. In principle, benzene could have been: (1) present in the phenylmagnesium bromide grignard reagent; (2) formed by quenching the phenylmagnesium bromide with $H_2O$ or; (3) formed by possible proton abstraction from the solvent, THF in this case. To confirm the absence of benzene from the phenyl magnesium bromide, the Grignard reagent was quenched with $D_2O$. The result was complete conversion of phenylmagnesium bromide to deuterated benzene ($C_6H_5D$), as determined by GC-MS, giving a *m/z* peak at 79.1. To verify the origin of the hydrogen atom obtained by the phenylmagnesium bromide, the filtrate from the reaction mixture of phenylmagnesium bromide with benzoquinone in THF was quenched with $D_2O$. No $C_6H_5D$ was observed, instead the phenyl radical abstracts a hydrogen atom more easily from THF to form non-deuterated benzene with a *m/z* peak at 78.1.

## Synthesis and Stability of PIL/PhMgBr solution

To a solution of PIL-$C_9H_{19}COO$ (5 ml) a small amount of ethereal solvent (1 ml) was added to raise the freezing point of the solution and lower the viscosity in order to facilitate stirring. The resulting mixture was cooled to -78°C, and to it an aliquot of Grignard reagent (5.0 ml) in THF was added dropwise. The solution was warmed to room temperature and the co-solvent was completely removed under vacuum and the absence of co-solvent was confirmed by NMR studies. The Grignard reagent dissolved in the PIL-$C_9H_{19}COO$ is persistent with no evidence for significant decay over two months. The stability of PIL-$C_9H_{19}COO$ was confirmed by $^{31}P$ NMR, which gave a single peak at 33.5 ppm with the absence of any phosphines. The stability of the PIL-$C_9H_{19}COO$/PhMgBr solution was also chemically analyzed as detailed below.

To PIL-$C_9H_{19}COO$ (5 mL) with a few drops of THF (up to 1 mL), commercially available 1 M phenylmagnesium bromide (5.0 mL) in THF was added at -78 °C. The mixture was stirred and then warmed to room temperature. THF was removed *in vacuo* leaving a viscous pale yellow or orange solution to which toluene (1.0 mL) was added to reduce viscosity. Treatment of this solution with either bromine or N,N'-dimethylformamide followed by quenching with saturated aqueous ammonium chloride and addition of water followed by extraction with dichloromethane resulted in the formation of bromobenzene (98%) and benzaldehyde (99%), respectively, as determined by GC-MS studies. Identical reactivity studies were carried out with one-month-old PIL-$C_9H_{19}COO$/PhMgBr and the same results were obtained indicating that there is no decomposition of the PIL-$C_9H_{19}COO$.

One point that should be noted is that on addition of phenylmagnesium bromide to PIL-$C_9H_{19}COO$, the colour changed from pale yellow to orange-red going through a faint blue colour. Initially, we speculated that this could be due to solvated electrons, but careful examination of the Grignard solutions and the PILs separately showed that they were all diamagnetic materials.

As explained previously, PIL-$C_9H_{19}COO$/PhMgBr is a good source of the phenyl radical and addition of the nitrone spin trap, 5,5-dimethyl-1-pyrroline *N*-oxide (DMPO) produced a species with a well-resolved 6-line EPR spectrum, as shown in Figure S2. The EPR spectrum exhibits distinctive $^1H$ and $^{14}N$ hyperfine couplings.

The same experiment was repeated with ethylmagnesium bromide in PIL-$C_9H_{19}COO$ and when DMPO was added to the reaction mixture a similar 6-line spectrum was obtained, consistent with the ethyl DMPO adduct.
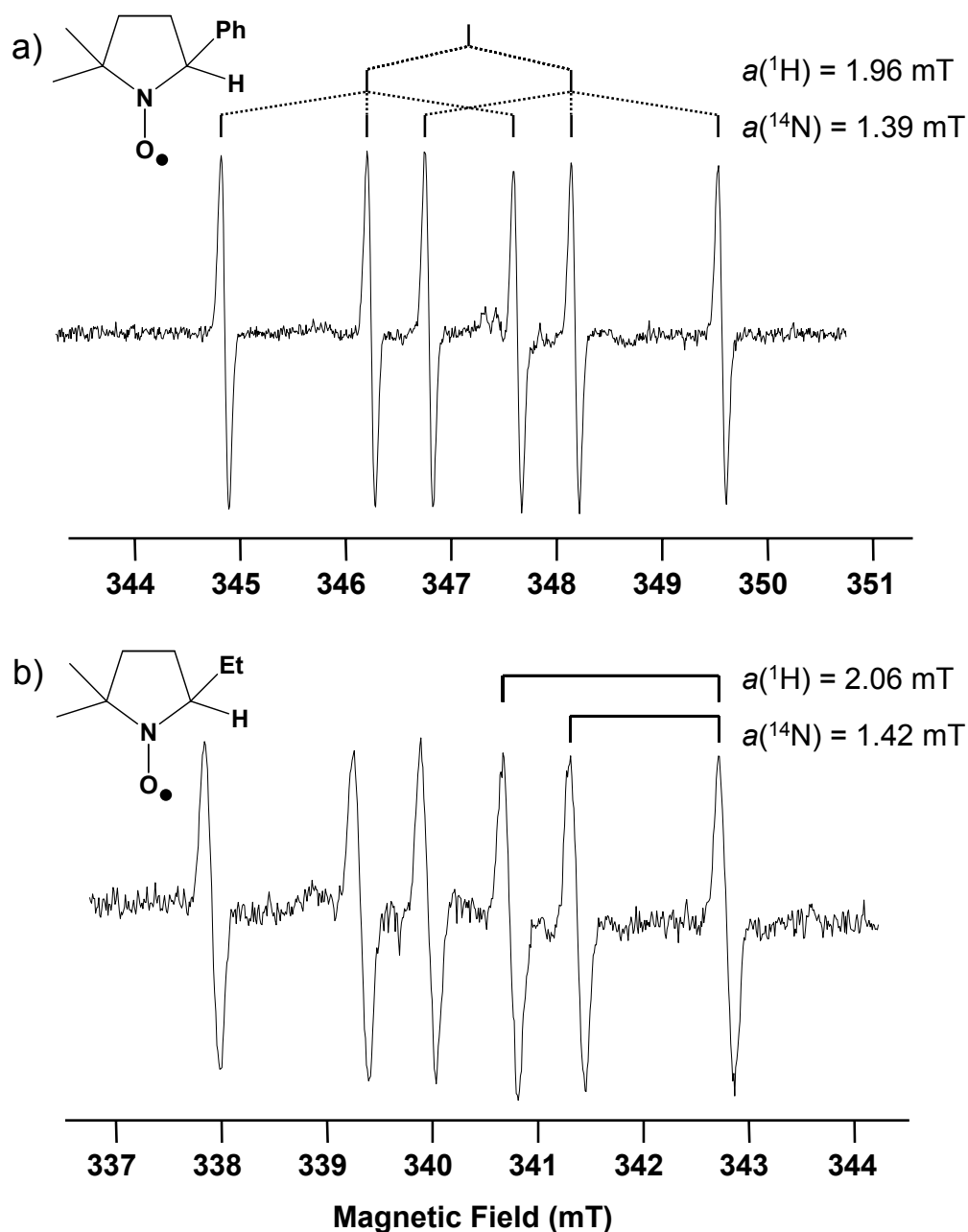
*Figure S2:* EPR spectrum of: a) PIL-C$_9$H$_{19}$COO/PhMgBr with DMPO; b) PIL-C$_9$H$_{19}$COO/EtMgBr, both diluted with toluene. *Experimental Conditions:* a) Modulation amplitude: 0.025 mT, MW freq. = 9.82 GHz, scan time = 20.0 s, time const. = 5.12 ms, microwave power = 0.64 mW; b) Modulation amplitude: 0.1 mT, MW freq. = 9.63GHz, scan time = 671.089 s, time const. = 327.68 ms, microwave power = 0.64 mW.

**Reaction of *p*-benzoquinone with phenylmagnesium bromide in PIL-C$_9$H$_{19}$COO⁻**

*p*-Benzoquinone (0.54 g, 5.0 mmol) was dissolved in PIL-C$_9$H$_{19}$COO/PhMgBr solution

(1.0 M, 5.0 mL) with a few drops of toluene to decrease viscosity. A spontaneous colour change was observed from orange to brownish blue. An EPR study was carried out on the sample and a broad five-line spectrum was observed, as shown in Figure S3.
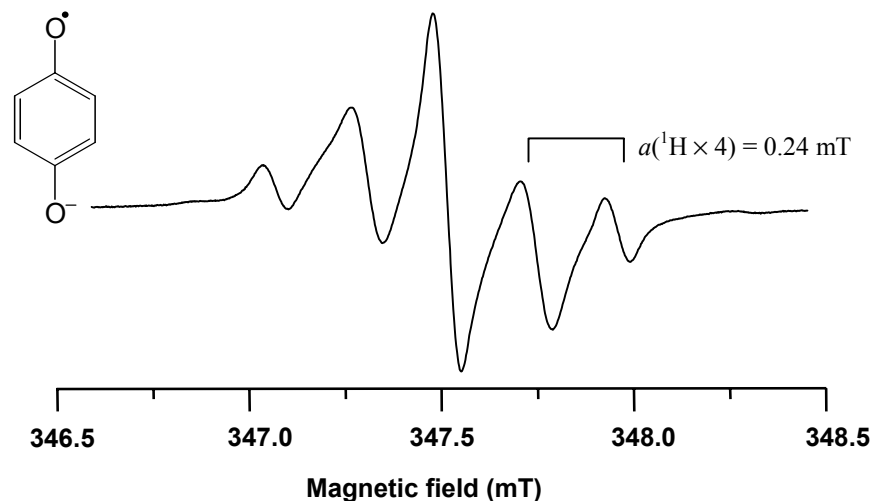


**Figure S3**: EPR Spectrum of PhMgBr + BQ in PIL-$C_9H_{19}COO^-$. *Experimental Conditions:* Modulation amplitude: 0.05 mT, MW freq. = 9.82 GHz, scan time = 41.94 s, time const. = 5.12 ms, microwave power = 0.64 mW

This EPR spectrum is consistent with the *p*-semiquinone radical anion ($BQ^{\bullet-}$), with hyperfine couplings from four equivalent protons of $a(^1H) = 0.23$ mT, in agreement with literature reports of $BQ^{\bullet-}$ in molecular solvents.[2] The presence of this radical anion is consistent with electron transfer from phenylmagnesium bromide to benzoquinone. The distorted line shapes are attributed to an underlying spectrum from a minor species. As shown in the main text (Figure 1) the EPR spectrum of PhMgBr + BQ in PIL-$C_9H_{19}COO$ correlates very closely with that of PhMgBr + BQ + 15% THF in Tetradecyl(trihexyl)phosphonium chloride (PIL-Cl). However, the solution with THF in PIL-Cl$^-$ has significantly better resolution allowing us to determine the identity of the underlying radical species and its concentration. Simulation of the spectrum indicates 80% $BQ^{\bullet-}$ and 20% of the second species, with proton hyperfine couplings of $a(^1H \times 2) = 0.242$ mT, $a(^1H \times 2) = 0.165$ mT, $a(^1H \times 2) = 0.066$ mT, $a(^1H) = 0.055$ mT (Figure S4). We anticipate that the pairs of larger couplings are from the semiquinone ring protons and the smaller couplings are from a phenyl group adducted via nucleophilic attack. The symmetry indicated by the pair-wise couplings of the semiquinone ring protons implies that the phenyl radical attacks at C1 and thus that the minor product is 4-hydroxy-4-phenyl-cyclohexa-2,5-dienone radical.

*Figure S4*: EPR Spectra of (A) BQ$^{\bullet-}$ (B) [BQ–Ph]$^{\bullet}$ (C) A+B (D) PhMgBr + BQ in PIL-Cl$^-$ *Simulation Parameters for A*: $a(^1H \times 2) = 0.230$ mT, $a(^1H \times 2) = 0.250$ mT, Linewidth 0.06 mT. *Simulation Parameters for B*: $a(^1H \times 2) = 0.242$ mT, $a(^1H \times 2) = 0.165$ mT, $a(^1H \times 2) = 0.066$ mT, $a(^1H) = 0.055$ mT, Linewidth 0.022 mT *Experimental Conditions:* Modulation amplitude: 0.025 mT, MW freq. = 9.82 GHz, scan time = 41.94 s, time const. = 20.48 ms, microwave power = 0.64 mW

After EPR studies the ionic-liquid mixture was quenched with saturated ammonium chloride and

then extracted with dichloromethane to give 4-hydroxy-4-phenyl-cyclohexa-2,5-dienone (15%) and dihydroxybenzene (85%), in good agreement with the concentration of the radical precursors characterised by EPR, and biphenyl (80%) but no benzene. For 4-hydroxy-4-phenyl-2,5-cyclohexadienone[3]: mp 102-103°C; IR (CHCl$_3$) 3418, 3371, 3030, 1656, 1599 cm$^{-1}$; $^1$H NMR (400 MHz, d$_6$-acetone) 5.042 (1H, s), 6.05 (2 H, d), 6.83 (2H, d), 7.28-7.45 (5H, m); $m/z$ (EI) 186.1. For dihydroxybenzene: $^1$H NMR (400 MHz, d$_6$-acetone) 6.657 (2 H), 7.66 (4 H); $m/z$ (EI) 110.1.

The same procedure was carried out with different Grignard reagents namely 2,4,6-trimethylphenylmagnesium bromide and ethylmagnesium bromide. Spectroscopic data for 4-hydroxy-4-2,4,6-timethylphenyl-2,5-cyclohexadiene: IR (CHCl$_3$) 3387, 3030, 1783, 1658, 1609, 1505 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) 2.33 (3H, s), 2.42 (6 H, s), 6.61 (2H, d), 6.69 (2H, d), 6.82 (2 H, s), 6.88 (2 H, s); $m/z$ (EI) 186.1. Spectroscopic data for 4-hydroxy-4-ethyl-2,5-cyclohexadiene: $m/z$ (EI) 139.2. All yields are shown in Table S1.

| | RMgBr | [BQ-RH] | Dihydroxybenzene | R-H | R-R |
|---|---|---|---|---|---|
| **In THF** | PhMgBr | 94[3] | 3 | 3 | Not observed |
| | MesMgBr | 97 | 3 | 4 | Not observed |
| | EtMgBr | 80[4] | 20 | Not observed | Not observed |
| **In** PIL-C$_9$H$_{19}$COO$^-$ | PhMgBr | 15 | 85 | Not observed | 80 |
| | MesMgBr | 20 | 80 | Not observed | 78 |
| | EtMgBr | 25 | 75 | Not observed | Not observed |

**Table S1**: Reaction of Grignard reagent with $p$-benzoquinone in molecular solvent (THF) and in PIL-C$_9$H$_{19}$COO where Ph = phenyl, Mes = 2,4,6-trimethylphenyl and Et = ethyl. The spectroscopic details for [BQ-RH], where R = Ph[3] and Et[4] have been reported in literature.

**Coupling reactions of Grignard reagents in PILs**

A stock solution of 1.0 M PhMgBr in THF (5 mL, 5 mmol) was added to cold PIL-C$_9$H$_{19}$COO (5.0 mL) at −78 ºC. The reaction mixture was warmed to room temperature and THF was removed *in vacuo*. Toluene (0.5 mL) was added to reduce viscosity, followed by the addition of one equivalent (with respect to PhMgBr) of: 4-fluorotoluene; 4-chlorotoluene; 4-bromotoluene; or 4-iodotoluene. To this solution, 0.05 mol percent of the complex bis[1,3-di(2′,6′-diisopropylphenyl)imidazolin-2-ylidene]nickel(0), prepared *in situ* by the reaction of nickel dicyclooctadiene and the free *N*-heterocyclic carbene in PIL-C$_9$H$_{19}$COO, was added as shown in Scheme S2. On addition of nickel dicyclooctadiene to *N*-heterocyclic carbene a colour change from pale yellow to dark green was observed. The reaction mixture was stirred for 18 hours at room temperature under nitrogen and then quenched with a few drops of methanol. Extraction was carried out using dichloromethane and water. The dichloromethane layer was then dried using anhydrous magnesium sulphate and then analyzed by GC-MS. Yields are shown in Table S2 below. In all cases a small amount (< 2 %) of biphenyl was observed.

X = F; yield = 42%
X = Cl; yield = 88%
X = Br; yield = 73%
X = I; yield = 74%
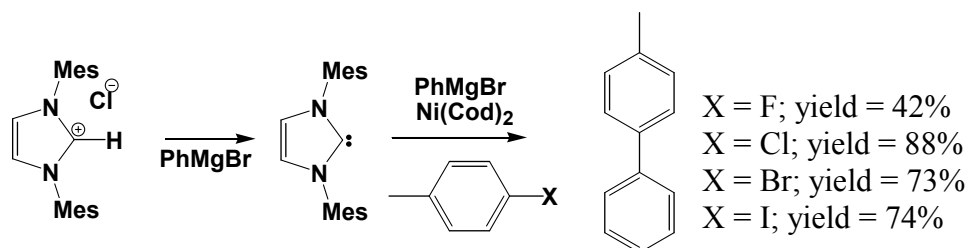
**Scheme S2**: Kumada-Corriu reaction in PILs.

| Aryl Halide | MePh-Ph | Me$_2$Ph$_2$ |
|---|---|---|
| 4-fluorotoluene | 42% | 0% |
| 4-chlorotoluene | 88% | 0% |
| 4-bromotoluene | 73% | 25% |
| 4-iodotoluene | 74% | 22% |

**Table S2:** Coupling of aryl-Grignard reagents with aryl halides in the presence of a Ni(0) complex of a nucleophilic carbene.

## Transmetallation reaction in PILs

Grignard reagents such as phenylmagnesium bromide and ethylmagnesium bromide are stable in PILs, as shown above, and show reactivity without degradation of the ionic liquid. Ethylmagnesium bromide in THF was added to cold PIL-C$_9$H$_{19}$COO and the molecular solvent was removed under vacuum. Bromobenzene was then added to this solution and stirred for six hours. To check whether transmetallation reaction occurred, benzaldehyde was added to the mixture followed by quenching with water and extraction using dichloromethane. The extract was analysed by GC-MS. Diphenyl-methanol was obtained in 83% yield and a very small amount of 1-phenyl-propan-1-ol was also obtained due to incomplete transmetallation and the nucleophilic attack of the ethylmagnesium bromide on benzaldehyde.

## References

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