# Grignard reagents in ionic solvents: electron transfer reactions and evidence for facile Br–Mg exchange†

**Taramatee Ramnial,[a] Stephanie A. Taylor,[a] Jason A. C. Clyburne[ab] and Charles J. Walsby[a]**

*Received (in Berkeley, CA, USA) 8th December 2006, Accepted 10th April 2007*
*First published as an Advance Article on the web 23rd April 2007*
**DOI: 10.1039/b617861h**

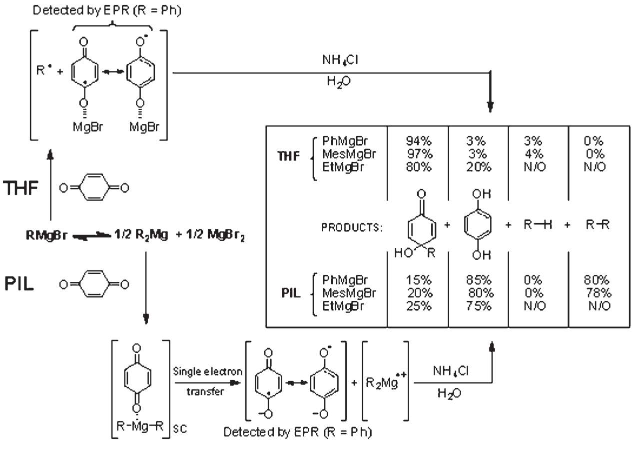
**Grignard reagents form persistent solutions in phosphonium ionic liquids possessing *O*-donor anions and these solutions are excellent reaction media for electron transfer processes and transmetallation reactions.**

This report describes the disparate reactivity of Grignard reagents in molecular and ionic solvents. Grignard reagents (RMgX) are among the most synthetically useful compounds.[1] Their diverse chemistry has been studied primarily, but not exclusively, in *molecular* solvents with the most common solvent being the broad class known as ethers. Recently we found that solutions of Grignard reagents dissolve and persist in phosphonium ionic liquids (PILs), specifically tetradecyl(trihexyl)phosphonium chloride (PIL-Cl) with ~15 mol% of THF as co-solvent.[2] In this work we demonstrate the potential general application of PILs to control selectivity in Grignard reactions by studying reactions with *p*-benzoquinone (BQ), a well-known electron acceptor that can react *via* an electron transfer mechanism. We have determined that the reaction selectivity of the Grignard reagent with BQ exhibits variability due to solvent-driven shifts in the Schlenk equilibrium. Specifically, we report: (1) formation of molecular-solvent free PIL solutions of Grignard reagents; (2) generation of persistent radicals in molecular solvents and PILs; (3) evidence for different reaction mechanisms of the Grignard reagent in molecular solvents and PILs; (4) synthetic utility of these solutions.

Imidazolium ionic liquids[3–7] are the most extensively studied ionic liquids, and typically react *via* acid–base reactions or electrochemically with basic/electron-rich reagents and hence the most common imidazolium ionic liquids, based on the 1-butyl-3-methylimidazolium cation, do not support traditional Grignard chemistry.[8] After our report of Grignard reactions in PILs,[2] Wilhelm *et al.*[9] and Handy[10] reported the use of new dihydroimidazolium and imidazolium-based ionic liquids, respectively, that were alkylated at $C_2$ in order to overcome the deprotonation problem commonly observed in imidazolium ionic liquids. Subsequently, Chan reported in this journal the preparation of Grignard reagents in pyridinium ionic liquids.[11]

Grignard reagents dissolved in PILs exhibit high reactivity (*vide infra*). For instance, $C_6H_5MgBr$ (PhMgBr) in THF or ether dissolves *exothermically* in anhydrous tetradecyl(trihexyl) phosphonium decanoate (PIL-$C_9H_{19}COO$) or anhydrous tetradecyl(trihexyl)phosphonium phosphinate. The highly exothermic dissolution suggests the formation of new strong interactions, most likely between the anion and the organomagnesium reagent. The ethereal co-solvent can be quantitatively removed by exhaustive evacuation, as indicated by NMR and GC–MS studies. These new PIL–Grignard solutions do not show any degradation over one month, as indicated by a one-month old solution of 1 M PhMgBr dissolved in PIL-$C_9H_{19}COO$ which, when treated with $Br_2$, gave bromobenzene in >95% yield. Organomagnesium halides and diorganomagnesium halides are Lewis acidic, and the metal centres strongly engage oxygen donor sites in ethereal solvents. We propose that the stability of these new solutions is the result of strong $Mg\cdots O$ interactions with the decanoate anion of PIL-$C_9H_{19}COO$.[12] Dissolution of THF solutions of PhMgBr in PIL-Cl is far less exothermic, consistent with weaker interactions between the chloride ions and the organomagnesium reagent.

Grignards are strong reducing agents. For example, the oxidation potential of PhMgBr in PIL-$C_9H_{19}COO$ was determined to be −0.10 V (*vs.* SCE, scan rate 300 mV $s^{-1}$, ferrocene as internal standard), close to the estimated value of −0.05 V of PhMgBr in THF.[1] It is generally accepted that electron transfer leads to a radical ion pair,[13] and the collapse of this pair in the solvent cage provides a mechanism for carbon–carbon bond formation. It is important to note that Grignard reagents are complex mixtures due to the Schlenk equilibrium, which is a dynamic interconversion between RMgX, $R_2Mg$ and $MgX_2$ (Scheme 1),[1] and several solvent complexes of these metal containing species are possible, such as $RMgX\cdot S_2$, $R_2Mg\cdot S_2$ and $MgX_2\cdot S_2$, where S is typically an *O*-donor solvent molecule.



**Scheme 1** Reaction of Grignard reagent with BQ in molecular and ionic solvents. N/O = not observable. Repeated yields have an error of ±2%.

---

[a] *Department of Chemistry, Simon Fraser University, 8888 University Drive, Burnaby, British Columbia, Canada V5A 1S6.*
*E-mail: cwalsby@sfu.ca; Fax: 604 291 3765; Tel: 604 291 4607*
[b] *Department of Chemistry, Saint Mary's University, 923 Robie Street, Halifax, Nova Scotia, B3H 3C3, Canada.*
*E-mail: jason.clyburne@smu.ca; Tel: 902 420-5649*

† Electronic supplementary information (ESI) available: Experimental details and EPR spectra. See DOI: 10.1039/b617861h

In THF, BQ reacts with PhMgBr to produce a blue solution over a blue precipitate (Scheme 1). The solution is paramagnetic and EPR studies showed a 9-line spectrum (Fig. 1 (A)) derived from two pairs of distinct $^1$H hyperfine couplings: $a(^1H \times 2) = 0.25$ mT, $a(^1H \times 2) = 0.22$ mT (for spectral simulation see ESI, Fig. S1). The distinctive splitting pattern and the size of the couplings (*cf.* 0.24 mT for the *p*-semiquinone radical)[14] lead us to conclude that this species is an asymmetric *p*-semiquinone radical adduct. Lack of extra hyperfine interactions indicates that the reduction in symmetry is due to an interacting atom with a low abundance of nuclear spin bearing isotopes. Mg has a 90% abundance of I = 0 isotopes and the data are consistent with an ionic-type interaction of a Mg centred cation derived from the Grignard reagent with the anionic oxygen of the radical. Thus, taken in total, the absence of further hyperfine structure is consistent with interaction with MgBr. The *solid* is also paramagnetic, giving a broad, unresolved EPR spectrum. Multiple washings of the solid with THF gave a blue solution with the same 9-line EPR spectrum found previously. Thus, the Mg···*p*-semiquinone radical adduct is the sole paramagnetic product of this reaction. Aqueous work-up of the mixture produced 4-hydroxy-4-phenyl-2,5-cyclohexadienone, dihydroxybenzene and a trace of benzene (Scheme 1). After filtration, the blue solution was quenched with water and then analyzed by GC–MS which showed the presence of a small amount of benzene and the *absence* of biphenyl. Reaction mixtures quenched with $D_2O$ do not contain $C_6H_5D$, suggestive of the assumed transient phenyl radical abstracting a hydrogen atom from the THF rather than unreacted PhMgBr reacting with the quenching reagents. Although this reactivity appears to be a *formal* nucleophilic attack, it is more likely that electron transfer occurs and the resulting radical pair collapses (persistent radical effect)[15] to form the observed product. The formation of benzene is also in accord with a radical pathway.[13]

In PILs a completely different reaction occurs (Scheme 1). Reaction of the PIL-$C_9H_{19}$COO–PhMgBr solution with BQ results in the formation of a dark blue solution. After stirring for three hours and aqueous work-up, the products of the reaction were dihydroxybenzene (85%) and a small amount of 4-hydroxy-4-phenyl-2,5-cyclohexadienone (15%). The EPR spectrum of the dark blue solution indicates the presence of two paramagnetic species (Fig. 1 (B)). The predominant species (~80%) exhibits a five-line spectrum consistent with hyperfine couplings from four equivalent protons with $a(^1H) = 0.24$ mT, in agreement with literature reports of $BQ^{\bullet -}$,[14] a product of the electron transfer mechanism in molecular solvents. Comparison of this spectrum with that of PhMgBr and benzoquinone in anhydrous PIL-Cl with 15% THF (Fig. 1 (C)) demonstrates that both solutions contain the same radical species in similar relative concentrations. The better resolution evident in the PIL-Cl–THF solution allows us to determine that both contain a small amount (~20%) of a *p*-semiquinone radical adduct which has been identified by simulation of the EPR spectrum (see ESI, Fig. S4) as the 4-hydroxy-4-phenyl-cyclohexa-2,5-dienone radical. This compound can be derived from the formal addition of a phenyl radical to BQ. The relative proportions of the radical species, as determined by EPR, are in close agreement with the corresponding species from aqueous work-up. Interestingly, this radical may be extracted from the blue solid by treatment of a suspension of the solid with added BQ. Most importantly, the fate of the Grignard reagent was found to be biphenyl (80%).

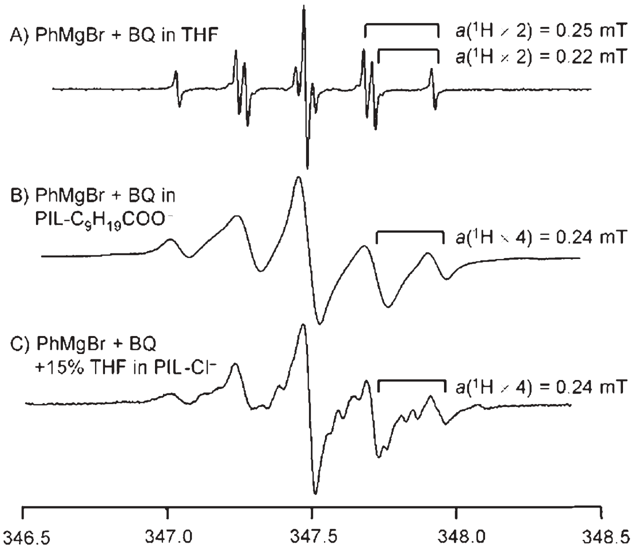


**Fig. 1** EPR spectra of radicals in molecular solvent compared to PILs.

As mentioned above, Grignard reagents engage in the Schlenk equilibrium, which is a dynamic interconversion between RMgX (the classical Grignard reagent), $R_2Mg$ and $MgX_2$. The position of the Schlenk equilibrium is dependent on the polarity of the solvent. We suggest that PIL-$C_9H_{19}$COO, being more polar, and the anion being a much stronger donor than THF (indeed, it is stronger than any other common neutral donor), shifts the Schlenk equilibrium towards $R_2Mg$, and likely exists as $R_2Mg{\cdot}S_2$, where S is now the donor component of the ionic liquid, *i.e.*, decanoate. We also note that $R_2Mg{\cdot}S$ may also be formed, since the carboxylate ligand may be either mono- or bidentate.

In molecular solvents oxidation of the Grignard potentially yields phenyl radical ($Ph^\bullet$), which typically scavenges hydrogen atoms from solvent to form benzene.[13] In PILs the observation of biphenyl indicates that $Ph^\bullet$ is not likely to be an intermediate. A reductive elimination from the postulated $PhMgPh^+$ intermediate is an alternative explanation and could lead to the observed products. Analogous studies of 2,4,6-trimethylphenylmagnesium bromide showed it to have the same kind of reactivity in PIL-$C_9H_{19}$COO, producing 2,2′,4,4′,6,6′-hexamethylbiphenyl.

Nevertheless, PIL–PhMgBr solutions are a good *source* of the *formal* phenyl radical. PIL-$C_9H_{19}$COO–PhMgBr solution reacts cleanly upon the addition of the spin trap, 5,5-dimethyl-1-pyrroline *N*-oxide (DMPO) giving a well-resolved, 6-line EPR spectrum with corresponding hyperfine coupling constants of $a(^{14}N) = 1.39$ mT and $a(^1H) = 1.96$ mT (Fig. 2, see also ESI, Fig. S2), in agreement with literature reports of the phenyl adduct of DMPO.[16,17] The spin trapping experiment indicates that the phenyl radical can be readily generated. However, the possibility of inverse spin trapping cannot be ruled out in this case. We note that formation of the tetraalkylphosphonyl radical, $R_4P^\bullet$ was not observed nor did work-up and GC–MS analysis of the reaction mixtures indicate breakdown of the PIL as would be suggested by detection of alkenes and phosphines.[18]

Finally, these results suggest that PILs are ideal reaction media to promote electron transfer processes. For example, catalytic

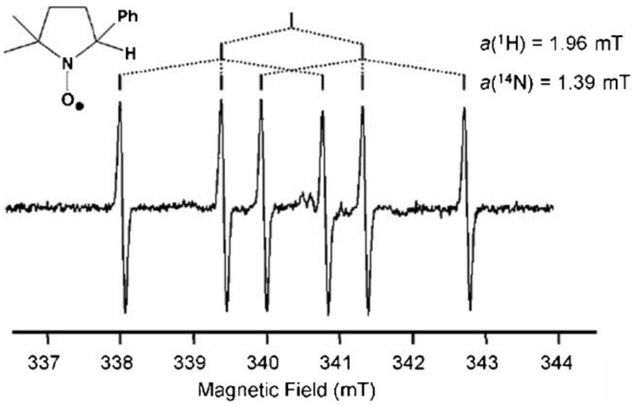
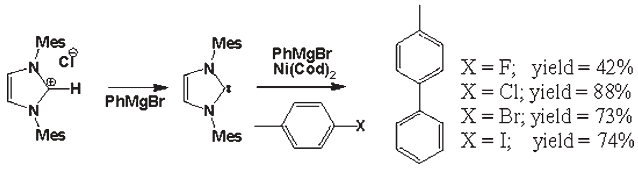


**Fig. 2** EPR spectrum of PIL-$C_9H_{19}COO$–PhMgBr with DMPO (diluted with toluene).



**Scheme 2** Kumada–Corriu reaction in PILs.

reactions that involve either radicals or charge-separated intermediates, which are important synthetic tools in carbon–carbon bond formation reactions. Unfortunately, some of the most active catalysts that support these reaction types involve species that are clearly incompatible with most ionic liquids, namely: (1) a low-valent metal centre in the presence of (2) a strongly nucleophilic ligand in (3) basic reaction media.[8] To illustrate the ability of our PIL–Grignard solutions to support such reactions, we examined the Kumuda–Corriu reaction, which involves coupling aryl-Grignard reagents with aryl halides in the presence of a Ni(0) complex of a nucleophilic carbene, as shown in Scheme 2.[19] The coupling reaction proceeds with high yield in the case of 4-bromotoluene and 4-iodotoluene, although transmetallation occurs with concomitant generation of ~25% 4,4′-dimethylbiphenyl.‡ The reaction also proceeds well for chlorotoluene, and surprisingly facilitates C–F bond activation.[20] The yield of the heterocoupling reaction in PILs is slightly lower than in molecular solvent (THF); however, different side products are obtained due to homocoupling, indicating that rapid transmetallation reactions are occurring.

Finally, the dramatic shift in the Schlenk equilibrium in favour of $R_2Mg{\cdot}S_2$, where S = decanoate, as well as the results from the Kumuda–Corriu reaction above, suggested to us that transmetallation reactions would be facile in the ionic liquid, recognizing the structural similarity to dialkylmagnesium compounds recently reported.[21] Indeed, transmetallations occur smoothly,‡ suggesting that PIL solutions of Grignard solutions are excellent reaction media for Mg–Br exchanges.[21]

In summary, ether-free solutions of Grignard reagents dissolved in PILs support a variety of strong bases and are good solvents for the generation of radicals. Ionic liquids may be used to evoke new chemistry for Grignard reagents. Reactions catalysed by transition metal complexes, proceeding either through radical or polar reaction pathways, also are supported in these new reaction media.

Funding was provided by the Natural Sciences and Engineering Council of Canada (NSERC) through the Discovery Grants Program to JACC and CJW. CJW is grateful for funding from Simon Fraser University. JACC acknowledges generous support from the Canada Research Chairs Program, the Canadian Foundation for Innovation and the Nova Scotia Research and Innovation Trust Fund.

## Notes and references

‡ **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-$C_9H_{19}COO$ (5.0 mL) at −78 °C. 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% 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 N-heterocyclic carbene, in PIL-$C_9H_{19}COO$, was added. On addition of nickel dicyclooctadiene 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 sulfate and then analyzed by GC–MS. In all cases a small amount (<2%) of biphenyl was observed.

**Mg–Br exchange**: For example, to cold PIL-$C_9H_{19}COO$, ethylmagnesium bromide in THF was added and the molecular solvent (THF) was removed under vacuum. To this ether free solution (as tested by $^1H$ NMR spectroscopy) bromobenzene was added and stirred for 6 hours. Benzaldehyde was added and the mixture was stirred for 16 hours. After an aqueous quench and extraction with dichloromethane, diphenylmethanol was detected in 83% yield. A small amount (6%) of 1-phenylpropan-1-ol was also observed in the reaction mixtures.

1 *Grignard Reagents: New Developments*, ed. H. G. Richey, Jr., John Wiley & Sons Inc., New York, 2000.
2 T. Ramnial, D. D. Ino and J. A. C. Clyburne, *Chem. Commun.*, 2005, 325.
3 M. Deetlefs and K. R. Seddon, *Chim. Oggi*, 2006, **24**, 16.
4 *Ionic Liquids: Industrial Applications for Green Chemistry*, ed. R. D. Rogers and K. R. Seddon, ACS Symp. Ser. 818, American Chemical Society, Washington, 2002.
5 D. Zhao, M. Wu, Y. Kou and E. Min, *Catal. Today*, 2002, **74**, 157.
6 R. X. Ren, A. Brenner, J. X. Wu and W. Ou, *Proc. Electrochem. Soc.*, 2002, **19**, 165.
7 P. J. Scammells, J. L. Scott and R. D. Singer, *Aust. J. Chem.*, 2005, **58**, 155.
8 J. Dupont and J. Spencer, *Angew. Chem., Int. Ed.*, 2004, **43**, 5296.
9 V. Jurcik and R. Wilhelm, *Green Chem.*, 2005, **7**, 844.
10 S. T. Handy, *J. Org. Chem.*, 2006, **71**, 4659.
11 M. C. Law, K.-Y. Wong and T. H. Chan, *Chem. Commun.*, 2006, 2457.
12 K. Maruyama and T. Katagiri, *J. Am. Chem. Soc.*, 1986, **108**, 6263.
13 J. McKinley, A. Aponick, J. C. Raber, C. Fritz, D. Montgomery and C. T. Wigal, *J. Org. Chem.*, 1997, **62**, 4874.
14 *Handbook of EPR spectra from quinones and quinols*, ed. J. A. Pedersen, CRC Press, Inc., Boca Raton, Florida, 1985.
15 A. Studer, *Chem.–Eur. J.*, 2001, **7**, 1159.
16 *Nitrones, Nitronates, and Nitroxides*, ed. E. Breuer, H. G. Aurich and A. Nielsen, John Wiley and Sons, Chichester, UK, 1989.
17 M. B. Kadiiska, K. S. De Costa, R. P. Mason and J. M. Mathews, *Chem. Res. Toxicol.*, 2000, **13**, 1082.
18 S. Marque and P. Tordo, *Top. Curr. Chem.*, 2005, **250**, 43.
19 V. P. W. Bohm, C. W. K. Gstottmayr, T. Weskamp and W. A. Herrmann, *Angew. Chem., Int. Ed.*, 2001, **40**, 3387.
20 J. Terao, A. Ikumi, H. Kuniyasu and N. Kambe, *J. Am. Chem. Soc.*, 2003, **125**, 5646.
21 A. Krasovskiy, B. F. Straub and P. Knochel, *Angew. Chem., Int. Ed.*, 2006, **45**, 159.