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Ionic Liquids *Very Important Paper*

The Formation of Imidazolium Salt Intimate (Contact) Ion Pairs in Solution**

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Abstract: *1-n-Butyl-2,3-dimethylimidazolium (BMMI) ionic liquids (ILs) associated with different anions undergo H/D exchange preferentially at 2-Me group of the imidazolium in deuterated solvents. This process is mainly related to the existence of ion pairs rather than the anion basicity. The H/D exchange occurs in solvents ($CDCl_3$ and MeCN for instance) in which intimate contact ion pairs are present and the anion possesses a labile H in its structure, such as hydrogen carbonate and prolinate. In D_2O, separated ion pairs are formed and the H/D exchange does not occur. A plausible catalytic cycle is that the IL behaves as a neutral base in the course of all H/D exchange processes. NMR experiments, density functional calculations, and molecular dynamics simulations corroborate these hypotheses.*

It is beyond doubt that the properties of neat imidazolium-based ILs,[1] either in condensate or gas phases,[2] can be ascribed to their structural organization, which involves the formation of supramolecular aggregates in which weak interactions (mainly hydrogen bonds) impose a high degree of directionality.[3,4] Moreover, this structural organization is maintained to a great extent even when these salts are mixed with other compounds. Indeed, it has been demonstrated that contact ion pairs are the main species of imidazolium salts associated with different anions when diluted in low polar solvents[5–7] such as chloroform[8–11] or in carbon dioxide.[12] In fact, only in higher polar solvents was the presence of solvent-separated ion pairs firmly established.[13] It is worth noting that, depending on the temperature, the formation of contact ion pairs can be re-established, as in the case of classical 1-*n*-butyl-3-methylimidazolium tetrafluoroborate ($BMI{\cdot}BF_4$), which is water-soluble at RT but becomes water-immiscible at temperatures around 4 °C.[14] Therefore, ion pairing appears to be a more general process in imidazolium ILs, but much less attention has been paid to the influence of these species during reactions performed in ILs. It is worth mentioning that such associated supramolecular species of other molecules in solution have been observed experimentally, in particular by ESI-MS.[15] More interestingly, ion-pairing effects are the key to the chiral transfer information from an ion to the transition state of a reaction at its prochiral counterion in the hydrogenation of a keto-functionalized IL.[16] Moreover, it appears that, depending on the anion basicity, 1-*n*-butyl-3-methylimidazolium ILs D/H exchange reactions were observed preferentially at C4 and C5 of the imidazolium cation in catalytic hydrogenation reactions.[17] In other words, it is enthalpically and entropically favorable for imidazolium ILs to be structured as pairs of ions, even when diluted in other substances.[5,7,8,10,18,19] Moreover, it has been observed that the H/D exchange reaction easily occurs at the C2 position of the imidazolium cation in deuterated solvents such as chloroform, acetone, and DMSO.[20] It should be noted that, depending on the imidazolium IL anion, the "latent" NCN carbenes[21,22] can be easily trapped in solution or in the gas phase with carbon dioxide or electron-deficient alkenes.[23,24] Therefore, the reactivity of imidazolium ILs as contact ion pairs should be more common than that reported to date. In fact, it is generally accepted that the formation of carbenes can be avoided by the protection of the C2 position of the imidazolium ring by the introduction of a methyl group, such as in the case of BMMI salts. However, in these cases, "abnormal" carbenes[25–30] (at positions 4 or 5 of the imidazolium ring) can be formed under relatively low basicity media.

We report herein that this H/D exchange reaction monitored by NMR is not directly related to the anion basicity but rather to the presence of the intimate ion pairs. Molecular dynamics simulations and DFT calculations were also performed to corroborate these hypotheses. Moreover, some imidazolium ILs can be used as "neutral" bases for the catalytic deuteration of compounds containing acidic hydrogen atoms using $CDCl_3$ as a D source.

The BMMI cation associated with anions of various pK_a (from −9 to 15.7; Table 1) were tested. A preferential deuteration of the C2 Me group (C11) was observed even in $BMMI{\cdot}HCO_3$ in $CDCl_3$ after 1 h (entry 2, Table 1), and almost no deuteration at the C4/C5 position of the imidazolium ring.

The ^{1}H NMR of $BMMI{\cdot}HCO_3$ clearly shows the decrease in the intensity of C11 hydrogen signals (originally singlet at 2.75 ppm) in $CDCl_3$, and the appearance of two triplets corresponding to CH_2D and CHD_2 (2.74 and 2.72 ppm). In the ^{13}C NMR spectrum, we observed the appearance of a septuplet at 9.8 ppm corresponding to the C11 carbon coupled to D and also a singlet at 77.4 ppm corresponding to

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Table 1: Degree [%][a] of deuteration of [BMMI][X] ILs in $CDCl_3$ after 1 h.[b]

Entry	X⁻	C11[a]	C4/C5[a]	pK_a of X/XH in H_2O[31]
1	$AlCl_4$/Br/Cl	0	0	[c]/−9/−8
2	HCO_3	38	0	3.6
3	HCO_2/N_3/OAc	0	0	3.77/4.72/4.76
4	Pro	76	0	1.95 and 10.64
5	bTri[d]/OH	0	0	11.9/15.7

[a] Determined by ^{1}H NMR spectroscopy. [b] Reaction conditions: RT, without stirring in a concentration of 0.2 mol L^{-1} except HCO_3 (ca. 0.05 M). [c] Data not available. [d] Benzotriazolate.

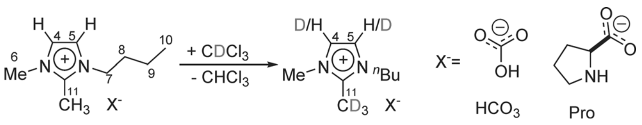
Table 2: Degree [%][a] of deuteration of [BMMI][HCO_3] ILs in different deuterated solvents after 1 h.[b]

Entry	Solvent	C11[a]	C4/C5[a]	Dielectric constant
1	$CDCl_3$	38	0	4.89
2	CD_3CN	79	96	37.5
3	[D_6]DMSO	32	32	46.45
4	D_2O	0	0	78.36

[a] Determined by ^{1}H NMR spectroscopy by the integral of the singlet of C11 methyl group and C4/C5 hydrogen atoms. [b] Reaction conditions: RT, without stirring, 0.1 M except in $CDCl_3$ (ca. 0.05 M).

the formed $CHCl_3$ (Supporting Information, Figure S1). In contrast, BMMI·HCO_3 does not undergo detectable deuterium incorporation in CD_2Cl_2 (Supporting Information, Figure S2). When 25 equiv of $CDCl_3$ was added to the latter solution, the C11 intensity was decreased by 10% and a multiplet at 2.75 ppm corresponding to CH_2D and CHD_2 appeared together with a singlet at 7.27 ppm, corresponding to the $CHCl_3$ peak (Supporting Information, Figure S2). However, noticeably, BMMI·HCO_3 is not stable in $CDCl_3$ and CD_2Cl_2 and starts to decompose after 10 min (Supporting Information, Figure S3).

It is also clear from the data shown in Table 1 that there is no direct relation between the basicity of the anion and the degree of deuteration, as no deuteration was observed in BMMI·Br (p$K_a = -9$, entry 1) and BMMI·OH (p$K_a = 15.7$, entry 5) under the same reaction conditions. The two cases in which H/D exchange was detected at C11 possess anions (HCO_3 and Pro) containing sites that can easily exchange H/D (Scheme 1).



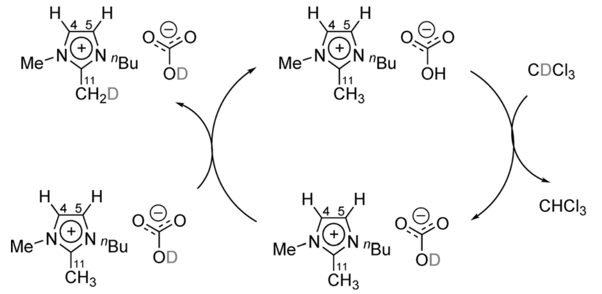
Scheme 1. H/D exchange reaction between BMMI ILs in $CDCl_3$.

It is noticeable that the H/D exchange in $CDCl_3$ preferentially occurs for the deuteration of C11 and not for the C4/C5 positions of the imidazolium ring (Table 1, entries 2 and 4). Notably a 97% deuteration is attained at C11 and only marginally at C4/C5 positions after 21 h (Supporting Information, Figure S3). This is a clear indication that positions C4/C5 are not easily accessible, and are probably blocked by interaction with the anion (see below).

More surprisingly, no deuteration products were observed after 1 h with BMMI ILs associated with Cl/HCO_3/HCO_2/Pro anions dissolved in highly polar D_2O. This is quite unexpected, as it is well-known that D incorporation is far more difficult to achieve in aprotic $CDCl_3$ than in protic polar solvents such as D_2O, which is partly due to the limited strength of bases in this medium.

In the case of BMMI·HCO_3, a high degree of deuteration at C11 was attained in CD_3CN (Table 2, entry 2) after 1 h. Also, a relatively low H/D exchange was detected at C11 in [D_6]DMSO (entry 3).

It is most probable that ILs acts as D transfer catalysts between $CDCl_3$ and the IL pair owing to the presence of a labile proton in its structure. Therefore, strong interaction between the cation and anion increases the basicity of the remote OH and NH groups of the hydrogen carbonate and prolinate anions, respectively. Although the intra-ion pair H/D exchange cannot be entirely discarded, it more plausible that these ILs would behave as a neutral base[32] during the course of all of the H/D exchange processes (Scheme 2).



Scheme 2. Proposed reaction pathways involved in the H/D exchange reaction between BMMI·HCO_3 and $CDCl_3$.

The high degree of H/D exchange in CD_3CN is probably due to the presence of the intimate ion pair IL structure and the resulting high basicity of the OH group, which is sufficient to deprotonate acetonitrile. In D_2O, the equilibrium is shifted towards solvent-separated ion pairs, thus liberating anions with low basicity that cannot catalyze the H/D exchange reaction. DMSO appears to be an intermediate case, where the equilibrium between contact ion pairs and solvent-separated ion pairs is maintained and displays intermediate reactivity (Table 2, compare entries 3 with entries 1 and 4).

To verify this hypothesis, NMR experiments for BMMI·HCO_3, DFT and molecular dynamics simulations were performed with BMMI·HCO_3 and BMMI·Cl in $CDCl_3$, DMSO, and water. ^{1}H,^{13}C HOESY experiments with ^{13}C-enriched BMMI·H*CO_3 were performed in CD_3CN in view of the low solubility and stability of the IL in $CDCl_3$. The HOESY results show a cation–anion interaction pattern (Figure 1) with a higher cross-peak intensity, corresponding to higher relative cross-relaxation rates between the H*CO3 anion and the hydrogens at C6 (N−Me), followed by the methylenic hydrogen atoms at the C7 (N−CH2) moiety.

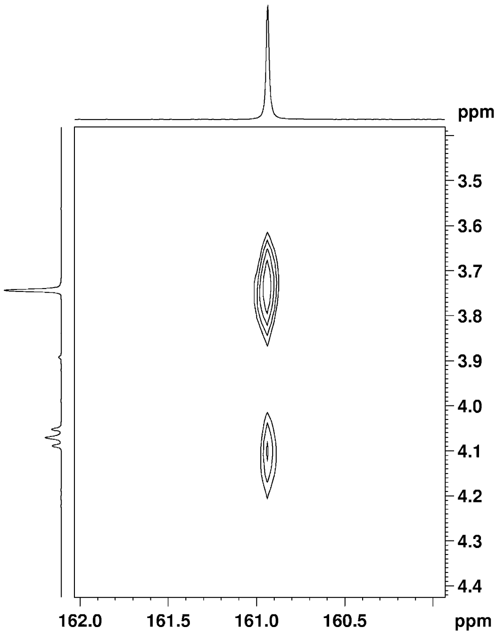


Figure 1. $^{13}C,^{1}H$ HOESY cross-peak of NCH_3 (C6) and NCH_2 (C7) with HCO_3 anions in CD_3CN (0.1 M).

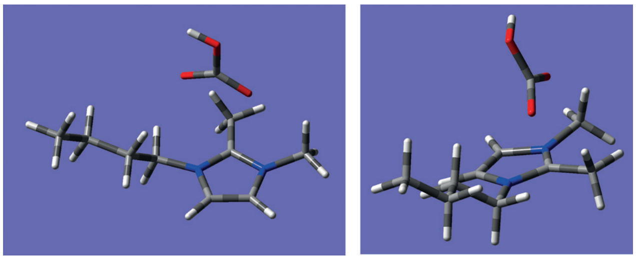


Figure 2. Most stable conformations of BMMI·HCO_3 obtained by DFT using the dispersion-corrected wB97xD functional. The distances between the O of the anion and H of the imidazolium ion (at C11, NCH_3 (C6), and $N(CH_2)$ (C7)) are in the range of 2.191 Å to 2.759 Å with angles between and 94.3° and 138.5°, typical of H-bonds.

This arrangement corresponds to the preferential sites for cation–anion interactions, in which HCO_3 is located closer to *N*-imidazolium substitutions C6 and C7. This structural arrangement (the HCO_3 is almost perpendicular and seated on the top of imidazolium ring) is similar to that obtained by DFT calculations (Figure 2). These computations also reveal moderate to strong hydrogen bonds between the carboxylic oxygen atoms of the anion and the methylic hydrogen atoms of the cation at C6 and C7. Furthermore, the CHELPG analysis provides a charge transfer of 0.19e from the anion to the cation, similar to values commonly calculated for ion pairs involving the imidazolium cation.[33]

No cross-peaks were observed in the HOESY experiments either at low or high concentrations of BMMI·H*CO_3 in D_2O, indicating that contact ion pairs are present in MeCN but not in D_2O. In [D$_6$]DMSO, contact ion pairs are observed at either high concentrations (0.05 M) or low concentrations (0.001 M; Supporting Information, Figure S4).

Molecular dynamics (MD) computer simulations were performed on single ion pairs containing the BMMI cation and Cl, formate, HCO_3, and prolinate anions in the solvents $CHCl_3$, DMSO, and water (298 K, 1 bar). A detailed analysis is presented for the solutions in $CHCl_3$.

We have computed the minimum distance between any atom of the BMMI cation and any atom of the paired anion along the simulation, as illustrated for the BMMI·HCO_3 and the BMMI·Pro ion pairs in Figure 3. We observed almost instantaneous ion separation in water, but stable ion pairs in $CHCl_3$ solution. In DMSO, the ion pairs dissociated rapidly, but, as becomes evident from Figure 3, there exists the possibility of ion pair reformation in this solvent. Note that the behavior depicted in Figure 3 is also representative of the other ion pairs, revealing stable ion pairs in $CHCl_3$, separated cations and anions in H_2O, and temporarily stable ion pairs in DMSO for ILs with the BMMI cation. These findings indicate that contact ion pair participation in the H/D exchange can be ignored in H_2O, but is possible in DMSO and, notably, in $CHCl_3$.

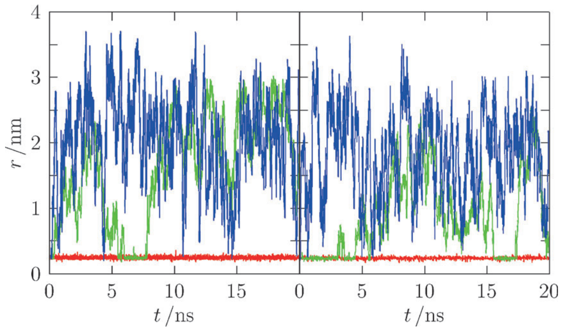


Figure 3. Time evolution of the minimum distances between the BMMI cation and the bicarbonate (left panel) and prolinate (right panel) anions in the solvents water (blue), DMSO (green), and chloroform (red).

Radial pair distribution functions (RDFs) for distances between the protons of the BMMI cation and the carboxylic oxygen in the formate, prolinate, and HCO_3 anions are given in the Supporting Information, Figure S5 (the chloride anion is included as a reference for a spherical anion). The anions mostly coordinate at the H4 and H5 protons of the cation. However, if the anion becomes less spherical, we observe more relevant coordination at the protons of the methyl substitutions at N3 and C2. All of these RDFs present a first peak at distances that correspond to the distance criterion for hydrogen bonding. If one assumes contact ion pair participation in the H/D exchange, the coordination patterns of the anions to the BMMI cation point to preferred exchange at C4, C5, and the two methyl groups at C6 and C2. However, the strong hydrogen bonding at H4 and H5 might significantly restrict the accessibility of these protons by the solvent molecules. Interestingly, the HCO_3 anion was weaker at H4 and H5, as indicated by the significantly lower amplitudes in the RDFs. Table 1 and 2 demonstrate that only in the case of this anion is it possible to observe H/D exchange in $CHCl_3$ at C4 and C5 within one hour.

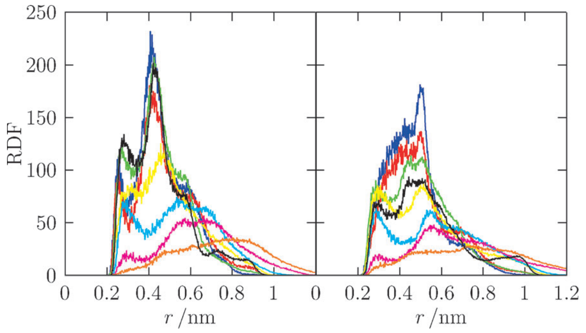
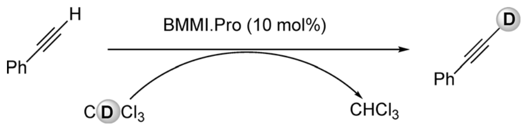


Figure 4. RDFs for distances between the protons of the BMMI cation and the oxygen atom of the HCO_3 hydroxy group (left panel) and the nitrogen atom of the prolinate amine group (right panel) in chloroform. The colors indicate correlations with the C4 (blue), C5 (red), C6 (green), C11 (black), C7 (yellow), C8 (cyan), C9(magenta), and C10 (orange) of the cation.

In the prolinate and HCO_3 anions, the nitrogen and hydroxy oxygen are additional heteroatoms with a partially negative charge and a hydrogen substitution. The RDFs for distances between these heteroatoms and BMMI hydrogen atoms (Figure 4) exhibit short-range flanks of the maximum within the reach of hydrogen bonding with most intense amplitudes for the methylic protons. Thus, the hydroxy oxygen of HCO_3 and the nitrogen of prolinate are involved in stronger short-range correlations with the methyl groups of BMMI. Note that these heteroatoms of the anions possess the hydrogen substitutions indicated by Scheme 2 in the H/D exchange reaction.

We did not detect any significant short-range correlation in the RDFs for distances between the hydrogen atoms of the cation and the proton and chlorines of the solvent. However, distinct solvation patterns of the anions with the $CHCl_3$ hydrogen atoms were found (Supporting Information, Figure S6). We observed strong correlations between the solvent hydrogen atoms and the most negatively charged atoms of the anions within the range of hydrogen-bonding distances. Correlations with other atoms of the anions are significantly weaker. However, we observed an additional peak within the range of hydrogen bonding with the oxygen of the hydroxy group in the BMMI·HCO_3 solution and the nitrogen atom in the BMMI·prolinate solution. The $CHCl_3$ molecules are thus strongly coordinated to the anions, facilitating an eventual proton abstraction/exchange.

Finally, BMMI·Pro is an active catalyst for the D-transfer from $CDCl_3$ to substrates containing acidic sites (Scheme 3). Indeed, an 85 % H/D exchange of phenylacetylene (1 mmol) was obtained after 1 h at RT using 10 mol % of BMMI·Pro in $CDCl_3$ (6 mmol).



Scheme 3. H/D exchange reaction of phenylacetylene and $CDCl_3$ catalyzed by BMMI·Pro.

In summary, we clearly demonstrated that solutions of imidazolium ILs not only maintain their intimate ion pair structure, but also behave as neutral species. In particular, in the case of anions containing remote basic sites, the ILs act as neutral bases. Therefore the presence of intimate ion pairs in the case of BMMI·HCO_3 and BMMI·Pro ILs in $CDCl_3$ and CD_3CN induces the augmentation of the remote basic sites; that is, OH and NH, respectively. Indeed, these species are active in the catalytic transfer of D from $CDCl_3$ to other substrates.

Experimental Section

BMMI·H*CO_3 was prepared in quantitative yield by reaction of BMMI·OH (prepared by anion exchange of BMMI·Cl and NaOH using a anionic Amberlist resin) with *CO_2 (3 bar) in water at RT for 26 h, and it was isolated by simple water removal under vacuum at RT. Recrystallization from MeCN affords BMMI·HCO_3 as a white crystalline solid.

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[1] T. Welton, *Chem. Rev.* **1999**, *99*, 2071–2083.
[2] B. A. DaSilveira Neto, L. S. Santos, F. M. Nachtigall, M. N. Eberlin, J. Dupont, *Angew. Chem. Int. Ed.* **2006**, *45*, 7251–7254; *Angew. Chem.* **2006**, *118*, 7409–7412.
[3] J. Dupont, *Acc. Chem. Res.* **2011**, *44*, 1223–1231.
[4] B. A. D. Neto, E. C. Meurer, R. Galaverna, B. J. Bythell, J. Dupont, R. G. Cooks, M. N. Eberlin, *J. Phys. Chem. Lett.* **2012**, *3*, 3435–3441.
[5] A. Mele, C. D. Tran, S. H. D. Lacerda, *Angew. Chem. Int. Ed.* **2003**, *42*, 4364–4366; *Angew. Chem.* **2003**, *115*, 4500–4502.
[6] A. G. Avent, P. A. Chaloner, M. P. Day, K. R. Seddon, T. Welton, *J. Chem. Soc. Dalton Trans.* **1994**, 3405–3413.
[7] C. S. Consorti, P. A. Z. Suarez, R. F. de Souza, R. A. Burrow, D. H. Farrar, A. J. Lough, W. Loh, L. H. M. da Silva, J. Dupont, *J. Phys. Chem. B* **2005**, *109*, 4341–4349.
[8] J. Dupont, P. A. Z. Suarez, R. F. De Souza, R. A. Burrow, J. P. Kintzinger, *Chem. Eur. J.* **2000**, *6*, 2377–2381.
[9] K. Fumino, P. Stange, V. Fossog, R. Hempelmann, R. Ludwig, *Angew. Chem. Int. Ed.* **2013**, *52*, 12439–12442; *Angew. Chem.* **2013**, *125*, 12667–12670.
[10] P. Stange, K. Fumino, R. Ludwig, *Angew. Chem. Int. Ed.* **2013**, *52*, 2990–2994; *Angew. Chem.* **2013**, *125*, 3064–3068.
[11] A. Wulf, K. Fumino, R. Ludwig, *Angew. Chem. Int. Ed.* **2010**, *49*, 449–453; *Angew. Chem.* **2010**, *122*, 459–463.
[12] M. C. Corvo, J. Sardinha, S. C. Menezes, S. Einloft, M. Seferin, J. Dupont, T. Casimiro, E. J. Cabrita, *Angew. Chem. Int. Ed.* **2013**, *52*, 13024–13027; *Angew. Chem.* **2013**, *125*, 13262–13265.
[13] Y. Lingscheid, S. Arenz, R. Giernoth, *ChemPhysChem* **2012**, *13*, 261–266.
[14] J. Dullius, P. Suarez, S. Einloft, R. de Souza, J. Dupont, J. Fischer, A. De Cian, *Organometallics* **1998**, *17*, 815–819.
[15] L. Santos, B. Neto, C. Consorti, C. Pavam, W. Almeida, F. Coelho, J. Dupont, M. Eberlin, *J. Phys. Org. Chem.* **2006**, *19*, 731–736.
[16] P. S. Schulz, N. Muller, A. Bosmann, P. Wasserscheid, *Angew. Chem. Int. Ed.* **2007**, *46*, 1293–1295; *Angew. Chem.* **2007**, *119*, 1315–1317.

[17] J. D. Scholten, G. Ebeling, J. Dupont, *Dalton Trans.* **2007**, 5554–5560.

[18] A. Berthod, J. J. Kozak, J. L. Anderson, J. Ding, D. W. Armstrong, *Theor. Chem. Acc.* **2007**, *117*, 127–135.

[19] J. D. Scholten, B. C. Leal, J. Dupont, *ACS Catal.* **2012**, *2*, 184–200.

[20] R. Giernoth, D. Bankmann, *Eur. J. Org. Chem.* **2008**, 2881–2886.

[21] M. Fèvre, P. Coupillaud, K. Miqueu, J. M. Sotiropoulos, J. Vignolle, D. Taton, *J. Org. Chem.* **2012**, *77*, 10135–10144.

[22] O. Hollóczki, D. Gerhard, K. Massone, L. Szarvas, B. Németh, T. Veszprémi, L. Nyulászi, *New J. Chem.* **2010**, *34*, 3004–3009.

[23] Y. E. Corilo, F. M. Nachtigall, P. V. Abdelnur, G. Ebeling, J. Dupont, M. N. Eberlin, *RSC Adv.* **2011**, *1*, 73–78.

[24] G. Gurau, H. Rodriguez, S. P. Kelley, P. Janiczek, R. S. Kalb, R. D. Rogers, *Angew. Chem. Int. Ed.* **2011**, *50*, 12024–12026; *Angew. Chem.* **2011**, *123*, 12230–12232.

[25] H. Lebel, M. K. Janes, A. B. Charette, S. P. Nolan, *J. Am. Chem. Soc.* **2004**, *126*, 5046–5047.

[26] D. Bacciu, K. Cavell, I. Fallis, L. Ooi, *Angew. Chem. Int. Ed.* **2005**, *44*, 5282–5284; *Angew. Chem.* **2005**, *117*, 5416–5418.

[27] C. E. Ellul, M. F. Mahon, O. Saker, M. K. Whittlesey, *Angew. Chem. Int. Ed.* **2007**, *46*, 6343–6345; *Angew. Chem.* **2007**, *119*, 6459–6461.

[28] S. Gründemann, A. Kovacevic, M. Albrecht, J. W. Faller, R. H. Crabtree, *Chem. Commun.* **2001**, 2274–2275.

[29] R. H. Crabtree, *Coord. Chem. Rev.* **2013**, *257*, 755–766.

[30] A. R. Chianese, A. Kovacevic, B. M. Zeglis, J. W. Faller, R. H. Crabtree, *Organometallics* **2004**, *23*, 2461–2468.

[31] D. H. Ripin and D. A. Evans, Harvard University, Chem 206, 2005, pKa's of inorganic and oxoacids, http://evans.harvard.edu/pdf/evans_pka.

[32] C. Sabot, K. A. Kumar, C. Antheaume, C. Mioskowski, *J. Org. Chem.* **2007**, *72*, 5001–5004.

[33] O. Hollóczki, F. Malberg, T. Welton, B. Kirchner, *Phys. Chem. Chem. Phys.* **2014**, *16*, 16880.