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The ionic liquid [bmim]Br as an alternative medium for the catalytic cleavage of aromatic C–F and C–Cl bonds

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ABSTRACT

The potential of [bmim]Br as an alternative to aprotic dipolar solvents in nickel-catalyzed hydrodehalogenation reactions is demonstrated. Hydrodechlorination of pentafluorochlorobenzene proceeds under the action of zinc in aqueous [bmim]Br. Under the above conditions aromatic C–F bonds also undergo slow cleavage. The reaction is significantly accelerated in the presence of nickel complexes with 2,2′-bipyridine or 1,10-phenanthroline. In the case of pentafluoroacetanilide highly regioselective *ortho*-hydrodefluorination leading to the formation of 3,4,5-trifluoroacetanilide is observed.

Incompletely halogenated aromatic compounds are useful substrates and precursors in a wide range of organic reactions[1] including the preparation of various functional materials.[2] Partially fluorinated aromatic compounds are of particular interest for the synthesis of biologically active substances.[3] An approach to the synthesis of incompletely halogenated compounds is based on the selective removal of one or more of the halogen atoms from fully halogenated substrates, which are more readily available for example in the case of polyfluorinated compounds.[4] Hence, the development of new methods for selective hydrodehalogenation of aromatic polyhalides is an interesting topic.

Ionic liquids (ILs) are low melting organic salts with properties useful in synthetic chemistry, catalysis, materials science, etc.[5] ILs are good solvents of both organic and inorganic substrates. In addition, the use of ionic liquids as solvents for transition metal catalyzed organic reactions makes it possible to isolate easily reaction products from the reaction mixtures and to recycle the catalyst-ionic liquid system.[5]

Numerous studies have been reported which describe catalytic reactions in ionic liquids.[5,6] At the same time, only a few examples of the catalytic activation of C–Hal bonds in aromatic halides are known to date with most being palladium-catalyzed reactions of aryl halides with unsaturated compounds (Heck reaction),[7,8] palladium-catalyzed reactions with organoboron compounds (Suzuki reaction),[8,9] carbonylation reactions,[10] nickel-catalyzed homocoupling reactions[11] as well as catalytic hydrodehalogenation of aryl halides.[12] However, there are no known examples of catalytic activation of aromatic C–F bonds in ionic liquids. In the present work we have found that an ionic liquid can be used as the reaction medium for the nickel-catalyzed activation of C–F and C–Cl bonds of aromatic polyfluorides.

Previously, we reported that hexafluorobenzene (**1**), octafluoronaphthalene (**2**), pentafluoropyridine (**3**),[13] pentafluorobenzoic acid (**4**) or their derivatives,[14] as well as pentafluoroaniline derivatives,[15,16] undergo hydrodefluorination under the action of zinc in the presence of catalytic amounts (5 mol % of the substrate) of nickel complexes with 2,2′-bipyridine (Bpy) or 1,10-phenanthroline (Phen). Mixtures of polar aprotic solvents (DMF, DMA or NMP) and water were used as the reaction media. The reaction pathway depends on the nature of the solvent, the catalytic complex and the substrate-zinc molar ratio. In the present work we studied the catalytic hydrodehalogenation reactions of polyfluorinated substrates in aqueous 1-butyl-3-methylimidazolium bromide ([bmim]Br).

We previously found that nickel complexes with two and three molecules of 2,2′-bipyridine or 1,10-phenanthroline as the ligands possessed the highest activity among the corresponding coordination compounds of nickel.[16] Therefore we chose the complexes $NiCl_2{\cdot}3Bpy$ and $NiCl_2{\cdot}2Phen$ as catalysts for the hydrodehalogenation. Hexafluorobenzene (**1**) undergoes smooth hydrodefluorination under reductive conditions in the presence of catalytic amounts of the nickel complexes in aqueous [bmim]Br to give a

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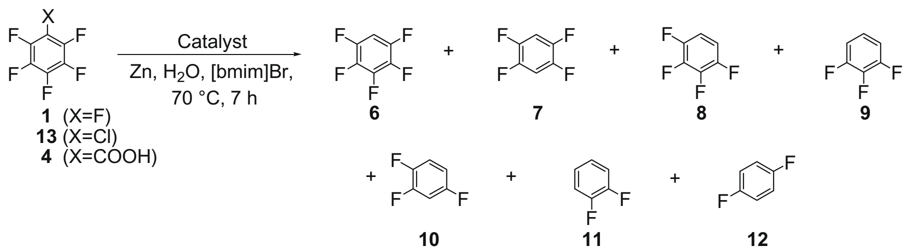


Scheme 1.

Table 1
Hydrodehalogenation of polyfluoroaromatic compounds **1**, **13**, and **4** in aqueous [bmim]Br[17]

Entry	Substrate	Catalyst	Conversion, %	Products[a] (selectivity, %)
1	**1**	None	35	**6** (99); **7** (1)
2	**1**	$NiCl_2$·3Bpy	96	**6** (10); **7** (22); **8** (21); **9** (17); **10** (19); **11** (3); **12** (8)
3	**1**	$NiCl_2$·2Phen	98	**6** (46); **7** (34); **8** (20)
4	**13**	None	100	**6** (96); **7** (1); **8** (3)
5	**13**	$NiCl_2$·3Bpy	100	**6** (34); **7** (27); **8** (29); **9** (4); **10** (6)
6	**13**	$NiCl_2$·2Phen	100	**6** (75); **7** (10); **8** (15)
7	**4**	None	100	**6** (52); **7** (48)
8	**4**	$NiCl_2$·3Bpy	100	**6** (50); **7** (38); **8** (6); **9** (6)
9	**4**	$NiCl_2$·2Phen	100	**6** (16); **7** (62); **8** (8); **9** (14)

[a] ^{19}F NMR data.

mixture of partially fluorinated benzenes **6**–**12** (Scheme 1; Table 1, entries 2 and 3). In polyfluorinated benzenes containing at least one hydrogen atom elimination of the next fluorine atom occurs at the *ortho*- and *para*-positions relative to the hydrogen atoms.

Under comparable conditions $NiCl_2$·2Phen (Table 1, entry 3) was less active than $NiCl_2$·3Bpy (Table 1, entry 2). In the presence of $NiCl_2$·2Phen a high conversion of **1** was observed, but only mono- and bis-defluorinated polyfluorobenzenes **6**, **7**, and **8** were detected as the reaction products. In the absence of the catalyst the conversion of **1** was only 35% (Table 1, entry 1) and pentafluorobenzene (**6**) was the major product.

In contrast to hexafluorobenzene (**1**), pentafluorochlorobenzene (**13**) underwent complete hydrodechlorination even in the absence of the catalyst (Scheme 1; Table 1, entry 4). This demonstrates that the aromatic C–Cl bond is much more reactive than the aromatic C–F bond. Addition of catalytic amounts of $NiCl_2$·3Bpy led to the formation of a mixture of partially fluorinated benzenes **6**–**10** (Table 1, entry 5). In the presence of $NiCl_2$·2Phen the formation of only small amounts of **7** and **8** was observed (Table 1, entry 6).

The hydrodefluorination reaction of pentafluorobenzoic acid (**4**) was accompanied by decarboxylation of substrate **4** and partially fluorinated benzoic acids. Only the formation of fluorinated benzenes **6**–**9** was observed (Scheme 1; Table 1, entries 7–9). This result differs from that obtained when the hydrodefluorination of acid **4** was carried out in DMF.[14] In the absence of the nickel complex the formation of pentafluorobenzene (**6**) and 1,2,4,5-tetrafluorobenzene (**7**) in approximately equal amounts was observed (Table 1, entry 7). The content of product **7** in the reaction mixture was significantly higher than that of the non-catalytic hydrodefluorination reactions of substrates **1** and **13**. Hence the hydrodefluorination reaction of **4** is faster than the decarboxylation reaction.

Without the catalyst the *para*-hydrodefluorination of **4** occurred similarly to that of the reaction of acid **4** in DMF[18] and aqueous ammonia.[19] Addition of catalytic amounts of $NiCl_2$·3Bpy or $NiCl_2$·2Phen led to a moderate increase in the selectivity of the *ortho*-hydrodefluorination reaction, but 1,2,4,5-tetrafluorobenzene (**7**) was the major product (Table 1, entries 8 and 9).

Table 2
Hydrodehalogenation of pentafluoropyridine (**3**) in aqueous [bmim]Br[17]

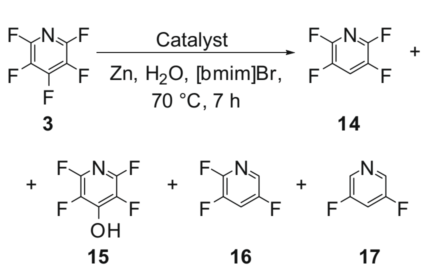
Entry	Catalyst	Products[a,b] (selectivity, %)
1	None	**14** (80); **15** (20)
2	$NiCl_2$·3Bpy	**14** (11); **15** (59); 16 (12); **17** (18)
3	$NiCl_2$·2Phen	**14** (38); **15** (38); **16** (22); **17** (2)

[a] Conversion of **3** was 100% in all cases.
[b] ^{19}F NMR data.

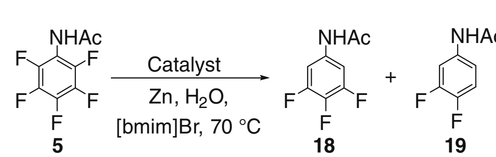
Table 3
Hydrodehalogenation of pentafluoroacetanilide **5** in aqueous [bmim]Br[17]

Entry	Catalyst	Time, h	Conversion, %	Products[a] (selectivity, %)
1	None	7	0	–
2	$NiCl_2$·3Bpy	0.5	100	**18** (65); **19** (35)
3	$NiCl_2$·2Phen	2	100	**18** (99); **19** (1)

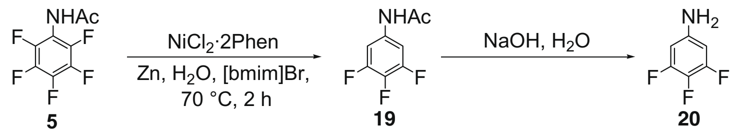
[a] ^{19}F NMR data.



Scheme 2.



Scheme 3.



Scheme 4.

In the absence of the catalyst, pentafluoropyridine (**3**) underwent two types of transformation with participation of the fluorine atom at C-4: non-catalytic hydrodefluorination to form 2,3,5,6-tetrafluoropyridine (**14**) and nucleophilic substitution with water to give 4-hydroxy-2,3,5,6-tetrafluoropyridine (**15**) (Scheme 2; Table 2, entry 1). In the presence of the nickel complexes the C–F bonds at positions 2 and 6 of substrate **3** were activated (Table 2, entries 2 and 3). In this reaction, $NiCl_2$·3Bpy was more active than $NiCl_2$·2Phen.

Unlike all the above described compounds, pentafluoroacetanilide (**5**) did not react with zinc in the aqueous [bmim]Br without the catalyst (Table 3, entry 1). In the presence of catalytic amounts of the nickel complexes highly regioselective activation of the aromatic C–F bonds *ortho* to the $NHCOCH_3$ group of acetanilide **5** was observed. 3,4,5-Trifluoroacetanilide (**18**) was the major product of the reaction (Scheme 3). A side reaction was the further hydrodefluorination of **18** to form 3,4-difluoroacetanilide (**19**). The rate of the side reaction depends on the nature of the nickel complex. In the presence of $NiCl_2$·3Bpy, the complete conversion of **5** was achieved in 30 min (Table 3, entry 2). Moreover, **19** was also formed with a selectivity of 35%. In this case $NiCl_2$·2Phen demonstrates the optimum catalytic activity and selectivity. Compound **5** was consumed completely in 2 h (Table 3, entry 3) and 3,4,5-trifluoroacetanilide (**18**) was obtained with a selectivity of 99%. A method for the preparation of 3,4,5-trifluoroaniline (**20**) from pentafluoroacetanilide **5** was developed based on this result (Scheme 4).[20]

We assume that the above-mentioned reactions involve the generation of zero-valent nickel complexes as a result of the interaction of Ni(II) compounds with Zn.[21] The Ni(0) species can react with the substrate in two ways. In the first case, the initial oxidative addition of the Ni(0) complex to the C–F bonds leads to the corresponding organonickel compounds which undergo hydrolysis with formation of the hydrodehalogenation product.[22] The second route involves formation of a hydride complex which acts as the reactive intermediate.[14]

Thus, in the present work we have demonstrated the potential of [bmim]Br as a solvent for hydrodehalogenation reactions. In general, chlorine atoms bonded to the aromatic ring are more reactive than fluorine atoms. As a consequence, hydrodechlorination occurs at a reasonable rate even in the absence of a catalyst, whereas the presence of nickel complexes with 2,2′-bipyridine or 1,10-phenanthroline ligands are required for the activation of aromatic C–F bonds. With pentafluorobenzoic acid, reductive defluorination was complicated by decarboxylation. Catalytic hydrodefluorination of pentafluoroacetanilide (**5**) leads to highly regioselective formation of 3,4,5-trifluoroacetanilide (**18**) in high yields. We have shown that [bmim]Br can serve as an alternative to the aprotic dipolar solvents.

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References and notes

1. (a) Kottirsch, G.; Szeimies, G. *Chem. Ber.* **1990**, *123*, 1495; (b) Indolese, A. F. *Tetrahedron Lett.* **1997**, *38*, 3513; (c) Desmarets, C.; Schneider, R.; Fort, Y. *Tetrahedron Lett.* **2000**, *41*, 2875; (d) Sonoda, M.; Inaba, A.; Itahashi, K.; Tobe, Y. *Org. Lett.* **2001**, *3*, 2419; (e) Burukin, A. S.; Vasil'ev, A. A.; Chizhov, A. O.; Zlotin, S. G. *Russ. Chem. Bull.* **2005**, *54*, 970; (f) Yoshikai, N.; Mashima, H.; Nakamura, E. *J. Am. Chem. Soc.* **2005**, *127*, 17978; (j) Yi, C.; Hua, R. *J. Org. Chem.* **2006**, *71*, 2535; (h) Yoshimura, T.; Inaba, A.; Sonoda, M.; Tahara, K.; Tobe, Y.; Williams, R. V. *Org. Lett.* **2006**, *8*, 2933; (i) Burukin, A. S.; Vasil'ev, A. A.; Merkulova, N. L.; Chizhov, A. O.; Mistryukov, E. A.; Zlotin, S. G. *Russ. Chem. Bull.* **2007**, *56*, 1467.
2. (a) Babudri, F.; Farinola, G. M.; Naso, F.; Ragni, R. *Chem. Commun.* **2007**, 1003; (b) Shirota, Y.; Kageyama, H. *Chem. Rev.* **2007**, *107*, 953; (c) Bunz, U. H. F.; Rubin, Y.; Tobe, Y. *Chem. Soc. Rev.* **1999**, *28*, 107.
3. Kirsch, P. *Modern Fluoroorganic Chemistry*; Wiley-VCH Verlag GmbH & Co.: Weinheim, 2004.
4. (a) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2002**, *102*, 4009; (b) Amii, H.; Uneyama, K. *Chem. Rev.* **2009**, *109*, 2119.
5. (a) Dyson, P. J.; Geldbach, T. J.. In *Metal Catalysed Reactions in Ionic Liquids*; Springer: Netherlands, 2005; Vol. 29; (b) Clare, B.; Sirwardana, A.; MacFarlane, D.. In *Ionic Liquids*; Springer: Berlin, Heidelberg, 2010; Vol. 290.
6. (a) Parvulescu, V. I.; Hardacre, C. *Chem. Rev.* **2007**, *107*, 2615; (b) Welton, T. *Chem. Rev.* **1999**, *99*, 2071; (c) Welton, T. *Coord. Chem. Rev.* **2004**, *248*, 2459.
7. (a) Kaufmann, D. E.; Nouroozian, M.; Henze, H. *Synlett* **1996**, 1091; (b) Carmichael, A. J.; Earle, M. J.; Holbrey, J. D.; McCormac, P. B.; Seddon, K. R. *Org. Lett.* **1999**, *1*, 997; (c) Xu, L.; Chen, W.; Xiao, J. *Organometallics* **2000**, *19*, 1123; (d) Selvakumar, K.; Zapf, A.; Beller, M. *Org. Lett.* **2002**, *4*, 3031; (e) Böhm, V. P. W.; Herrmann, W. A. *Chem. Eur. J.* **2000**, *6*, 1017; (f) Park, S. B.; Alper, H. *Org. Lett.* **2003**, *5*, 3209.
8. Wang, R.; Twamley, B.; Shreeve, J. N. M. *J. Org. Chem.* **2006**, *71*, 426.
9. Mathews, C. J.; Smith, P. J.; Welton, T. *J. Mol. Catal. A* **2004**, *214*, 27.
10. (a) Mizushima, E.; Hayashi, T.; Tanaka, M. *Green Chem.* **2001**, *3*, 76; (b) Mizushima, E.; Hayashi, T.; Tanaka, M. *Top. Catal.* **2004**, *29*, 163.
11. (a) Howarth, J.; James, P.; Dai, J. *Tetrahedron Lett.* **2000**, *41*, 10319; (b) Barhdadi, R.; Courtinard, C.; Nedelec, J. Y.; Troupel, M. *Chem. Commun.* **2003**, 1434.
12. (a) Calo, V.; Nacci, A.; Monopoli, A.; Damascelli, A.; Ieva, E.; Cioffi, N. *J. Organomet. Chem.* **2007**, *692*, 4397; (b) Ohlin, C. A.; Beni, Z.; Laurenczy, G.; Ruiz, N.; Masdeu-Bulto, A. M. *Appl. Organomet. Chem.* **2007**, *21*, 156; (c) Iranpoor, N.; Firouzabadi, H.; Azadi, R. *J. Organomet. Chem.* **2008**, *693*, 2469.
13. Adonin, N. Y.; Starichenko, V. F. *Mendeleev Commun.* **2000**, *10*, 60.
14. Adonin, N. Y.; Starichenko, V. F. *J. Fluorine Chem.* **2000**, *101*, 65.
15. Prikhod'ko, S. A.; Adonin, N. Y.; Babushkin, D. E.; Parmon, V. N. *Mendeleev Commun.* **2008**, *18*, 211.
16. Prikhod'ko, S. A.; Adonin, N. Y.; Parmon, V. N. *Russ. Chem. Bull.* **2009**, 2234.
17. *General procedure:* The nickel complexes were synthesized according to the literature method.[23] A 5 ml reaction vessel was charged with 0.025 mmol of $NiCl_2$·3Bpy or $NiCl_2$·2Phen, 327 mg (5 mmol) of Zn, 0.5 ml of molten [bmim]Br and 0.1 ml of H_2O. The mixture was stirred for 10 min and then 0.5 mmol of the corresponding substrate was added. The reaction mixture was heated with stirring at 70 °C. After cooling to ambient temperature the reaction mixture was analyzed by ^{19}F NMR spectroscopy. The NMR spectra of the dehalogenation products were in accord with the literature data.[15,24]
18. (a) Krasnov, V. I.; Platonov, V. E. *Zh. Org. Khim.* **1993**, *29*, 1078 (*Chem. Abstr.* **1994**, *120*, 191201); (b) Platonov, V. E.; Krasnov, V. I. *Zh. Org. Khim.* **1994**, *30*, 1271 (*Chem. Abstr.* **1995**, *123*, 285335).
19. Laev, S. S.; Shteingarts, V. D. *J. Fluorine Chem.* **1999**, *96*, 175.
20. *Preparation of 3,4,5-trifluoroaniline* (**20**): A 25 ml three-necked flask was charged with 300 mg (0.6 mmol) $NiCl_2$·2Phen, 8.01 g (122.4 mmol) of Zn, 13 ml of molten [bmim]Br and 2.5 ml of H_2O. The mixture was stirred at 70 °C for 10 min and 2.76 g (12.3 mmol) of **5** were added. The reaction mixture was heated with stirring at 70 °C for 2 h and then diluted with 10 ml of CH_3CN. The solid was removed by filtration and washed with CH_3CN. The solvent was evaporated and the product **18** was triturated with hot EtOAc (5×10 ml). The combined organics were evaporated under vacuum and the residue was mixed with 50 ml of H_2O and NaOH was added until pH 13–14. The resulting mixture was stirred for 1 h. The product **20** was isolated by steam distillation, after which 3,4,5-trifluoroaniline (1.25 g, 70% with respect to starting compound **5**) was obtained. ^1H NMR ($CDCl_3$, 300 MHz): δ 6.24 (ddd, 2H, J = 9.6, 9.5, 3.9 Hz. 2, 6-H), 3.69 (br s, 2H, NH_2). ^{19}F NMR ($CDCl_3$, 300 MHz): δ −136.1 (dd, 2F, J = 21.3, 9.3 Hz, 3,5-F), −176.0 (tt, 1F, J = 21.3, 5.6 Hz, 4-F).
21. (a) Tolman, C. A.; Seidel, W. C.; Gerlach, D. H. *J. Am. Chem. Soc.* **1972**, *94*, 2669; (b) Tolman, C. A.; Seidel, W. C.; Gosser, L. W. *J. Am. Chem. Soc.* **1974**, *96*, 53.

22. (a) Cronin, L.; Higgitt, C. L.; Karch, R.; Perutz, R. N. *Organometallics* **1997**, *16*, 4920; (b) Archibald, S. J.; Braun, T.; Gaunt, J. A.; Hobson, J. E.; Perutz, R. N. *J. Chem. Soc., Dalton Trans.* **2000**, 2013; (c) Braun, T.; Perutz, R. N. *Chem. Commun.* **2002**, 2749.
23. Ruiz-Perez, C.; Luis, P. A. L.; Lloret, F.; Julve, M. *Inorg. Chim. Acta* **2002**, *336*, 131.
24. Berger, S.; Braun, S.; Kalinowski, H.-O. *NMR-Spektroskopie von nichtmetallen*; Georg Thieme Verlag Stuttgart: New York, 1994. Band 4: ^{19}F NMR-Spektroskopie.