



Electrochemical hydrodefluorination of fluoroaromatic compounds



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ABSTRACT

The BH_4^- -promoted electrochemical hydrodefluorination of fluoroaromatic compounds was reported. Using platinum as electrodes in an undivided cell, the electrolysis was carried out at constant current at room temperature under air without the need of pretreatment of the solvent. This reaction could proceed smoothly on both nonactivated monofluoroarenes and perfluoroarenes with high yields and good selectivities.

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The fluorinated organic compounds (FOCs) have attracted great attention during the last few decades due to their extensive applications in modern pharmaceuticals, agrochemicals, materials science, and polymer chemistry.¹ C–F bonds are of high thermodynamic stability and kinetic inertness as the consequence of the small size ($r_{\text{W}} = 1.47 \text{ \AA}$) and high electronegativity ($\chi = 4$) of the fluorine atom.^{2,5} As a result, the organofluorine molecules are highly persistent in the environment and resistant to aerobic degradation.^{3,6a,n} The simplest and most efficient activation of the C–F bond in this regard is hydrodefluorination (HDF), by converting a C–F bond into the C–H bond. In the early studies of hydrodefluorination, efforts were focused on the relatively reactive perfluorobenzene derivatives, while nonactivated monofluoroarenes were less studied.⁴ Over the past two decades, the main group⁵ and transition metals⁶ have been employed and substantial progress has been made in the reaction of hydrodefluorination of fluoroarenes. Despite the tremendous progress made, it is still necessary to explore new approaches which are more simple, mild, and economical for hydrodefluorination.

Electrochemical methods have attracted great interest because of their significant environmental and economical advantages.^{7,8} However, electrochemical hydrodefluorination of simple fluoroaromatic compounds is less explored. Kariv-Miller developed an electrochemical method for hydrodefluorination of 1,3-difluorobenzene and fluorobenzene by using platinum foil anode and mercury pool cathode. The hydrodefluorination of fluorobenzene afforded benzene in a moderate yield of 76%. Their studies

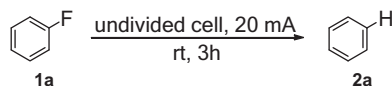
showed that the reaction was catalyzed by the ‘amalgam’ formed from the mercury and the dimethylpyrrolidinium ion (DMP^+).⁹ In Langer and Yurchak’s study, fluorobenzene underwent electrochemical hydrogenation on platinum black electrodes to give equal amounts of benzene and cyclohexane by using the H_2 as a reductant.¹⁰ In 2009, Trnková studied the electrochemical processes of hydrodefluorination of fluorobenzene on a platinum polycrystalline electrode in sulfuric acid by differential electrochemical mass spectrometry.¹¹ However, general, highly efficient, and selective electrochemical methods for hydrodefluorination of fluoroaromatics are still desirable. With our continuous interest in electrochemical synthesis,¹² herein we reported a highly efficient electrochemical method for hydrodefluorination of fluoroaromatics by using Pt electrodes.

We chose the hydrodefluorination of fluorobenzene as a model reaction. The reaction was initially investigated in a one-compartment cell with platinum foil as the anode and a platinum minigrad electrode (represented as Pt (g)) as the cathode in THF–0.2 M TBABF₄ (tetrabutylammonium tetrafluoroborate) solution at room temperature. After electrolysis for 3 h under a constant current (20 mA), only trace amount of benzene and about 90% of unreacted substrate were obtained (Table 1, entry 1). To our surprise, when NaBH_4 (2 equiv) was added, the yield of benzene increased to 39% (Table 1, entry 2). Then several other solvents were screened. The results showed that 1,4-dioxane, acetonitrile, and ethanol could give only trace amounts of desired product. Among all the tested solvents, diglyme turned out to be the best choice, giving the desired product in an excellent yield of 98% (Table 1, entries 2–9). It is important to note that NMP (*N*-methyl-2-pyrrolidone) could work as a convenient alternative solvent (Table 1, entry 8).

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Table 1
Optimization of the reaction conditions for the electrochemical hydrodefluorination of fluorobenzene^a



Entry	Electrode (anode/cathode)	Electrolyte	Additive (equiv)	Conversion ^b (%)	Yield ^b (%)
1	Pt–Pt (g)	THF–0.2 M TBABF ₄	–	10	Trace
2	Pt–Pt (g)	THF–0.2 M TBABF ₄	NaBH ₄ (2)	39	39
3	Pt–Pt (g)	Dioxane–0.2 M TBABF ₄	NaBH ₄ (2)	10	Trace
4	Pt–Pt (g)	EtOH–0.2 M TBABF ₄	NaBH ₄ (2)	10	8
5	Pt–Pt (g)	CH ₃ CN–0.2 M TBABF ₄	NaBH ₄ (2)	10	Trace
6	Pt–Pt (g)	DMF–0.2 M TBABF ₄	NaBH ₄ (2)	75	70
7	Pt–Pt (g)	DMSO–0.2 M TBABF ₄	NaBH ₄ (2)	25	11
8	Pt–Pt (g)	NMP–0.2 M TBABF ₄	NaBH ₄ (2)	100	95
9	Pt–Pt (g)	Diglyme–0.2 M TBABF ₄	NaBH ₄ (2)	100	98
10	Pt–Pt (g)	Diglyme–0.2 M TBABF ₄	TBABH ₄ (2)	100	97
11	Pt–Pt	Diglyme–0.2 M TBABF ₄	NaBH ₄ (2)	100	84
12	C ^c –RVC ^d	Diglyme–0.2 M TBABF ₄	NaBH ₄ (2)	98	82
13	Pt–RVC	Diglyme–0.2 M TBABF ₄	NaBH ₄ (2)	89	85
14	C ^c –Pt (g)	Diglyme–0.2 M TBABF ₄	NaBH ₄ (2)	86	84
15 ^e	Pt–Pt (g)	Diglyme–0.2 M TBABF ₄	NaBH ₄ (2)	100	95
16	Pt–Pt (g)	Diglyme–0.2 M TBABF ₄	–	14	13
17	Pt–Pt (g)	Diglyme–0.2 M TBABF ₄	NaBH ₄ (1)	82	82
18	Pt–Pt (g) ^f	Diglyme–0.2 M TBABF ₄	NaBH ₄ (2)	100	95

^a Conditions: fluorobenzene (0.5 mmol) in solvent (5 mL, commercial available AR grade solvent without further treatment) with 0.2 M electrolyte was electrolyzed at constant current (20 mA) in an undivided cell at rt, 3 h, air. Anode: Pt foil (1 × 1.5 cm²). The cathode is Pt (g): Pt minigrad electrode (52 meshes, 1 × 1.5 cm², 2 pieces in parallel).

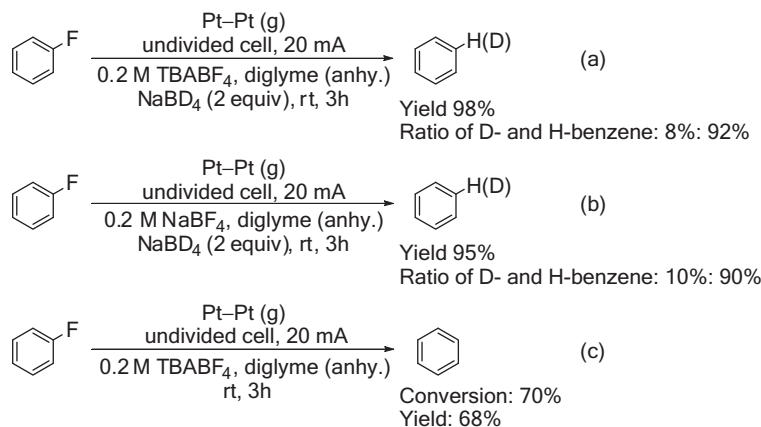
^b Base on NMR and GC analyses (see the ESI for details).

^c Graphite electrode.

^d Reticulated vitreous carbon.

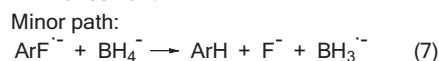
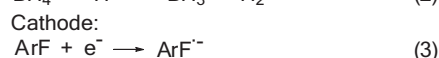
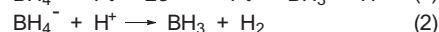
^e 40 °C.

^f Pt minigrad electrode (52 mesh, 1 × 1.5 cm², 1 piece).



Scheme 1. Further studies on the mechanistic aspects.

When tetrabutylammonium borohydride (TBABH₄) was used as a borohydride source instead of NaBH₄, the reaction could also afford an excellent yield of 97% (Table 1, entry 10). When the cathode was replaced with a piece of Pt foil (Table 1, entry 11), the yield of benzene decreased to 84% as the result of a smaller surface area of the cathode. Using graphite as electrodes instead of Pt, high yields of benzene could also be obtained (Table 1, entries 12–14), and it indicated that the metal (Pt) electrode does not catalyze or promote this reaction. Studies on the effect of temperature showed that when the reaction was carried out at a higher temperature (40 °C), the yield was slightly decreased (Table 1, entry 15). The reaction was also carried out in the absence of NaBH₄ (Table 1, entry 16) and most of the starting substrate was recovered and the yield of benzene was only 13%. Furthermore, when the loading



Scheme 2. Proposed reaction pathway.

Table 2
Electrochemical hydrodefluorination of fluoroaromatic compounds into aromatics^a


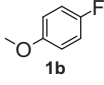



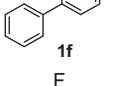

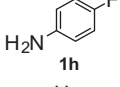

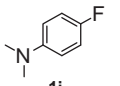
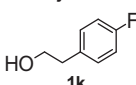





Entry	Substrates	Cond.	NaBH ₄ (equiv)	Temp (°C)	Yield ^b (%)
1		A	2	rt	98
2		A	2	rt	97 ^c
3		A	2	rt	99
4		A	2	rt	96
5		A	2	rt	98
6		B	3	40	86 ^c
7		B	3	40	80 ^{c,d}
8		B	6	60	70 ^c
9		B	6	60	87 ^c
10		B	6	60	89 ^c
11		A	3	rt	80 ^c
12		B	2	rt	87
13		B	6	rt	85
14		B	6	rt	88
15		B	4	rt	70 ^e

Table 2 (continued)

Entry	Substrates	Cond.	NaBH ₄ (equiv)	Temp (°C)	Yield ^b (%)
16		B	3	40	35 ^f

^a Conditions: Pt foil (1 × 1.5 cm²) as the anode, Pt minigrad electrode (52 mesh, 1 × 1.5 cm², 2 pieces in parallel) as the cathode. (A) Fluoroarenes (0.5 mmol) in diglyme (5 mL, commercially available AR grade solvent without further treatment) with 0.2 M TBABF₄ was electrolyzed at 20 mA in an undivided cell, 3 h, air; (B) fluoroarenes (0.5 mmol) in NMP (5 mL, commercial available AR grade solvent without further treatment) with 0.2 M NaBF₄ was electrolyzed at 30 mA in an undivided cell, 3 h, air.

^b Based on NMR and GC analyses (see the ESI for details). The substrates were completely consumed.

^c Isolated yields.

^d 1,2,3,4-tetrahydronaphthalene (10%) as by-product.

^e Benzene (70%) and partially hydrodefluorinated products of fluorobenzene (10%) and *o*-difluorobenzene (6%).

^f Toluene (35%) and α,α,α -trifluorotoluene (60%) were collected.

of NaBH₄ was reduced to 1 equiv, the yield decreased to 82% only (Table 1, entry 17). Hence, our optimized reaction conditions are shown in entry 9, Table 1 (Condition A). It is important to mention that we did not observe any cyclohexane, cyclohexene, and cyclohexadiene in the reaction under the optimized conditions.

Subsequently, the scope and limitation of the electrochemical hydrodefluorination of fluoroaromatic compounds were explored and the results are summarized in Table 2. Among the tested fluoroarenes, most of them could be reduced efficiently to give the desired products in high to excellent yields. Some of the fluoroarenes could give a higher yield when using the NMP as solvent and 0.2 M NaBF₄ as electrolyte (Condition B). The aromatic fluorides bearing electron-donating groups such as methyl- and methoxy- were converted to the corresponding arenes smoothly with excellent yields (Table 2, entries 2–5). Comparing the results of the *o*-, *m*-, and *p*-fluorotoluenes (1c–1e), steric factors seemed to have little influence on the reaction of electrochemical hydrodefluorination, since 1c gave a yield as high as 99% (Table 2, entries 3–5). In the case of 1-fluorobiphenyl (1f), the hydrodefluorination could also proceed smoothly to give the desired product in a good yield of 86% (Table 2, entry 6). 1-Fluoronaphthalene (1g) was hydrodefluorinated within 3 h to give 80% yield of naphthalene and about 10% yield of 1,2,3,4-tetrahydronaphthalene was also collected (Table 2, entry 7). Compounds with amine and hydroxyl groups (1h–1k) could also afford good yields of the desired products (Table 2, entries 8–11). The hydrodefluorination of polyfluorinated arenes was also tested. The reactions of *p*-, *o*-, and *m*-difluorobenzene (1l, 1m, and 1n), and 1,3,5-trifluorobenzene (1o) afforded benzene in moderate to good yields (Table 2, entries 12–15). As for 1o, a mixture of partially and completely hydrodefluorinated products was detected (Table 2, entry 15). Encouraged by these results, we also tried the hydrodefluorination of α,α,α -trifluorotoluene (1p). Only toluene was obtained as a completely hydrodefluorinated product in a low yield of 35%, which is consistent with the conclusion that benzylic C–F bonds were much more inert than aromatic C–F bonds (Table 2, entry 16).

Further studies on deuterium-labeling experiments were carried out (Scheme 1).¹³ Electrolysis of fluorobenzene in the presence of 2 equiv of NaBD₄ gave a mixture of C₆H₅D and C₆H₆ in a ratio of 8%:92% (Scheme 1a). Tributylamine was detected by GC–MS analysis on the product mixture. When using NaBF₄ as supporting electrolyte, a mixture of 10% C₆H₅D and 90% C₆H₆ was obtained

(Scheme 1b). These results indicated that both solvent and the TBABF₄ could be the proton donor for the product of benzene.

In the absence of NaBH₄, we observed that most of the starting substrate was recovered and the yield of benzene was only 13% (Table 1, entry 16). As the employed AR grade DME contained small amount of water ($\leq 0.05\%$, about 0.25 equiv of water in the reaction system), studies using anhydrous DME were carried out and the yield of the hydrodefluorination reaction increased to 68% with 70% of conversion (Scheme 1c). These results indicated that the water in the reaction mixture might have affected the rate of hydrodefluorination reaction. In contrast, in our reaction system with BH₄⁻, the yield was as high as 93% even if the water amount was increased to 1 equiv. To test if NaBH₄ could work as base to promote the current hydrodefluorination reaction, reactions were carried out by adding some other bases (Et₃N, NaOH, and Na₂CO₃) into the reaction system in the absence of NaBH₄. The yields were not improved and some of the reactions even gave lower conversions and lower yields (ESI, see Table S1).

The mechanism of electrochemical hydrodefluorination of fluoroaromatic compounds was tentatively proposed as shown in Scheme 2.^{14,15} BH₄⁻ worked as a sacrificial material for the anode oxidation (Scheme 2, Eqs. 1 and 2). Moreover, the produced BH₃ might have helped to remove the water in the solvent in a very fast rate. The fluoroarene was reduced to its radical anion at cathode, which was cleaved to produce a phenyl radical. The phenyl radical was further reduced and the resulting phenyl anion abstracted a proton from the solvent or the TBABF₄ (Scheme 2, Eqs. 3–6). According to the deuterium-labeling experiments, the reaction of Eq. 7 was proposed as a minor path.

In conclusion, a highly efficient electrochemical hydrodefluorination of monofluoroaromatic compounds promoted by NaBH₄ has been developed. The reaction proceeded with high selectivities and high yields in an undivided cell at ambient temperature under air. The mildness, simplicity, and environmental friendliness of the electrolysis procedure make it an attractive alternative for the hydrodefluorination of fluoroarenes. Further investigations to determine the mechanism of this reaction and to expand its scope are underway in our laboratory.

Acknowledgments

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Supplementary data

Supplementary data (detailed experimental procedure, cyclic voltammograms, and NMR data of the products) associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.tetlet.2015.02.022>.

These data include MOL files and InChIKeys of the most important compounds described in this article.

References and notes

- (a) Uneyama, K. *Organofluorine Chemistry*; Blackwell Publishing Ltd: Oxford, 2006; (b) *Handbook of Fluorous Chemistry*; Gladysz, J. A., Curran, D. P., Horváth, I. T., Eds.; Wiley-VCH: Weinheim, 2004; (c) Kirsch, P. *Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications*; Wiley-VCH: Weinheim, 2004; (d) Hiyama, T. *Organofluorine Compounds: Chemistry and Applications*; Springer: Berlin, 2000.
- (a) O'Hagan, D. *Chem. Soc. Rev.* **2008**, *37*, 308–319; (b) Blanksby, S. J.; Ellison, G. B. *Acc. Chem. Res.* **2003**, *36*, 255–263.
- (a) Victor, D. G.; MacDonald, G. J. *Climat. Change* **1999**, *42*, 633–662; (b) Ravishankara, A. R.; Turnipseed, A. A.; Jensen, N. R.; Barone, S.; Mills, M.; Howard, C. J.; Solomon, S. *Science* **1994**, *263*, 71–75.
- Fuchibe, K.; Ohshima, Y.; Mitomi, K.; Akiyama, T. *J. Fluorine Chem.* **2007**, *128*, 1158–1167.
- For review, see: Stahl, T.; Klare, H. F. T.; Oestreich, M. *ACS Catal.* **2013**, *3*, 1578–1587.
- For selected review articles, see: (a) Whittlesey, M. K.; Peris, E. *ACS Catal.* **2014**, *4*, 3152–3159; (b) Kuehnle, M. F.; Lentz, D.; Braun, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 3328–3348; (c) Nova, A.; Mas-Ballesté, R.; Lledós, A. *Organometallics* **2012**, *31*, 1245–1256; (d) Klahn, M.; Rosenthal, U. *Organometallics* **2012**, *31*, 1235–1244; (e) Braun, T.; Wehmeier, F. *Eur. J. Inorg. Chem.* **2011**, 613–625; (f) Hughes, R. P. *Eur. J. Inorg. Chem.* **2009**, 4591–4606; (g) Amii, H.; Uneyama, K. *Chem. Rev.* **2009**, *109*, 2119–2183; (h) Meier, G.; Braun, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 1546–1548; (i) Driver, T. G. *Angew. Chem., Int. Ed.* **2009**, *48*, 7974–7976; (j) Torrens, H. *Coord. Chem. Rev.* **2005**, *249*, 1957–1985; (k) Jones, W. D. *Dalton Trans.* **2003**, 3991–3995; (l) Braun, T.; Perutz, R. N. *Chem. Commun.* **2002**, 2749–2757; (m) Richmond, T. G. *Angew. Chem., Int. Ed.* **2000**, *39*, 3241–3244; (n) Burdeniuc, J.; Jedicka, B.; Crabtree, R. H. *Chem. Ber. Recueil* **1997**, *130*, 145–154; (o) Kiplinger, J. L.; Richmond, T. G.; Osterberg, C. E. *Chem. Rev.* **1994**, *94*, 373–431.
- (a) Morrow, G. W. In *Organic Electrochemistry*; Lund, H., Hammerich, O., Eds., fourth ed.; Marcel Dekker: New York, 2001; (b) Frontana-Urbe, B. A.; Little, R. D.; Ibanez, J. G.; Palma, A.; Vasquez-Medrano, R. *Green Chem.* **2010**, *12*, 2099–2119; (c) Yoshida, J.; Kataoka, K.; Horcajada, R.; Nagaki, A. *Chem. Rev.* **2008**, *108*, 2265–2299; (d) Sperry, J. B.; Wright, D. L. *Chem. Soc. Rev.* **2006**, *35*, 605–621; (e) Moeller, K. D. *Tetrahedron* **2000**, *56*, 9527–9554.
- For examples, see: (a) Elsler, B.; Schollmeyer, D.; Dyballa, K. M.; Franke, R.; Waldvogel, S. R. *Angew. Chem., Int. Ed.* **2014**, *53*, 5210–5213; (b) Nguyen, B. H.; Redden, A.; Moeller, K. D. *Green Chem.* **2014**, *16*, 69–72; (c) Kirste, A.; Elsler, B.; Schnakenburg, G.; Waldvogel, S. R. *J. Am. Chem. Soc.* **2012**, *134*, 3571–3576; (d) Hilt, G. *Angew. Chem., Int. Ed.* **2003**, *42*, 1720–1721; (e) Hilt, G.; Smolko, K. I. *Angew. Chem., Int. Ed.* **2001**, *40*, 3399–3402.
- Kariv-Miller, E.; Vajtner, Z. *J. Org. Chem.* **1985**, *50*, 1394–1399.
- Langer, S. H.; Yurchak, S. J. *Electrochem. Soc.* **1969**, *116*, 1228–1229.
- Musilová-Kebrlová, N.; Janderka, P.; Trnková, L. *Collect. Czech. Chem. Commun.* **2009**, *74*, 611–625.
- (a) Wu, W.-B.; Huang, J.-M. *J. Org. Chem.* **2014**, *79*, 10189–10195; (b) Qi, H.-L.; Chen, D.-S.; Ye, J.-S.; Huang, J.-M. *J. Org. Chem.* **2013**, *78*, 7482–7487; (c) Huang, J.-M.; Lin, Z.-Q.; Chen, D.-S. *Org. Lett.* **2012**, *14*, 22–25; (d) Huang, J.-M.; Wang, X.-X.; Dong, Y. *Angew. Chem., Int. Ed.* **2011**, *50*, 924–927.
- Deuterium incorporation was determined by using a developed Microsoft Excel program, see the Supporting information of: Young, K. J. H.; Meier, S. K.; Gonzales, J. M.; Oxgaard, J.; Goddard, W. A., III; Periana, R. A. *Organometallics* **2006**, *25*, 4734–4737.
- Liu, B. H.; Li, Z. P.; Suda, S. *Electrochim. Acta* **2004**, *49*, 3097–3105.
- (a) Campbell, B. H. *Anal. Chem.* **1972**, *44*, 1659–1663; (b) Kimura, M.; Miyahara, H.; Moritani, N.; Sawaki, Y. *J. Org. Chem.* **1990**, *55*, 3897–3902; (c) Koppang, M. D.; Ross, G. A.; Woolsey, N. F.; Bartak, D. E. *J. Am. Chem. Soc.* **1986**, *108*, 1441–1447.