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Electroorganic synthesis under solvent-free conditions. Highly regioselective anodic monofluorination of cyclic ethers, lactones, and a cyclic carbonate†

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Abstract—Regioselective anodic fluorination of cyclic ethers, lactones, and a cyclic carbonate in $Et_4NF{\cdot}nHF$ ($n=4$, 5) and $Et_3N{\cdot}5HF$ without a solvent was successfully carried out to give the corresponding monofluorinated products in moderate yields. This is the first report of direct electrochemical fluorination of cyclic ethers, lactones, and a cyclic carbonate using anodic fluorination. © 2002 Elsevier Science Ltd. All rights reserved.

Lactones, cyclic carbonates, and cyclic ethers are used as organic electrolytic solvents or additives for Li batteries and capacitors.[2,3] Introduction of fluorine atoms into these compounds is expected to improve their properties such as electrochemical stability, liquidus range, and non-flammability.[4–6] With these facts in mind, we attempted anodic fluorination of cyclic ethers, lactones and a cyclic carbonate. In this paper, we report the first successful regioselective anodic fluorination of cyclic ethers, lactones, and a cyclic carbonate.

At first, anodic fluorination of cyclic ethers was attempted in organic solvents at platinum electrodes under conventional conditions as follows. The anodic fluorination of tetrahydrofuran (**1**) was carried out at a constant current in acetonitrile and CH_2Cl_2 containing $Et_4NF{\cdot}4HF$ using an undivided cell. However, no fluorinated product was obtained and only unidentified polymerized products were formed. The anodic fluorination of dioxane (**3**) in CH_2Cl_2 provided the corresponding 2-fluorinated dioxane (**4**)[7] in a low yield of 19% along with complicated products due to carbon–carbon bond cleavage.

Recently, Momota et al. have shown that various substituted benzenes were anodically fluorinated with high current efficiency in $Et_4NF{\cdot}4HF$ without any solvents.[8] Yoneda et al. also reported that anodic fluorination of α-alkylcyclic ketones in $Et_3N{\cdot}5HF$ without a solvent resulted in the C–CO bond cleavage leading to ω-fluoroacylfluorides in high yields.[9] In these cases, a large excess amount of a fluoride salt was used as the solvent, fluorine source, and supporting salt. In consideration of this report of successful fluorination, anodic fluorination of **1** and **3** was conducted similarly in $Et_4NF{\cdot}4HF$ without any solvents. The fluorination proceeded, however, the yields of the fluorinated products **2** and **4** were as low as 12 and 28%, respectively. The low yields seem to be attributable to simultaneous oxidation of $Et_4NF{\cdot}4HF$ during the electrolysis. It was assumed that the substrate would be selectively oxidized, while the oxidation of $Et_4NF{\cdot}4HF$ would be suppressed by the decrease in the ratio of $Et_4NF{\cdot}4HF$ to the substrate. In order to confirm this assumption, a small amount of $Et_4NF{\cdot}4HF$ (only 1.5–1.7 equiv. of F^- to **1** and **3**) was used for the anodic fluorination. Thus, anodic fluorination of **1** and **3** was carried out at a high current density (150 mA/cm^2).[10] Surprisingly, 2-fluorotetrahydrofuran (**2**)[11] was formed in 80% yield (estimated by ^{19}F NMR) and with high current efficiency, as shown in Table 1 (run 1), when the theoretical amount of electricity (2 F/mol) for the monofluorination was passed.

1,4-Dioxane (**3**) was also efficiently fluorinated to give the corresponding monofluorodioxane (**4**) in a good yield of 77% (run 2). Anodic fluorination of 1,3-dioxolane (**5**) also proceeded similarly to provide the 2-fluorinated dioxolane **6**[12] predominantly in moderate yield (run 3). In both cases, the formation of carbon–carbon bond cleavage products was suppressed.

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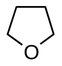
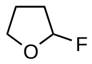
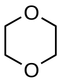
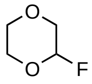
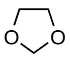
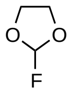
Table 1. Anodic fluorination of cyclic ethers[a]

run	substrate	product	yield (%)[b]
1	 **1**	 **2**	80 (56)
2	 **3**	 **4**	77(59)
3	 **5**	 **6**	45[c](20)

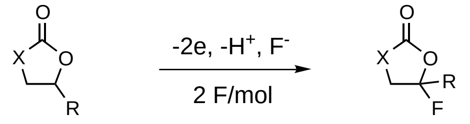
[a] A constant current (150 mA/cm^2) was applied.The reactions were carried out in $Et_4NF•4HF$ and stopped after 2 F/mol of charge was passed. [b] ^{19}F NMR yields based on ethers used. Isolated yields are shown in parentheses. [c] A trace amount of 4-fluoro-1,3-dioxolane was obtained.

Therefore, the fluorination under the conditions is highly selective. It was also notable that the fluorinated tetrahydrofuran **2** was easily isolated by simple distillation (bp 73°C) of the electrolytic solution after the electrolysis. The fluorinated dioxane **4** and dioxolane **6** were also easily separated by extracting the electrolytic solution using $CHCl_3$–hexane (10:1).

Next, anodic fluorination of γ-butyrolactone (**7**) was similarly carried out in $Et_4NF·4HF$, however, a large amount of the starting **7** was recovered, and the yield of the γ-fluorinated product **8**[13] was low (Table 2, run 1). It was found that the use of hardly oxidizable $Et_3N·5HF$ and $Et_4NF·5HF$ resulted in moderate conversion and better yields. Particularly when $Et_4NF·5HF$ was used, 75% yield of **8** based on the consumed **7** was obtained (run 3). Anodic fluorination of γ-valerolactone (**9**) also provided the corresponding γ-fluorinated lactone (**10**)[14] selectively in moderate yield (run 4). The fluorinated products **8** and **10** were easily isolated from the reaction mixture by silica gel column chromatography (hexane:ethyl acetate = 2:1). It is notable that a fluorine atom was introduced predominantly into the γ-position of lactones **7** and **9**.

Very recently, Sasaki and Ue et al. have reported the direct fluorination of **7** by fluorine gas giving a mixture of α-, β- and γ-fluoro-γ-butyrolactones in ca. 20% yield.[15] Using this method, γ-fluorinated product **8** was formed in only 5% yield (estimated by GC analysis),

Table 2. Anodic fluorination of γ-butyrolactone (**7**), γ-valerolactone (**9**) and ethylene carbonate (**11**)[a]



7,9,11 **8,10,12**

Run	Lactone			Supporting electrolyte[b]	Conversion (%)	Product	Yield (%)[c]
	No.	X	R				
1	**7**	CH_2	H	$Et_4NF·4HF$	50	**8**	35
2	**7**	CH_2	H	$Et_3N·5HF$	50	**8**	65
3	**7**	CH_2	H	$Et_4NF·5HF$	50	**8**	75 (61)
4	**9**	CH_2	Me	$Et_4NF·5HF$	51	**10**	51 (25)
5	**11**	O	H	$Et_4NF·5HF$	52	**12**	87 (76)

[a] A constant current (100 mA/cm^2) was applied. The reaction was stopped after 2 F/mol of charge was passed because product yields decreased after further electrolysis.

[b] 2.4 Equivalent amount of F^- to the substrate was used.

[c] ^{19}F NMR yields and isolated yields (in parentheses) based on the consumed lactones or carbonate.

which could not be separated from the reaction mixture. This method is obviously not suitable for the preparation of **8**. In contrast, the electrochemical fluorination of **7** is highly regioselective and **8** is readily isolable; therefore, this electrochemical method is much superior to the chemical fluorination.

Finally, this solvent-free electrolysis was applied to the anodic fluorination of ethylene carbonate (**11**). Previously, we reported the synthesis of monofluoroethylene carbonate (**12**) by fluorodesulfurization of 4-arylthio-1,3-dioxolane-2-ones.[16] Since **11**, devoid of an arylthio group, has an extremely high oxidation potential, it could not be fluorinated at all under the usual electrolytic conditions using organic solvents. In this case, organic solvents were predominantly oxidized. However, notably, anodic fluorination of **11** in $Et_4NF\cdot 5HF$ without a solvent provided **12** selectively in moderate yield (high yield based on the consumed **11**) (Table 2, run 5). Kobayashi et al. also reported the direct fluorination of **11** by fluorine gas providing **12** in moderate yield;[17] however, fluorine gas is hazardous.

In summary, we have successfully carried out for the first time selective anodic fluorination of cyclic ethers, lactones, and a cyclic carbonate under solvent-free conditions. Notably, 1.5–2.4 equiv. of F^- to a substrate is effective for the fluorination. It is noted that α-fluorotetrahydrofuran (**2**) was easily isolated in good yield by simple distillation of the electrolytic mixture. This is a completely solvent-free electrosynthetic process. The products seem to be highly useful as the electrolytic solutions for rechargeable Li batteries and building blocks. The scope and limitations of the present anodic fluorination are now under investigation.

Acknowledgements

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7. 2-Fluoro-1,4-dioxane (**4**): colorless oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.39 (d, $J=52$ Hz, 1H), 4.24 (m, 1H), 3.90–3.71 (m, 5H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 103.073 (d, $J=221$ Hz), 67.292 (d, $J=25.7$ Hz), 65.650, 60.671; ^{19}F NMR (254 MHz, $CDCl_3$) δ −61.1 (ddd, $J=52$, 35, 5.3 Hz); MS (*m/z*) 106 (M^+), 87 (M^+-F), 86, 73; HRMS *m/z* calcd for $C_4H_7FO_2$: 106.0430. Found: 106.0483.
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9. Yoneda, N.; Chen, S.-Q.; Hatakeyama, T.; Hara, S.; Fukuhara, T. *Chem. Lett.* **1994**, 849.
10. A typical procedure for the anodic fluorination is as follows. Anodic fluorination of **1** (4.90 g, 68.0 mmol) was carried out at platinum electrodes (2×2 cm^2) in 2.0 M $Et_4NF\cdot 4HF$ (1.5 equiv. of F^- to **1**, a total volume of **1** and $Et_4NF\cdot 4HF$ was 10 ml) in a cylindrical undivided cell under a nitrogen atmosphere at room temperature. Constant current (150 mA/cm^2) was applied. After 2 F/mol of charge was passed, the corresponding fluorinated compound **2** (3.43 g, 38.1 mmol) was isolated by simple distillation of the electrolytic solution (bp 73°C).
11. 2-Fluorotetrahydrofuran (**2**): colorless oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.88 (d, $J=67$ Hz, 1H), 4.26–4.14 (m, 1H), 4.02–3.91 (m, 1H), 2.35–1.65 (m, 4H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 112.6769 (d, $J=216$ Hz), 69.414, 46.122, 33.172 (d, $J=25.7$ Hz), 21.719; ^{19}F NMR (254 MHz, $CDCl_3$) δ −34.8 (m); MS (*m/z*) 71 (M^+-F), 69, 43; HRMS *m/z* calcd for C_4H_7O (M^+-F): 71.0497. Found: 71.0487.
12. 2-Fluoro-1,3-dioxolane (**6**): colorless oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.31 (d, $J=92$ Hz, 1H), 4.25–4.18 (m, 2H), 4.14–4.04 (m, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 117.209 (d, $J=249$ Hz), 63.153 (d, $J=16.7$ Hz); ^{19}F NMR (254 MHz, $CDCl_3$) δ −1.99 (d, $J=92.5$ Hz); MS (*m/z*) 73 (M^+-F); HRMS *m/z* calcd for $C_3H_5O_2$ (M^+-F): 73.0290. Found: 73.0263.
13. 5-Fluoro-5-pentanolide (**8**): colorless oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.20 (dd, $J=62.3$, 3.5 Hz, 1H), 2.82–2.63 (m, 1H), 2.57–2.32 (m, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 174.77 (d, $J=3.9$ Hz), 109.08 (d, $J=229$ Hz), 28.87 (d, $J=24.6$ Hz), 24.57; ^{19}F NMR (254 MHz, $CDCl_3$) δ −43.17 (br ddd, $J=61.0$, 27.7, 22.2 Hz); MS (*m/z*) 104 (M^+), 85; HRMS *m/z* calcd for $C_4H_5FO_2$: 104.0274. Found: 104.0219.
14. 5-Fluoro-5-methyl-5-pentanolide (**10**): colorless oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.82 (ddd, $J=18$, 11, 9.1 Hz, 1H), 2.63–2.42 (m, 2H), 2.24 (dddd, $J=32$, 14, 11, 9.7 Hz, 1H), 1.76 (d, $J=18$ Hz, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 174.75 (d, $J=1.7$ Hz), 118.22 (d, $J=226$ Hz), 33.29 (d, $J=28$ Hz), 27.34, 23.48 (d, $J=30$ Hz); ^{19}F NMR (254 MHz, $CDCl_3$) δ −16.6 (ddq, $J=31$, 13, 19 Hz); MS (*m/z*) 118 (M^+), 103, 99; HRMS *m/z* calcd for $C_5H_7FO_2$: 118.0430. Found: 118.0431.
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