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Electrolytic partial fluorination of organic compounds. Part 50: Highly selective anodic mono- and difluorination of 4-phenylthiomethyl-1,3-dioxolan-2-one and its synthetic application†

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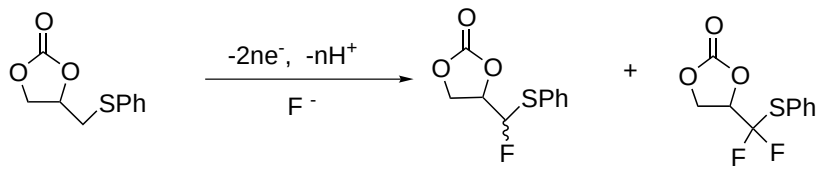
Abstract—Anodic fluorination of 4-phenylthiomethyl-1,3-dioxolan-2-ones was successfully carried out to provide the corresponding α-mono- and α,α-difluorinated products selectively, depending on the amount of the electricity passed. The fluorination was also greatly affected by solvents, temperature and current densities. The fluorinated products were readily converted into the corresponding fluorinated allyl alcohol and diols by treatment with an alkaline solution.

Fluorine-containing allyl alcohols and 1,2-diols are useful building blocks for the preparation of valuable organofluorine compounds such as fluorinated sugars.[2] However, their preparation is still limited.[3] Recently, electrochemical partial fluorination of organic compounds has been shown to be a new powerful method

Table 1. Anodic fluorination of 4-phenylthiomethyl-1,3-dioxolan-2-one (**1**)



1 **2** **3**

Run	Solvent	Supporting electrolyte	Electricity (F mol^{-1})	Temp. (°C)	Current density (mA cm^{-2})	Yield (%)[a]	
						2	**3**
1	MeCN	$Et_3N{\cdot}3HF$	2	20	10	0	0
2	CH_2Cl_2	$Et_3N{\cdot}3HF$	2	20	10	48	4
3	CH_2Cl_2	$Et_3N{\cdot}3HF$	4	20	10	6	26
4	DME	$Et_3N{\cdot}5HF$	2	20	10	24	5
5	DME	$Et_4NF{\cdot}4HF$	2	20	10	22	1
6	DME	$Et_3N{\cdot}3HF$	2	20	10	22	0
7	DME	$Et_3N{\cdot}3HF$	8	20	10	40	8
8	DME	$Et_3N{\cdot}3HF$	8	40	10	73	Trace
9	DME	$Et_3N{\cdot}3HF$	48	40	10	17	40
10	DME	$Et_3N{\cdot}3HF$	48	40	40	Trace	68
11	DME/MeCN (50/50)	$Et_3N{\cdot}3HF$	16	40	40	9	65

[a] Isolated yield.

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for selective fluorination.[4] We have reported selective anodic fluorination of various organo sulfur compounds.[5] With these in mind, we studied anodic fluorination of 4-phenylthiomethyl-1,3-dioxolan-2-ones (**1**) in order to synthesize fluorine-containing allyl alcohols and diols.

At first, we carried out anodic fluorination of **1** at platinum electrodes in an undivided cell under different conditions using various fluoride salts as a supporting electrolyte and a fluorine source.[6] Constant current was applied. The results are summarized in Table 1.

As shown in Table 1, no fluorinated product was formed in MeCN (run 1). In contrast, monofluorinated product **2** was obtained in moderate yield in CH_2Cl_2 (run 2). However, further oxidation of **2** resulted in a drastic decrease in the yield of **2** and the corresponding difluorinated product **3** was formed (run 3). On the other hand, the use of dimethoxyethane (DME) provided monofluorinated product **2** in reasonable yields regardless of the supporting fluoride salts (runs 4–6). In these cases, a large amount of the starting material **1** was recovered. Among the electrolytes used, $Et_3N{\cdot}3HF$ gave the best product selectivity (run 6). In order to increase the yield of **2**, the electrolysis of **1** was carried out by using $Et_3N{\cdot}3HF$/DME until the starting **1** was consumed. Thus, the product yield increased considerably when 8 F/mol of charge was passed (run 7).

Next, the electrolysis was investigated at a higher temperature. Interestingly, the anodic fluorination of **1** at 40°C gave monofluoro product **2** selectively in good yield (73%) (run 8). The increase of the yield of **2** can be accounted as follows. We have already proposed a Pummerer type mechanism for the anodic fluorination of sulfides.[7] Therefore, the anodic fluorination of **1** seems to proceed similarly as shown in Scheme 1.

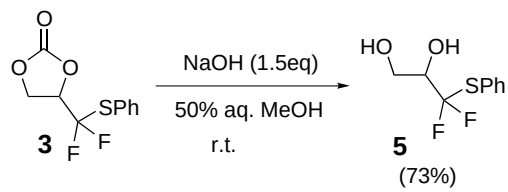
Elimination of hydrogen fluoride from the fluorosulfonium intermediate **A** should be facilitated at a higher temperature. Thus, we could obtain the desired monofluorinated product **2** in good yield. The product **2** was found to be a diastereoisomeric mixture (7:3).[8]

Further anodic oxidation at 40°C provided difluorinated product **3**[9] preferentially (run 9). In order to increase the yield of **3**, the applied current density was increased from 10 mA cm^{-2} to 40 mA cm^{-2} (run 10). Expectedly, the yield increased markedly to 70% and **3** was obtained predominantly. Thus, it was found that the electrolysis at a higher current density and higher temperature was suitable for the difluorination of **1**. Although, DME was suitable for anodic fluorination of **1**, a large excess amount of electricity was necessary for the formation of the difluorinated product **3** due to the simultaneous oxidation of DME. Next, we used a mixed solvent of DME/MeCN for the anodic fluorination in order to decrease the amount of the necessary electricity. Eventually, the required electricity was reduced to one-third by using DME/MeCN (50:50) and the desired difluorinated product **3** was obtained in an acceptable yield (run 11).

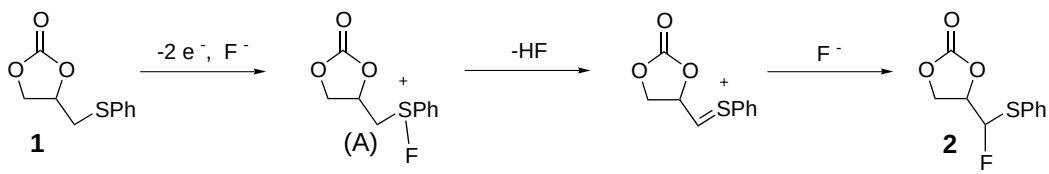
Finally, deprotection of the carbonate group of **2** and **3** was attempted. Alkaline hydrolysis of **2** resulted in decomposition of **2**. Therefore, **2** was converted into the corresponding sulfone and then alkaline hydrolysis was carried out at room temperature to provide the corresponding allyl alcohol derivative **4**[10] quantitatively (79% yield from **2**) as shown in Scheme 2.

On the other hand, difluorinated compound **3** was directly converted into the corresponding diol **5**[11] by alkaline hydrolysis at room temperature as shown in Scheme 3.

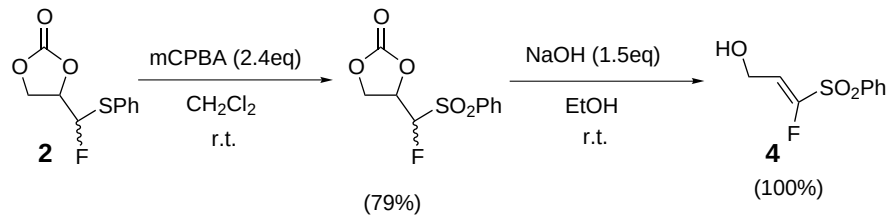
The compound **3** was also readily converted into the corresponding difluoro sulfonyl diol derivative **6**[12] by the oxidation of **3** with mCPBA followed by alkaline hydrolysis at room temperature as shown in Scheme 4.



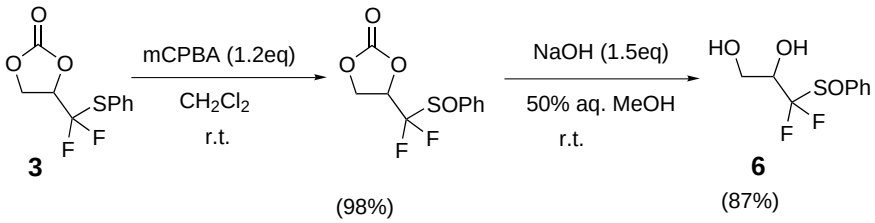
Scheme 3.



Scheme 1.



Scheme 2.



Scheme 4.

The products **4–6** have multi-functional groups. Therefore, they seem to be useful fluorinated building blocks.[13]

In conclusion, we successfully carried out selective anodic mono- and difluorination of 4-phenylthiomethyl-1,3-dioxolan-2-one and the fluorinated products were easily converted into monofluoro allyl alcohol and difluorodiol derivatives in good yields.

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5. Shaaban, M. R.; Ishii, H.; Fuchigami, T. *J. Org. Chem*. **2000**, 8685 and references cited therein.
6. Constant current electrolysis (10 or 40 mA cm^{-2}) of **1** (1 mmol) was carried out at platinum electrodes (2×2 cm^2) at 20 or 40°C in DME, MeCN or CH_2Cl_2 (10 ml) and DME/MeCN (5 ml/5 ml) containing 0.3 M fluoride salt using an undivided cell under a nitrogen atmosphere. After electrolysis, the supporting electrolyte was removed by silica gel short column chromatography. The products **2** and **3** were isolated by silica gel column chromatography (hexane:EtOAc = 9:1). Compounds **2** and **3** were converted to **4**, **5** and **6**, which were easily isolated by silica gel chromatography.
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8. **2** (more polar isomer): ^{1}H NMR ($CDCl_3$): δ 7.54–7.35 (m, 5H), 5.90 (dd, J = 53.5 Hz, 2.7 Hz), 5.00–4.91 (m, 1H), 4.56–4.36 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 153.6; 136.3; 130.6; 129.2; 129.0; 99.3 (d, J = 225.4 Hz); 75.4 (d, J = 26.2 Hz); 64.8 (d, J = 3.3 Hz); ^{19}F NMR ($CDCl_3$): δ −88.96 (dd, J = 53.6, 16.8 Hz); MS (m/z) 228 (M^+). HRMS calcd for $C_{10}H_9FO_3S$: 228.0256; found: 228.0252. **2** (less polar isomer): ^{1}H NMR ($CDCl_3$): δ 7.55–7.35 (m, 5H), 5.76 (dd, J = 51.7 Hz, 5.9 Hz), 4.92–4.80 (m, 1H), 4.57–4.38 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 153.8; 133.3; 133.1; 129.2; 129.4; 129.2; 99.6 (d, J = 226.5 Hz); 75.7 (d, J = 25.1 Hz); 65.6 (d, J = 3.3 Hz); ^{19}F NMR ($CDCl_3$): δ −83.73 (dd, J = 51.8, 13.0 Hz); MS (m/z) 228 (M^+). HRMS calcd for $C_{10}H_9FO_3S$: 228.0256; found: 228.0252.
9. **3**: ^{1}H NMR ($CDCl_3$): δ 7.64–7.41 (m, 5H), 4.86–4.61 (m, 1H), 4.58–4.50 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 153.2; 136.6; 130.8; 129.6; 125.8; 123.8; 74.8 (dd, J = 32.9, 28.0 Hz); 64.3; ^{19}F NMR ($CDCl_3$): δ −14.83–11.14 (m); MS (m/z) 246 (M^+). HRMS calcd for $C_{10}H_8F_2O_3S$: 246.0162; found: 246.0162.
10. **4**: ^{1}H NMR ($CDCl_3$): δ 7.96–7.55 (m, 5H), 6.40 (dt, J = 32.4, 6.2 Hz), 4.36 (dd, J = 6.2, 2.7 Hz); ^{13}C NMR ($CDCl_3$): δ 134.5; 129.4; 128.6; 126.1; 116.5 (d, J = 5.0 Hz); 55.5 (d, J = 3.9 Hz); ^{19}F NMR ($CDCl_3$): δ −47.72 (d, J = 31.5); HRMS calcd for $C_9H_9FO_3S$: 216.0256; found: 216.0249.
11. **5**: ^{1}H NMR ($CDCl_3$): δ 7.61–7.33 (m, 5H), 4.06–3.99 (m, 1H), 3.89–3.79 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 136.4; 130.0; 129.0; 128.7; 116.3 (d, J = 22.3 Hz); 73.9 (t, J = 26.8 Hz); 61.3 Hz; ^{19}F NMR ($CDCl_3$): δ −9.12–8.05 (m); −5.54 to 4.52 (m); MS (m/z) 220 (M^+). HRMS calcd for $C_9H_{10}F_2O_2S$: 220.0370; found: 220.0349.
12. **6**: ^{1}H NMR ($CDCl_3$): δ 7.63–7.54 (m, 5H), 4.19 (m, 1H), 3.90 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 134.6; 132.5; 129.0; 126.6; 116.5 (d, J = 4.4 Hz); 68.6 (dd, J = 26.7, 21.2 Hz); 60.0 (t, J = 5.0 Hz); ^{19}F NMR ($CDCl_3$): δ −40.84 (dd, J = 227.4, 7.4 Hz); −32.20 (dd, J = 225.6, 11.2 Hz); HRMS calcd for $C_9H_{10}F_2O_3S$: 236.0319; found: 236.0316.
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