Anodic Fluorination of (Poly)Heteroaromatic Compounds in Conventional Organic Solvents and Ionic Liquids

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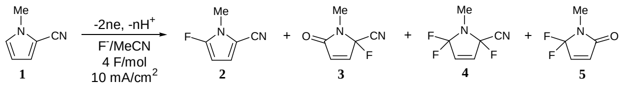
Fluorinated aromatic heterocyclic compounds have been of much interest because of their unique biological properties. Although direct fluorination of heteroaromatic rings is the simplest way to prepare fluorinated heterocycles, successful examples of the fluorination are limited. For example, the chemical fluorination of five-membered heteroaromatic compounds such as pyrroles, thiophenes, and furans was attempted, however the yields were extremely low (less than 6%) and the selectivity was also unsatisfactory in all cases.[1] Recently, electrochemical partial fluorination of organic compounds has been shown to be a new powerful method for selective fluorination. However, there have been few reports of direct fluorination of heteroaromatic compounds using an electrochemical method.[2] In most cases, yields of the fluorinated products are extremely low or unsatisfactory. On the other hand, we found that electron-withdrawing groups promoted the anodic fluorination of heterocyclic compounds. With these facts in mind, we attempted the direct anodic fluorination of (poly)heteroaromatic compounds having various electron-withdrawing groups in conventional organic solvents and ionic liquids.

At first, we investigated anodic fluorination of 2-cyano-1-methylpyrrole (**1**) using various fluoride supporting salts in MeCN. The results are summarized in Table 1.[3]

Table 1 Anodic Fluorination of 2-cyano-1-methylpyrrole **1**



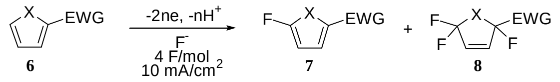
Run	Supporting electrolyte (1 M)	Yield(%)[a]			
		2	**3**	**4**	**5**
1	Et_3N-2HF	20	trace	32	trace
2	Et_3N-3HF	5	2	65	3
3	Et_3N-5HF	0	12	5	54
4	Et_4NF-4HF	0	21	6	28

[a] Determined by ^{19}F NMR spectroscopy.

Anodic fluorination of **1** took place efficiently to provide four fluorinated products **2**, **3**, **4** and **5** depending on the fluoride salts.

Next, anodic fluorination of *N*-substituted pyrrole and thiophene derivatives having electron-withdrawing groups at 2-position. The results are summarized in Table 2.[4]

Table 2 Anodic Fluorination of Pyrrole and Thiophene Derivatives



Run	X	EWG	Solvent	Supporting Electrolyte (1 M)	Yield (%)[a]	
					7	**8**
1	NPh	CN	MeCN	Et_3N-3HF	trace	43
2	NPh	CN	DME	Et_3N-3HF	30	18
3	NMe	$COCH_3$	MeCN	Et_3N-2HF	17	21
4	S	CN	MeCN	Et_4NF-4HF	trace	40
5	S	COOEt	MeCN	Et_4NF-4HF	trace	51

[a] Determined by ^{19}F NMR Spectroscopy.

We successfully synthesized for the first time monofluoropyrroles by anodic fluorination of *N*-substituted pyrroles having various electron-withdrawing groups at the 2-position. Moreover, we have shown that the trifluorinated product **8** was preferentially formed by the further electrochemical oxidation of **7** once formed during the electrolysis. The compounds **4**, **5** and **8** have a biologically interesting *gem*-difluoromethylene unit and an activated olefin in the molecule. Therefore, **4**, **5** and **8** seem to be highly useful building blocks for the preparation of various *gem*-difluoromethylene compounds.[5]

Electroconducting polymer films like polypyrrole and polythiophene films have received much attention because of their unique properties. Furthermore, one approach that is receiving increasing attention is electrochemical functionalization after polymerization. With these facts in mind, in the present work, we attempted the anodic fluorination of solid state polymer such as polypyrrole and polythiophene films. Such a fluorination offers the attractive possibility of developing useful materials since fluorinated π-conjugated materials exhibit excellent n-type semiconductivity.

Polypyrrole and polythiophene films were prepared by potential scanning method. For anodic fluorination of polypyrrole and polythiophene films, the polymer coated electrode was repeatedly potential scanned in 0.5 M Et_4NF-4HF / MeCN. As a typical example, the cyclic voltammogram of polythiophene in 0.5 M Et_4NF-4HF / MeCN is shown in Fig. 1.

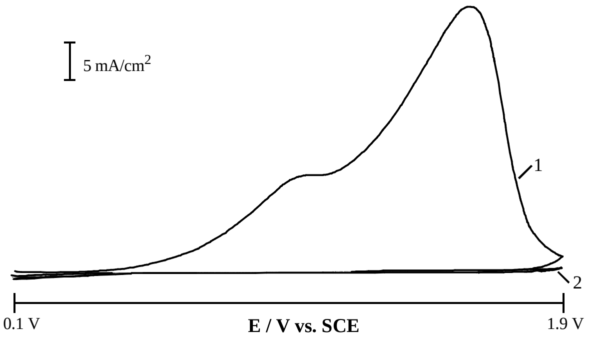


Fig. 1 Cyclic Voltammogram of Polythiophene in 0.5 M Et_4NF-4HF/MeCN

Polythiophene became electrochemically inactive after a single cycle of the potential to +1.9V in a F^--containing solution. Now, we are investigating the reactivation of polythiophene by electrochemical and chemical methods.

Fluorinated polymer films were subjected to elemental analysis, ^{19}F and ^{1}H NMR, IR, and UV-vis spectroscopy.

We have shown a potentially useful method for the introduction of fluorine atoms into the preformed conducting polymers.

References

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