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Selective anodic fluorination of electrophilic alkenes

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Abstract

Anodic fluorination of some electrophilic alkenes (conjugated with electron-withdrawn groups), ethyl cinnamates, R–C_6H_4–CH=CH–CO_2Et (R = H, CH_3, CH_3O, F and CF_3), cinnamonitrile, C_6H_4–CH=CH–CN, phenyl stryryl ketone, and *t*-butyl styryl ketone using ammonium fluorides as the fluorine source and supporting electrolyte, in CH_2Cl_2 as electrolytic solvent yields the expected *vicinal* difluoro compounds, as mixture of *erythro* and *threo* isomers. The anodic fluorination of phenyl 3,5-di-*t*-butyl-4-hydroxystyryl ketone yields two monofluoro compounds. A possible reaction mechanism is discussed.

Keywords: Electrochemical partial fluorination; Electrophilic alkenes; Amine–HF complexes

1. Introduction

The selective fluorination of organic molecules has attracted much interest because a number of partially fluorinated organic molecules are reported to show interesting chemical and physical properties and, in some cases, biological activities [1,2].

The electrochemical partial fluorination (ECPF) of organic compounds using $Et_3N{\cdot}n$HF (n = 2–4) as a fluorine source and supporting electrolyte has been developed in the last few years [3–5]. Recently, a new electrolyte, $Et_3N{\cdot}5$HF, has been found to be electrochemically highly stable and an excellent fluorinating agent for the electrochemical fluorination of aldehydes and ketones to produce the corresponding acylfluorides and alkylfluorides in good yields [6].

Continuing our efforts on the regioselective anodic fluorination of unsaturated compounds [7,8], we report in this paper the anodic fluorination of some electrophilic alkenes (alkenes conjugated with electron-withdrawing groups), such as α,β-unsaturated esters (ethyl cinnamates), cinnamonitrile, and α,β-unsaturated ketones (phenyl stryryl ketone, *t*-butyl styryl ketone, and phenyl 3,5-di-*t*-butyl-4-hydroxystyryl ketone) using $Et_3N{\cdot}n$HF (n = 3 and 5) and $Et_4NF{\cdot}n$HF (n = 2 and 4) as supporting electrolytes and fluorine sources in CH_2Cl_2 as electrolytic solvent. The influence of the nature of the fluorine sources and of the electrolytic temperature on the anodic fluorination was investigated.

2. Results and discussion

We first investigate the anodic fluorination of ethyl cinnamates **1A** (**a–e**), cinnamonitrile **1Ba**, phenyl stryryl ketone **1Ca**, and *t*-butyl styryl ketone **1Da** using various fluorine sources in CH_2Cl_2 (Scheme 1).

The experimental data are shown in Table 1. It was found that the anodic fluorination of these activated alkenes yields *vicinal* difluoro ester derivatives **2A** (**a–e**), **2Ba** and vicinal difluoro ketones **2Ca** and **2Da** as mixtures of two diastereoisomers, *erythro* and *threo*. Low yields were obtained when the electrochemical reaction occurs without using an electrolytic solvent (Entry 1) and in the presence of $Et_3N{\cdot}3$HF as fluorine source (Entries 1 and 2), CH_2Cl_2 was a suitable electrolytic solvent (Entries 3–16 and 19–20). High yields were obtained when the anodic fluorination occurs in the presence of $Et_3N{\cdot}5$HF, $Et_4NF{\cdot}2$HF, and $Et_4NF{\cdot}4$HF as fluorine sources and supporting electrolytes (Entries 3–12

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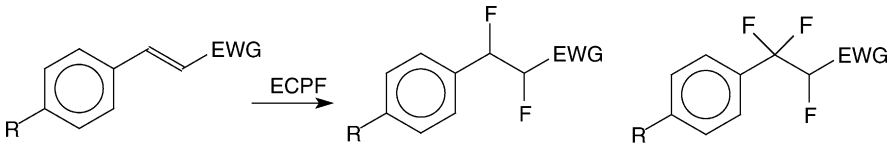


A: EWG = CO_2Et; **B**: EWG = CN; **C**: EWG = CO-*t*-Bu; **D**: EWG = COPh
a: R = H; **b**: R = CH_3; **c**: R = CH_3O; **d** : R = F; **e**: R = CF_3

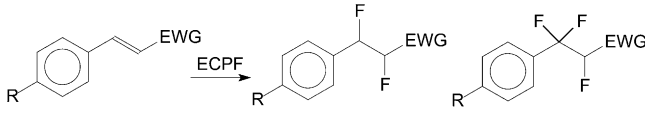
Scheme 1.

and 19–20). The electrolytic temperature generally was found not to be a great influence on the anodic fluorination of substrate **1Aa**. Room temperature (r.t.) seems to be a sufficient electrolytic temperature for these reactions (yield = 70%, Entries 5 and 8).

The substituent R influences the yields of reaction, better yields being obtained when substituent groups are electron withdrawing, F and CF_3 (Table 1, Entries 11 and 12); when substituent groups are electron donating ones, CH_3 and CH_3O, the substrates have lower anodic potentials due to the stabilized C^+ formed (higher reactivity for these systems), and the yields of the difluoro esters are lower (Table 1, Entries 9–10). Side products, like saturated trifluoro derivatives or unsaturated monofluoro derivatives, can be formed, as is shown in literature data [9], for these kind of reactions.

^{19}F NMR spectra show that the anodic fluorination of cinamonitrile **1B** yields the desired *vicinal* difluoro derivative **2Ba** as a mixture of two diastereoisomers, together with the trifluoro derivative **3Ba**. The trifluoro

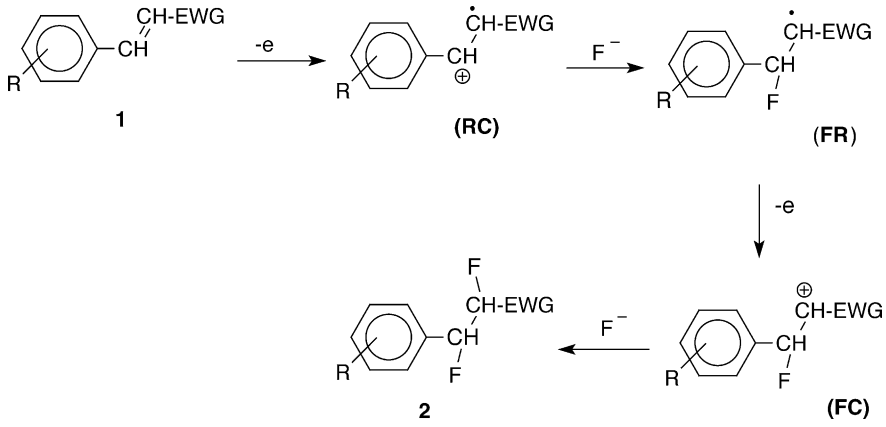
Table 1
Electrochemical partial fluorination of functionalized alkenes **1A–D**



A: EWG = CO_2Et; **B**: EWG = CN; **C**: EWG = CO-*t*-Bu; **D**: EWG = COPh
a: R = H; **b**: R = CH_3; **c**: R = CH_3O; **d**: R = F; **e**: R = CF_3

Entry	Compounds	R	Electrolyte	Solvent	Potential (V) vs. Ag/Ag^+	Charge passed (F/mol)	Temperature (°C)	Yield[a] (%)	
								2	**3Ba**
1	**1Aa**	H	$Et_3N{\cdot}3HF$	None	1.9	3.0	r.t.	1.5	
2	**1Aa**	H	$Et_3N{\cdot}3HF$	CH_2Cl_2	1.95	2.5	r.t.	16	
3	**1Aa**	H	$Et_3N{\cdot}5HF$	CH_2Cl_2	1.9	2.5	r.t.	58	
4	**1Aa**	H	$Et_4NF{\cdot}4HF$	CH_2Cl_2	1.95	3.5	r.t.	66	
5	**1Aa**	H	$Et_4NF{\cdot}2HF$	CH_2Cl_2	1.95	3.5	r.t.	70	
6	**1Aa**	H	$Et_4NF{\cdot}2HF$	CH_2Cl_2	1.95	3.5	0	66	
7	**1Aa**	H	$Et_4NF{\cdot}2HF$	CH_2Cl_2	1.95	3.5	−46	57	
8	**1Aa**	H	$Et_4NF{\cdot}2HF$	CH_2Cl_2	1.95	3.5	r.t.	70	
9	**1Ab**	CH_3	$Et_4NF{\cdot}2HF$	CH_2Cl_2	1.7	3.5	r.t.	57	
10	**1Ac**	CH_3O	$Et_4NF{\cdot}2HF$	CH_2Cl_2	1.4	3.0	r.t.	27	
11	**1Ad**	F	$Et_4NF{\cdot}2HF$	CH_2Cl_2	1.9	4.0	r.t.	63	
12	**1Ae**	CF_3	$Et_4NF{\cdot}2HF$	CH_2Cl_2	2.3	4.0	r.t.	58	
13	**1Ba**	H	$Et_4NF{\cdot}2HF$	CH_2Cl_2	1.85	3.0	r.t.	33	17
14	**1Ba**	H	$Et_3N{\cdot}3HF$	CH_2Cl_2	1.9	3.0	r.t.	27.5	5
15	**1Ba**	H	$Et_3N{\cdot}4HF$	CH_2Cl_2	1.8	2.5	r.t.	12	6
16	**1Ba**	H	$Et_3N{\cdot}5HF$	CH_2Cl_2	1.9	3.5	r.t.	27	23
17	**1Ba**	H	$Et_3N{\cdot}5HF$	AcOEt	1.9	3.5	r.t.	23	18
18	**1Ba**	H	$Et_3N{\cdot}5HF$	MeCN[b]	1.8	3.5	0	21	29
19	**1Ca**	H	$Et_4NF{\cdot}2HF$	CH_2Cl_2	1.9	4.0	r.t.	48	
20	**1Da**	H	$Et_4NF{\cdot}2HF$	CH_2Cl_2	1.9	5.0	r.t.	41	

Unfortunately, we were not able to isolate the pure fluoroacetamide derivative, which was not further investigated.
[a] Isolated yield.
[b] A fluoroacetamide derivative was obtained, 8% GC yield.



Scheme 2.

derivative **3Ba** was probably formed by dehydrofluorination–fluorination of **2**. Unfortunately, we were not able to isolate the pure trifluoro derivative **3Ba**, which was not further investigated.

The anodic fluorination of cinnamonitrile **1B** was performed in dichloromethane, ethylacetate, and acetonitrile as electrolytic solvents; no significant influence on the yields of electrolysis was found, as is shown in Table 1 (Entries 13–18). ^{19}F NMR shows that a fluoroacetamide derivative was obtained as a minor product (8% yield) when anodic fluorination occurred in acetonitrile as electrolytic solvent (Table 1, Entry 18); this compound was not further investigated.

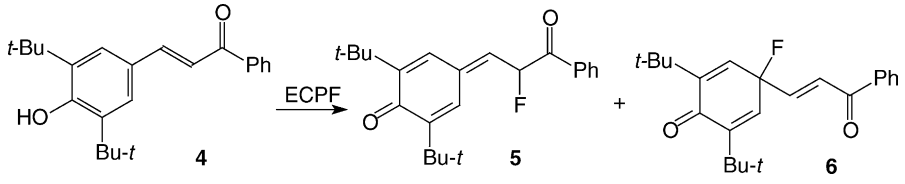
An EC_NEC_N (electrochemical–chemical–electrochemical–chemical) mechanism is widely accepted for electrochemical partial fluorination reactions [9,10], and most likely the reactions under our study follow the same pathway (Scheme 2).

The one-electron oxidation of the substrate **1** gave the radical cation species (RC), which was fluorinated by a nucleophilic attack of the fluoride ion to afford a fluorinated radical (FR). The subsequent oxidation of (FR) yielded the fluorocarbocation (FC). Finally, the *vicinal* fluorinated product **2** was formed by the nucleophilic attack of the fluoride ion toward (FC).

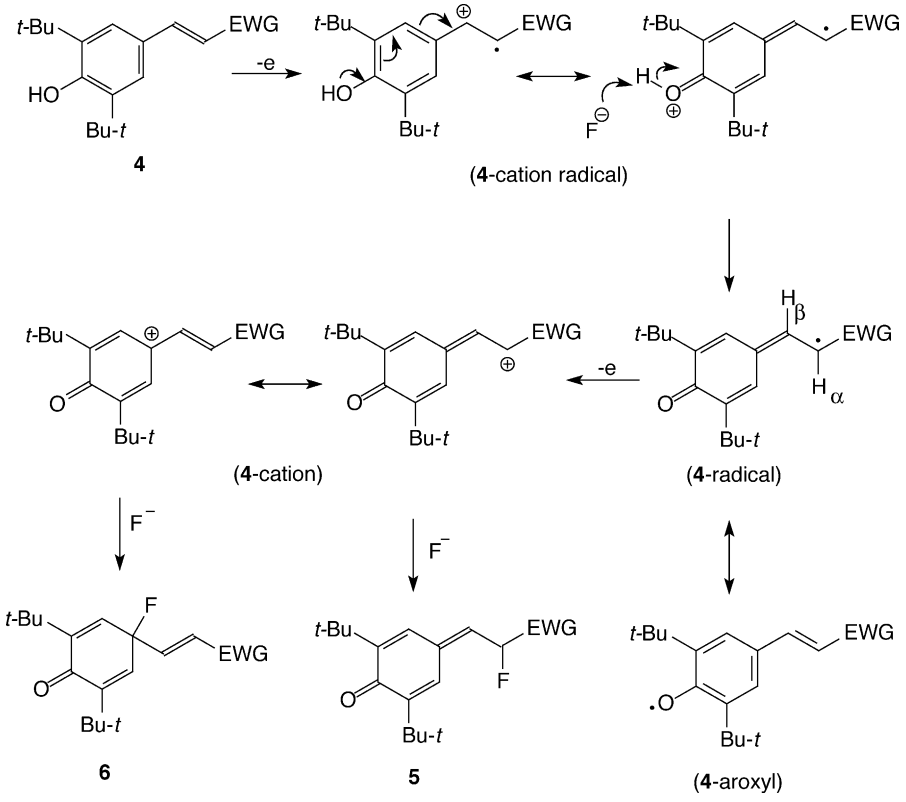
Calculations of the atomic orbital spin population in primary radical-cations formed by oxidation of cinnamic esters revealed that the highest spin density appears on the alpha-carbon atom, adjacent to the ester group, independently of the nature of *para*-substituents R in the benzene ring [9]. Therefore, the single electron in the radical cation is always located at this atom and consequently, nucleophilic attack of the fluoride ion takes place on the benzylic beta-carbon atom. It is known that the most positive charge in the radical-cation is always located on the carbonyl carbon atom, but nucleophilic attack on this atom is fully reversible and does not lead to any products [7,9]. The second high value of positive charge is located at beta-carbon atom, so the first fluorination occurs at the benzylic carbon atom.

An interesting fluorination occurs when phenyl 3,5-di-*t*-butyl-4-hydroxystyryl ketone **4** (a hindered phenol containing chalcone), synthesized from 3,5-di-*t*-butyl-4-hydroxybenzaldehyde and acetophenone in acidic conditions, was anodically fluorinated in the presence of $Et_4NF{\cdot}2HF$ as fluorine source and supporting electrolyte, and in CH_2Cl_2 as electrolytic solvent (Scheme 3). To our pleasant surprise, unlike our previous finding that fluorination occurs to yield *vic*-difluoro ketones, in this case ^{1}H and ^{19}F NMR spectra show that this reaction yields a mixture of two monofluoro derivatives **5** and **6** in ratio 1:1 (yields are 30% for each). Compounds **5** and **6** have the C=O stretching bands at 1630–1640 cm^{-1}, and do not have phenolic OH stretching bands. We believe that the electron-donating hindered phenolic group changed the reaction mechanism of anodic fluorination of this ketone derivative and two monofluoro derivatives were obtained.

We assume that this unexpected fluorination can be explained by the reaction mechanism shown in Scheme 4, in which the one-electron oxidation of chalcone **4** generates the (**4**-radical-cation) that exists in two tautomers structures in which the positive charge is located at carbon or oxygen atom. The nucleophilic fluoride attacks the proton from hydroxy group and the (**4**-radical) is formed; this radical has



Scheme 3.



Scheme 4.

a resonant structure, (4-aroxyl) that is a stable free radical (aroxyl) due to the presence of the bulky *t*-butyl groups in *ortho*, *ortho*′-positions. The hyperfine coupling constants (hfcs), determined by the EPR spectra are the highest (0.64 mT) on the styryl proton Hα, adjacent to the carbonyl group, indicating a higher contribution of hyperconjugative limiting structures placing high spin densities on these protons [11], and carbon radical is formed. The subsequent oxidation yields the corresponding (**4**-carbon cation), which exist in the tautomeric forms. The nucleophilic attack of fluoride ion on these cations yields the monofluoro derivatives **5** and **6** in same ratio.

In summary, we have reported a selective electrochemical fluorination of some electrophilic alkenes, i.e. ethyl cinnamates, cinnamonitrile, phenyl stryryl ketone, *t*-butyl styryl ketone, and phenyl 3,5-di-*t*-butyl-4-hydroxystyryl ketone using $Et_3N{\cdot}n$HF (n = 3 and 5) and $Et_4NF{\cdot}n$HF (n = 2 and 4) as supporting electrolytes and fluorine sources. Anodic fluorination of ethyl cinnamates, cinnamonitrile, phenyl stryryl ketone, and *t*-butyl styryl ketone yield *vicinal* difluoro esters or difluoro ketones, as mixtures of two diastereoisomers, *erythro* and *threo*. In the anodic fluorination of cinnamonitrile, the trifluoro derivative **3B** was also formed. The highest yields were obtained when $Et_4NF{\cdot}2HF$, $Et_4NF{\cdot}4HF$, and $Et_3N{\cdot}5HF$ were used as fluorine sources in the ECF of ethyl cinnamates **1A** (**a**–**e**) and when $Et_4NF{\cdot}2HF$, $Et_3N{\cdot}3HF$, and $Et_3N{\cdot}5HF$ were used in ECF of ethyl cinnamonitrile **1Ba**.

The anodic fluorination of phenyl 3,5-di-*t*-butyl-4-hydroxystyryl ketone yielded two monofluoro derivatives. Room temperature was found to be a sufficient electrolytic temperature for these reactions.

3. Experimental

The electrolytes, $Et_3N{\cdot}n$HF and $Et_4NF{\cdot}n$HF, were kind gifts of Morita Chemical Industries Co. Ltd. (Japan) and were used without purification.

Caution: They are toxic and contact with skin causes serious burns. Therefore, it is recommended that rubber gloves be used.

3.1. Anodic fluorination of unsaturated esters and ketones

Typical anodic difluorination conditions were as follows. Anodic oxidation of **1A** (1 mmol) and **1B** (1 mmol) was carried out with an undivided cell with a platinum anode and cathode (2 cm × 2 cm) in 15 mL fluorine source or in 8 mL fluorine source and 8 mL CH_2Cl_2 or MeCN. Anodic potentials were determined by cyclic voltammertry. The reference electrode was $Ag/AgNO_3$ (0.01 M) in MeCN containing $Et_4N{\cdot}BF_4$ (0.1 M).

Since positive oxidative potentials were involved, careful handling of the solvent supporting electrolyte system was

needed, moisture avoided, to ensure polymerization-free electrolysis.

The electrolytic mixture was diluted with water and extracted with three portions of CH_2Cl_2. The organic phase was washed with brine and dried over $MgSO_4$. After the removal of $MgSO_4$ by filtration, the products were isolated by column chromatography on silica gel and identified by ^1H- and ^{19}F NMR spectra, IR spectra, MS spectra and HMRS. Melting points were obtained on a Mel-Temp melting point apparatus and are uncorrected. IR spectra were obtained on FT/IR-410 Jasco spectometer. ^1H NMR and ^{19}F NMR spectra were recorded, in $CDCl_3$ as a solvent, on a JEOL Datum (400 MHz) spectrometer. The chemical shifts for ^1H NMR are reported in δ ppm downfield from internal TMS, and those for ^{19}F NMR are given in δ ppm downfield from internal C_6F_6, $\delta(CFCl_3)$ of the C_6F_6 reference being -162.2 ppm. All reactions with air-sensitive compounds were carried out under a nitrogen atmosphere. Column chromatography was conducted with silica gel. GC analyses were performed using a Hitachi G-5000 instrument (flame ionization detector, FID) with a 30 m column Neutra Bond.

The mass spectra of compounds **2A** (**a**–**e**), and **2Ba** contained the M^+ or $(M–HF)^+$ ions of low intensity and a number of strong, characteristic fragmentation ions (Table 2) allowed assignment of the structures.

All compounds were characterized by ^1H and ^{19}F NMR spectra, which confirmed their structure. The *threo* and *erythro* configurations of difluoro-compounds were unambigously demonstrated by the magnitude of vicinal H–F coupling constants (ca. 23–26 and 12–13 Hz, respectively) in their ^1H and ^{19}F NMR spectra. These values are characteristic for such structures as is shown in literature data [9].

*Ethyl 2,3-difluoro-3-phenylpropionate (**2Aa**)* was purified by flash chromatography on silica gel, eluting with 5:1 mixture of hexane and ethyl acetate to give a colorless oil.

threo: ^1H NMR: 1.31 (t, $J = 7$ Hz, 3H); 4.23 (q, $J = 7$ Hz, 2H); 5.06 (ddd, $J = 47.1$ Hz, $J = 25.6$ Hz, $J = 2.9$ Hz, 1H); 5.85 (ddd, $J = 44.6$ Hz, $J = 23.2$ Hz, $J = 2.9$ Hz, 1H); 7.1–7.4 (m, 5H). ^{19}F NMR: -15.2 (m, 1F); -41.7 (m, 1F). IR (neat, cm^{-1}) 1766 ($\nu_{C=O}$). HRMS: calcd. for $C_{11}H_{12}F_2O_2$ *m/e* 214.0805, found 214.0795.

Table 2
The most characteristic ions in the mass spectra of compounds **2A** and **B**

Compound	Ion; *m/z* (relative intensity)			
	M^+	$(M–HF)^+$	$(R–Ph–CHF–CHF)^+$	$(R–Ph–CHF)^+$
2Aa	214 (5)	194 (23)	141 (10)	109 (100)
2Ab	228 (10)	208 (25)	155 (9)	123 (100)
2Ad	232 (4)	212 (22)	159 (10)	127 (100)
2Ae	282 (10)	262 (20)	209 (14)	177 (100)

Compound	M^+	$(M–HF)^+$	$(Ph–CHF)^+$
2Ba	167 (28)	147 (17)	109 (100)

Compound **2Ac** could not be isolated and it was not further investigated.

erythro: ^1H NMR: 1.31 (t, $J = 7$ Hz, 3H); 4.26 (q, $J = 7$ Hz, 2H); 5.30 (ddd, $J = 49.3$ Hz, $J = 12.9$ Hz, $J = 3.4$ Hz, 1H); 5.83 (ddd, $J = 44.1$ Hz, $J = 20.7$ Hz, $J = 3.4$ Hz, 1H); 7.1–7.4 (m, 5H). ^{19}F NMR: -29.7 (m, 1F); -43.2 (m, 1F). IR (neat, cm^{-1}) 1766 ($\nu_{C=O}$). HRMS: calcd. for $C_{11}H_{12}F_2O_2$ *m/e* 214.0805, found 214.0795.

*Ethyl 2,3-difluoro-3-[4-methylphenyl] propionate (**2Ab**)* was purified by flash chromatography on silica gel, eluting with 5:1 mixture of hexane and ethyl acetate to give a colorless oil.

threo: ^1H NMR: 1.22 (t, $J = 7$ Hz, 3H); 2.32 (s, 3H); 4.28 (q, $J = 7$ Hz, 2H); 5.28 (ddd, $J = 47.3$ Hz, $J = 22.8$ Hz, $J = 3.4$ Hz, 1H); 5.78 (ddd, $J = 48.2$ Hz, $J = 23.2$ Hz, $J = 3.4$ Hz, 1H); 7.1–7.4 (m, 4H). ^{19}F NMR: -23.7 (m, 1F); -40.8 (m, 1F). IR (neat, cm^{-1}) 1767 ($\nu_{C=O}$). HRMS: calcd. for $C_{12}H_{14}F_2O_2$ *m/e* 228.0962, found 228.0949.

erythro: ^1H NMR: 1.23 (t, $J = 7$ Hz, 3H); 2.32 (s, 3H); 4.31 (q, $J = 7$ Hz, 2H); 4.98 (ddd, $J = 49.3$ Hz, $J = 12.2$ Hz, $J = 3.2$ Hz, 1H); 5.76 (ddd, $J = 44.2$ Hz, $J = 20.7$ Hz, $J = 3.2$ Hz, 1H); 7.1–7.4 (m, 4H). ^{19}F NMR: -28.3 (m, 1F); -42.1 (m, 1F). IR (neat, cm^{-1}) 1767 ($\nu_{C=O}$). HRMS: calcd. for $C_{12}H_{14}F_2O_2$ *m/e* 228.0962, found 228.0949.

*Ethyl 2,3-difluoro-3-[4-methoxyphenyl]propionate (**2Ac**)* was purified by flash chromatography on silica gel, eluting with 5:1 mixture of hexane and ethyl acetate to give a colorless oils. Only the *threo* isomer was isolated.

threo: ^1H NMR: 1.31 (t, $J = 7$ Hz, 3H); 3.82 (s, 3H); 4.28 (q, $J = 7$ Hz, 2H); 5.03 (ddd, $J = 47.3$ Hz, $J = 24.7$ Hz, $J = 3.2$ Hz, 1H); 5.77 (ddd, $J = 44.4$ Hz, $J = 22.7$ Hz, $J = 3.2$ Hz, 1H); 7.1–7.4 (m, 4H). ^{19}F NMR: -25 (m, 1F); -42.1 (m, 1F). IR (neat, cm^{-1}) 1767 ($\nu_{C=O}$). HRMS: calcd. for $C_{12}H_{14}F_2O_3$ *m/e* 244.0911, found 244.0886.

*Ethyl 2,3-difluoro-3-[4-fluorophenyl]propionate (**2Ad**)* was purified by flash chromatography on silica gel, eluting with 5:1 mixture of hexane and ethyl acetate to give a colorless oil.

threo: ^1H NMR: 1.27 (t, $J = 7$ Hz, 3H); 4.26 (q, $J = 7$ Hz, 2H); 5.02 (ddd, $J = 47.1$ Hz, $J = 25.4$ Hz, $J = 3$ Hz, 1H); 5.83 (ddd, $J = 44.4$ Hz, $J = 23.2$ Hz, $J = 3$ Hz, 1H); 7.1–7.4 (m, 4H). ^{19}F NMR: -28.2 (m, 1F); -43.3 (m, 1F); 50.1 (s, 1F). IR (neat, cm^{-1}) 1767 ($\nu_{C=O}$). HRMS: calcd. for $C_{11}H_{11}F_3O_2$ *m/e* 232.0711, found 232.0694.

erythro: ^1H NMR: 1.28 (t, $J = 7$ Hz, 3H); 4.28 (q, $J = 7$ Hz, 2H); 5.24 (ddd, $J = 49.3$ Hz, $J = 12$ Hz, $J = 3.4$ Hz, 1H); 5.87 (ddd, $J = 43.7$ Hz, $J = 21.5$ Hz, $J = 3.4$ Hz, 1H); 7.1–7.4 (m, 4H). ^{19}F NMR: -22.9 (m, 1F); -42.2 (m, 1F); 50.1 (s, 1F). IR (neat, cm^{-1}) 1767 ($\nu_{C=O}$). HRMS: calcd. for $C_{11}H_{11}F_3O_2$ *m/e* 232.0711, found 232.0694.

*Ethyl 2,3-difluoro-3-[4-tri-fluoromethylpheny]propionate (**2Ae**)* was purified by flash chromatography on silica gel, eluting with 5:1 mixture of hexane and ethyl acetate to give a colorless oil.

threo: ^1H NMR: 1.30 (t, $J = 7$ Hz, 3H); 4.29 (q, $J = 7$ Hz, 2H); 5.06 (ddd, $J = 46.8$ Hz, $J = 26.8$ Hz, $J = 2.7$ Hz, 1H); 5.83 (ddd, $J = 44.4$ Hz, $J = 23.6$ Hz, $J = 2.7$ Hz, 1H); 7.1–

7.4 (m, 4H). ^{19}F NMR: −98.6 (s, 3F); −131.3 (m, 1F); −142.9 (m, 1F). IR (neat, cm^{-1}) 1767 ($\nu_{C=O}$). HRMS: calcd. for $C_{12}H_{11}F_5O_2$ *m/e* 282.0679, found 282.0693.

erythro: ^{1}H NMR: 1.26 (t, J = 7 Hz, 3H); 4.30 (q, J = 7 Hz, 2H); 5.33 (ddd, J = 49.0 Hz, J = 13.4 Hz, J = 3.2 Hz, 1H); 5.94 (ddd, J = 44.2 Hz, J = 21.2 Hz, J = 3.2 Hz, 1H); 7.1–7.4 (m, 4H). ^{19}F NMR: −98.6 (s, 3F); −125.7 (m, 1F); −139.7 (m, 1F). IR (neat, cm^{-1}) 1767 ($\nu_{C=O}$). HRMS: calcd. for $C_{12}H_{11}F_5O_2$ *m/e* 282.0679, found 282.0693.

*2,3-Difluoro-3-phenylpropionitril (**2Ba**)* was purified by flash chromatography on silica gel, eluting with 10:1 mixture of hexane and ethyl acetate to give a colorless oil.

threo: ^{1}H NMR: 1.22 (t, J = 7 Hz, 3H); 4.26 (q, J = 7 Hz, 2H); 5.22 (ddd, J = 46.1 Hz, J = 17.8 Hz, J = 3.4 Hz, 1H); 5.82 (ddd, J = 45.6 Hz, J = 17.1 Hz, J = 3.4 Hz, 1H); 7.1–7.4 (m, 4H). ^{19}F NMR: −27.9 (m, 1F); −30.4 (m, 1F). IR (neat, cm^{-1}) 1767 ($\nu_{C=O}$). HRMS: calcd. for $C_9H_7F_2N$ *m/e* 167.0546, found 167.0561.

erythro: ^{1}H NMR: 1.26 (t, J = 7 Hz, 3H); 4.23 (q, J = 7 Hz, 2H); 5.34 (ddd, J = 46.8 Hz, J = 12.2 Hz, J = 5.7 Hz, 1H); 5.70 (ddd, J = 46.9 Hz, J = 12.2 Hz, J = 5.7 Hz, 1H); 7.1–7.4 (m, 4H). ^{19}F NMR: −23.7 (m, 1F); −31.94 (m, 1F). IR (neat, cm^{-1}) 1767 ($\nu_{C=O}$). HRMS: calcd. for $C_9H_7F_2N$ *m/e* 167.0546, found 167.0561.

*t-Butyl, 1,2-difluoro-2-phenyl-ethyl ketone (**2Ca**)* was purified by flash chromatography on silica gel, eluting with 20:1 mixture of hexane and ethyl acetate to give a colorless oil.

threo: ^{1}H NMR: 1.48 (s, 9H); 5.14 (ddd, J = 47.3 Hz, J = 27.1 Hz, J = 2.9 Hz, 1H); 5.96 (ddd, J = 44.6 Hz, J = 23.9 Hz, J = 2.9 Hz, 1H); 7.30–7.90 (m, 5H). ^{19}F NMR: −194.0 (m, 1F); −200.4 (m, 1F). IR (neat, cm^{-1}) 1698 ($\nu_{C=O}$). MS *m/z* 226 (M^+), 141 (Ph–CHF–CHF)$^+$, 109 (Ph–CHF)$^+$, 77 (Ph)$^+$. HRMS: calcd. for $C_{13}H_{16}F_2O$ *m/e* 226.1169, found 226.1167.

erythro: ^{1}H NMR: 1.49 (s, 9H); 5.37 (ddd, J = 49.2 Hz, J = 10.7 Hz, J = 4.1 Hz, 1H); 5.83 (ddd, J = 43.6 Hz, J = 20.9 Hz, J = 4.1 Hz, 1H); 7.30–7.90 (m, 5H). ^{19}F NMR: −187.9 (m, 1F); −198.4 (m, 1F). IR (neat, cm^{-1}) 1698 ($\nu_{C=O}$). MS *m/z* 226 (M^+), 141 (Ph–CHF–CHF)$^+$, 109 (Ph–CHF)$^+$, 77 (Ph)$^+$; HRMS: calcd. for $C_{13}H_{16}F_2O$ *m/e* 226.1169, found 226.1167.

*Phenyl, 1,2-difluoro-2-phenyl-ethyl ketone (**2Da**)* was purified by flash chromatography on silica gel, eluting with 20:1 mixture of hexane and ethyl acetate to give a colorless oil.

threo: ^{1}H NMR: 5.57 (ddd, J = 47.6 Hz, J = 25.4 Hz, J = 3.2 Hz, 1H); 6.02 (ddd, J = 44.9 Hz, J = 23.0 Hz, J = 3.2 Hz, 1H); 7.36–7.90 (m, 10H). ^{19}F NMR: −192.5 (m, 1F); −199.3 (m, 1F). IR (neat, cm^{-1}) 1698 ($\nu_{C=O}$). MS *m/z* 244 (M^+), 105 (Ph–CO)$^+$, 77 (Ph). HRMS: calcd. for $C_{15}H_{10}F_2O$ *m/e* 244.0700, found 244.0692.

erythro: ^{1}H NMR: 5.84 (ddd, J = 42.0 Hz, J = 6.3 Hz, J = 2.2 Hz, 1H); 5.98 (ddd, J = 44.2 Hz, J = 18.8 Hz, J = 2.2 Hz, 1H); 7.36–7.90 (m, 10H). ^{19}F NMR: −186.5 (m, 1F); −196.9 (m, 1F). IR (neat, cm^{-1}) 1698 ($\nu_{C=O}$). MS *m/z* 244 (M^+), 105 (Ph–CO)$^+$, 77 (Ph). HRMS: calcd. for $C_{15}H_{10}F_2O$ *m/e* 244.0700, found 244.0692.

*4-(2-Fluoro-3-oxo-3-phenylpropylidene)-2,6-di-t-butyl-cyclohexa-2,5-dien-1-one (**5**)* was purified by flash chromatography on silica gel, eluting with 20:1 mixture of hexane and ethyl acetate to give a yellowish-brown oil that crystallizes as yellowish-brown crystals (EtOH), mp 145 °C.

^{1}H NMR (400 MHz, $CDCl_3$): 1.24 (s, 9H); 6.33 (t, J = 15 Hz, 1H); 6.79 (s, 1H); 7.37 (dd, J = 15 Hz, 1H); 7.50 (t, J = 8Hz); 7.66 (t, J = 8Hz, 1H); 8.02 (d, J = 8Hz, 1H). ^{19}F NMR (400 MHz, $CDCl_3$): 71.6 (s, 1F). IR (neat, cm^{-1}) 1630 ($\nu_{C=O}$). HRMS: calcd. for $C_{23}H_{27}FO_2$ *m/e* 354.1995, found 354.1972.

*4-Fluoro-2,6-di-t-butyl-4-[(**1E**)-3-oxo-3-phenylprop-1-enyl]cyclohexa-2,5-dien-1-one (**6**)* was purified by flash chromatography on silica gel, eluting with 20:1 mixture of hexane and ethyl acetate to give a yellowish oil that crystallizes as yellow crystals (EtOH), mp 137–139 °C. ^{1}H NMR: 1.25 (s, 9H); 6.48 (s, 1H); 6.63 (dd, J = 15.2 Hz, J = 19 Hz, 1H); 7.31 (d, J = 15.2 Hz, 1H); 7.49 (t, J = 8 Hz, 1H); 7.58 (t, J = 8 Hz); 7.66 (t, J = 8 Hz, 1H); 7.96 (d, J = 8 Hz, 1H). ^{19}F NMR: 9.2 (s, 1F). IR (neat, cm^{-1}) 1640 ($\nu_{C=O}$). HRMS: calcd. for $C_{23}H_{27}FO_2$ *m/e* 354.1995, found 354.1962.

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