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Decarboxylative fluorination of β-Ketoacids with *N*-fluorobenzenesulfonimide (NFSI) for the synthesis of α-fluoroketones: Substrate scope and mechanistic investigation

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Dedicated to Prof. Dr. Antonio Togni on the occasion of his receipt of the ACS Award for Creative Work in Fluorine Chemistry 2017

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ABSTRACT

Cesium carbonate (Cs_2CO_3)-mediated decarboxylative fluorination of β-ketoacids using NFSI in the MeCN/H_2O mixed solvent system affords α-fluoroketones with a broad scope. Both electron-rich and electron-deficient α-non-substituted β-ketoacids are amenable to this protocol. The mechanistic study indicates that the reaction proceeds through electrophilic fluorination followed by decarboxylation, which is different from the decarboxylative fluorination of normal carboxylic acids.

1. Introduction

Organofluorine compounds are widely applied in pharmaceutical and agrochemical research owing to the unique effect of the fluorine in enhancing the bioactivity of organic molecules [1–4]. Carbon − fluorine bond formation has attracted increasing attention as an effective strategy for selective introduction of fluorine atoms [5–10]. Among many methods developed for this purpose, fluorinations via functional group transformation, such as deoxyfluorination [8], Balz-Schiemann fluorination [9] and halex fluorination [10], are among the most reliable ones due to their predictable site-selectivity. However, the extension of site-selective fluorination to other common functional groups, such as carboxylic acids, would provide new opportunities to access desired fluorinated compounds.

Carboxylic acids, which are ubiquitous organic compounds, have been frequently used as attractive synthetic precursors for site-specific decarboxylative functionalization reactions [11–13]. Recently, decarboxylative fluorination of aliphatic carboxylic acids has been well established to be efficient for the synthesis of alkyl fluorides under mild conditions [6,14–17]. Mechanistically, these reactions proceed through decarboxylation followed by radical fluorination [18]. During our investigation of the decarboxylative fluoroalkylation of α,β- and β,γ-unsaturated carboxylic acids (Scheme 1a) [19–22], we demonstrated that these reactions occur in a different manner, that is, via fluoroalkylation followed by decarboxylation.

Considering that the enol form of β-ketoacids are a special type of α,β-unsaturated carboxylic acids (Scheme 1b), we envisioned that β-ketoacids can undergo similar reactions as we previously reported. Indeed, β-ketoacids have been widely used as promising precursors for the generation of ketone enolate equivalents under very mild reaction conditions [23]. In 2015, Deng and coworkers reported the decarboxylative fluorination of β-ketoacids for the synthesis of α-fluoro ketones by using Selectfluor under phase-transfer conditions; however, the method is limited to electron-neutral and electron-rich substrates [24]. Herein, we report an improved method for the synthesis of α-fluoro ketones via transition-metal-free, fluorination-initiated decarboxylation of β-ketoacids with *N*-fluorobenzenesulfonimide (NFSI) (Scheme 1c).

2. Results and discussion

At the onset of our investigation, we chose β-ketoacid **1a** as a model substrate to survey the reaction conditions (Table 1). We screened the reaction conditions using different combinations of electrophilic fluorination reagent, solvent and base. When Selectfluor was used as the reagent, the reaction of **1a** in MeCN at room temperature for 12 h resulted in the complete conversion of **1a** and produced α-fluoro acetophenone (**2a**) in only trace amount (~2% yield) (Table 1, entry 1); however, α,α-difluoro acetophenone was formed in 31% yield, which probably arose from further fluorination of the monofluorinated β-ketoacid followed by decarboxylation [25]. In light of the amount of

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Scheme 1. Decarboxylative fluoroalkylation and fluorination of unsaturated carboxylic acids.

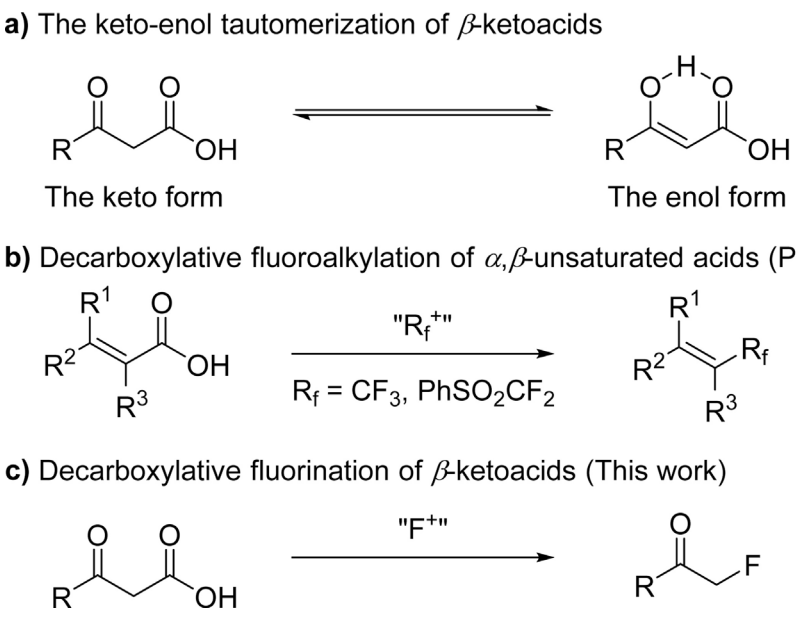
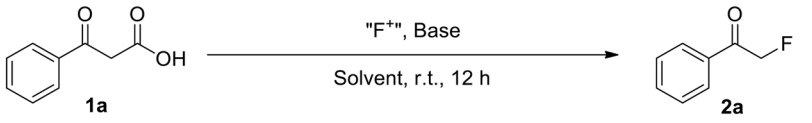


Table 1
Optimization of reaction conditions for decarboxylative fluorination of **1a**[a].



Entry	"F+" (equiv)	Solvent	Base (equiv)	Yield (%)[b]
1	Selectflour (1.0)	MeCN	-	~2[c]
2	Selectflour (1.0)/Quinine (1.0)	MeCN	-	77
3	NFSI (1.0)	MeCN	-	0
4	NFSI (1.0)	MeCN	K_2CO_3 (2.0)	72
5	NFSI (1.0)	THF	K_2CO_3 (2.0)	62
6	NFSI (1.0)	DMF	K_2CO_3 (2.0)	47
7	NFSI (1.0)	EtOAc	K_2CO_3 (2.0)	61
8	NFSI (1.0)	$CHCl_3$	K_2CO_3 (2.0)	7
9	NFSI (1.0)	$PhCH_3$	K_2CO_3 (2.0)	22
10	NFSI (1.0)	MeCN	Li_2CO_3 (2.0)	10
11	NFSI (1.0)	MeCN	Na_2CO_3 (2.0)	57
12	NFSI (1.0)	MeCN	$NaHCO_3$ (2.0)	27
13	NFSI (1.0)	MeCN	Cs_2CO_3 (2.0)	75
14	NFSI (1.0)	MeCN	iPr_2NH (2.0)	58
15	NFSI (1.0)	MeCN	Et_3N (2.0)	26
16	NFSI (1.2)	MeCN	Cs_2CO_3 (2.0)	76
17	NFSI (1.5)	MeCN	Cs_2CO_3 (2.0)	52
18	NFSI (1.0)	MeCN	Cs_2CO_3 (1.0)	65
19	NFSI (1.0)	MeCN	Cs_2CO_3 (3.0)	81
20	NFSI (1.0)	MeCN	Cs_2CO_3 (4.0)	74
21	NFSI (1.0)	MeCN	Cs_2CO_3 (3.0)	79[d]

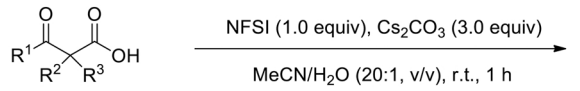
[a] All reactions were performed on 0.2 mmol scale in solvent (2.0 mL).
[b] Yield was determined by ^{19}F NMR spectroscopy using $PhSO_2CF_2H$ as an internal standard.
[c] $PhCOCF_2H$ was formed in 31% yield.
[d] Reaction time was 1 h.

Selectfluor used (only 1 equivalent), the over-fluorination indicates that Selectfluor is of high electrophilicity. To alleviate the reactivity of Selectfluor, we tried to add a tertiary amine as an additive to form a relatively weak "N-F" fluorinating reagent [26]. Thus, when Selectfluor was mixed with the same equivalent of quinine in advance, the fluorination of **1a** proceeded smoothly to give **2a** in good yield (77%) (Table 1, entry 2). Encouraged by the above preliminary results, we turned our attention to the use of NFSI, which contains a neutral fluorinated nitrogen atom and thus is expected to be a milder fluorinating reagent. The reaction conducted in the absence of a base, however, failed to give any fluorination product (Table 1, entry 3). The addition of K_2CO_3 promoted the reaction smoothly at room temperature, affording **2a** in 72% yield (Table 1, entry 4). A survey on the influence of solvent revealed that MeCN was the most suitable solvent (Table 1, entries 4–9). In terms of the base, Cs_2CO_3 was established to be slightly superior to K_2CO_3 (Table 1, entries 10–15). The molar ratio **1a**/NFSI/Cs_2CO_3 was further optimized to 1.0:1.0:3.0, and **2a** was obtained in 81% yield as the only fluorinated ketone product (Table 1, entries 16–20). An additional investigation showed that the reaction time could be shortened to 1 h without significant loss of the yield (Table 1, entries 21).

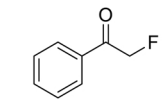
Then we continued to examine the substrate scope of the reaction between *β*-ketoacids **1** and NFSI. Initially, we applied the optimized reaction conditions (as described in Table 1, entry 21) to other *β*-ketoacids such as **1b**; however, we quickly realized that the reaction is sensitive to the solubility of **1** in MeCN and a relatively low solubility usually led to decreased yield. We found that adding water to improve the solubility is beneficial for the desired fluorination. Therefore, we modified the optimized conditions as listed under entry 21 (Table 1) by using water as a co-solvent and the scope of aryl substituted *β*-ketoacids are shown in Table 2. Various substituents on the aryl ring at the *β*-position, both electron-donating (**1a-1f**) and electron-withdrawing (**1g-1j**), are compatible with the reaction conditions, and the monofluorination products were obtained in good yields. Moreover, fully aliphatic substrates also worked well after a slight modification of reaction conditions, which is exemplified by the reaction of **1k** to give **2k** in moderate yield. Compared with the recently reported method using Selectfluor in aqueous media [24], our method is more suitable for the decarboxylative monofluorination of *β*-ketoacids bearing an electron-deficient *β*-aryl substituent such as F, Cl, Br, and CF_3. However, the current protocol is not compatible with α-substituted *β*-ketoacids such as 2-methyl-3-oxo-3-phenylpropanoic acid (**1l**) and 2,2-dimethyl-3-oxo-3-phenylpropanoic acid (**1r**). The reaction of **1 l** afforded the desired monofluorination product **2 l** in only 24% yield, whereas the reaction of **1r** failed to afford any fluorination products. As a complementary, we achieved the decarboxylative monofluorination of α-monosubstituted *β*-ketoacids **1l-1p** by using Selectfluor instead of NFSI (Table 3). In all cases, no difluorination products were detected.

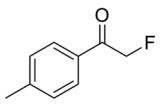
To gain insight into the reaction mechanism, we monitored the progress of the reaction of *β*-ketoacid **1a** and NFSI by variable-

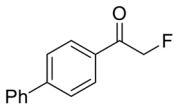
Table 2
Decarboxylative fluorination of various β-ketoacids with NFSI[a].

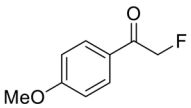


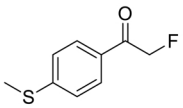
1 **2**

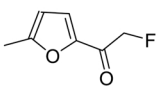

2a, 74%

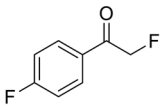

2b, 84%

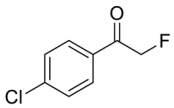

2c, 85%

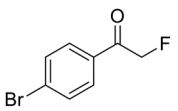

2d, 78%

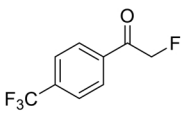

2e, 72%

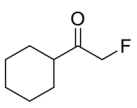

2f, 77%

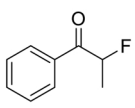

2g, 76%

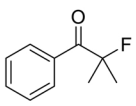

2h, 76%


2i, 76%


2j, 76%


2k, 66%[b,c]


2l, 24%[c]

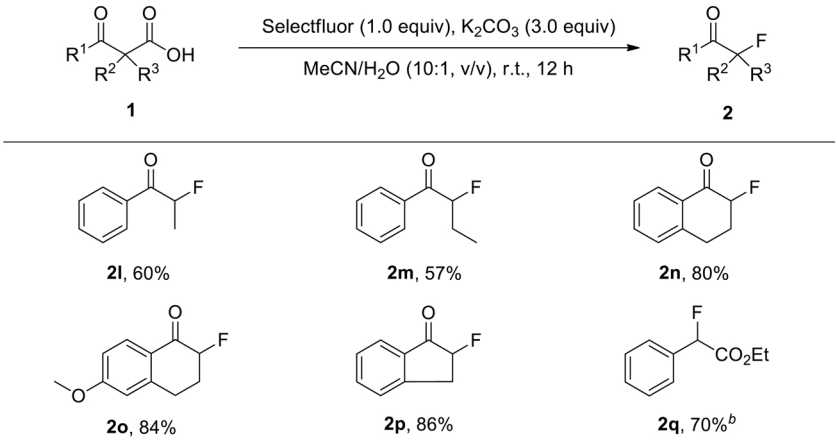

2r, 0%

[a] General conditions: **1** (0.5 mmol), NFSI (0.5 mmol), Cs_2CO_3 (1.5 mmol), MeCN/H_2O (20:1, v/v, 10.5 mL), r.t., 1 h. Unless otherwise noted, isolated yields were given.

[b] The reaction was performed at r.t. for 2 h, then at 60 °C for 40 min.

[c] ^{19}F NMR yield with $PhOCF_3$ as an internal standard.

Table 3
Decarboxylative fluorination of α-monosubstituted β-ketoacids with Selectfluor[a].



[a] Conditions: **1** (0.5 mmol), Selectfluor (0.5 mmol), K_2CO_3 (1.5 mmol), MeCN/H_2O (10:1, v/v, 11 mL), r.t., 12 h. Unless otherwise noted, isolated yields were given.
[b] ^{19}F NMR yield with $PhOCF_3$ as an internal standard.

temperature (VT) ^{19}F NMR spectroscopy (Fig. 1). When **1a**, NFSI and Cs_2CO_3 were mixed in a 1.0:1.0:3.0 ratio in MeCN/H_2O (20:1, v/v) at 0 °C, a fast consumption of NFSI [δ −39.4 ppm (s)] led to the generation of α-fluoro-β-ketocarboxylate salt **3a** [δ −179.7 ppm (d, $^2J_{H\text{-}F}$ = 56 Hz)] as the major intermediate product (Fig. 1a-1b). The decarboxylation of **3a** to form **2a** [δ −233.4 ppm (t, $^2J_{H\text{-}F}$ = 47 Hz)] was slow at 0 °C (Fig. 1c-1d); however, an increase in the temperature significantly accelerated the formation of **2a** (Fig. 1e-1f). This experiment indicated that: (1) the monofluorination of β-ketoacid **1a** is much faster than the decarboxylation of both **1a** itself and the fluorinated intermediate **3a**, and (2) the further fluorination of α-fluoro-β-ketocarboxylate salt **3a** is much slower than the fluorination of the carboxylate salt of **1a**, probably due to the steric hindrance of a fluorine substitution, which is in line with the aforementioned sluggish fluorination of β-ketoacid **1 l** with NFSI.

Based on the above experimental results, we proposed that the decarboxylative fluorination of α-nonsubstituted β-ketoacids with NFSI might proceed via the mechanism as depicted in Scheme 2. Initially, β-ketoacid **1,** which was in equilibrium with its enol form, was deprotonated by Cs_2CO_3 to give a dianion intermediate **4**. Subsequently,

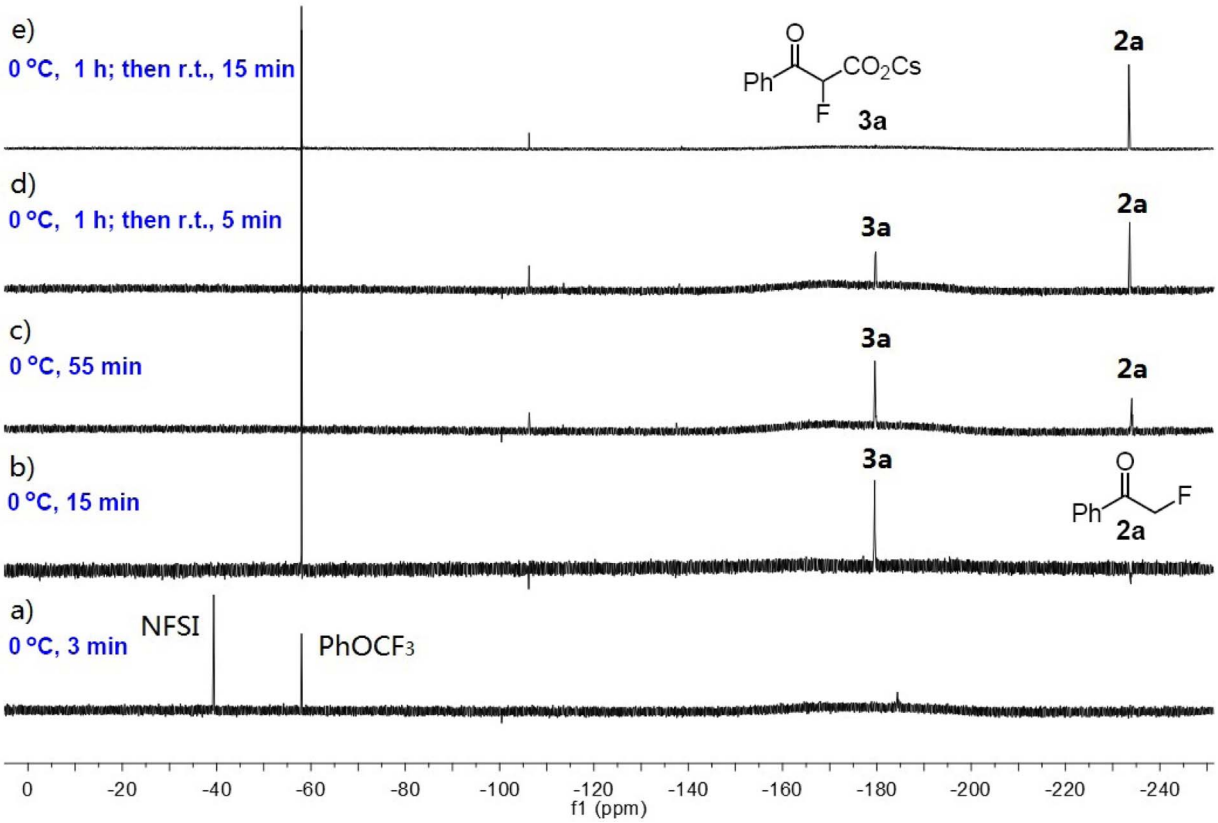
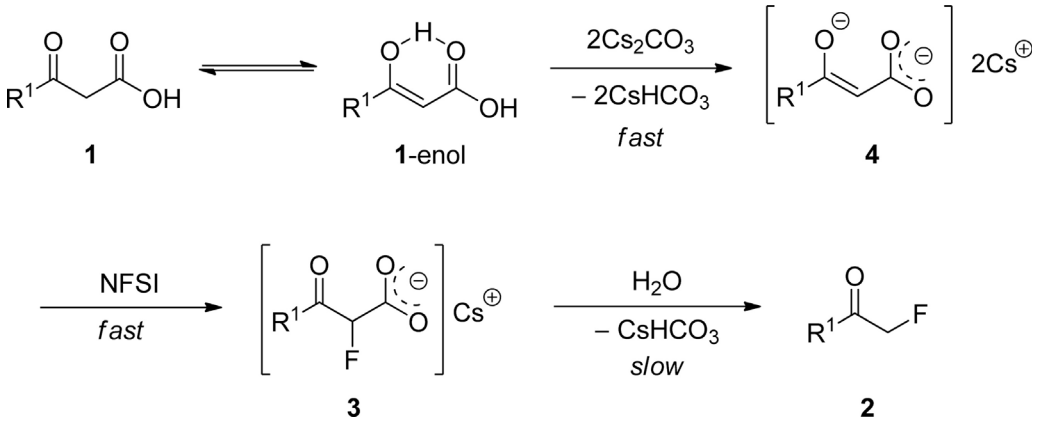


Fig. 1. Monitoring of the reaction of **1a**, NFSI and Cs_2CO_3 in MeCN/H_2O by VT ^{19}F NMR spectroscopy. $PhOCF_3$ was used as an internal standard. a–c) Reaction was performed at 0 °C for 3, 15 and 55 min, respectively; d–e) Reaction was performed at 0 °C for 1 h, then at r.t. for 5 and 15 min, respectively.



Scheme 2. Proposed mechanism.

intermediate **4** underwent a fast electrophilic fluorination with NFSI to afford α-fluoro-*β*-ketocarboxylate salt **3**. Finally, the slow decarboxylation of intermediate **3** resulted in the final product α-fluoroketone **2**. The compatibility of this protocol with electron-deficient *β*-ketoacids can be attributed to the moderate reactivity of NFSI in the mixed solvent system of MeCN/H_2O, which can readily fluorinate various α-nonsubstituted *β*-ketoacids with high selectivity.

3. Conclusion

In summary, we have described a new protocol for the synthesis of α-fluoroketones, that is, Cs_2CO_3-mediated decarboxylative fluorination of *β*-ketoacids using NFSI in the mixed solvent system MeCN/H_2O. Both electron-rich and electron-deficient α-nonsubstituted *β*-ketoacids could be converted into the corresponding α-fluoroketones in good yields. The mechanistic study by variable temperature ^{19}F NMR shows that the reaction proceeded through electrophilic fluorination (C-F bond formation) followed by decarboxylation, which is different from the decarboxylative fluorination of normal carboxylic acids.

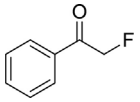
4. Experimental

Unless otherwise mentioned, solvents and reagents were purchased from commercial sources and used as received. The solvents MeCN and DMF were distilled over CaH_2. The solvents THF and toluene were distilled over sodium. All the *β*-ketoacids were prepared according to reported procedures [27,28]. ^1H, ^{19}F and ^{13}C NMR spectra were recorded on a Bruker AM-300 NMR, VarianMercury-300, or Agilent MR-400 NMR spectrometer. ^1H NMR chemical shifts were determined relative to internal $(CH_3)_4Si$ (TMS) at *δ* 0.0 or to the signal of a residual protonated solvent $CDCl_3$ at *δ* 7.26. ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ at *δ* 0.0. ^{13}C NMR chemical shifts were determined relative to internal $(CH_3)_4Si$ (TMS) at *δ* 0.0. MS (EI-MS) were obtained on an Agilent 5975C gas chromatography and HP5989A mass spectrometer. MS (ESI) were obtained on an AGILENT1100 mass spectrometer. HRMS(EI) were recorded on a Waters Micromass GCT Premier mass spectrometer.

4.1. Typical procedures for decarboxylation fluorination of α-nonsubstituted β-ketoacids with NFSI

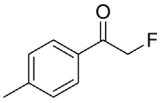
Into a 20-mL Schlenk flask equipped with a stirring bar were added *β*-ketoacid **1a** (82.0 mg, 0.5 mmol), *N*-fluorobenzenesulfonimide (NFSI) (167.7 mg, 0.5 mmol), Cs_2CO_3 (188.7 mg, 1.5 mmol), MeCN (10 mL), and H_2O (0.5 mL). The mixture was stirred for 1 h at room temperature and then filtered through Celite layer. The filtrate was concentrated *in vacuo* and purified using flash column chromatography (silica gel; petroleum ether/diethyl ether, 5:1, v/v) to give **2a** (51.1 mg, 74% yield) as colorless oil.

4.1.1. 2-Fluoro-1-phenylethanone (2a)[29,30]



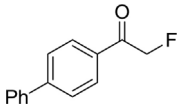
51.1 mg, 74% yield, colorless oil. ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.89–7.87 (m, 2H), 7.62–7.59 (m, 1H), 7.50–7.46 (m, 2H), 5.51 (d, *J* = 47.0 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$): *δ* −230.8 (t, *J* = 46.9 Hz, 1F); MS (EI, *m/z*, %): 138 (M^+, 10.05), 105 (100.00). The ^1H and ^{19}F NMR data are consistent with previous reports [29,30].

4.1.2. 2-Fluoro-1-(p-tolyl)ethanone (2b) [29]



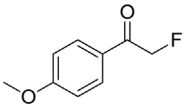
64.0 mg, 84% yield, white solid. ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.79 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 5.51 (d, *J* = 47.0 Hz, 2H), 2.43 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): *δ* −229.8 (t, *J* = 47.1 Hz); MS (EI, *m/z*, %): 152 (M^+, 21.50), 119 (100.00). The ^1H and ^{19}F NMR data are consistent with previous report [29].

4.1.3. 1-([1,1′-Biphenyl]-4-yl)-2-fluoroethanone (2c) [30]



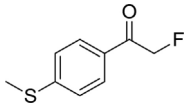
90.9 mg, 85% yield, white solid. ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.98–7.96 (m, 2H), 7.71–7.69 (m, 2H), 7.63–7.60 (m, 2H), 7.49–7.45 (m, 2H), 7.43–7.39 (m, 1H), 5.54 (d, *J* = 46.9 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$): *δ* −230.35 (t, *J* = 47.0 Hz, 1F); MS (EI, *m/z*, %): 214 (M^+, 29.64), 181 (100.00). The ^1H and ^{19}F NMR data are consistent with previous report [30].

4.1.4. 2-Fluoro-1-(4-methoxyphenyl)ethanone (2d) [29,30]



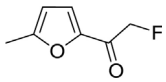
65.5 mg, 78% yield, white solid. ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.88 (d, *J* = 8.9 Hz, 2H), 6.95 (d, *J* = 8.9 Hz, 2H), 5.46 (d, *J* = 47.1 Hz, 2H), 3.87 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): *δ* −229.86 (t, *J* = 47.0 Hz, 1F); MS (EI, *m/z*, %): 168 (M^+, 13.28), 135 (100.00). The ^1H and ^{19}F NMR data are consistent with previous reports [29,30].

4.1.5. 2-Fluoro-1-(4-(methylthio)phenyl)ethanone (2e)



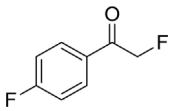
66.3 mg, 72% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, J = 8.7 Hz, 2H), 7.29 (d, J = 8.5 Hz, 2H), 5.48 (d, J = 47.0 Hz, 2H), 2.53 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ −230.15 (t, J = 47.0 Hz, 1F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.4 (d, J = 15.6 Hz), 147.5, 129.8 (s), 128.2 (d, J = 2.8 Hz), 125.1, 83.5 (d, J = 182.3 Hz), 14.6; MS (EI, m/z, %): 184 (M^+, 34.74), 151 (100.00); HRMS (EI): Calcd. For C_9H_9OFS: 184.0358; Found: 184.0359.

4.1.6. 2-Fluoro-1-(5-methylfuran-2-yl)ethanone (2f)



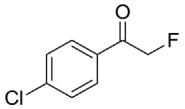
54.6 mg, 77% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.30 (m, 1H), 6.22–6.21 (m, 1H), 5.26 (d, J = 47.1 Hz, 2H), 2.41 (s, 3H); ^{19}F NMR (282 MHz, $CDCl_3$): δ −234.25 (t, J = 47.2 Hz, 1F); ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.9 (d, J = 17.8 Hz), 159.0, 148.6, 121.6 (d, J = 7.0 Hz), 109.4 (d, J = 1.3 Hz), 83.1 (d, J = 183.0 Hz), 14.0; MS (EI, m/z, %): 142 (M^+, 26.19), 109 (100.00). HRMS (EI): Calcd. For $C_7H_7O_2F$: 142.0430; Found: 142.0424.

4.1.7. 2-Fluoro-1-(4-fluorophenyl)ethanone (2g) [30]



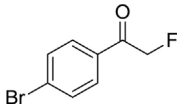
59.1 mg, 76% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98–7.94 (m, 2H), 7.74–7.16 (m, 2H), 5.48 (d, J = 47.0 Hz, 2H); ^{19}F NMR (282 MHz, $CDCl_3$): δ −102.76 (s, 1F), −229.23 (t, J = 46.9 Hz, 1F); MS (EI, m/z, %): 156 (M^+, 6.01), 123 (100.00). The ^{1}H and ^{19}F NMR data are consistent with previous report [30].

4.1.8. 1-(4-Chlorophenyl)-2-fluoroethanone (2 h) [30]



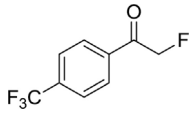
65.7 mg, 76% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, J = 8.5 Hz, 2H), 7.48 (d, J = 8.7 Hz, 2H), 5.48 (d, J = 46.9 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$): δ −229.69 (t, J = 46.9 Hz, 1F); MS (EI, m/z): 172 (M^+, 9.22), 139 (100.00). The ^{1}H and ^{19}F NMR data are consistent with previous report [30].

4.1.9. 1-(4-Bromophenyl)-2-fluoroethanone (2i) [30]



81.8 mg, 76% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 8.7 Hz, 2H), 5.47 (d, J = 46.9 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −229.79 (t, J = 46.2 Hz, 1F); MS (ESI, m/z, %): 214.90 (M-H$^-$, 100.00). The ^{1}H and ^{19}F NMR data are consistent with previous report [30].

4.2. -Fluoro-1-(4-(trifluoromethyl)phenyl)ethenone (2j) [31]

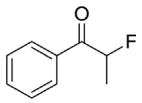


78.4 mg, 76% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.2 Hz, 2H), 7.76 (d, J = 8.2 Hz, 2H), 5.52 (d, J = 46.8 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.82 (s, 3F), −230.30 (t, J = 46.8 Hz, 1F); MS (ESI, m/z, %): 205.0 (M^+-H, 100.00). The ^{1}H and ^{19}F NMR data are consistent with previous report [31].

4.3. Typical procedures for decarboxylation fluorination of α-monosubstituted β-ketoacids with selectfluor

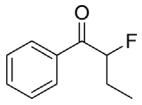
Into a 20-mL Schlenk flask equipped with a stirring bar were added β-ketoacid **11** (89.0 mg, 0.5 mmol), 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (Selectfluor) (177.3 mg, 0.5 mmol), K_2CO_3 (207.3 mg, 1.5 mmol), and MeCN (10 mL), and H_2O (1 mL). The mixture was stirred at room temperature for 12 h and then filtered through Celite layer. The filtrate was concentrated *in vacuo* and purified using flash column chromatography (silica gel; petroleum ether/diethyl ether, 5:1, v/v) to give **2 l** (53.9 mg, 78% yield).

4.3.1. 2-Fluoro-1-phenylpropan-1-one (2l)[32]



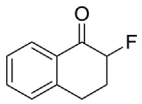
45.8 mg, 60% yield, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99–7.96 (m, 2H), 7.63–7.44 (m, 3H), 5.71 (dq, J = 48.6, 6.8 Hz, 1H), 1.67 (dd, J = 24.0, 6.8 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −181.50 (dq, J = 48.2, 24.0 Hz, 1F); Ms (ESI, m/z, %): 175.05 (M + Na^+, 100.00). The ^{1}H and ^{19}F NMR data are consistent with previous reports [32].

4.3.2. -Fluoro-1-phenylbutan-1-one (2m) [33]



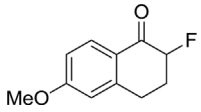
47.1 mg, 57% yield, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00–7.97 (m, 2H), 7.65–7.46 (m, 3H), 5.54 (ddd, J = 49.3, 7.7, 4.5 Hz, 1H), 2.17–1.92 (m, 2H), 1.11 (t, J = 7.4 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −191.0 (m, 1F); Ms (ESI, m/z, %): 189.10 (M + Na^+, 100.00). The ^{1}H and ^{19}F NMR data are consistent with previous report [33].

4.3.3. 2-Fluoro-3,4-dihydronaphthalen-1(2H)-one (2n) [30]



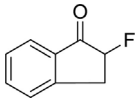
65.6 mg, 80% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 7.9 Hz, 1H), 7.53 (td, J = 7.6, 1.3 Hz, 1H), 7.36 (t, J = 7.6 Hz, 1H), 7.31–7.24 (m, 1H), 5.15 (ddd, J = 47.9, 12.8, 5.2 Hz, 1H), 3.14 (dd, J = 9.2, 4.0 Hz, 2H), 2.60–2.55 (m, 1H), 2.41–2.31 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −190.8 (m, 1F); Ms (ESI, m/z, %): 187.10 (M + Na^+, 100.00). The ^{1}H and ^{19}F NMR data are consistent with previous report [30].

4.3.4. 2-Fluoro-6-methoxy-3,4-dihydronaphthalen-1(2H)-one (**2o**) [34]



81.6 mg, 84% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.8 Hz, 1H), 6.85 (dd, J = 8.8, 2.5 Hz, 1H), 6.69 (d, J = 2.4 Hz, 1H), 5.08 (ddd, J = 48.0, 12.4, 5.1 Hz, 1H), 3.85 (s, 3H), 3.07 (dd, J = 9.1, 4.1 Hz, 2H), 2.57–2.50 (m, 1H), 2.31 (tdt, J = 12.5, 9.5, 7.1 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −190.9 (m, 1F); Ms (ESI, *m/z*, %): 195.05 (M + H^+, 100.00). The ^{1}H and ^{19}F NMR data are consistent with previous report [34].

4.3.5. 2-Fluoro-2,3-dihydro-1H-inden-1-one (**2p**)[33]



64.6 mg, 86% yield, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 7.7 Hz, 1H), 7.63 (t, J = 7.5 Hz, 1H), 7.44–7.37 (m, 2H), 5.22 (ddd, J = 51.0, 7.8, 4.3 Hz, 1H), 3.63–3.52 (m, 1H), 3.22–3.11 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −194.47 (ddd, J = 51.0, 23.4, 7.2 Hz, 1F); Ms (ESI, *m/z*, %): 173.05 (M + Na^+, 100.00). The ^{1}H and ^{19}F NMR data are consistent with previous report [33].

Acknowledgements

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