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Palladium-catalyzed direct mono-α-arylation of α-fluoroketones with aryl halides or phenyl triflate

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ABSTRACT

A palladium catalyzed Negishi-type α-arylation of α-fluoroketones with electron-rich and electron-deficient aryl halides or phenyl triflate has been developed. This direct mono-α-arylation method generate a variety of ternary α-aryl-α-monofluoroketones easily in good to excellent yields using XPhos as ligand and Cs_2CO_3 as mild base.

1. Introduction

Fluorinated compounds have been extensively used as pharmaceuticals, agrochemicals, fine chemicals and material science [1]. In particular, 5–15% of the total number of drugs launched worldwide over the past 50 years bear fluorinated substituents [2]. α-Fluoroketones are extremely valuable building blocks in medicinal and biological chemistry and can be easily transformed into chiral β-fluoroamines [3], β-fluoroalcohols [4] and a large number of interesting molecules [5]. Accordingly, several methods have been developed for the preparation of α-aryl-α-fluoroketones via direct electrophilic/nucleophilic fluorination methods or building block strategies (Scheme 1) [6]. These transformations, however, have some practical drawbacks, such as low functionality compatibility or high cost of fluorinated reagents.

Pioneered by the groups of Buchwald [7], Hartwig [8] and Miura [9], transition-metal-catalyzed direct α-arylation of ketones has emerged as a general methodology for the formation of C(sp^3)-C (sp^2) bonds and employed in the arylation of esters, amides, lactones and aldehydes. Shreeve described that the cyclic α-fluoroketone could be directly coupled with aryl bromides, however the arylation of open-chain α-fluoroketone failed [10]. Qing group reported palladium-catalyzed direct α-arylation of α-monofluorinated ketones and α,α-difluoroketones with aryl bromides, which afford quaternary fluorinated α-aryl ketones [11]. Knauber developed an efficient Pd/Xphos-catalyzed α-arylation of acyclic sulfones and sulfonamides in the presence of tmp·ZnCl·LiCl which promised high monoselectivity for the arylation [12]. Recently, we have developed a practical and efficient route to α-fluoroketones from trifluoromethyl β-diketones through decarboxylation process [13]. Herein we report an efficient palladium-catalyzed direct monoselective α-arylation of terminal α-fluoroketones with aryl halides or phenyl triflate (Scheme 1). This method provides an efficient and straightforward access to a variety of ternary α-aryl-α-monofluoroketones.

2. Results and discussion

Initial direct α-arylation conditions were optimized using 2-fluoro-1-phenylethan-1-one **1a** with bromobenzene **2a** as model compounds and the results were shown in Table 1. Generally the arylation of α-fluorinated ketones required weak base, such as $K_3PO_4·3H_2O$ [11], for α-fluorinated ketones suffered from the problem of defluorination in harsh basic circumstances [14]. Unfortunately, the reaction was complicated when $K_3PO_4·3H_2O$ was used as base (Table 1, entries 1–2). When cesium carbonate was used, the desired monoarylation product **3aa** was isolated in 16% yield associated with overarylated side product **4aa** (11%) (entry 5). Further investigation revealed that both the catalytic activity and monoselectivity were highly sensitive to the components of the catalyst system. Replacement of $Pd(OAc)_2$ with either $Pd_2(dba)_3$ or $Pd(dba)_2$ resulted in inferior yields of **3aa** (entries 7–9). In addition, the choice of ligand proved to be quite

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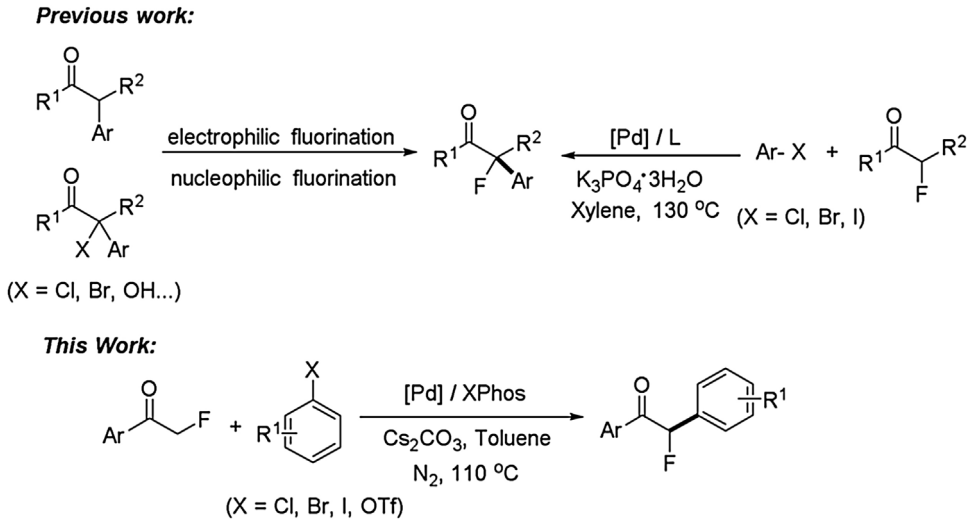
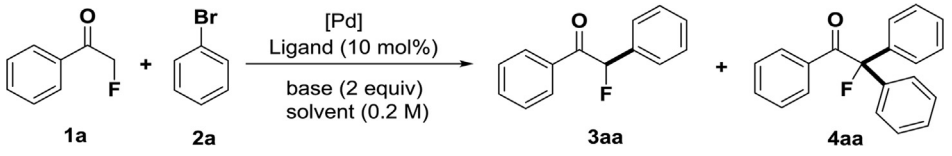
0022-1139/



Scheme 1. Synthetic strategies to α-aryl-α-fluoroketones.

Table 1
Screen proper bases and ligands for Pd-catalyzed mono-α-arylation of α-fluoroketone **1a** with bromobenzene.[a]



Entry	[Pd] (mol%)	Ligand	Base	Solvent	T/°C	t/h	Yield/%[b]	
							3aa	**4aa**
1	$Pd(OAc)_2$ (5.0)	PPh_3	$K_3PO_4·3H_2O$	Xylene	130	10	Complicated	
2	$Pd(OAc)_2$ (5.0)	BINAP	$K_3PO_4·3H_2O$	Xylene	130	10	Complicated	
3	$Pd(OAc)_2$ (5.0)		Cs_2CO_3	Xylene	130	10	N.R.	
4	$Pd_2(dba)_3$ (5.0)		Cs_2CO_3	Xylene	130	10	trace	
5	$Pd(OAc)_2$ (5.0)	PPh_3	Cs_2CO_3	Xylene	130	10	16	11
6	$Pd(OAc)_2$ (5.0)	BINAP	Cs_2CO_3	Xylene	130	10	34	10
7	$Pd(OAc)_2$ (5.0)	Xphos	Cs_2CO_3	Xylene	130	10	88	3
8	$Pd_2(dba)_3$ (2.5)	Xphos	Cs_2CO_3	Xylene	130	10	30	6
9	$Pd(dba)_2$ (5.0)	Xphos	Cs_2CO_3	Xylene	130	10	41	38
10	XphosPdG2 (2.0)		Cs_2CO_3	Toluene	110	10	69	4
11	XphosPdG2 (5.0)		Cs_2CO_3	Toluene	110	10	74	5
12	**$Pd(OAc)_2$ (5.0)**	**Xphos**	**Cs_2CO_3**	**Toluene**	**110**	**10**	**91**	**2**
13	$Pd(OAc)_2$ (5.0)	Xphos	Cs_2CO_3	Toluene	110	8	90	2
14	$Pd(OAc)_2$ (10.0)	Xphos	Cs_2CO_3	Toluene	110	8	89	8
15[c]	$Pd(OAc)_2$ (5.0)	Xphos	Cs_2CO_3	Toluene	110	8	90	5

[a] Reaction conditions: 0.2 mmol **1a**, 0.24 mmol **2a**, 10 mol% ligand, 2.0 equiv base, solvent (0.2 mol·L^{-1} of **1a**).
[b] Isolated yield.
[c] 0.4 mmol **2a** was used.

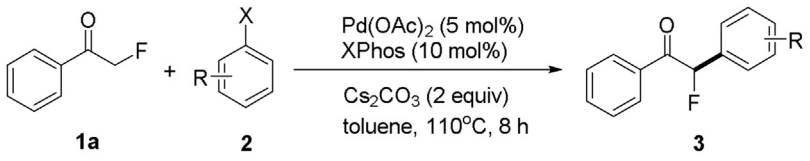
significant, as no products were isolated without ligand (entries 3–4). Next opitimization revealed that superior yields of **3aa** were achieved when Xphos was used as ligand instead of PPh_3 or BINAP (entries 5–7). When XphosPdG2 was used as combined catalyst, the reaction of **1a** with **2a** in toluene at 110 °C proceed smoothly to give **3aa** in 69% and 74% yields, respectively (entries 10–11). Notably, the reaction temperature could be lowered to 110 °C in toluene with good yields and preserved monoarylation selectivity (entries 12–15).

With 5 mol% $Pd(OAc)_2$ and 10 mol% Xphos as catalyst mixture for the addition of **1a** to **2a** in the presence of Cs_2CO_3 (2 equiv) at 110 °C as the optimized monoarylation conditions, we sought to explore the scope of the reaction for other aryl halides, heteroaromatic halides or phenyl triflate. As shown in Table 2, the arylation of α-fluoroketone **1a** with electron-rich and electron-poor aryl halide substrates **2** proceeded to the corresponding monoarylated α-fluoroketones **3** in good to excellent yields. Surprisingly the substrate 4-bromobenzonitrile was proved to be much more problematic (**3ae**, 21% yield) [15]. Next, various α-fluoro aryl ketones with aryl halides or phenyl triflate were examined for this transformation, and the results were presented in Table 3. We were pleased to find that the reaction between α-fluoroketones **1** and a broad range of aryl halides or phenyl triflate **2** led to formation of the desired α-fluoro-α-aryl ketones in good to excellent yields, and overarylation was not detected.

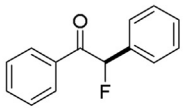
3. Conclusion

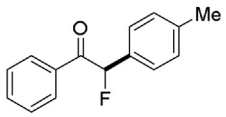
In summary, we have developed a convenient method of Pd-catalyzed monoselective α-arylation of α-fluoroketones with

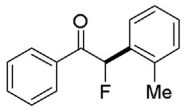
Table 2
Pd-catalyzed α-monoarylation of **1a** with aryl halides or phenyl triflate. [a,b]

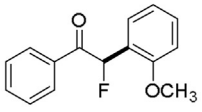


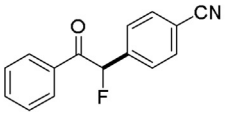
1a 2 3

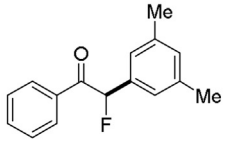

3aa: 86% (X = Cl)
91% (X = Br)
97% (X = I)
94% (X = OTf)

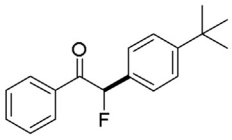

3ab: 82% (X = Cl)
93% (X = Br)

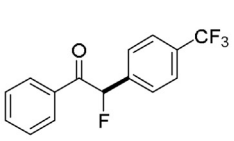

3ac: 94% (X = Br)

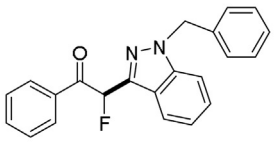

3ad: 90% (X = Br)
98% (X = I)


3ae: 21% (X = Br)


3af: 72% (X = Br)


3ag: 87% (X = Br)


3ah: 74% (X = Br)


3ai: 89% (X = Br)

[a] Reaction conditions: 5 mol% $Pd(OAc)_2$, 10 mol% XPhos, 1.2 equiv aryl halide or phenyl triflate, 2.0 equiv Cs_2CO_3, toluene (0.2 mol L^{-1} of **1a**), 110 °C, 8 h, at 0.2 mmol scale.
[b] Isolated yield.

various aryl halides or phenyl triflate. In view of the ease of conducting such reactions and the relative mild reaction conditions, we expect this protocol to be widely adapted in synthetic chemistry.

4. Experimental

4.1. General

All reactions were carried out in oven-dried glassware under a nitrogen atmosphere. α-Fluoroketones were prepared according to literature procedures [13]. All commercially available reagents were used without further purification, unless specified otherwise.

All new compounds were characterized by ^1H NMR, ^{19}F NMR, ^{13}C NMR and IR spectroscopy, in addition to high-resolution mass spectroscopy (HRMS) and low-resolution mass spectroscopy (LRMS). IR spectra (KBr) were recorded on a Nicolet 6700 spectrophotometer. LRMS and HRMS Mass Spectra were recorded on a Waters GCT Premier mass spectrometer with electron impact (70 eV). ^1H (400 MHz) and ^{13}C (101 MHz) NMR spectra were recorded on a Bruker AM-400 spectrometer with Me_4Si as an internal standard. ^{19}F NMR spectra were obtained on a Bruker AM-400 (376 MHz) spectrometer in $CDCl_3$ with $CFCl_3$ as an external standard, in which downfield shifts were designated as negative. All chemical shifts (δ) are expressed in parts per million and coupling constants (*J*) are given in hertz.

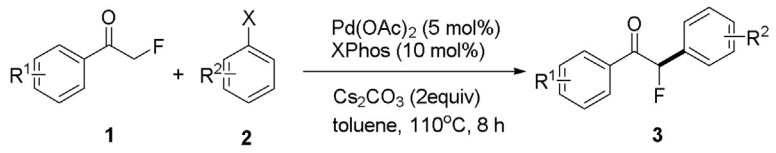
4.2. General procedure for Pd-catalyzed mono-α-arylation of α-fluoroketones with aryl halides or phenyl triflate

An oven-dried Schlenk tube containing a magnetic stirring bar was charged with $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), XPhos (9.6 mg, 0.02 mmol), and Cs_2CO_3 (130.0 mg, 0.4 mmol). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with nitrogen for three times. Toluene (2 mL) was added through the septum via syringe and the resulting mixture was stirred at room temperature for 15 min. Then α-fluoroketone **1** (0.2 mmol) and aryl halides or phenyl triflate **2** (0.24 mmol) were added. The Schlenk tube was sealed and the reaction mixture was heated at 110 °C with vigorous stirring for 8 h. The reaction mixture was cooled to room temperature and quenched with enough saturated aqueous NH_4Cl. The solution was extracted with ethyl acetate (3–10 mL), and the combined organic layers were washed with saturated brine, dried over anhydrous sodium sulfate, filtered, and concentrated in a vacuum. The crude product was purified by flash column chromatography on silica gel using petroleum ether/ethyl acetate or petroleum ether/dichloromethane as eluent.

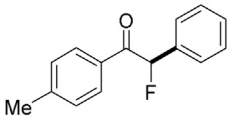
4.2.1. 2-Fluoro-1,2-diphenylethan-1-one (***3aa***) [16]

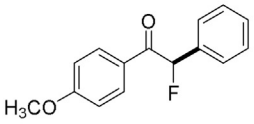
^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.4 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.49 (dd, *J* = 6.3, 1.4 Hz, 2H), 7.46–7.34 (m, 5H), 6.51 (d, *J* = 48.6 Hz, 1H). IR (neat, cm^{-1}): 3065, 2923, 1722, 1456, 1266, 959, 706.

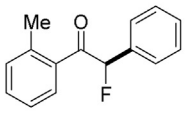
Table 3
Pd-catalyzed α-monoarylation of α-fluoroketones **1** with aryl halides or phenyl triflate **2**.[a,b]

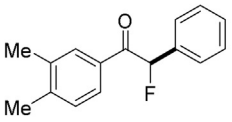


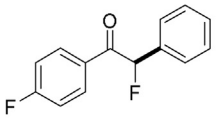
1 **2** **3**

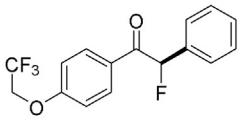

3ba: 97% (X = Br)

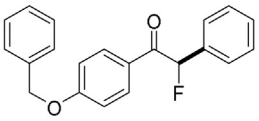

3ca: 94% (X = Br)
95% (X = I)

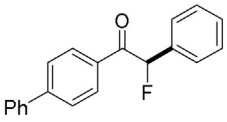

3da: 95% (X = Br)
92% (X = OTf)

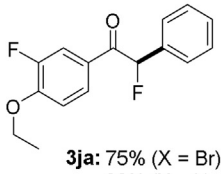

3ea: 91% (X = Br)

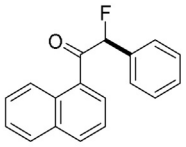

3fa: 93% (X = Br)
96% (X = I)

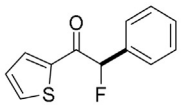

3ga: 88% (X = Br)
90% (X = OTf)

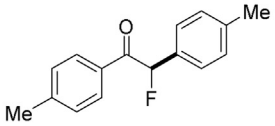

3ha: 83% (X = Br)
79% (X = Cl)

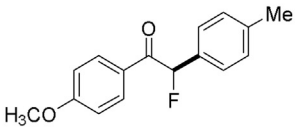

3ia: 98% (X = Br)

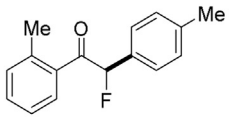

3ja: 75% (X = Br)
82% (X = I)
78% (X = OTf)

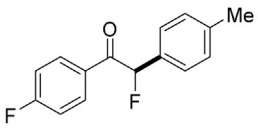

3ka: 80% (X = Br)

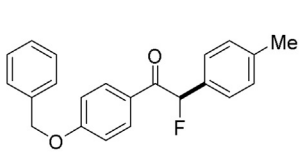

3la: 70% (X = Br)
56% (X = Cl)


3bb: 83% (X = Br)


3cb: 76% (X = Br)


3db: 81% (X = Br)


3fb: 80% (X = Br)
74% (X = Cl)



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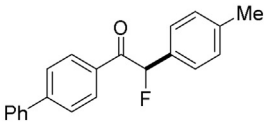
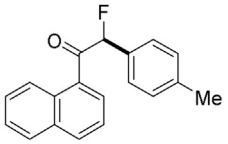
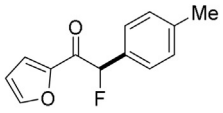


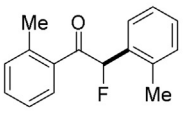
3ib: 85% (X = Br)



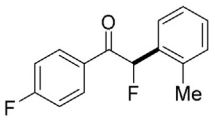
3kb: 76% (X = Br)



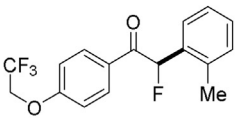
3mb: 85% (X = Br)
78% (X = Cl)



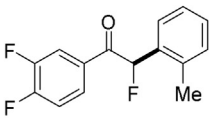
3dc: 74% (X = Br)



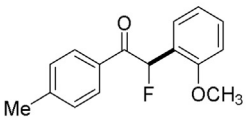
3fc: 98% (X = Br)



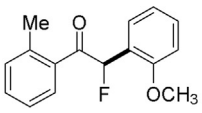
3gc: 94% (X = Br)



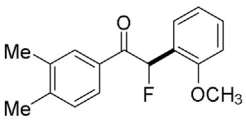
3nc: 89% (X = Br)



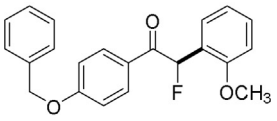
3bd: 93% (X = Br)
96% (X = I)



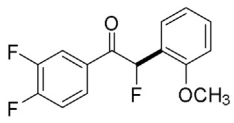
3dd: 78% (X = Br)



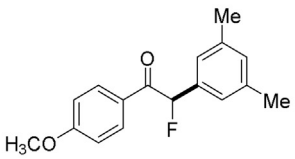
3ed: 89% (X = Br)



3hd: 73% (X = Br)
79% (X = I)



3md: 88% (X = Br)
84% (X = I)



3nd: 73% (X = Br)

[a] Reaction conditions: 5 mol% $Pd(OAc)_2$, 10 mol% XPhos, 1.2 equiv aryl halide or phenyl triflate, 2.0 equiv Cs_2CO_3, toluene (0.2 mol L^{-1} of **1**), 110 °C, 8 h, at 0.2 mmol scale.
[b] Isolated yield.

*4.2.2. -Fluoro-1-phenyl-2-(*p*-tolyl)ethan-1-one (**3ab**) [17]*

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 7.4 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.44–7.33 (m, 4H), 7.20 (d, J = 7.9 Hz, 2H), 6.50 (d, J = 48.7 Hz, 1H), 2.33 (d, J = 1.6 Hz, 3H). IR (neat, cm^{-1}): 3058, 2924, 1696, 1596, 1448, 1226, 1059, 968, 720.

*4.2.3. 2-Fluoro-1-phenyl-2-(*o*-tolyl)ethan-1-one (**3ac**)*

White solid. m.p.: 72.6–73.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94–7.84 (m, 2H), 7.59–7.51 (m, 1H), 7.42 (dd, J = 10.7, 4.8 Hz, 2H), 7.33–7.22 (m, 3H), 7.18 (dd, J = 10.7, 4.7 Hz, 1H), 6.71 (d, J = 48.1 Hz, 1H), 2.52 (d, J = 1.5 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −175.42 (d, J = 48.7 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.86 (d, J = 21.1 Hz), 137.37, 134.47, 133.69, 132.74 (d, J = 18.3 Hz), 131.33, 130.01, 128.83, 128.73, 128.65, 126.57, 91.76 (d, J = 183.7 Hz), 19.32. IR (neat, cm^{-1}): 3057, 2970, 2949, 1695, 1447, 1226, 1057, 958, 756. MS (EI): m/z (%) 77 (21), 105 (100), 228 (1.65, M^+). HRMS: Calcd. for $C_{15}H_{13}FO$: 228.0950; found: 228.0951.

*4.2.4. 2-Fluoro-2-(2-methoxyphenyl)-1-phenylethan-1-one (**3ad**)*

Yellow solid. m.p.: 83.6–84.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98–7.92 (m, 2H), 7.51 (d, J = 7.4 Hz, 1H), 7.45–7.31 (m, 4H), 7.03 (d, J = 48.0 Hz, 1H), 6.94 (d, J = 8.0 Hz, 2H), 3.91 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −177.85 (d, J = 47.9 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.39 (d, J = 21.0 Hz), 156.72, 134.22, 133.61, 131.51, 129.33, 128.59, 122.93, 122.74, 121.21, 111.34, 87.49 (d, J = 180.9 Hz), 55.74. IR (neat, cm^{-1}): 3068, 2986, 2839, 1693, 1492, 1222, 966, 760. MS (EI): m/z (%) 77 (18), 91 (39), 119 (100), 244 (5.0, M^+). HRMS: Calcd. for $C_{15}H_{13}FO_2$: 244.0900; found: 244.0901.

*4.2.5. 4-(1-Fluoro-2-oxo-2-phenylethyl)benzonitrile (**3ae**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98–7.90 (m, 2H), 7.70 (d, J = 8.1 Hz, 2H), 7.65–7.56 (m, 3H), 7.51–7.42 (m, 2H), 6.51 (d, J = 48.2 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −181.40 (d, J = 48.6 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.58 (d, J = 21.6 Hz), 139.22 (d, J = 20.3 Hz), 134.33, 133.64, 132.73, 129.25, 128.91, 127.20, 118.13, 113.34, 93.32 (d, J = 189.2 Hz). IR (neat, cm^{-1}): 3068, 2926, 2230, 1697, 1598, 1224, 1068, 968, 694. MS (EI): m/z (%) 77 (29), 105 (100), 239 (0.15, M^+). HRMS: Calcd. for $C_{15}H_{10}NFO$: 239.0746; found: 239.0748.

*4.2.6. 2-(3,5-Dimethylphenyl)-2-fluoro-1-phenylethan-1-one (**3af**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99–7.91 (m, 2H), 7.58–7.49 (m, 1H), 7.42 (dd, J = 10.6, 4.8 Hz, 2H), 7.10 (s, 2H), 7.01 (s, 1H), 6.45 (d, J = 48.8 Hz, 1H), 2.30 (s, 6H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −174.47 (d, J = 49.3 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.35 (d, J = 21.4 Hz), 138.87, 134.10, 133.93, 133.72, 131.44, 129.08, 128.69,

125.29, 94.01 (d, J = 185.0 Hz), 21.27. IR (neat, cm^{-1}): 3062, 2921, 2860, 1700, 1602, 1448, 1254, 1215, 1062, 843, 691. MS (EI): m/z (%) 77 (16), 105 (100), 137 (7), 224 (6), 242 (3, M^+). HRMS: Calcd. for $C_{16}H_{15}FO$: 242.1107; found: 242.1108.

*4.2.7. 2-(4-(Tert-butyl)phenyl)-2-fluoro-1-phenylethan-1-one (**3ag**)*

Light yellow solid. m.p.: 95.4–96.1 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.4 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.47–7.38 (m, 6H), 6.51 (d, J = 48.8 Hz, 1H), 1.29 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −174.21 (d, J = 48.7 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.33 (d, J = 21.5 Hz), 152.90, 134.10, 133.73, 131.16 (d, J = 20.2 Hz), 129.12, 128.70, 127.34, 126.13, 93.76 (d, J = 184.8 Hz), 34.74, 31.21. IR (neat, cm^{-1}): 3062, 2961, 2869, 1699, 1596, 1447, 1263, 1056, 964, 824. MS (EI): m/z (%) 77 (13), 91 (7), 105 (100), 119 (6), 252 (7), 270 (0.56, M^+). HRMS: Calcd. for $C_{18}H_{19}FO$: 270.1420; found: 270.1422.

*4.2.8. 2-Fluoro-1-phenyl-2-(4-(trifluoromethyl)phenyl)ethan-1-one (**3ah**)*

Yellow solid. m.p.: 78.3–79.2 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.6 Hz, 2H), 7.67 (d, J = 8.5 Hz, 2H), 7.73–7.54 (m, 3H), 7.46 (t, J = 7.7 Hz, 2H), 6.53 (d, J = 48.3 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.85 (s, 3F), −179.81 (d, J = 49.0 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.86 (d, J = 21.5 Hz), 138.11(d, J = 21.4 Hz), 134.18, 133.75, 131.56 (q, J = 33.3 Hz), 129.21, 128.86, 127.17, 126.01, 123.74 (q, J = 273.4 Hz), 93.41 (d, J = 187.8 Hz). IR (neat, cm^{-1}): 3062, 2924, 1687, 1595, 1449, 1219, 1072, 821, 695. MS (EI): m/z (%) 77 (29), 105 (100), 119 (4), 282 (0.91, M^+). HRMS: Calcd. for $C_{15}H_{10}F_4O$: 282.0668; found: 282.0666.

*4.2.9. 2-(1-Benzyl-1H-indazol-3-yl)-2-fluoro-1-phenylethanone (**3ai**)*

Yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.0 Hz, 2H), 7.83 (d, J = 8.0 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.37 (t, J = 7.8 Hz, 2H), 7.32 (t, J = 7.6 Hz, 2H), 7.26–7.21 (m, 3H), 7.20–7.14 (m, 1H), 7.11(d, J = 48.0 Hz, 1H), 7.09–7.07 (m, 2H), 5.59 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −181.13 (d, J = 47.6 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.32 (d, J = 21.1 Hz), 140.84, 138.13 (d, J = 26.0 Hz), 136.27, 133.78, 129.05, 128.75, 128.59, 127.89, 127.08, 127.00, 122.20, 121.97, 120.90, 109.65, 88.44 (d, J = 181.7 Hz), 53.13. IR (neat, cm^{-1}): 3060, 2921, 2857, 1689, 1601, 1441, 1267, 1173, 1058, 963, 821. MS (EI): m/z (%) 77 (12), 91 (11), 105 (100), 116 (6), 344 (0.35, M^+). HRMS: Calcd. for $C_{22}H_{17}FN_2O$: 344.3816; found: 344.3815.

*4.2.10. 2-Fluoro-2-phenyl-1-(p-tolyl)ethan-1-one (**3ba**) [17]*

^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.2 Hz, 2H), 7.52–7.45 (m, 2H), 7.39 (dt, J = 12.5, 3.4 Hz, 3H), 7.22 (d, J = 8.1 Hz, 2H), 6.50 (d, J = 48.7 Hz, 1H), 2.37 (s, 3H). IR (neat, cm^{-1}): 3065, 2925, 2854, 1694, 1606, 1454, 1229, 1060, 966, 699.

*4.2.11. 2-Fluoro-1-(4-methoxyphenyl)-2-phenylethan-1-one (**3ca**)*

White solid. m.p.: 85.2–85.9 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.9 Hz, 2H), 7.49 (dd, J = 6.5, 1.1 Hz, 2H), 7.44–7.31 (m, 3H), 6.88 (t, J = 5.8 Hz, 2H), 6.47 (d, J = 48.8 Hz, 1H), 3.83 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −175.45 (d, J = 48.8 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.70 (d, J = 21.1 Hz), 163.98, 134.68 (d, J = 20.0 Hz), 131.54, 129.54, 129.06, 127.32, 126.86, 113.96, 93.91 (d, J = 185.0 Hz), 55.51. IR (neat, cm^{-1}): 3068, 2934, 2842, 1687, 1600, 1511, 1261, 1173, 968, 700. MS (EI): m/z (%) 65 (6), 91 (34), 119 (100), 228 (0.1, M^+). HRMS: Calcd. for $C_{15}H_{13}FO$: 228.0950; found: 228.0952.

*4.2.12. 2-Fluoro-2-phenyl-1-(o-tolyl)ethan-1-one (**3da**)*

Yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 7.9 Hz, 1H), 7.43–7.32 (m, 6H), 7.24–7.18 (m, 2H), 6.39 (d, J = 48.4 Hz, 1H), 2.32 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −177.47 (d, J = 48.4 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.11 (d, J = 22.4 Hz), 138.85, 134.94, 133.90 (d, J = 20.4 Hz), 131.83, 129.43, 128.93, 128.36, 126.98, 125.44, 94.31 (d, J = 187.8 Hz), 20.56. IR (neat, cm^{-1}): 3064, 2927, 2854, 1701, 1600, 1454, 1222, 1056, 964, 699. MS (EI): m/z (%) 65 (6), 91 (34), 119 (100), 228 (0.1, M^+). HRMS: Calcd. for $C_{15}H_{13}FO$: 228.0950; found: 228.0952.

*4.2.13. 1-(3,4-Dimethylphenyl)-2-fluoro-2-phenylethan-1-one (**3ea**)*

Light yellow solid. m.p.: 41.8–42.7 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.66 (d, J = 7.9 Hz, 1H), 7.48 (dd, J = 6.3, 1.3 Hz, 2H), 7.42–7.32 (m, 3H), 7.16 (d, J = 7.9 Hz, 1H), 6.51 (d, J = 48.7 Hz, 1H), 2.28 (s, 3H), 2.27 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −175.59 (d, J = 49.0 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.01 (d, J = 21.0 Hz), 143.65, 137.24, 134.56 (d, J = 20.0 Hz), 131.89, 130.10, 129.86, 129.53, 129.04, 127.44, 126.82, 93.74 (d, J = 185.0 Hz), 20.11, 19.79. IR (neat, cm^{-1}): 3068, 2921, 2863, 1693, 1605, 1452, 1217, 1063, 981, 808. MS (EI): m/z (%) 77 (5), 91 (1), 105 (18), 133 (100), 242 (0.15, M^+). HRMS: Calcd. for $C_{16}H_{15}FO$: 242.1107; found: 242.1104.

*4.2.14. 2-Fluoro-1-(4-fluorophenyl)-2-phenylethan-1-one (**3fa**)*

Yellow solid. m.p.: 58.1–58.6 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.07–7.92 (m, 2H), 7.47 (d, J = 5.9 Hz, 2H), 7.41 (d, J = 5.6 Hz, 3H), 7.10 (t, J = 8.5 Hz, 2H), 6.45 (d, J = 48.7 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −103.18 (s, 1F), −175.97 (d, J = 48.9 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.88 (d, J = 22.0 Hz), 165.99 (d, J = 256.7 Hz), 134.14 (d, J = 19.9 Hz), 131.97, 130.35, 129.70, 129.16, 127.13, 115.96 (d, J = 22.0 Hz), 94.25 (d, J = 186.4 Hz). IR (neat, cm^{-1}): 3069, 2925, 1699, 1599, 1454, 1232, 1061, 970, 870, 699. MS (EI): m/z (%) 75 (3), 95 (20), 109 (4), 123 (100), 232 (0.33, M^+). HRMS: Calcd. for $C_{14}H_{10}F_2O$: 232.0700; found: 232.0701.

*4.2.15. 2-Fluoro-2-phenyl-1-(4-(2,2,2-trifluoroethoxy)phenyl)ethan-1-one (**3ga**)*

White solid. m.p.: 81.1–81.7 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.9 Hz, 2H), 7.48–7.38 (m, 5H), 6.94 (d, J = 8.9 Hz, 2H), 6.45 (d, J = 48.7 Hz, 1H), 4.38 (q, J = 7.9 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −73.78 (t, J = 8.4 Hz, 3F), −175.87 (d, J = 49.0 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.73 (d, J = 21.4 Hz), 161.18, 134.38 (d, J = 19.9 Hz), 131.70, 131.07, 129.62, 129.11, 127.18, 122.94 (q, J = 277.9 Hz), 114.63, 94.16 (d, J = 186.0 Hz), 65.44 (d, J = 36.2 Hz). IR (neat, cm^{-1}): 3080, 2925, 2854, 1681, 1599, 1457, 1259, 1173, 968, 870, 699. MS (EI): m/z (%) 92 (3), 111 (5), 175 (5), 203 (100), 312 (0.1, M^+). HRMS: Calcd. for $C_{16}H_{12}F_4O_2$: 312.0773; found: 312.0775.

*4.2.16. 1-(4-(Benzyloxy)phenyl)-2-fluoro-2-phenylethan-1-one (**3ha**)*

Light yellow solid. m.p.: 82.4–83.1 °C. ^1H NMR (400 MHz, CDCl3) δ 8.00–7.94 (m, 2H), 7.54–7.48 (m, 2H), 7.45–7.34 (m, 8H), 7.03–6.96 (m, 2H), 6.48 (d, J = 48.8 Hz, 1H), 5.12 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −175.52 (d, J = 49.0 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.69 (d, J = 21.0 Hz), 163.12, 135.93, 131.58, 129.50, 129.05, 128.74, 128.34, 127.48, 127.27, 114.76, 93.99 (d, J = 185.3 Hz), 70.19. IR (neat, cm^{-1}): 3064, 2926, 2854, 1688, 1599, 1454, 1259, 1172, 967, 866, 698. MS (EI): m/z (%) 91 (70), 121 (10), 211 (100), 320 (0.1, M^+). HRMS: Calcd. for $C_{21}H_{17}FO_2$: 320.1213; found: 320.1219.

*4.2.17. 1-([1,1′-Biphenyl]-4-yl)-2-fluoro-2-phenylethan-1-one (**3ia**)*

White solid. m.p.: 78.4–79.1 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.4 Hz, 2H), 7.69–7.61 (m, 2H), 7.59 (dd, J = 8.3, 1.3 Hz, 2H), 7.55–7.50 (m, 2H), 7.50–7.38 (m, 6H), 6.54 (d, J = 48.7 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −175.76 (d, J = 48.8 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.85 (d, J = 21.4 Hz), 146.47, 139.57, 134.35 (d, J = 19.9 Hz), 132.64, 129.71 (dd, J = 6.1, 2.7 Hz), 129.16, 129.01, 128.46, 127.40, 127.30, 94.08 (d, J = 185.7 Hz). IR (neat, cm^{-1}): 3065, 2925, 1694, 1586, 1391, 1277, 1158, 976, 843, 700. MS (EI): m/z (%) 91 (2), 152 (24), 181 (100), 290 (0.15, M^+). HRMS: Calcd. for $C_{20}H_{15}FO$: 290.1107; found: 290.1106.

*4.2.18. 1-(4-Ethoxy-3-fluorophenyl)-2-fluoro-2-phenylethan-1-one (**3ja**)*

Light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80–7.65 (m, 2H), 7.51–7.44 (m, 2H), 7.44–7.33 (m, 3H), 6.92 (t, J = 8.5 Hz, 1H), 6.42 (d, J = 48.7 Hz, 1H), 4.14 (q, J = 7.0 Hz, 2H), 1.46 (t, J = 7.0 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −133.15 (dd, J = 12.4, 9.3 Hz, 1F), −175.66 (d, J = 49.0 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.05 (d, J = 21.6 Hz), 151.93 (d, J = 248.5 Hz), 151.93 (d, J = 11.1 Hz), 134.36 (d, J = 20.0 Hz), 129.63, 129.11, 127.14, 126.76, 116.95, 116.75, 113.19, 94.13 (d, J = 186.1 Hz), 64.97, 14.54. IR (neat, cm^{-1}): 3068, 2984, 2937, 2924, 1692, 1609, 1517, 1437, 1278, 1143, 1036, 896, 807. MS (EI): m/z (%) 83 (6), 111 (11), 139 (65), 167 (100), 276 (0.35, M^+). HRMS: Calcd. for $C_{16}H_{14}F_2O_2$: 276.0962; found: 276.0964.

*4.2.19. 2-Fluoro-1-(naphthalen-2-yl)-2-phenylethan-1-one (**3ka**)*

Yellow solid. m.p.: 114.3–115.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 8.2 Hz, 1H), 7.98 (d, J = 8.2 Hz, 1H), 7.89–7.78 (m, 2H), 7.59–7.49 (m, 2H), 7.46 (t, J = 7.7 Hz, 3H), 7.40–7.30 (m, 3H), 6.58 (d, J = 48.4 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −175.87 (d, J = 49.0 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.78 (d, J = 22.4 Hz), 134.06 (d, J = 20.3 Hz), 133.87, 133.32, 132.59, 130.56, 129.47, 128.98, 128.48, 128.27, 128.13, 127.01, 126.73, 125.25, 124.09, 94.38 (d, J = 188.2 Hz). IR (neat, cm^{-1}): 3062, 2926, 1695, 1592, 1456, 1237, 1178, 1038, 943, 864, 779, 696. MS (EI): m/z (%) 77 (3), 127 (44), 155 (100), 264 (1, M^+). HRMS: Calcd. for $C_{18}H_{13}FO$: 264.0950; found: 264.0952.

*4.2.20. 2-Fluoro-2-phenyl-1-(thiophen-2-yl)ethanone (**3la**) [18]*

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dt, J = 3.8, 1.1 Hz, 1H), 7.70 (dd, J = 4.9, 0.6 Hz, 1H), 7.52 (dd, J = 6.5, 1.4 Hz, 2H), 7.40 (dd, J = 7.2, 3.5 Hz, 3H), 7.13 (dd, J = 4.8, 4.0 Hz, 1H), 6.26 (d, J = 48.4 Hz, 1H). IR (neat, cm^{-1}): 3063, 2925, 1699, 1472, 1249, 961, 711.

*4.2.21. 2-Fluoro-1,2-di-*p*-tolylethanone (**3bb**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.2 Hz, 2H), 7.37 (dd, J = 8.0, 1.5 Hz, 2H), 7.20 (t, J = 7.0 Hz, 4H), 6.48 (d, J = 48.8 Hz, 1H), 2.37 (s, 3H), 2.33 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −173.88 (d, J = 48.8 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.86 (d, J = 21.2 Hz), 144.73, 139.73, 131.57, 131.40, 129.79, 129.38, 129.15, 127.61, 93.68 (d, J = 184.6 Hz), 21.72, 21.27. IR (neat, cm^{-1}): 3041, 2925, 2853, 1693, 1607, 1411, 1265, 1182, 1063, 967, 814. MS (EI): m/z (%) 91 (20), 119 (100), 224 (3), 242 (0.56, M^+). HRMS: Calcd. for $C_{16}H_{15}FO$: 242.1107; found: 242.1108.

*4.2.22. 2-Fluoro-1-(4-methoxyphenyl)-2-(*p*-tolyl)ethan-1-one (**3cb**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 5.8 Hz, 2H), 7.37 (d, J = 6.8 Hz, 2H), 7.19 (d, J = 7.9 Hz, 2H), 6.87 (t, J = 5.8 Hz, 2H), 6.45 (d, J = 48.9 Hz, 1H), 3.82 (s, 3H), 2.33 (d, J = 1.4 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −173.66 (d, J = 48.9 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.74 (d, J = 21.2 Hz), 163.91, 139.69, 131.70 (d, J = 20.1 Hz), 131.46, 129.79, 127.54, 126.91, 113.93, 93.68 (d, J = 184.4 Hz), 55.50, 21.28. IR (neat, cm^{-1}): 3056, 2961, 2933, 2842, 1689, 1599, 1422, 1262, 1173, 1061, 968, 819. MS (EI): m/z (%) 77 (6), 92 (4), 107 (6), 135 (100), 191 (10), 258 (0.21, M^+). HRMS: Calcd. for $C_{16}H_{15}FO_2$: 258.1056; found: 258.1057.

*4.2.23. 2-Fluoro-1-(o-tolyl)-2-(*p*-tolyl)ethan-1-one (**3db**)*

Yellow solid. m.p.: 73.2–73.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04–7.92 (m, 2H), 7.35 (dd, J = 8.1, 1.5 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.13–7.03 (m, 2H), 6.43 (d, J = 48.8 Hz, 1H), 2.34 (d, J = 1.7 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −175.57 (d, J = 48.4 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.14 (d, J = 22.5 Hz), 139.50, 138.85, 135.02, 131.86, 131.70, 130.93 (d, J = 20.7 Hz), 129.64, 128.36, 127.14, 125.41, 94.20 (d, J = 187.0 Hz), 21.27, 20.61. IR (neat, cm^{-1}): 3061, 2928, 2855, 1598, 1597, 1452, 1226, 10549, 837, 759. MS (EI): m/z (%) 77 (2), 91 (25), 119 (100), 242 (0.41, M^+). HRMS: Calcd. for $C_{16}H_{15}FO$: 242.1107; found: 242.1106.

*4.2.24. 2-Fluoro-1-(4-fluorophenyl)-2-(*p*-tolyl)ethan-1-one (**3fb**)*

Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04–7.89 (m, 2H), 7.35 (dd, J = 8.1, 1.5 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.13–7.03 (m, 2H), 6.43 (d, J = 48.8 Hz, 1H), 2.34 (d, J = 1.7 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −103.35 (s, 1F), −174.02 (d, J = 49.5 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.89 (d, J = 21.8 Hz), 165.93 (d, J = 256.4 Hz), 139.93, 131.89 (dd, J = 9.5, 3.0 Hz), 131.15 (d, J = 20.1 Hz), 130.42, 129.88, 127.36, 115.92 (d, J = 21.9 Hz), 94.00 (d, J = 185.8 Hz), 21.28. IR (neat, cm^{-1}): 3080, 2925, 2854, 1694, 1599, 1507, 1413, 1232, 1156, 1077, 842. MS (EI): m/z (%) 77 (3), 95 (14), 123 (100), 246 (0.97, M^+). HRMS: Calcd. for $C_{15}H_{12}F_2O$: 264.0856; found: 264.0857.

*4.2.25. 1-(4-(Benzyloxy)phenyl)-2-fluoro-2-(*p*-tolyl)ethan-1-one (**3hb**)*

Yellow solid. m.p.: 85.2–85.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97–7.89 (m, 2H), 7.45–7.34 (m, 7H), 7.20 (d, J = 8.0 Hz, 2H), 7.00–6.93 (m, 2H), 6.44 (d, J = 48.9 Hz, 1H), 5.09 (s, 2H), 2.34 (d, J = 1.7 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −173.60 (d, J = 48.9 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.85, 163.05, 139.65, 135.96, 131.49, 129.77, 128.73, 128.33, 127.49, 127.14, 114.74, 93.76 (d, J = 184.6 Hz), 70.18, 21.28. IR (neat, cm^{-1}): 3068, 2923, 2866, 1688, 1598, 1509, 1455, 1257, 1172, 1062, 967, 812. MS (EI): m/z (%) 65 (3), 91 (60), 211 (100), 334 (0.1, M^+). HRMS: Calcd. for $C_{22}H_{19}FO_2$: 334.1369; found: 334.1366.

*4.2.26. 1-([1,1′-Biphenyl]-4-yl)-2-fluoro-2-(*p*-tolyl)ethan-1-one (**3ib**)*

White solid. m.p.: 80.7–81.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.4 Hz, 2H), 7.67–7.61 (m, 2H), 7.58 (dd, J = 5.3, 3.3 Hz, 2H), 7.50–7.43 (m, 2H), 7.40 (d, J = 7.5 Hz, 3H), 7.22 (d, J = 7.9 Hz, 2H), 6.52 (d, J = 48.7 Hz, 1H), 2.35 (d, J = 1.7 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −173.94 (d, J = 48.8 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.86 (d, J = 21.5 Hz), 146.37, 139.86, 139.61, 132.70, 131.37 (d, J = 20.0 Hz), 129.87, 129.67, 128.99, 128.43, 127.60, 127.28, 93.88 (d, J = 185.1 Hz), 21.30. IR (neat, cm^{-1}): 3061, 2928, 2857, 1689, 1590, 1387, 1256, 1164, 971, 833, 698. MS (EI): m/z (%) 119 (1), 152 (21), 181 (100), 304 (0.1, M^+). HRMS: Calcd. for $C_{21}H_{17}FO$: 304.1263; found: 304.1265.

*4.2.27. 2-Fluoro-1-(naphthalen-2-yl)-2-(*p*-tolyl)ethan-1-one (**3kb**)*

White solid. m.p.: 117.4–118.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, J = 8.5 Hz, 1H), 7.97 (d, J = 8.3 Hz, 1H), 7.88–7.77 (m, 2H), 7.54 (dddd, J = 19.5, 8.0, 6.9, 1.4 Hz, 2H), 7.44 (dd, J = 8.1, 7.4 Hz, 1H), 7.35 (d, J = 6.9 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 6.56 (d, J = 48.4 Hz, 1H), 2.30 (d, J = 1.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −173.88 (d, J = 49.0 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.81 (d, J = 22.5 Hz), 139.59, 133.89, 133.26, 132.67, 131.09 (d, J = 20.6 Hz), 130.58, 129.72, 128.48, 128.25, 128.12, 127.22, 126.70, 125.33, 124.10, 94.24 (d, J = 187.4 Hz), 21.25. IR (neat, cm^{-1}): 3062, 2958, 2925, 1697, 1607, 1265, 1185, 1066, 974, 813, 765. MS (EI): m/z (%) 77 (2), 127 (36), 155 (100), 260 (6), 278 (0.6, M^+). HRMS: Calcd. for $C_{19}H_{15}FO$: 278.1107; found: 278.1106.

*4.2.28. 2-Fluoro-1-(furan-2-yl)-2-(*p*-tolyl)ethan-1-one (**3mb**)*

White solid. m.p.: 75.9–76.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 1.1 Hz, 1H), 7.43–7.33 (m, 3H), 7.20 (d, J = 8.0 Hz, 2H), 6.54 (dd, J = 3.6, 1.7 Hz, 1H), 6.27 (d, J = 47.9 Hz, 1H), 2.34 (d, J = 1.5 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −179.08 (d, J = 48.0 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.26 (d, J = 24.3 Hz), 149.85, 147.45, 139.75, 131.16 (d, J = 20.5 Hz), 129.62, 127.27, 120.35, 112.55, 93.55 (d, J = 185.6 Hz), 21.28. IR (neat, cm^{-1}): 3091, 2963, 2923, 1680, 1589, 1441, 1281, 1155, 1065, 801, 765. MS (EI): m/z (%) 77 (5), 91 (26), 105 (8), 119 (100), 123 (20), 218 (5, M^+). HRMS: Calcd. for $C_{13}H_{11}FO_2$: 218.0743; found: 218.0742.

*4.2.29. 2-Fluoro-1,2-di-o-tolylethan-1-one (**3dc**)*

Yellow solid. m.p.: 74.2–74.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 7.6 Hz, 1H), 7.37–7.28 (m, 2H), 7.23 (t, J = 3.7 Hz, 1H), 7.17

(dd, *J* = 11.0, 7.7 Hz, 4H), 6.57 (d, *J* = 47.8 Hz, 1H), 2.33 (s, 3H), 2.31 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −175.94 (d, *J* = 47.8 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 198.55 (d, *J* = 22.4 Hz), 138.44, 136.83, 135.45, 132.24 (d, *J* = 19.1 Hz), 131.73 (d, *J* = 19.0 Hz), 131.11, 129.70, 128.08, 126.43, 125.45, 91.97 (d, *J* = 186.0 Hz), 20.40, 19.35. IR (neat, cm^{-1}): 3068, 2928, 2863, 1702, 1571, 1458, 1222, 1056, 965, 754. MS (EI): *m*/*z* (%) 65 (4), 91 (27), 119 (100), 242 (0.2, M^+). HRMS: Calcd. for $C_{16}H_{15}FO$: 242.1107; found: 242.1106.

*4.2.30. 2-Fluoro-1-(4-fluorophenyl)-2-(*o*-tolyl)ethan-1-one (**3fc**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.98–7.89 (m, 2H), 7.33–7.23 (m, 3H), 7.22–7.14 (m, 1H), 7.12–7.04 (m, 2H), 6.64 (d, *J* = 48.0 Hz, 1H), 2.49 (d, *J* = 1.5 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −103.36 (s), −175.09 (d, *J* = 48.7 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 193.40 (d, *J* = 21.5 Hz), 165.92 (d, *J* = 256.4 Hz), 137.37, 132.64 (d, *J* = 18.3 Hz), 131.70, 131.41, 130.81, 130.11, 128.53, 126.61, 115.98 (d, *J* = 22.0 Hz), 91.95 (d, *J* = 184.2 Hz), 19.33. IR (neat, cm^{-1}): 3071, 2923, 2854, 1703, 1599, 1504, 1270, 1231, 1155, 1072, 837, 756. MS (EI): *m*/*z* (%) 95(13), 123(100), 246(1.27, M^+). HRMS: Calcd. for $C_{15}H_{12}F_2O$: 246.0856; found: 246.0859.

*4.2.31. 2-Fluoro-2-(*o*-tolyl)-1-(4-(2,2,2-trifluoroethoxy)phenyl) ethan-1-one (**3gc**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.90 (d, *J* = 8.9 Hz, 2H), 7.34–7.21 (m, 3H), 7.15 (dd, *J* = 8.0, 8.0 Hz, 1H), 6.93 (d, *J* = 8.9 Hz, 2H), 6.64 (d, *J* = 48.1 Hz, 1H), 4.37 (q, *J* = 8.0 Hz, 2H), 2.49 (d, *J* = 1.2 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −73.79 (t, *J* = 7.9 Hz, 3F), −175.13 (d, *J* = 48.1 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 193.28 (d, *J* = 21.2 Hz), 161.12, 137.38, 132.94, 132.76, 131.38, 130.03, 128.89, 128.56, 126.56, 122.99 (q, *J* = 277.9 Hz), 114.65, 91.81 (d, *J* = 183.6 Hz), 65.40 (q, *J* = 36.2 Hz), 19.29. IR (neat, cm^{-1}): 3080, 2958, 2925, 2857, 1693, 1600, 1509, 1457, 1287, 1240, 1169, 1072, 970, 867, 761. MS (EI): *m*/*z* (%) 91 (4), 111 (4), 175 (4), 203 (100), 326 (0.1, M^+). HRMS: Calcd. for $C_{17}H_{14}F_4O_2$: 326.0930; found: 326.0932.

*4.2.32. 1-(3,4-Difluorophenyl)-2-fluoro-2-(*o*-tolyl)ethan-1-one (**3nc**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.86–7.73 (m, 1H), 7.73–7.62 (m, 1H), 7.35–7.14 (m, 5H), 6.59 (d, *J* = 47.9 Hz, 1H), 2.48 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −126.05–-129.19 (m, 1F), −135.29 (ddd, *J* = 20.8, 9.9, 8.4 Hz, 1F), −175.13 (d, *J* = 48.6 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 192.58 (d, *J* = 21.9 Hz), 153.89 (dd, *J* = 258.6, 12.8 Hz), 150.38 (dd, *J* = 251.4, 13.0 Hz), 137.34, 132.30 (d, *J* = 18.3 Hz), 131.50, 131.35, 130.24, 128.38, 126.66, 126.20, 92.16 (d, *J* = 185.0 Hz), 19.31. IR (neat, cm^{-1}): 3074, 2946, 2826, 1702, 1610, 1512, 1462, 1283, 1160, 1046, 757. MS (EI): *m*/*z* (%) 113 (23), 141 (100), 264 (0.95, M^+). HRMS: Calcd. for $C_{15}H_{11}F_3O$: 264.0762; found: 264.0764.

*4.2.33. 2-Fluoro-2-(2-methoxyphenyl)-1-(*p*-tolyl)ethan-1-one (**3bd**)*

Yellow solid. m.p.: 83.8–84.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.85 (d, *J* = 8.3 Hz, 2H), 7.38-7.31 (m, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 48.0 Hz, 1H), 6.96-6.92 (m, 2H), 3.91 (s, 3H), 2.36 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −177.87 (d, *J* = 47.5 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 193.95 (d, *J* = 20.9 Hz), 156.72, 144.53, 131.73, 131.38, 129.28, 128.69, 123.06 (d, *J* = 19.7 Hz), 121.20, 111.30, 87.30 (d, *J* = 180.5 Hz), 55.74, 21.71. IR (neat, cm^{-1}): 3080, 2972, 2943, 2842, 1690, 1602, 1492, 1255, 1187, 1059, 1027, 968, 81, 757. MS (EI): *m*/*z* (%) 91 (23), 119 (100), 240 (12), 258 (1.26, M^+). HRMS: Calcd. for $C_{16}H_{15}FO_2$: 258.1056; found: 258.1057.

*4.2.34. 2-Fluoro-2-(2-methoxyphenyl)-1-(*o*-tolyl)ethan-1-one (**3dd**)*

Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.59 (d, *J* = 7.7 Hz, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.32 (dq, *J* = 3.3, 1.6 Hz, 2H), 7.23–7.13 (m, 2H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 44.0 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 3.77 (s, 3H), 2.43 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −178.60 (d, *J* = 47.7 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 197.85 (d, *J* = 22.0 Hz), 156.68, 138.89, 134.98, 131.74, 131.62, 131.16, 128.98, 128.59, 125.28, 122.86 (d, *J* = 20.0 Hz), 121.00, 111.15, 88.77 (d, *J* = 183.0 Hz), 55.53, 20.79. IR (neat, cm^{-1}): 3068, 2964, 2925, 2842, 1701, 1601, 1493, 1463, 1251, 1049, 1026, 965, 756. MS (EI): *m*/*z* (%) 65 (5), 91 (30), 119 (100), 240 (9), 258 (1.28, M^+). HRMS: Calcd. for $C_{16}H_{15}FO_2$: 258.1056; found: 258.1057.

*4.2.35. 1-(3,4-Dimethylphenyl)-2-fluoro-2-(2-methoxyphenyl)ethan-1-one (**3ed**)*

Yellow solid. m.p.: 85.3–85.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.77 (s, 1H), 7.66 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.407.30 (m, 2H), 7.14 (d, *J* = 7.9 Hz, 1H), 7.04 (d, *J* = 47.5 Hz, 1H), 6.94 (dd, *J* = 7.9, 4.5 Hz, 2H), 3.93 (s, 3H), 2.26 (d, *J* = 1.6 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −178.04 (d, *J* = 47.9 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 194.10 (d, *J* = 20.8 Hz), 156.63, 143.34, 136.96, 132.05, 131.32, 129.79, 129.68, 129.21, 126.28, 123.12 (d, *J* = 19.8 Hz), 121.20, 111.26, 87.10 (d, *J* = 180.2 Hz), 55.69, 20.08, 19.78. IR (neat, cm^{-1}): 3068, 2970, 2942, 2839, 1694, 1604, 1493, 1252, 1106, 1023, 972, 756. MS (EI): *m*/*z* (%) 79 (4), 91 (4), 105 (14), 133 (100), 272 (0.45, M^+). HRMS: Calcd. for $C_{17}H_{17}FO_2$: 272.1213; found: 272.1214.

*4.2.36. 1-(4-(Benzyloxy)phenyl)-2-fluoro-2-(2-methoxyphenyl) ethan-1-one (**3hd**)*

Yellow solid. m.p.: 88.5–89.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.95 (d, *J* = 8.9 Hz, 2H), 7.37 (ddd, *J* = 10.9, 8.8, 3.6 Hz, 7H), 6.98 (dd, *J* = 28.1, 25.7 Hz, 5H), 5.09 (s, 2H), 3.92 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −177.57 (d, *J* = 47.8 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 192.84 (d, *J* = 20.9 Hz), 163.00, 156.67, 136.03, 131.39, 130.98, 129.23, 128.74, 128.32, 127.49, 127.36, 123.14 (d, *J* = 19.9 Hz), 121.22, 114.66, 111.31, 87.06 (d, *J* = 180.1 Hz), 70.14, 55.79. IR (neat, cm^{-1}): 3066, 2925, 2842, 1689, 1600, 1509, 1494, 1254, 1173, 1024, 868, 755. MS (EI): *m*/*z* (%) 91 (81), 121 (13), 211 (100), 350 (5.9, M^+). HRMS: Calcd. for $C_{22}H_{19}FO_3$: 350.1318; found: 350.1320.

*4.2.37. 1-(3,4-Difluorophenyl)-2-fluoro-2-(2-methoxyphenyl)ethan-1-one (**3md**)*

Yellow solid. m.p.: 57.4–58.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.88–7.80 (m, 1H), 7.79–7.71 (m, 1H), 7.37 (ddd, *J* = 13.9, 7.8, 4.6 Hz, 2H), 7.19 (dd, *J* = 17.4, 8.6 Hz, 1H), 7.05–6.81 (m, 3H), 3.92 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −123.60–-131.27 (m, 1F), −132.18–-140.41 (m, 1F), −177.69 (d, *J* = 47.6 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 192.06 (d, *J* = 21.3 Hz), 156.47, 153.84 (dd, *J* = 258.0, 12.9 Hz), 150.28 (dd, *J* = 250.9, 13.0 Hz), 131.77, 131.48–130.67 (m), 129.22, 125.76, 122.35 (d, *J* = 20.0 Hz), 121.37, 118.07 (d, *J* = 18.5 Hz), 117.63 (d, *J* = 17.9 Hz), 111.43, 87.59 (d, *J* = 182.4 Hz), 55.73. IR (neat, cm^{-1}): 3071, 2948, 2829, 1705, 1611, 1517, 1493, 1287, 1162, 1049, 756. MS (EI): *m*/*z* (%) 91 (79), 113 (31), 121 (45), 141 (100), 281 (3.1, M^+). HRMS: Calcd. for $C_{15}H_{11}F_3O_2$: 280.0711; found: 280.0712.

*4.2.38. 2-(3,5-Dimethylphenyl)-2-fluoro-1-(4-methoxyphenyl)ethan-1-one (**3nd**)*

White solid. m.p.: 56.9–57.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.00–7.91 (m, 2H), 7.09 (s, 2H), 6.99 (s, 1H), 6.96–6.83 (m, 2H), 6.40 (d, *J* = 49.0 Hz, 1H), 3.84 (s, 3H), 2.30 (s, 6H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −174.34 (d, *J* = 49.4 Hz, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 192.79 (d, *J* = 21.1 Hz), 163.91, 138.76, 134.46 (d, *J* = 20.2 Hz), 131.51, 131.27, 126.97, 125.13, 113.92, 94.00 (d, *J* = 184.6 Hz), 55.49, 21.27. IR (neat, cm^{-1}): 3071, 2955, 2922, 2850, 1688, 1599, 1511, 1462, 1256, 1173, 1027, 847, 703. MS (EI): *m*/*z* (%) 77 (6), 92 (4), 107 (5), 135 (100), 272 (0.39, M^+). HRMS: Calcd. for $C_{17}H_{17}FO_2$: 272.1213; found: 272.1211.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jfluchem.2016.09.016.

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