Facile Synthesis of 2-Fluoro-1,3-dicarbonyl Compounds with Aqueous Hydrofluoric Acid Mediated by Iodosylarenes

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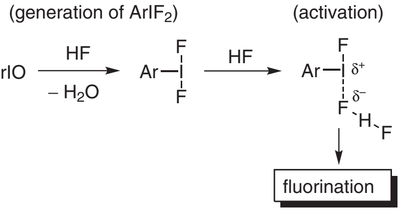
Abstract: Direct fluorination of 1,3-dicarbonyl compounds including 1,3-diketones, 3-oxo esters, and 3-oxoamides was conducted using aqueous hydrofluoric acid with the aid of iodosylarenes, giving the corresponding 2-fluorinated products in good to high yields. Among the used iodosylarenes, *o*-iodosyltoluene was found to be the most effective, and the yield of 2-fluorinated products was improved.

Key words: fluorination, hypervalent iodine, 1,3-dicarbonyl compound, iodosylarene, hydrofluoric acid

Organofluorine compounds have attracted much attention, since they are applicable to pharmaceuticals, agrochemicals and functional materials due to their unique properties. There are two major processes for the synthesis of organofluorine compounds:[1] (a) direct replacement of an atom or group by a fluorine atom and (b) indirectly using a fluorinated component as a building block. Since the fluorinated building blocks are prepared by direct fluorination, the development of methods for the introduction of fluorine atoms remains important. Although direct fluorination reactions have been conducted using molecular fluorine or other electrophilic fluorinating reagents, some drawbacks remain, namely the possibility of explosion due to instability, difficulty of handling, and the requirement for specific apparatus.

Recent remarkable progress in the chemistry of hypervalent iodine compounds has been proven that hypervalent iodine compounds are useful in organic synthesis.[2] (Difluoroiodo)arenes ($ArIF_2$) are stable and low toxic, and they have attract much attention as useful reagents because they can reduce the drawbacks found in direct fluorination reactions.[3] However, most (difluoroiodo)arenes are prepared by fluorination of iodoarenes with powerful fluorinating reagents, such as fluorine[4] or xenon difluoride,[5] they are conveniently prepared by direct replacement in (dichloroiodo)arenes with hydrogen fluoride in the presence of mercury(II) oxide,[6] and they are more simply prepared by reaction of iodosylarenes with hydrofluoric acid.[7] In addition, (difluoroiodo)arenes must be activated by a hydrofluoric acid reagent such as hydrofluoric acid–amine complexes for fluorination reactions.[3,8] Accordingly, hydrofluoric acid is essential for both the preparation and activation of (difluoroiodo)arenes in fluorination reactions. To develop a convenient one-pot fluorination reaction, we envisaged achieving both the preparation of a (difluoroiodo)arene and its activation for fluorination. In the fluorination reaction, aqueous hydrofluoric acid was considered to play both roles: (1) as the reagent for the generation of the (difluoroiodo)arene and (2) as the activating agent for the fluorination reaction, as shown in Scheme 1.



Scheme 1 Generation and activation of (difluoroiodo)arenes by hydrofluoric acid

In order to achieve one-pot fluorination reactions, we examined the fluorination of 1,3-dicarbonyl compounds. Synthesis of 2-fluoro-1,3-dicarbonyl compounds has so far been performed by the fluorination of 1,3-dicarbonyl compounds with molecular fluorine[9] and various fluorinating agents such as xenon difluoride,[10] fluoroxy compounds,[11] and fluoronitrogen compounds,[12] however, many of these reagents are dangerous or expensive. The fluorination of 1,3-dicarbonyl compounds with 4-(difluoroiodo)toluene was recently reported by Hara and Yoneda.[13] 4-(Difluoroiodo)toluene, in this case, was prepared by the reaction of 4-iodosyltoluene (*p*-TolIO) with aqueous hydrofluoric acid.[7] According to the above hypothesis, we examined direct fluorination of 1,3-dicarbonyl compounds using commercially available aqueous hydrofluoric acid in the presence of a hypervalent iodine compound and found that iodosylarenes (ArIO) were effective for the fluorination of 1,3-dicarbonyl compounds with aqueous hydrofluoric acid.[14] Here we would like to report a facile synthesis of 2-fluoro-1,3-dicarbonyl compounds,

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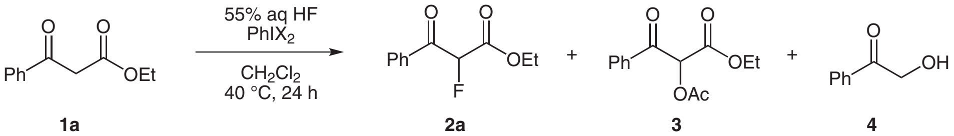
Table 1 Optimization of Fluorination Reaction of **1a**[a]



Entry	$PhIX_2$	Yield (%)[b]		
		2a	**3**	**4**
1	$PhI(OAc)_2$	39	41	16
2	$PhI(OCOCF_3)_2$	7	–	31
3	PhIO	98	–	0

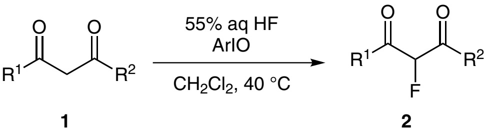
[a] Conditions: 55% aq HF (10 mmol HF), $PhIX_2$ (1.2 mmol), **1a** (1 mmol), CH_2Cl_2 (2 mL), 40 °C, 24 h.
[b] Isolated yield.

emphasizing that 2-iodosyltoluene is the most effective for mediating the fluorination reaction.

In this fluorination reaction, ethyl 3-oxo-3-phenylpropanoate (**1a**) was chosen as a model substrate and the fluorination reaction with aqueous hydrofluoric acid was investigated using hypervalent iodine compounds, (diacetoxyiodo)benzene, bis[(trifluoroacetoxy)iodo]benzene, or iodosylbenzene.

First, (diacetoxyiodo)benzene was employed because it was the most stable hypervalent iodine reagent among them and it is easy to handle. The reaction of **1a** (1 mmol) with a mixture of (diacetoxyiodo)benzene (1.2 mmol) and aqueous hydrofluoric acid (55%, 10 mmol HF) was conducted in dichloromethane (2 mL) at 40 °C for 24 hours (Table 1, entry 1). The fluorinated product, ethyl 2-fluoro-3-oxo-3-phenylpropanoate (**2a**), was obtained in 39% yield. In addition, ethyl 2-acetoxy-3-oxo-3-phenylpropanoate (**3**) and 2-hydroxyacetophenone (**4**) were also obtained in 41 and 16% yields, respectively. This result suggests that the substitution reaction by the acetate ion competes with this fluorination reaction. Next, we conducted the fluorination reaction with bis[(trifluoroacetoxy)iodo]benzene bearing a less nucleophilic trifluoroacetate. However, the reaction with bis[(trifluoroacetoxy)iodo]benzene gave **2a** only in 7% yield and **4** in 31% yield (entry 2). The formation of **4** was considered to be derived from over-oxidation by bis[(trifluoroacetoxy)iodo]benzene. Finally, it was found that iodosylbenzene was the best reagent. The reaction using iodosylbenzene under the same conditions gave **2a** in 98% yield (entry 3).

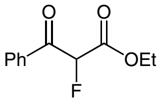
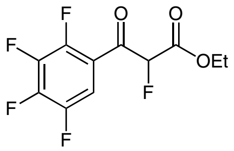
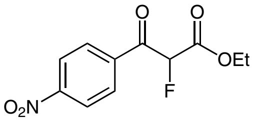
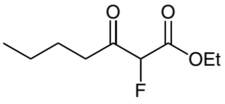
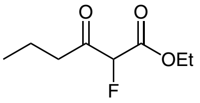
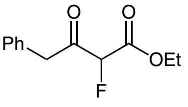
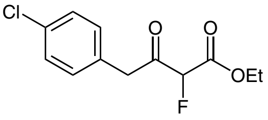
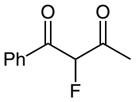
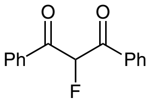
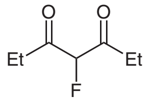
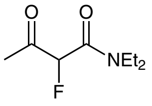
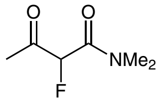
To find the scope of the fluorination reaction, several 1,3-dicarbonyl compounds were examined using the optimized conditions (Scheme 2); the results are given in Table 2. In addition to ethyl 3-oxo-3-phenylpropanoate (**1a**) (entry 1), 2,3,4,5-tetrafluoro- and 4-nitrophenyl derivatives **1b** and **1c**, aliphatic 3-oxo esters **1d** and **1e**, and 4-aryl-3-oxobutanoates **1f** and **1g** underwent the fluorination reaction to give good to high yields of 2-fluorinated 3-oxo esters **2b**–**g** (entries 3, 4, 7–10). Among them, aliphatic 3-oxo esters showed higher reactivity than aromatic ones. In addition to 3-oxo esters, 1,3-diketones **1f**–**h** and 3-oxoamides **1i** and **1j** also underwent the fluorination reaction to give the corresponding 2-fluorinated products **2f**–**j** (entries 11, 14, 16, 18, 20). However, the fluorination reaction of **1c**,**h**,**j**,**k**,**l** using iodosylbenzene did not give satisfactory results.



Scheme 2 Iodosylarene-mediated fluorination of **1** with aqueous hydrofluoric acid

In order to improve the yield, we further examined on the performance of other iodosylarenes for the fluorination reaction. 4-Iodosyltoluene (*p*-TolIO) was found to be a better reagent for fluorination than iodosylbenzene. In the case of the fluorination of **1c**, 4-iodosyltoluene improved the yield of **2c** from 58 to 78% (entry 5). However, only a slight increase in the yield of **2h** was observed in the case of **1h** (entry 12). Then, we examined about the capability of 2-iodosyltoluene (*o*-TolIO) for the fluorination. Surprisingly, 2-iodosyltoluene was found to give much better results. Although the fluorination of **1a** and **2j** with 2-iodosyltoluene resulted in a similar result to that with iodosylbenzene (entries 2 and 15), that of **1c** and **1h** was much improved to give **2c** and **2h** in 90 and 84% yields, respectively (entries 6 and 13). Although the fluorination of aliphatic 1,3-diketone **1j** gave a moderate yield (54%) of **2j** (entry 17), the fluorination of 3-oxoamides **1k** and **1l** was much improved to give **2k** and **2l** in 93 and 68% yields, respectively (entries 19 and 21). When triethylamine–pentahydrofluoride ($Et_3N{\cdot}5\,HF$) was used as the fluorinating agent in the case of **1l**, the fluorination reaction gave **2l** in 91% yield (entry 22). The high performance of iodosyltoluenes in the present fluorination reaction may be attributed to the good solubility of the hypervalent iodine reagents, (difluoroiodo)toluenes. The *ortho*-methyl group may increase the reactivity due to its steric repulsion. The fluorination of **2** using *o*- or *m*-iodosylanisole did not give the desired fluorinated products, but resulted in recovery of the starting materials and the reduced iodoanisoles. To explore the scope of the reaction further, we examined the fluorination of ethyl 2-oxocyclohexanecarboxylate as a 2-substituted oxo ester and diethyl malonate as a β-diester. However, both substrates did not give the desired fluorinated products.

Table 2 Iodosylarene-Mediated Fluorination of 1,3-Dicarbonyl Compounds[a]

Entry	ArIO	Time (h)	Product	Yield[b] (%)
1	PhIO	24	 **2a**	98
2	*o*-TolIO	24	**2a**	95
3	PhIO	24	 **2b**	70
4	PhIO	24	 **2c**	58
5	*p*-TolIO	24	**2c**	78
6	*o*-TolIO	24	**2c**	90
7	PhIO	1	 **2d**	73
8	PhIO	1	 **2e**	93
9	PhIO	24	 **2f**	100
10	PhIO	24	 **2g**	71
11	PhIO	24	 **2h**	47
12	*p*-TolIO	24	**2h**	56
13	*o*-TolIO	24	**2h**	84
14	PhIO	36	 **2i**	90
15	*o*-TolIO	24	**2i**	96
16[c]	PhIO	2	 **2j**	34[d]
17[c]	*o*-TolIO	24	**2j**	54[d]
18	PhIO	2	 **2k**	52
19	*o*-TolIO	4	**2k**	93
20	PhIO	2	 **2l**	25
21	*o*-TolIO	2	**2l**	68
22[e]	*o*-TolIO	2	**2l**	91

[a] Reaction conditions: substrate (1 mmol), ArIO (1.2 mmol), 55% aq HF (10 mmol HF), CH_2Cl_2 (2 mL), 40 °C.

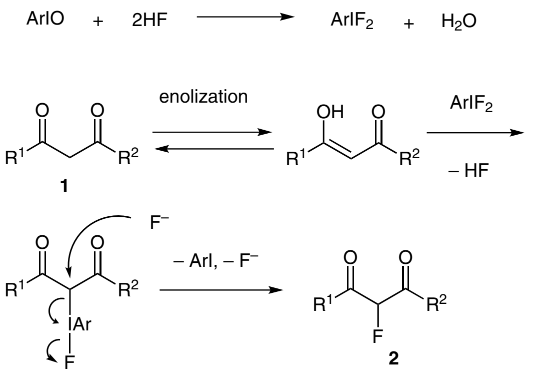
[b] Isolated yields.

[c] At r.t.

[d] Determined by ^{1}H NMR.

[e] $Et_3N·5\ HF$ (2 mmol) was used instead of 55% aq HF.

In order to understand the reaction mechanism, we performed the isolation of (difluoroiodo)benzene under the reaction conditions without 1,3-dicarbonyl compounds **1**. After mixing iodosylbenzene with aqueous hydrofluoric acid in dichloromethane, extraction with dichloromethane gave (difluoroiodo)benzene in 72% yield as a solid. Therefore, it is suggested that a (difluoroiodo)arene ($ArIF_2$) is a key fluorinating agent. A possible mechanism is shown in Scheme 3. The reaction of (difluoroiodo)arene with **1** is considered to proceed effectively after enolization of **1** because it has been reported that the enol form of **1** reacts with hypervalent iodine compounds.[3] The resulting 2-iodanyl-1,3-dicarbonyl compound readily undergoes displacement by a fluoride ion due to the high leaving ability of the phenyliodonio group, to give the fluorine-containing product **2**.



Scheme 3 A possible mechanism for fluorination of 1,3-dicarbonyl compounds

In summary, we have developed an efficient and convenient fluorination reaction of 1,3-dicarbonyl compounds mediated by iodosylarenes. The fluorination reaction was performed by mixing the substrate with aqueous hydrofluoric acid and iodosylarene. This simple and easy procedure was applied to the fluorination of 1,3-diketones, 3-oxo esters, and 3-oxoamides. Although the fluorination of 3-oxo esters proceeded with iodosylbenzene to give good yields of the products, aliphatic 1,3-diketones and 3-oxoamides did not undergo the fluorination well. Iodosyltoluenes, especially 2-iodosyltoluene, improved the fluorination reaction to give good results even in the case of 3-oxoamides.

All solvents and starting materials were used as received without further purification unless otherwise indicated. ^{1}H (300 MHz), ^{13}C (75 MHz), and ^{19}F NMR (282 MHz) spectra were recorded on a Jeol JNM-Al 300 FT-NMR spectrometer in CDCl$_3$ soln. Melting points were measured with a Yanaco micro melting apparatus and are uncorrected. Column chromatographic separations were carried out using silica gel as the stationary phase. Pre-coated plates (silica gel 60 F$_{254}$, MERCK) were used for TLC examination.

Ethyl 2-Fluoro-3-oxo-3-phenylpropanoate (2a); Typical Procedure

To a PFA test tube were added the hypervalent iodine reagent, PhI(OAc)$_2$ or PhI(OCOCF$_3$)$_2$, (1.2 mmol), 55% aq HF soln (0.64 mL, 10 mmol HF), and CH$_2$Cl$_2$ (2 mL). After stirring for 15 min at r.t., **1a** (1 mmol) was added and then the mixture was stirred at 40 °C for 12 or 24 h. The mixture was poured into H$_2$O (20 mL), neutralized with NaHCO$_3$, and extracted with CH$_2$Cl$_2$ (3 × 6 mL). The combined organic layers were washed with sat. NaCl and dried (anhydrous Na$_2$SO$_4$). After evaporation of the solvent, purification of the residue by column chromatography (silica gel, EtOAc–hexane or CH$_2$Cl$_2$–hexane) gave **2a**[15] as a colorless oil; yield: 206 mg (98%, Table 1, entry 3).

IR: 1762 (C=O), 1697 cm^{-1} (C=O).

^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.26 (t, J = 7.2 Hz, 3 H, Me), 4.30 (q, J = 7.2 Hz, 2 H, CH$_2$), 5.87 (d, J = 48 Hz, 1 H, CHF), 7.48–7.53 (m, 2 H, H$_{Ar}$), 7.61–7.67 (m, 1 H, H$_{Ar}$), 8.03–8.06 (m, 2 H, H$_{Ar}$).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 13.8, 62.6, 90.0 (d, J = 196.0 Hz), 128.8, 129.4 (d, J = 3.8 Hz), 133.4 (d, J = 1.9 Hz), 134.4, 164.8 (d, J = 24.2 Hz), 189.5 (d, J = 19.7 Hz).

^{19}F NMR (282 MHz, CDCl$_3$): δ = –190.57 (d, J = 48 Hz).

Ethyl 2-Acetoxy-3-oxo-3-phenylpropanoate (3)[16]

Colorless oil; yield: 103 mg (41%, Table 1, entry 1).

^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.21 (t, J = 7.2 Hz, 3 H, Me), 2.22 (s, 3 H, MeCO), 4.25 (q, J = 7.2 Hz, 2 H, CH$_2$), 6.33 (s, 1 H, CH), 7.47–7.52 (m, 2 H, H$_{Ar}$), 7.60–7.65 (m, 1 H, H$_{Ar}$), 7.98–8.02 (m, 2 H, H$_{Ar}$).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 13.8, 20.4, 62.4, 74.4, 128.7, 129.1, 134.1, 134.2, 165.1, 169.4, 189.6.

2-Hydroxyacetophenone (4)[17]

Colorless crystals; yield: 42 mg (31%, Table 1, entry 2); mp 83.5–84.5 °C (hexane–EtOH).

^{1}H NMR (300 MHz, CDCl$_3$): δ = 3.51 (br s, 1 H, OH), 4.88 (s, 2 H, CH$_2$), 7.48–7.53 (m, 2 H, H$_{Ar}$), 7.61–7.66 (m, 1 H, H$_{Ar}$), 7.91–7.94 (m, 2 H, H$_{Ar}$).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 65.4, 127.7, 129.0, 133.4, 134.3, 198.4.

2-Fluoro-1,3-Dicarbonyl Compounds 2a–l; General Procedure

To a PFA test tube were added ArIO (1.2 mmol), 55% aq HF soln (0.64 mL, 10 mmol HF), and CH$_2$Cl$_2$ (2 mL). After stirring for 15 min at r.t., a 1,3-dicarbonyl compound **1** (1 mmol) was added and then the mixture was stirred at 40 °C for the time given in Table 2. The mixture was poured into H$_2$O (20 mL), neutralized with NaHCO$_3$, and extracted with CH$_2$Cl$_2$ (3 × 6 mL) The combined organic layers were washed with sat. NaCl and dried (anhydrous Na$_2$SO$_4$). After evaporation of the solvent, the product was isolated by column chromatography (silica gel, EtOAc–hexane).

Ethyl 2-Fluoro-3-oxo-3-(2,3,4,5-tetrafluorophenyl)propanoate (2b)[14]

Colorless oil; yield: 198 mg (70%, Table 2, entry 3).

IR (KBr): 1771 (C=O), 1717 cm^{-1} (C=O).

^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.26–1.32 (m, 3 H, Me), 4.28–4.36 (m, 2 H, CH$_2$), 5.89 (d, J = 47 Hz, 1 H, CHF), 7.53–7.62 (m, 1 H, H$_{Ar}$).

^{19}F NMR (282 MHz, CDCl$_3$): δ = –135.46, –137.15, –145.56, –153.94, –195.69 (dd, J = 15.0, 47 Hz).

Ethyl 2-Fluoro-3-(4-nitrophenyl)-3-oxopropanoate (2c)[18]

Pale yellow oil; yield: 230 mg (90%, Table 2, entry 6).

IR (KBr): 1766 (C=O), 1713 cm^{-1} (C=O).

^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.29 (t, J = 7.2 Hz, 3 H, Me), 4.34 (dq, J = 1.5, 7.2 Hz, 2 H, CH$_2$), 5.95 (d, J = 49 Hz, 1 H, CHF), 8.22–8.38 (m, 4 H, H$_{Ar}$).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 13.8, 63.0, 90.1 (d, J = 197.2 Hz), 123.8, 130.6 (d, J = 4.4 Hz), 137.6 (d, J = 2.5 Hz), 164.7 (d, J = 23.5 Hz), 188.5 (d, J = 21.0 Hz).

^{19}F NMR (282 MHz, CDCl$_3$): δ = –191.81 (d, J = 49 Hz).

Ethyl 2-Fluoro-3-oxo-heptanoate (2d)[19]

Colorless oil; yield: 139 mg (73%, Table 2, entry 7).

IR (KBr): 1760 (C=O), 1733 cm^{-1} (C=O).

^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.84 (t, J = 7.2 Hz, 3 H, Me), 1.25 (t, J = 7.2 Hz, 3 H, Me), 1.26 (sext, J = 7.2 Hz, 2 H, CH$_2$), 1.52 (quint, J = 72 Hz, 2 H, CH$_2$), 2.57–2.64 (m, 2 H, CH$_2$), 4.23 (q, J = 7.2 Hz, 2 H, CH$_2$), 5.16 (d, J = 49 Hz, 1 H, CHF).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 13.6, 13.9, 22.0, 24.7, 38.1, 62.5, 91.3 (d, J = 196.6 Hz), 164.2 (d, J = 23.5 Hz), 201.3 (d, J = 22.3 Hz).

^{19}F NMR (282 MHz, CDCl$_3$): δ = –195.99 (d, J = 49 Hz).

Ethyl 2-Fluoro-3-oxohexanoate (2e)[20]
Colorless oil; yield: 164 mg (93%, Table 2, entry 8).

IR (KBr): 1760 (C=O), 1732 cm^{-1} (C=O).

^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.86 (t, J = 7.3 Hz, 3 H, Me), 1.25 (t, J = 7.2 Hz, 3 H, Me), 1.58 (sext, J = 7.2 Hz, 2 H, CH$_2$), 2.55–2.62 (m, 2 H, CH$_2$), 4.23 (q, J = 7.2 Hz, 2 H, CH$_2$), 5.16 (d, J = 49 Hz, 1 H, CHF).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 13.3, 13.8, 16.1, 40.2, 62.5, 91.3 (d, J = 196.0 Hz), 164.1 (d, J = 24.1 Hz), 201.1 (d, J = 22.2 Hz).

^{19}F NMR (282 MHz, CDCl$_3$): δ = –195.95 (d, J = 49 Hz).

Ethyl 2-Fluoro-3-oxo-4-phenylbutanoate (2f)
Colorless oil; yield: 224 mg (100%, Table 2, entry 9).

^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.26 (t, J = 7.2 Hz, 3 H, Me), 4.02 (d, J = 3.0 Hz, 2 H, CH$_2$), 4.26 (q, J = 7.2 Hz, 2 H, CH$_2$), 5.33 (d, J = 48.9 Hz, 1 H, CHF), 7.25–7.38 (m, 5 H, H$_{Ar}$).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 13.7 (d, J = 3.8 Hz), 45.1, 62.5, 90.6 (d, J = 197.2 Hz), 127.3, 128.5 (d, J = 3.8 Hz), 129.5 (d, J = 3.8 Hz), 131.7, 163.8 (d, J = 20.1 Hz), 198.2 (d, J = 22.9 Hz).

HRMS (EI): m/z [M]$^+$ calcd for C$_{12}$H$_{13}$FO$_3$: 224.0849; found: 224.0845.

Ethyl 4-(4-Chlorophenyl)-2-fluoro-3-oxobutanoate (2g)
Colorless oil; yield: 184 mg (71%, Table 2, entry 10).

^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.26 (t, J = 7.2 Hz, 3 H, Me), 3.94 (d, J = 3.0 Hz, 2 H, CH$_2$), 4.24 (q, J = 7.2 Hz, 2 H, CH$_2$), 5.28 (d, J = 48.9 Hz, 1 H, CHF), 7.10–7.30 (m, 4 H, H$_{Ar}$).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 13.8 (d, J = 3.8 Hz), 44.3 (d, J = 3.8 Hz), 62.6, 90.7 (d, J = 197.2 Hz), 128.7 (d, J = 3.1 Hz), 130.2 (d, J = 1.3 Hz), 131.0 (d, J = 3.8 Hz), 133.3, 163.7 (d, J = 23.5 Hz), 197.9 (d, J = 22.9 Hz).

HRMS (EI): m/z [M]$^+$ calcd for C$_{12}$H$_{12}$ClFO$_3$: 258.0459; found: 258.0461.

2-Fluoro-1-phenylbutane-1,3-dione (2h)[20]
Colorless oil; yield: 151 mg (84%, Table 2, entry 13).

IR (KBr): 1736 (C=O), 1695 cm^{-1} (C=O).

^{1}H NMR (300 MHz, CDCl$_3$): δ = 2.34 (d, J = 4.2 Hz, 3 H, Me), 5.95 (d, J = 49 Hz, 1 H, CHF), 7.46–8.03 (m, 5 H, H$_{Ar}$).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 25.9, 96.5 (d, J = 197.2 Hz), 128.7, 129.6 (d, J = 3.1 Hz), 133.4, 134.6, 190.2 (d, J = 19.1 Hz), 200.5 (d, J = 23.5 Hz).

^{19}F NMR (282 MHz, CDCl$_3$): δ = –182.54 (dq, J = 4.2, 49 Hz).

2-Fluoro-1,3-diphenylpropane-1,3-dione (2i)[20]
Pale yellow crystals; yield: 233 mg (96%, Table 2, entry 15); mp 66.5–67.7 °C (hexane).

IR (KBr): 1701 (C=O), 1683 cm^{-1} (C=O).

^{1}H NMR (300 MHz, CDCl$_3$): δ = 6.54 (d, J = 49 Hz, 1 H, CHF), 7.43–7.50 (m, 4 H, H$_{Ar}$), 7.56–7.63 (m, 2 H, H$_{Ar}$), 8.07–8.10 (m, 4 H, H$_{Ar}$).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 96.5 (d, J = 197.2 Hz), 128.7, 129.7 (d, J = 3.1 Hz), 133.5 (d, J = 1.8 Hz), 134.5, 191.1 (d, J = 19.8 Hz).

^{19}F NMR (282 MHz, CDCl$_3$): δ = –188.20 (d, J = 49 Hz).

4-Fluoroheptane-3,5-dione (2j)[21]
Colorless oil; yield: 45 mg (31%, Table 2, entry 17).

^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.08 (t, J = 7.2 Hz, 6 H, Me), 2.49–2.82 (m, 4 H, CH$_2$), 5.30 (d, J = 50 Hz, 1 H, CHF).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 6.7 (d, J = 2.5 Hz), 32.2, 98.1 (d, J = 197.8 Hz), 202.3 (d, J = 24.3 Hz).

^{19}F NMR (282 MHz, CDCl$_3$): δ = –196.55 (d, J = 50 Hz).

***N*,*N*-Diethyl-2-fluoro-3-oxobutanamide (2k)**[22]
Yellow oil; yield: 163 mg (93%, Table 2, entry 19).

^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.05 (t, J = 7.2 Hz, 3 H, Me), 1.11 (t, J = 7.2 Hz, 3 H, Me), 2.24 (d, J = 5.2 Hz, 3 H, Me), 3.22–3.39 (m, 4 H, CH$_2$), 5.33 (d, J = 50 Hz, 1 H, CHF).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 10.0, 11.7, 23.5, 38.3, 39.3 (d, J = 3.7 Hz), 89.2 (d, J = 194.1 Hz), 160.6 (d, J = 19.7 Hz), 199.6 (d, J = 24.8 Hz).

^{19}F NMR (282 MHz, CDCl$_3$): δ = –189.29 (d, J = 50 Hz).

***N*,*N*-Dimethyl-2-fluoro-3-oxobutanamide (2l)**[20]
Yellow oil; yield: 134 mg (91%, Table 2, entry 22).

^{1}H NMR (300 MHz, CDCl$_3$): δ = 2.3 (d, J = 4.2 Hz, 3 H, Me), 3.00 (d, J = 1.2 Hz, 3 H, Me), 3.11 (d, J = 1.5 Hz, 3 H, Me), 5.51 (d, J = 50 Hz, 1 H, CHF).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 26.0, 36.0, 36.9 (d, J = 4.4 Hz), 91.4 (d, J = 193.5 Hz), 163.6 (d, J = 19.8 Hz), 201.8 (d, J = 24.2 Hz).

^{19}F NMR (282 MHz, CDCl$_3$): δ = –189.71 (d, J = 50 Hz).

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