Supporting Information

Photocatalytic Site-Selective C–H Difluoroalkylation of Aromatic Aldehydes

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1. General information

All the reactions were conducted in oven-dried Schlenk tubes. All solvents were obtained from commercial suppliers. Flash column chromatographic purification of products was accomplished using forced-flow chromatography on Silica Gel (200-300 mesh).

¹H NMR (600 Hz), ¹³C NMR (150 Hz) and ¹⁹F NMR (564 Hz) were recorded in CDCl₃ using TMS as internal standard. Data for ¹H NMR are reported as follows: chemical shift (ppm, scale), multiplicity, coupling constant (Hz), and integration. Data for ¹³C NMR are reported in terms of chemical shift (ppm, scale), multiplicity, and coupling constant (Hz). Gas chromatographic (GC) analyses were performed on a GC equipped with a flameionization detector and an Rtx@-65 (30 m × 0.32 mm ID × 0.25 µm df) column. GC-MS analyses were performed on a GC-MS with an EI mode. High-resolution mass spectra were obtained by EI and ESI on a TOF mass analyzer.

2. Reaction optimization for para-difluoroalkylation of benzaldehydes

Table S1. Screen of photoredox catalyst

Сн	• Br F OEt • Br OEt Ar, rt, 18 h 0 18 W blue L	→ ED RO₂CF	² CHO 3a, R = Ft
1a	2		
entry	PC	time (h)	yield (%)
			[p/(o+m)]
1	$Ru(bpy)_3(PF_6)_2$	18	< 8
2	[Ru(bpy) ₃]Cl ₂ ·6H ₂ O	18	trace
3	Eosin Y	18	0
4	ArCH ⁺ ClO ₄ ⁻	18	0
5	$Ru(bpy)_3Cl_2$	18	0
6	Rose Bengal	18	0
7	Rhodamine B	18	0
8	<i>fac</i> -Ir(ppy) ₃	18	30 (0.9/1)
9	[Co(dmgH) ₂ pySnPh ₃]	18	< 5

^{*a*}reaction conditions: **1a** (0.1 mmol), BrCF₂CO₂Et **2** (1 mmol), K₂CO₃ (6 equiv), photoredox catalyst (PC, 3 mol %) in 2 mL TFE at room temperature under an argon atmosphere and a 18 W blue LED, unless otherwise noted. ^{*b*}Yields are calculated for the isolated products, selectivities [p/(o+m)] were determined by ¹H NMR.





entry	solvents	time	yield (%)
		(h)	[p/(o+m)]
1	TFE	18	30 (0.9/1)
2	DCM	18	37 (1.0/1.0)
3	HFIP	18	29 (1.0/1.0)
4	EtOH	18	55 (0.8/1.0)
5	<i>n</i> -hexane	18	18 (0.7/1.0)
6	acetone	18	70 (1.9/1.0)
7	<i>t</i> -BuOH (0.5 mL)	18	64 (4.3/1.0)
8	MeOH	18	< 15 (2.0/1.0)
9	H ₂ O	18	< 10 (0.1/1.0)
10	MeOH/TFE (17/3)	18	40 (7.0/1.0)
11	MeOH/acetone (17/3)	18	58 (2.8/1.0)
12	MeOH/HFIP (17/3)	18	38 (7.0/1.0)

^{*a*} reaction conditions: **1a** (0.1 mmol), BrCF₂CO₂Et **2** (1 mmol), K₂CO₃ (6 equiv), the *fac*-Ir(ppy)₃ (3 mol %) in solvents (2 mL) at room temperature under an argon atmosphere and a 18 W blue LED, unless otherwise noted. ^{*b*} Yields are calculated for the isolated products, selectivities [p/(o+m)] were determined by ¹H NMR. (*3a'* was obtained in the presence of MeOH)

Table S3. Screen of base

la	,⊂HO +		ac-lr(ppy) ₃ base (6 MeOH/ (2 mL, Ar, rt, 18 W blu	(3 mol %) equiv) TFE 17/3) 18 h Je LED	MeO ₂ CF ₂ C 3a'	,⊂HO
	entry	bas	e	time (h)	yield (%)	
					[p/(o+m)]	
	1	K ₂ C	O ₃	18	40 (7/1)	
	2	KO	Ac	18	63 (7/1)	
	3	KO	Н	18	< 10	
	4	NE	t ₃	18	trace	
	5	ⁱ Pr ₂ N	JEt	18	trace	

^{*a*}reaction conditions: **1a** (0.1 mmol), BrCF₂CO₂Et **2** (1 mmol), base (6 equiv), the *fac*-Ir(ppy)₃ (3 mol %) in a mixture of MeOH/TFE (2 mL, 17/3) at room temperature under an argon atmosphere and a 18 W blue LED, unless otherwise noted. ^{*b*}Yields are calculated for the isolated products, selectivities [p/(o+m)] were determined by ¹H NMR. (*3a' was obtained in the presence of MeOH*)

Table S4. Screen of the amount of KOAc or 2

la	_CHO +		Hr(ppy) ₃ (3 mol %) base (6 equiv) HeOH/CF ₃ CH ₂ OH (2 mL, 17/3) Ar, rt, 18 h 18 W blue LED	MeO ₂ CF ₂ C	СНО
	entry	2	KOAc	yield (%)	—
		(eq.)	(eq.)		
	1	10	6	63	_
	2	5	6	30	
	3	2	6	<15	
	4	10	4	42	
	5	10	2	20	_

^{*a*} reaction conditions: **1a** (0.1 mmol), BrCF₂CO₂Et **2** (X eq.), KOAc (6 equiv), the *fac*-Ir(ppy)₃ (3 mol %) in a mixture of MeOH/TFE (2 mL, 17/3) at room temperature under an argon atmosphere and a 18 W blue LED, unless otherwise noted. ^{*b*} Yields are calculated for the isolated products. (*3a'* was obtained in the presence of MeOH)

Table S1, entry 10, ¹H NMR spectrum.



3. General procedures for para-difluoroalkylation of benzaldehydes



Procedure 1 (1a, 1b, 1d-1g, 1p-1q, and 1t): To a 25 mL of Schlenk tube *fac*-Ir(ppy)₃ (3 mol %), KOAc (6 equiv) under air. The mixture was evacuated and backfilled with Ar (3 times). The benzaldehyde **1a** (0.1 mmol) and BrCF₂CO₂Et **2** (1 mmol) and degassed MeOH/TFE (2 mL, 17/3)

were added successively. The mixture was stirred at room temperature for 18 hours while irradiated by 18 W blue LED. The reaction mixture was quenched with 1N HCl aqueous and extracted with E_2O (20 mL x 3). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4 and concentrated in vacuo. The organic layer was concentrated and purified directly by column chromatography to afford the products.

Procedure 2 (1c): To a 25 mL of Schlenk tube *fac*-Ir(ppy)₃ (3 mol %), Fe(OAc)₂ (1.2 equiv) and KOAc (6 equiv) under air. The mixture was evacuated and backfilled with Ar (3 times). The benzaldehyde **1c** (0.1 mmol) and BrCF₂CO₂Et **2** (1 mmol) and degassed MeOH/TFE (2 mL, 17/3) were added successively. The mixture was stirred at room temperature for 18 hours while irradiated by 18 W blue LED. The reaction mixture was quenched with 1N HCl aqueous and extracted with Et₂O (20 mL x 3). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄ and concentrated in vacuo. The organic layer was concentrated and purified directly by column chromatography to afford the products



Procedure 3 (1h-1o): To a 25 mL of Schlenk tube *fac*-Ir(ppy)₃ (1 mol %) and K₂CO₃ (4 equiv) under air. The mixture was evacuated and backfilled with Ar (3 times). The benzaldehydes (**1j-1o**) (0.1 mmol) and BrCF₂CO₂Et **2** (1 mmol) and *t*-BuOH (*t*-BuOH/acetone) (0.5 mL) were added successively. The mixture was stirred at room temperature for 40 hours while irradiated by 18 W blue LED. EtOAc (20 mL) and H₂O (20 mL) were added to the reaction mixture at ambient temperature. The separated aqueous phase was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄ and concentrated in vacuo. The organic layer was concentrated and purified directly by column chromatography to afford the products (**3j-3o**).

4. Characterization of product 3.

Methyl 2,2-difluoro-2-(4-formylphenyl)acetate (3a'). Following general procedure, the product was purified by flash chromatography (PE/EA = 20:1) as a colorless oil (13.5 mg, 63%).

¹H NMR (600 MHz, CDCl₃) δ 10.02 (s, 1H), 7.91 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.2 Hz, 2H),

3.80 (s, 3H).

¹³C NMR (151 MHz, CDCl3) δ 191.23, 163.94 (t, *J* = 34.8 Hz), 138.14, 129.82, 126.36 (t, *J* = 6.1

Hz), 112.79 (t, *J* = 253.1 Hz), 53.86.

¹⁹F NMR (564 MHz, CDCl₃) δ -104.42 (s, 2F).

HRMS ESI (m/z): $[M+Na]^+$ calcd. for $C_{10}H_8F_2NaO_3$: 237.0334, found: 237.0334.



Methyl 2,2-difluoro-2-(4-formyl-2-methylphenyl)acetate (3b'). Following general procedure, the product was purified by flash chromatography (PE/EA = 10:1) as a colorless oil (11.1 mg, 49%).

¹H NMR (600 MHz, CDCl₃) δ 9.97 (s, 1H), 7.71 (q, *J* = 8.0 Hz, 2H), 7.67 (s, 1H), 3.80 (s, 3H),

2.42 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 191.51, 163.92 (t, *J* = 34.6 Hz), 137.85, 137.69 (t, *J* = 3.0 Hz),

136.54 (t, J = 23.3 Hz), 132.60, 127.23, 127.04 (t, J = 8.9 Hz), 113.52 (t, J = 252.6 Hz), 53.82,

19.61.

¹⁹F NMR (564 MHz, CDCl₃) δ -102.03 (s, 2F).

HRMS ESI (m/z): [M+Na]⁺ calcd. for C₁₁H₁₀F₂NaO₃: 251.0490, found: 251.0490



Methyl 2,2-difluoro-2-(4-formyl-2-methoxyphenyl)acetate (3c'). Following general procedure, the product was purified by flash chromatography (PE/EA = 10:1) as a colorless oil (19.5 mg, 80%).

¹H NMR (600 MHz, CDCl₃) δ 10.04 (s, 1H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.46 (s, 1H), 3.91 (s, 3H), 3.87 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 191.19, 163.78 (t, *J* = 33.7 Hz), 157.34 (t, *J* = 4.7 Hz), 139.64, 127.53 (t, *J* = 24.0 Hz), 127.20 (t, *J* = 7.6 Hz), 123.71, 111.53 (t, *J* = 249.5 Hz), 109.78, 56.16, 53.47.

¹⁹F NMR (564 MHz, CDCl₃) δ -103.61 (s, 2F).

HRMS ESI (m/z): [M+Na]⁺ calcd. for C₁₁H₁₀F₂NaO₄: 267.0439, found: 267.0433.

ethyl 2,2-difluoro-2-(4-formyl-2-methoxyphenyl)acetate (3c). Following general procedure, the product was purified by flash chromatography (PE/EA = 10:1) as a colorless oil (20 mg, 78%). ¹H NMR (600 MHz, CDCl₃) δ 10.03 (s, 1H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.45 (s, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.90 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 191.31, 163.32, 157.29, 139.57, 127.72 (t, *J* = 23.7 Hz), 127.25 (t, *J* = 7.6 Hz), 123.86, 111.58 (t, *J* = 249.8 Hz), 109.53, 62.94, 56.03, 13.92.

¹⁹F NMR (564 MHz, CDCl₃) δ -103.65 (s, 2F).

Methyl 2,2-difluoro-2-(4-formyl-2-(trifluoromethoxy)phenyl)acetate (3d'). Following general procedure, the product was purified by flash chromatography (PE/EA = 10:1) as a colorless oil (8.9 mg, 30%).

¹H NMR (600 MHz, CDCl₃) δ 10.00 (s, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H),

7.77 (s, 1H), 3.83 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 189.58, 162.91 (t, *J* = 33.3 Hz), 139.71, 130.50, 128.40 (t, *J* = 7.8

Hz), 127.90, 120.06 (d, *J* = 261.6 Hz), 118.78, 110.89 (t, *J* = 252.4 Hz), 109.98, 53.84.

¹⁹F NMR (564 MHz, CDCl₃) δ -57.05 (s, 3F), -102.57 (s, 2F).

HRMS (ESI) m/z calc. for C₁₁H₈F₅O₄ [M+H]⁺ 299.0337, found 299.0337.



Methyl 2,2-difluoro-2-(2-fluoro-4-formylphenyl)acetate (3e'). Following general procedure, the product was purified by flash chromatography (PE/EA = 10:1) as a colorless oil (7.8 mg, 34%). ¹H NMR (600 MHz, CDCl₃) δ 9.98 (s, 1H), 7.79 (t, *J* = 7.3 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 10.0 Hz, 1H), 3.85 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 189.77, 162.96 (t, *J* = 33.6 Hz), 160.12 (d, *J* = 256.1 Hz), 140.31 (d, *J* = 6.5 Hz), 128.20 (t, *J* = 6.1 Hz), 125.76 (d, *J* = 3.5 Hz), 116.23, 116.09, 111.00 (t, *J* = 252.6 Hz), 53.99.

¹⁹F NMR (564 MHz, CDCl₃) δ -102.64 (s, 2F), -112.34 (s, 1F).

HRMS (ESI) m/z calc. for $C_{10}H_8F_3O_4$ [M+H]⁺ 233.0420, found 233.0420.

Methyl-4-(3-chlorophenyl)-2,2-difluorobut-3-enoate (3f'). Following general procedure, the product was purified by flash chromatography (PE/EA = 20:1) as a colorless oil (9.8 mg, 40%). ¹H NMR (600 MHz, CDCl₃) δ 10.05 (s, 1H), 7.95 (d, *J* = 8.7 Hz, 2H), 7.91 (d, *J* = 8.0 Hz, 1H), 3.91 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 189.87, 162.92 (t, *J* = 33.7 Hz), 139.05, 136.27, 133.32, 131.00,

128.25 (t, J = 8.5 Hz), 128.01, 111.58 (t, J = 252.1 Hz), 54.01.

¹⁹F NMR (564 MHz, CDCl₃) δ -102.84 (s, 2F).

HRMS (EI) (m/z): calcd. for C₁₀H₇ClF₂O₃: 248.0052, found: 248.0046.

Methyl 2-(2-bromo-4-formylphenyl)-2,2-difluoroacetate (3g'). Following general procedure, the product was purified by flash chromatography (PE/EA = 20:1) as a colorless oil (11.3 mg, 39%).

¹H NMR (600 MHz, CDCl₃) δ 9.97 (s, 1H), 8.07 (s, 1H), 7.87 (q, *J* = 8.1 Hz, 2H), 3.84 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 189.79, 162.83 (t, *J* = 33.5 Hz), 138.99, 137.92 (t, *J* = 24.1 Hz),

134.52, 128.51 (t, J = 8.9 Hz), 128.48, 121.44 (t, J = 4.1 Hz), 112.16 (t, J = 251.9 Hz), 54.03.

¹⁹F NMR (564 MHz, CDCl₃) δ -102.23 (s, 2F).

HRMS EI (m/z): $[M-Br]^+$ calcd. for $C_{10}H_7F_2O_3$: 213.0358, found: 213.0356; $[M-C_2H_3O_2]^+$ calcd. for $C_8H_4F_2O$: 232.9408, found: 232.9408.

HRMS ESI (m/z): [M+H]⁺ calcd. for C₁₀H₈F₂O₃: 292.9619, found: 292.9615

Ethyl 2-(2,4-diformylphenyl)-2,2-difluoroacetate (3h). Following general procedure, the product was purified by flash chromatography (PE/EA = 5:1) as a yellow solid (9.5 mg, 38%).

¹H NMR (600 MHz, CDCl₃) δ 10.23 (s, 1H), 10.10 (s, 1H), 8.43 (s, 1H), 8.15 (d, J = 8.0 Hz, 1H),

7.96 (d, J = 8.0 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 1.27 (t, J = 7.1 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 190.10, 189.76, 162.63 (t, *J* = 33.1 Hz), 138.23, 137.86 (t, *J* = 25.1

Hz), 134.93, 133.76, 132.73, 127.83 (t, *J* = 9.6 Hz), 112.69 (t, *J* = 253.6 Hz), 63.67, 13.76.

¹⁹F NMR (564 MHz, CDCl₃) δ -98.71 (s, 2F).

HRMS ESI (m/z): [M+Na]⁺ calcd. for C₁₂H₁₀F₂NaO₄: 279.0439, found: 279.0440.

Ethyl 2-(2-cyano-4-formylphenyl)-2,2-difluoroacetate (3i). Following general procedure, the product was purified by flash chromatography (PE/EA = 5:1) as a yellow oil (3.8 mg, 15%).

¹H NMR (600 MHz, CDCl₃) δ 10.11 (s, 1H), 8.30 (s, 1H), 8.21 (d, J = 8.0 Hz, 1H), 7.99 (d, J = 8.1 Hz, 1H), 4.40 (q, J = 7.1 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 188.90, 162.19 – 161.60 (m), 140.25 (t, J = 25.1 Hz), 138.00, 135.09, 133.14, 128.07 (t, J = 7.5 Hz), 114.91, 111.92, 111.70 (t, J = 255.8 Hz), 64.29, 13.81. ¹⁹F NMR (564 MHz, CDCl₃) δ -101.90 (s, 2F).

HRMS (ESI) m/z calc. for $C_{12}H_{10}F_2NO_3$ [M+H]⁺ 254.0623, found 254.0627.



Ethyl 2,2-difluoro-2-(4-formyl-3-methylphenyl)acetate (3j). Following general procedure, the product was purified by flash chromatography (PE/EA = 30:1) as a colorless oil (16.9 mg, 70%). ¹H NMR (600 MHz, CDCl₃) δ 10.25 (s, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 8.1 Hz, 1H), 7.45 (s, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 2.65 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 191.86, 163.58 (t, *J* = 34.7 Hz), 141.08, 137.31 (t, *J* = 25.4 Hz), 135.76, 131.94, 128.79 (t, *J* = 5.9 Hz), 123.49 (t, *J* = 6.1 Hz), 112.75 (t, *J* = 253.1 Hz), 63.46, 19.60, 13.85.

¹⁹F NMR (564 MHz, CDCl3) δ -104.82 (s, 2F).

HRMS ESI (m/z): $[M+H]^+$ calcd. for $C_{12}H_{13}F_2O_3$: 243.0827, found: 243.0822.

Ethyl 2,2-difluoro-2-(4-formyl-3-methoxyphenyl)acetate (3k). Following general procedure, the product was purified by flash chromatography (PE/EA = 30:1) as a colorless oil (17.5 mg, 68%).

¹H NMR (600 MHz, CDCl3) δ 10.49 (s, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.27 (d, J = 8.0 Hz, 1H),

7.23 (s, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 3.99 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 189.02, 163.49 (t, *J* = 34.0 Hz), 161.57, 139.64 (t, *J* = 25.3 Hz),

128.97, 126.41, 117.72 (t, J = 6.0 Hz), 112.67 (t, J = 253.4 Hz), 108.99 (t, J = 6.4 Hz), 63.50,

¹⁹F NMR (564 MHz, CDCl₃) δ -104.90 (s, 2F).

HRMS (EI) (m/z): calcd. for C₁₂H₁₂F₂O₄: 258.0704, found: 258.0698.



Ethyl 2,2-difluoro-2-(4-formyl-3-(trifluoromethoxy)phenyl)acetate (31). Following general procedure, the product was purified by flash chromatography (PE/EA = 20:1) as a colorless oil (15.5 mg, 50%).

¹H NMR (600 MHz, CDCl₃) δ 10.40 (s, 1H), 8.07 (d, J = 8.1 Hz, 1H), 7.69 (d, J = 8.2 Hz, 1H),

7.63 (s, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 186.58, 162.84 (t, *J* = 33.4 Hz), 150.58, 139.90 (t, *J* = 26.0 Hz), 130.11, 129.58, 124.55 (t, *J* = 6.0 Hz), 121.09, 119.16 (t, *J* = 6.5 Hz), 111.95 (t, *J* = 254.2 Hz),

¹⁹F NMR (564 MHz, CDCl₃) δ -57.83 (s, 3F), -104.68 (s, 2F).

HRMS (EI) (m/z): calcd. for C₁₂H₉F₅O₄: 312.0421, found: 312.0417.



Ethyl 2,2-difluoro-2-(3-fluoro-4-formylphenyl)acetate (3m). Following general procedure, the product was purified by flash chromatography (PE/EA = 30:1) as a colorless oil (9.3 mg, 38%). ¹H NMR (600 MHz, CDCl₃) δ 10.40 (s, 1H), 7.98 (t, *J* = 7.4 Hz, 1H), 7.53 (d, *J* = 8.1 Hz, 1H), 7.48 (d, *J* = 10.3 Hz, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 186.26, 165.01, 163.29, 162.98 (t, *J* = 34.3 Hz), 140.46 (d, *J* = 8.5 Hz), 129.30 (d, *J* = 2.2 Hz), 125.70, 121.85 (d, *J* = 4.0 Hz), 114.60 (t, *J* = 6.3 Hz), 114.44 (t, *J* = 6.4 Hz), 63.75, 13.84.

¹⁹F NMR (564 MHz, CDCl₃) δ -104.70 (s), -120.02 (s).

HRMS (EI) (m/z): calcd. for C₁₁H₉F₃O₃: 246.0504, found: 246.0489.

Ethyl 2-(3-chloro-4-formylphenyl)-2,2-difluoroacetate (3n). Following general procedure, the product was purified by flash chromatography (PE/EA = 30:1) as a colorless oil (15.0 mg, 57%). ¹H NMR (600 MHz, CDCl₃) δ 10.51 (s, 1H), 8.01 (d, *J* = 8.1 Hz, 1H), 7.73 (s, 1H), 7.64 (d, *J* = 8.1 Hz, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 188.86, 163.00 (t, *J* = 34.5 Hz), 139.20 (t, *J* = 26.1 Hz), 138.09,

134.05, 129.72, 128.00 (t, *J* = 6.4 Hz), 124.52 (t, *J* = 5.9 Hz), 112.00 (t, *J* = 254.2 Hz), 63.76,

13.85.

¹⁹F NMR (564 MHz, CDCl₃) δ -104.90 (s, 2F).

HRMS (ESI) m/z calc. for C₁₁H₁₀ClF₂O₃ [M+H]⁺ 263.0281, found 263.0281.



Ethyl 2-(3-bromo-4-formylphenyl)-2,2-difluoroacetate (30). Following general procedure, the product was purified by flash chromatography (PE/EA = 20:1) as a colorless oil (18 mg, 59%). ¹H NMR (600 MHz, CDCl₃) δ 10.39 (s, 1H), 8.00 (d, *J* = 8.1 Hz, 1H), 7.92 (s, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 190.91, 163.02 (t, *J* = 34.4 Hz), 139.26 (t, *J* = 25.8 Hz), 135.15, 131.15 (t, *J* = 6.3 Hz), 130.07, 126.91, 125.15 (t, *J* = 5.8 Hz), 111.89 (t, *J* = 254.2 Hz), 63.77,

13.86.

¹⁹F NMR (564 MHz, CDCl3) δ -104.81 (s, 2F).

HRMS (EI) (m/z): calcd. for C₁₁H₉BrF₂O₃: 305.9703, found: 305.9699.



Methyl 2,2-difluoro-2-(4-formyl-2,6-dimethylphenyl)acetate (3p'). Following general procedure, the product was purified by flash chromatography (PE/EA = 10:1) as a white solid (12.3 mg, 51%).

¹H NMR (600 MHz, CDCl₃) δ 9.98 (s, 1H), 7.56 (s, 2H), 3.89 (s, 3H), 2.54 (t, *J* = 4.4 Hz, 6H). ¹³C NMR (151 MHz, CDCl₃) δ 191.77, 164.17 (t, *J* = 34.7 Hz), 139.01 (t, *J* = 3.2 Hz), 136.76, 135.19 (t, *J* = 22.2 Hz), 131.15, 115.44 (t, *J* = 253.9 Hz), 53.83, 21.74 (t, *J* = 6.1 Hz).

¹⁹F NMR (564 MHz, CDCl₃) δ -95.89 (s, 2F).

HRMS ESI (m/z): [M+Na]⁺ calcd. for C₁₂H₁₂F₂NaO₃: 265.0647, found: 265.0655.



Methyl 2-(2,6-dichloro-4-formylphenyl)-2,2-difluoroacetate (3q'). Following general procedure, the product was purified by flash chromatography (PE/EA = 10:1) as a colorless oil (8.2 mg, 29%). ¹H NMR (600 MHz, CDCl₃) δ 9.98 (s, 1H), 7.87 (s, 2H), 3.92 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 188.47, 162.66 (t, *J* = 32.8 Hz), 138.07, 136.02, 133.10, 130.71,

112.55 (t, J = 256.5 Hz), 54.13.

¹⁹F NMR (564 MHz, CDCl₃) δ -97.60 (s, 2F).

HRMS (ESI) m/z calc. for C₁₀H₇Cl₂F₂O₃ [M+H]⁺ 282.9735, found 282.9731.

MeO₂CF₂C MeO N CHO

methyl 2,2-difluoro-2-(6-formyl-2-methoxypyridin-3-yl)acetate (3t'). Following general procedure, the product was purified by flash chromatography (PE/EA = 5:1) as a colorless oil (14.8 mg, 60%).

¹H NMR (600 MHz, CDCl₃) δ 9.91 (s, 1H), 8.03 (d, *J* = 7.6 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 4.00 (s, 3H), 3.81 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 191.95, 163.16 (t, *J* = 33.6 Hz), 160.87 (t, *J* = 4.6 Hz), 151.97,

136.78 (t, J = 6.9 Hz), 120.75 (t, J = 25.4 Hz), 114.77, 111.06 (t, J = 250.4 Hz), 54.34, 53.66.

¹⁹F NMR (564 MHz, CDCl₃) δ -104.57 (s, 2F).

5. Table S5. Optimization of ortho-C-H difluoromethylation of 5a^{a,b}

Hm Me 5a 0.1 mm	$Ho \qquad \begin{array}{c} Br CF_2 CO_2 Et \\ (1.5 \text{ mmol}) \\ fac-lr(ppy)_3 \\ (2 \text{ mol} \%) \\ KOAc (4 \text{ equiv}) \\ solvent (2 \text{ mL}) \\ Ar, \text{ rt, 30 h} \\ 18 \text{ W blue LED} \end{array}$	Hm CHO Me F F Ga R = CO ₂ Et Ga' R = CO ₂ Me
entry	solvent	yield (%)
	(2 mL)	(<i>o/m</i>)
1	CF ₃ CH ₂ OH	27.4/4.6
2 MeOH		< 10
3	acetone	36/34
4	DMSO	41.7/8.3
5	DMSO/DMF (19/1)	51.6/6.4

^{*a*} Reaction conditions: **5a** (0.1 mmol), BrCF₂CO₂Et **2** (1.5 mmol), KOAc (4 equiv) in solvent (2 mL) at room temperature under an argon atmosphere and a 18 W blue light bulb, unless otherwise noted. ^{*b*} Isolated yields. ^{*c*} The ratio of selectivity determined by ¹H NMR.

Table S5. entry 1, 1H NMR spectrum:



6. General procedures for *ortho*-difluoroalkylation of *para*-substituted benzaldehydes



To a 25 mL of Schlenk tube *fac*-Ir(ppy)₃ (2 mol %) and KOAc (4 equiv) under air. The mixture was evacuated and backfilled with Ar (3 times). The *para*-substituted benzaldehydes **5** (0.1 mmol) and BrCF₂CO₂Et **2** (1 mmol) and the mixture of degassed DMSO/DMF (19:1, 2 mL) were added

successively. The mixture was stirred at room temperature for 40 hours while irradiated by 18 W blue LED. EtOAc (20 mL) and H₂O (20 mL) were added to the reaction mixture at ambient temperature. The separated aqueous phase was extracted with EtOAc (3×20 mL). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄ and concentrated in vacuo. The organic layer was concentrated and purified directly by column chromatography to afford the product **6**.

7. Characterization of product 6.



Ethyl 2,2-difluoro-2-(2-formyl-5-methylphenyl)acetate (6a). Following general procedure, the product was purified by flash chromatography (PE/EA = 40:1) as a colorless oil (14 mg, 58%). ¹H NMR (600 MHz, CDCl₃) δ 10.14 (s, 1H), 7.89 (d, J = 7.8 Hz, 1H), 7.64 (s, 1H), 7.48 (d, J = 7.8 Hz, 1H), 4.35 (q, J = 7.1 Hz, 2H), 2.50 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 190.68, 163.30 (t, J = 33.5 Hz), 145.14, 132.89, 132.83, 131.75, 131.67, 127.55 (t, J = 9.7 Hz), 113.19 (t, J = 252.2 Hz), 63.23, 21.88, 13.85. ¹⁹F NMR (564 MHz, CDCl₃) δ -98.64 (s, 2F).

HRMS (ESI) m/z calc. for C₁₂H₁₃F₂O₃ [M+H]⁺ 243.0827, found 0827.

Ethyl 2-(5-ethyl-2-formylphenyl)-2,2-difluoroacetate (6b). Following general procedure, the product was purified by flash chromatography (PE/EA = 40:1) as a colorless solid (15.4 mg, 60%). ¹H NMR (600 MHz, CDCl₃) δ 7.66 (d, *J* = 6.4 Hz, 1H), 7.35 (s, 1H), 7.12 (t, *J* = 8.3 Hz, 1H), 7.02 – 6.90 (m, 1H), 6.24 (dt, *J* = 16.2, 11.2 Hz, 1H), 4.36 (dd, *J* = 14.2, 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 163.63 (t, *J* = 34.7 Hz), 159.67 (d, *J* = 251.1 Hz), 134.35 (t, *J* = 9.3 Hz), 132.38, 131.83 (d, *J* = 3.9 Hz), 128.12 (d, *J* = 7.3 Hz), 120.08 (t, *J* = 25.1 Hz), 116.87 (d, *J* = 22.9 Hz), 112.30 (t, *J* = 249.0 Hz), 109.73 (d, *J* = 21.6 Hz), 63.25, 13.95.

¹⁹F NMR (564 MHz, CDCl₃) δ -103.46 (s, 2F), -105.29 (s, 1F).

HRMS (EI) (m/z): calcd. for C₁₃H₁₄F₂O₃: 256.0911, found: 256.0907.

Ethyl 2-(5-(*tert*-butyl)-2-formylphenyl)-2,2-difluoroacetate (6c). Following general procedure, the product was purified by flash chromatography (PE/EA = 20:1) as a colorless solid (20 mg, 70%).

¹H NMR (600 MHz, CDCl₃) δ 10.15 (s, 1H), 7.93 (d, J = 8.1 Hz, 1H), 7.84 (s, 1H), 7.69 (d, J =

6.9 Hz, 1H), 4.36 (q, J = 7.1 Hz, 2H), 1.38 (s, 9H), 1.35 (t, J = 7.1 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 190.80, 163.36 (t, *J* = 33.7 Hz), 158.00, 132.74, 132.62 (t, *J* = 24.1 Hz), 131.54, 128.12, 123.90 (t, *J* = 9.8 Hz), 113.40 (t, *J* = 252.2 Hz), 63.22, 35.57, 30.93, 13.87.
¹⁹F NMR (564 MHz, CDCl₃) δ -98.27 (s, 2F).

HRMS (ESI) m/z calc. for $C_{15}H_{19}F_2O_3$ [M+H]⁺ 285.1297, found 285.1297.



Ethyl 2,2-difluoro-2-(2-formyl-5-(methylthio)phenyl)acetate (6d). Following general procedure, the product was purified by flash chromatography (PE/EA = 10:1) as a colorless solid (8.8 mg, 32%).

¹H NMR (600 MHz, CDCl₃) δ 10.05 (s, 1H), 7.88 (d, J = 8.1 Hz, 1H), 7.62 (s, 1H), 7.44 (d, J =

8.1 Hz, 1H), 4.35 (q, J = 7.2 Hz, 2H), 2.58 (s, 3H), 1.34 (t, J = 7.2 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 189.97, 162.97 (t, J = 33.4 Hz), 148.22, 133.16, 133.14 (d, J =

49.1 Hz), 129.95, 126.59, 123.02 (t, *J* = 10.3 Hz), 112.88 (t, *J* = 252.6 Hz), 63.28, 14.60, 13.83.

¹⁹F NMR (564 MHz, CDCl₃) δ -99.08 (s, 2F).

HRMS (EI) (m/z): calcd. for C₁₂H₁₂F₂O₃S: 274.0475, found: 274.0471.

Ethyl 2,2-difluoro-2-(5-fluoro-2-formylphenyl)acetate (6e). Following general procedure, the product was purified by flash chromatography (PE/EA = 20:1) as a colorless solid (11.00 mg, 45%).

¹H NMR (600 MHz, CDCl₃) δ 10.13 (s, 1H), 8.05 (dd, *J* = 8.4, 5.6 Hz, 1H), 7.56 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.38 (t, *J* = 6.8 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.2 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 189.34, 165.49 (d, *J* = 258.4 Hz), 162.70 (t, *J* = 33.1 Hz), 135.44

(d, J = 9.6 Hz), 118.21 (d, J = 21.5 Hz), 115.25 (t, J = 10.3 Hz), 115.08 (t, J = 10.3 Hz), 112.26 (t, J = 10.3 Hz), 112.

J = 253.5 Hz), 63.53, 13.82.

¹⁹F NMR (564 MHz, CDCl₃) δ -98.77 (s), -101.20 (s).

HRMS ESI (m/z): [M+H]⁺ calcd. for C₁₁H₁₀F₃O₃: 247.0577, found: 247.0577.



Ethyl 2,2-difluoro-2-(2-formyl-5-iodophenyl)acetate (6f). Following general procedure, the product was purified by flash chromatography (PE/EA = 10:1) as a white solid (6.4 mg, 18%). ¹H NMR (600 MHz, CDCl₃) δ 10.14 (s, 1H), 8.17 (s, 1H), 8.08 (d, *J* = 8.1 Hz, 1H), 7.69 (d, *J* = 8.1 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 190.16, 162.79 (t, *J* = 33.3 Hz), 140.68, 135.89 (t, *J* = 10.2 Hz),

134.02 (t, J = 25.2 Hz), 133.25, 133.20, 112.21 (t, J = 253.7 Hz), 101.70, 63.58, 13.84.

¹⁹F NMR (564 MHz, CDCl₃) δ -98.65 (s, 2F).

HRMS ESI (m/z): [M+H]⁺ calcd. for C₁₁H₁₀F₂IO₃: 354.9637, found: 354.9637.

MeO₂C CHO CF₂CO₂Et

Methyl 3-(2-ethoxy-1,1-difluoro-2-oxoethyl)-4-formylbenzoate (6g). Following general procedure, the product was purified by flash chromatography (PE/EA = 10:1) as a colorless oil (43%, o/m = 2:1).

¹H NMR (600 MHz, CDCl₃) δ 10.31 (s, 1H), 8.46 (s, 1H), 8.32 (d, J = 8.0 Hz, 1H), 8.08 (d, J =

7.9 Hz, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 3.99 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 190.14 (t, J = 2.9 Hz), 165.11, 163.01 (t, J = 33.5 Hz), 137.10,

134.65, 133.52 (t, *J* = 25.5 Hz), 132.27, 131.77, 127.98 (t, *J* = 9.7 Hz), 112.92 (t, J = 253.5 Hz),

63.60, 52.78, 13.81.

¹⁹F NMR (564 MHz, CDCl₃) δ -98.09 (s, 2F).

HRMS ESI (m/z): [M+H]⁺ calcd. for C₁₃H₁₃F₂O₅: 287.0726, found: 287.0723.

OHC CF₂CO₂Et

Ethyl 2-(2,5-diformylphenyl)-2,2-difluoroacetate (6h). Following general procedure, the product was purified by flash chromatography (PE/EA = 5:1) as a colorless oil (7.4 mg, 29%). ¹H NMR (600 MHz, CDCl₃) δ 10.33 (s, 1H), 10.17 (s, 1H), 8.33 (s, 1H), 8.20 (s, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 190.33, 190.13, 162.88 (t, *J* = 33.3 Hz), 139.16, 137.76, 134.20 (t, *J* = 25.6 Hz), 132.26 (d, *J* = 98.6 Hz), 127.93 (t, *J* = 9.6 Hz), 112.73 (t, *J* = 253.7 Hz), 63.75, 13.84.

HRMS (EI) (m/z): calcd. for C₁₂H₁₀F₂O₄: 256.0547, found: 256.0541.

Ethyl 2-(2-acetyl-5-methylphenyl)-2,2-difluoroacetate (6j). Following general procedure, the product was purified by flash chromatography (PE/EA = 10:1) as a colorless oil (7.9 mg, 31%). ¹H NMR (600 MHz, CDCl₃) δ 7.76 (d, J = 7.9 Hz, 1H), 7.69 (s, 1H), 7.39 (d, J = 7.8 Hz, 1H), 4.36 (q, J = 7.1 Hz, 2H), 2.57 (s, 3H), 2.47 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 199.16, 163.27 (t, J = 33.2 Hz), 143.33, 136.09, 131.02, 130.45, 129.13, 128.03, 113.38 (t, J = 249.8 Hz), 62.56, 27.90, 21.65, 13.89. ¹⁹F NMR (564 MHz, CDCl₃) δ -99.74 (s, 2F). HRMS ESI (m/z): [M+Na]⁺ calcd. for C₁₃H₁₄F₂NaO₃: 279.0803, found: 279.0805.



Ethyl 2,2-difluoro-2-(3-formylthiophen-2-yl)acetate (6k). Following general procedure, the product was purified by flash chromatography (PE/EA = 20:1) as a colorless oil (11.0 mg, 46%). ¹H NMR (600 MHz, CDCl₃) δ 10.14 (s, 1H), 7.59 (d, *J* = 5.2 Hz, 1H), 7.46 (d, *J* = 5.2 Hz, 1H),

4.37 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 184.43, 162.32 (t, J = 34.5 Hz), 141.12 (t, J = 30.8 Hz), 140.50,

128.37, 127.70, 111.78 (t, *J* = 253.1 Hz), 64.03, 13.79.

¹⁹F NMR (564 MHz, CDCl₃) δ -90.84 (s, 2F).

HRMS (ESI) m/z calc. for $C_9H_9F_2O_3S$ [M+H]⁺ 235.0235, found 235.0235.

Methyl 2-(2-ethoxy-1,1-difluoro-2-oxoethyl)thiophene-3-carboxylate (6l). Following general procedure, the product was purified by flash chromatography (PE/EA = 10:1) as a colorless oil (10.0 mg, 38%).

¹H NMR (600 MHz, CDCl₃) δ 7.48 (d, *J* = 5.2 Hz, 1H), 7.39 (d, *J* = 5.2 Hz, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 3.80 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 162.17 (t, *J* = 33.7 Hz), 161.98, 141.39 (t, *J* = 28.4 Hz), 131.53 (t,

J = 5.1 Hz), 129.84, 126.42, 111.49 (t, *J* = 248.2 Hz), 63.14, 51.96, 13.79.

¹⁹F NMR (564 MHz, CDCl₃) δ -91.15 (s, 2F).

HRMS (ESI) m/z calc. for $C_{10}H_{11}F_2O_4S$ [M+H]⁺ 265.0341, found 265.0341.

8. Post-synthetic modification of 3c



Procedure for preparation of 7*c* (*Angew. Chem., Int. Ed.* 2016, *55*, 2934): To a solution of 3*c* (0.2 mmol) in dry DCM (2 mL) was added 1-Aminopiperidine (1.4 equiv) and anhydrous MgSO₄ (80 mg). The resulting reaction mixture was stirred at room temperature until it was completed (by TLC). Filtration on a flash chromatography with DCM as eluent, then removing of the solvent under reduced pressure, afforded the desired product 7*c*.



ethyl (E)-2,2-difluoro-2-(2-methoxy-4-((piperidin-1-ylimino)methyl)phenyl)acetate (7c):

¹H NMR (600 MHz, CDCl₃) δ 7.50 (d, *J* = 7.9 Hz, 1H), 7.41 (s, 1H), 7.22 (s, 1H), 7.04 (d, *J* = 7.9 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.76 (s, 3H), 3.14 – 3.10 (m, 4H), 1.68 (d, *J* = 4.8 Hz, 4H), 1.51 – 1.46 (m, 2H), 1.21 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 164.05 (t, *J* = 34.1 Hz), 156.90 (t, *J* = 4.9 Hz), 141.04, 132.30, 126.39 (t, *J* = 7.4 Hz), 119.05, 112.29 (t, *J* = 247.8 Hz), 107.11, 62.55, 55.63, 51.85, 25.03, 23.96, 13.90.

¹⁹F NMR (564 MHz, CDCl₃) δ -102.33 (s, 2F).

Procedure for preparation of 8c (Synthetic Commun. 2018, 48, 1068): A 25-mL oven-dried Schlenk tube was sequentially added a mixture of aldehyde derivatives 3c (0.2 mmol), dry CH₃OH (2 mL), and Eosin Y (2 mol%). The tube was evacuated and backfilled with nitrogen (three times). The reaction mixture was stirred under a 36 W green LED irradiation at room temperature for 12 h. The resulting mixture was diluted with EtOAc (8 mL). After completion of the reaction, phenylhydrazine was added to react with the excess benzaldehyde. The resulting crude product was washed with sodium hydroxide solution thrice. Subsequently, anhydrous sodium sulfate was added to remove water and the resulting mixture was filtered to collect the filtrate. The solvent in the filtrate was partially removed by rotary evaporation and the remaining product was purified by column chromatography (ethyl acetate/petroleum ether), followed by another round of rotary evaporation to afford the corresponding compounds.



ethyl 2-(4-(dimethoxymethyl)-2-methoxyphenyl)-2,2-difluoroacetate (**8c**): ¹H NMR (600 MHz, CDCl₃) δ 7.55 (d, *J* = 7.9 Hz, 1H), 7.05 (d, *J* = 7.9 Hz, 1H), 6.99 (s, 1H), 5.31 (s, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 3.75 (s, 3H), 3.27 (s, 6H), 1.21 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 163.91 (t, *J* = 33.9 Hz), 156.74 (t, *J* = 4.9 Hz), 142.84, 126.16 (t, *J* = 7.3 Hz), 121.93 (t, *J* = 24.2 Hz), 118.96, 112.11 (t, *J* = 248.2 Hz), 109.50, 102.41, 62.58, 55.69, 52.79, 13.85.

¹⁹F NMR (564 MHz, CDCl₃) δ -102.69 (s, 2F).

Procedure for preparation of 9c (*J. Org. Chem.* 2017, 82, 1591): A methanol suspension (2 mL) of 3c (0.2 mmol) and (NH₄)₂S₂O₈ (1.5 equiv) was stirred at 60 °C for 12 h. After cooling to room temperature, distilled water (10 mL) was used to dissolve the solid and the product was extracted by ethyl acetate (3 × 10 mL). The combined organic extract was concentrated and then purified by column chromatography on silica gel (petroleum ether/ethyl acetate 10:1) provided 9c.



methyl 4-(2-ethoxy-1,1-difluoro-2-oxoethyl)-3-methoxybenzoate (**9c**): ¹H NMR (600 MHz, CDCl₃) δ 7.65 (q, *J* = 8.0 Hz, 2H), 7.53 (s, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 3H), 3.80 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 166.07, 163.47 (t, J = 33.6 Hz), 156.66 (t, J = 4.7 Hz), 133.95,

126.50 (t, J = 7.5 Hz), 126.18 (t, J = 24.1 Hz), 121.84, 112.07, 111.74 (t, J = 249.2 Hz), 62.79,

55.95, 52.45, 13.87.

¹⁹F NMR (564 MHz, CDCl₃) δ -103.53 (s, 2F).

9. Mechanistic Studies

a) Intermolecular competition experiments



Scheme S1. Intermolecular competition experiments of 1c and 1e

A suspension of *fac*-Ir(ppy)₃ (3 mol %), KOAc (6 equiv), **1c** (0.1 mmol), **1e** (0.1 mmol) and BrCF₂CO₂Et **2** (1 mmol) in degassed MeOH/TFE (2 mL, 17/3) was stirred under Ar for 18 h. The reaction mixture was quenched with 1N HCl aqueous and extracted with Et₂O (20 mL x 3). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄ and concentrated in vacuo. The organic layer was concentrated and purified directly by column chromatography to afford the products. The remaining residue was purified by column chromatography on silica gel (PE/EA = 10:1) to yield a mixture of **3c'** and **3e'** in a ratio of 7:1 as determined by ¹H NMR spectroscopy.



Scheme S2. Intermolecular competition experiments of 1c and 1b



A suspension of fac-Ir(ppy)₃ (3 mol %), KOAc (6 equiv), 1c (0.1 mmol), 1b (0.1 mmol) and BrCF₂CO₂Et 2 (1 mmol) in degassed MeOH/TFE (2 mL, 17/3) was stirred under Ar for 18 h. The

reaction mixture was quenched with 1N HCl aqueous and extracted with Et_2O (20 mL x 3). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄ and concentrated in vacuo. The organic layer was concentrated and purified directly by column chromatography to afford the products. The remaining residue was purified by column chromatography on silica gel (PE/EA = 10:1) to yield a mixture of **3c'** and **3b'** in a ratio of 5:1 as determined by ¹H NMR spectroscopy.



Scheme S3. Intermolecular competition experiments of 1c and 10



A suspension of *fac*-Ir(ppy)₃ (2 mol %), KOAc (6equiv), **1c** (0.1 mmol), **10** (0.1 mmol) and BrCF₂CO₂Et **2** (1 mmol) in MeOH/TFE (2 mL, 17/3) was stirred under Ar for 18 h. However, a mixture of difluoroalkylation products **11'** was obtained without any site-selectivity, which indicated that the arene-bound aldehyde group is highly essential in realizing the *para*-selective C–H difluoroalkylation reaction.

b) Radical mechanism experiment

Scheme S4. Radical mechanism experiment



We subsequently introduced the radical scavenger, TEMPO or 1,1-diphenylethylene, which could trap the ·CFR radical generated in situ in the reaction. As expected, a TEMPO-CF₂R adduct or the byproduct 12 were detected by GC-MS, and only a trace amount of 3a was observed. These results suggested that a ·CF₂R radical was involved in the reaction pathway.

c) The computational studies of the regio-selectivity of benzaldehyde

CHO CF ₂ CO ₂ N p/(o+m) = 7.0/	le EtO ₂ CF 1.0 3a _	CHO H 2 C para site TS 19.3	CI CI Sa_	$\begin{bmatrix} \mathbf{CF}_{2}\mathbf{CO}_{2}\mathbf{Et} \\ \mathbf{H} \end{bmatrix}^{\ddagger}$	CH CH 3a_m	• H • CF ₂ CO ₂ Et • teta site TS 21.2
	Ortho site TS energy (hartrees)	Meta site TS energy (hartrees)	Para site TS energy (hartrees)	TS energy difference (Para&Ortho, kcal/mol)	TS energy difference (Para&Meta, kcal/mol)	Expt. Selectivity
CHO ortho meta para	-850.913374	-850.910937	-850.914095	0.4	1.9	7/1 [<i>p</i> /(o+m)]

Scheme S5. The computational studies of the regio-selectivity of benzaldehyde

Ortho site TS		
C -2.94174000	-1.17195800	-0.57561700
C -2.77270900	1.15633900	0.29719500
C -2.10187600	2.37402400	0.38595400
C -2.21107200	0.08814800	-0.41323000
C -0.86272500	2.54731700	-0.26560900
Н -2.54777300	3.20184100	0.92957000
C -0.88916500	0.21029700	-0.95514000
C -0.27880400	1.50142100	-0.95803300
Н -0.37419800	3.51755100	-0.23852900
Н -0.56884500	-0.52486800	-1.69151300
Н 0.66843200	1.64111500	-1.46998700
Н -2.43260600	-1.93884900	-1.18951900
O -4.05063100	-1.40241200	-0.09640200
C 1.59018400	-1.05620800	-0.01094400
O 1.83191900	-2.02875100	-0.70806500
O 2.41762800	-0.04825200	0.25512300
C 3.74672000	-0.11514700	-0.35076500

Н 4.22974600	-1.03466300	-0.00883900
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C 0.23596900	-0.80909800	0.55788100
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Н 4.60158000	1.15947300	1.17459500
Н 5.50364500	1.10421800	-0.35339200
Н 3.99275700	2.03281000	-0.25397300
F -0.47309400	-1.92578200	0.75425100
F 0.17476100	-0.01944800	1.63203900
Н -3.75183300	1.03013700	0.75041800
Meta site TS		
C -4.07399000	-0.30600000	0.25040700
C -2.40817800	1.55219000	-0.00615200
C -1.18422700	2.02237400	-0.49393100
C -2.75974500	0.19691200	-0.19133200
C -0.29817300	1.15817900	-1.12407700
Н -0.93643800	3.07630800	-0.40128000
C -1.88293100	-0.67923400	-0.82343900
C -0.57580200	-0.24491600	-1.20534000
Н 0.63620500	1.53658900	-1.52809700
Н -2.17405200	-1.71358400	-0.98510500
Н -0.03491400	-0.83906800	-1.93948200
H -4.26401800	-1.37580100	0.03622000
O -4.92158700	0.37165000	0.81854800
C 1.99825600	-0.94002000	-0.04939400
O 2.57451800	-1.73713800	-0.77410500
O 2.48996400	0.21576500	0.39644600
C 3.84184600	0.55915400	-0.03834600
Н 4.51666700	-0.23864200	0.28411000
Н 3.84542700	0.60246200	-1.13148100
C 0.56932900	-1.10321500	0.33076700
C 4.19003000	1.89110100	0.58844300
Н 4.17241800	1.82999600	1.68194500
Н 5.19952900	2.18222900	0.27712100
Н 3.49224200	2.67196300	0.26714300
F 0.16600600	-2.38066300	0.34489800
F 0.18212400	-0.47722600	1.44876700
Н -3.10833400	2.22043600	0.48548200
Para site TS		
C -4.38213100	-0.66457400	0.13796300
C -2.63268100	0.96773200	-0.59569300
C -1.34893200	1.24238300	-1.01818900
C -3.01858800	-0.36059900	-0.30002400

С-	0.37323800	0.19858400	-1.08867200
Н-	1.05715500	2.25897500	-1.26379300
C -	2.08986500	-1.41105600	-0.46064900
C -	0.80042800	-1.14848400	-0.88430600
Н	0.53480000	0.37857100	-1.65997200
Н-	2.40631800	-2.43409600	-0.27054900
Н-	0.09462900	-1.96079600	-1.02843100
Н-	4.58798200	-1.73560900	0.32947500
0 -	5.26866000	0.17315900	0.29642400
С	1.89182200	-0.31621600	0.68950400
0	1.82998200	-1.44092800	1.16028300
0	2.90844100	0.19735800	-0.00041700
С	4.05837200	-0.67860600	-0.21392500
Н	4.44457800	-0.97710800	0.76461000
Н	3.71043200	-1.57060600	-0.74259100
С	0.73547300	0.61869300	0.71810800
С	5.07569500	0.10202300	-1.01578500
Н	5.39827400	0.99938300	-0.47686600
Н	5.95399000	-0.52958700	-1.18961100
Н	4.66784000	0.40057100	-1.98755400
F -	0.13041000	0.39353200	1.70429000
	1.01025000	1 92015200	0.61912700
F	1.01935900	1.92013200	0.01/12/00
F Н -	3.37073800	1.76004400	-0.50980600
F H - Ph	3.37073800 CHO	1.76004400	-0.50980600
F H - Ph C -	1.01935900 3.37073800 CHO 1.98443600	1.76004400 0.47187900	-0.50980600 -0.00000100
F H - Ph C - C -	1.01933900 3.37073800 CHO 1.98443600 0.53601400	1.76004400 0.47187900 0.21083400	-0.50980600 -0.00000100 0.00000000
F H - Ph C - C - C -	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700	1.76004400 0.47187900 0.21083400 -1.10596700	-0.50980600 -0.00000100 0.00000000 0.00000000
F H - Ph C - C - C - C	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700 1.32896700	1.76004400 0.47187900 0.21083400 -1.10596700 -1.33230300	-0.50980600 -0.00000100 0.00000000 0.00000000 0.00000000
F H - Ph C - C - C - C C	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700 1.32896700 2.21639100	1.76004400 0.47187900 0.21083400 -1.10596700 -1.33230300 -0.24749900	-0.50980600 -0.00000100 0.00000000 0.00000000 0.00000000
F H - Ph C - C - C - C C C C	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700 1.32896700 2.21639100 1.73222800	1.76004400 0.47187900 0.21083400 -1.10596700 -1.33230300 -0.24749900 1.06410700	-0.50980600 -0.00000100 0.00000000 0.00000000 0.00000000
F H - Ph C - C - C C C C C C C C C	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700 1.32896700 2.21639100 1.73222800 0.35677100	1.76004400 0.47187900 0.21083400 -1.10596700 -1.33230300 -0.24749900 1.06410700 1.29403600	-0.50980600 -0.00000100 0.00000000 0.00000000 0.00000000
F H - Ph C - C - C C C C C C C C H -	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700 1.32896700 2.21639100 1.73222800 0.35677100 0.74616100	1.76004400 0.47187900 0.21083400 -1.10596700 -1.33230300 -0.24749900 1.06410700 1.29403600 -1.93414300	-0.50980600 -0.00000100 0.00000000 0.00000000 0.00000000
F H - Ph C - C - C C C C C C C H - H	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700 1.32896700 2.21639100 1.73222800 0.35677100 0.74616100 1.71340100	1.76004400 0.47187900 0.21083400 -1.10596700 -1.33230300 -0.24749900 1.06410700 1.29403600 -1.93414300 -2.34850200	-0.50980600 -0.00000100 0.00000000 0.00000000 0.00000000 0.00000000
F H - Ph C - C - C - C - C - C - C - C - C - C -	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700 1.32896700 2.21639100 1.73222800 0.35677100 0.74616100 1.71340100 3.28822500	1.76004400 0.47187900 0.21083400 -1.10596700 -1.33230300 -0.24749900 1.06410700 1.29403600 -1.93414300 -2.34850200 -0.42761600	-0.50980600 -0.50980600 0.00000000 0.00000000 0.00000000 0.00000000
F H - Ph C - C - C C C C C C H - H H H	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700 1.32896700 2.21639100 1.73222800 0.35677100 0.74616100 1.71340100 3.28822500 2.42510600	1.76004400 0.47187900 0.21083400 -1.10596700 -1.33230300 -0.24749900 1.06410700 1.29403600 -1.93414300 -2.34850200 -0.42761600 1.90087100	-0.50980600 -0.00000100 0.00000000 0.00000000 0.00000000 0.00000000
F H- Ph C- C- C C C C C C H- H H H	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700 1.32896700 2.21639100 1.73222800 0.35677100 0.74616100 1.71340100 3.28822500 2.42510600 0.03189000	1.76004400 0.47187900 0.21083400 -1.10596700 -1.33230300 -0.24749900 1.06410700 1.29403600 -1.93414300 -2.34850200 -0.42761600 1.90087100 2.30983100	-0.50980600 -0.50980600 0.00000000 0.00000000 0.00000000 0.00000000
F H- Ph C- C- C C C C C C H- H H H H- H-	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700 1.32896700 2.21639100 1.73222800 0.35677100 0.74616100 1.71340100 3.28822500 2.42510600 0.03189000 2.26942100	1.76004400 0.47187900 0.21083400 -1.10596700 -1.33230300 -0.24749900 1.06410700 1.29403600 -1.93414300 -2.34850200 -0.42761600 1.90087100 2.30983100 1.54230400	-0.50980600 -0.00000100 0.00000000 0.00000000 0.00000000 0.00000000
F H- C- C- C C C C C C C H H H H H H - H O-	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700 1.32896700 2.21639100 1.73222800 0.35677100 0.74616100 1.71340100 3.28822500 2.42510600 0.03189000 2.26942100 2.85032600	1.76004400 0.47187900 0.21083400 -1.10596700 -1.33230300 -0.24749900 1.06410700 1.29403600 -1.93414300 -2.34850200 -0.42761600 1.90087100 2.30983100 1.54230400 -0.39665900	-0.50980600 -0.50980600 0.00000000 0.00000000 0.00000000 0.00000000
F H- C- C- C- C C C C C C H H H H H - H -	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700 1.32896700 2.21639100 1.73222800 0.35677100 0.74616100 1.71340100 3.28822500 2.42510600 0.03189000 2.26942100 2.85032600 2COOEt radi	1.76004400 0.47187900 0.21083400 -1.10596700 -1.33230300 -0.24749900 1.06410700 1.29403600 -1.93414300 -2.34850200 -0.42761600 1.90087100 2.30983100 1.54230400 -0.39665900 cal	-0.50980600 -0.50980600 0.00000000 0.00000000 0.00000000 0.00000000
F H- Ph C- C- C C C C C C C H H H H - H C F C	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700 1.32896700 2.21639100 1.73222800 0.35677100 0.74616100 1.71340100 3.28822500 2.42510600 0.03189000 2.26942100 2.85032600 2COOEt radi 0.31262100	1.76004400 0.47187900 0.21083400 -1.10596700 -1.33230300 -0.24749900 1.06410700 1.29403600 -1.93414300 -2.34850200 -0.42761600 1.90087100 2.30983100 1.54230400 -0.39665900 cal 0.88628700	-0.50980600 -0.50980600 0.00000000 0.00000000 0.00000000 0.00000000
F H- Ph C- C- C C C C C C C C C H H H H - H C - C C C C	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700 1.32896700 2.21639100 1.73222800 0.35677100 0.74616100 1.71340100 3.28822500 2.42510600 0.03189000 2.26942100 2.85032600 2COOEt radii 0.31262100 1.51471300	1.76004400 0.47187900 0.21083400 -1.10596700 -1.33230300 -0.24749900 1.06410700 1.29403600 -1.93414300 -2.34850200 -0.42761600 1.90087100 2.30983100 1.54230400 -0.39665900 cal 0.88628700 0.68421900	-0.50980600 -0.50980600 0.00000000 0.00000000 0.00000000 0.00000000
F H- Ph C- C C C C C C C C C C H H H H - C F C O O O	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700 1.32896700 2.21639100 1.73222800 0.35677100 0.74616100 1.71340100 3.28822500 2.42510600 0.03189000 2.26942100 2.85032600 2COOEt radi 0.31262100 1.51471300 0.29008200	1.76004400 0.47187900 0.21083400 -1.10596700 -1.33230300 -0.24749900 1.06410700 1.29403600 -1.93414300 -2.34850200 -0.42761600 1.90087100 2.30983100 1.54230400 -0.39665900 cal 0.88628700 0.68421900 2.08353700	-0.50980600 -0.50980600 -0.00000000 0.00000000 0.00000000 0.00000000
F H Phu C C - C - C - C - C - C - C - C - C	1.01933900 3.37073800 CHO 1.98443600 0.53601400 0.04334700 1.32896700 2.21639100 1.73222800 0.35677100 0.74616100 1.71340100 3.28822500 2.42510600 0.03189000 2.26942100 2.85032600 2COOEt radii 0.31262100 1.51471300 0.29008200 0.58052300	1.76004400 0.47187900 0.21083400 -1.10596700 -1.33230300 -0.24749900 1.06410700 1.29403600 -1.93414300 -2.34850200 -0.42761600 1.90087100 2.30983100 1.54230400 -0.39665900 cal 0.88628700 0.68421900 2.08353700 3.24164400	-0.50980600 -0.50980600 -0.0000000 0.00000000 0.00000000 0.00000000

Н	1.09007900	3.15986000	-0.98674400
С-	0.64066700	-0.18739400	0.19025300
С-	0.29285000	4.47503400	0.05667300
Н-	0.79468900	4.54390200	1.02788200
Н	0.33200400	5.36586700	-0.07175400
Н-	1.05189400	4.46978100	-0.73315900
F -	0.24526700	-1.43752600	0.26656700
F -	1.91260500	-0.00961900	0.47317400

10. Copies of NMR spectra




















































0 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 f1 (ppm)





^{10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170} f1 (ppm)









6 0.86-

0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 f1 (ppm)









210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 fl (ppm)


























