

Supporting Information

Photocatalyst-free EDA complex-enabled radical difluoroalkylation/cyclization for access to difluoroalkylated polycyclic coumarin derivatives

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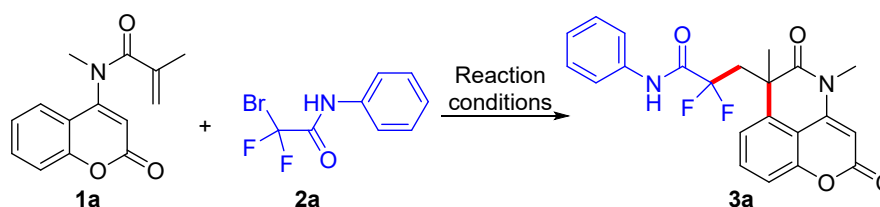
1 Experimental section

1.1 General information

All chemicals were commercially available and used as received without further. Column chromatography was performed using 300-400 mesh silica. Nuclear magnetic resonance spectra were recorded on Bruker Avance 500 MHz spectrometer. ^1H NMR spectra are recorded in parts per million from tetramethylsilane. ^{13}C NMR spectra were recorded in parts per million from tetramethylsilane. ^{19}F NMR spectra were recorded in parts per million with fluorobenzene as external standard. High resolution mass spectra (HR MS) were performed using an Agilent 6546 LC/Q-TOF mass spectrometer. IR spectra were recorded on WQF-510 Fourier transform infrared spectrophotometer. Melting points were measured on an XT4A microscopic apparatus uncorrected. The photochemical reactions were conducted on RLH-18 8-position Photo Reaction System under a blue LED (10 W, 455 nm and 430 nm).

1.2 Optimization of reaction conditions

Table S1. Optimization of reaction conditions^a



Entry	Oxidant (equiv.)	Base (equiv.)	Solvent	Yield (%) ^b
1	$\text{K}_2\text{S}_2\text{O}_8$ (1.5)	TMEDA (1.5)	MeCN	70
2 ^c	$\text{K}_2\text{S}_2\text{O}_8$ (1.5)	TMEDA (1.5)	MeCN	60
3 ^d	$\text{K}_2\text{S}_2\text{O}_8$ (1.5)	TMEDA (1.5)	MeCN	75
4 ^e	$\text{K}_2\text{S}_2\text{O}_8$ (1.5)	TMEDA (1.5)	MeCN	75
5	$(\text{NH}_4)_2\text{S}_2\text{O}_8$ (1.5)	TMEDA (1.5)	MeCN	70
6	Selectfluor (1.5)	TMEDA (1.5)	MeCN	50
7	PIFA (1.5)	TMEDA (1.5)	MeCN	30
8	PIDA (1.5)	TMEDA (1.5)	MeCN	30

9	K ₂ S ₂ O ₈ (1.0)	TMEDA (1.5)	MeCN	70
10	K ₂ S ₂ O ₈ (2.0)	TMEDA (1.5)	MeCN	80
11	K ₂ S ₂ O ₈ (2.5)	TMEDA (1.5)	MeCN	80
12	K ₂ S ₂ O ₈ (2.0)	Et ₃ N (1.5)	MeCN	10
13	K ₂ S ₂ O ₈ (2.0)	DBU (1.5)	MeCN	0
14	K ₂ S ₂ O ₈ (2.0)	DIPEA(1.5)	MeCN	10
15	K ₂ S ₂ O ₈ (2.0)	NHCO ₃ (1.5)	MeCN	0
16	K ₂ S ₂ O ₈ (2.0)	K ₃ PO ₄ (1.5)	MeCN	0
17	K ₂ S ₂ O ₈ (2.0)	K ₂ HPO ₄ (1.5)	MeCN	0
18	K ₂ S ₂ O ₈ (2.0)	TMEDA (1.0)	MeCN	60
19	K ₂ S ₂ O ₈ (2.0)	TMEDA (2.0)	MeCN	85
20	K ₂ S ₂ O ₈ (2.0)	TMEDA (2.5)	MeCN	80
21	K ₂ S ₂ O ₈ (2.0)	TMEDA (2.0)	DMF	80
22	K ₂ S ₂ O ₈ (2.0)	TMEDA (2.0)	DMSO	80
23	K ₂ S ₂ O ₈ (2.0)	TMEDA (2.0)	THF	0
24	K ₂ S ₂ O ₈ (2.0)	TMEDA (2.0)	2-MeTHF	0
25	K ₂ S ₂ O ₈ (2.0)	TMEDA (2.0)	H ₂ O	0
26	K ₂ S ₂ O ₈ (2.0)	TMEDA (2.0)	MeCN-H ₂ O (1:1, v/v)	80
27	K ₂ S ₂ O ₈ (2.0)	TMEDA (2.0)	MeCN-H ₂ O (2:1, v/v)	90
28 ^f	K ₂ S ₂ O ₈ (2.0)	TMEDA (2.0)	MeCN-H ₂ O (2:1, v/v)	80
29 ^g	K ₂ S ₂ O ₈ (2.0)	TMEDA (2.0)	MeCN-H ₂ O (2:1, v/v)	90
30	-	TMEDA (2.0)	MeCN-H ₂ O (2:1, v/v)	0
31	K ₂ S ₂ O ₈ (2.0)	-	MeCN-H ₂ O (2:1, v/v)	0
32 ^h	K ₂ S ₂ O ₈ (2.0)	TMEDA (2.0)	MeCN-H ₂ O (2:1, v/v)	0
33	K ₂ S ₂ O ₈ (2.0)	TMEDA (2.0)	MeCN-H ₂ O (2:1, v/v)	20

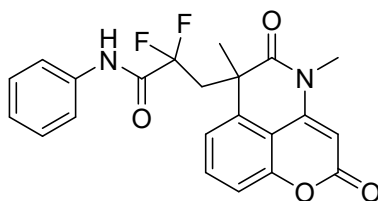
^a Reaction conditions: *N*-methyl-*N*-(2-oxo-2*H*-chromen-4-yl)methacrylamide **1a** (0.2 mmol, 48.6 mg), BrCF₂CONHPh **2a** (0.3 mmol, 74.7 mg), oxidant, base, and solvent (2 mL), 10 W blue LEDs (430 nm) for 6 h at room temperature under N₂ atmosphere. ^b Isolated yield. ^c The molar ratio of **1a** and **2a** is 1:1. ^d The molar ratio of **1a** and **2a** is 1:2. ^e The molar ratio of **1a** and **2a** is 1:2.5. ^f 5 h. ^g 7 h. ^h Without blue LEDs irradiation, strictly avoid

light under full dark conditions. ⁱ In air atmosphere.

1.3 General procedure for the synthesis of 2,2-difluoroalkylated pyrano[2,3,4-*ij*]isoquinoline derivatives (3)

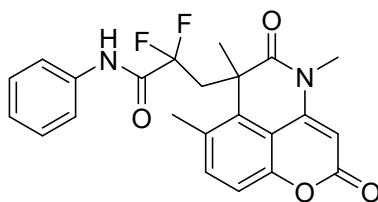
A Schlenk-tube equipped with a magnetic stir bar was charged with *N*-(2-oxo-2*H*-chromen-4-yl)methacrylamides **1** (0.2 mmol), BrCF₂CONHPh **2a** (0.4 mmol, 99.6 mg), K₂S₂O₈ (0.4 mmol, 108 mg), TMEDA (0.4 mmol, 46.4 mg) and MeCN-H₂O (2 mL, v/v, 2:1). The tube was stirred under the irradiation of 10 W blue LEDs (430 nm) at room temperature under N₂ atmosphere. After 6 hours, the mixture was transferred into a 100 mL separating funnel which contained 20 mL saturated sodium chloride solution. The mixture was extracted with ethyl acetate (10 mL × 2). The combined organic phase was dried over anhydrous Na₂SO₄ and concentrated under vacuum. The residue was purified by flash column chromatography using a mixture of ethyl acetate /petroleum ether as eluent to give the desired products **3**.

3-(4,6-Dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-2,2-difluoro-*N*-phenylpropanamide (3a)



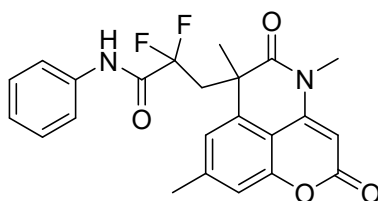
White solid (74.2 mg, 90%), m.p. 220.3-221.3 °C, R_f = 0.26 (EA/DCM/PE = 1:3:4). IR (KBr) ν (cm⁻¹): 3279, 1680, 1613, 1542, 1436, 1347, 1281, 1182, 1075. ¹H NMR (500 MHz, DMSO-*d*₆) δ : 10.1 (s, 1H), 7.58-7.55 (m, 2H), 7.44 (d, *J*_{H-H} = 7.9 Hz, 2H), 7.28 (t, *J*_{H-H} = 7.7 Hz, 2H), 7.18 (dd, *J*_{H-H} = 6.9 Hz, *J*_{H-H} = 2.1 Hz, 1H), 7.11 (t, *J*_{H-H} = 7.3 Hz, 1H), 5.98 (s, 1H), 3.44 (s, 3H), 3.38-3.11 (m, 2H), 1.64 (s, 3H). ¹³C NMR (126 MHz, DMSO-*d*₆) δ : 172.2 (C=O), 161.5 (t, *J*_{F-C} = 29.0 Hz, C=O), 161.3 (C=O), 151.8, 148.9, 137.5, 137.3, 132.8, 128.9, 125.2, 123.0, 121.0, 116.9 (dd, *J*_{F-C} = 252.0 Hz, *J*_{F-C} = 252.0 Hz), 114.9, 108.8, 92.9, 44.9 (t, *J*_{F-C} = 22.1 Hz), 43.3 (d, *J*_{F-C} = 3.2 Hz), 31.8, 29.9. ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ : -97.5 (d, *J*_{F-C} = 255.5 Hz, 1F), -102.7 (d, *J*_{F-C} = 255.5 Hz, 1F). HR MS (ESI) *m/z*: calcd for C₂₂H₁₉F₂N₂O₄ [M + H]⁺ 413.1307, found 413.1305.

2,2-Difluoro-*N*-phenyl-3-(4,6,7-trimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)propanamide (3b)



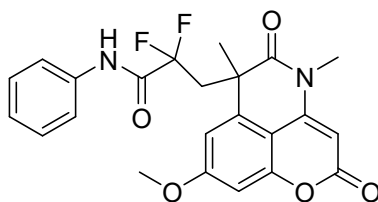
White solid (55.4 mg, 65%), m.p. 182.4-183.4 °C, $R_f = 0.321$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3284, 2924, 1677, 1614, 1565, 1445, 1350, 1270, 1160. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ : 10.18 (s, 1H), 7.42 (d, $J_{\text{H-H}} = 7.9$ Hz, 2H), 7.37 (d, $J_{\text{H-H}} = 8.6$ Hz, 1H), 7.28 (t, $J_{\text{H-H}} = 7.7$ Hz, 2H), 7.13-7.09 (m, 2H), 5.97 (s, 1H), 3.54-3.48 (m, 1H), 3.27-3.20 (m, 1H), 2.50 (s, 6H), 1.74 (s, 3H). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ : 173.3 (C=O), 161.2 (t, $J_{\text{F-C}} = 29.1$ Hz, C=O), 161.1 (C=O), 151.0, 149.1, 137.6, 137.3, 133.7, 132.6, 129.0, 125.3, 121.0, 109.5, 92.8, 44.4 (d, $J_{\text{F-C}} = 5.4$ Hz), 41.5 (t, $J_{\text{F-C}} = 22.4$ Hz), 30.4, 27.7, 22.2. ^{19}F NMR (471 MHz, $\text{DMSO-}d_6$) δ : -97.7 (d, $J_{\text{F-C}} = 256.4$ Hz, 1F), -105.2 (d, $J_{\text{F-C}} = 256.4$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{23}\text{H}_{21}\text{F}_2\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 427.1464, found 427.1455.

2,2-Difluoro-N-phenyl-3-(4,6,8-trimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)propanamide (3c)



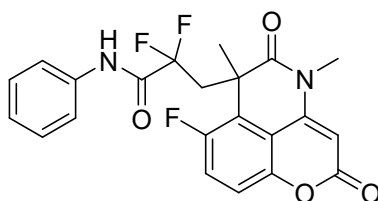
White solid (61.3 mg, 72%), m.p. 185.0-186.0 °C, $R_f = 0.323$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3282, 2917, 2850, 1686, 1615, 1548, 1445, 1425, 1347, 1296, 1142, 1082. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ : 10.12 (s, 1H), 7.44 (d, $J_{\text{H-H}} = 7.9$ Hz, 2H), 7.34 (s, 1H), 7.28 (t, $J_{\text{H-H}} = 7.6$ Hz, 2H), 7.11 (t, $J_{\text{H-H}} = 7.4$ Hz, 1H), 6.94 (s, 1H), 5.93 (s, 1H), 3.33 (s, 3H), 3.28-3.09 (m, 2H), 2.20 (s, 3H), 1.61 (s, 3H). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ : 171.3 (C=O), 160.5 (t, $J_{\text{F-C}} = 28.3$ Hz, C=O), 160.4 (C=O), 152.8, 147.9, 142.5, 136.3, 135.7, 127.8, 124.1, 122.7, 119.7, 114.4 (d, $J_{\text{F-C}} = 256.0$ Hz), 105.4, 90.9, 43.8 (t, $J_{\text{F-C}} = 21.8$ Hz), 42.2 (d, $J_{\text{F-C}} = 5.1$ Hz), 30.7, 28.8, 20.5. ^{19}F NMR (471 MHz, $\text{DMSO-}d_6$) δ : -95.8 (d, $J_{\text{F-C}} = 255.9$ Hz, 1F), -104.4 (d, $J_{\text{F-C}} = 255.9$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{23}\text{H}_{20}\text{F}_2\text{N}_2\text{O}_4\text{Na}$ $[\text{M} + \text{Na}]^+$ 449.1283, found 449.1261.

2,2-Difluoro-3-(8-methoxy-4,6-dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-N-phenylpropanamide (3d)



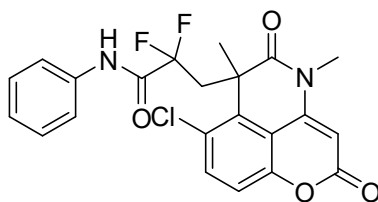
White solid (62.8 mg, 71%), m.p. 177.1-178.1 °C, $R_f = 0.33$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3275, 2918, 1685, 1606, 1548, 1424, 1347, 1140. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ : 10.14 (s, 1H), 7.44 (d, $J_{\text{H-H}} = 8.2$ Hz, 2H), 7.28 (t, $J_{\text{H-H}} = 7.8$ Hz, 2H), 7.11 (t, $J_{\text{H-H}} = 6.4$ Hz, 2H), 6.74 (d, $J_{\text{H-H}} = 1.6$ Hz, 1H), 5.84 (s, 1H), 3.70 (s, 3H), 3.32-3.26 (m, 4H), 3.16-3.07 (m, 1H), 1.62 (s, 3H). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ : 172.3 (C=O), 163.0 (C=O), 161.6 (t, $J_{\text{F-C}} = 28.9$ Hz, C=O), 153.8, 149.2, 138.5, 137.3, 128.9, 125.2, 120.9, 110.7, 102.2, 100.1, 90.3, 56.2, 44.7 (t, $J_{\text{F-C}} = 22.2$ Hz), 43.5 (d, $J_{\text{F-C}} = 3.6$ Hz), 31.8, 29.8. ^{19}F NMR (471 MHz, $\text{DMSO-}d_6$) δ : -95.9 (d, $J_{\text{F-C}} = 255.5$ Hz, 1F), -104.5 (d, $J_{\text{F-C}} = 255.5$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{23}\text{H}_{20}\text{F}_2\text{N}_2\text{O}_5\text{Na}$ $[\text{M} + \text{Na}]^+$ 465.1232, found 465.1240.

2,2-Difluoro-3-(7-fluoro-4,6-dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-*N*-phenylpropanamide (3e)



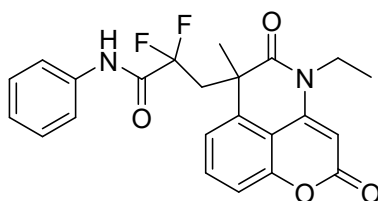
White solid (58.5 mg, 68%), m.p. 193.5-194.5 °C, $R_f = 0.314$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3293, 2917, 2851, 1680, 1610, 1556, 1494, 1449, 1354, 1233, 1171. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ : 10.32 (s, 1H), 7.50 (t, $J_{\text{H-H}} = 8.5$ Hz, 1H), 7.45 (d, $J_{\text{H-H}} = 8.0$ Hz, 2H), 7.34-7.33 (m, 1H), 7.32-7.27 (m, 2H), 7.12 (t, $J_{\text{H-H}} = 7.3$ Hz, 1H), 6.07 (s, 1H), 3.27 (s, 3H), 3.24-3.18 (m, 2H), 1.70 (s, 3H). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ : 171.5 (C=O), 161.2 (t, $J_{\text{F-C}} = 28.8$ Hz, C=O), 161.0 (C=O), 156.9, 155.0, 148.4, 137.2, 129.0, 125.3, 122.4 (d, $J_{\text{F-C}} = 12.5$ Hz), 121.0, 120.9 (d, $J_{\text{F-C}} = 25.9$ Hz), 117.8 (dd, $J_{\text{F-C}} = 250.0$ Hz, $J_{\text{F-C}} = 250.0$ Hz), 110.0 (d, $J_{\text{F-C}} = 5.6$ Hz), 93.8, 42.5, 41.5, 30.3, 28.2 (d, $J_{\text{F-C}} = 3.6$ Hz). ^{19}F NMR (471 MHz, $\text{DMSO-}d_6$) δ : -99.1 (d, $J_{\text{F-C}} = 255.6$ Hz, 1F), -103.4 (d, $J_{\text{F-C}} = 255.6$ Hz, 1F), -116.0 (s, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{22}\text{H}_{18}\text{F}_3\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 431.1213, found 431.1199.

3-(7-Chloro-4,6-dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-2,2-difluoro-*N*-phenylpropanamide (3f)



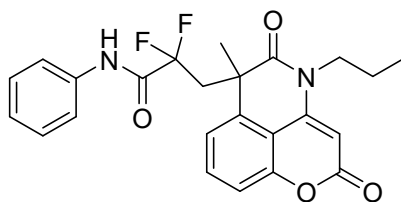
White solid (55.3 mg, 62%), m.p. 166.2-167.2 °C, $R_f = 0.31$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3297, 2953, 2915, 1729, 1693, 1612, 1556, 1488, 1459, 1376, 1357, 1265, 1180. ^1H NMR (500 MHz, CDCl_3) δ : 7.85 (s, 1H), 7.55 (d, $J_{\text{H-H}} = 8.9$ Hz, 1H), 7.42 (d, $J_{\text{H-H}} = 7.9$ Hz, 2H), 7.32 (t, $J_{\text{H-H}} = 7.7$ Hz, 2H), 7.20-7.15 (m, 2H), 5.82 (s, 1H), 4.05-3.95 (m, 1H), 3.41 (s, 3H), 3.37-3.30 (m, 1H), 1.92 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ : 172.2 (C=O), 160.8 (C=O), 160.7 (t, $J_{\text{F-C}} = 27.6$ Hz, C=O), 151.4, 148.0, 135.8, 135.7, 132.7, 129.2, 128.3, 125.7, 120.0, 118.7, 116.7 (t, $J_{\text{F-C}} = 257.0$ Hz), 110.7, 93.3, 44.3, 40.1 (t, $J_{\text{F-C}} = 21.4$ Hz), 30.2, 26.7. ^{19}F NMR (471 MHz, CDCl_3) δ : -99.3 (d, $J_{\text{F-C}} = 256.2$ Hz, 1F), -103.4 (d, $J_{\text{F-C}} = 256.2$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{22}\text{H}_{18}\text{ClF}_2\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 447.0918, found 447.0912.

3-(4-Ethyl-6-methyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-ij]isoquinolin-6-yl)-2,2-difluoro-N-phenylpropanamide (3g)



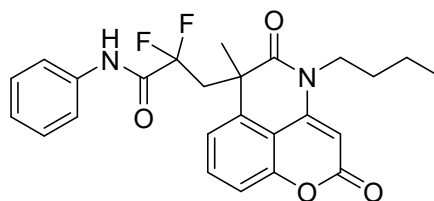
White solid (72.4 mg, 85%), m.p. 186.8-187.8 °C, $R_f = 0.332$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3280, 1685, 1607, 1537, 1496, 1448, 1384, 1251, 1086. ^1H NMR (500 MHz, $\text{DMSO}-d_6$) δ : 10.20 (s, 1H), 7.60-7.56 (m, 2H), 7.46 (d, $J_{\text{H-H}} = 7.9$ Hz, 2H), 7.29 (t, $J_{\text{H-H}} = 7.6$ Hz, 2H), 7.20 (dd, $J_{\text{H-H}} = 7.2$ Hz, $J_{\text{H-H}} = 1.6$ Hz, 1H), 7.12 (t, $J_{\text{H-H}} = 7.4$ Hz, 1H), 6.07 (s, 1H), 4.10-4.02 (m, 1H), 3.97-3.90 (m, 1H), 3.32-3.14 (m, 2H), 1.65 (s, 3H), 1.15 (t, $J_{\text{H-H}} = 6.9$ Hz, 3H). ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$) δ : 170.8 (C=O), 160.5 (t, $J_{\text{F-C}} = 28.8$ Hz, C=O), 160.4 (C=O), 150.9, 146.6, 136.6, 136.2, 131.7, 127.9, 124.2, 121.9, 120.0, 115.9 (t, $J_{\text{F-C}} = 257.0$ Hz), 114.1, 107.8, 91.4, 43.7 (t, $J_{\text{F-C}} = 21.9$ Hz), 42.1 (d, $J_{\text{F-C}} = 3.4$ Hz), 36.6, 30.8, 10.5. ^{19}F NMR (471 MHz, $\text{DMSO}-d_6$) δ : -97.1 (d, $J_{\text{F-C}} = 256.5$ Hz, 1F), -102.8 (d, $J_{\text{F-C}} = 256.5$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{23}\text{H}_{21}\text{F}_2\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 427.1464, found 427.1470.

2,2-Difluoro-3-(6-methyl-2,5-dioxo-4-propyl-2,4,5,6-tetrahydropyrano[2,3,4-ij]isoquinolin-6-yl)-N-phenylpropanamide (3h)



White solid (73.9 mg, 84%), m.p. 176.4-177.4 °C, $R_f = 0.316$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3312, 1720, 1687, 1616, 1603, 1548, 1448, 1358, 1282, 1239, 1083. ^1H NMR (500 MHz, DMSO- d_6) δ : 10.21 (s, 1H), 7.60-7.56 (m, 2H), 7.47 (d, $J_{\text{H-H}} = 7.9$ Hz, 2H), 7.30 (t, $J_{\text{H-H}} = 7.6$ Hz, 2H), 7.21 (dd, $J_{\text{H-H}} = 6.9$ Hz, $J_{\text{H-H}} = 2.0$ Hz, 1H), 7.12 (t, $J_{\text{H-H}} = 7.4$ Hz, 1H), 6.07 (s, 1H), 3.95-3.88 (m, 2H), 3.33-3.15 (m, 2H), 1.65 (s, 3H), 1.61-1.58 (m, 2H), 0.94 (t, $J_{\text{H-H}} = 7.4$ Hz, 3H). ^{13}C NMR (126 MHz, DMSO- d_6) δ : 172.2 (C=O), 161.6 (t, $J_{\text{F-C}} = 28.8$ Hz, C=O), 161.5 (C=O), 152.0, 148.0, 137.6, 137.3, 132.7, 128.9, 125.2, 123.0, 121.1, 117.0 (dd, $J_{\text{F-C}} = 257.0$ Hz, $J_{\text{F-C}} = 257.0$ Hz), 115.2, 108.9, 92.7, 44.6 (t, $J_{\text{F-C}} = 22.2$ Hz), 43.9, 43.3 (d, $J_{\text{F-C}} = 3.6$ Hz), 32.1, 19.5, 11.4. ^{19}F NMR (471 MHz, DMSO- d_6) δ : -97.1 (d, $J_{\text{F-C}} = 256.6$ Hz, 1F), -102.8 (d, $J_{\text{F-C}} = 256.6$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{24}\text{H}_{23}\text{F}_2\text{N}_2\text{O}_4$ [M + H] $^+$ 441.1620, found 441.1613.

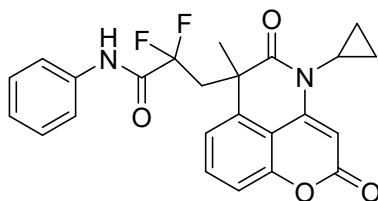
3-(4-Butyl-6-methyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-ij]isoquinolin-6-yl)-2,2-difluoro-N-phenylpropanamide (3i)



White solid (72.6 mg, 80%), m.p. 155.8-156.8 °C, $R_f = 0.32$ (EA/PE = 1:3). IR (KBr) $\nu(\text{cm}^{-1})$: 3278, 2953, 1682, 1612, 1545, 1500, 1445, 1380, 1281, 1188. ^1H NMR (500 MHz, CDCl_3) δ : 10.20 (s, 1H), 7.60-7.55 (m, 2H), 7.46 (d, $J_{\text{H-H}} = 8.1$ Hz, 2H), 7.29 (t, $J_{\text{H-H}} = 7.7$ Hz, 2H), 7.21 (dd, $J_{\text{H-H}} = 7.1$ Hz, $J_{\text{H-H}} = 1.5$ Hz, 1H), 7.12 (t, $J_{\text{H-H}} = 7.4$ Hz, 1H), 6.02 (s, 1H), 3.98-3.87 (m, 2H), 3.32-3.14 (m, 2H), 1.64 (s, 3H), 1.58-1.48 (m, 2H), 1.40-1.35 (m, 2H), 0.90 (t, $J_{\text{H-H}} = 7.3$ Hz, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ : 172.2 (C=O), 161.6 (t, $J_{\text{F-C}} = 31.2$ Hz, C=O), 161.4 (C=O), 152.0, 147.9, 137.6, 137.3, 132.8, 129.0, 125.2, 123.0, 121.1, 117.0 (dd, $J_{\text{F-C}} = 250.9$ Hz, $J_{\text{F-C}} = 250.9$ Hz), 115.2, 108.9, 92.6, 44.6 (t, $J_{\text{F-C}} = 21.2$ Hz), 43.3 (d, $J_{\text{F-C}} = 3.0$ Hz), 42.2, 32.1, 28.2, 19.8, 14.2. ^{19}F NMR (471 MHz, CDCl_3) δ : -97.0 (d, $J_{\text{F-C}} = 256.5$ Hz, 1F), -102.6 (d, $J_{\text{F-C}} = 256.5$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{25}\text{H}_{25}\text{F}_2\text{N}_2\text{O}_4$ [M + H] $^+$ 455.1777, found 455.1770.

3-(4-Cyclopropyl-6-methyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-ij]isoquinolin-6-yl)-2,2-

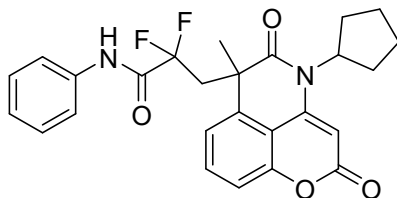
difluoro-*N*-phenylpropanamide (3j)



White solid (43.8 mg, 50%), m.p. 204.4-205.4 °C, $R_f = 0.27$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3334, 2921, 1683, 1618, 1546, 1489, 1449, 1413, 1335, 1278, 1170. $^1\text{H NMR}$ (500 MHz, $\text{DMSO-}d_6$) δ : 10.17 (s, 1H), 7.55-7.52 (m, 2H), 7.43 (d, $J_{\text{H-H}} = 7.8$ Hz, 2H), 7.28 (t, $J_{\text{H-H}} = 7.7$ Hz, 2H), 7.17 (d, $J_{\text{H-H}} = 7.0$ Hz, 1H), 7.12 (d, $J_{\text{H-H}} = 7.4$ Hz, 1H), 6.18 (s, 1H), 3.26-3.04 (m, 2H), 2.73 (bs, 1H), 1.59 (s, 3H), 1.20-1.16 (m, 2H), 0.79-0.77 (m, 1H), 0.68-0.66 (m, 1H). $^{13}\text{C NMR}$ (126 MHz, $\text{DMSO-}d_6$) δ : 173.1 (C=O), 161.4 (t, $J_{\text{F-C}} = 28.8$ Hz, C=O), 161.3 (C=O), 151.8, 150.0, 137.7, 137.3, 132.7, 129.0, 125.3, 123.0, 121.1, 115.1, 109.2, 93.4, 43.9 (d, $J_{\text{F-C}} = 3.6$ Hz), 31.5, 26.3, 10.4, 9.8. $^{19}\text{F NMR}$ (471 MHz, $\text{DMSO-}d_6$) δ : -96.8 (d, $J_{\text{F-C}} = 256.6$ Hz, 1F), -102.6 (d, $J_{\text{F-C}} = 256.6$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{24}\text{H}_{20}\text{F}_2\text{N}_2\text{O}_4\text{Na}$ [M + Na] $^+$ 461.1283, found 461.1249.

3-(4-Cyclopentyl-6-methyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-2,2-

difluoro-*N*-phenylpropanamide (3k)

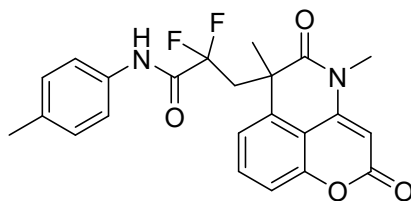


White solid (68.0 mg, 73%), m.p. 162.1-163.1 °C, $R_f = 0.32$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3295, 2915, 1682, 1616, 1560, 1545, 1497, 1446, 1400, 1281, 1190. $^1\text{H NMR}$ (500 MHz, $\text{DMSO-}d_6$) δ : 10.21 (s, 1H), 7.56 (bs, 2H), 7.49 (d, $J_{\text{H-H}} = 6.8$ Hz, 2H), 7.32 (t, $J_{\text{H-H}} = 7.7$ Hz, 2H), 7.21-7.20 (m, 1H), 7.15-7.13 (m, 1H), 6.26 (s, 1H), 4.86 (s, 1H), 3.29-3.20 (m, 2H), 1.96-1.91 (m, 6H), 1.65 (s, 3H), 1.60 (bs, 2H). $^{13}\text{C NMR}$ (126 MHz, $\text{DMSO-}d_6$) δ : 172.2 (C=O), 161.7 (C=O), 161.6 (t, $J_{\text{F-C}} = 28.4$ Hz, C=O), 151.9, 149.4, 137.6, 137.4, 132.6, 128.9, 125.2, 122.9, 121.2, 117.1 (t, $J_{\text{F-C}} = 256.0$ Hz), 115.2, 93.1, 56.9, 44.2 (t, $J_{\text{F-C}} = 21.1$ Hz), 44.0 (d, $J_{\text{F-C}} = 3.6$ Hz), 31.9, 28.5, 28.0, 26.2, 26.0. $^{19}\text{F NMR}$ (471 MHz, $\text{DMSO-}d_6$) δ : -96.5 (d, $J_{\text{F-C}} = 256.9$ Hz, 1F), -103.0 (d, $J_{\text{F-C}} = 256.9$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{26}\text{H}_{25}\text{F}_2\text{N}_2\text{O}_4$ [M + H] $^+$ 467.1777, found 467.1779.

1.4 General procedure for the synthesis of 2,2-difluoroalkylated pyrano[2,3,4-ij]isoquinoline derivatives (4)

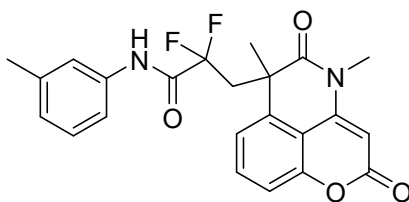
A Schlenk-tube equipped with a magnetic stir bar was charged with *N*-methyl-*N*-(2-oxo-2*H*-chromen-4-yl)methacrylamide **1a** (0.2 mmol, 48.6 mg), BrCF₂COR² (0.4 mmol), K₂S₂O₈ (0.4 mmol, 108 mg), TMEDA (0.4 mmol, 46.4 mg) and MeCN-H₂O (2 mL, v/v, 2:1). The tube was stirred under the irradiation of 10 W blue LEDs (430 nm) at room temperature under N₂ atmosphere. After 6 hours, the mixture was transferred into a 100 mL separating funnel which contained 20 mL saturated sodium chloride solution. The mixture was extracted with ethyl acetate (10 mL × 2). The combined organic phase was dried over anhydrous Na₂SO₄ and concentrated under vacuum. The residue was purified by flash column chromatography using a mixture of ethyl acetate /petroleum ether as eluent to give the desired products **4**.

3-(4,6-Dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-2,2-difluoro-*N*-(*p*-tolyl)propanamide (4a)



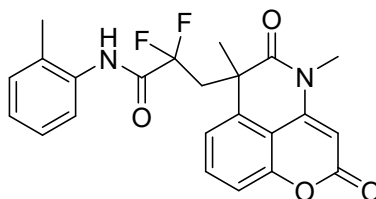
White solid (72.4 mg, 85%), m.p. 205.4-206.4 °C, R_f = 0.29 (EA/DCM/PE = 1:3:3). IR (KBr) ν (cm⁻¹): 3340, 1679, 1607, 1526, 1351, 1279, 1179, 1075. ¹H NMR (500 MHz, DMSO-*d*₆) δ : 10.1 (s, 1H), 7.58-7.55 (m, 2H), 7.31 (d, *J*_{H-H} = 8.4 Hz, 2H), 7.21-7.19 (m, 1H), 7.08 (d, *J*_{H-H} = 8.3 Hz, 2H), 5.98 (s, 1H), 3.33 (s, 3H), 3.27-3.12 (m, 2H), 2.24 (s, 3H), 1.64 (s, 3H). ¹³C NMR (126 MHz, DMSO-*d*₆) δ : 172.2 (C=O), 161.3 (t, *J*_{F-C} = 32.3 Hz, C=O), 151.8, 148.9, 137.5, 134.8, 134.3, 132.8, 129.3, 123.0, 121.0, 116.9 (t, *J*_{F-C} = 257.4 Hz), 114.9, 108.8, 92.9, 44.9 (t, *J*_{F-C} = 22.6 Hz), 43.3, 31.8, 29.9, 20.9. ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ : -97.5 (d, *J*_{F-C} = 255.3 Hz, 1F), -102.6 (d, *J*_{F-C} = 255.3 Hz, 1F). HR MS (ESI) *m/z*: calcd for C₂₃H₂₁F₂N₂O₄ [M + H]⁺ 427.1464, found 427.1466.

3-(4,6-Dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-2,2-difluoro-*N*-(*m*-tolyl)propanamide (4b)



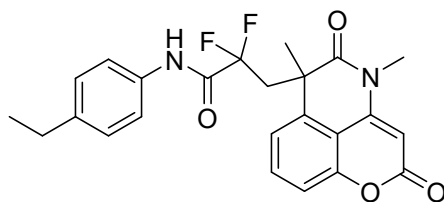
White solid (59.6 mg, 70%), m.p. 205.6-206.6 °C, $R_f = 0.296$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3253, 2920, 1682, 1617, 1559, 1500, 1425, 1257, 1184, 1083. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ : 10.1 (s, 1H), 7.60-7.55 (m, 2H), 7.22-7.13 (m, 4H), 6.93 (d, $J_{\text{H-H}} = 7.4$ Hz, 1H), 5.99 (s, 1H), 3.33 (s, 3H), 3.30-3.09 (m, 2H), 2.25 (s, 3H), 1.63 (s, 3H). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ : 172.2 (C=O), 161.4 (t, $J_{\text{F-C}} = 30.2$ Hz, C=O), 161.3 (C=O), 151.8, 148.9, 138.1, 137.5, 137.2, 132.8, 128.8, 125.9, 123.0, 121.6, 118.2, 116.8 (t, $J_{\text{F-C}} = 257.4$ Hz), 115.1, 108.8, 92.9, 45.0 (t, $J_{\text{F-C}} = 22.6$ Hz), 43.2 (d, $J_{\text{F-C}} = 3.6$ Hz), 31.9, 30.0, 21.5. ^{19}F NMR (471 MHz, $\text{DMSO-}d_6$) δ : -97.3 (d, $J_{\text{F-C}} = 255.2$ Hz, 1F), -102.7 (d, $J_{\text{F-C}} = 255.2$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{23}\text{H}_{20}\text{F}_2\text{N}_2\text{O}_4\text{Na}$ [$\text{M} + \text{Na}$] $^+$ 449.1283, found 449.1264.

3-(4,6-Dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-ij]isoquinolin-6-yl)-2,2-difluoro-N-(o-tolyl)propanamide (4c)



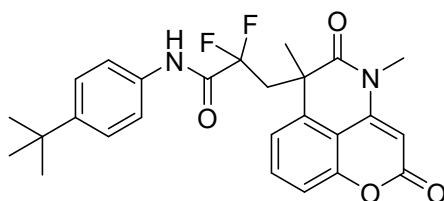
White solid (53.7 mg, 63%), m.p. 173.1-174.1 °C, $R_f = 0.291$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3293, 2917, 1709, 1687, 1618, 1560, 1529, 1501, 1425, 1353, 1203, 1079. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ : 9.99 (s, 1H), 7.69 (t, $J_{\text{H-H}} = 8.0$ Hz, 1H), 7.63 (d, $J_{\text{H-H}} = 7.9$ Hz, 1H), 7.34 (d, $J_{\text{H-H}} = 8.2$ Hz, 1H), 7.22-7.21 (m, 1H), 7.17-7.16 (m, 2H), 6.98-6.96 (m, 1H), 6.01 (s, 1H), 3.36 (s, 3H), 3.30-3.13 (m, 2H), 2.04 (s, 3H), 1.65 (s, 3H). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ : 172.4 (C=O), 162.1 (t, $J_{\text{F-C}} = 28.3$ Hz, C=O), 161.3 (C=O), 151.9, 149.0, 138.1, 134.5, 134.2, 132.9, 130.8, 127.3, 127.0, 126.5, 123.1, 117.3 (t, $J_{\text{F-C}} = 251.1$ Hz), 115.2, 108.7, 92.8, 44.6 (t, $J_{\text{F-C}} = 22.6$ Hz), 43.3, 31.9, 30.0, 17.8. ^{19}F NMR (471 MHz, $\text{DMSO-}d_6$) δ : -99.0 (d, $J_{\text{F-C}} = 256.6$ Hz, 1F), -102.1 (d, $J_{\text{F-C}} = 256.6$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{23}\text{H}_{21}\text{F}_2\text{N}_2\text{O}_4$ [$\text{M} + \text{H}$] $^+$ 427.1464, found 427.1464.

3-(4,6-Dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-ij]isoquinolin-6-yl)-N-(4-ethylphenyl)-2,2-difluoropropanamide (4d)



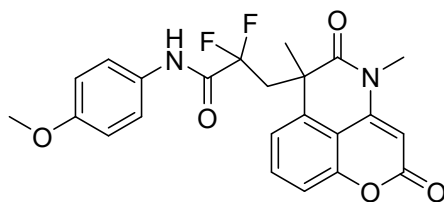
White solid (74.8 mg, 85%), m.p. 157.1-158.1 °C, $R_f = 0.314$ (EA/PE = 1:2.5). IR (KBr) $\nu(\text{cm}^{-1})$: 3275, 2952, 1681, 1612, 1532, 1425, 1345, 1284, 1189, 1077. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ : 10.1 (s, 1H), 7.61-7.56 (m, 2H), 7.35 (d, $J_{\text{H-H}} = 8.4$ Hz, 2H), 7.21 (d, $J_{\text{H-H}} = 7.5$ Hz, 1H), 7.12 (d, $J_{\text{H-H}} = 8.4$ Hz, 2H), 5.99 (s, 1H), 3.34 (s, 3H), 3.31-3.11 (m, 2H), 2.57-2.51 (m, 2H), 1.64 (s, 3H), 1.15 (t, $J_{\text{H-H}} = 7.6$ Hz, 3H). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ : 172.2 (C=O), 161.4 (t, $J_{\text{F-C}} = 28.8$ Hz, C=O), 161.3 (C=O), 151.8, 148.9, 140.7, 137.6, 135.0, 132.8, 128.1, 123.0, 121.1, 117.0 (dd, $J_{\text{F-C}} = 252.0$ Hz, $J_{\text{F-C}} = 252.0$ Hz), 115.1, 108.8, 92.8, 44.9 (t, $J_{\text{F-C}} = 22.3$ Hz), 43.3 (d, $J_{\text{F-C}} = 2.6$ Hz), 31.8, 29.9, 28.0, 16.0. ^{19}F NMR (471 MHz, $\text{DMSO-}d_6$) δ : -97.7 (d, $J_{\text{F-C}} = 255.4$ Hz, 1F), -102.5 (d, $J_{\text{F-C}} = 255.4$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{24}\text{H}_{23}\text{F}_2\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 441.1620, found 441.1618.

***N*-(4-(*tert*-Butyl)phenyl)-3-(4,6-dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-2,2-difluoropropanamide (4e)**



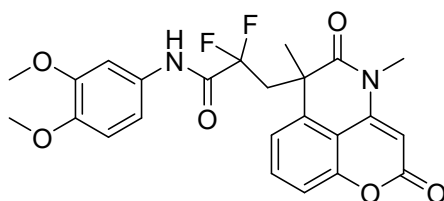
White solid (57.1 mg, 61%), m.p. 172.5-173.5 °C, $R_f = 0.295$ (EA/PE = 1:3). IR (KBr) $\nu(\text{cm}^{-1})$: 3340, 2951, 1744, 1702, 1677, 1604, 1542, 1498, 1427, 1350, 1261, 1187. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) : 10.1 (s, 1H), 7.62-7.57 (m, 2H), 7.37 (d, $J_{\text{H-H}} = 8.7$ Hz, 2H), 7.30 (d, $J_{\text{H-H}} = 8.7$ Hz, 2H), 7.21 (d, $J_{\text{H-H}} = 7.5$ Hz, 1H), 5.99 (s, 1H), 3.35 (s, 3H), 3.31-3.11 (m, 2H), 1.65 (s, 3H), 1.25 (s, 9H). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ : 172.2 (C=O), 161.4 (t, $J_{\text{F-C}} = 28.8$ Hz, C=O), 161.3 (C=O), 151.8, 148.9, 147.6, 137.6, 148.9, 147.6, 137.6, 134.7, 132.8, 125.6, 123.0, 120.8, 117.0 (t, $J_{\text{F-C}} = 256.0$ Hz), 115.1, 108.8, 92.9, 44.9 (t, $J_{\text{F-C}} = 22.6$ Hz), 43.3 (d, $J_{\text{F-C}} = 3.3$ Hz), 34.9, 31.9, 31.5, 29.9. ^{19}F NMR (471 MHz, $\text{DMSO-}d_6$) δ : -98.0 (d, $J_{\text{F-C}} = 256.6$ Hz, 1F), -102.2 (d, $J_{\text{F-C}} = 256.6$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{26}\text{H}_{27}\text{F}_2\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 469.1933, found 469.1930.

3-(4,6-Dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-2,2-difluoro-*N*-(4-methoxyphenyl)propanamide (4f)



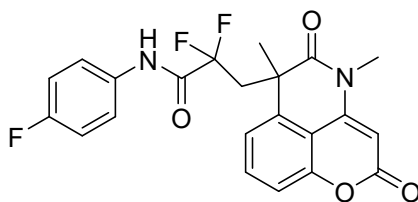
White solid (48.6 mg, 55%), m.p. 100.1-101.1 °C, $R_f = 0.28$ (EA/DCM/PE = 1:5:4). IR (KBr) $\nu(\text{cm}^{-1})$: 3294, 3056, 1683, 1613, 1507, 1411, 1350, 1244, 1181, 1078. $^1\text{H NMR}$ (500 MHz, $\text{DMSO-}d_6$) δ : 10.0 (s, 1H), 7.59-7.55 (m, 2H), 7.34 (d, $J_{\text{H-H}} = 8.9$ Hz, 2H), 7.21 (d, $J_{\text{H-H}} = 6.8$ Hz, 1H), 6.84 (d, $J_{\text{H-H}} = 8.9$ Hz, 2H), 5.99 (s, 1H), 3.71 (s, 3H), 3.33 (s, 3H), 3.27-3.08 (m, 2H), 1.64 (s, 3H). $^{13}\text{C NMR}$ (126 MHz, $\text{DMSO-}d_6$) δ : 172.2 (C=O), 161.3 (C=O), 156.6 (C=O), 151.8, 148.9, 137.5, 132.8, 130.3, 123.0, 122.5, 115.1, 114.0, 108.8, 92.9, 55.6, 43.3, 31.8, 29.9. $^{19}\text{F NMR}$ (471 MHz, $\text{DMSO-}d_6$) δ : -97.4 (d, $J_{\text{F-C}} = 255.0$ Hz, 1F), -102.7 (d, $J_{\text{F-C}} = 255.0$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{23}\text{H}_{21}\text{F}_2\text{N}_2\text{O}_5$ [M + H]⁺ 443.1413, found 443.1409.

***N*-(3,4-Dimethoxyphenyl)-3-(4,6-dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-2,2-difluoropropanamide (4g)**



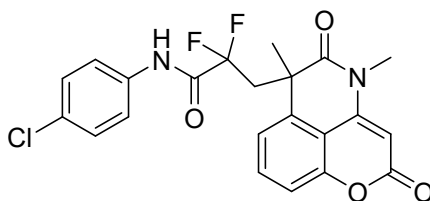
White solid (66.1 mg, 70%), m.p. 126.3-127.3 °C, $R_f = 0.32$ (EA/PE = 1:1). IR (KBr) $\nu(\text{cm}^{-1})$: 3578, 3095, 1681, 1621, 1561, 1513, 1452, 1425, 1347, 1229, 1135, 1077. $^1\text{H NMR}$ (500 MHz, $\text{DMSO-}d_6$) δ : 10.0 (s, 1H), 7.60-7.55 (m, 1H), 7.19 (d, $J_{\text{H-H}} = 7.6$ Hz, 1H), 7.07-7.04 (m, 2H), 6.85 (d, $J_{\text{H-H}} = 8.7$ Hz, 1H), 5.98 (s, 1H), 3.72 (s, 3H), 3.69 (s, 3H), 3.34 (s, 3H), 3.30-3.09 (m, 2H), 1.63 (s, 3H). $^{13}\text{C NMR}$ (126 MHz, $\text{DMSO-}d_6$) δ : 172.2 (C=O), 161.3 (C=O), 161.0 (C=O), 151.8, 148.9, 148.5, 146.2, 137.4, 132.7, 130.6, 123.0, 117.0 (t, $J_{\text{F-C}} = 251.1$ Hz), 115.1, 112.9, 111.8, 108.8, 105.7, 92.9, 56.0, 55.6, 45.0 (t, $J_{\text{F-C}} = 22.6$ Hz), 43.2 (d, $J_{\text{F-C}} = 3.3$ Hz), 31.8, 29.9. $^{19}\text{F NMR}$ (471 MHz, $\text{DMSO-}d_6$) δ : -97.1 (d, $J_{\text{F-C}} = 256.6$ Hz, 1F), -103.0 (d, $J_{\text{F-C}} = 256.6$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{24}\text{H}_{23}\text{F}_2\text{N}_2\text{O}_6$ [M + H]⁺ 473.1519, found 473.1521.

3-(4,6-Dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-2,2-difluoro-*N*-(4-fluorophenyl)propanamide (4h)



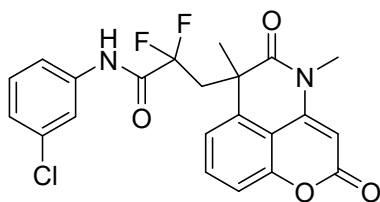
White solid (64.5 mg, 75%), m.p. 225.4-226.4 °C, $R_f = 0.33$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3288, 2916, 1697, 1678, 1620, 1563, 1532, 1506, 1425, 1282, 1209, 1063. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ : 10.2 (s, 1H), 7.58-7.54 (m, 2H), 7.46-7.44 (m, 2H), 7.18 (dd, $J_{\text{H-H}} = 6.8$ Hz, $J_{\text{H-H}} = 2.5$ Hz, 1H), 7.12 (t, $J_{\text{H-H}} = 8.1$ Hz, 2H), 5.98 (s, 1H), 3.33 (s, 3H), 3.31-3.09 (m, 2H), 1.63 (s, 3H). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ : 172.2 (C=O), 161.5 (t, $J_{\text{F-C}} = 28.8$ Hz, C=O), 161.3 (C=O), 159.3 (d, $J_{\text{F-C}} = 242.2$ Hz), 151.8, 148.9, 137.4, 133.7 (d, $J_{\text{F-C}} = 2.5$ Hz), 132.7, 123.0 (d, $J_{\text{F-C}} = 21.7$ Hz), 122.8, 116.9 (dd, $J_{\text{F-C}} = 252.0$ Hz, $J_{\text{F-C}} = 252.0$ Hz), 115.6 (d, $J_{\text{F-C}} = 22.3$ Hz), 115.1, 108.8, 92.9, 45.0 (t, $J_{\text{F-C}} = 22.5$ Hz), 43.2 (d, $J_{\text{F-C}} = 3.9$ Hz), 31.8, 29.9. ^{19}F NMR (471 MHz, $\text{DMSO-}d_6$) δ : -97.2 (d, $J_{\text{F-C}} = 255.4$ Hz, 1F), -103.1 (d, $J_{\text{F-C}} = 255.4$ Hz, 1F), -117.2 (s, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{22}\text{H}_{18}\text{F}_3\text{N}_2\text{O}_4$ [$\text{M} + \text{H}$] $^+$ 431.1213, found 431.1207.

***N*-(4-Chlorophenyl)-3-(4,6-dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-2,2-difluoropropanamide (4i)**



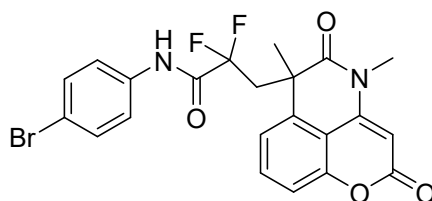
White solid (71.4 mg, 80%), m.p. 221.7-222.7 °C, $R_f = 0.274$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3295, 1681, 1613, 1526, 1354, 1280, 1184, 1079. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ : 10.3 (s, 1H), 7.59-7.54 (m, 2H), 7.48 (d, $J_{\text{H-H}} = 8.8$ Hz, 2H), 7.35 (t, $J_{\text{H-H}} = 8.8$ Hz, 2H), 7.18 (dd, $J_{\text{H-H}} = 7.0$ Hz, $J_{\text{H-H}} = 1.7$ Hz, 1H), 5.99 (s, 1H), 3.34 (s, 3H), 3.29-3.10 (m, 2H), 1.64 (s, 3H). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ : 172.2 (C=O), 161.7 (t, $J_{\text{F-C}} = 28.9$ Hz, C=O), 161.3 (C=O), 151.8, 148.9, 137.3, 136.3, 132.8, 129.0, 128.9, 123.0, 122.5, 122.4, 116.9 (t, $J_{\text{F-C}} = 252.0$ Hz), 115.2, 108.8, 92.9, 44.9 (t, $J_{\text{F-C}} = 22.7$ Hz), 43.3 (d, $J_{\text{F-C}} = 3.2$ Hz), 31.8, 30.0. ^{19}F NMR (471 MHz, $\text{DMSO-}d_6$) δ : -97.1 (d, $J_{\text{F-C}} = 255.8$ Hz, 1F), -103.2 (d, $J_{\text{F-C}} = 255.8$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{22}\text{H}_{18}\text{ClF}_2\text{N}_2\text{O}_4$ [$\text{M} + \text{H}$] $^+$ 447.0918, found 447.0906.

***N*-(3-Chlorophenyl)-3-(4,6-dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-2,2-difluoropropanamide (4j)**



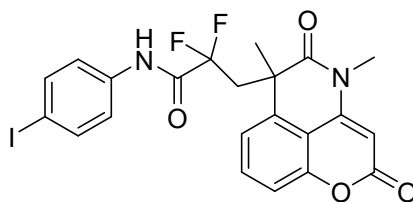
White solid (53.5 mg, 60%), m.p. 223.8-224.8 °C, $R_f = 0.305$ (EA/PE = 1.5:1). IR (KBr) $\nu(\text{cm}^{-1})$: 3291, 2993, 1684, 1606, 1428, 1540, 1347, 1276, 1183, 1077. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ : 10.3 (s, 1H), 7.57 (d, $J_{\text{H-H}} = 5.8$ Hz, 3H), 7.40 (d, $J_{\text{H-H}} = 8.3$ Hz, 1H), 7.32 (t, $J_{\text{H-H}} = 8.1$ Hz, 1H), 7.20-7.16 (m, 2H), 6.00 (s, 1H), 3.36 (s, 3H), 3.33-3.12 (m, 2H), 1.66 (s, 3H). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ : 172.2 (C=O), 161.8 (t, $J_{\text{F-C}} = 28.6$ Hz, C=O), 161.2 (C=O), 151.8, 148.9, 138.7, 137.3, 133.2, 132.7, 130.6, 125.0, 123.0, 120.4, 119.3, 116.7 (t, $J_{\text{F-C}} = 252.0$ Hz), 115.1, 108.8, 93.0, 45.0 (t, $J_{\text{F-C}} = 22.5$ Hz), 43.2 (d, $J_{\text{F-C}} = 3.9$ Hz), 31.8, 29.9. ^{19}F NMR (471 MHz, $\text{DMSO-}d_6$) δ : -97.2 (d, $J_{\text{F-C}} = 255.7$ Hz, 1F), -103.3 (d, $J_{\text{F-C}} = 255.7$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{22}\text{H}_{18}\text{ClF}_2\text{N}_2\text{O}_4$ [M + H] $^+$ 447.0918, found 447.0911.

***N*-(4-Bromophenyl)-3-(4,6-dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-2,2-difluoropropanamide (4k)**



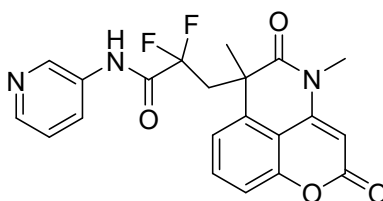
White solid (70.6 mg, 72%), m.p. 206.3-207.3 °C, $R_f = 0.279$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3300, 1699, 1681, 1619, 1562, 1528, 1491, 1427, 1400, 1353, 1279, 1062. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ : 10.3 (s, 1H), 7.59-7.55 (m, 2H), 7.48 (d, $J_{\text{H-H}} = 8.9$ Hz, 2H), 7.43 (d, $J_{\text{H-H}} = 8.9$ Hz, 2H), 7.19 (dd, $J_{\text{H-H}} = 6.8$ Hz, $J_{\text{H-H}} = 2.5$ Hz, 1H), 6.00 (s, 1H), 3.34 (s, 3H), 3.30-3.11 (m, 2H), 1.64 (s, 3H). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ : 172.2 (C=O), 161.6 (t, $J_{\text{F-C}} = 29.0$ Hz, C=O), 161.3 (C=O), 151.8, 148.9, 137.4, 136.7, 132.8, 131.8, 123.0, 122.8, 117.2, 116.8 (dd, $J_{\text{F-C}} = 251.9$ Hz, $J_{\text{F-C}} = 251.9$ Hz), 115.2, 108.8, 92.9, 44.9 (t, $J_{\text{F-C}} = 22.6$ Hz), 43.3 (d, $J_{\text{F-C}} = 3.5$ Hz), 31.8, 30.0. ^{19}F NMR (471 MHz, $\text{DMSO-}d_6$) δ : -97.1 (d, $J_{\text{F-C}} = 256.0$ Hz, 1F), -103.1 (d, $J_{\text{F-C}} = 256.0$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{22}\text{H}_{18}\text{BrF}_2\text{N}_2\text{O}_4$ [M + H] $^+$ 491.0413, found 491.0409.

3-(4,6-Dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-2,2-difluoro-*N*-(4-iodophenyl)propanamide (4l)



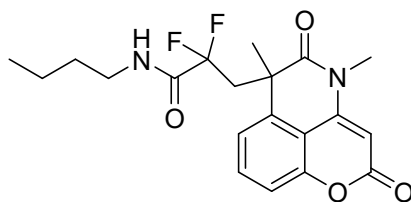
White solid (76.4 mg, 71%), m.p. 114.3-115.3 °C, $R_f = 0.285$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3005, 1684, 1614, 1534, 1457, 1342, 1316, 1181, 1084. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ : 10.3 (s, 1H), 7.63 (d, $J_{\text{H-H}} = 8.7$ Hz, 2H), 7.59-7.54 (m, 2H), 7.28 (d, $J_{\text{H-H}} = 8.7$ Hz, 2H), 7.19 (d, $J_{\text{H-H}} = 7.4$ Hz, 1H), 5.99 (s, 1H), 3.33 (s, 3H), 3.28-3.10 (m, 2H), 1.64 (s, 3H). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ : 172.2 (C=O), 161.6 (t, $J_{\text{F-C}} = 28.6$ Hz, C=O), 161.3 (C=O), 151.8, 148.9, 137.7, 137.4, 137.2, 132.8, 123.1, 123.0, 122.9, 116.9 (t, $J_{\text{F-C}} = 252.0$ Hz), 115.2, 108.8, 92.9, 89.6, 44.9 (t, $J_{\text{F-C}} = 22.5$ Hz), 43.2, 31.8, 30.0. ^{19}F NMR (471 MHz, $\text{DMSO-}d_6$) δ : -97.2 (d, $J_{\text{F-C}} = 256.1$ Hz, 1F), -103.0 (d, $J_{\text{F-C}} = 256.1$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{22}\text{H}_{18}\text{F}_2\text{IN}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 539.0274, found 539.0278.

3-(4,6-Dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-ij]isoquinolin-6-yl)-2,2-difluoro-N-(pyridin-3-yl)propanamide (4m)



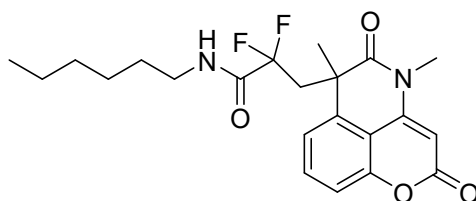
White solid (70.2 mg, 85%), m.p. 203.8-204.8 °C, $R_f = 0.274$ (EA/PE = 3:1). IR (KBr) $\nu(\text{cm}^{-1})$: 3387, 3055, 1680, 1610, 1551, 1483, 1420, 1342, 1271, 1180, 1021. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ : 10.4 (s, 1H), 8.62 (d, $J_{\text{H-H}} = 1.5$ Hz, 1H), 8.34 (d, $J_{\text{H-H}} = 4.5$ Hz, 1H), 7.85 (d, $J_{\text{H-H}} = 8.2$ Hz, 1H), 7.57-7.55 (m, 2H), 7.36-7.33 (m, 1H), 7.17-7.15 (m, 1H), 6.02 (s, 1H), 3.43 (s, 3H), 3.36-3.14 (m, 2H), 1.66 (s, 3H). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ : 172.2 (C=O), 162.1 (t, $J_{\text{F-C}} = 28.6$ Hz, C=O), 161.3 (C=O), 151.8, 148.9, 146.1, 142.4, 137.3, 134.1, 132.7, 128.0, 123.9, 123.1, 116.8 (t, $J_{\text{F-C}} = 252.0$ Hz), 115.2, 108.9, 93.0, 44.9 (t, $J_{\text{F-C}} = 22.5$ Hz), 43.3 (d, $J_{\text{F-C}} = 3.9$ Hz), 31.8, 30.0. ^{19}F NMR (471 MHz, $\text{DMSO-}d_6$) δ : -96.7 (d, $J_{\text{F-C}} = 255.8$ Hz, 1F), -103.6 (d, $J_{\text{F-C}} = 255.8$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{21}\text{H}_{18}\text{F}_2\text{N}_3\text{O}_4$ $[\text{M} + \text{H}]^+$ 414.1260, found 414.1263.

N-Butyl-3-(4,6-dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-ij]isoquinolin-6-yl)-2,2-difluoropropanamide (4n)



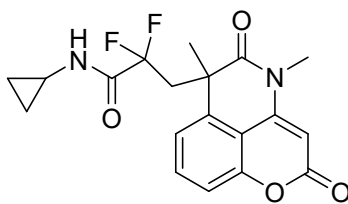
White solid (59.6 mg, 76%), m.p. 139.3-140.3 °C $R_f = 0.33$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3344, 2916, 1723, 1686, 1620, 1545, 1504, 1465, 1350, 1255, 1184, 1073. ^1H NMR (500 MHz, CDCl_3) δ : 7.62-7.58 (m, 1H), 7.30-7.25 (m, 2H), 6.19 (bs, 1H), 5.82 (s, 1H), 3.44 (s, 3H), 3.31-3.20 (m, 1H), 3.12-2.98 (m, 3H), 1.67 (s, 3H), 1.38-1.35 (m, 2H), 1.27-1.23 (m, 2H), 0.89 (t, $J_{\text{H-H}} = 6.7$ Hz, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ : 172.3 (C=O), 163.1 (t, $J_{\text{F-C}} = 30.1$ Hz, C=O), 161.7 (C=O), 152.2, 148.6, 136.9, 132.4, 122.1, 116.4 (t, $J_{\text{F-C}} = 253.8$ Hz), 115.5, 108.5, 92.8, 44.4 (t, $J_{\text{F-C}} = 22.3$ Hz), 43.4 (d, $J_{\text{F-C}} = 3.2$ Hz), 39.3, 32.2, 31.0, 29.6, 19.8, 13.6. ^{19}F NMR (471 MHz, CDCl_3) δ : -99.5 (d, $J_{\text{F-C}} = 260.3$ Hz, 1F), -105.2 (d, $J_{\text{F-C}} = 260.3$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{20}\text{H}_{22}\text{F}_2\text{N}_2\text{O}_4\text{Na}$ $[\text{M} + \text{Na}]^+$ 415.1440, found 415.1442.

3-(4,6-Dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-ij]isoquinolin-6-yl)-2,2-difluoro-N-hexylpropanamide (4o)



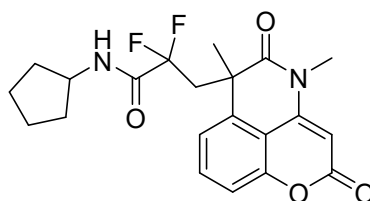
White solid (66.4 mg, 79%), m.p. 109.7-110.7 °C, $R_f = 0.31$ (EA/PE = 1:3). IR (KBr) $\nu(\text{cm}^{-1})$: 3328, 2970, 1682, 1618, 1557, 1503, 1347, 1255, 1190, 1076. ^1H NMR (500 MHz, CDCl_3) δ : 7.60 (t, $J_{\text{H-H}} = 8.1$ Hz, 1H), 7.29-7.25 (m, 2H), 6.18 (s, 1H), 5.81 (s, 1H), 3.43 (s, 3H), 3.30-3.21 (m, 1H), 3.12-2.94 (m, 3H), 1.67 (s, 3H), 1.38-1.35 (m, 2H), 1.27-1.23 (m, 6H), 0.86 (t, $J_{\text{H-H}} = 6.6$ Hz, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ : 172.2 (C=O), 163.1 (t, $J_{\text{F-C}} = 27.7$ Hz, C=O), 161.6 (C=O), 152.1, 148.6, 136.9, 132.4, 122.1, 116.4 (t, $J_{\text{F-C}} = 256.4$ Hz), 115.5, 108.5, 92.8, 44.4 (t, $J_{\text{F-C}} = 22.6$ Hz), 43.4 (d, $J_{\text{F-C}} = 3.3$ Hz), 39.5, 32.2, 31.3, 29.6, 28.9, 26.3, 22.4, 13.9. ^{19}F NMR (471 MHz, CDCl_3) δ : -99.5 (d, $J_{\text{F-C}} = 260.3$ Hz, 1F), -105.2 (d, $J_{\text{F-C}} = 260.3$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{22}\text{H}_{27}\text{F}_2\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 421.1933, found 421.1938.

N-Cyclopropyl-3-(4,6-dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-ij]isoquinolin-6-yl)-2,2-difluoropropanamide (4p)



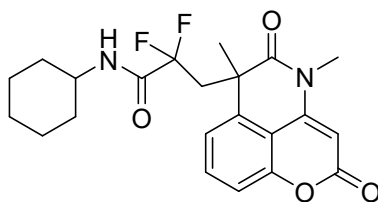
White solid (55.6 mg, 74%), m.p. 224.1-225.1 °C, Rf = 0.293 (EA/PE = 1:1.5). IR (KBr) $\nu(\text{cm}^{-1})$: 3349, 2981, 1719, 1682, 1618, 1562, 1526, 1500, 1426, 1353, 1185, 1068. ^1H NMR (500 MHz, DMSO- d_6) δ : 8.40 (d, $J_{\text{H-H}} = 4.2$ Hz, 1H), 7.66 (t, $J_{\text{H-H}} = 8.0$ Hz, 1H), 7.53 (d, $J_{\text{H-H}} = 7.9$ Hz, 1H), 7.32 (d, $J_{\text{H-H}} = 8.0$ Hz, 1H), 5.99 (s, 1H), 3.35 (s, 3H), 3.18-2.96 (m, 2H), 2.42-2.40 (m, 1H), 1.61 (s, 3H), 0.57-0.48 (m, 2H), 0.37-0.31 (m, 2H). ^{13}C NMR (126 MHz, DMSO- d_6) δ : 172.3 (C=O), 164.0 (t, $J_{\text{F-C}} = 28.4$ Hz, C=O), 161.4 (C=O), 151.8, 149.0, 137.6, 132.8, 123.1, 116.9 (dd, $J_{\text{F-C}} = 252.0$ Hz, $J_{\text{F-C}} = 252.0$ Hz), 115.1, 108.8, 92.8, 44.8 (t, $J_{\text{F-C}} = 22.3$ Hz), 43.2 (d, $J_{\text{F-C}} = 3.2$ Hz), 31.8, 29.9, 22.9. ^{19}F NMR (471 MHz, DMSO- d_6) δ : -97.6 (d, $J_{\text{F-C}} = 255.2$ Hz, 1F), -104.1 (d, $J_{\text{F-C}} = 255.2$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{19}\text{H}_{19}\text{F}_2\text{N}_2\text{O}_4$ [M + H] $^+$ 377.1307, found 377.1309.

***N*-Cyclopentyl-3-(4,6-dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-2,2-difluoropropanamide (4q)**



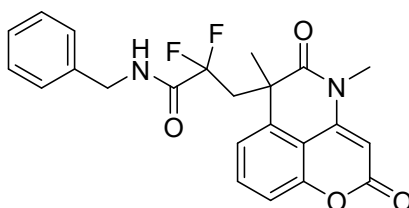
White solid (63.8 mg, 79%), m.p. 154.9-155.9 °C, Rf = 0.307 (EA/PE = 1:1.5). IR (KBr) $\nu(\text{cm}^{-1})$: 3270, 2966, 1716, 1668, 1620, 1563, 1502, 1427, 1352, 1251, 1077. ^1H NMR (500 MHz, DMSO- d_6) δ : 8.31-8.27 (m, 1H), 7.66 (t, $J_{\text{H-H}} = 8.1$ Hz, 1H), 7.52 (d, $J_{\text{H-H}} = 7.8$ Hz, 1H), 7.32 (d, $J_{\text{H-H}} = 8.2$ Hz, 1H), 5.99 (s, 1H), 3.69-3.62 (m, 1H), 3.36 (s, 3H), 3.20-2.97 (m, 2H), 1.70-1.64 (m, 1H), 1.61 (s, 3H), 1.58-1.50 (m, 3H), 1.44-1.36 (m, 2H), 1.31-1.17 (m, 2H). ^{13}C NMR (126 MHz, DMSO- d_6) δ : 172.3 (C=O), 162.5 (t, $J_{\text{F-C}} = 30.9$ Hz, C=O), 161.4 (C=O), 151.8, 149.0, 137.5, 132.7, 123.2, 116.9 (t, $J_{\text{F-C}} = 256.8$ Hz), 115.1, 108.8, 92.7, 50.9, 44.8 (t, $J_{\text{F-C}} = 22.1$ Hz), 43.2 (d, $J_{\text{F-C}} = 3.2$ Hz), 32.1, 31.8, 31.6, 29.9, 24.0. ^{19}F NMR (471 MHz, DMSO- d_6) δ : -96.6 (d, $J_{\text{F-C}} = 256.2$ Hz, 1F), -104.2 (d, $J_{\text{F-C}} = 256.2$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{21}\text{H}_{23}\text{F}_2\text{N}_2\text{O}_4$ [M + H] $^+$ 405.1620, found 405.1616.

***N*-Cyclohexyl-3-(4,6-dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-2,2-difluoropropanamide (4r)**



White solid (68.6 mg, 82%), m.p. 181.7-182.7 °C, R_f = 0.31 (EA/PE = 1:3). IR (KBr) ν (cm⁻¹): 3270, 2920, 2853, 1712, 1656, 1617, 1559, 1428, 1348, 1257, 1187, 1080. ¹H NMR (500 MHz, DMSO-*d*₆) δ : 8.26 (d, *J*_{H-H} = 7.9 Hz, 1H), 7.66 (t, *J*_{H-H} = 8.0 Hz, 1H), 7.54 (d, *J*_{H-H} = 7.9 Hz, 1H), 7.32 (d, *J*_{H-H} = 8.2 Hz, 1H), 5.99 (s, 1H), 3.35 (s, 3H), 3.27-2.97 (m, 3H), 1.63 (bs, 5H), 1.61-1.51 (m, 2H), 1.41-1.39 (m, 1H), 1.19-1.08 (m, 5H). ¹³C NMR (126 MHz, DMSO-*d*₆) δ : 172.3 (C=O), 162.1 (t, *J*_{F-C} = 28.4 Hz, C=O), 161.3 (C=O), 151.8, 149.0, 137.8, 132.8, 123.1, 117.0 (dd, *J*_{F-C} = 251.2 Hz, *J*_{F-C} = 251.2 Hz), 115.1, 108.8, 92.6, 48.7, 44.7 (t, *J*_{F-C} = 22.1 Hz), 43.2 (d, *J*_{F-C} = 3.2 Hz), 32.1, 31.8, 29.9, 25.4, 25.1. ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ : -97.8 (d, *J*_{F-C} = 255.5 Hz, 1F), -103.3 (d, *J*_{F-C} = 255.5 Hz, 1F). HR MS (ESI) *m/z*: calcd for C₂₂H₂₅F₂N₂O₄ [M + H]⁺ 419.1777, found 419.1776.

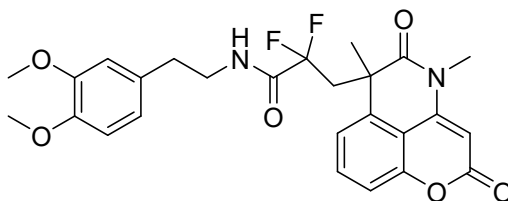
***N*-Benzyl-3-(4,6-dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]isoquinolin-6-yl)-2,2-difluoropropanamide (4s)**



White solid (63.9 mg, 75%), m.p. 157.8-158.8 °C, R_f = 0.28 (EA/PE = 1:2). IR (KBr) ν (cm⁻¹): 3255, 2984, 1720, 1679, 1621, 1562, 1499, 1300, 1258, 1141, 1082. ¹H NMR (500 MHz, DMSO-*d*₆) δ : 9.00 (t, *J*_{H-H} = 5.9 Hz, 1H), 7.67 (t, *J*_{H-H} = 8.0 Hz, 1H), 7.57 (d, *J*_{H-H} = 7.9 Hz, 1H), 7.34-7.28 (m, 3H), 7.22 (t, *J*_{H-H} = 7.2 Hz, 1H), 7.13 (d, *J*_{H-H} = 7.5 Hz, 2H), 6.01 (s, 1H), 4.12-4.07 (m, 1H), 3.96-3.92 (m, 1H), 3.36 (s, 3H), 3.24-3.02 (m, 2H), 1.63 (s, 3H). ¹³C NMR (126 MHz, DMSO-*d*₆) δ : 172.3 (C=O), 163.3 (t, *J*_{F-C} = 28.3 Hz, C=O), 161.4 (C=O), 151.8, 149.0, 138.5, 137.6, 132.7, 128.7, 127.6, 127.4, 123.1, 117.2 (dd, *J*_{F-C} = 251.1 Hz, *J*_{F-C} = 251.1 Hz), 115.2, 108.8, 92.8, 44.8 (t, *J*_{F-C} = 22.6 Hz), 43.2 (d, *J*_{F-C} = 3.5 Hz), 42.5, 31.7, 29.9. ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ : -98.2 (d, *J*_{F-C} = 255.4 Hz, 1F), -103.9 (d, *J*_{F-C} = 255.4 Hz, 1F). HR MS (ESI) *m/z*: calcd for C₂₃H₂₁F₂N₂O₄ [M + H]⁺ 427.1464, found 427.1461.

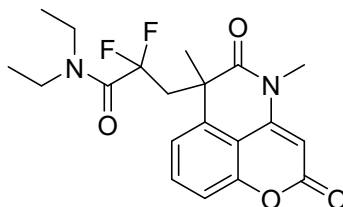
***N*-(3,4-Dimethoxyphenethyl)-3-(4,6-dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-**

***ij*]-isoquinolin-6-yl)-2,2-difluoropropanamide (4t)**



White solid (75.0 mg, 75%), m.p. 158.7-159.7 °C, $R_f = 0.297$ (EA/PE = 1.5:1). IR (KBr) $\nu(\text{cm}^{-1})$: 3274, 2919, 1685, 1622, 1562, 1512, 1455, 1425, 1352, 1257, 1187, 1075. ^1H NMR (500 MHz, CDCl_3) δ : 7.59 (t, $J_{\text{H-H}} = 8.1$ Hz, 1H), 7.29-7.23 (m, 2H), 6.78 (d, $J_{\text{H-H}} = 7.9$ Hz, 1H), 6.63 (d, $J_{\text{H-H}} = 8.1$ Hz, 2H), 6.27 (s, 1H), 5.78 (s, 1H), 3.84 (s, 3H), 3.82 (s, 3H), 3.40 (s, 3H), 3.37-3.32 (m, 1H), 3.27-3.15 (m, 2H), 3.05-2.95 (m, 1H), 2.64 (t, $J_{\text{H-H}} = 7.0$ Hz, 2H), 1.66 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ : 172.2 (C=O), 163.2 (t, $J_{\text{F-C}} = 28.1$ Hz, C=O), 161.6 (C=O), 152.1, 148.9, 148.5, 147.7, 136.8, 132.4, 130.3, 122.1, 120.5, 116.3 (d, $J_{\text{F-C}} = 254.2$ Hz), 115.5, 111.7, 111.3, 108.5, 92.7, 55.9, 55.7, 44.3 (t, $J_{\text{F-C}} = 22.3$ Hz), 43.4 (d, $J_{\text{F-C}} = 3.1$ Hz), 40.7, 34.6, 32.2, 29.6. ^{19}F NMR (471 MHz, CDCl_3) δ : -99.4 (d, $J_{\text{F-C}} = 260.6$ Hz, 1F), -105.0 (d, $J_{\text{F-C}} = 260.6$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{26}\text{H}_{27}\text{F}_2\text{N}_2\text{O}_6$ [$\text{M} + \text{H}$] $^+$ 501.1832, found 501.1828.

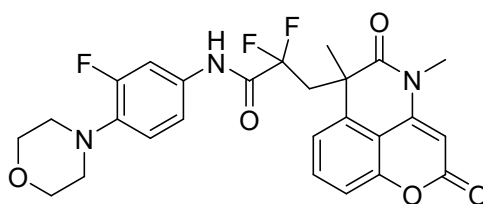
3-(4,6-Dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-*ij*]-isoquinolin-6-yl)-*N,N*-diethyl-2,2-difluoropropanamide (4u)



White solid (62.7 mg, 80%), m.p. 156.5-157.4 °C, $R_f = 0.286$ (EA/PE = 1:2). IR (KBr) $\nu(\text{cm}^{-1})$: 3088, 2979, 1716, 1679, 1650, 1614, 1559, 1500, 1451, 1430, 1345, 1258, 1189, 1094. ^1H NMR (500 MHz, CDCl_3) δ : 7.59 (t, $J_{\text{H-H}} = 8.1$ Hz, 1H), 7.29-7.25 (m, 2H), 5.84 (s, 1H), 3.51-3.40 (m, 4H), 3.29-3.24 (m, 4H), 3.03-2.93 (m, 1H), 1.71 (s, 3H), 1.08-1.02 (m, 6H). ^{13}C NMR (126 MHz, CDCl_3) δ : 167.7 (C=O), 157.1 (C=O), 157.0 (t, $J_{\text{F-C}} = 28.1$ Hz, C=O), 147.4, 144.0, 133.1, 127.5, 117.5, 113.4 (t, $J_{\text{F-C}} = 257.7$ Hz), 110.5, 103.8, 87.9, 40.7 (t, $J_{\text{F-C}} = 20.5$ Hz), 38.3 (d, $J_{\text{F-C}} = 1.7$ Hz), 36.9 (t, $J_{\text{F-C}} = 6.5$ Hz), 27.5, 24.8, 9.3, 7.4. ^{19}F NMR (471 MHz, CDCl_3) δ : -101.2 (d, $J_{\text{F-C}} = 278.9$ Hz, 1F), -103.1 (d, $J_{\text{F-C}} = 278.9$ Hz, 1F). HR MS (ESI) m/z : calcd for $\text{C}_{20}\text{H}_{23}\text{F}_2\text{N}_2\text{O}_4$ [$\text{M} + \text{H}$] $^+$ 393.1620, found 393.1618.

1.6 Synthesis of 3-(4,6-Dimethyl-2,5-dioxo-2,4,5,6-tetrahydropyrano[2,3,4-ij]isoquinolin-6-yl)-2,2-difluoro-N-(3-fluoro-4-morpholinophenyl)propanamide (8)

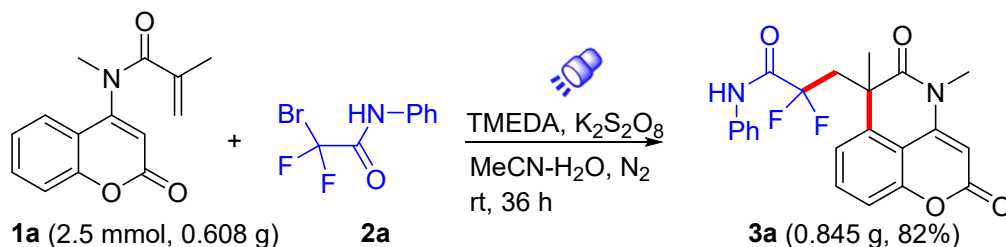
A Schlenk-tube was charged with *N*-methyl-*N*-(2-oxo-2*H*-chromen-4-yl)methacrylamide **1a** (0.2 mmol, 48.6 mg), 2-bromo-2,2-difluoro-*N*-(3-fluoro-4-morpholinophenyl)acetamide **2a** (0.4 mmol, 140.8 mg), K₂S₂O₈ (0.4 mmol, 108 mg), TMEDA (0.4 mmol, 46.4 mg) and MeCN-H₂O (3 mL, v/v, 2:1). The tube was stirred under the irradiation of 10 W blue LEDs (430 nm) at room temperature under N₂ atmosphere. After 6 hours, the mixture was transferred into a 100 mL separating funnel which contained 20 mL saturated sodium chloride solution. The mixture was extracted with ethyl acetate (10 mL × 2). The combined organic phase was dried over anhydrous Na₂SO₄ and concentrated under vacuum. The residue was purified by flash column chromatography using a mixture of ethyl acetate /petroleum ether as eluent to give the desired product **8**.



White solid (41.2 mg, 40%), m.p. 137.1-138.1 °C, R_f = 0.289 (EA/PE = 1:1). IR (KBr) ν (cm⁻¹): 2853, 1729, 1686, 1521, 1560, 1545, 1502, 1427, 1351, 1259, 1207, 1182. ¹H NMR (500 MHz, DMSO-*d*₆) δ : 10.2 (s, 1H), 7.60-7.55 (m, 2H), 7.31-7.28 (m, 1H), 7.21-7.18 (m, 2H), 6.95 (t, *J*_{H-H} = 9.5 Hz, 1H), 5.99 (s, 1H), 3.74-3.72 (m, 4H), 3.34 (s, 3H), 3.31-3.09 (m, 2H), 2.97-2.95 (m, 4H), 1.64 (s, 3H). ¹³C NMR (126 MHz, DMSO-*d*₆) δ : 172.2 (C=O), 161.3 (t, *J*_{F-C} = 256.0 Hz, C=O), 161.0 (C=O), 154.3 (d, *J*_{F-C} = 243.7 Hz), 151.8, 148.9, 137.4, 136.9 (d, *J*_{F-C} = 8.5 Hz), 132.7, 132.1 (d, *J*_{F-C} = 10.7 Hz), 123.0, 119.1 (d, *J*_{F-C} = 3.8 Hz), 117.0 (t, *J*_{F-C} = 251.0 Hz), 116.9, 115.1, 109.1, 108.9 (d, *J*_{F-C} = 15.2 Hz), 92.9, 66.6, 51.0 (d, *J*_{F-C} = 2.6 Hz), 45.0 (t, *J*_{F-C} = 22.6 Hz), 43.2 (d, *J*_{F-C} = 3.3 Hz), 31.8, 30.0. ¹⁹F NMR (471 MHz, DMSO-*d*₆) δ : -97.2 (d, *J*_{F-C} = 256.6 Hz, 1F), -103.0 (d, *J*_{F-C} = 256.6 Hz, 1F), -121.5 (s, 1F). HR MS (ESI) *m/z*: calcd for C₂₆H₂₅F₃N₃O₅ [M + H]⁺ 516.1741, found 516.1734.

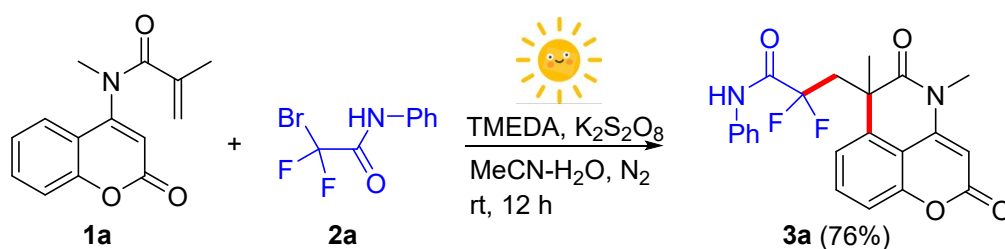
2 Gram scale experiment and natural sunlight experiment

2.1 Gram scale experiment



A Schlenk-flask equipped with a magnetic stir bar was charged with *N*-methyl-*N*-(2-oxo-2*H*-chromen-4-yl)methacrylamide **1a** (2.5 mmol, 0.608 g), BrCF₂CONHPh **2a** (5.0 mmol, 1.245 g), K₂S₂O₈ (5.0 mmol, 1.350 g), TMEDA (5.0 mmol, 0.580 g) and MeCN-H₂O (60 mL, v/v, 2:1). The flask was stirred under the irradiation of 10 W blue LEDs (430 nm) at room temperature under N₂ atmosphere. After 36 hours, the mixture was transferred into a 250 mL separating funnel which contained 80 mL saturated sodium chloride solution. The mixture was extracted with ethyl acetate (80 mL × 2). The combined organic phase was dried over anhydrous Na₂SO₄ and concentrated under vacuum. The residue was purified by flash column chromatography using a mixture of ethyl acetate /petroleum ether as eluent to give the desired product **3a** (0.845 g, 82%).

2.2 Natural sunlight experiment



A Schlenk-tube was charged with *N*-methyl-*N*-(2-oxo-2*H*-chromen-4-yl)methacrylamide **1a** (0.2 mmol, 48.6 mg), BrCF₂CONHPh **2a** (0.4 mmol, 99.6 mg), K₂S₂O₈ (0.4 mmol, 108 mg), TMEDA (0.4 mmol, 46.4 mg) and MeCN-H₂O (3 mL, v/v, 2:1). The tube was stirred under the irradiation of natural sunlight at room temperature under N₂ atmosphere. After 12 hours, the mixture was transferred into a 100 mL separating funnel which contained 20 mL saturated sodium chloride solution. The mixture was extracted with ethyl acetate (10 mL × 2). The combined organic phase

was dried over anhydrous Na_2SO_4 and concentrated under vacuum. The residue was purified by flash column chromatography using a mixture of ethyl acetate /petroleum ether as eluent to give the desired product **3a** (62.6 mg, 76%).

3 Mechanistic study

3.1 UV-vis spectroscopic measurement

UV-vis spectra were performed on UV visible spectrophotometer (recorded in 1 cm path quartz cuvettes using TU-1901 Visible spectrophotometer)

Solution 1: $\text{BrCF}_2\text{CONHPh}$ **2a** (1×10^{-4} M) in MeCN (3 mL)

Solution 2: $\text{K}_2\text{S}_2\text{O}_8$ (1×10^{-4} M) in MeCN (3 mL)

Solution 3: TMEDA (1×10^{-4} M) in MeCN (3 mL)

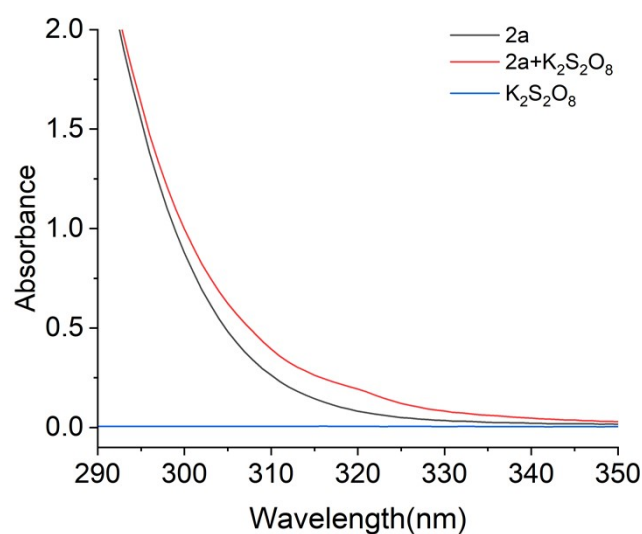


Fig. S1 Absorption spectra of **2a** (1×10^{-4} M), $\text{K}_2\text{S}_2\text{O}_8$ (1×10^{-4} M) and **2a** (1×10^{-4} M)- $\text{K}_2\text{S}_2\text{O}_8$ (1×10^{-4} M) in MeCN

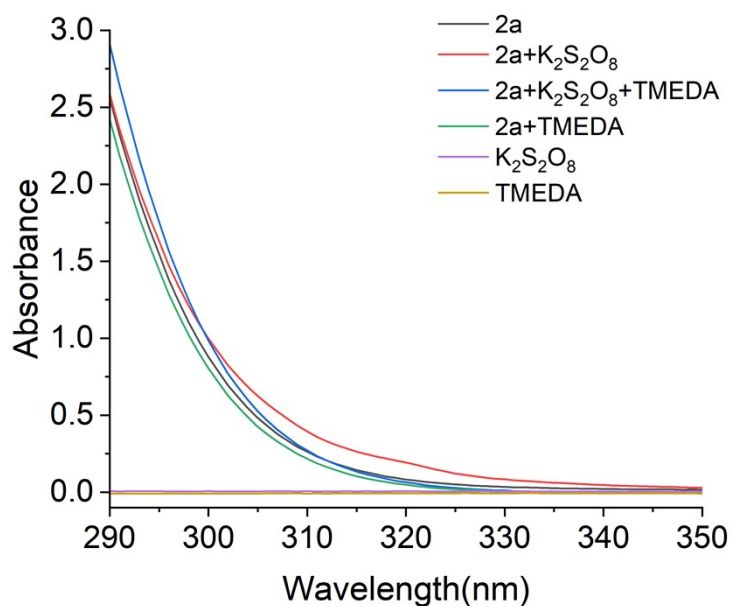
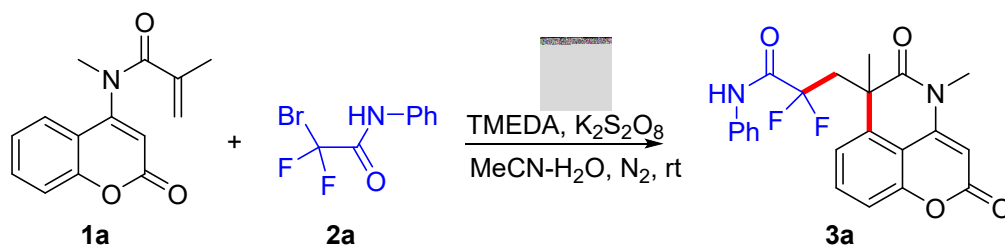


Fig. S2 Absorption spectra of **2a** (1×10^{-4} M), TMEDA (1×10^{-4} M), $K_2S_2O_8$ (1×10^{-4} M), **2a** (1×10^{-4} M)- $K_2S_2O_8$ (1×10^{-4} M), **2a** (1×10^{-4} M)-TMEDA (1×10^{-4} M), and **2a** (1×10^{-4} M)- $K_2S_2O_8$ (1×10^{-4} M)-TMEDA (1×10^{-4} M) in MeCN

3.2 Light on/off experiment



A Schlenk-tube was charged with *N*-methyl-*N*-(2-oxo-2*H*-chromen-4-yl)methacrylamide **1a** (0.2 mmol, 48.6 mg), $BrCF_2CONHPh$ **2a** (0.4 mmol, 99.6 mg), $K_2S_2O_8$ (0.4 mmol, 108 mg), TMEDA (0.4 mmol, 46.4 mg) and MeCN- H_2O (3 mL, v/v, 2:1). The tube was stirred under the irradiation of 10 W blue LEDs (430 nm) at room temperature under N_2 atmosphere, and the reaction was placed in light and dark in every alternative 1 h. The yield of product **3a** was determined by ^{19}F NMR.

Entry	Time (h)	Light source	Yield (%)
1	2	on	30
2	2	off	30
3	2	on	70
4	2	off	70
5	2	on	90
6	2	off	90

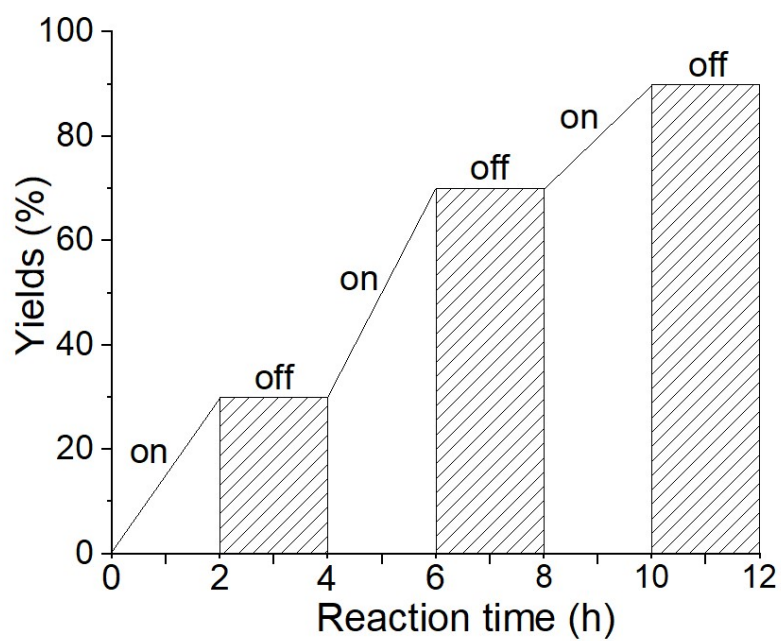


Fig. S3 Visible light irradiation on/off experiment

3.3 HR MS spectra of the adducts

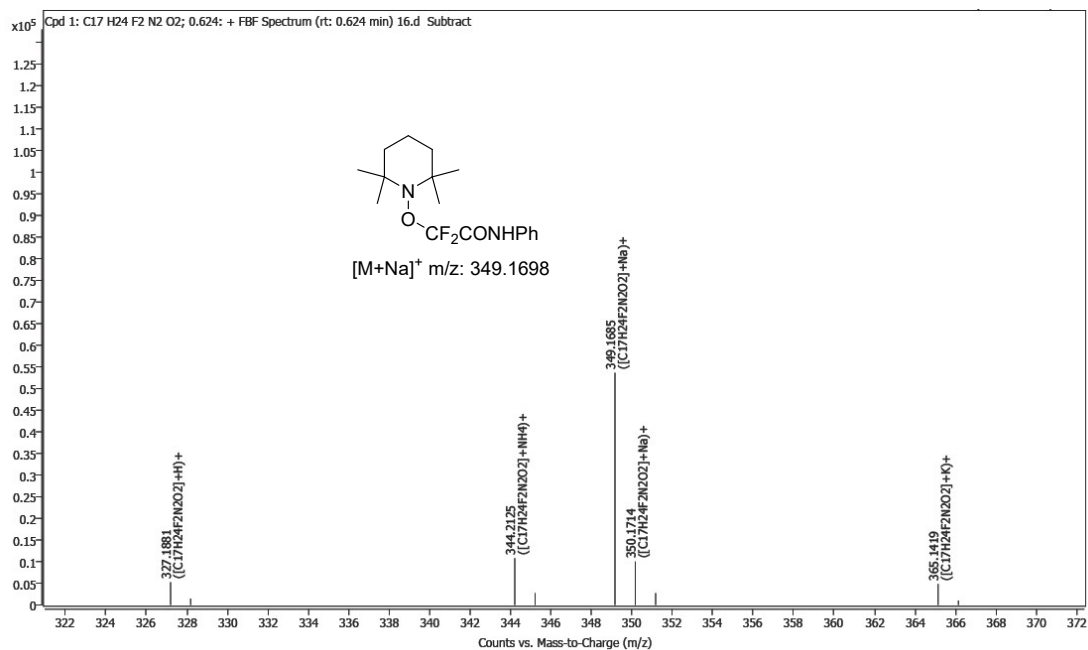


Fig. S4 HR MS spectrum of the adduct TEMPO-CF₂CONHPh (9)

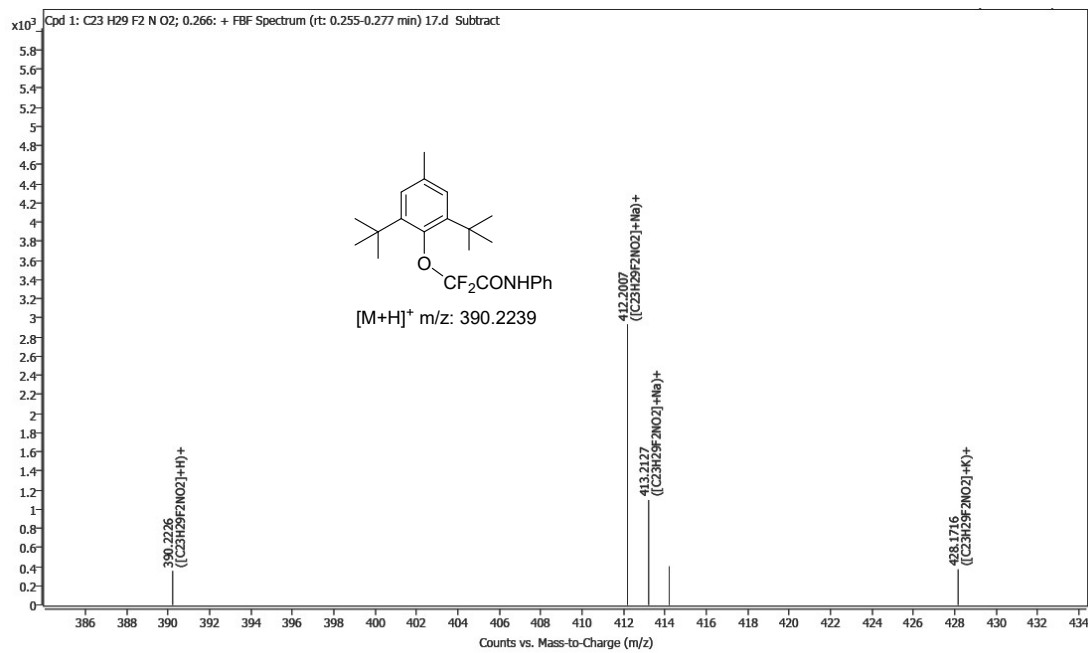


Fig. S5 HR MS spectrum of the adduct BHT-CF₂CONHPh (10)

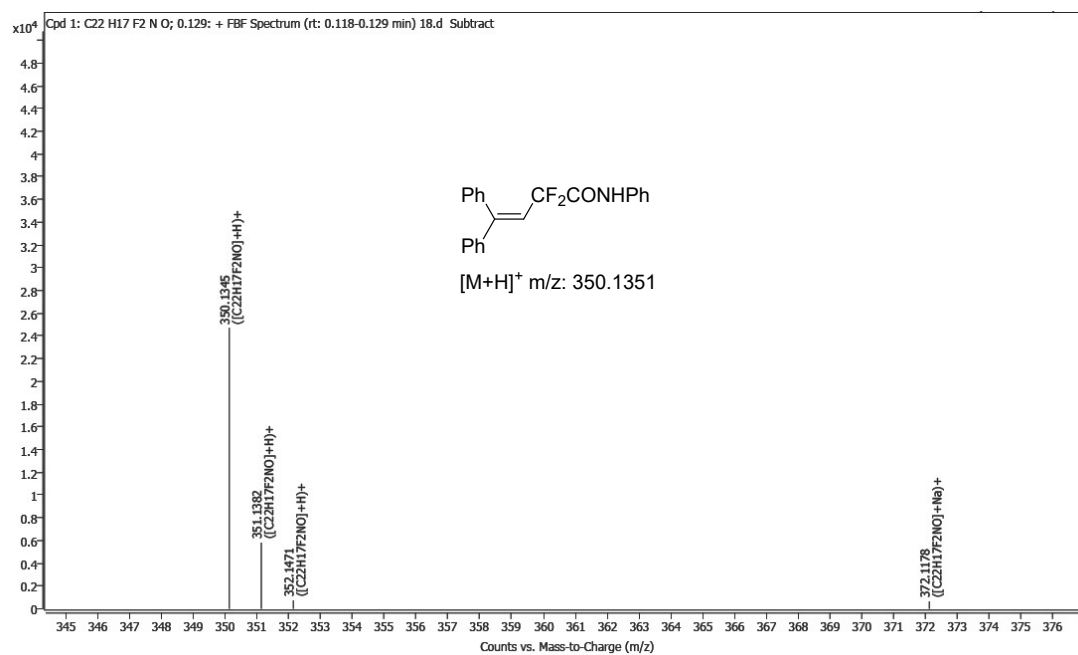
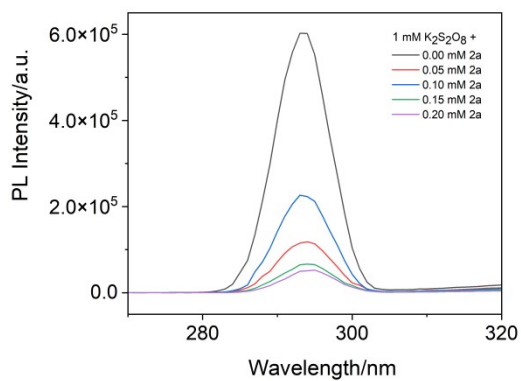


Fig. S6 HR MS spectrum of the adduct DPE- CF_2CONHPh (**11**)

3.4 Stern-Volmer quenching experiments

(a) Fluorescence quenching



(b) Stern-Volmer plots

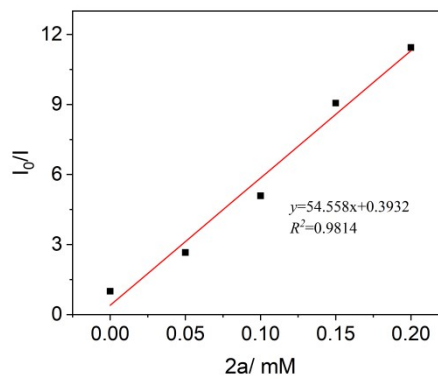


Figure. S7 (a) Fluorescence quenching of $K_2S_2O_8$ by bromodifluoroacetamide in $CH_3CN/H_2O(2:1)$ (left); (b) Stern-Volmer plots of $K_2S_2O_8$ by bromodifluoroacetamide (right).

In addition, a typical fluorescence quenching experiment, in which the excitation peak intensity of $K_2S_2O_8$ gradually decreased as the concentration of bromodifluoroacetamide 2a increased, indicates efficient quenching of $K_2S_2O_8$ by bromodifluoroacetamide (Figure S7a, left). The linear correlation observed in the corresponding Stern-Volmer plot provided additional evidence for the EDA interaction of 2a with $K_2S_2O_8$ (Figure S7b, right).

4 Copies of spectra of desired products

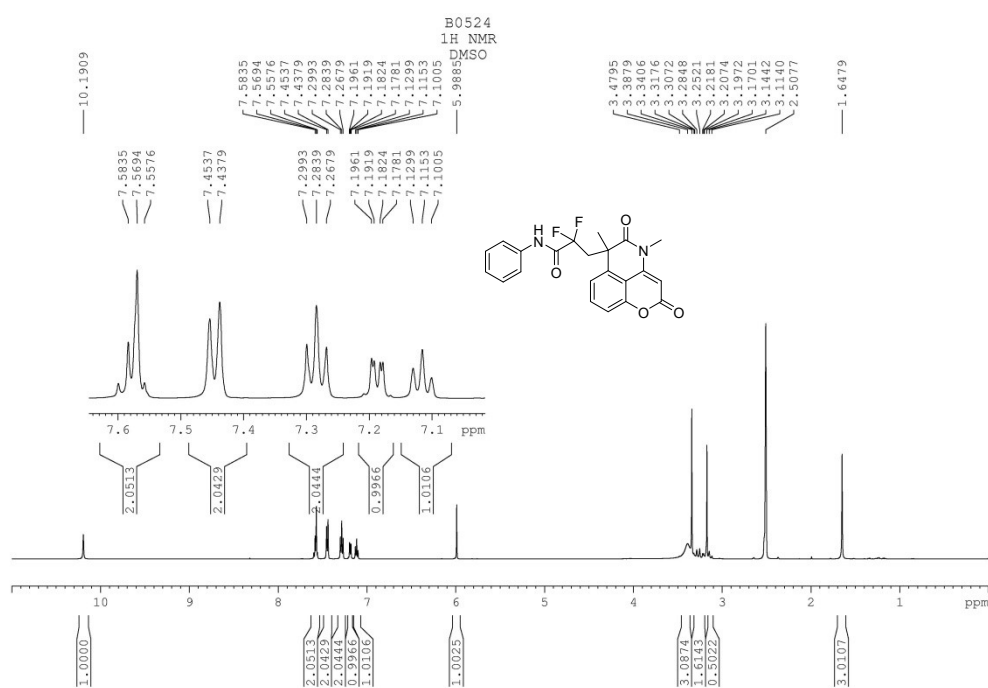


Fig. S8 1H NMR (500 MHz) spectrum of compound **3a**

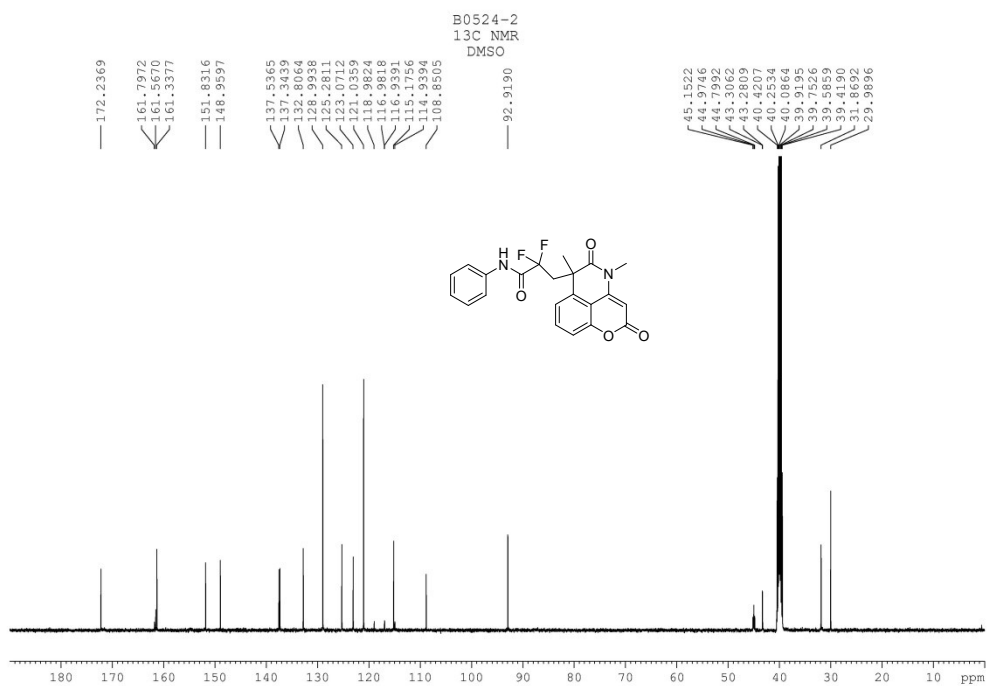


Fig. S9 ¹³C NMR (126 MHz) spectrum of compound 3a

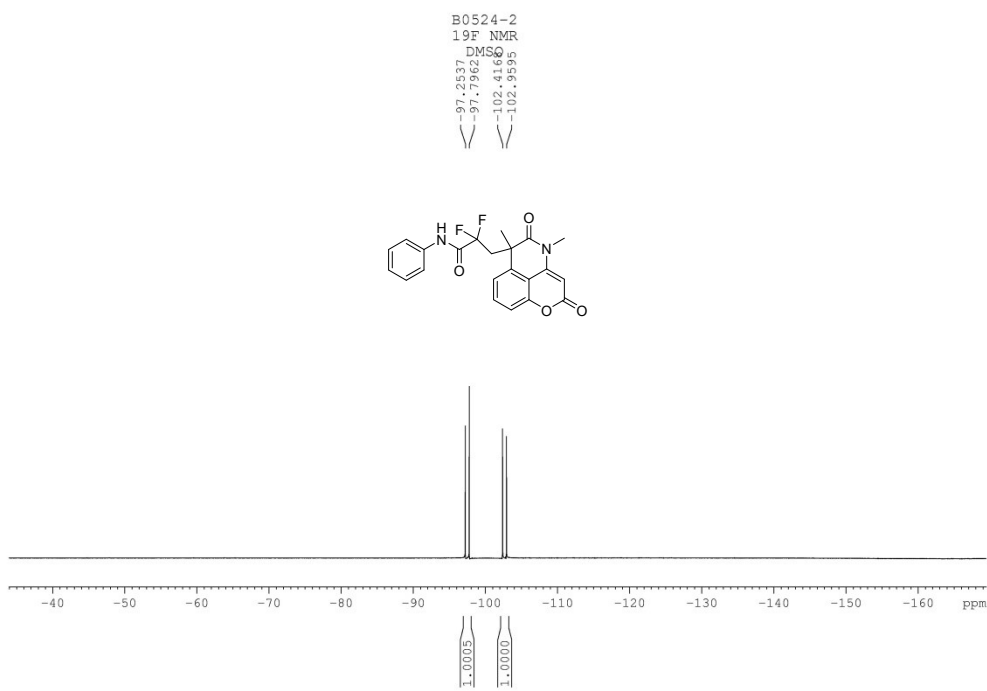


Fig. S10 ¹⁹F NMR (471 MHz) spectrum of compound 3a

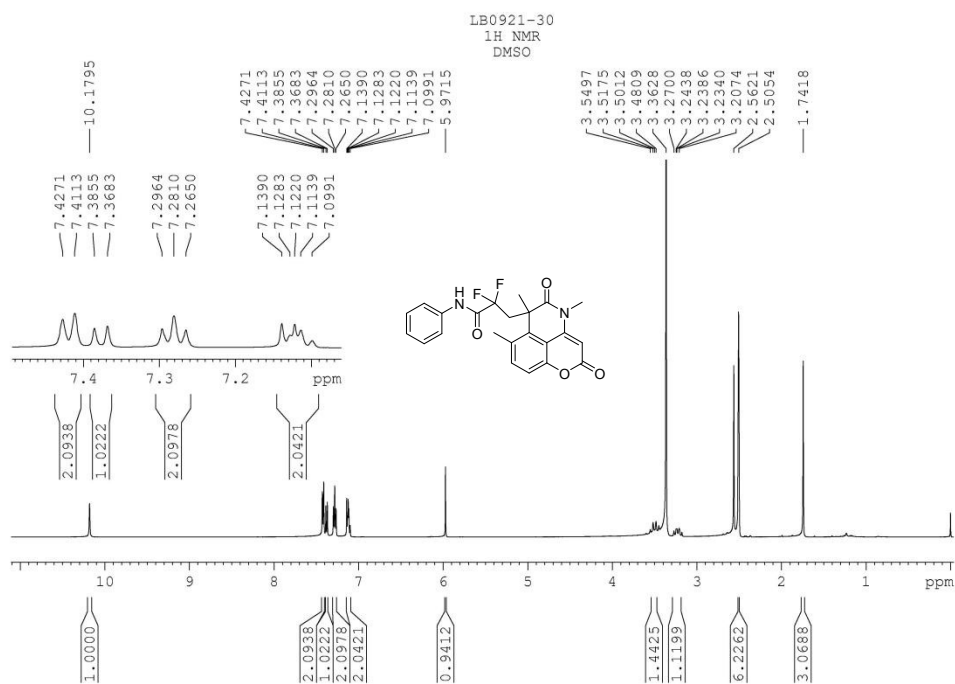


Fig. S11 ¹H NMR (500 MHz) spectrum of compound 3b

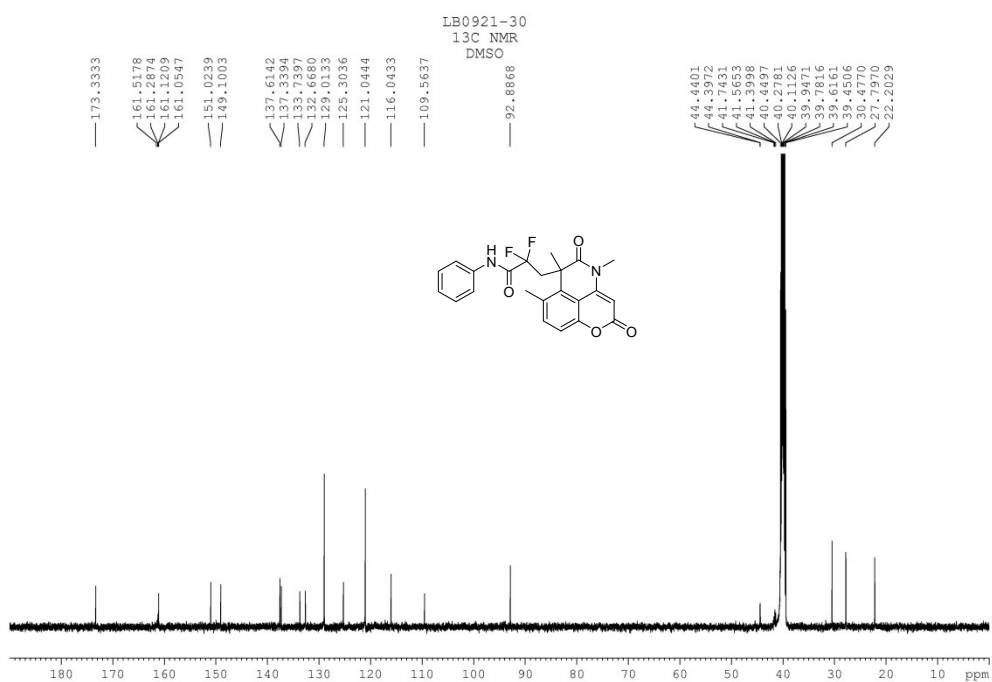


Fig. S12 ¹³C NMR (126 MHz) spectrum of compound 3b



Fig. S13 ¹⁹F NMR (471 MHz) spectrum of compound 3b

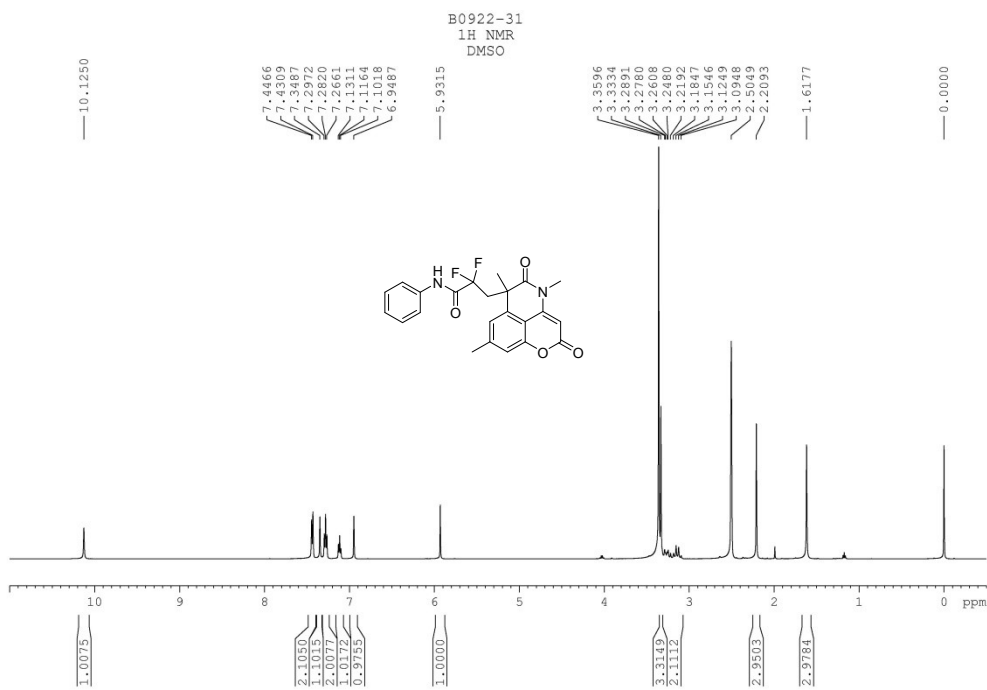


Fig. S14 ¹H NMR (500 MHz) spectrum of compound 3c

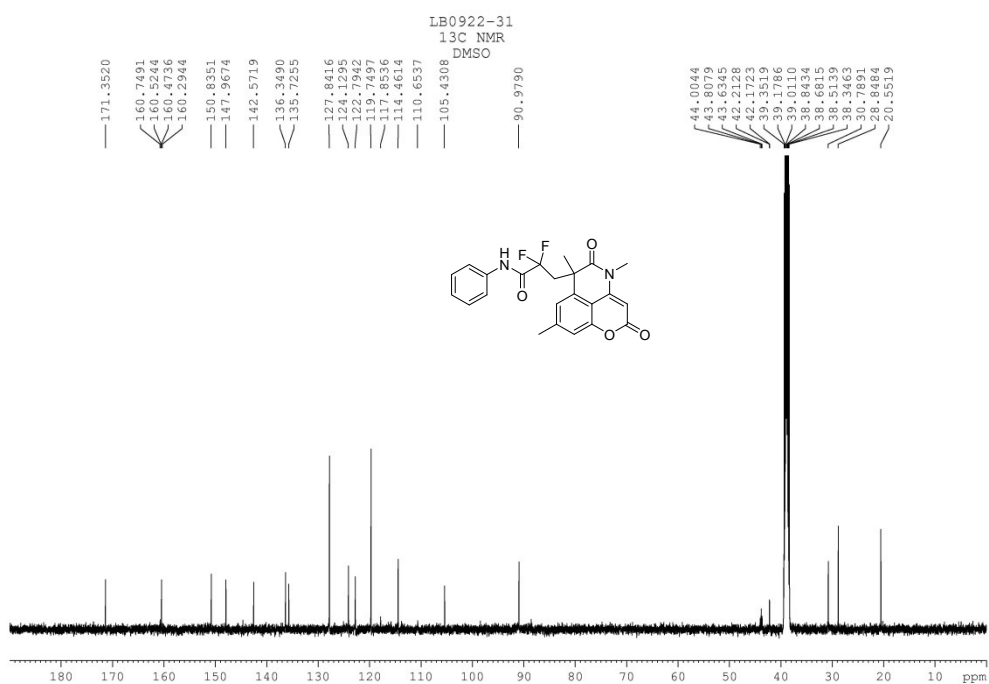


Fig. S15 ¹³C NMR (126 MHz) spectrum of compound 3c

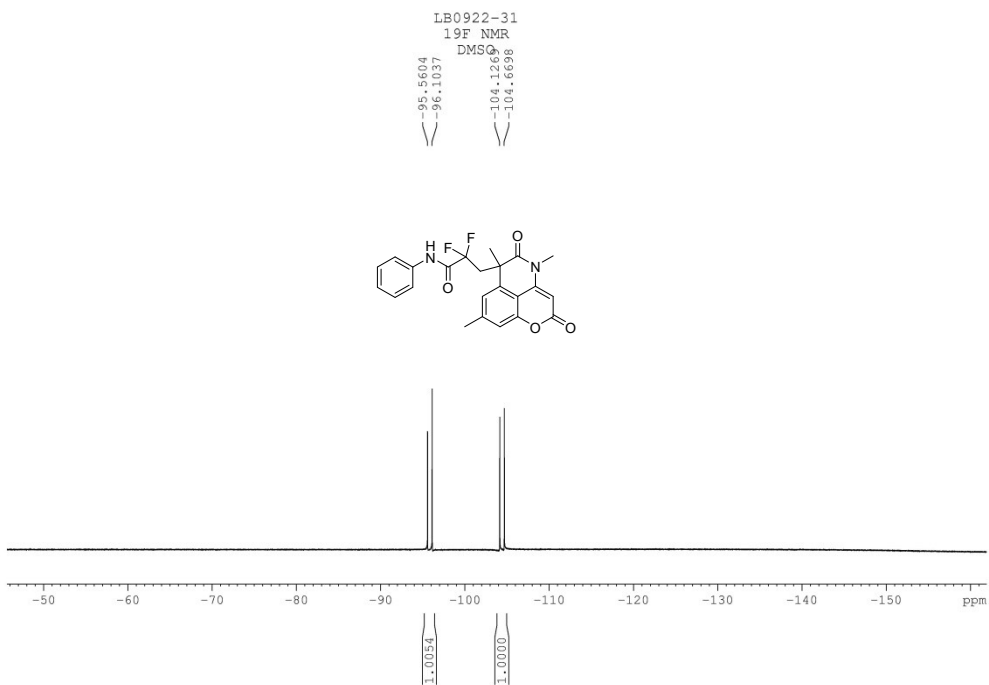


Fig. S16 ¹⁹F NMR (471 MHz) spectrum of compound 3c

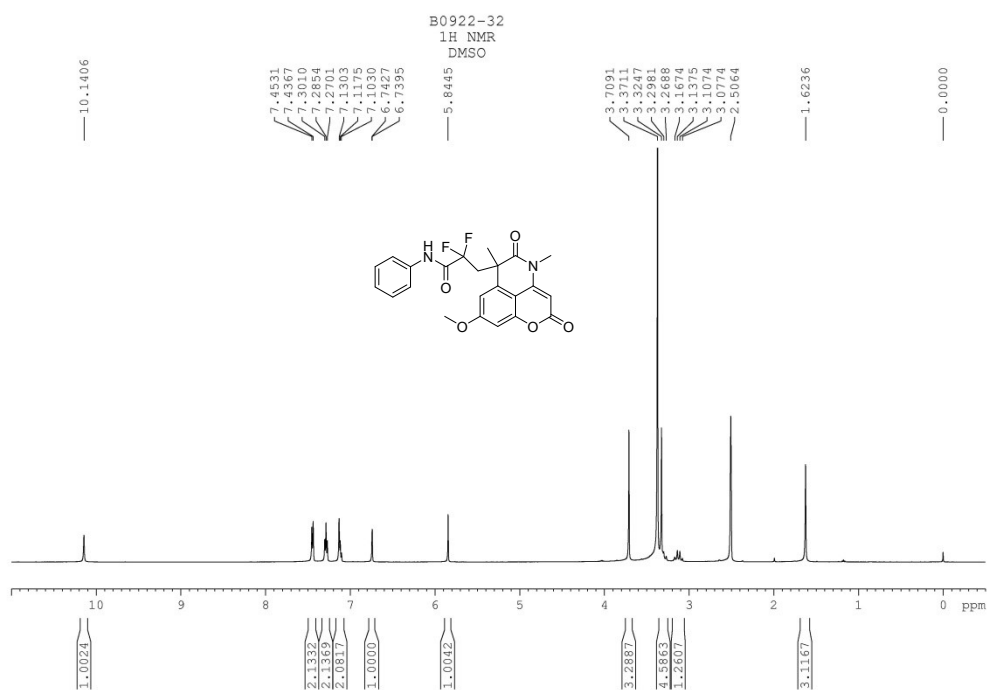


Fig. S17 ¹H NMR (500 MHz) spectrum of compound 3d

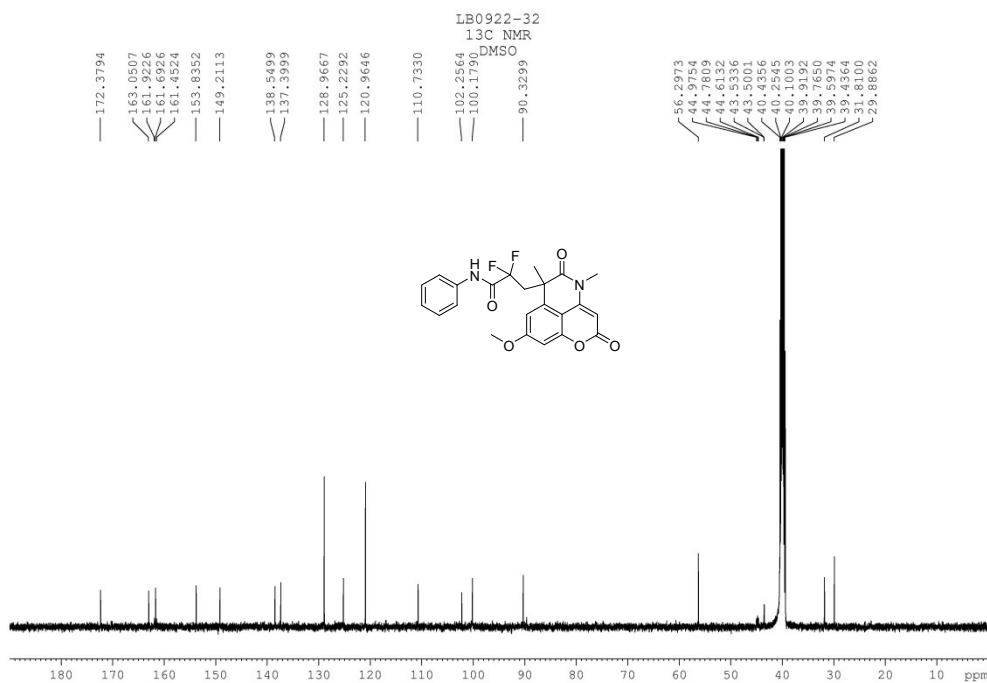


Fig. S18 ¹³C NMR (126 MHz) spectrum of compound 3d

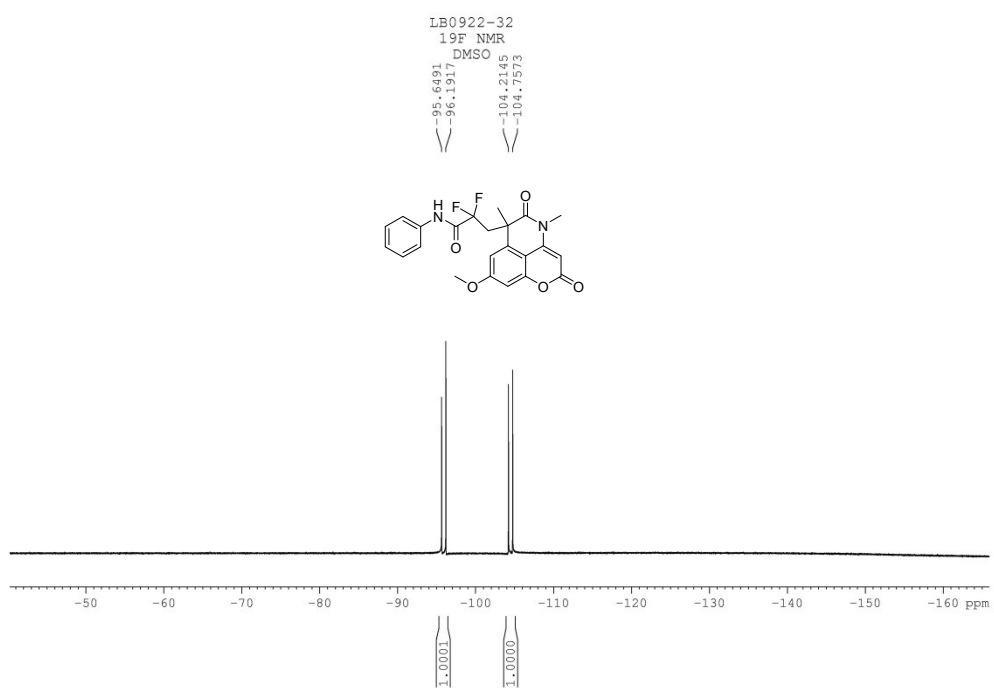


Fig. S19 ¹⁹F NMR (471 MHz) spectrum of compound 3d

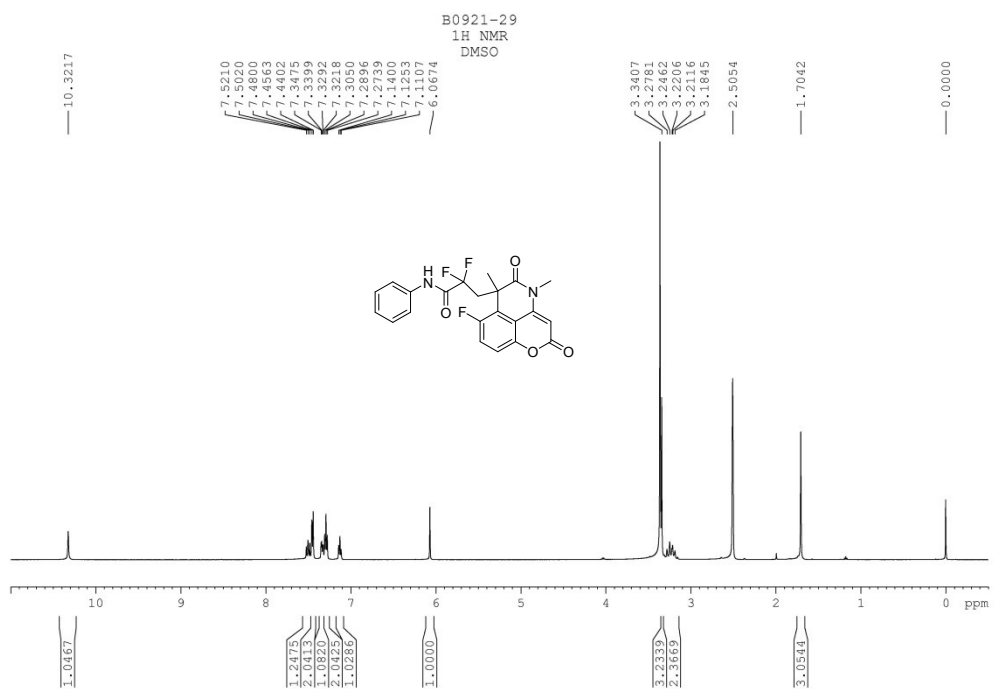


Fig. S20 ¹H NMR (500 MHz) spectrum of compound 3e

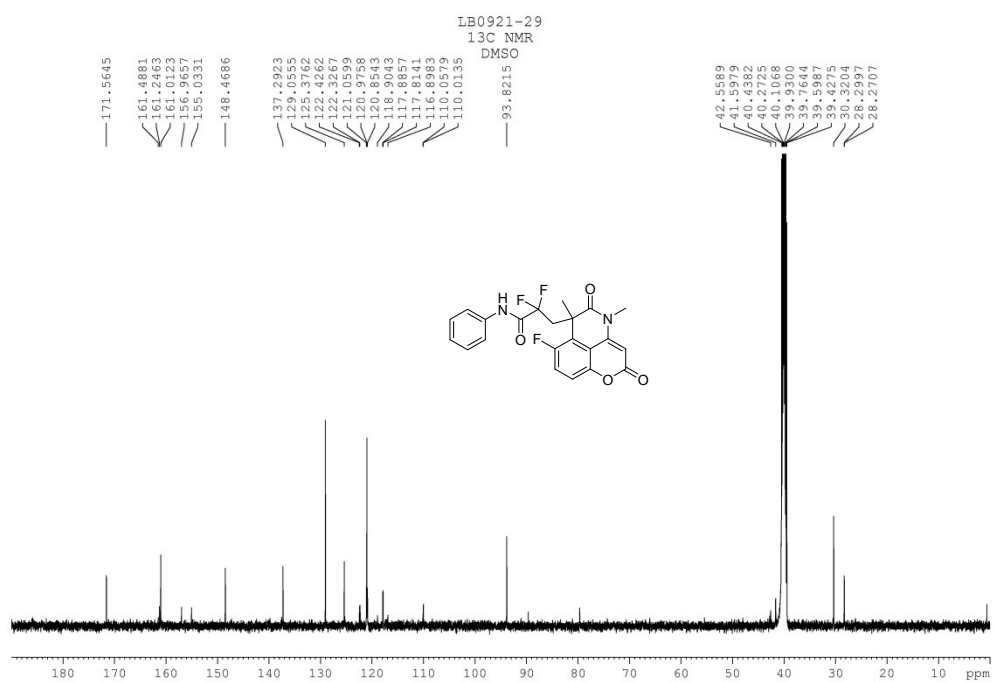


Fig. S21 ¹³C NMR (126 MHz) spectrum of compound 3e

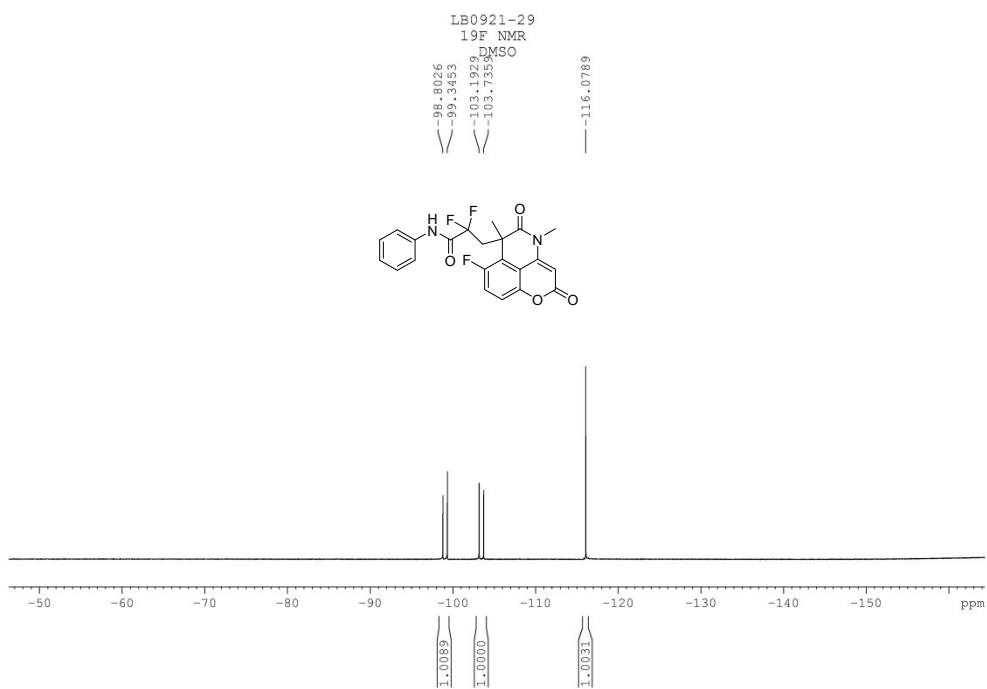


Fig. S22 ¹⁹F NMR (471 MHz) spectrum of compound 3e

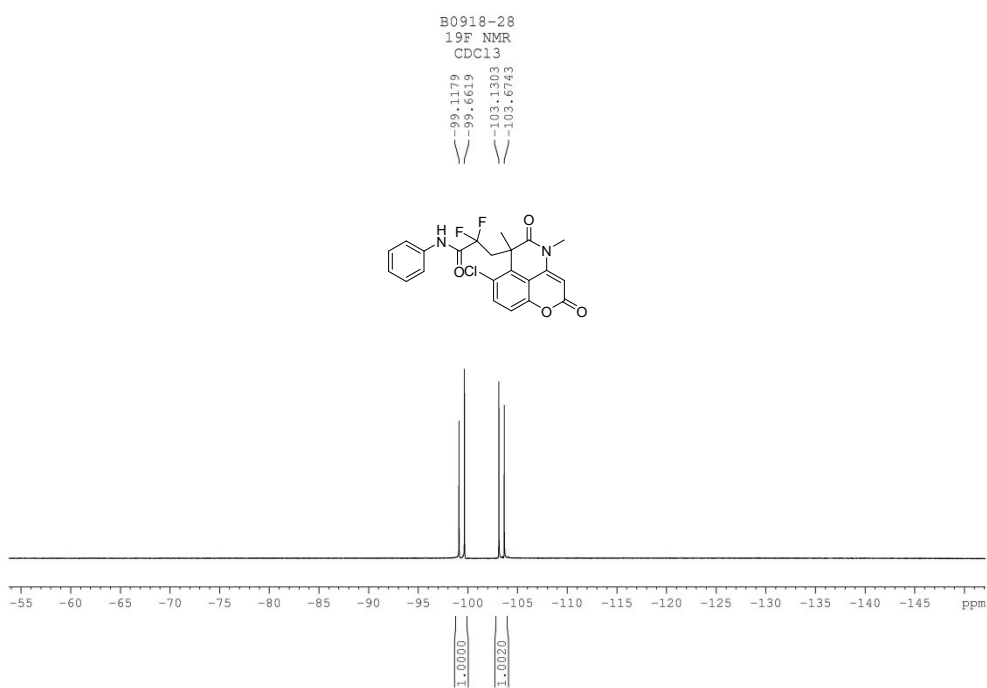


Fig. S25 ¹⁹F NMR (471 MHz) spectrum of compound **3f**

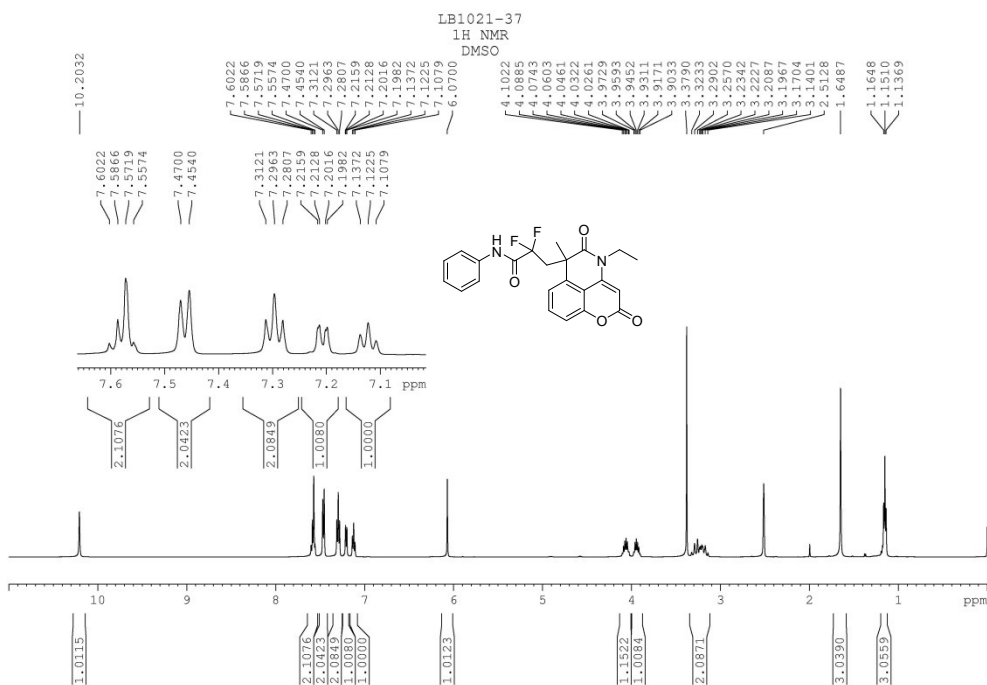


Fig. S26 ¹H NMR (500 MHz) spectrum of compound **3g**

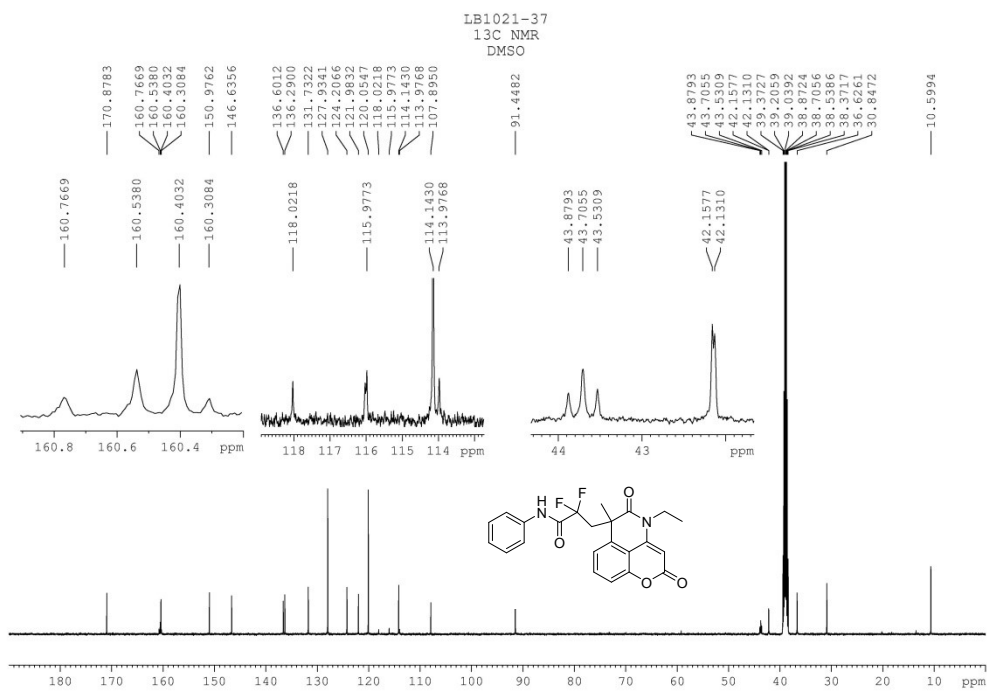


Fig. S27 ¹³C NMR (126 MHz) spectrum of compound 3g

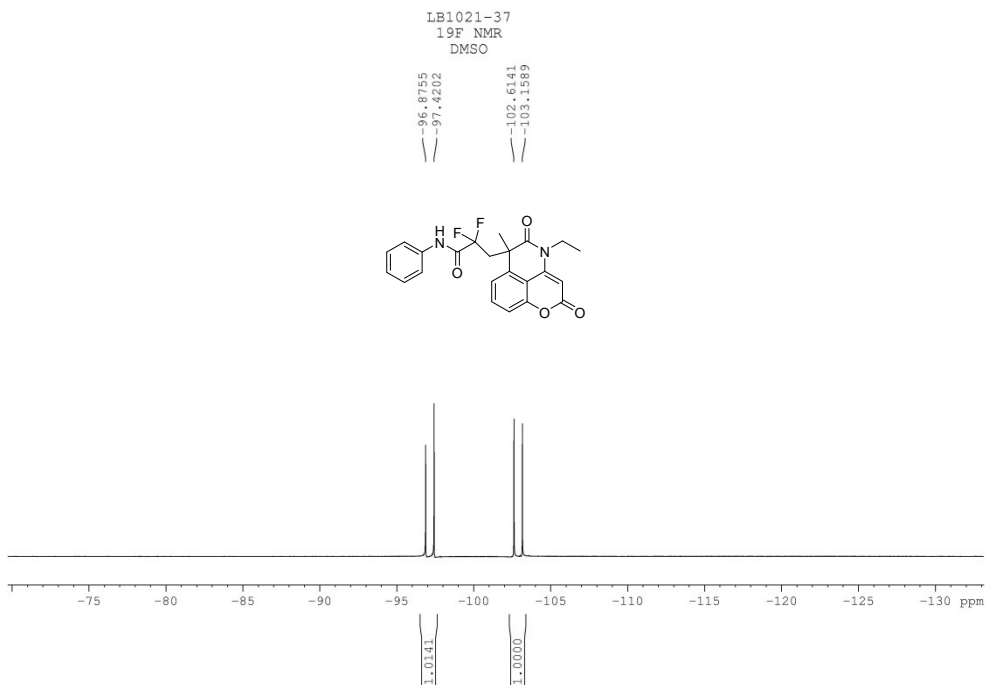


Fig. S28 ¹⁹F NMR (471 MHz) spectrum of compound 3g

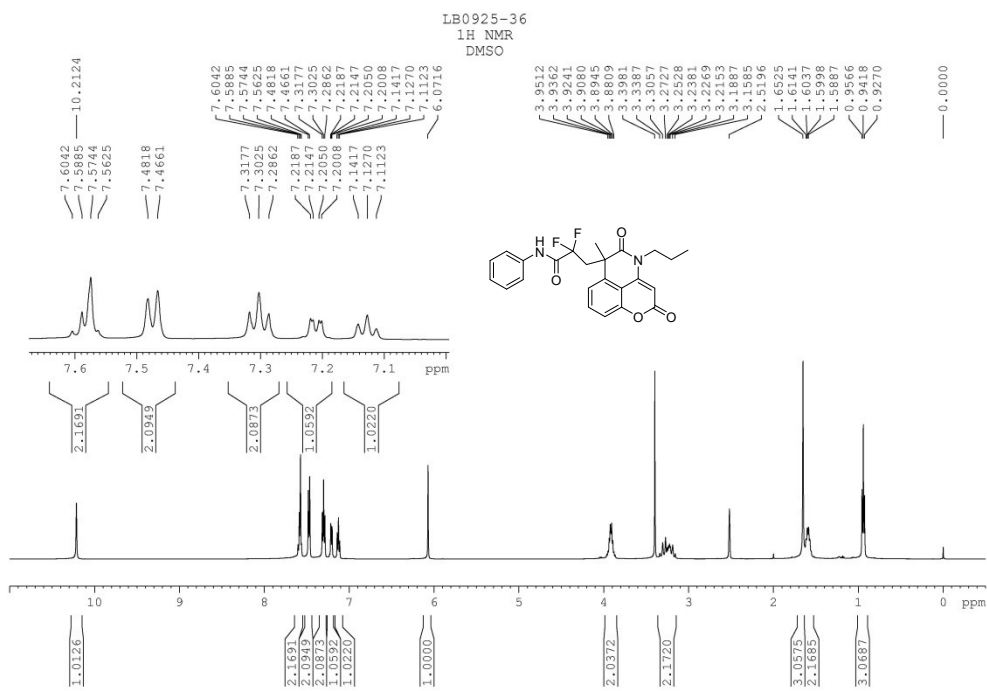


Fig. S29 ¹H NMR (500 MHz) spectrum of compound 3h

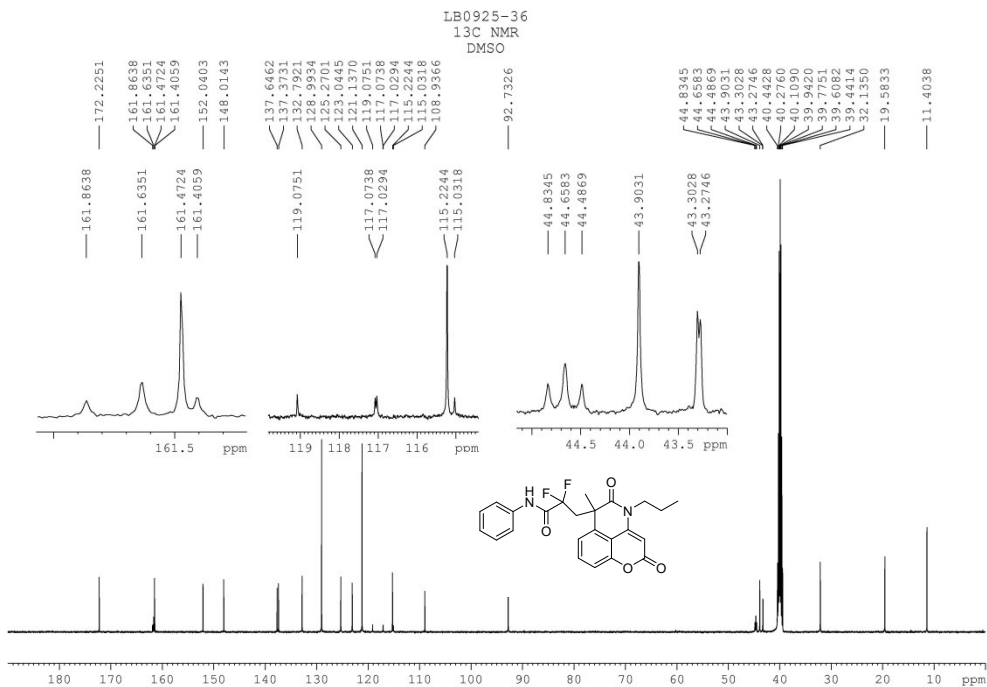


Fig. S30 ¹³C NMR (126 MHz) spectrum of compound 3h



Fig. S31 ¹⁹F NMR (471 MHz) spectrum of compound **3h**

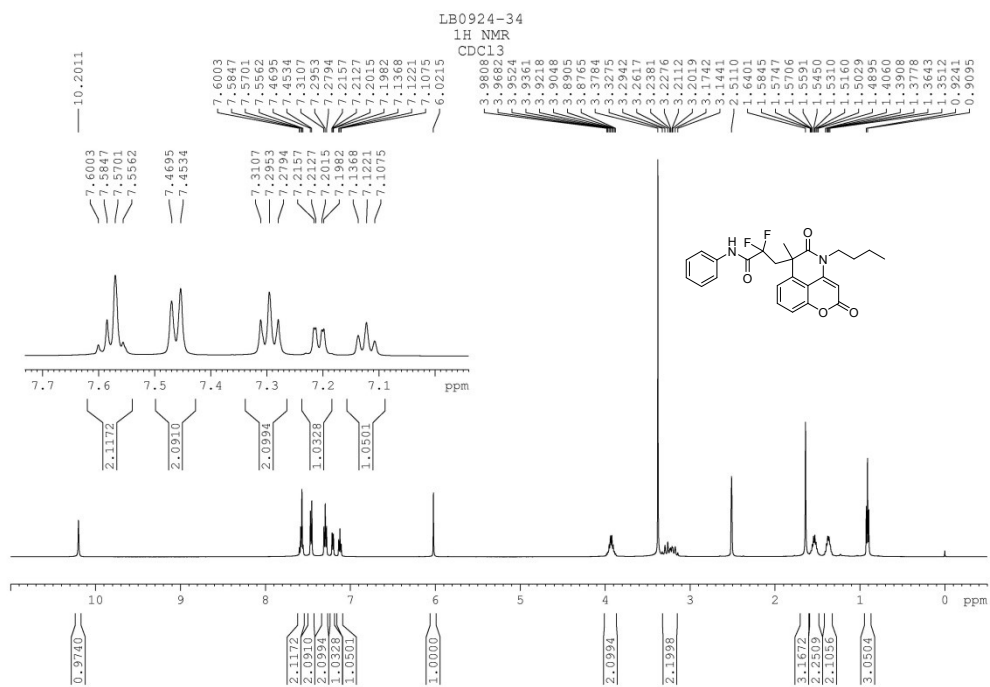


Fig. S32 ¹H NMR (500 MHz) spectrum of compound **3i**

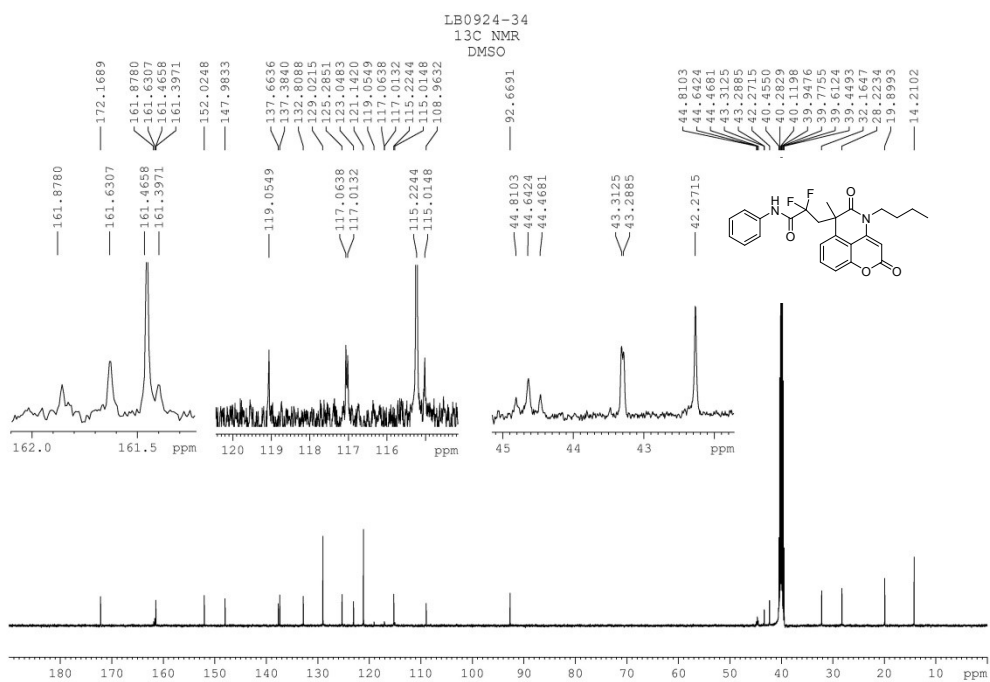


Fig. S33 ¹³C NMR (126 MHz) spectrum of compound 3i



Fig. S34 ¹⁹F NMR (471 MHz) spectrum of compound 3i

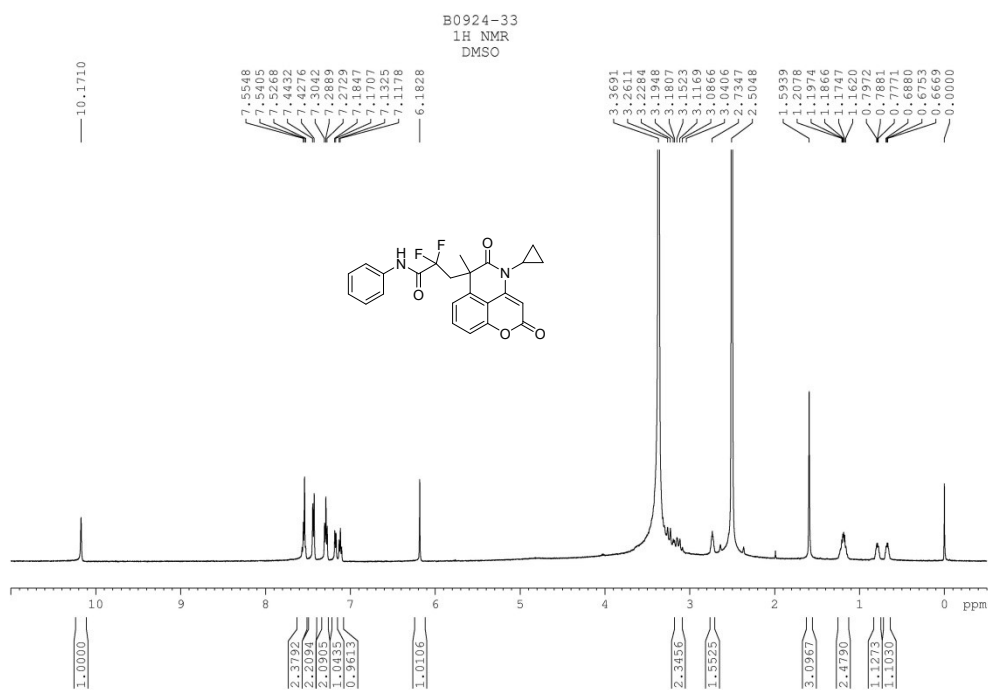


Fig. S35 ¹H NMR (500 MHz) spectrum of compound 3j

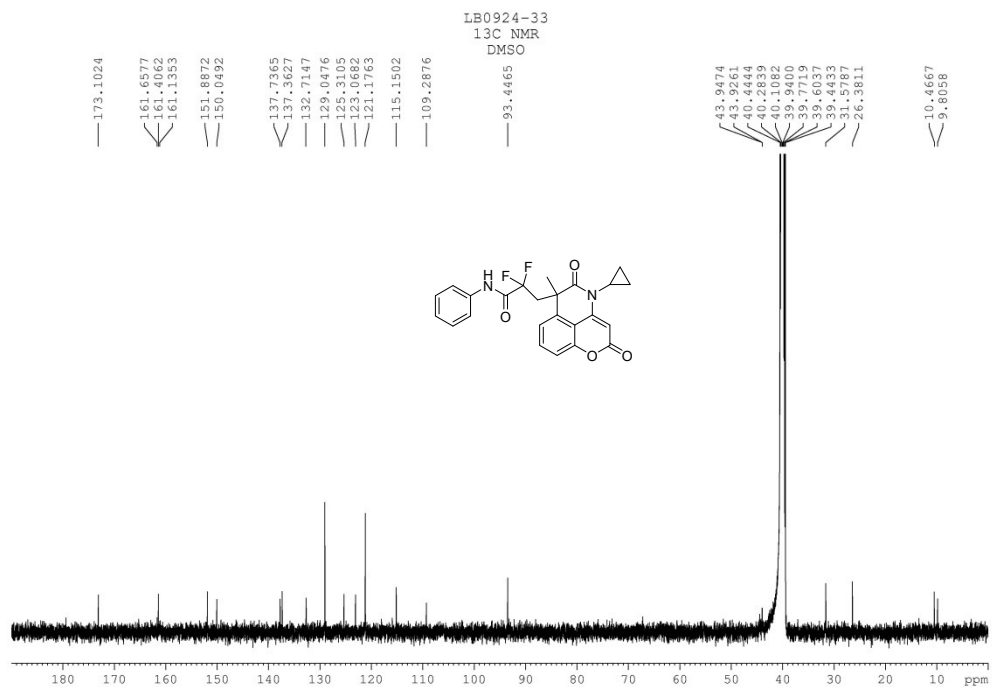


Fig. S36 ¹³C NMR (126 MHz) spectrum of compound 3j

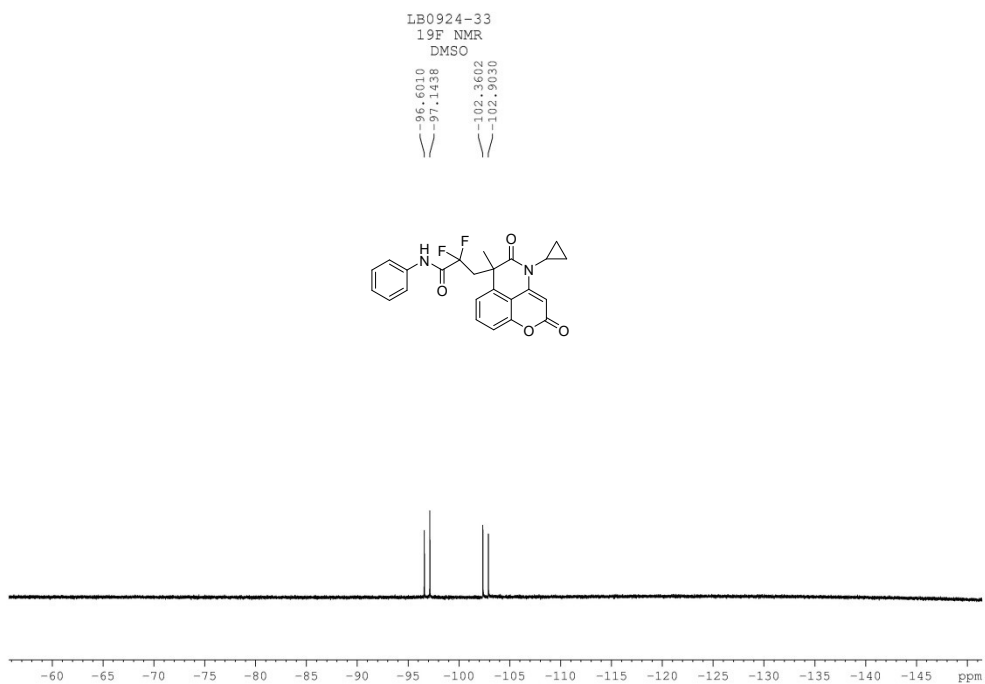


Fig. S37 ¹⁹F NMR (471 MHz) spectrum of compound **3j**

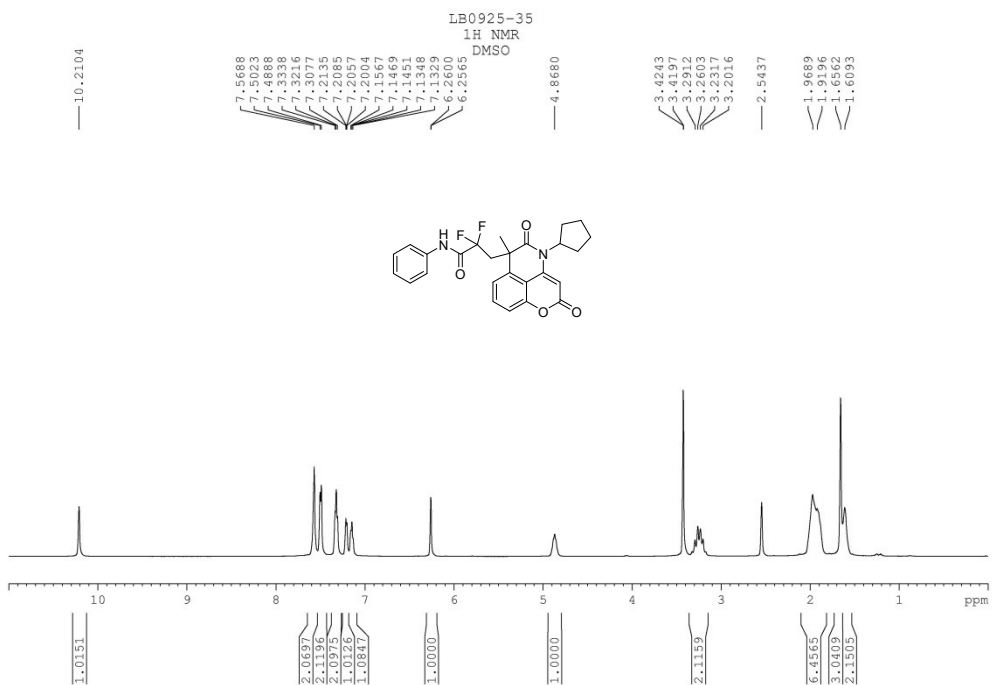


Fig. S38 ¹H NMR (500 MHz) spectrum of compound **3k**

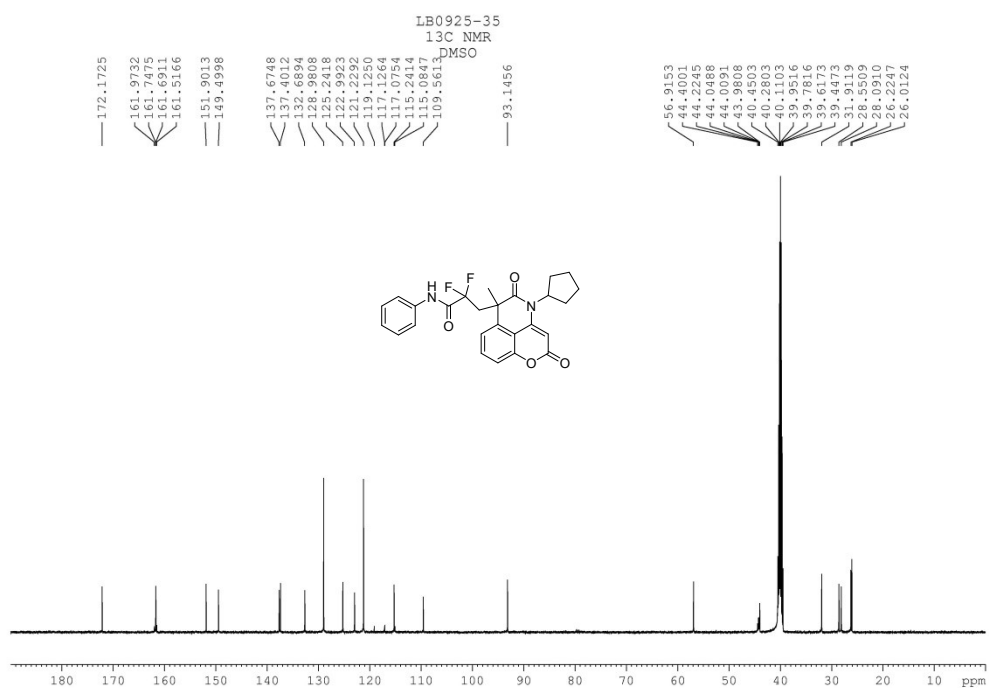


Fig. S39 ¹³C NMR (126 MHz) spectrum of compound 3k

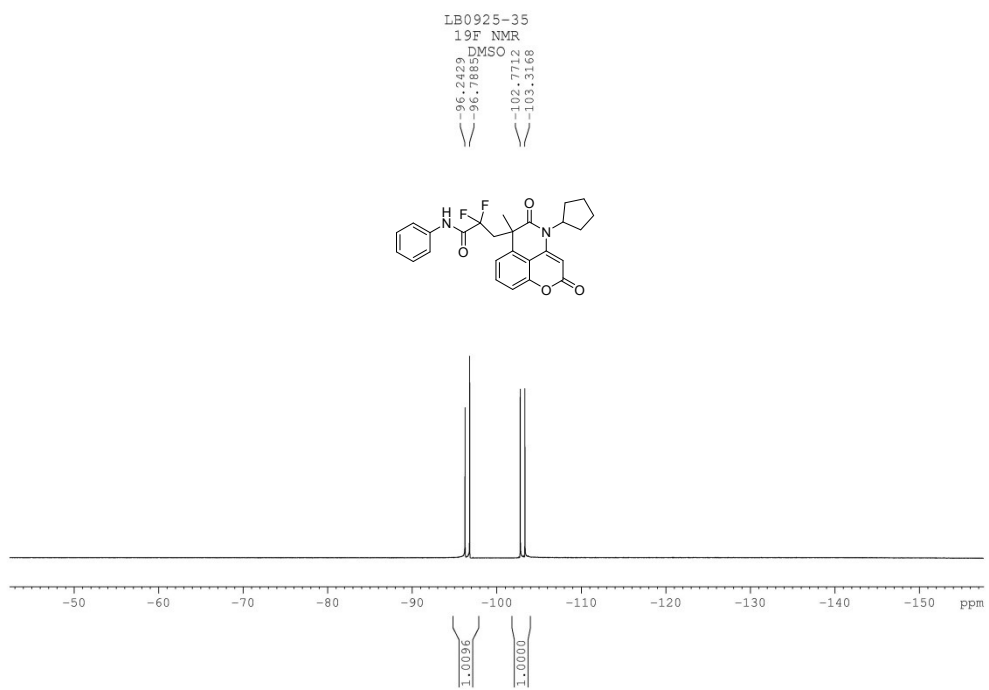


Fig. S40 ¹⁹F NMR (471 MHz) spectrum of compound 3k

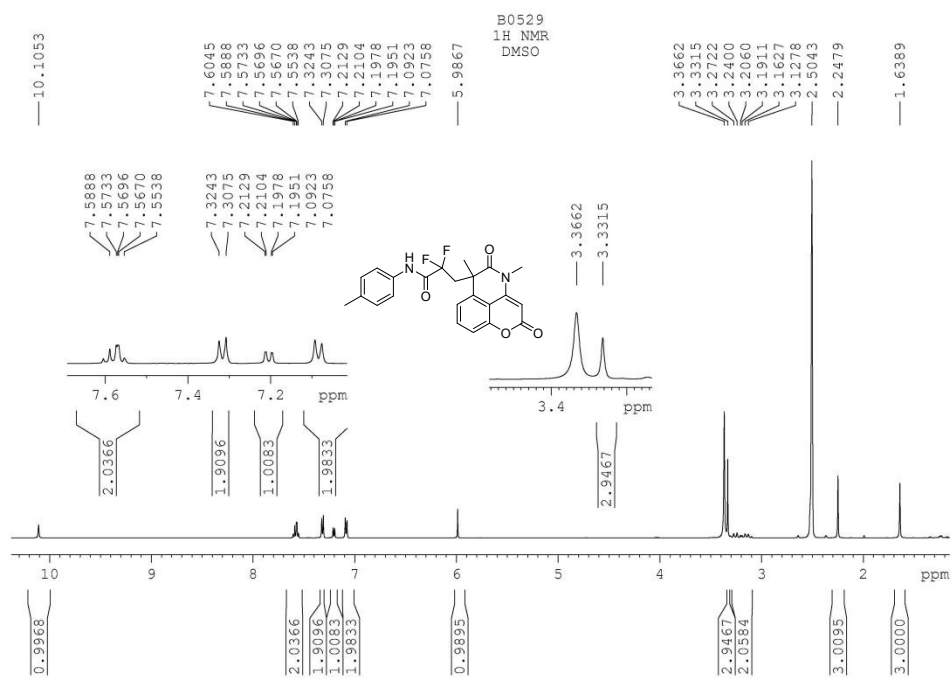


Fig. S41 ^1H NMR (500 MHz) spectrum of compound 4a

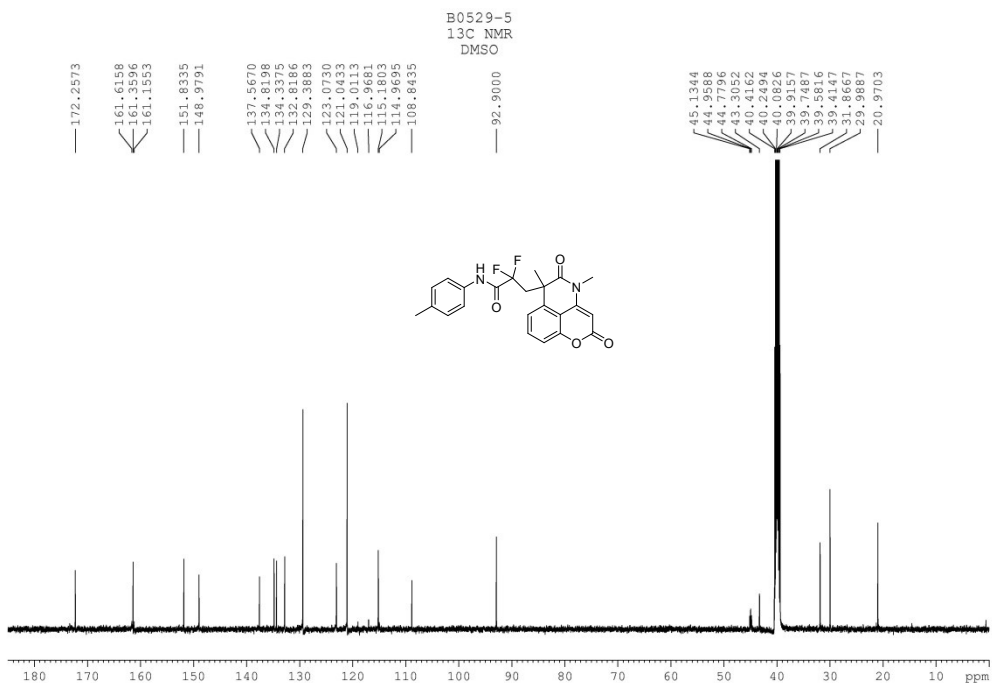


Fig. S42 ^{13}C NMR (126 MHz) spectrum of compound 4a

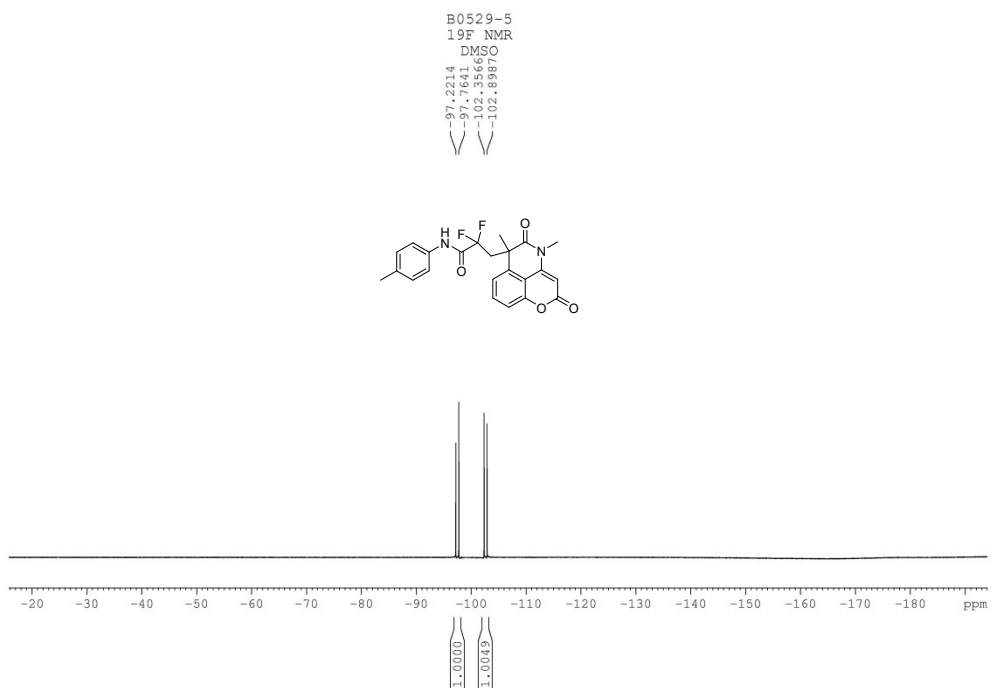


Fig. S43 ¹⁹F NMR (471 MHz) spectrum of compound 4a

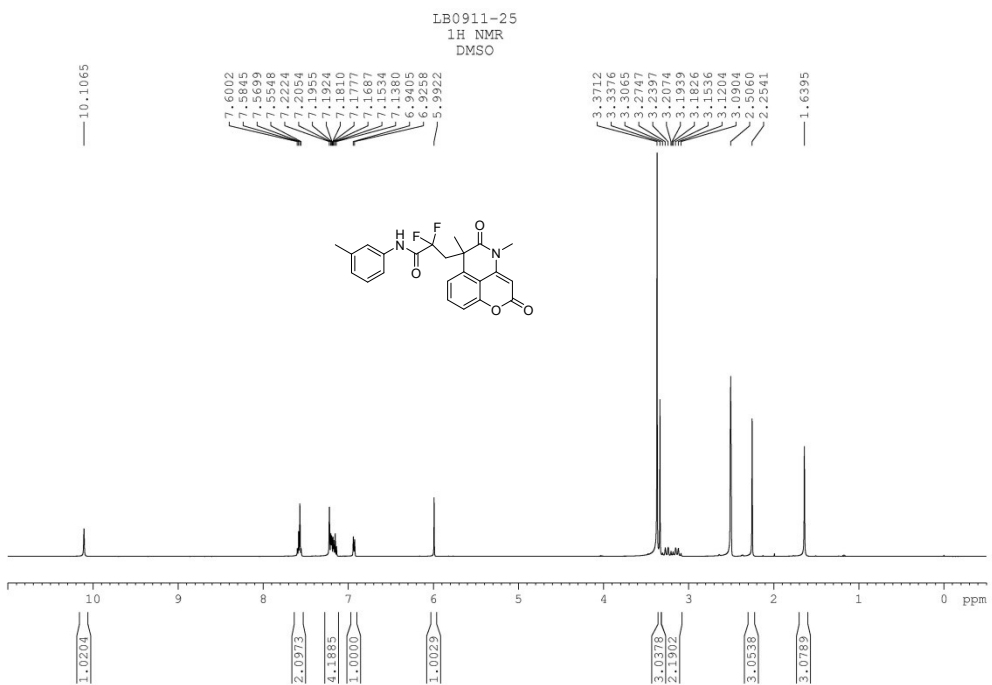


Fig. S44 ¹H NMR (500 MHz) spectrum of compound 4b

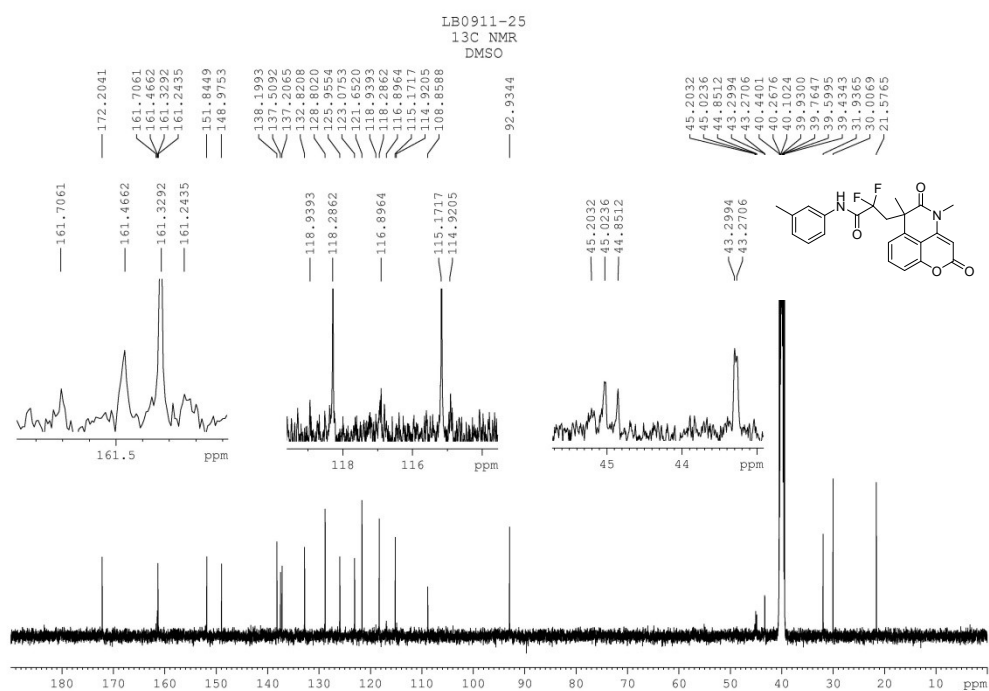


Fig. S45 ¹³C NMR (126 MHz) spectrum of compound 4b

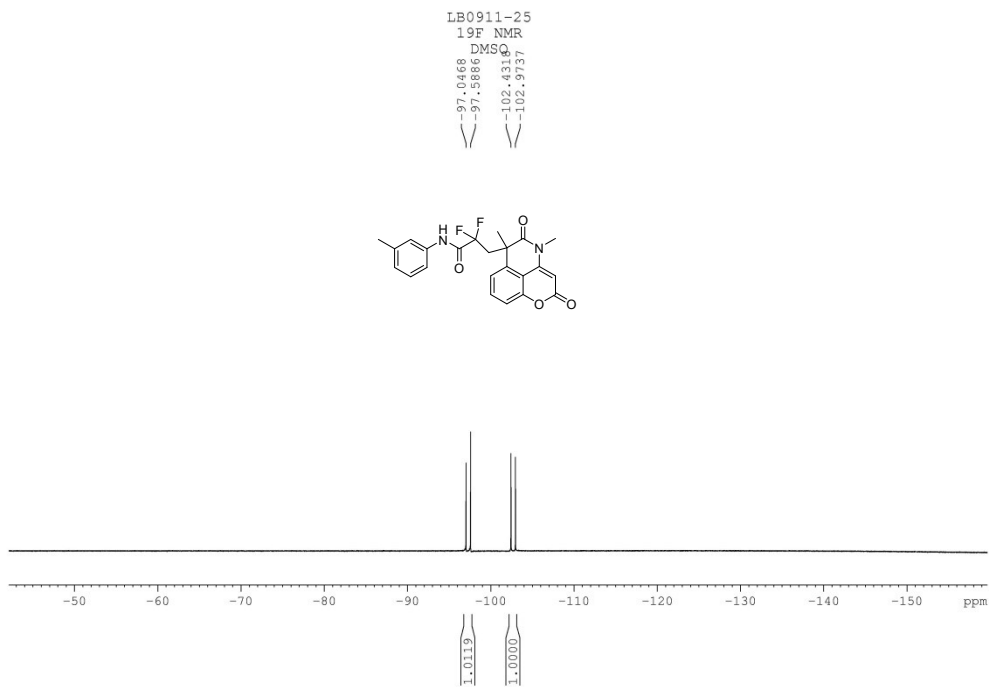


Fig. S46 ¹⁹F NMR (471 MHz) spectrum of compound 4b

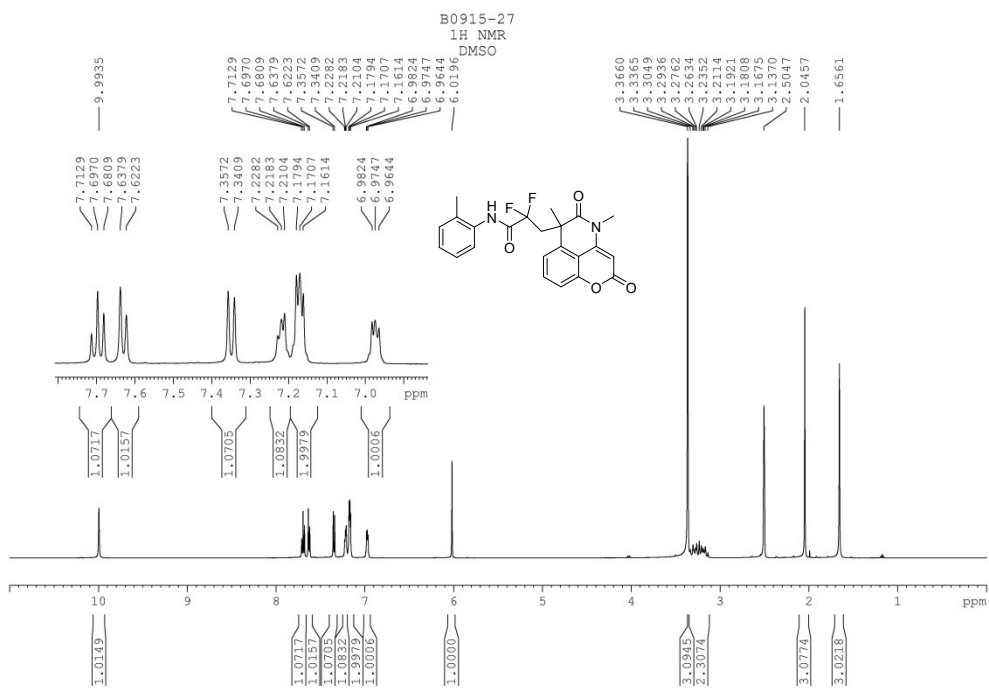


Fig. S47 ¹H NMR (500 MHz) spectrum of compound 4c

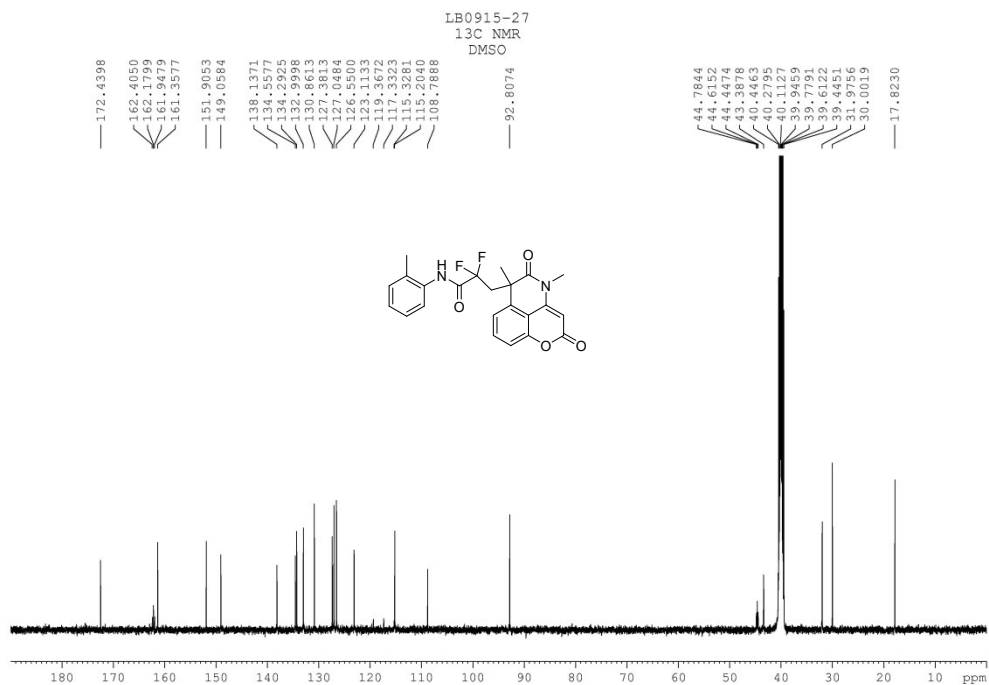


Fig. S48 ¹³C NMR (126 MHz) spectrum of compound 4c

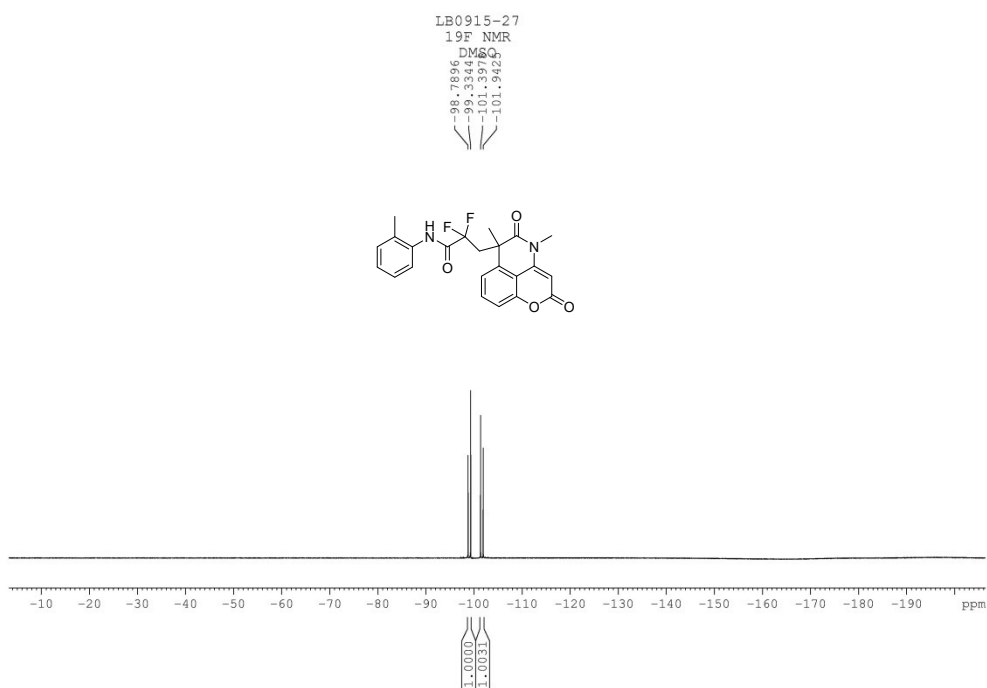


Fig. S49 ¹⁹F NMR (471 MHz) spectrum of compound 4c

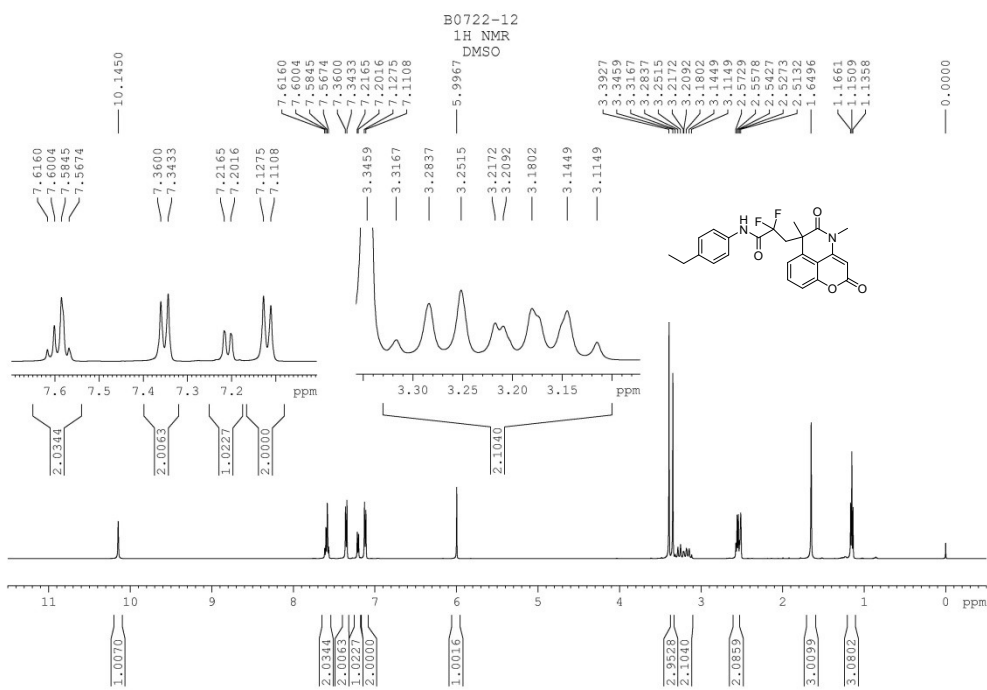


Fig. S50 ¹H NMR (500 MHz) spectrum of compound 4d

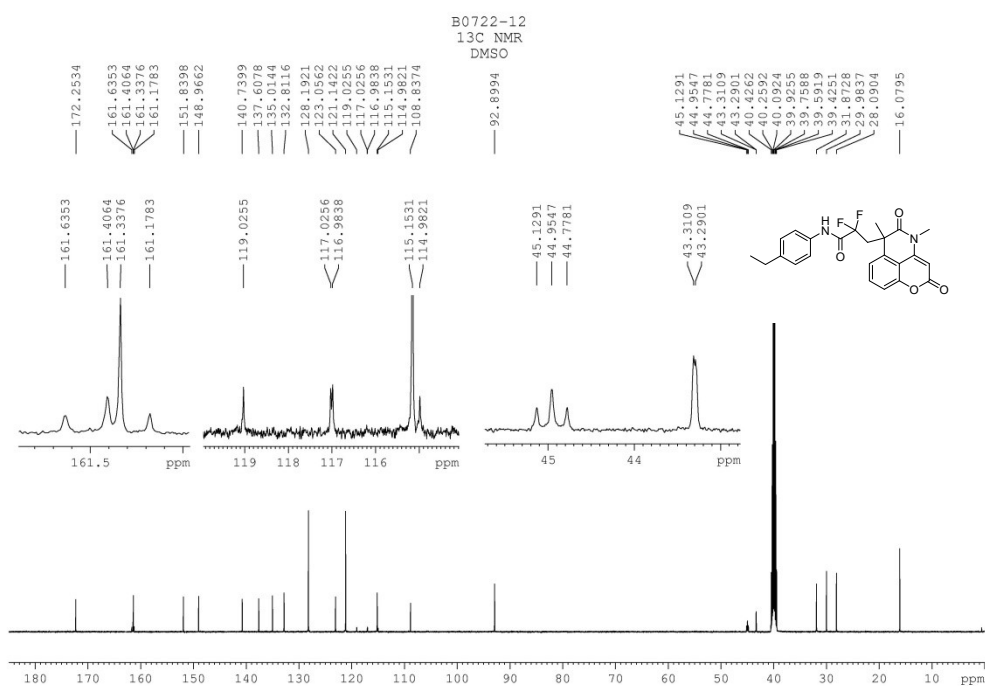


Fig. S51 ¹³C NMR (126 MHz) spectrum of compound 4d

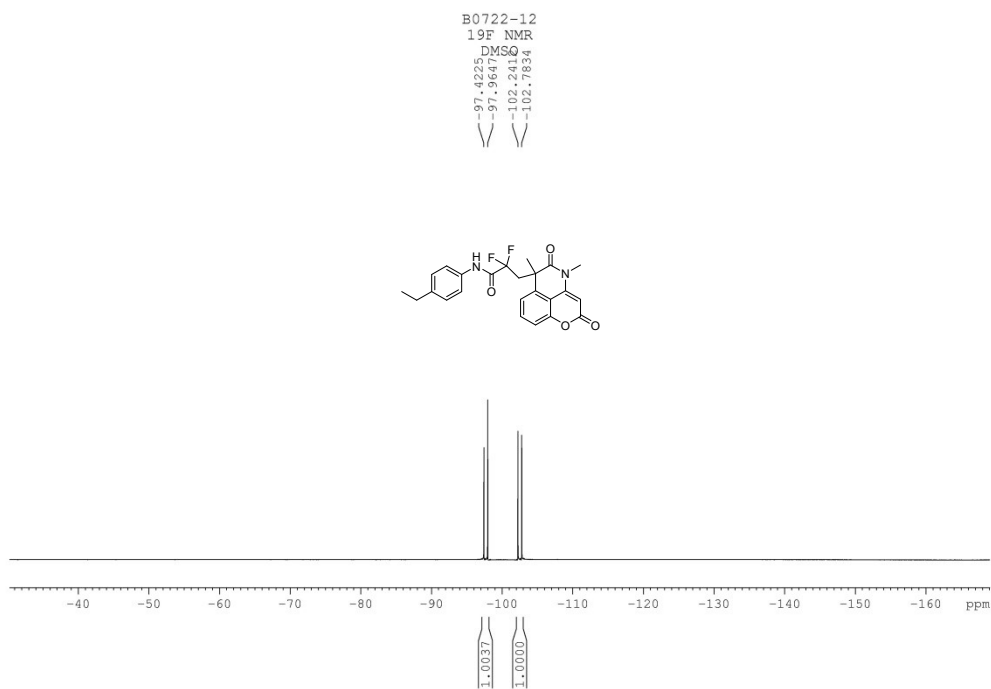


Fig. S52 ¹⁹F NMR (471 MHz) spectrum of compound 4d

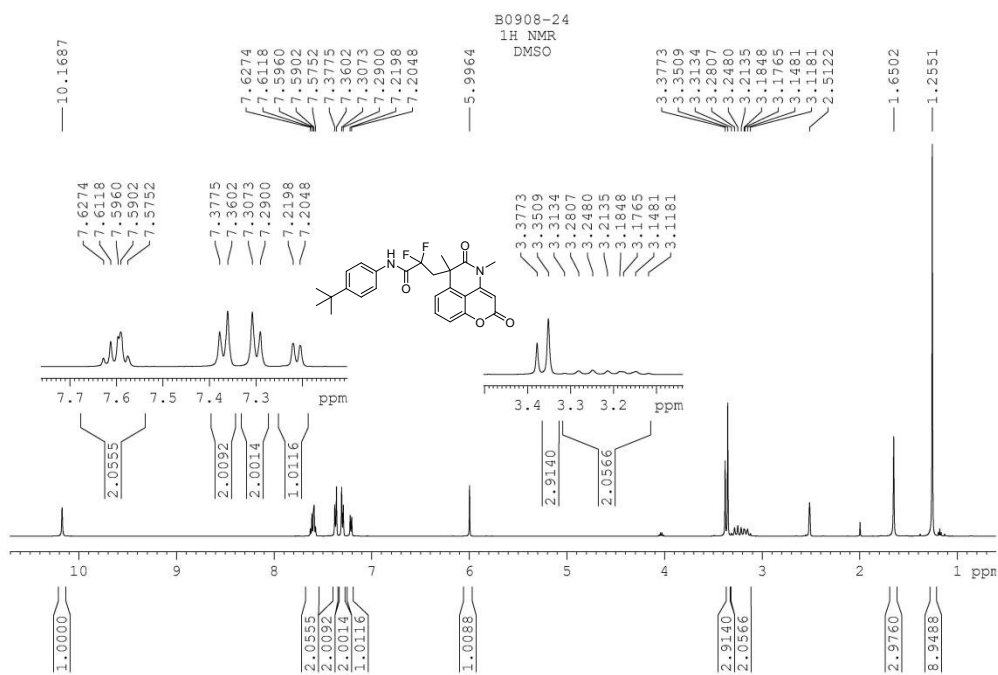


Fig. S53 ¹H NMR (500 MHz) spectrum of compound 4e

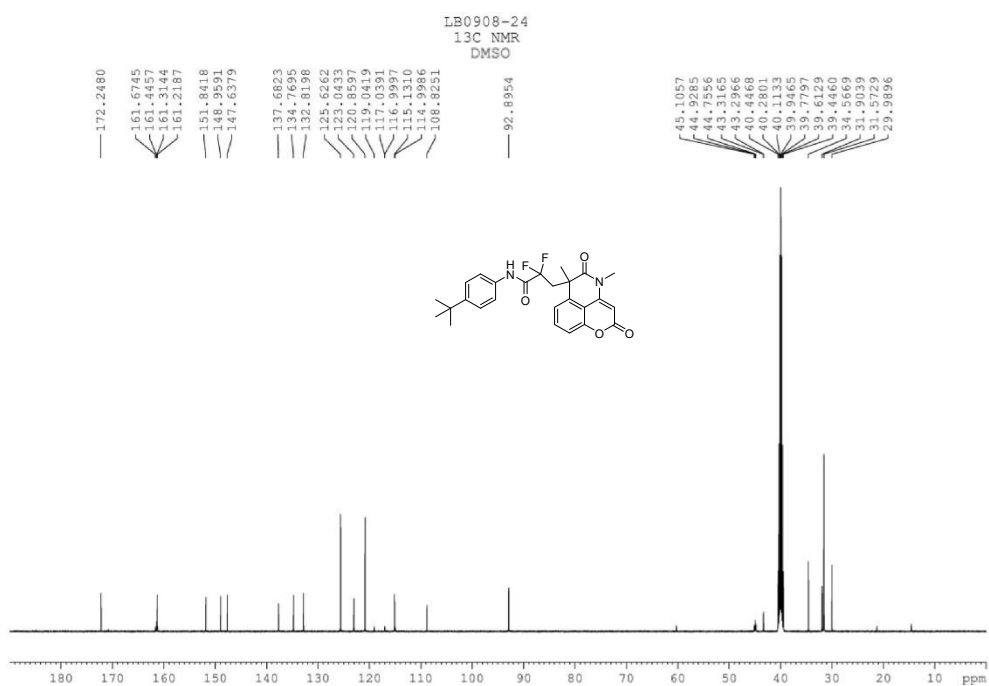


Fig. S54 ¹³C NMR (126 MHz) spectrum of compound 4e

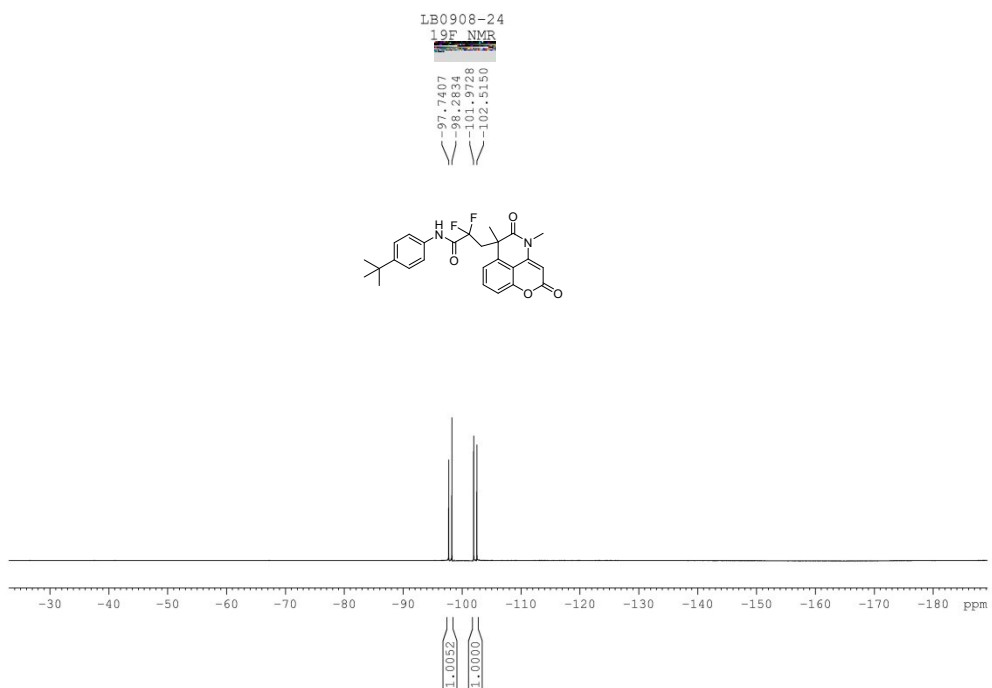


Fig. S55 ¹⁹F NMR (471 MHz) spectrum of compound 4e

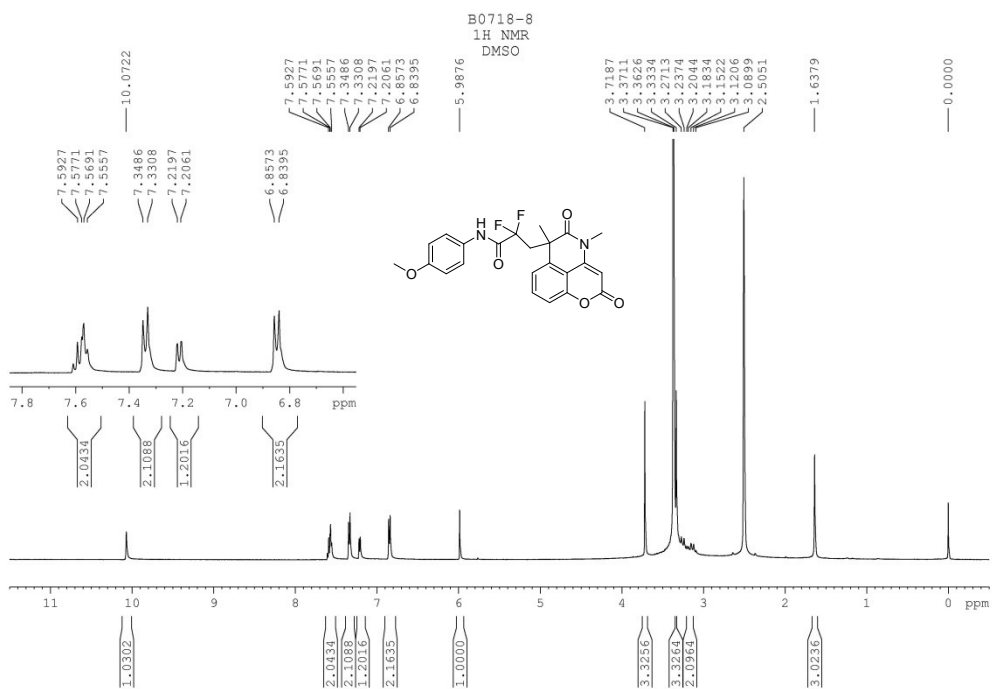


Fig. S56 ¹H NMR (500 MHz) spectrum of compound 4f

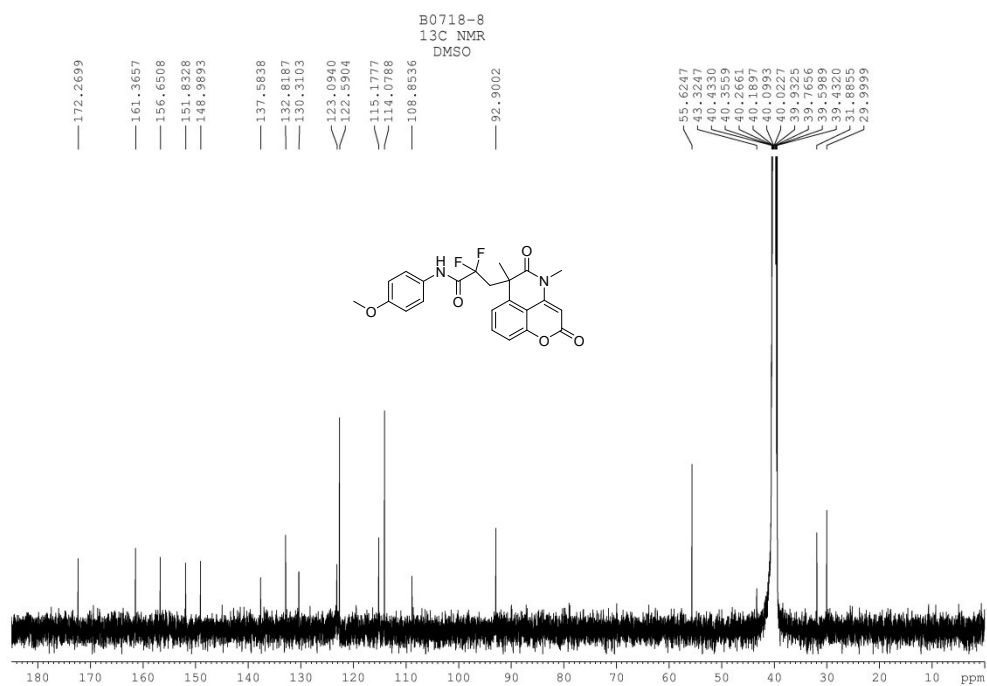


Fig. S57 ¹³C NMR (126 MHz) spectrum of compound 4f

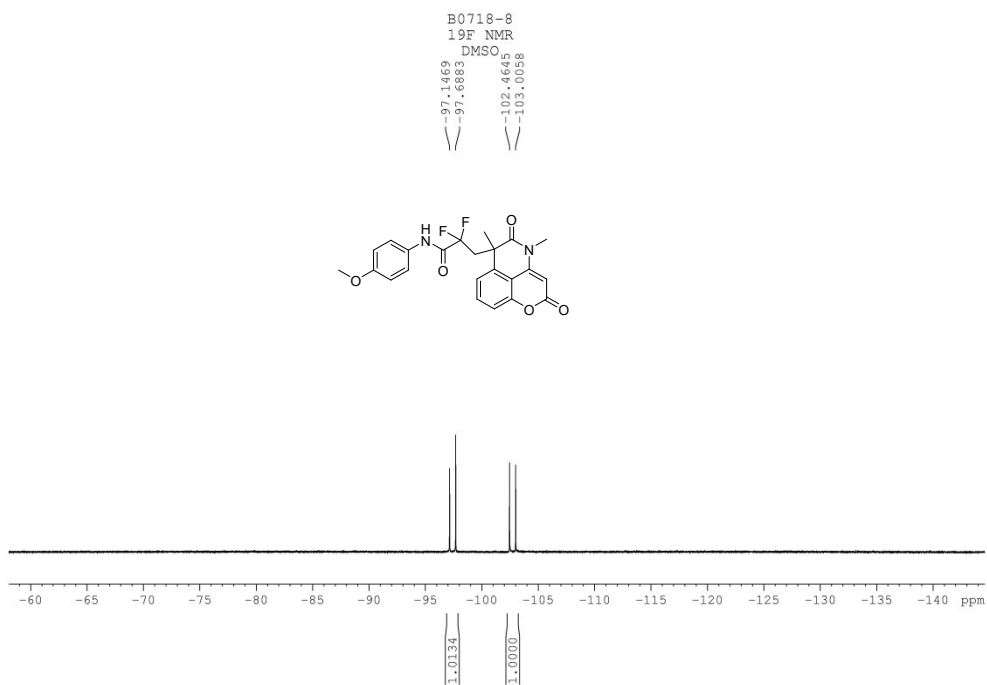


Fig. S58 ¹⁹F NMR (471 MHz) spectrum of compound 4f

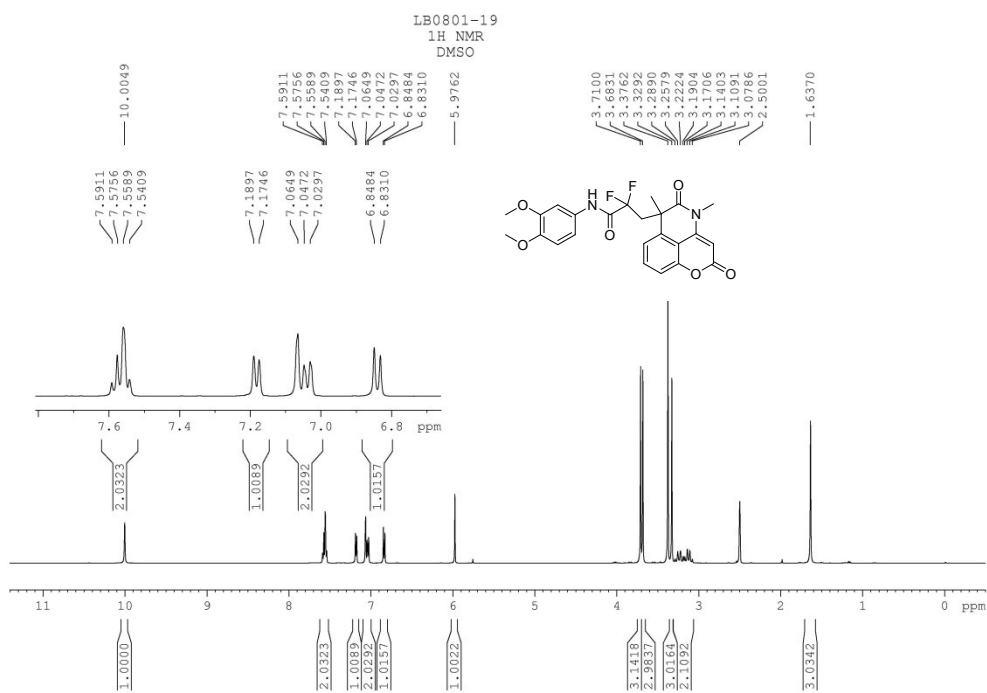


Fig. S59 ¹H NMR (500 MHz) spectrum of compound 4g

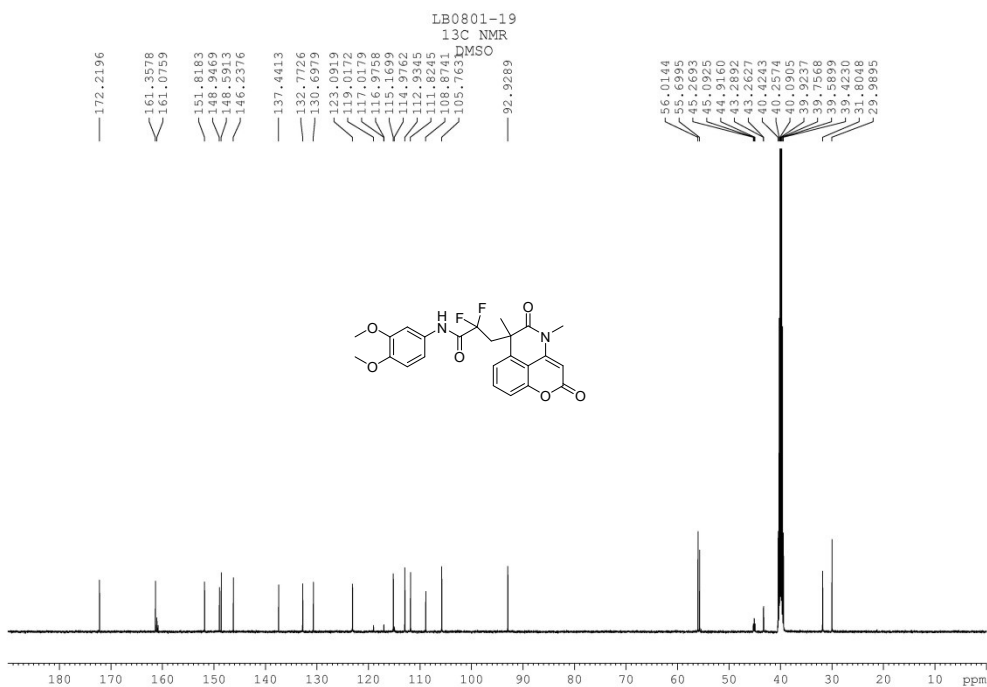


Fig. S60 ¹³C NMR (126 MHz) spectrum of compound 4g

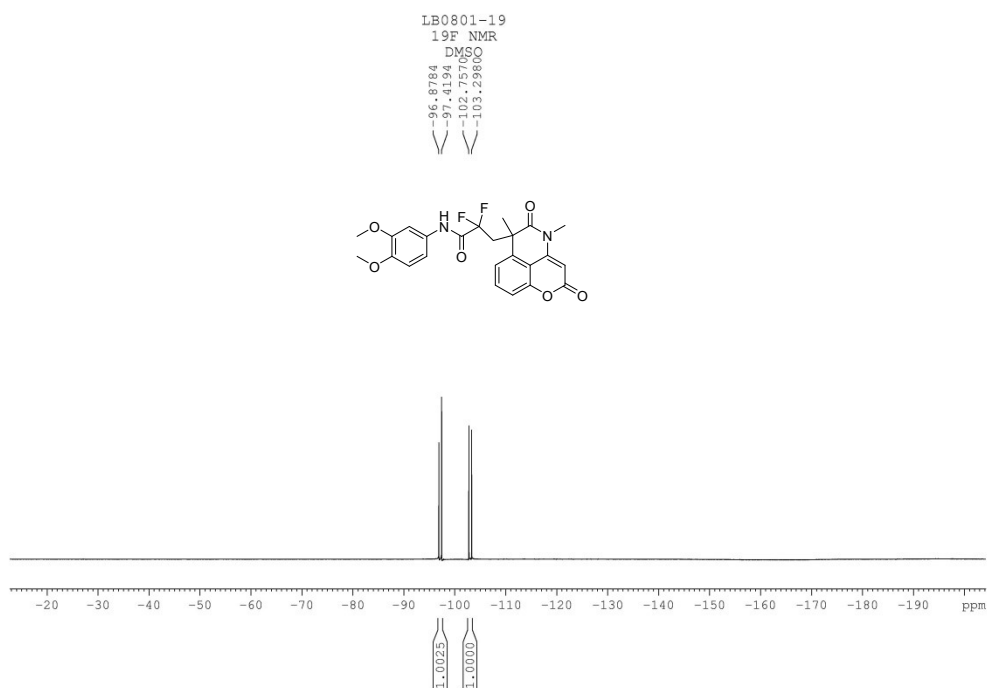


Fig. S61 ¹⁹F NMR (471 MHz) spectrum of compound 4g

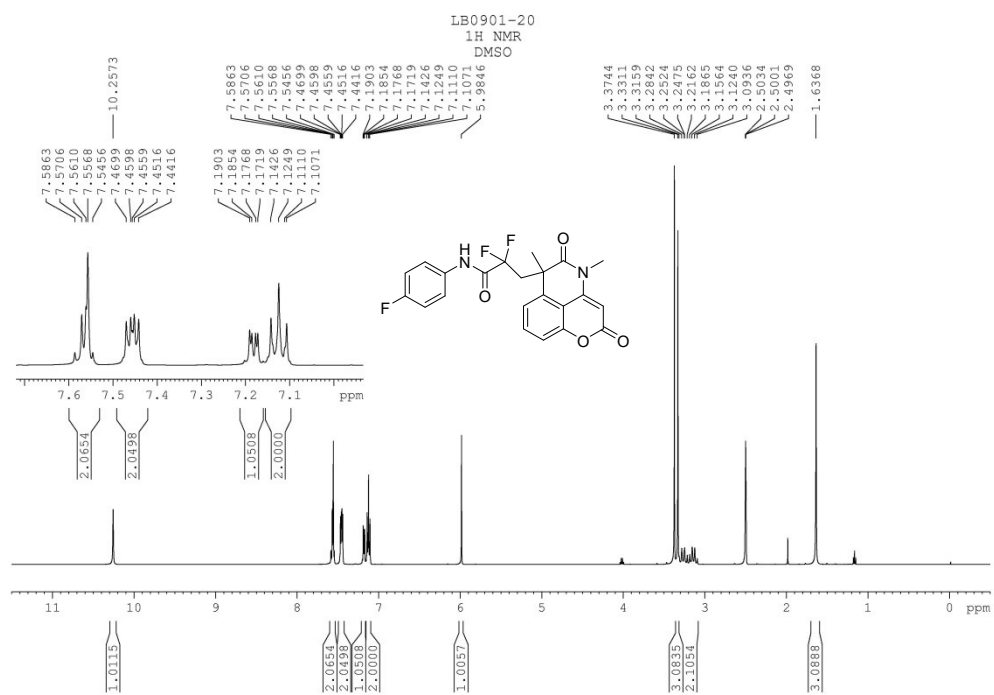


Fig. S62 ¹H NMR (500 MHz) spectrum of compound 4h

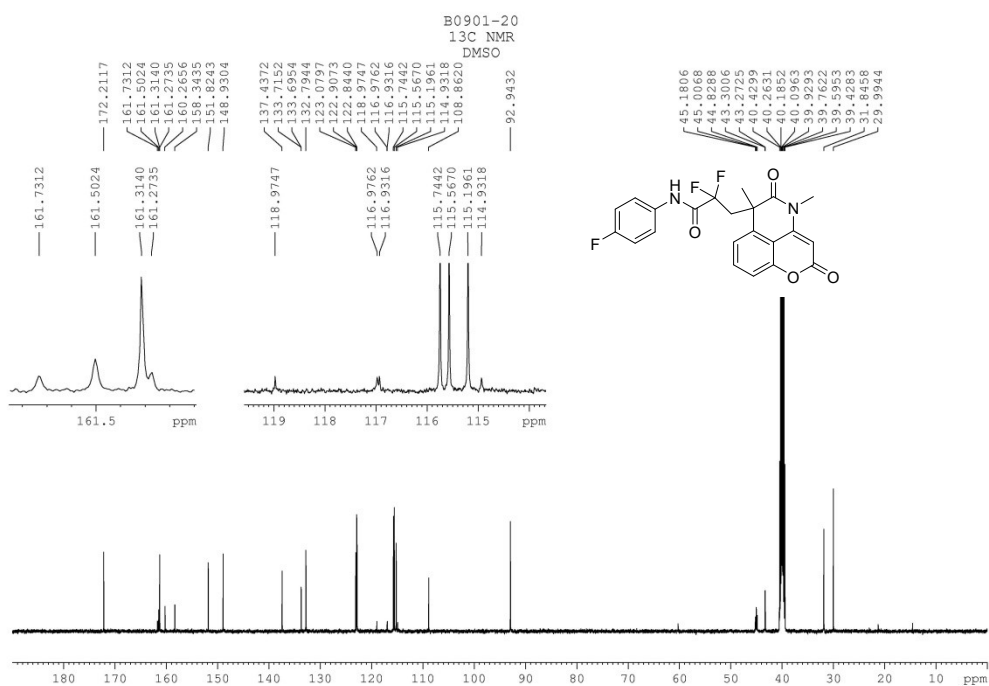


Fig. S63 ¹³C NMR (126 MHz) spectrum of compound 4h

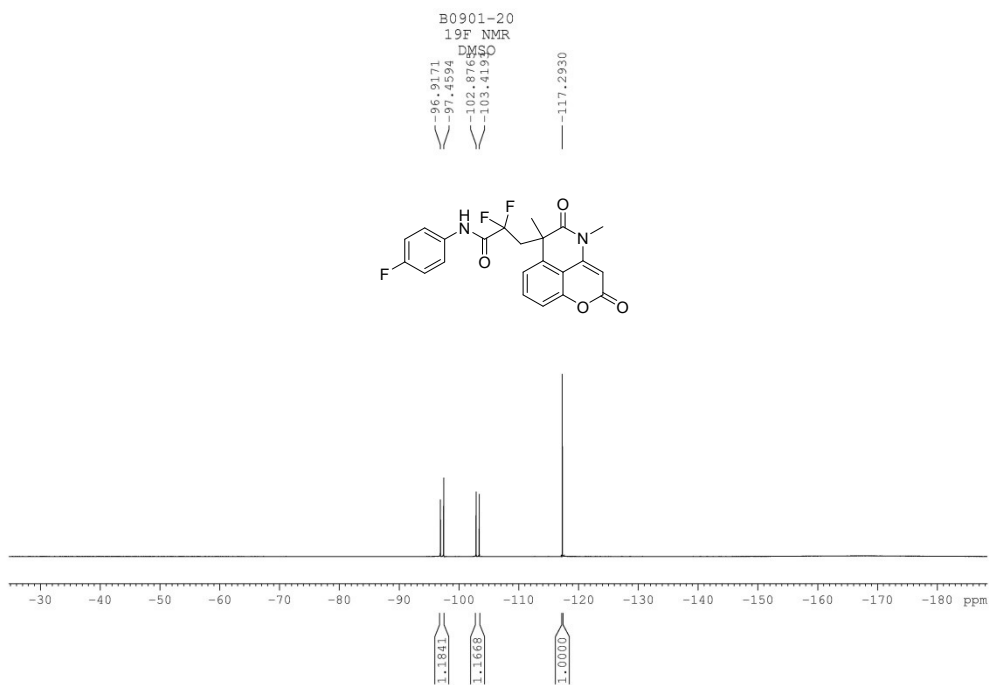


Fig. S64 ¹⁹F NMR (471 MHz) spectrum of compound 4h

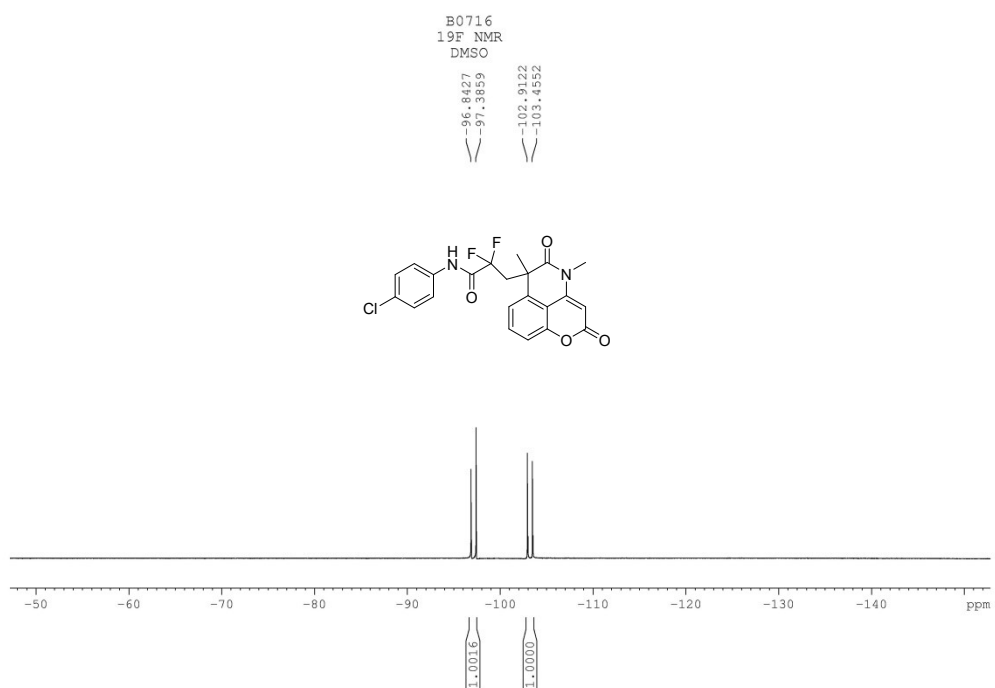


Fig. S67 ¹⁹F NMR (471 MHz) spectrum of compound 4i

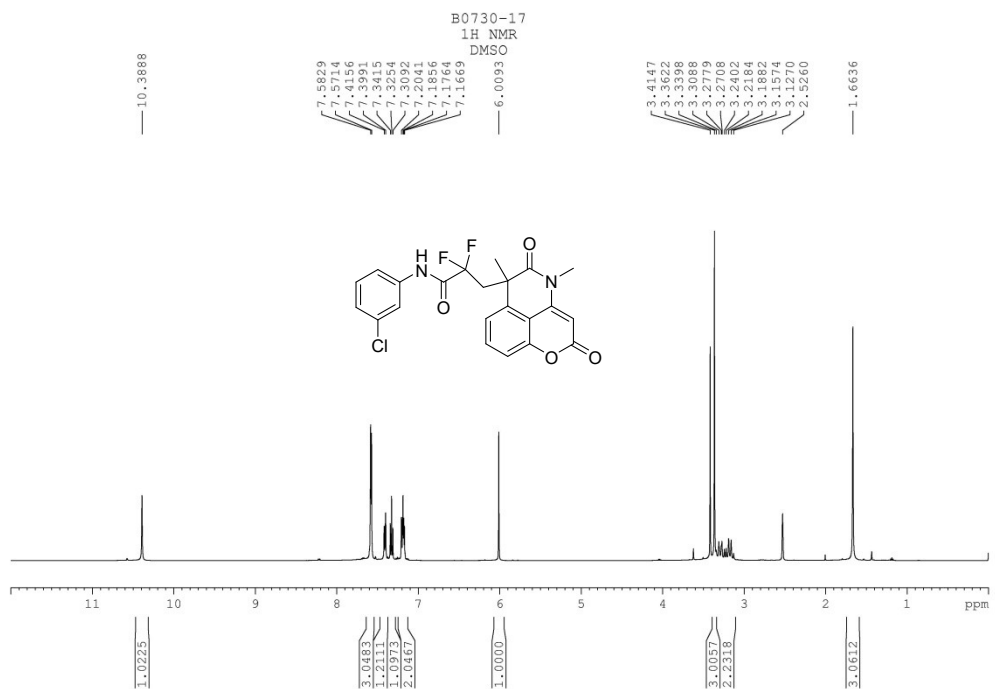


Fig. S68 ¹H NMR (500 MHz) spectrum of compound 4j

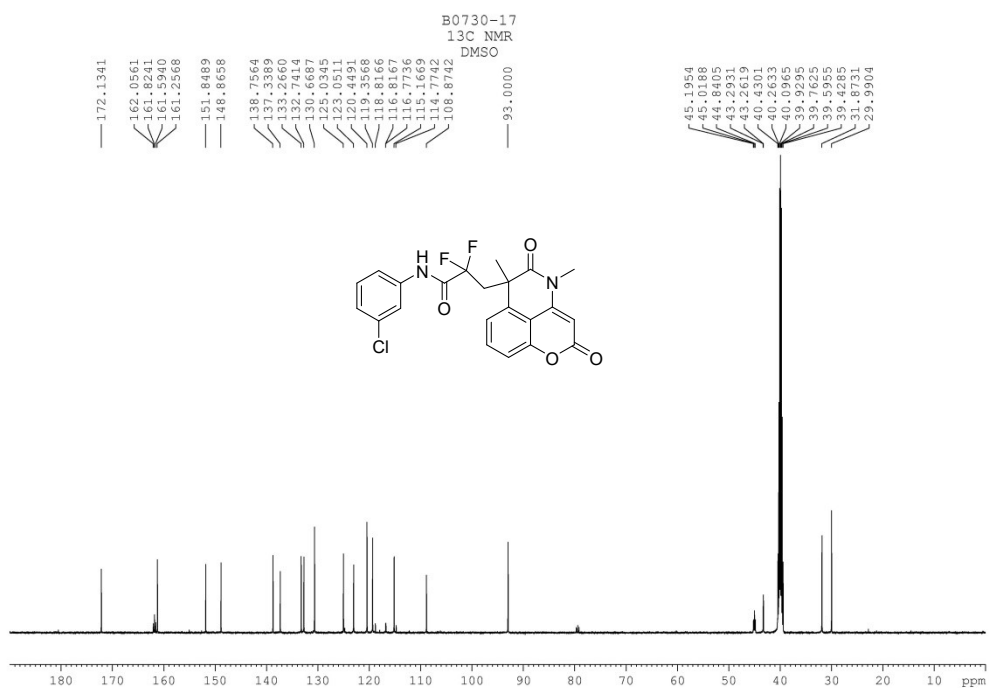


Fig. S69 ¹³C NMR (126 MHz) spectrum of compound 4j

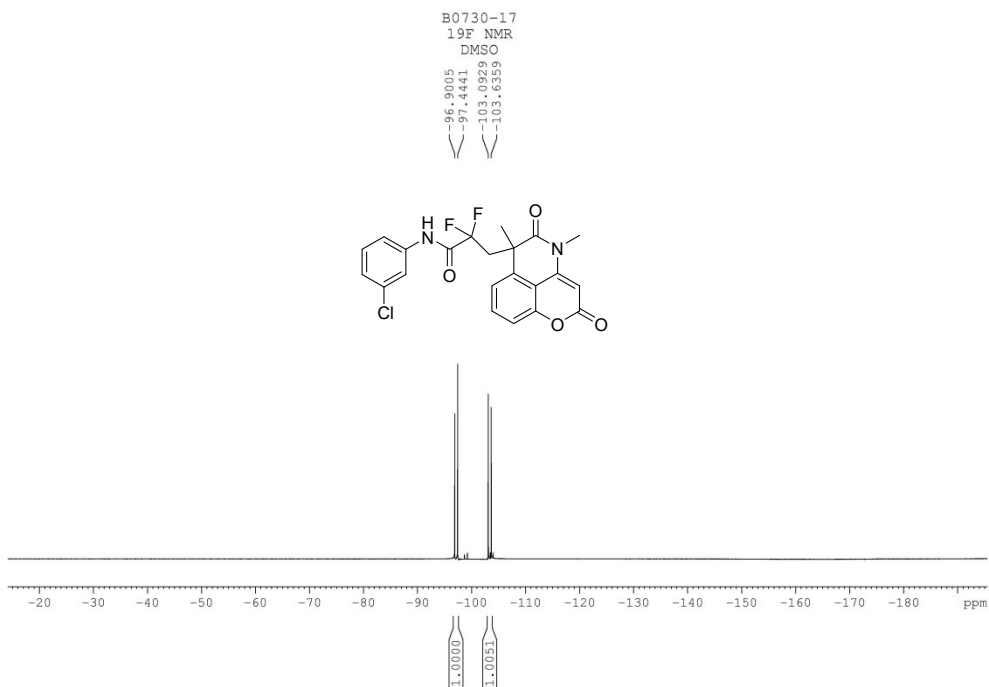


Fig. S70 ¹⁹F NMR (471 MHz) spectrum of compound 4j

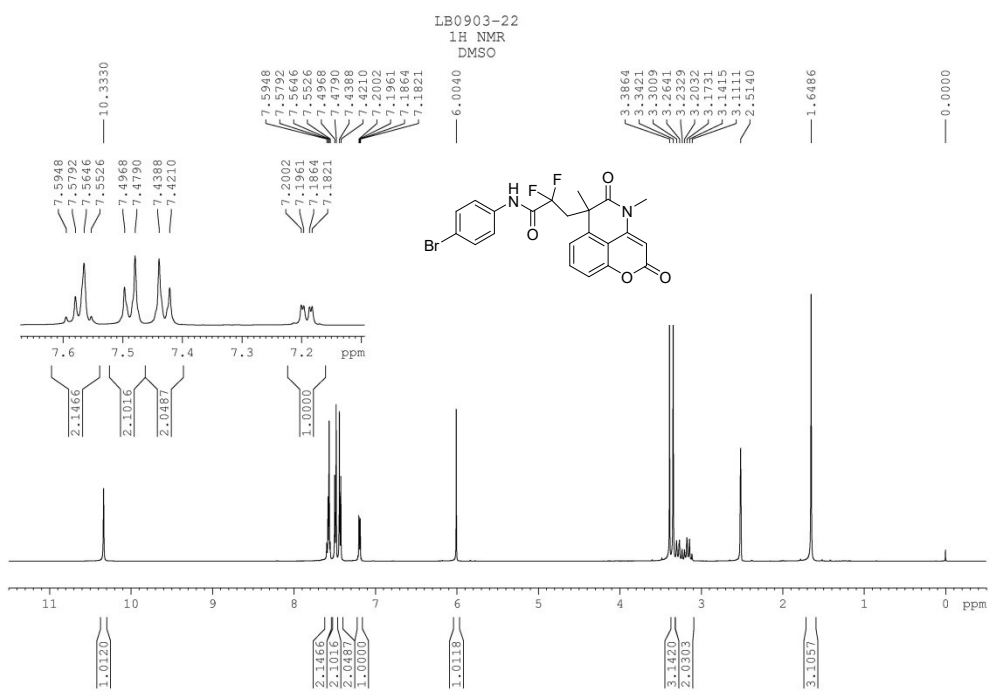


Fig. S71 ¹H NMR (500 MHz) spectrum of compound 4k

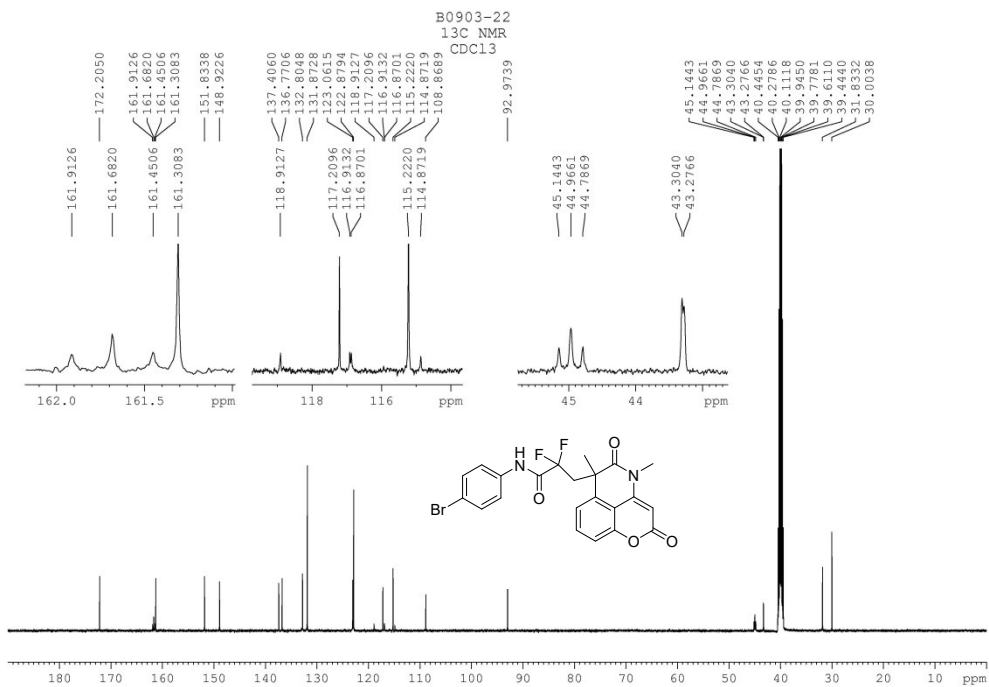


Fig. S72 ¹³C NMR (126 MHz) spectrum of compound 4k

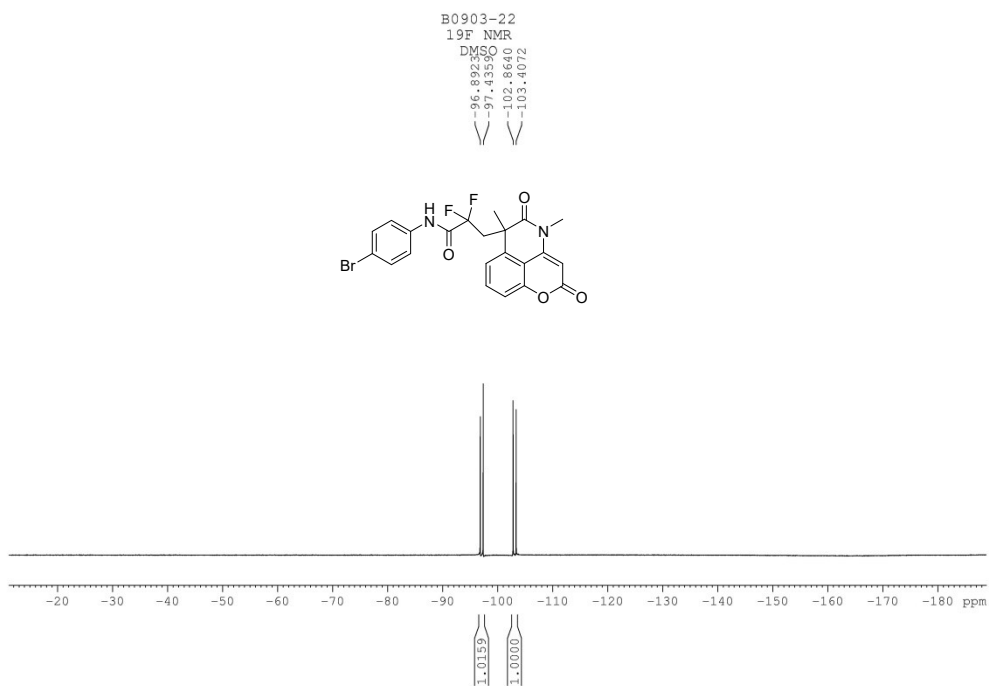


Fig. S73 ¹⁹F NMR (471 MHz) spectrum of compound 4k

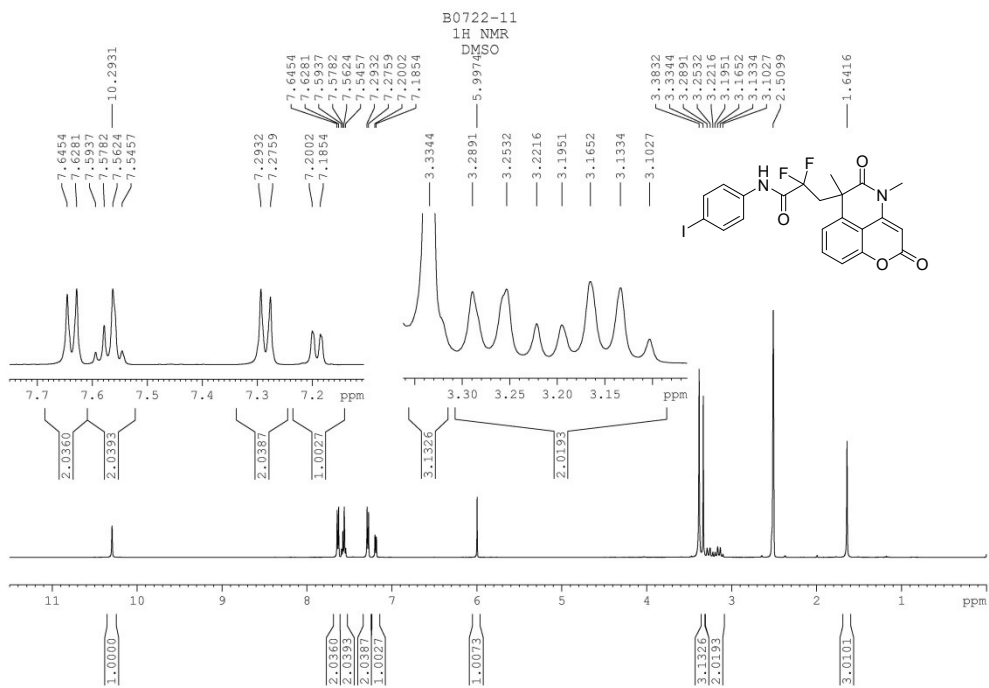


Fig. S74 ¹H NMR (500 MHz) spectrum of compound 4l

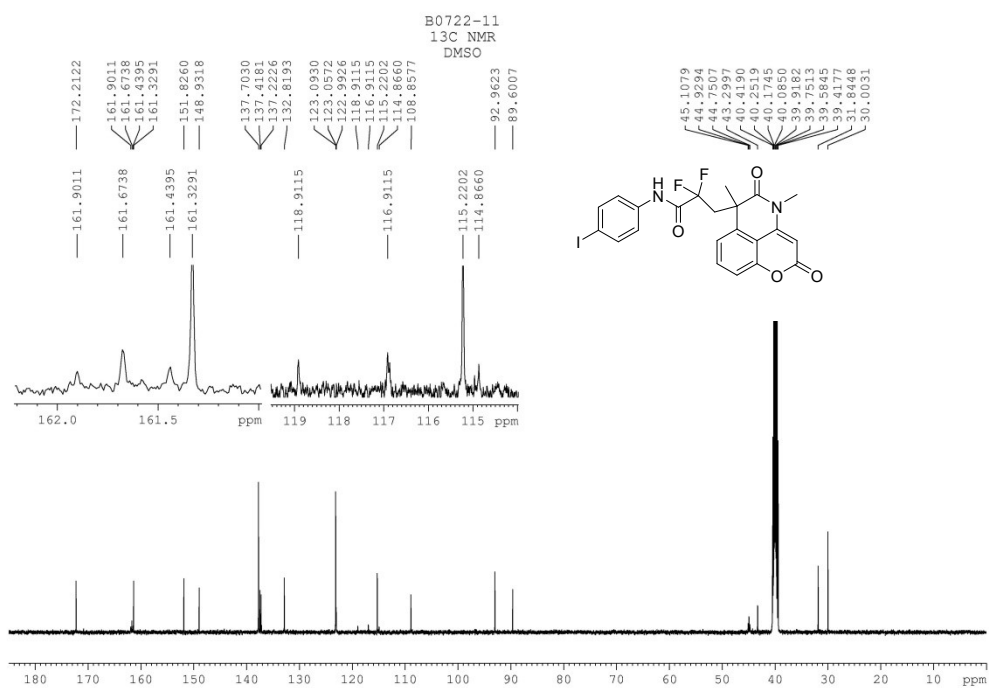


Fig. S75 ¹³C NMR (126 MHz) spectrum of compound 41

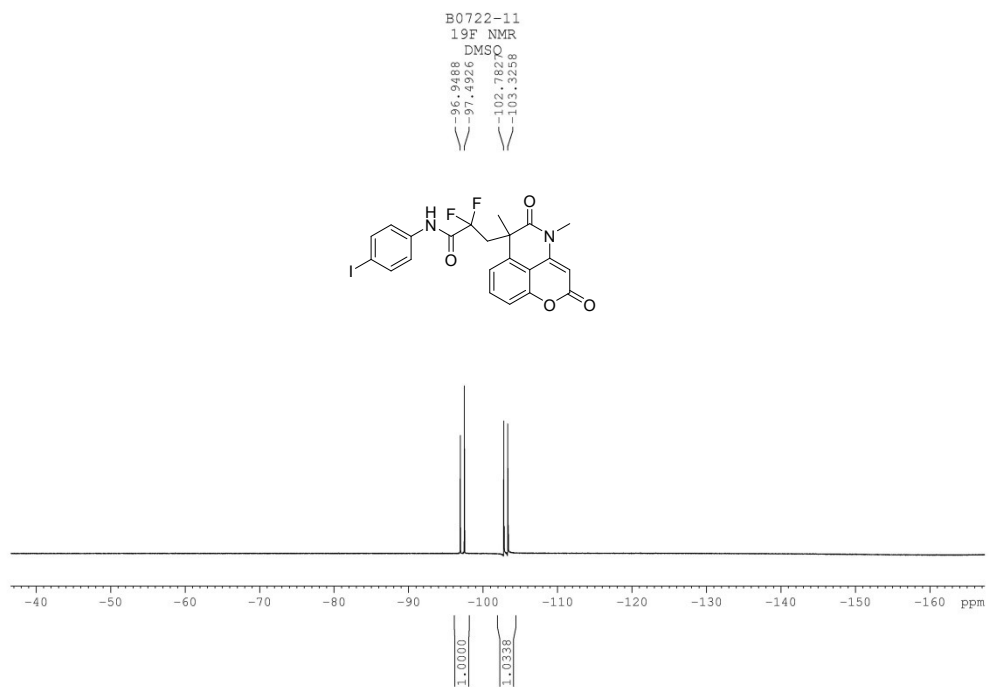


Fig. S76 ¹⁹F NMR (471 MHz) spectrum of compound 41

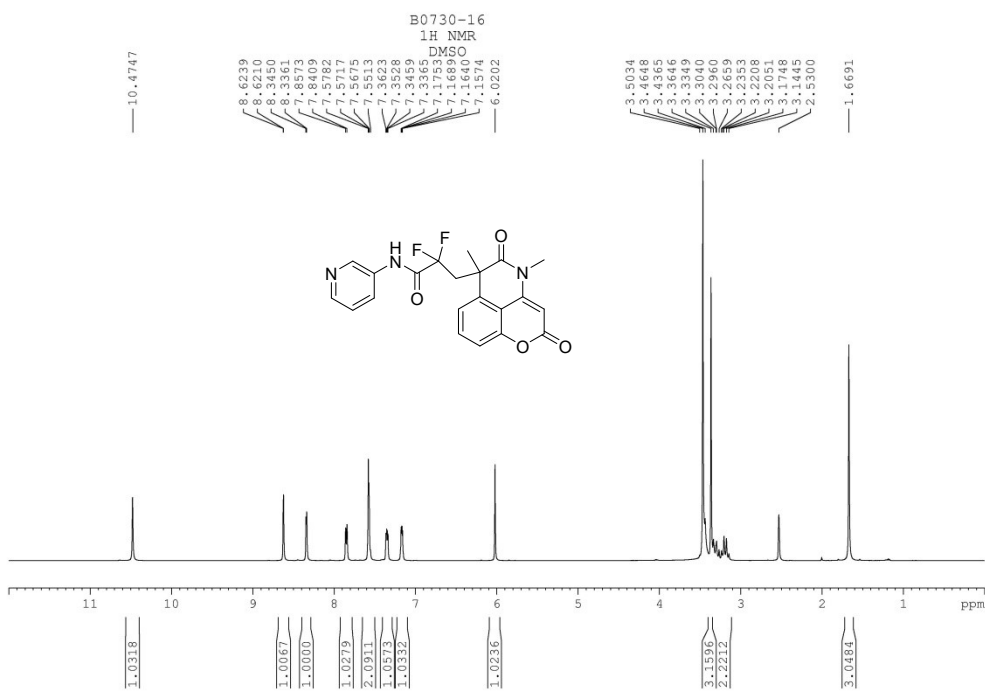


Fig. S77 ¹H NMR (500 MHz) spectrum of compound 4m

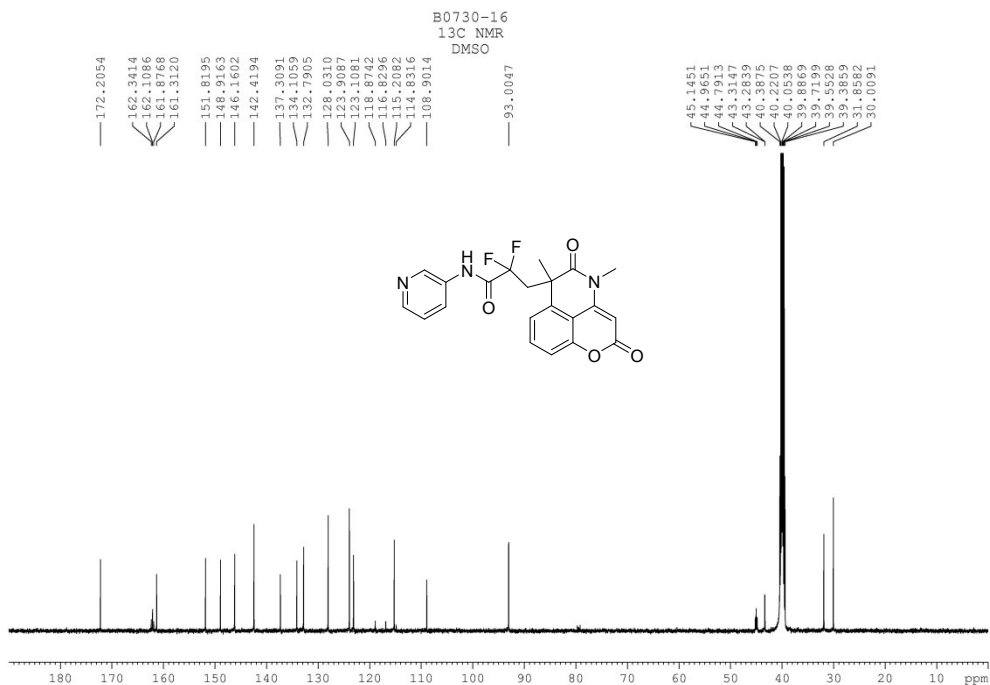


Fig. S78 ¹³C NMR (126 MHz) spectrum of compound 4m

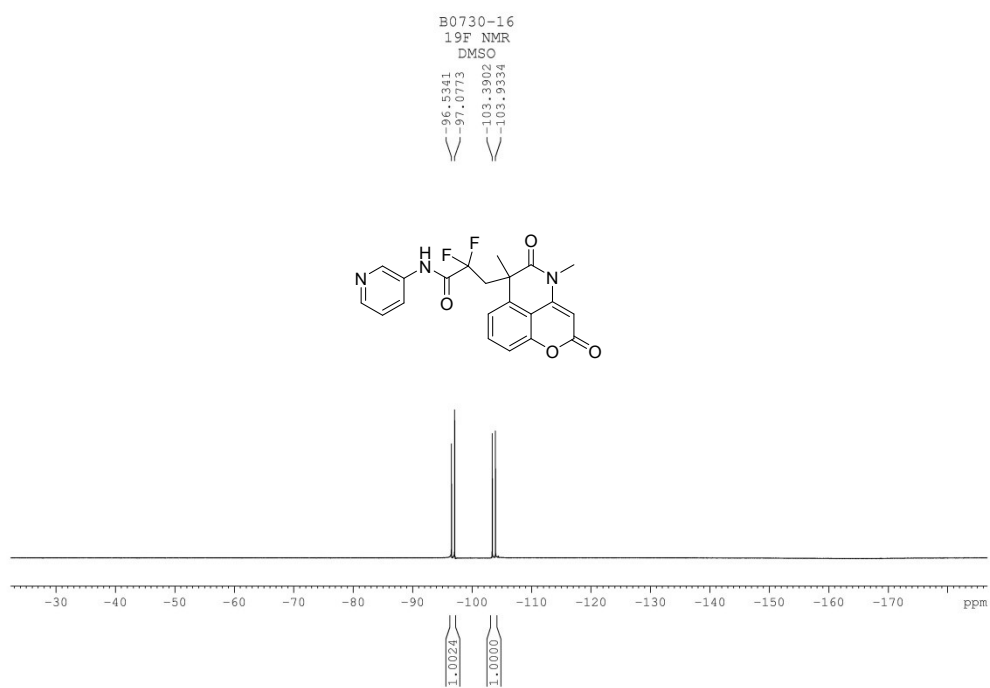


Fig. S79 ¹⁹F NMR (471 MHz) spectrum of compound 4m

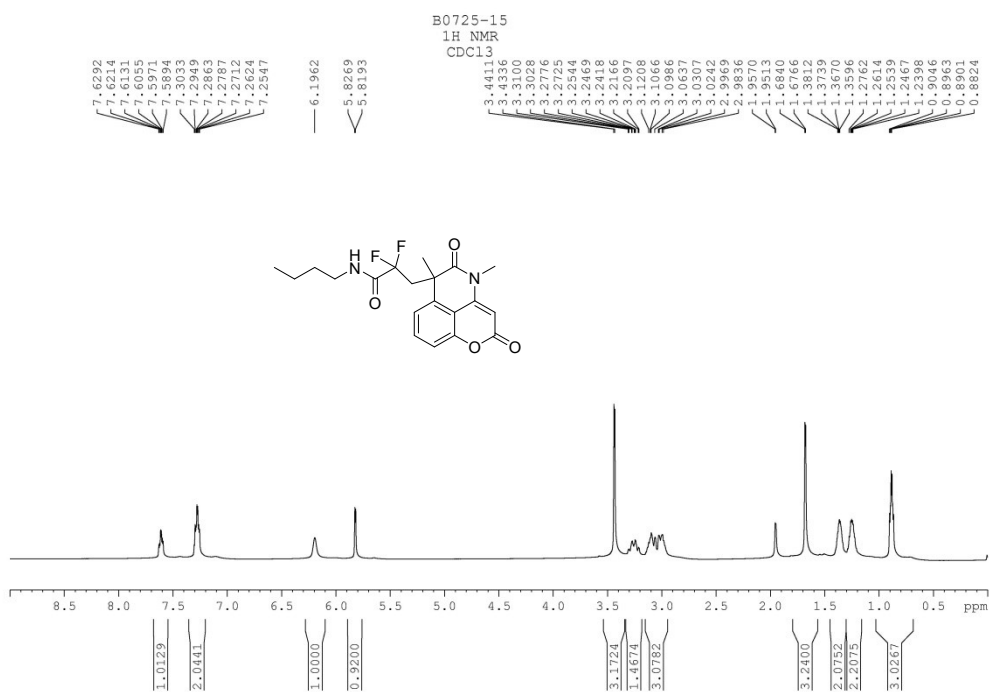


Fig. S80 ¹H NMR (500 MHz) spectrum of compound 4n

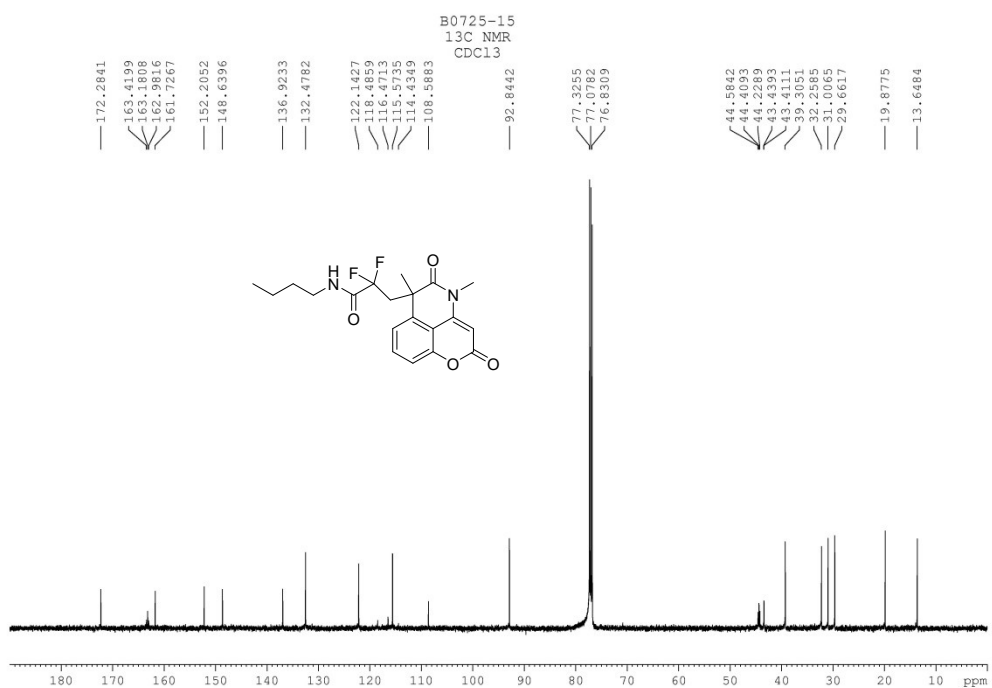


Fig. S81 ¹³C NMR (126 MHz) spectrum of compound 4n

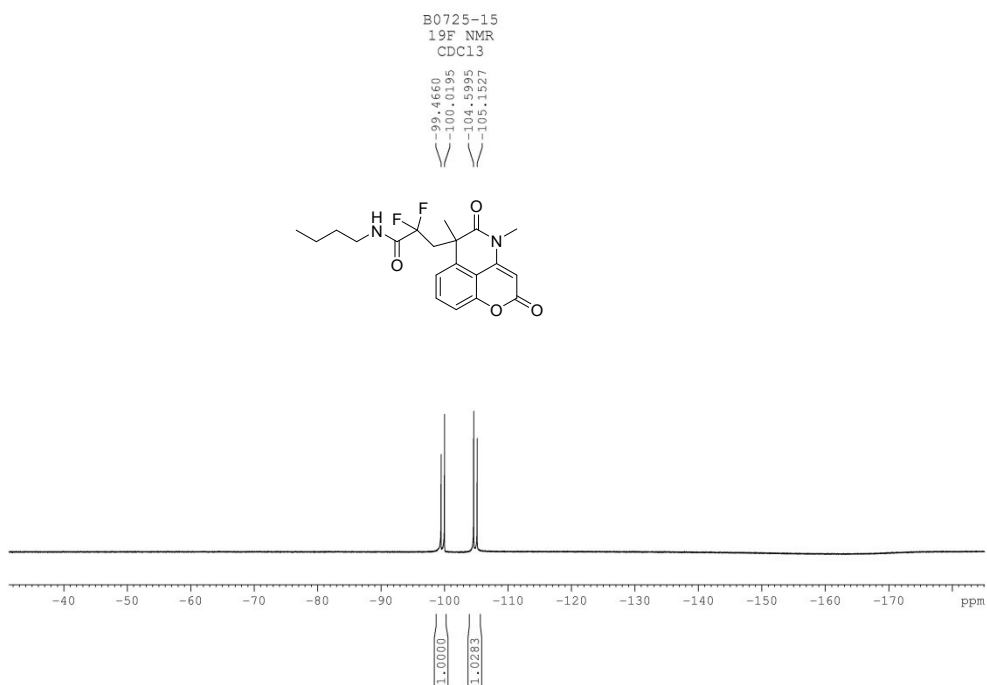


Fig. S82 ¹⁹F NMR (471 MHz) spectrum of compound 4n

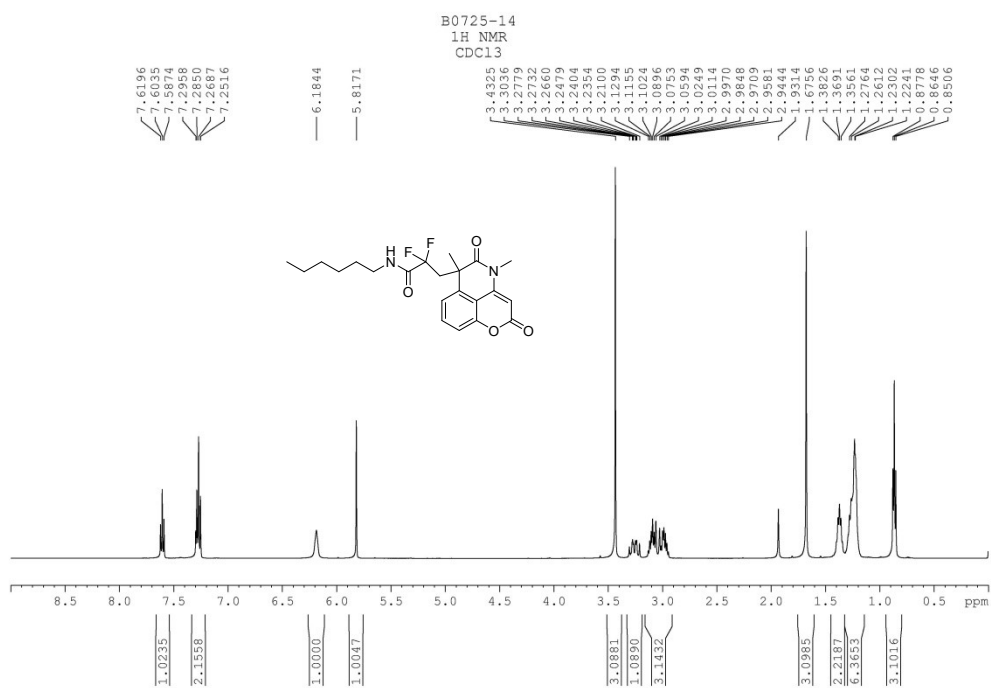


Fig.S S82 ¹H NMR (500 MHz) spectrum of compound 4o

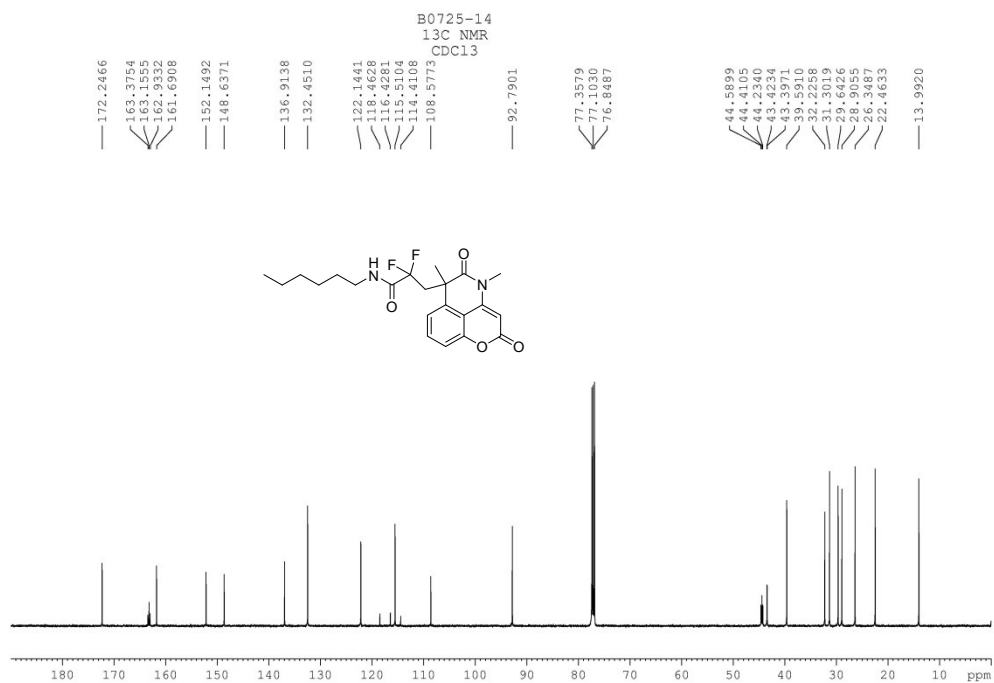


Fig. S83 ¹³C NMR (126 MHz) spectrum of compound 4o

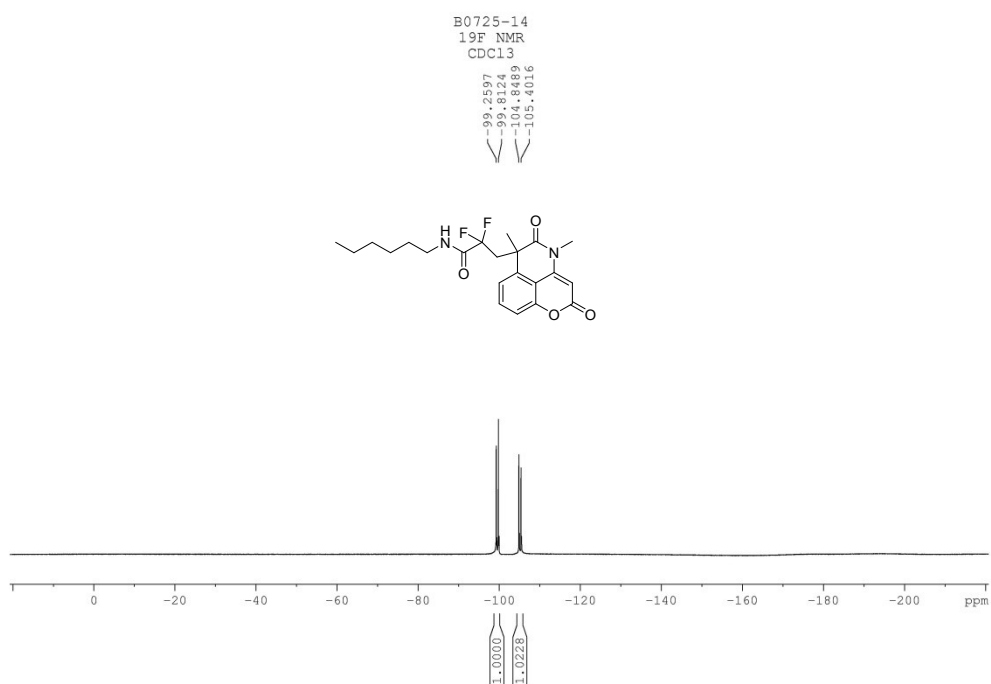


Fig. S84 ¹⁹F NMR (471 MHz) spectrum of compound 4o

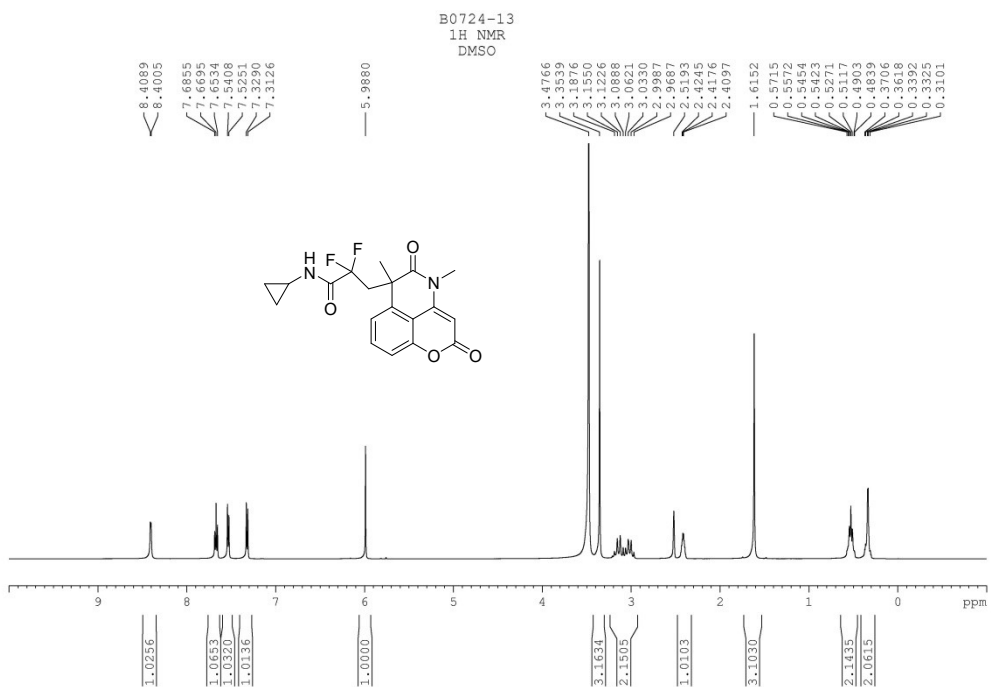


Fig. S85 ¹H NMR (500 MHz) spectrum of compound 4p

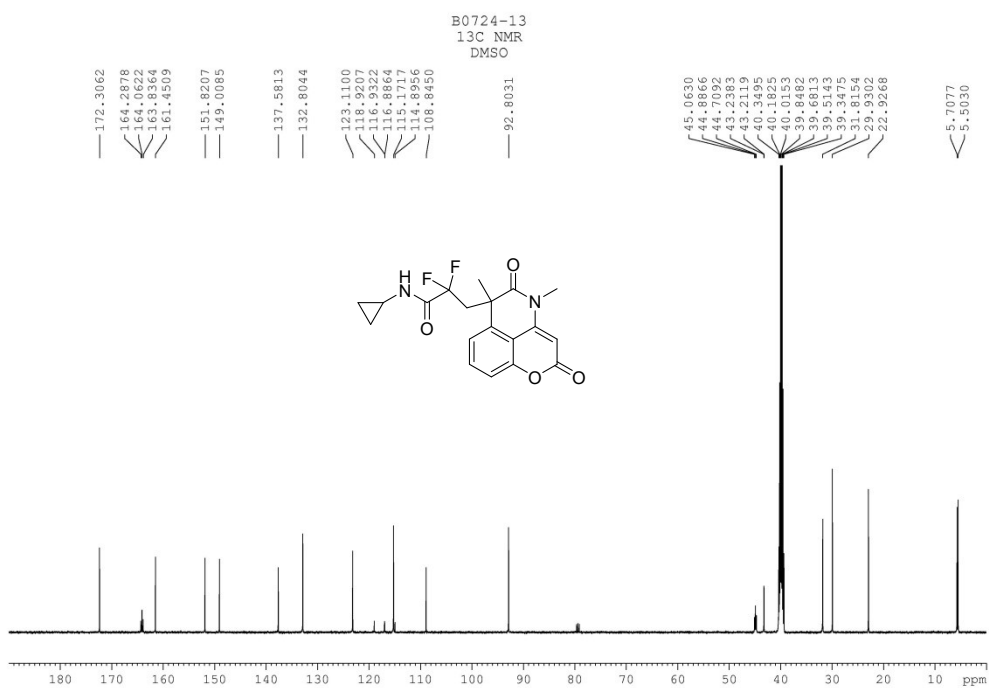


Fig. S86 ¹³C NMR (126 MHz) spectrum of compound 4p

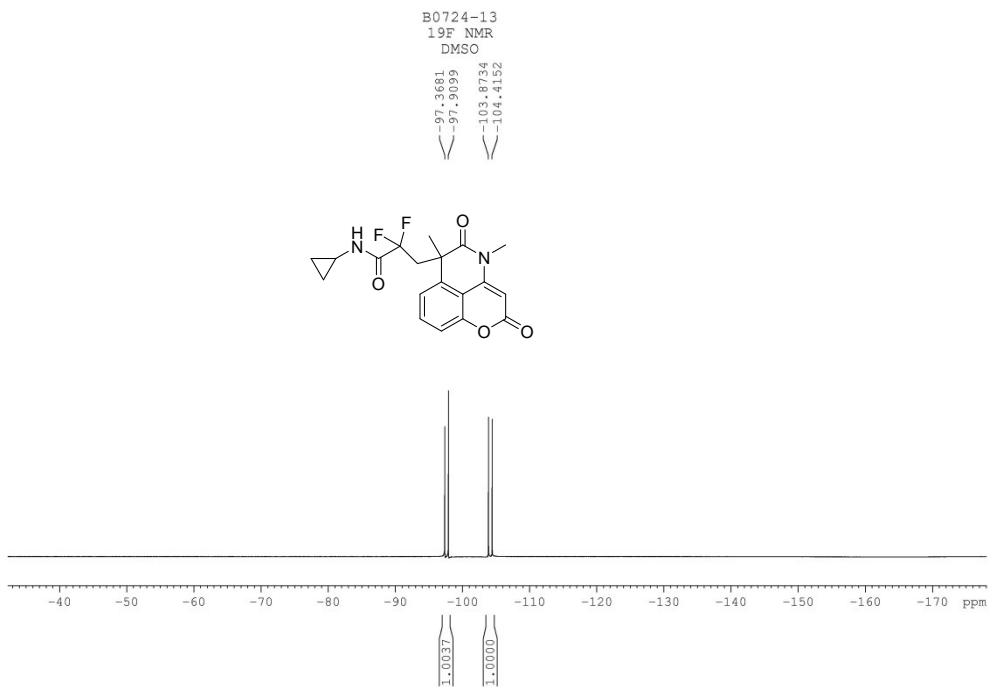


Fig. S87 ¹⁹F NMR (471 MHz) spectrum of compound 4p

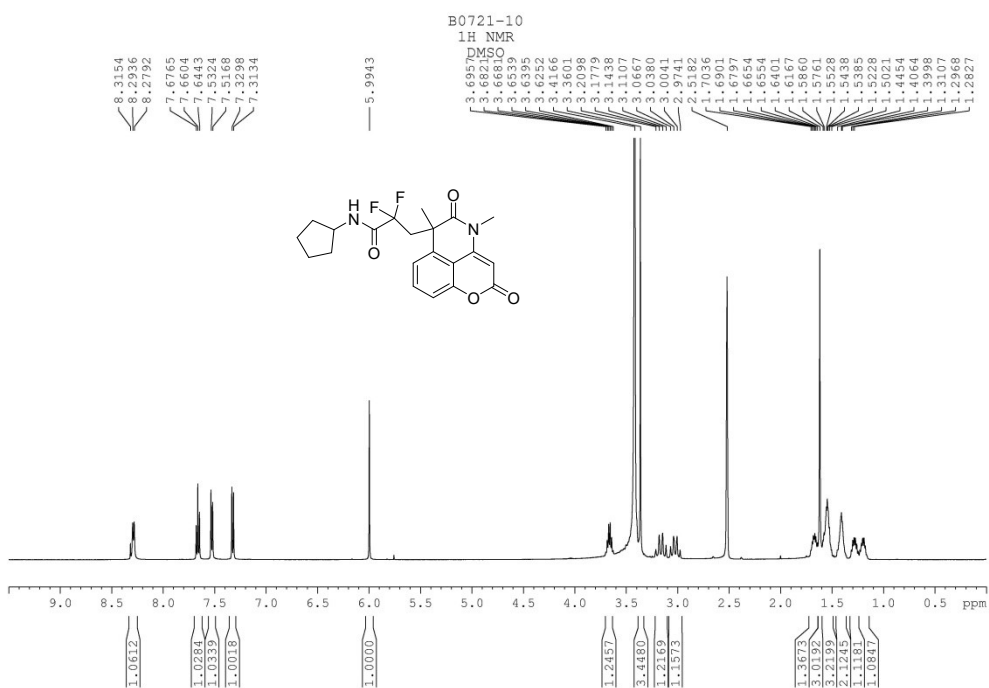


Fig. S88 ¹H NMR (500 MHz) spectrum of compound 4q

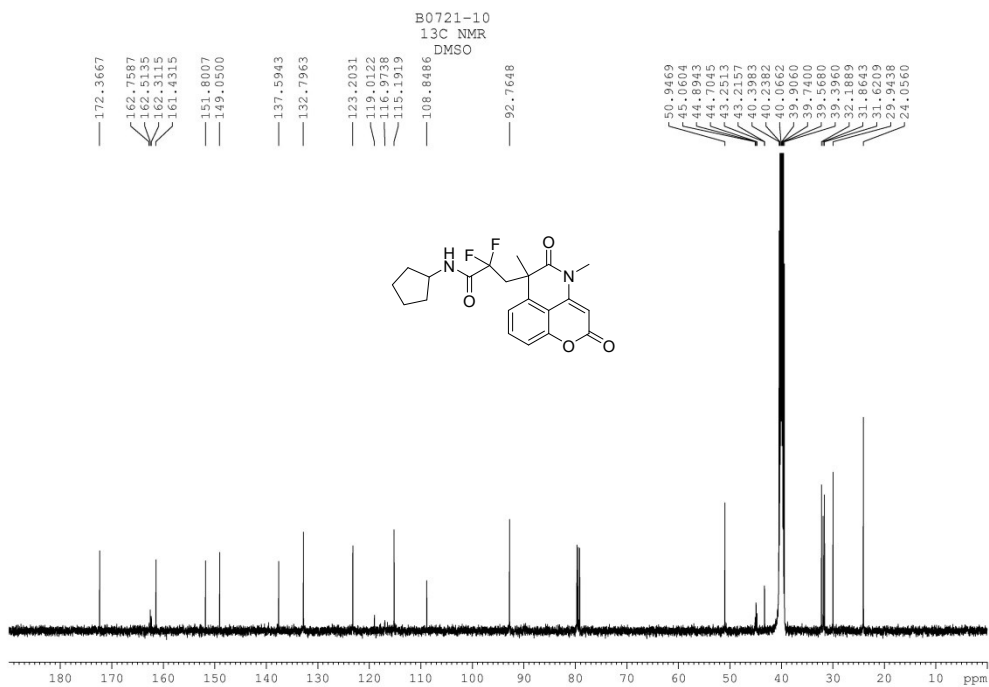


Fig. S89 ¹³C NMR (126 MHz) spectrum of compound 4q

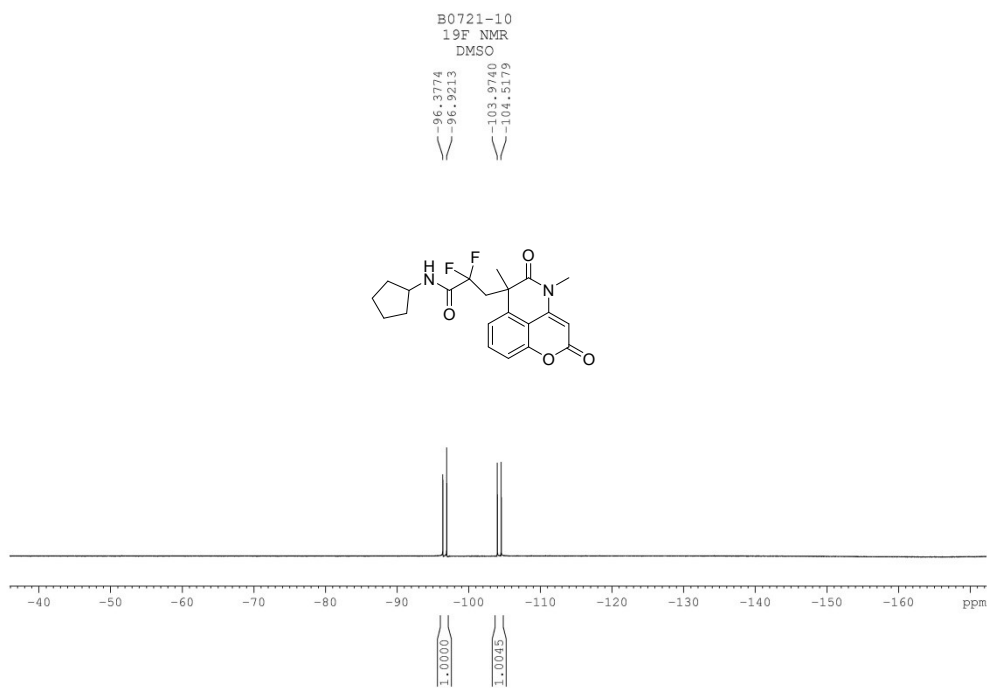


Fig. S90 ¹⁹F NMR (471 MHz) spectrum of compound 4q

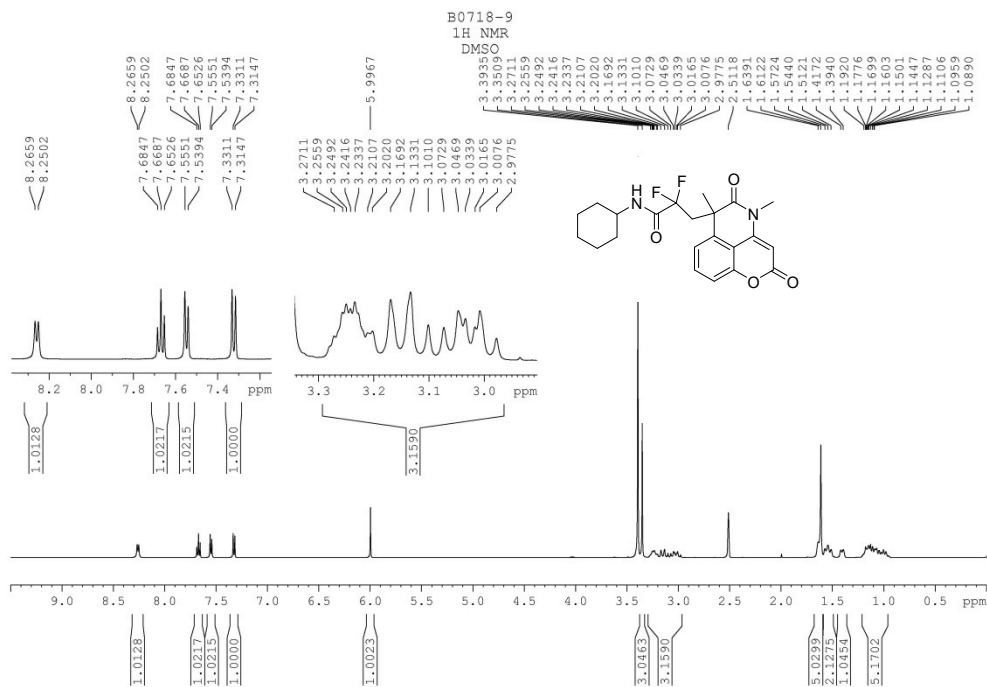


Fig. S91 ¹H NMR (500 MHz) spectrum of compound 4r

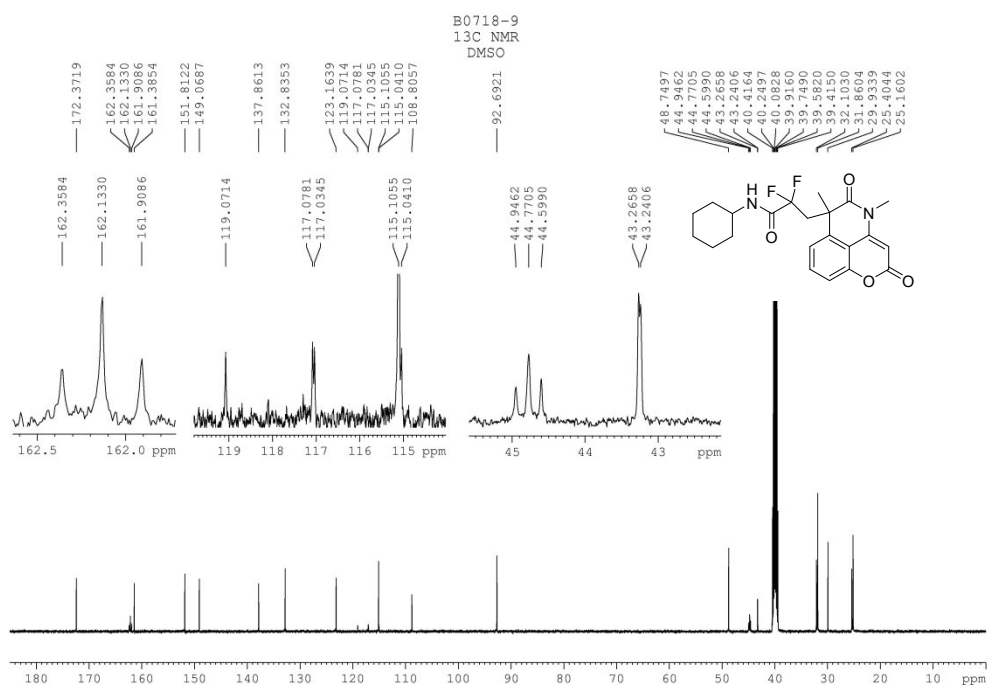


Fig. S92 ¹³C NMR (126 MHz) spectrum of compound 4r

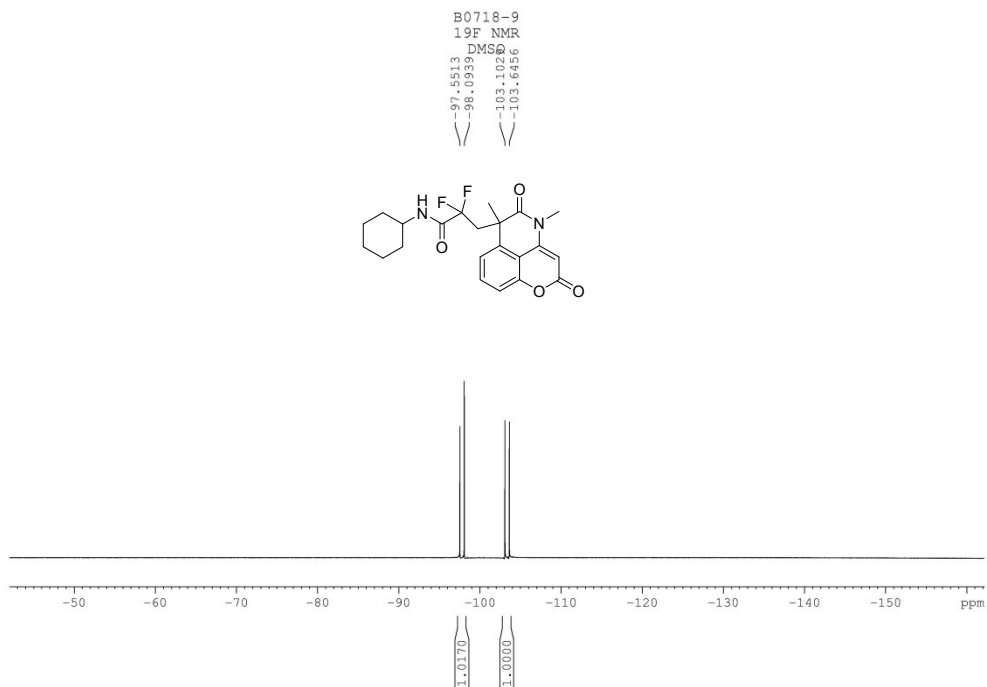


Fig. S93 ¹⁹F NMR (471 MHz) spectrum of compound 4r

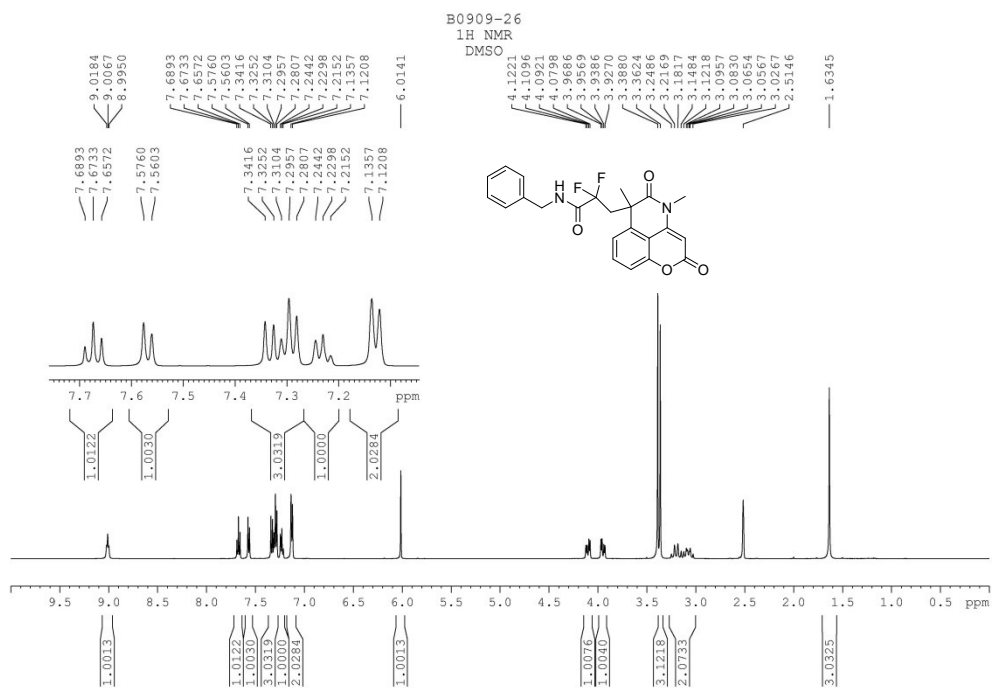


Fig. S94 ¹H NMR (500 MHz) spectrum of compound 4s

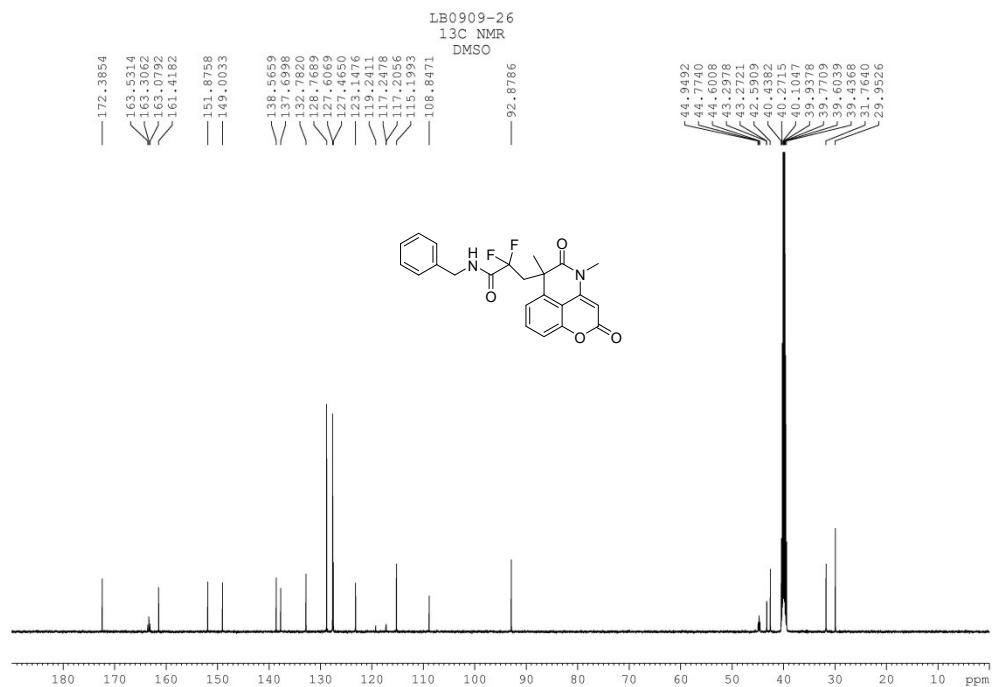


Fig. S95 ¹³C NMR (126 MHz) spectrum of compound 4s

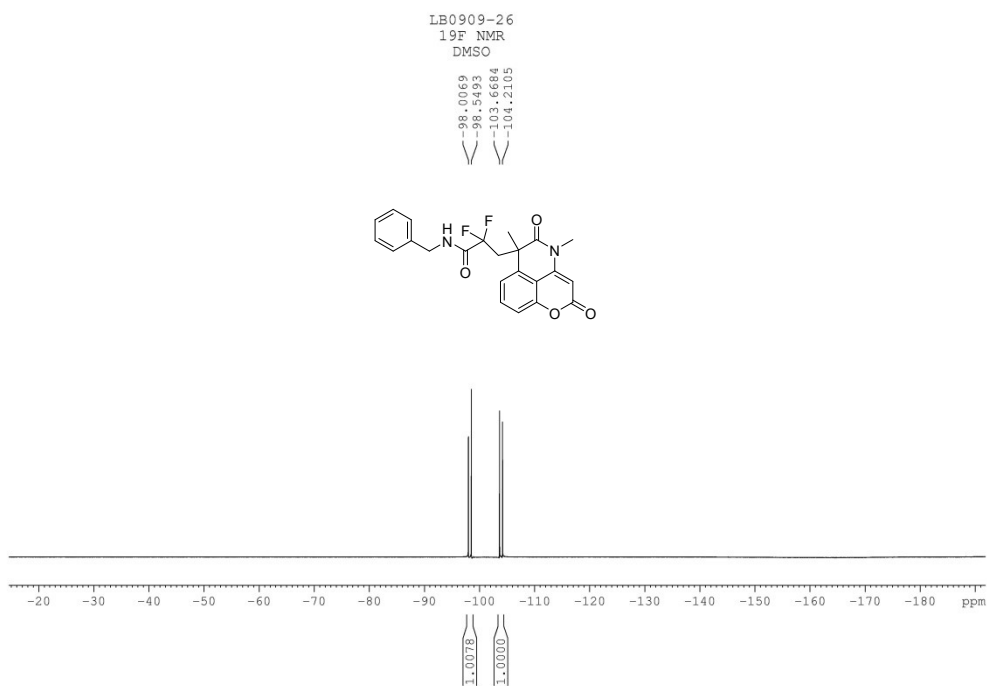


Fig. S96 ¹⁹F NMR (471 MHz) spectrum of compound 4s

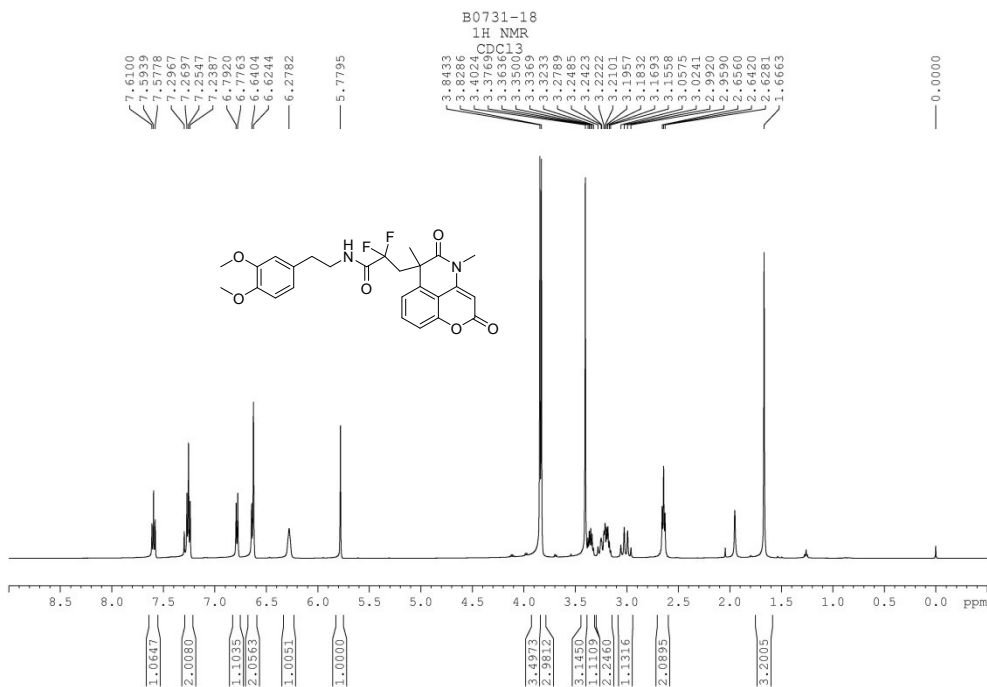


Fig. S97 ¹H NMR (500 MHz) spectrum of compound 4t

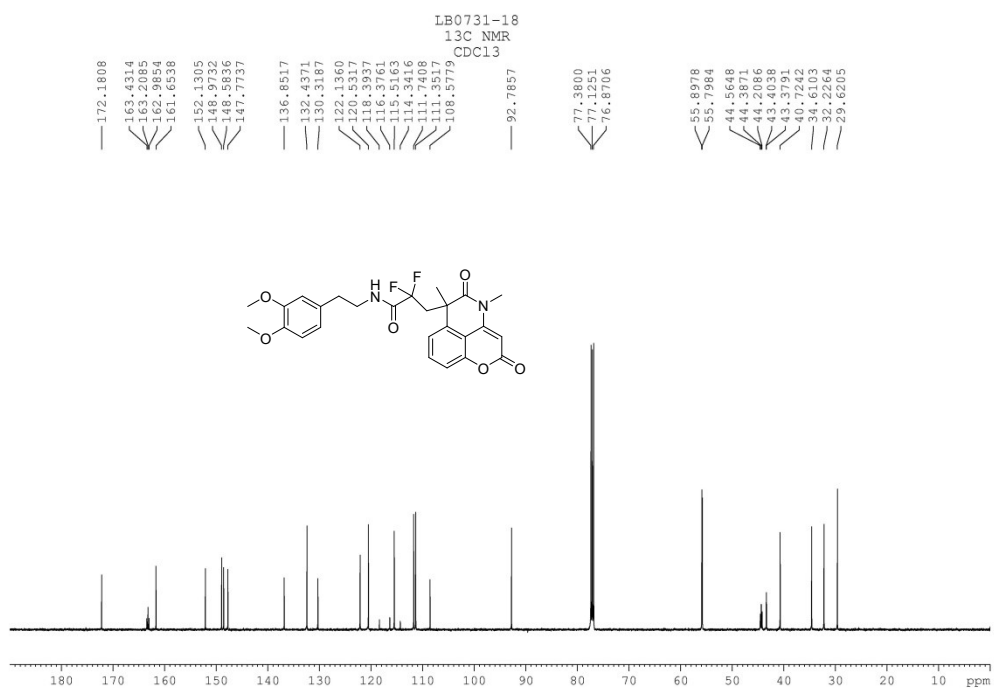


Fig. S98 ¹³C NMR (126 MHz) spectrum of compound 4t

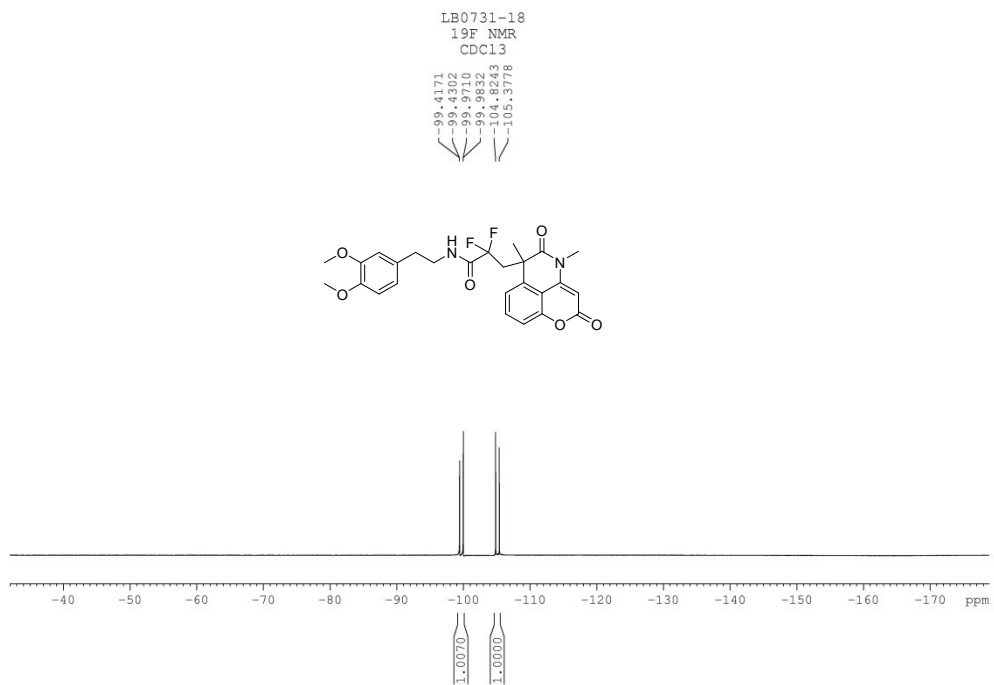


Fig. S99 ¹⁹F NMR (471 MHz) spectrum of compound 4t

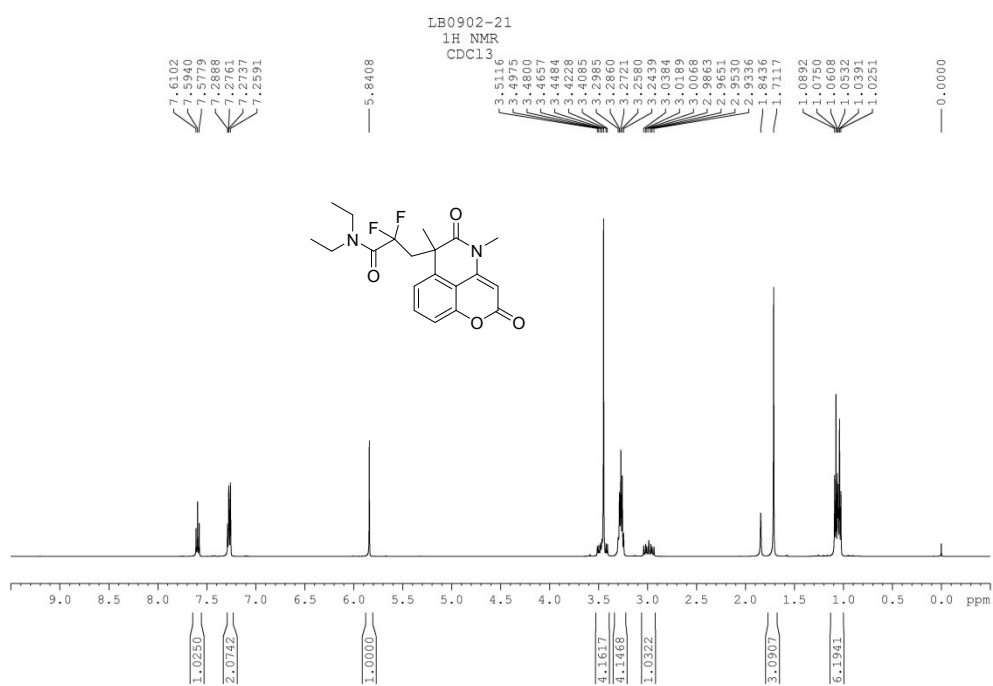


Fig. S100 ¹H NMR (500 MHz) spectrum of compound **4u**

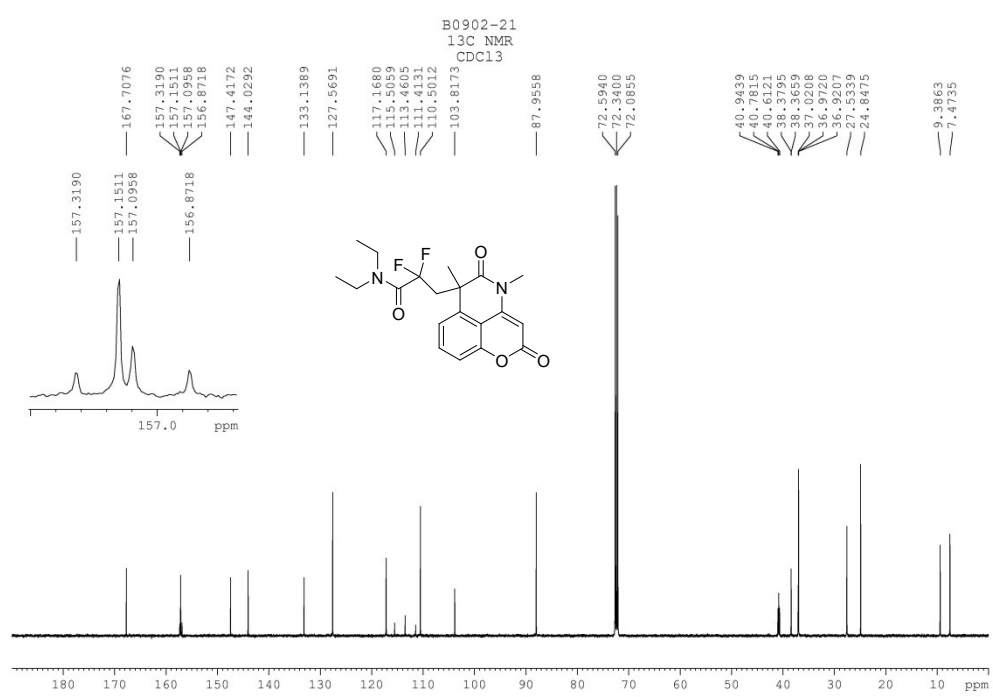


Fig. S101 ¹³C NMR (126 MHz) spectrum of compound **4u**

B0902-21
19F NMR
CDCl3
100.9663
101.5566
102.8846
103.4763

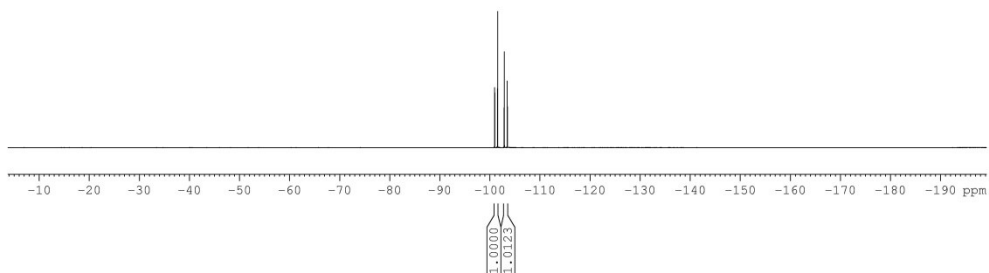
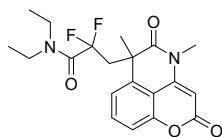


Fig. S102 ^{19}F NMR (471 MHz) spectrum of compound **4u**

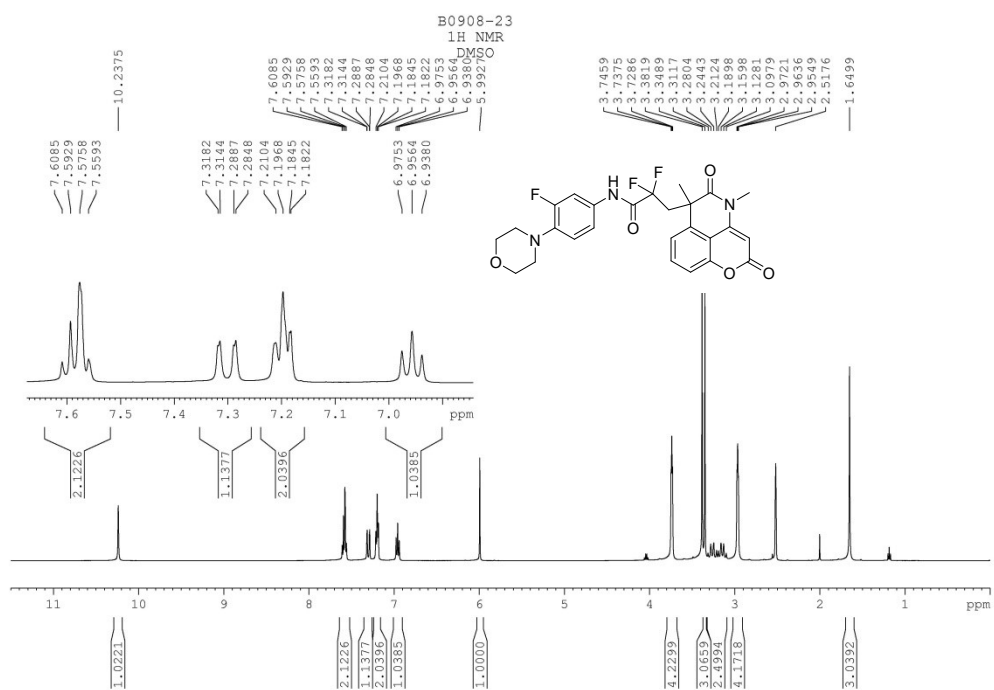


Fig. S103 ¹H NMR (500 MHz) spectrum of compound 8

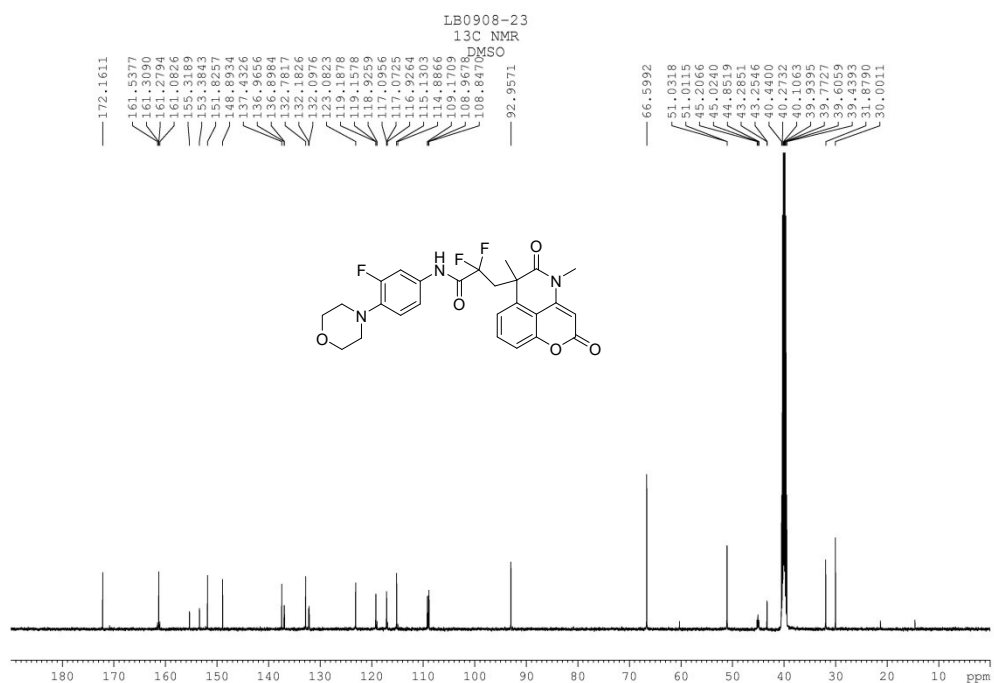


Fig. S104 ¹³C NMR (126 MHz) spectrum of compound 8



Fig. S105 ^{19}F NMR (471 MHz) spectrum of compound **8**