A Physico-chemical Investigation on Fluorine-Enriched Quinolines

Supporting Information

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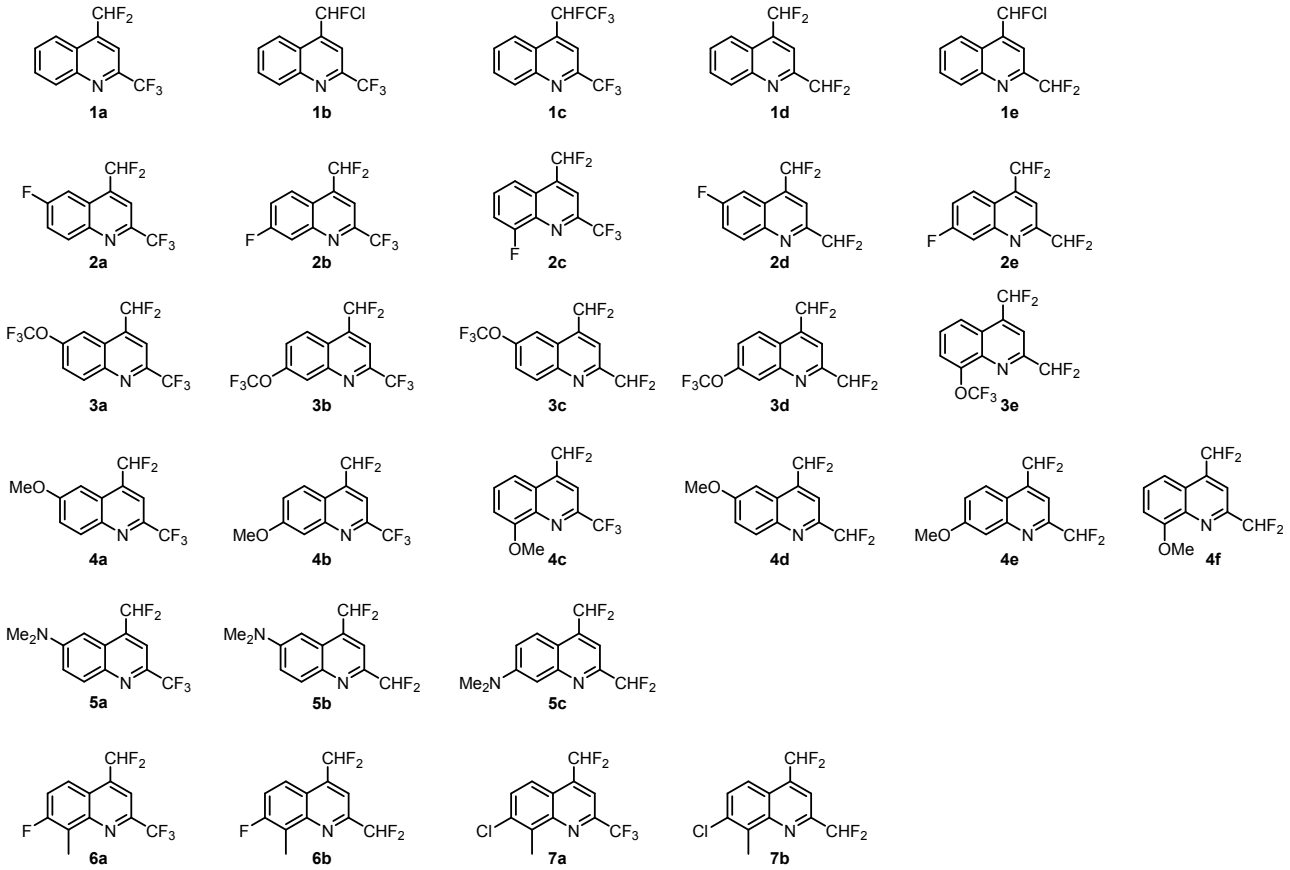
Supplementary material

(53 pages including this one)



Scheme S1. Chemical structures of the fluorinated quinolines considered in this work.

Spectrophotometric Absorption Studies

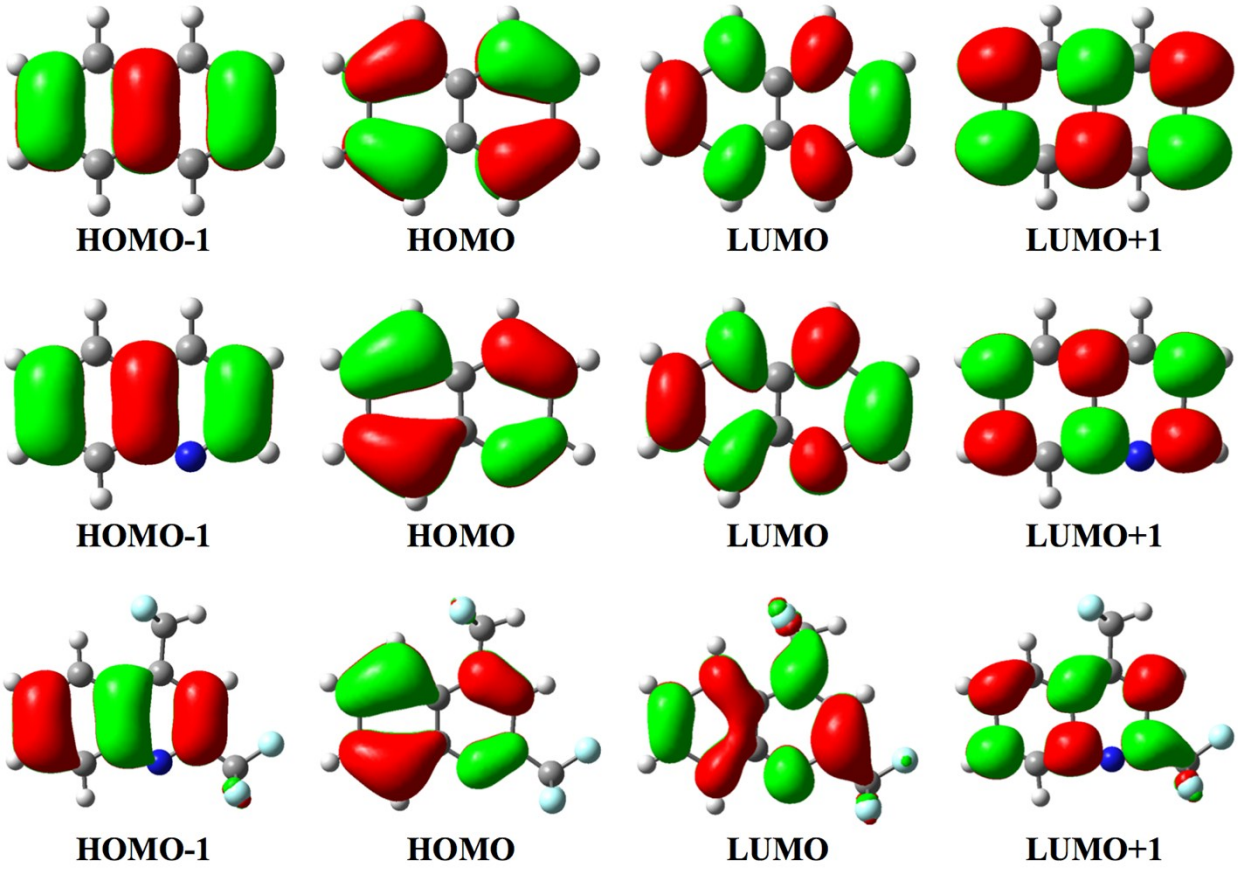


Figure S1. Molecular orbitals (HOMO, HOMO-1, LUMO and LUMO+1) of naphthalene, quinoline and **1a** calculated using the B3LYP/6-311++G(2d,p)//B3LYP/6-311++G(d,p) level of theory.

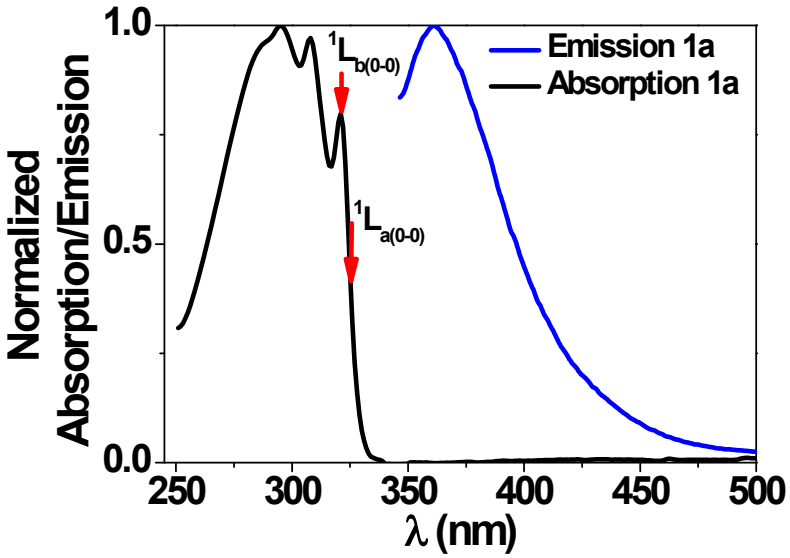


Figure S2. Normalized absorption (black) and emission (blue) spectra of compound **1a** in 1,2-dichloroethane. The origin band (0-0) energies of the two lowest lying ^1L_a and ^1L_b singlet states are indicated with red arrows. The $^1L_{b(0-0)}$ is observed as a sharp transition, while the $^1L_{a(0-0)}$ has been estimated by averaging the energies of the absorption and emission bands maxima, respectively.

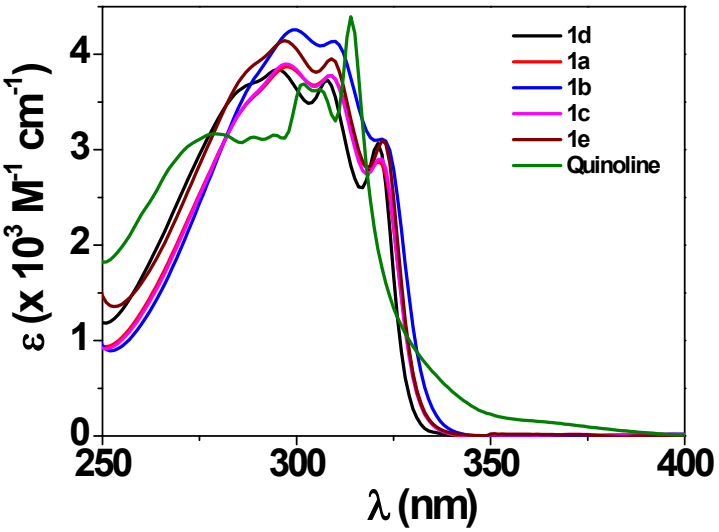


Figure S3. Electronic absorption spectra of fluorinated (CHF_2, CHFCl, CF_3 or $CHFCF_3$) quinolines substituted at C2 and C4 positions (**1a**, **1b**, **1c**, **1d** and **1e**, see Scheme S1 for the corresponding chemical structures). Solvent: 1,2-dichloroethane; *T* = 25 °C.

Table S1. Absorption properties for quinoline derivatives (quinoline, **1a-e**) substituted at C2 and C4 positions by fluorinated groups.

Compound	π-π*	
	λ (nm)	ε (x 10^3 M^{-1} cm^{-1})
quinoline	278	3.167
	289	3.134
	294	3.154
	302	3.688
	306	3.634
	314	4.395
1a	288	sh
	298	3.869
	309	3.777
	321	2.876
1b	289	sh
	299	4.256
	309	4.138
	322	3.112
1c	287	sh
	298	3.898
	309	3.778
	322	2.904
1d	285	sh
	295	3.843
	308	3.732
	321	3.067
1e	287	sh
	297	4.142
	309	3.955
	322	3.095

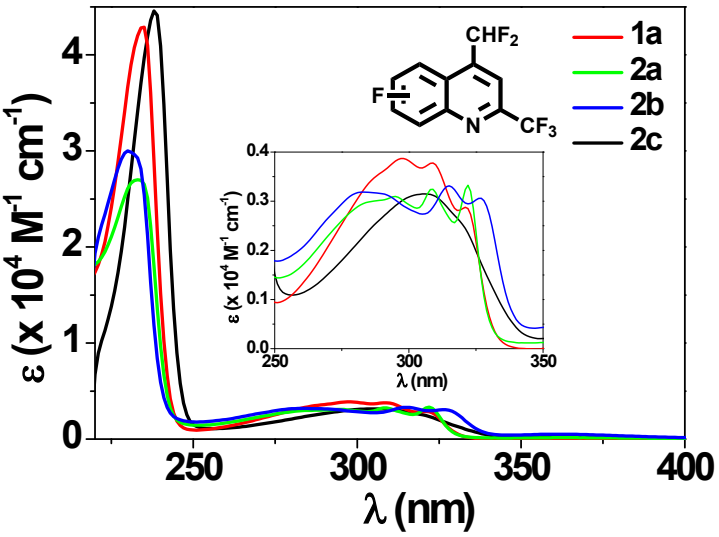


Figure S4. Change of absorption spectra as a function of the fluorine substitution position: C6 (**2a**), C7 (**2b**) or C8 (**2c**) of a quinoline derivative bearing a CF_3 group at C2 position and a CHF_2 group at C4 position (**1a** as a scaffold reference). Solvent: 1,2-dichloroethane, *T* = 25.0(2) °C. The inset shows a spectral expansion from 250 nm to 350 nm.

Table S2. Electronic absorption properties for a quinoline derivative (**1a**) substituted by a fluorine group on either C6 (**2a**), C7 (**2b**) or C8 (**2c**) position and bearing a CF_3 group at C2 position and a CHF_2 group at C4 position (see Figure S4). Solvent: 1,2-dichloroethane, *T* = 25.0(2) °C.

Compound	Band III λ (ε)	Band I (^1L_b) λ (ε)	Band II (^1L_a) λ (ε)
1a	235 (4.29)		287 (0.347) 298 (0.387) 309 (0.378) 321 (0.287)
2a	233 (2.70)		283 (0.295) 295 (0.310) 309 (0.324) 322 (0.332)
2b	230 (3.00)		283 (0.318) 290 sh 315 (0.331) 327 (0.306)
2c	238 (4.458)		306 (0.315) 320 sh
Solvent: 1,2-dichloroethane; *T* = 25 °C; λ in nm; ε in x 10^4 M^{-1} cm^{-1}. The errors on λ and ε are given as ± 1 nm and 10%, respectively.			

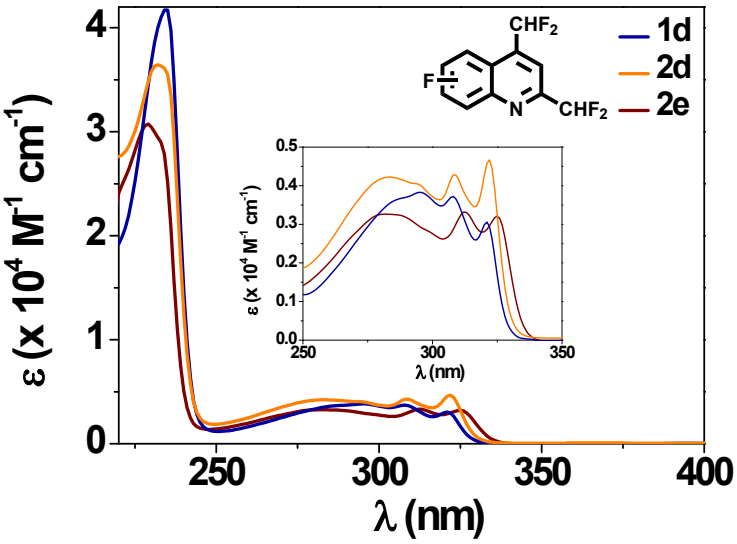


Figure S5. Change of absorption spectra as a function of the fluorine substitution position: C6 (**2d**) or C7 (**2e**) positions for a quinoline derivative bearing CHF_2 groups at both C2 and C4 positions (**1d** as a scaffold reference). Solvent: 1,2-dichloroethane, *T* = 25.0(2) °C. The inset shows a spectral expansion from 250 nm to 350 nm.

Table S3. Electronic absorption properties for a quinoline derivative (**1d**) substituted by fluorine group on either C6 (**2d**) or C7 (**2e**) positions and bearing CHF_2 groups at both C2 and C4 positions. Solvent: 1,2-dichloroethane, *T* = 25.0(2) °C.

Compound	Band III λ (ε)	Band I (^1L_b) λ (ε)	Band II (^1L_a) λ (ε)
1d	234 (4.172)		284 sh 295 (0.383) 308 (0.372) 321 (0.306)
2d	232 (3.645)		284 (0.422) 294 (0.403) 309 (0.428) 322 (0.467)
2e	229 (3.074)		282 (0.326) 288 sh 312 (0.331) 325 (0.321)
Solvent: 1,2-dichloroethane; *T* = 25 °C; λ in nm; ε in x 10^4 M^{-1} cm^{-1}. The errors on λ and ε are given as ± 1 nm and 10%, respectively.			

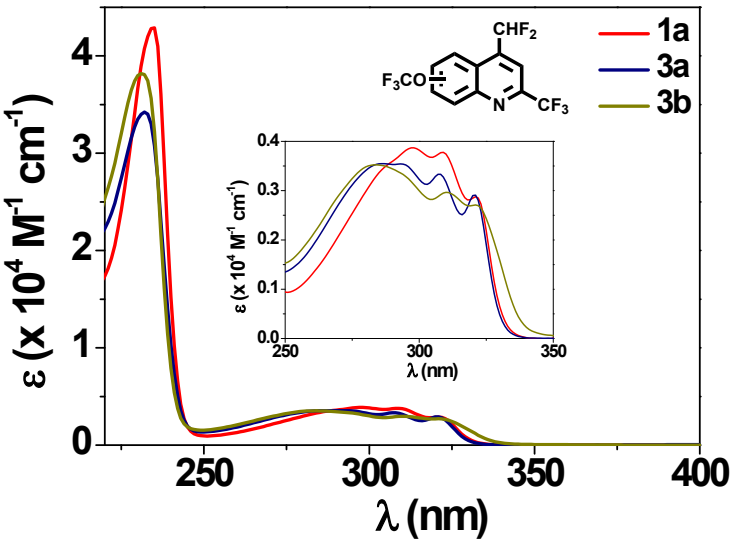


Figure S6. Change of absorption spectra as a function of the trifluoromethoxy group position: C6 (**3a**) or C7 (**3b**) positions of a quinoline derivative bearing a CF_3 group at C2 position and a CHF_2 group in C4 position (**1a** as a scaffold reference). Solvent: 1,2-dichloroethane, *T* = 25.0(2) °C. The inset shows a spectral expansion from 250 nm to 350 nm.

Table S4. Electronic absorption properties for a quinoline derivative (**1a**) substituted by a trifluoromethoxy group at either C6 (**3a**) or C7 (**3b**) positions and bearing a CF_3 group at C2 position and a CHF_2 group at C4 position. Solvent: 1,2-dichloroethane, *T* = 25.0(2) °C.

Compound	Band III λ (ε)	Band I (^1L_b) λ (ε)	Band II (^1L_a) λ (ε)
1a	235 (4.29)		287 (0.347) 298 (0.387) 309 (0.378) 321 (0.287)
3a	232 (3.422)		286 (0.355) 293 (0.354) 308 (0.333) 321 (0.291)
3b	232 (3.422)		284 (0.352) 310 (0.296) 321 (0.271)
Solvent: 1,2-dichloroethane; *T* = 25 °C; λ in nm; ε in x 10^4 M^{-1} cm^{-1}. The errors on λ and ε are given as ± 1 nm and 10%, respectively.			

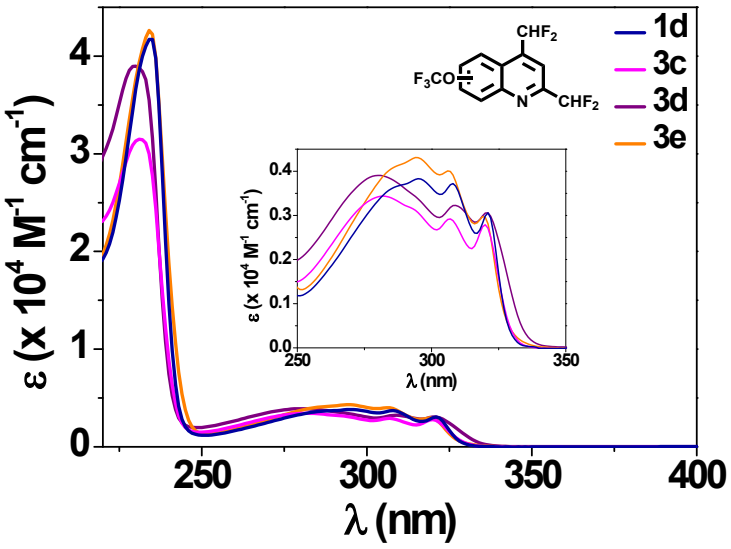


Figure S7. Change of absorption spectra as a function of the trifluoromethoxy group position: C6 (**3c**), C7 (**3d**) or C8 (**3e**) positions of a quinoline derivative bearing CHF_2 groups at both C2 and C4 positions (**1d** as a scaffold reference). Solvent: 1,2-dichloroethane, *T* = 25.0(2) °C. The inset shows a spectral expansion from 250 nm to 350 nm.

Table S5. Electronic absorption properties for a quinoline derivative (**1d**) substituted by a trifluoromethoxy group at either C6 (**3c**), C7 (**3d**) or C7 (**3e**) positions and bearing CHF_2 groups at both C2 and C4 positions. Solvent: 1,2-dichloroethane, *T* = 25.0(2) °C.

Compound	Band III λ (ε)	Band I (^1L_b) λ (ε)	Band II (^1L_a) λ (ε)
1d	234 (4.172)		284 sh 295 (0.383) 308 (0.372) 321 (0.306)
3c	231 (3.148)		282 (0.344) 293 sh 307 (0.292) 320 (0.279)
3d	230 (3.897)		280 (0.391) 294 sh 309 (0.323) 321 (0.306)
3e	234 (4.264)		284 sh 294 (0.431) 306 (0.401) 319 (0.297)
Solvent: 1,2-dichloroethane; *T* = 25 °C; λ in nm; ε in x 10^4 M^{-1} cm^{-1}. The errors on λ and ε are given as ± 1 nm and 10%, respectively.			

Table S6. Absorption properties of 6-substituted quinoline derivatives bearing a CF_3 at C2 position and a CHF_2 at C4 position.

Compound	Band III λ (ε)	Band I (^1L_b) λ (ε)	Band II (^1L_a) λ (ε)
1a	235 (4.29)		287 (0.347) 298 (0.387) 309 (0.378) 321 (0.287)
2a	233 (4.29)		283 (0.295) 295 (0.310) 309 (0.324) 322 (0.332)
3a	232 (3.42)		285 (0.354) 294 (0.354) 307 (0.333) 321 (0.291)
4a	247 (3.17)	287 (0.230) 330 (0.456) 340 (0.499)	440 (0.026)
5a	270 (2.8)	312 (0.664) 324 (0.723)	406 (0.740)
Solvent: 1,2-dichloroethane; *T* = 25 °C; λ in nm; ε in x 10^4 M^{-1} cm^{-1}. The errors on λ and ε are given as ± 1 nm and 10%, respectively.			

Table S7. ^{13}C NMR chemical shifts of 6-substituted quinoline derivatives bearing a CF_3 at C2 position and a CHF_2 at C4 position (**1a** series). Solvent: $CDCl_3$; T = 298 K.

Compound	^{13}C δ (ppm)							
	6-R	C_2	C_3	C_4	C_5	C_6	C_7	C_8
1a	H	147.94	114.14	140.33	123.44	130.06	131.39	131.29
2a	F	147.31	115.09	139.92	107.68	162.40	122.01	133.96
3a	OCF_3	148.41	115.36	140.46	113.97	149.50	125.35	133.66
4a	OMe	144.95	114.59	138.21	101.06	160.35	124.42	132.56
5a	NMe_2	142.35	114.48	136.12	98.92	150.28	120.46	131.80

Table S8. ^{13}C NMR chemical shifts of 6-substituted quinoline derivatives bearing CHF_2 at both C2 and C4 positions (**1d** series). Solvent: $CDCl_3$; T = 298 K.

Compound	^{13}C δ (ppm)							
	6-R	C_2	C_3	C_4	C_5	C_6	C_7	C_8
1d	H	152.70	114.24	139.93	123.55	129.33	130.91	130.83
2d	F	152.09	115.28	139.56	107.84	162.01	121.43	133.46
3c	OCF_3	153.23	115.56	140.06	114.32	148.97	124.89	133.17
4d	OMe	149.93	114.70	138.02	101.35	159.77	123.71	132.11
5b	NMe_2	147.42	114.64	136.29	99.55	149.96	120.03	131.36

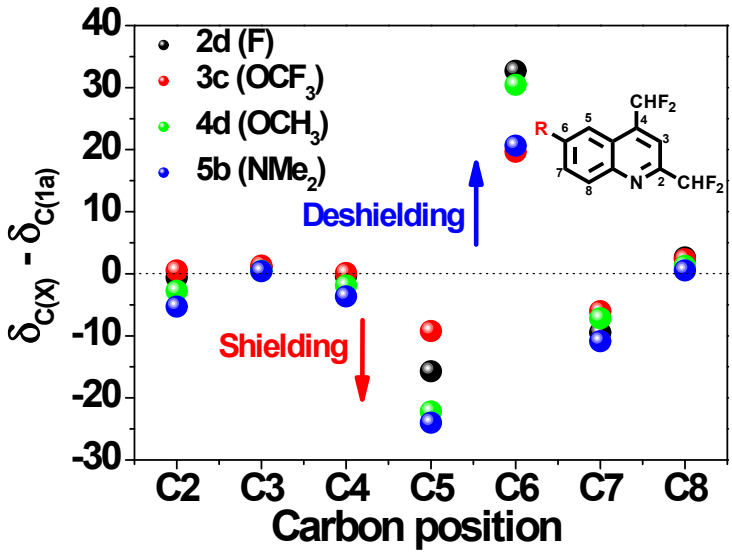


Figure S8. Variation of the ^{13}C NMR shifts of the quinoline carbons as a function of the nature of the substituent at position C6 for the **1d**-derived compounds series. Solvent: $CDCl_3$; *T* = 298 K.

Table S9. ^{13}C NMR chemical shifts of 7-substituted quinoline derivatives bearing CHF_2 at both C2 and C4 positions (**1d** series). Solvent: $CDCl_3$; T = 298 K.

Compound	^{13}C δ (ppm)							
	7-R	**C_2**	**C_3**	**C_4**	**C_5**	**C_6**	**C_7**	**C_8**
1d	H	152.70	114.24	139.93	123.55	129.33	130.91	130.83
2e	F	153.93	113.86	140.17	126	119.91	163.60	114.58
3d	OCF_3	154.12	114.72	140.14	125.76	123.13	150.58	120.02
4e	OMe	152.86	111.80	139.56	124.33	122.45	161.45	108.24
5c	NMe_2	152.95	109.73	139.30	124.08	107.26	151.69	118.49

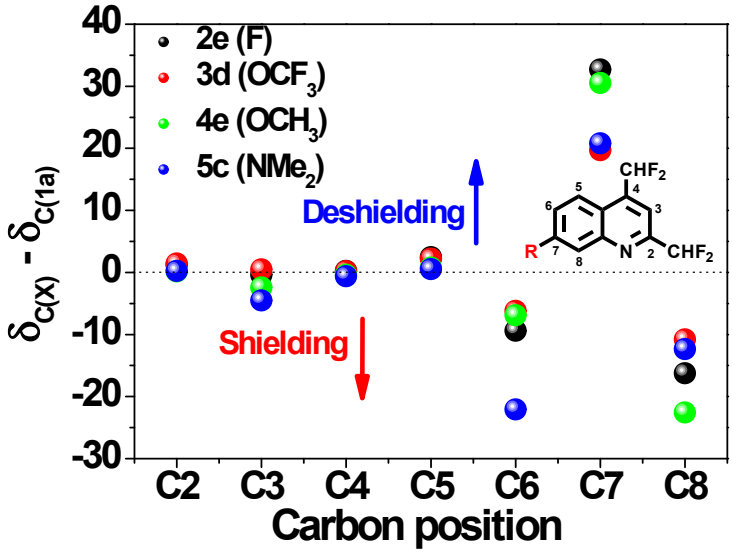


Figure S9. Variation of the ^{13}C NMR shifts of the quinoline carbons as a function of the nature of the substituent at position C7 for the **1d**-derived compounds series. Solvent: $CDCl_3$; *T* = 298 K.

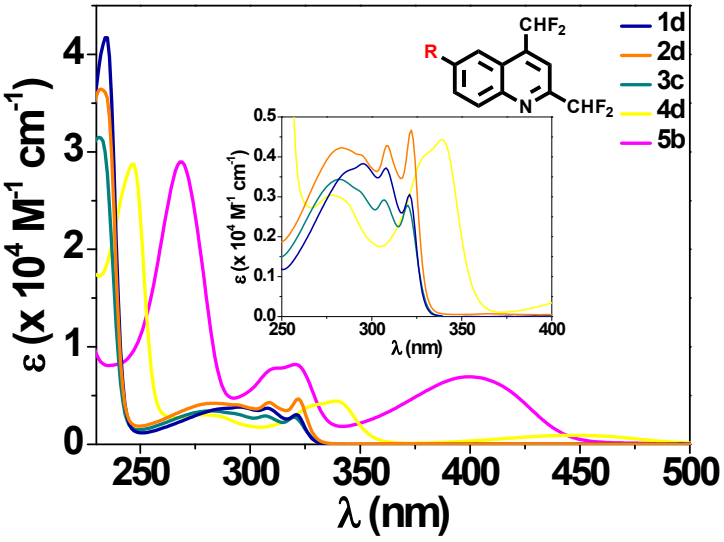


Figure S10. Change in the absorption spectra as a function of the nature of the substituent at the C6 position (**2d** = F, **3c** = OCF_3, **4d** = OCH_3, **5b** = NMe_2) for a quinoline derivative bearing CHF_2 groups in both C2 and C4 positions (**1d** as a scaffold reference). Solvent: 1,2-dichloroethane, *T* = 25.0(2) °C. The inset shows a spectral expansion from 250 nm to 400 nm.

Table S10. Electronic absorption properties for 6-substituted quinoline derivatives (**2d** = F, **3c** = OCF_3, **4d** = OCH_3, **5b** = NMe_2) bearing CHF_2 groups at both C2 and C4 positions. Solvent: 1,2-dichloroethane, *T* = 25.0(2) °C.

Compound	Band III λ (ε)	Band I (^1L_b) λ (ε)	Band II (^1L_a) λ (ε)
1d	234 (4.172)		284 sh 295 (0.383) 308 (0.372) 321 (0.306)
2d	232 (3.645)		284 (0.422) 294 (0.403) 309 (0.428) 322 (0.467)
3c	231 (3.140)		282 (0.344) 293 sh 307 (0.292) 320 (0.277)
4d	247 (2.874)	277 (0.303) 329 (0.402) 339 (0.443)	446 (0.093)
5b	269 (2.897)	311 (0.778) 321 (0.820)	400 (0.693)
Solvent: 1,2-dichloroethane; *T* = 25 °C; λ in nm; ε in x 10^4 M^{-1} cm^{-1}. The errors on λ and ε are given as ± 1 nm and 10%, respectively.			

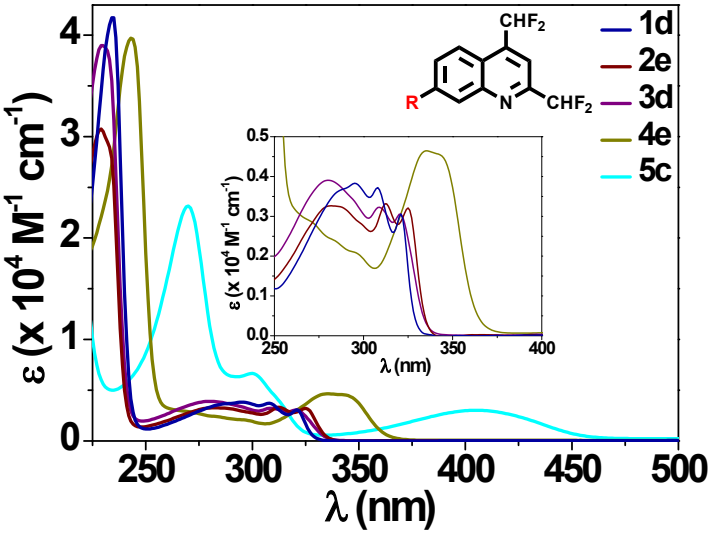


Figure S11. Change in the absorption spectra as a function of the nature of the substituent at the C7 position (**2e** = F, **3d** = OCF_3, **4e** = OCH_3, **5c** = NMe_2) for a quinoline derivative bearing CHF_2 groups at both C2 and C4 positions (**1d** as a scaffold reference). Solvent: 1,2-dichloroethane, *T* = 25.0(2) °C. The inset shows a spectral expansion from 250 nm to 400 nm.

Table S11. Electronic absorption properties for 7-substituted quinoline derivatives (**2e** = F, **3d** = OCF_3, **4e** = OCH_3, **5c** = NMe_2) bearing CHF_2 groups at both C2 and C4 positions. Solvent: 1,2-dichloroethane, *T* = 25.0(2) °C.

Compound	Band III λ (ε)	Band I (^1L_b) λ (ε)	Band II (^1L_a) λ (ε)
1d	234 (4.172)		284 sh 295 (0.383) 308 (0.372) 321 (0.306)
2e	229 (3.074)		282 (0.326) 289 sh 312 (0.331) 325 (0.321)
3d	230 (3.896)		280 (0.391) 295 sh 309 (0.323) 321 (0.306)
4e	243 (3.968)	271 sh 295 sh 335 (0.464) 342 (0.456)	-
5c	270 (2.316)	300 (0.665) 313 sh	405 (0.303)
Solvent: 1,2-dichloroethane; *T* = 25 °C; λ in nm; ε in x 10^4 M^{-1} cm^{-1}. The errors on λ and ε are given as ± 1 nm and 10%, respectively.			

Spectrofluorimetric Studies

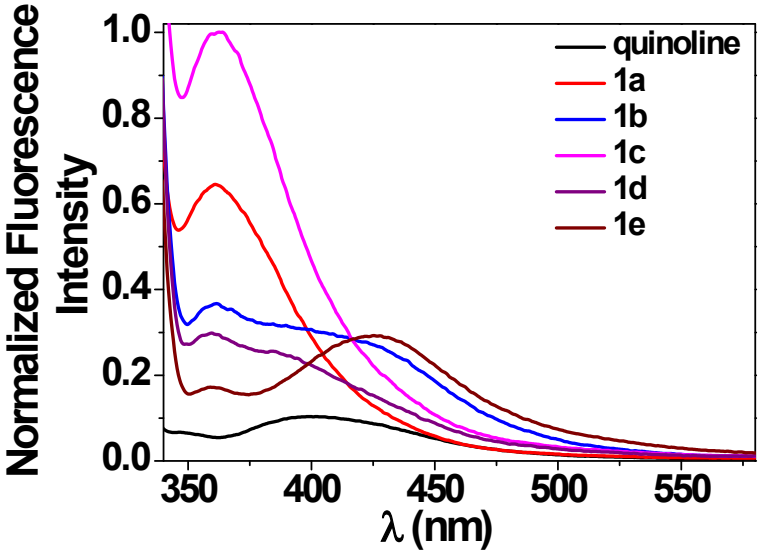


Figure S12. Fluorescence emission spectra of fluorinated (CHF_2, CHFCl, CF_3 or $CHFCF_3$) quinolines substituted at C2 and C4 positions (**1a**, **1b**, **1c**, **1d** and **1e**, see Scheme S1 for the corresponding chemical structures). Solvent: 1,2-dichloroethane; *T* = 25 °C. Emission and excitation band widths = 15 and 20 nm, respectively. The emission intensities have been normalized with respect to the absorbances of the quinoline solutions and therefore reflect the relative emission quantum yields. The absorbances at excitation wavelength are always below 0.1 to prevent inner filter effects.

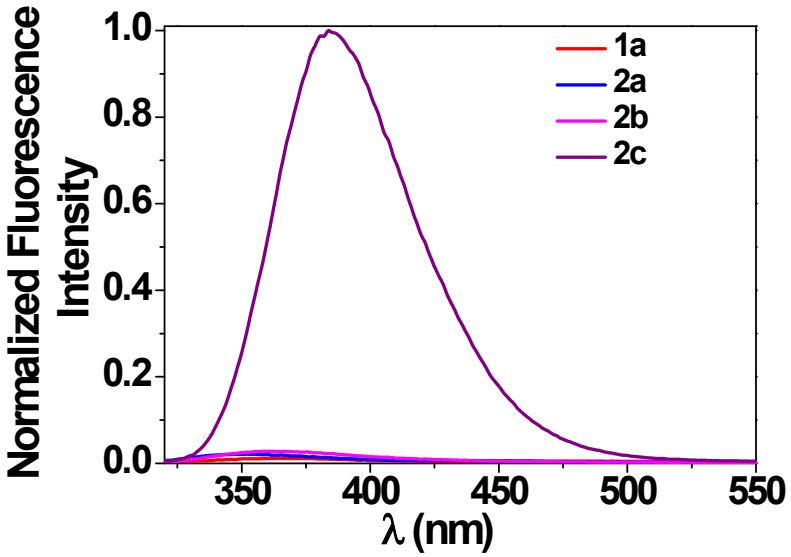


Figure S13. Influence on the emission spectra of fluorine substitution on either C6 (**2a**), C7 (**2b**) or C8 (**2c**) positions of a quinoline derivative bearing a CHF_2 group at C2 and a CF_3 group at C4 position (**1a** as a scaffold reference). Solvent: 1,2-dichloroethane; *T* = 25 °C. Emission and excitation band widths = 15 and 20 nm, respectively; band-pass filter at 290 nm; 1% attenuator. The emission intensities have been normalized with respect to the absorbances of the quinoline solutions (λ_{exc} = 300 nm) and therefore reflect the relative emission quantum yields. The absorbances at excitation wavelength are always below 0.1 to prevent inner filter effects.

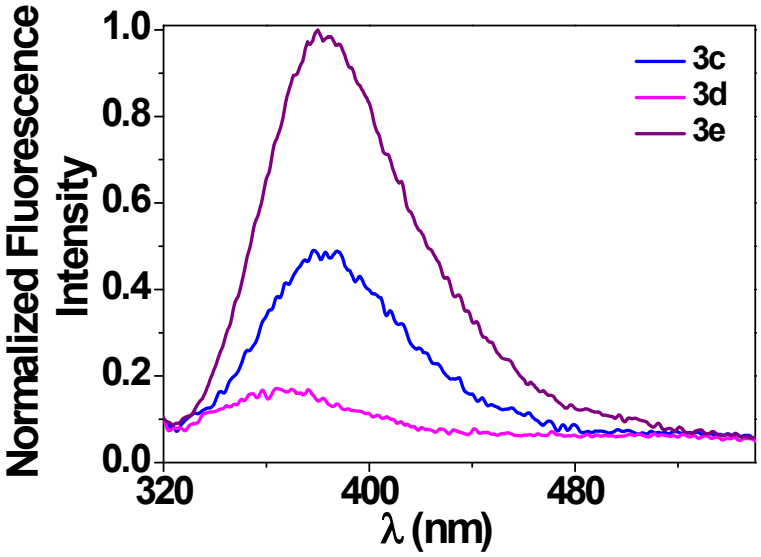


Figure S14. Influence on the emission spectra of trifluoromethoxy substitution on either C6 (**3c**), C7 (**3d**) or C8 (**3e**) positions of a quinoline derivative bearing a CHF_2 group at both C2 and C4 positions (**1d** as a scaffold reference). Solvent: 1,2-dichloroethane; *T* = 25 °C. Emission and excitation band widths = 15 and 20 nm, respectively; band-pass filter at 290 nm; 1% attenuator. The emission intensities have been normalized with respect to the absorbances of the quinoline solutions (λ_{exc} = 300 nm) and therefore reflect the relative emission quantum yields. The absorbances at excitation wavelength are always below 0.1 to prevent inner filter effects.

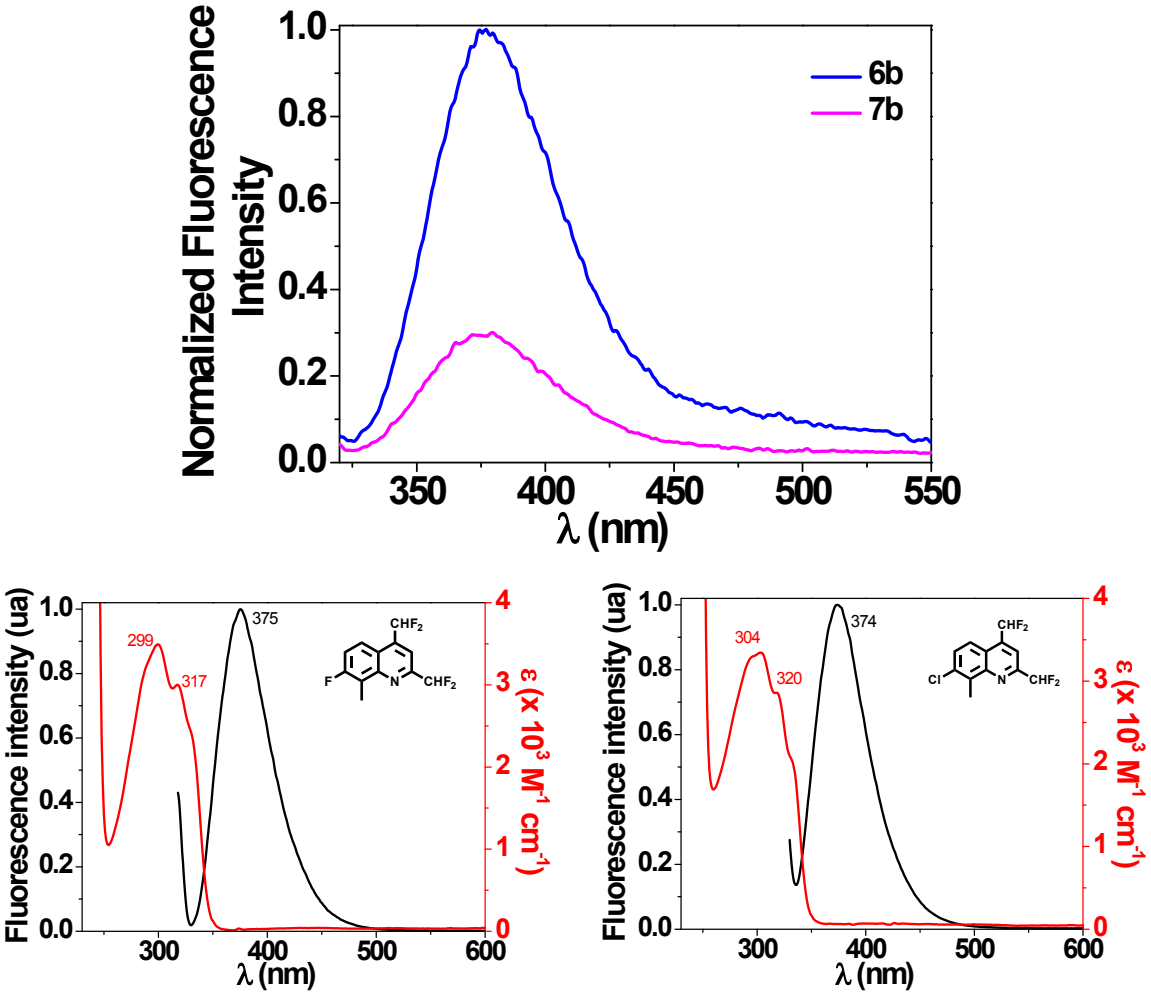


Figure S15. Influence on the emission spectra of the C7- and C8-substitution (**6b**, C7 = F, C8 = CH_3; **7b**, C7 = Cl, C8 = CH_3) of a quinoline derivative bearing CHF_2 groups at both C2 and C4 positions (**1d** as a scaffold reference). Solvent: 1,2-dichloroethane; *T* = 25 °C. Emission and excitation band widths = 15 and 20 nm, respectively; band-pass filter at 290 nm; 1% attenuator. The emission intensities have been normalized with respect to the absorbances of the quinoline (λ_{exc} = 300 nm) solutions and therefore reflect the relative emission quantum yields. The absorbances at excitation wavelength are always below 0.1 to prevent inner filter effects.

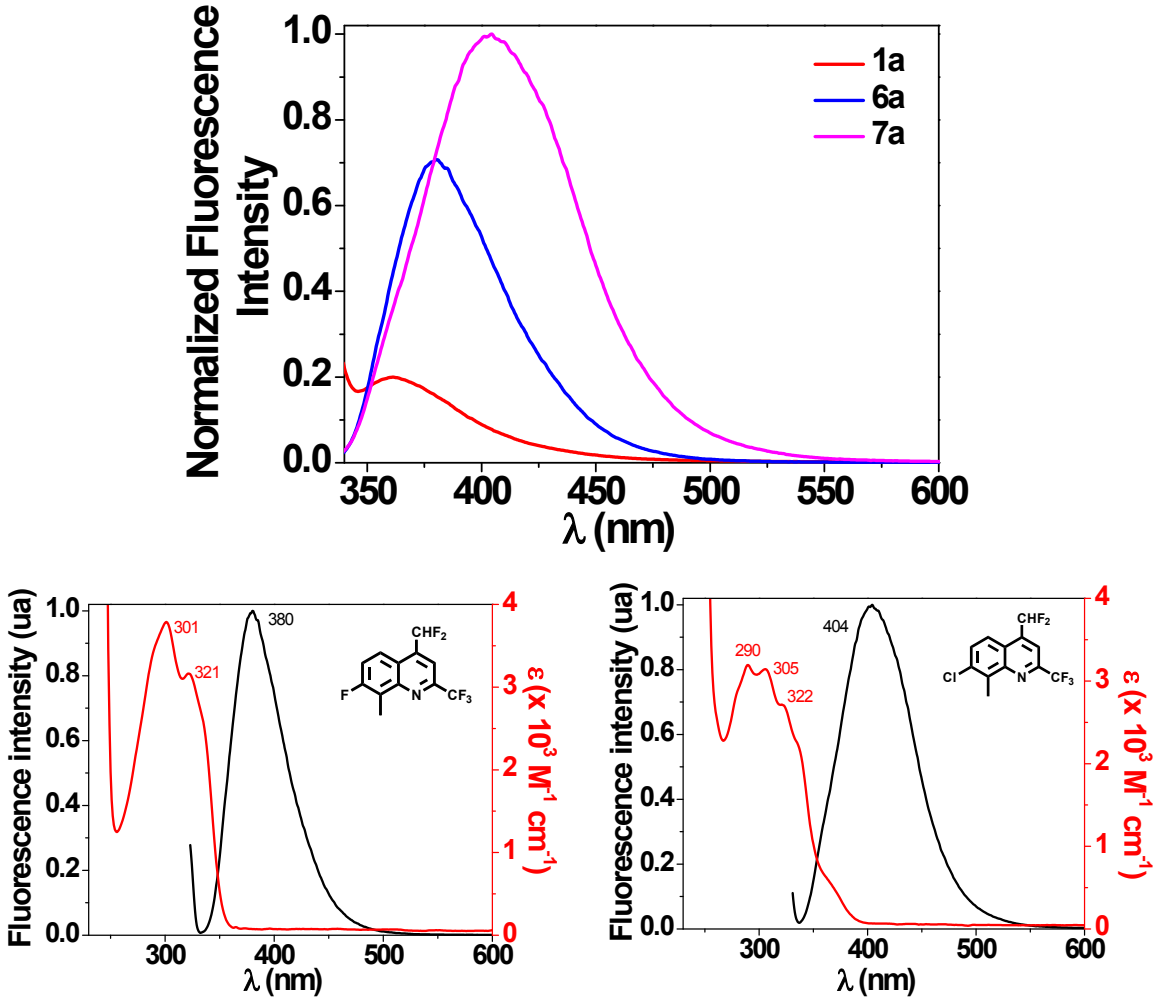


Figure S16. Influence on the emission spectra of the C7- and C8-substitution (**6a**, C7 = F, C8 = CH_3; **7a**, C7 = Cl, C8 = CH_3) of a quinoline derivative bearing a CHF_2 group at C2 position and a CF_3 group at C4 position (**1a** as a scaffold reference). Solvent: 1,2-dichloroethane; *T* = 25 °C. Emission and excitation band widths = 15 and 20 nm, respectively. The emission intensities have been normalized with respect to the absorbances of the quinoline solutions and therefore reflect the relative emission quantum yields. The absorbances at excitation wavelength are always below 0.1 to prevent inner filter effects.

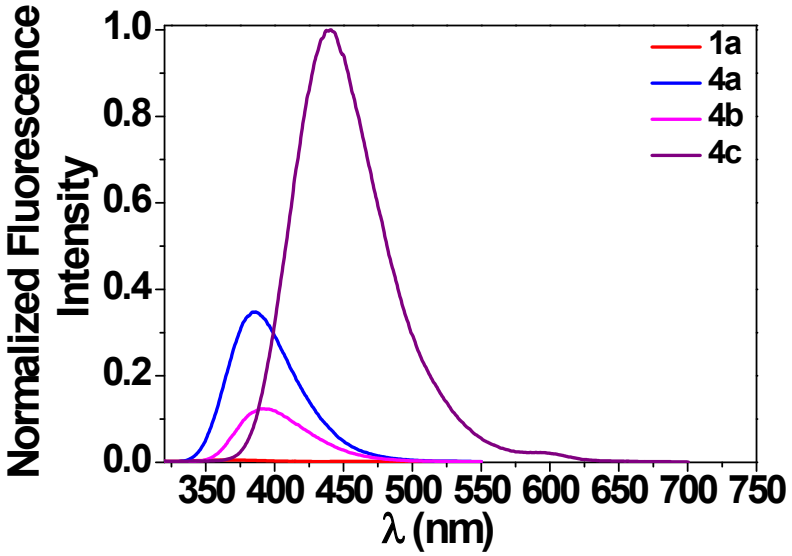


Figure S17. Influence on the emission spectra of methoxy substitution on either C6 (**4a**), C7 (**4b**) or C8 (**4c**) positions of a quinoline derivative bearing a CHF_2 group at C2 and a CF_3 group at C4 positions (**1a** as a scaffold reference). Solvent: 1,2-dichloroethane; *T* = 25 °C. Emission and excitation band widths = 15 and 20 nm, respectively; band-pass filter at 290 nm; 1% attenuator. The emission intensities have been normalized with respect to the absorbances of the quinoline (λ_{exc} = 300 nm) solutions and therefore reflect the relative emission quantum yields. The absorbances at excitation wavelength are always below 0.1 to prevent inner filter effects.

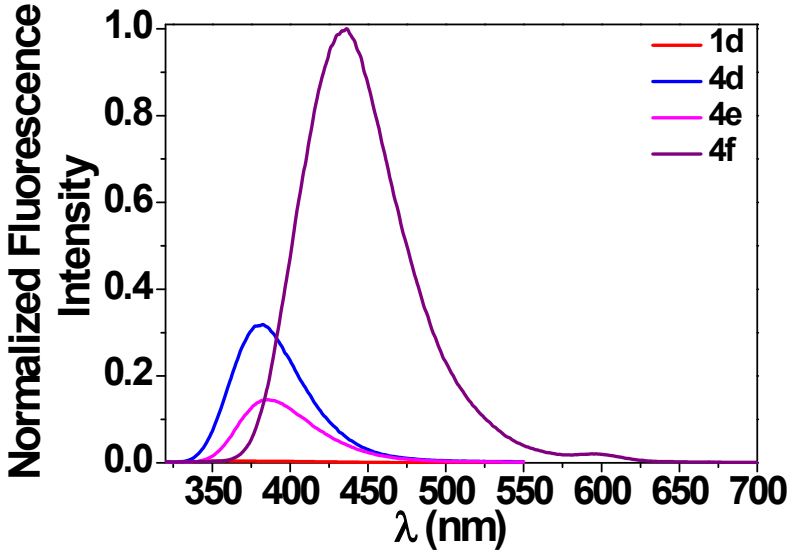


Figure S18. Influence on the emission spectra of methoxy substitution on either C6 (**4d**), C7 (**4e**) or C8 (**4f**) positions of a quinoline derivative bearing a CHF_2 group at both C2 and C4 positions (**1d** as a scaffold reference). Solvent: 1,2-dichloroethane; *T* = 25 °C. Emission and excitation band widths = 15 and 20 nm, respectively; band-pass filter at 290 nm; 1% attenuator. The emission intensities have been normalized with respect to the absorbances of the quinoline (λ_{exc} = 300 nm) solutions and therefore reflect the relative emission quantum yields. The absorbances at excitation wavelength are always below 0.1 to prevent inner filter effects.

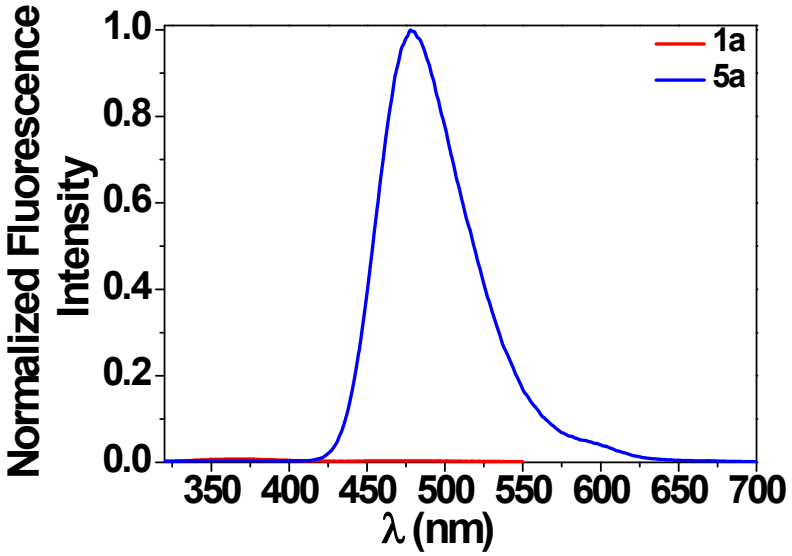


Figure S19. Influence on the emission spectra of dimethylamino substitution on the C6 (**5a**) position of a quinoline derivative bearing a CHF_2 group at C2 and a CF_3 group at C4 positions (**1a** as a scaffold reference). Solvent: 1,2-dichloroethane; *T* = 25 °C. Emission and excitation band widths = 15 and 20 nm, respectively; band-pass filter at 290 nm; 1% attenuator. The emission intensities have been normalized with respect to the absorbances of the quinoline (λ_{exc} = 300 nm) solutions and therefore reflect the relative emission quantum yields. The absorbances at excitation wavelength are always below 0.1 to prevent inner filter effects.

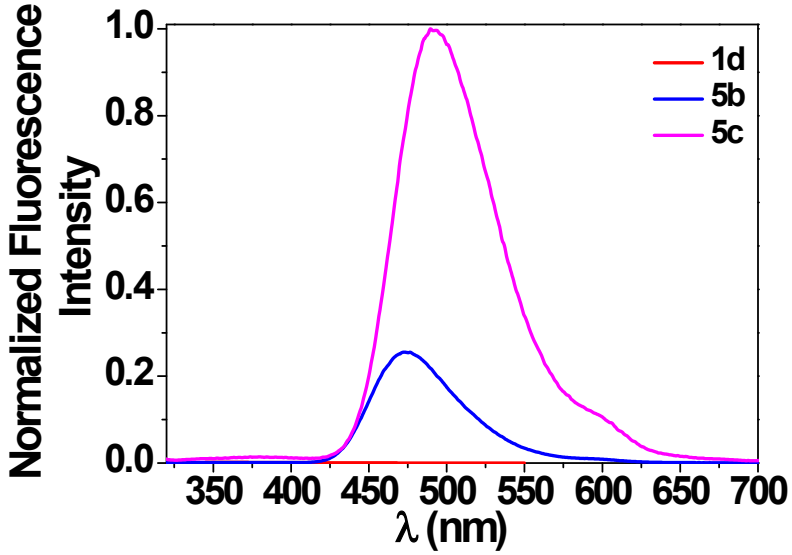


Figure S20. Influence on the emission spectra of dimethylamino substitution on either C6 (**5b**), C7 (**5c**) positions of a quinoline derivative bearing a CHF_2 group at both C2 and C4 positions (**1d** as a scaffold reference). Solvent: 1,2-dichloroethane; *T* = 25 °C. Emission and excitation band widths = 15 and 20 nm, respectively; band-pass filter at 290 nm; 1% attenuator. The emission intensities have been normalized with respect to the absorbances of the quinoline (λ_{exc} = 300 nm) solutions and therefore reflect the relative emission quantum yields. The absorbances at excitation wavelength are always below 0.1 to prevent inner filter effects.

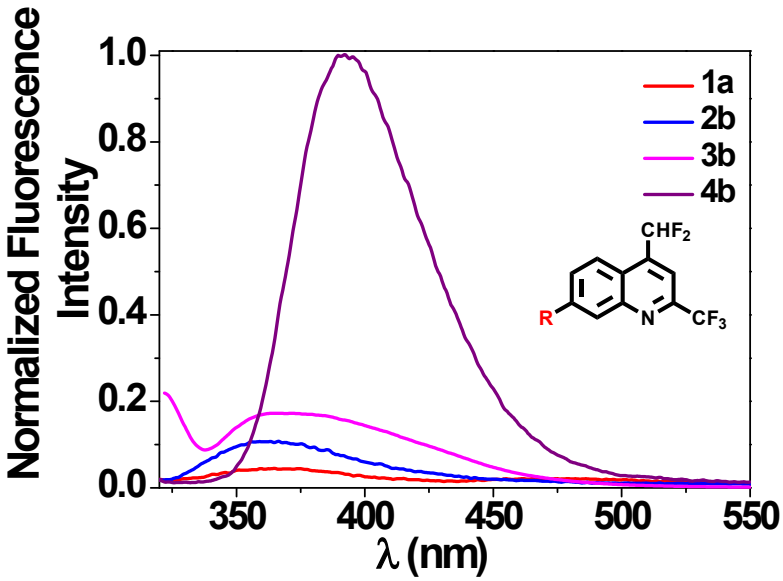


Figure S21. Influence on the emission spectra of the substitution on the C7 position for quinoline derivatives bearing a CF_3 at C2 and a CHF_2 at C4 positions (derivative **1a** as a scaffold reference). Solvent: 1,2-dichloroethane, *T* = 25.0(2) °C. Emission and excitation band widths = 15 and 20 nm, respectively; band-pass filter at 290 nm; 1% attenuator. The emission intensities have been normalized with respect to the absorbances of the quinoline (λ_{exc} = 300 nm) solutions and therefore reflect the relative emission quantum yields. The absorbances at excitation wavelength are always below 0.1 to prevent inner filter effects.

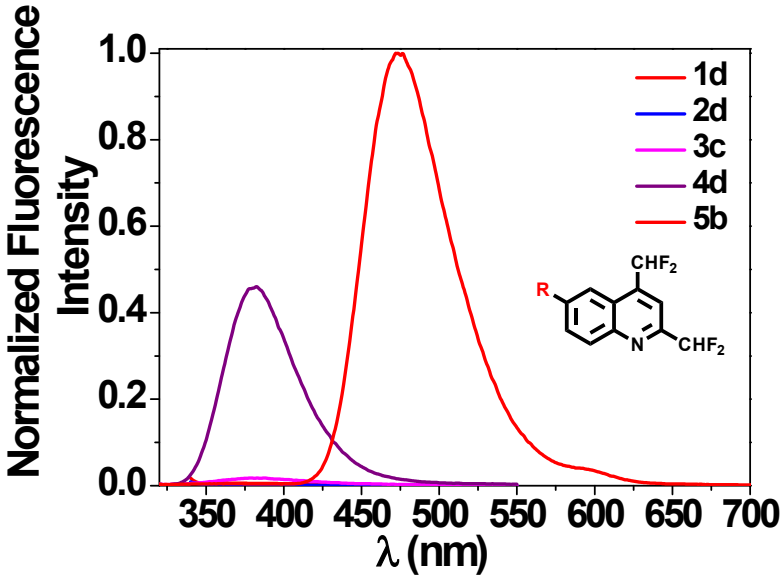


Figure S22. Influence on the emission spectra of the substitution on the C6 position for quinoline derivatives bearing a CHF_2 group at both C2 and C4 positions (derivative **1d** as a scaffold reference). Solvent: 1,2-dichloroethane, *T* = 25.0(2) °C. Emission and excitation band widths = 15 and 20 nm, respectively; band-pass filter at 290 nm; 1% attenuator. The emission intensities have been normalized with respect to the absorbances of the quinoline (λ_{exc} = 300 nm) solutions and therefore reflect the relative emission quantum yields. The absorbances at excitation wavelength are always below 0.1 to prevent inner filter effects.

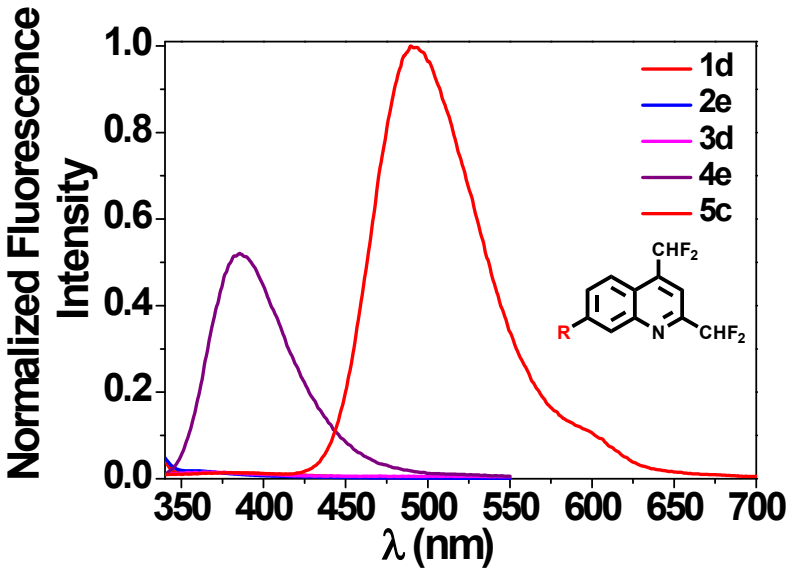


Figure S23. Influence on the emission spectra of the substitution on the C7 position for quinoline derivatives bearing CHF_2 at both C2 and C4 positions (derivative **1d** as a scaffold reference). Solvent: 1,2-dichloroethane, *T* = 25.0(2) °C. Emission and excitation band widths = 15 and 20 nm, respectively; band-pass filter at 290 nm; 1% attenuator. The emission intensities have been normalized with respect to the absorbances of the quinoline (λ_{exc} = 300 nm) solutions and therefore reflect the relative emission quantum yields. The absorbances at excitation wavelength are always below 0.1 to prevent inner filter effects.

CV Electrochemical Studies

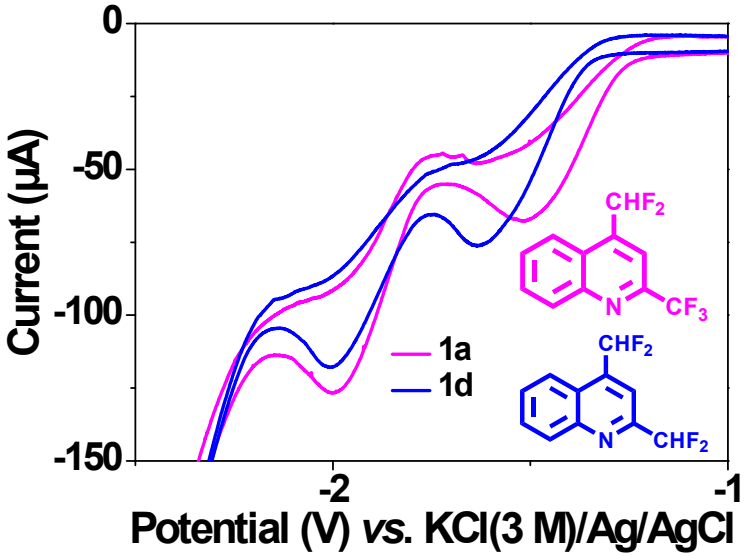


Figure S24. Cyclic voltammograms of **1a** and **1d** measured at a sweep rate of 200 mV s^{-1}. Solvent: 1,2-dichloroethane; *T* = 25.0(2) °C; *I* = 0.1 M (NBu_4BF_4); reference electrode = KCl(3 M)/Ag/AgCl; working electrode = glassy carbon disk of 0.07 cm^2 area. The compounds concentrations are about 1 mM.

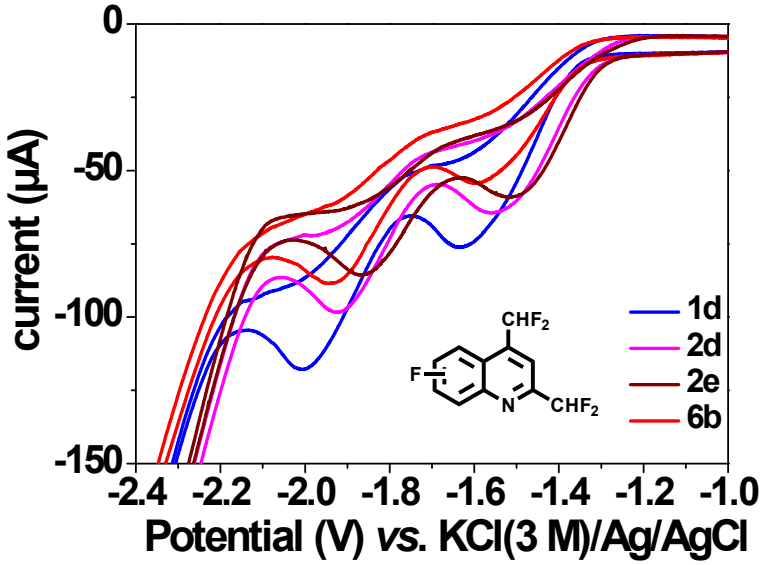


Figure S25. Influence on the cyclic voltammograms of the fluorine substitution at the C6 (**2d**) and C7 (**2e**) positions of a quinoline derivative bearing CHF_2 groups at both C2 and C4 positions (**1d** as a scaffold reference) as well as the introduction of a methyl group at the C8 position (**6b**). *v* = 200 mV s^{-1}; solvent: 1,2-dichloroethane; *T* = 25.0(2) °C; *I* = 0.1 M (NBu_4BF_4); reference electrode = KCl(3 M)/Ag/AgCl; working electrode = glassy carbon disk of 0.07 cm^2 area. The compounds concentrations are about 1 mM.

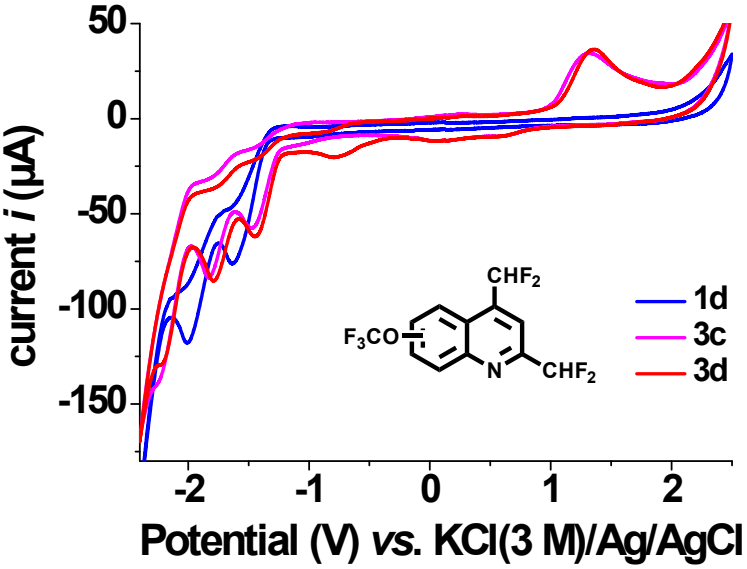


Figure S26. Influence on the cyclic voltammograms of the trifluoromethoxy substitution at the C6 (**3c**) and C7 (**3d**) positions of a quinoline derivative bearing CHF_2 groups at both C2 and C4 positions (**1d** as a scaffold reference). *v* = 200 mV s^{-1}; solvent: 1,2-dichloroethane; *T* = 25.0(2) °C; *I* = 0.1 M (NBu_4BF_4); reference electrode = KCl(3 M)/Ag/AgCl; working electrode = glassy carbon disk of 0.07 cm^2 area. The compounds concentrations are about 1 mM.

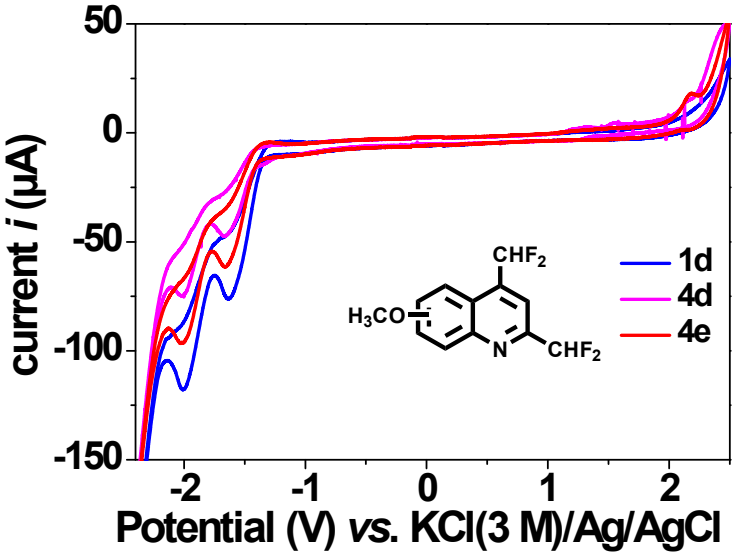


Figure S27. Influence on the cyclic voltammograms of the methoxy substitution at the C6 (**4d**) and C7 (**4e**) positions of a quinoline derivative bearing CHF_2 groups at both C2 and C4 positions (**1d** as a scaffold reference). *v* = 200 mV s^{-1}; solvent: 1,2-dichloroethane; *T* = 25.0(2) °C; *I* = 0.1 M (NBu_4BF_4); reference electrode = KCl(3 M)/Ag/AgCl; working electrode = glassy carbon disk of 0.07 cm^2 area. The compounds concentrations are about 1 mM.

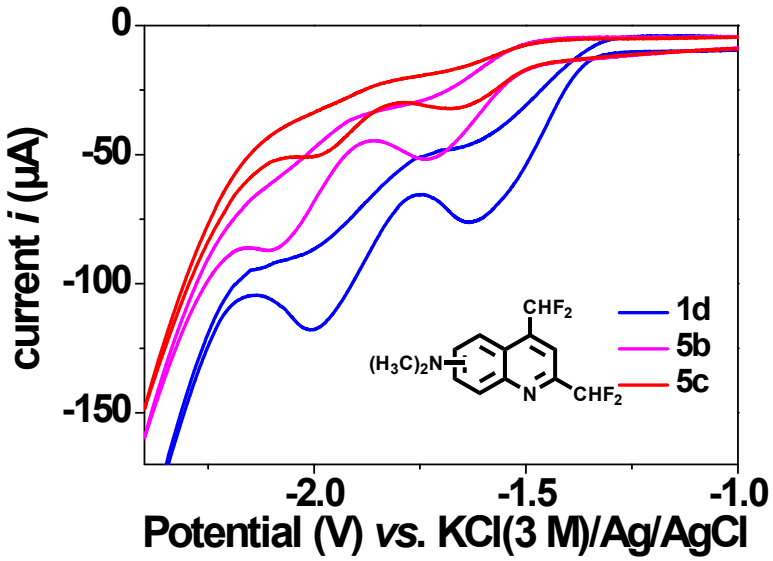


Figure S28. Influence on the cyclic voltammograms of the dimethylamino substitution at the C6 (**5b**) and C7 (**5c**) positions of a quinoline derivative bearing CHF_2 groups at both C2 and C4 positions (**1d** as a scaffold reference). v = 200 mV s^{-1}; solvent: 1,2-dichloroethane; T = 25.0(2) °C; I = 0.1 M (NBu_4BF_4); reference electrode = KCl(3 M)/Ag/AgCl; working electrode = glassy carbon disk of 0.07 cm^2 area. The compounds concentrations are about 1 mM.

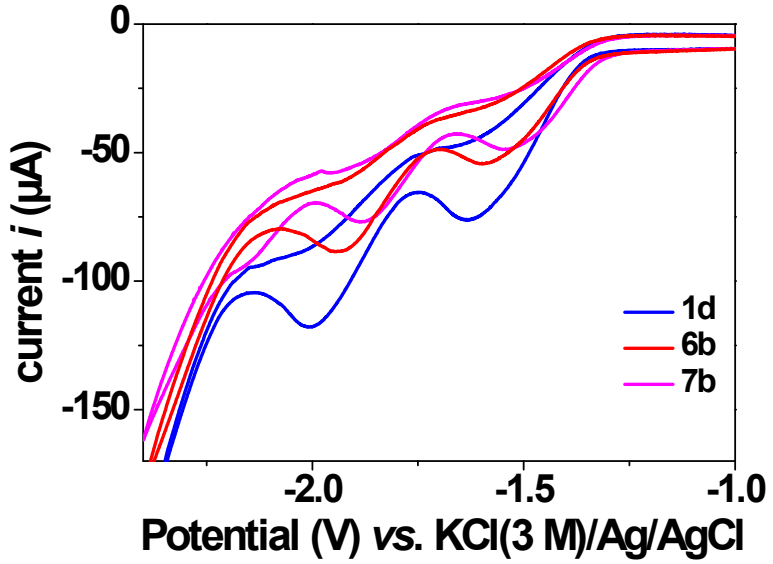
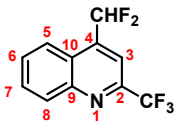


Figure S29. Influence on the cyclic voltammograms of the halogen substitution (F, **6b** and Cl, **7b**) at the C6 positions of a quinoline derivative bearing CHF_2 groups at both C2 and C4 positions and a CH_3 group at the C8 position (**1d** as a scaffold reference). v = 200 mV s^{-1}; solvent: 1,2-dichloroethane; T = 25.0(2) °C; I = 0.1 M (NBu_4BF_4); reference electrode = KCl(3 M)/Ag/AgCl; working electrode = glassy carbon disk of 0.07 cm^2 area. The compounds concentrations are about 1 mM.

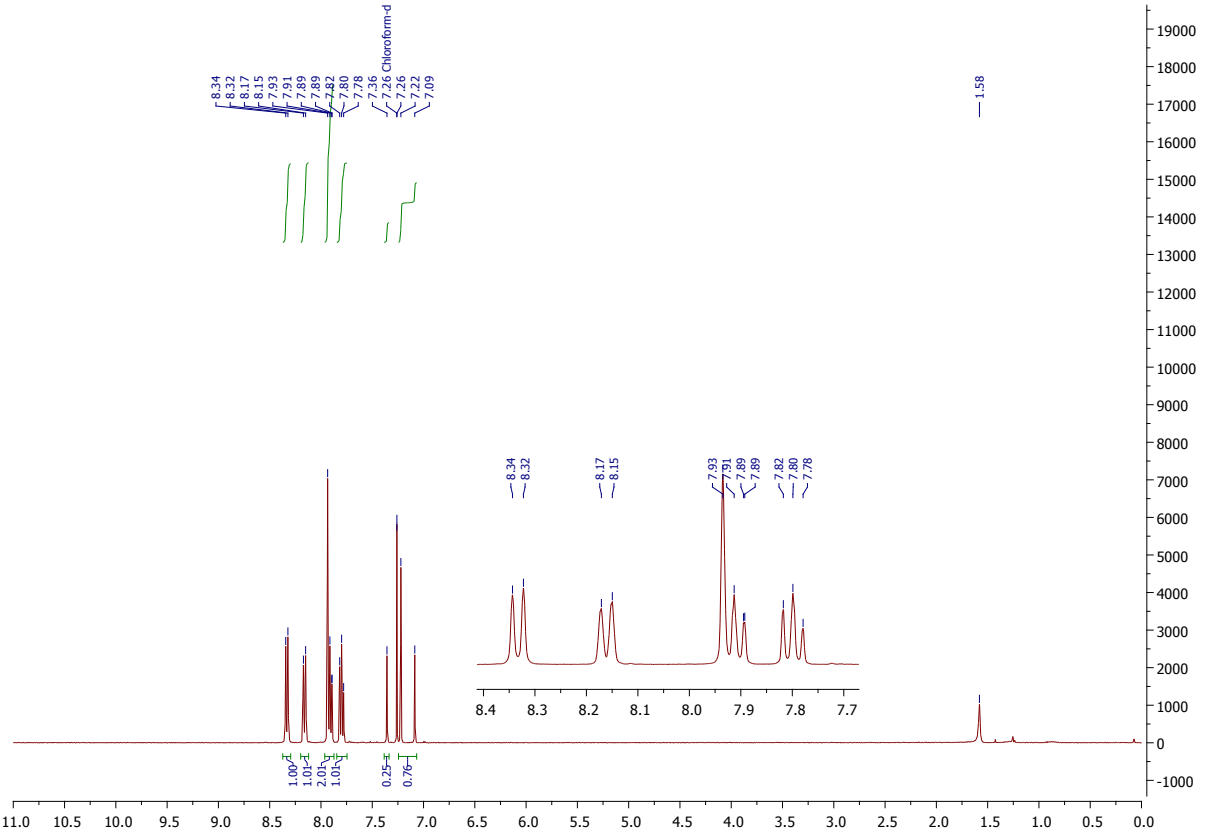
Figure S30. NMR (^{1}H, ^{13}C and ^{19}F) and characterization data of compound **1a**.

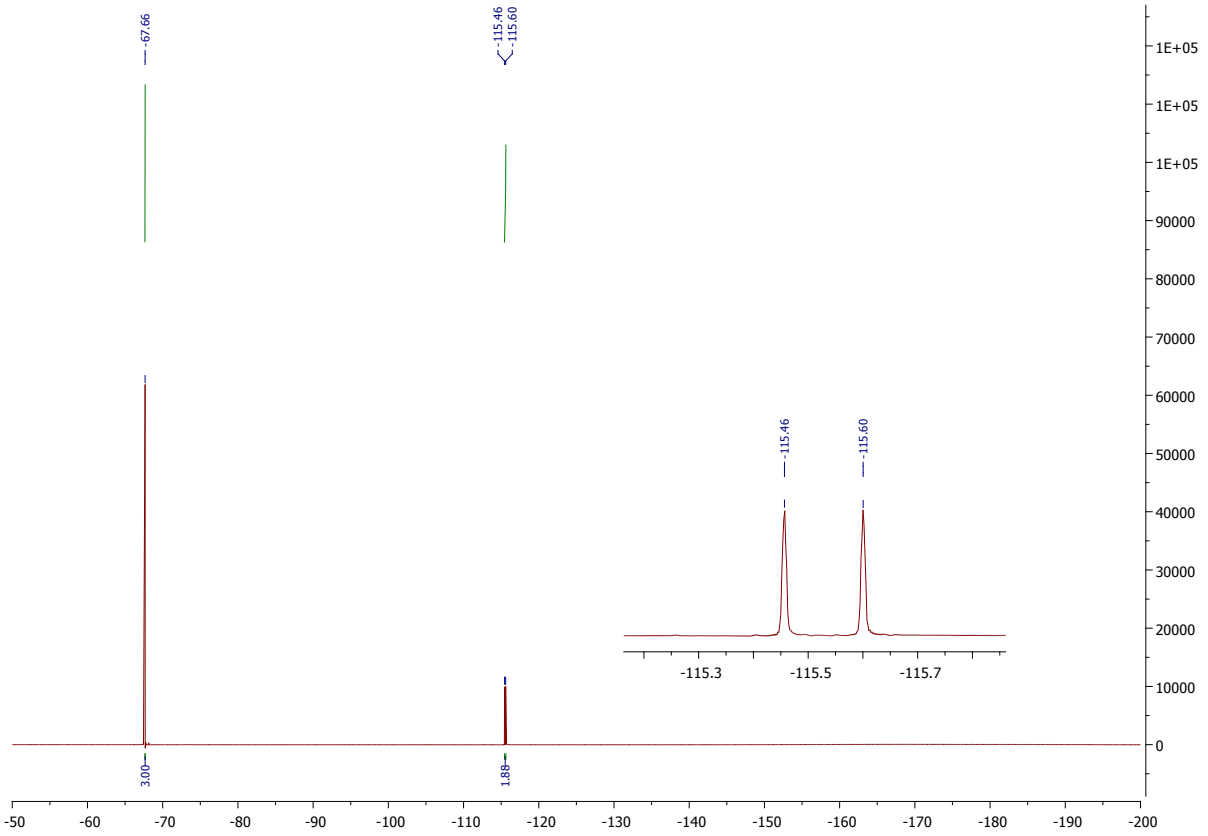
4-(Difluoromethyl)-2-(trifluoromethyl)quinoline 1a



1a
Chemical Formula: $C_{11}H_6F_5N$
Exact Mass: 247,04 g/mol
Yellow solid

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.33 (d, $^{3}J_{H-H}$ = 8.5 Hz, 1H, C_8H), 8.16 (d, $^{3}J_{H-H}$ = 8.5 Hz, 1H, C_5H), 7.93 (s, 1H, C_3H), 7.92 – 7.87 (m, 1H, C_7H), 7.80 (t, $^{3}J_{H-H}$ = 7.7 Hz, 1H, C_6H), 7.22 (t, $^{2}J_{H-F}$ = 54.2 Hz, 1H, C_4CHF_2) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -67.66 (s, C_2CF_3), -115.53 (d, $^{2}J_{F-H}$ = 54.1 Hz, C_4CHF_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 147.94 (q, $^{2}J_{C-F}$ = 35.3 Hz, C_2), 147.87 (t, C_9), 140.33 (t, $^{2}J_{C-F}$ = 22.3 Hz, C_4), 131.39 (s, C_7), 131.29 (s, C_8), 130.06 (s, C_6), 125.09 (s, C_{10}), 123.44 (s, C_5), 121.33 (q, $^{1}J_{C-F}$ =275.73Hz, C_2CF_3), 114.14 (td, $^{3}J_{C-F}$ = 7.9, $^{3}J_{C-F}$ = 2.1 Hz, C_3), 112.74 (t, $^{1}J_{C-F}$ = 241.5 Hz, C_4CHF_2) ppm. HRMS (ESI positive) for $C_{11}H_7F_5N$ [M^+]: calcd 248.0493, found 248.0520. $C_{11}H_6F_5N$ (247): calcd (%) N 5.66, C 53.40, H 2.43, found N 5.73, C 53.83, H 2.58. MP: 64 – 65.1 °C.

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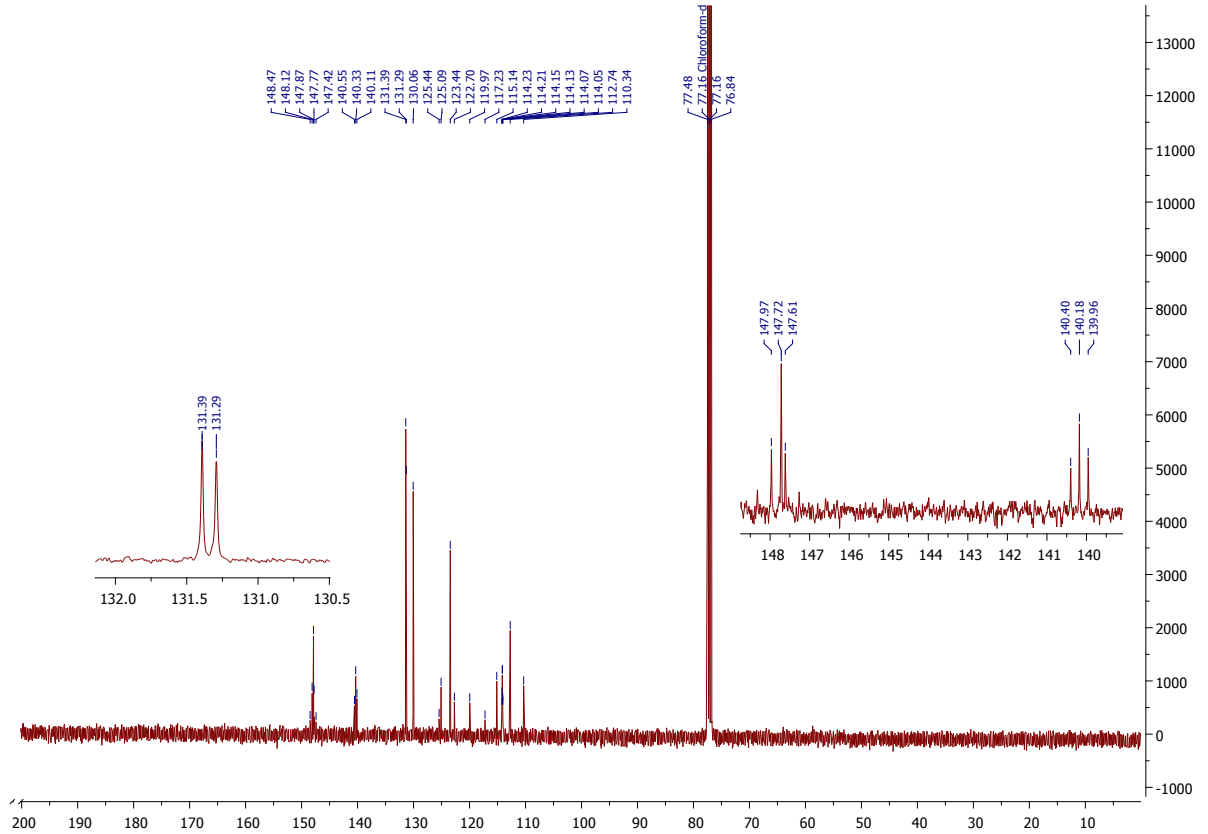
-115.46
-115.60
-115.3
-115.5
-115.7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147.77
147.42
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140.11
131.39
131.29
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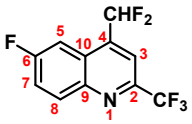
123.44
122.70
119.97
117.23
115.14
114.23
114.21
114.15
114.13
114.07
114.05
112.74
110.34
77.48
77.16 Chloroform-d
77.16
76.84
147.97
147.72
147.61
140.40
140.18
139.96
131.39
131.29
132.0
131.5
131.0
130.5
148
147
146
145
144
143
142
141
140

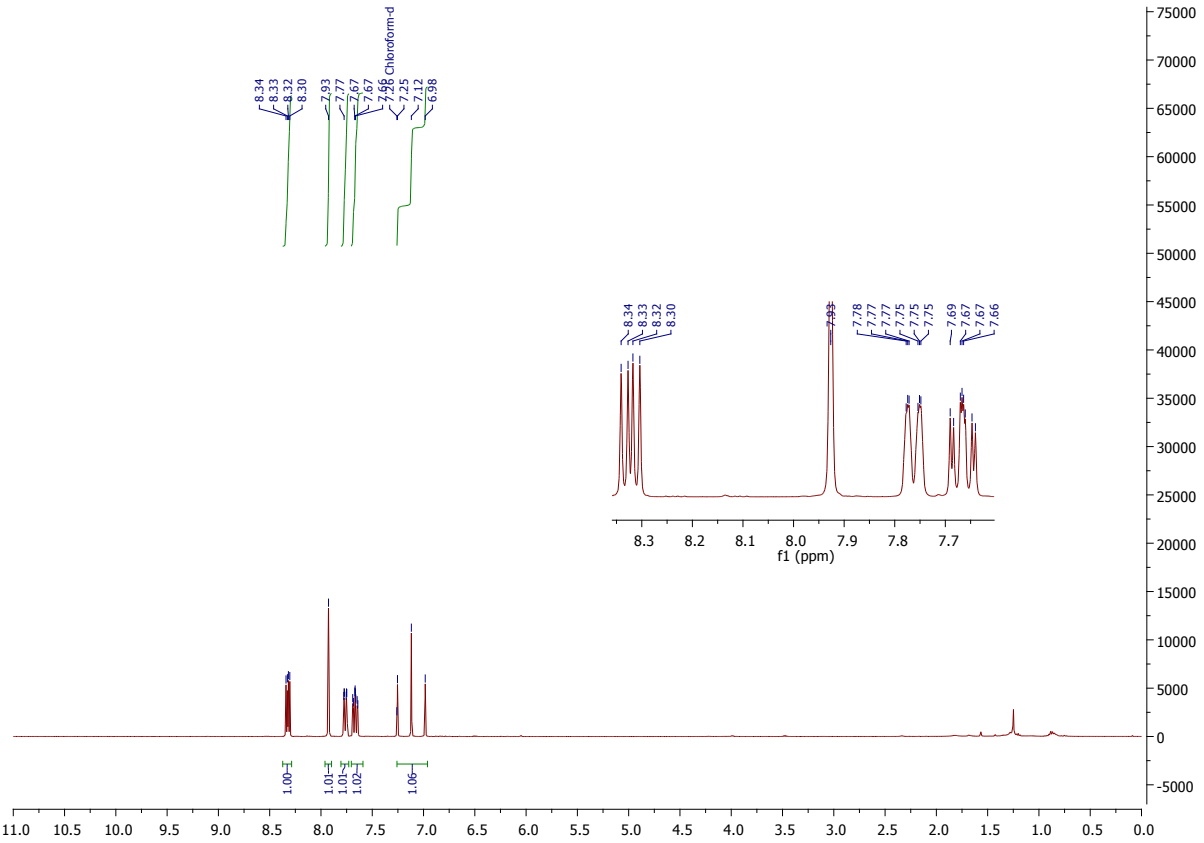
Figure S31. NMR (^{1}H, ^{13}C and ^{19}F) and characterization data of compound **2a**.

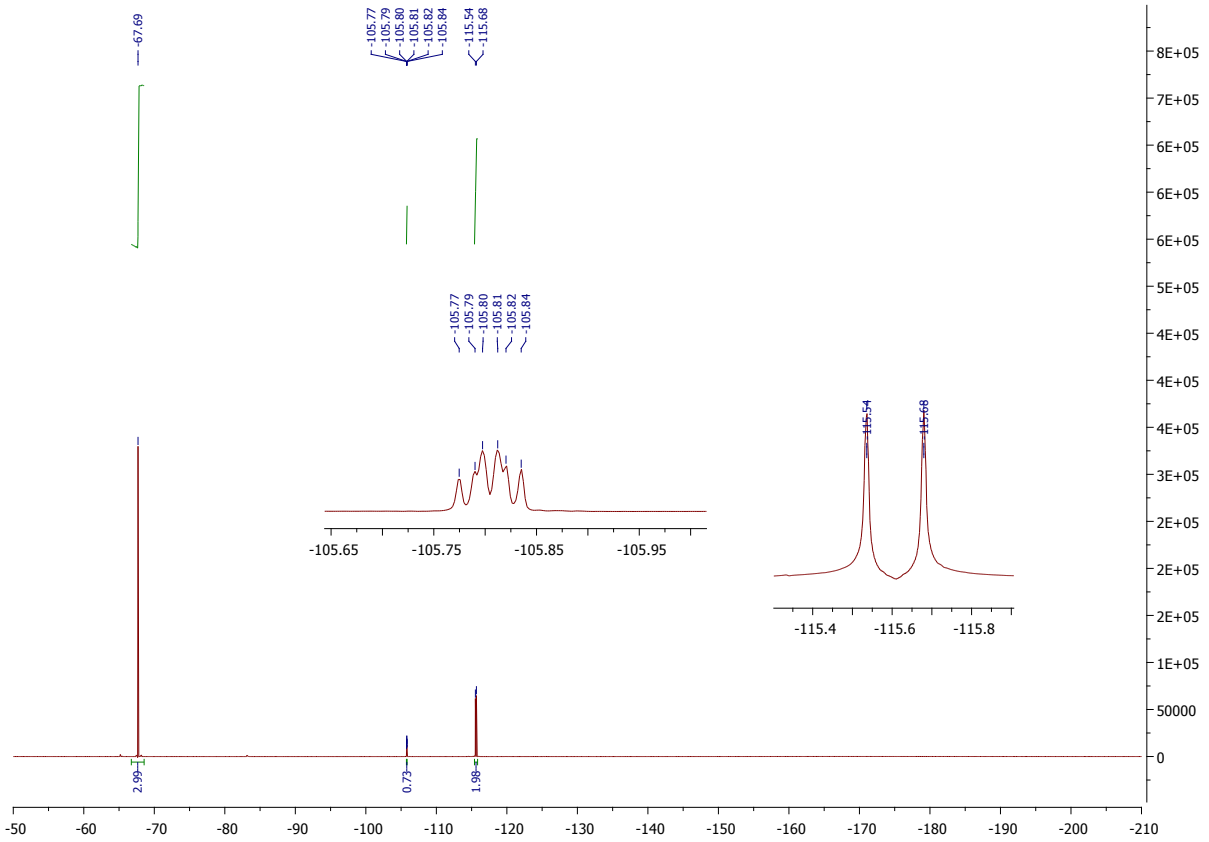
4-(Difluoromethyl)-6-fluoro-2-(trifluoromethyl)quinoline 2a



2a
Chemical Formula: $C_{11}H_5F_6N$
Exact Mass: 265,03 g/mol
Yellow solid

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.32 (dd, $^{3}J_{H-H}$ = 9.3, $^{4}J_{H-F}$ = 5.5 Hz, 1H, C_8H), 7.93 (s, 1H, C_3H), 7.81 – 7.73 (m, 1H, C_5H), 7.67 – 7.66 (m, 1H, C_7H), 7.12 (t, $^{2}J_{H-F}$ = 54.1 Hz, 1H, C_4CHF_2) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -67.69 (s, C_2CF_3), 105.84 - -105.77 (m, C_6F), -115.61 (d, $^{2}J_{F-H}$ = 54.1 Hz, C_4CHF_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 162.40 (d, $^{1}J_{C-F}$ = 254.3 Hz, C_6), 147.31 (qd, $^{2}J_{C-F}$ = 35.7, $^{6}J_{C-F}$ = 3.2 Hz, C_2), 145.05 (s, C_9), 139.92 (td, $^{2}J_{C-F}$ = 22.5, $^{4}J_{C-F}$ = 6.2 Hz, C_4), 133.96 (d, $^{3}J_{C-F}$ = 9.8 Hz, C_8), 126.06 (d, $^{3}J_{C-F}$ = 10.7 Hz, C_{10}), 122.01 (d, $^{2}J_{C-F}$ = 26.0 Hz, C_7), 121.24 (q, $^{1}J_{C-F}$ = 275.1 Hz, C_2CF_3), 115.17 – 115.02 (m, C_3), 112.74 (t, $^{1}J_{C-F}$ = 237.4 Hz, C_4CHF_2), 107.68 (d, $^{2}J_{C-F}$ = 24.1 Hz, C_5) ppm. HRMS (ESI positive) for $C_{11}H_6F_6N$ $[M^+]$: calcd 266.0399, found 266.0387. MP: 68.2 – 69.8 °C.

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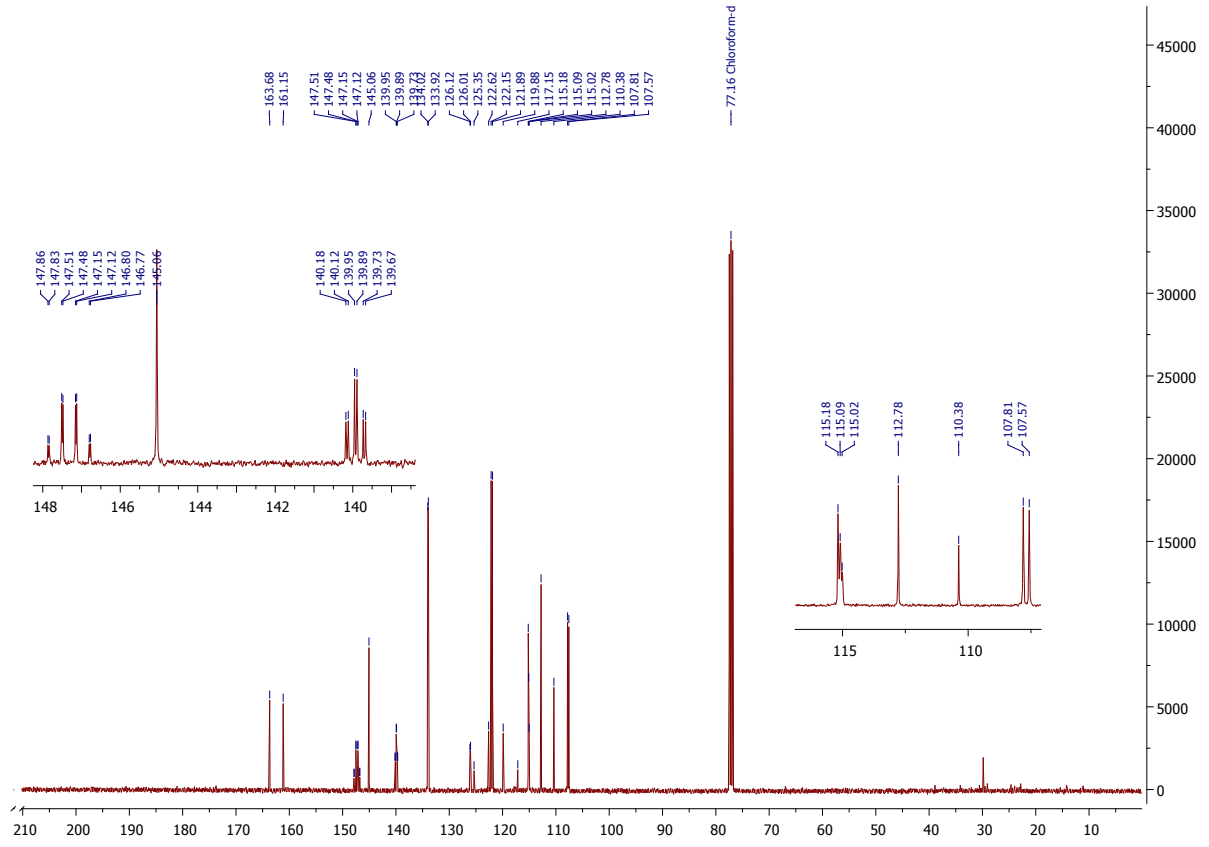
1.98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147.12
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139.95
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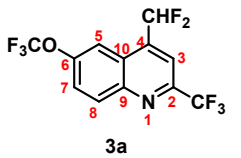
133.92
126.12
126.01
125.35
122.62
122.15
121.89
119.88
117.15
115.18
115.09
115.02
112.78
110.38
107.81
107.57
77.16 Chloroform-d

Figure S32. NMR (^{1}H, ^{13}C and ^{19}F) and characterization data of compound **3a**.

4-(Difluoromethyl)-6-(trifluoromethoxy)-2-(trifluoromethyl)quinoline 3a

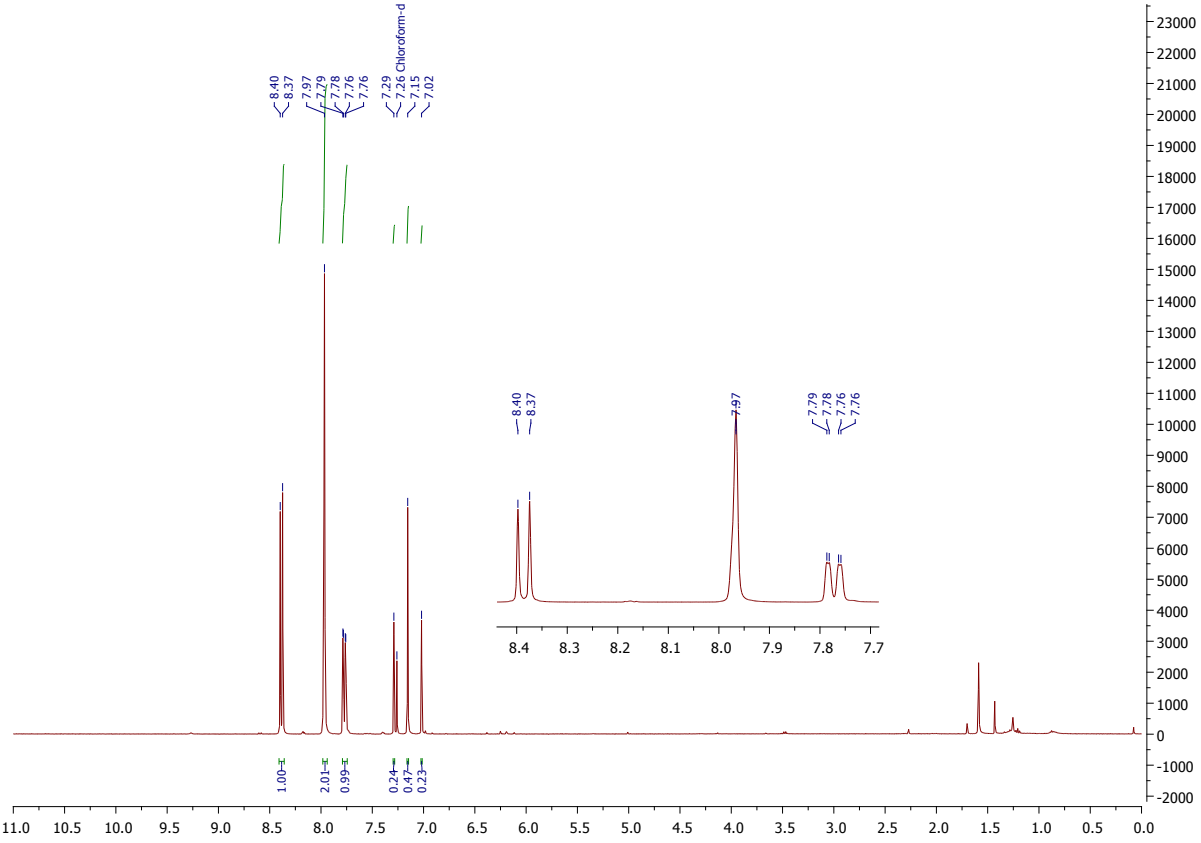


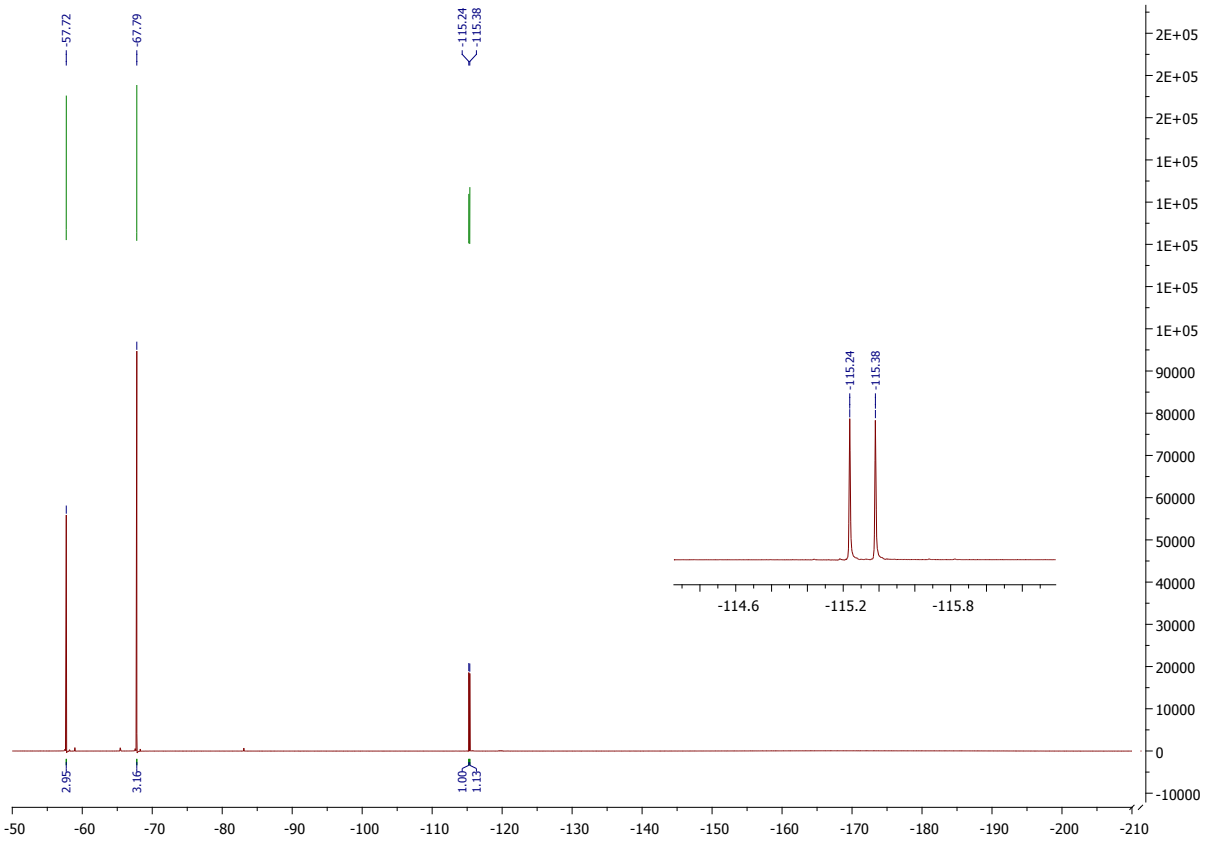
3a

Chemical Formula: $C_{12}H_5F_8NO$
Exact Mass: 331,02 g/mol
Yellow solid

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.39 (d, $^{3}J_{H\text{-}H}$ = 9.3 Hz, 1H, C_8H), 7.97 (s, 2H, $_5$H), 7.77 (dd, $^{3}J_{H\text{-}H}$ = 9.3, $^{4}J_{H\text{-}H}$ = 1.9 Hz, 1H, C_7H), 7.15 (t, $^{2}J_{H\text{-}F}$ = 54.0 Hz, 1H, C_4CHF_2) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -57.72 (s, C_6OCF_3), -67.79 (s, C_2CF_3), -115.31 (d, $^{2}J_{F\text{-}H}$ = 53.9 Hz, C_4CHF_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) 149.50 (s, C_6), 148.41 (q, $^{2}J_{C\text{-}F}$ = 35.9 Hz, C_2), 146.02 (s, C_9), 140.46 (t, $^{2}J_{C\text{-}F}$ = Hz, C_4), 133.66 (s, C_8), 125.52 (s, C_{10}), 125.35 (s, C_7), 121.12 (q, $^{1}J_{C\text{-}F}$ = 276.4 C_2CF_3), 120.74 (q, $^{1}J_{C\text{-}F}$ = 260.6 Hz, C_6OCF_3), 115.36 (td, $^{3}J_{C\text{-}F}$ = 8.0, $^{3}J_{C\text{-}F}$ = 2.1 C_3), 113.97 (s, C_5), 112.67 (t, $^{1}J_{C\text{-}F}$ = 242.0 Hz, C_4CHF_2) ppm. $C_{12}H_5F_8NO$ (331): calcd (%) N 4.23, C 43.48, H 1.51, found N 4.20, C 43.77, H 1.83. MP: 42.2 – 43.8 °C.

C_3, δ_C = 22.6 Hz, Hz,

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1.13
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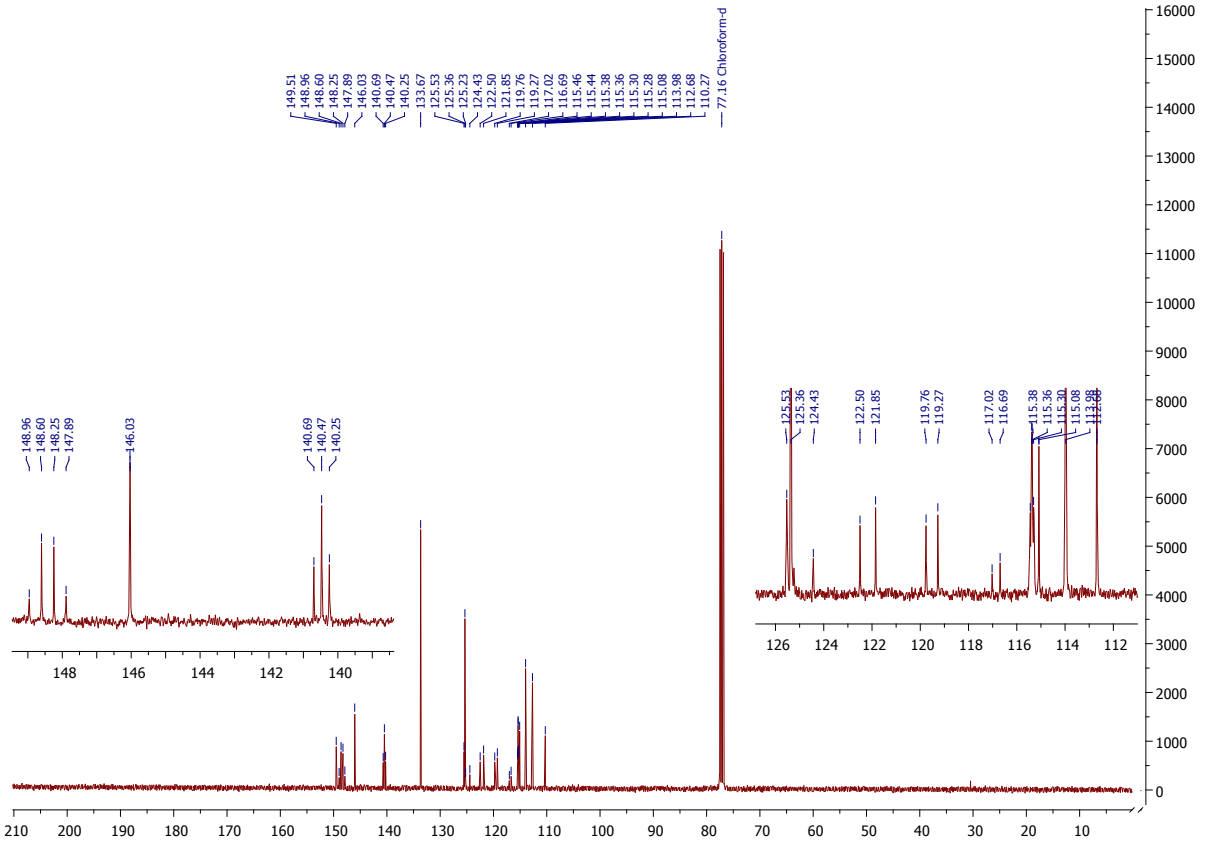
-115.8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119.76
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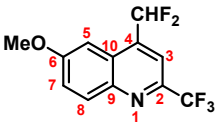
117.02
116.69
115.38
115.36
115.30
115.08

Figure S33. NMR (^{1}H, ^{13}C and ^{19}F) and characterization data of compound **4a**.

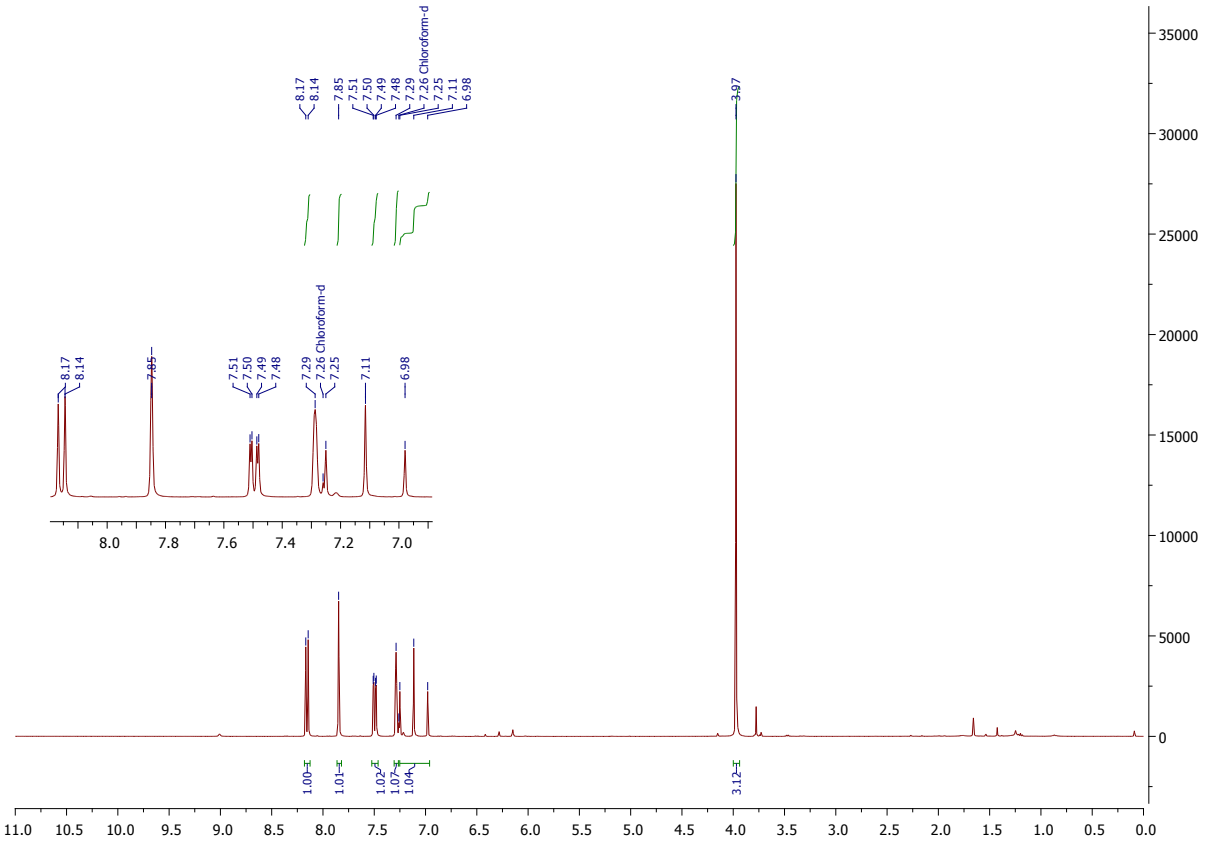
4-(Difluoromethyl)-6-methoxy-2-(trifluoromethyl)quinoline 4a

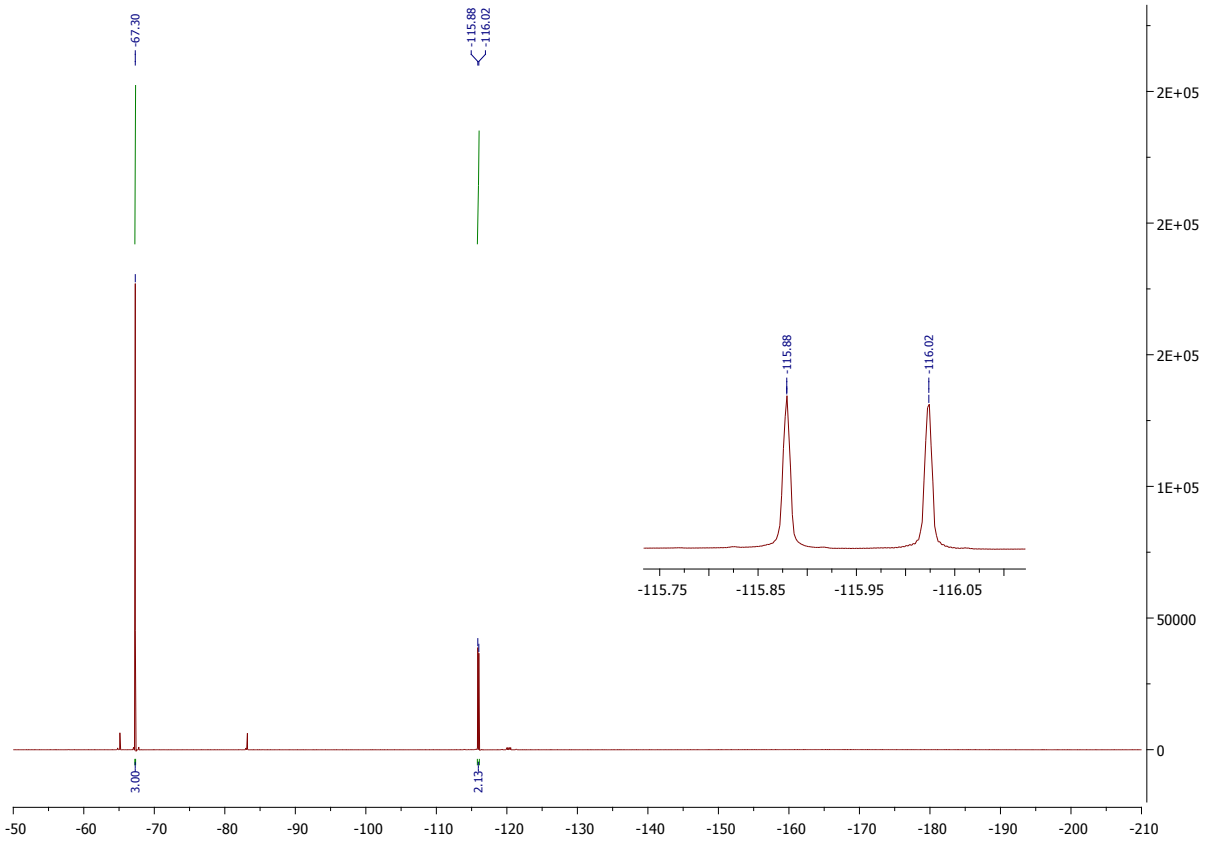


4a

Chemical Formula: $C_{12}H_8F_5NO$
Exact Mass: 277,05 g/mol
Brown solid

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.16 (d, $^{3}J_{H\text{-}H}$ = 9.3 Hz, 1H, C_8H), 7.85 (s, 1H, C_3H), 7.50 (dd, $^{3}J_{H\text{-}H}$ = 9.3, $^{4}J_{H\text{-}H}$ = 2.6 Hz, 1H, C_7H), 7.29 (s, 1H, C_5H), 7.11 (t, $^{2}J_{H\text{-}F}$ = 54.3 Hz, 1H, C_4CHF_2), 3.97 (s, 3H, C_6OCH_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -67.30 (s, C_2CF_3), -115.95 (d, $^{2}J_{F\text{-}H}$ = 54.4 Hz, C_4CHF_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 160.35 (s, C_6), 144.95 (q, $^{2}J_{C\text{-}F}$ = 35.4 Hz, C_2), 144.11 (s, C_9), 138.21 (t, $^{2}J_{C\text{-}F}$ = 22.1 Hz, C_4), 132.56 (s, C_8), 126.63 (s, C_{10}), 124.40 (s, C_7), 121.43 (q, $^{1}J_{C\text{-}F}$ = 274.7 Hz, C_2CF_3), 114.59 (td, $^{3}J_{C\text{-}F}$ = 8.1, $^{3}J_{C\text{-}F}$ = 2.3 Hz, C_3), 113.17 (t, $^{1}J_{C\text{-}F}$ = 241.1 Hz, C_4CHF_2), 101.06 (s, C_5), 55.88 (s, C_6OCH_3) ppm. $C_{12}H_8F_5NO$ (277): calcd (%) N 5.05, C 51.95, H 2.88, found N 5.03, C 51.64, H 2.80. MP: 105.9 – 108.2 °C.




-67.30
-115.88
-116.02
3.00
2.13
-115.75
-115.85
-115.95
-116.05
2E+05
1E+05
50000
0
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210

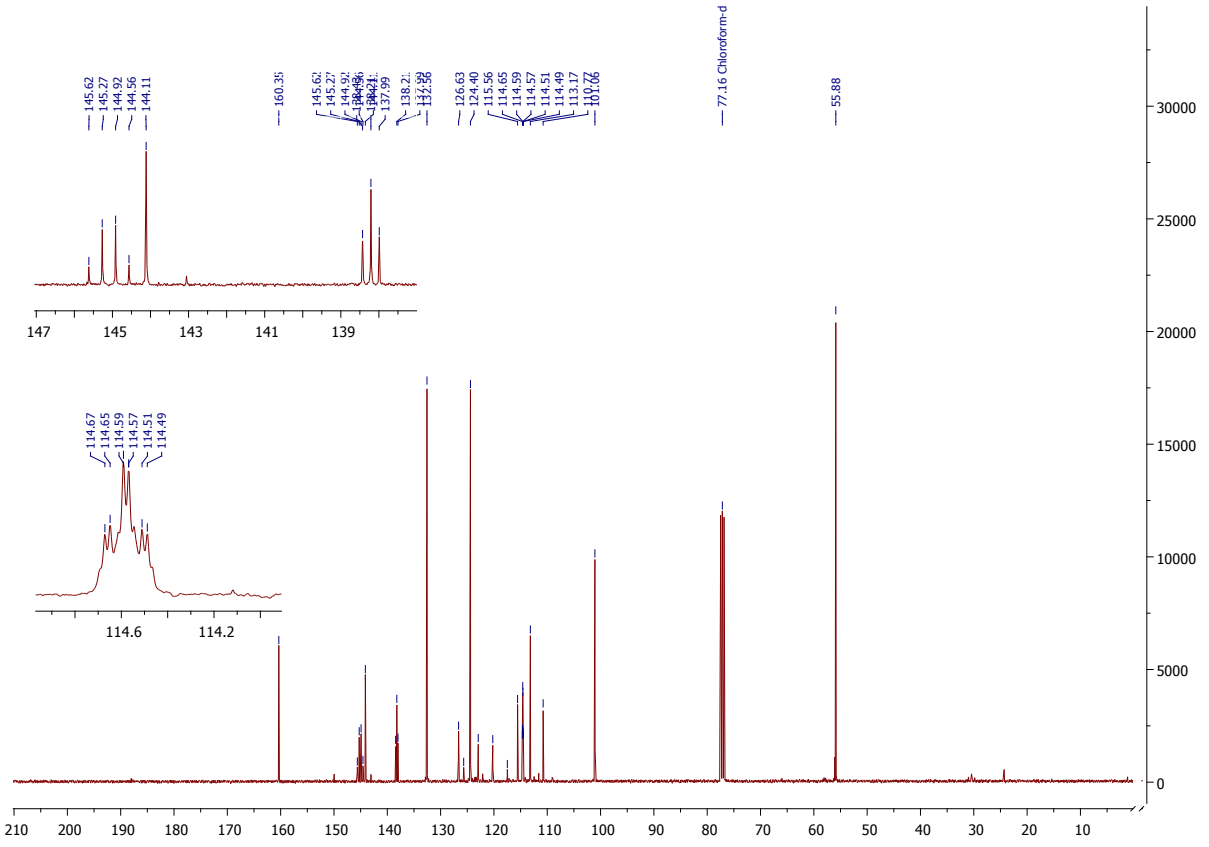
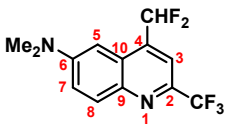

145.62
145.27
144.92
144.56
144.11
160.35
137.99
126.63
124.40
115.56
114.65
114.59
114.57
114.51
114.49
113.17
77.16 Chloroform-d
55.88
114.67
114.65
114.59
114.57
114.51
114.49
147
145
143
141
139
114.6
114.2
30000
25000
20000
15000
10000
5000
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

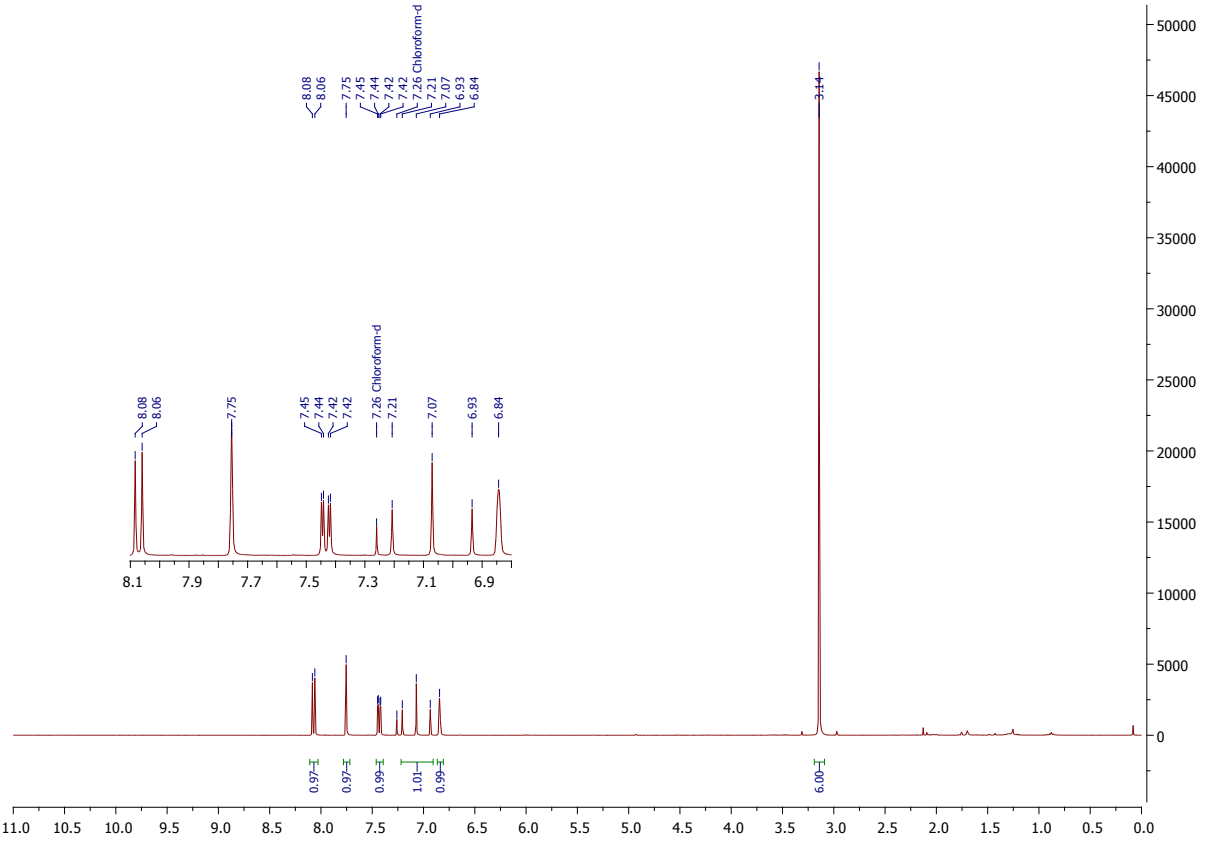
Figure S34. NMR (^{1}H, ^{13}C and ^{19}F) and characterization data of compound **5a**.

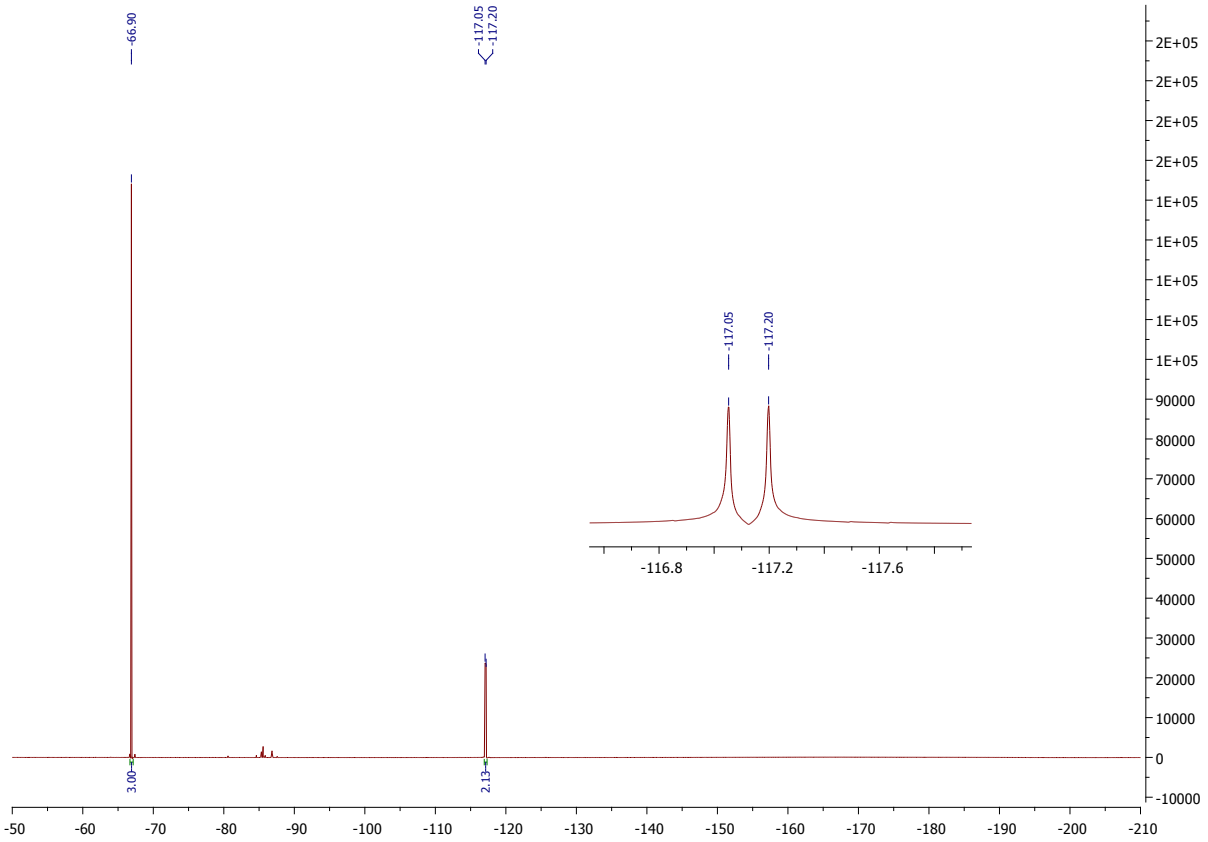
4-(Difluoromethyl)-*N,N*-dimethyl-2-(trifluoromethyl)quinolin-6-amine 5a



5a
Chemical Formula: $C_{13}H_{11}F_5N_2$
Exact Mass: 290,08 g/mol
Yellow solid

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.07 (d, $^{3}J_{H\text{-}H}$ = 9.5 Hz, 1H, C_8H), 7.75 (s, 1H, C_3H), 7.43 (dd, $^{3}J_{H\text{-}H}$ = 9.5, $^{4}J_{H\text{-}H}$ = 2.8 Hz, 1H, C_7H), 7.07 (t, $^{2}J_{H\text{-}F}$ = 54.5 Hz, 1H, C_4CHF_2), 6.84 (s, 1H, C_5H), 3.14 (s, 1H, $C_6N(CH_3)_2$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -66.90 (s, C_2CF_3), -117.13 (d, $^{2}J_{F\text{-}H}$ = 54.7 Hz, C_4CHF_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 150.28 (s, C_6), 143.01 – 141.69 (m, C_2 + C_9), 136.12 (t, $^{2}J_{C\text{-}F}$ = 21.6 Hz, C_4), 131.80 (s, C_8), 127.25 (t, $^{3}J_{C\text{-}F}$ = 2.5 Hz, C_{10}), 121.98 (q, $^{1}J_{C\text{-}F}$ = 274.0 Hz, C_2CF_3), 120.46 (s, C_7), 114.48 (td, $^{3}J_{C\text{-}F}$ = 8.2, $^{3}J_{C\text{-}F}$ = 2.3 Hz, C_3), 113.29 (t, $^{1}J_{C\text{-}F}$ = 240.4 Hz, C_4CHF_2), 98.92 (s, C_5), 40.46 (s, $C_6N(CH_3)_2$) ppm. $C_{13}H_{11}F_5N_2$ (290): calcd (%) N 9.65, C 53.75, H 3.79, found N 9.42, C 53.55, H 3.81. MP: 107.5 – 108.4 °C.




-66.90
-117.05
-117.20
3.00
2.13
-116.8
-117.2
-117.6

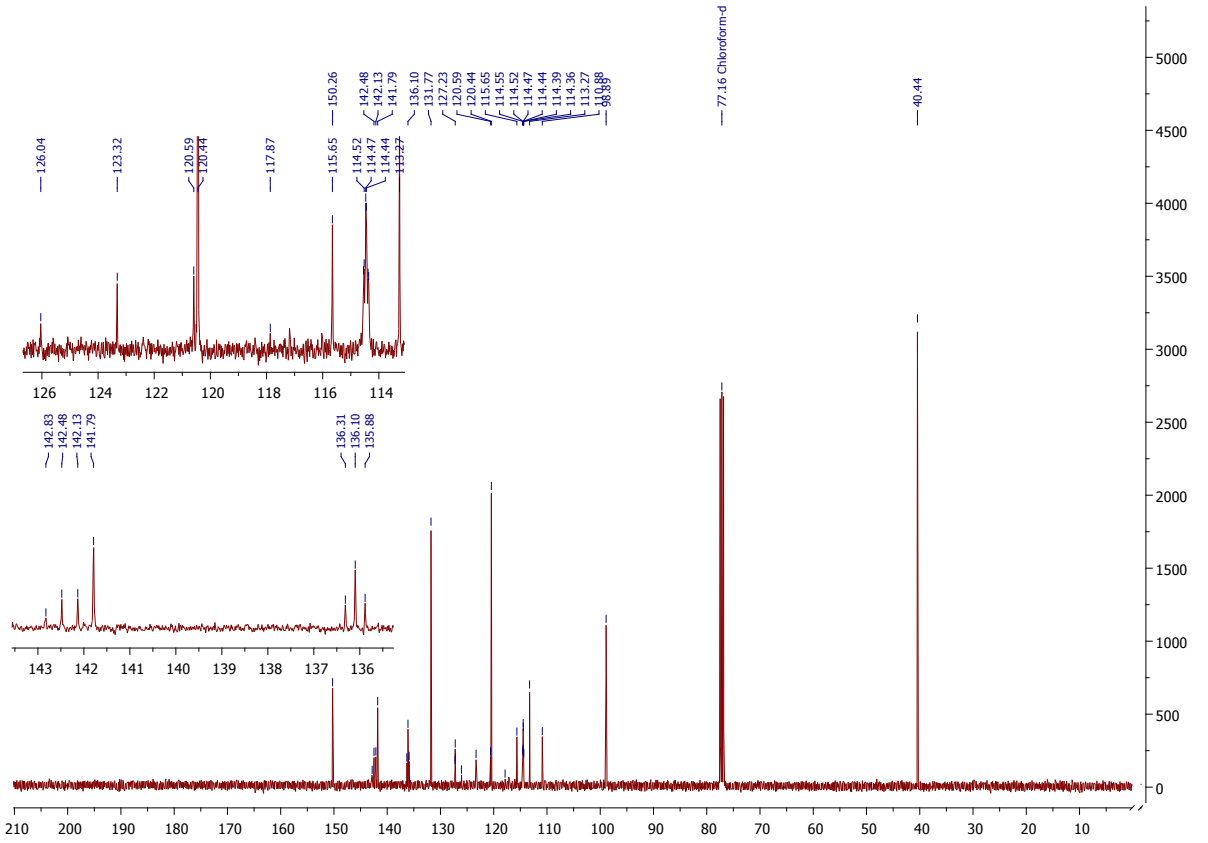
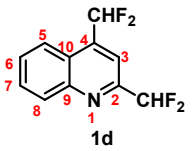

150.26
142.48
142.13
141.79
136.10
131.77
127.23
120.59
120.44
115.65
114.55
114.52
114.47
114.44
114.39
114.36
113.27
77.16 Chloroform-d
40.44
126.04
123.32
120.59
120.44
117.87
115.65
114.52
114.47
114.44
142.83
142.48
142.13
141.79
136.31
136.10
135.88

Figure S35. NMR (^{1}H, ^{13}C and ^{19}F) and characterization data of compound **1d**.

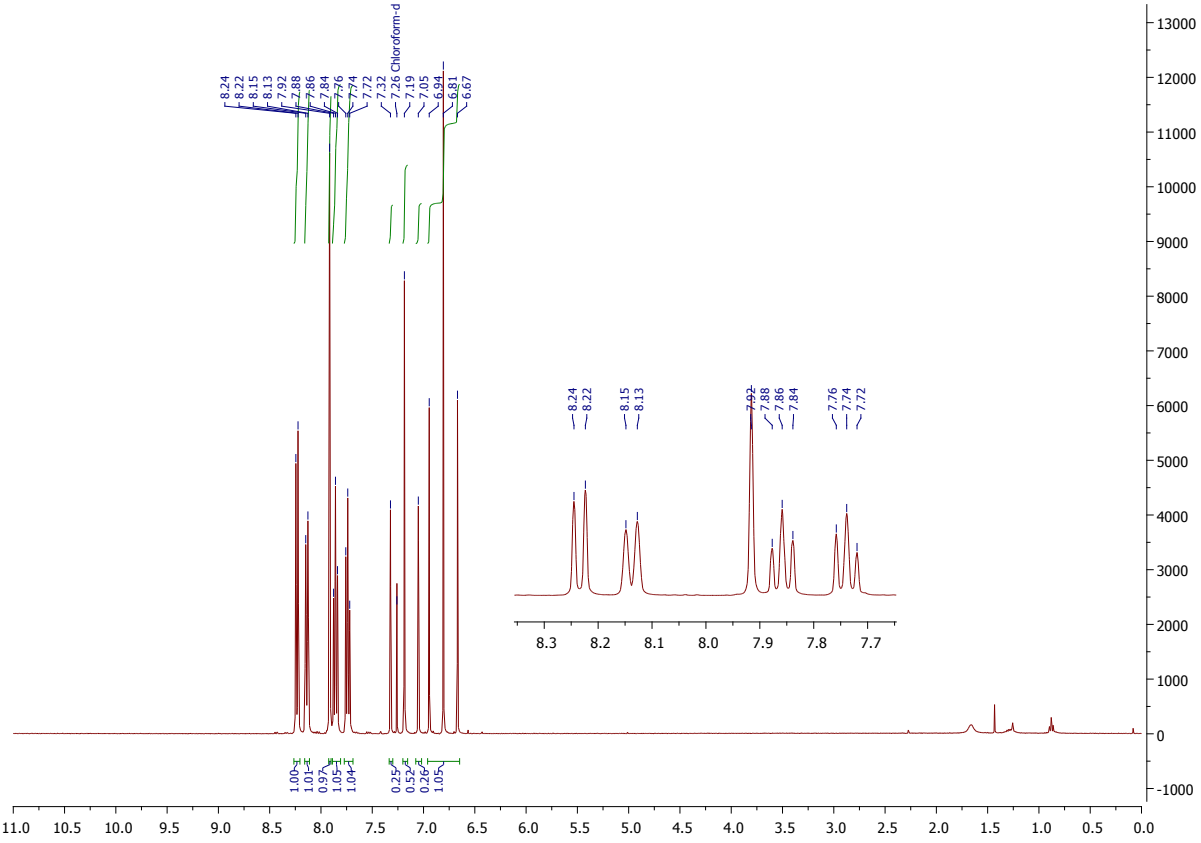
2,4-Bis(difluoromethyl)quinoline 1d

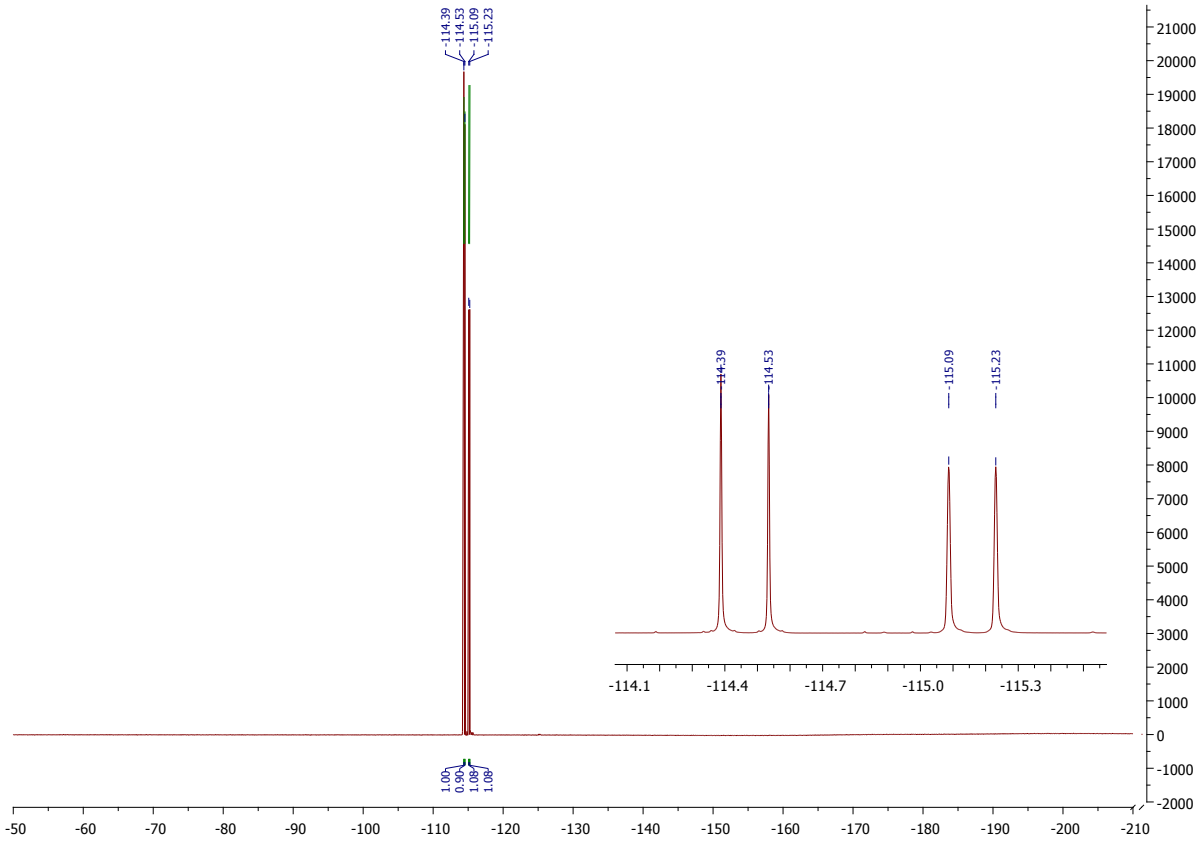


1d

Chemical Formula: $C_{11}H_7F_4N$
Exact Mass: 229,05 g/mol
Yellow solid

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.23 (d, $^{3}J_{H-H}$ = 8.5 Hz, 1H, C_8H), 8.14 (d, $^{3}J_{H-H}$ = 8.5 Hz, 1H, C_5H), 7.92 (s, 1H, C_3H), 7.86 (t, $^{3}J_{H-H}$ = 7.7 Hz, 1H, C_7H), 7.74 (t, $^{3}J_{H-H}$ = 7.7 Hz, 1H, C_6H), 7.19 (t, $^{2}J_{H-F}$ = 54.3 Hz, 1H, C_4CHF_2), 6.81 (t, $^{2}J_{H-F}$ = 55.1 Hz, C_2CHF_2) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ_F =-114.46 (d, $^{2}J_{F-H}$ = 55.1 Hz, C_2CHF_2), -115.16 (d, $^{2}J_{F-H}$ = 54.3 Hz, C_4CHF_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 152.70 (t, $^{2}J_{C-F}$ = 27.1 Hz, C_2), 147.80 (s, C_9), 139.93 (t, $^{2}J_{C-F}$ = 22.2 Hz, C_4), 130.91 (s, C_7), 130.83 (s, C_8), 129.33 (s, C_6), 124.84 (s, C_{10}), 123.55 (s, C_5), 114.37 (t, $^{1}J_{C-F}$ = 242.0 Hz, C_4CHF_2), 114.32 – 114.17 (m, C_3), 113.13 (t, $^{1}J_{C-F}$ = 241.2 Hz, C_2CHF_2) ppm. $C_{11}H_7F_4N$ (229): calcd (%) N 6.10, C 57.60, H 3.05, found N 6.20, C 57.56, H 2.96. MP: 48.2 – 49.7 °C.




-114.39
-114.53
-115.09
-115.23
1.00
0.90
1.08
1.08

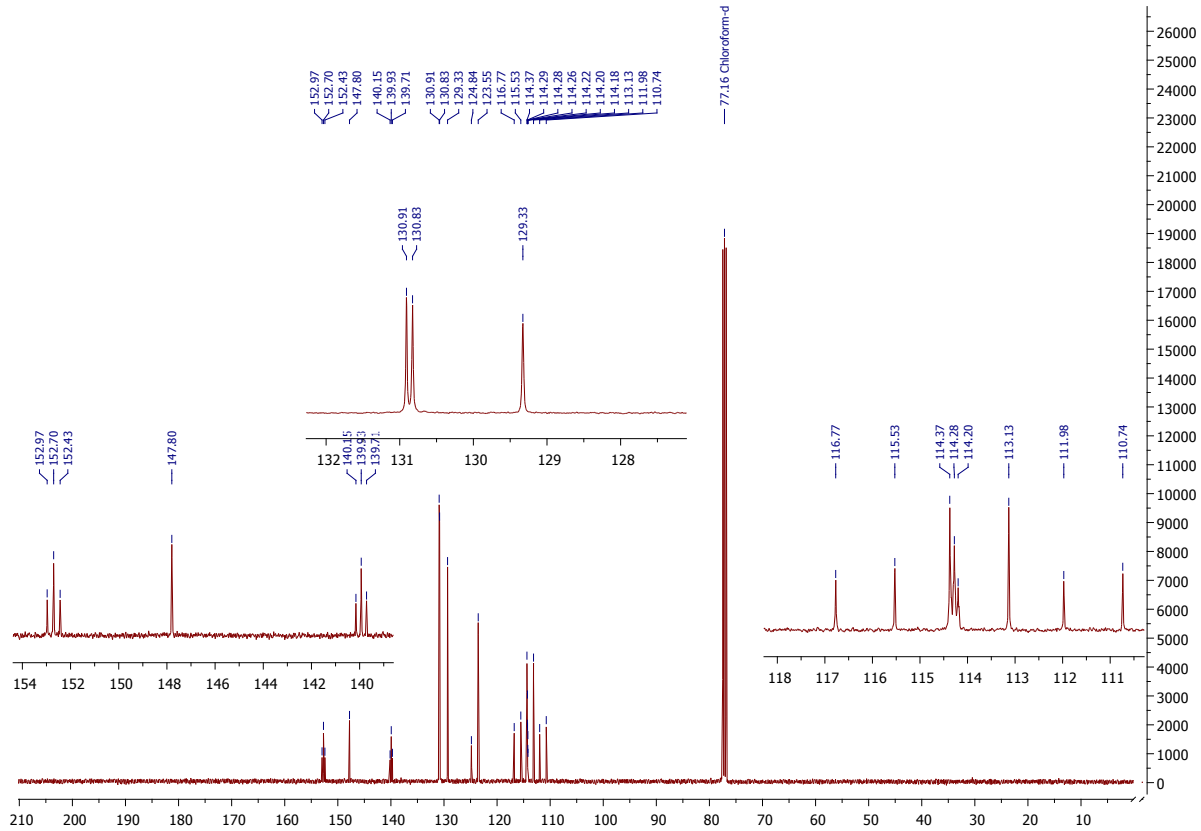
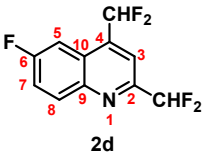

152.97
152.70
152.43
147.80
140.15
139.93
139.71
130.91
130.83
129.33
124.84
123.55
116.77
115.53
114.37
114.29
114.28
114.26
114.22
114.20
114.18
113.13
111.98
110.74
77.16 Chloroform-d

Figure S36. NMR (^{1}H, ^{13}C and ^{19}F) and characterization data of compound **2d**.

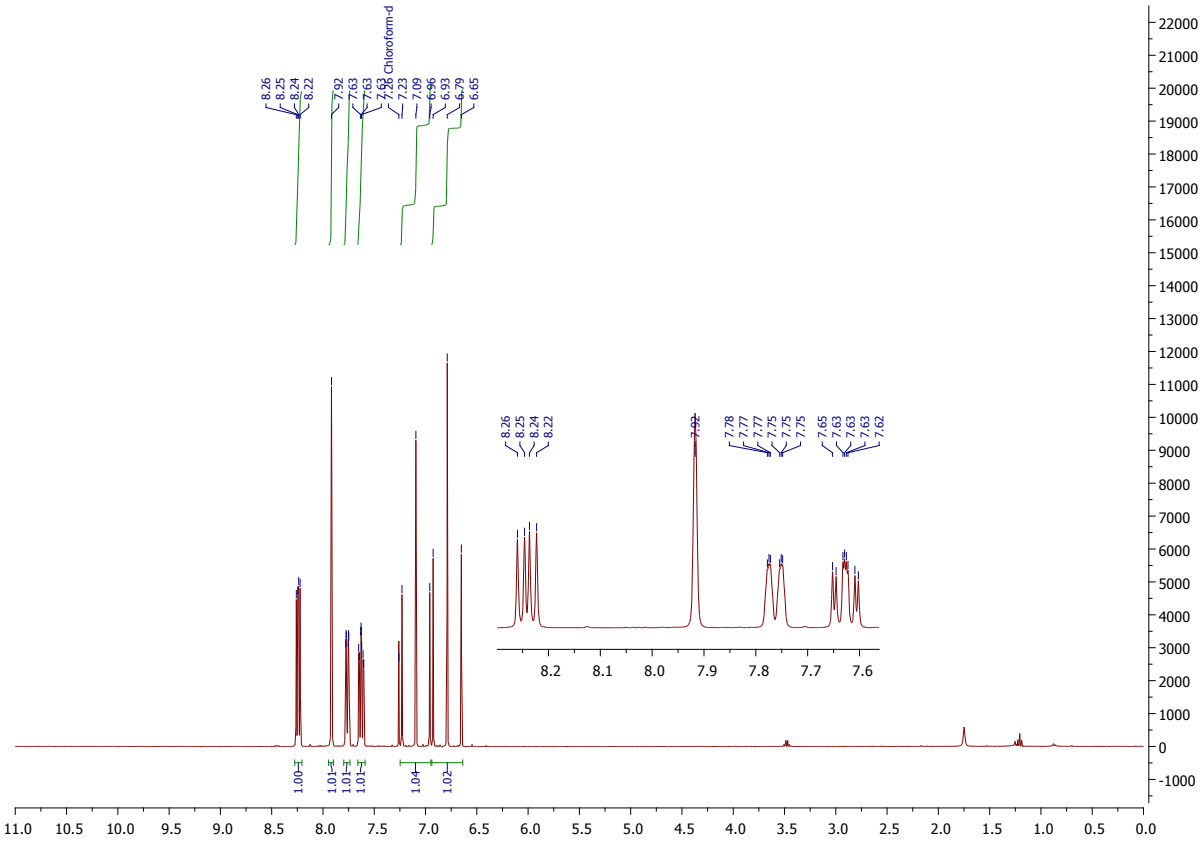
2,4-Bis(difluoromethyl)-6-fluoroquinoline 2d

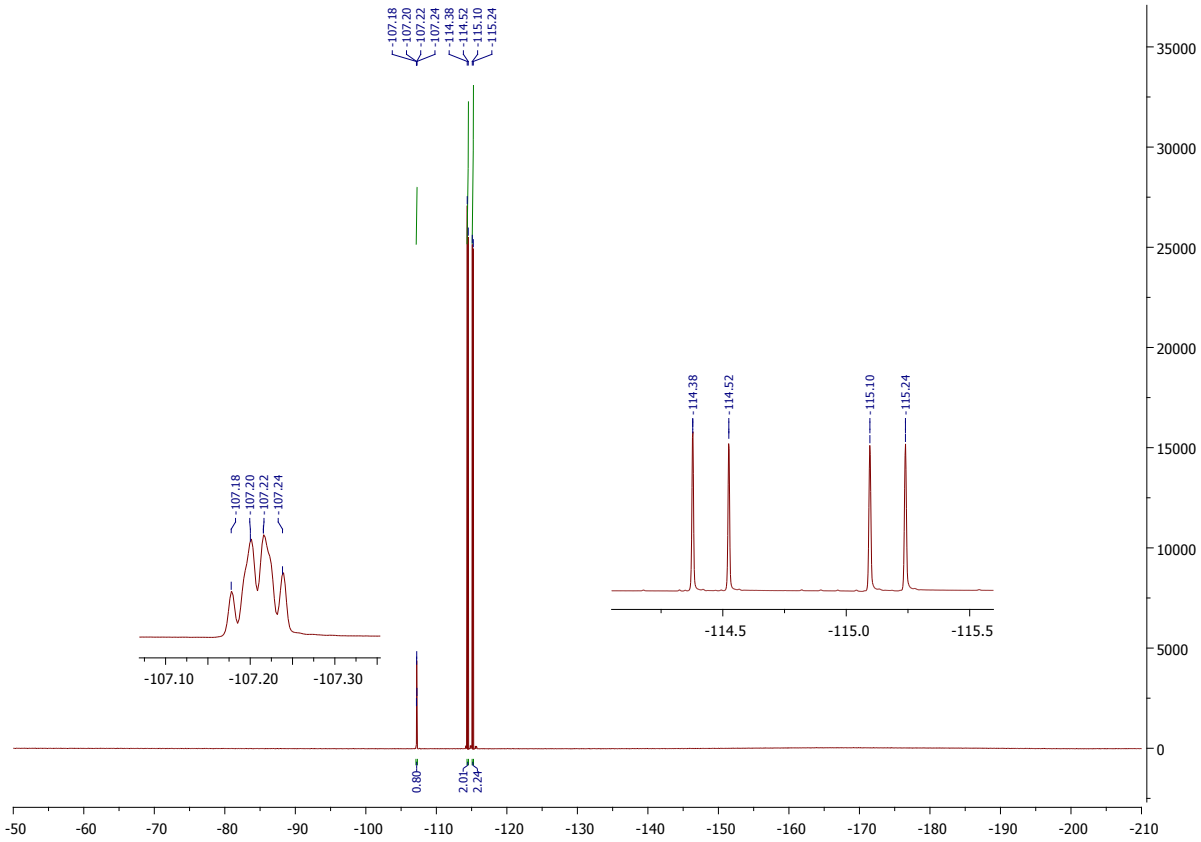


2d

Chemical Formula: $C_{11}H_6F_5N$
Exact Mass: 247,04 g/mol
Yellow solid

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.24 (dd, $^{3}J_{H\text{-}H}$ = 9.3, $^{4}J_{H\text{-}F}$ = 5.5 Hz, 1H, C_8H), 7.92 (s, 1H, C_3H), 7.80 – 7.74 (m, 1H, C_5H), 7.65 – 7.60 (m, 1H, C_7H), 7.09 (t, $^{2}J_{H\text{-}F}$ = 54.2 Hz, 1H, C_4CHF_2), 6.79 (t, $^{2}J_{H\text{-}F}$ = 55.0 Hz, 1H, C_2CHF_2) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -107.18 - -107.24 (m, C_6F), -114.45 (d, $^{2}J_{F\text{-}H}$ = 55.0 Hz, C_2CHF_2), -115.17 (d, $^{2}J_{F\text{-}H}$ = 54.2 Hz, C_4CHF_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 162.01 (d, $^{1}J_{C\text{-}F}$ = 252.9 Hz, C_6), 152.09 (td, $^{2}J_{C\text{-}F}$ = 27.3, $^{6}J_{C\text{-}F}$ = 3.1 Hz, C_2), 144.98 (s, C_9), 139.56 (td, $^{2}J_{C\text{-}F}$ = 22.4, $^{4}J_{C\text{-}F}$ = 6.1 Hz, C_4), 133.46 (d, $^{3}J_{C\text{-}F}$ = 9.6 Hz, C_8), 125.76 (d, $^{3}J_{C\text{-}F}$ = 10.4 Hz, C_{10}), 121.43 (d, $^{2}J_{C\text{-}F}$ = 25.8 Hz, C_7), 115.28 (t, $^{3}J_{C\text{-}F}$ = 7.8 Hz, C_3), 114.21 (t, $^{1}J_{C\text{-}F}$ = 241.3 Hz, C_2CHF_2), 110.78 (t, $^{1}J_{C\text{-}F}$ = 242.0 Hz, C_4CHF_2), 107.84 (d, $^{2}J_{C\text{-}F}$ = 24.0 Hz, C_5) ppm. $C_{11}H_6F_5N$ (247): calcd (%) N 5.66, C 53.41, H 2.43, found N 5.67, C 53.42, H 2.57. HRMS (ESI positive) for $C_{11}H_7F_5N$ [M$^+$]: calcd 248.0493, found 248.0497. MP: 68.7 – 71.2 °C.




-107.18
-107.20
-107.22
-107.24
-114.38
-114.52
-115.10
-115.24
0.80
2.01
2.24

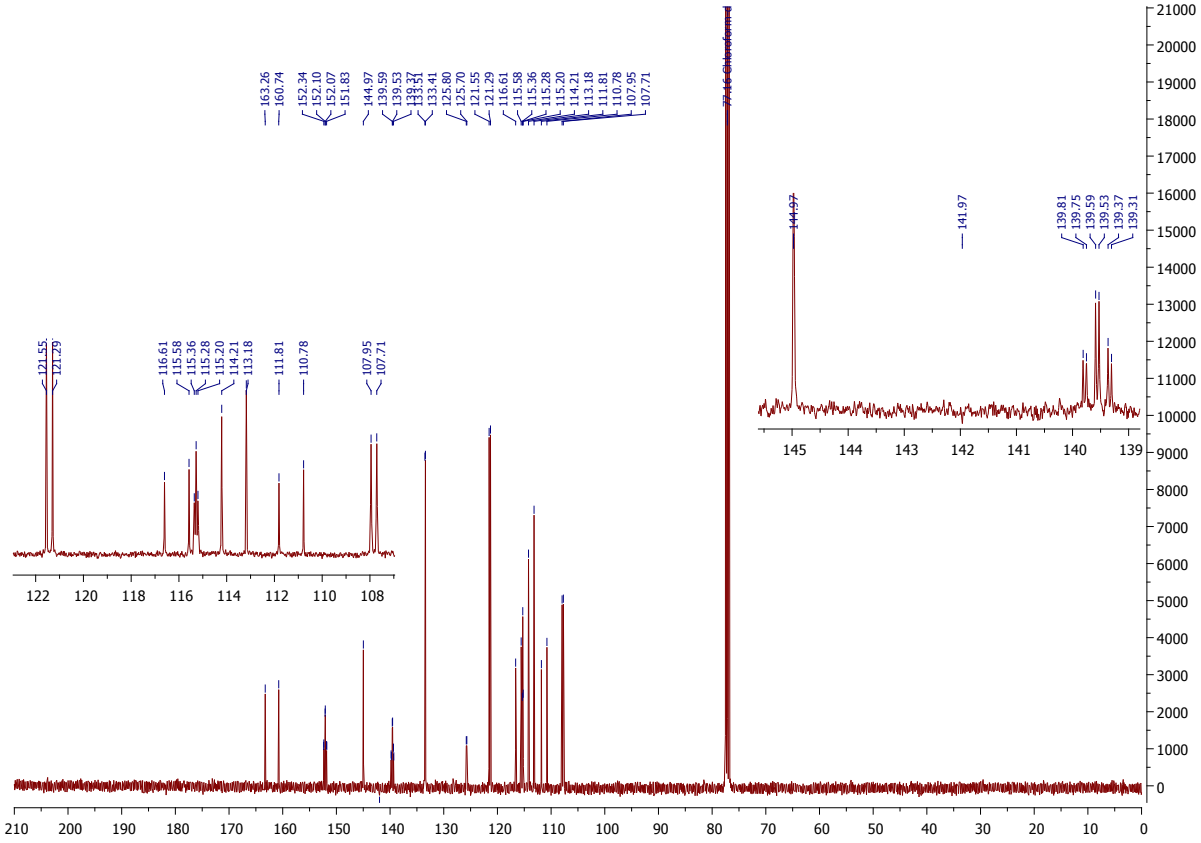
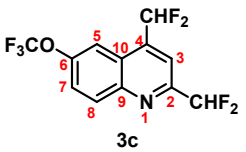

163.26
160.74
152.34
152.10
152.07
151.83
144.97
139.59
139.53
139.37
133.41
125.80
125.70
121.55
121.29
116.61
115.58
115.36
115.28
115.20
114.21
113.18
111.81
110.78
107.95
107.71
77.16 CHloroform
141.97
139.81
139.75
139.59
139.53
139.37
139.31

Figure S37. NMR (^{1}H, ^{13}C and ^{19}F) and characterization data of compound **3c**.

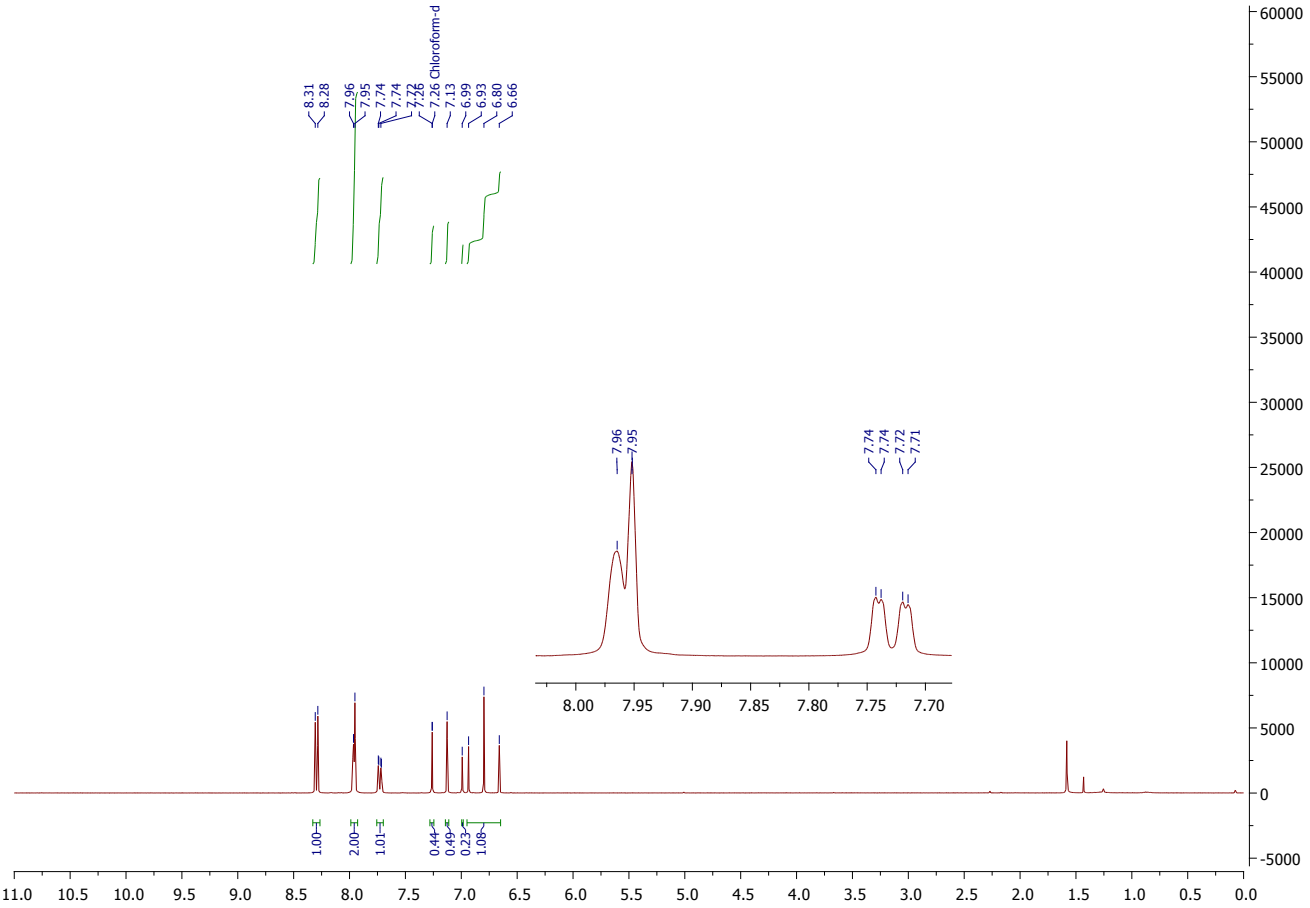
2,4-Bis(difluoromethyl)-6-(trifluoromethoxy)quinoline 3c

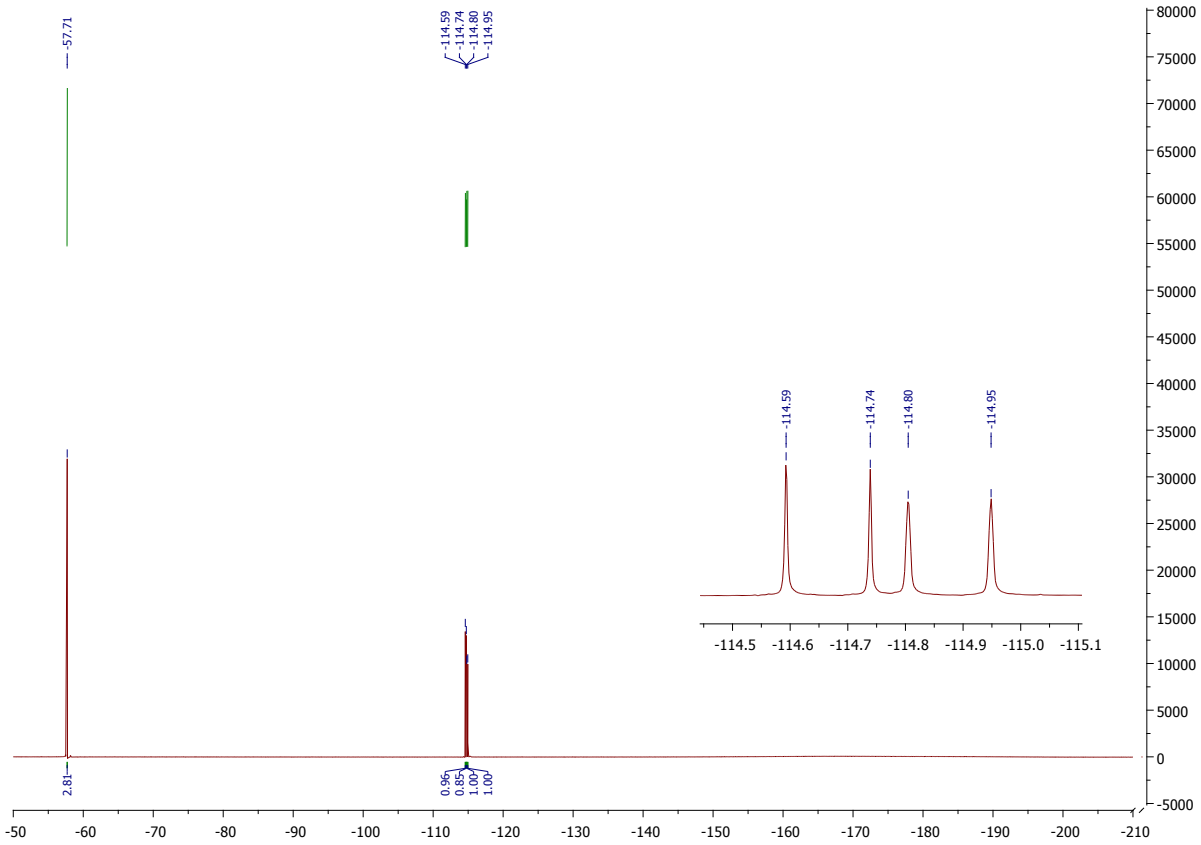


3c

Chemical Formula: $C_{12}H_6F_7NO$
Exact Mass: 313,03 g/mol
Yellow solid

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.30 (d, $^{3}J_{H\text{-}H}$ = 9.3 Hz, 1H, C_8H), 7.96 – 7.95 (m, 2H, $C_{3,5}H$), 7.73 (dd, $^{3}J_{H\text{-}H}$ = 9.3, $^{4}J_{H\text{-}H}$ = 1.8 Hz, 1H, C_7H), 7.13 (t, $^{2}J_{H\text{-}F}$ = 56.0 Hz, 1H, $C_4\mathit{CHF_2}$), 6.80 (t, $^{2}J_{H\text{-}F}$ = 55.0 Hz, 1H, $C_2\mathit{CHF_2}$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -57.71 (s, $C_6\mathit{OCF_3}$), -114.67 (d, $^{2}J_{F\text{-}H}$ = 55.0 Hz, $C_2\mathit{CHF_2}$), -114.88 (d, $^{2}J_{F\text{-}H}$ = 54.1 Hz, $C_4\mathit{CHF_2}$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 153.23 (t, $^{2}J_{C\text{-}F}$ = 27.5 Hz, C_2), 148.97 (s, C_6), 146.01 (s, C_9), 140.06 (t, $^{2}J_{C\text{-}F}$ = 22.5 Hz, C_4), 133.17 (s, C_8), 125.23 (s, C_{10}), 124.89 (s, C_7), 120.59 (q, $^{1}J_{C\text{-}F}$ = 259.2 Hz, $C_6\mathit{OCF_3}$), 115.64 – 115.49 (m, C_3), 114.32 (s, C_5), 114.08 (t, $^{1}J_{C\text{-}F}$ = 241.6 Hz, $C_2\mathit{CHF_2}$), 113.09 (t, $^{1}J_{C\text{-}F}$ = 240.0 Hz, $C_4\mathit{CHF_2}$) ppm. $C_{12}H_6F_7NO$ (313): calcd (%) N 4.47, C 45.98, H 1.92, found N 4.49, C 46.35, H 2.07. MP: 47.5 – 48.2 °C.




-57.71
-114.59
-114.74
-114.80
-114.95
2.81
0.96
0.85
1.00
1.00
-114.5 -114.6 -114.7 -114.8 -114.9 -115.0 -115.1

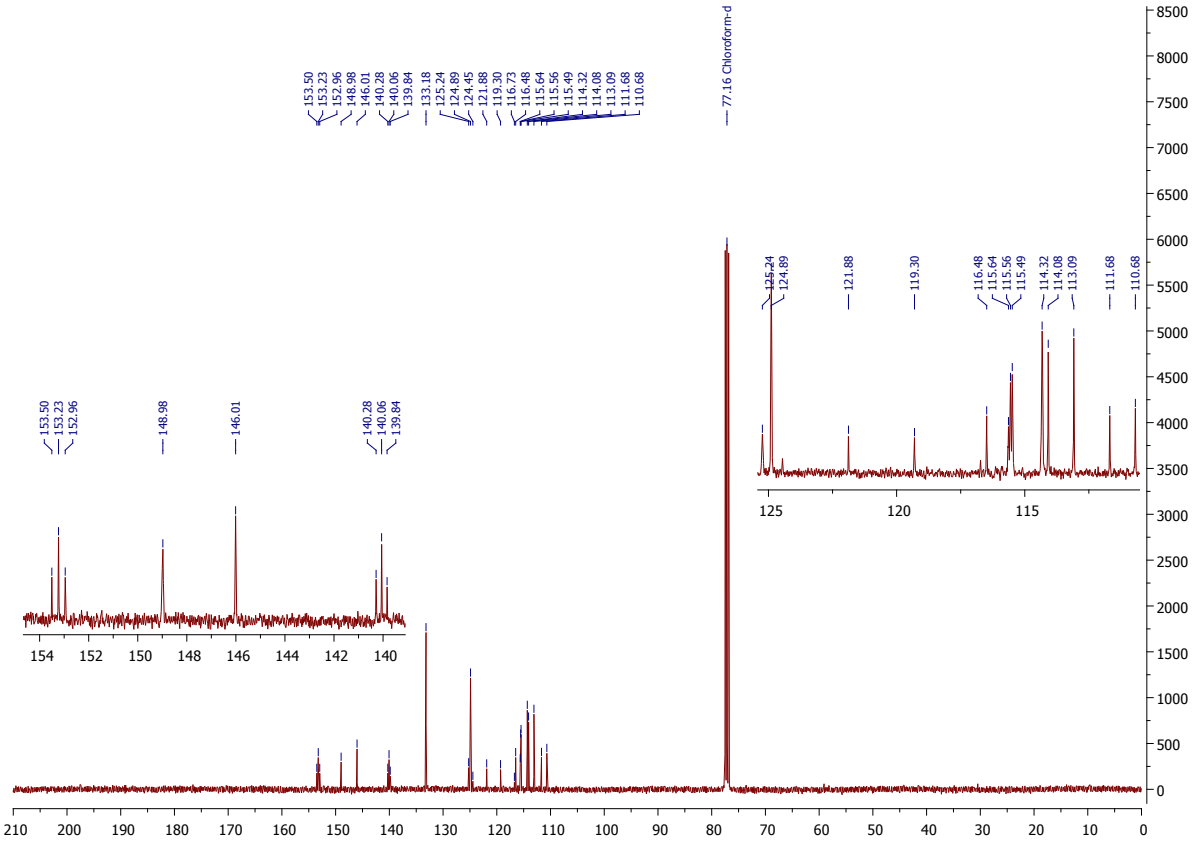
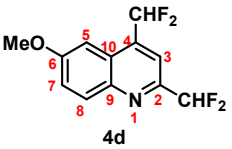

153.50
153.23
152.96
148.98
146.01
140.28
140.06
139.84
133.18
125.24
124.89
124.45
121.88
119.30
116.73
116.48
115.64
115.56
115.49
114.32
114.08
113.09
111.68
110.68
77.16 Chloroform-d
154 152 150 148 146 144 142 140
125 120 115

Figure S38. NMR (^{1}H, ^{13}C and ^{19}F) and characterization data of compound **4d**.

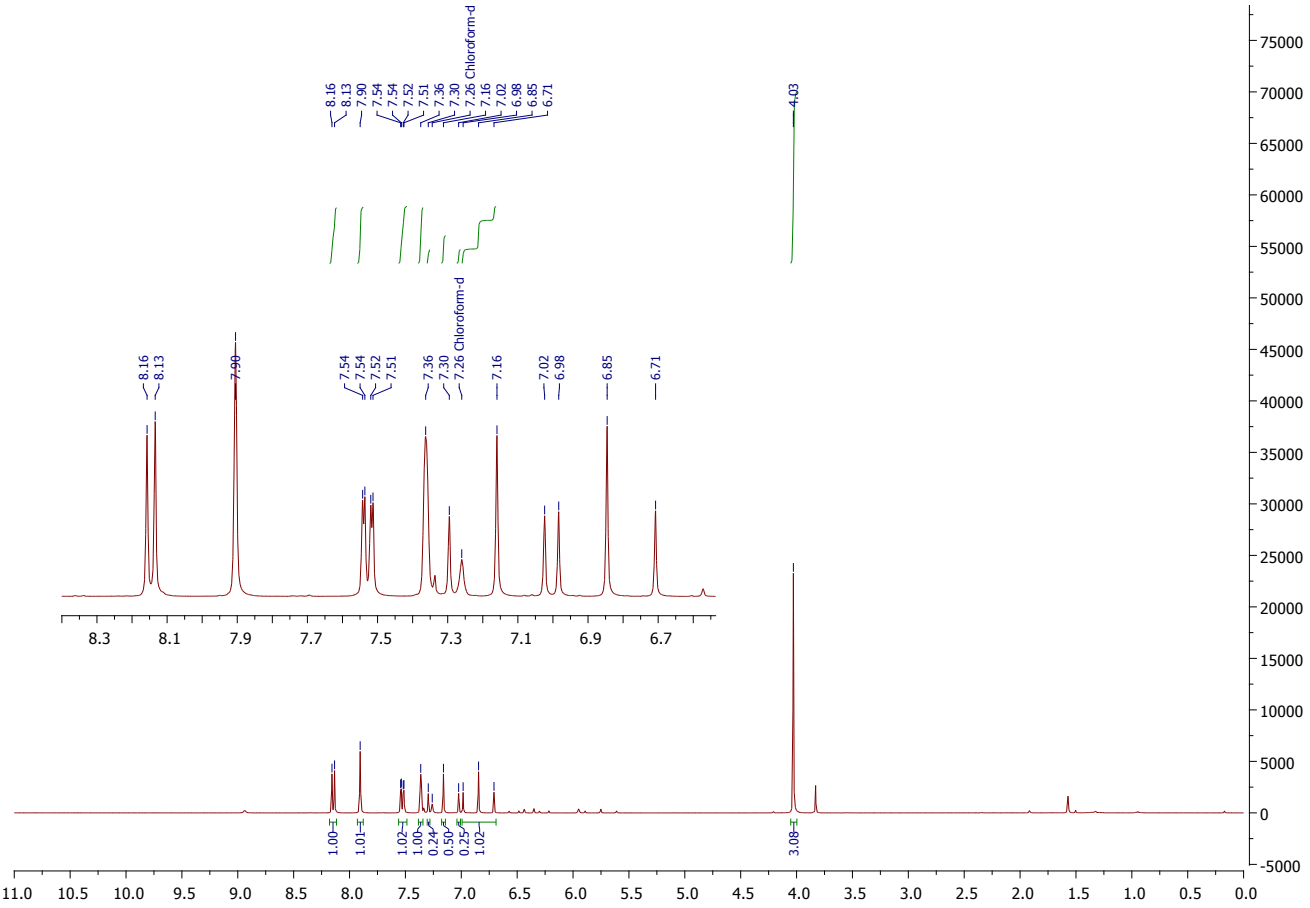
2,4-Bis(difluoromethyl)-6-methoxyquinoline 4d

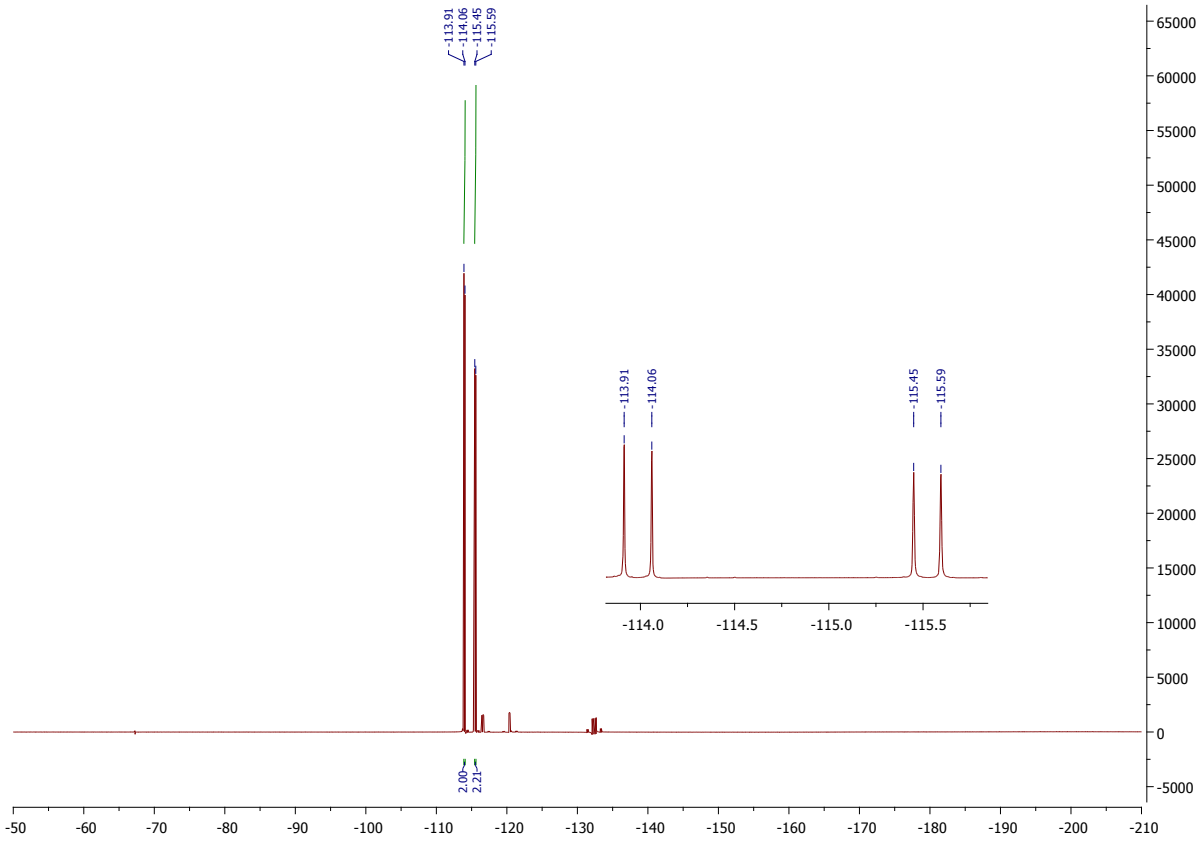


4d

Chemical Formula: $C_{12}H_9F_4NO$
Exact Mass: 259,06 g/mol
Orange solid

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.15 (d, $^{3}J_{H\text{-}H}$ = 9.3 Hz, 1H, C_8H), 7.90 (s, 1H, C_3H), 7.53 (dd, $^{3}J_{H\text{-}H}$ = 9.3, $^{4}J_{H\text{-}H}$ = 2.5 Hz, 1H, C_7H), 7.36 (s, 1H, C_5H), 7.16 (t, $^{2}J_{H\text{-}F}$ = 54.4 Hz, 1H, $C_4\mathit{CHF_2}$), 6.85 (t, $^{2}J_{H\text{-}F}$ = 55.2 Hz, 1H, $C_2\mathit{CHF_2}$), 4.03 (s, 3H, $C_8\mathit{OCH_3}$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -113.99 (d, $^{2}J_{F\text{-}H}$ = 55.3 Hz, $C_2\mathit{CHF_2}$), -115.52 (d, $^{2}J_{F\text{-}H}$ = 54.4 Hz, $C_4\mathit{CHF_2}$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 159.77 (s, C_6), 149.93 (t, $^{2}J_{C\text{-}F}$ = 27.0 Hz, C_2), 143.966 (s, C_9), 138.02 (t, $^{2}J_{C\text{-}F}$ = 22.0 Hz, C_4), 132.11 (s, C_8), 126.21 (s, C_{10}), 123.71 (s, C_7), 114.70 (tt, $^{3}J_{C\text{-}F}$ = 8.0, $^{3}J_{C\text{-}F}$ = 1.8 Hz, C_3), 114.51 (t, $^{1}J_{C\text{-}F}$ = 241.9 Hz, $C_2\mathit{CHF_2}$,), 113.57 (t, $^{1}J_{C\text{-}F}$ = 240.8 Hz, $C_4\mathit{CHF_2}$), 101.35 (s, C_5), 55.79 (s, $C_8\mathit{OCH_3}$) ppm. $C_{12}H_9F_4NO$ (259): calcd (%) N 5.40, C 55.55, H 3.47, found N 5.43, C 55.24, H 3.30. MP: 93.5 – 97.2 °C.




-113.91
-114.06
-115.45
-115.59
2.00
2.21

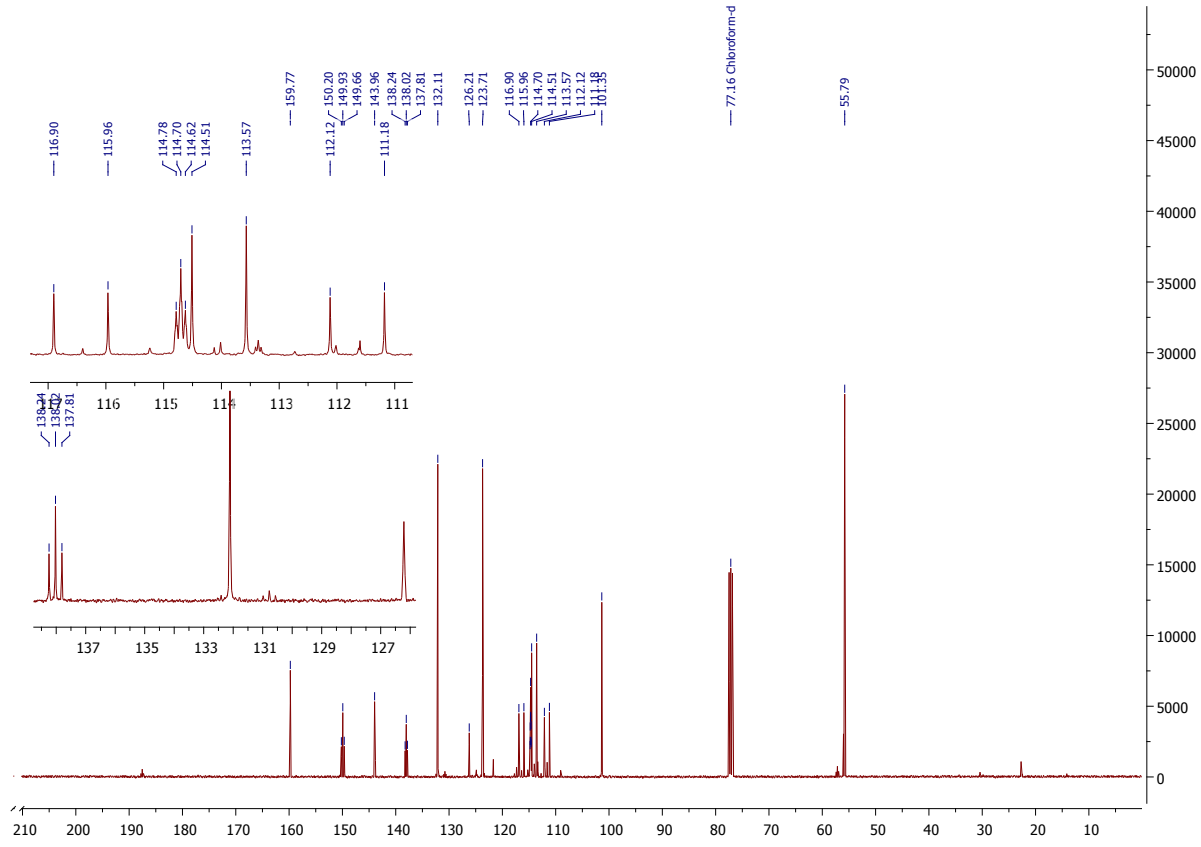
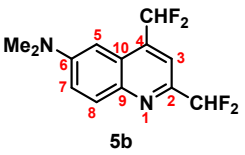

116.90
115.96
114.78
114.70
114.62
114.51
113.57
159.77
150.20
149.93
149.66
143.96
138.24
138.02
137.81
132.11
126.21
123.71
116.90
115.96
114.70
114.51
113.57
112.12
77.16 Chloroform-d
55.79

Figure S39. NMR (^{1}H, ^{13}C and ^{19}F) and characterization data of compound **5b**.

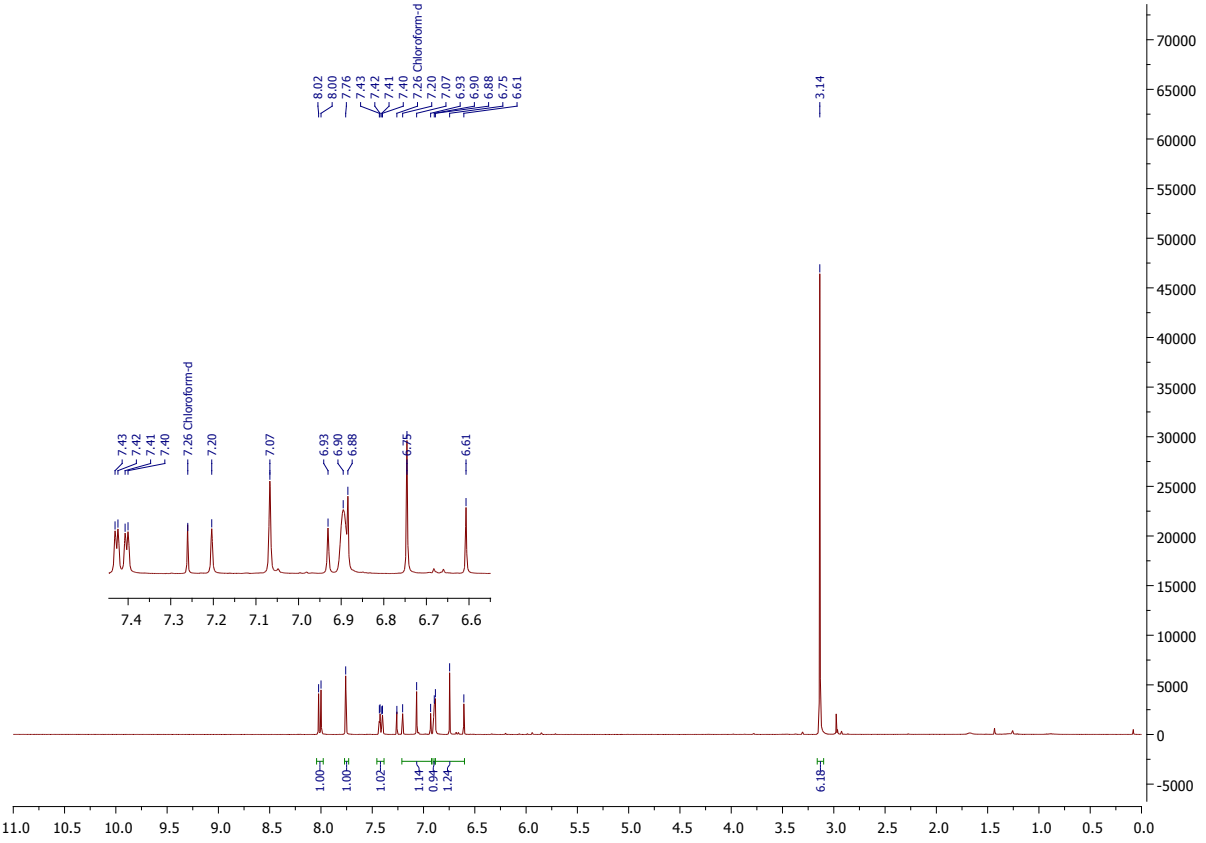
2,4-Bis(difluoromethyl)-*N,N*-dimethylquinolin-6-amine 5b

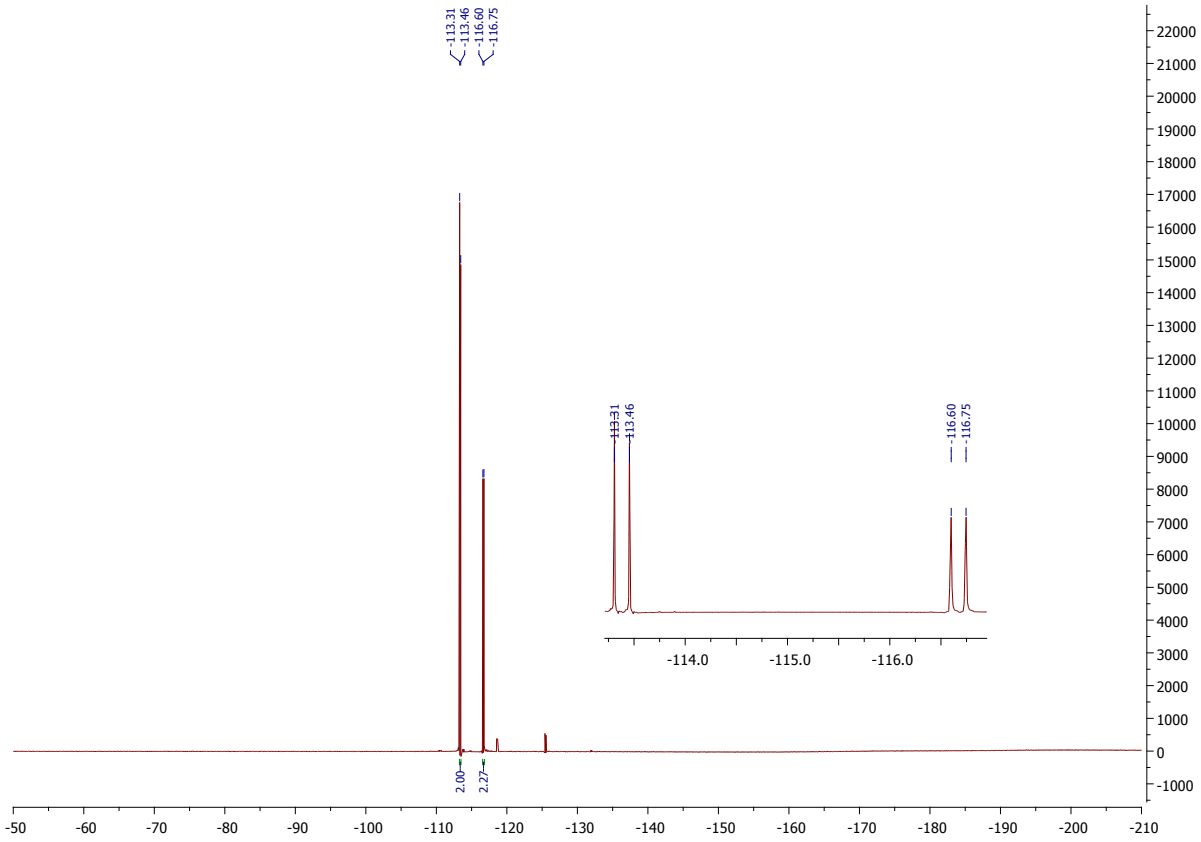


5b

Chemical Formula: $C_{13}H_{12}F_4N_2$
Exact Mass: 272,09 g/mol
Orange solid

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.01 (d, $^{3}J_{H\text{-}H}$ = 9.4 Hz, 1H, C_8H), 7.76 (s, 1H, C_3H), 7.42 (dd, $^{3}J_{H\text{-}H}$ = 9.5, $^{4}J_{H\text{-}H}$ = 2.7 Hz, 1H, C_7H), 7.07 (t, $^{2}J_{H\text{-}F}$ = 54.6 Hz, 1H, C_4CHF_2), 6.90 (s, 1H, C_5H), 6.75 (t, $^{2}J_{H\text{-}F}$ = 55.5 Hz, 1H, C_2CHF_2), 3.14 (s, 1H, $C_6N(CH_3)_2$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -113.38 (d, $^{2}J_{F\text{-}H}$ = 55.5 Hz, C_2CHF_2), -116.67 (d, $^{2}J_{F\text{-}H}$ = 54.6 Hz, C_4CHF_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 149.96 (s, C_6), 147.42 (t, $^{2}J_{C\text{-}F}$ = 26.8 Hz, C_2), 141.73 (s, C_9), 136.29 (t, $^{2}J_{C\text{-}F}$ = 21.5 Hz, C_4), 131.36 (s, C_8), 126.89 (s, C_{10}), 120.03 (s, C_7), 114.90 (t, $^{1}J_{C\text{-}F}$ = 239.9 Hz, C_2CHF_2), 114.64 (t, $^{3}J_{C\text{-}F}$ = 8.1 Hz, C_3), 113.69 (t, $^{1}J_{C\text{-}F}$ = 241.4 Hz, C_4CHF_2), 99.55 (s, C_5), 40.53 (s, $C_6N(CH_3)_2$) ppm. $C_{13}H_{12}F_4N_2$ (272): calcd (%) N 10.20, C 57.30, H 4.41, found N 10.09, C 56.86, H 4.40. MP: 115.6 – 116.9 °C.




-113.31
-113.46
-116.60
-116.75
2.00
2.27
-114.0
-115.0
-116.0

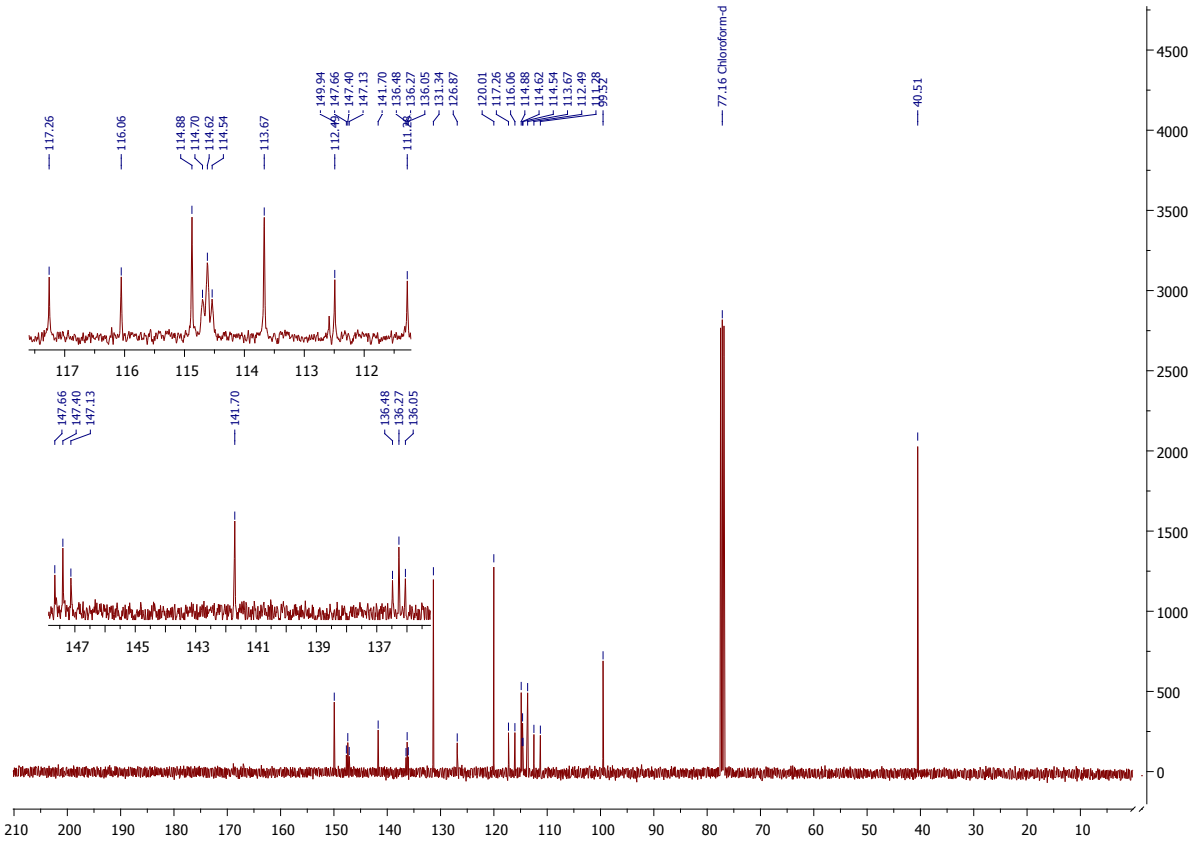
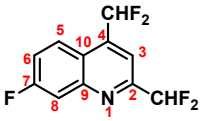

77.16 Chloroform-d
40.51
117.26
116.06
114.88
114.70
114.62
114.54
113.67
149.94
147.66
147.40
147.13
141.70
136.48
136.27
136.05
131.34
126.87
120.01
117.26
116.06
114.88
114.62
114.54
113.67
112.49
99.52
147.66
147.40
147.13
141.70
136.48
136.27
136.05

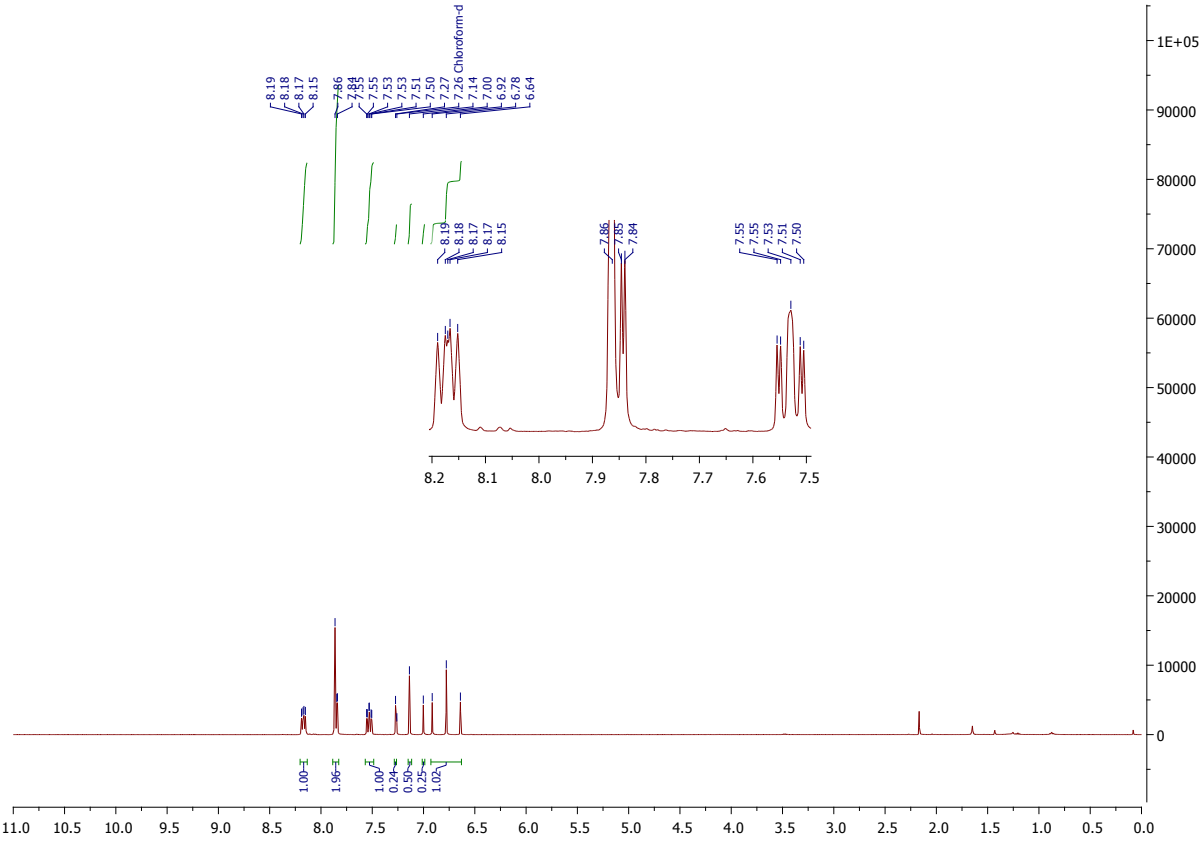
Figure S40. NMR (^{1}H, ^{13}C and ^{19}F) and characterization data of compound **2e**.

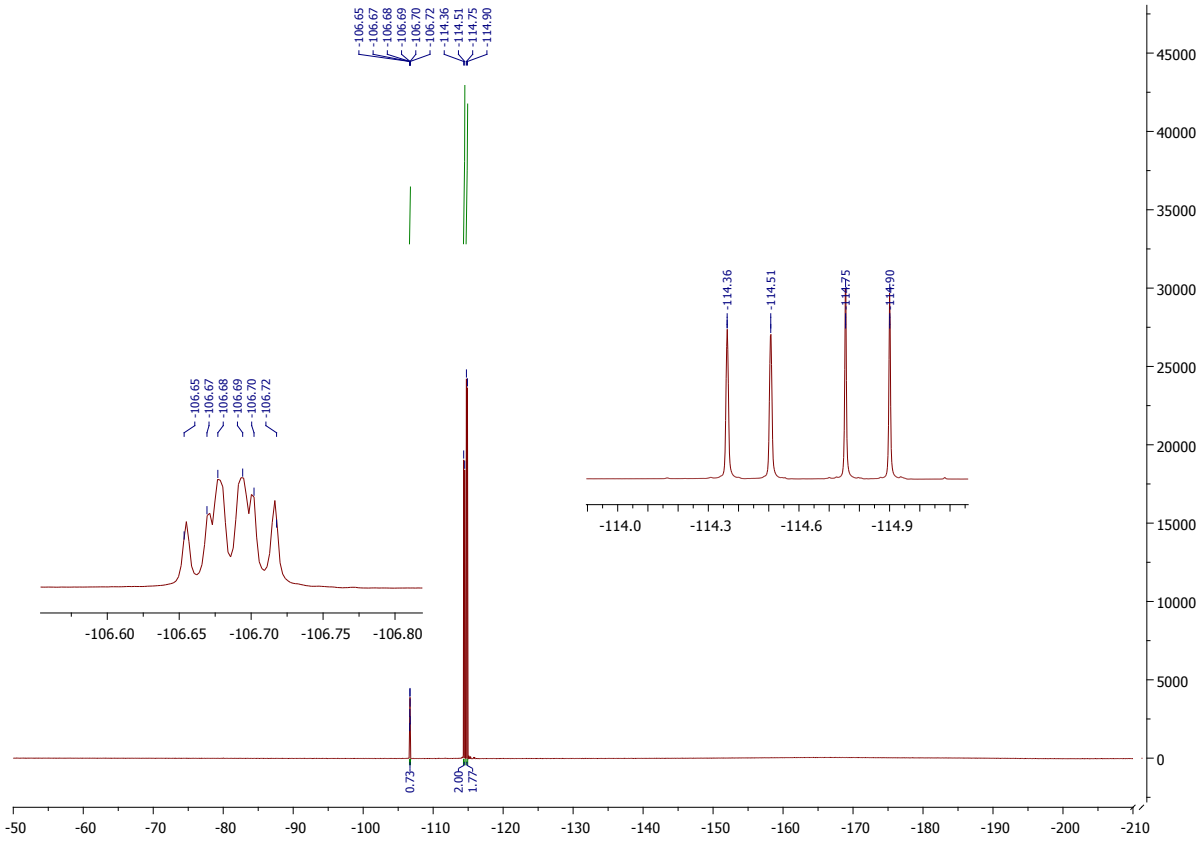
2,4-Bis(difluoromethyl)-7-fluoroquinoline 2e



2e
Chemical Formula: $C_{11}H_6F_5N$
Exact Mass: 247,04 g/mol
Yellow solid

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.17 (dd, $^{4}J_{H\text{-}H}$ = 9.3, $^{3}J_{H\text{-}F}$ = 5.7 Hz, 1H, C_8H), 7.86 (s, 1H, C_3H), 7.84 (s, 1H, C_5H), 7.57 – 7.49 (m, 1H, C_6H), 7.14 (t, $^{2}J_{H\text{-}F}$ = 54.2 Hz, 1H, C_4CHF_2), 6.78 (t, $^{2}J_{H\text{-}F}$ = 55.0 Hz, 1H, C_2CHF_2) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -106.41 – -106.96 (m, C_7F), -114.43 (d, $^{2}J_{F\text{-}H}$ = 54.2 Hz, C_2CHF_2), -114.83 (d, $^{2}J_{F\text{-}H}$ = 55.0 Hz, C_4CHF_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 163.60 (d, $^{1}J_{C\text{-}F}$ = 253.6 Hz, C_7), 153.93 (t, $^{2}J_{C\text{-}F}$ = 27.3 Hz, C_2), 149.21 (d, $^{3}J_{C\text{-}F}$ = 12.7 Hz, C_9), 140.17 (td, $^{2}J_{C\text{-}F}$ = 22.4, $^{5}J_{C\text{-}F}$ = 1.1 Hz, C_4), 126.00 (d, $^{3}J_{C\text{-}F}$ = 9.8 Hz, C_5), 121.79 (d, $^{4}J_{C\text{-}F}$ = 1.0 Hz, C_{10}), 119.91 (d, $^{2}J_{C\text{-}F}$ = 25.39 Hz, C_6), 114.54 (d, $^{2}J_{C\text{-}F}$ = 20.56 Hz, C_8), 114.12 (t, $^{1}J_{C\text{-}F}$ = 242.9 Hz, C_2CHF_2), 113.86 (m, C_3), 113.23 (t, $^{1}J_{C\text{-}F}$ = 241.5 Hz, C_4CHF_2) ppm. $C_{11}H_6F_5N$ (247): calcd (%) N 5.66, C 53.41, H 2.43, found N 5.79, C 53.54, H 2.69. MP: 73.2 – 74.6 °C.




-106.65
-106.67
-106.68
-106.69
-106.70
-106.72
-114.36
-114.51
-114.75
-114.90
0.73
2.00
1.77

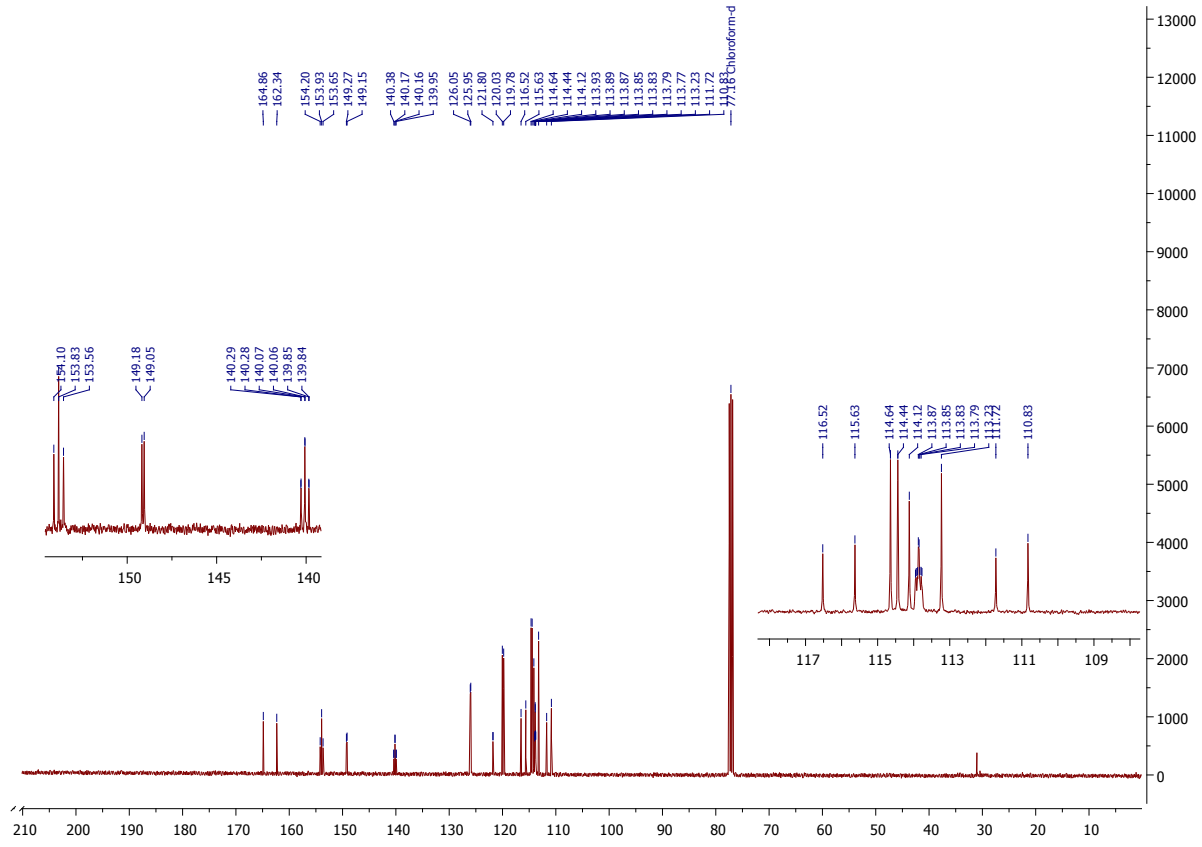
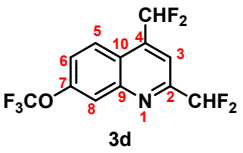

164.86
162.34
154.20
153.93
153.65
149.27
149.15
140.38
140.17
140.16
139.95
126.05
125.95
121.80
120.03
119.78
116.52
115.63
114.64
114.44
114.12
113.93
113.89
113.87
113.85
113.83
113.79
113.77
113.23
111.72
110.83
77.16 chloroform-d

Figure S41. NMR (^{1}H, ^{13}C and ^{19}F) and characterization data of compound **3d**.

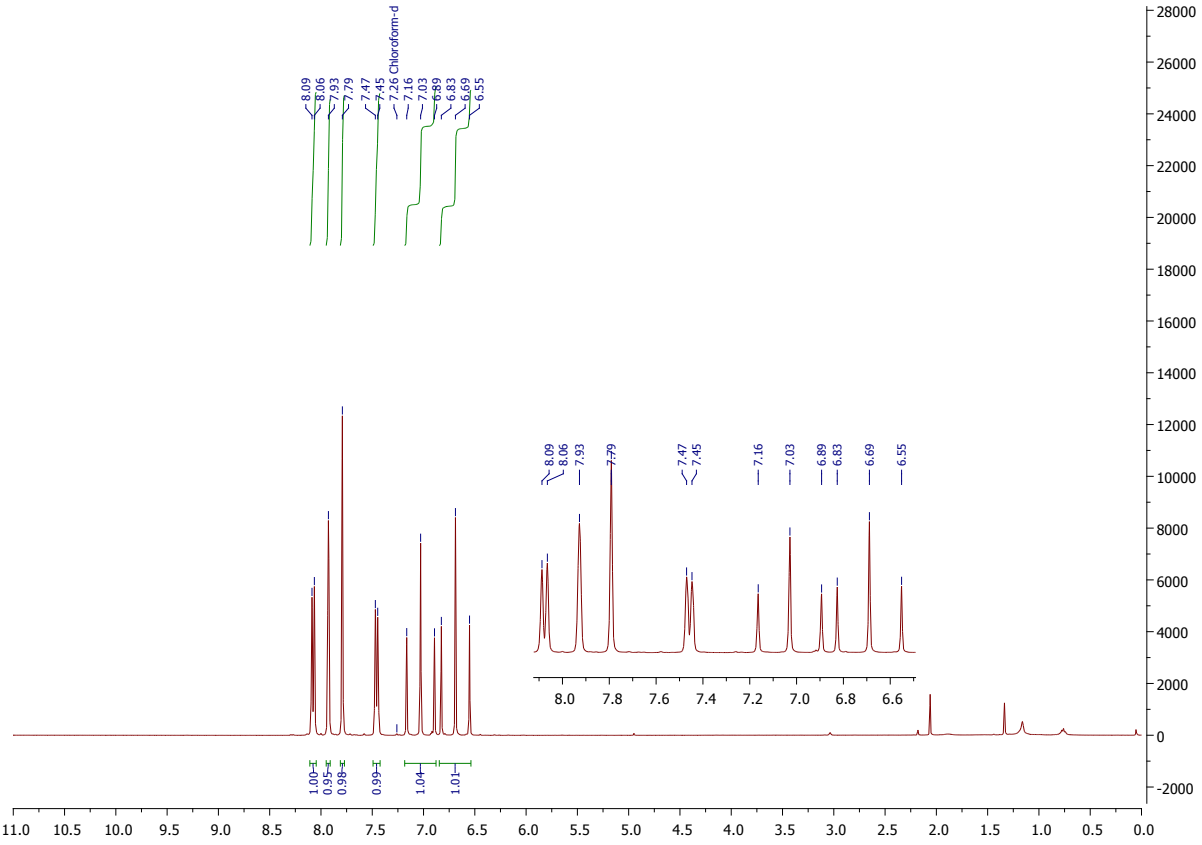
2,4-Bis(difluoromethyl)-7-(trifluoromethoxy)quinoline 3d

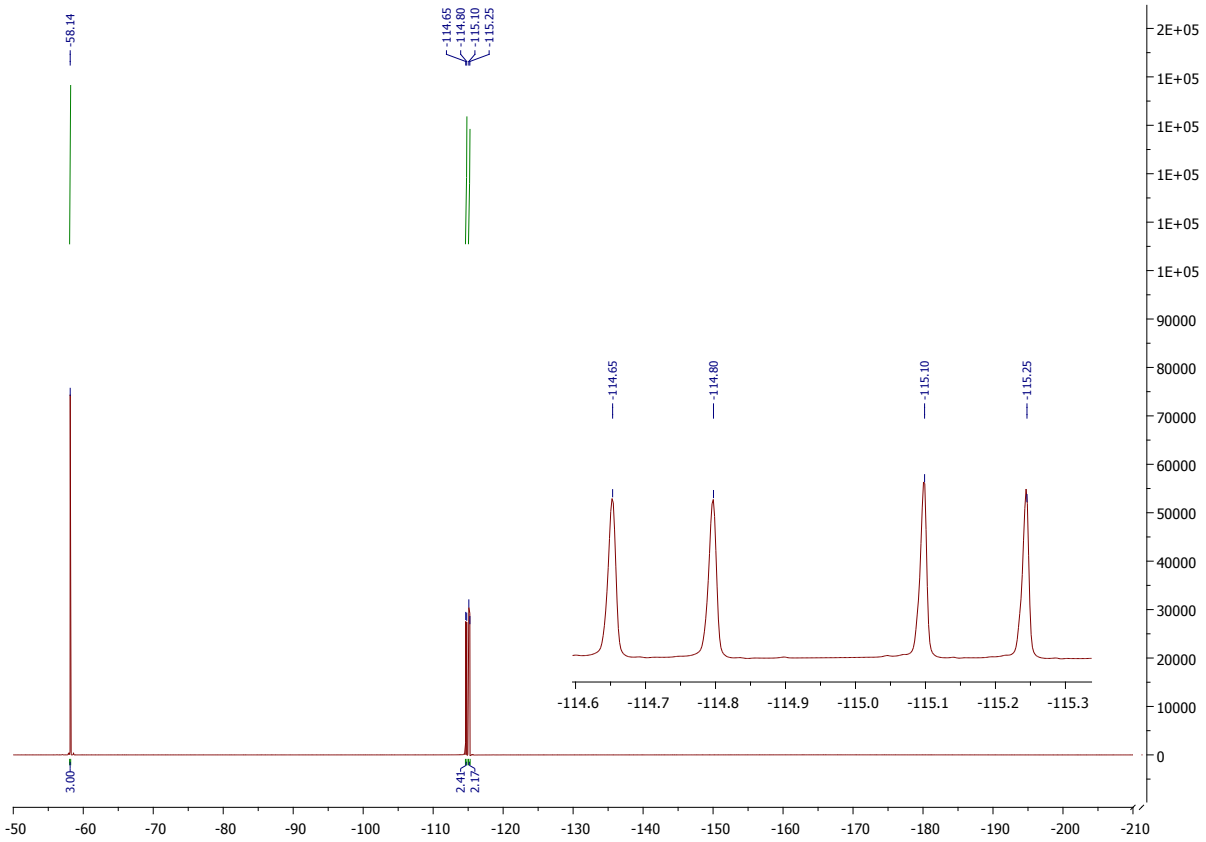


3d

Chemical Formula: $C_{12}H_6F_7NO$
Exact Mass: 313,03 g/mol
Light brown liquid

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 8.08 (d, $^{3}J_{H\text{-}H}$ = 9.2 Hz, 1H, C_5H), 7.93 (s, 1H, C_8H), 7.79 (s, 1H, C_3H), 7.46 (d, $^{3}J_{H\text{-}H}$ = 9.2 Hz, 1H, C_6H), 7.03 (t, $^{2}J_{H\text{-}F}$ = 54.2 Hz, 1H, C_4CHF_2), 6.69 (t, $^{2}J_{H\text{-}F}$ = 55.0 Hz, 1H, C_2CHF_2) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -58.14 (s, C_7OCF_3), -114.72 (d, $^{2}J_{F\text{-}H}$ = 54.1 Hz, C_2CHF_2), -115.17 (d, $^{2}J_{F\text{-}H}$ = 54.9 Hz, C_4CHF_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 154.12 (t, $^{2}J_{C\text{-}F}$ = 27.3 Hz, C_2), 150.58 (s, C_7), 148.46 (s, C_9), 140.14 (t, $^{2}J_{C\text{-}F}$ = 22.5 Hz, C_4), 125.76 (s, C_5), 123.13 (s, C_6), 122.95 (s, C_{10}), 120.58 (q, $^{1}J_{C\text{-}F}$ = 259.4 Hz, C_7OCF_3), 120.02 (s, C_8), 114.72 (tt, $^{3}J_{C\text{-}F}$ = 8, $^{3}J_{C\text{-}F}$ = 1.8 Hz, C_3), 114.04 (t, $^{1}J_{C\text{-}F}$ = 242.4 Hz, C_2CHF_2), 113.12 (t, $^{1}J_{C\text{-}F}$ = 241.4 Hz, C_4CHF_2) ppm. $C_{12}H_6F_7NO$ (313): calcd (%) N 4.47, C 45.98, H 1.92, found N 4.49, C 46.13, H 2.15.




-58.14
-114.65
-114.80
-115.10
-115.25
3.00
2.41
2.17

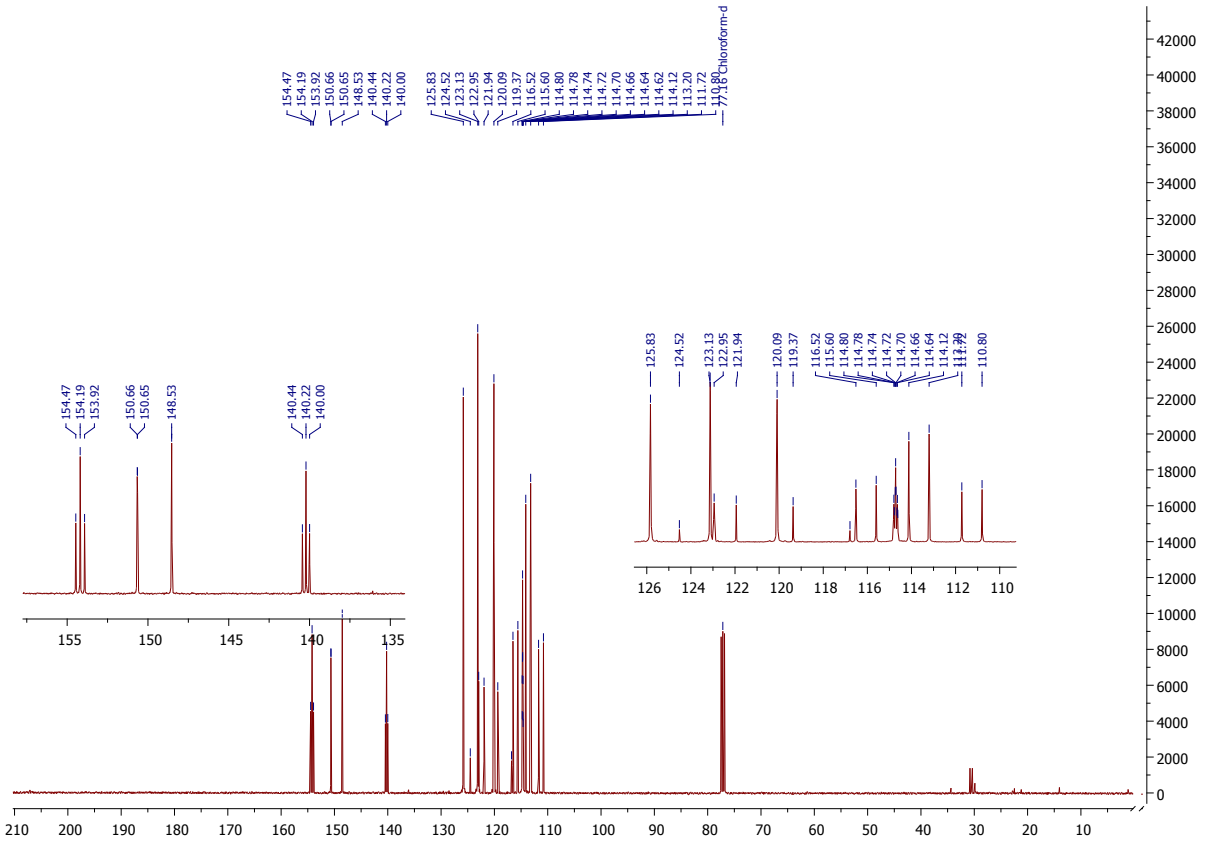
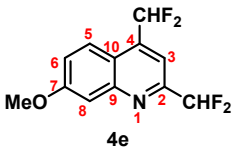

154.47
154.19
153.92
150.66
150.65
148.53
140.44
140.22
140.00
125.83
124.52
123.13
122.95
121.94
120.09
119.37
116.52
115.60
114.80
114.78
114.74
114.72
114.70
114.66
114.64
114.12
110.80
77.16 Chloroform-d

Figure S42. NMR (^{1}H, ^{13}C and ^{19}F) and characterization data of compound **4e**.

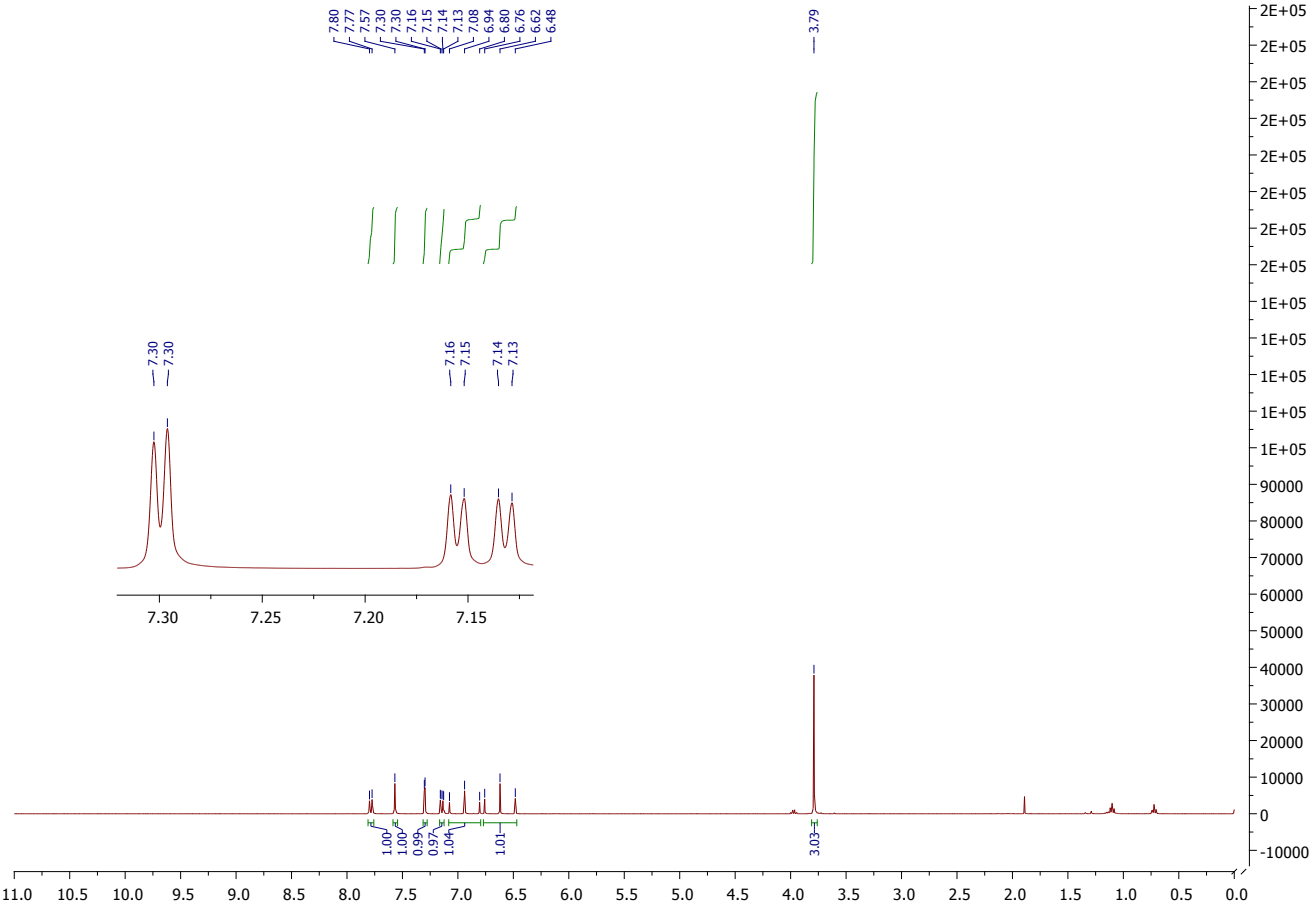
2,4-Bis(difluoromethyl)-7-methoxyquinoline 4e

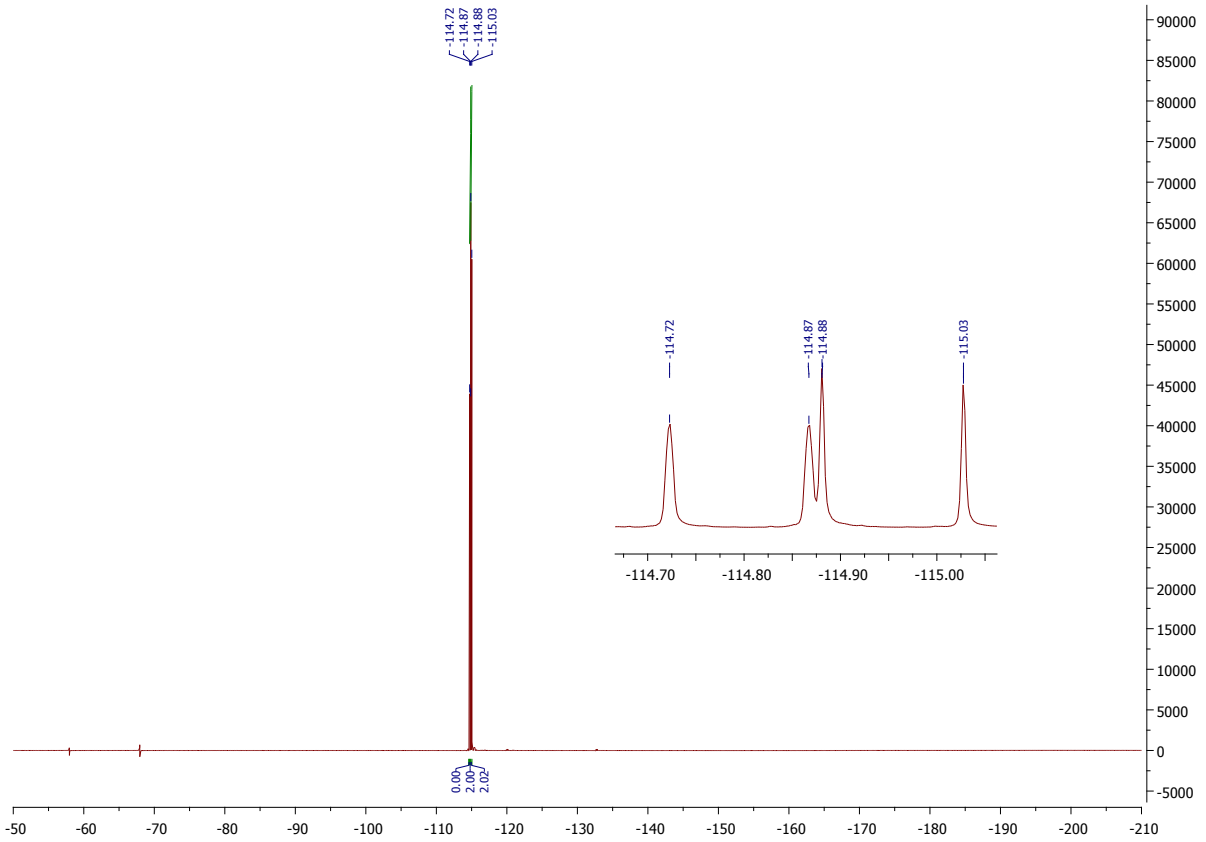


4e

Chemical Formula: $C_{12}H_9F_4NO$
Exact Mass: 259,06 g/mol
Yellow solid

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 7.79 (d, $^{3}J_{H\text{-}H}$ = 9.3 Hz, 1H, C_5H), 7.57 (s, 1H, C_3H), 7.30 (d, $^{4}J_{H\text{-}H}$ = 2.6 Hz, 1H, C_8H), 7.14 (dd, $^{3}J_{H\text{-}H}$ = 9.3, $^{4}J_{H\text{-}H}$ = 2.6 Hz, 1H, C_6H), 6.94 (t, $^{2}J_{H\text{-}F}$ = 54.4 Hz, 1H, C_4CHF_2), 6.62 (t, $^{2}J_{H\text{-}F}$ = 55.2 Hz, 1H, C_2CHF_2), 3.79 (s, 3H, C_8OCH_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -114.79 (d, $^{2}J_{F\text{-}H}$ = 54.4 Hz, C_2CHF_2), -114.95 (d, $^{2}J_{F\text{-}H}$ = 55.3 Hz, C_4CHF_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 161.45 (s, C_7), 152.86 (t, $^{2}J_{C\text{-}F}$ = 26.7 Hz, C_2), 149.83 (s, C_9), 139.56 (t, $^{2}J_{C\text{-}F}$ = 22.2 Hz, C_4), 124.33 (s, C_5), 122.45 (s, C_6), 119.77 (t, $^{3}J_{C\text{-}F}$ = 2.8 Hz, C_{10}), 114.25 (t, $^{1}J_{C\text{-}F}$ = 242.4 Hz, C_2CHF_2), 113.18 (t, $^{1}J_{C\text{-}F}$ = 241.0 Hz, C_4CHF_2), 111.89 – 111.70 (m, C_3), 108.24 (s, C_8), 55.60 (s, C_8OCH_3) ppm. $C_{12}H_9F_4NO$ (259): calcd (%) N 5.40, C 55.55, H 3.47, found N 5.55, C 55.57, H 3.67. MP: 55.4 – 56.9 °C.




-114.72
-114.87
-114.88
-115.03
0.00
2.00
2.02

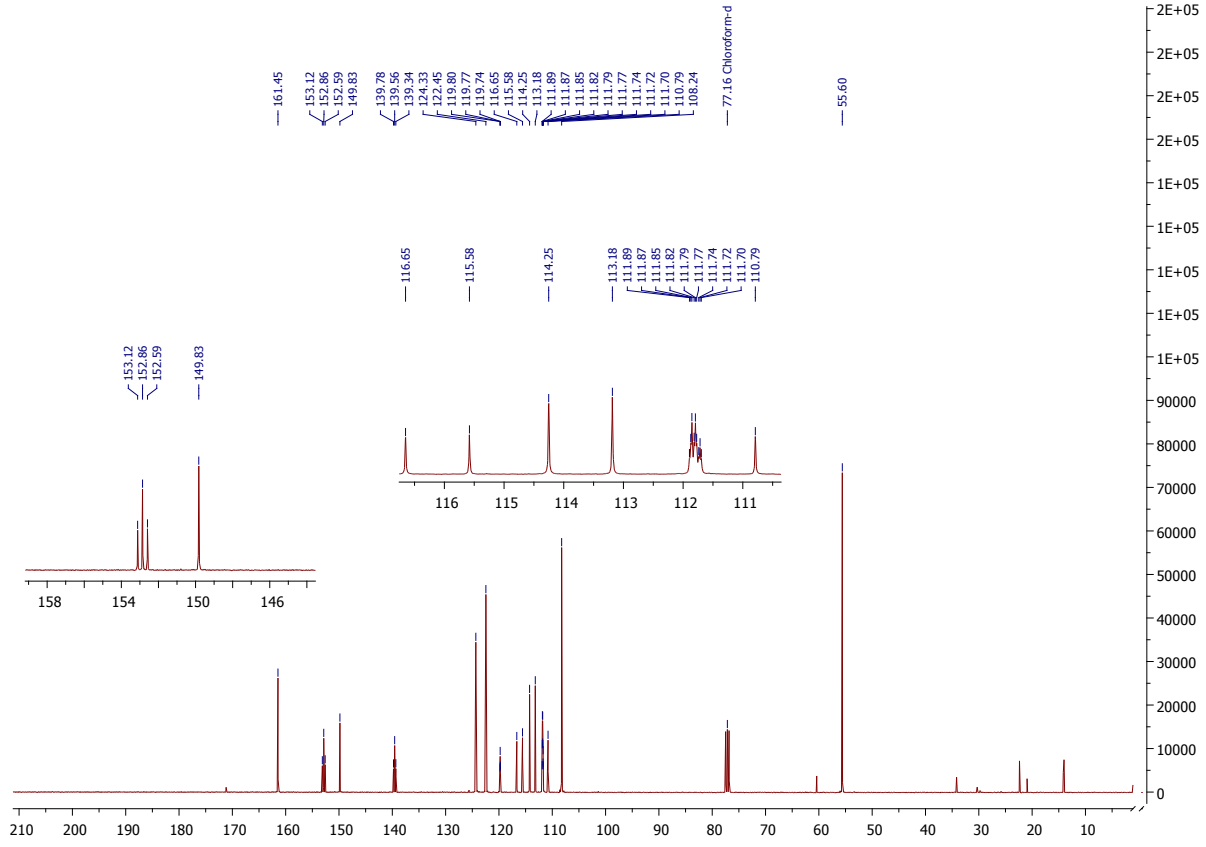
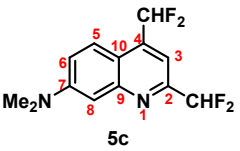

161.45
153.12
152.86
152.59
149.83
139.78
139.56
139.34
124.33
122.45
119.80
119.77
119.74
116.65
115.58
114.25
113.18
111.89
111.87
111.85
111.82
111.79
111.77
111.74
111.72
111.70
110.79
108.24
77.16 Chloroform-d
55.60

Figure S43. NMR (^{1}H, ^{13}C and ^{19}F) and characterization data of compound **5c**.

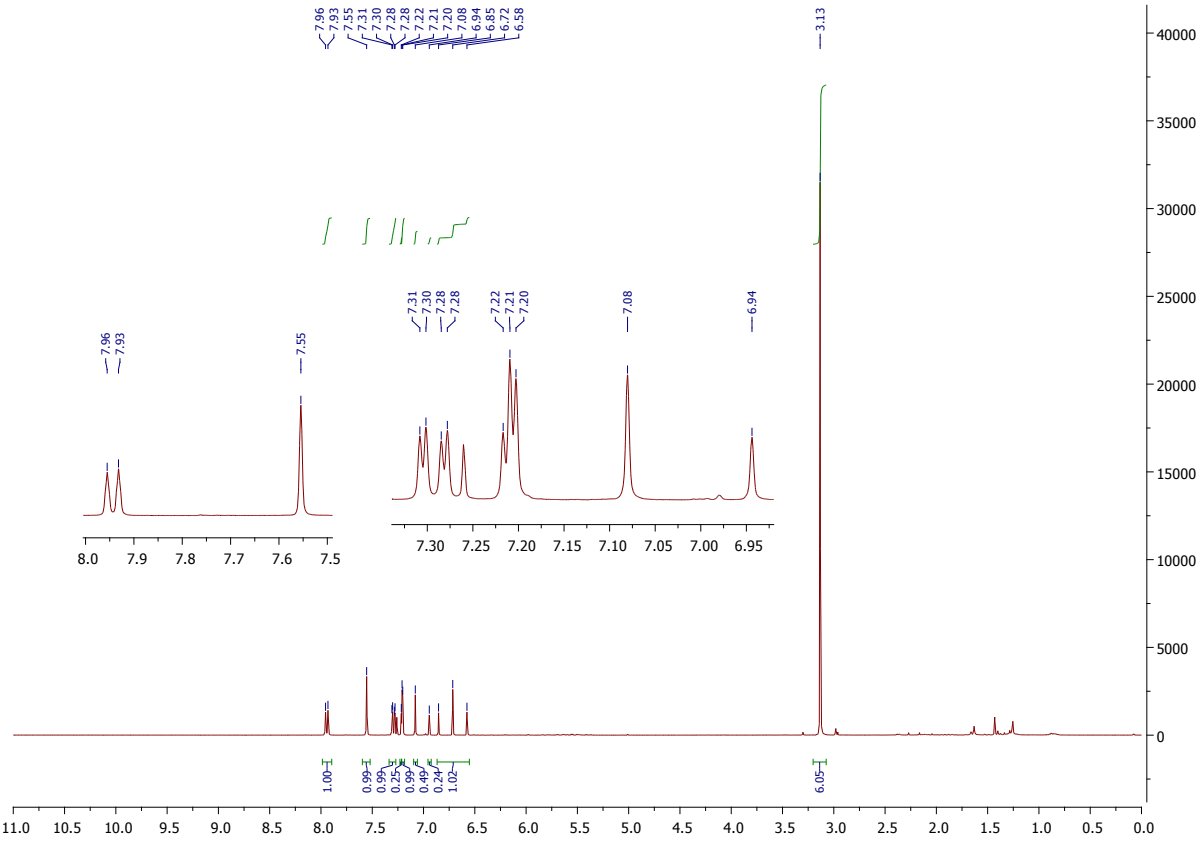
2,4-Bis(difluoromethyl)-*N,N*-dimethylquinolin-7-amine 5c

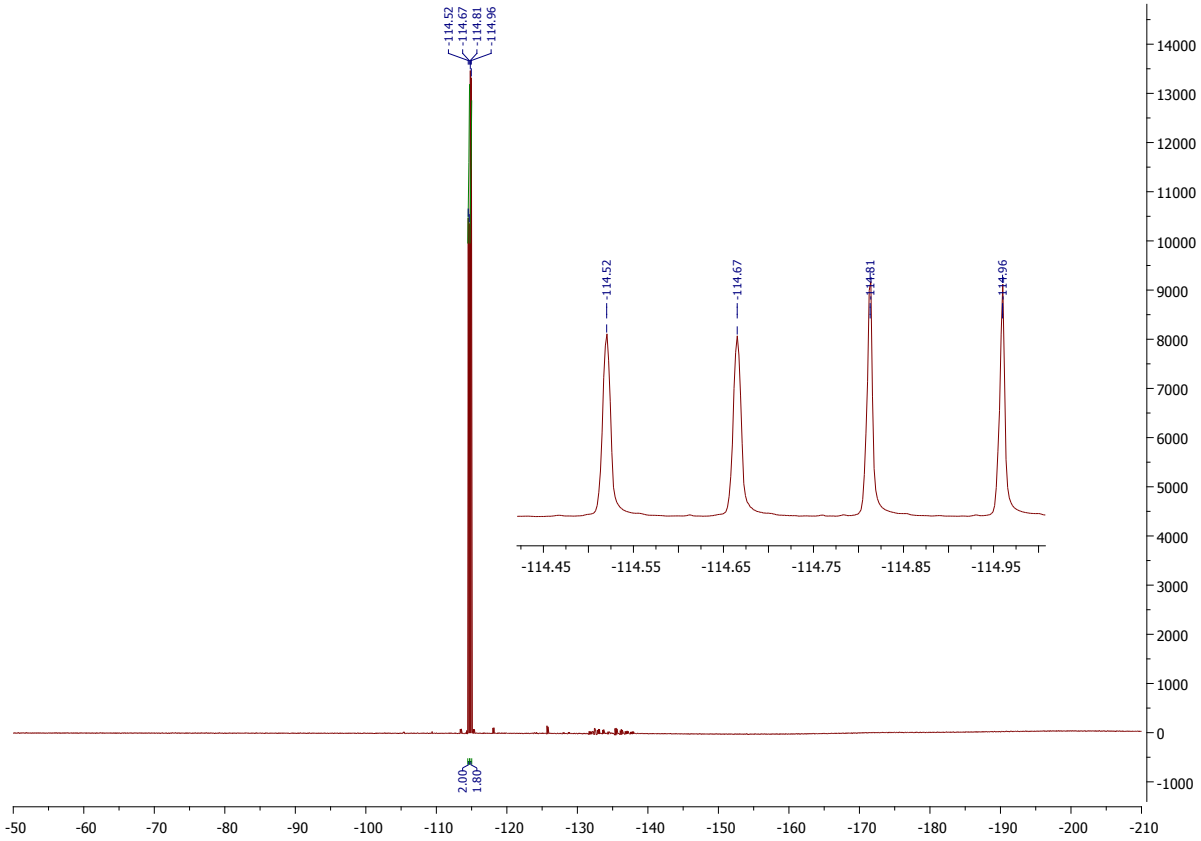


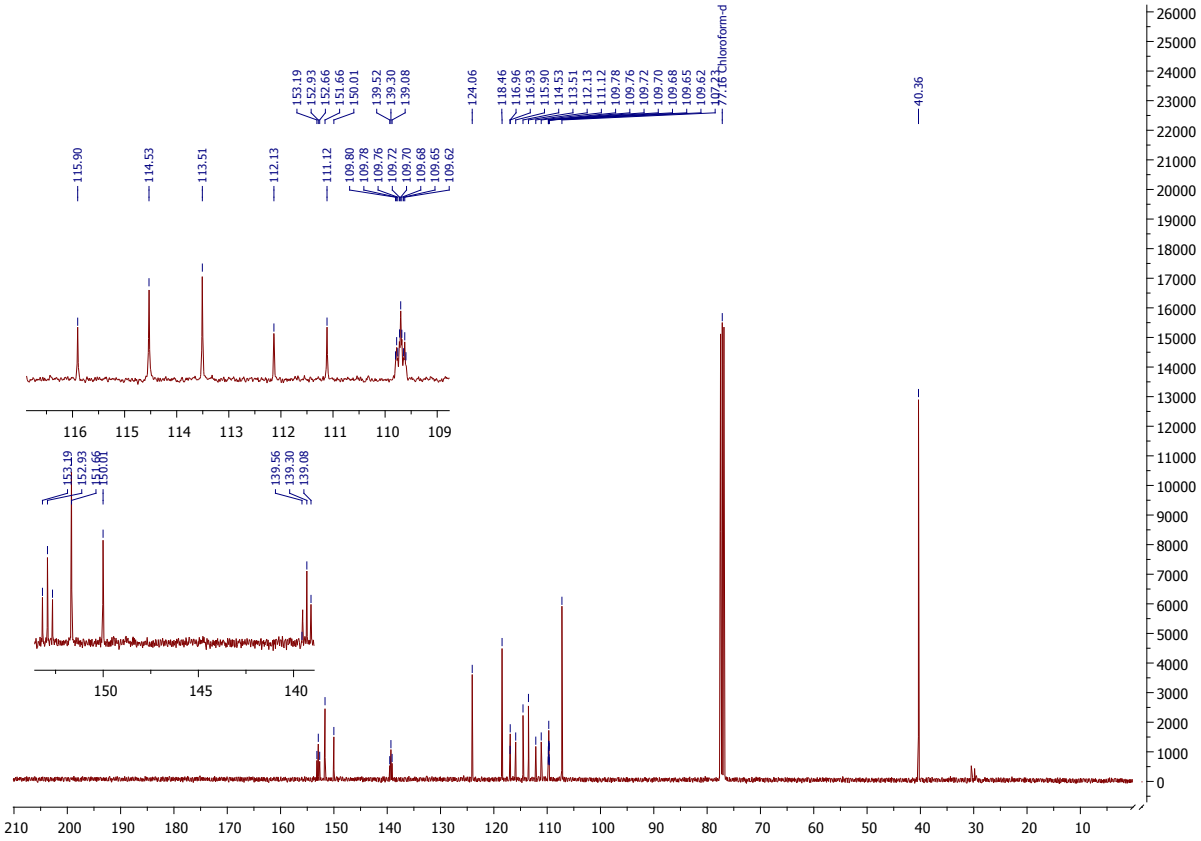
5c

Chemical Formula: $C_{13}H_{12}F_4N_2$
Exact Mass: 272,09 g/mol
Brown solid

^{1}H NMR (400 MHz, $CDCl_3$) δ_H = 7.94 (d, $^{3}J_{H\text{-}H}$ = 9.4 Hz, 1H, C_5H), 7.55 (s, 1H, C_8H), 7.29 (dd, $^{3}J_{H\text{-}H}$ = 9.4, $^{4}J_{H\text{-}H}$ = 2.7 Hz, 1H, C_6H), 7.21 (d, $^{4}J_{H\text{-}F}$ = 2.7 Hz, 1H, C_3H), 7.08 (t, $^{2}J_{H\text{-}F}$ = 54.6 Hz, 1H, C_4CHF_2), 6.72 (t, $^{2}J_{H\text{-}F}$ = 55.4 Hz, 1H, C_2CHF_2), 3.13 (s, 6H, $C_7N(CH_3)_2$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ_F = -114.59 (d, $^{2}J_{F\text{-}H}$ = 54.6 Hz, C_2CHF_2), -114.89 (d, $^{2}J_{F\text{-}H}$ = 55.4 Hz, C_4CHF_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ_C = 152.95 (t, $^{2}J_{C\text{-}F}$ = 26.5 Hz, C_2), 151.69 (s, C_7), 150.03 (s, C_9), 139.30 (t, $^{2}J_{C\text{-}F}$ = 23.9 Hz, C_4), 124.08 (s, C_5), 118.49 (s, C_8), 116.98 (s, C_{10}), 114.56 (t, $^{1}J_{C\text{-}F}$ = 264.0 Hz, C_2CHF_2), 113.54 (t, $^{1}J_{C\text{-}F}$ = 240.8 Hz, C_4CHF_2), 109.73 (tt, $^{3}J_{C\text{-}F}$ = 8.0, $^{3}J_{C\text{-}F}$ = 2.2 Hz, C_3), 107.26 (s, C_6), 40.38 (s, $C_7N(CH_3)_2$) ppm. $C_{13}H_{12}F_4N_2$ (272): calcd (%) N 10.20, C 57.30, H 4.41, found N 10.06, C 57.26, H 4.41. MP: 83.7 – 84.7 °C.




-114.52
-114.67
-114.81
-114.96
-114.45
-114.55
-114.65
-114.75
-114.85
-114.95
2.00
1.80


153.19
152.93
152.66
151.66
150.01
139.52
139.30
139.08
124.06
118.46
116.96
116.93
115.90
114.53
113.51
112.13
111.12
109.80
109.78
109.76
109.72
109.70
109.68
109.65
109.62
77.16 Chloroform-d
40.36