



Supporting Information

for

Synthesis of aryl 2-bromo-2-chloro-1,1-difluoroethyl ethers through the base-mediated reaction between phenols and haloethane

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Beilstein J. Org. Chem. **2021**, *17*, 89–96. doi:10.3762/bjoc.17.9

Characterization data for 2b–p and copies of ^1H , ^{13}C , and ^{19}F NMR spectra

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1. Characterization data for 2b–p

2-Bromo-2-chloro-1,1-difluoroethyl *p*-methoxyphenyl ether (2b): The title product (2b) was purified by column chromatography (hexane:CHCl₃ = 19:1 to hexane:AcOEt = 9:1) and was obtained in 79% yield (237.2 mg). A yellow oil; ¹H NMR (400 MHz, CDCl₃) δ: 3.81 (3H, s), 5.90 (1H, t, *J* = 5.0 Hz), 6.88 (2H, d, *J* = 9.1 Hz), 7.15 (2H, d, *J* = 9.1 Hz); ¹³C NMR (100 MHz, CDCl₃) δ: 53.5 (t, *J* = 42.1 Hz), 55.7, 114.6, 119.7 (t, *J* = 267.1 Hz), 123.2, 142.9, 157.9; ¹⁹F NMR (376 MHz, CDCl₃) δ: -78.2 (1F, dd, *J* = 137.5, 5.0 Hz), -78.5 (1F, dd, *J* = 137.5, 5.0 Hz); MS (EI) *m/z*: 300 (M⁺); HRMS (EI) Calcd. for C₉H₈BrClF₂O₂: 299.9364 (M⁺), Found: 299.9361.

2-Bromo-2-chloro-1,1-difluoroethyl *o*-*t*-butylphenyl ether (2c): The title product (2c) was purified by column chromatography and preparative TLC (hexane only). 2c was obtained in 47% yield (155.2 mg). A colorless oil; ¹H NMR (400 MHz, CDCl₃) δ: 1.41 (9H, s), 5.97 (1H, t, *J* = 5.2 Hz), 7.13 (1H, ddd, *J* = 7.5, 7.5, 1.2 Hz), 7.18-7.24 (1H, m), 7.37-7.43 (2H, m); ¹³C NMR (100 MHz, CDCl₃) δ: 30.5, 35.0, 54.0 (t, *J* = 42.1 Hz), 119.1 (t, *J* = 3.6 Hz), 120.0 (t, *J* = 270.8 Hz), 125.0, 127.2, 127.8, 140.0, 149.6; ¹⁹F NMR (376 MHz, CDCl₃) δ: -76.9 (1F, ddd, *J* = 134.3, 5.2, 2.1 Hz), -77.2 (1F, ddd, *J* = 134.3, 5.2, 2.1 Hz); MS (EI) *m/z*: 326 (M⁺); HRMS (EI) Calcd. for C₁₂H₁₄BrClF₂O: 325.9885 (M⁺), Found: 325.9879.

2-Bromo-2-chloro-1,1-difluoroethyl *p*-nitrophenyl ether (2d): The title product (2d) was purified by column chromatography and preparative TLC (hexane:AcOEt = 19:1). 2d was obtained in 3% yield (10.7 mg). A yellow oil; ¹H NMR (400 MHz, CDCl₃) δ: 5.95 (1H, t, *J* = 5.1 Hz), 7.39 (2H, d, *J* = 8.4 Hz), 8.29 (2H, d, *J* = 8.4 Hz); ¹³C NMR (100 MHz, CDCl₃) δ: 52.9 (t, *J* = 40.6 Hz), 119.8 (t, *J* = 272.0 Hz), 121.8, 125.7, 145.8, 154.4; ¹⁹F NMR (376 MHz, CDCl₃) δ: -78.1 (1F, dd, *J* = 134.9, 4.9 Hz), -78.5 (1F, dd, *J* = 134.9, 4.9 Hz); MS (EI) *m/z*: 315 (M⁺); HRMS (EI) Calcd. for C₈H₅BrClF₂NO₃: 314.9109 (M⁺), Found: 314.9106.

2-Bromo-2-chloro-1,1-difluoroethyl *p*-trifluoromethylphenyl ether (2e): The title product (2e) was purified by column chromatography (hexane only). 2e was obtained in 48% yield (163.3 mg). A pale yellow oil; ¹H NMR (400 MHz, CDCl₃) δ: 5.93 (1H, t, *J* = 5.0 Hz), 7.35 (2H, d, *J* = 8.3 Hz), 7.67 (2H, d, *J* = 8.3 Hz); ¹³C NMR (100 MHz, CDCl₃) δ: 53.1 (t, *J* = 40.8 Hz), 119.8 (t, *J* = 270.2 Hz), 121.9, 123.9 (q, *J* = 272.3 Hz), 127.2 (q, *J* = 3.5 Hz), 128.8 (q, *J* = 33.0 Hz), 152.2; ¹⁹F NMR (376 MHz, CDCl₃) δ: -62.2 (3F, s), -78.0 (1F, dd, *J* = 136.2, 4.9 Hz), -78.3 (1F, dd, *J* = 136.2, 4.9 Hz); MS (EI) *m/z*: 338 (M⁺); HRMS (EI) Calcd. for C₉H₅BrClF₅O: 337.9132 (M⁺), Found: 337.9135.

Ethyl *p*-(2-bromo-2-chloro-1,1-difluoroethoxy)benzoate (2f): The title product (2f) was purified by column chromatography and preparative TLC (hexane:AcOEt = 15:1). 2f was obtained in 47% yield (161.0 mg). A pale yellow oil; ¹H NMR (400 MHz, CDCl₃) δ: 1.40 (3H, t, *J* = 7.1 Hz), 4.39 (2H, q, *J* = 7.1 Hz), 5.92 (3H, t, *J* = 5.1 Hz), 7.29 (2H, d, *J* = 8.4 Hz), 8.08 (2H, d, *J* = 8.4 Hz); ¹³C NMR (100 MHz, CDCl₃) δ: 14.5, 53.3 (t, *J* = 41.2 Hz), 61.3, 119.7 (t, *J* = 270.1 Hz), 121.2, 128.7, 131.5, 153.2, 165.7; ¹⁹F NMR (376 MHz, CDCl₃) δ: -78.0 (1F, dd, *J* = 136.5, 5.1 Hz), -78.3 (1F, dd, *J* = 136.5, 5.1 Hz); MS (EI) *m/z*: 342 (M⁺); HRMS (EI) Calcd. for C₁₁H₁₀BrClF₂O₃: 341.9470 (M⁺), Found: 341.9473.

2-Bromo-2-chloro-1,1-difluoroethyl *o*-phenylphenyl ether (2h): The title product (2h) was purified by column chromatography and preparative TLC (hexane only). 2h was obtained in 71% yield (247.1 mg). A colorless oil; ¹H NMR (400 MHz, CDCl₃) δ: 5.64 (1H, t, *J* = 5.2 Hz), 7.30-7.49 (9H, m); ¹³C NMR (100 MHz, CDCl₃) δ: 53.4 (t, *J* = 41.2 Hz), 119.6 (t, *J* = 268.8 Hz), 122.4, 126.7, 127.6, 128.2, 128.6, 129.7, 131.5, 135.9, 137.4, 146.7; ¹⁹F NMR (376

MHz, CDCl₃) δ : -77.5 (2F, dd, J = 5.2, 3.1 Hz); MS (EI) m/z : 346 (M⁺); HRMS (EI) Calcd. for C₁₄H₁₀BrClF₂O: 345.9572 (M⁺), Found: 345.9562.

2-Bromo-2-chloro-1,1-difluoroethyl *m*-phenylphenyl ether (2i): The title product (2i) was purified by column chromatography and preparative TLC (hexane only). 2i was obtained in 79% yield (275.9 mg). A pale yellow oil; ¹H NMR (400 MHz, CDCl₃) δ : 5.94 (1H, t, J = 5.1 Hz), 7.19-7.24 (1H, m), 7.35-7.53 (6H, m), 7.56-7.61 (2H, m); ¹³C NMR (100 MHz, CDCl₃) δ : 53.5 (t, J = 41.7 Hz), 119.7 (t, J = 269.6 Hz), 120.5, 120.6, 125.3, 127.3, 128.0, 129.1, 130.0, 140.0, 143.2, 150.0; ¹⁹F NMR (376 MHz, CDCl₃) δ : -77.7 (1F, dd, J = 136.9, 5.1 Hz), -78.1 (1F, dd, J = 136.9, 5.1 Hz); MS (EI) m/z : 346 (M⁺); HRMS (EI) Calcd. for C₁₄H₁₀BrClF₂O: 345.9572 (M⁺), Found: 345.9567.

2-Bromo-2-chloro-1,1-difluoroethyl *p*-phenylphenyl ether (2j): The title product (2j) was purified by column chromatography (hexane only) and was obtained in 88% yield (304.4 mg). White solid; mp: 46.0-46.5 °C; ¹H NMR (400 MHz, CDCl₃) δ : 5.93 (1H, t, J = 4.8 Hz), 7.30 (2H, d, J = 7.9 Hz), 7.37 (1H, t, J = 7.2 Hz), 7.45 (2H, dd, J = 7.9, 7.2 Hz), 7.58 (4H, t, J = 8.4 Hz); ¹³C NMR (100 MHz, CDCl₃) δ : 53.5 (t, J = 41.6 Hz), 119.7 (t, J = 267.7 Hz), 122.1, 127.2, 127.7, 128.4, 129.0, 139.7, 140.1, 149.1; ¹⁹F NMR (376 MHz, CDCl₃) δ : -78.0 (1F, dd, J = 137.1, 4.8 Hz), -78.1 (1F, dd, J = 137.1, 4.8 Hz); MS (EI) m/z : 346 (M⁺); HRMS (EI) Calcd. for C₁₄H₁₀BrClF₂O: 345.9572 (M⁺), Found: 345.9566.

2-Bromo-2-chloro-1,1-difluoroethyl 1-naphthyl ether (2k): The title product (2k) was purified by column chromatography (hexane only). 2k was obtained in 85% yield (275.3 mg). A colorless oil; ¹H NMR (400 MHz, CDCl₃) δ : 6.09 (1H, t, J = 4.8 Hz), 7.39-7.49 (2H, m), 7.51-7.60 (2H, m), 7.74-7.80 (1H, m), 7.84-7.91 (1H, m), 8.21-8.29 (1H, m); ¹³C NMR (100 MHz, CDCl₃) δ : 53.7 (t, J = 41.7 Hz), 117.4, 120.1 (t, J = 268.1 Hz), 122.0, 125.3, 126.5, 126.8, 126.9, 127.7, 127.9, 134.8, 145.5; ¹⁹F NMR (376 MHz, CDCl₃) δ : -77.5 (1F, dd, J = 136.6, 4.8 Hz), -78.0 (1F, dd, J = 136.6, 4.8 Hz); MS (EI) m/z : 320 (M⁺); HRMS (EI) Calcd. for C₁₂H₈BrClF₂O: 319.9415 (M⁺), Found: 319.9416.

2-Bromo-2-chloro-1,1-difluoroethyl *o*-iodophenyl ether (2l): The title product (2l) was purified by column chromatography (hexane only) and was obtained in 67% yield (266.7 mg). A yellow oil; ¹H NMR (400 MHz, CDCl₃) δ : 6.01 (1H, t, J = 5.6 Hz), 6.97-7.03 (1H, m), 7.30-7.40 (2H, m), 7.86 (1H, dd, J = 8.4, 1.6 Hz); ¹³C NMR (100 MHz, CDCl₃) δ : 53.5 (t, J = 40.3 Hz), 89.9, 119.9 (t, J = 270.5 Hz), 122.0, 127.9, 129.6, 140.3, 149.9; ¹⁹F NMR (376 MHz, CDCl₃) δ : -77.4 (1F, ddd, J = 135.0, 5.8, 1.1 Hz), -77.8 (1F, ddd, J = 135.0, 5.8, 1.1 Hz); MS (EI) m/z : 396 (M⁺); HRMS (EI) Calcd. for C₈H₅BrClF₂IO: 395.8225 (M⁺), Found: 395.8231.

***o*-Allylphenyl 2-bromo-2-chloro-1,1-difluoroethyl ether (2m):** The title product (2m) was purified by column chromatography (hexane only) and was obtained in 81% yield (253.4 mg). A colorless oil; ¹H NMR (400 MHz, CDCl₃) δ : 3.49 (2H, d, J = 6.8 Hz), 5.06-5.14 (2H, m), 5.95 (1H, t, J = 4.6 Hz), 5.96 (1H, ddt, J = 17.6, 9.4, 6.7 Hz), 7.17-7.32 (4H, m); ¹³C NMR (100 MHz, CDCl₃) δ : 34.2, 53.7 (t, J = 41.8 Hz), 116.5, 119.9 (t, J = 268.9 Hz), 121.8, 126.5, 127.5, 130.8, 133.2, 136.2, 147.7; ¹⁹F NMR (376 MHz, CDCl₃) δ : -77.3 (1F, dd, J = 137.1, 4.6 Hz), -77.6 (1F, dd, J = 137.1, 4.6 Hz); MS (EI) m/z : 310 (M⁺); HRMS (EI) Calcd. for C₁₁H₁₀BrClF₂O: 309.9572 (M⁺), Found: 309.9568.

2-Bromo-2-chloro-1,1-difluoroethyl *o*-propenylphenyl ether (2n): The title product (2n) was purified by column chromatography and preparative TLC (hexane only). 2n was obtained an inseparable mixture of *cis-trans* isomers (1:2.2) in 71% yield (219.9 mg). A colorless oil; ¹H NMR (400 MHz, CDCl₃) δ : 1.81 (dd, J = 7.0, 1.7 Hz, *cis*-isomer)

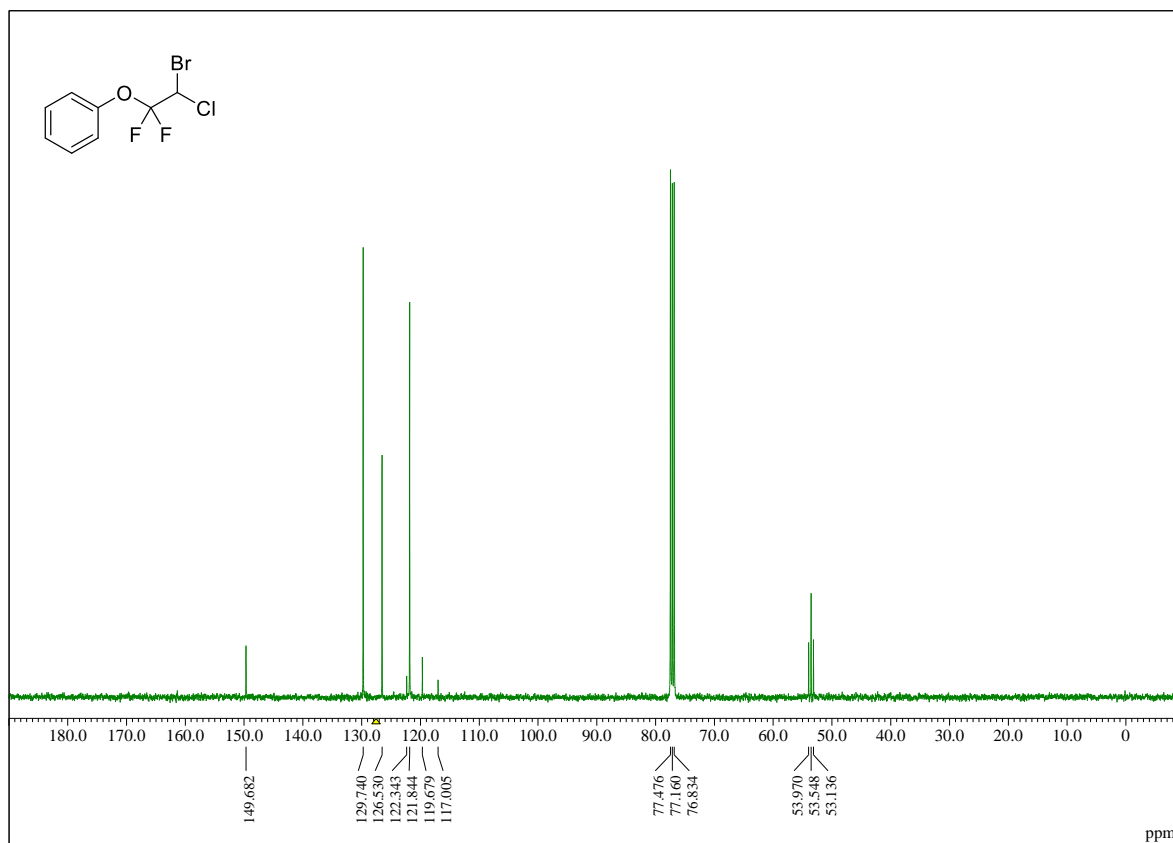
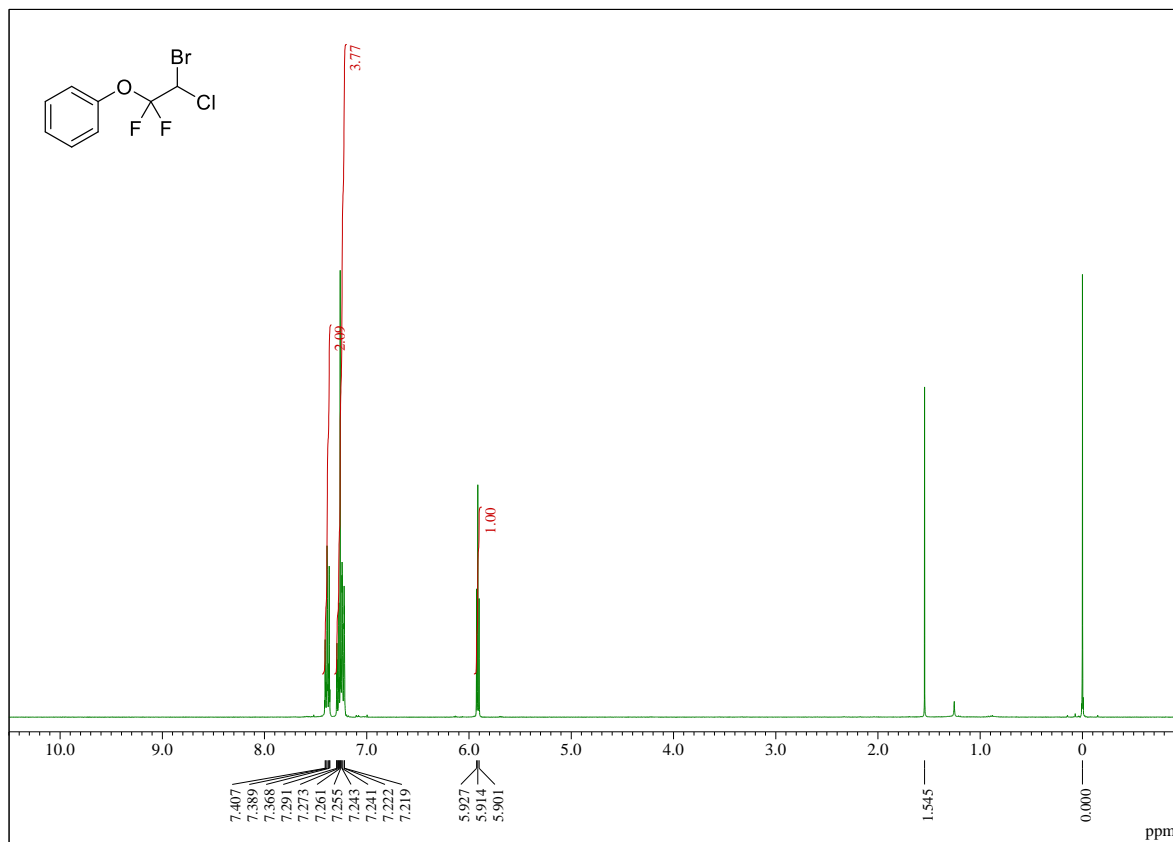
and 1.91 (dd, $J = 6.7, 1.7$ Hz, *trans*-isomer) (3H), 5.88 (dq, $J = 11.4, 7.0$ Hz, *cis*-isomer) and 6.26 (dd, $J = 15.7, 6.7$ Hz, *trans*-isomer) (1H), 5.93 (t, $J = 5.0$ Hz, *cis*-isomer) and 5.98 (t, $J = 4.8$ Hz, *trans*-isomer) (1H), 6.54 (dq, $J = 11.4, 1.7$ Hz, *cis*-isomer) and 6.76 (d, $J = 15.7$ Hz, *trans*-isomer) (1H), 7.17-7.31 (3H, m), 7.33-7.38 (m, *cis*-isomer) and 7.49-7.57 (m, *trans*-isomer) (1H); ^{13}C NMR (100 MHz, CDCl_3) δ : 14.7 (*cis*-isomer), 19.0 (*trans*-isomer), 53.6 (t, $J = 41.8$ Hz, *cis*-isomer), 53.7 (t, $J = 41.8$ Hz, *trans*-isomer), 119.77 (t, $J = 267.9$ Hz, *cis*-isomer), 119.81 (t, $J = 268.0$ Hz, *trans*-isomer), 122.2 (*cis*-isomer), 122.4 (*trans*-isomer), 124.5, 126.0 (*cis*-isomer), 126.4 (*trans*-isomer), 126.6 (*trans*-isomer), 127.7 (*trans*-isomer), 127.9 (*cis*-isomer), 128.4 (*trans*-isomer), 128.8 (*cis*-isomer), 130.9 (*cis*-isomer), 131.4 (*cis*-isomer), 131.9 (*trans*-isomer), 146.1 (*trans*-isomer), 147.2 (*cis*-isomer); ^{19}F NMR (376 MHz, CDCl_3) δ : -77.2 (1F, dd, $J = 137.1, 4.8$ Hz, *trans*-isomer), -77.6 (1F, dd, $J = 137.1, 4.8$ Hz, *trans*-isomer), -77.51 (1F, dd, $J = 9.0, 5.0$ Hz, *cis*-isomer), -77.53 (1F, dd, $J = 9.0, 5.0$ Hz, *cis*-isomer); MS (EI) m/z : 310 (M^+); HRMS (EI) Calcd. for $\text{C}_{11}\text{H}_{10}\text{BrClF}_2\text{O}$: 309.9572 (M^+), Found: 309.9568.

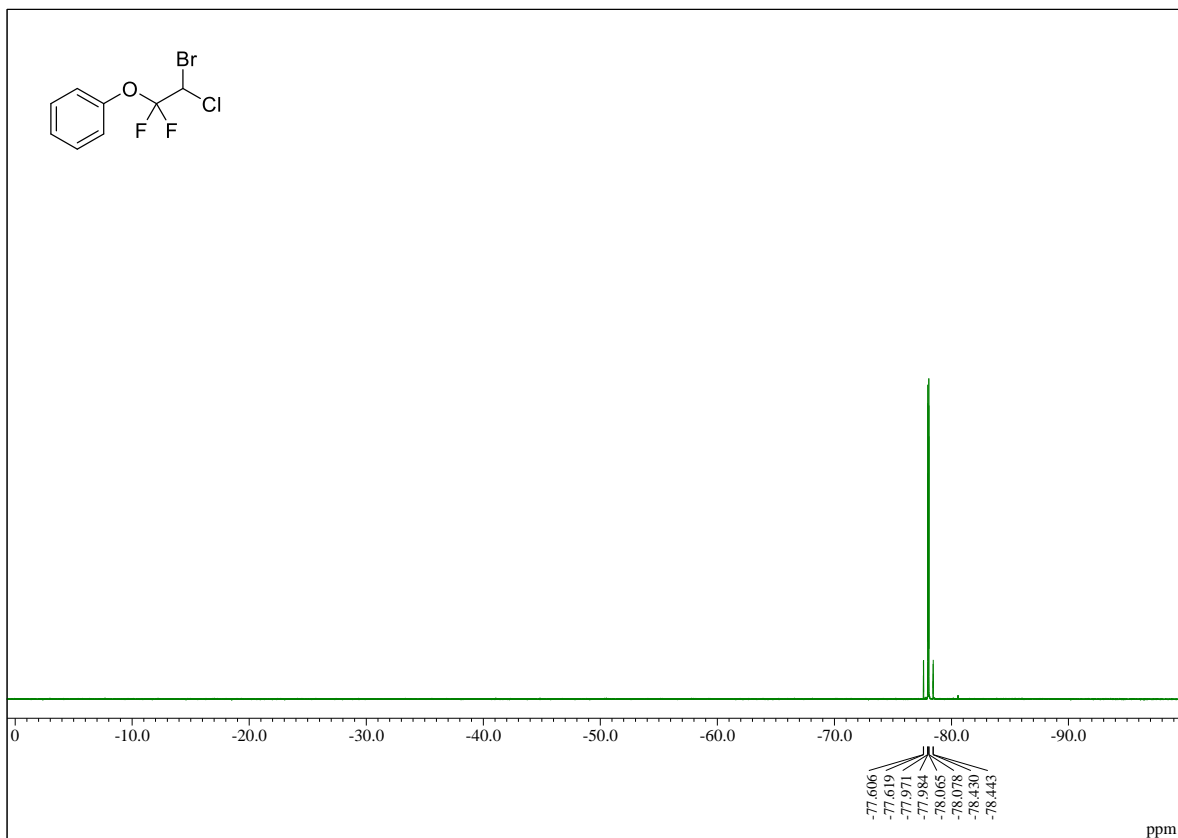
(*E*)-2'-(2-Bromo-2-chloro-1,1-difluoroethoxy)-chalcone (2o): The title product (**2o**) was purified by column chromatography and preparative TLC (hexane: AcOEt = 9:1). **2o** was obtained in 56% yield (225.0 mg). A yellow solid; mp: 66.5-67.1 °C; ^1H NMR (400 MHz, CDCl_3) δ : 5.97 (1H, t, $J = 4.8$ Hz), 7.32-7.39 (2H, m), 7.41-7.54 (4H, m), 7.55-7.62 (1H, m), 7.79-7.84 (1H, m), 7.96-8.01 (2H, m), 8.14 (1H, d, $J = 16.0$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 53.2 (t, $J = 41.0$ Hz), 119.9 (t, $J = 269.4$ Hz), 122.7, 125.0, 126.9, 127.7, 128.6, 128.8, 129.0, 131.5, 132.9, 138.1, 138.5, 148.4, 191.2; ^{19}F NMR (376 MHz, CDCl_3) δ : -77.2 (1F, dd, $J = 136.4, 4.8$ Hz), -77.8 (1F, dd, $J = 136.4, 4.8$ Hz); MS (EI) m/z : 400 (M^+); HRMS (EI) Calcd. for $\text{C}_{17}\text{H}_{12}\text{BrClF}_2\text{O}_2$: 399.9677 (M^+), Found: 399.9670.

***o*-Aminophenyl 2-bromo-2-chloro-1,1-difluoroethyl ether (2p):** The title product (**2p**) was purified by column chromatography (hexane: AcOEt = 9:1) and was obtained in 51% yield (145.3 mg). A yellow oil; ^1H NMR (400 MHz, CDCl_3) δ : 3.93 (2H, br s), 5.98 (1H, t, $J = 4.4$ Hz), 6.72 (1H, dd, $J = 7.6, 1.2$ Hz), 6.79 (1H, dd, $J = 8.0, 1.6$ Hz), 7.06 (1H, dd, $J = 7.6, 1.6$ Hz), 7.16 (2H, dd, $J = 8.0, 1.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ : 53.7 (t, $J = 41.9$ Hz), 116.7, 118.4, 120.2 (t, $J = 267.4$ Hz), 122.6, 127.4, 136.5, 139.9; ^{19}F NMR (376 MHz, CDCl_3) δ : -77.7 (1F, dd, $J = 137.1, 4.4$ Hz), -78.5 (1F, dd, $J = 137.1, 4.4$ Hz); MS (EI) m/z : 285 (M^+); HRMS (EI) Calcd. for $\text{C}_8\text{H}_7\text{BrClF}_2\text{NO}$: 284.9368 (M^+), Found: 284.9363.

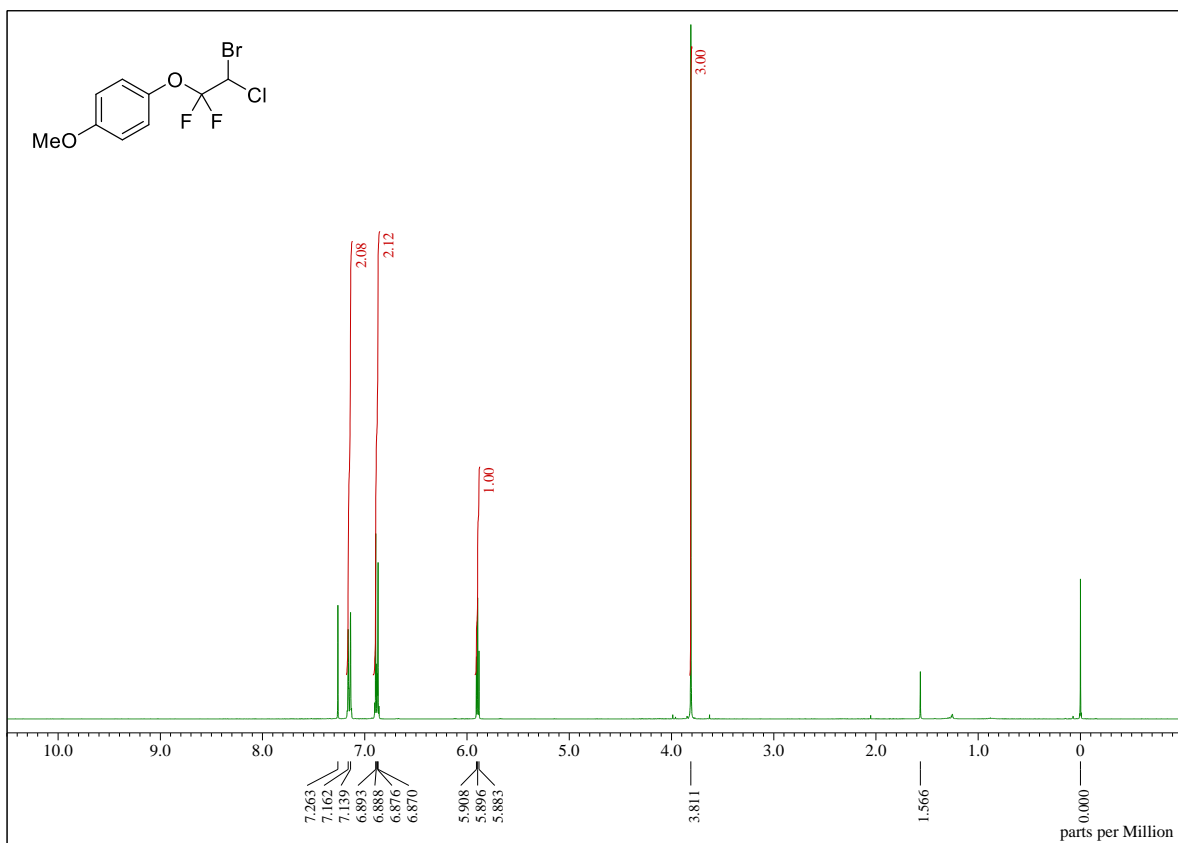
2. ^1H , ^{13}C and ^{19}F NMR spectra

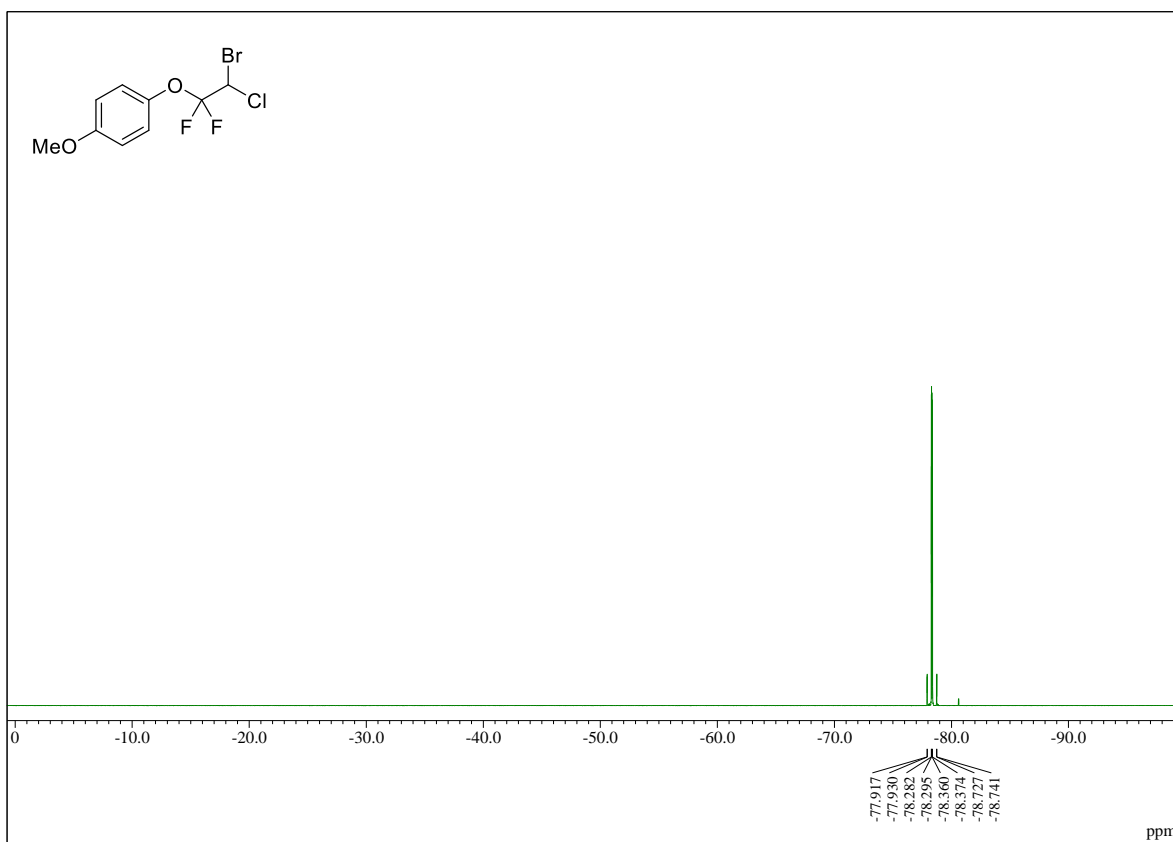
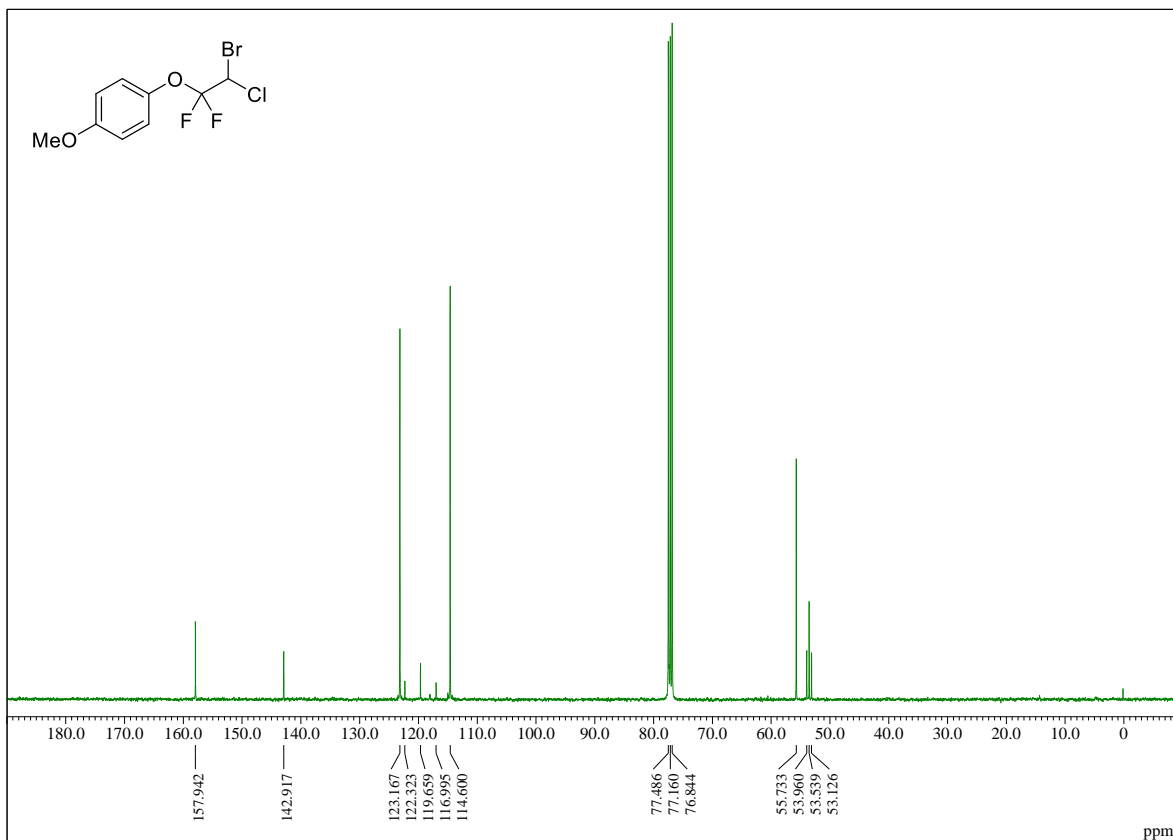
2-Bromo-2-chloro-1,1-difluoroethyl phenyl ether (2a)



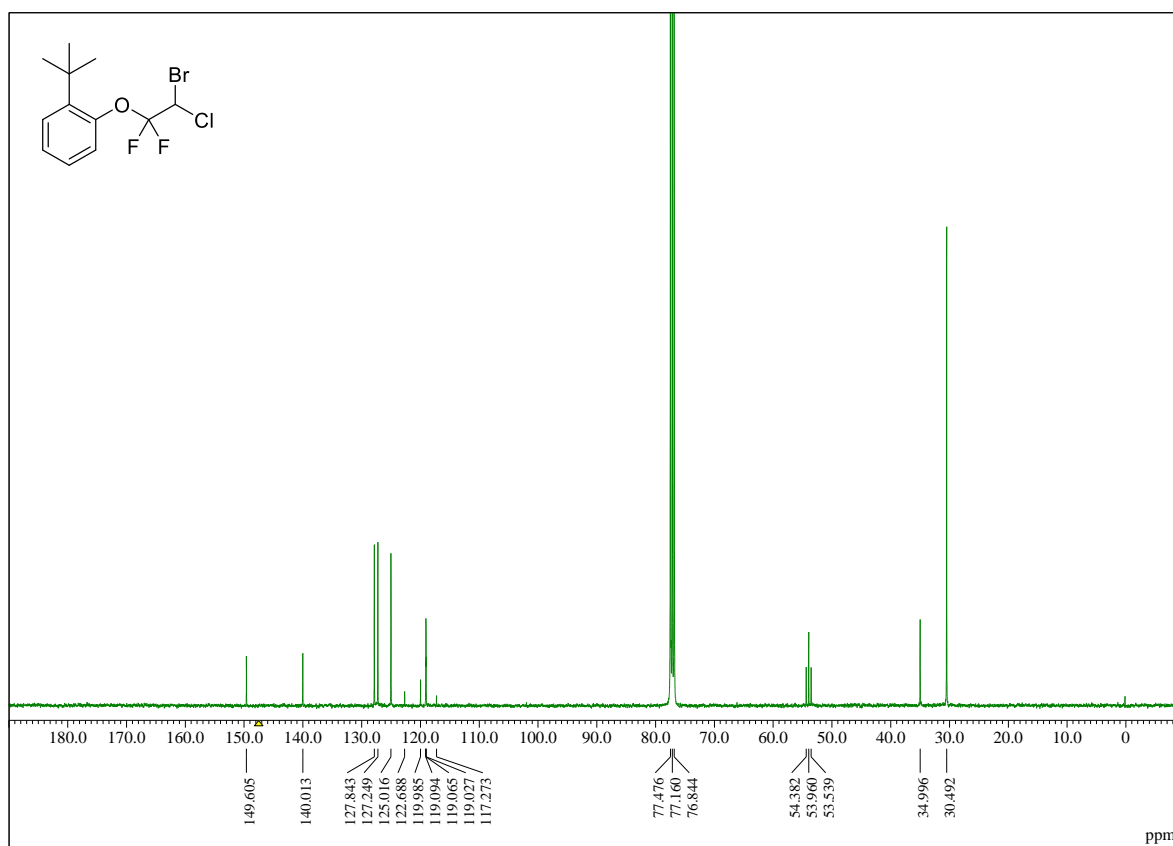
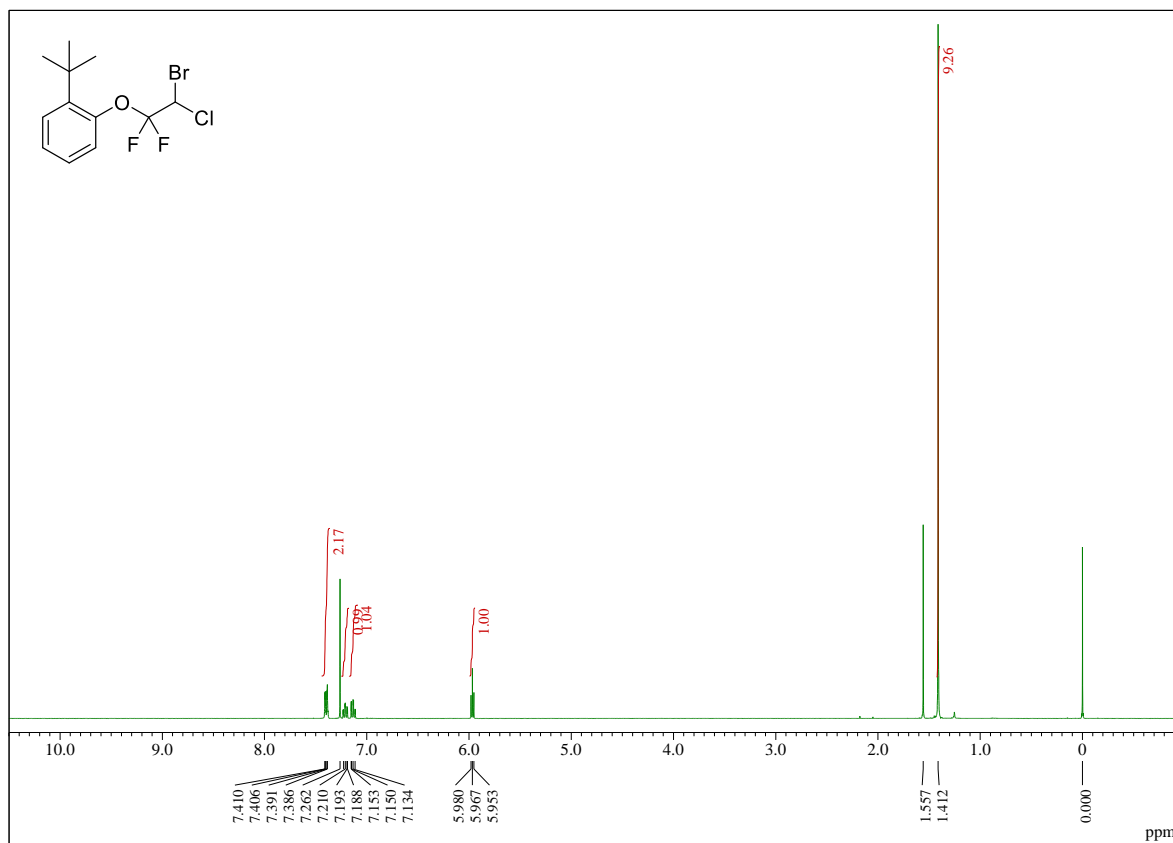


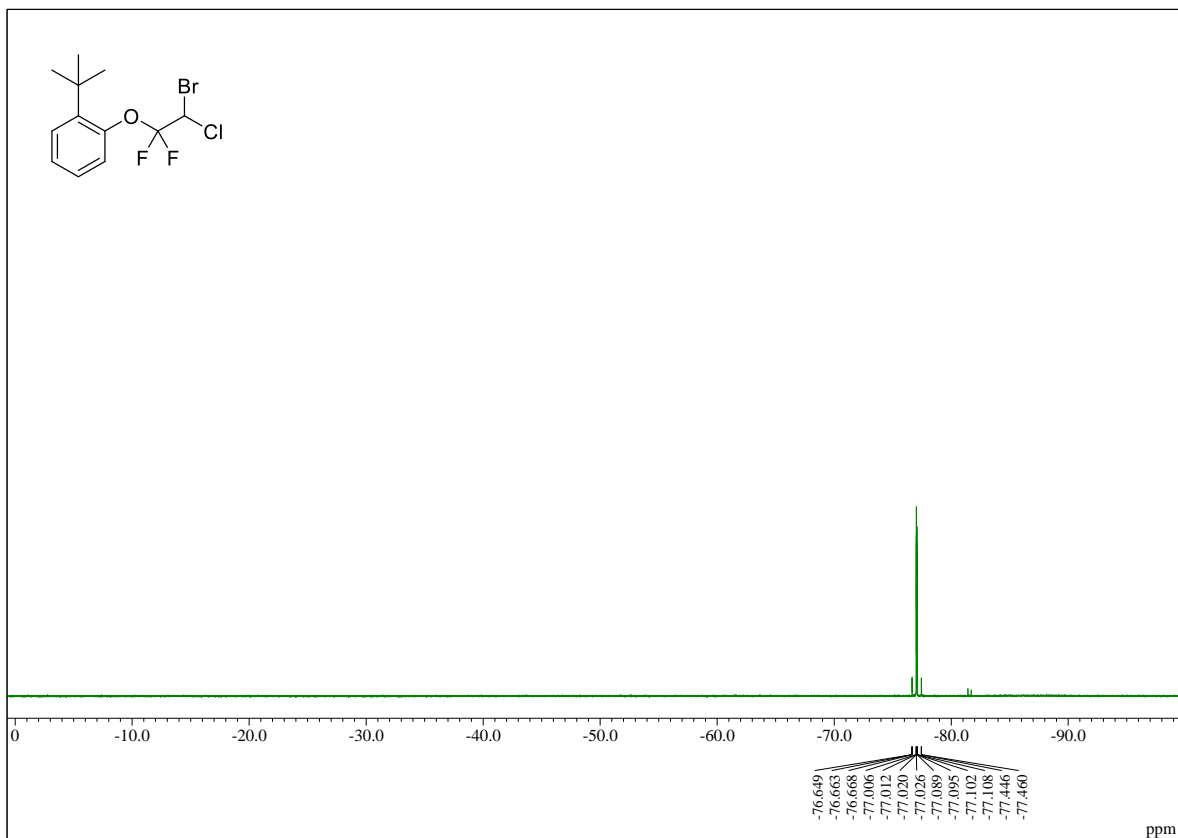
2-Bromo-2-chloro-1,1-difluoroethyl *p*-methoxyphenyl ether (2b)



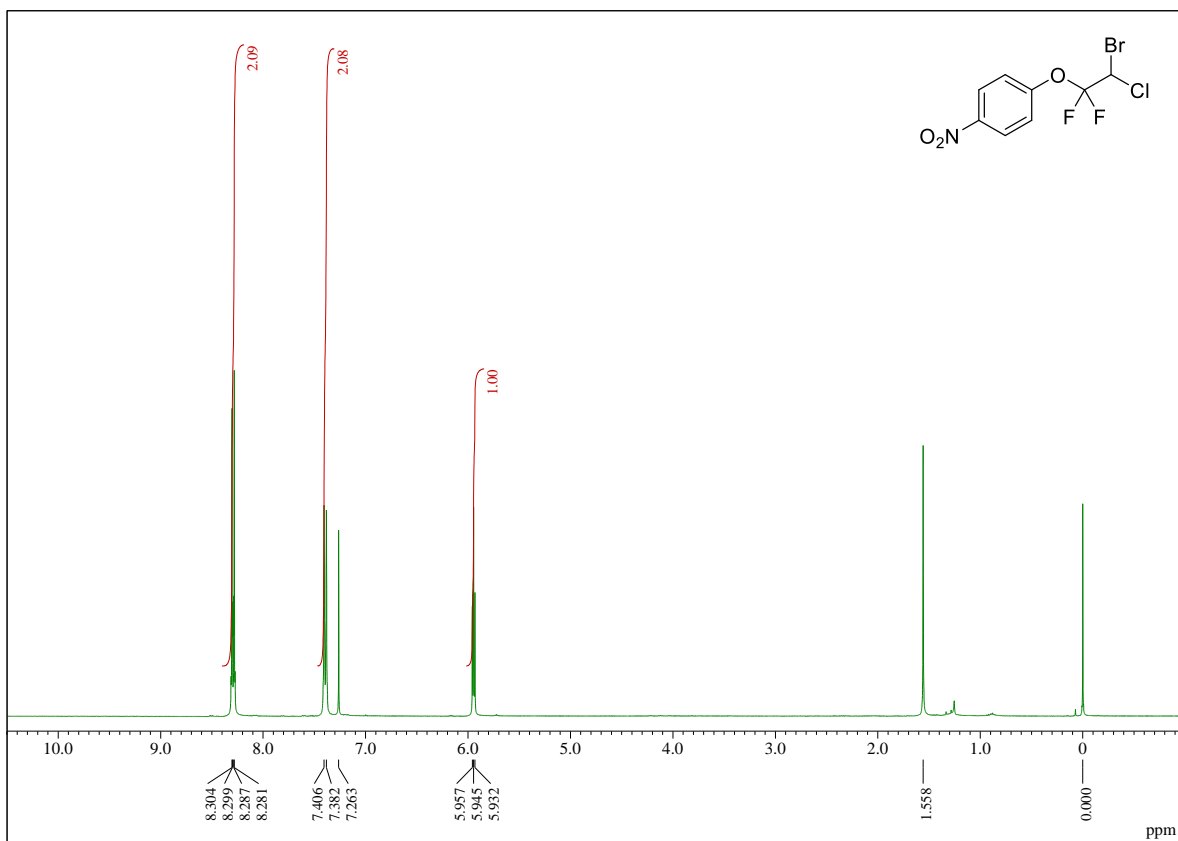


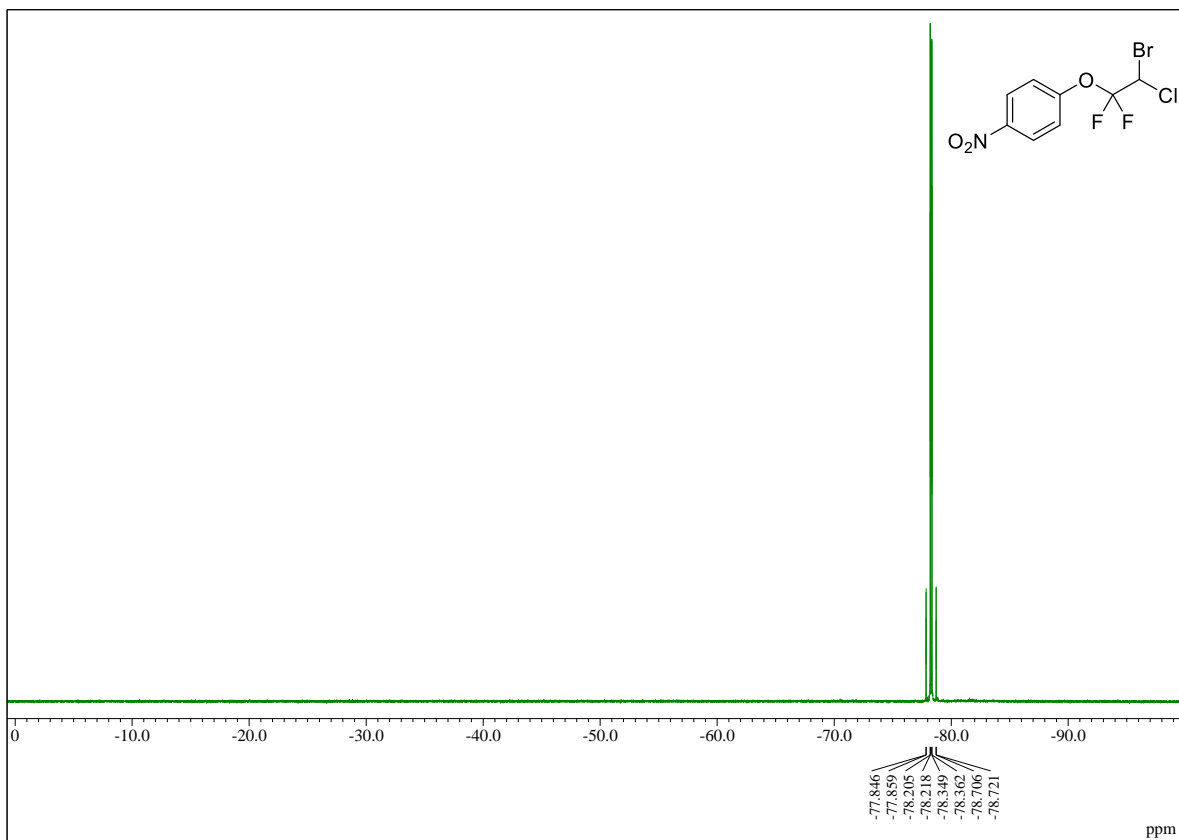
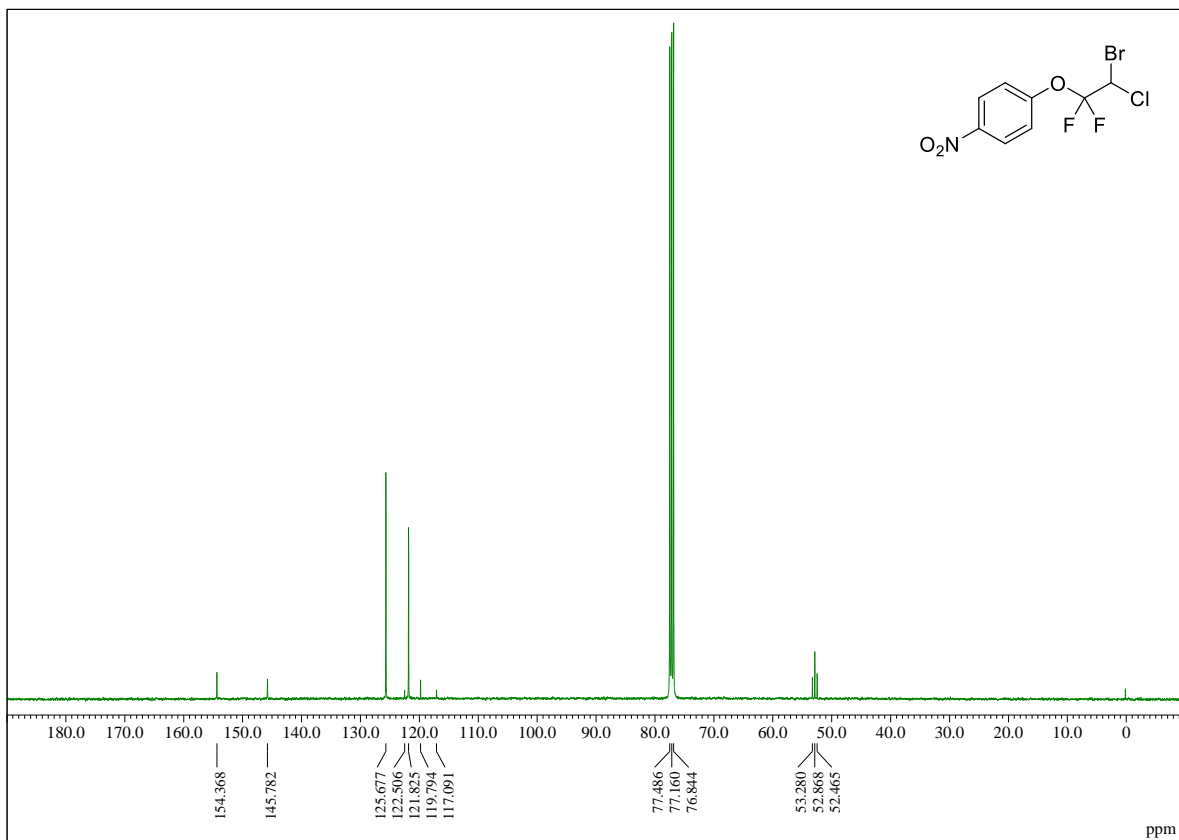
2-Bromo-2-chloro-1,1-difluoroethyl *o*-*t*-butylphenyl ether (2c)



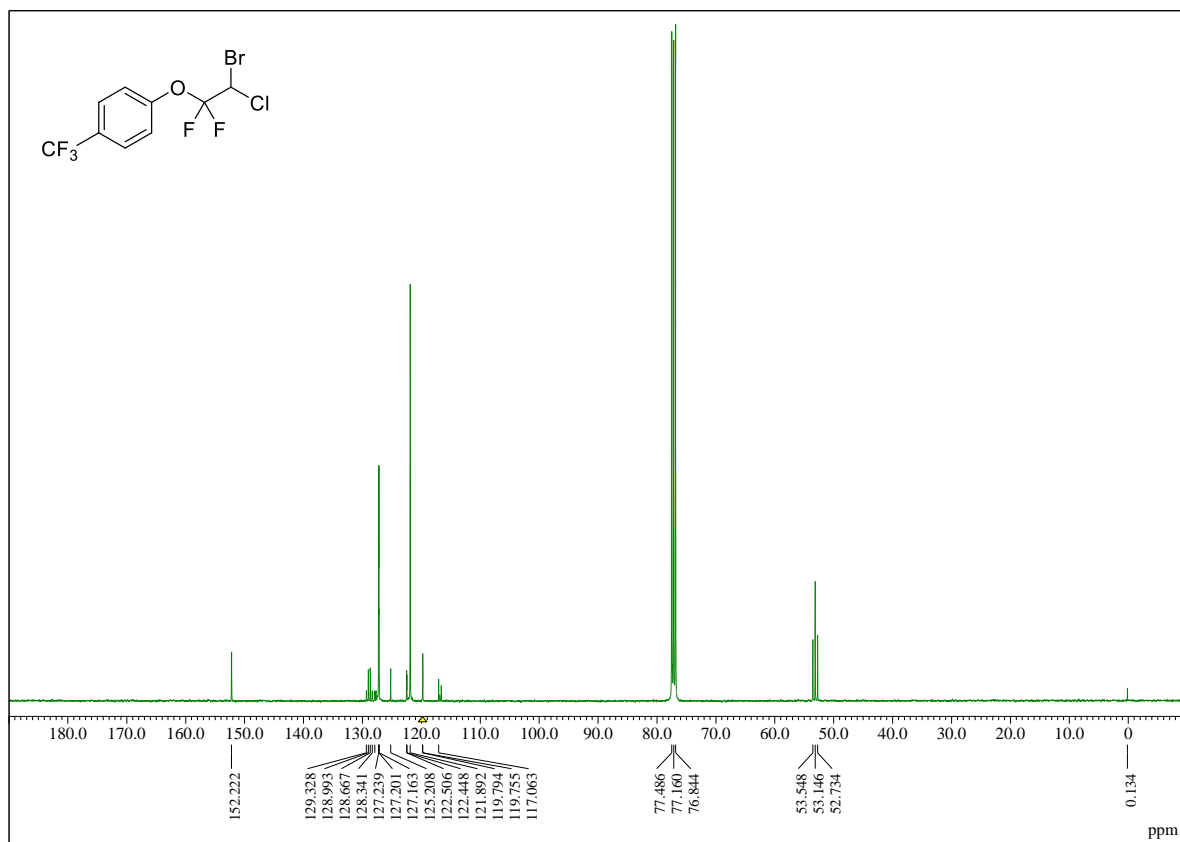
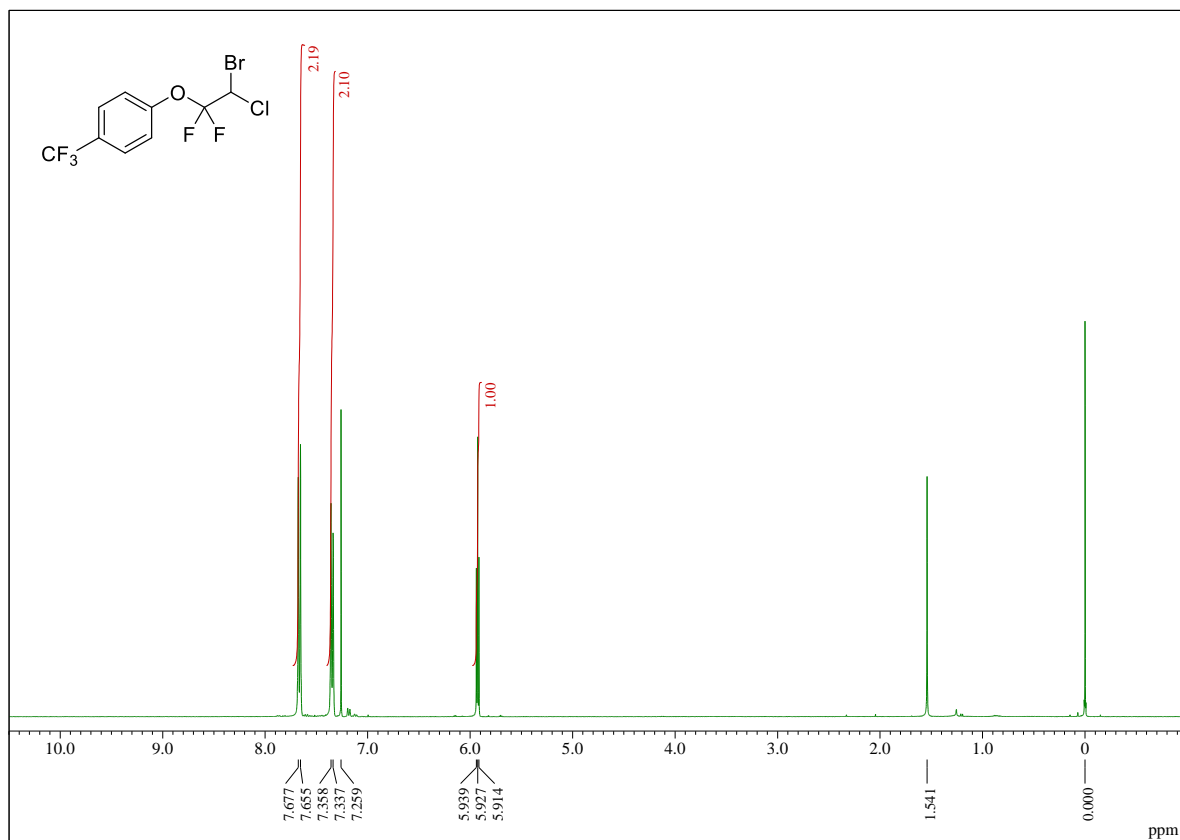


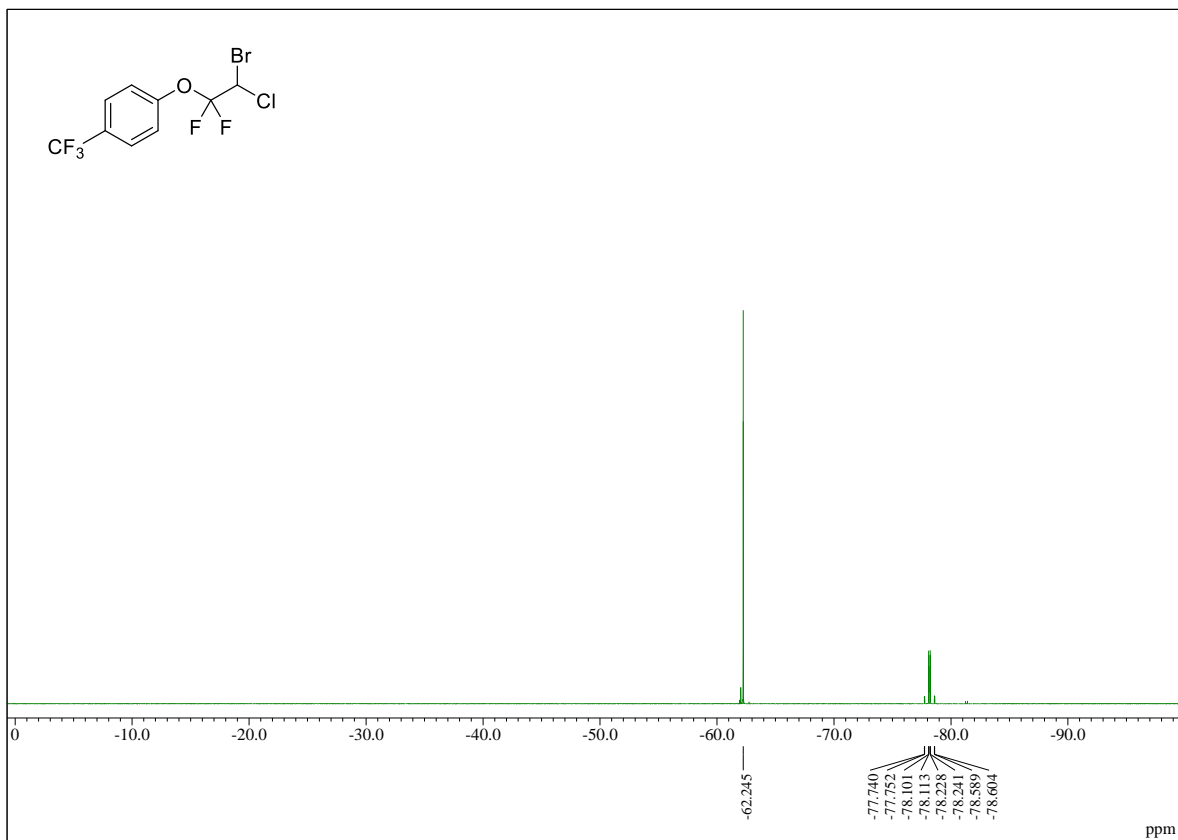
2-Bromo-2-chloro-1,1-difluoroethyl *p*-nitrophenyl ether (2d)



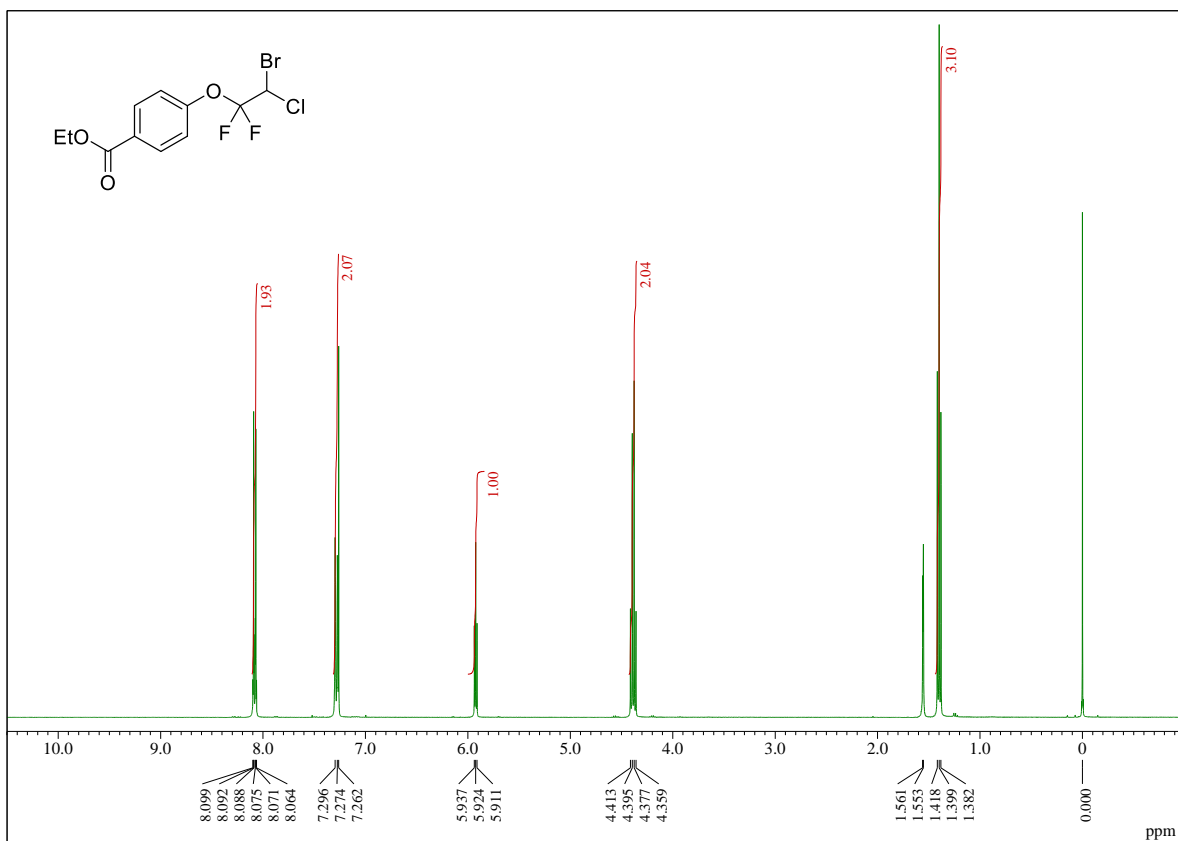


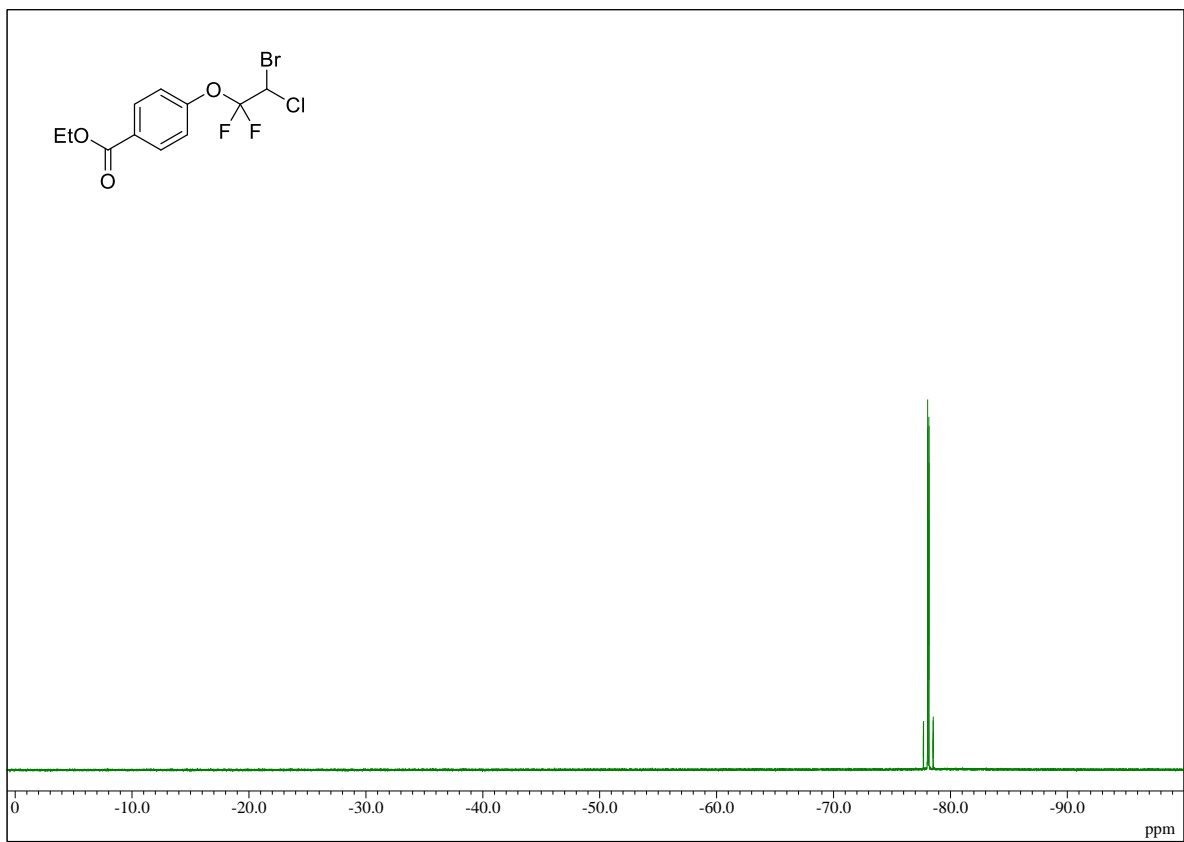
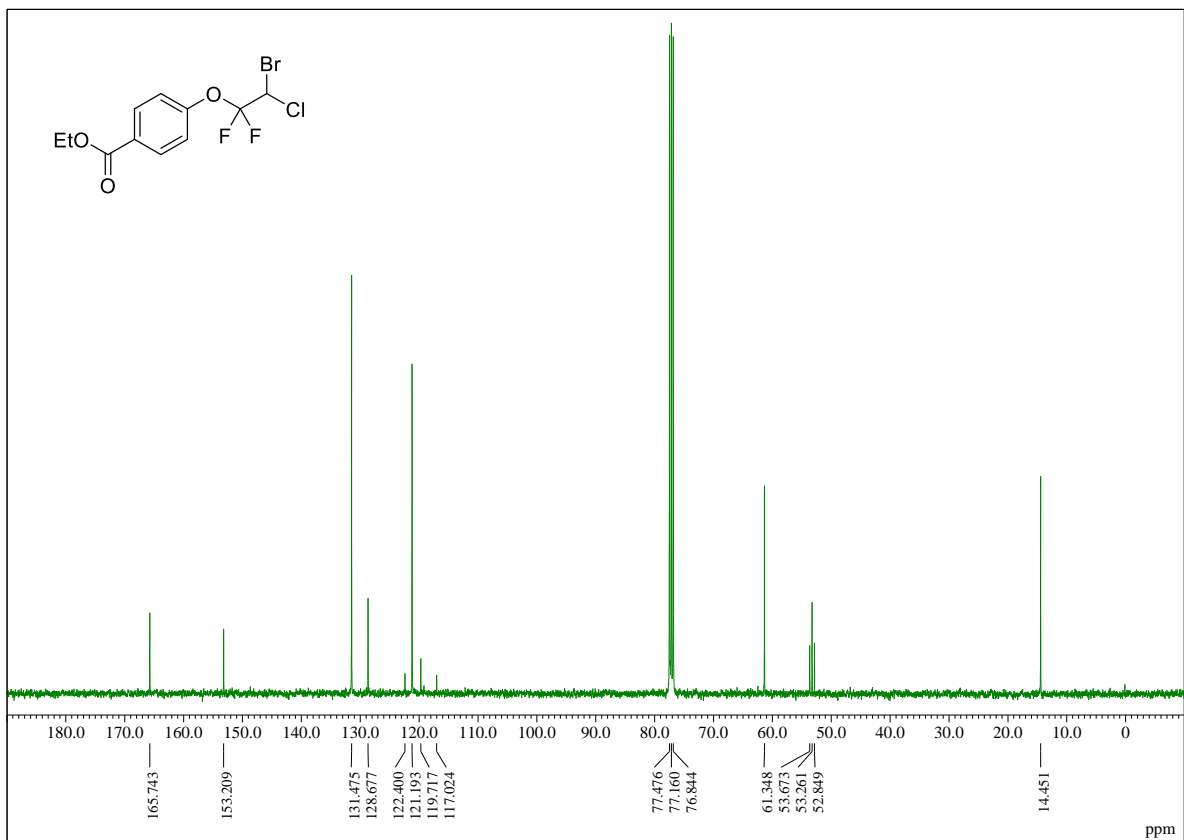
2-Bromo-2-chloro-1,1-difluoroethyl *p*-trifluoromethylphenyl ether (2e)



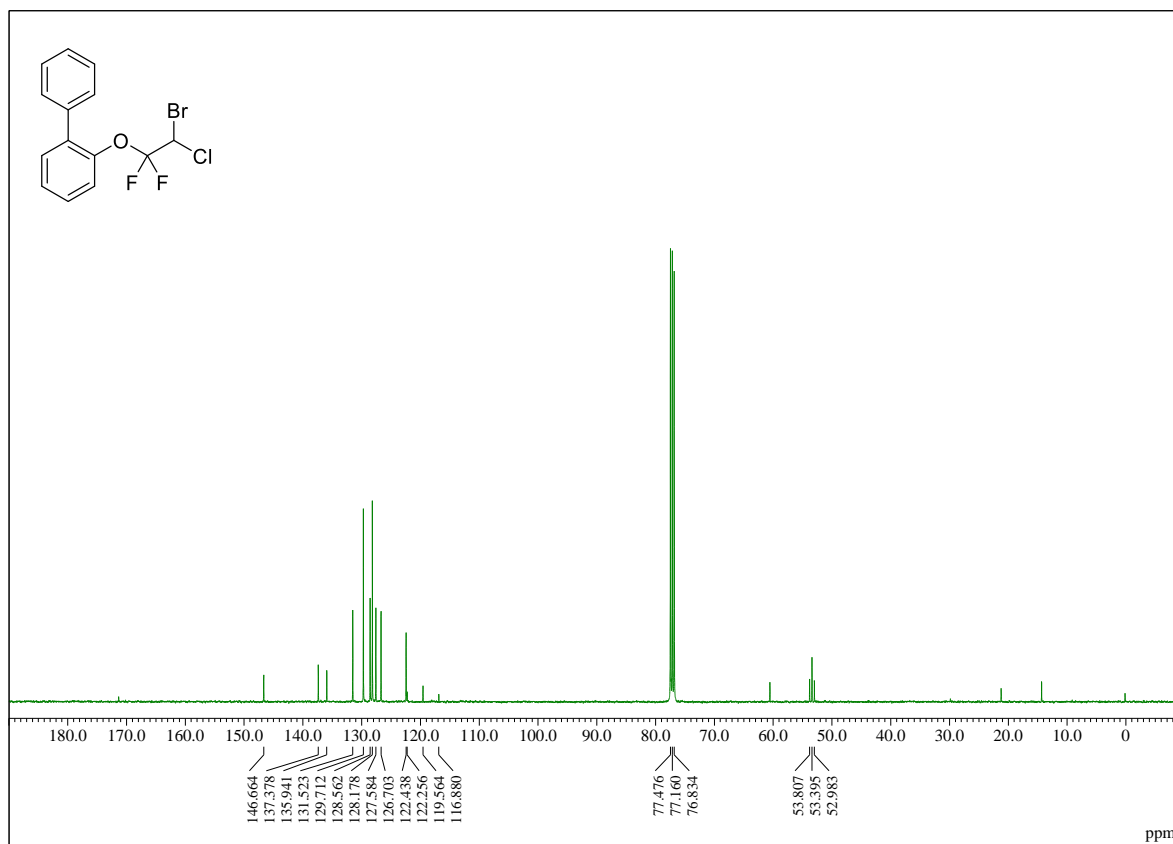
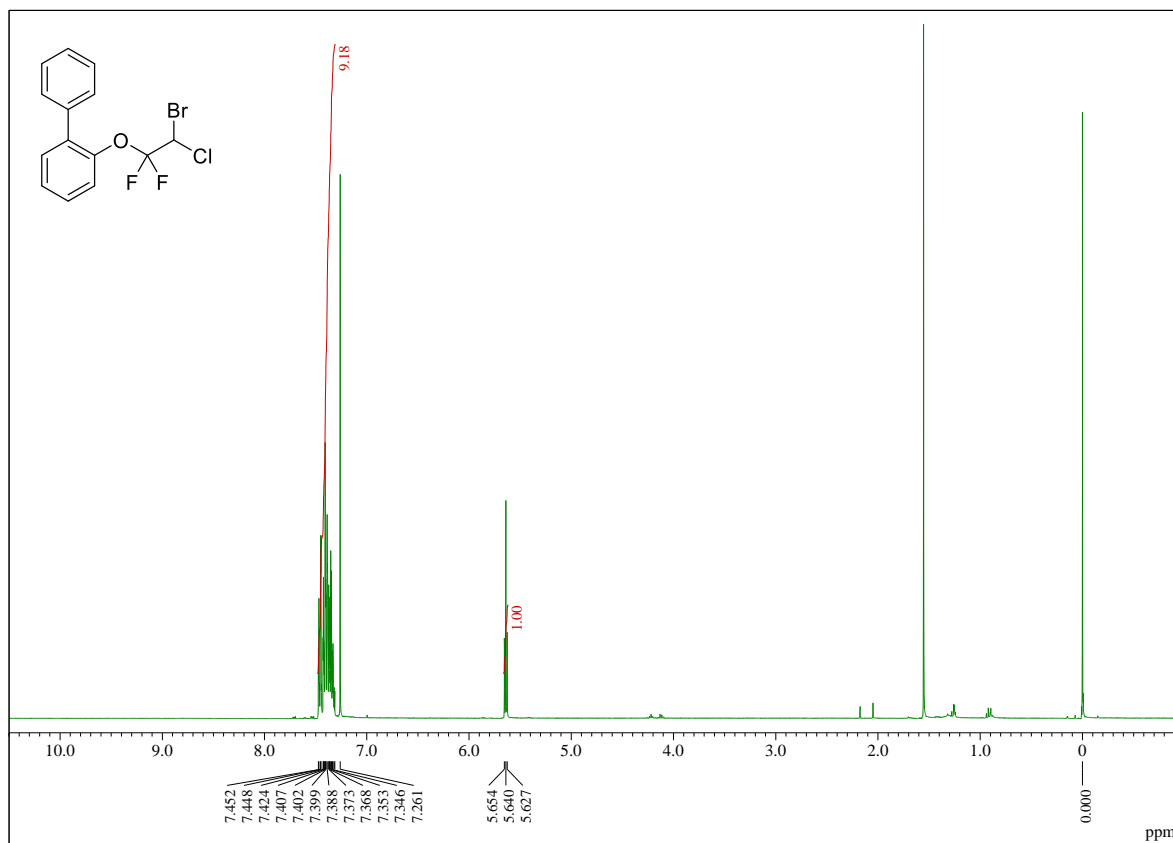


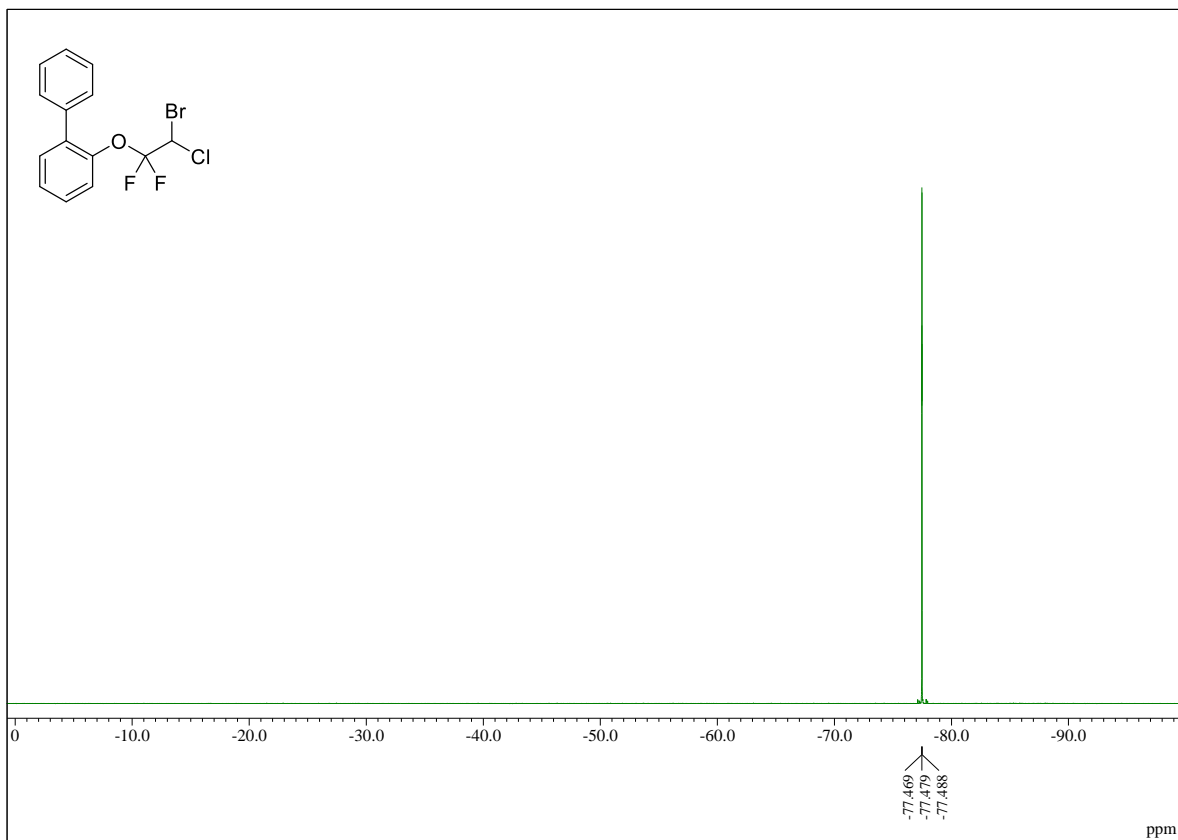
Ethyl *p*-(2-bromo-2-chloro-1,1-difluoroethoxy)benzoate (2f)



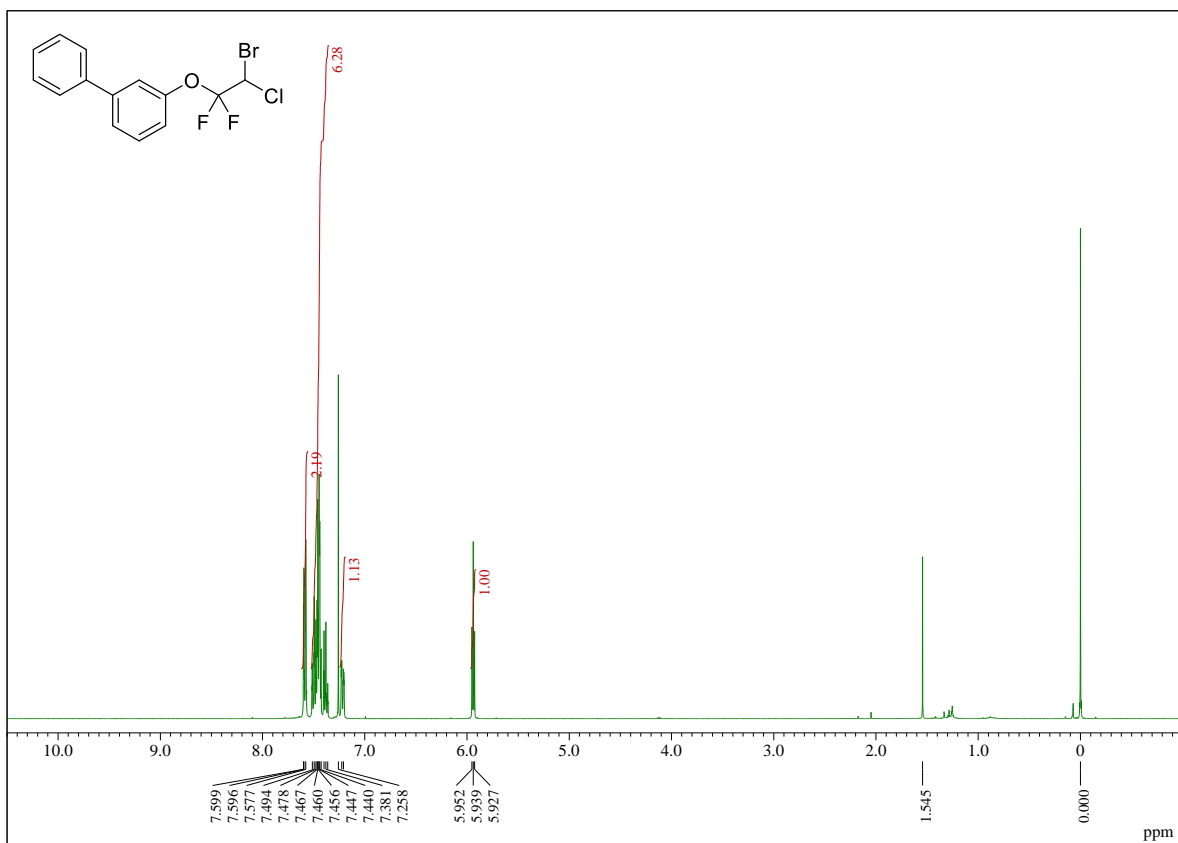


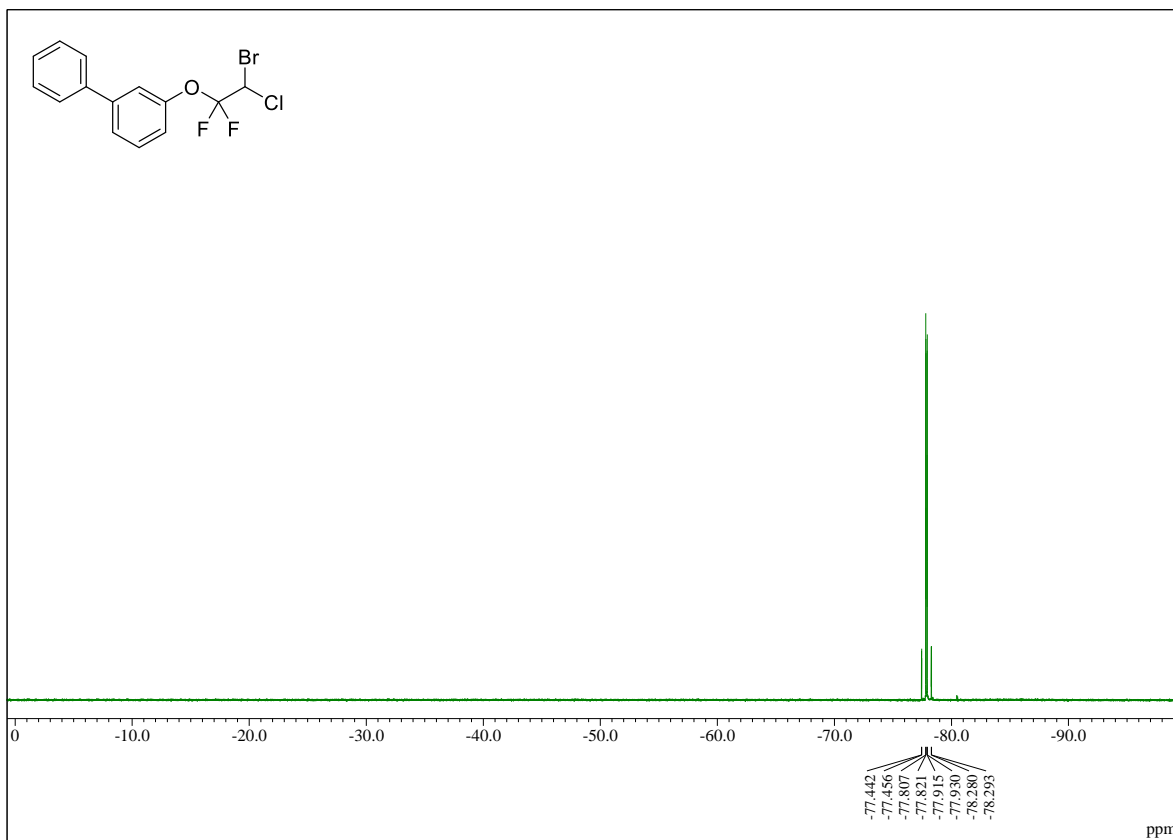
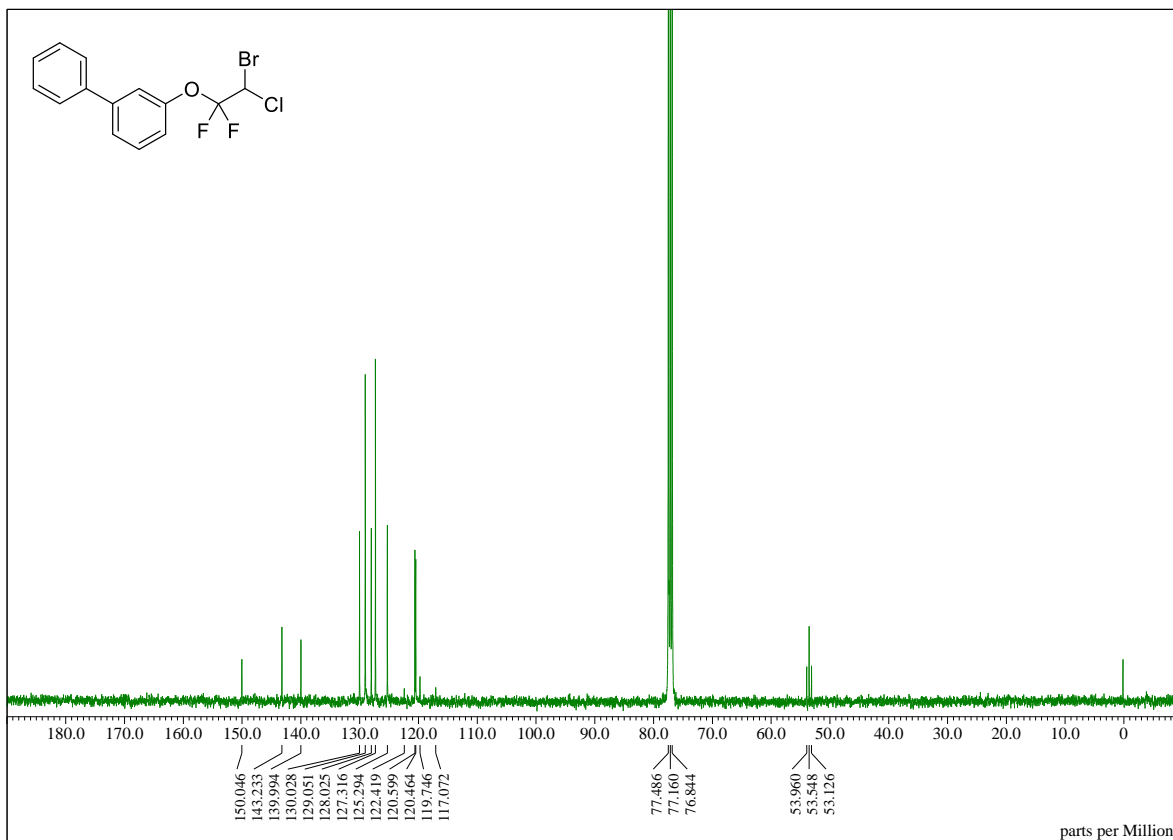
2-Bromo-2-chloro-1,1-difluoroethyl *o*-phenylphenyl ether (2h)



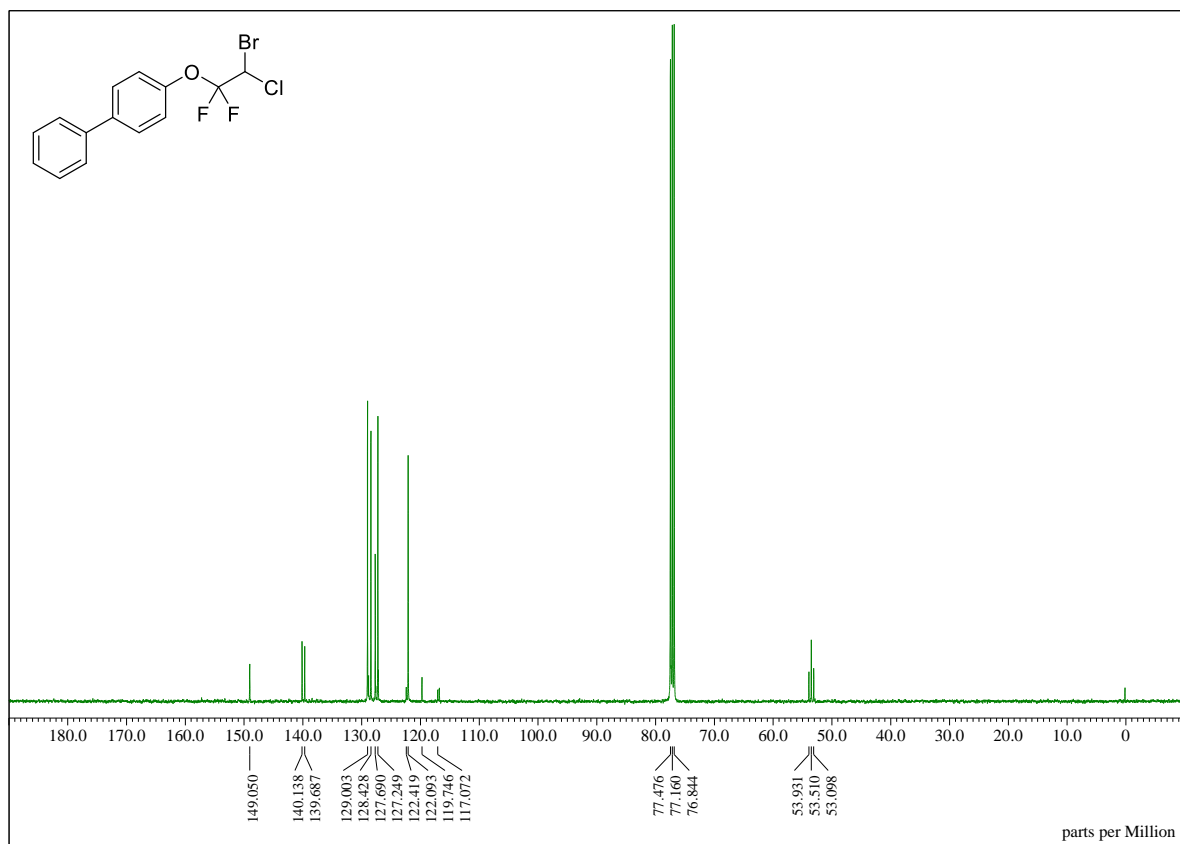
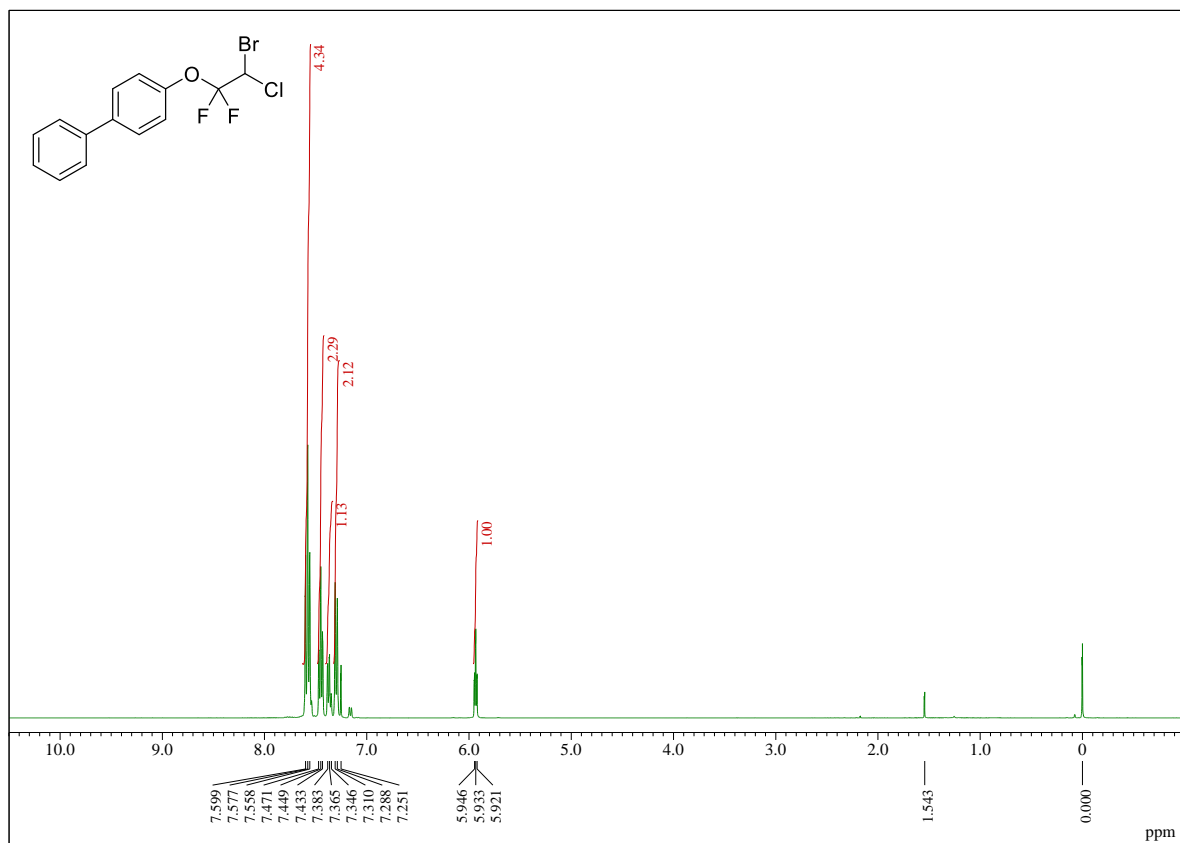


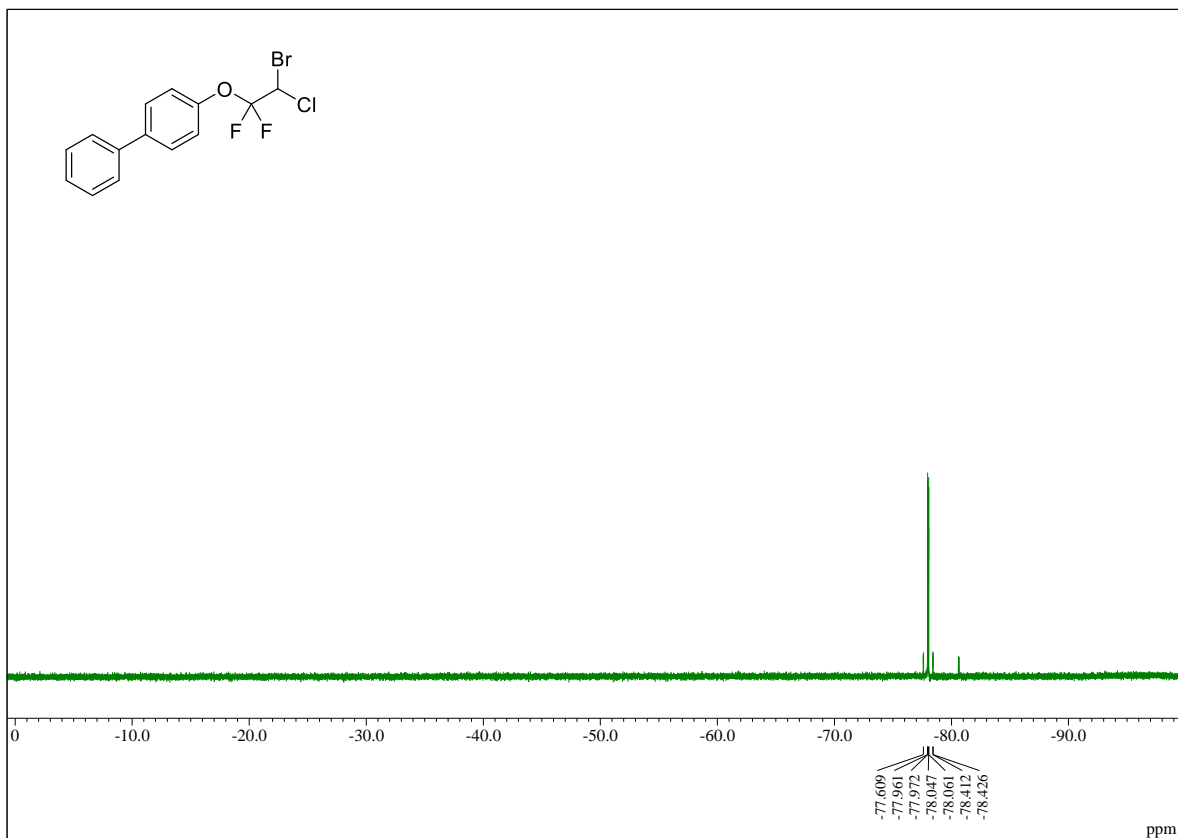
2-Bromo-2-chloro-1,1-difluoroethyl *m*-phenylphenyl ether (2i)



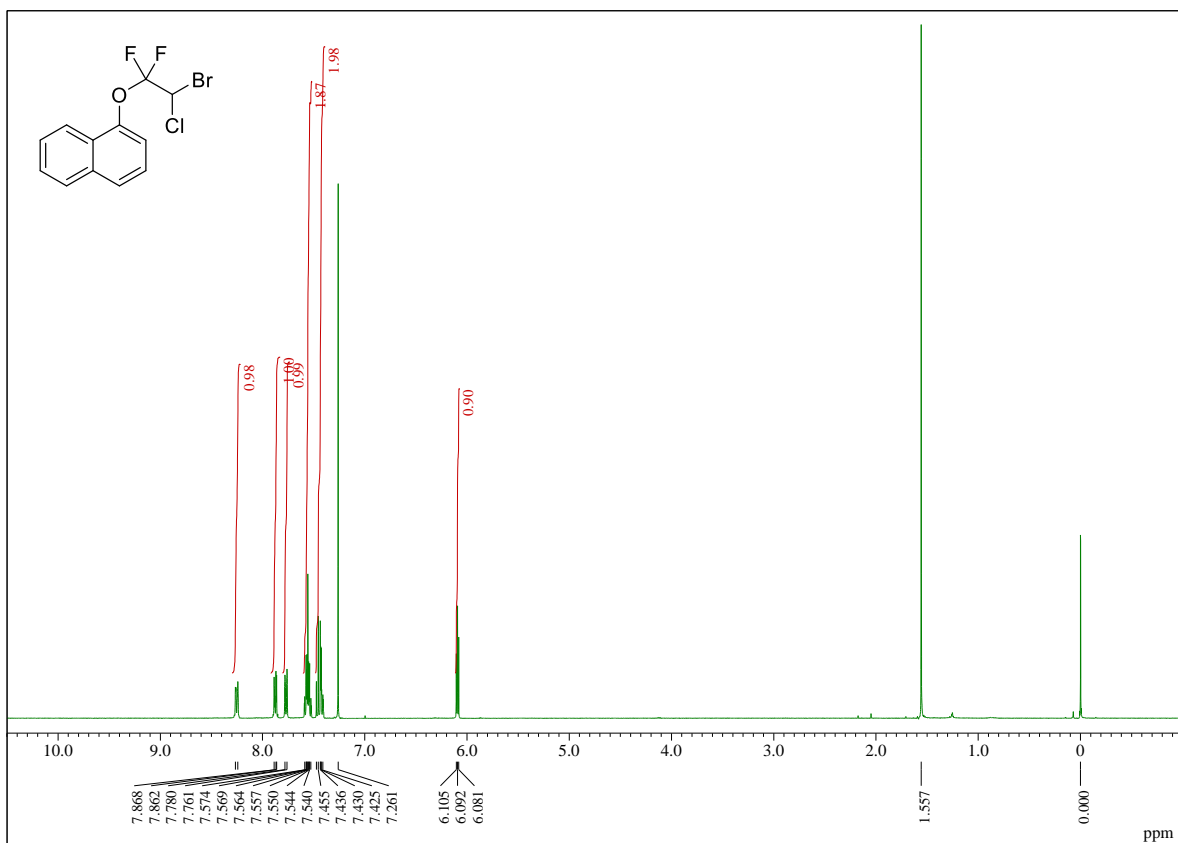


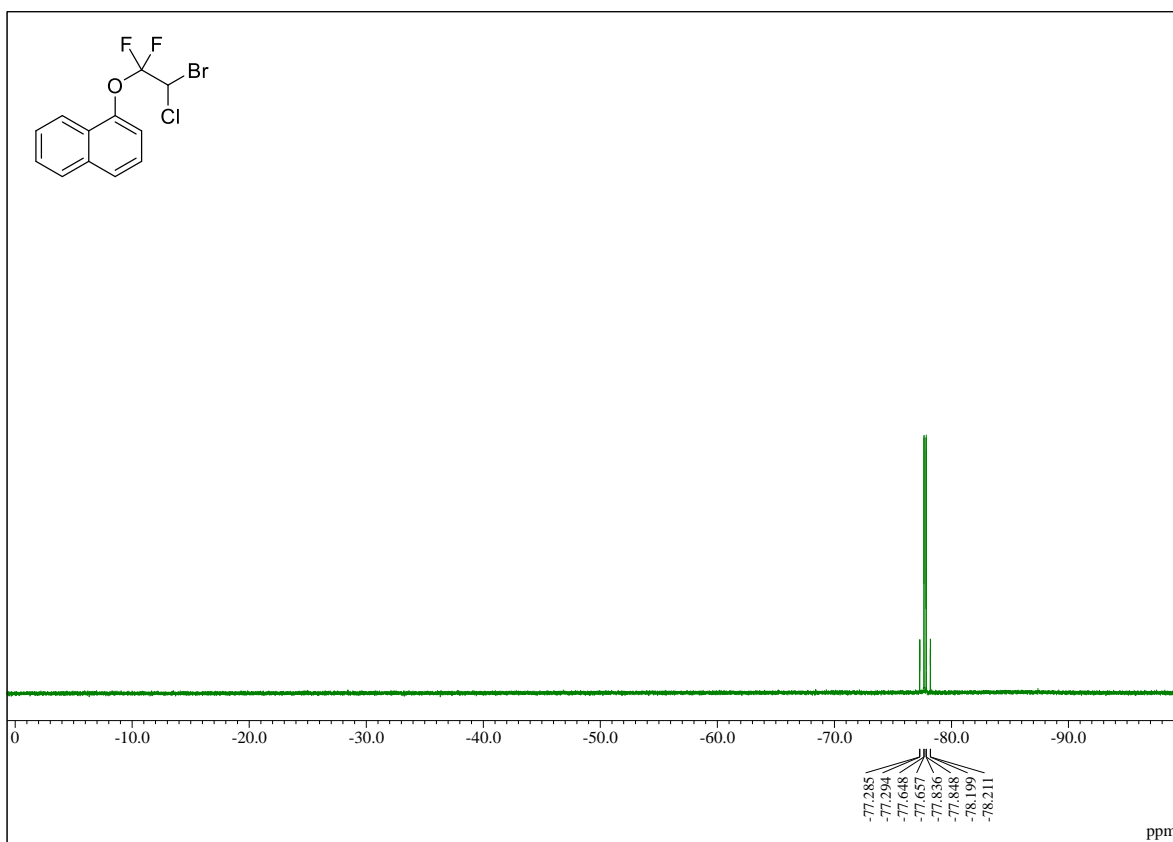
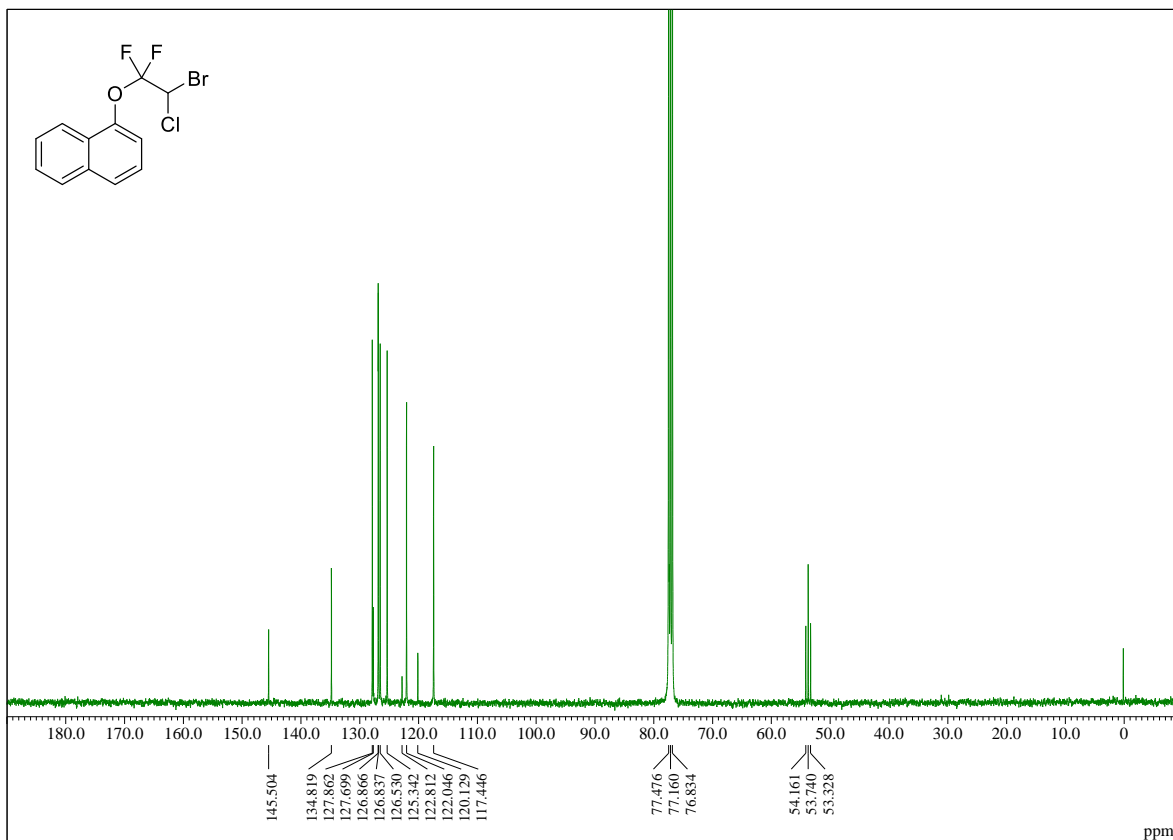
2-Bromo-2-chloro-1,1-difluoroethyl *p*-phenylphenyl ether (2j)



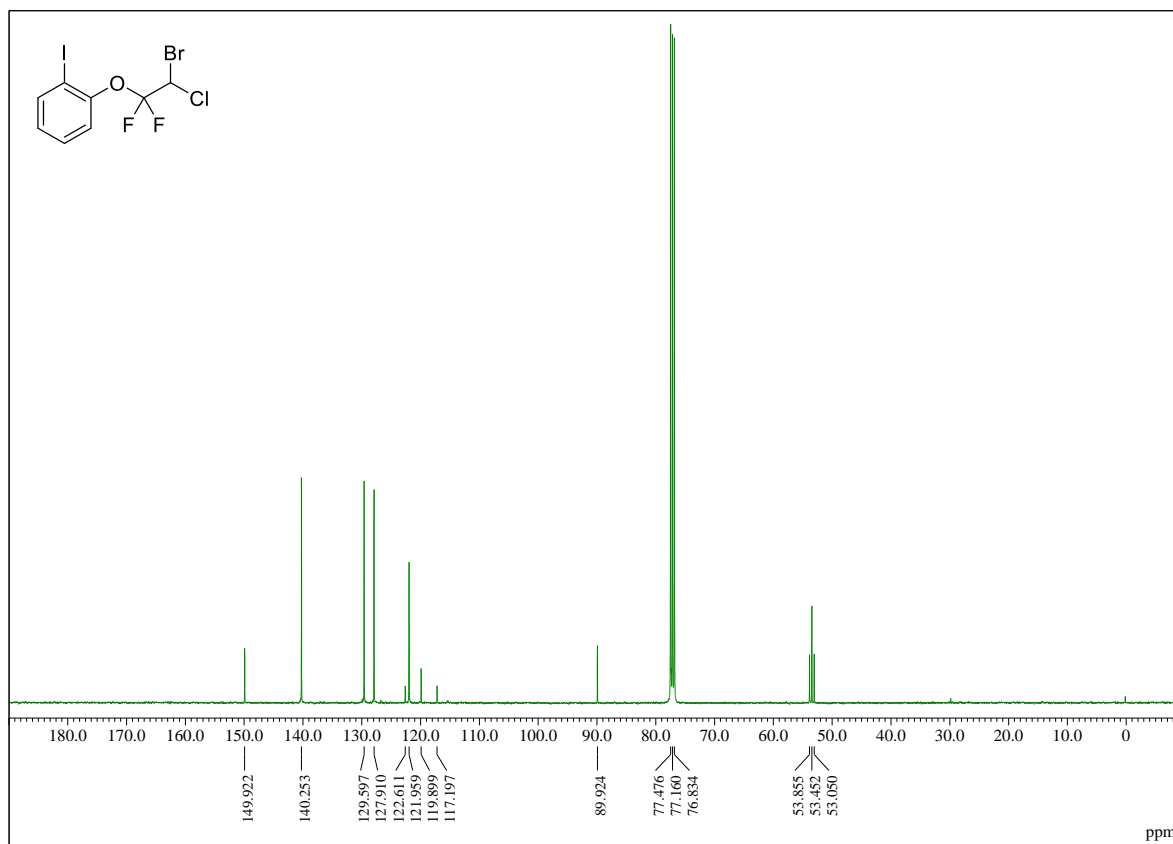
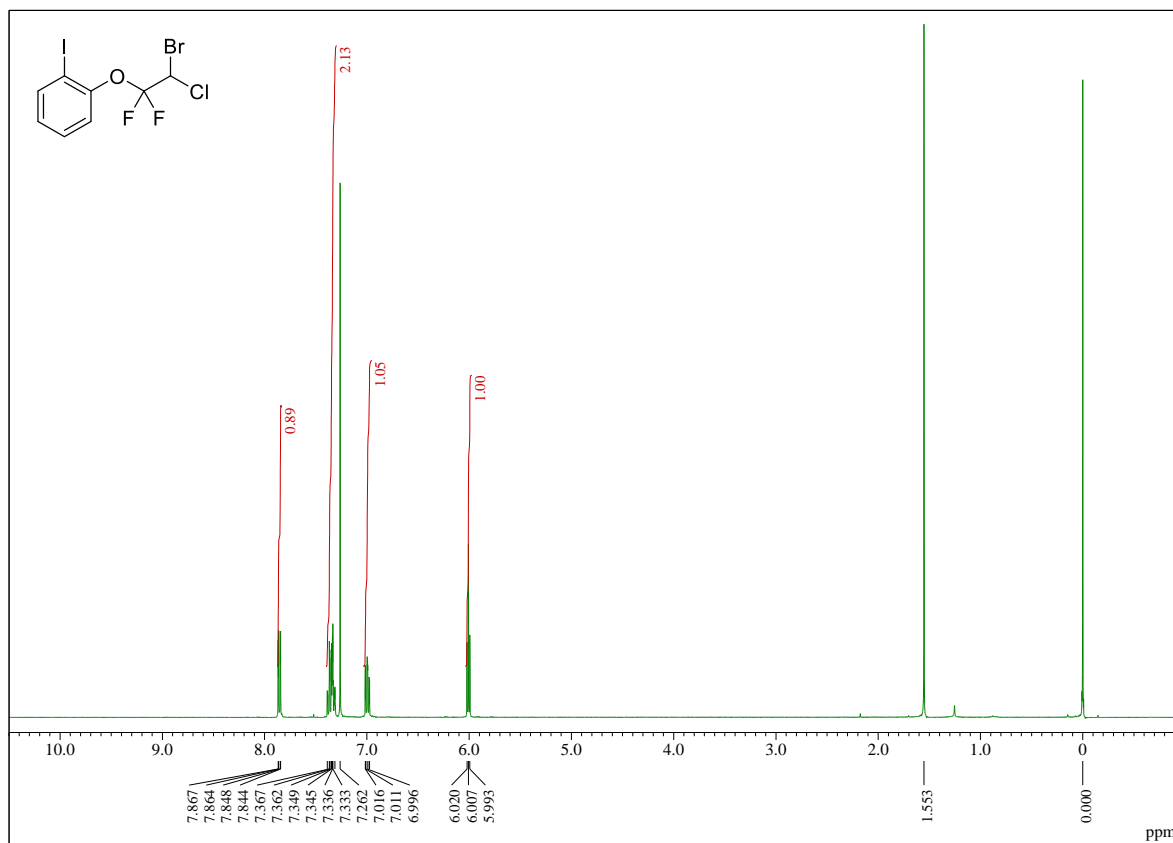


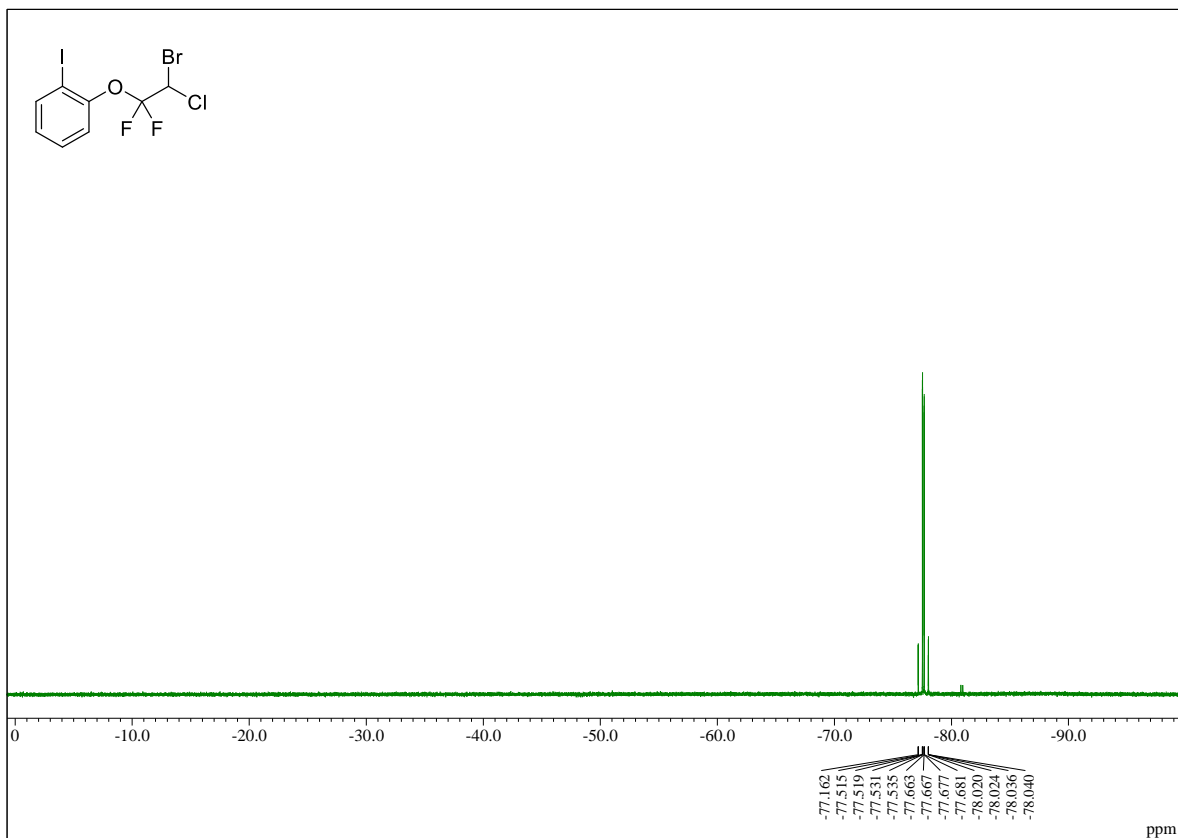
2-Bromo-2-chloro-1,1-difluoroethyl 1-naphthyl ether (2k)



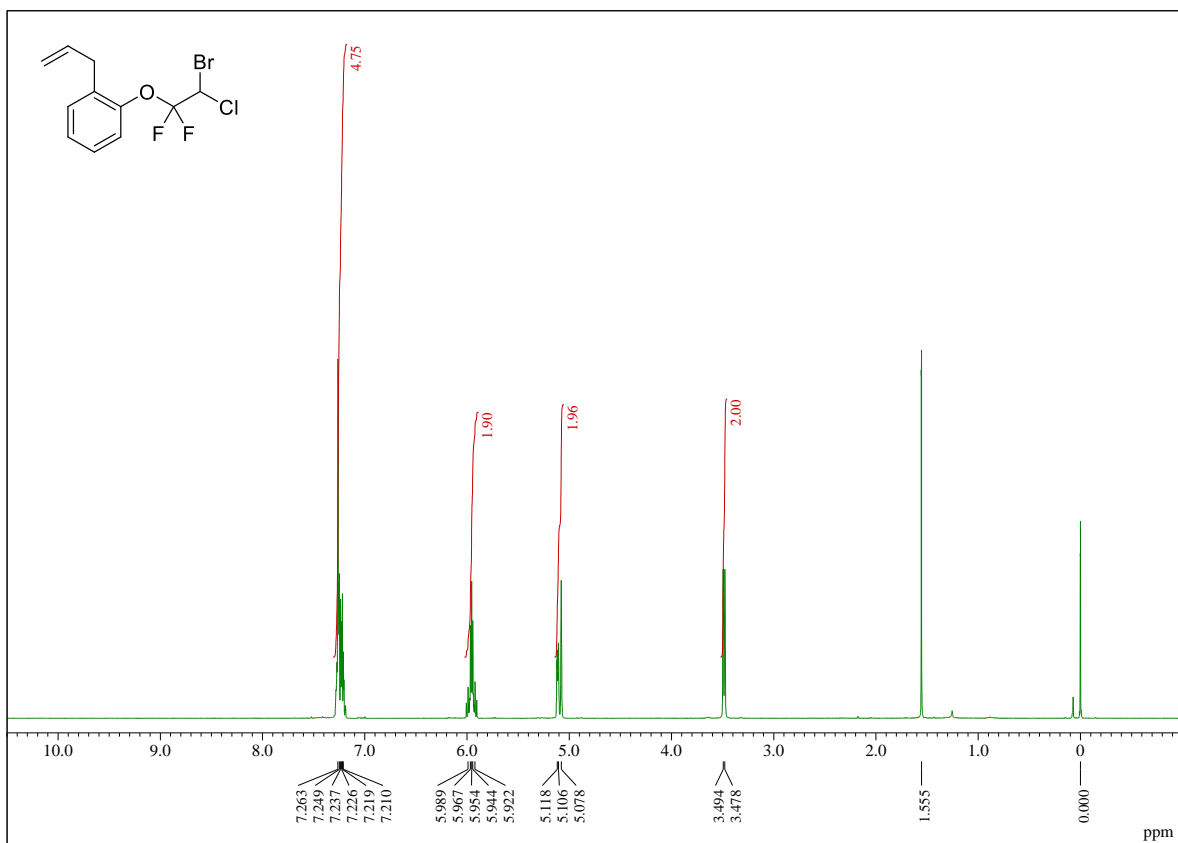


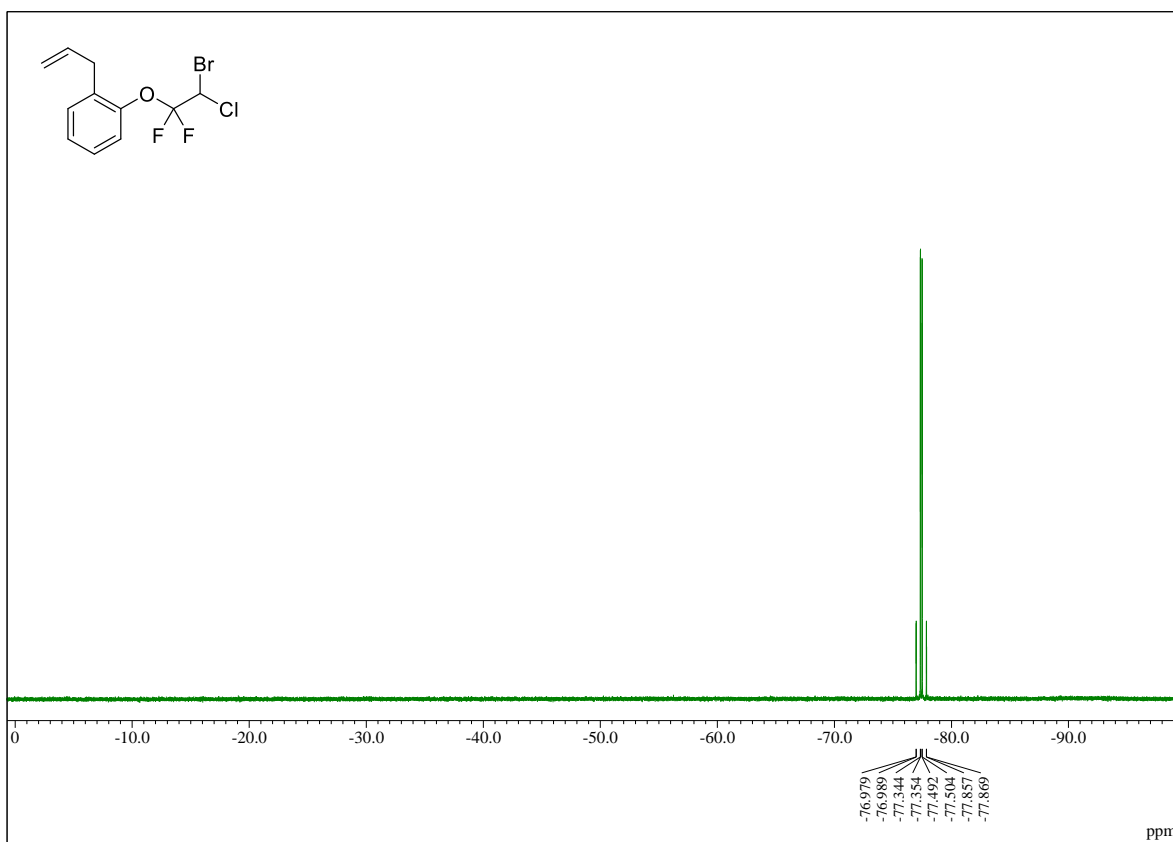
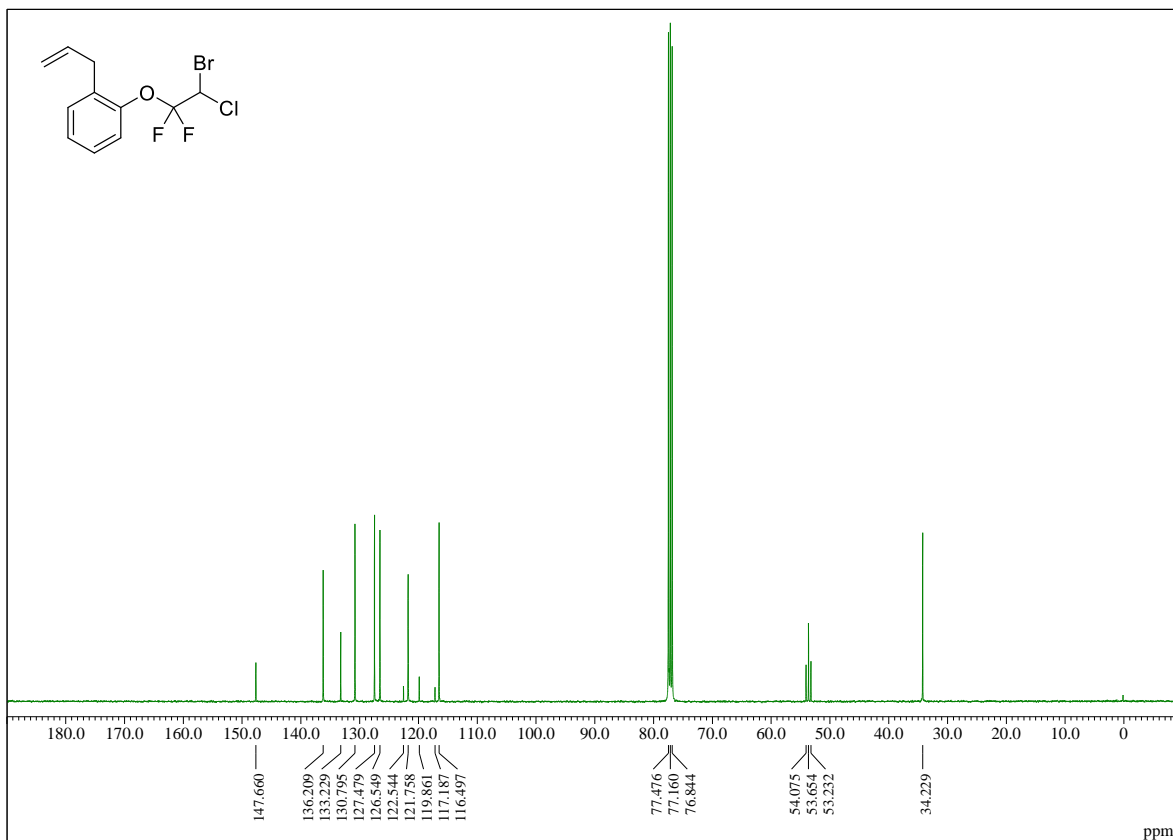
2-Bromo-2-chloro-1,1-difluoroethyl *o*-iodophenyl ether (2I)



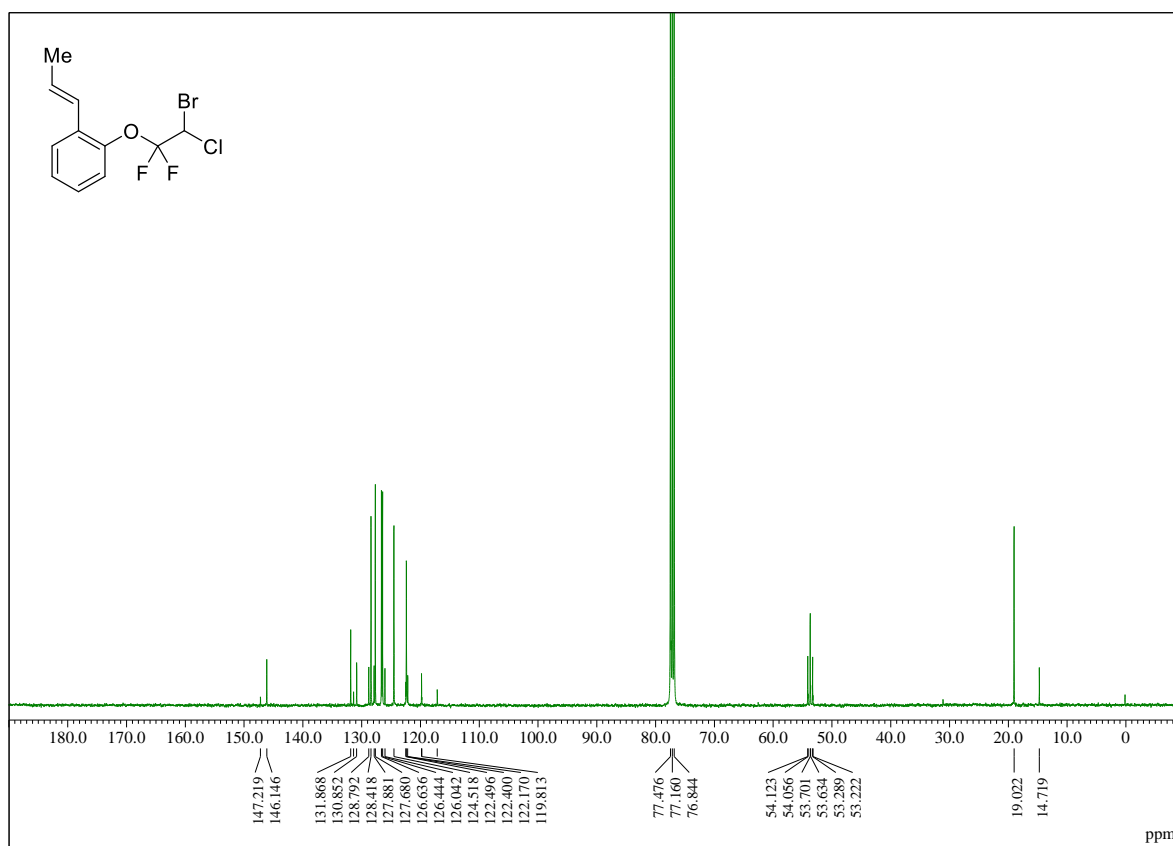
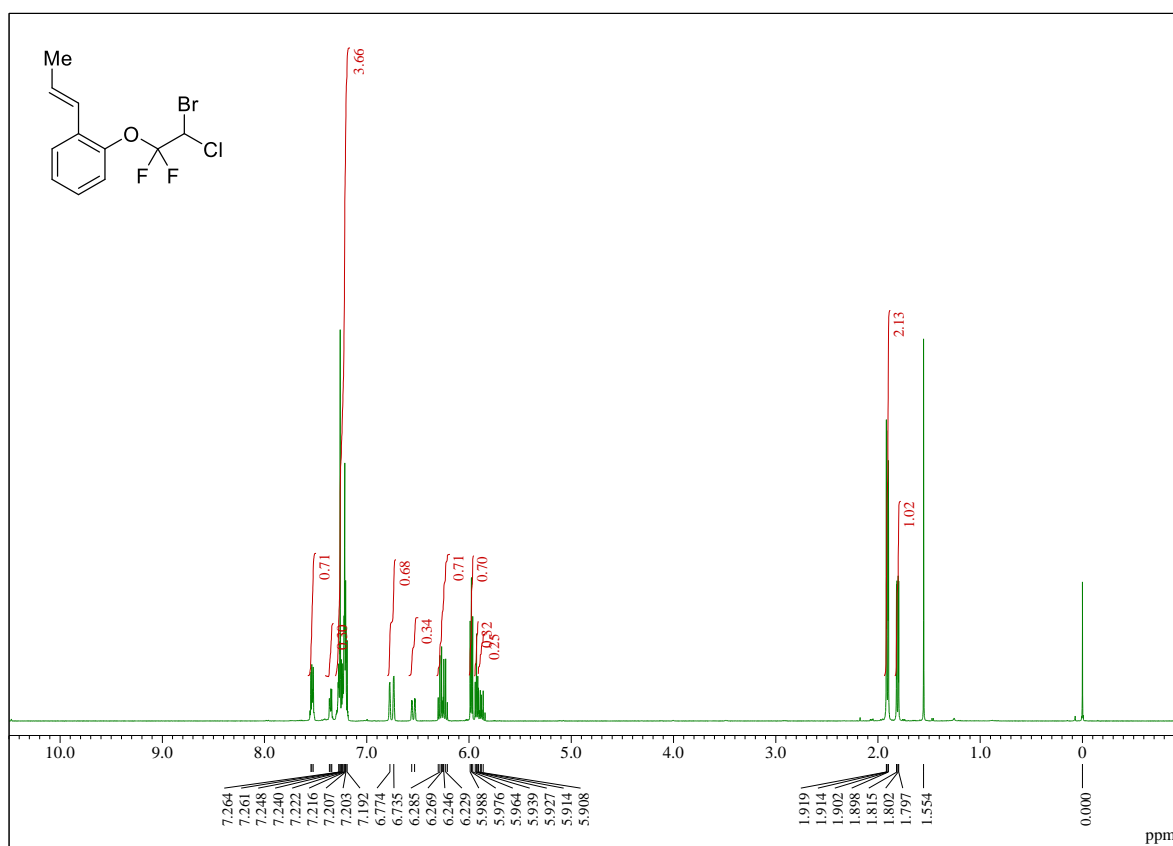


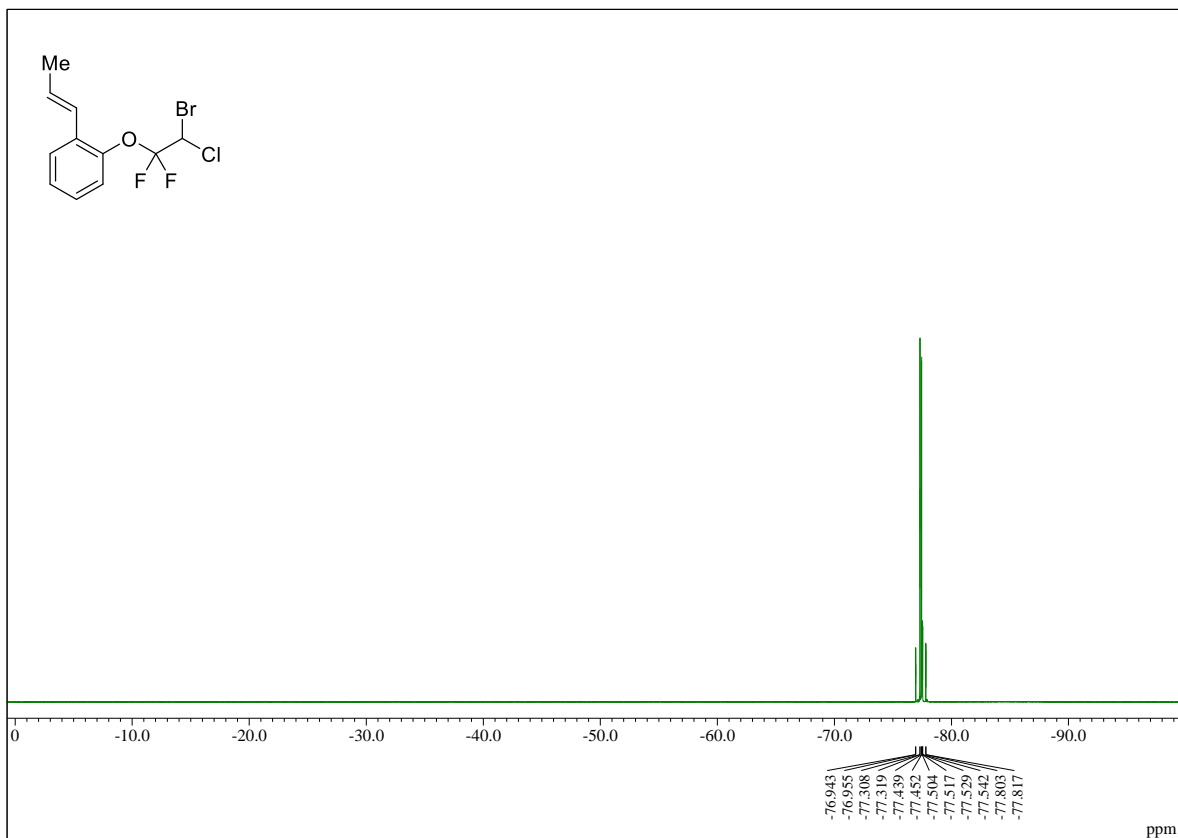
***o*-Allylphenyl 2-bromo-2-chloro-1,1-difluoroethyl ether (2m)**



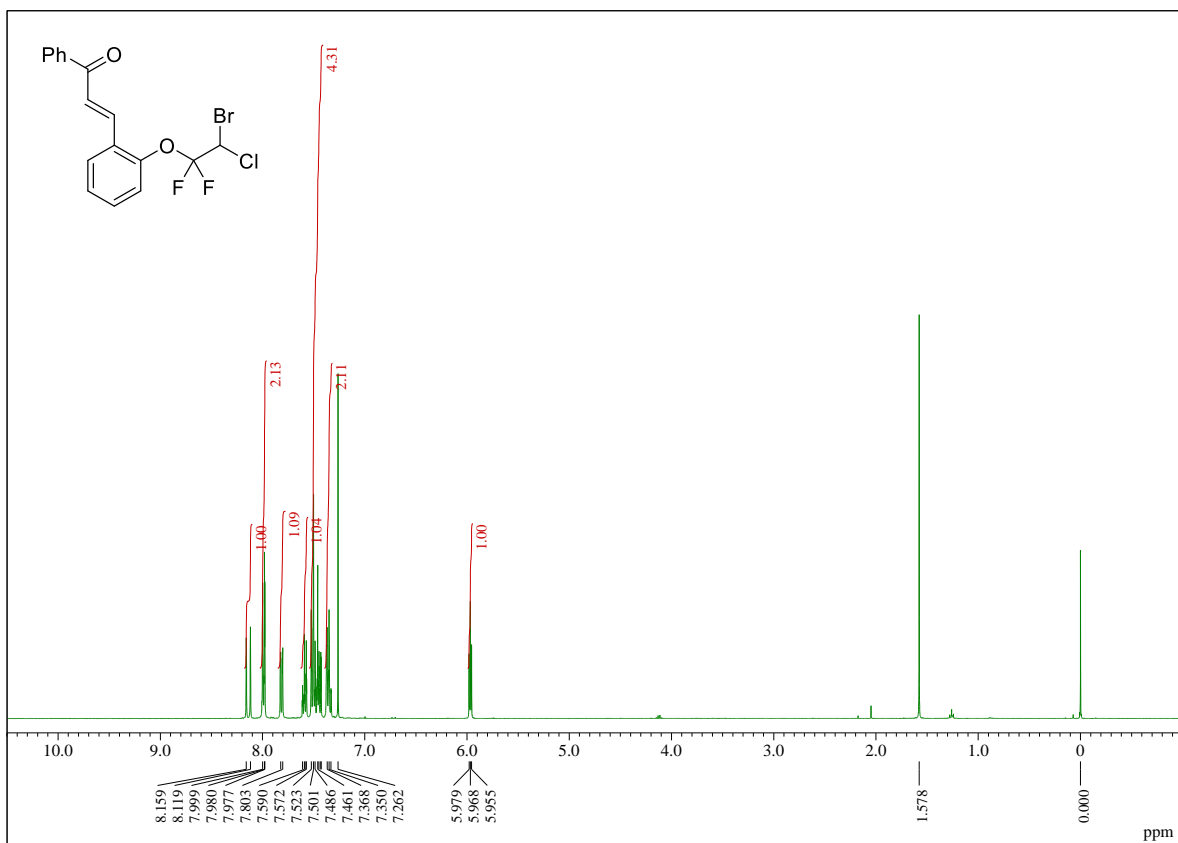


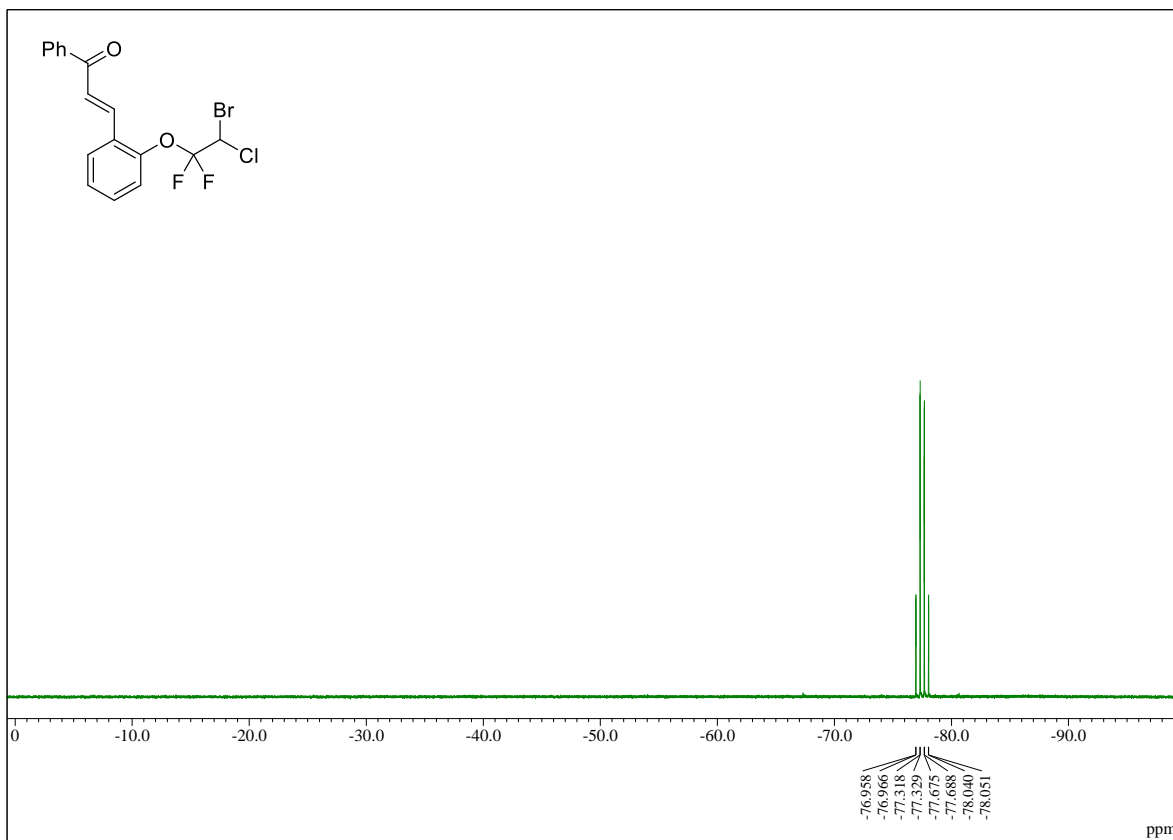
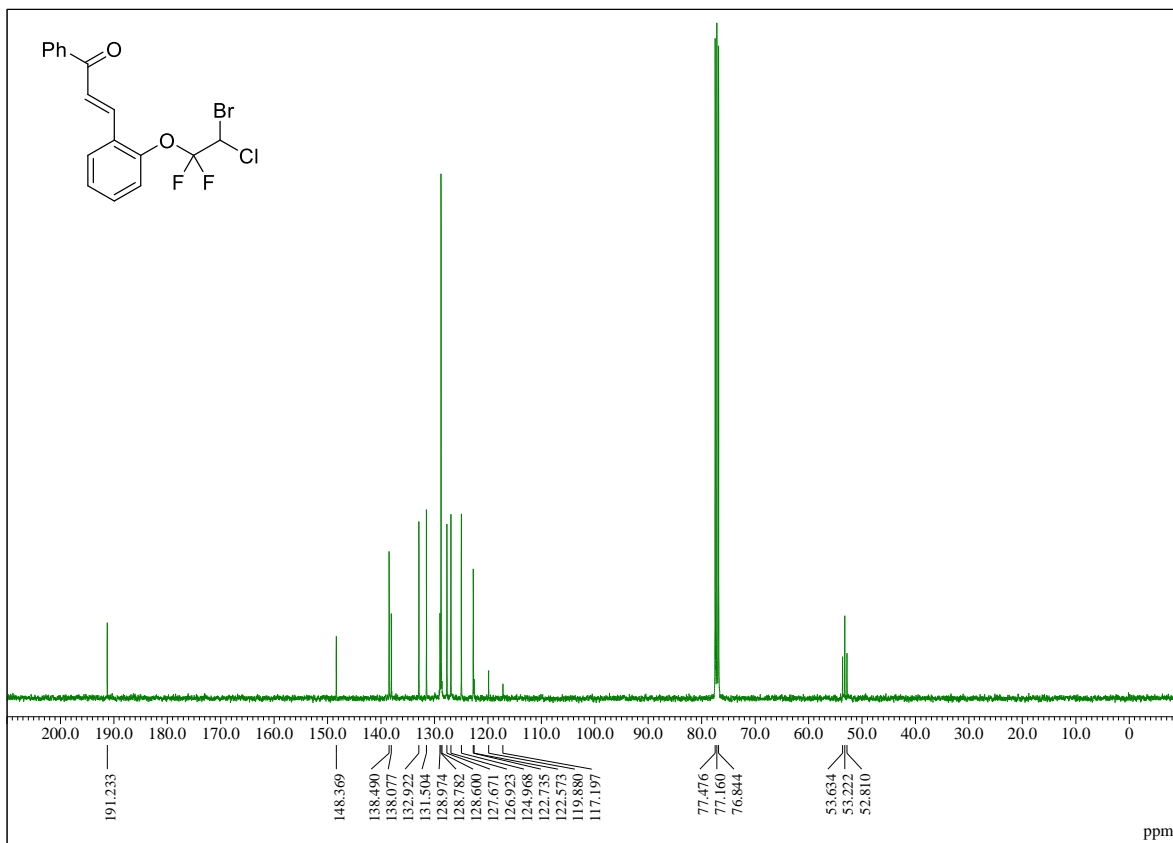
2-Bromo-2-chloro-1,1-difluoroethyl *o*-propenylphenyl ether (2n)



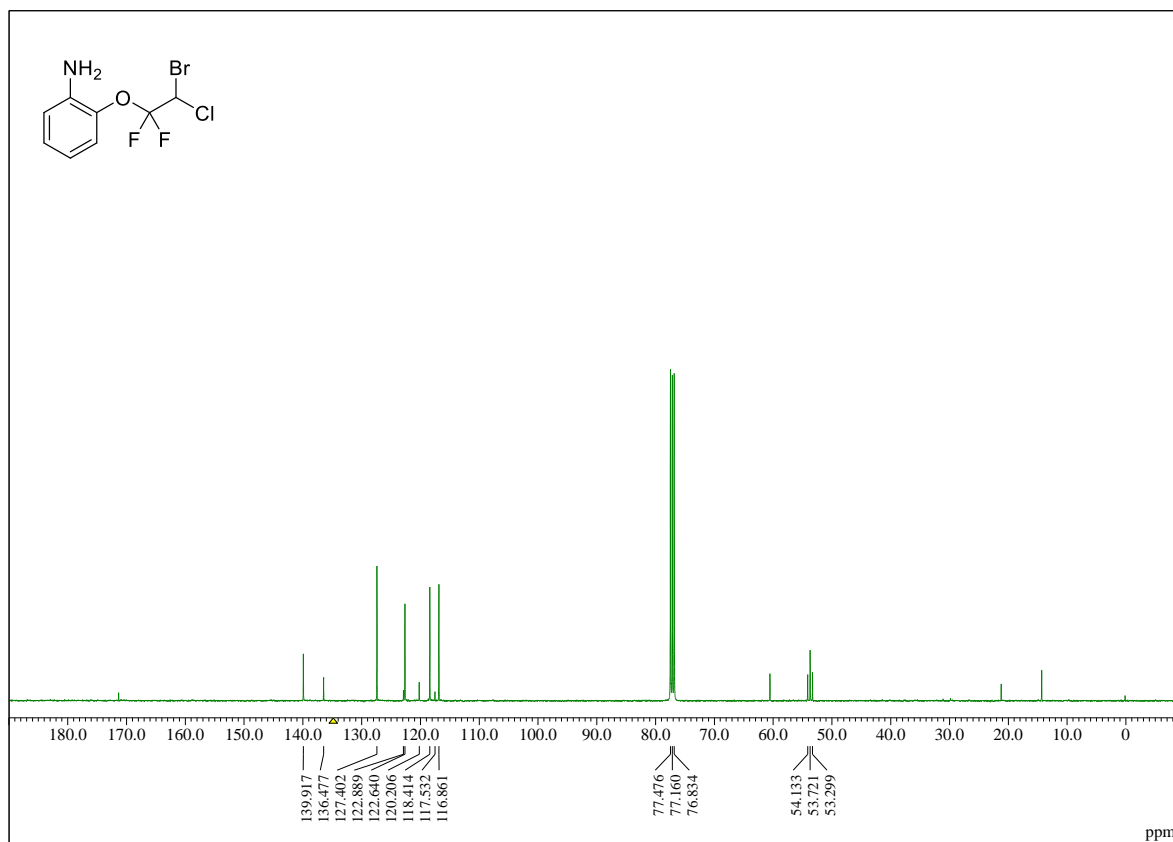
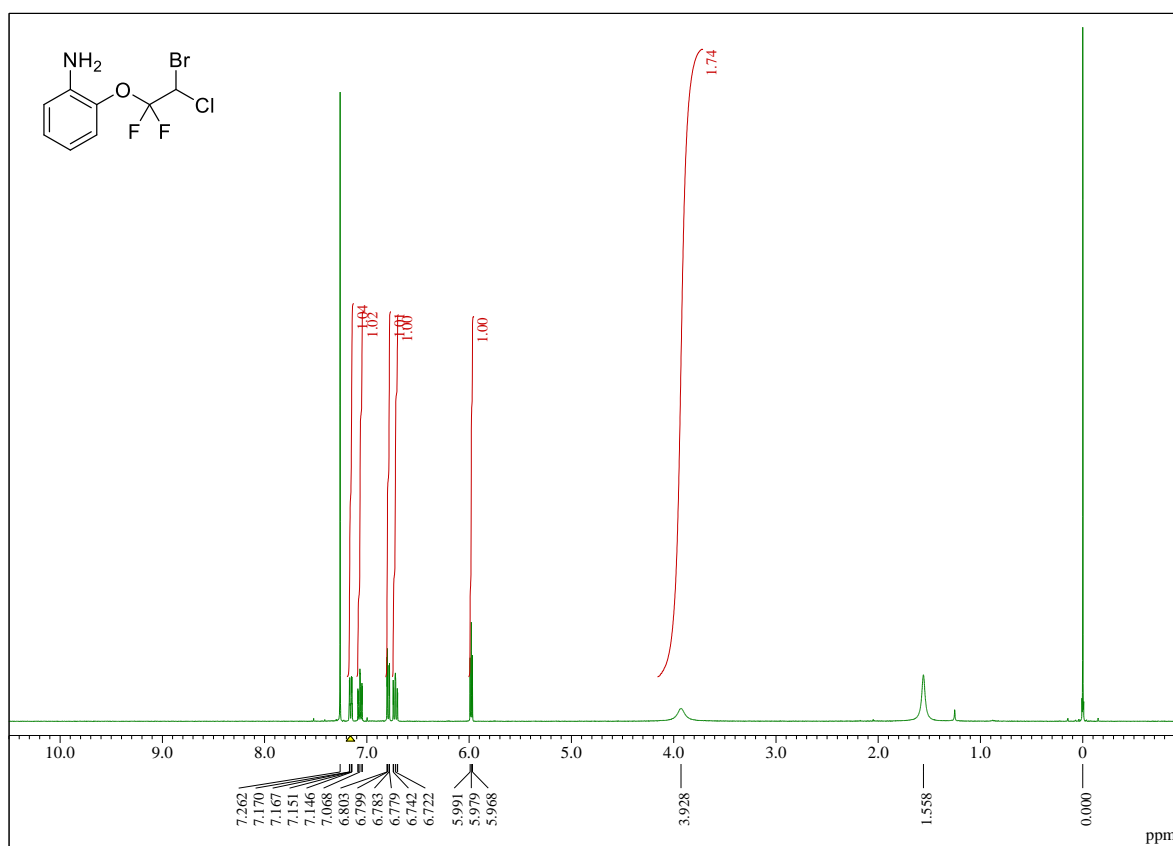


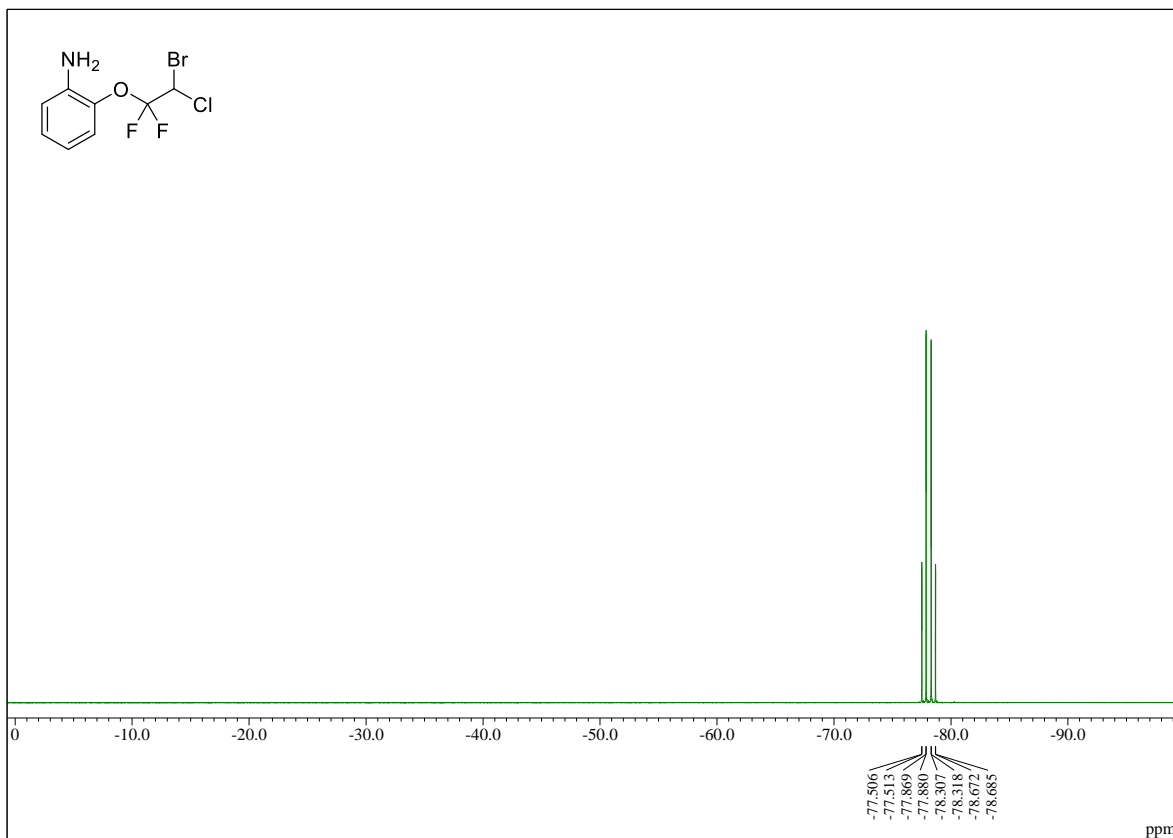
(E)-2'-(2-Bromo-2-chloro-1,1-difluoroethoxy)-chalcone (2o)





***o*-Aminophenyl 2-bromo-2-chloro-1,1-difluoroethyl ether (2p)**





4-Benzoylmethyl-3-chloro-2,2-difluorochromane (3)

