Iridium-Catalyzed Radiosynthesis of Branched Allylic [^{18}F]Fluorides

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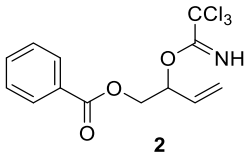
Supporting Information

Instrumentation. All proton (^{1}H) nuclear magnetic resonance spectra were recorded on a 400 or 500 MHz spectrometer. All carbon (^{13}C) nuclear magnetic resonance spectra were recorded on a 101 or 125 MHz NMR spectrometer. All fluorine (^{19}F) nuclear magnetic resonance spectra were recorded on a 376 MHz NMR spectrometer. Chemical shifts are expressed in parts per million (δ scale) and are referenced to residual $CHCl_3$ (^{1}H: δ 7.26 ppm, ^{13}C: δ 77.16 ppm) and C_6D_6 (^{1}H: δ 7.16 ppm, ^{13}C: δ 128.06 ppm). Data are presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and bs = broad singlet), integration, and coupling constant in hertz (Hz). Infrared (IR) spectra were reported in cm^{-1}. High resolution TOF mass spectrometry utilizing electrospray ionization in positive mode or electron ionization was performed to confirm the identity of the compounds.

General Procedure for the Synthesis of Allylic Trichloroacetimidates

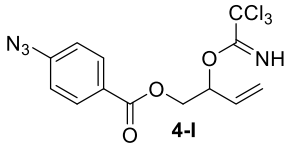
Secondary Allylic trichloroacetimidates **2**, **5-I**, **6-I**, **7-I**, **8-I**, **9-I**, **10-I**, **11-I**, **12-I**, **13-I**, **14-I**, **15-I**, **17-I**, **18-I**, **19-I, 21** and **22** have been previously prepared.[1-3]



2

We have previously reported the synthesis of compound **2**.[1]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.43 (s, 1H), 8.10 – 7.95 (m, 2H), 7.64 – 7.51 (m, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 6.06 – 5.88 (m, 1H), 5.81 (dtd, *J* = 7.3, 3.8, 1.8 Hz, 1H), 5.57 (dt, *J* = 17.3, 1.3 Hz, 1H), 5.39 (dd, *J* = 10.6, 1.3 Hz, 1H), 4.61 (dd, *J* = 11.9, 3.6 Hz, 1H), 4.50 (dd, *J* = 12.0, 7.3 Hz, 1H).

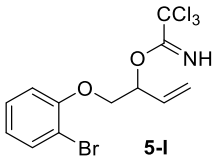


4-I

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.43 (s, 1H), 8.10 – 7.97 (m, 2H), 7.10 (t, *J* = 8.7 Hz, 2H), 5.96 (ddd, *J* = 17.3, 10.7, 5.6 Hz, 1H), 5.80 (dtd, *J* = 7.3, 3.7, 1.8 Hz, 1H), 5.56 (dt, *J* = 17.3, 1.3 Hz, 1H), 5.39 (dt, *J* = 10.6, 1.2 Hz, 1H), 4.60 (dd, *J* = 11.9, 3.6 Hz, 1H), 4.49 (dd, *J* = 11.9, 7.3 Hz, 1H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ =165.3, 161.8, 145.0, 131.5, 131.4, 126.3, 119.2, 118.9, 91.4, 76.6, 64.9.

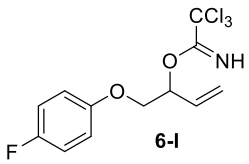
HRMS (FTMS ESI+): calc. for $C_{13}H_{11}O_3N_4Cl_3Na$ $(M+Na)^+$: 398.9789; found: 398.9789.



5-I

We have previously reported the synthesis of compound **5-I**.[2]

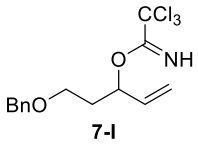
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.45 (s, 1H), 7.56 – 7.49 (m, 1H), 7.30 – 7.20 (m, 1H), 6.94 (dd, *J* = 8.3, 1.4 Hz, 1H), 6.85 (td, *J* = 7.6, 1.4 Hz, 1H), 6.06 (ddd, *J* = 17.3, 10.7, 5.7 Hz, 1H), 5.91 – 5.77 (m, 1H), 5.57 (dt, *J* = 17.3, 1.3 Hz, 1H), 5.40 (dt, *J* = 10.7, 1.3 Hz, 1H), 4.33 – 4.18 (m, 2H).



6-I

We have previously reported the synthesis of compound **6-I**.[1]

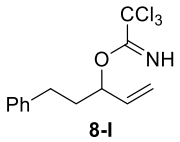
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.44 (s, 1H), 7.04 – 6.91 (m, 2H), 6.92 – 6.80 (m, 2H), 6.00 (ddd, *J* = 17.2, 10.7, 5.7 Hz, 1H), 5.81 – 5.70 (m, 1H), 5.54 (dt, *J* = 17.4, 1.4 Hz, 1H), 5.38 (dt, *J* = 10.8, 1.2 Hz, 1H), 4.24 – 4.09 (m, 2H).



7-I

We have previously reported the synthesis of compound **7-I**.[2]

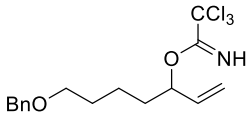
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.33 (s, 1H), 7.38 – 7.26 (m, 5H), 5.90 (ddd, *J* =17.3, 10.6, 5.8 Hz, 1H), 5.67 – 5.53 (m, 1H), 5.38 (dt, *J* =17.3, 1.3 Hz, 1H), 5.23 (dt, *J* =10.6, 1.2 Hz, 1H), 4.51 (s, 2H), 3.69 – 3.56 (m, 2H), 2.17 – 1.99 (m, 2H).



8-I

We have previously reported the synthesis of compound **8-I**.[1]

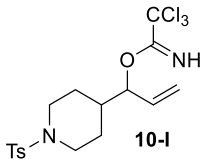
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.32 (s, 1H), 7.35 – 7.24 (m, 3H), 7.24 – 7.14 (m, 3H), 5.90 (ddd, *J* =17.2, 10.6, 5.8 Hz, 1H), 5.46 – 5.34 (m, 2H), 5.25 (dt, *J* =10.6, 1.2 Hz, 1H), 2.89 – 2.67 (m, 3H), 2.26 – 1.96 (m, 2H).



9-I

We have previously reported the synthesis of compound **9-I**.[2]

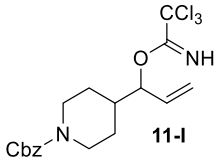
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.25 (s, 1H), 7.34 – 7.23 (m, 5H), 5.89 – 5.77 (m, 1H), 5.40 – 5.29 (m, 2H), 5.19 (dt, *J*=11, 1 Hz, 1H), 4.46 (s, 2H), 3.45 (t, *J*=6 Hz, 2H), 1.86 – 1.40 (m, 6H).



10-I

We have previously reported the synthesis of compound **10-I**.[3]

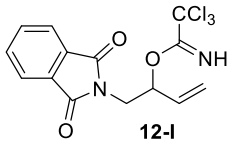
^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.30 (s, 1H), 7.63 (d, *J*=8 Hz, 2H), 7.31 (d, *J*=8 Hz, 2H), 5.75 (ddd, *J*=17, 11, 6 Hz, 1H), 5.35 (d, *J*=17 Hz, 1H), 5.28 (d, *J*=11 Hz, 1H), 5.19 (t, *J*=6 Hz, 1H), 3.84 (d, *J*=10 Hz, 2H), 2.43 (s, 3H), 2.23 (td, *J*=12, 2 Hz, 2H), 1.89 (d, *J*=13 Hz, 2H), 1.76 (d, *J*=13 Hz, 2H), 1.68 – 1.58 (m, 1H), 1.51 (m, 2H).



11-I

We have previously reported the synthesis of compound **11-I**.[3]

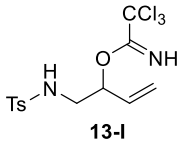
^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.30 (s, 1H), 7.39-7.27 (m, 5H), 5.80 (ddd, *J*=17, 11, 6 Hz, 1H), 5.43-5.25 (m, 2H), 5.22 (t, *J*=6 Hz, 1H), 5.12 (s, 2H), 4.32-4.14 (br m, 2H), 2.85-2.65 (br m, 2H), 1.92-1.85 (m, 2H), 1.73-1.71 (m, 1H), 1.39-1.27 (m, 2H).



12-I

We have previously reported the synthesis of compound **12-I**.[1]

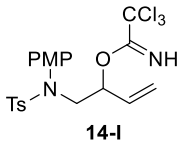
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.32 (s, 1H), 7.85 (dd, J = 5.4, 3.1 Hz, 2H), 7.72 (dd, J = 5.5, 3.0 Hz, 2H), 5.94 (ddd, J = 17.0, 10.6, 6.1 Hz, 1H), 5.83 – 5.70 (m, 1H), 5.51 (dt, J = 17.3, 1.1 Hz, 1H), 5.35 (dt, J = 10.7, 1.0 Hz, 1H), 4.14 (dd, J = 14.2, 8.5 Hz, 1H), 3.92 (dd, J = 14.2, 4.6 Hz, 1H).



13-I

We have previously reported the synthesis of compound **13-I**.[3]

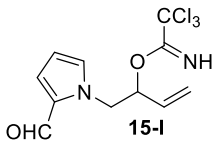
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.39 (s, 1H), 7.74 (d, *J*=8 Hz, 2H), 7.30 (d, *J*=8 Hz, 2H), 5.82 – 5.71 (m, 1H), 5.43 – 5.27 (m, 3H), 4.95 (t, *J*=6 Hz, 1H), 3.39 – 3.31 (m, 1H), 3.26-3.19 (m, 1H), 2.42 (s, 3H).



14-I

We have previously reported the synthesis of compound **14-I**.[3]

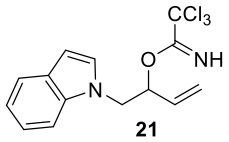
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.28 (s, 1H), 7.46 (d, *J*=8 Hz, 2H), 7.25 – 7.22 (m, 2H), 6.96 – 6.91 (m, 2H), 6.82 – 6.76 (m, 2H), 5.89 (ddd, *J*=17, 11, 6 Hz, 1H), 5.45 – 5.38 (m, 2H), 5.35 – 5.31 (m, 1H), 3.93 (dd, *J*=14, 7 Hz, 1H), 3.79 (s, 3H), 3.73 (dd, *J*=14, 5 Hz, 1H), 2.42 (s, 3H).



15-I

We have previously reported the synthesis of compound **15-I**.[3]

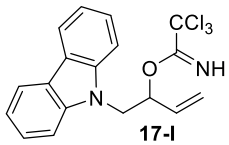
^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.57 (s, 1H), 8.31 (s, 1H), 7.07 (s, 1H), 6.95 (dd, *J*=4, 1 Hz, 1H), 6.22 (dd, *J*=4, 3 Hz, 1H), 5.93 (ddd, *J*=17, 11, 5 Hz, 1H), 5.73 - 5.70 (m, 1H), 5.50 (d, *J*=17 Hz, 1H), 5.32 (d, *J*=11 Hz, 1H), 4.88 (dd, *J*=14, 3 Hz, 1H), 4.46 (dd, *J*=14, 8 Hz, 1H).



21

We have previously reported the synthesis of compound **21**.[3]

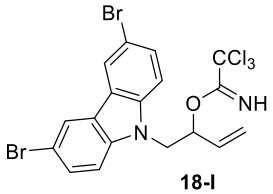
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.41 (s, 1H), 7.64 (d, *J*=8 Hz, 1H), 7.47 (d, *J*=8 Hz, 1H), 7.25 (t, *J*=8 Hz, 1H), 7.20 (d, *J*=3 Hz, 1H), 7.14 (t, *J*=7 Hz, 1H), 6.52 (d, *J*=3 Hz, 1H), 5.89 (ddd, *J*=17, 11, 6 Hz, 1H), 5.75 (q, *J*=6 Hz, 1H), 5.51 – 5.29 (m, 2H), 4.53 (dd, *J*=15, 7 Hz, 1H), 4.40 (dd, *J*=15, 5 Hz, 1H).



17-I

We have previously reported the synthesis of compound **17-I**.[3]

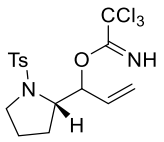
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.40 (s, 1H), 8.08 (dd, *J*=8, 1 Hz, 2H), 7.57 (d, *J*=8 Hz, 2H), 7.47 (ddd, *J*=8, 7, 1 Hz, 2H), 7.29 – 7.20 (m, 2H), 6.01 – 5.81 (m, 2H), 5.48 (dt, *J*=17, 1 Hz, 1H), 5.30 (dt, *J*=10, 1 Hz, 1H), 4.73 (dd, *J*=15, 7 Hz, 1H), 4.49 (dd, *J*=15, 6 Hz, 1H).



18-I

We have previously reported the synthesis of compound **18-I**.[3]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.40 (s, 1H), 8.10 (d, *J*=2 Hz, 2H), 7.55 (dd, *J*=9, 2 Hz, 2H), 7.42 (d, *J*=9 Hz, 2H), 5.89 (ddd, *J*=17, 11, 6 Hz, 1H), 5.81 – 5.74 (m, 1H), 5.44 (dt, *J*=17, 1 Hz, 1H), 5.30 (dd, *J*=11, 1 Hz, 1H), 4.64 (dd, *J*=15, 7 Hz, 1H), 4.41 (dd, *J*=15, 6 Hz, 1H).

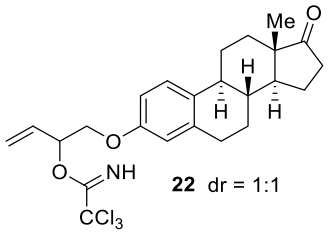


19-I dr >25:1

We have previously reported the synthesis of compound **19-I**.[3]

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.40 (s, 1H), 7.71 (d, *J*=8 Hz, 2H), 7.28 (d, *J*=8 Hz, 2H), 5.86 – 5.78 (m, 2H), 5.44 – 5.38 (m, 1H), 5.32 – 5.28 (m, 1H), 3.93 (dt, *J*=9, 3 Hz, 1H), 3.37 (dt, *J*=10,

6 Hz, 1H), 3.33 – 3.24 (m, 1H), 2.41 (s, 3H), 2.09 – 1.99 (m, 2H), 1.66 (ddt, *J*=13, 9, 4 Hz, 1H), 1.55 (h, *J*=7, 5 Hz, 1H).



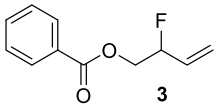
22 dr = 1:1

We have previously reported the synthesis of compound **22**.[2]

^{1}H NMR (CDCl$_3$, 400 MHz): δ = 8.42 (s, 1H), 7.19 (dd, *J* = 8.6, 1.0 Hz, 1H), 6.83 – 6.70 (m, 1H), 6.68 (d, *J* = 2.7 Hz, 1H), 6.01 (ddd, *J* = 17.3, 10.7, 5.7 Hz, 1H), 5.82 – 5.69 (m, 1H), 5.53 (dt, *J* = 17.3, 1.3 Hz, 1H), 5.36 (dt, *J* = 10.7, 1.3 Hz, 1H), 4.27 – 4.07 (m, 2H), 2.94 – 2.79 (m, 2H), 2.50 (dd, *J* = 18.8, 8.5 Hz, 1H), 2.43 – 2.32 (m, 1H), 2.33 – 2.18 (m, 1H), 2.20 – 1.89 (m, 4H), 1.69 – 1.33 (m, 6H), 0.91 (s, 3H).

General Procedure for the Synthesis of Allylic [^{19}F]Fluorides

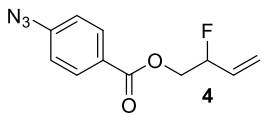
Secondary Allylic Fluorides **3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19,** and **20** have been previously prepared.[1-3]



3

We have previously reported the synthesis of compound **3**.[1]

^{1}H NMR (CDCl$_3$, 400 MHz): δ = 8.08 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.62 – 7.54 (m, 1H), 7.51 – 7.40 (m, 2H), 5.96 (dddd, *J* = 17.3, 15.0, 10.7, 5.7 Hz, 1H), 5.52 (ddt, *J* = 17.3, 2.7, 1.3 Hz, 1H), 5.40 (dt, *J* = 10.8, 1.3 Hz, 1H), 5.25 (dtdd, *J* = 48.8, 5.6, 3.0, 1.5 Hz, 1H), 4.62 – 4.33 (m, 2H).



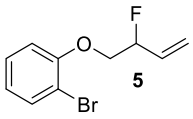
4

^{1}H NMR (CDCl$_3$, 400 MHz): δ = 8.08 – 8.03 (m, 2H), 7.10 – 7.05 (m, 2H), 5.95 (dddd, *J*=17, 15, 11, 6 Hz, 1H), 5.52 (ddt, *J*=17, 3, 1 Hz, 1H), 5.40 (dt, *J*=11, 1 Hz, 1H), 5.33 – 5.14 (m, 1H), 4.58 – 4.32 (m, 2H).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 165.4, 145.1, 131.9 (d, *J*=19 Hz), 131.6, 126.1, 119.5 (d, *J*=11 Hz), 118.9, 90.7 (d, $J_{C\text{-}F}$ =174 Hz), 65.9 (d, *J*=23 Hz).

^{19}F NMR ($CDCl_3$, 376 MHz): δ = -186.1.

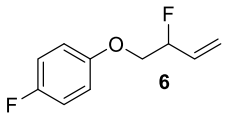
HRMS (FTMS ESI+): calc. for $C_{11}H_{11}O_2N_3F$ $(M+H)^+$: 236.0830; found: 236.0837.



5

We have previously reported the synthesis of compound **5**.[2]

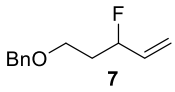
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.55 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.31 – 7.21 (m, 1H), 6.94 – 6.82 (m, 2H), 6.06 (dddd, *J* = 17.1, 14.8, 10.8, 5.9 Hz, 1H), 5.54 (ddt, *J* = 17.3, 3.0, 1.3 Hz, 1H), 5.43 – 5.19 (m, 2H), 4.27 – 4.08 (m, 2H).



6

We have previously reported the synthesis of compound **6**.[1]

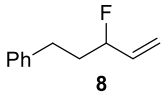
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.03 – 6.92 (m, 2H), 6.93 – 6.83 (m, 2H), 5.99 (dddd, *J* = 17.3, 14.9, 10.8, 5.8 Hz, 1H), 5.52 (ddt, *J* = 17.3, 2.8, 1.3 Hz, 1H), 5.39 (dt, *J* = 10.8, 1.2 Hz, 1H), 5.35 – 5.12 (m, 1H), 4.16 – 3.95 (m, 2H).



7

We have previously reported the synthesis of compound **7**.[2]

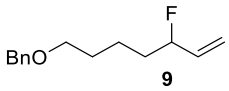
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.41 – 7.27 (m, 5H), 5.92 (dddd, *J* = 17.1, 14.3, 10.7, 6.0 Hz, 1H), 5.35 (ddt, *J* = 17.1, 3.3, 1.4 Hz, 1H), 5.24 (dt, *J* = 10.7, 1.4 Hz, 1H), 5.21 – 4.99 (m, 1H), 4.53 (d, *J* = 2.9 Hz, 2H), 3.72 – 3.53 (m, 2H), 2.10 – 1.87 (m, 2H).



8

We have previously reported the synthesis of compound **8**.[1]

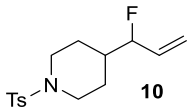
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.36 – 7.27 (m, 2H), 7.24 – 7.16 (m, 3H), 5.91 (dddd, *J* = 17.2, 14.2, 10.7, 6.0 Hz, 1H), 5.33 (ddt, *J* = 17.3, 3.5, 1.4 Hz, 1H), 5.24 (dt, *J* = 10.7, 1.3 Hz, 1H), 5.03 – 4.77 (m, 1H), 2.85 – 2.63 (m, 2H), 2.16 – 1.82 (m, 2H).



9

We have previously reported the synthesis of compound **9**.[2]

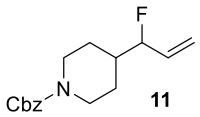
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.46 – 7.06 (m, 5H), 5.85 (dddd, *J*=17, 14, 11, 6 Hz, 1H), 5.28 (ddt, *J*=17, 4, 1 Hz, 1H), 5.19 (dt, *J*=11, 1 Hz, 1H), 4.84 (dddd, *J*=49, 7, 6, 5 Hz, 1H), 4.48 (s, 2H), 3.46 (t, *J*=6 Hz, 2H), 1.87 – 1.33 (m, 6H).



10

We have previously reported the synthesis of compound **10**.[3]

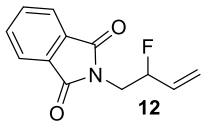
^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.65 (d, *J*=8 Hz, 2H), 7.33 (d, *J*=8 Hz, 2H), 5.79 (dddd, *J*=17, 14, 11, 7 Hz, 1H), 5.38 – 5.25 (m, 2H), 4.60 (dt, *J*=47, 6 Hz, 1H), 3.91 – 3.78 (m, 1H), 2.44 (s, 3H), 2.22 (tt, *J*=12, 2 Hz, 2H), 1.90 (d, *J*=13 Hz, 1H), 1.66 (d, *J*=12 Hz, 1H), 1.47 (m, 3H).



11

We have previously reported the synthesis of compound **11**.[3]

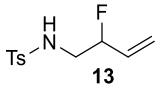
^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.43-7.27 (m, 5H), 5.84 (dddd, *J*=17,14,11,7 Hz), 5.38-5.27 (m, 2H), 5.13 (s, 2H), 4.62 (dt, *J*=48, 7 Hz, 1H), 4.35-4.15 (br m, 2H), 2.76 (br m, 2H), 2.82-2.65 (m, 1H), 1.78-1.67 (m, 1H), 1.66-1.58 (m, 1H), 1.40-1.17 (m, 2H).



12

We have previously reported the synthesis of compound **12**.[1]

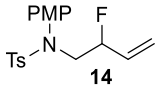
1H NMR (CDCl3, 400 MHz): δ = 7.86 (dd, J = 5.4, 3.1 Hz, 2H), 7.73 (dd, J = 5.5, 3.1 Hz, 2H), 5.93 (dddd, J = 17.0, 14.5, 10.7, 6.0 Hz, 1H), 5.45 (ddt, J = 17.3, 3.3, 1.3 Hz, 1H), 5.34 (dt, J = 10.6, 1.2 Hz, 1H), 5.30 – 5.09 (m, 1H), 4.03 (td, J = 13.9, 8.2 Hz, 1H), 3.82 (ddd, J = 26.3, 14.3, 4.0 Hz, 1H).



13

We have previously reported the synthesis of compound **13**.[3]

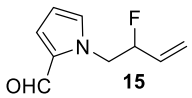
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.75 (d, *J*=8 Hz, 2H), 7.32 (d, *J*=8 Hz, 2H), 5.88 – 5.65 (m, 1H), 5.42 – 5.34 (m, 1H), 5.32 (d, *J*=11 Hz, 1H), 5.03 – 4.84 (m, 1H), 4.79 – 4.69 (m, 1H), 3.28 (m, 1H), 3.17 – 3.04 (m, 1H), 2.44 (s, 1H).



14

We have previously reported the synthesis of compound **14**.[3]

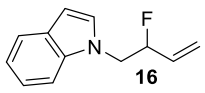
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.51 – 7.47 (m, 2H), 7.27 – 7.23 (m, 2H), 6.98 – 6.94 (m, 2H), 6.81 (d, *J*=9 Hz, 2H), 5.85 (dddd, *J*=17, 15, 11, 6 Hz, 1H), 5.38 (ddt, *J*=17, 3, 1 Hz, 1H), 5.31 (dt, *J*=11, 1 Hz, 1H), 5.06 – 4.87 (m, 1H), 3.80 (s, 3H), 3.78 – 3.61 (m, 2H), 2.42 (s, 3H).



15

We have previously reported the synthesis of compound **15**.[3]

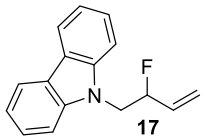
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.54 (s, 1H), 7.04 – 6.95 (m, 2H), 6.28 – 6.24 (m, 1H), 5.90 (dtd, *J*=17, 11, 5 Hz, 1H), 5.45 (d, *J*=17 Hz, 1H), 5.32 (d, *J*=11 Hz, 1H), 5.17 (dt, *J*=49, 6 Hz, 1H), 4.79 (ddd, *J*=30, 14, 3 Hz, 1H), 4.32 (ddd, *J*=19, 15, 8 Hz, 1H).



16

We have previously reported the synthesis of compound **16**.[3]

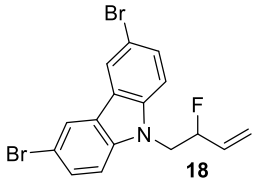
^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.67 (d, *J*=8 Hz, 1H), 7.37 (d, *J*=8 Hz, 1H), 7.25 (t, *J*=8 Hz, 1H), 7.18 – 7.13 (m, 2H), 6.56 (d, *J*=3 Hz, 1H), 5.91 (dddd, *J*=17, 15, 11, 6 Hz, 1H), 5.50 – 5.43 (m, 1H), 5.36 (d, *J*=11 Hz, 1H), 5.22 (dq, *J*=48, 6 Hz, 1H), 4.41 – 4.33 (m, 2H).



17

We have previously reported the synthesis of compound **17**.[3]

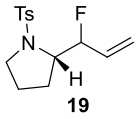
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.13 (d, *J*=8 Hz, 2H), 7.49 (dt, *J*=15, 8 Hz, 4H), 7.29 (d, *J*=15 Hz, 2H), 6.01 (dddd, *J*=17, 15, 11, 6 Hz, 1H), 5.55 – 5.46 (m, 1H), 5.39 (dq, *J*= 48, 6 Hz, 1H), 5.37 (d, *J*=11 Hz, 1H), 4.66 – 4.46 (m, 2H).



18

We have previously reported the synthesis of compound **18**.[3]

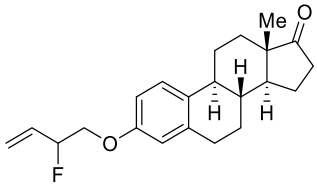
^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.10 (s, 2H), 7.56 (d, *J*=8 Hz, 2H), 7.27 (d, *J*=9 Hz, 2H), 5.93 (dt, *J*=18, 10 Hz, 1H), 5.50-5.22 (m, 3H), 4.49 – 4.37 (m, 2H).



19

We have previously reported the synthesis of compound **19**.[3]

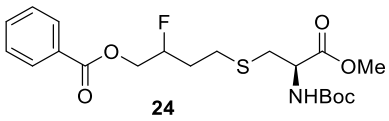
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.74 (t, *J*=8 Hz, 3H), 7.33 (dd, *J*=8, 5 Hz, 3H), 6.06 – 5.95 (m, 0.5H), 5.86 (dddd, *J*=23, 17, 11, 5 Hz, 1H), 5.50 – 5.43 (m, 1H), 5.42 – 5.32 (m, 2H), 5.31 – 5.23 (m, 1.5H) 3.91 (tt, *J*=8, 4 Hz, 0.5H), 3.82 – 3.68 (m, 1H), 3.45 – 3.31 (m, 2H), 3.28 – 3.15 (m, 1.5H), 2.44 (s, 1.5H), 2.43 (s, 3H), 1.99 – 1.85 (m, 3H), 1.80 – 1.70 (m, 1H), 1.64 – 1.42 (2H, m).



20

We have previously reported the synthesis of compound **20**.[2]

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.24 – 7.13 (m, 1H), 6.81 – 6.60 (m, 2H), 6.08 – 5.85 (m, 1H), 5.57 – 5.43 (m, 1H), 5.43 – 5.32 (m, 1H), 5.24 (dddd, *J* = 48.7, 7.6, 3.8, 1.9 Hz, 1H), 4.16 – 3.96 (m, 2H), 3.00 – 2.81 (m, 2H), 2.51 (dd, *J* = 19.0, 8.7 Hz, 1H), 2.39 (td, *J* = 7.6, 2.9 Hz, 1H), 2.33 – 2.20 (m, 1H), 2.20 – 1.89 (m, 4H), 1.73 – 1.36 (m, 6H), 0.91 (s, 3H).



24

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.06 (d, J = 7.3 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.7 Hz, 2H), 5.36 (d, J = 5.8 Hz, 1H), 5.03 – 4.84 (m, 1H), 4.60 – 4.35 (m, 3H), 3.76 (s, 3H), 3.06 – 2.92 (m, 2H), 2.81 – 2.63 (m, 2H), 2.15 – 2.05 (m, 1H), 1.96 – 1.80 (m, 1H), 1.44 (s, 9H).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 171.4, 166.2, 155.1, 133.3, 129.7, 129.6, 128.4, 89.6 (d, J = 174.0 Hz), 80.2, 65.8 (d, J = 22.3 Hz), 53.3, 52.6, 34.7, 34.7, 31.5 (dd, J = 21.3, 2.1 Hz), 29.7, 28.3, 28.0 (d, J = 4.2 Hz).

^{19}F NMR (471 MHz, CDCl3): δ -189.38, -189.44.

HRMS (FTMS ESI+): calc. for $C_{20}H_{28}O_6NFSNa$ $(M+Na)^+$: 452.1525; found: 452.1509.

General Procedure for the Synthesis of Allylic [^{18}F]Fluorides

Procedure for [F-18]KF·Kryptofix Preparation: The [^{18}F]fluoride ion was prepared by the $^{18}O(p,n)^{18}F$ reaction using >95% oxygen-18 enriched water as the target material with a Havar window and niobium target body. The target was rinsed with [^{16}O]H_2O to reclaim residual [^{18}F]fluoride from an earlier production run. The target rinse was pushed to the hot cell with helium pressure and the aqueous [^{18}F]fluoride was trapped on an anion exchange resin (Waters QMA). The [^{18}F]fluoride was then eluted with a potassium carbonate [2,2,2] Kryptofix® solution (5.5 mg K_2CO_3, 30 mg of Kryptofix per mL of acetonitrile:water = 19:1). The resulting [^{18}F]KF•Kryptofix

[2,2,2] solution was dried by azeotropic distillation with acetonitrile at 105°C (3 x 1 mL). The dried [^{18}F]KF•Kryptofix complex was taken up in THF (0.5-1.5 mL depending on activity).

Procedure for Fluorine-18 Allylic Fluorination: A glass v-vial was charged with a solution of allylic trichloroacetimidate (45 µmol in 0.4 mL THF) and catalyst (15 mol% to imidate, stored and weighed in glovebox). A portion of the [^{18}F]KF•Kryptofix [2,2,2] (~3 mCi) / THF (0.1 mL) stock solution was added to the v-vial. The v-vial was capped under ambient air, agitated via micro-pipette, and then allowed to stir at room temperature for 15 min. Upon completion of the reaction, the crude mixture was spotted on silica gel TLC plates (2 µL) to determine the radiochemical conversion (RCC). The remaining solution was diluted with acetonitrile (1 mL). An analytical portion of the crude reaction was analyzed by analytical HPLC with UV and radio detection, which confirmed the presence of the fluorine-18 labeled allylic fluorination compound and the identity of the product was confirmed via UV with a fluorine-19 labeled reference standard.

Procedure for radiochemical yield determination of fluorine-18 allylic fluorides: A glass v-vial was charged with a solution of allylic trichloroacetimidate (45 µmol in 0.4 mL THF) and $[IrMeO(COD)]_2$ (15 mol% to imidate, stored and weighed in glovebox). A portion of the [^{18}F]KF•Kryptofix [2,2,2] (~3 mCi) / THF (0.1 mL) stock solution was added to the v-vial. The v-vial was capped under ambient air, agitated via micro-pipette, and then allowed to stir at room temperature for 15 min. Upon completion of the reaction, the crude mixture was spotted on silica gel TLC plates (2 µL) to determine the radiochemical conversion (RCC). The reaction mixture was diluted in H_2O (6 mL) and passed over a C-18 SepPak (Waters), preconditioned with 10 mL of water. The SepPak was further washed with 10 mL of HPLC-grade water and eluted with acetonitrile (2 x 1 mL). The eluate was diluted with water (1 mL) and injected onto a semi-prep HPLC. The product was isolated and further characterized by TLC and analytical HPLC (UV and radio detection).

General Procedure for Thiol-ene Reactions: A glass v-vial was charged with a solution of allylic trichloroacetimidate (45 µmol in 0.4 mL THF) and $[IrMeO(COD)]_2$ (15 mol% to imidate, stored and weighed in glovebox). A portion of the [^{18}F]KF•Kryptofix [2,2,2] (~3 mCi) / THF (0.1 mL) stock solution was added to the v-vial. The v-vial was capped under ambient air, agitated via micro-pipette, and then allowed to stir at room temperature for 15 min. Upon completion of the

reaction the crude mixture was spotted on silica gel TLC plates (2 µL) to determine the radiochemical conversion (RCC). The reaction mixture was diluted in water (6 mL) and passed over a C-18 SepPak (Waters), preconditioned with 10 mL of water. The SepPak was further washed with 10 mL of HPLC-grade water and eluted with acetonitrile (1 mL). The eluate was added to a mixture of $(Ir[dF(CF_3)ppy]_2(dtbpy))PF_6$ (1 mg) and *N*-(*tert*-Butoxycarbonyl)-L-cysteine methyl ester (0.34 mmol, 0.07 mL). The solution was placed in a Penn Optical Coatings Photoreactor m1 for 15 min (450 nm, 2000 rpm). The subsequent solution was diluted with water (6 mL) and passed over a C-18 SepPak (Waters), preconditioned with 10 mL of water. The SepPak was further washed with 10 mL of HPLC-grade water and eluted with acetonitrile (2 x 1 mL). The eluate was diluted with water (1 mL) and injected onto a semi-prep HPLC. The product was isolated and further characterized by TLC and analytical HPLC (UV and radio detection).

HPLC Conditions:

Method 1 (Analytical Method):

Condition: 20-95% gradient of (MeOH) in (0.1M NH_4OAc (aq)) pH 6.3 – 6.6

Flow rate: 1 mL/min

Column: Phenomenex Gemini C-18 Column 150 x 4.6 mm; 5 µm

0-3 min 20% MeOH / 80% 0.1M NH_4OAc (aq)	Isocratic
3-10 min 20% to 95% MeOH	Linear increase
10-15 min 95% MeOH	Isocratic
15-20 min 20% MeOH / 80% 0.1M NH_4OAc (aq)	Isocratic

Method 2 (Analytical Method):

Condition: 20-95% gradient of (MeOH) in (0.1M NH_4OAc (aq)) pH 6.3 – 6.6

Flow rate: 1 mL/min

Column: Phenomenex Gemini C-18 Column 150 x 4.6 mm; 5 µm

0-3 min 20% MeOH / 80% 0.1M NH_4OAc (aq)	Isocratic
3-10 min 20% to 80% MeOH	Linear increase
10-20 min 80% MeOH	Isocratic
20-24 min 80% to 95% MeOH	Linear increase
24-25 min 95% MeOH	Isocratic
25-30 min 95% to 20% MeOH	Linear decrease

Method 3 (Prep. Method):

Condition: 60% isocratic of (CH_3CN) in (0.1M NH_4OAc (aq)) pH 6.3 – 6.6

Flow rate: 3 mL/min

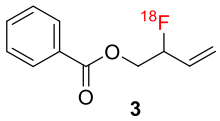
Column: Phenomenex Gemini C-18 Column 150 x 10 mm, 5 µm

Method 4 (Prep. Method):

Condition: 75% isocratic of (CH_3CN) in (0.1M NH_4OAc (aq)) pH 6.3 – 6.6

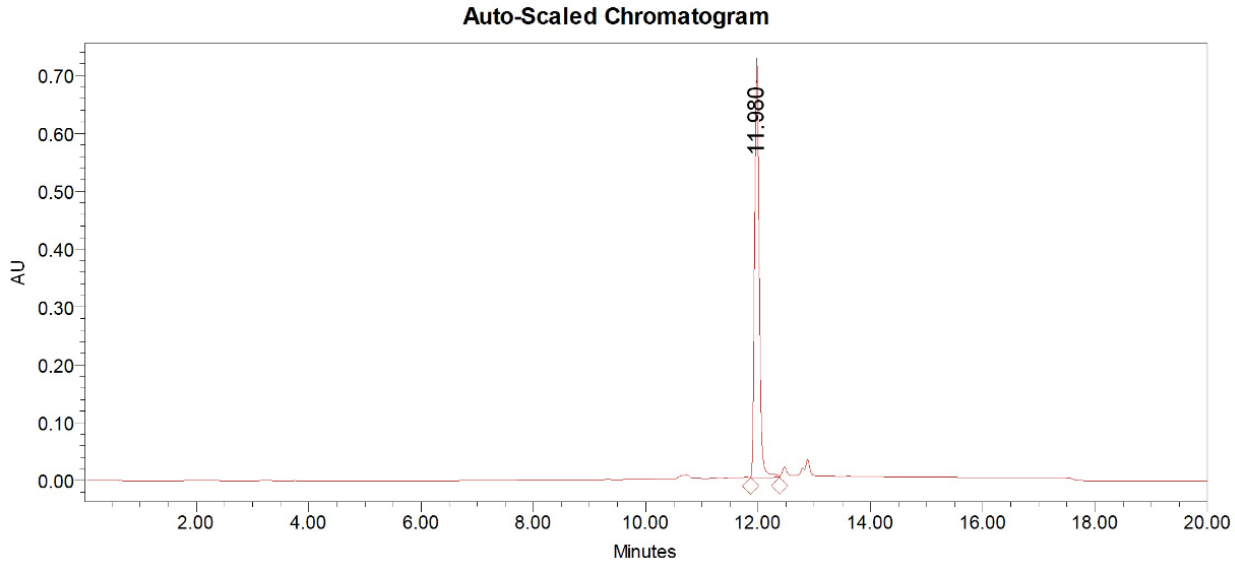
Flow rate: 3 mL/min

Column: Phenomenex Gemini C-18 Column 150 x 10 mm, 5 µm



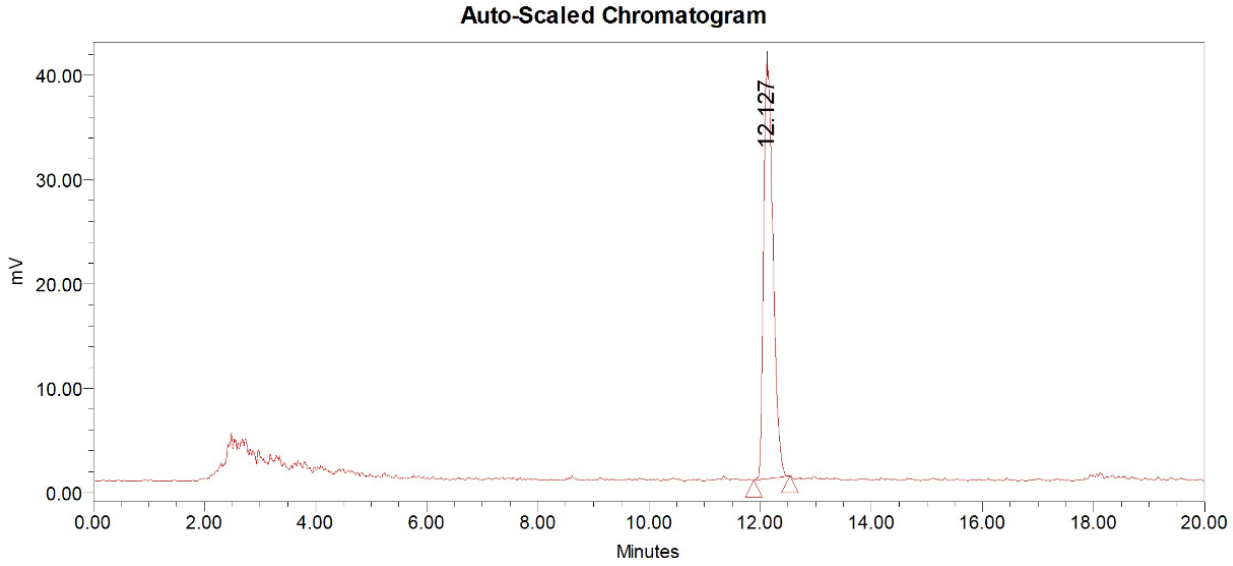
3

[^{19}F] Standard Allylic Fluoride

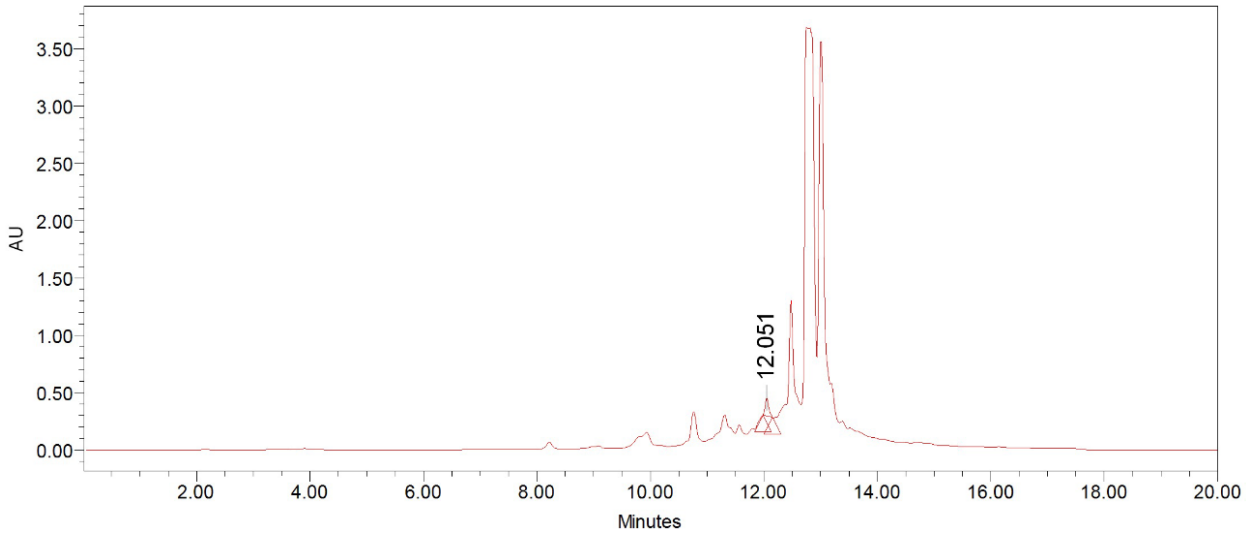


Allylic Fluoride [^{19}F] Standard Retention Time: 11.980 min. (Method 1)

[^{18}F] Rad. Allylic Fluoride



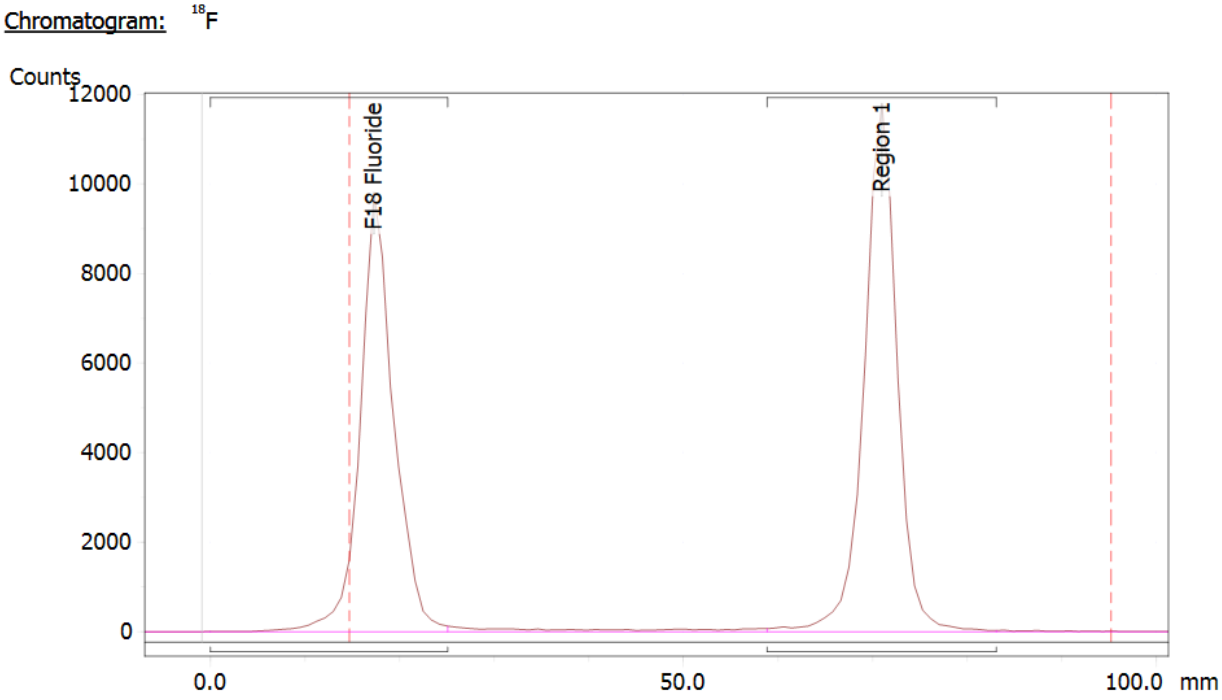
Allylic Fluoride [^{18}F] Rad. Retention Time: 12.127 min. (Method 1)



Crude Allylic Fluoride [^{18}F] UV Retention Time: 12.051 min. (Method 1)

[^{18}F] Rad. TLC

TLC Conditions: 8:2 Hex/EA



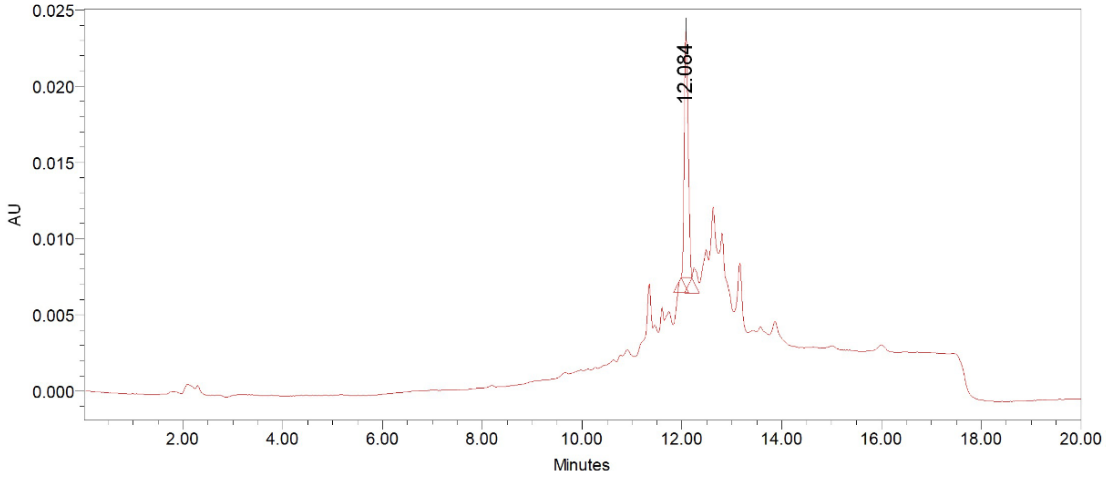
Radio TLC Trials:

Trial	RCC
1	44%
2	53%
3	51%

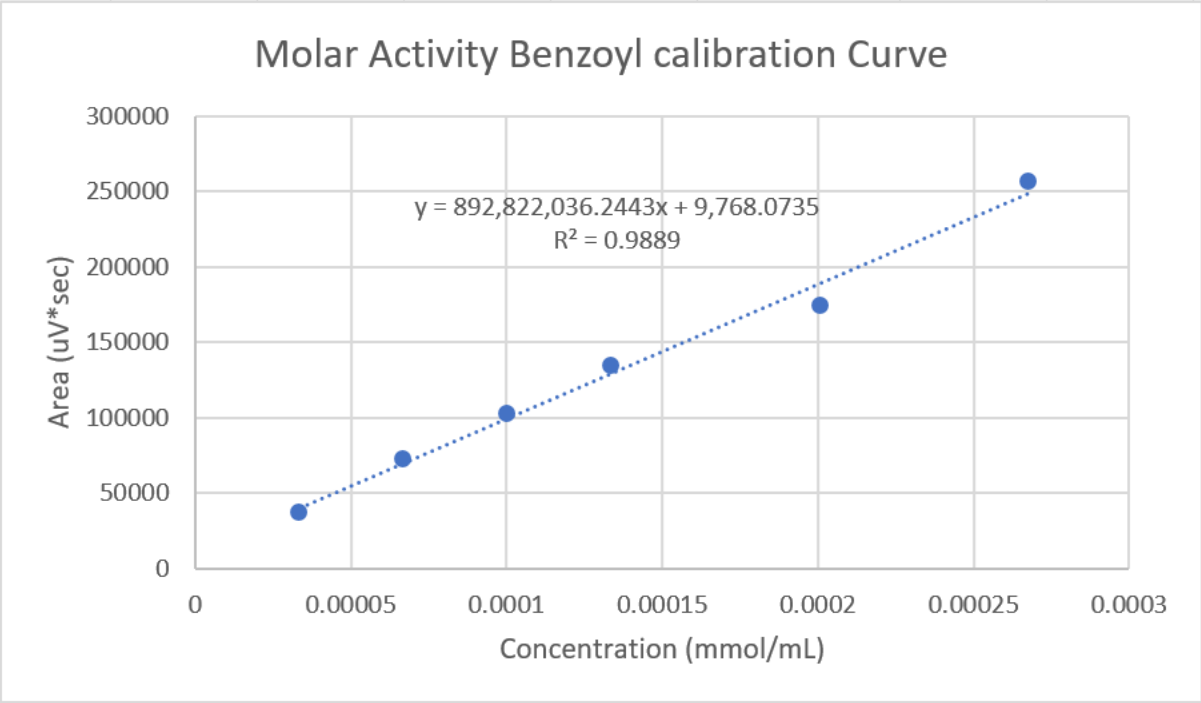
Average: 49% +/- 5% (n = 3)

Molar Activity Benzoyl Substrate

A standard calibration curve was generated from the injection of known standard solutions (each run in duplicate). An aliquot of the sample (5.5 mCi, 3.2 mCi, 3.4 mCi) was injected onto an analytical HPLC using Method 1. The UV peak corresponding to the radiofluorinated product was determined by comparing the UV and RAD traces. The UV area was then used to calculate the concentration of the product based on linear regression analysis of appropriate allylic fluoride standards. This provided the concentration of the ^{19}F standard product in mmol/mL. Dividing the activity concentration (Ci/mL) factoring in the RCC by the HPLC-derived concentration of product (mmol/mL) provided the molar activity in Ci/mmol.



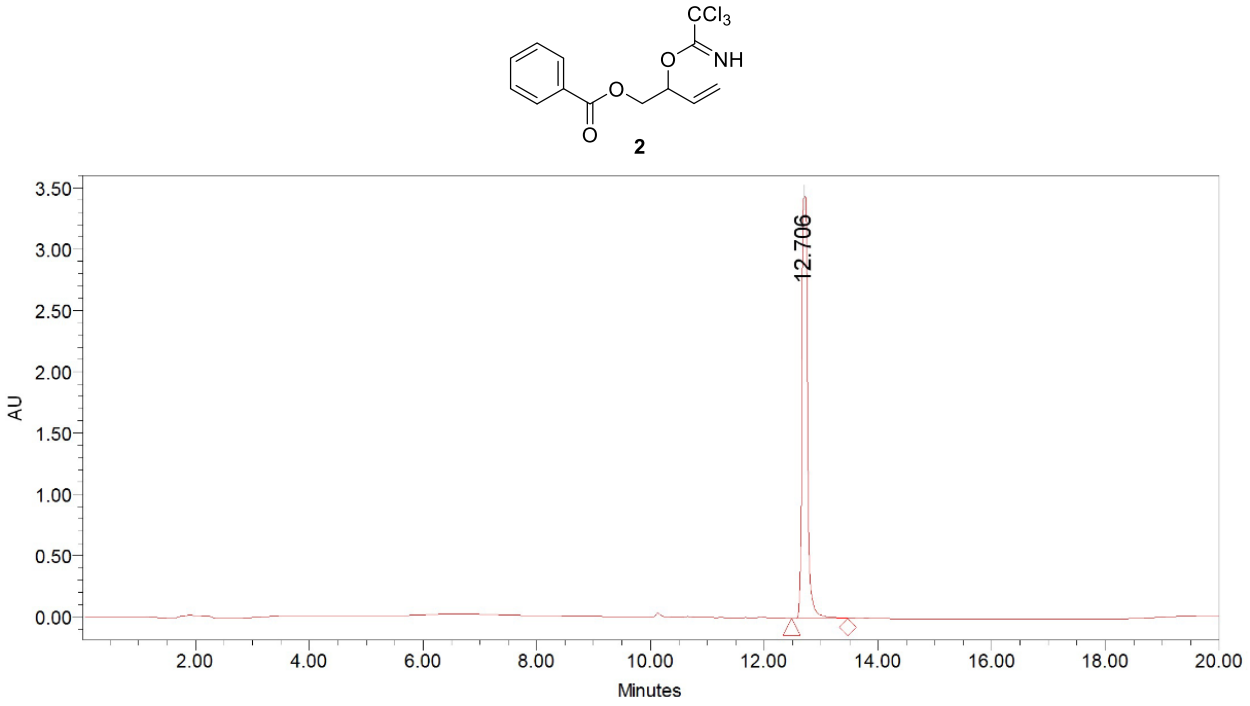
Allylic Fluoride [^{18}F] UV. Retention Time: 12.084 min. (Method 1) for Molar Activity Calculation



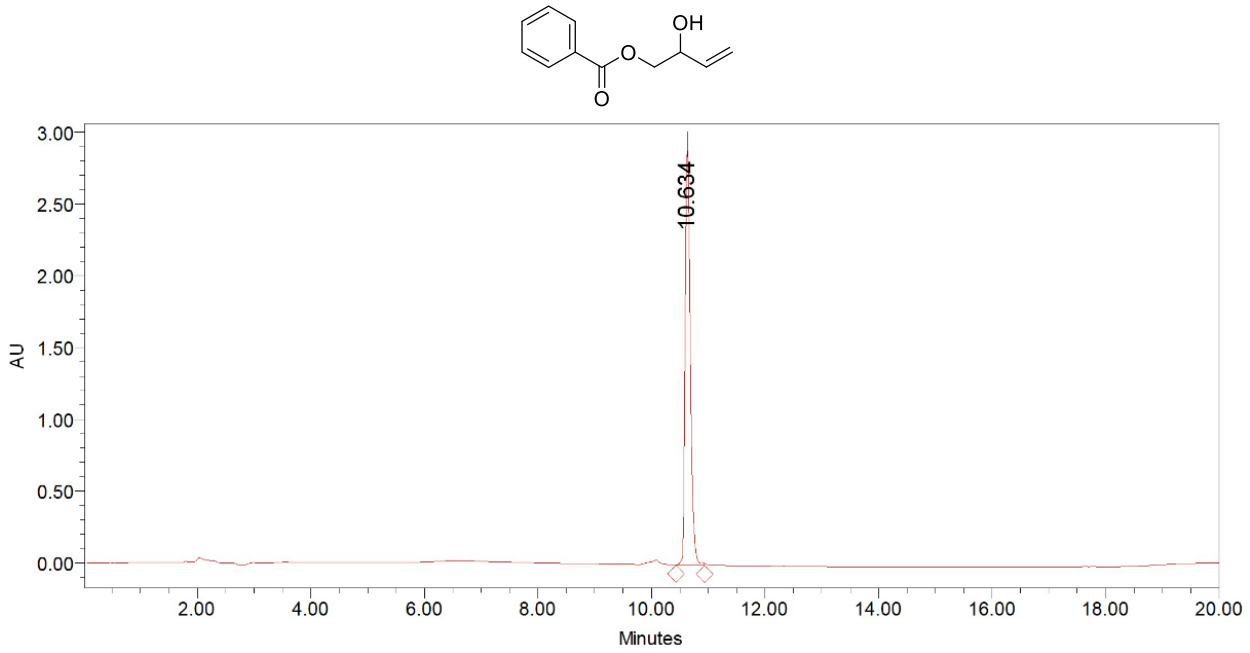
Molar Activity:

Trial	M.A.
1	24 Ci/mmol
2	15 Ci/mmol
3	25 Ci/mmol

Average: 21 +/- 5 Ci/mmol (n = 3)



Allylic Trichloroacetimidate UV Retention Time: 12.706 min. (Method 1)

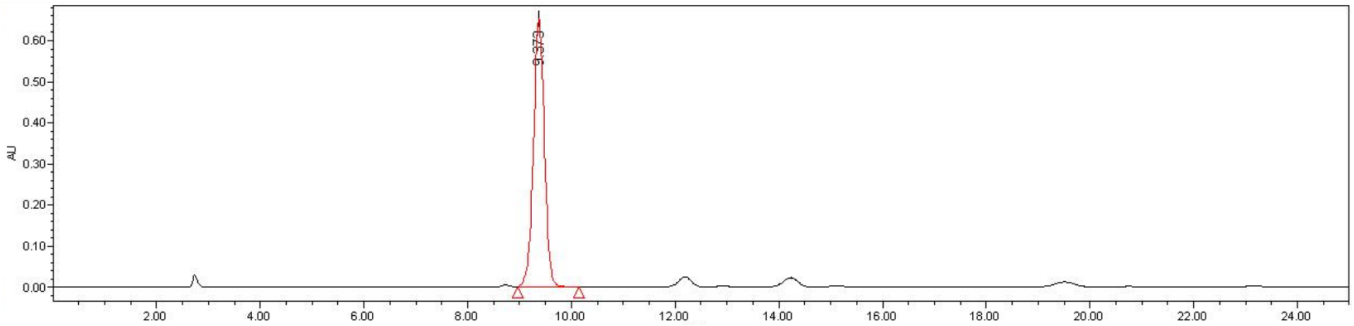


Allylic Alcohol UV Retention Time: 10.634 min. (Method 1)

Radiochemical Yield Determination using Prep. HPLC:

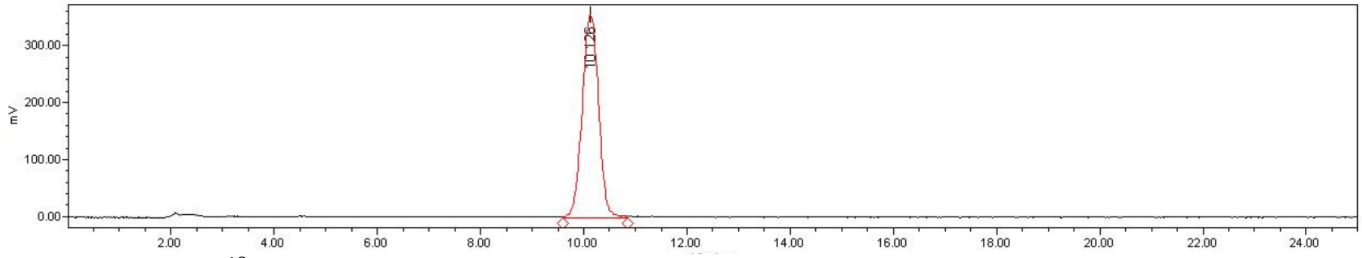
An isocratic Prep-HPLC method was used for the isolation of the desired [18F] allylic fluoride in order to have a double verification of the product being analyzed by two different HPLC eluent systems and methods.

[^{19}F] Standard Allylic Fluoride Prep HPLC

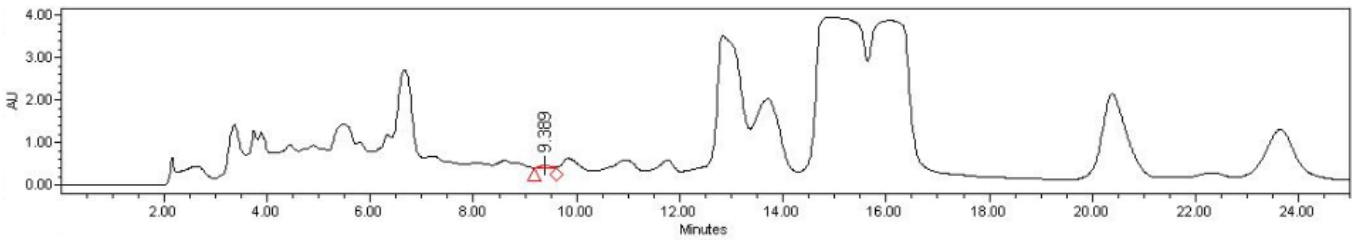


Allylic Fluoride [^{18}F] Standard Retention Time: 9.373 min. (Method 3)

[^{18}F] Standard Allylic Fluoride Prep HPLC



Allylic Fluoride [^{18}F] Rad. Retention Time: 10.126 min. (Method 3)



Allylic Fluoride [^{18}F] UV Retention Time: 9.389 min. (Method 3)

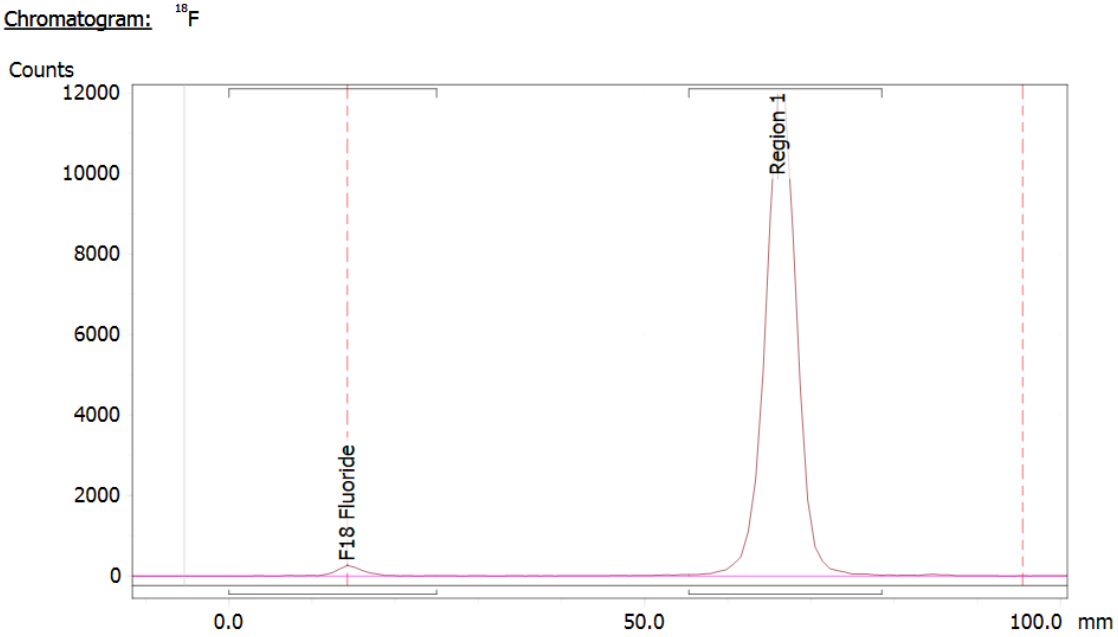
Radiochemical Yield Trials:

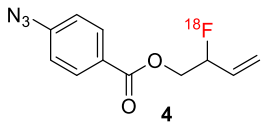
Trial	RCY
1	32%
2	33%
3	29%

Average: 31% +/- 2% (n = 3)

[^{18}F] Rad. TLC RCY (Isolated Product)

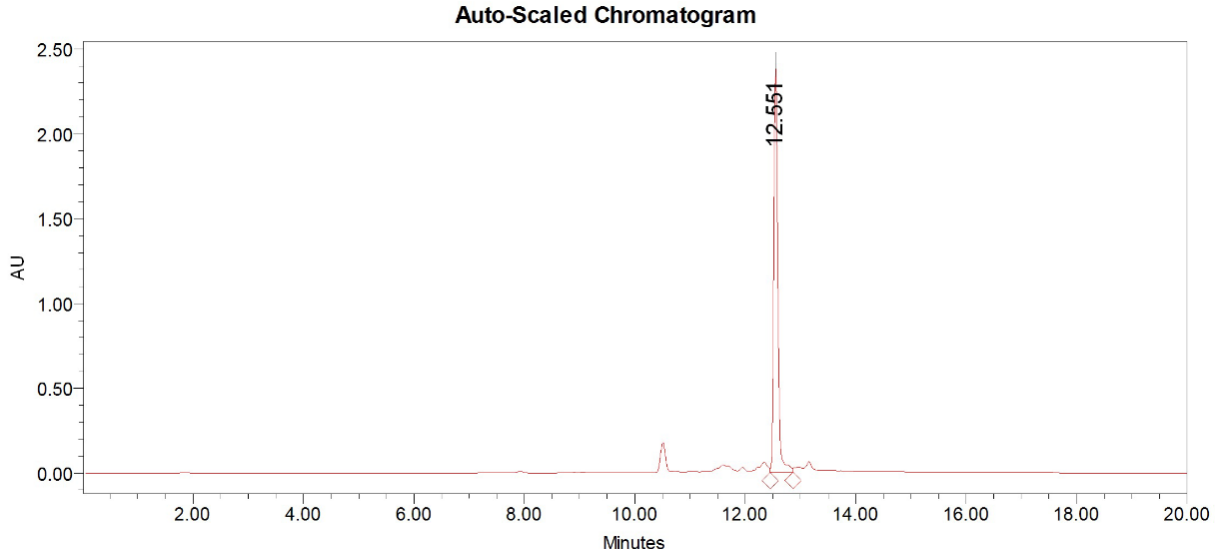
TLC Conditions: 8:2 Hex/EA





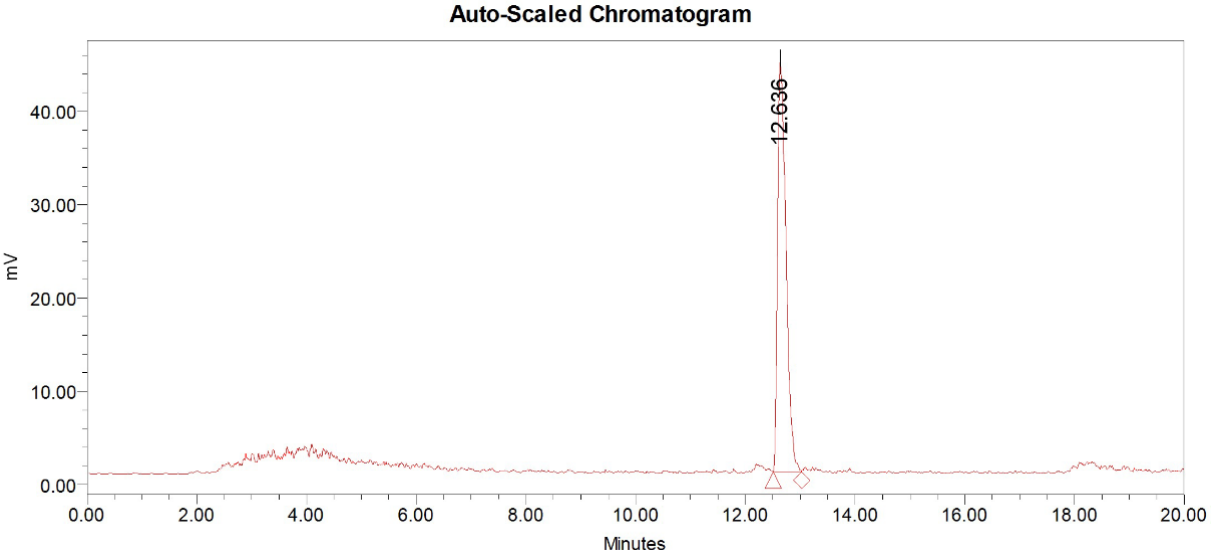
4

[^{19}F] Standard Allylic Fluoride

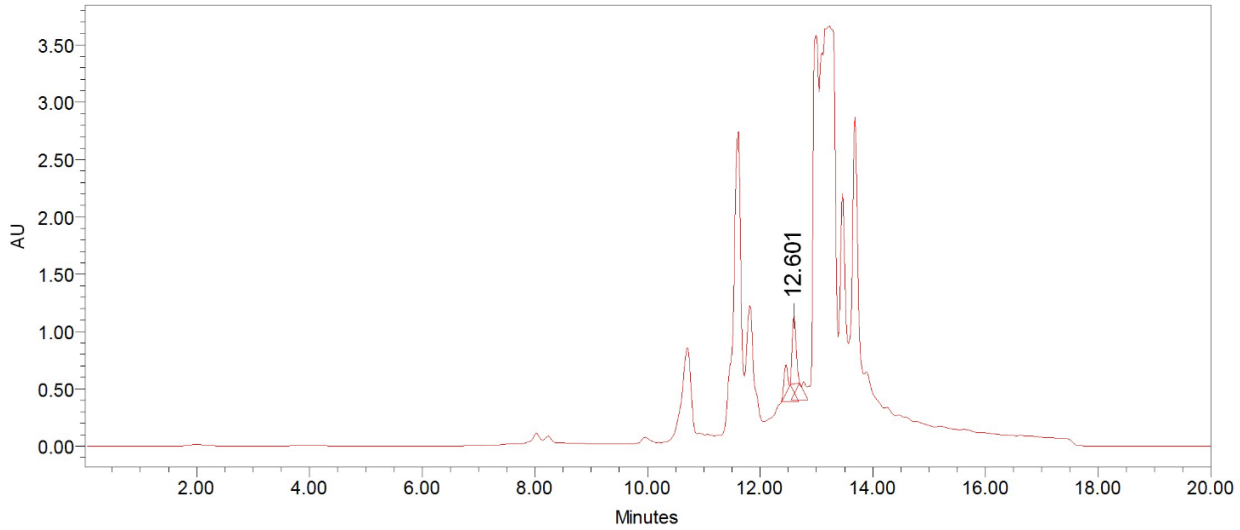


Allylic Fluoride [^{19}F] Standard Retention Time: 12.551 min. (Method 1)

[^{18}F] Rad. Allylic Fluoride



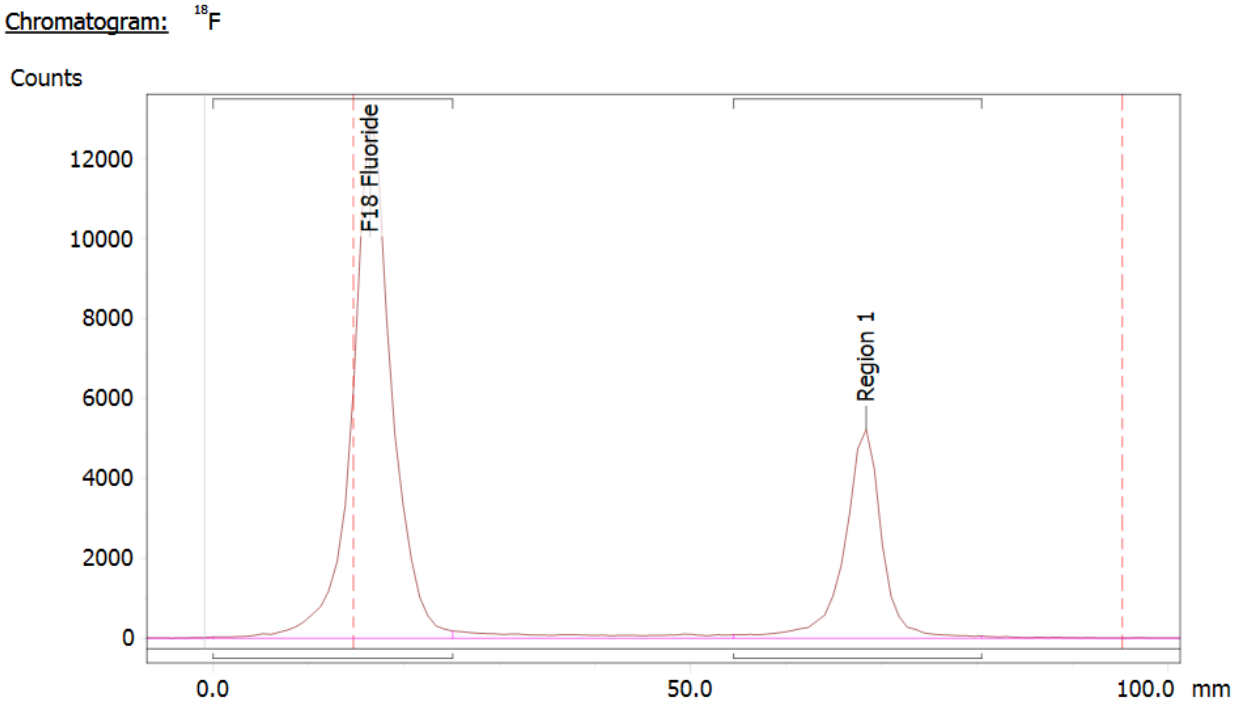
Allylic Fluoride [^{18}F] Rad. Retention Time: 12.636 min. (Method 1)



Crude Allylic Fluoride [^{18}F] UV Retention Time: 12.601 min. (Method 1)

[^{18}F] Rad. TLC

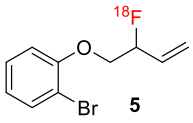
TLC Conditions: 8:2 Hex/EA



Radio TLC Trials:

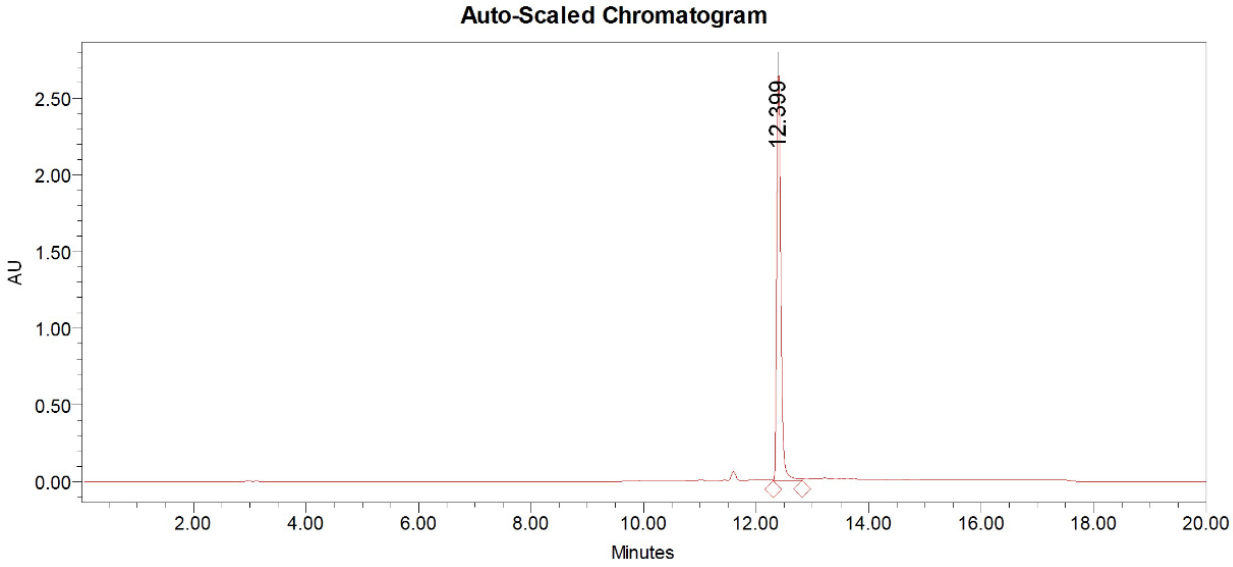
Trial	RCC
1	17%
2	20%
3	25%
4	27%
5	23%

Average: 23% +/- 4% (n = 5)



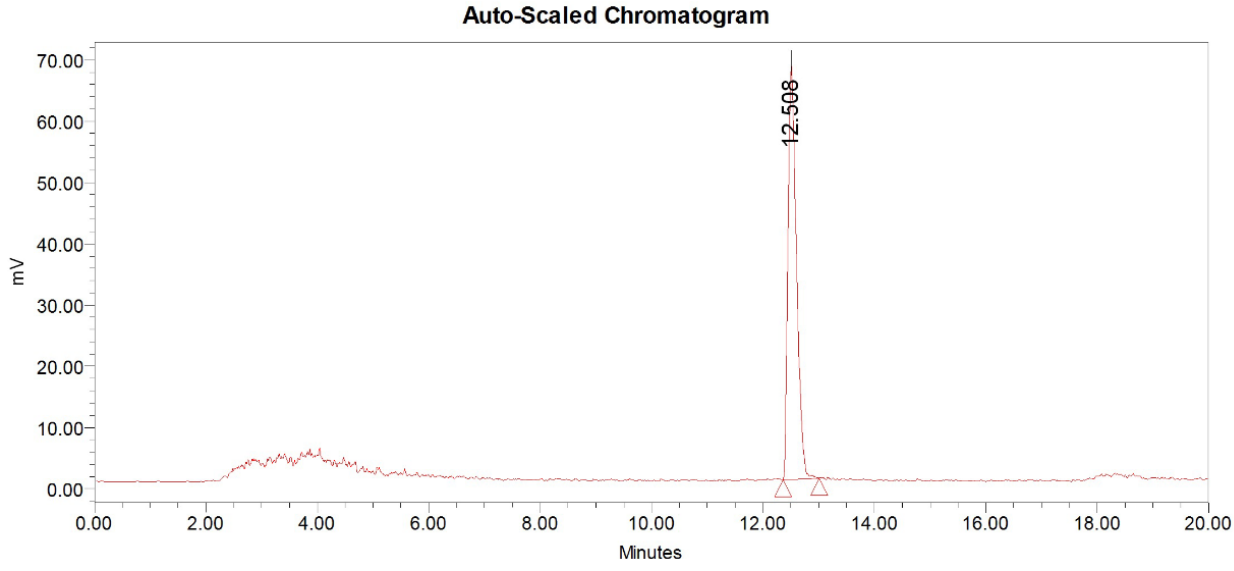
5

[19F] Standard Allylic Fluoride

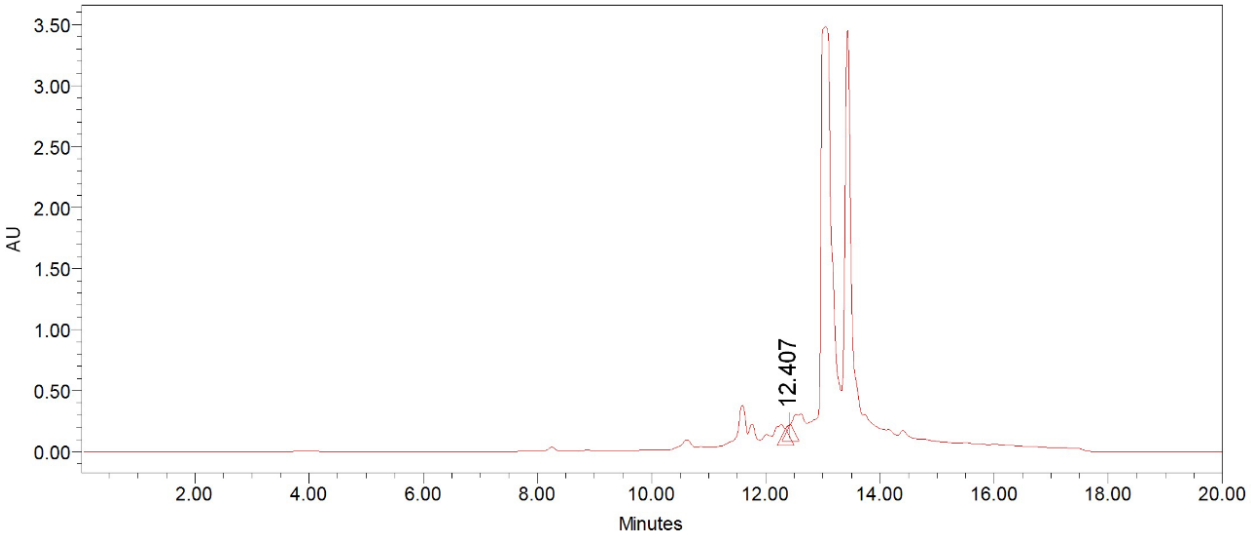


Allylic Fluoride [19F] Standard Retention Time: 12.399 min. (Method 1)

[18F] Rad. Allylic Fluoride



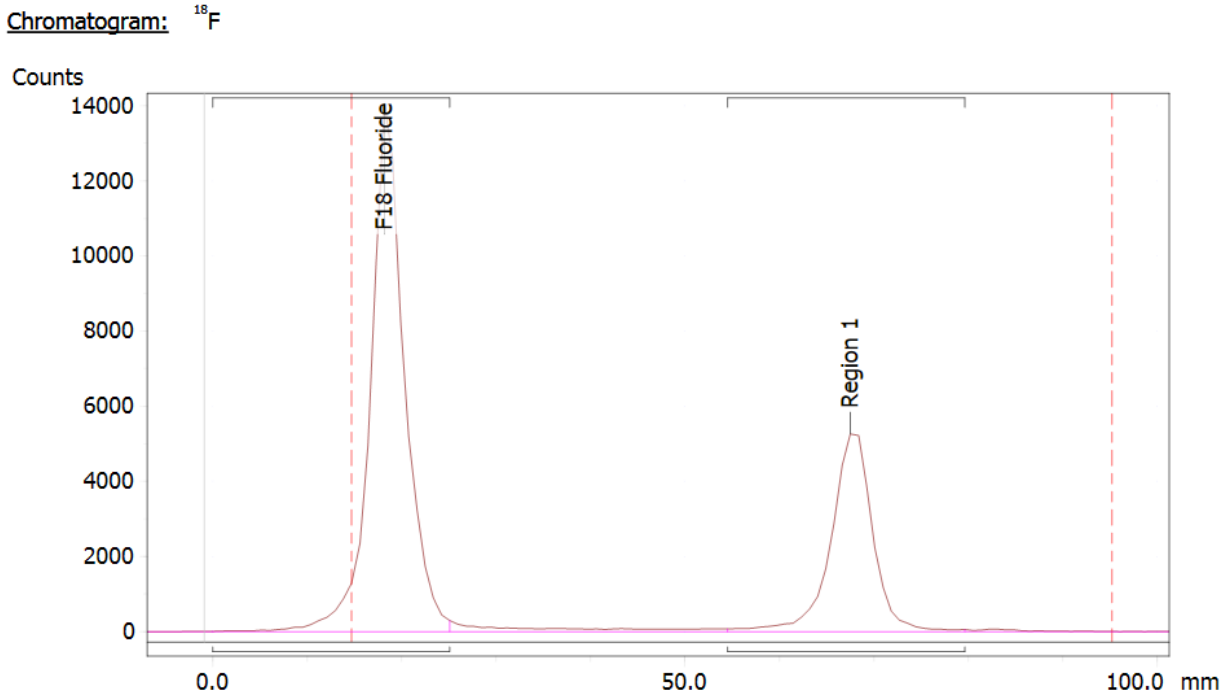
Allylic Fluoride [18F] Rad. Retention Time: 12.508 min. (Method 1)



Crude Allylic Fluoride [^{18}F] UV Retention Time: 12.407 min. (Method 1)

[^{18}F] Rad. TLC

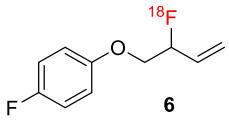
TLC Conditions: 8:2 Hex/EA



Radio TLC Trials:

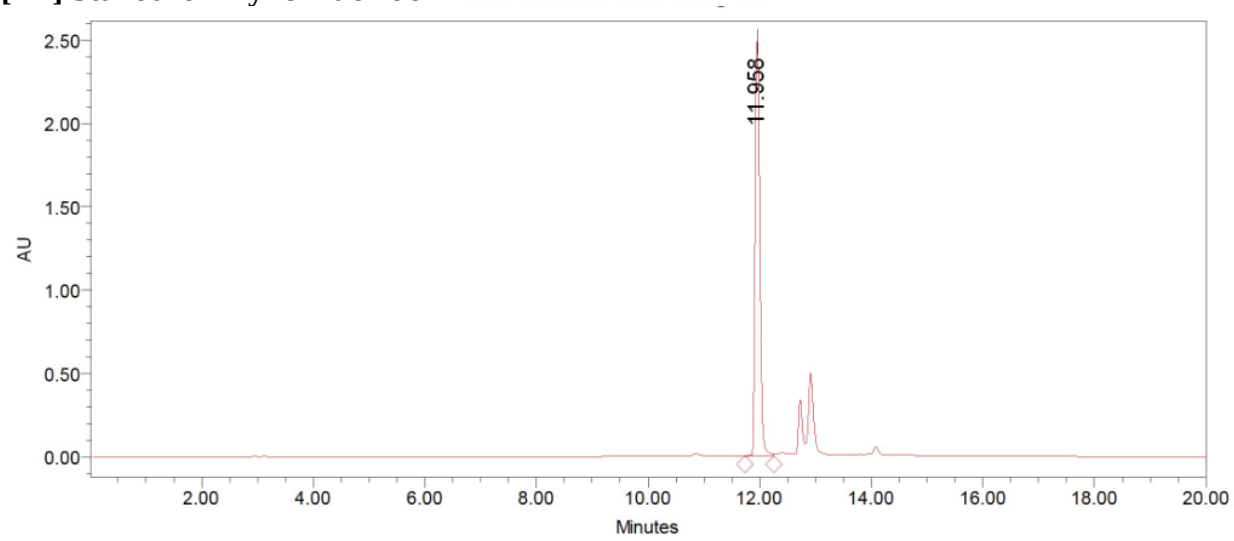
Trial	RCC
1	29%
2	34%
3	33%
4	45%
5	29%

Average: 34% +/- 6% (n = 5)



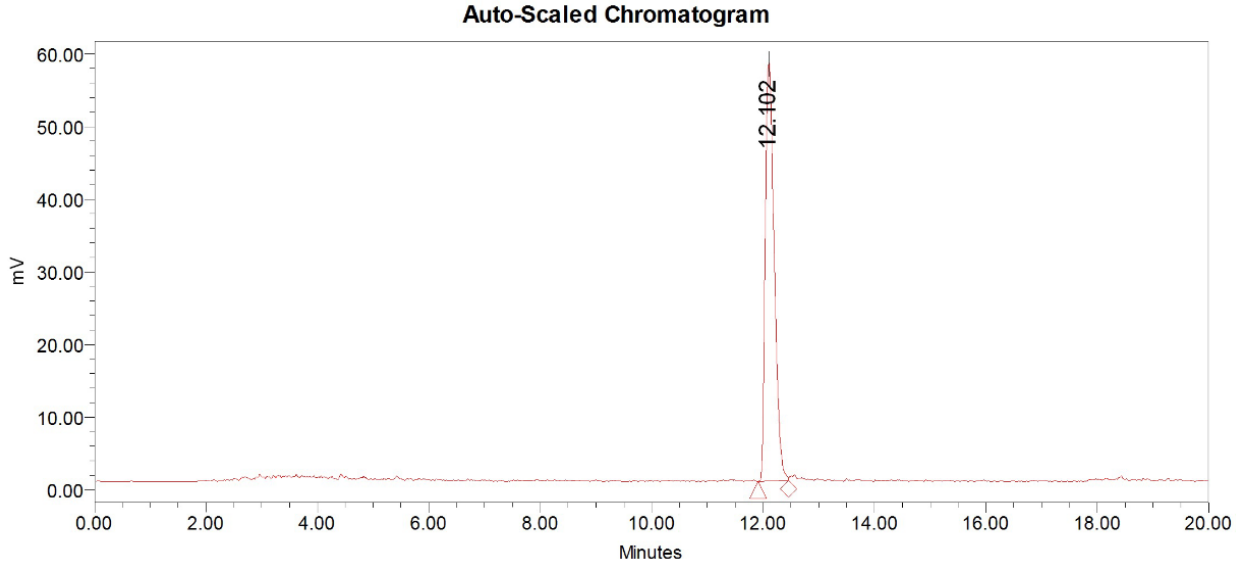
6

[^{19}F] Standard Allylic Fluoride

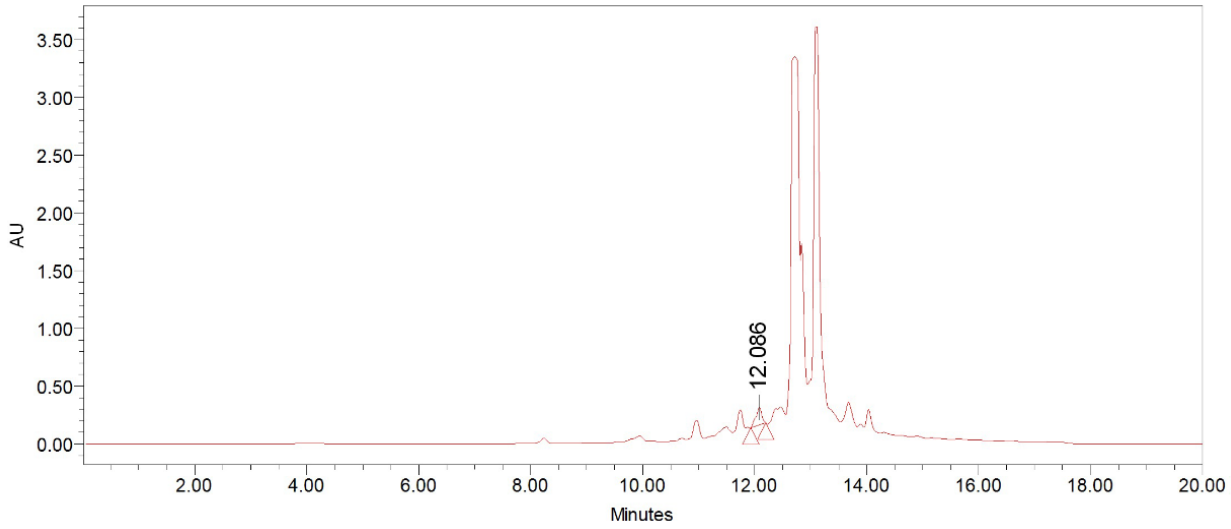


Allylic Fluoride [^{19}F] Standard Retention Time: 11.958 min. (Method 1)

[^{18}F] Rad. Allylic Fluoride



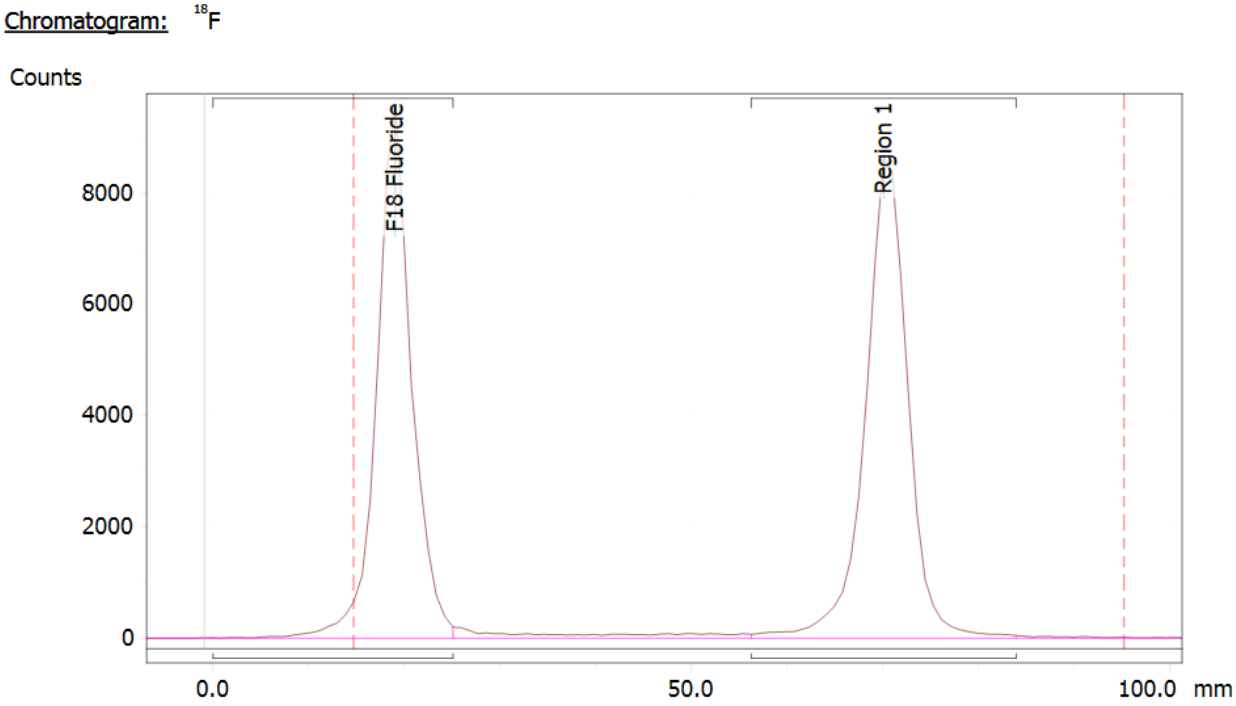
Allylic Fluoride [^{18}F] Rad. Retention Time: 12.102 min. (Method 1)



Crude Allylic Fluoride [^{18}F] UV Retention Time: 12.086 min. (Method 1)

[^{18}F] Rad. TLC

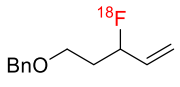
TLC Conditions: 8:2 Hex/EA



Radio TLC Trials:

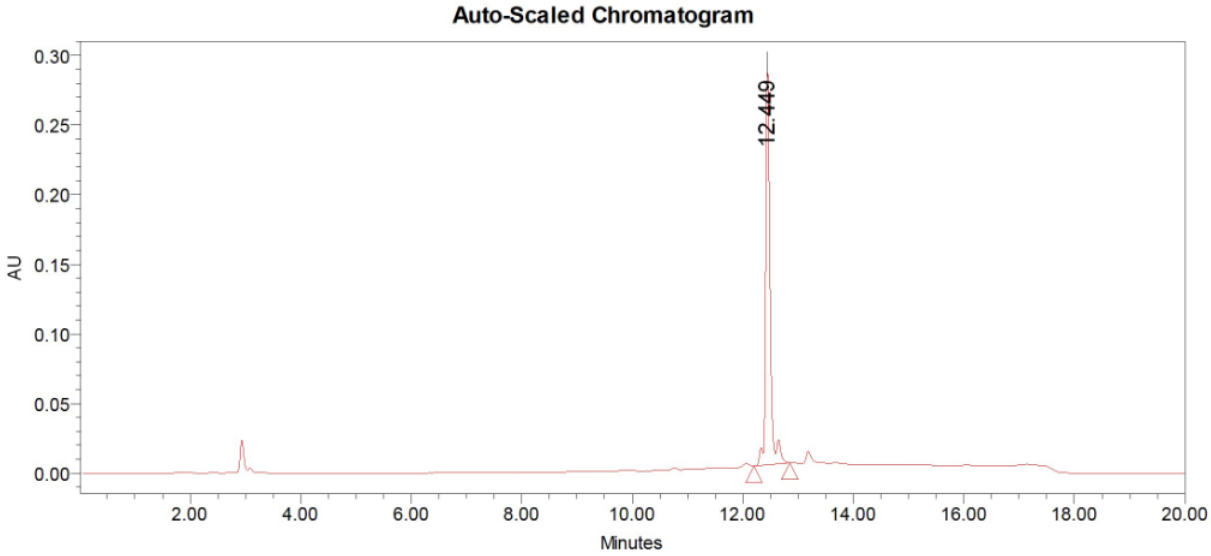
Trial	RCC
1	55%
2	54%
3	54%
4	54%
5	45%

Average: 53% +/- 4% (n = 5)



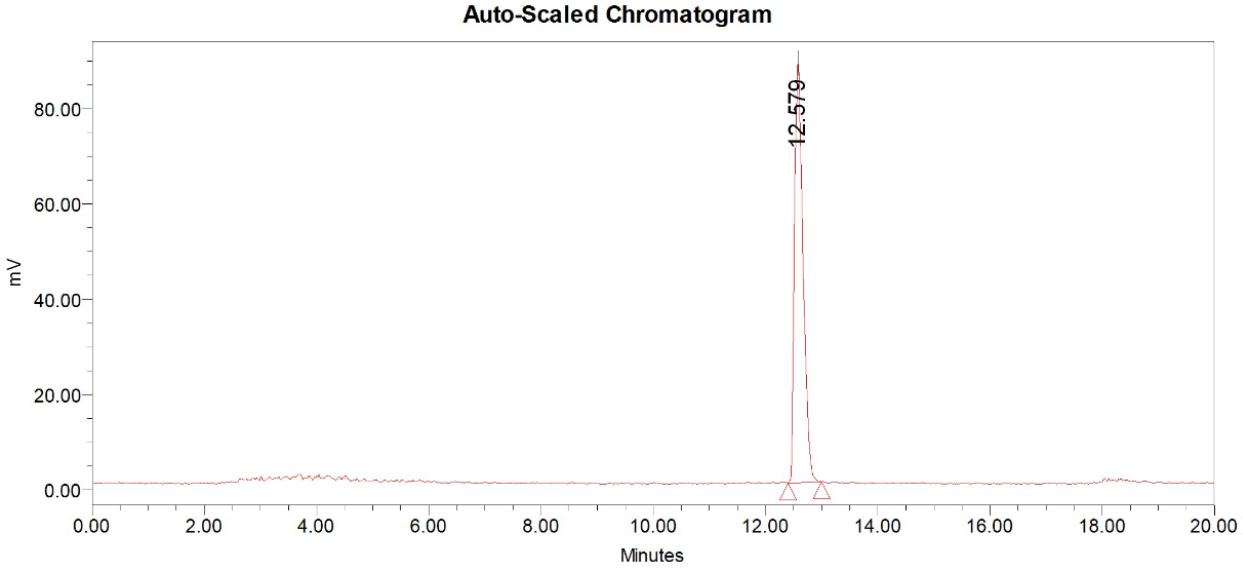
7

[^{19}F] Standard Allylic Fluoride

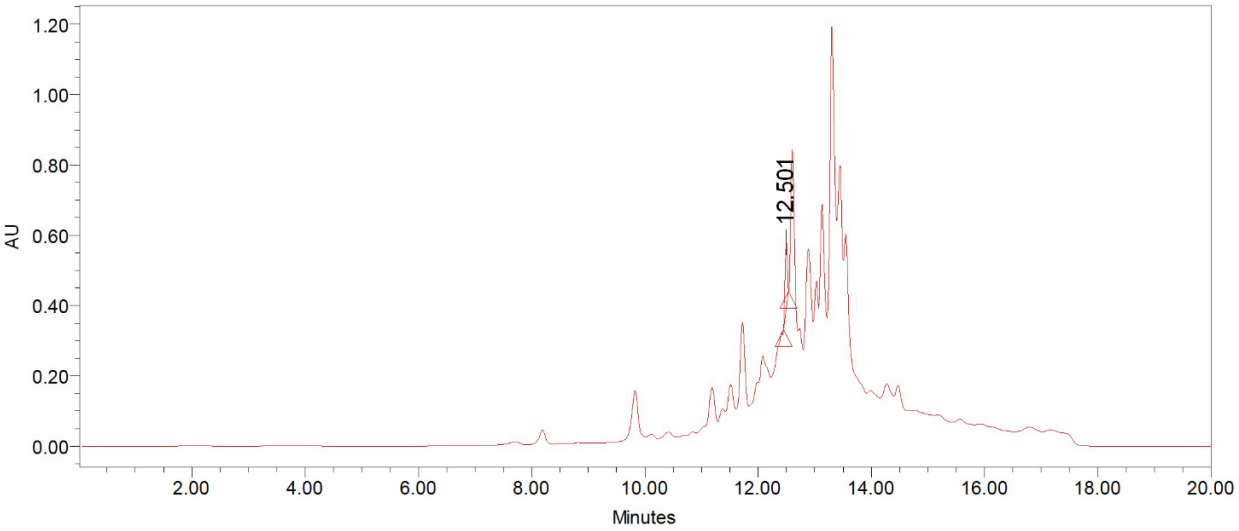


Allylic Fluoride [^{19}F] Standard Retention Time: 12.449 min. (Method 1)

[^{18}F] Rad. Allylic Fluoride



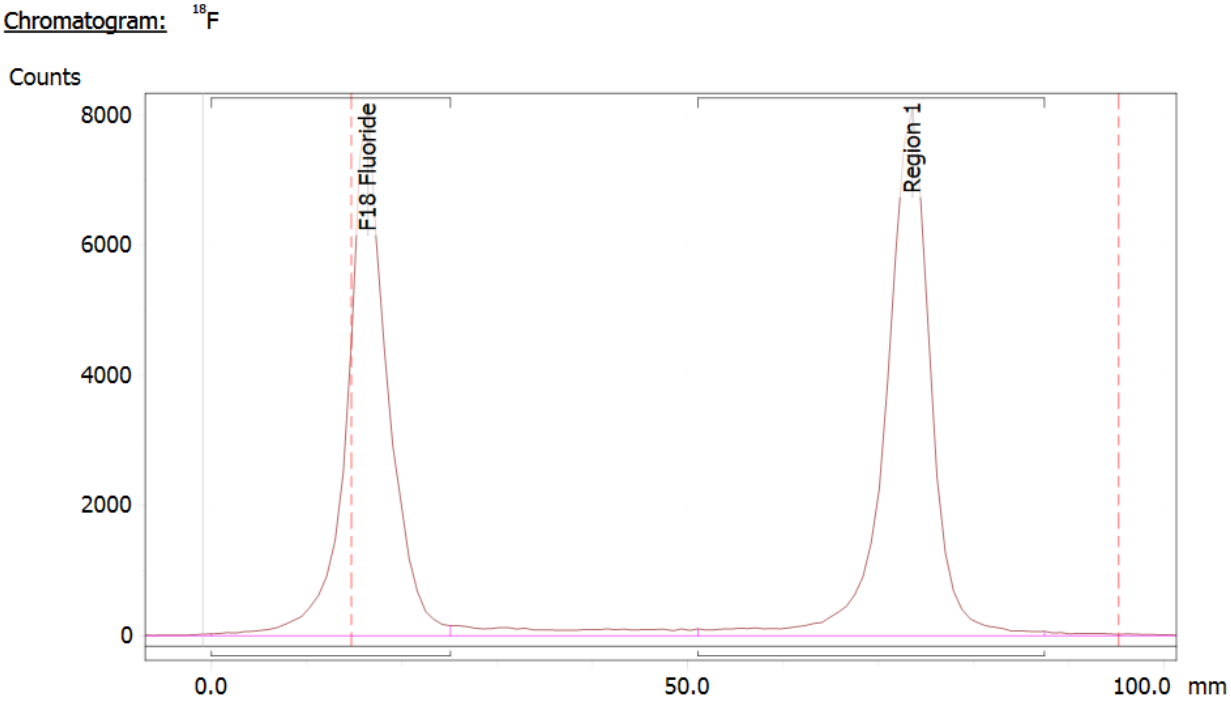
Allylic Fluoride [^{18}F] Rad. Retention Time: 12.579 min. (Method 1)



Crude Allylic Fluoride [^{18}F] UV Retention Time: 12.501 min. (Method 1)

[^{18}F] Rad. TLC

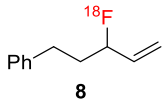
TLC Conditions: 8:2 Hex/EA



Radio TLC Trials:

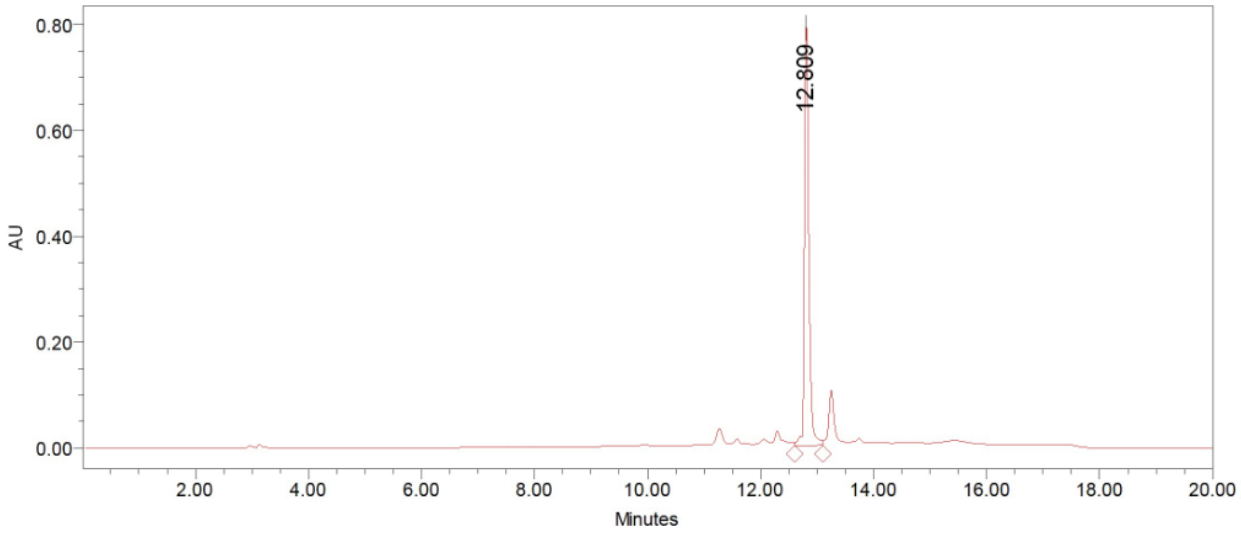
Trial	RCC
1	54%
2	39%
3	53%
4	54%
5	40%

Average: 48% +/- 8% (n = 5)



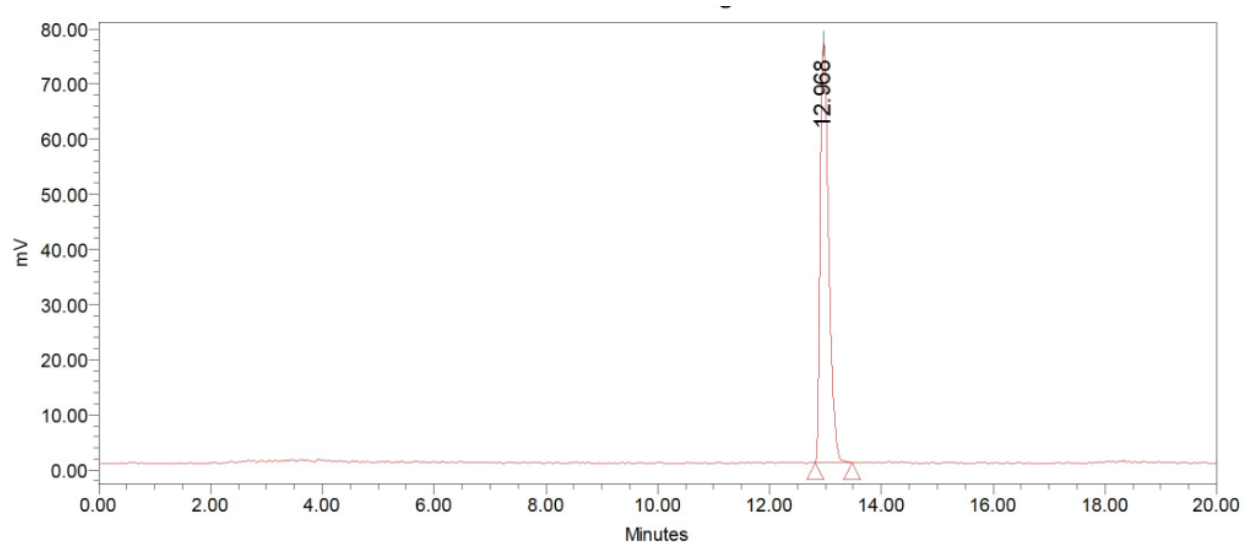
8

[19F] Standard Allylic Fluoride

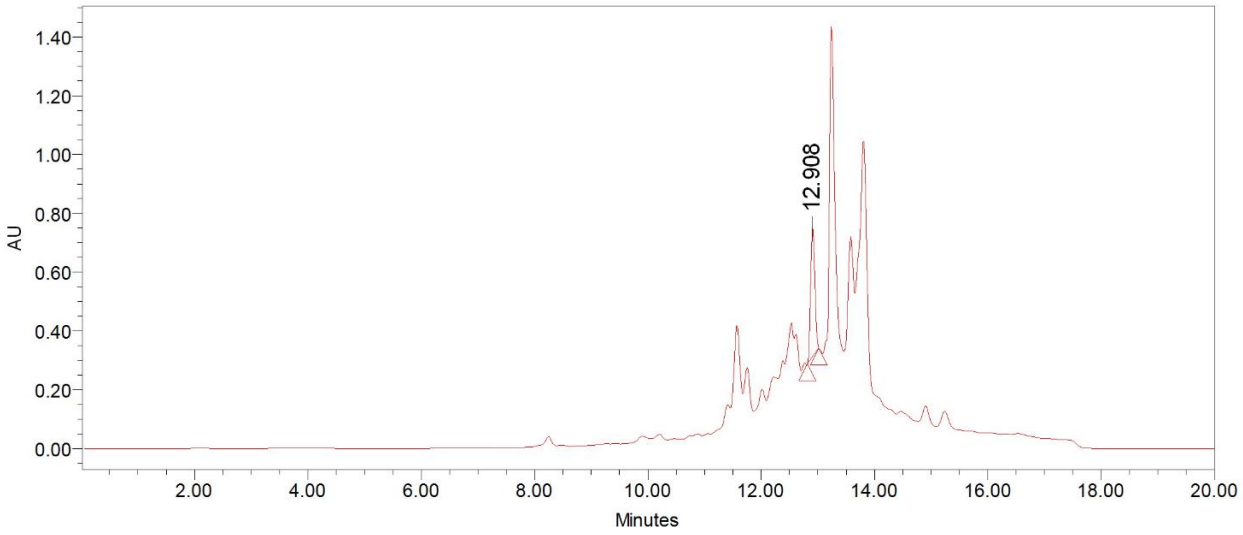


Allylic Fluoride [19F] Standard Retention Time: 12.809 min. (Method 1)

[18F] Rad. Allylic Fluoride



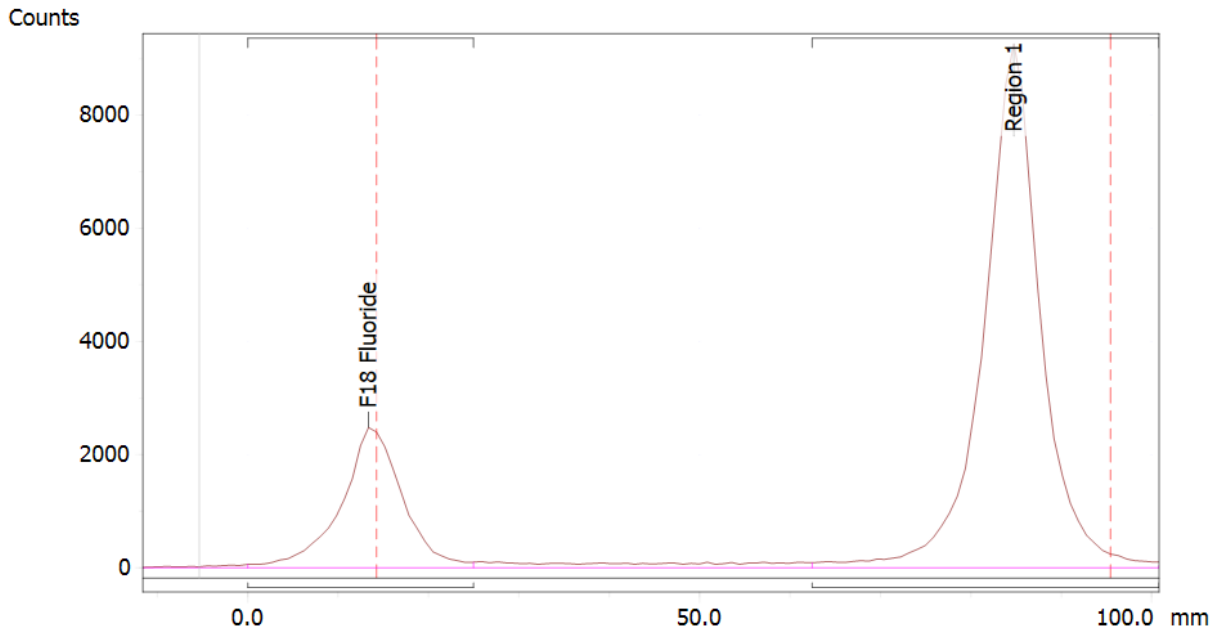
Allylic Fluoride [18F] Rad. Retention Time: 12.968 min. (Method 1)



Crude Allylic Fluoride [^{18}F] UV Retention Time: 12.908 min. (Method 1)

[^{18}F] Rad. TLC

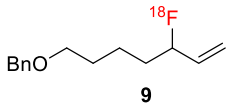
TLC Conditions: 8:2 Hex/EA



Radio TLC Trials:

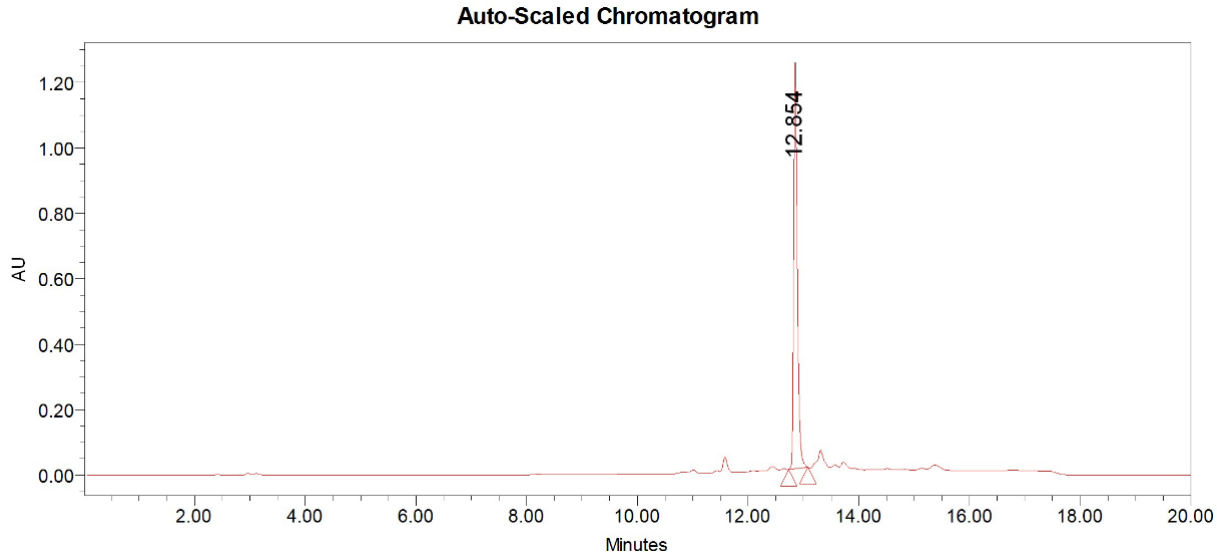
Trial	RCC
1	73%
2	71%
3	69%
4	72%
5	67%

Average: 71% +/- 2% (n = 5)



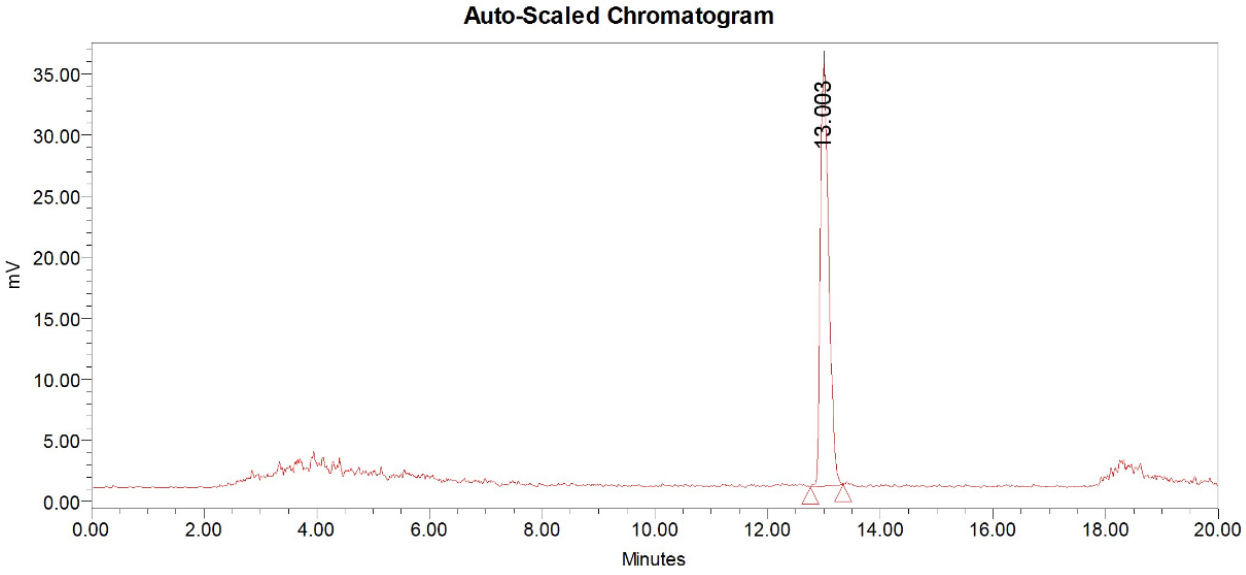
9

[^{19}F] Standard Allylic Fluoride

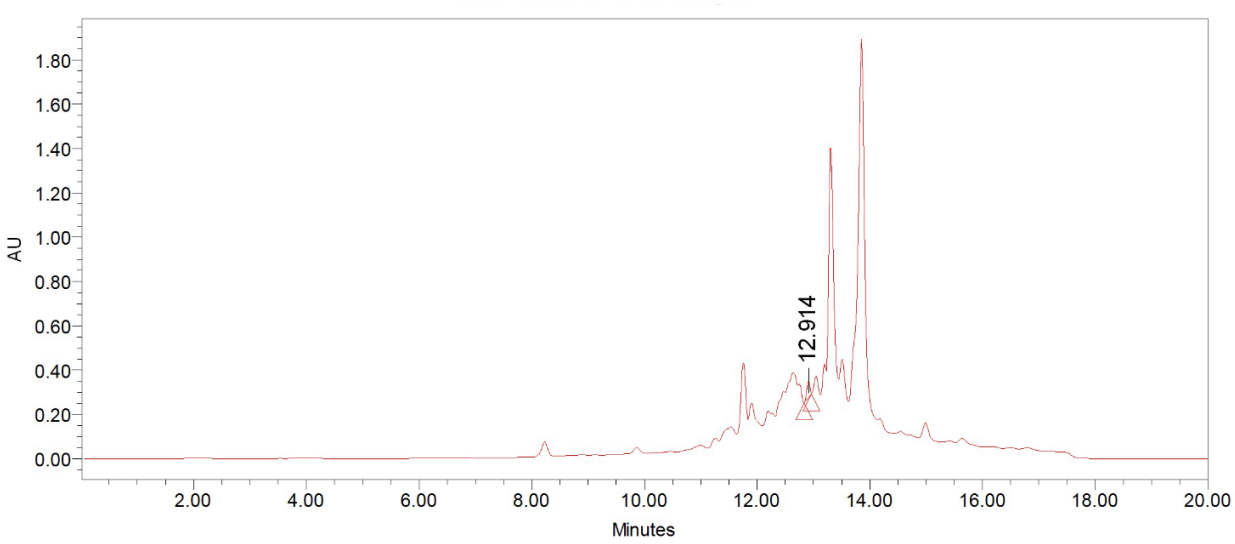


Allylic Fluoride [^{19}F] Standard Retention Time: 12.854 min. (Method 1)

[^{18}F] Rad. Allylic Fluoride



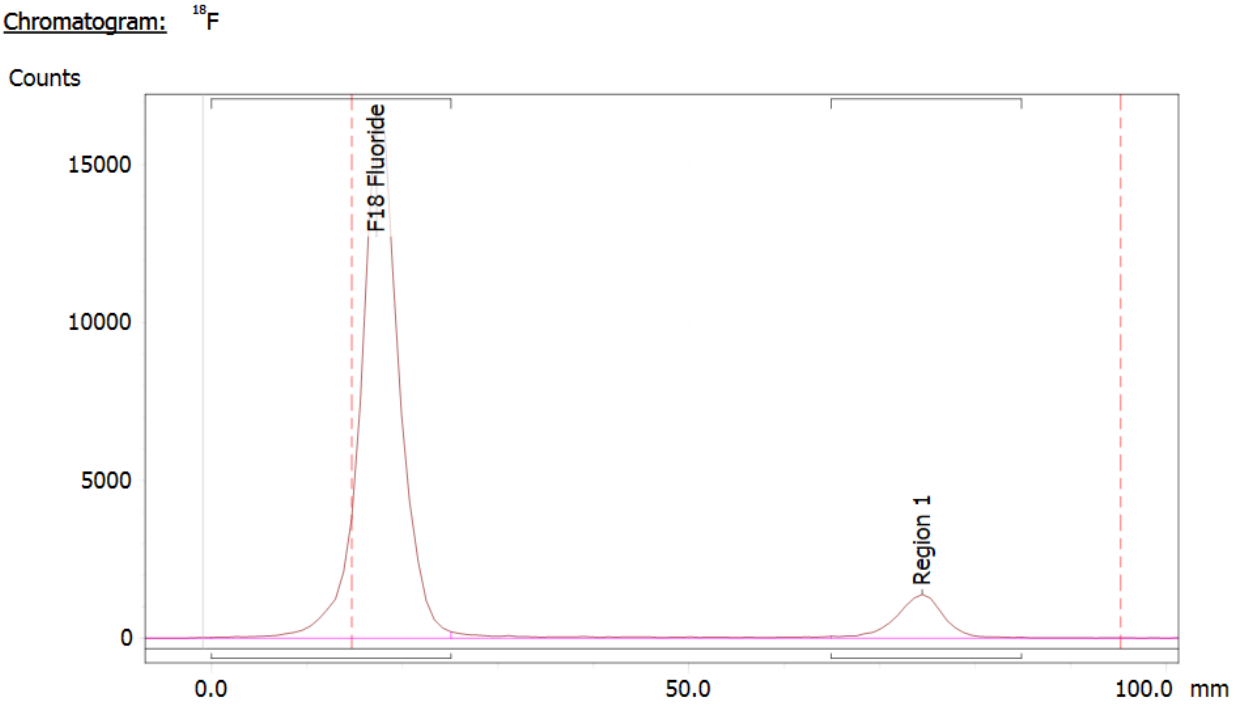
Allylic Fluoride [^{18}F] Rad. Retention Time: 13.003 min. (Method 1)



Crude Allylic Fluoride [^{18}F] UV Retention Time: 12.914 min. (Method 1)

[^{18}F] Rad. TLC

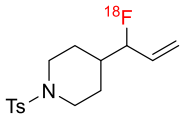
TLC Conditions: 8:2 Hex/EA



Radio TLC Trials:

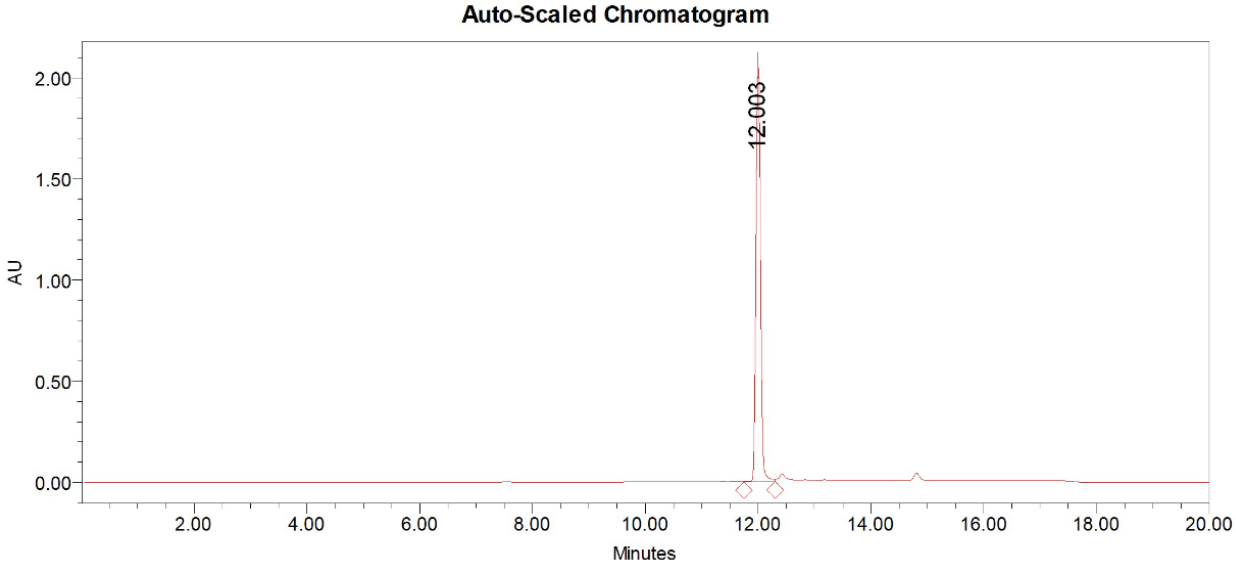
Trial	RCC
1	9%
2	9%
3	12%
4	13%
5	11%

Average: 11% +/- 2% (n = 5)



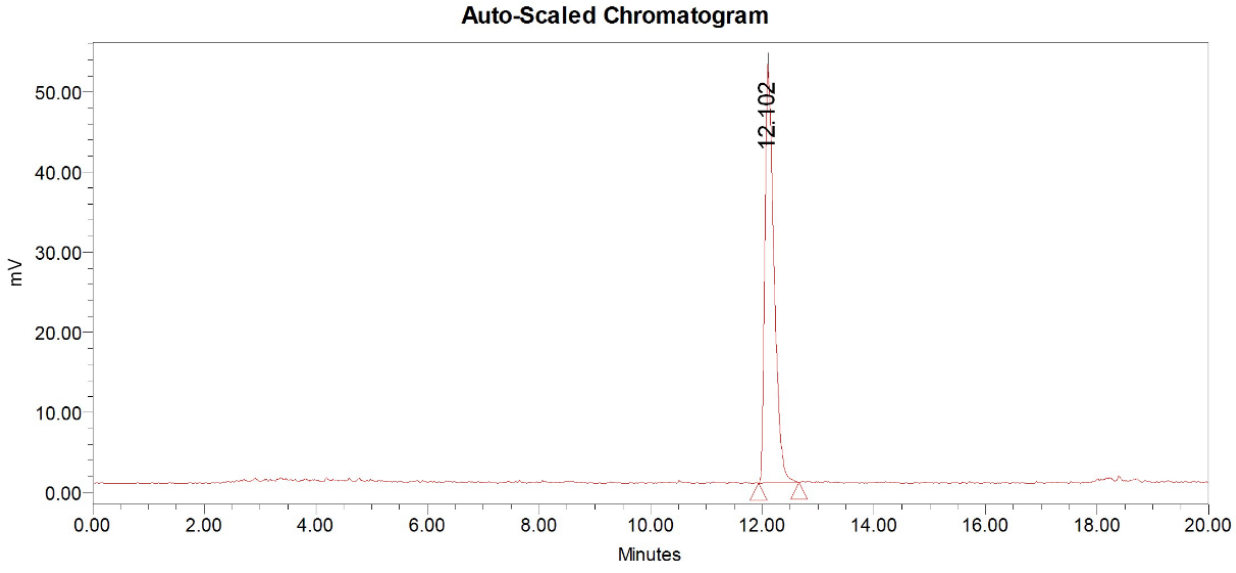
10

[^{19}F] Standard Allylic Fluoride

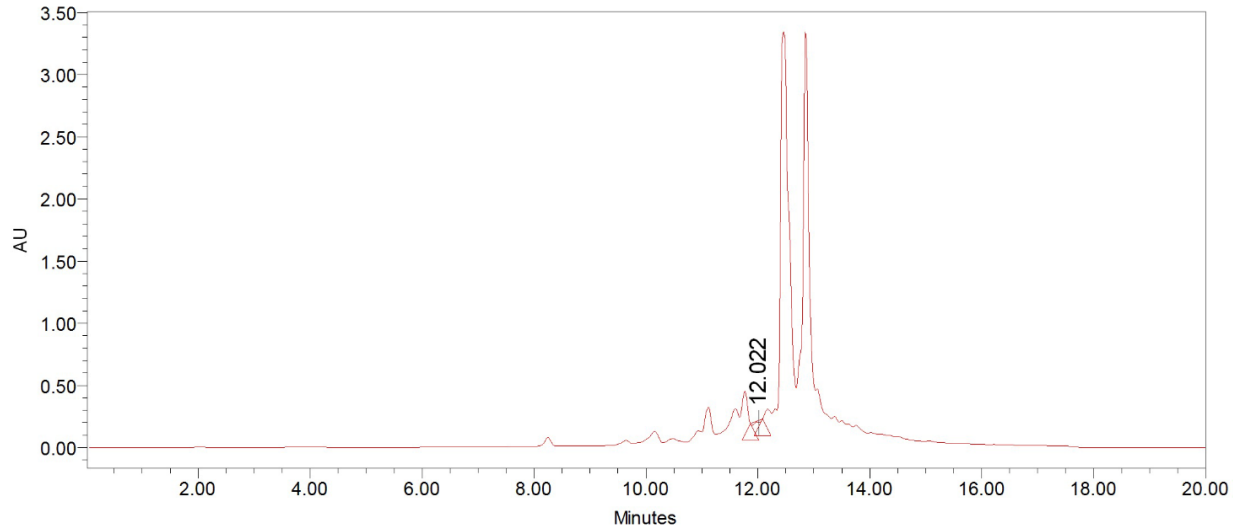


Allylic Fluoride [^{19}F] Standard Retention Time: 12.003 min. (Method 1)

[^{18}F] Rad. Allylic Fluoride



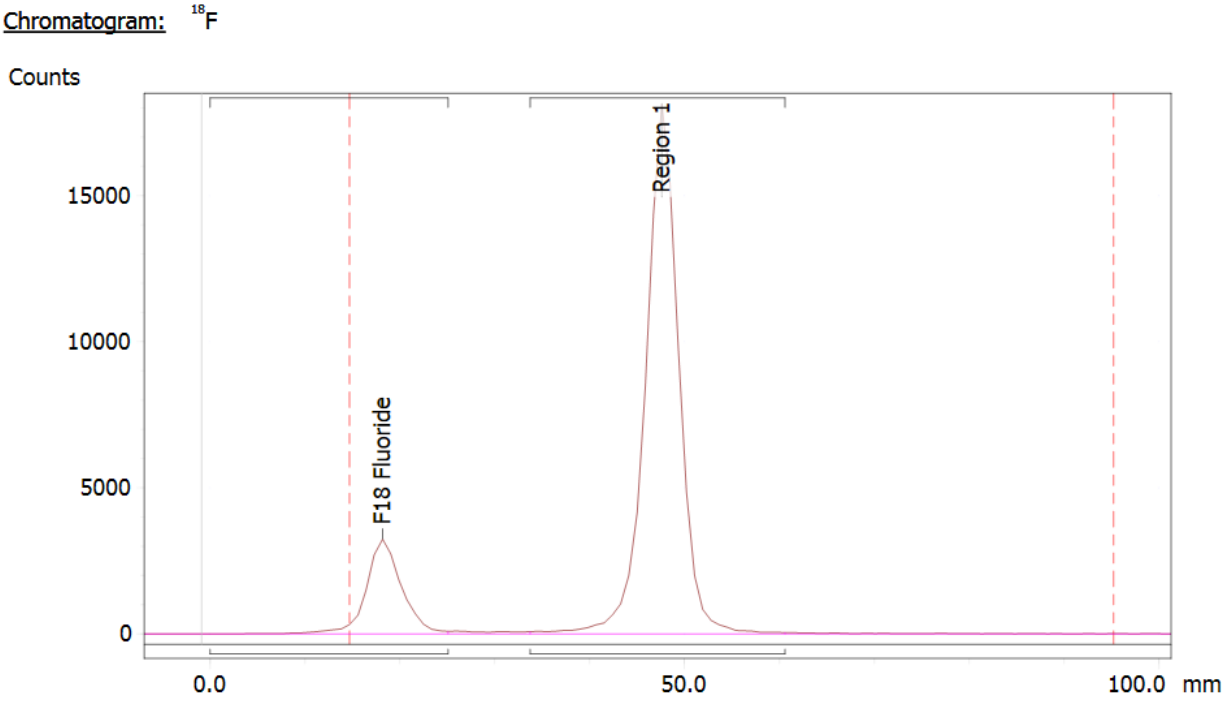
Allylic Fluoride [^{18}F] Rad. Retention Time: 12.102 min. (Method 1)



Crude Allylic Fluoride [^{18}F] UV Retention Time: 12.022 min. (Method 1)

[^{18}F] Rad. TLC

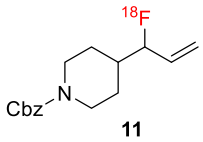
TLC Conditions: 8:2 Hex/EA



Radio TLC Trials:

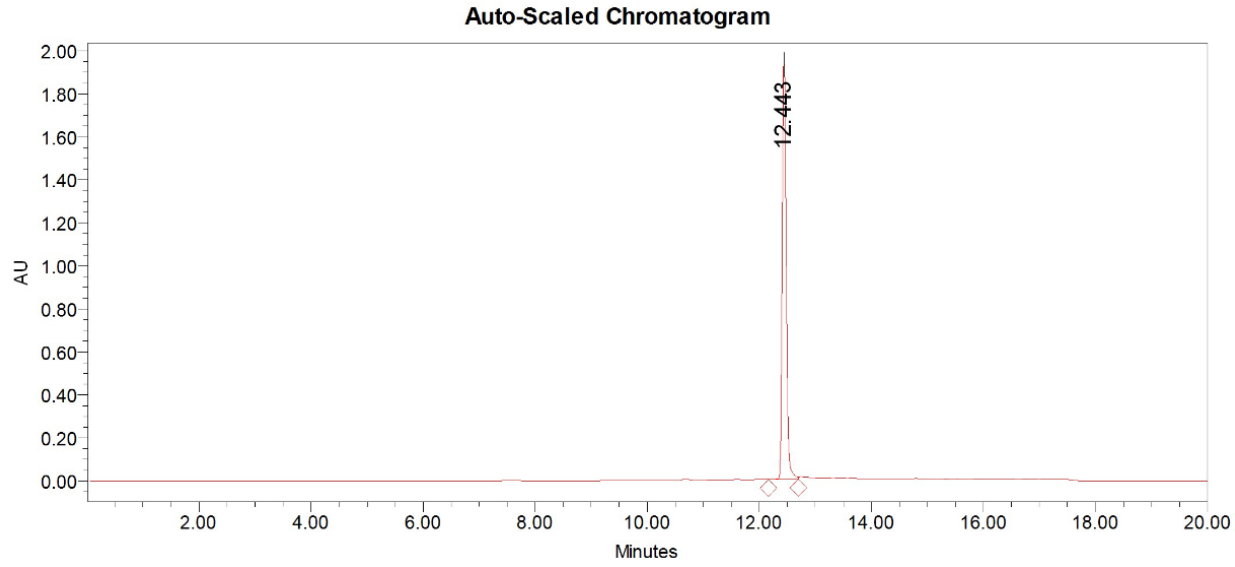
Trial	RCC
1	77%
2	83%
3	61%
4	59%
5	82%

Average: 73% +/- 12% (n = 5)



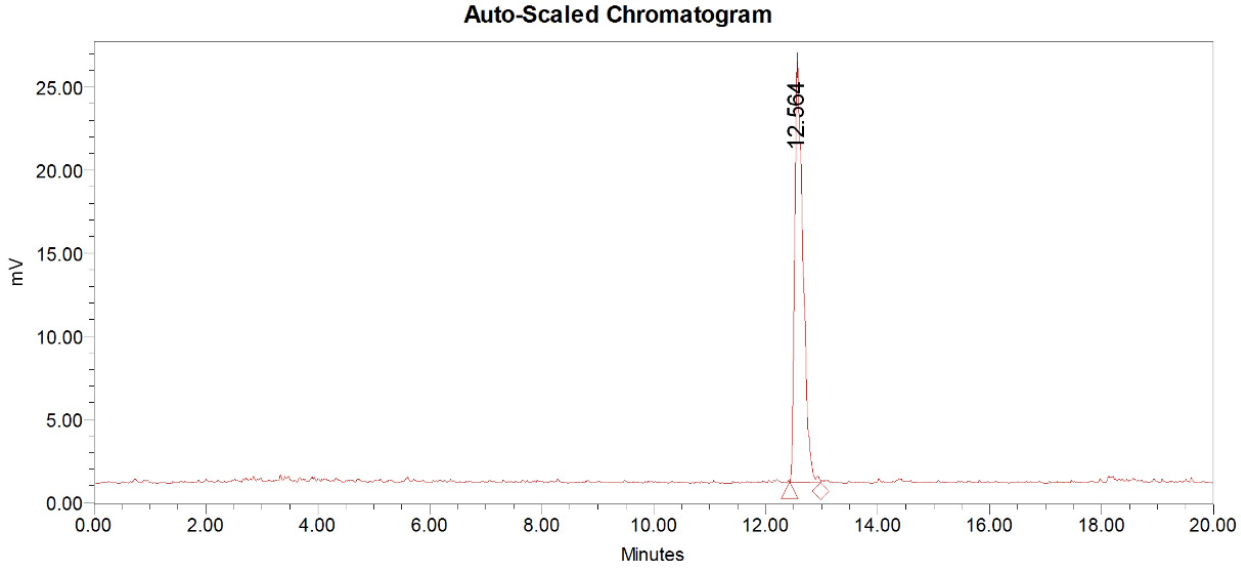
11

[^{19}F] Standard Allylic Fluoride

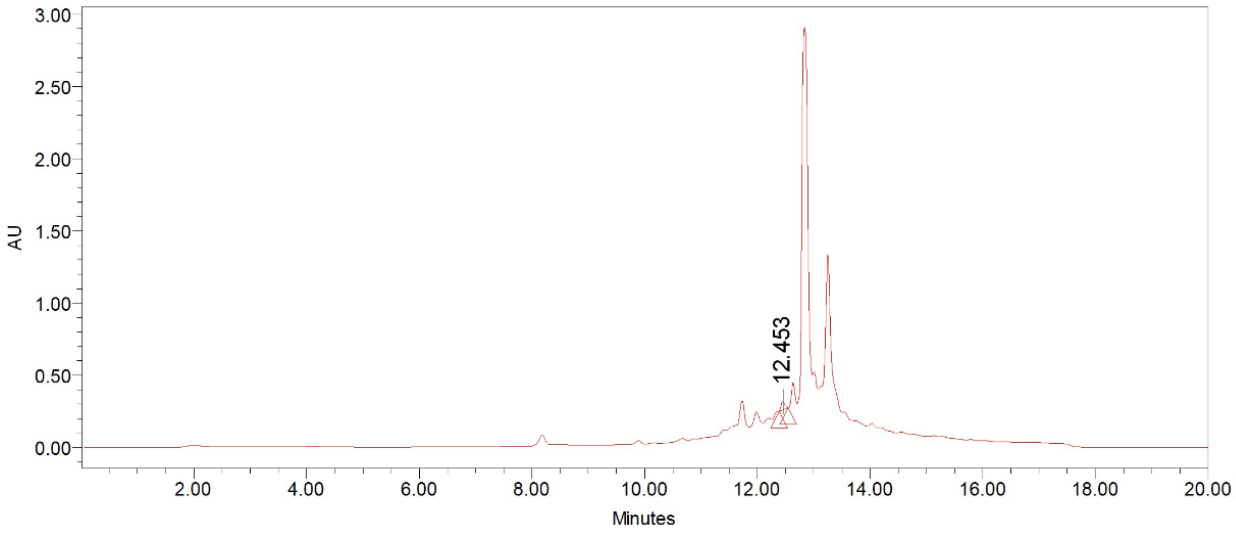


Allylic Fluoride [^{19}F] Standard Retention Time: 12.443 min. (Method 1)

[^{18}F] Rad. Allylic Fluoride



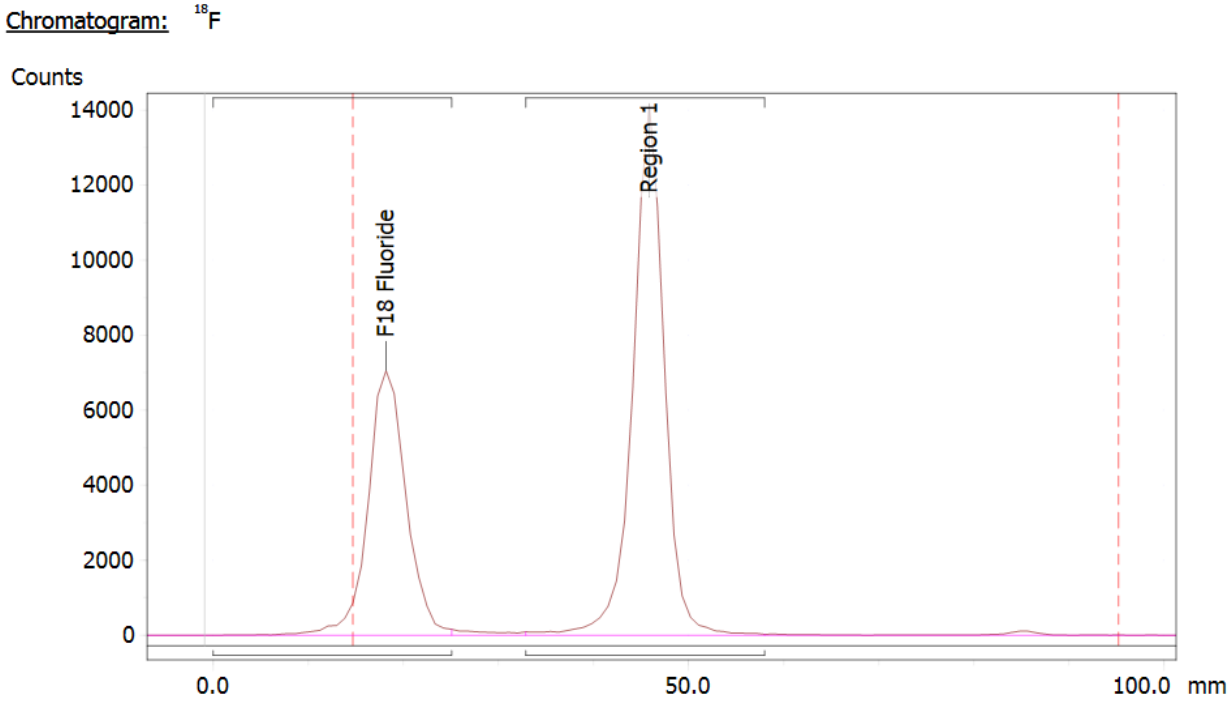
Allylic Fluoride [^{18}F] Rad. Retention Time: 12.564 min. (Method 1)



Crude Allylic Fluoride [^{18}F] UV Retention Time: 12.453 min. (Method 1)

[^{18}F] Rad. TLC

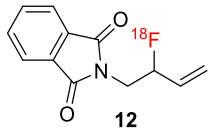
TLC Conditions: 8:2 Hex/EA



Radio TLC Trials:

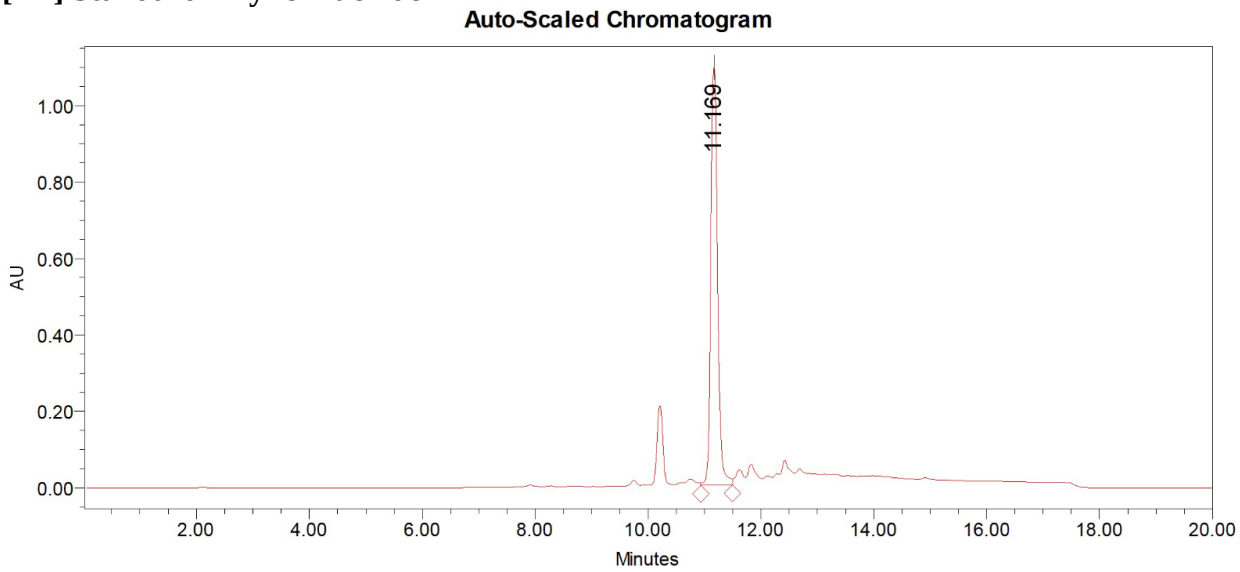
Trial	RCC
1	51%
2	61%
3	57%
4	55%
5	72%

Average: 59% +/- 8% (n = 5)



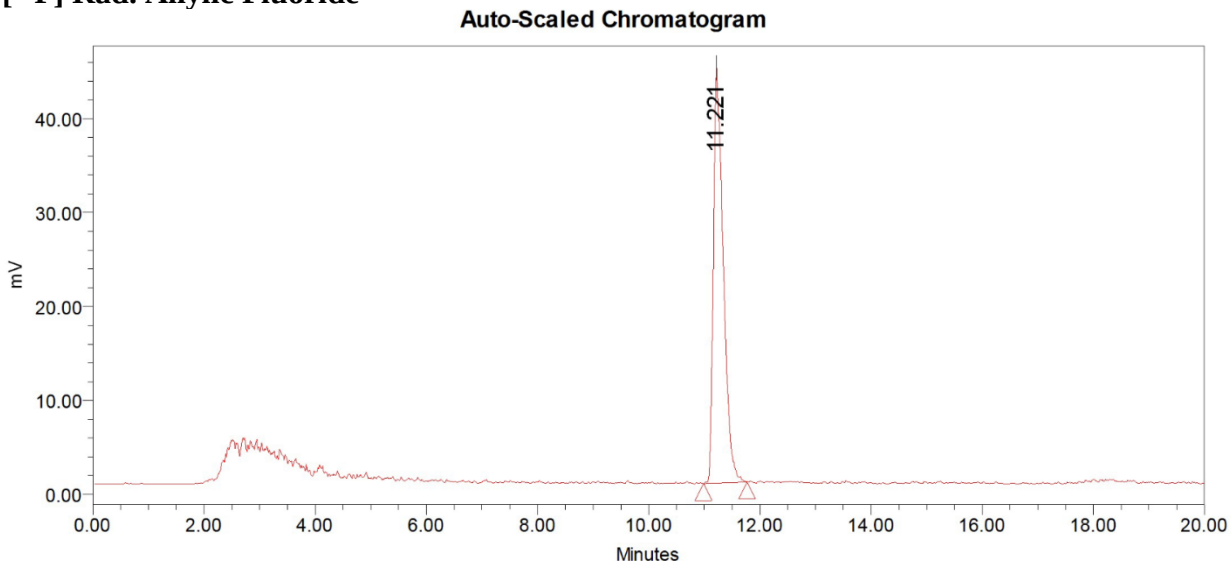
12

[^{19}F] Standard Allylic Fluoride

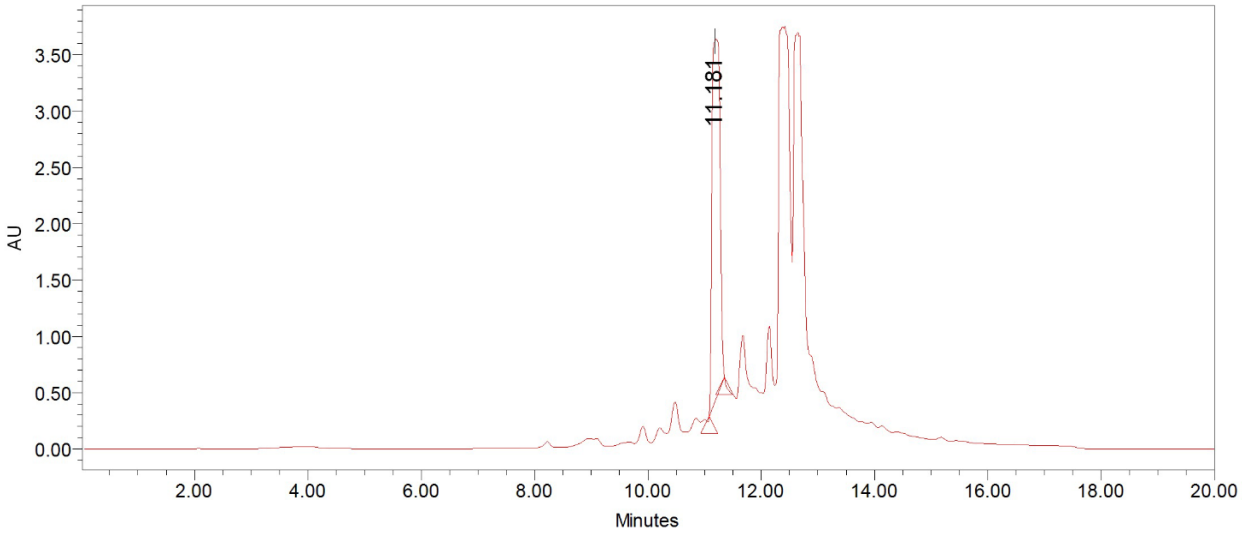


Allylic Fluoride [^{19}F] Standard Retention Time: 11.169 min. (Method 1)

[^{18}F] Rad. Allylic Fluoride



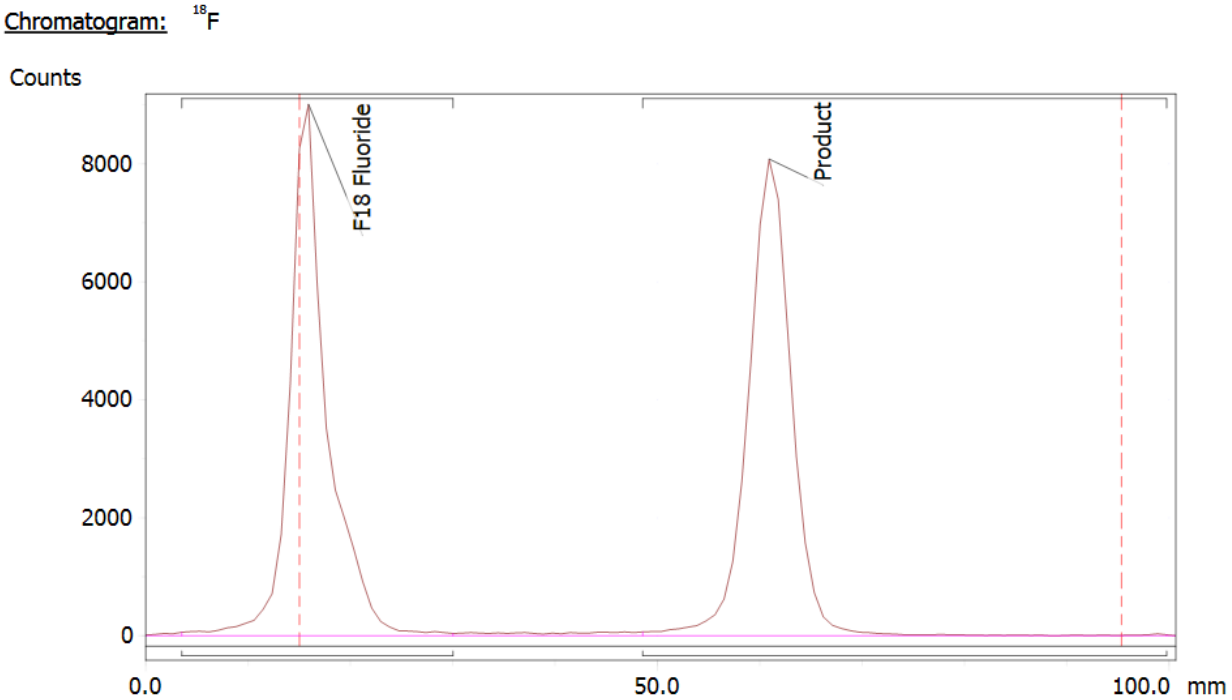
Allylic Fluoride [^{18}F] Rad. Retention Time: 11.221 min. (Method 1)



Crude Allylic Fluoride [^{18}F] UV Retention Time: 11.181 min. (Method 1)

[^{18}F] Rad. TLC

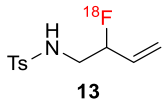
TLC Conditions: 8:2 Hex/EA



Radio TLC Trials:

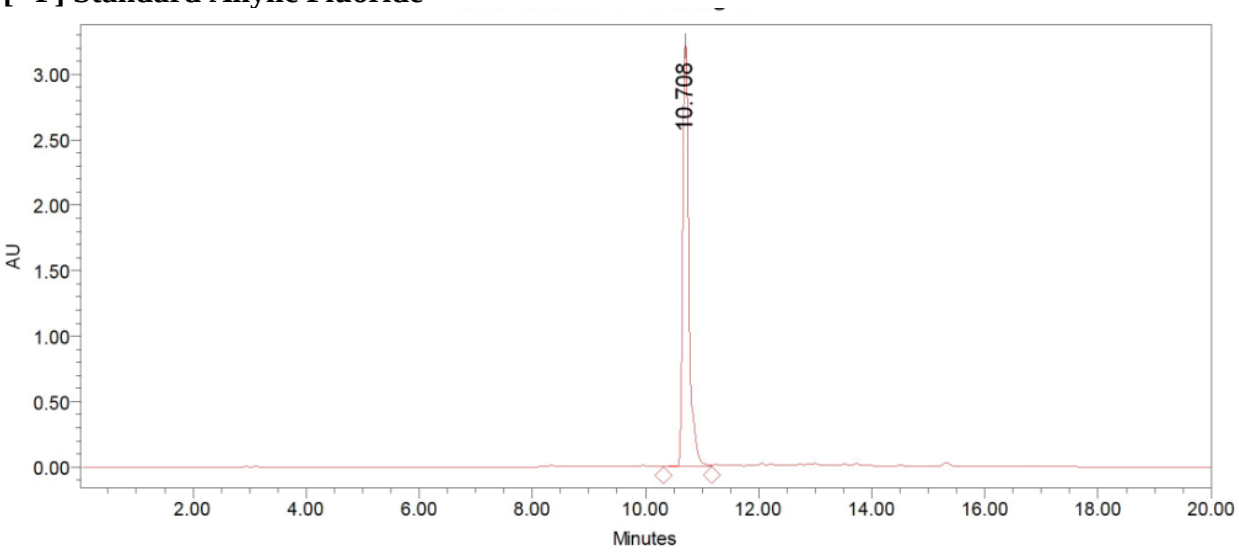
Trial	RCC
1	51%
2	51%
3	50%
4	55%
5	34%

Average: 48% +/- 8% (n = 5)



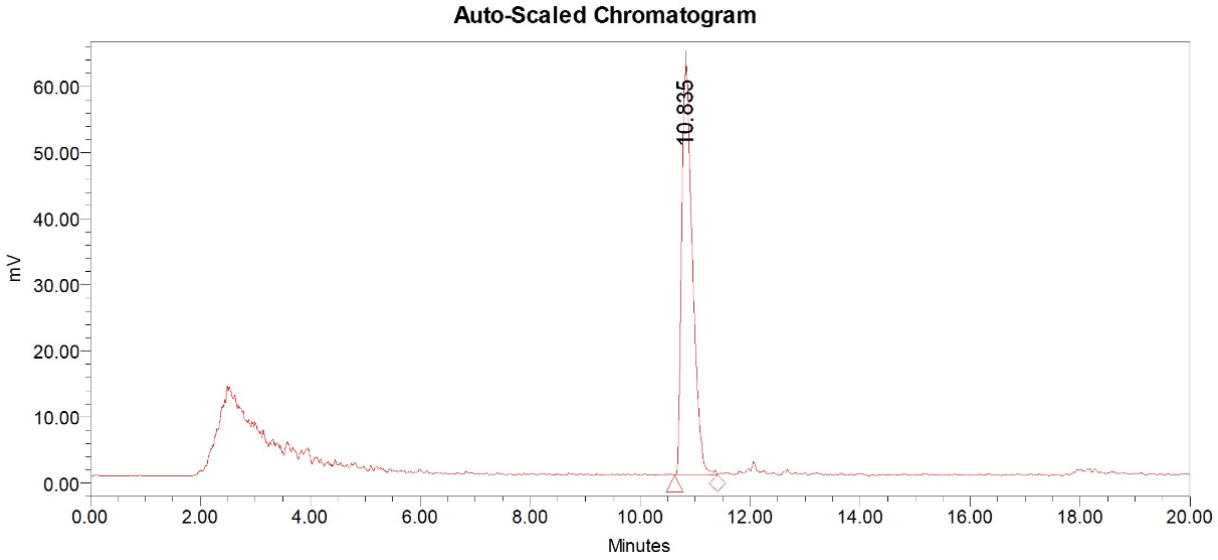
13

[^{19}F] Standard Allylic Fluoride

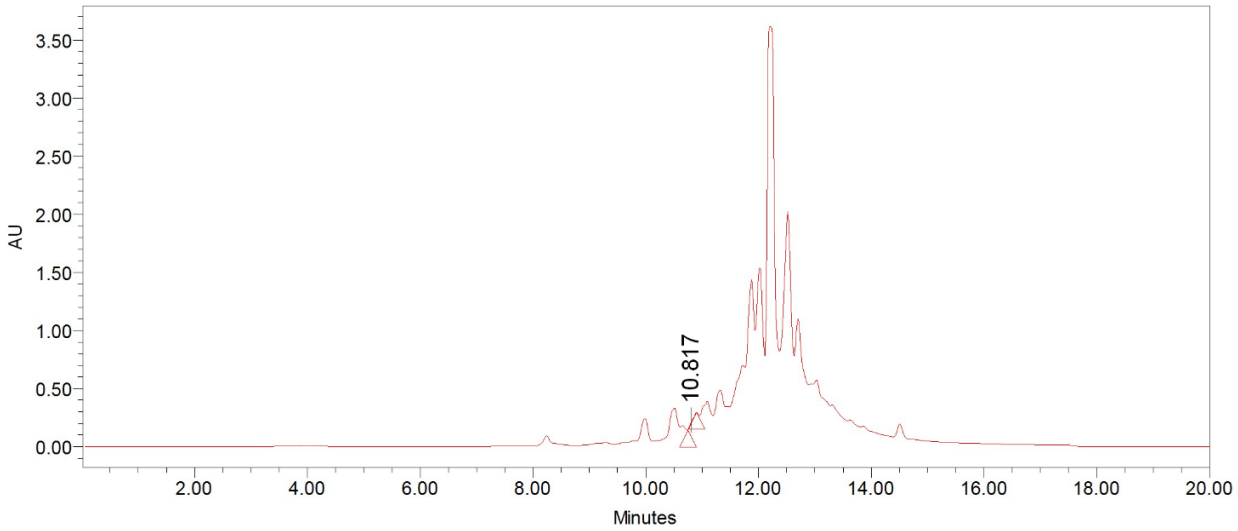


Allylic Fluoride [^{19}F] Standard Retention Time: 10.715 min. (Method 1)

[^{18}F] Rad. Allylic Fluoride



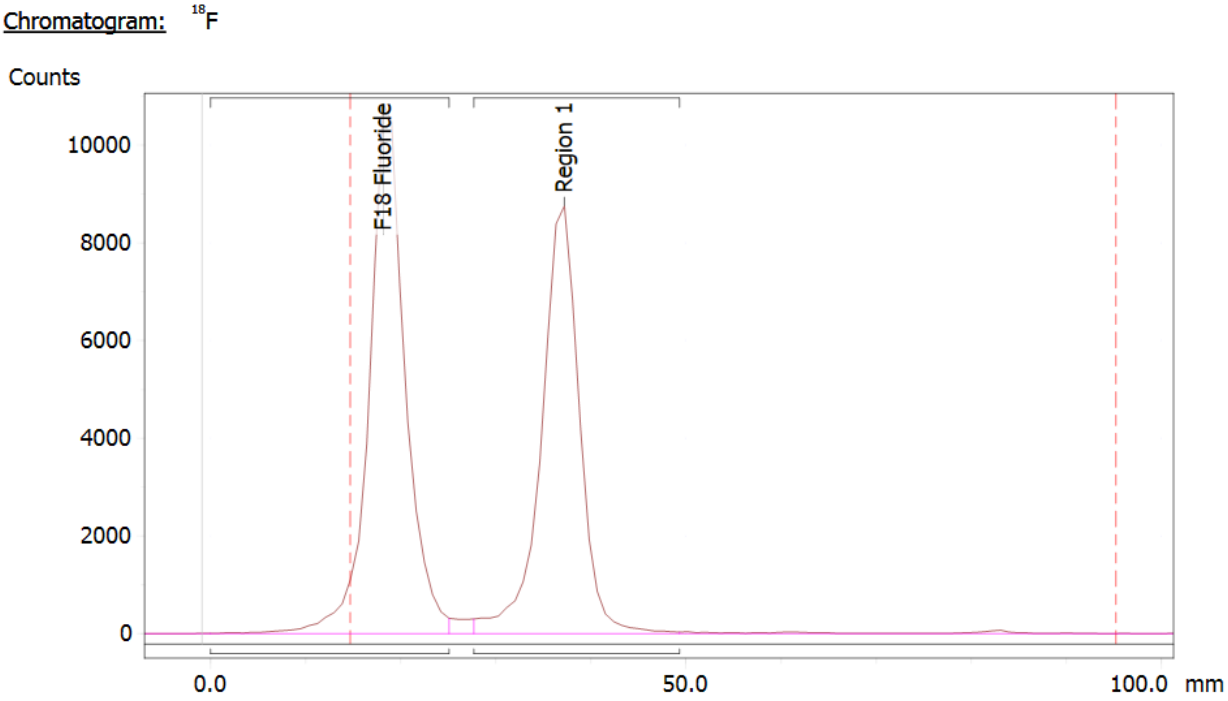
Allylic Fluoride [^{18}F] Rad. Retention Time: 10.835 min. (Method 1)



Crude Allylic Fluoride [^{18}F] UV Retention Time: 10.817 min. (Method 1)

[^{18}F] Rad. TLC

TLC Conditions: 8:2 Hex/EA

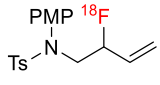


Radio TLC Trials:

Trial	RCC (5 min)	RCC (15 min)
1	21%	42%
2	21%	43%
3	27%	56%
4	33%	50%
5	20%	49%

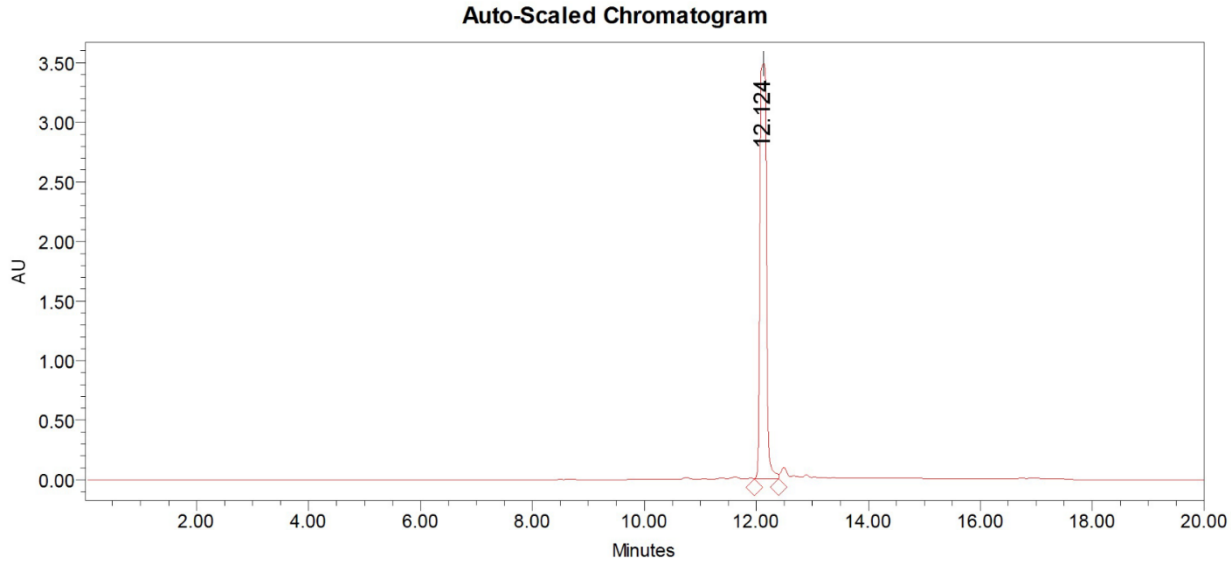
Average (5 min): 24% +/- 6% (n = 5)

Average (15 min): 48% +/- 6% (n = 5)



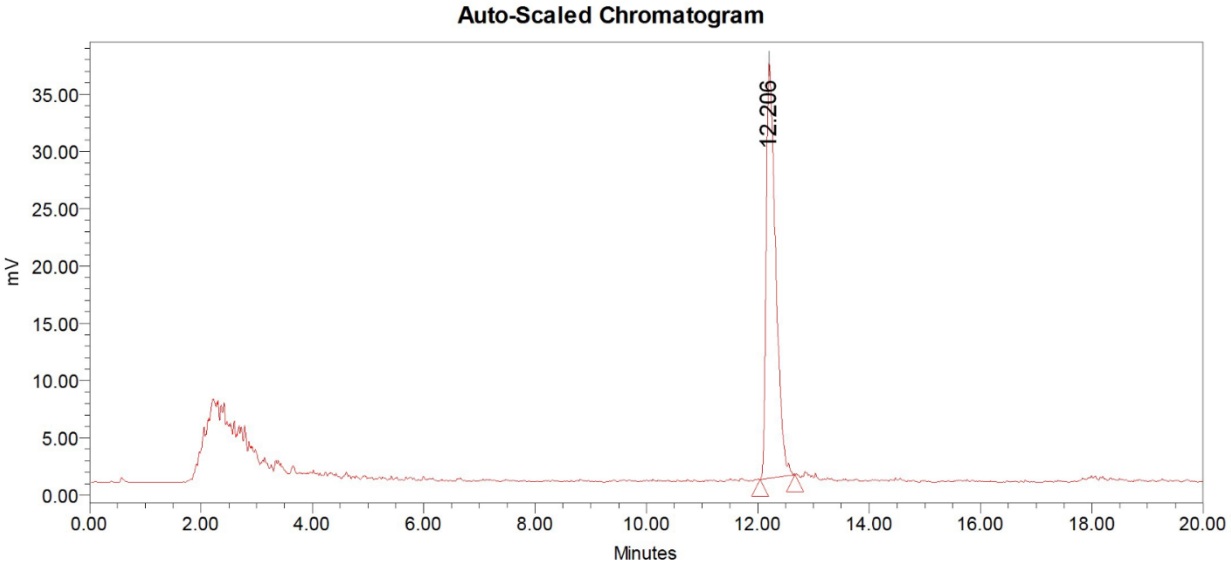
14

[^{19}F] Standard Allylic Fluoride

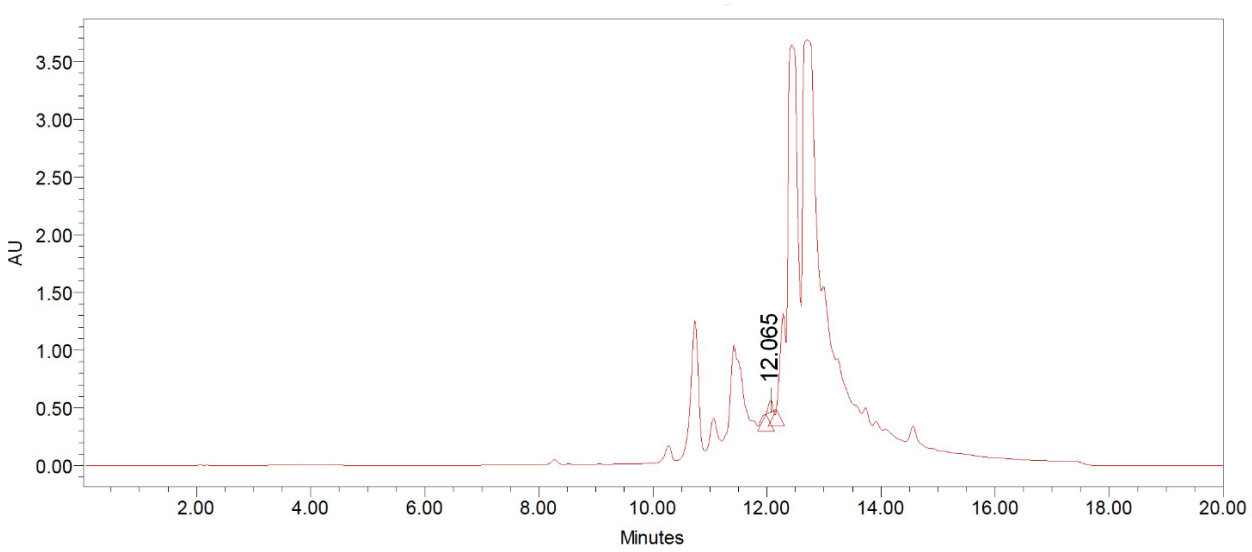


Allylic Fluoride [^{19}F] Standard Retention Time: 12.124 min. (Method 1)

[^{18}F] Rad. Allylic Fluoride



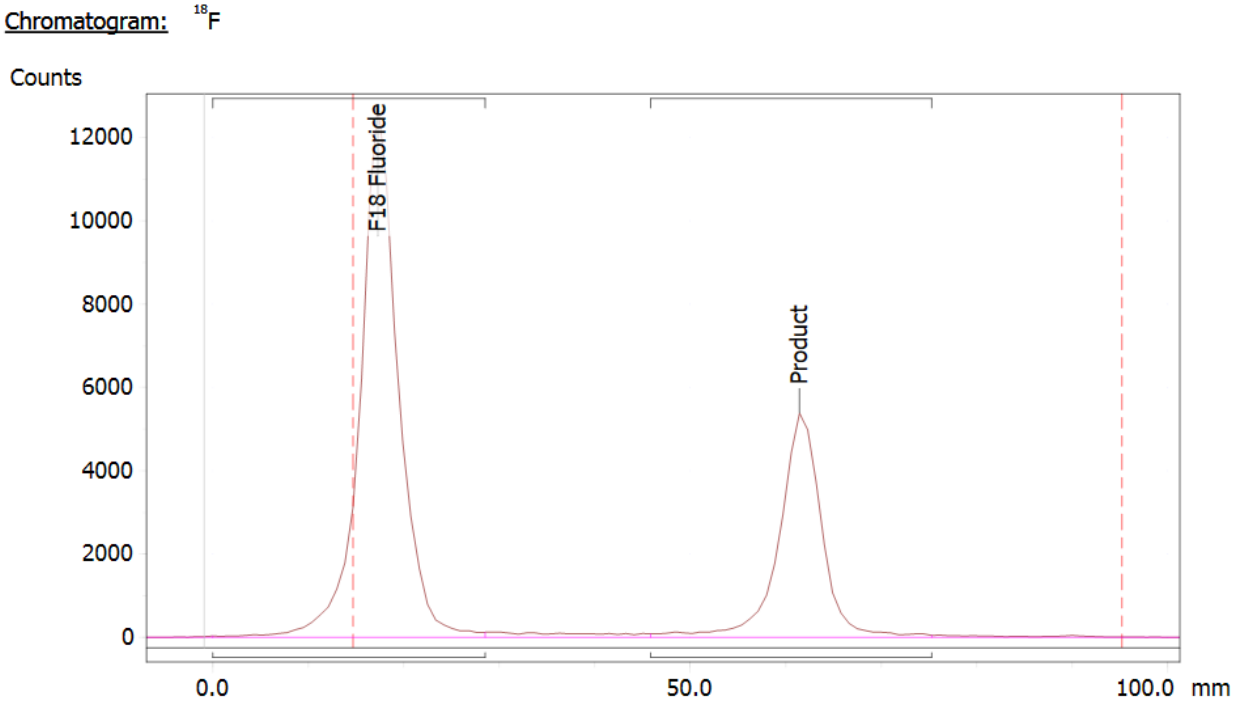
Allylic Fluoride [^{18}F] Rad. Retention Time: 12.206 min. (Method 1)



Crude Allylic Fluoride [^{18}F] UV Retention Time: 12.065 min. (Method 1)

[^{18}F] Rad. TLC

TLC Conditions: 7:3 Hex/EA

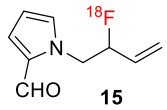


Radio TLC Trials:

Trial	RCC (5 min)	RCC (15 min)
1	28%	44%
2	32%	38%
3	27%	42%
4	31%	44%
5	31%	38%

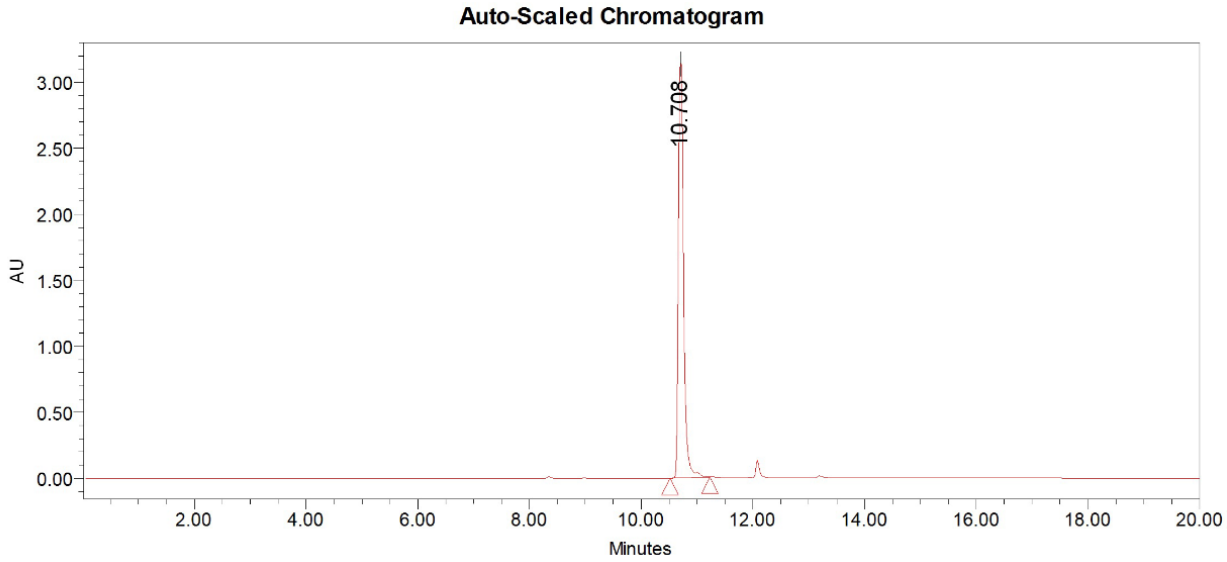
Average (5 min): 30% +/- 2% (n = 5)

Average (15 min): 41% +/- 3% (n = 5)



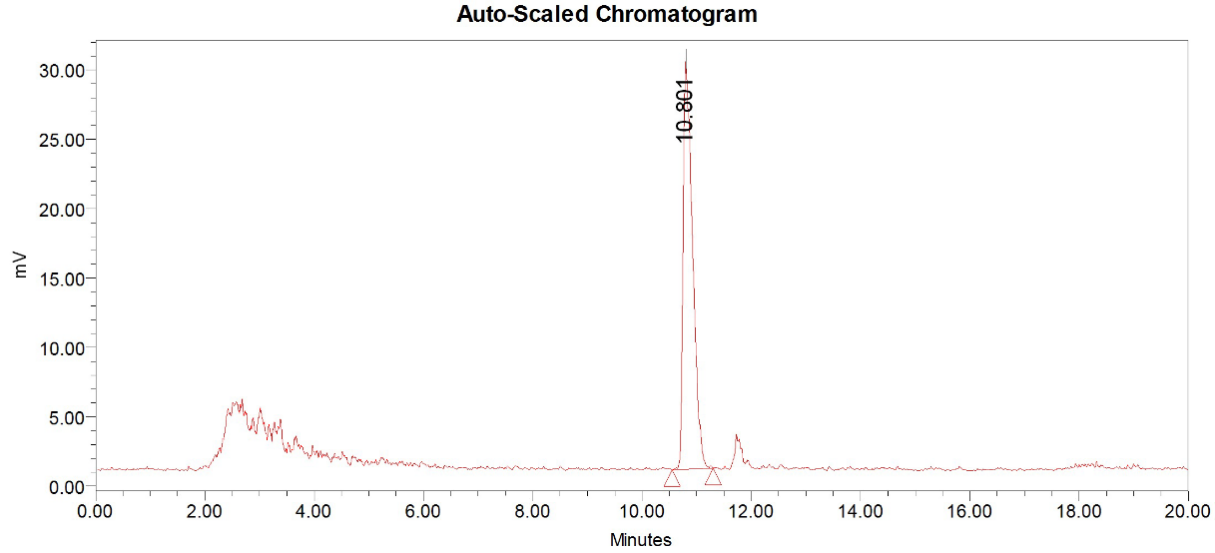
15

[19F] Standard Allylic Fluoride

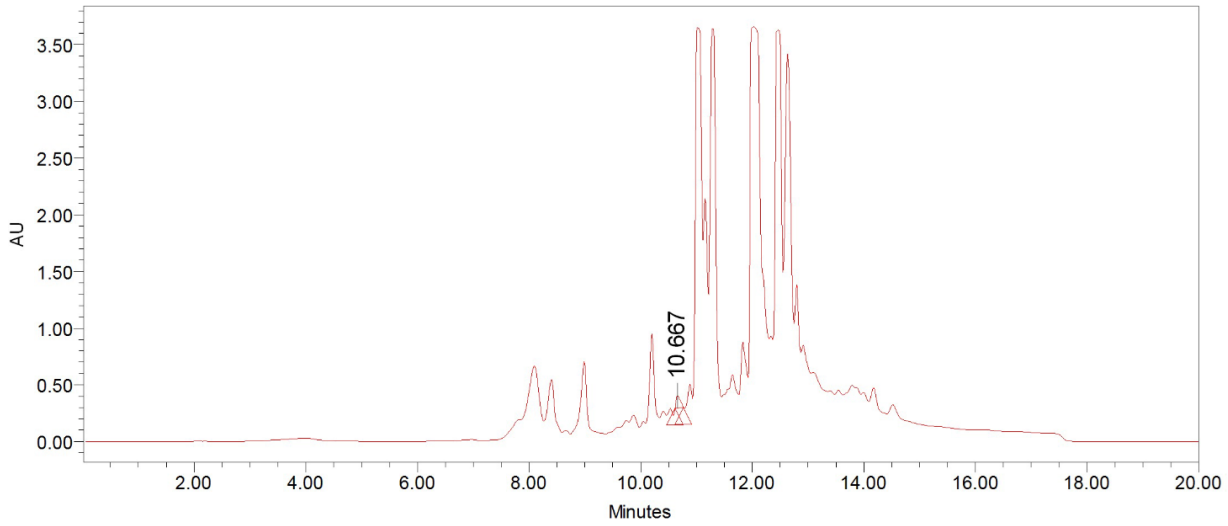


Allylic Fluoride [19F] Standard Retention Time: 10.708 min. (Method 1)

[18F] Rad. Allylic Fluoride



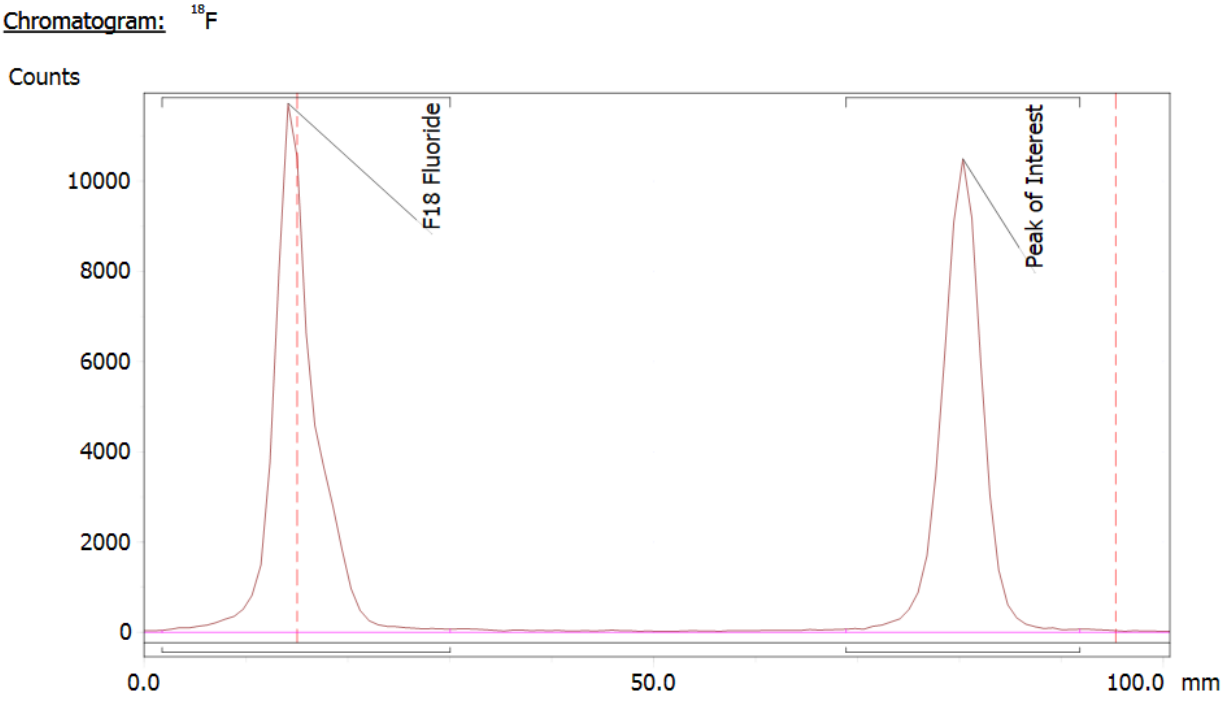
Allylic Fluoride [18F] Standard Retention Time: 10.801 min. (Method 1)



Crude Allylic Fluoride [^{18}F] UV Retention Time: 10.667 min. (Method 1)

[^{18}F] Rad. TLC

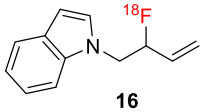
TLC Conditions: 6:4 Hex/EA



Radio TLC Trials:

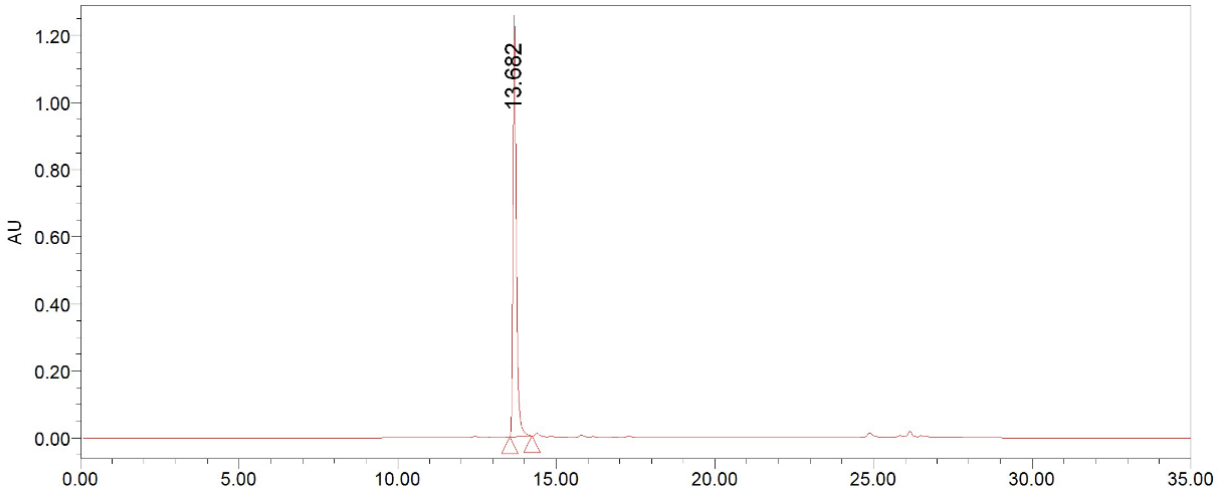
Trial	RCC
1	45%
2	47%
3	45%
4	48%
5	55%

Average: 48% +/- 4% (n = 5)



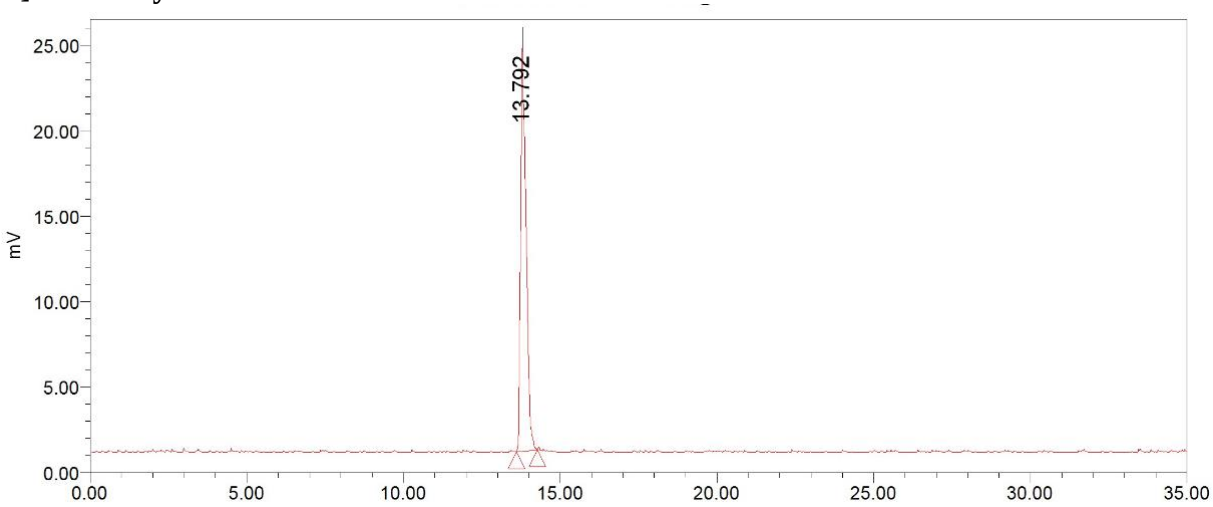
16

[^{19}F] Standard Allylic Fluoride

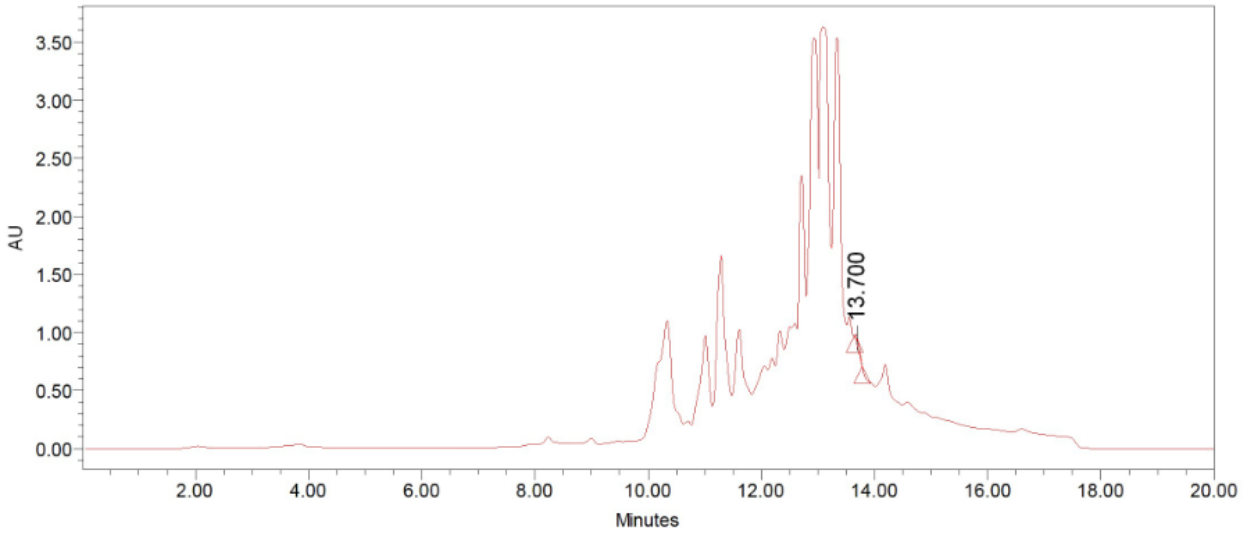


Allylic Fluoride [^{19}F] Standard Retention Time: 13.682 min. (Method 2)

[^{18}F] Rad. Allylic Fluoride



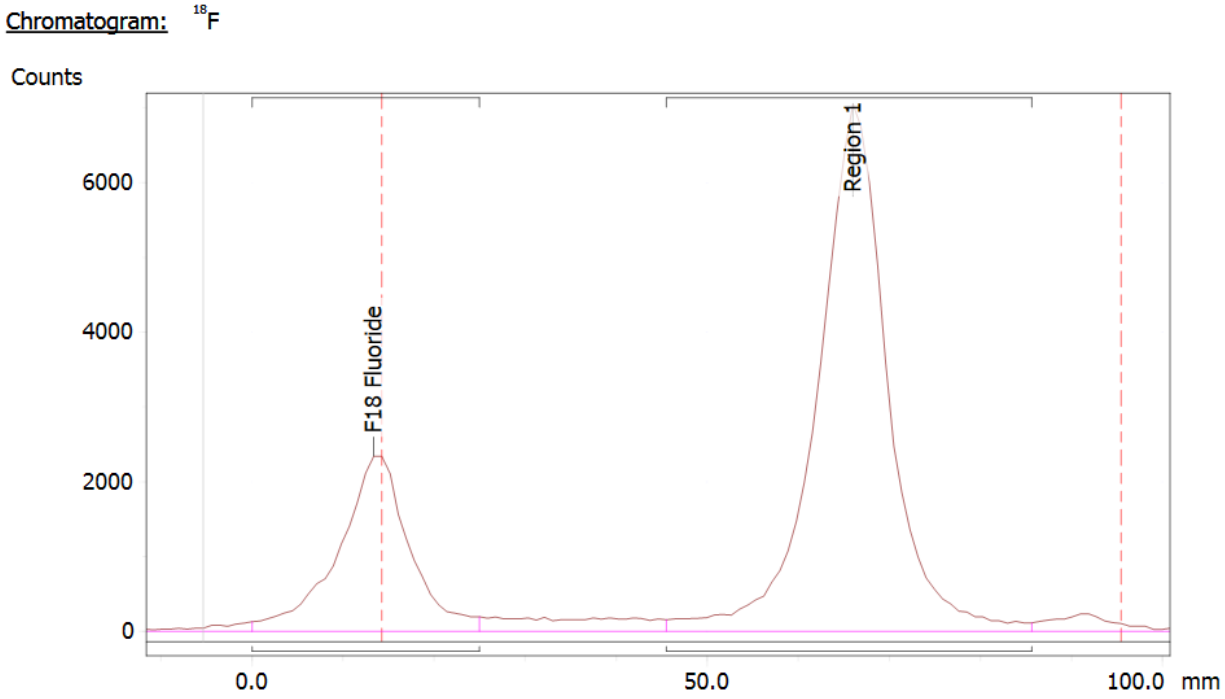
Allylic Fluoride [^{18}F] Rad. Retention Time: 13.792 min. (Method 2)



Allylic Fluoride [^{18}F] UV Retention Time: 13.700 min. (Method 2)

[^{18}F] Rad. TLC Conversion (Crude Product)

TLC Conditions: 8:2 Hex/EA



Radio TLC Trials:

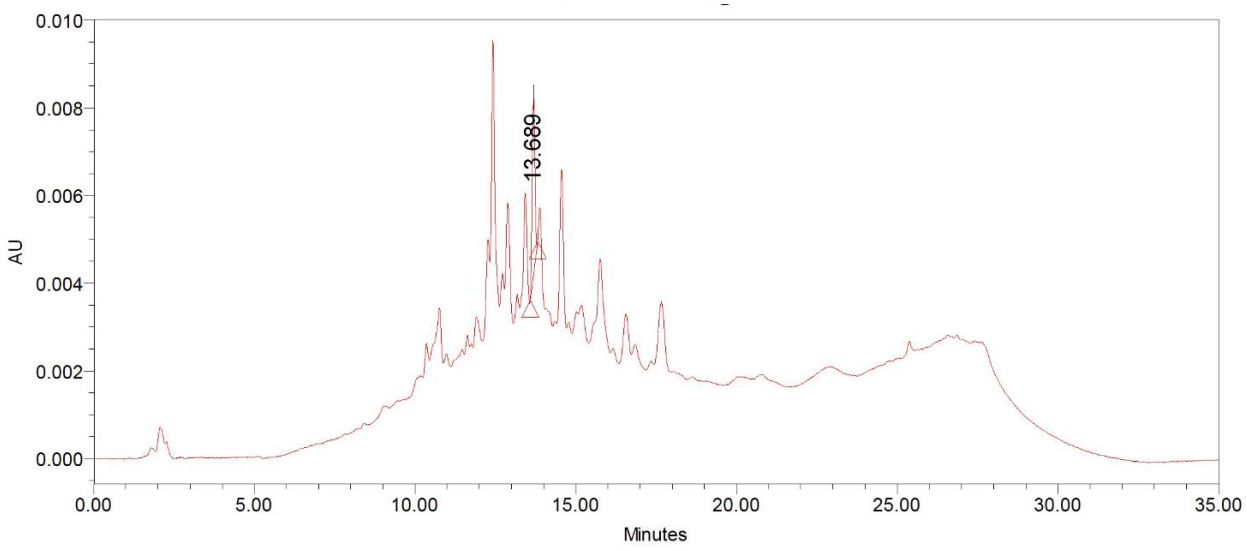
Trial	RCC (5 min)	RCC (15 min)
1	20%	66%
2	23%	63%
3	23%	65%
4	32%	69%
5	25%	70%

Average (5 min): 25% +/- 5% (n = 5)

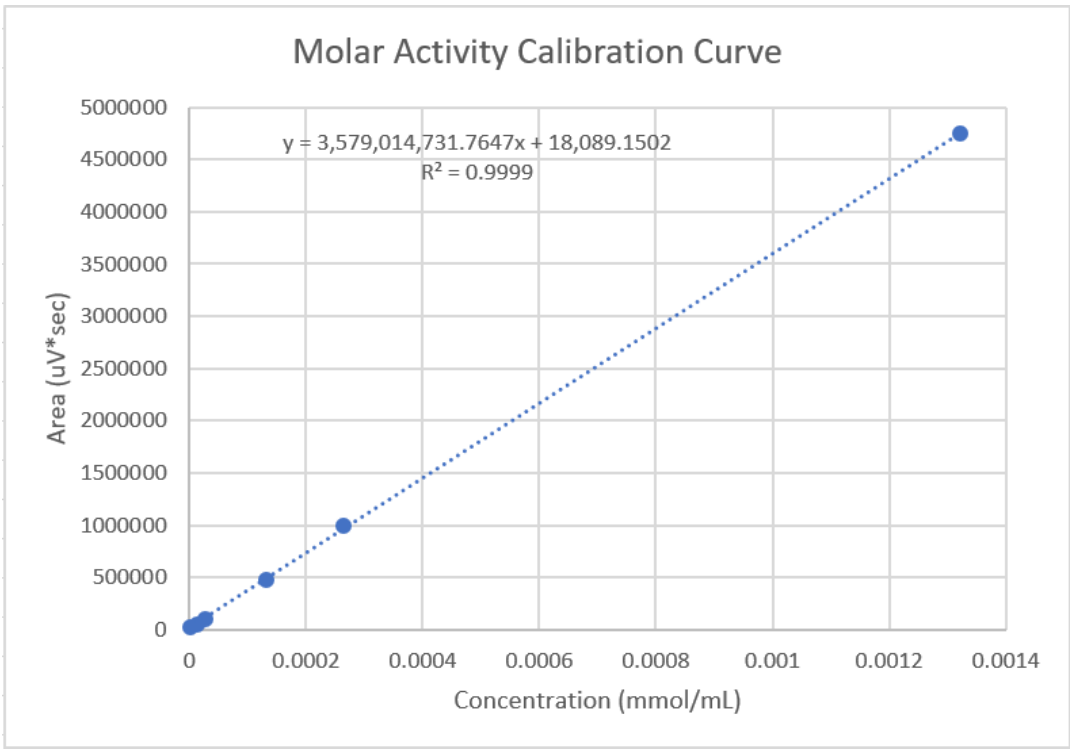
Average (15 min): 67% +/- 3% (n = 5)

Molar Activity:

A standard calibration curve was generated from the injection of known standard solutions (each run in duplicate). An aliquot of the sample (6.8 mCi, 7.7 mCi, 4.1 mCi) was injected onto an analytical HPLC using Method 1. The UV peak corresponding to the radiofluorinated product was determined by comparing the UV and RAD traces. The UV area was then used to calculate the concentration of the product based on linear regression analysis of appropriate allylic fluoride standards. This provided the concentration of the ^{19}F standard product in mmol/mL. Dividing the activity concentration (Ci/mL) factoring in the RCC by the HPLC-derived concentration of product (mmol/mL) provided the molar activity in Ci/mmol.



Allylic Fluoride [^{18}F] UV Retention Time: 13.689 min. (Method 2) for Molar Activity Calculation



Molar Activity:

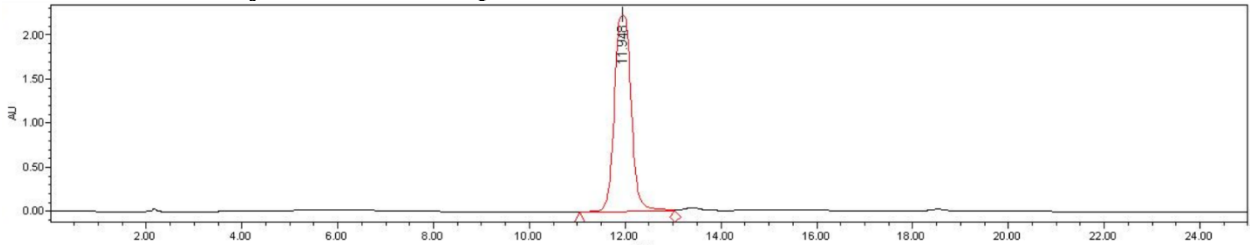
Trial	M.A.
1	410 Ci/mmol
2	253 Ci/mmol
3	442 Ci/mmol

Average: 368 +/- 101 Ci/mmol (n = 3)

Radiochemical Yield Determination using Prep. HPLC:

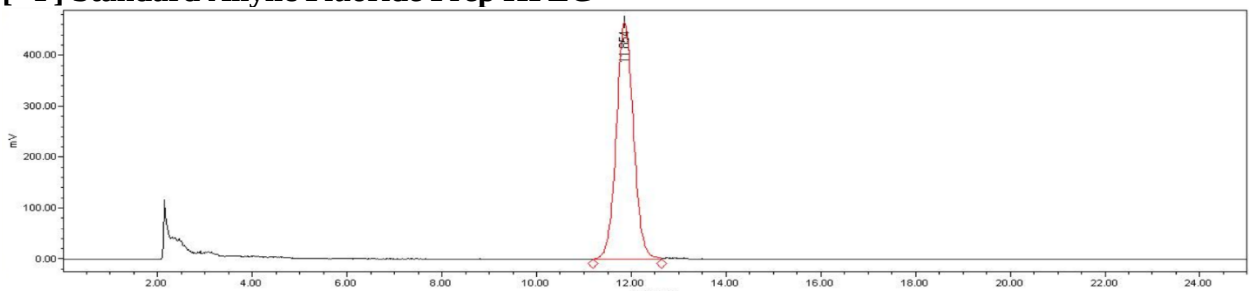
An isocratic Prep-HPLC method was used for the isolation of the desired [^{18}F] allylic fluoride in order to have a double verification of the product being analyzed by two different HPLC eluent systems and methods.

[^{19}F] Standard Allylic Fluoride Prep HPLC

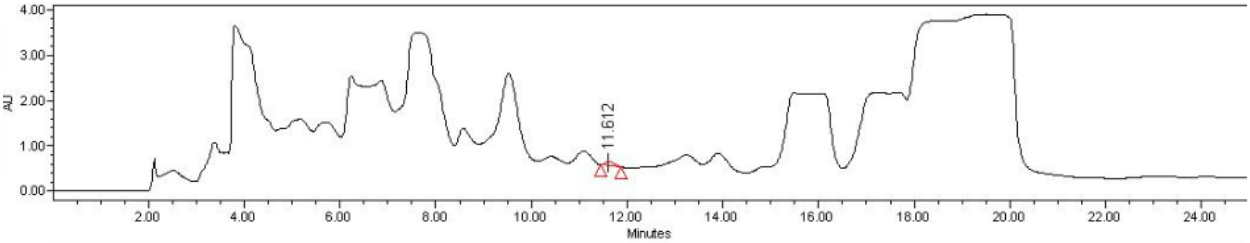


Allylic Fluoride [^{18}F] Standard Retention Time: 11.948 min. (Method 3)

[^{18}F] Standard Allylic Fluoride Prep HPLC



Allylic Fluoride [^{18}F] Rad. Retention Time: 11.854 min. (Method 3)



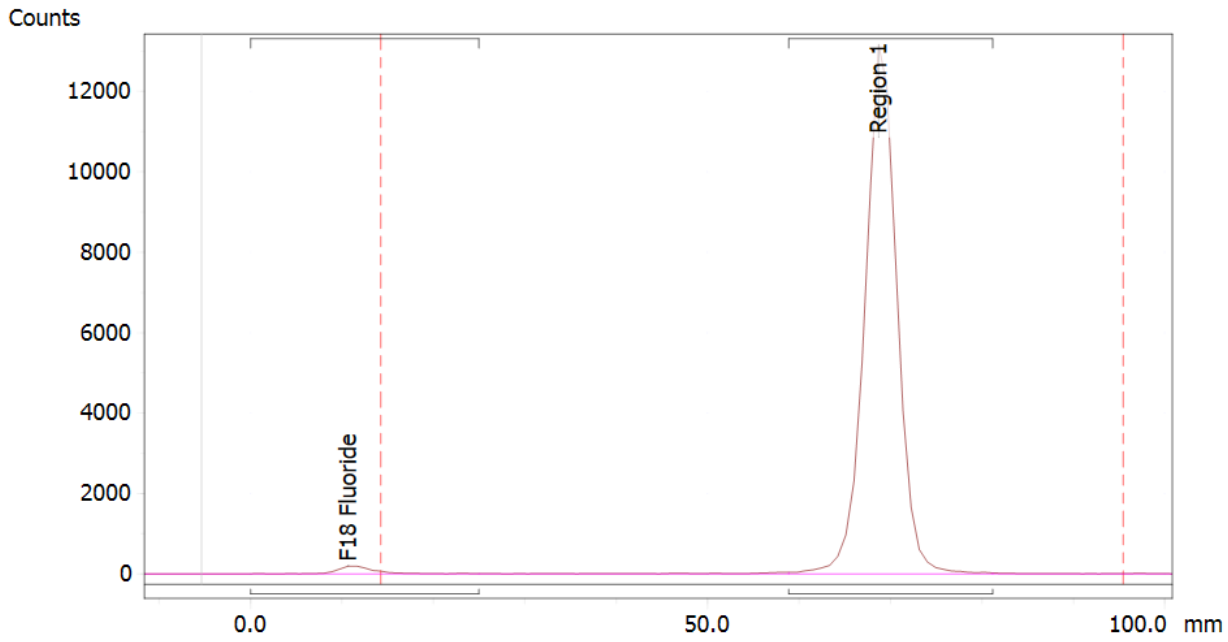
Allylic Fluoride [^{18}F] UV Retention Time: 11.612 min. (Method 3)

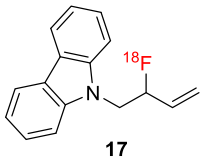
Radiochemical Yield Trials:

Trial	RCY
1	39%
2	39%
3	34%

Average: 37% +/- 3% (n = 3)

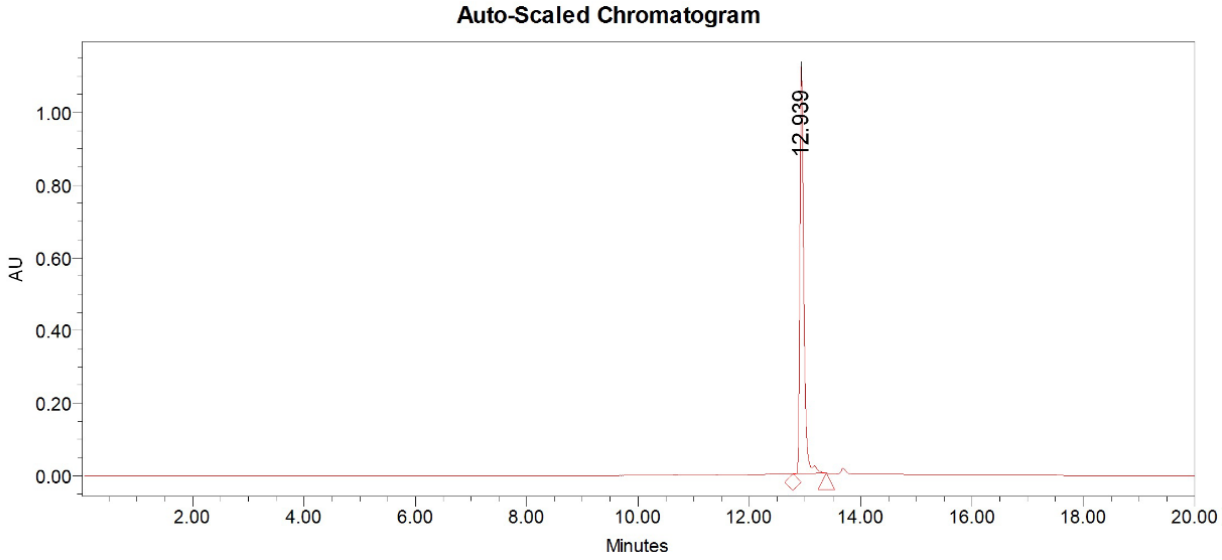
[^{18}F] Rad. TLC RCY (Isolated Product)
TLC Conditions: 8:2 Hex/EA





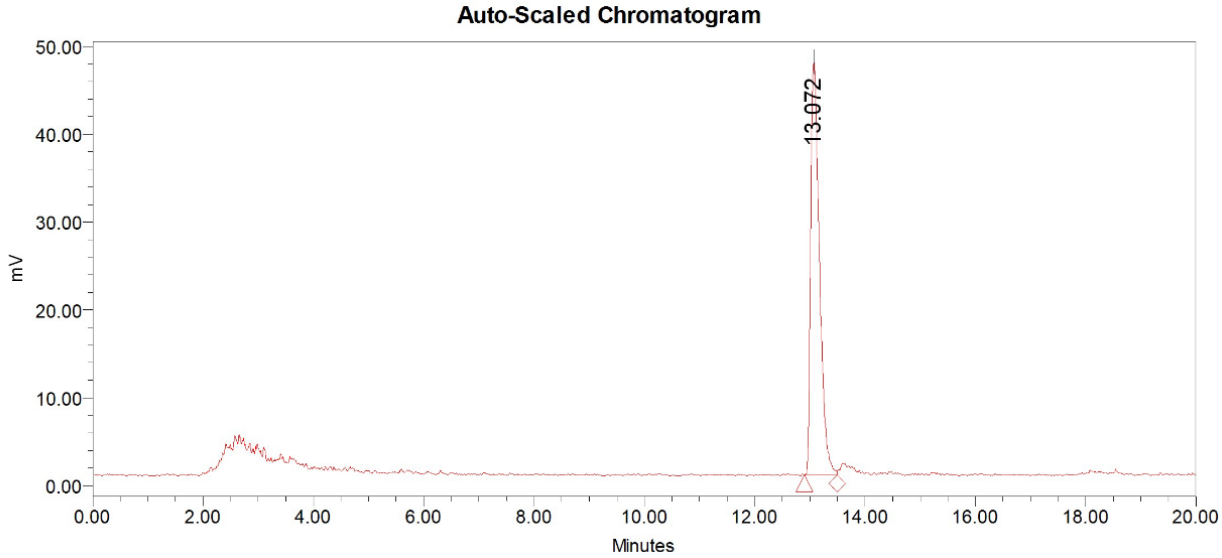
17

[19F] Standard Allylic Fluoride

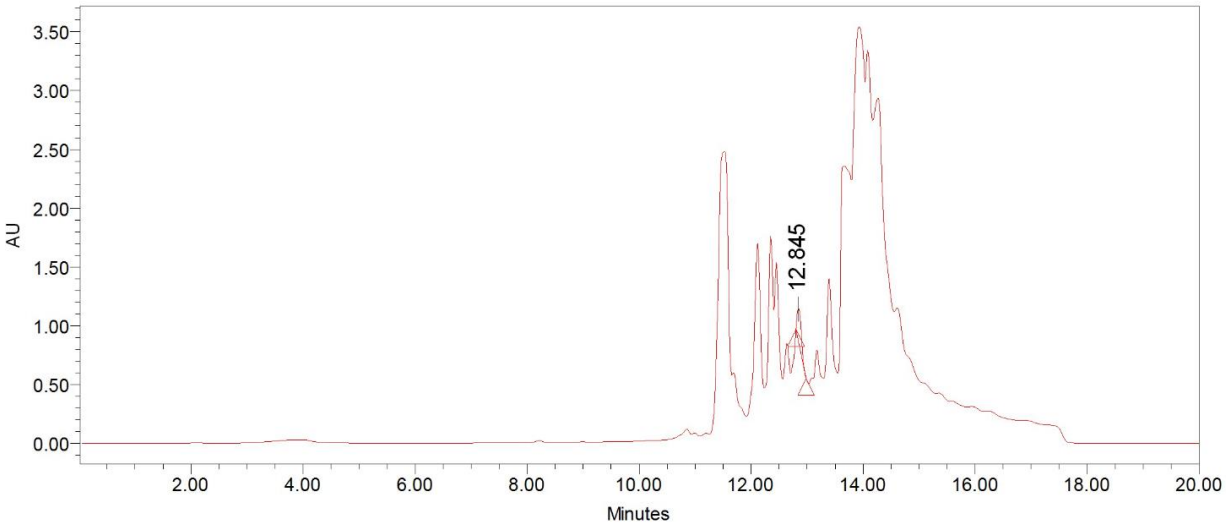


Allylic Fluoride [19F] Standard Retention Time: 12.939 min. (Method 1)

[18F] Rad. Allylic Fluoride



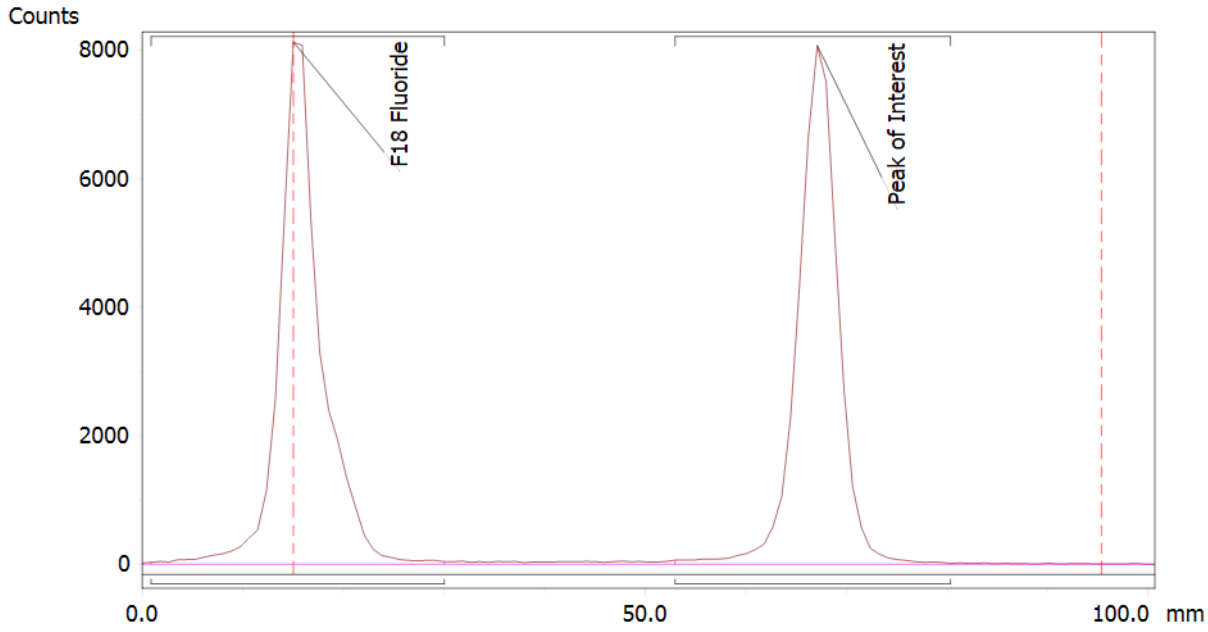
Allylic Fluoride [18F] Standard Retention Time: 13.072 min. (Method 1)



Crude Allylic Fluoride [^{18}F] UV Retention Time: 12.845 min. (Method 1)

[^{18}F] Rad. TLC

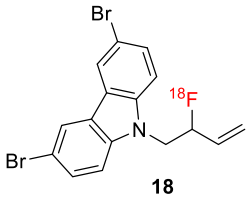
Chromatogram: ^{18}F



Radio TLC Trials:

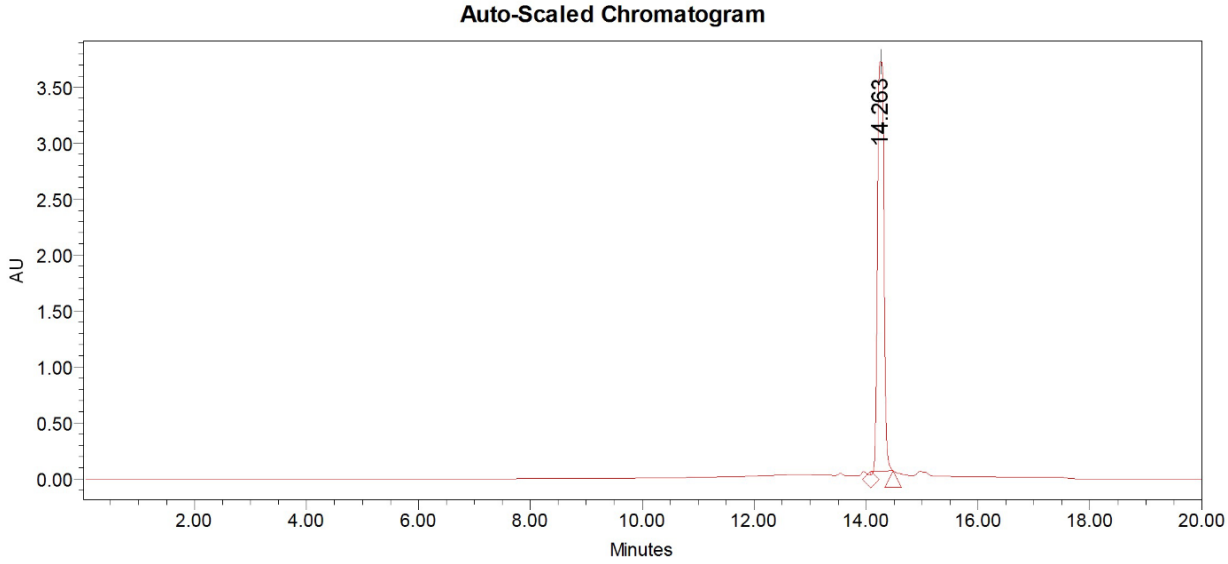
Trial	RCC
1	39%
2	50%
3	45%
4	49%
5	45%

Average: 46% +/- 4% (n = 5)



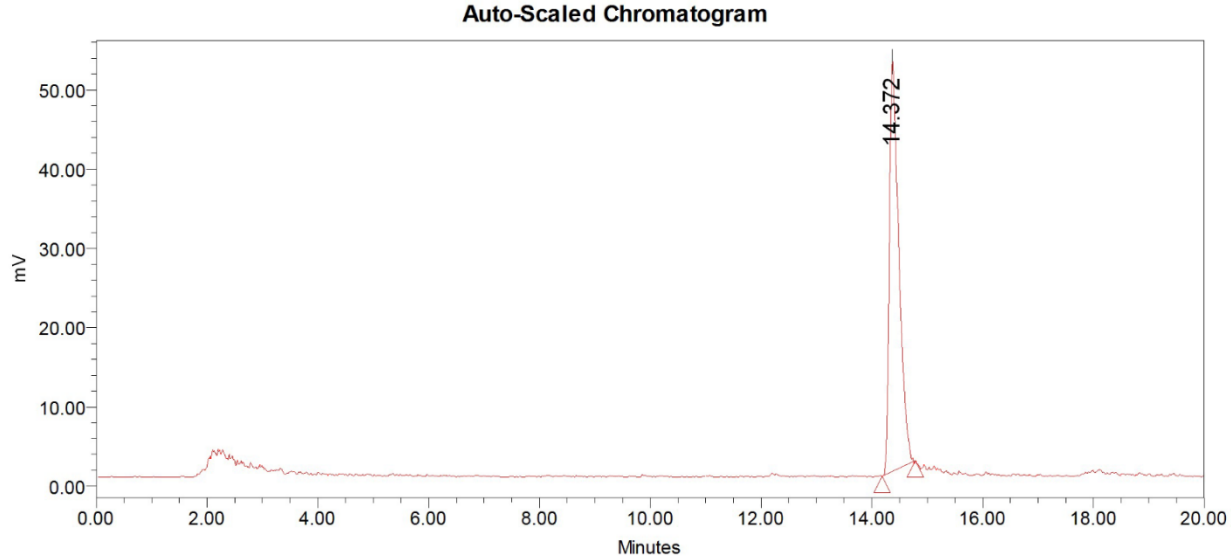
18

[19F] Standard Allylic Fluoride

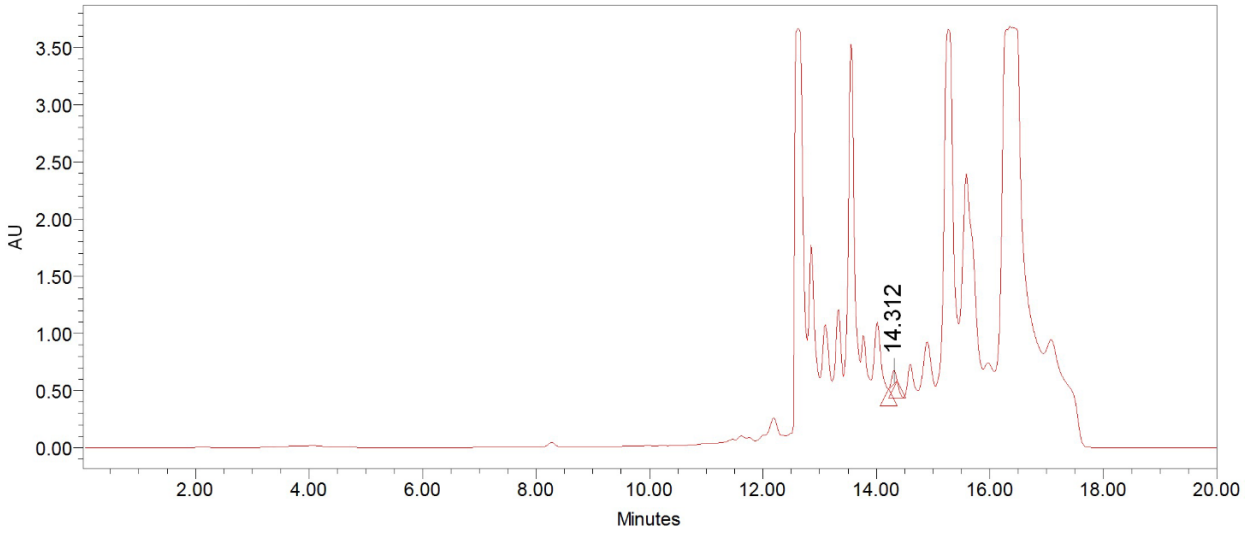


Allylic Fluoride [19F] Standard Retention Time: 14.263 min. (Method 1)

[18F] Rad. Allylic Fluoride



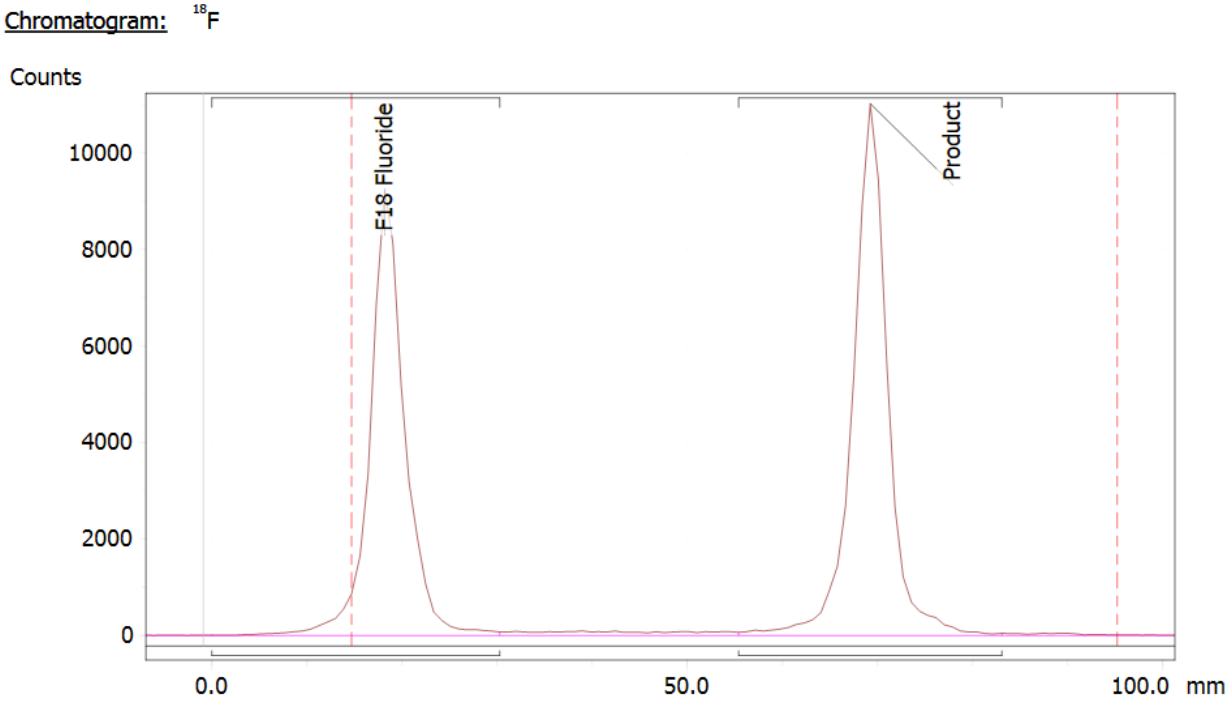
Allylic Fluoride [18F] Rad. Retention Time: 14.372 min. (Method 1)



Crude Allylic Fluoride [^{18}F] UV Retention Time: 14.312 min. (Method 1)

[^{18}F] Rad. TLC

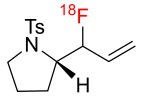
TLC Conditions: 8:2 Hex/EA



Radio TLC Trials:

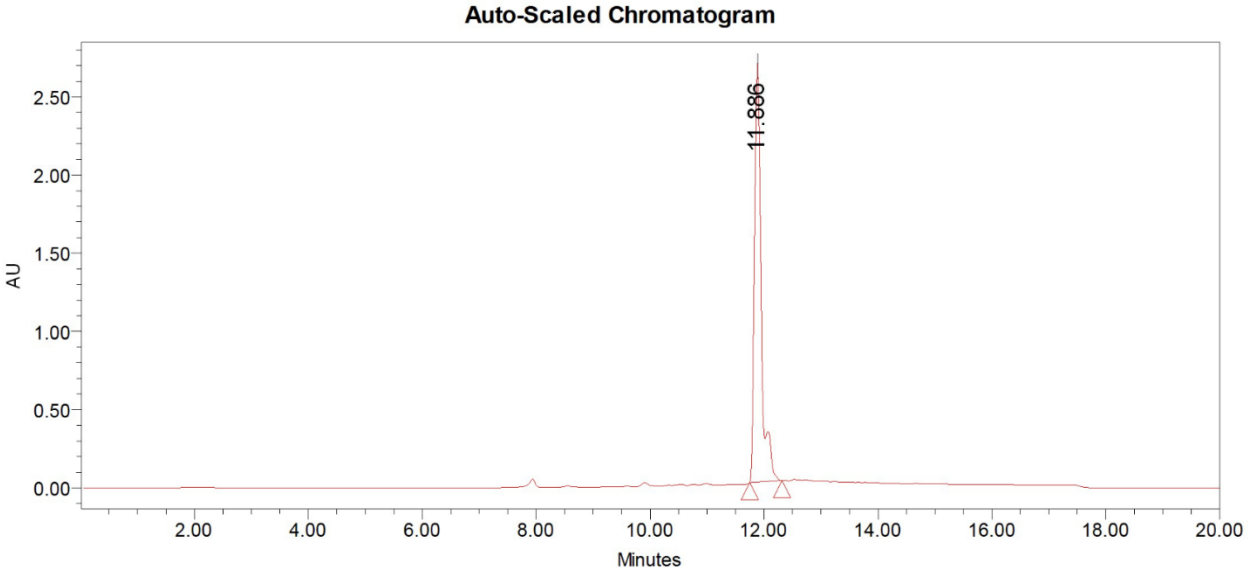
Trial	RCC
1	50%
2	57%
3	54%
4	57%
5	56%

Average: 56% +/- 4% (n = 5)



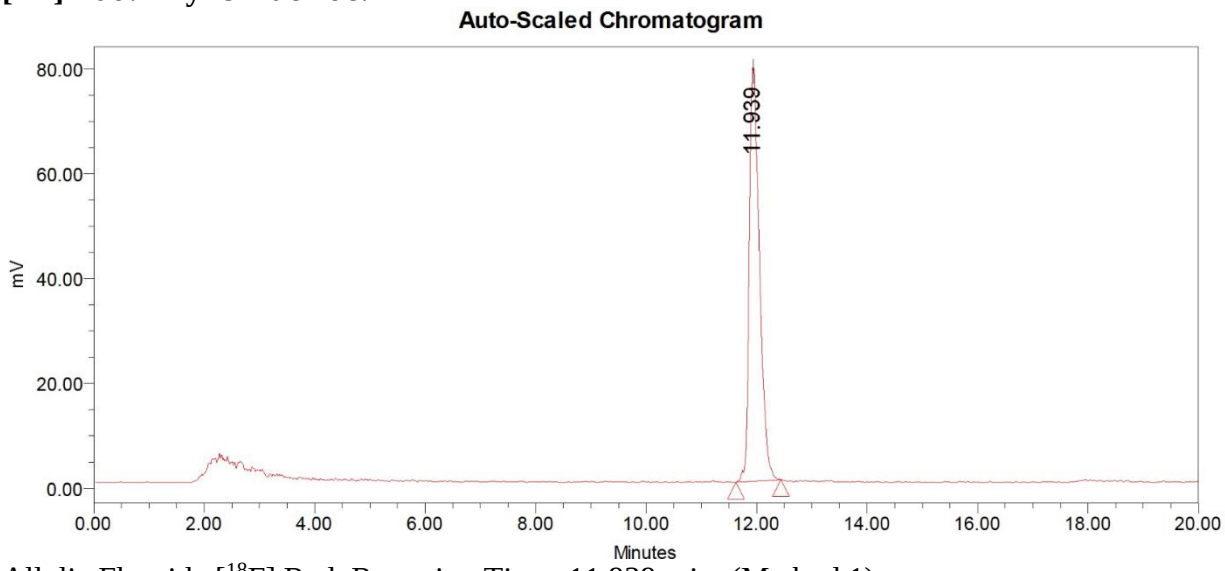
19

[^{19}F] Standard Allylic Fluoride

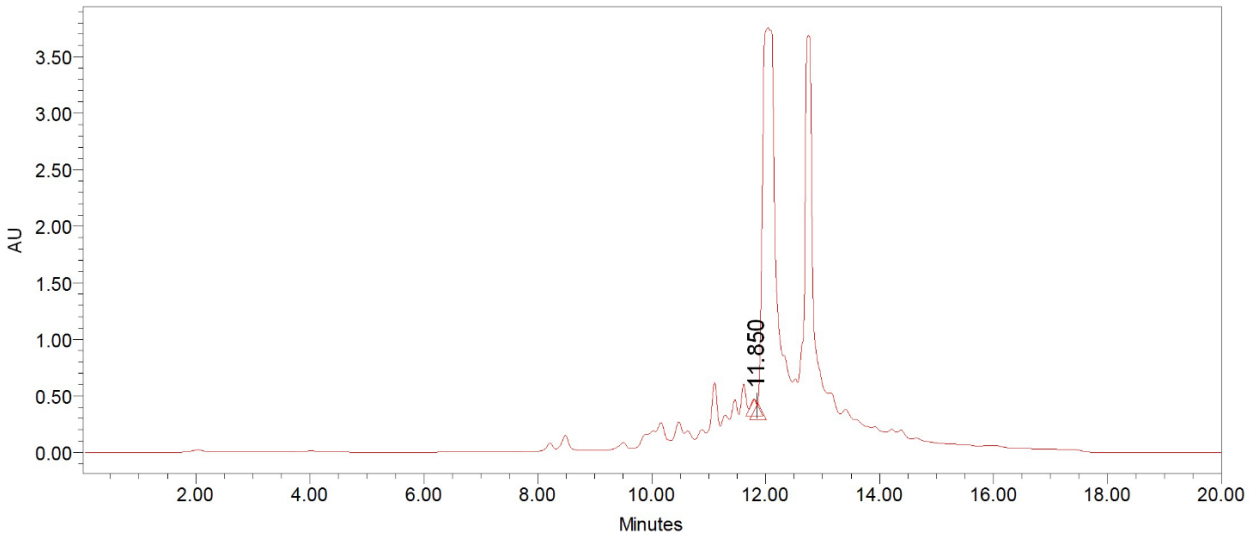


Allylic Fluoride [^{19}F] Standard Retention Time: 11.886 min. (Method 1)

[^{18}F] Rad. Allylic Fluoride:



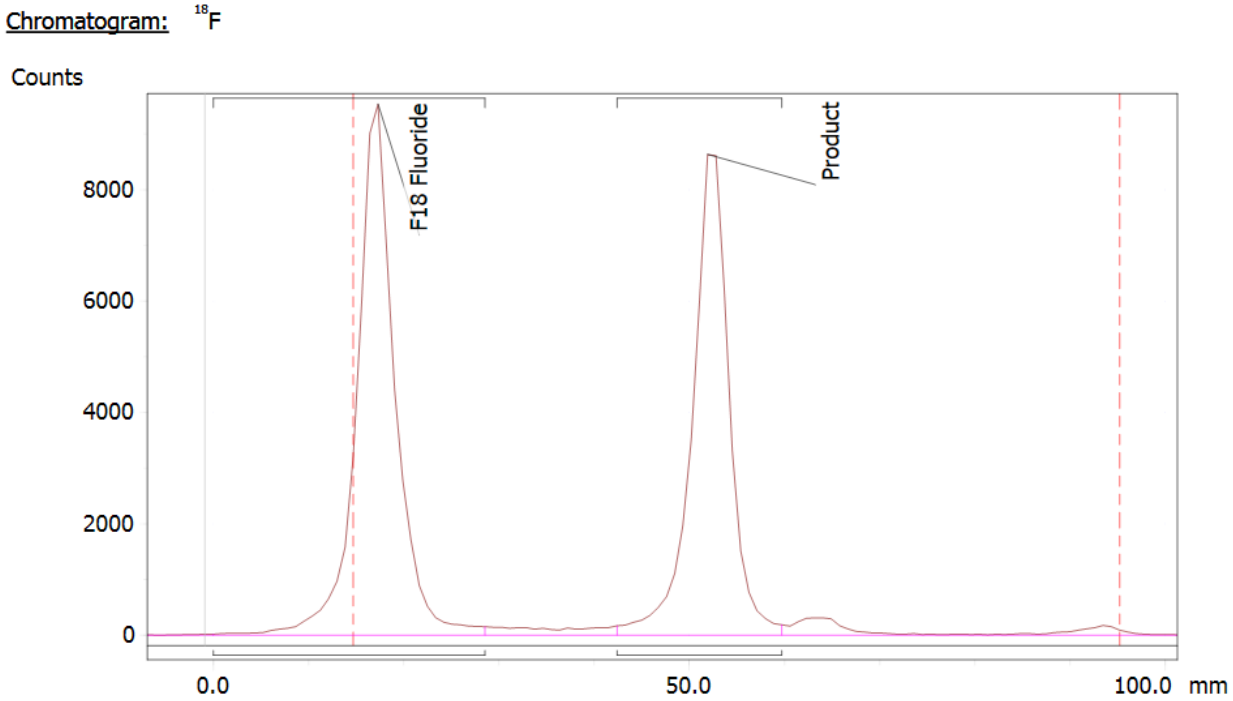
Allylic Fluoride [^{18}F] Rad. Retention Time: 11.939 min. (Method 1)



Crude Allylic Fluoride [^{18}F] UV Retention Time: 11.850 min. (Method 1)

[^{18}F] Rad. TLC

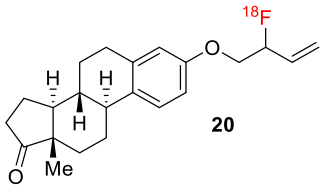
TLC Conditions: 8:2 Hex/EA



Radio TLC Trials:

Trial	RCC
1	51%
2	45%
3	45%
4	39%
5	45%

Average: 45% +/- 4% (n = 5)



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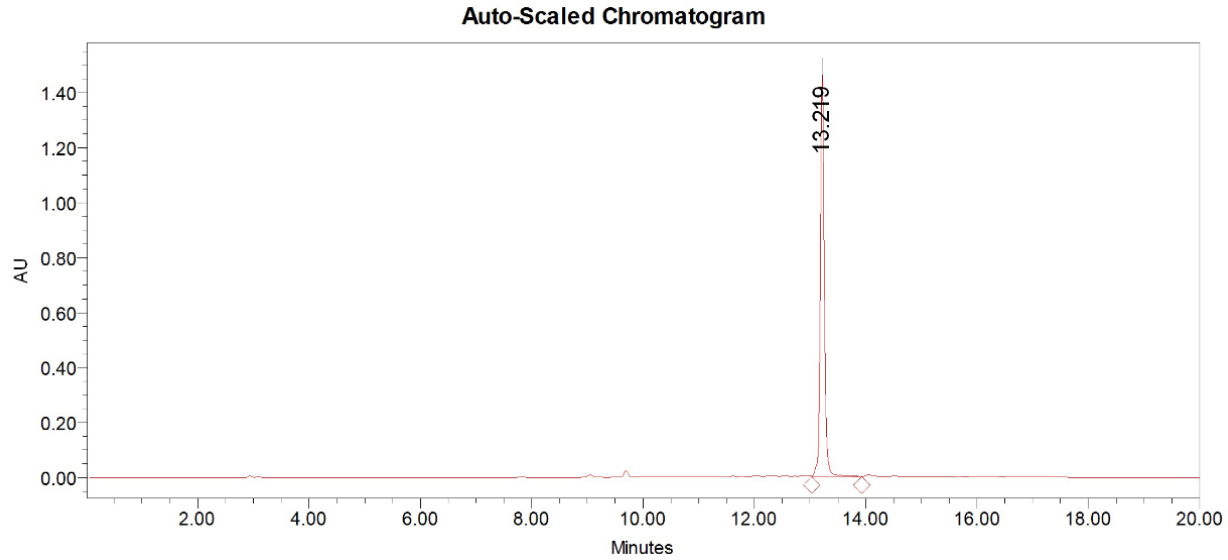
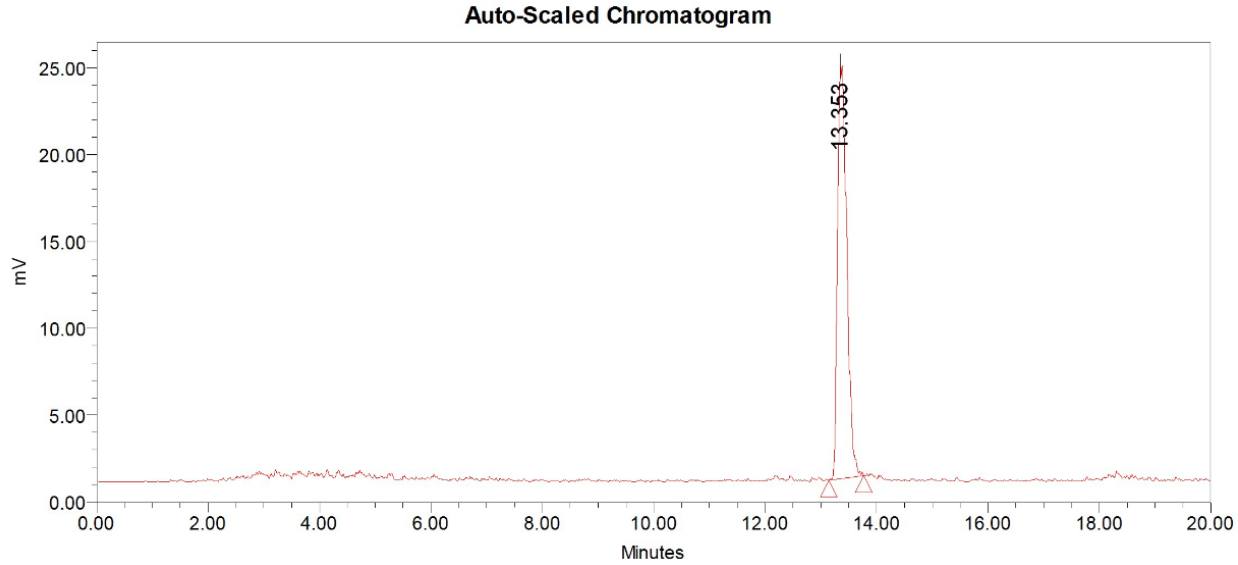
[^{19}F] Standard Allylic Fluoride

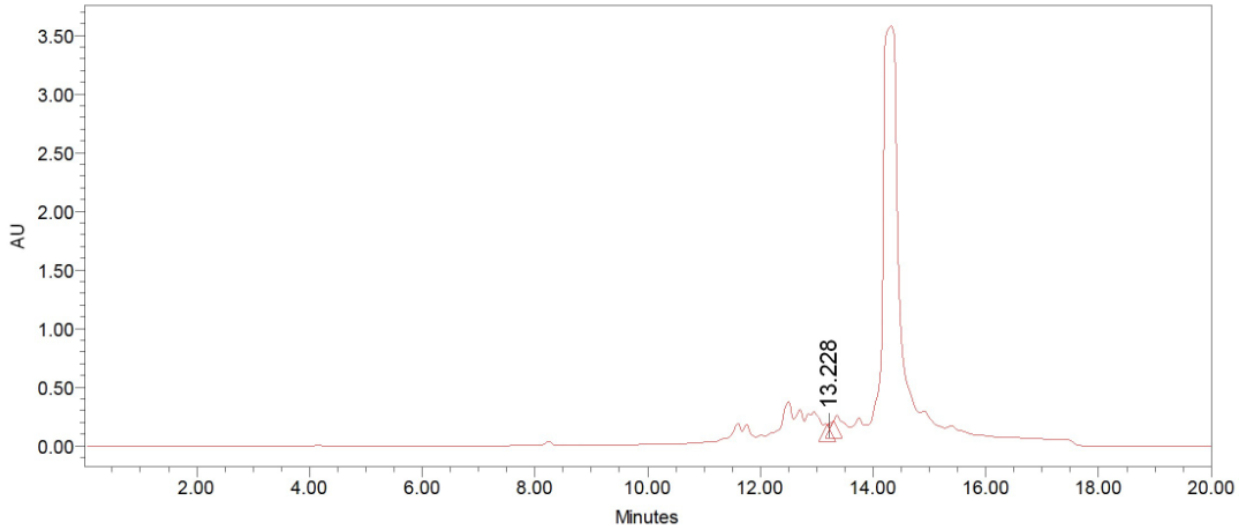


Allylic Fluoride [^{19}F] Standard Retention Time: 13.219 min. (Method 1)

[^{18}F] Rad. Allylic Fluoride



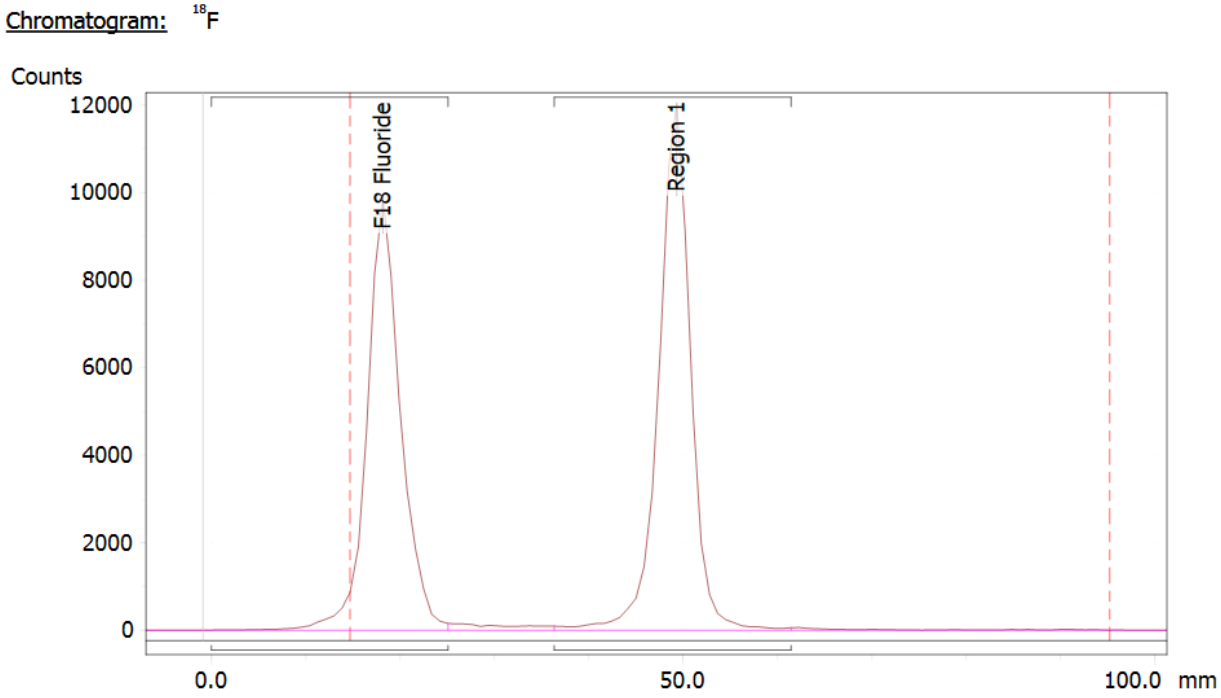
Allylic Fluoride [^{18}F] Rad. Retention Time: 13.353 min. (Method 1)



Allylic Fluoride [^{18}F] UV Retention Time: 13.228 min. (Method 1)

[^{18}F] Rad. TLC

TLC Conditions: 8:2 Hex/EA



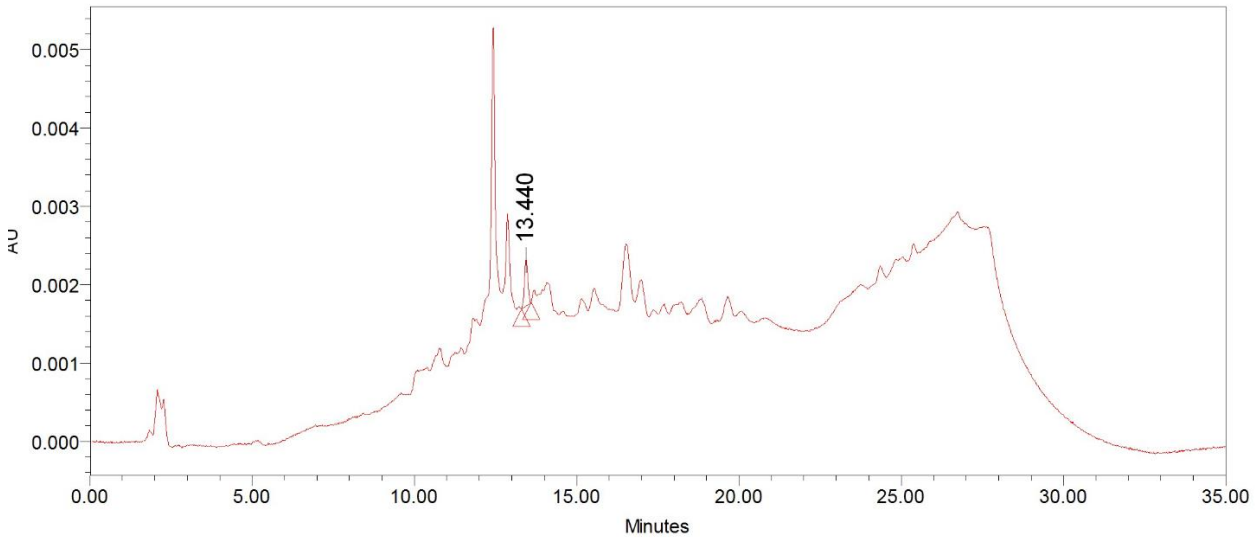
Radio TLC Trials:

Trial	RCC
1	52%
2	50%
3	49%
4	53%
5	54%

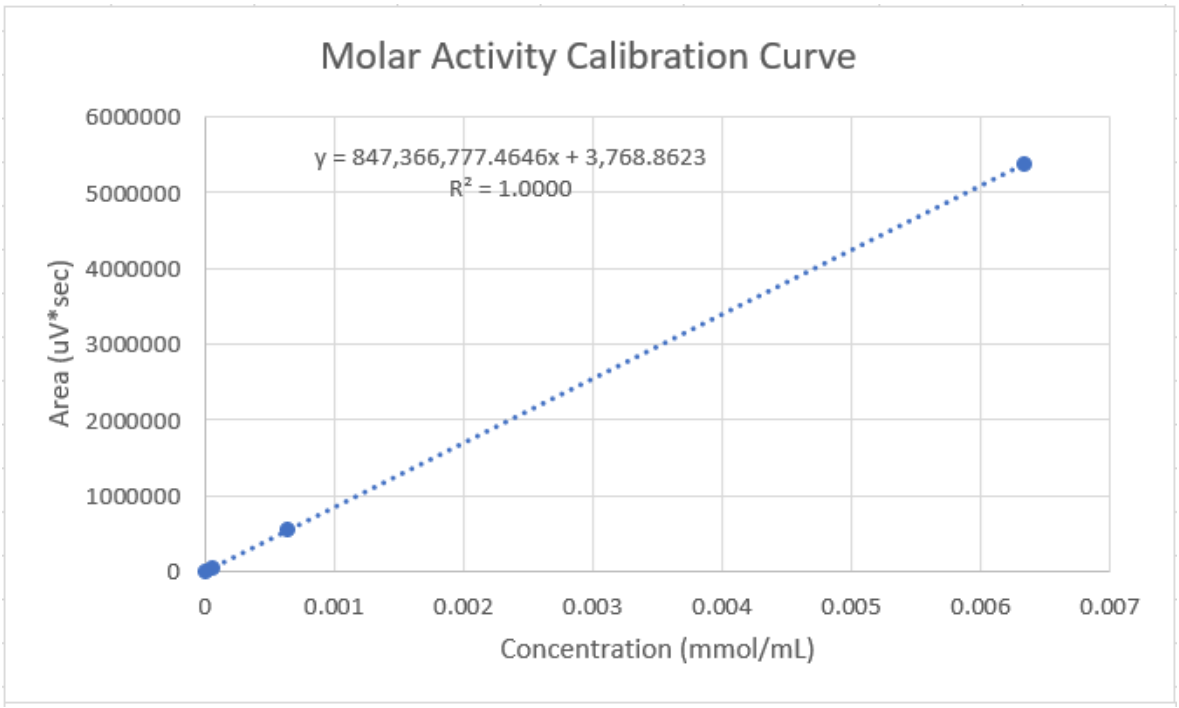
Average: 51% +/- 2% (n = 5)

Molar Activity

A standard calibration curve was generated from the injection of known standard solutions (each run in duplicate). An aliquot of the sample (5.1 mCi, 6.7 mCi, 2.6 mCi) was injected onto an analytical HPLC using Method 1. The UV peak corresponding to the radiofluorinated product was determined by comparing the UV and RAD traces. The UV area was then used to calculate the concentration of the product based on linear regression analysis of appropriate allylic fluoride standards. This provided the concentration of the ^{19}F standard product in mmol/mL. Dividing the activity concentration (Ci/mL) factoring in the RCC by the HPLC-derived concentration of product (mmol/mL) provided the molar activity in Ci/mmol.



Allylic Fluoride [^{18}F] UV Retention Time: 13.440 min. (Method 2) for Molar Activity Calculation



Molar Activity:

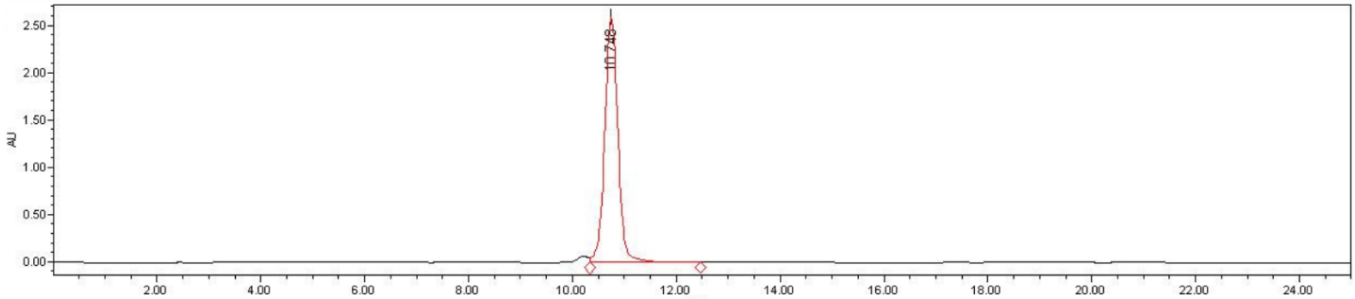
Trial	M.A.
1	96 Ci/mmol
2	79 Ci/mmol
3	71 Ci/mmol

Average: 82 +/- 13 Ci/mmol (n = 3)

Radiochemical Yield Determination using Prep. HPLC:

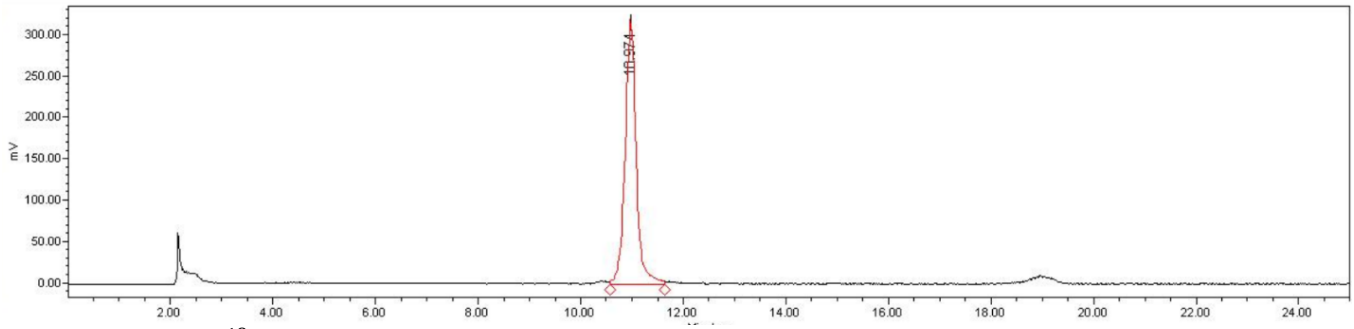
An isocratic Prep-HPLC method was used for the isolation of the desired [^{18}F] allylic fluoride in order to have a double verification of the product being analyzed by two different HPLC eluent systems and methods.

[^{19}F] Standard Allylic Fluoride Prep HPLC

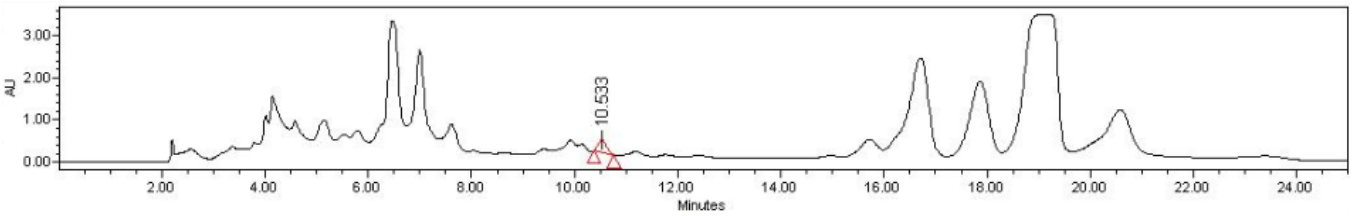


Allylic Fluoride [^{18}F] Standard Retention Time: 10.748 min. (Method 4)

[^{18}F] Standard Allylic Fluoride Prep HPLC



Allylic Fluoride [^{18}F] Rad. Retention Time: 10.974 min. (Method 4)



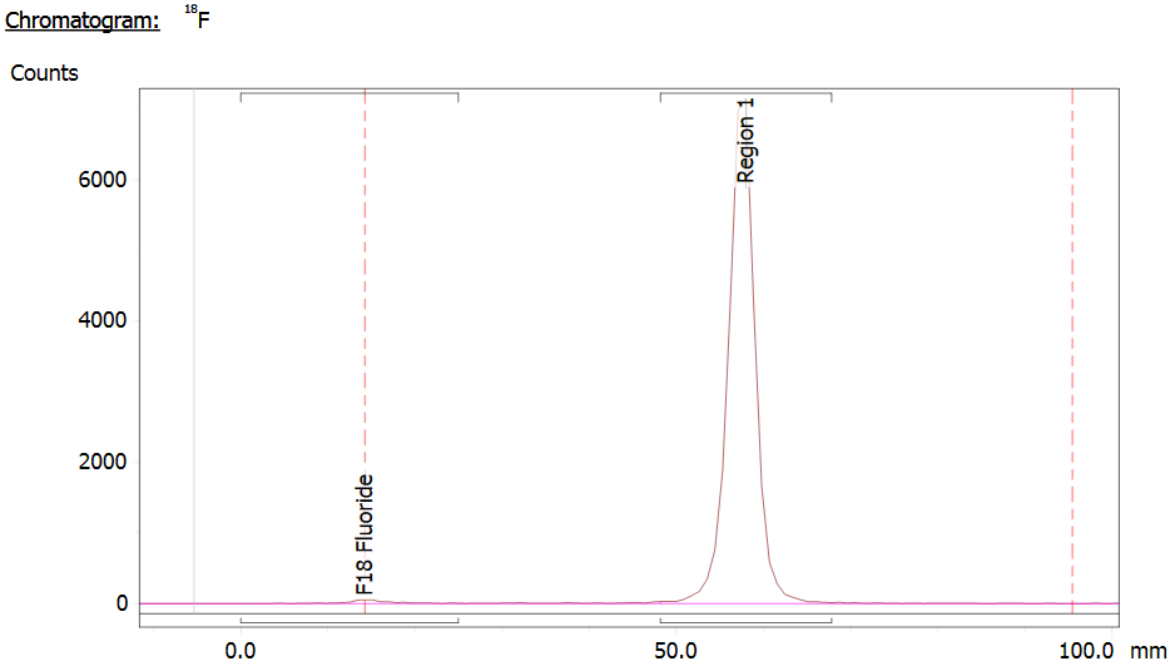
Allylic Fluoride [^{18}F] UV Retention Time: 10.533 min. (Method 4)

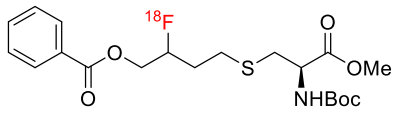
Radiochemical Yield Trials:

Trial	RCY
1	28%
2	30%
3	26%

Average: 28% +/- 2% (n = 3)

[^{18}F] Rad. TLC RCY (Isolated Product)
TLC Conditions: 8:2 Hex/EA





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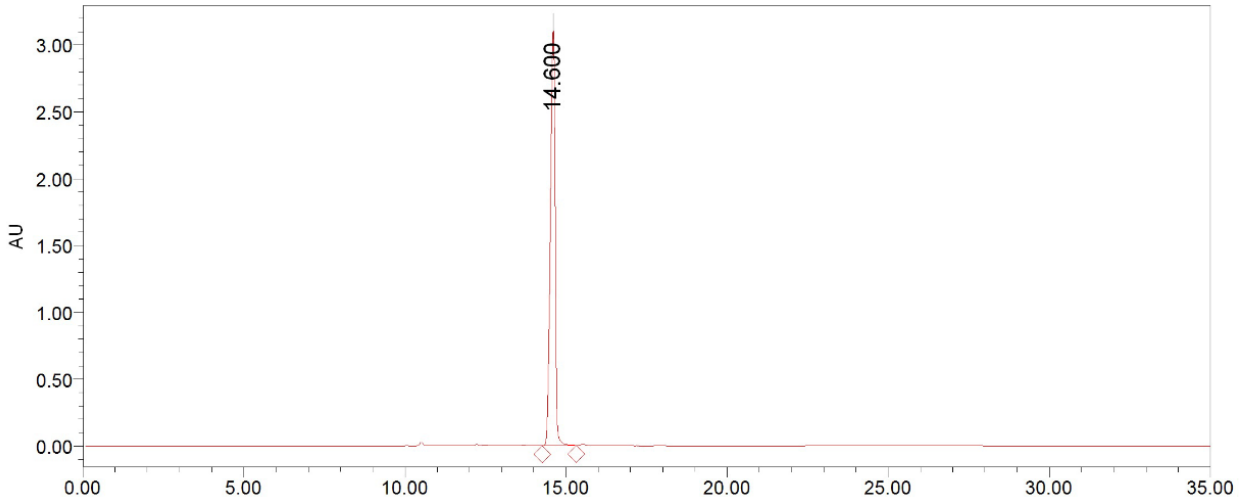
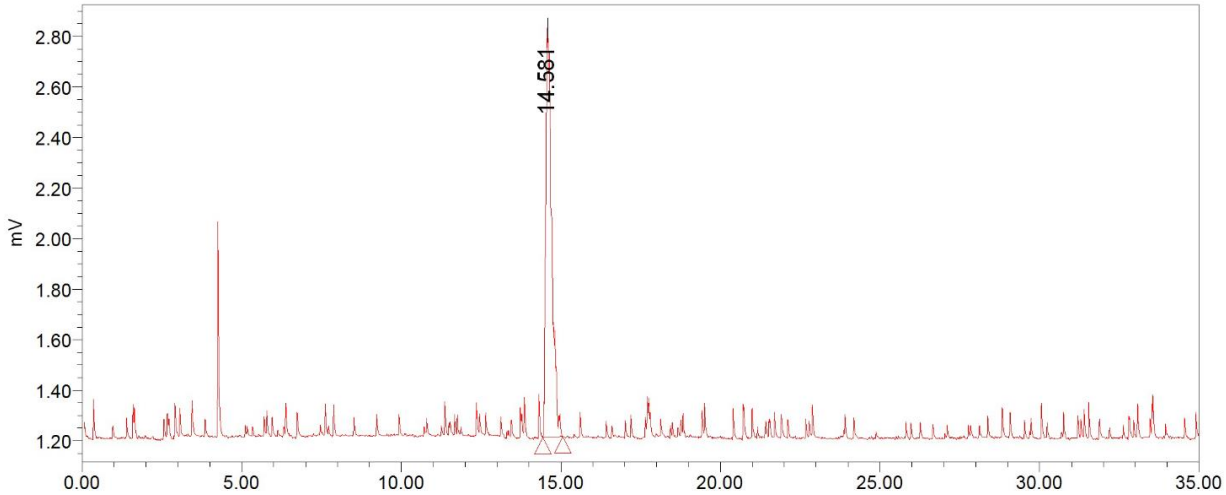
[^{19}F] Standard Allylic Fluoride

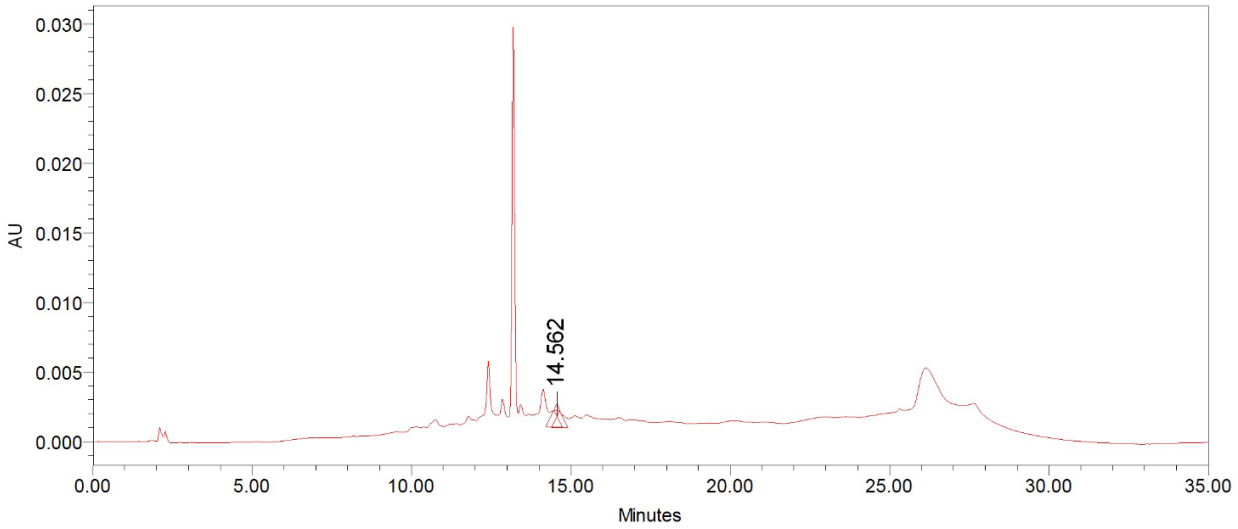


Allylic Fluoride [^{19}F] Standard Retention Time: 14.600 min. (Method 2)

[^{18}F] Rad. Allylic Fluoride:

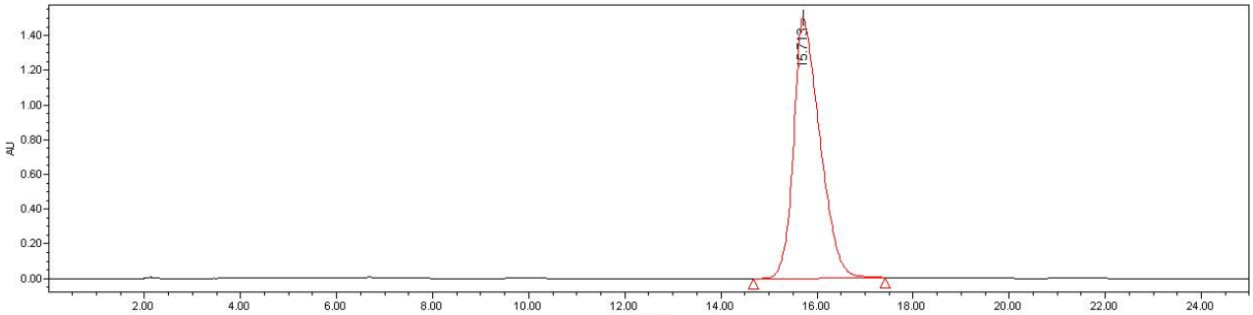


Allylic Fluoride [^{18}F] Rad. Retention Time: 14.581 min. (Method 2)



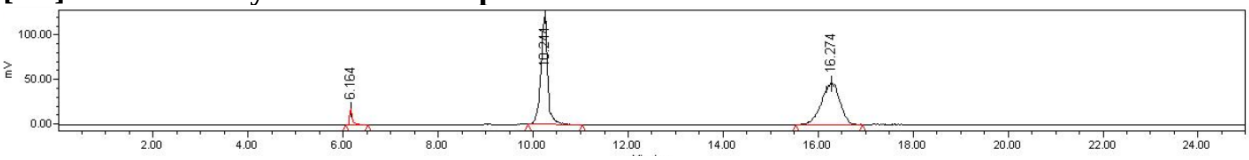
Allylic Fluoride [^{18}F] UV Retention Time: 14.562 min. (Method 1)

[^{19}F] Standard Allylic Fluoride Prep HPLC

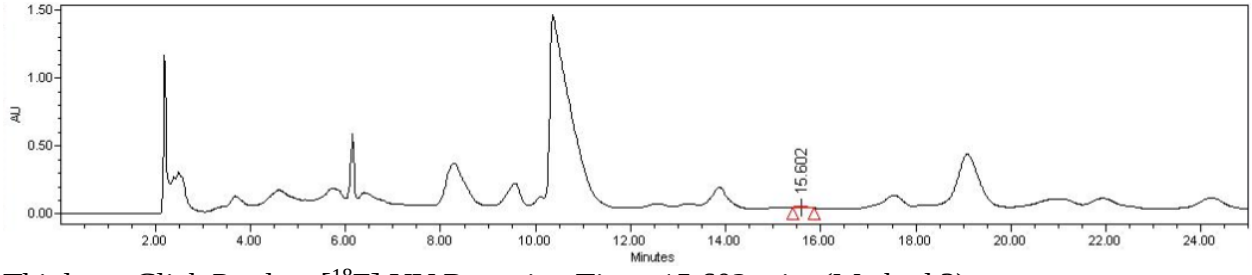


Thiol-ene Click Product [^{18}F] Rad. Retention Time: 15.713 min. (Method 3)

[^{18}F] Standard Allylic Fluoride Prep HPLC



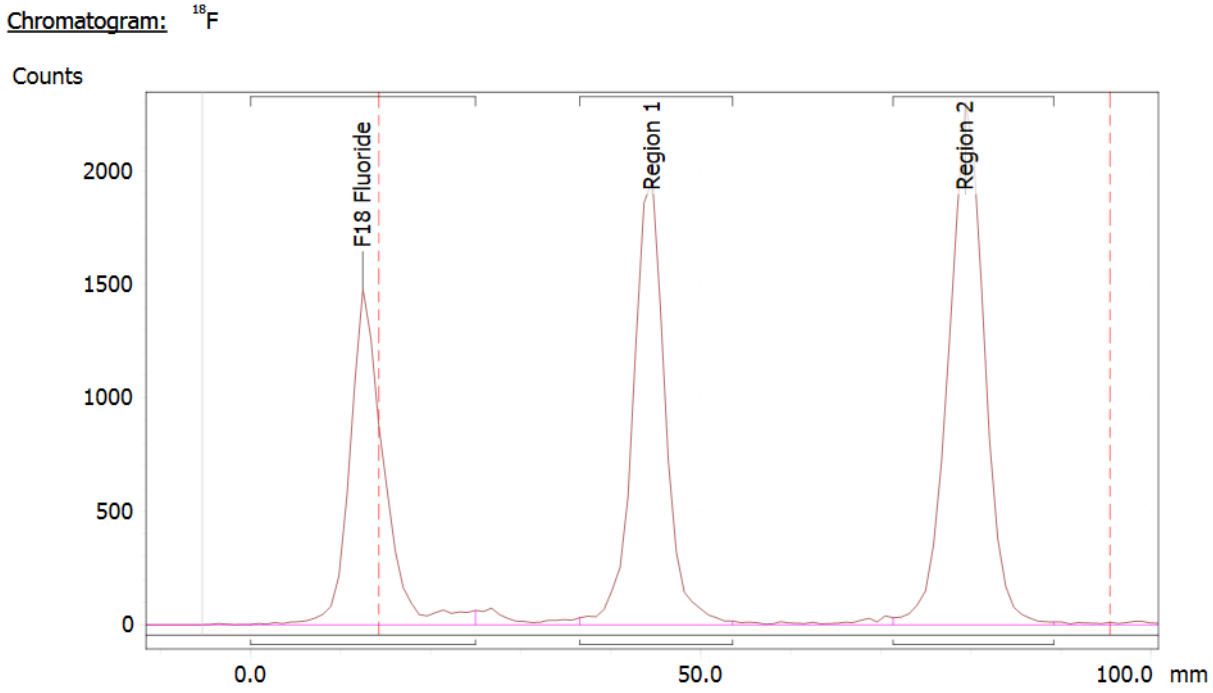
Allylic Fluoride [^{18}F] Rad. Retention Time: 10.244 min. (Method 3)
Thiol-ene Click Product [^{18}F] Rad. Retention Time: 16.274 min. (Method 3)



Thiol-ene Click Product [^{18}F] UV Retention Time: 15.602 min. (Method 3)

Run Activity: 3.02 mCi, 4.01 mCi, 3.97 mCi

[^{18}F] Rad. TLC Conversion (Crude Mixture)
TLC Conditions: 8:2 Hex/EA



Region 1: Thiol-ene click product
Region 1: Residual allylic fluoride

Radio TLC Trials:

Trial	Allylic Fluor. RCC	Thiol-ene RCC	Overall RCC
1	51%	44%	22%
2	48%	39%	19%
3	46%	40%	19%

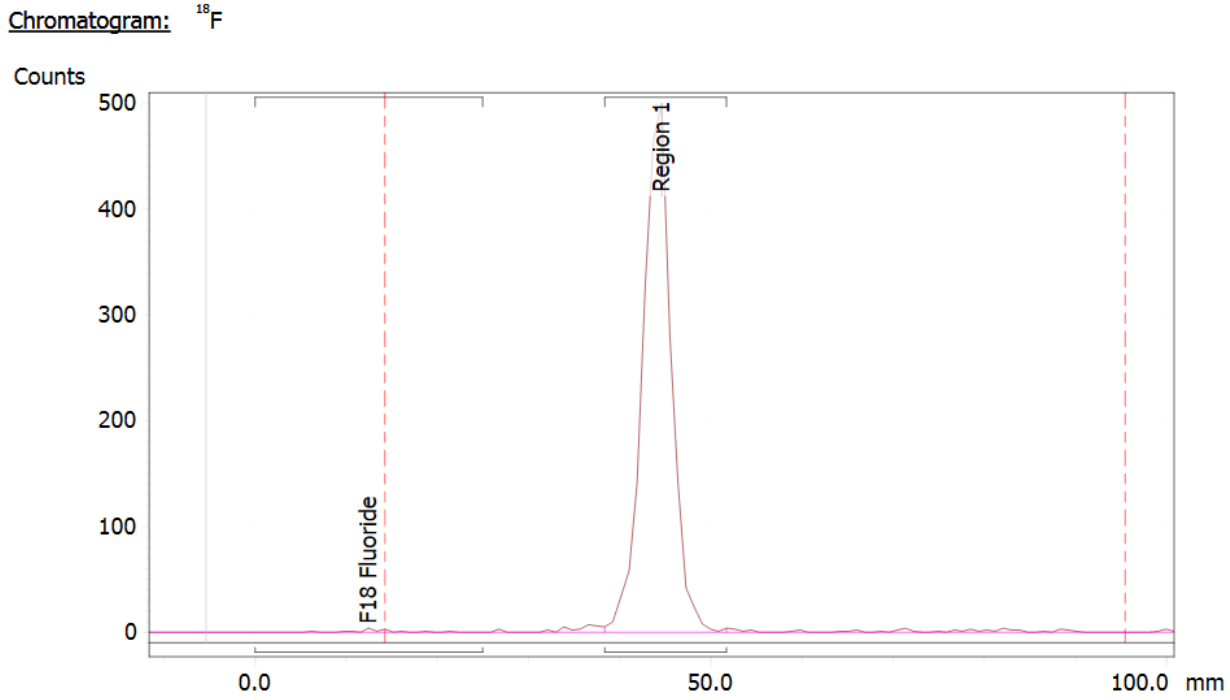
Avg Allylic Fluor RCC: 48% +/- 3% (n = 5)

Avg Thiol-ene RCC: 41% +/- 3% (n = 5)

Overall RCC: 20% +/- 2% (n = 5)

[^{18}F] Rad. TLC RCY (Purified Product)

TLC Conditions: 8:2 Hex/EA



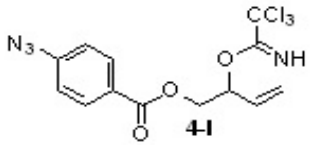
Radiochemical Yield Trials:

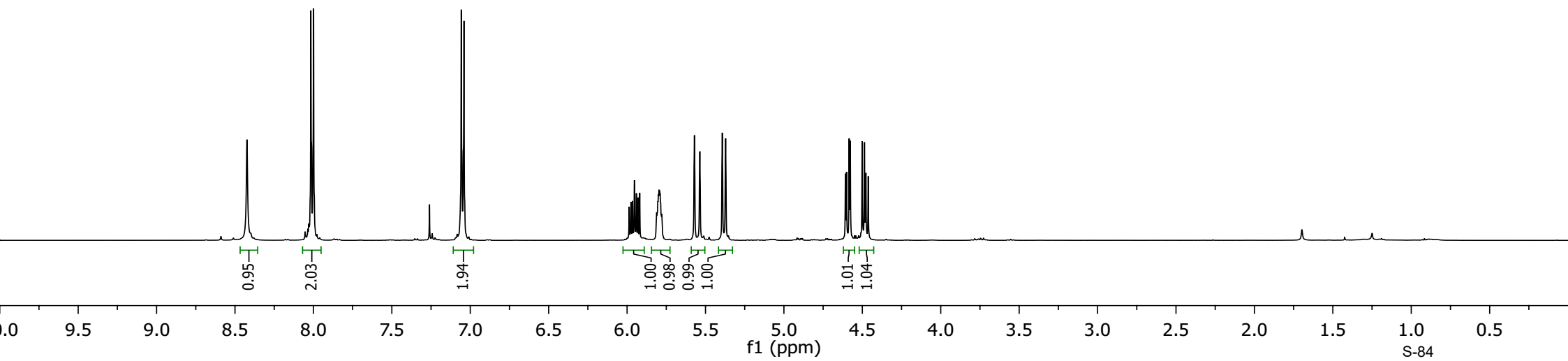
Trial	RCY
1	5%
2	4%
3	4%

Average: 4% +/- 1% (n = 3)

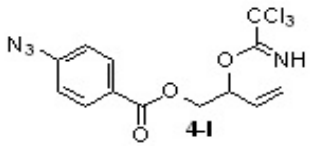
Citations:

1. J. J. Topczewski, T. J. Tewson and H. M. Nguyen, *J. Am. Chem. Soc.*, 2011, **133**, 19318-19321.
2. Q. Zhang, D. P. Stockdale, J. C. Mixdorf, J. J. Topczewski and H. M. Nguyen, *J. Am. Chem. Soc.*, 2015, **137**, 11912-11915.
3. J. C. Mixdorf, A. M. Sorlin, Q. Zhang and H. M. Nguyen, *ACS Catal.*, 2018, **8**, 790-801.

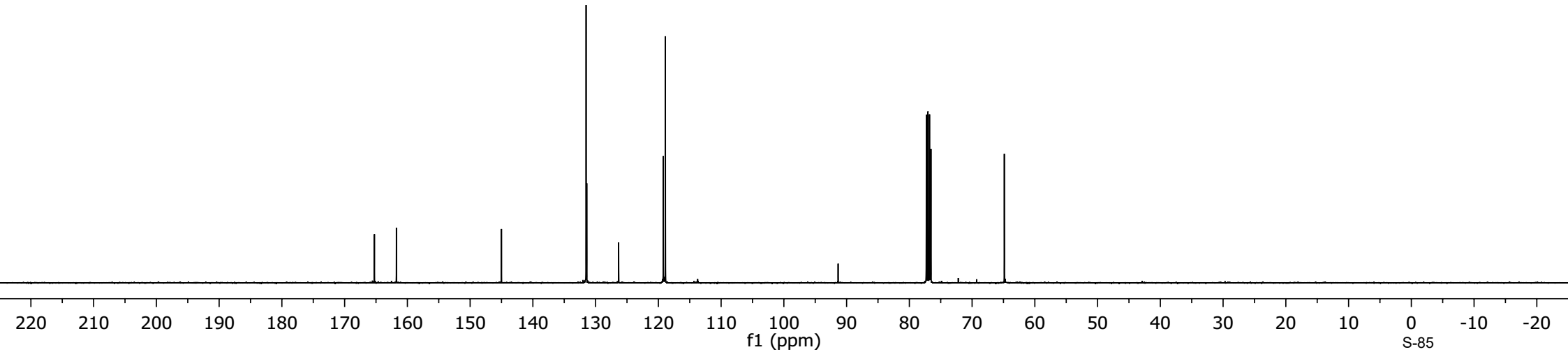




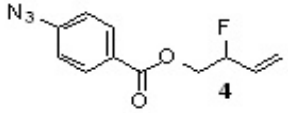
500 MHz, $CDCl_3$

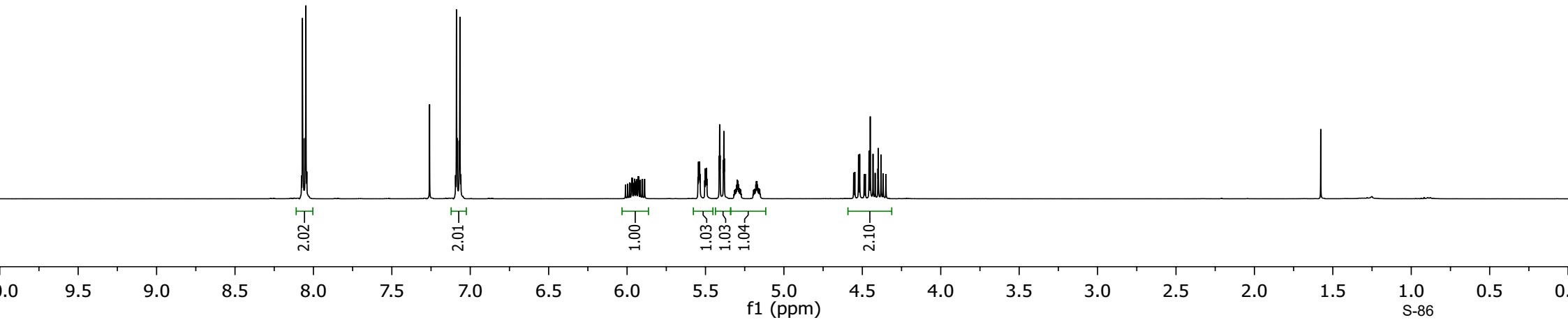


165.2
161.7
145.0
131.5
131.4
126.3
119.2
118.9
91.4
76.6
64.9

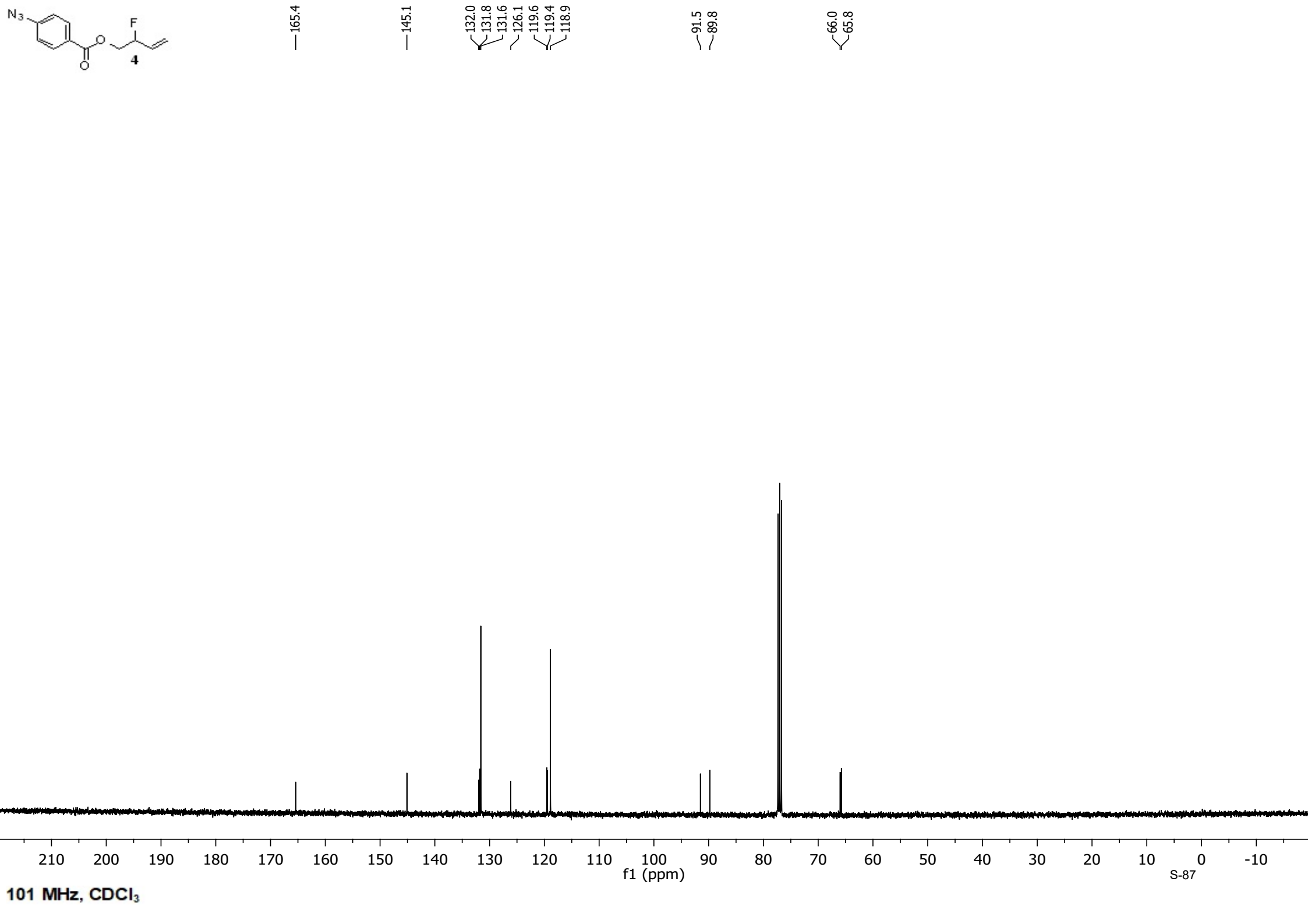


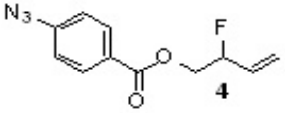
126 MHz, $CDCl_3$





400 MHz, $CDCl_3$


N3
F
O
O
4
165.4
145.1
132.0
131.8
131.6
126.1
119.6
119.4
118.9
91.5
89.8
66.0
65.8
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
101 MHz, CDCl3

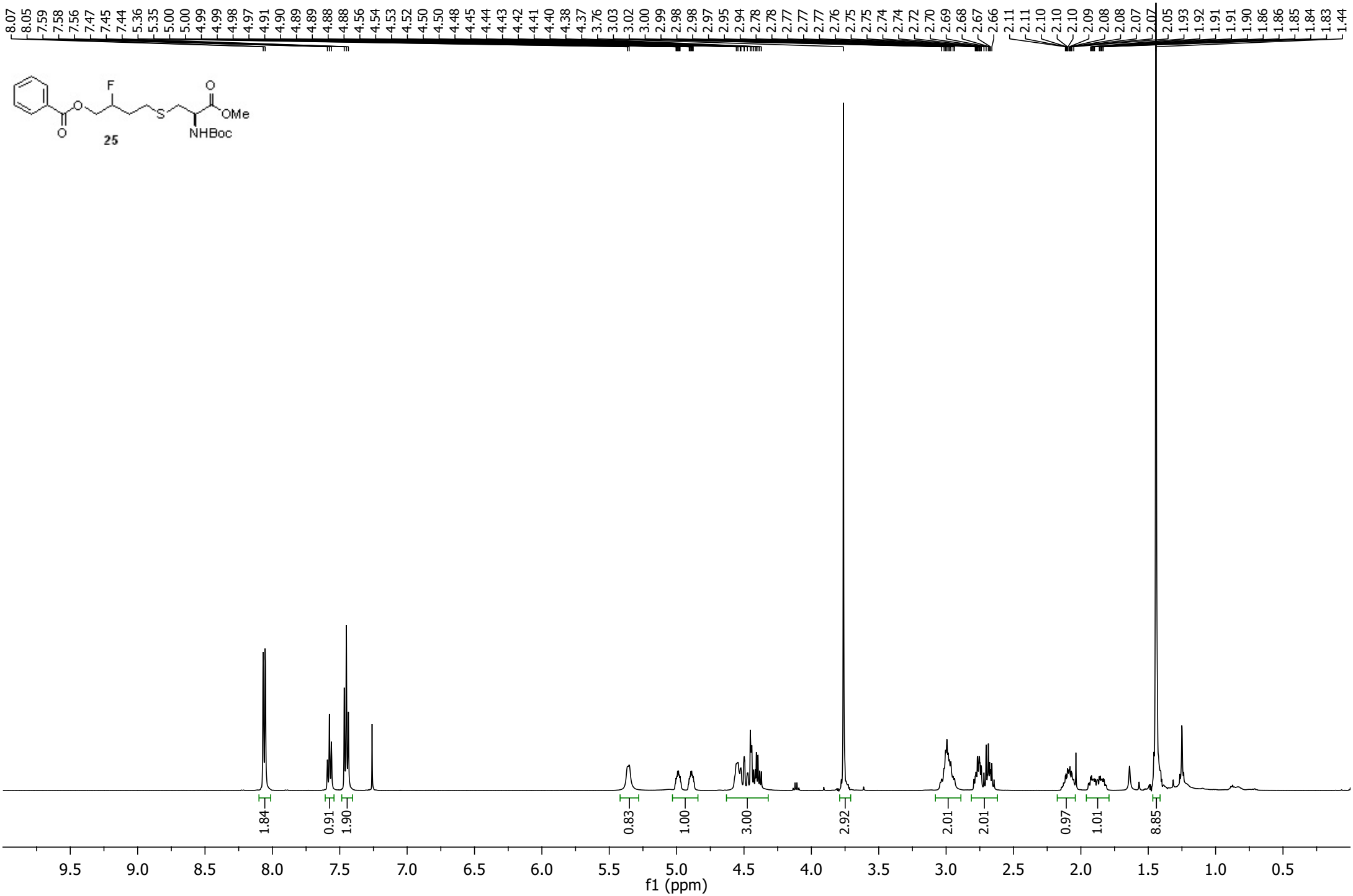


-186.1

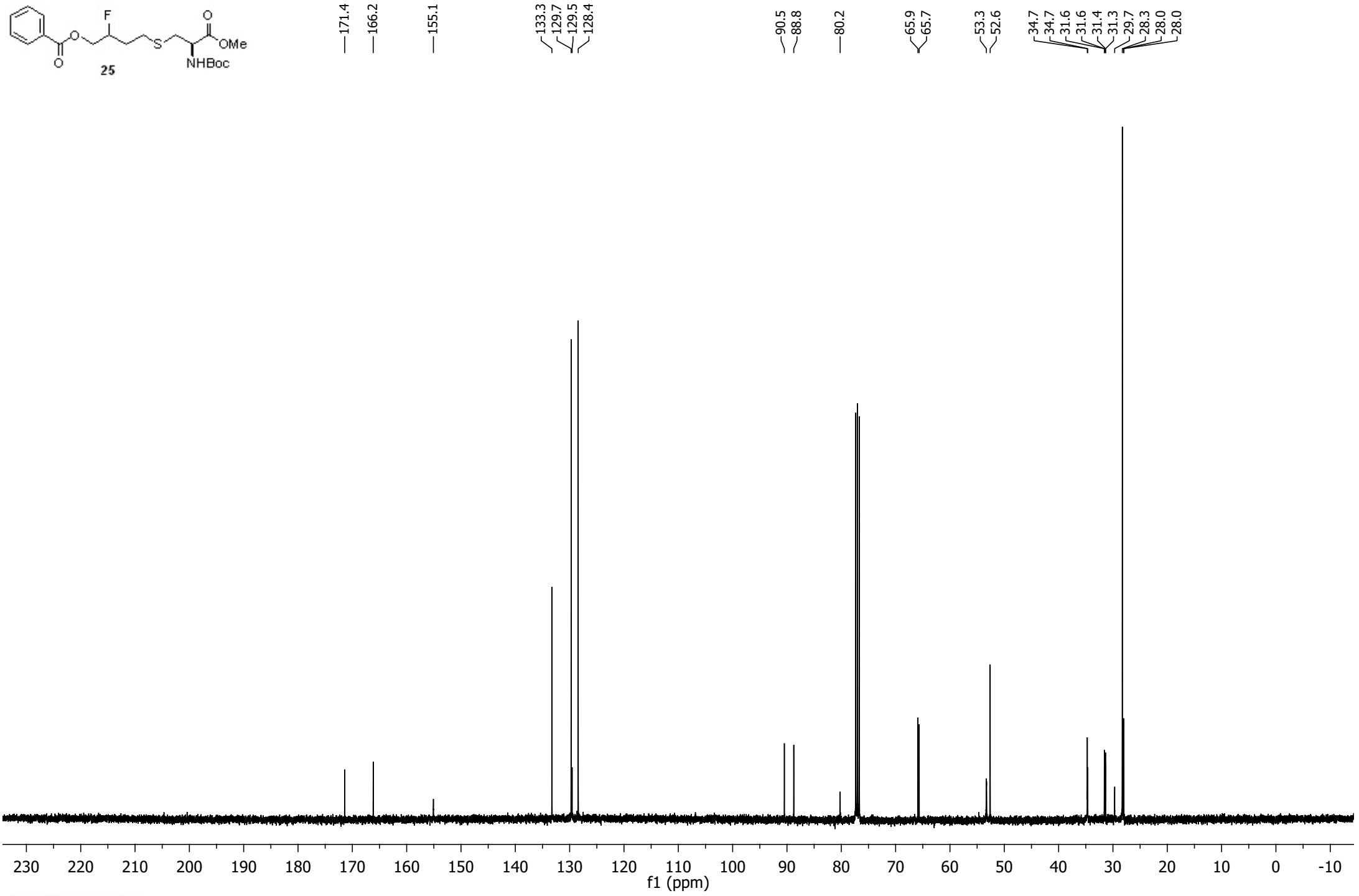
-20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240

f1 (ppm)

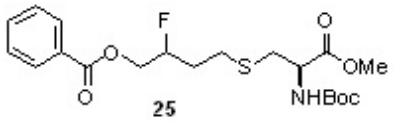
376 MHz, $CDCl_3$



500 MHz, $CDCl_3$



101 MHz, $CDCl_3$



25

-189.38
-189.44

-30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230
f1 (ppm)

471 MHz, $CDCl_3$