

Supporting information

Insights into Elution of Anion Exchange Cartridges: Opening the Path towards Aliphatic ^{18}F -Radiolabeling of Base-Sensitive Tracers

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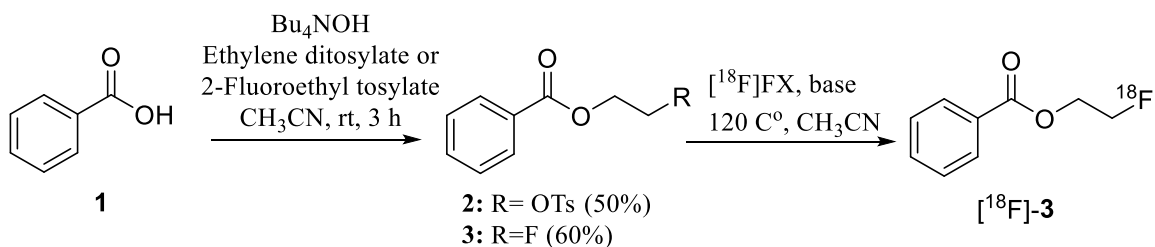
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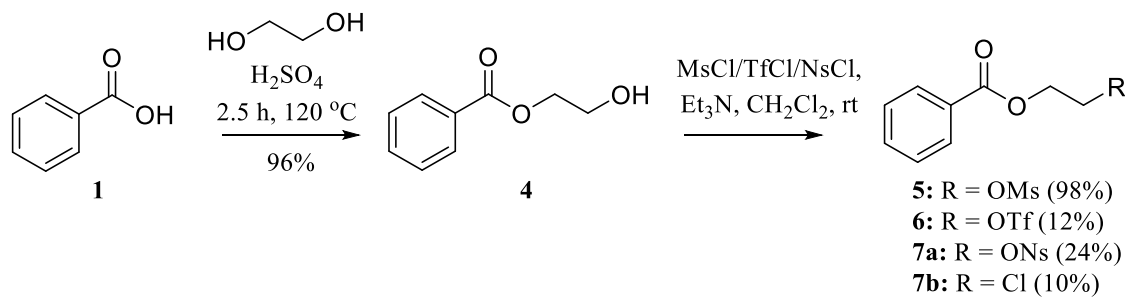
General Experimental Information, organic synthesis

Commercial reagents were used without further purification. Analytical TLC was performed using silica gel 60 F₂₅₄ (Merck) with detection by UV absorption and/or by charring following immersion in a KMnO₄ solution (1.5 g of KMnO₄, 10 g of K₂CO₃, and 1.25 mL of 10% NaOH in 200 mL of water). Purification of compounds was carried out by column chromatography on silica gel (40–60 μm, 60 Å). NMR spectra were acquired on a 600 MHz Bruker Avance III HD (600 MHz for ¹H and 151 MHz for ¹³C), a 400 MHz Bruker Avance II (400 MHz for ¹H, 376 MHz for ¹⁹F, 162 MHz for ³¹P, and 101 MHz for ¹³C), samples were measured at 300K. Chemical shift (δ) are expressed in parts per million and relative to tetramethylsilane and calibrated using solvent residual peak $\delta^1\text{H}$ 7.26, $\delta^{13}\text{C}$ 77.16. for CDCl₃ and $\delta^1\text{H}$ 2.50 and $\delta^{13}\text{C}$ 39.42 for *d*₆-DMSO. The resonance multiplicity is abbreviated as: s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet) and was analyzed using MestReNova 12.0.1. Analytical HPLC method: Thermo Fisher UltiMate 3000 with a C-18 column (Luna 5 μm C18(2) 100 Å, 150 mm × 4.6 mm). Eluents: A, H₂O with 0.1% TFA; B, MeCN with 0.1% TFA. Gradient from 100% A to 100% B over 15 min, back to 100% A over 4 min, flow rate 1.5 mL/min. Detection by UV absorption at λ = 254 nm if nothing else stated on a UVD 170U detector. Preparative high-performance liquid chromatography (HPLC) was performed on a Thermo Scientific Dionex 3000 UltiMate instrument connected to a Thermo Scientific Dionex 3000 Diode Array Detector using a Gemini-NX 5μ RP C18 column (250 × 21.2 mm) with UV detection at 254 nm. Mobile phase A: 0.1% TFA in water. Mobile phase B: 0.1% TFA, 10% water in MeCN. Flow rate: 20 mL/min, using a gradient from 100% A → 100% B over 15 min. Melting points were determined using a Büchi Melting Point B-540 apparatus. High resolution mass spectrometry (HRMS) was performed as matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF). Analyses were performed in either positive or negative ion mode with ionization on a ThermoQExactive Orbitrap mass spectrometer (Thermo Scientific) equipped with an AP-SMALDI 10 ion source (TransmitMIT) and operated with mass resolving power 140,000 at *m/z* 200 and lock-mass for internal mass calibration. Samples were dissolved in a matrix consisting of 2,5-dihydroxybenzoic acid, 20 mg/mL, (positive mode) or 1,5-diaminonaphthalene, 5 mg/mL (negative mode). All the reference compounds and precursors were tested for purity using analytical HPLC-UV. Analytical HPLC method: Thermo Fisher UltiMate 3000 with a C-18 column (Luna 5 μm C18(2) 100 Å, 150 mm × 4.6 mm). Eluents: A, H₂O with 0.1% TFA; B, MeCN with 0.1% TFA. Gradient from 100% A to 100% B over 15 min, back to 100% A over 4 min, flow rate 1.5 mL/min. Detection by UV absorption at λ = 254 nm if nothing else stated on a UVD 170U detector. All the compounds showed a purity \geq 95%. Chemicals were purchased from ABX, PharmaSynth Fluorochem, Sigma or Merck and used as received.

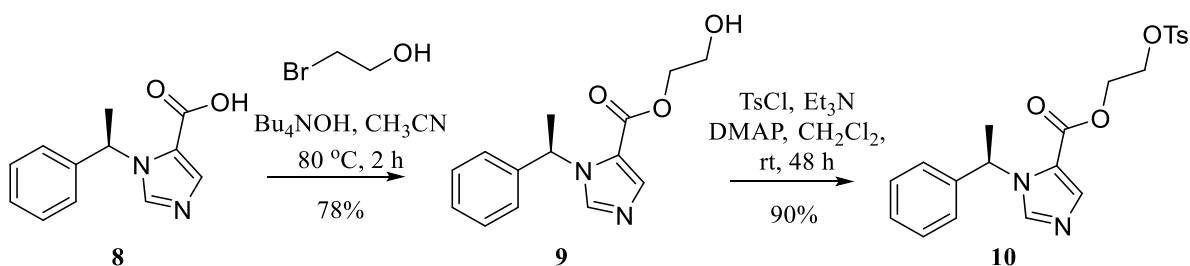
Synthetic schemes for precursor and references



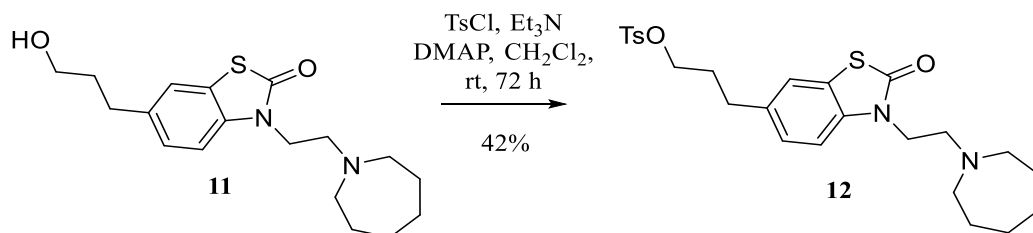
Scheme S1 Synthesis and radiolabeling of precursor **2**.



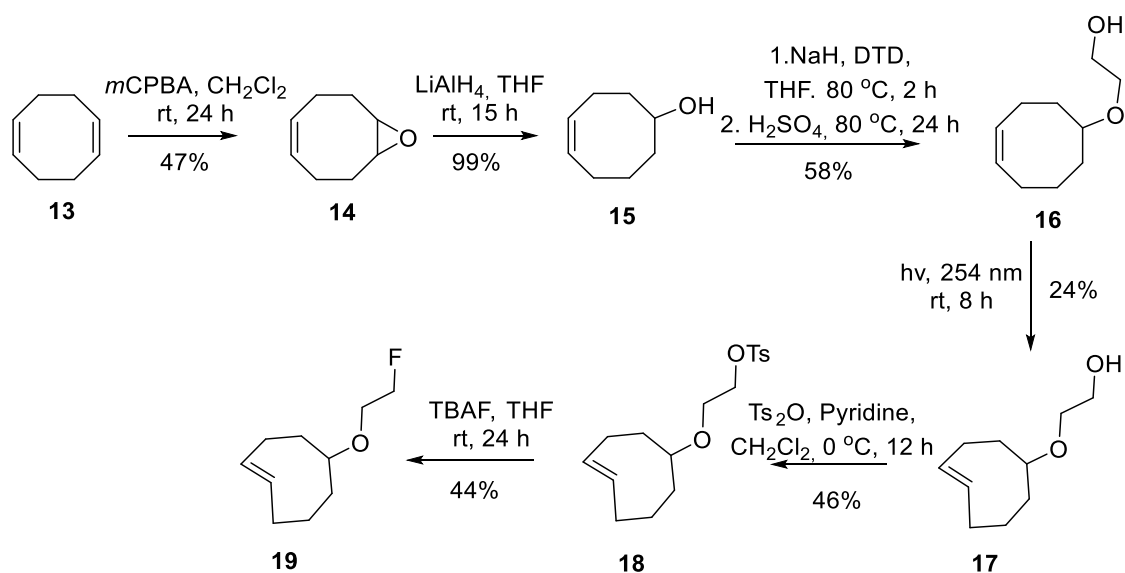
Scheme S2 Synthesis of precursors **5**, **6** and **7a-b** to investigate the influence of different leaving groups.



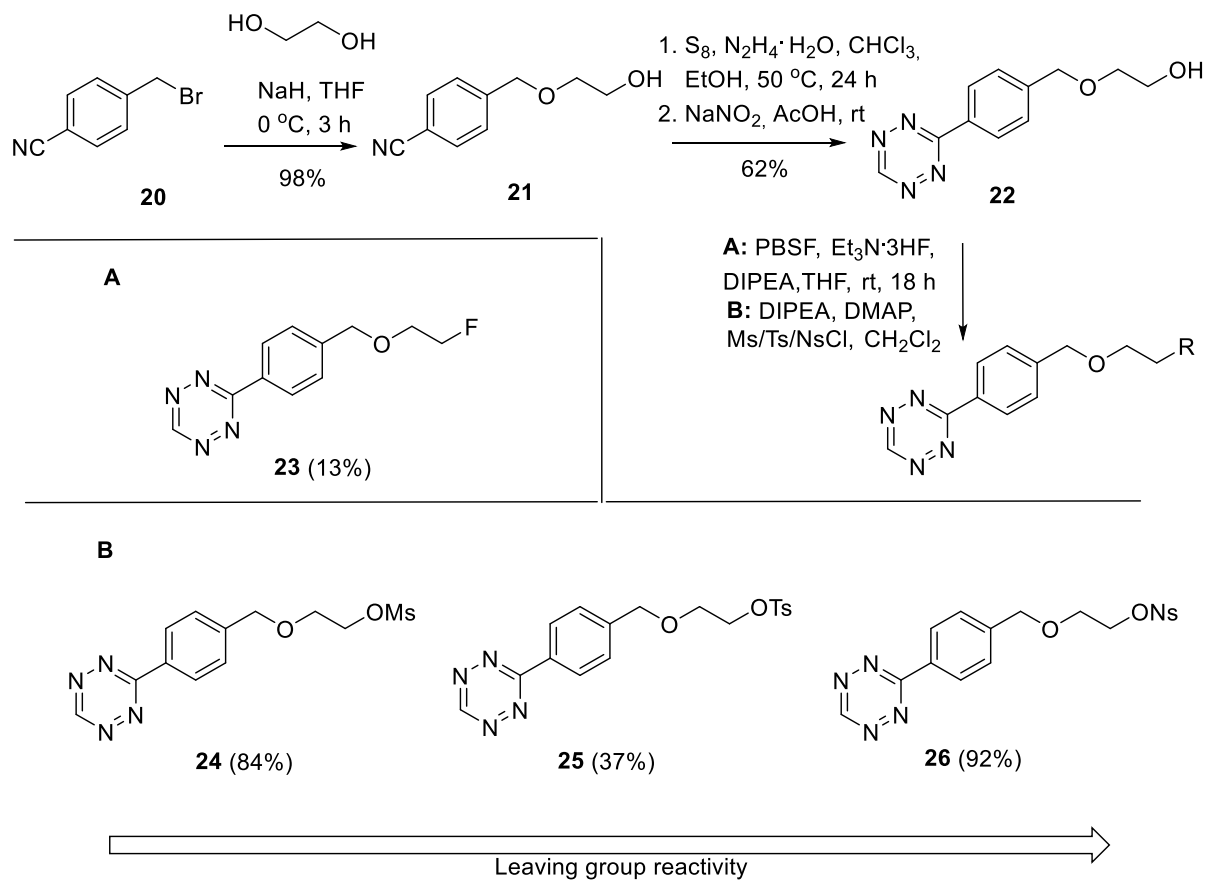
Scheme S3 Synthetic route to obtain $[\text{}^{18}\text{F}]\text{FETO}$ precursor **10**.



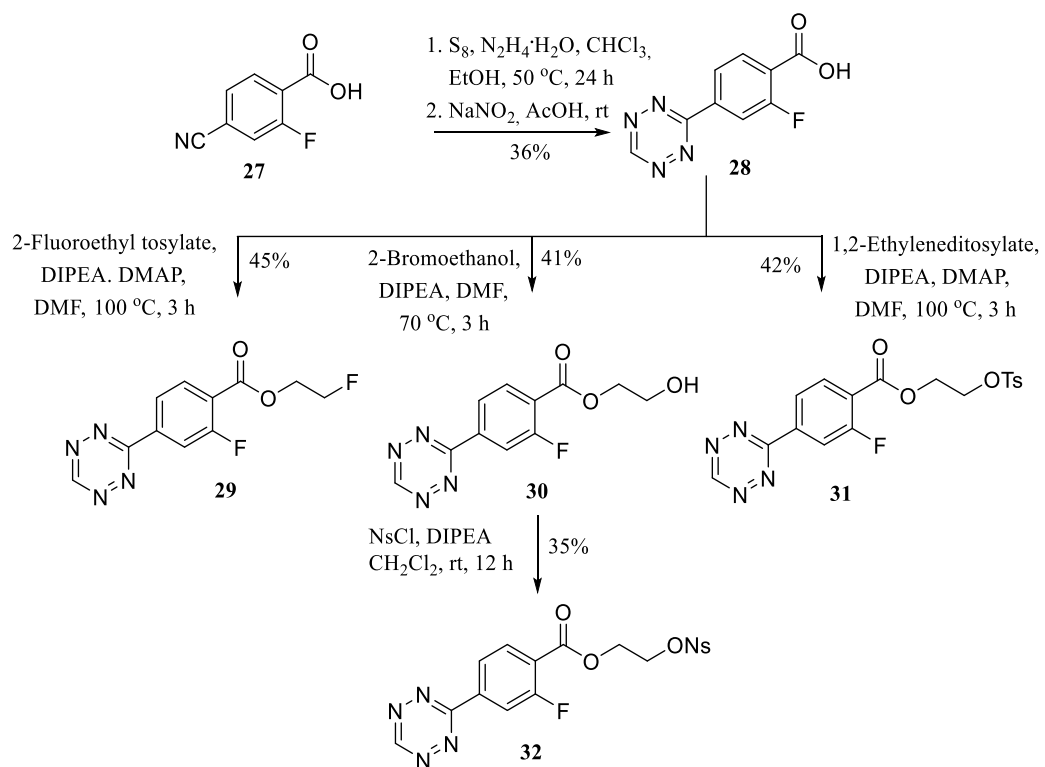
Scheme S4 Synthetic route to obtain $[\text{}^{18}\text{F}]\text{FTC-146}$ precursor **12**.



Scheme S5 Synthetic route to obtain precursor **18** and reference **19** for labeling of [¹⁸F]-2-fluoroethyl-TCO.



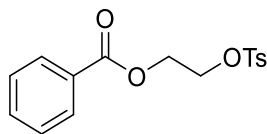
Scheme S6 Synthetic route to obtain reference **23** and precursors **24, 25** and **26**.



Scheme S7 Synthesis of reference **29** and precursors **31** and **32**.

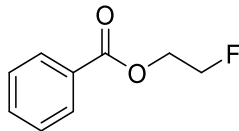
Organic synthesis of precursors and references

2-(Tosyloxy)ethyl benzoate (2)



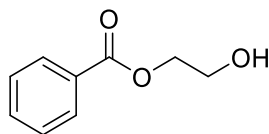
Benzoic acid (150 mg, 1.23 mmol 1.00 equiv.) was mixed with Bu₄NOH (40% wt in MeOH, 1.20 mL, 1.84 mmol, 1.50 equiv.). Subsequently, H₂O (2 mL) and toluene (2 mL) were added and the resulting mixture was stirred for 5 minutes. The volatiles were then removed under reduced pressure. The residue was redissolved in 5 mL of dry MeCN and cooled to 0 °C. Ethane-1,2-diyl bis(4-methylbenzenesulfonate) (683 mg, 1.84 mmol, 1.50 equiv.) was dissolved in 10 mL of dry MeCN and added to the reaction. The mixture was allowed to slowly reach room temperature and left for 3 additional hours. The reaction was then quenched with NH₄Cl (sat., 20 mL) and extracted with EtOAc (3 x 20 mL). The organic phase was washed with brine (2 x 20 mL), dried over MgSO₄ and concentrated under reduced pressure. Purification by flash chromatography (n-heptane/EtOAc 70:30) yielded 2-(tosyloxy)ethyl benzoate (195 mg, 0.61 mmol, 50%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 7.98 – 7.91 (m, 2H), 7.82 – 7.75 (m, 2H), 7.61 – 7.54 (m, 1H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.30 – 7.23 (m, 2H), 4.52 – 4.32 (m, 4H), 2.38 (s, 3H); ¹³C NMR (151 MHz, CDCl₃) δ 166.18, 145.13, 133.45, 132.96, 130.06, 129.91, 129.53, 128.52, 128.08, 67.88, 62.21, 21.79; HRMS (MALDI-TOF) calculated for C₁₆H₁₆O₅S⁺ [M+Na]⁺: 343.0610, found: 343.0610; Mp: 72-74 °C.

2-Fluoroethyl benzoate (3)



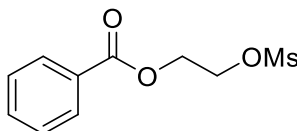
Benzoic acid (47 mg, 0.38 mmol 1.00 equiv.) was mixed with Bu₄NOH (40% wt in MeOH, 408 μL, 0.57 mmol, 1.5 equiv.). Subsequently, H₂O (2 mL) and toluene (2 mL) were added and the resulting mixture was stirred for 5 minutes. The volatiles were then removed under reduced pressure. The residue was redissolved in 5 mL of dry MeCN and cooled to 0 °C. 2-Fluoroethyltosylate (100 mg, 0.46 mmol, 1.2 equiv.) was dissolved in 1 mL of dry MeCN and added to the reaction dropwise under argon. The mixture was allowed to slowly reach room temperature and left for 3 additional hours. The reaction was diluted with EtOAc (20 mL) and washed with brine (2 x 20 mL) and water (2 x 20 mL). The organic phase was dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (n-heptane/EtOAc 70:30) yielded 2-fluoroethyl benzoate (36 mg, 0.21 mmol, 56%) as a clear liquid. ¹H NMR (400 MHz, CDCl₃) δ 8.16 – 8.06 (m, 2H), 7.64 – 7.53 (m, 1H), 7.51 – 7.40 (m, 2H), 4.85 – 4.75 (m, 1H), 4.72 – 4.65 (m, 1H), 4.63 – 4.58 (m, 1H), 4.56 – 4.50 (m, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 166.53, 133.38, 129.91, 129.85, 128.57, 81.58 (*J*_{C-F} = 170.8 Hz), 63.98 (*J*_{C-F} = 20.2 Hz); ¹⁹F NMR (376 MHz, CDCl₃) δ -224.53; HRMS (MALDI-TOF) calculated for C₉H₉FO₂⁺ [M+H]⁺: 169.0659, found: 169.0653.

2-Hydroxyethyl benzoate (4)



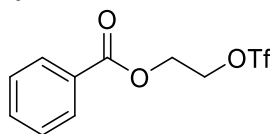
Sulfuric acid (0.5 mL, 0.5 equiv.) was added to a mixture of benzoic acid (2.40 g, 19.65 mmol, 1.00 equiv.) and ethylene glycol (5.40 g, 87.00 mmol, 4.43 equiv.). The mixture was heated to 120 °C and left stirring for 2.5 h. The mixture was cooled and quenched carefully with H₂O (40 mL). The mixture was neutralized with a sat. solution of NaHCO₃, further diluted with 60 mL of H₂O and extracted with EtOAc (3 x 100 mL). The organic phase was dried over MgSO₄, filtered, and concentrated under reduced pressure yielding 2-hydroxyethyl benzoate (3.14 g, 18.90 mmol, 96%) as a pale semisolid. The compound was used without further purification in the following reactions.

2-((Methylsulfonyl)oxy)ethyl benzoate (5)



2-Hydroxyethyl benzoate (400 mg, 2.41 mmol, 1.00 equiv.) was dissolved in 5 mL of dry CH₂Cl₂. Et₃N (504 μL, 3.61 mmol, 1.50 equiv.) and methanesulfonyl chloride (280 μL, 3.61 mmol, 1.50 equiv.) were added at 0 °C under argon atmosphere. The reaction was allowed to reach room temperature and then stirred for additional 60 minutes. The crude was diluted with 30 mL of CH₂Cl₂ and then quenched with 20 mL of H₂O. The aqueous phase was extracted with CH₂Cl₂ (2 x 20 mL) and the combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (n-heptane/EtOAc, 50:50) yielded 2-((methylsulfonyl)oxy)ethyl benzoate (580 mg, 2.37 mmol, 98%) as an off-white solid. ¹H NMR (600 MHz, CDCl₃) δ 8.06 (dt, *J* = 8.4, 1.1 Hz, 2H), 7.59 (ddt, *J* = 7.8, 6.9, 1.3 Hz, 1H), 7.49 – 7.43 (m, 2H), 4.62 – 4.58 (m, 2H), 4.58 – 4.54 (m, 2H), 3.06 (s, 3H); ¹³C NMR (151 MHz, CDCl₃) δ 166.28, 133.56, 129.89, 129.51, 128.66, 67.25, 62.48, 37.97; HRMS (MALDI-TOF) calculated for C₁₀H₁₂O₅S⁺ [M+Na]⁺: 267.0297, found: 267.0299; Mp: 53 °C.

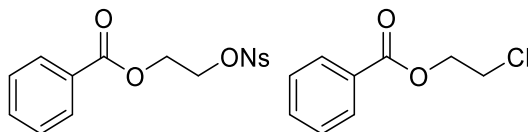
2-(((Trifluoromethane)sulfonyl)oxy)ethyl benzoate (6)



2-Hydroxyethyl benzoate (400 mg, 2.41 mmol, 1.00 equiv.) was dissolved in 5 mL of dry CH₂Cl₂ and Et₃N (504 μL, 3.61 mmol, 1.50 equiv.) and trifluoromethanesulfonyl chloride (381 μL, 3.61 mmol, 1.50 equiv.) was added at 0 °C under argon atmosphere. The reaction was allowed to reach room temperature and then stirred for additional 3 hours. The crude was diluted with 30 mL of CH₂Cl₂ and then quenched with 20 mL H₂O. The aqueous phase was extracted with CH₂Cl₂ (2 x 20 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (n-heptane/EtOAc, 70:30) yielded 2-(((trifluoromethane)sulfonyl)oxy)ethyl benzoate (85 mg, 0.29 mmol, 12%) as a pale semisolid. ¹H NMR (400 MHz, CDCl₃) δ 8.11 – 8.04 (m, 2H), 7.58

(td, $J = 7.3, 1.3$ Hz, 1H), 7.50 – 7.41 (m, 2H), 4.58 (dd, $J = 6.3, 5.2$ Hz, 2H), 3.82 (dd, $J = 6.3, 5.2$ Hz, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 166.34, 133.42 (2C), 129.90, 129.79, 128.59, 64.60, 41.82; ^{19}F NMR (376 MHz, CDCl_3) δ -78.40; HRMS (MALDI-TOF) calculated for $\text{C}_{10}\text{H}_{10}\text{F}_3\text{O}_5\text{S}$ $[\text{M}+\text{H}]^+$: 299.0195, found: 299.0197.

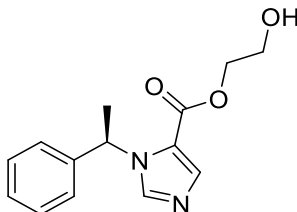
2-[[4-Nitrobenzene)sulfonyl]oxy]ethyl benzoate (7a) and 2-Chloroethyl benzoate (7b)



2-Hydroxyethyl benzoate (150 mg, 0.90 mmol, 1.00 equiv.) and nitrobenzenesulfonyl chloride (600 mg, 2.71 mmol, 3.00 equiv.) were dissolved in 10 mL of dry CH_2Cl_2 under argon at 0 °C. A mixture of DIPEA (629 μL , 3.61 mmol, 4.00 equiv.) and DMAP (22 mg, 0.18 mmol, 0.20 equiv.) in 3 mL of dry CH_2Cl_2 was subsequently added under argon and the reaction was slowly allowed to reach room temperature and stirred for additional 3 hours. The reaction was diluted with 10 mL of CH_2Cl_2 and washed with a saturated solution of NH_4Cl (20 mL) and H_2O (2 x 20 mL). The organic phase was dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. Purification by flash chromatography (n-heptane/EtOAc, 60:40) and recrystallization in EtOAc/n-heptane yielded 2-[[4-nitrobenzene)sulfonyl]oxy]ethyl benzoate (76 mg, 0.22 mmol, 24%) as an off-white solid. ^1H NMR (600 MHz, CDCl_3) δ 8.27 – 8.21 (m, 2H), 8.10 – 8.04 (m, 2H), 7.90 – 7.84 (m, 2H), 7.58 (tt, $J = 7.4, 1.3$ Hz, 1H), 7.45 – 7.37 (m, 2H), 4.55 – 4.50 (m, 4H). ^{13}C NMR (151 MHz, CDCl_3) δ 165.97, 150.77, 141.78, 133.81, 129.74, 129.27, 129.12, 128.62, 124.58, 69.16, 61.90.; HRMS (MALDI-TOF) calculated for $\text{C}_{15}\text{H}_{13}\text{NO}_7\text{S}$ $[\text{M}+\text{H}]^+$: 352.0485, found: 352.0490; Mp: 135-137 °C.

During flash chromatography 2-chloroethyl benzoate was also isolated (17 mg, 0.09 mmol, 10%) as a clear liquid. ^1H NMR (600 MHz, CDCl_3): δ 8.09 – 8.05 (m, 2H), 7.60 – 7.55 (m, 1H), 7.48 – 7.42 (m, 2H), 4.60 – 4.55 (m, 2H), 3.84 – 3.79 (m, 2H); ^{13}C NMR (151 MHz, CDCl_3) δ 166.31, 133.40, 129.88, 129.77, 128.58, 64.58, 41.80; HRMS (MALDI-TOF) calculated for $\text{C}_9\text{H}_9\text{ClO}_2$ $[\text{M}+\text{H}]^+$: 184.0291, found: 184.0285.

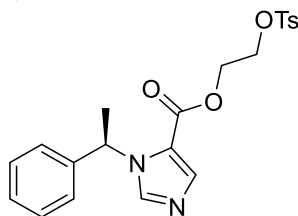
2-Hydroxyethyl 1-[(1R)-1-phenylethyl]-1H-imidazole-5-carboxylate (9)



(*R*)-1-(1-phenylethyl)-1*H*-imidazole-5-carboxylic acid (30 mg, 0.14 mmol, 1.00 equiv.) was dissolved in CH_2Cl_2 (2 mL) and Bu_4NOH (40% in MeOH, 99 μL , 0.15 mmol, 1.10 equiv.) was added. The solution was concentrated under reduced pressure. The residue was dissolved in 2 mL CH_2Cl_2 and concentrated again two times. The dried reagents were redissolved in 2 mL of dry MeCN under argon. 2-Bromoethanol (43 μL , 0.61 mmol, 4.40 equiv.) was dissolved in 0.5 mL of dry MeCN and added to the reaction under argon. The reaction was heated to reflux for 2 h. The solution was diluted with CH_2Cl_2 (10 mL) and washed with sat. NaHCO_3 solution (10 mL). The organic phase was dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. Purification by flash chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 95:5)

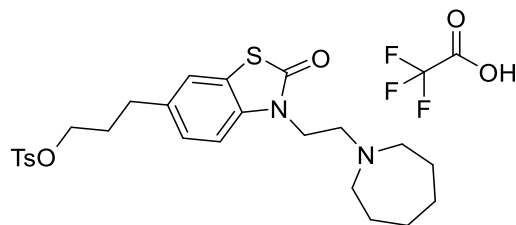
yielded 2-hydroxyethyl 1-[(1*R*)-1-phenylethyl]-1*H*-imidazole-5-carboxylate (28 mg, 0.11 mmol, 78%) as a clear oil. ¹H NMR (400 MHz, CDCl₃) δ 7.84 – 7.73 (m, 2H), 7.36 – 7.24 (m, 3H), 7.21 – 7.14 (m, 2H), 6.33 (q, *J* = 7.1 Hz, 1H), 4.41 – 4.25 (m, 2H), 3.85 (t, *J* = 4.6 Hz, 2H), 3.79 (s, 1H), 1.84 (d, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 160.31, 140.84, 139.85, 137.81, 129.01, 128.25, 126.39, 122.47, 66.54, 60.72, 55.72, 22.25; HRMS (MALDI-TOF) calculated for C₁₄H₁₆N₂O₃ [M+H]⁺: 261.1233, found: 261.1236.

2-(Tosyloxy)ethyl (*R*)-1-(1-phenylethyl)-1*H*-imidazole-5-carboxylate (10)



2-Hydroxyethyl 1-[(1*R*)-1-phenylethyl]-1*H*-imidazole-5-carboxylate (28 mg, 0.11 mmol, 1.00 equiv.) and tosyl chloride (92 mg, 0.48 mmol, 5.00 equiv.) were dissolved in dry CH₂Cl₂ (2 mL). Et₃N (67 μL, 0.48 mmol, 5.00 equiv.) and DMAP (1 mg, 0.01 mmol, 0.10 equiv.) were solubilized in 0.5 mL of dry CH₂Cl₂ and added under argon at 0 °C. The reaction was allowed to reach room temperature and left stirring for additional 2 days. The reaction was then diluted with CH₂Cl₂ (10 mL), washed with a NH₄Cl saturated solution (10 mL) and H₂O (2 x 10 mL). The organic phase was dried over Na₂SO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (CH₂Cl₂/MeOH, 97:3) yielded 2-(tosyloxy)ethyl (*R*)-1-(1-phenylethyl)-1*H*-imidazole-5-carboxylate (36 mg, 0.09 mmol, 90%) as a pale semisolid. ¹H NMR (600 MHz, CDCl₃) δ 7.87 – 7.82 (m, 1H), 7.79 – 7.74 (m, 2H), 7.67 (d, *J* = 1.1 Hz, 1H), 7.37 – 7.27 (m, 5H), 7.20 – 7.15 (m, 2H), 6.28 (q, *J* = 7.1 Hz, 1H), 4.39 (qdd, *J* = 12.5, 5.1, 4.0 Hz, 2H), 4.28 (ddd, *J* = 5.6, 3.7, 1.5 Hz, 2H), 2.43 (s, 3H), 1.85 (d, *J* = 7.3 Hz, 3H); ¹³C NMR (151 MHz, CDCl₃): δ 159.33, 145.33, 140.57, 139.88, 137.73, 132.84, 130.08, 129.12, 128.42, 128.03, 126.43, 121.94, 67.45, 61.79, 56.01, 22.26, 21.79; HRMS (MALDI-TOF) calculated for C₂₁H₂₂N₂O₅S [M+H]⁺: 415.1322, found: 415.1321.

1-(2-(2-Oxo-6-(3-(tosyloxy)propyl)benzo[*d*]thiazol-3(2*H*)-yl)ethyl)azepan-1-ium 2,2,2-trifluoroacetate (12)



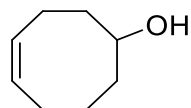
Tosyl chloride (103 mg, 0.54 mmol, 3.00 equiv.) was dissolved in 2 mL of dry CH₂Cl₂, DIPEA (125 μL, 0.72 mmol, 4.00 equiv.) and DMAP (5 mg, 0.04 mmol, 0.20 equiv.) were then added. 3-(2-(Azepan-1-yl)-6-(3-hydroxypropyl)benzo[*d*]thiazol-2(3*H*)-one (60 mg, 0.18 mmol) was dissolved in 1 mL of dry CH₂Cl₂ and added dropwise under argon. The resulting mixture was left at room temperature for 3 days.

The crude was diluted with CH₂Cl₂ (20 mL) and washed with a NH₄Cl saturated solution (10 mL) and water (2 x 10 mL). The organic phase was dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by preparative HPLC (gradient: MeCN/H₂O + 0.1% TFA 0:100 → 90:10), yielded 3-(3-(2-(azepan-1-yl)ethyl)-2-oxo-2,3-dihydrobenzo[*d*]-thiazol-6-yl)propyl 4-methylbenzenesulfonate as a TFA salt (46 mg, 0.08 mmol, 42%, yellow oil). Starting material was also recovered during the purification (20 mg). ¹H NMR (600 MHz, CDCl₃) δ 11.32 (s, 1H), 7.82 – 7.77 (m, 2H), 7.42 – 7.35 (m, 3H), 7.13 (d, *J* = 1.7 Hz, 1H), 7.11 (dd, *J* = 8.3, 1.8 Hz, 1H), 4.52 (dd, *J* = 8.8, 6.7 Hz, 2H), 4.02 (t, *J* = 6.1 Hz, 2H), 3.65 (ddt, *J* = 13.2, 8.0, 2.5 Hz, 2H), 3.40 – 3.33 (m, 2H), 3.11 (dddd, *J* = 13.2, 8.9, 6.8, 2.0 Hz, 2H), 2.71 – 2.64 (m, 2H), 2.47 (s, 3H), 2.17 – 2.04 (m, 2H), 1.99 – 1.81 (m, 6H), 1.69 (td, *J* = 9.7, 5.1 Hz, 2H); ¹³C NMR (151 MHz, CDCl₃) δ 170.84, 158.81 (q, *J*_{C-F} = 41.6 Hz, TFA), 145.10, 136.94, 134.12, 133.17, 130.09, 128.05, 127.63, 122.82, 122.52, 114.86 (q, *J*_{C-F} = 286.0 Hz, TFA), 111.57, 69.32, 55.49, 53.18, 37.57, 31.24, 30.68, 26.57, 23.75, 21.83; HRMS (MALDI-TOF) calculated for C₂₅H₃₂N₂O₄S₂ [M+H]⁺: 489.1876, found: 489.1881.

(*Z*)-9-Oxabicyclo[6.1.0]non-4-ene (14)

(*Z*)-9-Oxabicyclo[6.1.0]non-4-ene was prepared by the following procedure adapted from Clark et al¹. *Cis,cis*-1,5-cyclooctadiene (22.0 g, 203.36 mmol, 1.00 equiv.) and dry CH₂Cl₂ (300 mL) were added to a 500 mL round-bottom flask. The mixture was cooled to 0 °C with an ice bath and mCPBA (45.57 g, 203.36 mmol, 1.00 equiv.) was added portion wise to give a white suspension. The mixture was allowed to reach room temperature and left stirring overnight. The mixture was filtered and washed with NaHCO₃ saturated solution (3 x 100 mL) and NaCl saturated solution (100 mL). The organic layer was collected, dried with MgSO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (n-heptane/EtOAc, 90:10) yielded (*Z*)-9-oxabicyclo[6.1.0]non-4-ene (11.82 g, 95.16 mmol, 47%) as a colorless oil. ¹H NMR (600 MHz, CDCl₃) δ 5.69 – 5.48 (m, 2H), 3.15 – 2.91 (m, 2H), 2.55 – 2.35 (m, 2H), 2.21 – 2.08 (m, 2H), 2.08 – 1.86 (m, 4H); ¹³C NMR (151 MHz, CDCl₃) δ 129.00, 56.87, 28.25, 23.82. ¹H and ¹³C NMR spectroscopic data for **14** were identical to that previously reported.¹

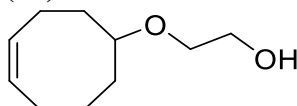
(*Z*)-Cyclooct-4-enol (15)



(*Z*)-Cyclooct-4-enol was prepared by the following procedure adapted from Kurra et al². Lithium aluminum hydride tablets (3.26 g, 85.93 mmol, 3.00 equiv.) were added to an oven-dried 500 mL three-necked round-bottom flask. The flask was sealed and flushed with argon. The flask was cooled to 0 °C using an ice-bath and dry THF (120 mL) was added slowly while vigorously stirring to give a grey suspension. (*Z*)-9-Oxabicyclo[6.1.0]non-4-ene (3.56 g, 28.64 mmol, 1.00 equiv.) in dry THF (10 mL) was added dropwise and the mixture was allowed to reach room temperature and stirred overnight. The mixture was cooled to 0 °C in an ice bath and quenched with EtOAc (120 mL). A saturated solution of Rochelle salt (100 mL) was added and the mixture was stirred vigorously for 10 minutes. The mixture

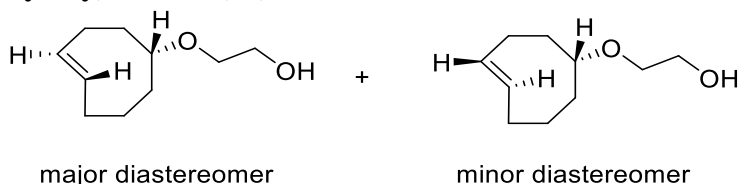
was transferred to a separatory funnel and the organic layer was collected. The aqueous layer was extracted with CH₂Cl₂ (3 x 150 mL). The combined organic layers were washed with H₂O (200 mL), dried over MgSO₄, filtered and concentrated under reduced pressure to give (Z)-cyclooct-4-enol (3.49 g, 28.45 mmol, 99%) ¹H NMR (600 MHz, CDCl₃) δ 5.75 – 5.63 (m, 1H), 5.61 – 5.52 (m, 1H), 3.86 – 3.75 (m, 1H), 2.36 – 2.24 (m, 1H), 2.20 – 2.04 (m, 3H), 1.97 (s, 1H), 1.93 – 1.88 (m, 1H), 1.86 – 1.81 (m, 1H), 1.75 – 1.68 (m, 1H), 1.67 – 1.59 (m, 1H), 1.56 – 1.46 (m, 2H); ¹³C NMR (151 MHz, CDCl₃) δ 130.23, 129.63, 72.85, 37.75, 36.36, 25.75, 24.97, 22.88. ¹H and ¹³C NMR spectroscopic data for **15** were identical to that previously reported.¹

(Z)-2-(Cyclooct-4-en-1-yloxy)ethanol (16)



(Z)-2-(Cyclooct-4-en-1-yloxy)ethanol was prepared by the following procedure adapted from Collins et al.³ Sodium hydride (60% dispersion in mineral oil, 633 mg, 15.84 mmol, 2.00 equiv.) was added to an oven-dried vial and flushed with argon. Dry THF (10 mL) was added to give a grey suspension. A solution of (Z)-cyclooct-4-enol (1.00 g, 7.92 mmol, 1.00 equiv.) in dry THF (4 mL) was added and the mixture was heated to 80 °C for 1 hour. The mixture was cooled to 0 °C with an ice bath and a solution of ethylene sulfate (1.96 g, 15.84 mmol, 2.00 equiv.) in dry THF (5 mL) was added slowly to the mixture. The reaction was heated to 80 °C and stirred for 1.5 hours. The mixture solidified partially and dry THF (10 mL) was added. The solution was cooled to 50 °C and stirred overnight. TLC showed presence of starting material and the mixture was heated to 80 °C and stirred for two hours. The reaction was cooled to room temperature and H₂O (1 mL) was added dropwise, followed by the dropwise addition of conc. H₂SO₄ (1 mL). The mixture was heated to 80 °C and stirred overnight. The reaction was cooled to room temperature and the mixture was neutralized with 5M NaOH. The solution was transferred to a separatory funnel and the organic layer was collected and the aqueous layer was extracted with CH₂Cl₂ (3 x 20 mL). The combined organic layers were washed with H₂O (30 mL) and dried, filtered and concentrated to give the crude product as a yellow oil (1.464 g). The yellow oil was purified by flash chromatography (n-heptane/EtOAc, 70:30) to give the desired product as a colorless oil (782 mg, 58%). ¹H NMR (600 MHz, CDCl₃) δ 5.70 – 5.64 (m, 1H), 5.63 – 5.56 (m, 1H), 3.73 – 3.63 (m, 2H), 3.60 – 3.51 (m, 1H), 3.51 – 3.45 (m, 1H), 3.42 – 3.35 (m, 1H), 2.42 – 2.29 (m, 1H), 2.23 – 2.10 (m, 2H), 2.05 (tdd, *J* = 10.2, 6.9, 3.9 Hz, 1H), 2.01 – 1.88 (m, 1H), 1.87 – 1.63 (m, 3H), 1.51 (s, 1H), 1.48 – 1.31 (m, 1H); ¹³C NMR (151 MHz, CDCl₃) δ 130.15, 129.64, 81.11, 69.40, 62.26, 34.30, 33.51, 25.95, 25.71, 22.75. ¹H and ¹³C NMR spectroscopic data for **16** were identical to that previously reported.³

(E)-2-(Cyclooct-4-en-1-yloxy)ethanol (17)



(E)-2-(Cyclooct-4-en-1-yloxy)ethanol was prepared by the following procedure adapted from Royzen et al.⁴

Photoreactor Preparations: The photochemical set-up is shown above. The bottom of a 40 g column (Flash Cartridge, Screw Top, Luer Lock end fittings, includes top and bottom frit, o-ring, dispersing insert) was packed with dry silica gel (8 cm), and the top was packed with silver impregnated silica (10% AgNO₃, ~17 g). The column was attached to the pump and the Rayonet® reactor by PTFE tubing and the column was flushed with a diethyl ether/n-heptane mixture (ratio 9:1, 500 mL) at a flow rate of 100 mL/min. The column was covered with aluminum to protect the silver from light, see *Figure S1*. The photoreactor and cooler were turned on and the solvent was pumped through the system for 10 minutes. After 10 minutes, the photoreactor was turned off.



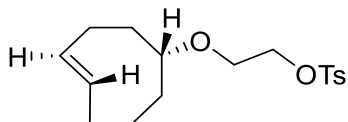
Figure S1. Photo of the set-up of the photoreactor used for trapping and isomerization of the TCOs.

Experimental Procedure

(Z)-2-(Cyclooct-4-en-1-yloxy)ethanol (782 mg, 4.59 mmol, 1.00 equiv.) was dissolved in a diethyl ether/n-heptane mixture (ratio 9:1, 500 mL) and was added to a 1500 mL quartz flask. Methyl benzoate (10 mL, 5.00 mmol, 1.09 equiv.) was added to the mixture. The FMI pump was set at a flowrate of 100 mL/min and the Rayonet® reactor equipped with 16x 254nm lamps (RPR-2537A) was turned on and photolysis was carried out for 8 hours. After 8 hours, the photoreactor was turned off, and the column was flushed with an additional 200 mL of ether/n-heptane (ratio 9:1) and dried with a stream of compressed air. The silica was poured into a 500 mL Erlenmeyer flask and NH₄OH (200 mL) and CH₂Cl₂ (200 mL) were added. The mixture was stirred vigorously for 10 minutes. The silica was filtered off and the residue was transferred to a separatory funnel. The organic layer was collected, and the aqueous layer was back extracted with CH₂Cl₂ (200 mL). The combined organic layers were washed with H₂O (200 mL), dried over MgSO₄, filtered, and concentrated to give the crude product as a colorless oil (458 mg). The oil was purified using flash chromatography (n-heptane/EtOAc 70:30) to give the desired compound as separated diastereomers (235 mg, major isomer 24.3%, minor isomer 5.8%). Major product. ¹H NMR (600 MHz, CDCl₃) δ 5.58 (ddd, *J* = 15.3, 11.3, 3.6 Hz, 1H), 5.38 (ddd, *J* = 15.8, 11.1, 3.6 Hz, 1H), 3.67 (ddd, *J* = 5.5, 3.7, 1.6 Hz, 2H), 3.49 (ddd, *J* = 9.4, 5.4, 3.8 Hz, 1H), 3.39 (ddd, *J* = 9.6, 5.4, 3.9 Hz, 1H), 3.03 (ddt, *J* = 10.7, 5.1, 1.4 Hz, 1H), 2.44 – 2.31 (m, 2H), 2.24 (qd, *J* = 11.9, 5.2 Hz, 1H), 2.14 – 2.07 (m, 1H), 2.02 – 1.91 (m, 2H), 1.89 – 1.73 (m, 2H), 1.58 – 1.42 (m, 2H); ¹³C NMR (151 MHz, CDCl₃) δ

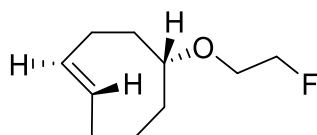
135.49, 132.43, 86.23, 69.29, 62.22, 40.95, 37.98, 34.65, 33.12, 31.85. Minor product. ^1H NMR (600 MHz, CDCl_3) δ 5.62 – 5.54 (m, 1H), 5.53 – 5.43 (m, 1H), 3.79 – 3.71 (m, 2H), 3.66 – 3.58 (m, 1H), 3.55 (ddd, $J = 9.2, 5.0, 4.0$ Hz, 1H), 3.44 (ddd, $J = 9.6, 5.5, 4.1$ Hz, 1H), 2.39 – 2.28 (m, 2H), 2.26 – 2.22 (m, 1H), 2.22 – 2.15 (m, 1H), 2.08 – 1.99 (m, 1H), 1.87 – 1.71 (m, 3H), 1.55 – 1.47 (m, 1H), 1.28 – 1.15 (m, 1H); ^{13}C NMR (151 MHz, CDCl_3) δ 135.95, 131.50, 75.17, 69.82, 62.33, 40.34, 34.59, 33.11, 29.95, 27.77. ^1H and ^{13}C NMR spectroscopic data for **17** were identical to that previously reported.³

(*E*)-2-(Cyclooct-4-enyloxy)ethyl 4-methylbenzenesulfonate (18)



(*E*)-2-(Cyclooct-4-enyloxy)ethyl 4-methylbenzenesulfonate was prepared by the following procedure adapted from Collins et al.³ Dry CH_2Cl_2 (5 mL) and (*E*)-2-(Cyclooct-4-en-1-yloxy)ethanol (major isomer, 190 mg, 1.12 mmol, 1.00 equiv.) were added to a 20 mL microwave vessel and the mixture was cooled to 0 °C using an ice bath and anhydrous pyridine (180 μL , 2.23 mmol, 2.00 equiv.) was added. The mixture was stirred for 5 minutes and 4-methylbenzenesulfonic acid anhydride (389 mg, 1.19 mmol, 1.07 equiv.) was added. The mixture was allowed to reach room temperature and stirred overnight. CH_2Cl_2 (10 mL) was added, and the mixture was washed with H_2O (25 mL), 1M HCl (25 mL), sat. NaHCO_3 (25 mL) and sat. NaCl (25 mL). The organic layer was collected, dried over MgSO_4 , filtered and concentrated. The crude product (252 mg) was purified by flash chromatography (n-heptane/EtOAc; 90:10), to give the desired product as a colorless oil (165 mg, 46%). ^1H NMR (400 MHz, CDCl_3) δ 7.79 (d, $J = 8.4$ Hz, 2H), 7.33 (d, $J = 8.1$ Hz, 2H), 5.54 (ddd, $J = 15.3, 11.3, 3.6$ Hz, 1H), 5.33 (ddd, $J = 15.7, 10.9, 3.6$ Hz, 1H), 4.11 (t, $J = 4.9$ Hz, 2H), 3.61 – 3.37 (m, 2H), 2.97 – 2.92 (m, 1H), 2.44 (s, 3H), 2.38 – 2.30 (m, 2H), 2.26 – 2.11 (m, 1H), 2.01 – 1.85 (m, 3H), 1.82 – 1.63 (m, 2H), 1.47 – 1.35 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 144.85, 135.43, 133.35, 132.41, 129.91, 128.13, 86.45, 69.70, 65.77, 40.72, 37.76, 34.61, 33.04, 31.81, 21.78. ^1H and ^{13}C NMR spectroscopic data for **18** were identical to that previously reported.³

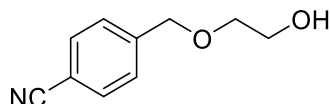
(*E*)-5-(2-Fluoroethoxy)cyclooct-1-ene (19)



(*E*)-5-(2-Fluoroethoxy)cyclooct-1-ene methylbenzenesulfonate was prepared by the following procedure adapted from Collins et al.³ To an oven-dried 5 mL microwave vessel, dry THF (1.5 mL) and (*E*)-2-(cyclooct-4-enyloxy)ethyl 4-methylbenzenesulfonate (30 mg, 0.0925 mmol, 1.00 equiv.) were added. The vessel was sealed and flushed with argon. TBAF (1M in THF, 278 μL , 0.28 mmol, 3.00 equiv.) was added and the mixture was protected from light and stirred at room temperature for 24 hours. The crude product was directly subjected to column chromatography (n-heptane/EtOAc 90:10) to give the desired product as a colorless oil (7 mg, 44%). ^1H NMR (400 MHz, CDCl_3) δ 5.58 (ddd, $J = 15.2, 11.1, 3.6$ Hz, 1H), 5.37 (ddd, $J = 16.0, 11.0, 3.6$ Hz, 1H), 4.56 (t, $J = 4.3$ Hz, 1H), 4.44 (t, $J = 4.3$ Hz, 1H), 3.73 – 3.39 (m, 2H), 3.11 – 2.99 (m, 1H), 2.49 – 2.32 (m, 2H), 2.30 – 2.15 (m, 1H), 2.11 (dd, $J = 13.2, 5.0$ Hz, 1H), 2.08 – 1.78 (m, 4H), 1.65 – 1.43 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 135.53, 132.41, 86.40, 83.41

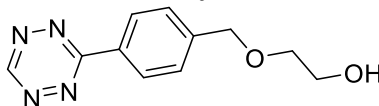
(J_{C-F} = 168.9 Hz), 67.42 (J_{C-F} = 19.8 Hz), 40.87, 37.87, 34.65, 33.13, 31.88; ^{19}F NMR (376 MHz, CDCl_3) δ -223.17. ^1H and ^{13}C NMR spectroscopic data for **19** were identical to that previously reported.³

4-[(2-Hydroxyethoxy)methyl]benzonitrile (**21**)



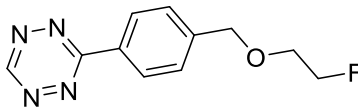
NaH (90% wt, 445 mg, 16.83 mmol, 1.10 equiv.) was suspended in dry THF (10 mL) and ethylene glycol (8.56 mL, 153.0 mmol, 10.00 equiv.) was added dropwise under argon at 0 °C. The solution was left for 30 min at 0 °C before dropwise addition of 4-(bromomethyl)benzonitrile (3000 mg, 15.30 mmol, 1.00 equiv.) in dry THF (30 mL) under argon at 0 °C. The reaction was slowly heated to room temperature and left for 3 hours. The reaction was quenched by adding EtOAc (50 mL) and the crude was washed with NH_4Cl saturated solution (50 mL x2) and water (50 mL). The organic phase was dried over Na_2SO_4 , filtered and concentrated under reduced pressure. Purification by flash chromatography (n-heptane/EtOAc, 40:60) yielded 4-[(2-hydroxyethoxy)methyl]benzonitrile (2662 mg, 15.02 mmol, 98%) as a colorless liquid. ^1H NMR (600 MHz, CDCl_3) δ 7.67 – 7.62 (m, 2H), 7.48 – 7.42 (m, 2H), 4.62 (s, 2H), 3.82 – 3.77 (m, 2H), 3.66 – 3.61 (m, 2H); ^{13}C NMR (151 MHz, CDCl_3) δ 143.71, 132.42, 127.91, 118.89, 111.62, 72.40, 72.09, 62.00. HRMS (MALDI-TOF) calculated for $\text{C}_{10}\text{H}_{11}\text{NO}_2$ $[\text{M}+\text{Na}]^+$: 200.0682, found: 200.0687.

4-[(2-Hydroxyethoxy)methyl]-1,2,4,5-tetrazin-3-yl}benzene (**22**)



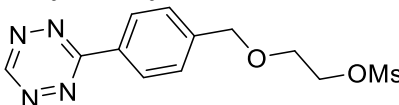
4-[(2-Hydroxyethoxy)methyl]benzonitrile (250 mg, 1.41 mmol, 1.00 equiv.), CH_2Cl_2 (0.109 mL, 1.69 mmol, 1.20 equiv.), sulfur (91 mg, 0.35 mmol, 0.25 equiv.) and ethanol (3.0 mL) were mixed together in a microwave reaction vial. Hydrazine monohydrate (0.550 mL, 14.11 mmol, 10.00 equiv.) was added dropwise with stirring. The vessel was sealed, and the reaction mixture was heated at 50 °C for 24 hours. The reaction was diluted with 3 mL of CH_2Cl_2 and sodium nitrite (974 mg, 14.11 mmol, 10.00 equiv.) in 20 mL of H_2O was added dropwise to the mixture under cooling. Excess acetic acid (2.5 mL) was then added slowly during which the solution turned bright red in color. The reaction mixture was extracted with CH_2Cl_2 (3 x 100 mL). The organic phase was dried over MgSO_4 , filtered and concentrated under reduced pressure. The resulting residue was purified using flash chromatography (n-heptane/EtOAc, 60:40) and recrystallized from n-heptane/EtOAc to give 4-[(2-hydroxyethoxy)methyl]-1,2,4,5-tetrazin-3-yl}benzene (204 mg, 0.88 mmol, 62%) as a pink solid. ^1H NMR (600 MHz, CDCl_3) δ 10.21 (s, 1H), 8.64 – 8.59 (m, 2H), 7.58 (d, J = 8.1 Hz, 2H), 4.70 (s, 2H), 3.85 – 3.80 (m, 2H), 3.70 – 3.66 (m, 2H), ^{13}C NMR (151 MHz, CDCl_3) δ 166.48, 157.95, 143.81, 131.10, 128.62, 128.38, 72.79, 71.99, 62.09; HRMS (MALDI-TOF) calculated for (*in situ* reduced to dihydro tetrazine) $\text{C}_{11}\text{H}_{14}\text{N}_4\text{O}_2$ $[\text{M}+\text{H}]^+$: 235.1189, found: 235.1192; Mp: 98-100 °C.

4-[[2-(2-Fluoroethoxy)methyl]-1,2,4,5-tetrazin-3-yl]benzene (23)



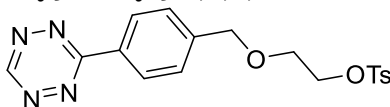
4-[[2-(2-Hydroxyethoxy)methyl]-1,2,4,5-tetrazin-3-yl]benzene (30 mg, 0.13 mmol, 1.00 equiv.) was dissolved in 3 mL of dry THF and PBSF (78 mL, 0.26 mmol, 2.00 equiv.) and DIPEA (135 μ L, 0.78 mmol, 6.00 equiv.) were added. Et₃N*3HF (42 μ L, 0.26 mmol, 2.00 equiv.) was dissolved in 1 mL of THF and added dropwise. The reaction was left at room temperature for 18 hours. The reaction was diluted with 10 mL CH₂Cl₂ and washed with sat. NH₄Cl (20 mL). The aqueous phase was extracted with CH₂Cl₂ (2 x 10 mL) and the combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (n-heptane/EtOAc, 50:50) yielded 4-[[2-(2-fluoroethoxy)methyl]-1,2,4,5-tetrazin-3-yl]benzene (4 mg, 0.02 mmol, 13%) as a pink solid as well as recovered starting material (4 mg, 0.02 mmol). ¹H NMR (400 MHz, CDCl₃) δ 10.21 (s, 1H), 8.68 – 8.57 (m, 2H), 7.60 (d, *J* = 8.1 Hz, 2H), 4.77 – 4.67 (m, 3H), 4.62 – 4.55 (m, 1H), 3.89 – 3.83 (m, 1H), 3.80 – 3.75 (m, 1H); ¹⁹F NMR (376 MHz, CDCl₃) δ -222.93; ¹³C NMR (101 MHz, CDCl₃) δ 166.51, 157.96, 143.70, 131.10, 128.62, 128.34, 127.86, 83.25 (*J*_{C-F} = 169.6 Hz), 72.89, 69.88 (*J*_{C-F} = 19.7 Hz). HRMS (MALDI-TOF) calculated for C₁₁H₁₁FN₄O [M+H]⁺: 235.0989, found: 235.0995; Mp: 55-57 °C.

4-[[2-[[2-[(Methane)sulfonyl]oxy]ethoxy]methyl]-1,2,4,5-tetrazin-3-yl]benzene (24)



4-[[2-(2-Hydroxyethoxy)methyl]-1,2,4,5-tetrazin-3-yl]benzene (50 mg, 0.22 mmol, 1.00 equiv.) was mixed with methanesulfonyl chloride (50 μ L, 0.65 mmol, 3.00 equiv.) and dissolved in 4 mL of dry CH₂Cl₂ under argon. A mixture of DIPEA (150 μ L, 0.86 mmol, 4 equiv.) and DMAP (5 mg, 0.04 mmol, cat.) in 1 mL dry CH₂Cl₂ was added at 0 °C under argon. The reaction was allowed to reach room temperature and left stirring for additional 1.5 hours. The reaction was diluted with 10 mL of CH₂Cl₂ and washed with sat. NH₄Cl (20 mL) and H₂O (2 x 20 mL). The organic phase was dried over Na₂SO₄, filtered and concentrated under reduced pressure. Purification by flash chromatography (n-heptane/EtOAc, 70:30) yielded 4-[[2-[[2-[(methane)sulfonyl]oxy]ethoxy]methyl]-1,2,4,5-tetrazin-3-yl]benzene (56 mg, 0.18 mmol, 84%) as a pink liquid that solidified over time. ¹H NMR (600 MHz, CDCl₃) δ 10.22 (s, 1H), 8.65 – 8.60 (m, 2H), 7.58 (d, *J* = 8.3 Hz, 2H), 4.71 (s, 2H), 4.47 – 4.42 (m, 2H), 3.85 – 3.81 (m, 2H), 3.06 (s, 3H); ¹³C NMR (151 MHz, CDCl₃) δ 166.43, 157.98, 143.16, 131.29, 128.66, 128.38, 72.87, 68.97, 68.50, 37.88; HRMS (MALDI-TOF) calculated for C₁₂H₁₄N₄O₄S [M+Na]⁺: 333.0628, found: 333.0627; Mp: 96-98 °C.

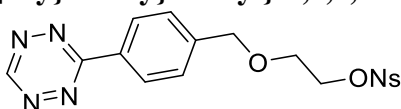
4-[[2-[[2-[(Toluene)sulfonyl]oxy]ethoxy]methyl]-1,2,4,5-tetrazin-3-yl]benzene (25)



4-[[2-(2-Hydroxyethoxy)methyl]-1,2,4,5-tetrazin-3-yl]benzene (50 mg, 0.22 mmol, 1.00 equiv.) was mixed with tosyl chloride (123 mg, 0.65 mmol, 3.00 equiv.) and dissolved in 4 mL dry CH₂Cl₂ under

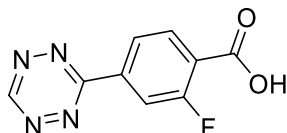
argon. A mixture of DIPEA (150 μ L, 0.86 mmol, 4 equiv.) and DMAP (5 mg, 0.04 mmol, cat.) in 1 mL dry CH_2Cl_2 was added at 0 $^\circ\text{C}$ under argon. The reaction was allowed to reach room temperature and left stirring for additional 20 hours. The reaction was diluted with 10 mL CH_2Cl_2 and washed with sat. NH_4Cl (20 mL) and H_2O (2 x 20 mL). The organic phase was dried over N_2SO_4 and concentrated under reduced pressure. Purification by flash chromatography (n-heptane/EtOAc, 70:30) 4-{{2-{{[(toluene)sulfonyl]oxy}ethoxy}methyl]-1,2,4,5-tetrazin-3-yl}benzene (31 mg, 0.08 mmol, 37%) as a pink solid. ^1H NMR (600 MHz, CDCl_3) δ 10.22 (d, J = 1.1 Hz, 1H), 8.61 – 8.57 (m, 2H), 7.84 – 7.80 (m, 2H), 7.52 – 7.48 (m, 2H), 7.35 – 7.31 (m, 2H), 4.62 (s, 2H), 4.28 – 4.23 (m, 2H), 3.78 – 3.73 (m, 2H), 2.44 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ 166.47, 157.97, 145.04, 143.41, 133.19, 131.10, 130.00, 128.55, 128.21, 128.14, 72.73, 69.30, 68.22, 21.81; HRMS (MALDI-TOF) calculated for $\text{C}_{18}\text{H}_{18}\text{N}_4\text{O}_4\text{S}$ $[\text{M}+\text{Na}]^+$: 409.0941, found: 409.0941; Mp: 100-102 $^\circ\text{C}$.

4-{{2-{{[(4-Nitrobenzene)sulfonyl]oxy}ethoxy}methyl]-1,2,4,5-tetrazin-3-yl}benzene (26)



4-{{2-{{[(2-Hydroxyethoxy)methyl]-1,2,4,5-tetrazin-3-yl}benzene (50 mg, 0.22 mmol, 1.00 equiv.) was mixed with nitrobenzenesulfonyl chloride (143 mg, 0.65 mmol, 3.00 equiv.) and dissolved in 4 mL dry CH_2Cl_2 under argon. A mixture of DIPEA (150 μ L, 0.86 mmol, 4 equiv.) and DMAP (5 mg, 0.04 mmol, cat.) in 1 mL dry CH_2Cl_2 was added at 0 $^\circ\text{C}$ under argon. The reaction was allowed to reach room temperature and left stirring for additional 3 hours. The reaction was diluted with 10 mL CH_2Cl_2 and washed with sat. NH_4Cl (20 mL) and H_2O (2 x 20 mL). The organic phase was dried over N_2SO_4 , filtered and concentrated under reduced pressure. Purification by flash chromatography (n-heptane/EtOAc, 60:40) yielded 4-{{2-{{[(4-nitrobenzene)sulfonyl]oxy}ethoxy}-methyl]-1,2,4,5-tetrazin-3-yl}benzene (83 mg, 0.20 mmol, 92%) as a pink solid. ^1H NMR (600 MHz, CDCl_3) δ 10.24 (s, 1H), 8.61 – 8.57 (m, 2H), 8.32 – 8.28 (m, 2H), 8.12 – 8.08 (m, 2H), 7.46 (dd, J = 7.4, 1.1 Hz, 2H), 4.58 (s, 2H), 4.41 – 4.37 (m, 2H), 3.79 – 3.75 (m, 2H); ^{13}C NMR (151 MHz, CDCl_3): δ 166.34, 158.01, 150.80, 142.86, 142.05, 131.39, 129.38, 128.57, 128.32, 124.45, 72.83, 70.58, 68.04.; HRMS (MALDI-TOF) calculated for $\text{C}_{17}\text{H}_{15}\text{N}_5\text{O}_6\text{S}$ $[\text{M}+\text{Na}]^+$: 440.0635, found: 440.0636; Mp: 126-128 $^\circ\text{C}$.

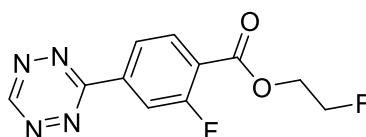
2-Fluoro-4-(1,2,4,5-tetrazin-3-yl)benzoic acid (28)



2-Fluoro-4-cyanobenzoic acid (0.99 g, 6.00 mmol, 1 equiv.), CH_2Cl_2 (6.00 mmol, 0.385 mL, 1 equiv.), sulfur (0.385 g, 1.50 mmol, 0.25 equiv.) and ethanol (6.0 mL) were mixed together in 3 x 20 mL microwave reaction tubes. Hydrazine monohydrate (2.34 mL, 48.00 mmol, 8 equiv.) was added slowly under stirring. The vessel was sealed, and the reaction mixture was heated to 50 $^\circ\text{C}$ for 24 hours. CH_2Cl_2 (3 mL) and sodium nitrite (4.14 g, 60.00 mmol, 10 equiv.) in 60 mL of H_2O were added to the mixture. Excess acetic acid (21 mL) was then added slowly and the solution turned bright red in color. The reaction mixture was extracted with CH_2Cl_2 (3 x 20 mL). The organic phase was dried over MgSO_4 ,

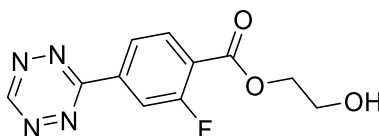
filtered and concentrated under reduced pressure. The resulting residue was purified using flash chromatography (30/70 n-heptane/EtOAc) to afford 2-fluoro-4-(1,2,4,5-tetrazin-3-yl)benzoic acid as a pink solid. $^1\text{H-NMR}$ (MeOD, 600 MHz): 10.44 (s, 1H), 8.50 (dd, $J = 1.6, 8.1$ Hz), 8.40 (dd, $J = 1.6, 11.5$ Hz, 1H), 8.20 (t, $J = 7.74$ Hz, 1H); $^{19}\text{F NMR}$ (376 MHz, MeOD) δ -110.27; $^{13}\text{C NMR}$ (151 MHz, MeOD) δ 165.11 ($J_{\text{C-F}} = 3.3$ Hz), 165.04 ($J_{\text{C-F}} = 2.7$ Hz), 162.10 ($J_{\text{C-F}} = 259.0$ Hz), 158.24 ($J_{\text{C-F}} = 10.2$ Hz), 137.97 ($J_{\text{C-F}} = 8.8$ Hz), 132.85 ($J_{\text{C-F}} = 1.2$ Hz), 123.10 ($J_{\text{C-F}} = 4.0$ Hz), 122.84 ($J_{\text{C-F}} = 10.7$ Hz), 115.83 ($J_{\text{C-F}} = 25.7$ Hz); HRMS (MALDI-TOF) calculated for $\text{C}_9\text{H}_5\text{FN}_4\text{O}_2$ $[\text{M-H}]^-$: 219.0323, found: 219.0318; Mp: 227-229 °C.

2-Fluoro-4-(1,2,4,5-tetrazin-3-yl)-2-fluoroethyl-benzoate (29)



2-Fluoro-4-(1,2,4,5-tetrazin-3-yl)benzoic acid (10 mg, 0.05 mmol, 1.00 equiv.) and 2-fluoroethyl 4-methylbenzenesulfonate (30 mg, 0.14 mmol, 3.00 equiv.) were dissolved in 2 mL dry DMF and DIPEA (20 μL , 0.10 mmol, 2.00 equiv.) was added. The reaction was left at 100 °C overnight. The reaction was diluted with Et_2O (15 mL) and washed with sat. NH_4Cl (20 mL) and H_2O (2 x 10 mL). The organic phase was dried over MgSO_4 , filtered and concentrated under reduced pressure. Purification by flash chromatography (toluene) yielded 2-Fluoro-4-(1,2,4,5-tetrazin-3-yl)-2-fluoroethyl-benzoate (6.5 mg, 0.02 mmol, 45%) as a pink liquid that solidified over time. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 10.31 (s, 1H), 8.51 (dd, $J = 8.2, 1.6$ Hz, 1H), 8.45 (dd, $J = 11.2, 1.6$ Hz, 1H), 8.21 (dd, $J = 8.2, 7.1$ Hz, 1H), 4.88 – 4.79 (m, 1H), 4.77 – 4.65 (m, 2H), 4.65 – 4.57 (m, 1H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 165.23, 163.49, 162.49 ($J_{\text{C-F}} = 262.2$ Hz), 158.34, 137.83, 133.38, 123.67 ($J_{\text{C-F}} = 4.1$ Hz), 122.26, 116.96 ($J_{\text{C-F}} = 25.5$ Hz), 81.23 ($J_{\text{C-F}} = 171.3$ Hz), 64.65 ($J_{\text{C-F}} = 20.4$ Hz); $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -106.87, -224.63; HRMS (MALDI-TOF) calculated for (*in situ* reduced to dihydro tetrazine) $\text{C}_{11}\text{H}_{10}\text{F}_2\text{N}_4\text{O}_2$ $[\text{M+H}]^+$: 269.0844, found: 269.0848; Mp: 96-98 °C.

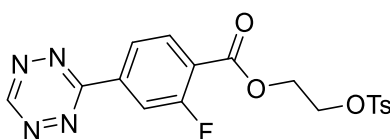
2-Fluoro-4-(1,2,4,5-tetrazin-3-yl)-2-hydroxyethyl-benzoate (30)



2-Fluoro-4-(1,2,4,5-tetrazin-3-yl)benzoic acid (0.07 g, 0.32 mmol, 1.00 equiv.) and 2-bromoethanol (0.07 mL, 0.97 mmol, 3.00 equiv.) were dissolved in 3 mL of dry DMF. DIPEA (0.17 mL, 0.97 mmol, 3.00 equiv.) was dissolved in 1 mL DMF and added dropwise and the reaction was left at 70 °C. After the reaction was completed, it was cooled down, diluted with water (30 mL) and extracted with CH_2Cl_2 (2 x 20 mL). The organic phase was dried over MgSO_4 , filtered, and concentrated under reduced pressure. The crude was purified by flash chromatography (60/40 n-heptane/EtOAc) to give 2-fluoro-4-(1,2,4,5-tetrazin-3-yl)-2-hydroxyethyl-benzoate (35 mg, 41%) as a red solid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 10.30 (s, 1H), 8.46 (dd, $J = 8.3, 1.7$ Hz, 1H), 8.38 (dd, $J = 11.3, 1.7$ Hz, 1H), 8.16 (t, $J = 7.7$ Hz, 1H), 4.58 –

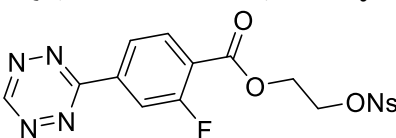
4.45 (m, 2H), 3.99 (t, $J = 4.7$ Hz, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 164.99 ($J_{\text{C-F}} = 2.7$ Hz), 163.84 ($J_{\text{C-F}} = 3.9$ Hz), 162.12 ($J_{\text{C-F}} = 261.1$ Hz), 158.14, 137.51 ($J_{\text{C-F}} = 9.0$ Hz), 133.24, 123.52 ($J_{\text{C-F}} = 4.0$ Hz), 122.35 ($J_{\text{C-F}} = 10.5$ Hz), 116.70 ($J_{\text{C-F}} = 25.7$ Hz), 67.31, 60.98; HRMS (MALDI-TOF) calculated for $\text{C}_{11}\text{H}_9\text{FN}_4\text{O}_3$ $[\text{M}+\text{H}]^+$: 266.0615, found: 266.0617; Mp: 101-103 °C.

2-Fluoro-4-(1,2,4,5-tetrazin-3-yl)- 2-[[{(tolouene)sulfonyl]oxy}ethyl -benzoate (31)



2-Fluoro-4-(1,2,4,5-tetrazin-3-yl)benzoic acid (300 mg, 1.36 mmol, 1.00 equiv) and ethylene di(*p*-toluenesulfonate) (1514 mg, 4.09 mmol, 3.00 equiv.) were dissolved in 30 mL of dry DMF. DIPEA (0.340 mL, 2.18 mmol, 1.60 equiv.) was dissolved in 4 mL of dry DMF and added dropwise to the reaction which was left at 100 °C for 3 hours. The crude was diluted with Et_2O (30 mL) and washed with sat. NH_4Cl (20 mL) and H_2O (2 x 30 mL). The organic phase was dried over MgSO_4 , filtered and concentrated under reduced pressure. Purification by flash chromatography (toluene/ EtOAc , 95:5) yielded 2-fluoro-4-(1,2,4,5-tetrazin-3-yl)- 2-[[{(tolouene)-sulfonyl]oxy}ethyl-benzoate (242 mg, 0.58 mmol, 42%) as a pink liquid that solidified over time. ^1H NMR (600 MHz, CDCl_3) δ 10.32 (d, $J = 1.5$ Hz, 1H), 8.52 – 8.46 (m, 1H), 8.42 (dt, $J = 11.2, 1.6$ Hz, 1H), 8.10 (td, $J = 7.8, 7.2, 1.5$ Hz, 1H), 7.81 (dd, $J = 8.3, 1.7$ Hz, 2H), 7.32 (d, $J = 7.9$ Hz, 2H), 4.59 – 4.54 (m, 2H), 4.42 – 4.36 (m, 2H), 2.41 (s, 3H); ^{19}F NMR (376 MHz, CDCl_3) δ -106.68; ^{13}C NMR (151 MHz, CDCl_3) δ 165.16 ($J_{\text{C-F}} = 2.7$ Hz), 163.07 ($J_{\text{C-F}} = 3.9$ Hz), 162.44 ($J_{\text{C-F}} = 262.6$ Hz), 158.34 ($J_{\text{C-F}} = 2.5$ Hz), 145.24, 137.85 ($J_{\text{C-F}} = 9.0$ Hz), 133.39, 132.90, 130.07, 128.10, 123.61 ($J_{\text{C-F}} = 3.9$ Hz), 121.93 ($J_{\text{C-F}} = 9.9$ Hz), 116.86 ($J_{\text{C-F}} = 25.3$ Hz), 67.44, 62.90, 21.79; HRMS (MALDI-TOF) calculated for (*in situ* reduced to dihydro tetrazine): $\text{C}_{18}\text{H}_{18}\text{FN}_4\text{O}_5\text{S}$ $[\text{M}+\text{H}]^+$: 421.0982, found: 421.0970; Mp: 104-106 °C.

2-Fluoro-4-(1,2,4,5-tetrazin-3-yl)- 2-[[{(4-nitrobenzene)sulfonyl]oxy}ethyl -benzoate (32)



To a solution of 2-fluoro-4-(1,2,4,5-tetrazin-3-yl)-2-hydroxyethyl-benzoate (0.05 g, 0.10 mmol) and DIPEA (0.07 mL, 0.43 mmol) in CH_2Cl_2 (20 mL) nosyl chloride (0.072 g, 0.32 mmol) and DMAP (0.002 g, 0.02 mmol) were added. The reaction was stirred at room temperature for 4 hours. The volatiles were removed under reduced pressure. Purification by flash chromatography (75/25 *n*-heptane/ EtOAc) yielded semi-pure product (60 mg) as a red solid. Recrystallization from EtOAc/n -heptane afforded 2-fluoro-4-(1,2,4,5-tetrazin-3-yl)- 2-[[{(4-nitrobenzene)sulfonyl]oxy}ethyl -benzoate (35 mg, 0.078 mmol, 35%) as a red solid. ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ 10.73 (s, 1H), 8.43 (dd, $J = 8.2, 1.7$ Hz, 1H), 8.40 – 8.36 (m, 2H), 8.34 (dd, $J = 11.5, 1.6$ Hz, 1H), 8.22 – 8.18 (m, 2H), 8.03 (t, $J = 7.8$ Hz, 1H), 4.59 – 4.54 (m, 4H); ^{13}C NMR (151 MHz, DMSO) δ 164.58, 162.73 ($J_{\text{C-F}} = 3.5$ Hz), 160.72, 158.96, 150.98, 140.99, 138.80 ($J_{\text{C-F}} = 8.9$ Hz), 133.39, 129.82, 125.35, 124.08 ($J_{\text{C-F}} = 3.8$ Hz), 121.34 ($J_{\text{C-F}} = 10.5$ Hz), 116.38 ($J_{\text{C-F}} = 24.7$ Hz), 70.38, 63.21; ^{19}F NMR (376 MHz, $\text{DMSO}-d_6$) δ -108.44; HRMS (MALDI-TOF) calculated for $\text{C}_{17}\text{H}_{12}\text{FN}_5\text{O}_7\text{S}$ $[\text{M}+\text{H}]^+$: 450.0514, found: 450.0515; Mp: 103-105 °C.

Radiochemistry general

[¹⁸F]Fluoride was produced by proton irradiation of [¹⁸O]H₂O via a (p,n) reaction using a cyclotron (CTI Siemens Eclipse or Scanditronix MC32). Samples were analyzed by analytical HPLC (Thermo Fisher® UltiMate 3000) with a C-18 column (Luna® 5u C18(2) 100Å, 150 x 4.6 mm). Eluents: A: H₂O with 0.1% TFA, B: MeCN with 0.1% TFA. Gradient from 100% A → 100% B over 15 minutes, back to 100% A over 4 minutes, flow rate 1.5 mL/min. Detection by UV-absorption at λ = 254 nm on a UVD 170U detector if nothing else stated, radioactivity was analyzed using a flow-through GM tube based radiodetector (Scansys). Radio TLC was performed on silica gel 60 F₂₅₄ (Merck), radioactivity was detected using photostimulated luminescence plates (PSP) (Perkin Elmer) by incubating the TLC-plates on the PSP for 5 min. PSP were read in a cyclone reader (Cyclone Plus Phosphor Imager, PerkinElmer, Inc.) and analyzed using Optiquant. Automated synthesis was performed on a Scansys Laboratorieteknik synthesis module with purification by semipreparative HPLC using a C-18 column (Luna® 5µm C18(2) 100Å, 250 x 10 mm). SPE purification was carried out on C18 cartridges (Sep-Pak C18 Plus Short types) preconditioned by rinsing with EtOH (10 mL) followed by H₂O (10 mL) and then dried with air. Anion exchange cartridge (Sep-Pak® Light QMA cartridge 130 mg sorbent, chloride as counter ion) were prepared by flushing with EtOH (2 mL) followed by a solution of the appropriate preconditioning anion (0.5 M solution, 10 mL). The cartridge was then washed with H₂O (10 mL) and dried with air.

General method for elution experiments

[¹⁸F]fluoride was delivered from the cyclotron and received in a 10 mL glass vial. Activity concentration was adjusted to 100-300 MBq/mL by diluting with milliQ water. The [¹⁸F]Fluoride solution was applied to the cartridge (0.2-2 mL, 20-100 MBq) using a 1 mL syringe followed by flushing the cartridge with air and activity stuck to the cartridge was measured using a dose calibrator. The cartridge was then eluted in the same direction using 1 mL of the eluting anion solution. The cartridge was flushed with air and activity was measured of both the eluted cartridge and the collected eluate. [¹⁸F]Fluoride recovery was calculated as the decay corrected activity difference between the cartridge before elution and the vial with the eluate. The results from the different elution experiments are presented in *Table S1*. Obtained experimental elution curves (% eluted [¹⁸F]fluoride plotted against eluting base concentration) were fitted to the Hill equation:

$$\%EL = 100\% \times \frac{C_b^n}{C_b^n + dc50^n},$$

where C_b is the concentration of the eluting base in mmol/L, %EL is the experimentally determined [¹⁸F]fluoride elution efficiency, dc50 is the eluting base concentration leading to 50% elution efficiency, and n is the Hill slope coefficient. The concentration of the base leading to 90% elution efficiency (dc90) was then calculated from the dc50 value using the following formula:

$$dc90 = dc50 \times \sqrt[n]{9}$$

General method for manual radiolabeling experiments

[¹⁸F]Fluoride solution was prepared in the same manner as for the elution experiments. Anion exchange cartridge was eluted into a 4 mL V-shaped glass vial, for the cases where kryptands or crown ethers were added, 1.3 equivalents were used to the eluting anion concentration. The vial was placed in a heating

block and heated to 100 °C under a stream of nitrogen for 10 min to remove the eluting solvent. Azeotropic drying by MeCN added 2x0.5 mL followed by 5 min drying at 100 °C under a stream of nitrogen. The activity of the dried fluoride was measured in a dose calibrator to determine if any fluoride was lost during the drying process. In case of elution by methanolic solutions, the cartridge was flushed with air (10 mL syringe) before elution, to remove residual water. The drying was then conducted at 100 °C under nitrogen flow for 5 minutes without addition of MeCN.

Precursor dissolved in the reaction solvent was added to the dried [¹⁸F]fluoride and the cap of the reaction vial was switched to a new one. The reaction vial was placed back in the heating block at the desired reaction temperature. When the reaction was finished the reaction vial was removed from the heating block and was allowed to cool down for 1 min. The activity of the reaction vial was measured in a dose calibrator, the reaction solution was moved to a new vial containing 0.3 mL of H₂O to quench the reaction using a 1 mL syringe. To dissolve any residual [¹⁸F]fluoride stuck to the glass wall, 0.3 mL H₂O was added to the empty reaction vial and it was shaken gently. The activity of both vials were measured in a dose calibrator to determine how much activity was in solution by the end of the reaction. An analytical sample (0.1 mL) was taken from the quenched reaction (crude RCC). The quenched reaction mixture was then moved back to the original reaction vial using the same syringe, the solution was mixed, and another analytical sample was taken (0.1 mL) (resolubilized RCC). The samples were analyzed by analytical HPLC (for identification) and TLC (for quantification). Region for the desired product was integrated as well as free [¹⁸F]fluoride (base line, rf: 0) for quantification. Results were given as percent of activity of the integrated region versus the activity of total lane. This did not require for all potential byproducts to be integrated however this resulted in a slightly lower percentage of the integrated product resulting in lower pRCY as it did not account for the lane background not containing any radioactive species.

The workflow for aliphatic radiolabeling experiments can be seen in *Figure S2*.

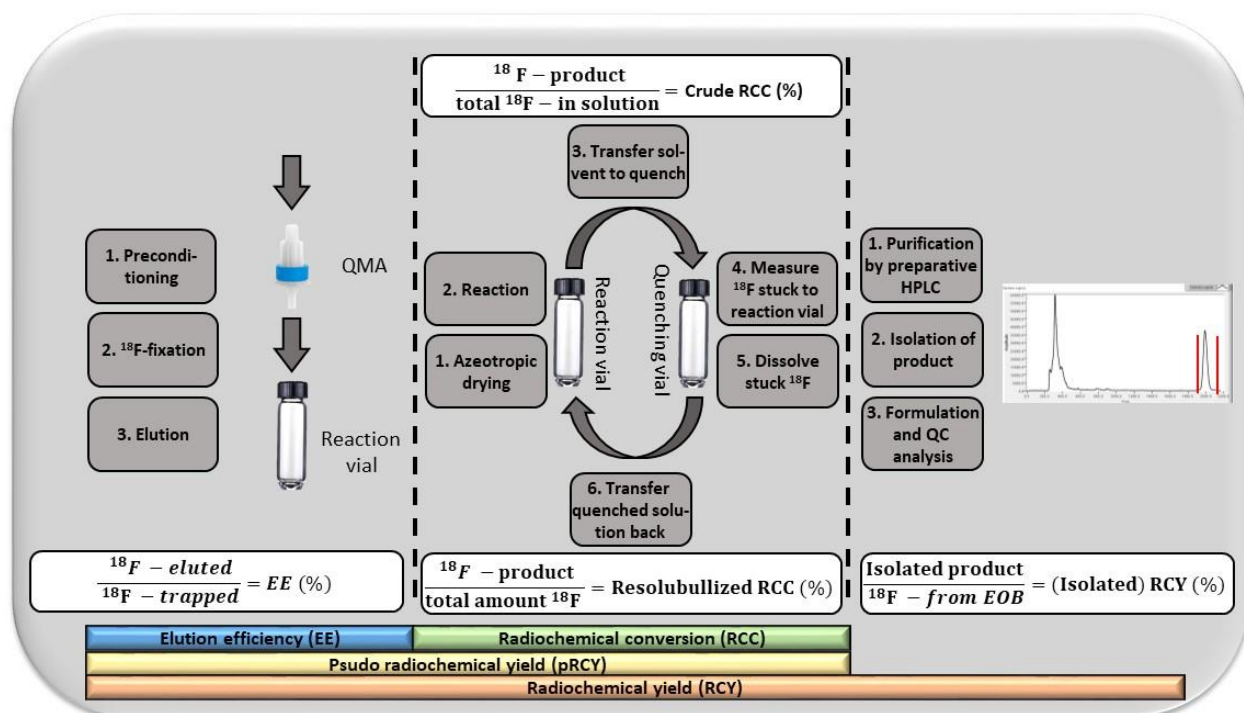


Figure S2. Workflow for elution, reaction and purification of aliphatic ^{18}F -fluorination reactions. For automated synthesis to determine isolated RCY the elution and reaction part was performed automated and the EE and pRCY was not determined.

Results from initial screening of anion exchange cartridge

Experiments conducted according to the general method for elution experiments, results displayed in *Table S1*.

Table S1 Results from the elution experiments with different concentrations of bases for various preconditioning anions, cartridges and solvents.

Exp id	Cartridge	Preconditioning anion	Eluting base	Eluting concentration	Co-solvent	% co-solvent	% eluted
1	QMA	Cl^-	$\text{K}_2\text{CO}_3/\text{K}_{222}$	100	MeCN	90	98
2	QMA	Cl^-	$\text{K}_2\text{CO}_3/\text{K}_{222}$	75	MeCN	90	98
3	QMA	Cl^-	$\text{K}_2\text{CO}_3/\text{K}_{222}$	50	MeCN	90	94
4	QMA	Cl^-	$\text{K}_2\text{CO}_3/\text{K}_{222}$	33	MeCN	90	68
5	QMA	Cl^-	$\text{K}_2\text{CO}_3/\text{K}_{222}$	25	MeCN	90	53
6	QMA	Cl^-	$\text{K}_2\text{CO}_3/\text{K}_{222}$	10	MeCN	90	3
7	QMA	Cl^-	$\text{K}_2\text{CO}_3/\text{K}_{222}$	5	MeCN	90	1
8	QMA	HCO_3^-	$\text{K}_2\text{CO}_3/\text{K}_{222}$	100	MeCN	90	98
9	QMA	HCO_3^-	$\text{K}_2\text{CO}_3/\text{K}_{222}$	75	MeCN	90	97
10	QMA	HCO_3^-	$\text{K}_2\text{CO}_3/\text{K}_{222}$	50	MeCN	90	95
11	QMA	HCO_3^-	$\text{K}_2\text{CO}_3/\text{K}_{222}$	33	MeCN	90	87
12	QMA	HCO_3^-	$\text{K}_2\text{CO}_3/\text{K}_{222}$	25	MeCN	90	82
13	QMA	HCO_3^-	$\text{K}_2\text{CO}_3/\text{K}_{222}$	10	MeCN	90	43
14	QMA	HCO_3^-	$\text{K}_2\text{CO}_3/\text{K}_{222}$	5	MeCN	90	11
15	QMA	HCO_3^-	$\text{K}_2\text{CO}_3/\text{K}_{222}$	100	none	0	99
16	QMA	HCO_3^-	$\text{K}_2\text{CO}_3/\text{K}_{222}$	75	none	0	99

17	QMA	HCO ₃ ⁻	K ₂ CO ₃ /K ₂₂₂	50	none	0	99
18	QMA	HCO ₃ ⁻	K ₂ CO ₃ /K ₂₂₂	33	none	0	98
19	QMA	HCO ₃ ⁻	K ₂ CO ₃ /K ₂₂₂	25	none	0	99
20	QMA	HCO ₃ ⁻	K ₂ CO ₃ /K ₂₂₂	10	none	0	78
21	QMA	HCO ₃ ⁻	K ₂ CO ₃ /K ₂₂₂	5	none	0	17
22	QMA	Cl ⁻	K ₂ CO ₃ /K ₂₂₂	100	none	0	94
23	QMA	Cl ⁻	K ₂ CO ₃ /K ₂₂₂	75	none	0	98
24	QMA	Cl ⁻	K ₂ CO ₃ /K ₂₂₂	50	none	0	98
25	QMA	Cl ⁻	K ₂ CO ₃ /K ₂₂₂	33	none	0	97
26	QMA	Cl ⁻	K ₂ CO ₃ /K ₂₂₂	25	none	0	97
27	QMA	Cl ⁻	K ₂ CO ₃ /K ₂₂₂	10	none	0	50
28	QMA	Cl ⁻	K ₂ CO ₃ /K ₂₂₂	5	none	0	2
29	QMA	HCO ₃ ⁻	K ₂ CO ₃ /K ₂₂₂	100	MeCN	50	98
30	QMA	HCO ₃ ⁻	K ₂ CO ₃ /K ₂₂₂	75	MeCN	50	99
31	QMA	HCO ₃ ⁻	K ₂ CO ₃ /K ₂₂₂	50	MeCN	50	99
32	QMA	HCO ₃ ⁻	K ₂ CO ₃ /K ₂₂₂	33	MeCN	50	99
33	QMA	HCO ₃ ⁻	K ₂ CO ₃ /K ₂₂₂	25	MeCN	50	99
34	QMA	HCO ₃ ⁻	K ₂ CO ₃ /K ₂₂₂	10	MeCN	50	95
35	QMA	HCO ₃ ⁻	K ₂ CO ₃ /K ₂₂₂	5	MeCN	50	57
36	QMA	Cl ⁻	K ₂ CO ₃	50	MeCN	50	97
37	QMA	Cl ⁻	K ₂ CO ₃	50	MeCN	10	98
38	QMA	Cl ⁻	K ₂ CO ₃	50	MeCN	90	0
39	QMA	Cl ⁻	KHCO ₃ /K ₂₂₂	100	MeCN	90	89
40	QMA	Cl ⁻	KHCO ₃ /K ₂₂₂	75	MeCN	90	82
41	QMA	Cl ⁻	KHCO ₃ /K ₂₂₂	50	MeCN	90	70
42	QMA	Cl ⁻	KHCO ₃ /K ₂₂₂	33	MeCN	90	54
43	QMA	Cl ⁻	KHCO ₃ /K ₂₂₂	25	MeCN	90	25
44	QMA	Cl ⁻	KHCO ₃ /K ₂₂₂	10	MeCN	90	3
45	QMA	Cl ⁻	KHCO ₃ /K ₂₂₂	5	MeCN	90	0
46	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	100	MeCN	90	96
47	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	75	MeCN	90	90
48	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	50	MeCN	90	86
49	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	33	MeCN	90	78
50	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	25	MeCN	90	77
51	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	10	MeCN	90	33
52	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	5	MeCN	90	8
53	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	100	none	0	93
54	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	75	none	0	99
55	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	50	none	0	99
56	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	33	none	0	100
57	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	25	none	0	99
58	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	10	none	0	99
59	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	5	none	0	85
60	QMA	Cl ⁻	KHCO ₃ /K ₂₂₂	100	none	0	95
61	QMA	Cl ⁻	KHCO ₃ /K ₂₂₂	75	none	0	96
62	QMA	Cl ⁻	KHCO ₃ /K ₂₂₂	50	none	0	96
63	QMA	Cl ⁻	KHCO ₃ /K ₂₂₂	33	none	0	96
64	QMA	Cl ⁻	KHCO ₃ /K ₂₂₂	25	none	0	96
65	QMA	Cl ⁻	KHCO ₃ /K ₂₂₂	10	none	0	62
66	QMA	Cl ⁻	KHCO ₃ /K ₂₂₂	5	none	0	9
67	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	100	MeCN	50	99

68	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	75	MeCN	50	99
69	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	50	MeCN	50	99
70	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	33	MeCN	50	99
71	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	25	MeCN	50	99
72	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	10	MeCN	50	76
73	QMA	HCO ₃ ⁻	KHCO ₃ /K ₂₂₂	5	MeCN	50	20
74	QMA	Cl ⁻	KHCO ₃ /18C6	100	MeCN	90	78
75	QMA	Cl ⁻	KHCO ₃ /18C6	75	MeCN	90	70
76	QMA	Cl ⁻	KHCO ₃ /18C6	50	MeCN	90	52
77	QMA	Cl ⁻	KHCO ₃ /18C6	33	MeCN	90	11
78	QMA	Cl ⁻	KHCO ₃ /18C6	25	MeCN	90	2
79	QMA	Cl ⁻	KHCO ₃ /18C6	10	MeCN	90	0
80	QMA	Cl ⁻	KHCO ₃ /18C6	5	MeCN	90	0
81	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	100	MeCN	90	88
82	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	75	MeCN	90	76
83	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	50	MeCN	90	70
84	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	33	MeCN	90	51
85	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	25	MeCN	90	43
86	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	10	MeCN	90	10
87	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	5	MeCN	90	4
88	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	100	none	0	96
89	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	75	none	0	96
90	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	50	none	0	94
91	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	33	none	0	96
92	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	25	none	0	96
93	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	10	none	0	68
94	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	5	none	0	7
95	QMA	Cl ⁻	KHCO ₃ /18C6	100	none	0	97
96	QMA	Cl ⁻	KHCO ₃ /18C6	75	none	0	97
97	QMA	Cl ⁻	KHCO ₃ /18C6	50	none	0	97
98	QMA	Cl ⁻	KHCO ₃ /18C6	33	none	0	96
99	QMA	Cl ⁻	KHCO ₃ /18C6	25	none	0	95
100	QMA	Cl ⁻	KHCO ₃ /18C6	10	none	0	53
101	QMA	Cl ⁻	KHCO ₃ /18C6	5	none	0	6
102	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	100	MeCN	50	99
103	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	75	MeCN	50	99
104	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	50	MeCN	50	99
105	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	33	MeCN	50	99
106	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	25	MeCN	50	97
107	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	10	MeCN	50	62
108	QMA	HCO ₃ ⁻	KHCO ₃ /18C6	5	MeCN	50	7
109	QMA	Cl ⁻	Et ₄ NHCO ₃	100	MeCN	90	52
110	QMA	Cl ⁻	Et ₄ NHCO ₃	75	MeCN	90	45
111	QMA	Cl ⁻	Et ₄ NHCO ₃	50	MeCN	90	35
112	QMA	Cl ⁻	Et ₄ NHCO ₃	33	MeCN	90	22
113	QMA	Cl ⁻	Et ₄ NHCO ₃	25	MeCN	90	6
114	QMA	Cl ⁻	Et ₄ NHCO ₃	10	MeCN	90	2
115	QMA	Cl ⁻	Et ₄ NHCO ₃	5	MeCN	90	1
116	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	100	MeCN	90	90
117	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	75	MeCN	90	80
118	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	50	MeCN	90	75

119	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	33	MeCN	90	65
120	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	25	MeCN	90	50
121	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	10	MeCN	90	22
122	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	5	MeCN	90	8
123	QMA	Cl ⁻	Et ₄ NHCO ₃	100	none	0	99
124	QMA	Cl ⁻	Et ₄ NHCO ₃	75	none	0	98
125	QMA	Cl ⁻	Et ₄ NHCO ₃	50	none	0	98
126	QMA	Cl ⁻	Et ₄ NHCO ₃	33	none	0	97
127	QMA	Cl ⁻	Et ₄ NHCO ₃	25	none	0	94
128	QMA	Cl ⁻	Et ₄ NHCO ₃	10	none	0	25
129	QMA	Cl ⁻	Et ₄ NHCO ₃	5	none	0	2
130	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	100	none	0	99
131	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	75	none	0	99
132	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	50	none	0	99
133	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	33	none	0	99
134	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	25	none	0	98
135	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	10	none	0	54
136	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	5	none	0	7
137	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	100	MeCN	50	100
138	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	75	MeCN	50	99
139	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	50	MeCN	50	99
140	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	33	MeCN	50	96
141	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	25	MeCN	50	94
142	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	10	MeCN	50	35
143	QMA	HCO ₃ ⁻	Et ₄ NHCO ₃	5	MeCN	50	2
144	QMA	Cl ⁻	Cs ₂ CO ₃	100	MeCN	90	7
145	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	100	none	0	99
146	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	75	none	0	99
147	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	50	none	0	99
148	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	33	none	0	99
149	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	25	none	0	100
150	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	10	none	0	98
151	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	5	none	0	50
152	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	100	none	0	99
153	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	75	none	0	98
154	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	50	none	0	98
155	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	33	none	0	98
156	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	25	none	0	98
157	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	10	none	0	91
158	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	5	none	0	25
159	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	100	MeCN	50	98
160	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	75	MeCN	50	98
161	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	50	MeCN	50	98
162	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	33	MeCN	50	98
163	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	25	MeCN	50	98
164	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	10	MeCN	50	96
165	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	5	MeCN	50	67
166	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	100	MeCN	50	97
167	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	75	MeCN	50	97
168	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	50	MeCN	50	97
169	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	33	MeCN	50	97

170	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	25	MeCN	50	97
171	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	10	MeCN	50	61
172	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	5	MeCN	50	12
173	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	100	MeCN	90	96
174	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	75	MeCN	90	98
175	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	50	MeCN	90	96
176	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	33	MeCN	90	90
177	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	25	MeCN	90	86
178	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	10	MeCN	90	94
179	QMA	HCO ₃ ⁻	K ₂ C ₂ O ₄ /18C6	5	MeCN	90	32
180	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	100	MeCN	90	87
181	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	75	MeCN	90	81
182	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	50	MeCN	90	76
183	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	33	MeCN	90	67
184	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	25	MeCN	90	43
185	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	10	MeCN	90	2
186	QMA	Cl ⁻	K ₂ C ₂ O ₄ /18C6	5	MeCN	90	2
187	QMA	HCO ₃ ⁻	NaOAc	100	none	0	100
188	QMA	HCO ₃ ⁻	NaOAc	20	none	0	84
189	QMA	HCO ₃ ⁻	NaOAc	10	none	0	40
190	QMA	HCO ₃ ⁻	NaOAc	5	none	0	24
191	QMA	Cl ⁻	DBU	100	MeCN	90	9
192	QMA	Cl ⁻	DBU	75	MeCN	90	7
193	QMA	Cl ⁻	DBU	50	MeCN	90	4
194	QMA	Cl ⁻	DBU	33	MeCN	90	2
195	QMA	Cl ⁻	DBU	25	MeCN	90	1
196	QMA	Cl ⁻	DBU	10	MeCN	90	0
197	QMA	Cl ⁻	DBU	5	MeCN	90	0
198	QMA	Cl ⁻	DBU	5	none	0	81
199	QMA	Cl ⁻	DBU	10	none	0	79
200	QMA	Cl ⁻	DBU	20	none	0	95
201	QMA	Cl ⁻	DBU	33	none	0	97
202	QMA	Cl ⁻	DBU	50	none	0	98
203	QMA	Cl ⁻	DBU	75	none	0	98
204	QMA	Cl ⁻	DBU	100	none	0	98
205	QMA	HCO ₃ ⁻	DBU	2	none	0	2
206	QMA	HCO ₃ ⁻	DBU	3,3	none	0	7
207	QMA	HCO ₃ ⁻	DBU	5	none	0	22
208	QMA	HCO ₃ ⁻	DBU	5	none	0	24
209	QMA	HCO ₃ ⁻	DBU	5	none	0	16
210	QMA	HCO ₃ ⁻	DBU	10	none	0	87
211	QMA	HCO ₃ ⁻	DBU	20	none	0	99
212	QMA	HCO ₃ ⁻	DBU	50	none	0	99
213	QMA	HCO ₃ ⁻	DBU	5	none	0	98
214	QMA	HCO ₃ ⁻	DBU	5	none	0	98
215	QMA	HCO ₃ ⁻	DBU	10	none	0	97
216	QMA	HCO ₃ ⁻	DBU	20	none	0	99
217	QMA	Cl ⁻	DBU	5	none	0	10
218	QMA	Cl ⁻	DBU	10	none	0	61
219	QMA	HCO ₃ ⁻	DBU	100	MeCN	50	100
220	QMA	HCO ₃ ⁻	DBU	75	MeCN	50	100

221	QMA	HCO ₃ ⁻	DBU	50	MeCN	50	100
222	QMA	HCO ₃ ⁻	DBU	33	MeCN	50	100
223	QMA	HCO ₃ ⁻	DBU	25	MeCN	50	100
224	QMA	HCO ₃ ⁻	DBU	10	MeCN	50	46
225	QMA	HCO ₃ ⁻	DBU	5	MeCN	50	3
226	QMA	HCO ₃ ⁻	DBU	100	MeCN	90	87
227	QMA	HCO ₃ ⁻	DBU	75	MeCN	90	84
228	QMA	HCO ₃ ⁻	DBU	50	MeCN	90	80
229	QMA	HCO ₃ ⁻	DBU	33	MeCN	90	76
230	QMA	HCO ₃ ⁻	DBU	25	MeCN	90	74
231	QMA	HCO ₃ ⁻	DBU	100	MeCN	90	87
232	QMA	HCO ₃ ⁻	DBU	100	MeCN	50	100
233	QMA	HCO ₃ ⁻	DBU	10	MeCN	90	63
234	QMA	HCO ₃ ⁻	DBU	10	MeCN	50	95
235	QMA	HCO ₃ ⁻	DBU	100	MeCN	10	100
236	QMA	HCO ₃ ⁻	DBU	10	none	0	98
237	QMA	HCO ₃ ⁻	DBU	10	MeCN	90	29
238	QMA	HCO ₃ ⁻	DBU	5	MeCN	90	6
239	QMA	Cl ⁻	Et ₃ N	100	MeCN	90	0
240	QMA	Cl ⁻	Et ₃ N	75	MeCN	90	0
241	QMA	Cl ⁻	Et ₃ N	50	MeCN	90	0
242	QMA	Cl ⁻	Et ₃ N	33	MeCN	90	0
243	QMA	Cl ⁻	Et ₃ N	25	MeCN	90	0
244	QMA	Cl ⁻	Et ₃ N	10	MeCN	90	0
245	QMA	Cl ⁻	Et ₃ N	5	MeCN	90	0
246	QMA	HCO ₃ ⁻	Et ₃ N	100	MeCN	90	2
247	QMA	HCO ₃ ⁻	Et ₃ N	75	MeCN	90	1
248	QMA	HCO ₃ ⁻	Et ₃ N	50	MeCN	90	0
249	QMA	HCO ₃ ⁻	Et ₃ N	33	MeCN	90	0
250	QMA	HCO ₃ ⁻	Et ₃ N	25	MeCN	90	0
251	QMA	HCO ₃ ⁻	Et ₃ N	10	MeCN	90	0
252	QMA	HCO ₃ ⁻	Et ₃ N	5	MeCN	90	0
253	QMA	HCO ₃ ⁻	Et ₃ N	100	MeCN	90	3
254	QMA	HCO ₃ ⁻	Et ₃ N	100	MeCN	50	97
255	QMA	HCO ₃ ⁻	Et ₃ N	100	MeCN	10	99
256	QMA	Cl ⁻	Et ₃ N	5	none	0	2
257	QMA	Cl ⁻	Et ₃ N	10	none	0	10
258	QMA	Cl ⁻	Et ₃ N	20	none	0	39
259	QMA	Cl ⁻	Et ₃ N	33	none	0	44
260	QMA	Cl ⁻	Et ₃ N	50	none	0	55
261	QMA	Cl ⁻	Et ₃ N	75	none	0	59
262	QMA	Cl ⁻	Et ₃ N	100	none	0	71
263	QMA	HCO ₃ ⁻	Et ₃ N	5	MeCN	50	8
264	QMA	HCO ₃ ⁻	Et ₃ N	10	MeCN	50	50
265	QMA	HCO ₃ ⁻	Et ₃ N	20	MeCN	50	81
266	QMA	HCO ₃ ⁻	Et ₃ N	33	MeCN	50	84
267	QMA	HCO ₃ ⁻	Et ₃ N	50	MeCN	50	93
268	QMA	HCO ₃ ⁻	Et ₃ N	75	MeCN	50	92
269	QMA	HCO ₃ ⁻	Et ₃ N	100	MeCN	50	93
270	QMA	HCO ₃ ⁻	Et ₃ N	5	none	0	21
271	QMA	HCO ₃ ⁻	Et ₃ N	10	none	0	28

272	QMA	HCO ₃ ⁻	Et ₃ N	20	none	0	97
273	QMA	HCO ₃ ⁻	Et ₃ N	33	none	0	99
274	QMA	HCO ₃ ⁻	Et ₃ N	50	none	0	100
275	QMA	HCO ₃ ⁻	Et ₃ N	75	none	0	99
276	QMA	HCO ₃ ⁻	Et ₃ N	100	none	0	99
277	QMA	Cl ⁻	DIPEA	5	none	0	12
278	QMA	Cl ⁻	DIPEA	10	none	0	80
279	QMA	Cl ⁻	DIPEA	25	none	0	94
280	QMA	Cl ⁻	DIPEA	33	none	0	95
281	QMA	Cl ⁻	DIPEA	50	none	0	97
282	QMA	Cl ⁻	DIPEA	75	none	0	97
283	QMA	Cl ⁻	DIPEA	75	none	0	81
284	QMA	Cl ⁻	DIPEA	100	none	0	97
285	QMA	Cl ⁻	DIPEA	5	MeCN	90	0
286	QMA	Cl ⁻	DIPEA	10	MeCN	90	0
287	QMA	Cl ⁻	DIPEA	25	MeCN	90	0
288	QMA	Cl ⁻	DIPEA	33	MeCN	90	1
289	QMA	Cl ⁻	DIPEA	50	MeCN	90	0
290	QMA	Cl ⁻	DIPEA	75	MeCN	90	2
291	QMA	Cl ⁻	DIPEA	100	MeCN	90	0
292	QMA	HCO ₃ ⁻	DIPEA	5	MeCN	90	0
293	QMA	HCO ₃ ⁻	DIPEA	10	MeCN	90	1
294	QMA	HCO ₃ ⁻	DIPEA	25	MeCN	90	1
295	QMA	HCO ₃ ⁻	DIPEA	33	MeCN	90	3
296	QMA	HCO ₃ ⁻	DIPEA	50	MeCN	90	0
297	QMA	HCO ₃ ⁻	DIPEA	75	MeCN	90	6
298	QMA	HCO ₃ ⁻	DIPEA	100	MeCN	90	4
299	QMA	HCO ₃ ⁻	DIPEA	5	MeCN	50	9
300	QMA	HCO ₃ ⁻	DIPEA	10	MeCN	50	76
301	QMA	HCO ₃ ⁻	DIPEA	25	MeCN	50	93
302	QMA	HCO ₃ ⁻	DIPEA	33	MeCN	50	98
303	QMA	HCO ₃ ⁻	DIPEA	50	MeCN	50	94
304	QMA	HCO ₃ ⁻	DIPEA	75	MeCN	50	99
305	QMA	HCO ₃ ⁻	DIPEA	100	MeCN	50	96
306	QMA	HCO ₃ ⁻	DIPEA	5	none	0	55
307	QMA	HCO ₃ ⁻	DIPEA	10	none	0	91
308	QMA	HCO ₃ ⁻	DIPEA	25	none	0	100
309	QMA	HCO ₃ ⁻	DIPEA	33	none	0	99
310	QMA	HCO ₃ ⁻	DIPEA	50	none	0	99
311	QMA	HCO ₃ ⁻	DIPEA	75	none	0	99
312	QMA	HCO ₃ ⁻	DIPEA	100	none	0	99
313	QMA	Cl ⁻	DMAP	100	MeCN	90	0
314	QMA	Cl ⁻	DMAP	75	MeCN	90	0
315	QMA	Cl ⁻	DMAP	50	MeCN	90	0
316	QMA	Cl ⁻	DMAP	33	MeCN	90	0
317	QMA	Cl ⁻	DMAP	25	MeCN	90	0
318	QMA	Cl ⁻	DMAP	10	MeCN	90	0
319	QMA	Cl ⁻	DMAP	5	MeCN	90	0
320	QMA	Cl ⁻	DMAP	100	MeOH	50	0
321	QMA	Cl ⁻	DMAP	100	MeCN	90	0
322	QMA	HCO ₃ ⁻	DMAP	100	MeCN	90	0

323	QMA	HCO ₃ ⁻	DMAP	75	MeCN	90	0
324	QMA	HCO ₃ ⁻	DMAP	50	MeCN	90	0
325	QMA	HCO ₃ ⁻	DMAP	33	MeCN	90	0
326	QMA	HCO ₃ ⁻	DMAP	25	MeCN	90	0
327	QMA	HCO ₃ ⁻	DMAP	10	MeCN	90	0
328	QMA	HCO ₃ ⁻	DMAP	5	MeCN	90	0
329	QMA	Cl ⁻	DMAP	100	none	0	13
330	QMA	Cl ⁻	DMAP	75	none	0	14
331	QMA	Cl ⁻	DMAP	50	none	0	7
332	QMA	Cl ⁻	DMAP	33	none	0	9
333	QMA	Cl ⁻	DMAP	25	none	0	4
334	QMA	Cl ⁻	DMAP	10	none	0	4
335	QMA	Cl ⁻	DMAP	5	none	0	2
336	QMA	HCO ₃ ⁻	DMAP	100	none	0	99
337	QMA	HCO ₃ ⁻	DMAP	75	none	0	99
338	QMA	HCO ₃ ⁻	DMAP	50	none	0	99
339	QMA	HCO ₃ ⁻	DMAP	33	none	0	99
340	QMA	HCO ₃ ⁻	DMAP	25	none	0	97
341	QMA	HCO ₃ ⁻	DMAP	10	none	0	52
342	QMA	HCO ₃ ⁻	DMAP	5	none	0	3
343	QMA	HCO ₃ ⁻	DMAP	100	MeCN	50	13
344	QMA	HCO ₃ ⁻	DMAP	75	MeCN	50	4
345	QMA	HCO ₃ ⁻	DMAP	50	MeCN	50	15
346	QMA	HCO ₃ ⁻	DMAP	33	MeCN	50	9
347	QMA	HCO ₃ ⁻	DMAP	25	MeCN	50	1
348	QMA	HCO ₃ ⁻	DMAP	10	MeCN	50	0
349	QMA	HCO ₃ ⁻	DMAP	5	MeCN	50	0
350	QMA	HCO ₃ ⁻	DMAP	100	MeCN	90	0
351	QMA	HCO ₃ ⁻	DMAP	100	MeCN	50	33
352	QMA	HCO ₃ ⁻	DMAP	100	MeCN	90	0
353	QMA	HCO ₃ ⁻	DMAP	100	MeCN	50	35
354	QMA	HCO ₃ ⁻	DMAP	100	none	0	94
355	QMA	HCO ₃ ⁻	DMAP	100	none	0	96
356	QMA	HCO ₃ ⁻	pyridine	100	MeCN	90	0
357	QMA	HCO ₃ ⁻	pyridine	100	MeCN	50	0
358	QMA	HCO ₃ ⁻	pyridine	500	none	0	1
359	QMA	HCO ₃ ⁻	pyridine	100	MeCN	10	0
360	QMA	HCO ₃ ⁻	Cu(OTf) ₂	20	none	0	62
361	QMA	HCO ₃ ⁻	Cu(OTf) ₂	100	none	0	98
362	QMA	Cl ⁻	(Bu ₄ N) ₂ SO ₄	5	MeCN	90	82
363	QMA	Cl ⁻	(Bu ₄ N) ₂ SO ₄	10	MeCN	90	81
364	QMA	Cl ⁻	(Bu ₄ N) ₂ SO ₄	20	MeCN	90	79
365	QMA	Cl ⁻	(Bu ₄ N) ₂ SO ₄	33	MeCN	90	85
366	QMA	Cl ⁻	(Bu ₄ N) ₂ SO ₄	50	MeCN	90	89
367	QMA	Cl ⁻	(Bu ₄ N) ₂ SO ₄	75	MeCN	90	91
368	QMA	Cl ⁻	(Bu ₄ N) ₂ SO ₄	100	MeCN	90	90
369	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	5	MeCN	90	56
370	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	10	MeCN	90	68
371	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	20	MeCN	90	78
372	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	33	MeCN	90	81
373	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	50	MeCN	90	81

374	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	75	MeCN	90	84
375	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	100	MeCN	90	84
376	QMA	Cl ⁻	(Bu ₄ N) ₂ SO ₄	5	none	0	64
377	QMA	Cl ⁻	(Bu ₄ N) ₂ SO ₄	10	none	0	71
378	QMA	Cl ⁻	(Bu ₄ N) ₂ SO ₄	20	none	0	83
379	QMA	Cl ⁻	(Bu ₄ N) ₂ SO ₄	33	none	0	87
380	QMA	Cl ⁻	(Bu ₄ N) ₂ SO ₄	50	none	0	89
381	QMA	Cl ⁻	(Bu ₄ N) ₂ SO ₄	75	none	0	87
382	QMA	Cl ⁻	(Bu ₄ N) ₂ SO ₄	100	none	0	89
383	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	5	none	0	74
384	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	10	none	0	91
385	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	20	none	0	94
386	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	33	none	0	88
387	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	50	none	0	94
388	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	75	none	0	94
389	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	100	none	0	93
390	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	5	MeCN	50	86
391	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	10	MeCN	50	89
392	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	20	MeCN	50	89
393	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	33	MeCN	50	90
394	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	50	MeCN	50	89
395	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	75	MeCN	50	89
396	QMA	HCO ₃ ⁻	(Bu ₄ N) ₂ SO ₄	100	MeCN	50	90
397	QMA	HCO ₃ ⁻	Bu ₄ NOMs	100	none	0	99
398	QMA	HCO ₃ ⁻	Bu ₄ NOMs	20	none	0	93
399	QMA	HCO ₃ ⁻	Bu ₄ NOMs	10	none	0	47
400	QMA	HCO ₃ ⁻	Bu ₄ NOMs	5	none	0	22
401	QMA	HCO ₃ ⁻	Bu ₄ NOMs	100	MeCN	50	100
402	QMA	HCO ₃ ⁻	Bu ₄ NOMs	75	MeCN	50	99
403	QMA	HCO ₃ ⁻	Bu ₄ NOMs	50	MeCN	50	98
404	QMA	HCO ₃ ⁻	Bu ₄ NOMs	33	MeCN	50	95
405	QMA	HCO ₃ ⁻	Bu ₄ NOMs	25	MeCN	50	90
406	QMA	HCO ₃ ⁻	Bu ₄ NOMs	10	MeCN	50	30
407	QMA	HCO ₃ ⁻	Bu ₄ NOMs	5	MeCN	50	5
408	QMA	HCO ₃ ⁻	Bu ₄ NOMs	100	none	0	98
409	QMA	HCO ₃ ⁻	Bu ₄ NOMs	75	none	0	99
410	QMA	HCO ₃ ⁻	Bu ₄ NOMs	50	none	0	98
411	QMA	HCO ₃ ⁻	Bu ₄ NOMs	33	none	0	99
412	QMA	HCO ₃ ⁻	Bu ₄ NOMs	25	none	0	95
413	QMA	HCO ₃ ⁻	Bu ₄ NOMs	10	none	0	73
414	QMA	HCO ₃ ⁻	Bu ₄ NOMs	5	none	0	6
415	QMA	Cl ⁻	Bu ₄ NOMs	100	none	0	98
416	QMA	Cl ⁻	Bu ₄ NOMs	75	none	0	97
417	QMA	Cl ⁻	Bu ₄ NOMs	50	none	0	95
418	QMA	Cl ⁻	Bu ₄ NOMs	33	none	0	92
419	QMA	Cl ⁻	Bu ₄ NOMs	25	none	0	84
420	QMA	Cl ⁻	Bu ₄ NOMs	10	none	0	23
421	QMA	Cl ⁻	Bu ₄ NOMs	5	none	0	0
422	QMA	HCO ₃ ⁻	Bu ₄ NOMs	100	MeCN	90	37
423	QMA	HCO ₃ ⁻	Bu ₄ NOMs	75	MeCN	90	55
424	QMA	HCO ₃ ⁻	Bu ₄ NOMs	50	MeCN	90	38

425	QMA	HCO ₃ ⁻	Bu ₄ NOMs	33	MeCN	90	4
426	QMA	HCO ₃ ⁻	Bu ₄ NOMs	25	MeCN	90	36
427	QMA	HCO ₃ ⁻	Bu ₄ NOMs	10	MeCN	90	1
428	QMA	HCO ₃ ⁻	Bu ₄ NOMs	5	MeCN	90	2
429	QMA	Cl ⁻	Bu ₄ NOMs	100	MeCN	90	3
430	QMA	Cl ⁻	Bu ₄ NOMs	75	MeCN	90	1
431	QMA	Cl ⁻	Bu ₄ NOMs	50	MeCN	90	1
432	QMA	Cl ⁻	Bu ₄ NOMs	33	MeCN	90	1
433	QMA	Cl ⁻	Bu ₄ NOMs	25	MeCN	90	2
434	QMA	Cl ⁻	Bu ₄ NOMs	10	MeCN	90	-1
435	QMA	Cl ⁻	Bu ₄ NOMs	5	MeCN	90	1
436	QMA	HCO ₃ ⁻	KOTf	100	none	0	100
437	QMA	HCO ₃ ⁻	KOTf	20	none	0	96
438	QMA	HCO ₃ ⁻	KOTf	10	none	0	51
439	QMA	HCO ₃ ⁻	KOTf	5	none	0	27
440	QMA	Cl ⁻	KOTf	5	none	0	14
441	QMA	Cl ⁻	KOTf	10	none	0	35
442	QMA	Cl ⁻	KOTf	20	none	0	87
443	QMA	Cl ⁻	KOTf	33	none	0	98
444	QMA	Cl ⁻	KOTf	50	none	0	99
445	QMA	Cl ⁻	KOTf	75	none	0	100
446	QMA	Cl ⁻	KOTf	100	none	0	99
447	QMA	HCO ₃ ⁻	KOTf	5	none	0	21
448	QMA	HCO ₃ ⁻	KOTf	10	none	0	42
449	QMA	HCO ₃ ⁻	KOTf	20	none	0	96
450	QMA	HCO ₃ ⁻	KOTf	33	none	0	99
451	QMA	HCO ₃ ⁻	KOTf	50	none	0	100
452	QMA	HCO ₃ ⁻	KOTf	75	none	0	100
453	QMA	HCO ₃ ⁻	KOTf	100	none	0	100
454	QMA	HCO ₃ ⁻	KOTf	5	MeCN	50	10
455	QMA	HCO ₃ ⁻	KOTf	10	MeCN	50	35
456	QMA	HCO ₃ ⁻	KOTf	20	MeCN	50	73
457	QMA	HCO ₃ ⁻	KOTf	33	MeCN	50	93
458	QMA	HCO ₃ ⁻	KOTf	50	MeCN	50	98
459	QMA	HCO ₃ ⁻	KOTf	75	MeCN	50	99
460	QMA	HCO ₃ ⁻	KOTf	100	MeCN	50	100
461	QMA	HCO ₃ ⁻	KOTf	5	MeCN	90	3
462	QMA	HCO ₃ ⁻	KOTf	10	MeCN	90	1
463	QMA	HCO ₃ ⁻	KOTf	20	MeCN	90	5
464	QMA	HCO ₃ ⁻	KOTf	100	MeCN	90	3
465	QMA	HCO ₃ ⁻	KOTf	200	MeCN	90	3
466	QMA	Cl ⁻	KOTf	5	MeCN	90	2
467	QMA	Cl ⁻	KOTf	100	MeCN	90	1
468	QMA	Cl ⁻	KOTf	200	MeCN	90	3
469	QMA	HCO ₃ ⁻	KOTf/18C6	20	MeCN	50	66
470	QMA	HCO ₃ ⁻	KOTf/18C6	50	MeCN	50	77
471	QMA	HCO ₃ ⁻	KOTf/18C6	100	MeCN	50	98
472	QMA	HCO ₃ ⁻	KOTf/18C6	20	MeCN	90	2
473	QMA	HCO ₃ ⁻	KOTf/18C6	50	MeCN	90	5
474	QMA	HCO ₃ ⁻	KOTf/18C6	100	MeCN	90	19

Screening and cold testing

Initial radiolabeling tests

Initial radiolabeling reactions comparing eluting bases from different classes of anions (standard, volatile and neutral). Reactions were performed according to the general method for manual radiolabeling experiments.

Table S2 Results from initial radiolabeling reactions comparing different eluting compounds for HCO₃⁻ and Cl⁻ preconditioned QMA with MeCN as a reaction solvent.

Initial radiolabeling tests								
Exp id	Type of sample	Eluting anion	Concentration eluting anion (mM)	Preconditioning anion	Expected elution (%)	Observed elution (%)	[¹⁸ F]-3 (%)	[¹⁸ F]F ⁻
1	Crude	K ₂ CO ₃ /K ₂₂₂	40	Cl ⁻	100	99	67.3	25.4
2	Resolubilized	K ₂ CO ₃ /K ₂₂₂	40	Cl ⁻	100	99	58.8	35.6
3	Crude	K ₂ CO ₃ /K ₂₂₂	30	Cl ⁻	90	99	61.2	33.1
4	Resolubilized	K ₂ CO ₃ /K ₂₂₂	30	Cl ⁻	90	99	38.8	56.9
5	Crude	K ₂ CO ₃ /K ₂₂₂	10	Cl ⁻	50	44	5.4	90.3
6	Resolubilized	K ₂ CO ₃ /K ₂₂₂	10	Cl ⁻	50	44	3.9	91.2
7	Crude	K ₂ CO ₃ /K ₂₂₂	7	Cl ⁻	20	8	0.2	98.1
8	Resolubilized	K ₂ CO ₃ /K ₂₂₂	7	Cl ⁻	20	8	0.4	97.5
9	Crude	K ₂ CO ₃ /K ₂₂₂	10	HCO ₃ ⁻	90	95	66.8	21.2
10	Resolubilized	K ₂ CO ₃ /K ₂₂₂	10	HCO ₃ ⁻	90	95	49.3	41.5
11	Crude	K ₂ CO ₃ /K ₂₂₂	10	HCO ₃ ⁻	90	100	71	21.8
12	Resolubilized	K ₂ CO ₃ /K ₂₂₂	10	HCO ₃ ⁻	90	100	48.3	46.8
13	Crude	K ₂ CO ₃ /K ₂₂₂	5	HCO ₃ ⁻	50	58	65	26.3
14	Resolubilized	K ₂ CO ₃ /K ₂₂₂	5	HCO ₃ ⁻	50	58	34.7	59.7
15	Crude	K ₂ CO ₃ /K ₂₂₂	2	HCO ₃ ⁻	20	10	59.9	29.6
16	Resolubilized	K ₂ CO ₃ /K ₂₂₂	2	HCO ₃ ⁻	20	10	26.7	68.6
17	Crude	K ₂ CO ₃ /K ₂₂₂	2	HCO ₃ ⁻	20	4	21.5	69.7
18	Resolubilized	K ₂ CO ₃ /K ₂₂₂	2	HCO ₃ ⁻	20	4	6	90.3
19	Crude	Et ₃ N	200	Cl ⁻	40	4	0	96.9
20	Resolubilized	Et ₃ N	200	Cl ⁻	40	4	0	97.8
21	Crude	Et ₃ N	20	Cl ⁻	20	1	0	95.6
22	Resolubilized	Et ₃ N	20	Cl ⁻	20	1	0	95.7
23	Crude	Et ₃ N	30	HCO ₃ ⁻	90	96	0	97.6
24	Resolubilized	Et ₃ N	30	HCO ₃ ⁻	90	96	0	98
25	Crude	Et ₃ N	6	HCO ₃ ⁻	10	9	0	97.9
26	Resolubilized	Et ₃ N	6	HCO ₃ ⁻	10	9	0	97.6
27	Crude	Bu ₄ NOMs	50	Cl ⁻	50	89	0.1	96.7
28	Resolubilized	Bu ₄ NOMs	50	Cl ⁻	50	89	0.1	96.1
29	Crude	Bu ₄ NOMs	20	Cl ⁻	20	24	0	97.3
30	Resolubilized	Bu ₄ NOMs	20	Cl ⁻	20	24	0	96.9
31	Crude	Bu ₄ NOMs	30	HCO ₃ ⁻	100	98	63.5	27.1
32	Resolubilized	Bu ₄ NOMs	30	HCO ₃ ⁻	100	98	53.5	37.2
33	Crude	Bu ₄ NOMs	20	HCO ₃ ⁻	90	92	65.7	21.2
34	Resolubilized	Bu ₄ NOMs	20	HCO ₃ ⁻	90	92	51.7	30
35	Crude	Bu ₄ NOMs	15	HCO ₃ ⁻	50	82	60.3	27.5
36	Resolubilized	Bu ₄ NOMs	15	HCO ₃ ⁻	50	82	51.8	36.2
37	Crude	Bu ₄ NOMs	6	HCO ₃ ⁻	20	22	62.4	30.7
38	Resolubilized	Bu ₄ NOMs	6	HCO ₃ ⁻	20	22	52.7	39.8

39	Crude	DIPEA	50	HCO ₃ ⁻	95	96	0	97.3
40	Resolubilized	DIPEA	50	HCO ₃ ⁻	95	96	0.2	97.1
41	Crude	DIPEA	30	HCO ₃ ⁻	90	94	0.2	97.5
42	Resolubilized	DIPEA	30	HCO ₃ ⁻	90	94	0.2	97.4
43	Crude	DBU	10	HCO ₃ ⁻	100	81	0	96.4
44	Resolubilized	DBU	10	HCO ₃ ⁻	100	81	0	97.1
45	Crude	DBU	5	HCO ₃ ⁻	90	20	0	96.5
46	Resolubilized	DBU	5	HCO ₃ ⁻	90	20	0	98.1

Comparison of UV-trace from crude reactions for reactions using Cl⁻ preconditioned QMA

Samples were taken from different reactions (entry 6, 32 and 36) and the retention time on the analytical HPLC was compared to confirm the formation of chlorinated precursor **7b** when using Cl⁻ preconditioned QMAs, *Figure S3*.

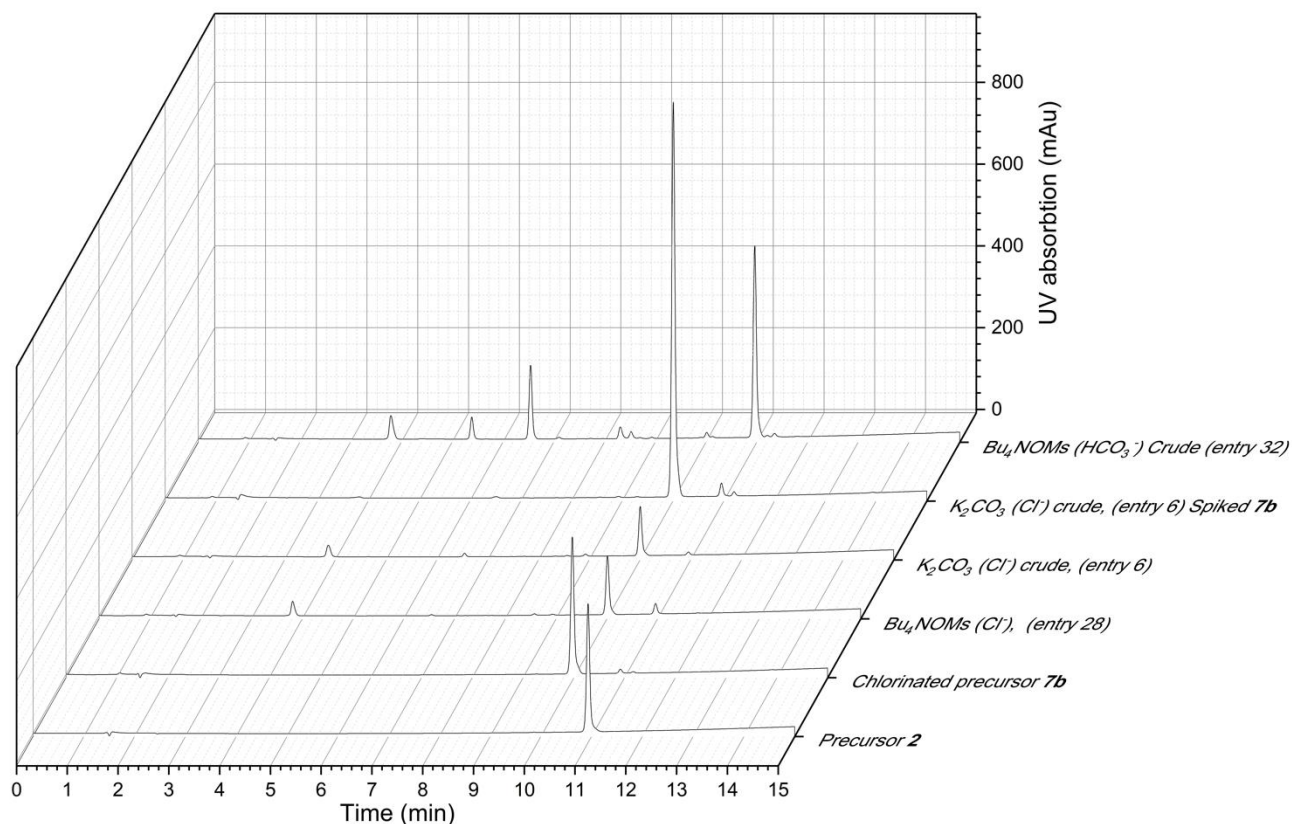


Figure S3 Chromatogram from analytical HPLC analysis (UV absorption, 254 nm) of reaction crudes for Cl⁻ preconditioned QMA, reference compounds or a reference reaction using a HCO₃⁻ preconditioned QMA eluted with Bu₄NOMs.

Non-basic elution of non-basic preconditioned QMA

Reactions were conducted according to the general procedure for manual radiolabeling experiments.

Table S3 Results from OMs⁻ and SO₄²⁻ preconditioned QMAs eluted with Bu₄NOMs or (Bu₄N)₂SO₄ with MeCN used as a reaction solvent.

Non-basic elutions with non-basic preconditioning								
Exp id	Type of sample	Eluting anion	Concentration eluting anion (mM)	Preconditioning anion	Expected elution (%)	Observed elution (%)	[¹⁸ F]-3 (%)	[¹⁸ F]F ⁻
47	Crude	(Bu ₄ N) ₂ SO ₄	10	SO ₄ ²⁻	90	83	0	100
48	Resolubilized	(Bu ₄ N) ₂ SO ₄	10	SO ₄ ²⁻	90	83	0	100
49	Crude	(Bu ₄ N) ₂ SO ₄	6	SO ₄ ²⁻	85	85	0	100
50	Resolubilized	(Bu ₄ N) ₂ SO ₄	6	SO ₄ ²⁻	85	85	0	100
51	Crude	Bu ₄ NOMs	20	SO ₄ ²⁻	90	96	0	100
52	Resolubilized	Bu ₄ NOMs	20	SO ₄ ²⁻	90	96	0	100
53	Crude	Bu ₄ NOMs	6	SO ₄ ²⁻	10	95	0	100
54	Resolubilized	Bu ₄ NOMs	6	SO ₄ ²⁻	10	95	0	100
55	Crude	(Bu ₄ N) ₂ SO ₄	10	OMs ⁻	90	82	0	100
56	Resolubilized	(Bu ₄ N) ₂ SO ₄	10	OMs ⁻	90	82	0	100
57	Crude	(Bu ₄ N) ₂ SO ₄	6	OMs ⁻	85	38	0	100
58	Resolubilized	(Bu ₄ N) ₂ SO ₄	6	OMs ⁻	85	38	0	100
59	Crude	Bu ₄ NOMs	6	OMs ⁻	10	0	0	100
60	Resolubilized	Bu ₄ NOMs	6	OMs ⁻	10	0	0	100
61	Crude	Bu ₄ NOMs	200	OMs ⁻	100	98	1.1	98.2
62	Resolubilized	Bu ₄ NOMs	200	OMs ⁻	100	98	0.7	95.7
63	Crude	Bu ₄ NOMs	20	OMs ⁻	30	25	5.6	60.4
64	Resolubilized	Bu ₄ NOMs	20	OMs ⁻	30	25	1.2	90.5
65	Crude	K ₂ SO ₄ /K ₂₂₂	10	SO ₄ ²⁻	90	96	3	88.6
66	Resolubilized	K ₂ SO ₄ /K ₂₂₂	10	SO ₄ ²⁻	90	96	0.9	95.9

Secondary addition of base to a non-basic preconditioning and elution

Reactions were performed according to the general method for manual radiolabeling reactions using **2** to yield [¹⁸F]**3** with a few exceptions. According to the method described by Lee *et al.* a the QMA was preconditioned using KOMs (0.2 M, 10 mL).⁵ The QMA was then eluted using either Bu₄NOMs (1 mL, 30-50 mM, MeCN/H₂O, 50:50) or KOMs/K₂₂₂ (0.7 mL, 25/50 mM, MeOH). To the reaction vial potassium bicarbonate, -carbonate or hydroxide dissolved in H₂O was added from a stock solution to give a range of concentrations. The resulting mixture was then dried azeotropically according to the general method for manual radiolabeling. The results from the reaction are presented in *Table S4*.

Table S4 Results from radiolabeling experiments using secondary addition of base

KOMs preconditioning Bu ₄ NOMs elution (50 mM) with addition of base					
Exp id	Type of sample	Concentration and type of base added	EE (%)	[¹⁸ F] 3 (%)	[¹⁸ F]F ⁻
67	Crude	1 μmol KHCO ₃	96	0	97.3
68	Resolubilized	1 μmol KHCO ₃	96	0	98.5
69	Crude	5 μmol KHCO ₃	92	13.2	75.6
70	Resolubilized	5 μmol KHCO ₃	92	1	97.3
71	Crude	10 μmol KHCO ₃	97	11.3	81.8
72	Resolubilized	10 μmol KHCO ₃	97	1.9	96.3
73	Crude	1 μmol K ₂ CO ₃	91	12.7	82.9
74	Resolubilized	1 μmol K ₂ CO ₃	91	7.3	90.4

75	Crude	5 μmol K_2CO_3	97	16	72.9
76	Resolubilized	5 μmol K_2CO_3	97	2	95.9
77	Crude	10 μmol K_2CO_3	95	23.3	68.2
78	Resolubilized	10 μmol K_2CO_3	95	3.6	94.7
Elution by 30 mM Bu_4NOMs					
79	Crude	1 μmol KHCO_3	25	5.6	60.4
80	Resolubilized	1 μmol KHCO_3	25	1.2	90.5
Elution by 25 mM KOMs/K_{222}					
81	Crude	7.8 μmol KOH	92	90.4	3.8
82	Resolubilized	7.8 μmol KOH	92	74.2	19.9
83	Crude	7.8 μmol K_2CO_3	90	92.7	2.5
84	Resolubilized	7.8 μmol K_2CO_3	90	64.8	28.4
85	Crude	7.8 μmol KHCO_3	87	70.2	22.2
86	Resolubilized	7.8 μmol KHCO_3	87	57.5	36.9
87	Crude	3.9 μmol KOH	90	83.6	9.4
88	Resolubilized	3.9 μmol KOH	90	73.8	20.6
89	Crude	3.9 μmol KHCO_3	88	89.2	7.5
90	Resolubilized	3.9 μmol KHCO_3	88	59.6	34.4
91	Crude	3.9 μmol KHCO_3 (with stirring)	86	62.9	28.5
92	Resolubilized	3.9 μmol KHCO_3 (with stirring)	86	23.4	70.3
93	Crude	1.85 μmol KOH	92	71.8	14.1
94	Resolubilized	1.85 μmol KOH	92	56.8	33.5
95	Crude	1.85 μmol KHCO_3	86	74.5	18.0
96	Resolubilized	1.85 μmol KHCO_3	86	37.6	56.0
97	Crude	1.85 μmol KHCO_3 (with stirring)	82	33.4	68.8
98	Resolubilized	1.85 μmol KHCO_3 (with stirring)	82	21.8	77.0

Using lower concentrations of added base resulted in lower and lower pRCY. This was due to a higher amount of [^{18}F]fluoride adsorbing to the glass vessel walls. This was especially pronounced for the less basic KHCO_3 compared to KOH indicating that this method is not suitable for low-base conditions (*Figure S4*). Performing the same reactions with stirring did not improve the fluorination efficiency (*Table S4*).

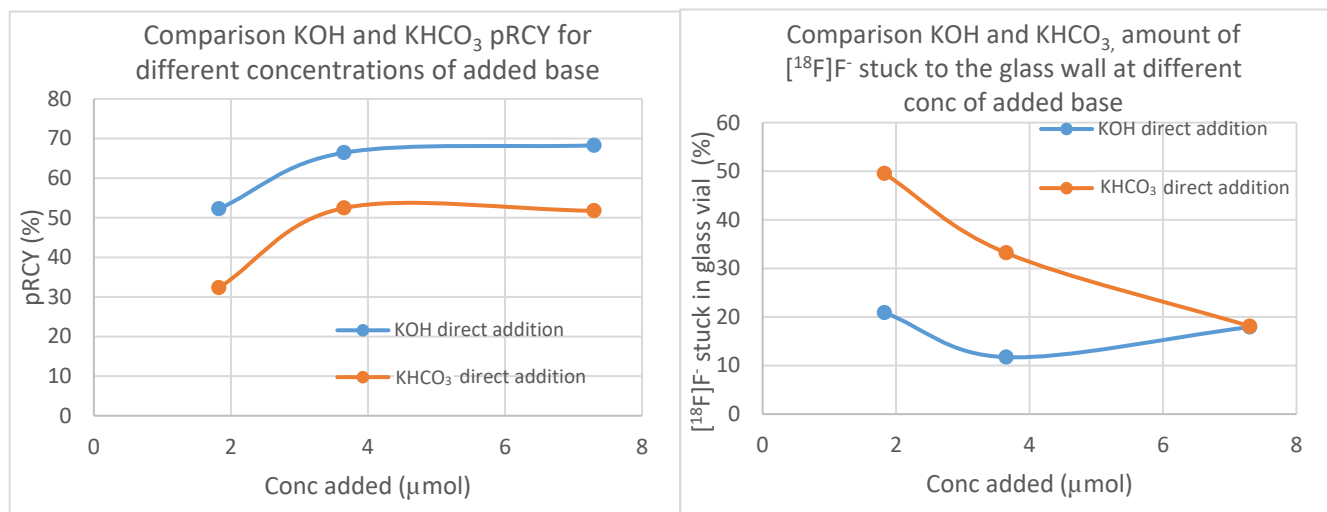


Figure S4 pRCY for reactions preconditioned with KOMs and eluted with KOMs/K₂₂₂ and different concentrations of base added to the eluate (left). Quantification of amount of [¹⁸F]F⁻ stuck to the glass wall at the end of the reaction after direct addition of base to the eluate (right).

Screening preconditioning anions of different pK_a and valency

Screening of different preconditioning anions with Bu₄NOMs (20 mM) used for elution and MeCN as the reaction solvent. Reactions were conducted according to the general method for manual radiolabeling reactions.

Table S5. Results for screening of different preconditioning anions with non-basic elution using Bu₄NOMs.

Screening of precondition anions with increasing pK _a using Bu ₄ NOMs elution								
Exp id	Type of sample	Eluting anion	Concentration eluting anion (mM)	Preconditioning anion	Expected elution (%)	Observed elution (%)	[¹⁸ F]-3 (%)	[¹⁸ F]F ⁻
29	Crude	Bu ₄ NOMs	20	Cl ⁻	20	24	0	97.3
30	Resolubilized	Bu ₄ NOMs	20	Cl ⁻	20	24	0	96.9
63	Crude	Bu ₄ NOMs	20	OMs ⁻	30	28	3.2	96.8
64	Resolubilized	Bu ₄ NOMs	20	OMs ⁻	30	28	3.1	96.7
51	Crude	Bu ₄ NOMs	20	SO ₄ ⁻²	90	96	0	100
52	Resolubilized	Bu ₄ NOMs	20	SO ₄ ⁻²	90	96	0	100
99	Crude	Bu ₄ NOMs	20	H ₂ PO ₄ ⁻	90	86	0	95.2
100	Resolubilized	Bu ₄ NOMs	20	H ₂ PO ₄ ⁻	90	86	0	94.4
101	Crude	Bu ₄ NOMs	20	C ₂ O ₄ ²⁻	90	99	6.7	85.1
102	Resolubilized	Bu ₄ NOMs	20	C ₂ O ₄ ²⁻	90	99	4.4	87
103	Crude	Bu ₄ NOMs	20	AcO ⁻	50	45	0.8	90.1
104	Resolubilized	Bu ₄ NOMs	20	AcO ⁻	50	45	0.9	88.5
105	Crude	Bu ₄ NOMs	20	HCO ₃ ⁻	90	98	63.5	27.1
106	Resolubilized	Bu ₄ NOMs	20	HCO ₃ ⁻	90	98	53.5	37.2
107	Crude	Bu ₄ NOMs	20	HCO ₃ ⁻	90	85	75.9	18.4
108	Resolubilized	Bu ₄ NOMs	20	HCO ₃ ⁻	90	85	71	23.5
109	Crude	Bu ₄ NOMs	20	HCO ₃ ⁻	100	90	52.6	43.2
110	Resolubilized	Bu ₄ NOMs	20	HCO ₃ ⁻	100	90	48.3	46.6
111	Crude	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	95	44.5	50.1
112	Resolubilized	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	95	46.3	49.1
113	Crude	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	97	56.4	38.9
114	Resolubilized	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	97	53.4	40.8

115	Crude	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	95	62.1	33.6
116	Resolubilized	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	95	60.1	34.7
117	Crude	Bu ₄ NOMs	20	CO ₃ ²⁻	90	83	66.8	20.8
118	Resolubilized	Bu ₄ NOMs	20	CO ₃ ²⁻	90	83	53.9	28
119	Crude	Bu ₄ NOMs	20	CO ₃ ²⁻	100	97	71.4	24.3
120	Resolubilized	Bu ₄ NOMs	20	CO ₃ ²⁻	100	97	56.1	39.6
121	Crude	Bu ₄ NOMs	20	CO ₃ ²⁻	100	96	73.2	22.1
122	Resolubilized	Bu ₄ NOMs	20	CO ₃ ²⁻	100	96	55.3	39.9
123	Crude	Bu ₄ NOMs	20	PO ₄ ³⁻	100	97	82.4	12.3
124	Resolubilized	Bu ₄ NOMs	20	PO ₄ ³⁻	100	97	79.7	14.4
125	Crude	Bu ₄ NOMs	20	PO ₄ ³⁻	100	97	88.4	8.5
126	Resolubilized	Bu ₄ NOMs	20	PO ₄ ³⁻	100	97	85	9.1
127	Crude	Bu ₄ NOMs	20	PO ₄ ³⁻	100	97	63.4	30.7
128	Resolubilized	Bu ₄ NOMs	20	PO ₄ ³⁻	100	97	58.1	34.9

Analysis of decayed reaction crudes with different preconditioning anions

Reactions performed according to the general method for manual radiolabeling showed different results depending on the preconditioning of the QMA. Nucleophilic anions substituted the precursor **2** competing with the [¹⁸F]fluoride resulting in very low incorporation. Results from the LCMS and UV-channel on the analytical HPLC can be seen in *Figure S5*.

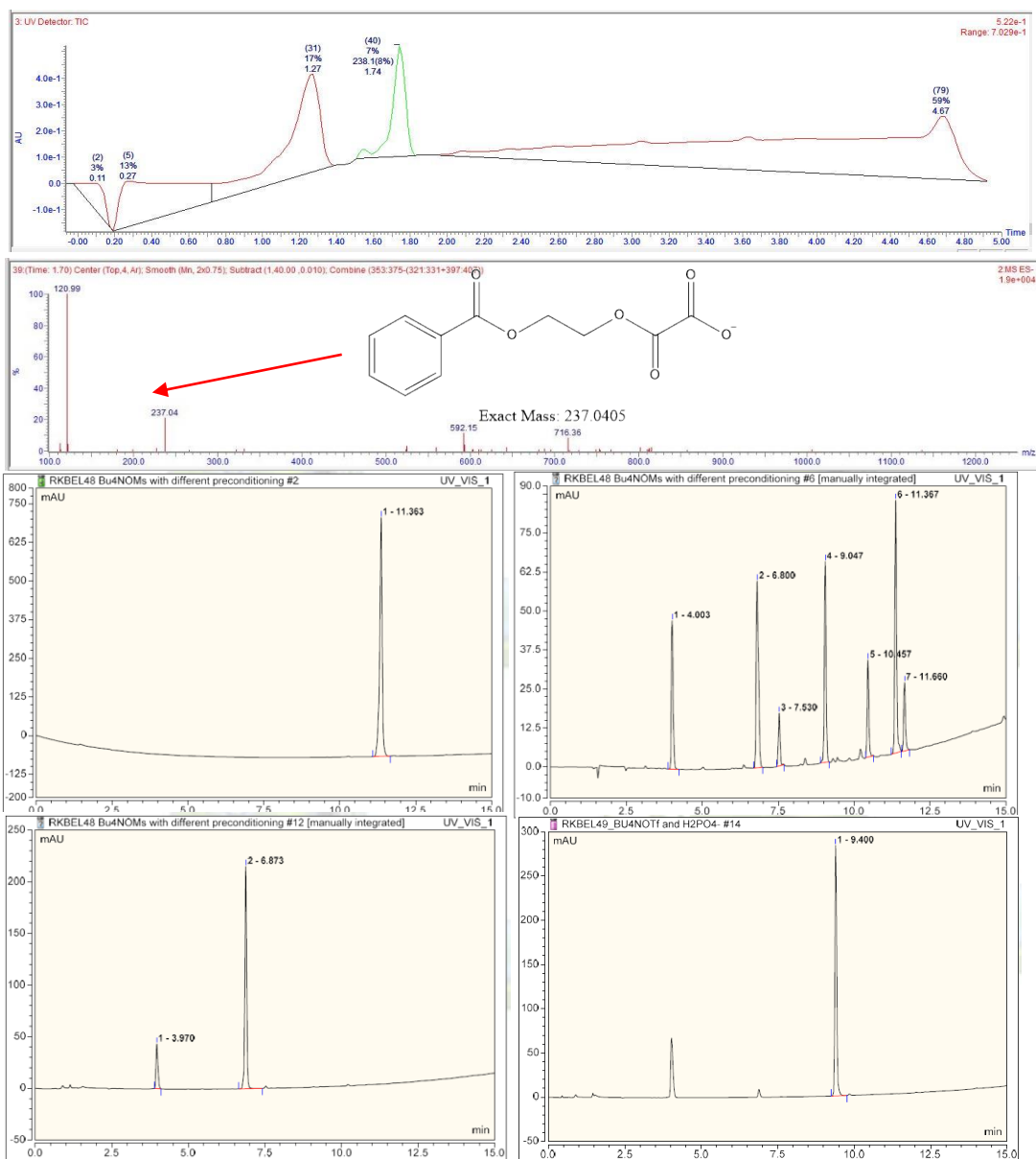


Figure S5 Chromatogram from LCMS analysis (UV and MS negative mode) of decayed analytical HPLC sample of $C_2O_4^{2-}$ preconditioned QMA eluted with Bu_4NOMs (top). Results from analytical HPLC of samples with different preconditioning. Middle left: Precursor **2** (1 mg/mL) for reference (rt: 11.36 min). Middle right: HCO_3^- preconditioned QMA eluted with Bu_4NOMs (20 mM), reference how degradation of precursor looks for a successful radiolabeling reaction. Bottom left: $C_2O_4^{2-}$ preconditioned QMA eluted with Bu_4NOMs (20 mM), resulting in 1 major UV active product (rt: 6.87 min) identified as the C_2O_4 -substituted precursor by LCMS. Bottom right: AcO^- preconditioned QMA eluted with Bu_4NOMs (20 mM), showing the same pattern as $C_2O_4^{2-}$ with one major UV active product (rt: 9.40 min) however, LCMS analysis was inconclusive.

“Cold” analysis of QMA using pH measurements and qNMR

Analysis using pH meter

Calibration curves were prepared by mixing different concentrations of the desired anion in solutions with MeCN /H₂O, 50:50. The solutions were then measured using a pH meter (Knick Portamess 913 pH Meter) and the results were plotted, (Figure S6-8).

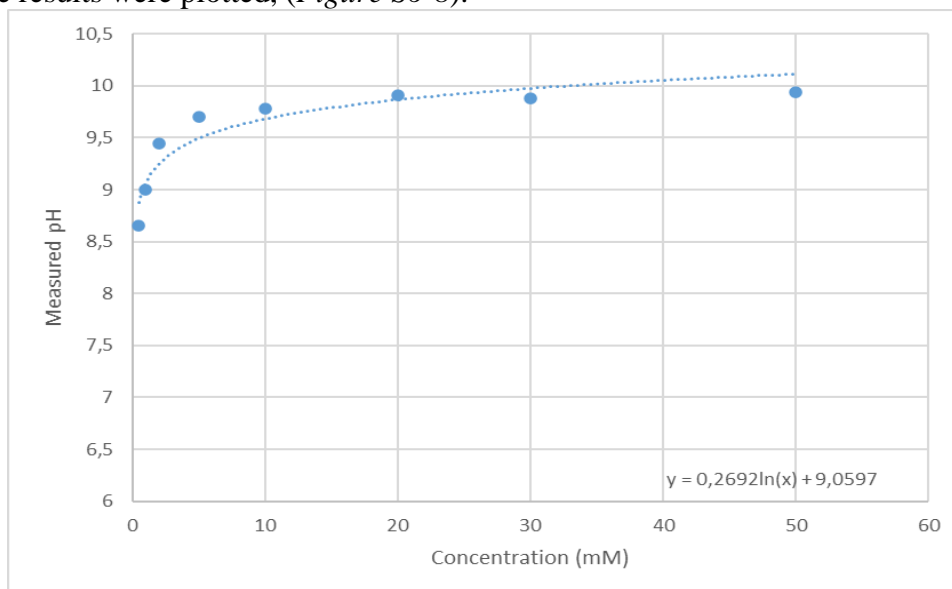


Figure S6 Calibration curve for KHCO₃.

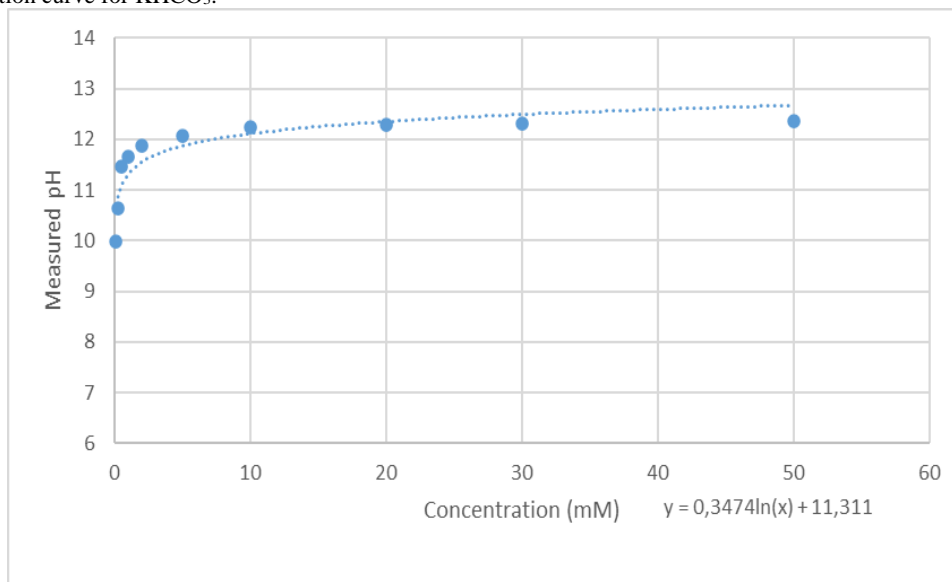


Figure S7 Calibration curve for K₂CO₃.

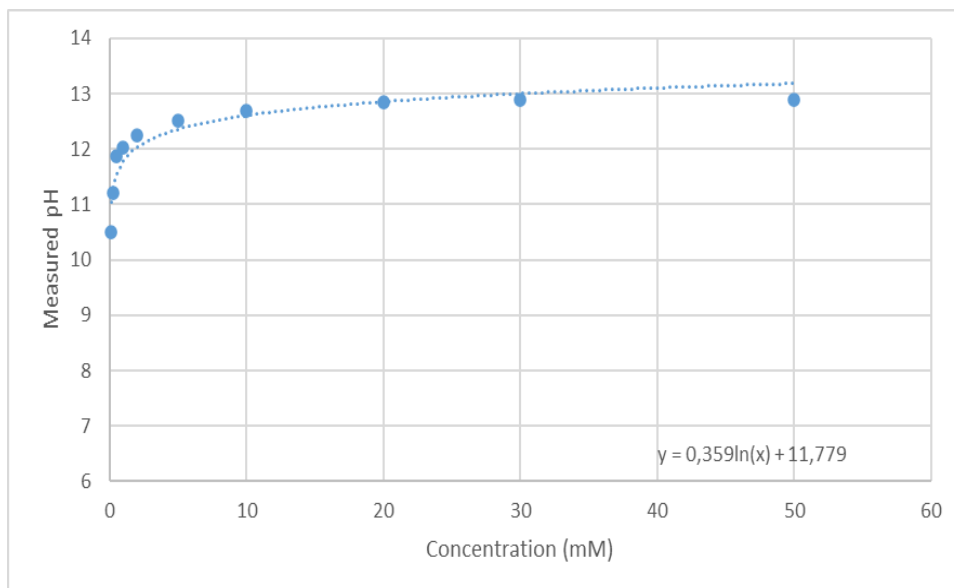


Figure S8 Calibration curve for K_3PO_4 .

QMA (Sep-Pak® Light QMA cartridge, chloride as counter ion) was preconditioned by flushing with EtOH (2 mL) followed by a solution of the appropriate preconditioning anion (0.5 M solution, 10 mL). The cartridge was then washed with H_2O (10 mL) and dried with air. Solutions of Bu_4NOMs at different concentrations were made and their pH was measured to make sure this didn't significantly influence pH (*Figure S9*).

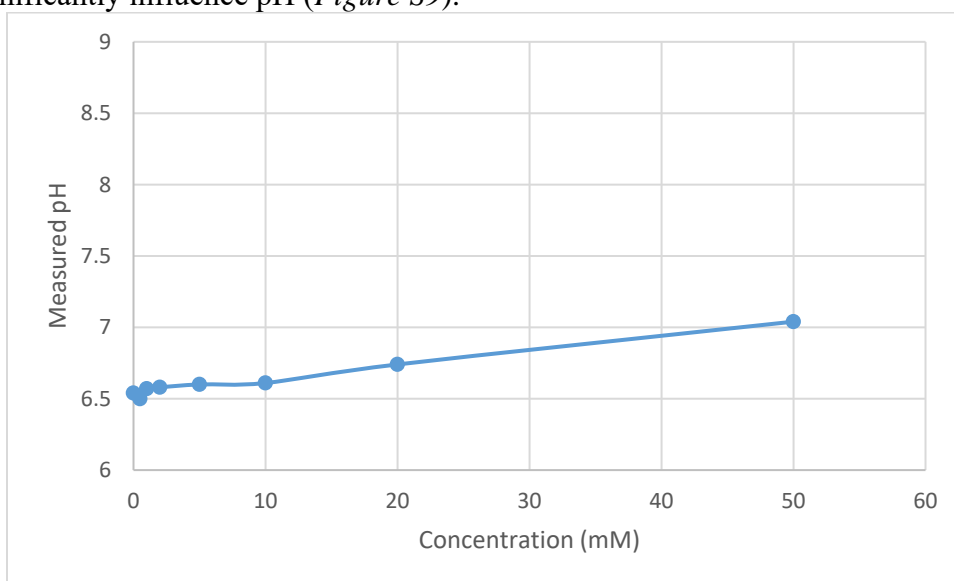


Figure S9 Checking different concentrations of Bu_4NOMs to determine that it doesn't influence pH significantly.

Control experiments were made with $KHCO_3$, K_2CO_3 , and K_3PO_4 (20 mM) mixed with Bu_3NOMs (20 mM) and the pH corresponded to the solutions not containing Bu_4OMs . The solutions of Bu_4OMs at different concentrations were used to elute the preconditioned QMAs into a 1.5 mL vial using a 1 mL syringe. Following elution, the QMA was flushed with 1 mL of air to make sure all of the liquid passed through. The pH of the eluate was measured using the pH meter and the concentration of the displaced

preconditioning anion was calculated using the equations derived from the corresponding calibration curves. The results are presented in *Table S6*.

Table S6 Results from “Cold” analysis of QMA using pH meter.

KHCO₃ preconditioned QMA		
Concentration of Bu₄NOMs	Measured pH	Calculated KHCO₃ conc in eluate (mM)
5	9.20	1.68
20	9.89	21.85
30	9.77	14.00
50	9.9	22.68
K₂CO₃ preconditioned QMA		
Concentration of Bu₄NOMs	Measured pH	Calculated K₂CO₃ conc in eluate (mM)
5	11.18	0.69
20	11.45	1.49
30	11.44	1.45
50	11.49	1.67
K₃PO₄ preconditioned QMA		
Concentration of Bu₄NOMs	Measured pH	Calculated K₃PO₄ conc in eluate (mM)
5	11.81	1.09
20	11.94	1.57
30	11.97	1.70
50	11.97	1.70

Analysis using qNMR

Calibration curves were made with solutions of Et₄NHCO₃ for HCO₃⁻ (¹³C-NMR) and Bu₄NH₂PO₄ for H₂PO₄⁻ (³¹P-NMR) and Bu₄NOMs for OMs⁻ (¹H-NMR) by dissolving the compounds at different concentrations in DMSO-d₆. Validation experiments were made with 2 different concentrations of calibration solutions. The relaxation delay (d1) was tested for ¹³C-, ³¹P- and ¹H-spectra (2.0 (1.0 for ¹H), 10.0, and 20.0 s) were 2.0 sec gave the most accurate results for ¹³C and ³¹P whereas 1.0 sec gave the most accurate result for ¹H. ¹³C- and ¹H-NMR was recorded on a 600 MHz Bruker Avance III HD at a spectrometer frequency of 150.83 MHz for ¹³C and 600 MHz for ¹H, running 512 and 64 scans respectively. ³¹P-NMR was recorded on a 400 MHz Bruker Avance II HD at a spectrometer frequency of 161.95 MHz running 512 scans.

¹³C calibration

The ¹³C NMR was analyzed using HSQC and the peak at offset 156.7 ppm was identified as the bicarbonate carbon. The peak was integrated and a calibration curve using the solvent as an internal standard was made (*Figure S10*), values were plotted using Excel.

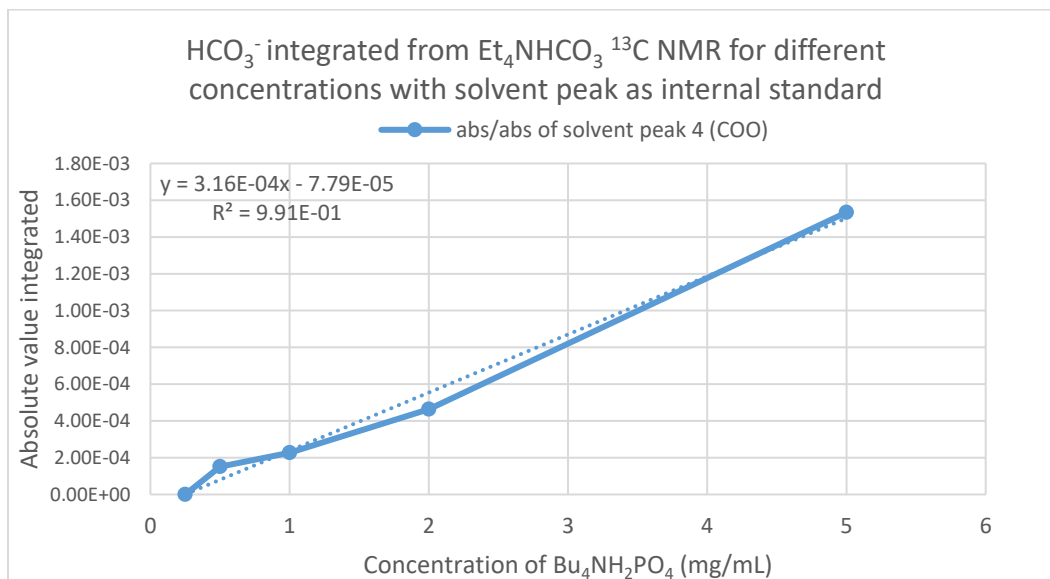


Figure S10 Calibration curves for HCO₃⁻ using Et₄NHCO₃ with solvent peak as internal standard.

¹H calibration

A calibration curve for the CH₃ peak of the OMs⁻ anion was made using different concentrations of Bu₄NOMs. The singlet peak was identified at 2.29 ppm and integration was divided by the solvent peak used as an internal standard. The results were plotted using excel, see *figure S11*.

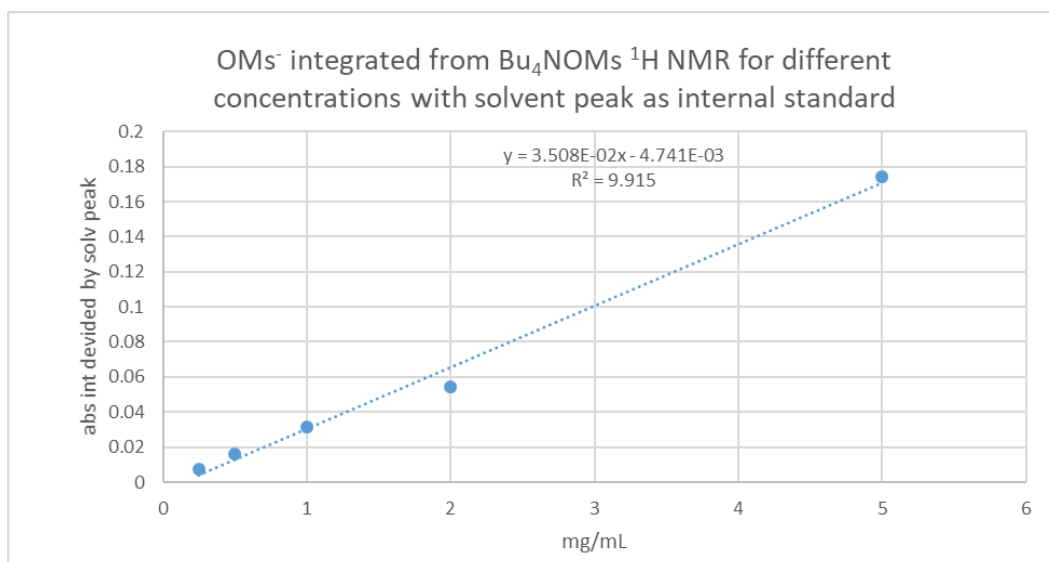


Figure S11 Calibration curve OMs⁻ using Bu₄NOMs with solvent peak as internal standard.

³¹P calibration

A calibration curve was made for H_2PO_4^- in the same manner were triphenyl phosphate (Ph_3PO_4) was used as an internal standard (1 mg/mL) in each sample. However, the internal standard (peak offset around -17 ppm in accordance with reference values)⁶ proved to be non-inert and the absolute value of the was heavily affected by different concentrations of $\text{Bu}_4\text{NH}_2\text{PO}_4$ while the absolute value of the phosphate peak identified as H_2PO_4^- (peak offset around 0 ppm) showed a very nice linear correlation over different concentrations (Figure S12). The ³¹P-values for H_2PO_4^- were compared with the ¹H-peak of CH_2 signal from the Bu_4N^+ counter ion for the same samples, which also confirmed the linear correlation (Figure S13). For higher concentrations of $\text{Bu}_4\text{NH}_2\text{PO}_4$ a second peak appeared which is believed to be HPO_4^{2-} why this interval was chosen (0.25-5 mg).

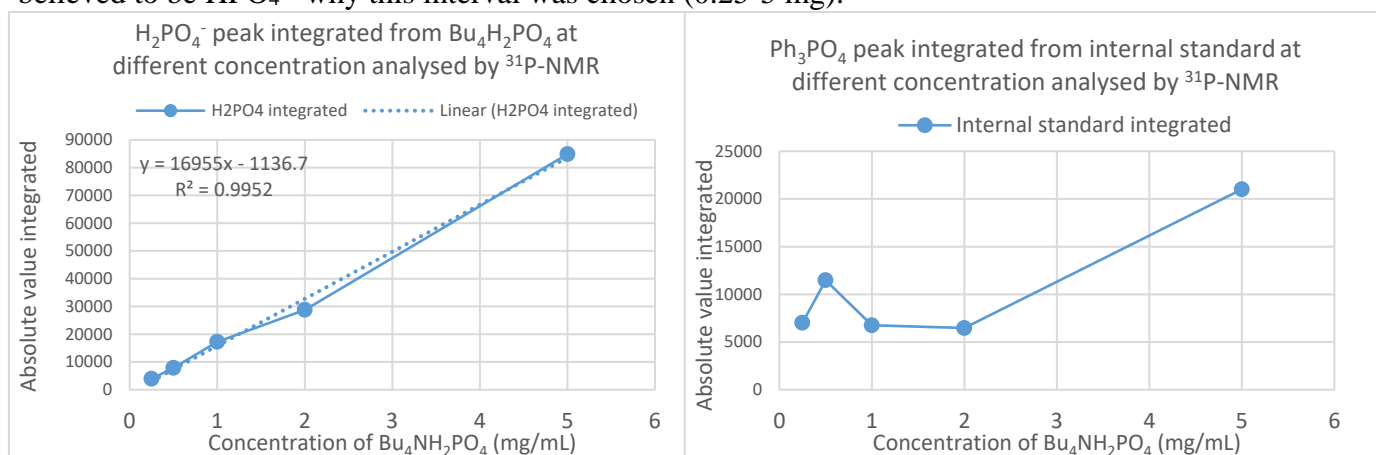


Figure S12 Calibration curves for H_2PO_4^- using $\text{Bu}_4\text{NH}_2\text{PO}_4$ with absolute values integrated for H_2PO_4^- (left) and the internal standard Ph_3PO_4 (1 mg/mL) at different concentrations of $\text{Bu}_4\text{NH}_2\text{PO}_4$ (right).

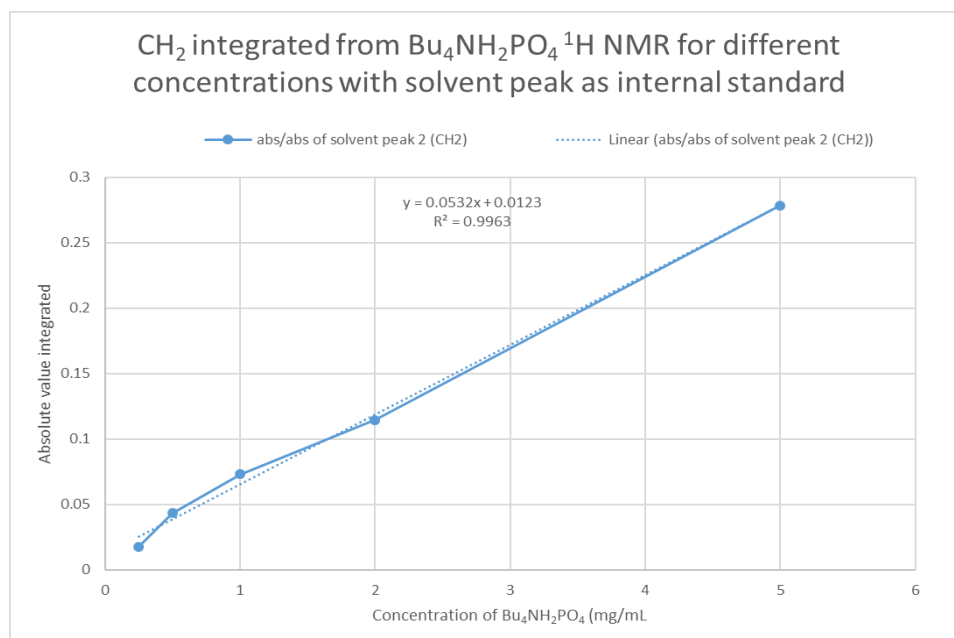


Figure S13 CH_2 -peak of $\text{Bu}_4\text{NH}_2\text{PO}_4$ at different concentrations divided by solvent peak integrated from ¹H NMR to confirm concentration accuracy of absolute integration of H_2PO_4^- from the ³¹P NMR.

qNMR analysis of QMA eluates

The QMAs were preconditioned in the same manner as for the pH measurement analysis. The QMA was eluted using 20 mM solutions of the investigated anion (MeCN /H₂O, 50:50) into a 4 mL vial. The vial was placed in a heating block and heated to 100 °C under a stream of nitrogen for 10 min to remove the eluting solvent. Azeotropic drying by MeCN added 2x0.5 mL followed by 5 min drying at 100 °C under a stream of nitrogen. To the dried vial 1 mL of d₆-DMSO was added and the vial was placed in a heating block at 120 °C for 5 min. The vial was allowed to cool for 1 min and 0.4 mL of the solvent was placed in a NMR tube and the solution was analyzed using the same sequences as for the calibration solutions. The results show that the lower valent anions are displaced to a higher extent compared to the multivalent anions from the QMA. This was corroborated by the fact that the eluting OMs⁻ anion concentration was lower for the HCO₃⁻ preconditioned QMA compared to the multivalent carbonate or phosphate preconditioned QMAs. This is because the difference in affinity to the resin for anions of the same valency is lower causing the OMs⁻ to displace the HCO₃⁻ preconditioning anion and it gets adsorbed to the QMA. Whereas for PO₄³⁻ preconditioned QMA the OMs⁻ anion passes through but is not able to displace the more strongly bound preconditioning anion and is thus not adsorbed to the QMA resulting in a higher concentration of OMs⁻ in the eluted sample, *Table S7*.

Table S7 Compiled results from the qNMR analysis of eluted QMA varying the preconditioning and eluting anions, all experiments were carried out in triplicates.

Eluting anion flow through	Eluting anion concentration (mM)			
	Bu ₄ NOMs [OMs ⁻]		Bu ₄ NH ₂ PO ₄ [H ₂ PO ₄ ⁻]	
Eluting anion				
HCO ₃ ⁻	1.33 ± 0.41		0.86 ± 0.42	
CO ₃ ²⁻	2.60 ± 0.51		0.77 ± 0.03	
HPO ₄ ²⁻	3.0 ± 0.35		5.40 ± 0.45	
PO ₄ ³⁻	3.44 ± 0.15		2.24 ± 3.17	
Preconditioning anion break through	Preconditioning anion concentration (mM)			
	HCO ₃ ⁻ [HCO ₃ ⁻]	CO ₃ ²⁻ [HCO ₃ ⁻]	HPO ₄ ²⁻ [H ₂ PO ₄ ⁻]	PO ₄ ³⁻ [H ₂ PO ₄ ⁻]
Eluting anion				
Bu ₄ NOMs	2.48 ± 0.16	1.16 ± 0.13	2.28 ± 0.17	0.76 ± 0.01
Bu ₄ NH ₂ PO ₄	1.76 ± 0.35	2.00 ± 0.13	5.40 ± 0.45	2.24 ± 3.17

The results from the qNMR analysis generally generate a lower value of the concentration of the eluted preconditioning anion than the pH-analysis method. This is expected as the eluates are azeotropically distilled using MeCN at 100 °C which could result in adsorption of anions to the glass walls. Another factor for reduction of HCO₃⁻ is the possible formation of CO₂ from H₂CO₃ at high temperatures under the slightly acidic conditions from Bu₄NH₂PO₄.

Comparing resolubilization capabilities of different cations

Comparing resolubilization between Bu_4^+ - and $\text{K}^+/\text{K}_{222}$ -salts for elution of HCO_3^- -preconditioned QMA. The reactions were conducted according to the general procedure for manual radiolabeling reactions, Table S8-S9.

Table S8 Results from comparing Bu_4^+ - and $\text{K}^+/\text{K}_{222}$ -salts for elution of HCO_3^- -preconditioned QMA with MeCN as a reaction solvent.

Testing resolubilization between $\text{K}^+/\text{K}_{222}$ - and Bu_4N -salts								
Exp id	Type of sample	Eluting anion	Concentration eluting anion (mM)	Preconditioning anion	Expected elution (%)	Observed elution (%)	$[\text{F}^{18}]$ -3 (%)	$[\text{F}^{18}]\text{F}^-$
31	Crude	Bu_4NOMs	30	HCO_3^-	100	98	63.5	27.1
32	Resolubilized	Bu_4NOMs	30	HCO_3^-	100	98	53.5	37.2
33	Crude	Bu_4NOMs	20	HCO_3^-	90	92	65.7	21.2
34	Resolubilized	Bu_4NOMs	20	HCO_3^-	90	92	51.7	30
35	Crude	Bu_4NOMs	15	HCO_3^-	50	82	60.3	27.5
36	Resolubilized	Bu_4NOMs	15	HCO_3^-	50	82	51.8	36.2
37	Crude	Bu_4NOMs	6	HCO_3^-	20	22	62.4	30.7
38	Resolubilized	Bu_4NOMs	6	HCO_3^-	20	22	52.7	39.8
129	Crude	$\text{K}_2\text{SO}_4/\text{K}_{222}$	30	HCO_3^-	90	99	53.7	38.1
130	Resolubilized	$\text{K}_2\text{SO}_4/\text{K}_{222}$	30	HCO_3^-	90	99	44.1	46.5
131	Crude	$\text{K}_2\text{SO}_4/\text{K}_{222}$	10	HCO_3^-	90	98	69.9	15.6
132	Resolubilized	$\text{K}_2\text{SO}_4/\text{K}_{222}$	10	HCO_3^-	90	98	50.2	42.2
133	Crude	$\text{K}_2\text{SO}_4/\text{K}_{222}$	5	HCO_3^-	85	53	59.4	25.8
134	Resolubilized	$\text{K}_2\text{SO}_4/\text{K}_{222}$	5	HCO_3^-	85	53	41.2	49.9
135	Crude	$\text{K}_2\text{SO}_4/\text{K}_{222}$	3	HCO_3^-	10	19	41.6	41.6
136	Resolubilized	$\text{K}_2\text{SO}_4/\text{K}_{222}$	3	HCO_3^-	10	19	23.4	61.3
137	Crude	$\text{KOMs}/\text{K}_{222}$	30	HCO_3^-	95	100	62.7	37.3
138	Resolubilized	$\text{KOMs}/\text{K}_{222}$	30	HCO_3^-	95	100	47.7	52.3
139	Crude	$\text{KOMs}/\text{K}_{222}$	20	HCO_3^-	90	85	64.3	35.7
140	Resolubilized	$\text{KOMs}/\text{K}_{222}$	20	HCO_3^-	90	85	49.9	50.1
141	Crude	$\text{KOMs}/\text{K}_{222}$	10	HCO_3^-	30	41	63.1	36.9
142	Resolubilized	$\text{KOMs}/\text{K}_{222}$	10	HCO_3^-	30	41	43.2	56.8
143	Crude	$\text{KOMs}/\text{K}_{222}$	6	HCO_3^-	10	9	67.3	32.7
144	Resolubilized	$\text{KOMs}/\text{K}_{222}$	6	HCO_3^-	10	9	60.9	39.1
145	Crude	$(\text{Bu}_4\text{N})_2\text{SO}_4$	20	HCO_3^-	100	97	11	85.2
146	Resolubilized	$(\text{Bu}_4\text{N})_2\text{SO}_4$	20	HCO_3^-	100	97	10.2	85.1
147	Crude	$(\text{Bu}_4\text{N})_2\text{SO}_4$	10	HCO_3^-	90	93	42.1	47.2
148	Resolubilized	$(\text{Bu}_4\text{N})_2\text{SO}_4$	10	HCO_3^-	90	93	36	51.2
149	Crude	$(\text{Bu}_4\text{N})_2\text{SO}_4$	5	HCO_3^-	85	58	49.1	40.2
150	Resolubilized	$(\text{Bu}_4\text{N})_2\text{SO}_4$	5	HCO_3^-	85	58	42.3	47.4

Table S9 Compiled results of the resolubilization calculated by dividing the amount of product obtained from the crude samples with the resolubilized samples.

Eluting neutral salt	Resolubilization (%)
Bu_4NOMs	85.9 ± 2.2 (n = 4)
$\text{KOMs}/\text{K}_{222}$	78.2 ± 9.1 (n = 4)
$(\text{Bu}_4\text{N})_2\text{SO}_4$	88.1 ± 4.0 (n = 3)
$\text{K}_2\text{SO}_4/\text{K}_{222}$	69.9 ± 10.6 (n = 4)

Multiparametric screening of elution conditions

Results from experiments with combination of different tetra alkyl salts with 4 different preconditioned QMA in various solvents. All reactions were performed according to the general procedure for manual radiolabeling. The results are presented in *Table S10*.

Table S10 Results from radiolabeling combinations from different tetra alkyl salts and preconditioned QMAs in various solvents.

Bu ₄ NOMs elution in MeCN								
Exp id	Type of sample	Eluting anion	Concentration eluting anion (mM)	Preconditioning anion	Expected elution (%)	Observed elution (%)	[¹⁸ F]-3 (%)	[¹⁸ F]F ⁻
105	Crude	Bu ₄ NOMs	20	HCO ₃ ⁻	90	98	63.5	27.1
106	Resolubilized	Bu ₄ NOMs	20	HCO ₃ ⁻	90	98	53.5	37.2
107	Crude	Bu ₄ NOMs	20	HCO ₃ ⁻	90	85	75.9	18.4
108	Resolubilized	Bu ₄ NOMs	20	HCO ₃ ⁻	90	85	71	23.5
109	Crude	Bu ₄ NOMs	20	HCO ₃ ⁻	90	90	52.6	43.2
110	Resolubilized	Bu ₄ NOMs	20	HCO ₃ ⁻	90	90	48.3	46.6
117	Crude	Bu ₄ NOMs	20	CO ₃ ²⁻	90	83	66.8	20.8
118	Resolubilized	Bu ₄ NOMs	20	CO ₃ ²⁻	90	83	53.9	28
119	Crude	Bu ₄ NOMs	20	CO ₃ ²⁻	100	97	71.4	24.3
120	Resolubilized	Bu ₄ NOMs	20	CO ₃ ²⁻	100	97	56.1	39.6
121	Crude	Bu ₄ NOMs	20	CO ₃ ²⁻	100	96	73.2	22.1
122	Resolubilized	Bu ₄ NOMs	20	CO ₃ ²⁻	100	96	55.3	39.9
131	Crude	Bu ₄ NOMs	20	PO ₄ ³⁻	100	97	82.4	12.3
132	Resolubilized	Bu ₄ NOMs	20	PO ₄ ³⁻	100	97	79.7	14.4
133	Crude	Bu ₄ NOMs	20	PO ₄ ³⁻	100	97	88.4	8.5
134	Resolubilized	Bu ₄ NOMs	20	PO ₄ ³⁻	100	97	85	9.1
135	Crude	Bu ₄ NOMs	20	PO ₄ ³⁻	100	97	63.4	30.7
136	Resolubilized	Bu ₄ NOMs	20	PO ₄ ³⁻	100	97	58.1	34.9
111	Crude	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	95	44.5	50.1
112	Resolubilized	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	95	46.3	49.1
113	Crude	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	97	56.4	38.9
114	Resolubilized	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	97	53.4	40.8
115	Crude	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	95	62.1	33.6
116	Resolubilized	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	95	60.1	34.7
Bu ₄ NOMs elution in DMSO								
151	Crude	Bu ₄ NOMs	20	HCO ₃ ⁻	100	95	71.2	22.3
154	Resolubilized	Bu ₄ NOMs	20	HCO ₃ ⁻	100	95	69	25.2
159	Crude	Bu ₄ NOMs	20	HCO ₃ ⁻	100	60	45	55
160	Resolubilized	Bu ₄ NOMs	20	HCO ₃ ⁻	100	60	53.3	46.6
161	Crude	Bu ₄ NOMs	20	HCO ₃ ⁻	100	86	72	23.3
162	Resolubilized	Bu ₄ NOMs	20	HCO ₃ ⁻	100	86	66.6	28.6
163	Crude	Bu ₄ NOMs	20	CO ₃ ²⁻	100	99	80.1	14.7
164	Resolubilized	Bu ₄ NOMs	20	CO ₃ ²⁻	100	99	74.3	20.5
165	Crude	Bu ₄ NOMs	20	CO ₃ ²⁻	100	99	88.9	7.7
166	Resolubilized	Bu ₄ NOMs	20	CO ₃ ²⁻	100	99	85.4	10.1
167	Crude	Bu ₄ NOMs	20	CO ₃ ²⁻	100	95	77.8	16.1
168	Resolubilized	Bu ₄ NOMs	20	CO ₃ ²⁻	100	95	71.8	23.5
169	Crude	Bu ₄ NOMs	20	PO ₄ ³⁻	100	100	78.8	16.4
170	Resolubilized	Bu ₄ NOMs	20	PO ₄ ³⁻	100	100	77.4	18.8
171	Crude	Bu ₄ NOMs	20	PO ₄ ³⁻	100	100	61.1	35.6
172	Resolubilized	Bu ₄ NOMs	20	PO ₄ ³⁻	100	100	60.7	35.8

173	Crude	Bu ₄ NOMs	20	PO ₄ ³⁻	100	97	88.3	5.4
174	Resolubilized	Bu ₄ NOMs	20	PO ₄ ³⁻	100	97	86.9	6.6
175	Crude	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	97	76.1	14.3
176	Resolubilized	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	97	58.1	37.6
177	Crude	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	99	49.6	45.2
178	Resolubilized	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	99	48.7	46
179	Crude	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	96	45.4	49.8
180	Resolubilized	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	96	45.6	50.2
Bu₄NOMs elution in tBuOH/MeCN (5:1)								
181	Crude	Bu ₄ NOMs	20	HCO ₃ ⁻	100	92	21.5	76
182	Resolubilized	Bu ₄ NOMs	20	HCO ₃ ⁻	100	92	21.9	75.2
183	Crude	Bu ₄ NOMs	20	CO ₃ ²⁻	100	97	19.8	77.9
184	Resolubilized	Bu ₄ NOMs	20	CO ₃ ²⁻	100	97	18.9	78.2
185	Crude	Bu ₄ NOMs	20	PO ₄ ³⁻	100	99	14.9	82.2
186	Resolubilized	Bu ₄ NOMs	20	PO ₄ ³⁻	100	99	18.2	78.4
187	Crude	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	99	15.5	80.7
188	Resolubilized	Bu ₄ NOMs	20	HPO ₄ ²⁻	100	99	13.8	82
Bu₄NOTf elution in MeCN								
189	Crude	Bu ₄ NOTf	20	HCO ₃ ⁻	10	4	55.4	30.8
190	Resolubilized	Bu ₄ NOTf	20	HCO ₃ ⁻	10	4	48.5	32.7
191	Crude	Bu ₄ NOTf	20	CO ₃ ²⁻	100	95	70	24.9
192	Resolubilized	Bu ₄ NOTf	20	CO ₃ ²⁻	100	95	48	44.9
193	Crude	Bu ₄ NOTf	20	CO ₃ ²⁻	100	89	39.6	60.4
194	Resolubilized	Bu ₄ NOTf	20	CO ₃ ²⁻	100	89	25.2	74.8
195	Crude	Bu ₄ NOTf	20	CO ₃ ²⁻	100	90	47.6	52.4
196	Resolubilized	Bu ₄ NOTf	20	CO ₃ ²⁻	100	90	36.1	63.9
197	Crude	Bu ₄ NOTf	20	PO ₄ ³⁻	100	99	65.2	30.1
198	Resolubilized	Bu ₄ NOTf	20	PO ₄ ³⁻	100	99	61	34.6
199	Crude	Bu ₄ NOTf	20	PO ₄ ³⁻	100	100	81	12.7
200	Resolubilized	Bu ₄ NOTf	20	PO ₄ ³⁻	100	100	79.5	13.8
201	Crude	Bu ₄ NOTf	20	PO ₄ ³⁻	100	100	72.6	18
202	Resolubilized	Bu ₄ NOTf	20	PO ₄ ³⁻	100	100	71.3	21.2
203	Crude	Bu ₄ NOTf	20	HPO ₄ ²⁻	100	85	5.3	92.1
204	Resolubilized	Bu ₄ NOTf	20	HPO ₄ ²⁻	100	85	5.1	91.8
205	Crude	Bu ₄ NOTf	20	HPO ₄ ²⁻	100	96	1	99
206	Resolubilized	Bu ₄ NOTf	20	HPO ₄ ²⁻	100	96	0.5	99.5
207	Crude	Bu ₄ NOTf	20	HPO ₄ ²⁻	100	93	2.4	95.2
208	Resolubilized	Bu ₄ NOTf	20	HPO ₄ ²⁻	100	93	1.3	96
Bu₄NOTf elution in DMSO								
209	Crude	Bu ₄ NOTf	20	HCO ₃ ⁻	10	4	69.9	16.6
210	Resolubilized	Bu ₄ NOTf	20	HCO ₃ ⁻	10	4	64.2	21.5
211	Crude	Bu ₄ NOTf	20	CO ₃ ²⁻	100	79	55.5	37.7
212	Resolubilized	Bu ₄ NOTf	20	CO ₃ ²⁻	100	79	51.9	42.4
213	Crude	Bu ₄ NOTf	20	CO ₃ ²⁻	100	100	79.9	13.7
214	Resolubilized	Bu ₄ NOTf	20	CO ₃ ²⁻	100	100	71.6	17.9
215	Crude	Bu ₄ NOTf	20	CO ₃ ²⁻	100	100	66.1	26.1
216	Resolubilized	Bu ₄ NOTf	20	CO ₃ ²⁻	100	100	55.1	39.4
217	Crude	Bu ₄ NOTf	20	PO ₄ ³⁻	100	99	91.1	5.2
218	Resolubilized	Bu ₄ NOTf	20	PO ₄ ³⁻	100	99	87.4	8.3
219	Crude	Bu ₄ NOTf	20	PO ₄ ³⁻	100	97	85	81.2
220	Resolubilized	Bu ₄ NOTf	20	PO ₄ ³⁻	100	97	81.2	10

221	Crude	Bu ₄ NOTf	20	PO ₄ ³⁻	100	93	80.2	14.4
222	Resolubilized	Bu ₄ NOTf	20	PO ₄ ³⁻	100	93	78	15.9
223	Crude	Bu ₄ NOTf	20	HPO ₄ ²⁻	100	67	57.2	36.8
224	Resolubilized	Bu ₄ NOTf	20	HPO ₄ ²⁻	100	67	57.1	38.6
225	Crude	Bu ₄ NOTf	20	HPO ₄ ²⁻	100	100	66.2	28.6
226	Resolubilized	Bu ₄ NOTf	20	HPO ₄ ²⁻	100	100	64.9	29.2
227	Crude	Bu ₄ NOTf	20	HPO ₄ ²⁻	100	99	67.7	26.6
228	Resolubilized	Bu ₄ NOTf	20	HPO ₄ ²⁻	100	99	67.8	25.2
Bu₄NOTf elution in tBuOH/MeCN (5:1)								
211	Crude	Bu ₄ NOTf	20	HCO ₃ ⁻	10	2	16.2	33.6
212	Resolubilized	Bu ₄ NOTf	20	HCO ₃ ⁻	10	2	15.3	34.9
213	Crude	Bu ₄ NOTf	20	CO ₃ ²⁻	100	76	3.3	90.09
214	Resolubilized	Bu ₄ NOTf	20	CO ₃ ²⁻	100	76	2.5	91.2
215	Crude	Bu ₄ NOTf	20	PO ₄ ³⁻	100	79	23	69
216	Resolubilized	Bu ₄ NOTf	20	PO ₄ ³⁻	100	79	22.4	70.1
217	Crude	Bu ₄ NOTf	20	HPO ₄ ²⁻	100	71	13.3	81.3
218	Resolubilized	Bu ₄ NOTf	20	HPO ₄ ²⁻	100	71	12.6	81.5
Bu₄NH₂PO₄ elution in MeCN								
219	Crude	Bu ₄ NH ₂ PO ₄	20	HCO ₃ ⁻	90	92	70.6	24.8
220	Resolubilized	Bu ₄ NH ₂ PO ₄	20	HCO ₃ ⁻	90	92	67.8	25.1
221	Crude	Bu ₄ NH ₂ PO ₄	20	HCO ₃ ⁻	100	100	77.6	18.2
222	Resolubilized	Bu ₄ NH ₂ PO ₄	20	HCO ₃ ⁻	100	100	77.8	15.7
223	Crude	Bu ₄ NH ₂ PO ₄	20	HCO ₃ ⁻	100	98	83.3	10.9
224	Resolubilized	Bu ₄ NH ₂ PO ₄	20	HCO ₃ ⁻	100	98	82.4	12.1
225	Crude	Bu ₄ NH ₂ PO ₄	20	CO ₃ ²⁻	100	100	88.4	6.4
226	Resolubilized	Bu ₄ NH ₂ PO ₄	20	CO ₃ ²⁻	100	100	84.9	7.3
227	Crude	Bu ₄ NH ₂ PO ₄	20	CO ₃ ²⁻	100	99	89.5	4.5
228	Resolubilized	Bu ₄ NH ₂ PO ₄	20	CO ₃ ²⁻	100	99	87.6	5.8
229	Crude	Bu ₄ NH ₂ PO ₄	20	CO ₃ ²⁻	100	97	89.2	6.9
230	Resolubilized	Bu ₄ NH ₂ PO ₄	20	CO ₃ ²⁻	100	97	86.9	8.9
231	Crude	Bu ₄ NH ₂ PO ₄	20	PO ₄ ³⁻	100	97	67.8	29
232	Resolubilized	Bu ₄ NH ₂ PO ₄	20	PO ₄ ³⁻	100	97	65.9	29.8
233	Crude	Bu ₄ NH ₂ PO ₄	20	PO ₄ ³⁻	100	98	26	69
234	Resolubilized	Bu ₄ NH ₂ PO ₄	20	PO ₄ ³⁻	100	98	24.8	69.9
235	Crude	Bu ₄ NH ₂ PO ₄	20	PO ₄ ³⁻	100	99	60.5	34.8
236	Resolubilized	Bu ₄ NH ₂ PO ₄	20	PO ₄ ³⁻	100	99	56.8	37.5
237	Crude	Bu ₄ NH ₂ PO ₄	20	HPO ₄ ²⁻	100	99	11.6	83.8
238	Resolubilized	Bu ₄ NH ₂ PO ₄	20	HPO ₄ ²⁻	100	99	11.9	83.4
239	Crude	Bu ₄ NH ₂ PO ₄	20	HPO ₄ ²⁻	100	99	3.6	91.6
240	Resolubilized	Bu ₄ NH ₂ PO ₄	20	HPO ₄ ²⁻	100	99	3.5	91.9
241	Crude	Bu ₄ NH ₂ PO ₄	20	HPO ₄ ²⁻	100	97	16.8	80.7
242	Resolubilized	Bu ₄ NH ₂ PO ₄	20	HPO ₄ ²⁻	100	97	16.9	80.5
Bu₄NH₂PO₄ elution in DMSO								
243	Crude	Bu ₄ NH ₂ PO ₄	20	HCO ₃ ⁻	100	88	83.4	13
244	Resolubilized	Bu ₄ NH ₂ PO ₄	20	HCO ₃ ⁻	100	88	80	15.9
245	Crude	Bu ₄ NH ₂ PO ₄	20	HCO ₃ ⁻	100	100	84.3	8.9
246	Resolubilized	Bu ₄ NH ₂ PO ₄	20	HCO ₃ ⁻	100	100	83.6	10.9
247	Crude	Bu ₄ NH ₂ PO ₄	20	HCO ₃ ⁻	100	99	75.3	19.4
248	Resolubilized	Bu ₄ NH ₂ PO ₄	20	HCO ₃ ⁻	100	99	74.5	20.4
249	Crude	Bu ₄ NH ₂ PO ₄	20	CO ₃ ²⁻	100	99	85.6	9.7
250	Resolubilized	Bu ₄ NH ₂ PO ₄	20	CO ₃ ²⁻	100	99	84	10.8

251	Crude	Bu ₄ NH ₂ PO ₄	20	CO ₃ ²⁻	100	99	86.2	9.1
252	Resolubilized	Bu ₄ NH ₂ PO ₄	20	CO ₃ ²⁻	100	99	84.7	11.2
253	Crude	Bu ₄ NH ₂ PO ₄	20	CO ₃ ²⁻	100	100	89.2	5.6
254	Resolubilized	Bu ₄ NH ₂ PO ₄	20	CO ₃ ²⁻	100	100	87.9	6.9
255	Crude	Bu ₄ NH ₂ PO ₄	20	PO ₄ ³⁻	100	98	60.9	33.6
256	Resolubilized	Bu ₄ NH ₂ PO ₄	20	PO ₄ ³⁻	100	98	59.7	34.5
257	Crude	Bu ₄ NH ₂ PO ₄	20	PO ₄ ³⁻	100	99	2.3	92.6
258	Resolubilized	Bu ₄ NH ₂ PO ₄	20	PO ₄ ³⁻	100	99	2.4	91.9
259	Crude	Bu ₄ NH ₂ PO ₄	20	PO ₄ ³⁻	100	100	14	81.1
260	Resolubilized	Bu ₄ NH ₂ PO ₄	20	PO ₄ ³⁻	100	100	13.2	82.4
261	Crude	Bu ₄ NH ₂ PO ₄	20	HPO ₄ ²⁻	100	98	39.7	56.1
262	Resolubilized	Bu ₄ NH ₂ PO ₄	20	HPO ₄ ²⁻	100	98	38.2	58.1
263	Crude	Bu ₄ NH ₂ PO ₄	20	HPO ₄ ²⁻	100	98	18.4	78.6
264	Resolubilized	Bu ₄ NH ₂ PO ₄	20	HPO ₄ ²⁻	100	98	19.7	76.3
265	Crude	Bu ₄ NH ₂ PO ₄	20	HPO ₄ ²⁻	100	95	17.6	79.4
266	Resolubilized	Bu ₄ NH ₂ PO ₄	20	HPO ₄ ²⁻	100	95	17.6	79.4
Bu₄NH₂PO₄ elution in MeCN/tBuOH (5:1)								
267	Crude	Bu ₄ NH ₂ PO ₄	20	HCO ₃ ⁻	100	97	18.9	71
268	Resolubilized	Bu ₄ NH ₂ PO ₄	20	HCO ₃ ⁻	100	97	18.9	72.6
269	Crude	Bu ₄ NH ₂ PO ₄	20	CO ₃ ²⁻	100	97	14.3	82.2
270	Resolubilized	Bu ₄ NH ₂ PO ₄	20	CO ₃ ²⁻	100	97	13.8	81.1
271	Crude	Bu ₄ NH ₂ PO ₄	20	PO ₄ ³⁻	100	98	4.4	91.1
272	Resolubilized	Bu ₄ NH ₂ PO ₄	20	PO ₄ ³⁻	100	98	4.8	87.1
273	Crude	Bu ₄ NH ₂ PO ₄	20	HPO ₄ ²⁻	100	94	16.6	76.9
274	Resolubilized	Bu ₄ NH ₂ PO ₄	20	HPO ₄ ²⁻	100	94	15.6	77.7
Et₄NHCO₃ elution in MeCN								
275	Crude	Et ₄ NHCO ₃	20	HCO ₃ ⁻	100	96	TLC Failed	
276	Resolubilized	Et ₄ NHCO ₃	20	HCO ₃ ⁻	100	96	82.3	12.6
277	Crude	Et ₄ NHCO ₃	20	HCO ₃ ⁻	100	95	83.7	8.6
278	Resolubilized	Et ₄ NHCO ₃	20	HCO ₃ ⁻	100	95	79.6	13.4
279	Crude	Et ₄ NHCO ₃	20	HCO ₃ ⁻	100	94	82.7	12.2
280	Resolubilized	Et ₄ NHCO ₃	20	HCO ₃ ⁻	100	94	71.6	24.1
281	Crude	Et ₄ NHCO ₃	20	CO ₃ ²⁻	100	100	83.9	9.7
282	Resolubilized	Et ₄ NHCO ₃	20	CO ₃ ²⁻	100	100	73.3	21.3
283	Crude	Et ₄ NHCO ₃	20	CO ₃ ²⁻	100	100	85.9	9
284	Resolubilized	Et ₄ NHCO ₃	20	CO ₃ ²⁻	100	100	77.5	16.7
285	Crude	Et ₄ NHCO ₃	20	CO ₃ ²⁻	100	100	91.1	4.7
286	Resolubilized	Et ₄ NHCO ₃	20	CO ₃ ²⁻	100	100	74.2	22.1
287	Crude	Et ₄ NHCO ₃	20	PO ₄ ³⁻	100	96	93.5	3.5
288	Resolubilized	Et ₄ NHCO ₃	20	PO ₄ ³⁻	100	96	86.3	10.4
289	Crude	Et ₄ NHCO ₃	20	PO ₄ ³⁻	100	98	77.2	14.7
290	Resolubilized	Et ₄ NHCO ₃	20	PO ₄ ³⁻	100	98	73.1	17.4
291	Crude	Et ₄ NHCO ₃	20	PO ₄ ³⁻	100	99	88.3	5.5
292	Resolubilized	Et ₄ NHCO ₃	20	PO ₄ ³⁻	100	99	81.4	12.8
293	Crude	Et ₄ NHCO ₃	20	HPO ₄ ²⁻	100	97	91.4	4.9
294	Resolubilized	Et ₄ NHCO ₃	20	HPO ₄ ²⁻	100	97	87.8	8.1
295	Crude	Et ₄ NHCO ₃	20	HPO ₄ ²⁻	100	95	76.8	23.2
296	Resolubilized	Et ₄ NHCO ₃	20	HPO ₄ ²⁻	100	95	67.9	32.1
297	Crude	Et ₄ NHCO ₃	20	HPO ₄ ²⁻	100	97	74.4	25.6
298	Resolubilized	Et ₄ NHCO ₃	20	HPO ₄ ²⁻	100	97	71.9	28.1
Et₄NHCO₃ elution in DMSO								

299	Crude	Et ₄ NHCO ₃	20	HCO ₃ ⁻	100	95	86.6	7.4
300	Resolubilized	Et ₄ NHCO ₃	20	HCO ₃ ⁻	100	95	74.6	18.7
301	Crude	Et ₄ NHCO ₃	20	HCO ₃ ⁻	100	93	84.9	8.7
302	Resolubilized	Et ₄ NHCO ₃	20	HCO ₃ ⁻	100	93	78	16.9
303	Crude	Et ₄ NHCO ₃	20	HCO ₃ ⁻	100	94	82.7	12.2
304	Resolubilized	Et ₄ NHCO ₃	20	HCO ₃ ⁻	100	94	71.6	24.1
305	Crude	Et ₄ NHCO ₃	20	CO ₃ ²⁻	100	100	63.2	33.9
306	Resolubilized	Et ₄ NHCO ₃	20	CO ₃ ²⁻	100	100	52.3	43
307	Crude	Et ₄ NHCO ₃	20	CO ₃ ²⁻	100	100	75.3	21
308	Resolubilized	Et ₄ NHCO ₃	20	CO ₃ ²⁻	100	100	54.6	41
309	Crude	Et ₄ NHCO ₃	20	CO ₃ ²⁻	100	99	80	12.8
310	Resolubilized	Et ₄ NHCO ₃	20	CO ₃ ²⁻	100	99	68	23.4
311	Crude	Et ₄ NHCO ₃	20	PO ₄ ³⁻	100	95	89.9	4.4
312	Resolubilized	Et ₄ NHCO ₃	20	PO ₄ ³⁻	100	95	82.9	9.7
313	Crude	Et ₄ NHCO ₃	20	PO ₄ ³⁻	100	100	87.8	7.6
314	Resolubilized	Et ₄ NHCO ₃	20	PO ₄ ³⁻	100	100	80.8	13.3
315	Crude	Et ₄ NHCO ₃	20	PO ₄ ³⁻	100	100	86.6	9.1
316	Resolubilized	Et ₄ NHCO ₃	20	PO ₄ ³⁻	100	100	76	19.4
317	Crude	Et ₄ NHCO ₃	20	HPO ₄ ²⁻	100	96	88.8	7.3
318	Resolubilized	Et ₄ NHCO ₃	20	HPO ₄ ²⁻	100	96	83	12.4
319	Crude	Et ₄ NHCO ₃	20	HPO ₄ ²⁻	100	100	83.9	13.3
320	Resolubilized	Et ₄ NHCO ₃	20	HPO ₄ ²⁻	100	100	81.8	14.3
321	Crude	Et ₄ NHCO ₃	20	HPO ₄ ²⁻	100	98	85	7.2
322	Resolubilized	Et ₄ NHCO ₃	20	HPO ₄ ²⁻	100	98	84.2	8.6
Et₄NHCO₃ elution in tBuOH/MeCN (5:1)								
323	Crude	Et ₄ NHCO ₃	20	HCO ₃ ⁻	100	95	15.2	76.6
324	Resolubilized	Et ₄ NHCO ₃	20	HCO ₃ ⁻	100	95	14.1	76.3
325	Crude	Et ₄ NHCO ₃	20	CO ₃ ²⁻	100	95	7.8	89.6
326	Resolubilized	Et ₄ NHCO ₃	20	CO ₃ ²⁻	100	95	8.1	88.3
327	Crude	Et ₄ NHCO ₃	20	PO ₄ ³⁻	100	95	13.8	79.1
328	Resolubilized	Et ₄ NHCO ₃	20	PO ₄ ³⁻	100	95	14	78.3
329	Crude	Et ₄ NHCO ₃	20	HPO ₄ ²⁻	100	94	9.3	87.3
330	Resolubilized	Et ₄ NHCO ₃	20	HPO ₄ ²⁻	100	94	8.6	87.9

Control experiments

Longer reaction times for [¹⁸F]3

The reactions were conducted according to the general procedure for manual radiolabeling as described above. Reaction was performed using Bu₄NOMs (20 mM) solutions for elution. The only major difference could be seen using the carbonate preconditioning anions were the pRCY increased from 5-10 minutes in MeCN and DMSO (*Figure S14*).

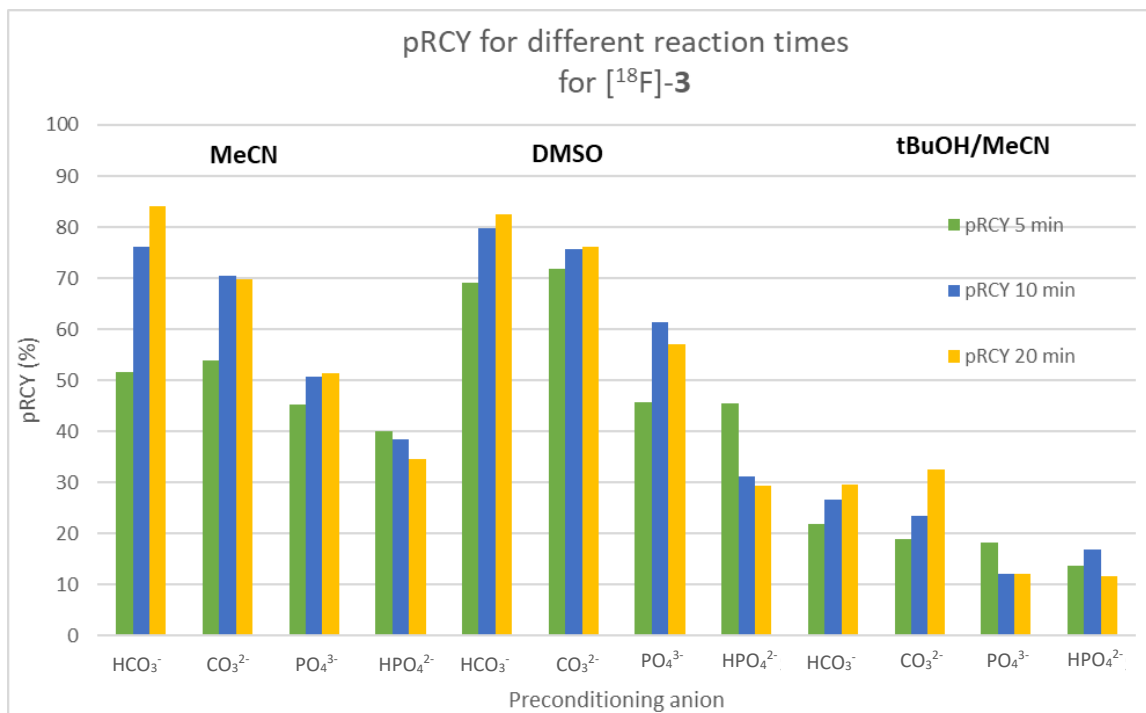


Figure S14 pRCY of [18F]-3 at different time points.

Remaining precursor analysis

The amount of precursor **2** remaining after the radiolabeling reaction was investigated for the same reactions by integrating the corresponding UV peak (254 nm, rt: 11.45 min) in the analytical chromatograms from the resolubilized samples. The concentration was calculated as a percentage of the original concentration of **2** (1 mg/mL) compensated for the dilution from quenching and dilution in the analytical HPLC vial. The data is plotted in *Figure S15*.

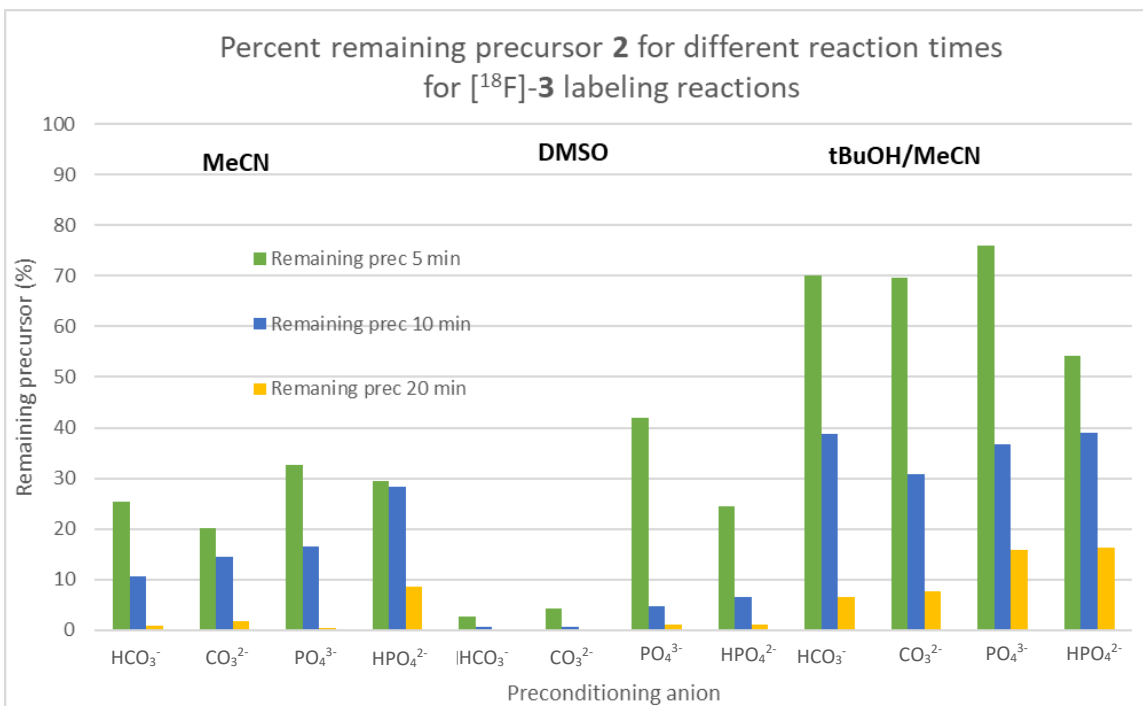


Figure S15 Percentage of remaining precursor 2 at the end of the radiolabeling reaction for different time points.

Testing different concentrations of precursor 2

Results from using higher and lower amounts of precursor for radiolabeling using conditions 4A in MeCN for precursor 2 to form [¹⁸F]3 can be seen in *Figure S16*.

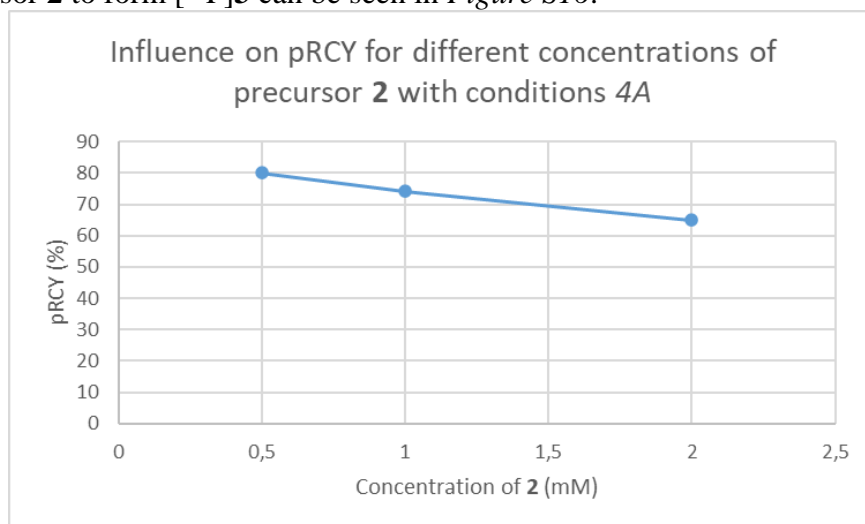


Figure S16 Influence on concentration of precursor 2 on the pRCY for [¹⁸F]3.

Temperature screening

A screening of different temperatures was made for different eluting anions using the general method for manual radiolabeling with 2 to form [¹⁸F]3 with a PO₄³⁻ preconditioned QMA with MeCN as a reaction solvent. The results from the experiments can be seen in *Figure S17*.

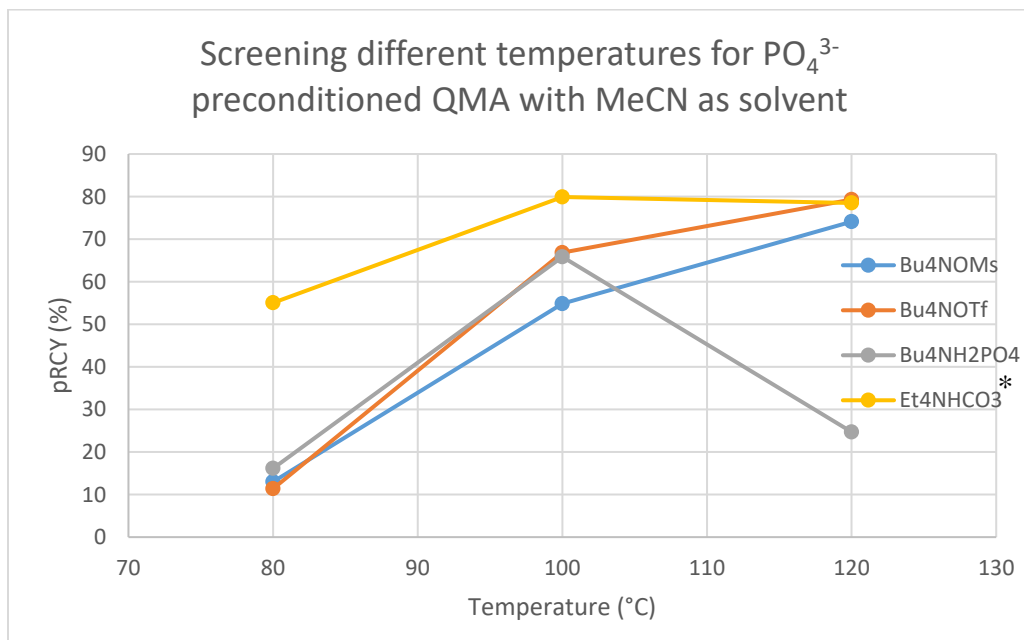


Figure S17 Results from screening of different temperatures using different eluting anions. *pRCY using 4C had a very high variability and thus no major conclusions could be drawn without further repetitions.

Leaving group screening

In order to test different how leaving groups influence of the pRCY in some of the derived conditions to form [¹⁸F]3 a set of new precursors were synthesized (*Scheme S1*)

The precursors were radiolabeled according to the general procedure for manual radiolabeling. To different derived conditions that were high yielding using the original tosylate precursor 2 (3C and 4A) were tested with the new precursors (*Figure S18*)

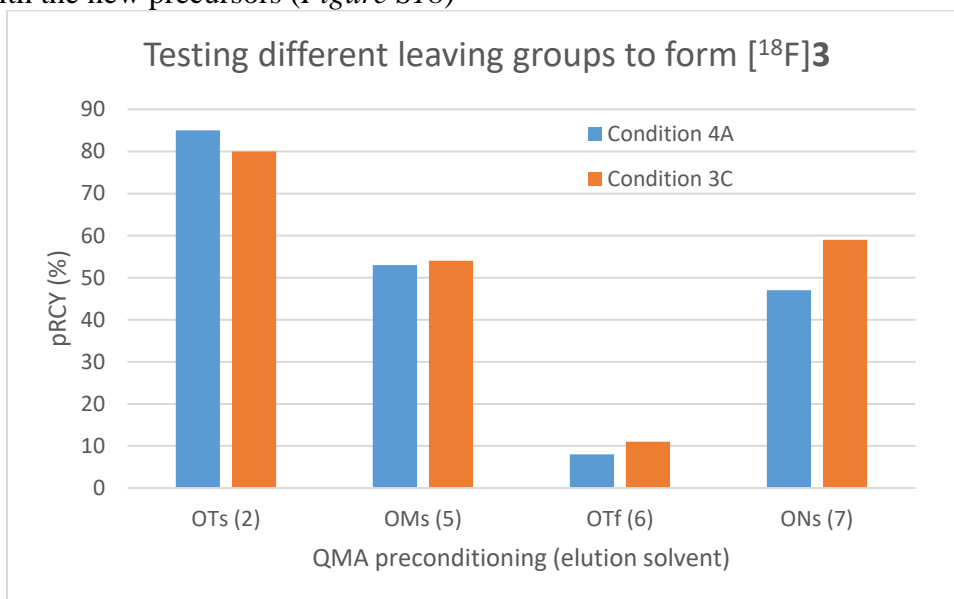


Figure S18 Results from radiolabeling reactions with precursors 5, 6 and 7 compared with the original tosylate precursor 2.

Switching eluting solvent

The reactions were conducted according to the general procedure for manual radiolabeling as described above. MeOH was used as solvent for elution instead of MeCN/H₂O resulting in a higher or comparable pRCY all the tested reactions, see *Figure S19*. Screening was conducted for Bu₄NOMs elution of all preconditioning anions in MeCN as well as for the conditions used for subsequent labelling of clinical tracers/synthons.

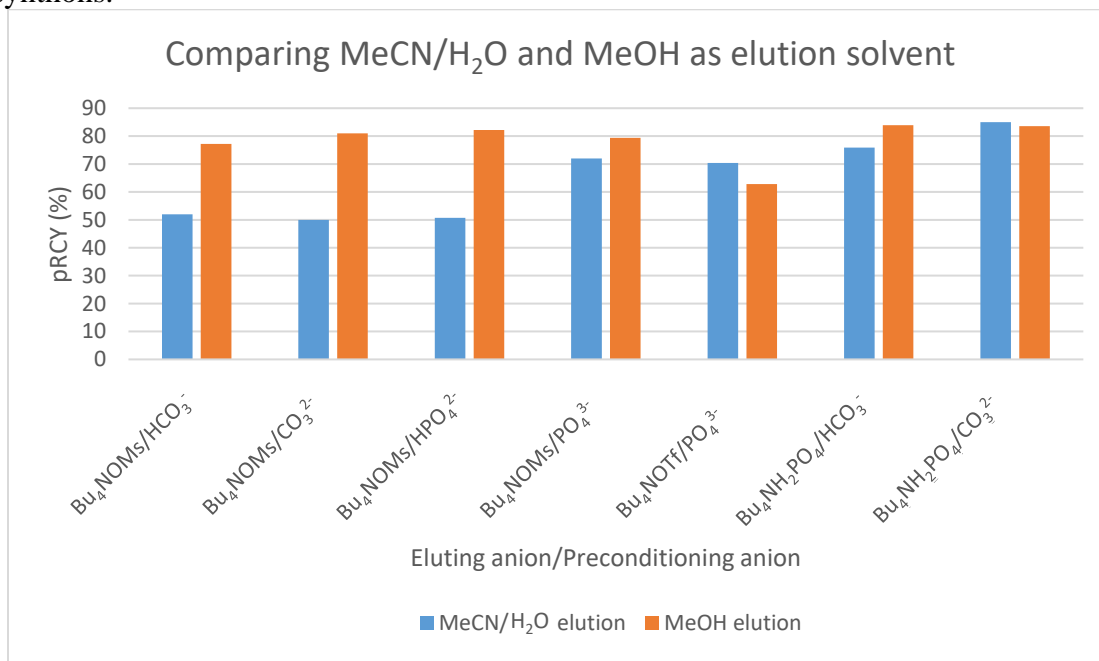


Figure S19 Switching to MeOH as a solvent for elution with Bu₄NOTf instead of MeCN/H₂O.

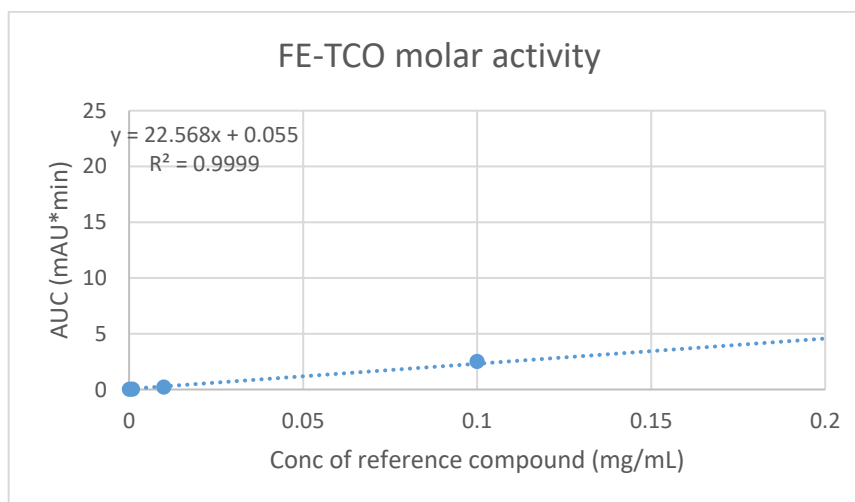
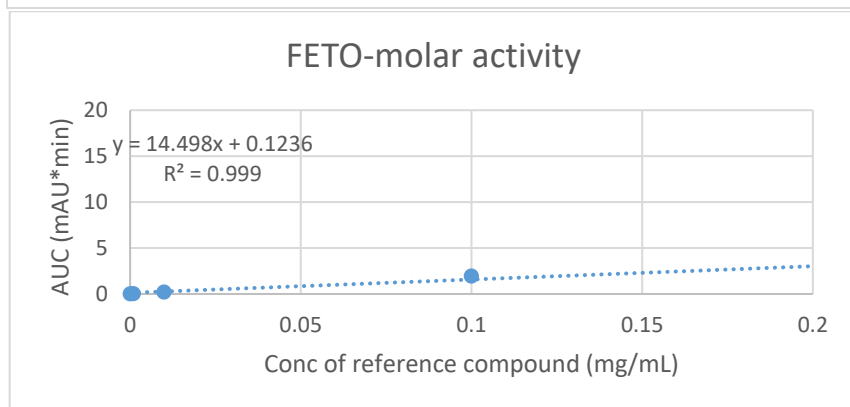
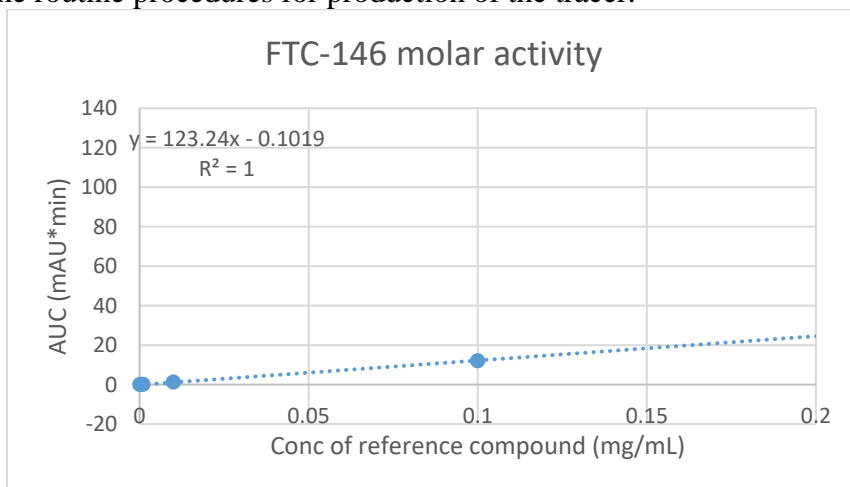
Automated radiosynthesis of clinically relevant tracers and synthons

Determination of molar activity (A_m)

The reference compound was dissolved in MeCN (1.0 mg/mL). A dilution series (10-fold dilution per sample) was made by diluting 100 μL of the concentrated solution in 900 μL of MeCN (1 mg/mL-0.0001 mg/mL). The samples were injected (10 μL) on the same analytical HPLC (using the general method for analytical HPLC) as the formulated tracers on the same day as the synthesis. The UV-trace of the chromatograms (wavelength specified for each tracer) were analyzed and the peak corresponding to the reference compound was integrated. The area under the curve was plotted in Excel and formula from the linear regression was used to determine the concentration of cold compound in the formulated tracer solutions. The concentration of radioactivity in the formulated tracers was determined by measuring the activity in a dose calibrator and dividing by the volume of the formulated tracer. Samples of 10 μL of the formulated tracers was injected and the decay corrected activity concentration was divided by the cold tracer concentration determined by the UV-trace and calculated from the standard curves. For dosimetry purposes and to be able to perform multiple syntheses in sequence relatively low starting activities (1-6 GBq) was used resulting in a slightly lower A_m than could be expected in clinical production.

Standard curves for determination of molar activity

The standard curves plotted for the different reference compounds is shown below, the x-axis has been zoomed in in order to better display the lower concentration data points. Linear regression is showed as the dashed line, the derived equation is displayed in the top left corner of the graph. Molar activity for [¹⁸F]FE-PE2I was determined by comparing to three injections of samples containing 1 µg/mL in accordance with the routine procedures for production of the tracer.



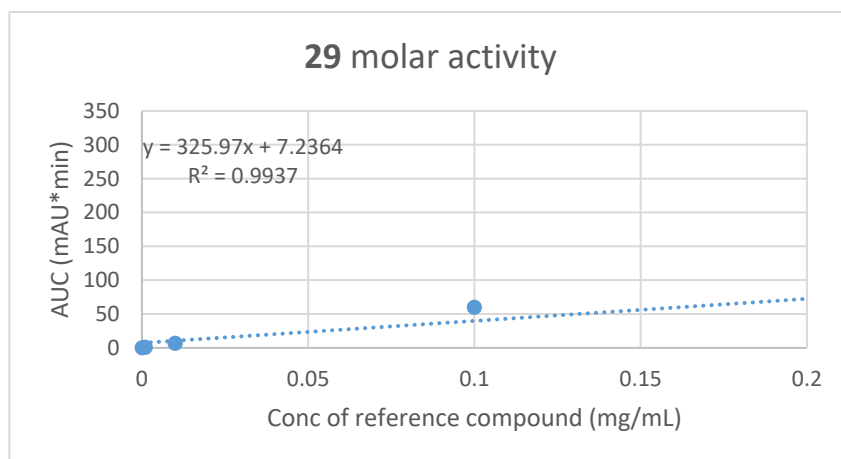
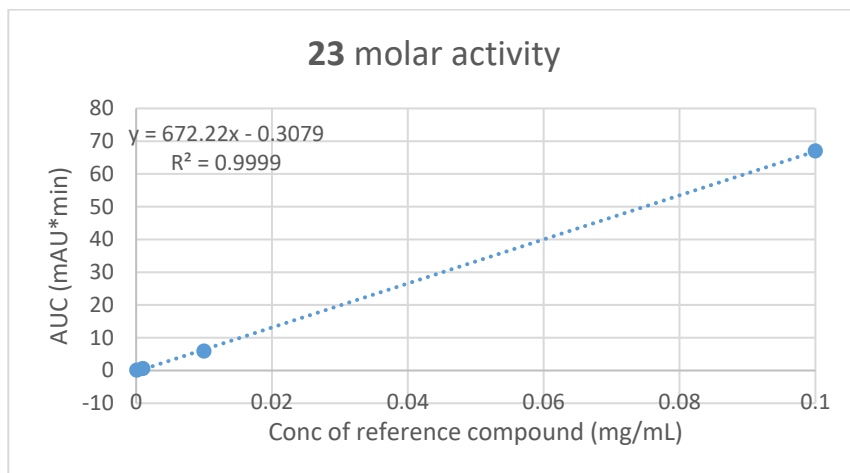
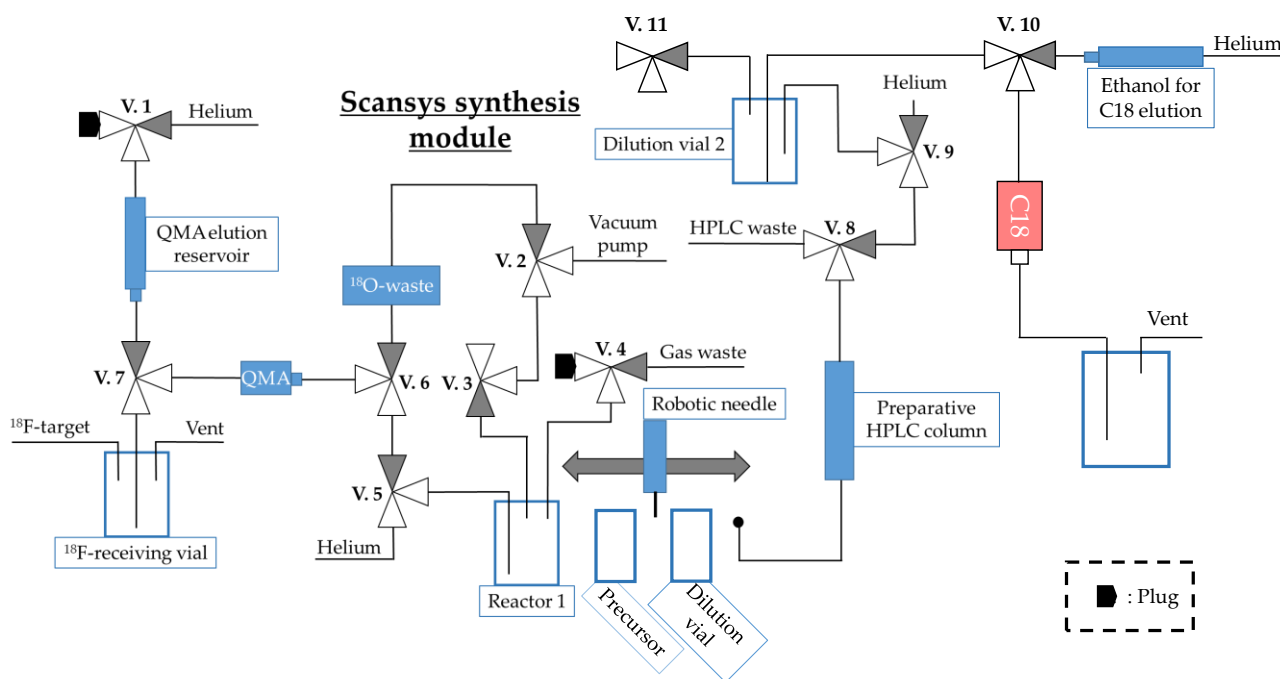


Figure S20 Calibration curves for molar activity of radiolabeled tracers. Curves zoomed in for clarity.

General method for automated radiosynthesis

The automated radiosynthesis was carried out using a Scansys research synthesis module (Scansys Laboratorieteknik) (*Scheme S8*). The ^{18}F -target water was received in the ^{18}F -receiving vial and subsequently trapped on the preconditioned QMA via vacuum over V.7, V.6 and V.2 removing the ^{18}O -water to the ^{18}O -waste. Once all the activity had been transferred the QMA-elution solution was passed over the QMA by helium flow (30 mL/min) eluting the activity via V.6. and V.5 while opening V.4 for ventilation to Reactor 1 for 40 seconds. Reactor 1 was then heated to 100 °C and the helium flow was increased to 500 mL/min for 3 min. Subsequently V.4 was closed and a vacuum was applied over the reactor via V.3 and V.2 while increasing the helium flow to 900 mL/min for 2 min. Once the reaction vial was dry the Robotic needle was used to transfer the precursor from the precursor vial to the reaction vial and the reaction was heated to the designated reaction temperature. The reaction was then cooled to 60 °C by airflow and the reaction was diluted with 0.1% TFA in H_2O (3 mL) from the dilution vial using the Robotic needle. The diluted reaction mixture was then injected on the preparative HPLC using the Robotic needle. Once the peak corresponding to the desired product was observed on the radio detector V.8 was used to collect the fraction to dilution vial 2 (100 mL), previously prepared with ca 60 mL H_2O for dilution. The lines were flushed by helium from V.9 which was then bubbled through the solution for mixing with V.11 open for ventilation. The diluted fraction was then transferred over a C18-cartridge by applying a pressure from V.9 using 1000 mL/min of helium. When all the activity had been trapped on the C18 V.10 was switched and the activity was eluted with 1 mL of EtOH with a helium flow (100 mL/min) eluting the desired product to the product vial previously prepared with the appropriate formulation solution.



Scheme S8. Flowchart for the Scansys automated synthesis module used for automated reactions.

[¹⁸F]FE-PE2I

The precursor and reference compound were purchased from PharmaSynth AS (Tartu Estonia). Manual radiosynthesis: The synthesis was performed according to the general procedure for manual labeling. Synthesis specific details:

Table S11. Details for [¹⁸F]FE-PE2I synthesis

Original procedure (Rigshospitalet, Copenhagen)	
Preconditioning of QMA	K ₂ CO ₃ (0.5M, 10 mL)
Elution of QMA	K ₂ CO ₃ (7.8 μmol) K ₂₂₂ (15.1 μmol), MeOH/H ₂ O 72:18
Reaction solvent and precursor concentration	DMSO (1 mL), 1.0 mg (1.6 μmol)
Reaction time and temperature	135 °C, 3 min
Derived conditions (4A)	
Preconditioning of QMA	K ₃ PO ₄ (0.5M, 10 mL)
Elution of QMA	Bu ₄ NOMs (20 μmol), MeCN/H ₂ O, 50:50
Reaction solvent and precursor concentration	DMSO (1 mL), 1.0 mg (1.6 μmol)
Reaction time and temperature	120 °C, 5 min

Automated synthesis: Synthesis was performed on a Scansys research module (Scansys Laboratorieteknik), reaction conditions from manual radiosynthesis (4A) were used. The reaction vial was quenched using 3 mL sodium ascorbate/ascorbic acid buffer (25 mM, pH 4.3). Purification by semipreparative HPLC using Onyx™ Monolithic Semi-Prep C18 (LC Column 100 x 10 mm), isocratic method (18% EtOH in sodium ascorbate/ascorbic acid buffer, 25 mM, pH 4.3, 6 mL/min, rt: 11 min). The fraction (10 mL) was collected in a 20 mL vial and diluted to a total volume of 20 mL with sterile water. Analytical HPLC for Manual radiosynthesis according to the general procedure, UV detection at 220 nm, rt (radio): 9.20 min. TLC eluent: n-heptane/EtOAc, 33:66, rf: 0.7. RCY: 47.8±7.9%, A_m: 110.8 – 762.2 GBq/μmol. (Higher value was a result of a high activity synthesis starting from 71 GBq)

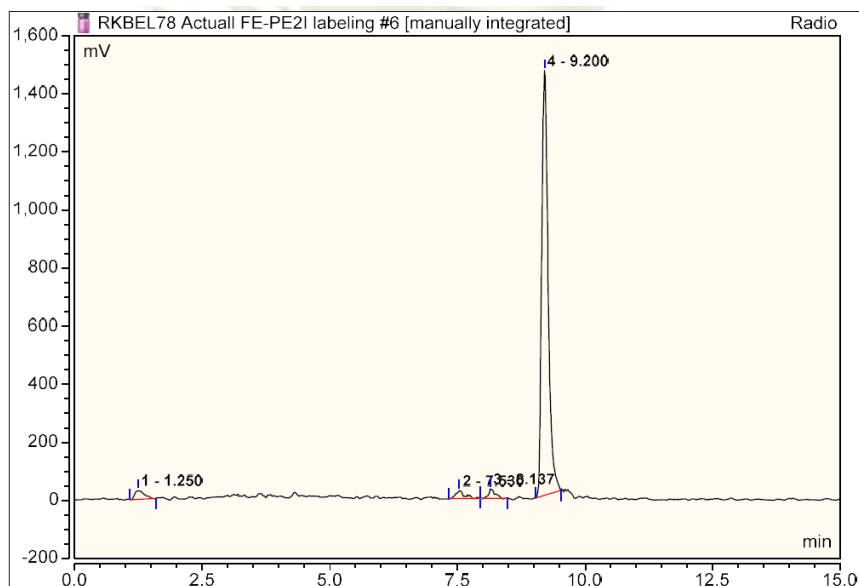


Figure S21. Analytical HPLC chromatogram of crude product (manual labeling), rt: 9.20 min.

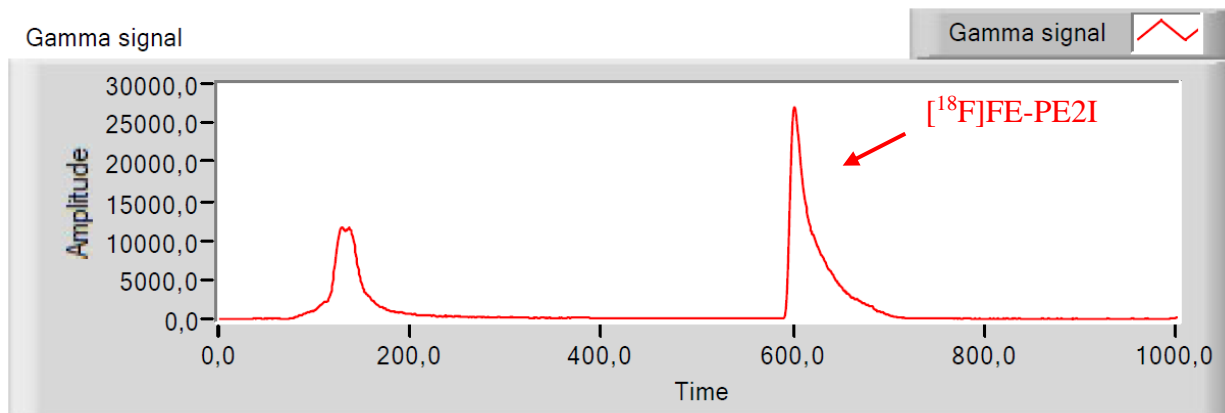


Figure S22. Preparative HPLC chromatogram of automated synthesis, rt: 10.0 min.

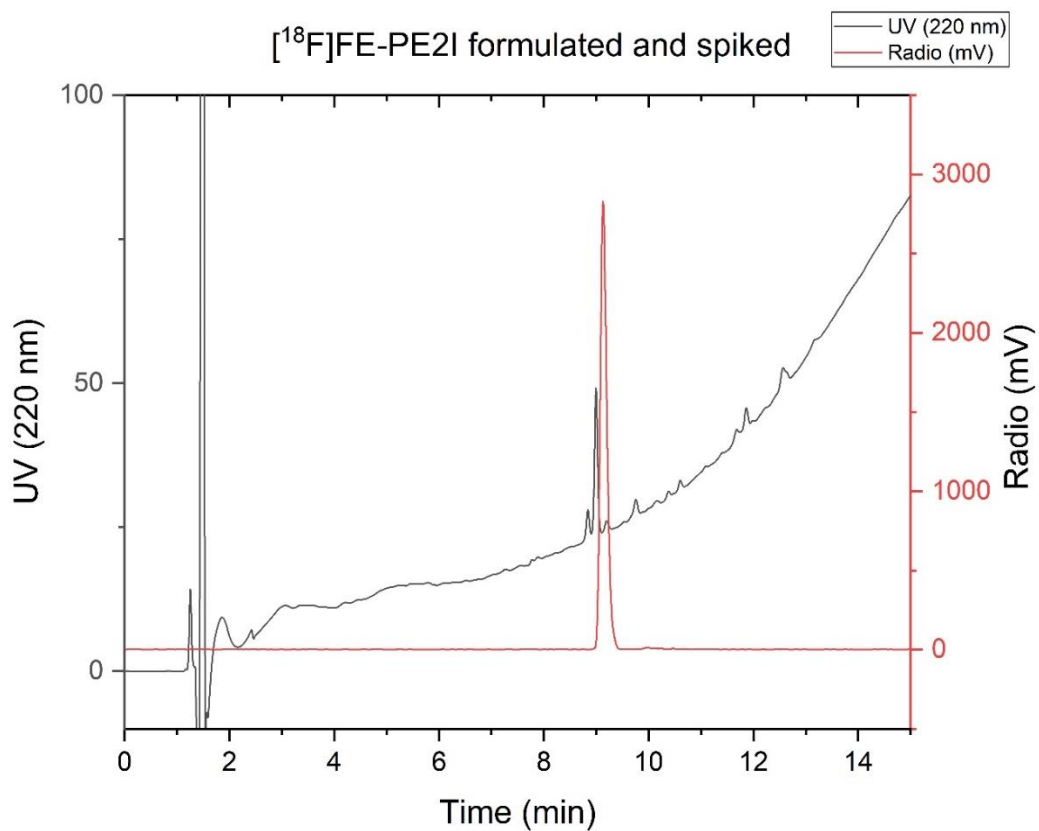


Figure S23. Analytical HPLC of formulated product [¹⁸F]FE-PE2I, spiked with ¹⁹F-reference.

[¹⁸F]FETO

The carboxylate precursor **9** and reference compound were purchased from ABX (Radeberg, Germany) and the tosylate precursor **10** was made in two steps according to *Scheme S3*. Manual radiosynthesis: The synthesis was performed according to the general procedure for manual labeling. Synthesis specific details:

Table S12. Details for [¹⁸F]FETO synthesis

Original procedure (Rahman et. al.) ⁷	
Preconditioning of QMA	K ₂ CO ₃ (0.5M, 10 mL)
Elution of QMA	K ₂ CO ₃ (25.0 μmol) K ₂₂₂ (26.6 μmol), MeCN/H ₂ O 66:33
Reaction solvent and precursor concentration	DMF (0.5 mL), 5.0 mg (12.1 μmol)
Reaction time and temperature	110 °C, 10 min
Derived conditions (IC)	
Preconditioning of QMA	KHCO ₃ (0.5M, 10 mL)
Elution of QMA	Bu ₄ NH ₂ PO ₄ (20 μmol), MeOH
Reaction solvent and precursor concentration	DMSO (1 mL), 1.3 mg (3.1 μmol)
Reaction time and temperature	120 °C, 5 min

Automated synthesis: Synthesis was performed on a Scansys research module (Scansys Laboratorieteknik) reaction conditions from Manual radiosynthesis (IC) were used. Reaction was quenched with 2 mL H₂O. Purification using semipreparative HPLC, with a C-18 column (Luna® 5μm C18(2) 100Å, 250 x 10 mm) used an isocratic method (70% MeOH in 25 mM NaH₂PO₄, 3.0 mL/min, rt: 11.5 min. Fraction was collected in 60 mL H₂O and applied to a Sep-Pak C18 Plus and subsequently formulated by eluting with 1 mL EtOH into 9 mL sterile water for injection. Analytical HPLC for manual and automated synthesis according to the general procedure. UV detection at 254 nm, rt (radio): 7.02 min, TLC eluent: n-heptane/EtOAc, 33:66, rf: 0.4. RCY: 54.5±7.0%, A_m: 4.42 ± 1.81 GBq/μmol.

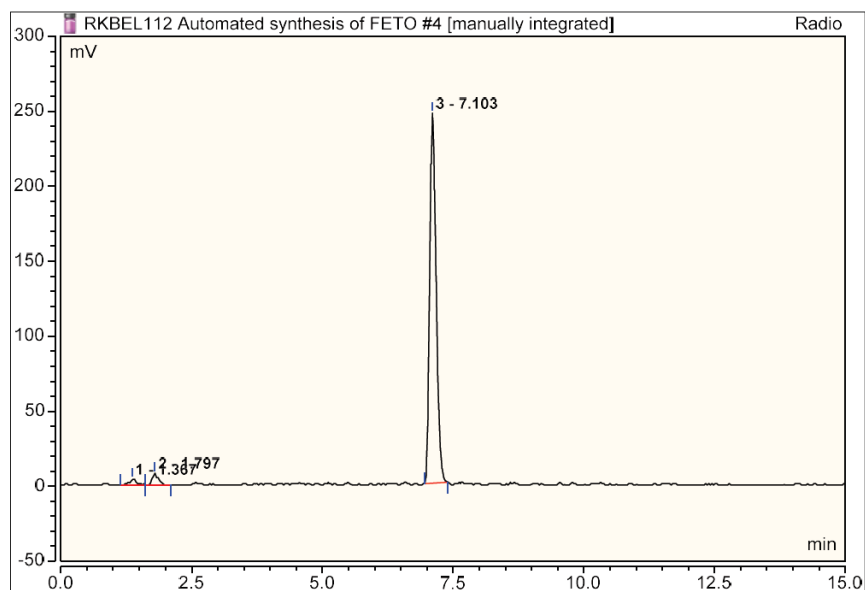


Figure S24. Analytical HPLC chromatogram of crude product, rt: 8.34 min.

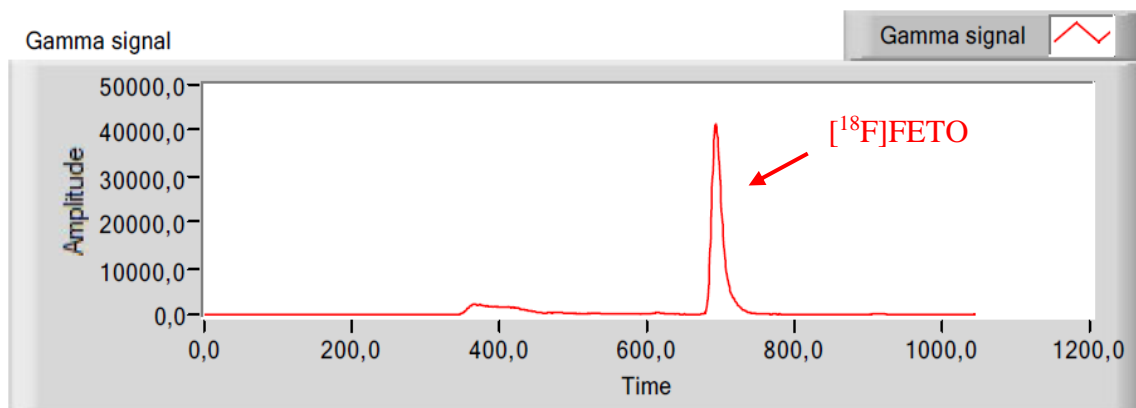


Figure S25. Preparative HPLC chromatogram of automated synthesis, rt: 11.5 min.

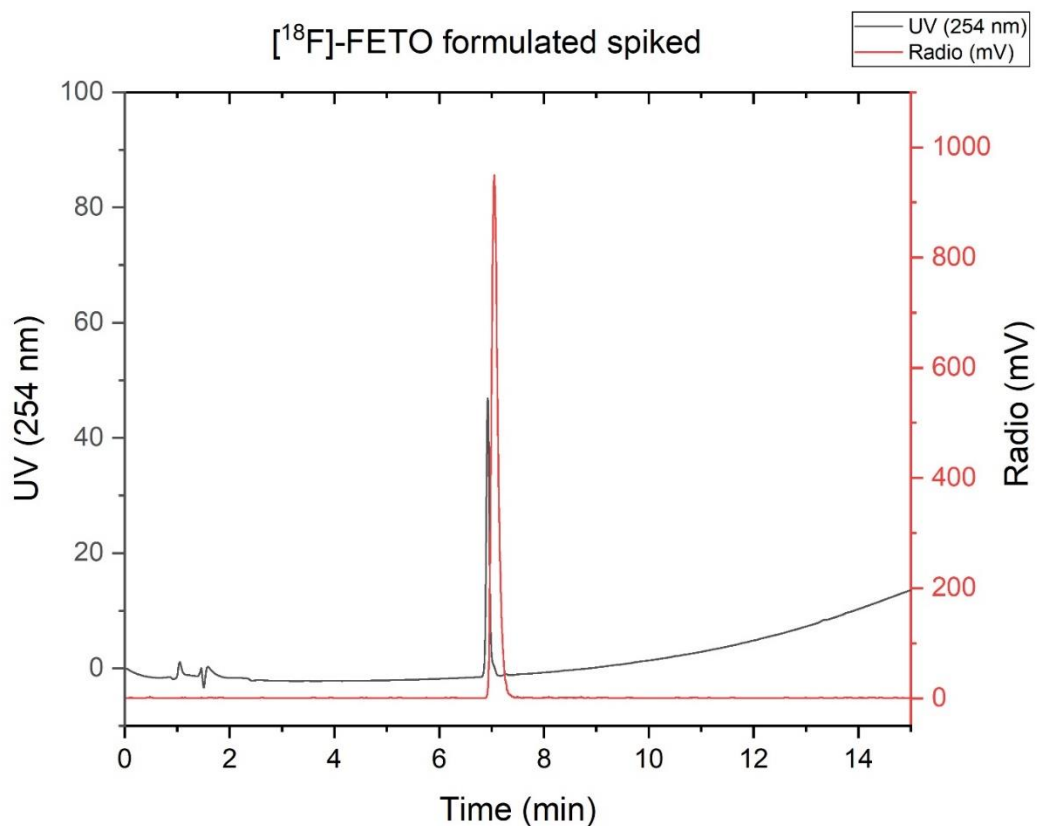


Figure S26. Analytical HPLC of formulated product [¹⁸F]FETO, spiked with ¹⁹F-reference.

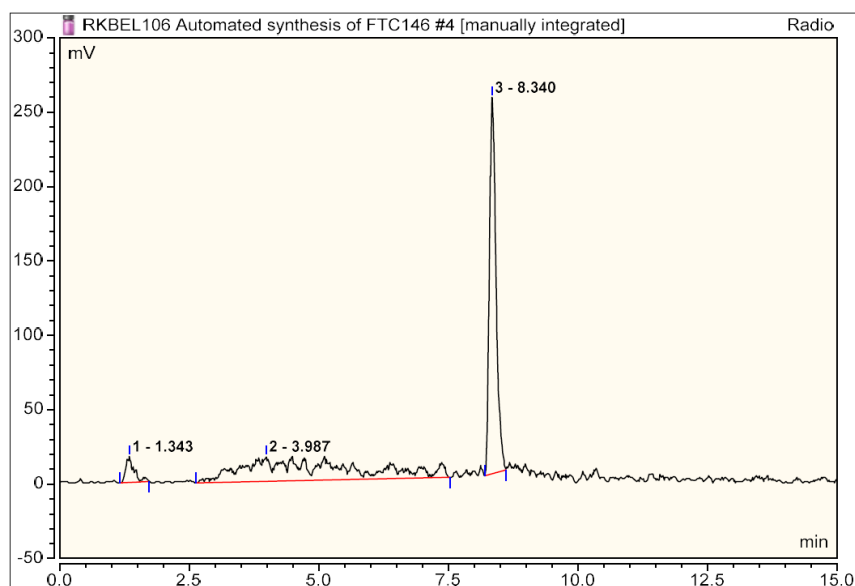
[¹⁸F]FTC-146

The alcohol precursor and reference compound were purchased from Merck and the tosylate precursor **12** was synthesized in one step according to *Scheme S4*. Manual radiosynthesis: The synthesis was performed according to the general procedure for manual labeling. Synthesis specific details:

Table S13. Details for [¹⁸F]FTC-146 synthesis

Original procedure (Collins et. al.) ³	
Preconditioning of QMA	K ₂ CO ₃ (0.5M, 10 mL)
Elution of QMA	K ₂ CO ₃ (25.4 μmol) K ₂₂₂ (40.0 μmol), MeCN/H ₂ O 90:10
Reaction solvent and precursor concentration	DMSO (1 mL), 3.0 mg (6.1 μmol)
Reaction time and temperature	185 °C, 15 min
Derived conditions (3C)	
Preconditioning of QMA	K ₂ CO ₃ (0.5M, 10 mL)
Elution of QMA	Bu ₄ NH ₂ PO ₄ (20 μmol), MeOH
Reaction solvent and precursor concentration	DMSO (1 mL), 1.5 mg (3.1 μmol)
Reaction time and temperature	120 °C, 5 min

Automated synthesis: Synthesis was performed on a Scansys research module (Scansys Laboratorieteknik) reaction conditions from Manual radiosynthesis (3C) were used. Reaction was quenched with 2 mL H₂O. Purification using semipreparative HPLC, with a C-18 column (Luna® 5μm C18(2) 100Å, 250 x 10 mm) used an isocratic method (60% MeCN with 0.1% Et₃N in H₂O (v/v) , 3.0 mL/min, rt: 25.8 min. Fraction was collected in 60 mL H₂O and applied to a Sep-Pak C18 Plus and subsequently formulated by eluting with 1 mL EtOH into 9 mL sterile water for injection. Analytical HPLC for manual and automated synthesis according to the general procedure. UV detection at 254 nm, rt (radio): 8.34 min, TLC eluent: EtOAc + 0.1% Et₃N (v/v), rf: 0.5. RCY: 24.6±2.7%, A_m: 22.1 ± 8.96 GBq/μmol.

**Figure S27.** Analytical HPLC chromatogram of crude product, rt: 8.34 min.

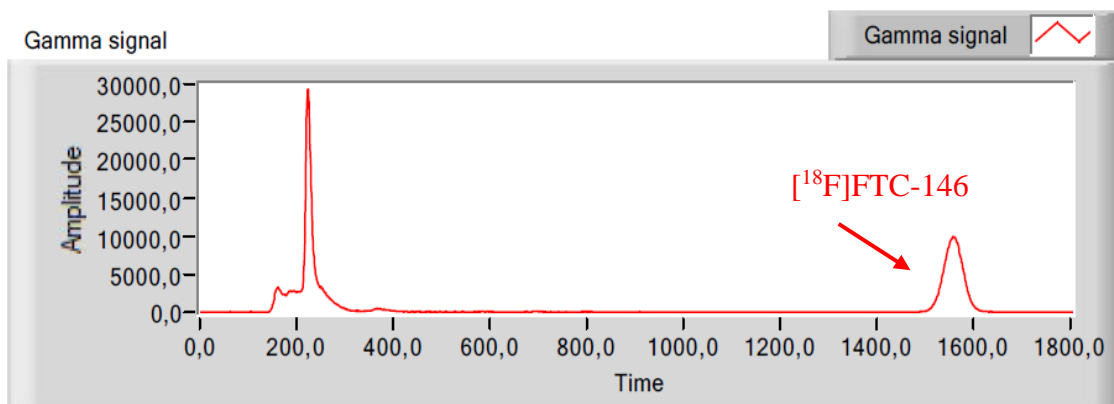


Figure S28. Preparative HPLC chromatogram of automated synthesis, rt: 25.8 min.

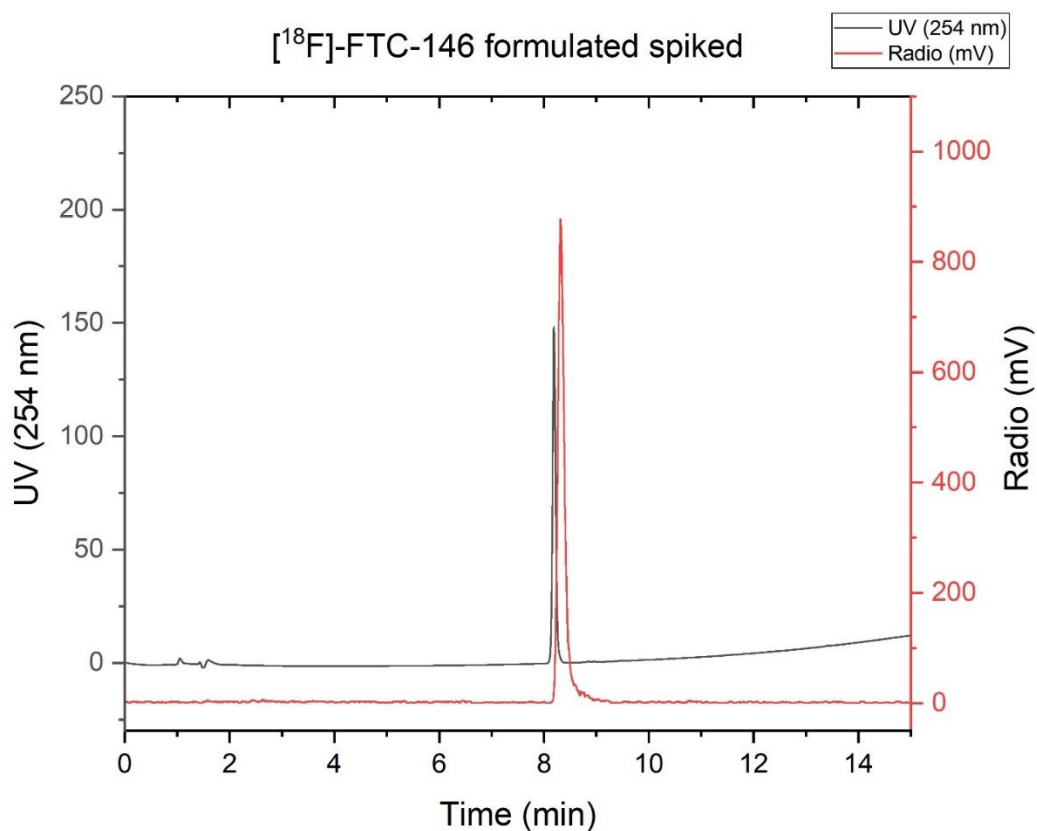


Figure S29. Analytical HPLC of formulated product $[^{18}\text{F}]\text{FTC-146}$, spiked with ^{19}F -reference.

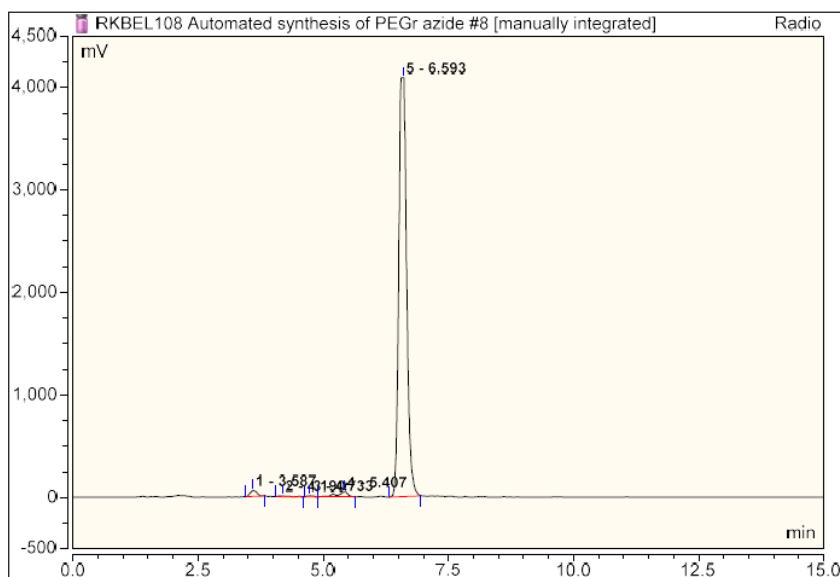
$[^{18}\text{F}]\text{F-PEG}_3\text{-azide}$

The precursor and reference compound were obtained according to Steen et. al.¹² Manual radiosynthesis: The synthesis was performed according to the general procedure for manual labeling. Synthesis specific details:

Table S14. Details for [¹⁸F]F-PEG₃-azide synthesis

Original procedure (Shen et. al.) ⁸	
Preconditioning of QMA	KHCO ₃ (PS-30), no modification
Elution of QMA	K ₂ CO ₃ (21.7 μmol) K ₂₂₂ (40.0 μmol), MeCN/H ₂ O 90:10
Reaction solvent and precursor concentration	DMSO (1 mL), 3.0 mg (8.0 μmol)
Reaction time and temperature	110 °C, 20 min
Derived conditions (3C)	
Preconditioning of QMA	K ₂ CO ₃ (0.5M, 10 mL)
Elution of QMA	Bu ₄ NH ₂ PO ₄ (20 μmol), MeOH
Reaction solvent and precursor concentration	DMSO (1 mL), 0.85 mg (2.3 μmol)
Reaction time and temperature	120 °C, 5 min

Automated synthesis: Synthesis was performed on a Scansys research module (Scansys Laboratorieteknik) reaction conditions from Manual radiosynthesis (3C) were used. Reaction was quenched with 2 mL H₂O. Purification using semipreparative HPLC, with a C-18 column (Luna® 5μm C18(2) 100Å, 250 x 10 mm) used an isocratic method, 30% MeCN in 0.1% TFA (v/v), 3.0 mL/min, rt: 17.5 min. Fraction was collected in 60 mL H₂O and applied to a Sep-Pak C18 Plus and subsequently formulated by eluting with 1 mL DMF. Analytical HPLC for manual and automated synthesis according to the general procedure. UV detection at 290 nm, rt (radio): 6.59 min, TLC eluent: EtOAc, rf: 0.8. RCY: 66.4±9.3%, A_m: not determined.

**Figure S30.** Analytical HPLC chromatogram of crude product, rt: 6.59 min.

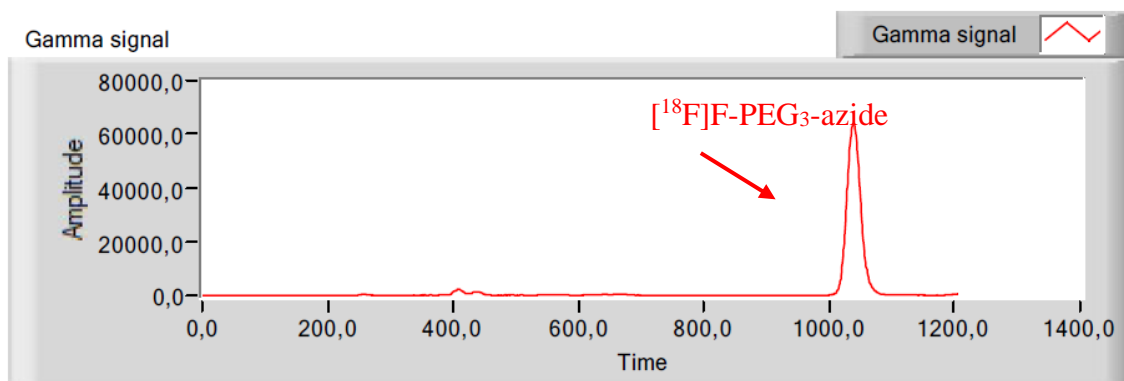


Figure S31. Preparative HPLC chromatogram of automated synthesis, rt: 17.5 min

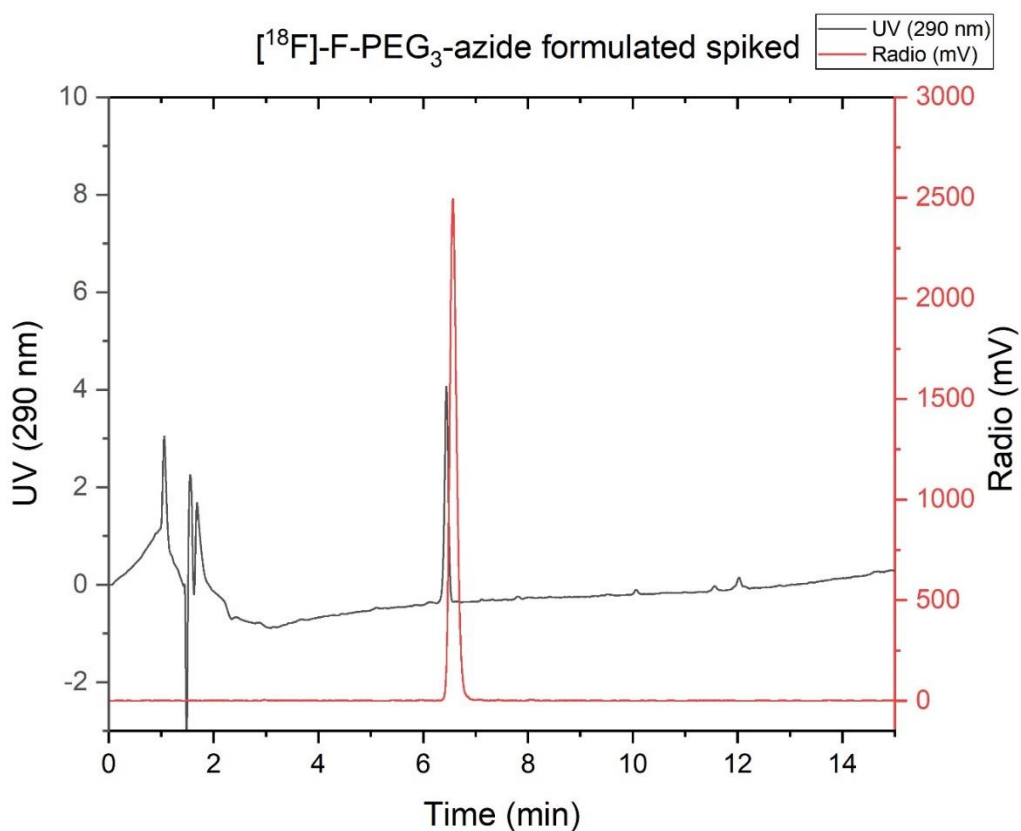


Figure S32. Analytical HPLC of formulated product [^{18}F]F-PEG₃-azide, spiked with ^{19}F -reference.

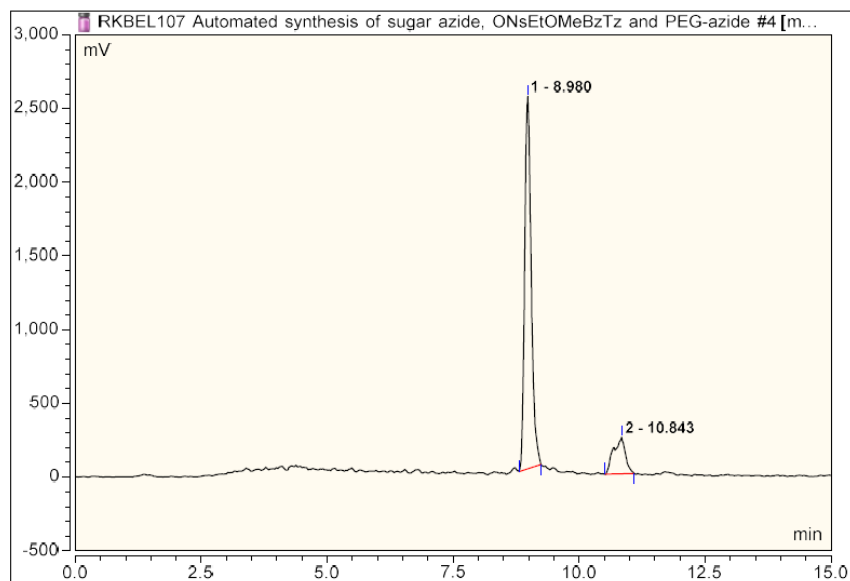
[^{18}F](2R,3R,4S,5R,6R)-2-Azido-6-(fluoromethyl)tetrahydro-2H-pyran-3,4,5-triyl triacetate ([^{18}F]sugarazide)

The precursor, alkyne tetrazine and tetrazine reference compound were obtained according to Steen et. al.¹² Manual radiosynthesis: The synthesis was performed according to the general procedure for manual labeling. Synthesis specific details:

Table S15. Details for [¹⁸F]Sugarazide synthesis.

Original procedure (Steen et al.) ¹²	
Preconditioning of QMA	NaCl (no modification of Cl preconditioned QMA)
Elution of QMA	K ₂ CO ₃ (36.2 μmol) K ₂₂₂ (88.8 μmol), MeOH/H ₂ O 96:4
Reaction solvent and precursor concentration	MeCN (0.5 mL), 11.0 mg (21.0 μmol)
Reaction time and temperature	100 °C, 7 min
Derived conditions (4B)	
Preconditioning of QMA	K ₃ PO ₄ (0.5M, 10 mL)
Elution of QMA	Bu ₄ NOTf (20 μmol), MeCN/H ₂ O, 50:50
Reaction solvent and precursor concentration	MeCN (1 mL), 3.2 mg (6.2 μmol)
Reaction time and temperature	100 °C, 5 min

Automated synthesis: Synthesis was performed on a Scansys research module (Scansys Laboratorieteknik) reaction conditions from Manual radiosynthesis (4B) were used. Reaction was quenched with 2 mL H₂O. Purification using semipreparative HPLC, with a C-18 column (Luna® 5μm C18(2) 100Å, 250 x 10 mm) used an isocratic method (40% MeCN in phosphate buffer 10 mM, pH 6, 3.0 mL/min, rt: 30 min. Fraction was collected in 60 mL H₂O and applied to a Sep-Pak C18 Plus and subsequently eluted with 1 mL 7N NH₃ in MeOH for deprotection. Analytical HPLC for manual and automated synthesis according to the general procedure. Identification by copper catalyzed click of the deprotected tracer to an alkyne-tetrazine. UV detection at 254 nm, rt (radio): 8.98 min for the TLC eluent: EtOAc, rf: 0.9. RCY: 41.8±7.8%, A_m: not determined for the [¹⁸F]sugarazide. Deprotected rt (radio): 2.35 min. Clicked to the alkyne-tetrazine rt (radio): 4.77 min.

**Figure S33.** Analytical HPLC chromatogram of crude product, rt: 8.98 min.

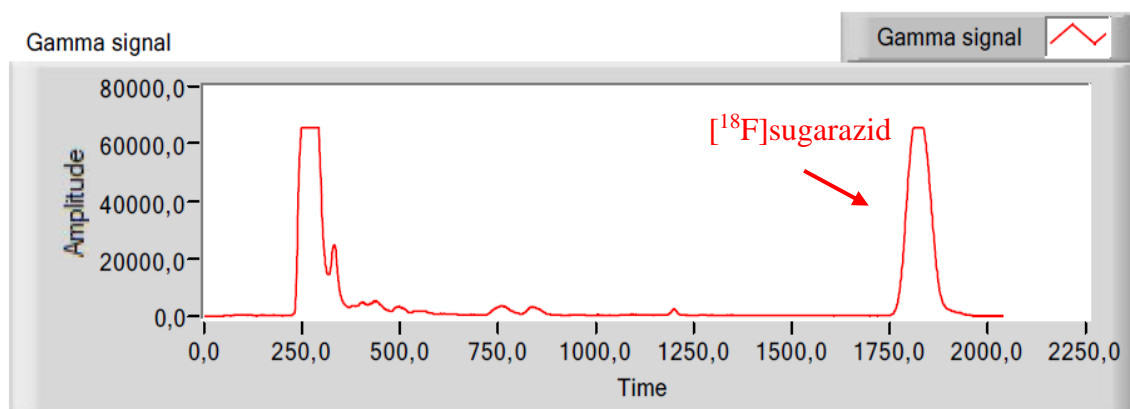


Figure S34. Preparative HPLC chromatogram of automated synthesis, rt: 30.0 min.

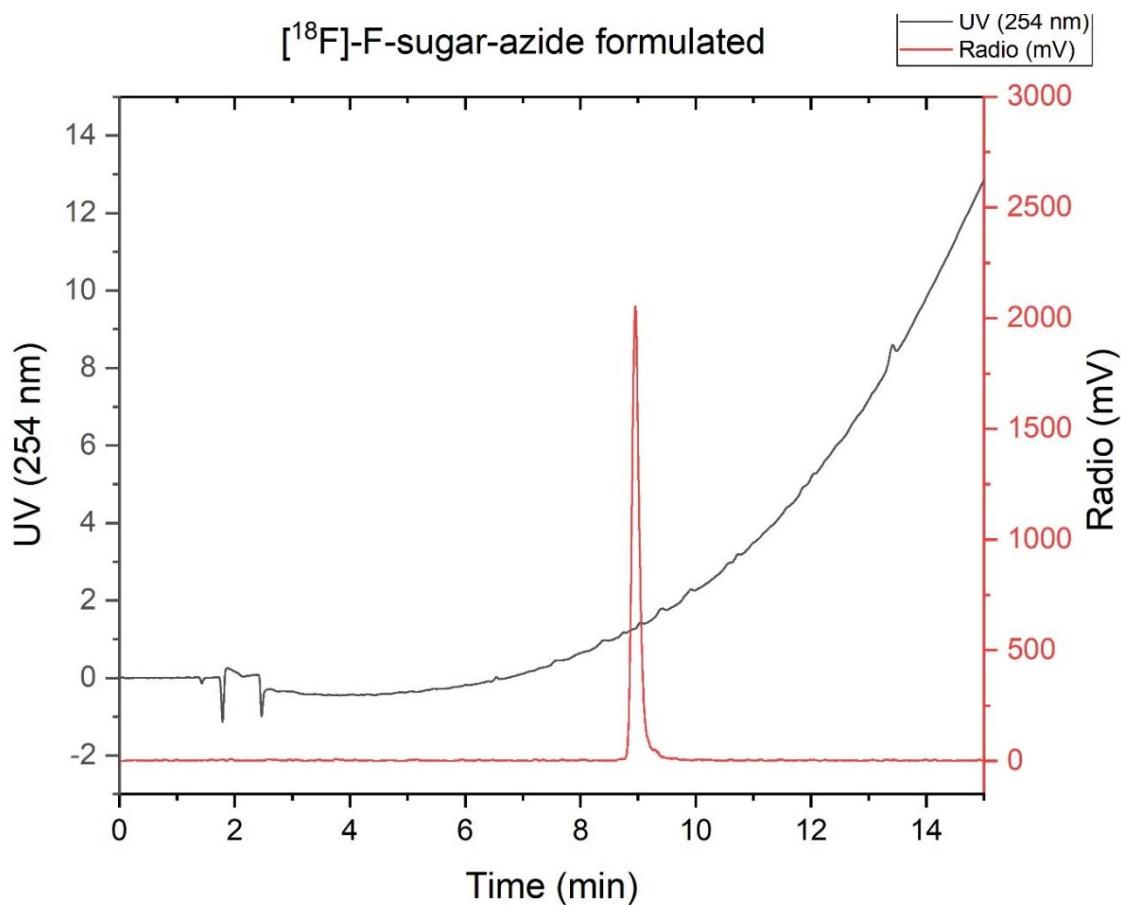


Figure S35. Analytical HPLC of formulated product [¹⁸F]sugarazide.

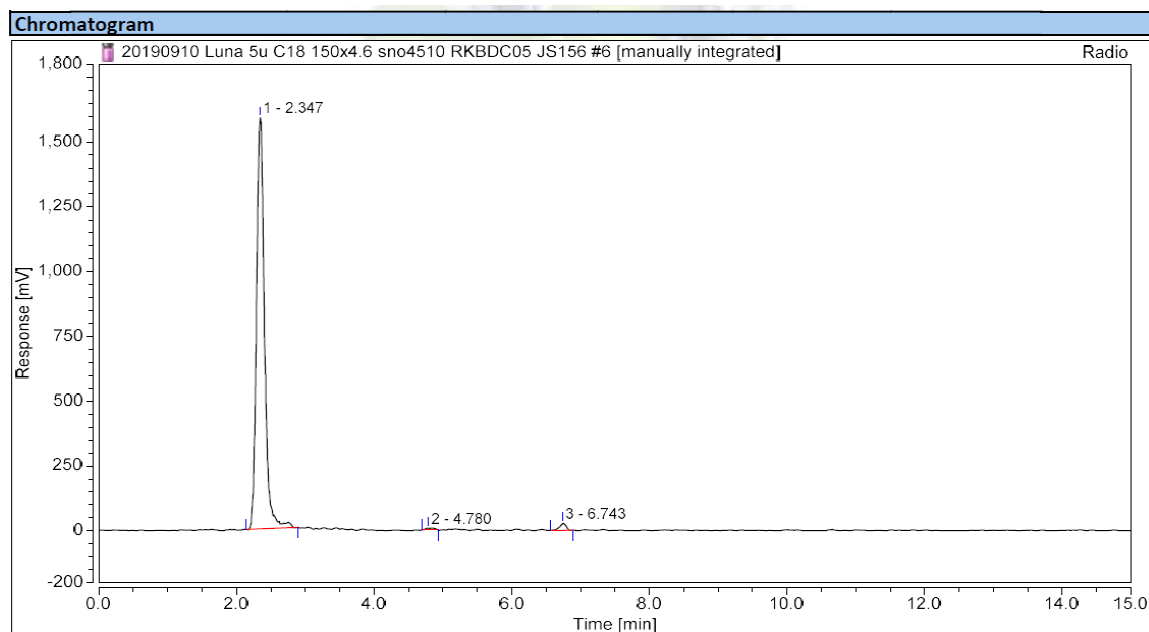


Figure S36. Chromatogram of the deprotected [^{18}F]sugarazide, rt: 2.35 min.

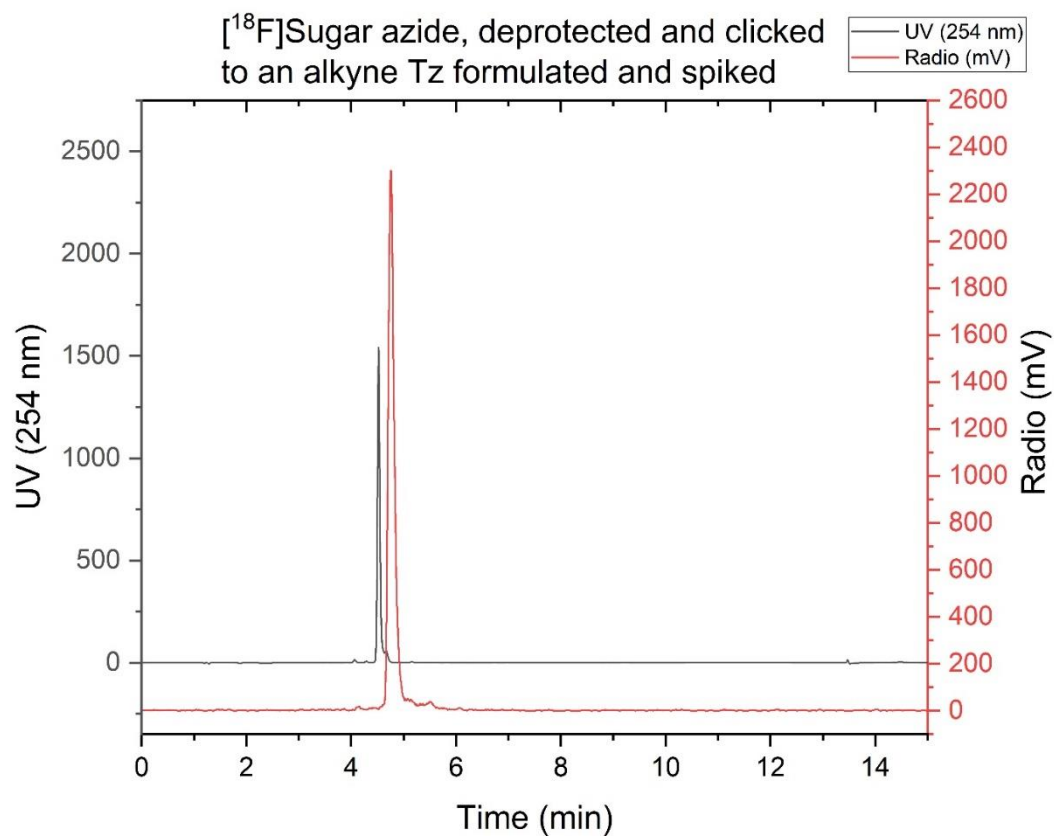


Figure S37. Analytical HPLC of formulated product [^{18}F]sugarazide deprotected and clicked to an alkyne tetrazine according to the procedures described in Steen et. al.

[¹⁸F]FE-TCO

The precursor (**18**) and reference compound (**19**) were synthesized according to *Scheme S5 Manual radiosynthesis*: The synthesis was performed according to the general procedure for manual labeling. Synthesis specific details:

Table S16. Details for [¹⁸F]FE-TCO synthesis

Original procedure (Collins et. al.) ³	
Preconditioning of QMA	K ₂ CO ₃ (0.5 M, 10 mL)
Elution of QMA	6.5 μL of 40% Bu ₄ NOH (10.0 μmol) MeCN/H ₂ O 30:50 (0.8 mL)
Reaction solvent and precursor concentration	MeCN (1 mL), 4.0 mg (12.3 μmol)
Reaction time and temperature	90 °C, 10 min
Derived conditions (3C)	
Preconditioning of QMA	K ₂ CO ₃ (0.5M, 10 mL)
Elution of QMA	Bu ₄ NH ₂ PO ₄ (20 μmol), MeOH
Reaction solvent and precursor concentration	MeCN (1 mL), 1.00 mg (3.1 μmol)
Reaction time and temperature	120° C, 5 min

Automated synthesis: Synthesis was performed on a Scansys research module (Scansys Laboratorieteknik) reaction conditions from Manual radiosynthesis (3C) were used. Reaction was quenched with 2 mL H₂O. Purification using semipreparative HPLC, with a C-18 column (Luna® 5μm C18(2) 100Å, 250 x 10 mm) used an isocratic method, 50% MeCN in 0.1% TFA (v/v), 6.0 mL/min, rt: 13.0 min. Fraction was collected in 60 mL H₂O and applied to a Sep-Pak C18 Plus and subsequently formulated by eluting with 1 mL EtOH and diluted in 9 mL H₂O. Analytical HPLC for manual and automated synthesis according to the general procedure. UV detection at 220 nm, rt (radio): 10.68 min, TLC eluent: Hep/EtOAc (30:70), rf: 0.6. RCY: 61.8±4.7%, A_m: 70.7 ± 27.9 GBq/μmol.

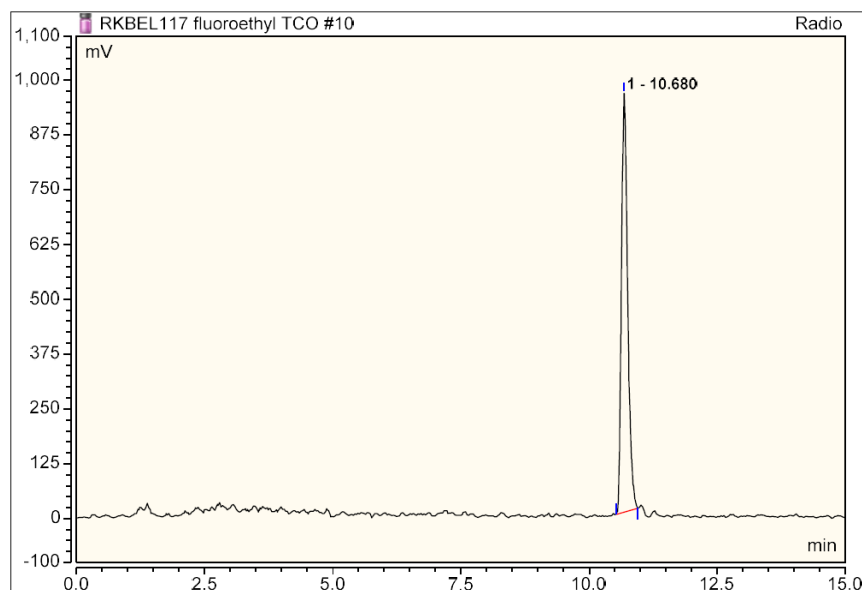


Figure S38. Analytical HPLC chromatogram of crude product, rt: 10.68 min.

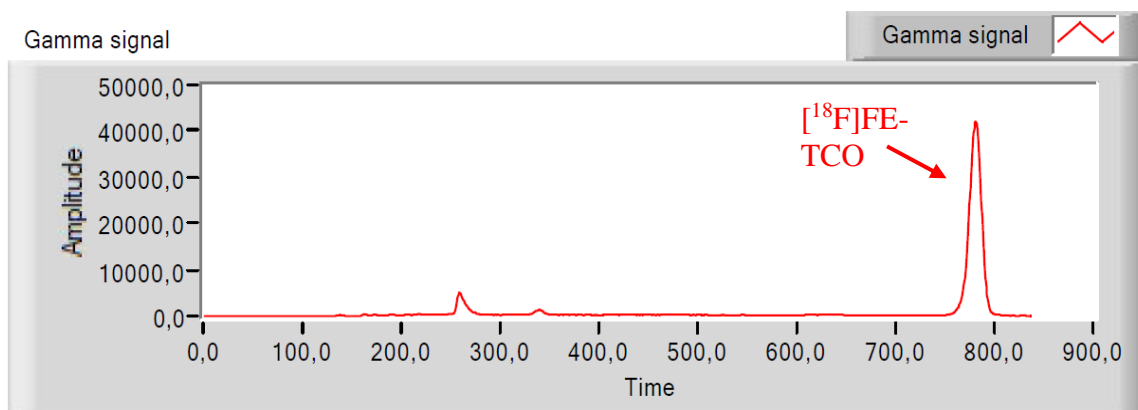


Figure S39. Preparative HPLC chromatogram of automated synthesis, rt: 13.00 min.

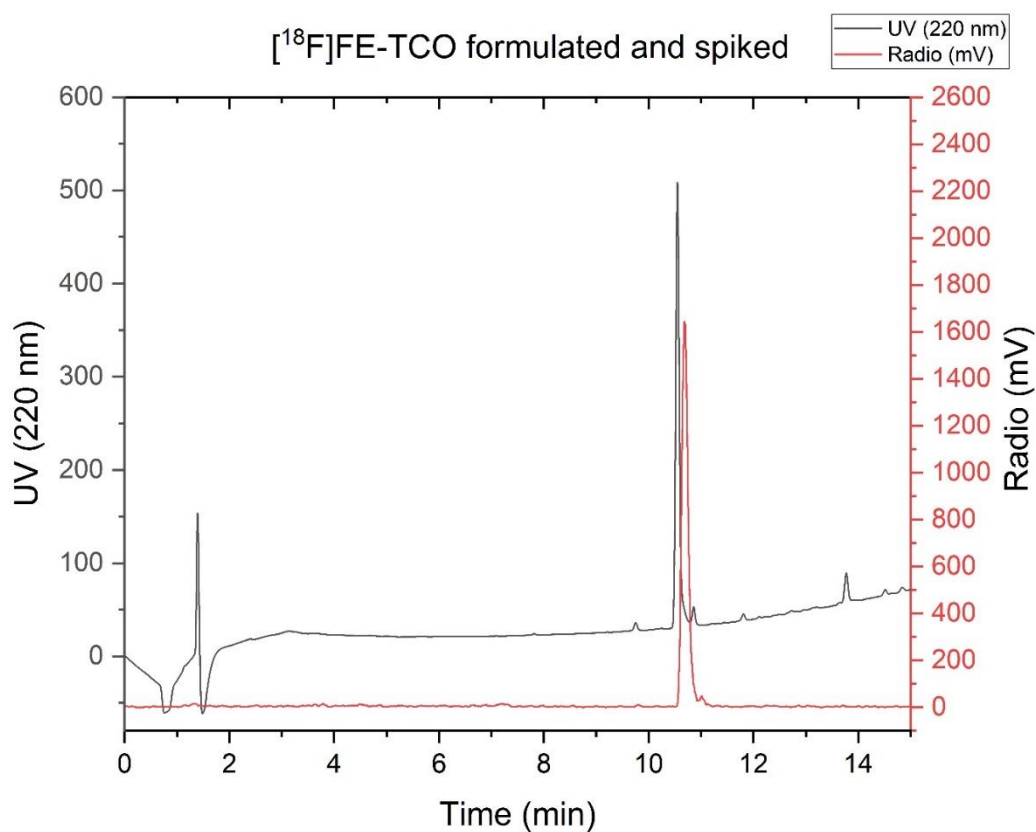


Figure S40. Analytical HPLC of formulated product $[^{18}\text{F}]\text{FE-TCO}$, spiked with ^{19}F -reference.

$[^{18}\text{F}]\text{FTHA}$

The precursor and reference compound were purchased from ABX (Radeberg, Germany). Manual radiosynthesis: The synthesis was performed according to the general procedure for manual labeling. However, following the reaction the solvent was removed by adding a ventilation needle to the vial and the reaction was heated at 130 °C for 5 min under a stream of nitrogen. Deprotection by adding 1 mL of

2N NaOH, reaction was left at 130 °C for 5 min. No separate analysis was made for crude and resolubilized fractions. Synthesis specific details:

Table S17. Details for [¹⁸F]FTHA synthesis.

Original procedure (Savisto et. al.) ⁹	
Preconditioning of QMA	K ₂ CO ₃ (0.5 M, 10 mL)
Elution of QMA	K ₂ CO ₃ (32.0 μmol) K ₂₂₂ (10.0 μmol), MeCN/H ₂ O 10:90
Reaction solvent and precursor concentration	MeCN (1 mL), 14.0 mg (8.7 μmol)
Reaction time and temperature	130 °C, 5 min
Derived conditions (4A)	
Preconditioning of QMA	K ₃ PO ₄ (0.5M, 10 mL)
Elution of QMA	Bu ₄ NOMs (20 μmol), MeOH
Reaction solvent and precursor concentration	MeCN (1 mL), 2.4 mg (3.1 μmol)
Reaction time and temperature	120 °C, 5 min

Automated synthesis: Synthesis was performed on a Scansys research module (Scansys Laboratorieteknik) reaction conditions from Manual radiosynthesis (4B) were used with deprotection as described for Manual radiosynthesis. Reaction was quenched with 300 μL MeOH, 300 μL H₂O and 166 μL AcOH. Purification using semipreparative HPLC, with a C-18 column (Luna® 5μm C18(2) 100Å, 250 x 10 mm) used an isocratic method MeOH/H₂O/AcOH, 85:15:4 (v/v/v), 3.0 mL/min, rt: 19.1 min. Fraction was collected in 60 mL H₂O and applied to a Sep-Pak C18 and subsequently formulated by eluting with 1 mL EtOH into 9 mL sterile water for injection. Analytical HPLC for manual and automated synthesis according to the general procedure. UV detection at 230 nm, rt (radio): 13.30 min, TLC eluent: n-heptane/EtOAc, (66:33) rf: 0.4. RCY: 26.5±4.8%, A_m: not determined.

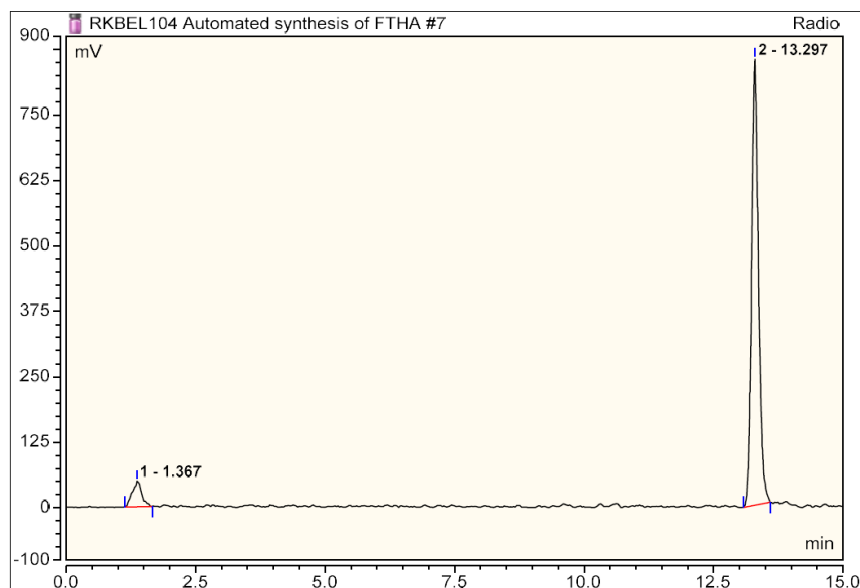


Figure S41. Analytical HPLC chromatogram of crude product after deprotection, rt: 13.30 min.

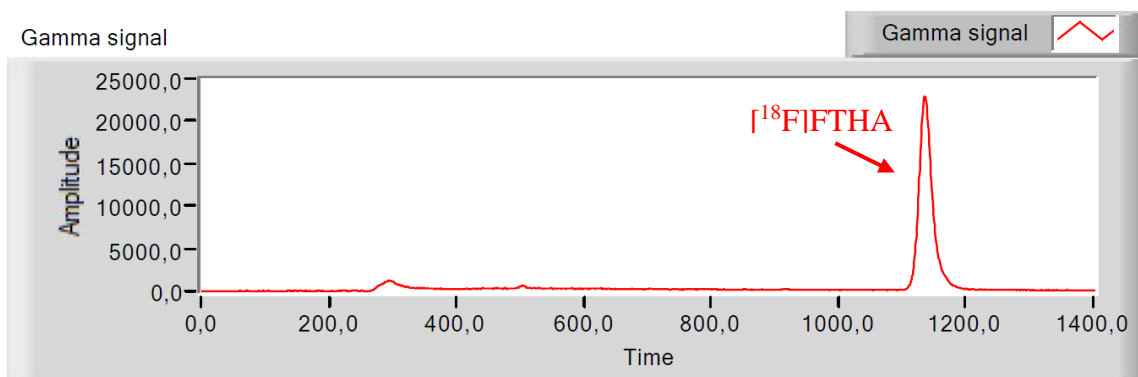


Figure S42. Preparative HPLC chromatogram of automated synthesis, rt: 19.1 min.

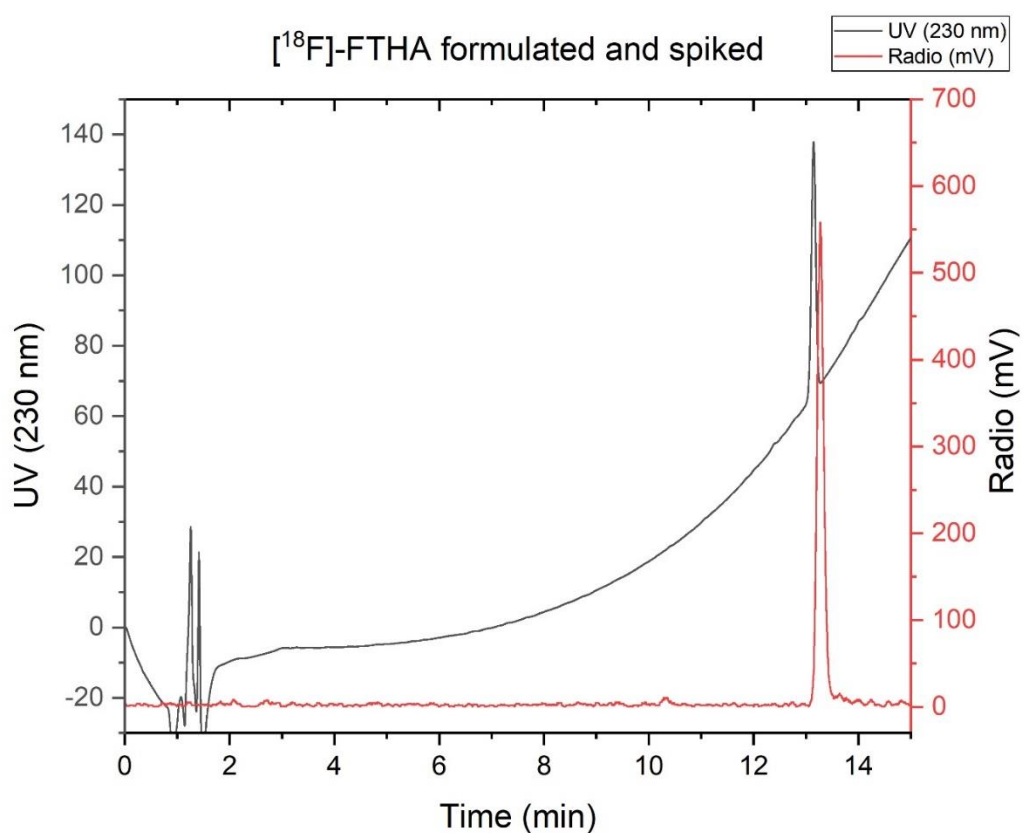


Figure S43. Analytical HPLC of formulated product [^{18}F]FTHA, spiked with ^{19}F -reference.

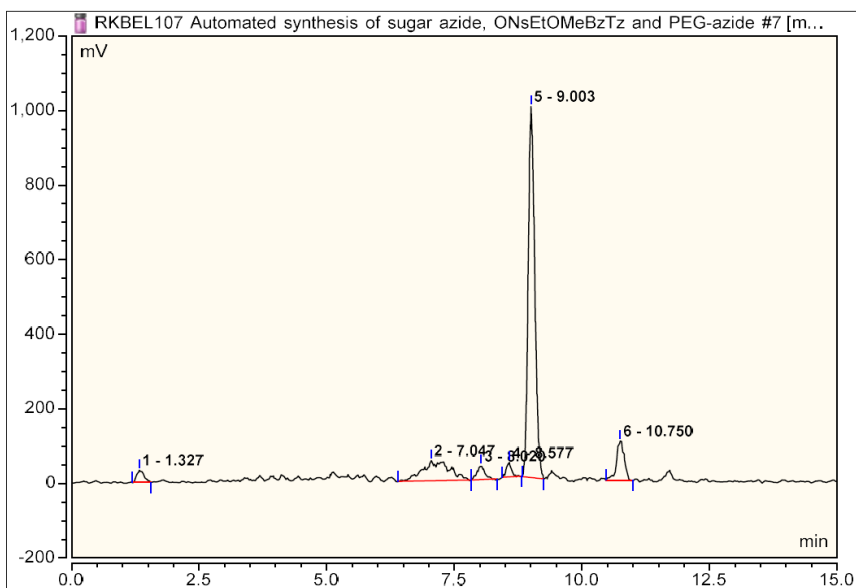
[^{18}F]4-[(2-Fluoroethoxy)methyl]-1,2,4,5-tetrazin-3-yl]benzene ([^{18}F]23)

The precursor (**26**) and reference compound (**23**) were synthesized according to *Scheme S6. Manual radiosynthesis*. The synthesis was performed according to the general procedure for manual labeling. Synthesis specific details:

Table S18. Details for [¹⁸F]23 synthesis

Original procedure (Li et. al.) ¹⁰	
Preconditioning of QMA	K ₂ CO ₃ (0.5M, 10 mL)
Elution of QMA	Et ₄ NHCO ₃ (20 μmol) MeCN/H ₂ O 50:50 (concentration not specified in ref)
Reaction solvent and precursor concentration	MeCN (1 mL), 3.0 mg (7.2 μmol) (concentration and volume not specified in ref)
Reaction time and temperature	85 °C, 15 min
Derived conditions (4A)	
Preconditioning of QMA	K ₃ PO ₄ (0.5M, 10 mL)
Elution of QMA	Bu ₄ NOMs (20 μmol), MeOH
Reaction solvent and precursor concentration	tBuOH/MeCN or tBuOH/DMSO, 86:14 (1 mL), 1.3 mg (3.1 μmol)
Reaction time and temperature	100 °C, 5 min

Automated synthesis: Synthesis was performed on a Scansys research module (Scansys Laboratorieteknik) reaction conditions from Manual radiosynthesis (4A) were used. Reaction was quenched with 2 mL 0.1% TFA in H₂O. Purification using semipreparative HPLC, with a C-18 column (Luna® 5μm C18(2) 100Å, 250 x 10 mm) used an isocratic method (45% MeCN with 0.1% TFA in H₂O (v/v) , 3.0 mL/min, rt: 16.5 min. Fraction was collected in 60 mL H₂O and applied to a Sep-Pak C18 Plus and subsequently formulated by eluting with 1 mL EtOH into 9 mL sterile water for injection. Analytical HPLC for manual and automated synthesis according to the general procedure. UV detection at 254 nm, rt: 9.00 min, TLC eluent: n-heptane/EtOAc, 66:34, rf: 0.6. RCY: 22.8±3.9%, A_m: 34.1 ± 14.0 GBq/μmol.

**Figure S44.** Analytical HPLC chromatogram of crude product, rt: 9.00 min

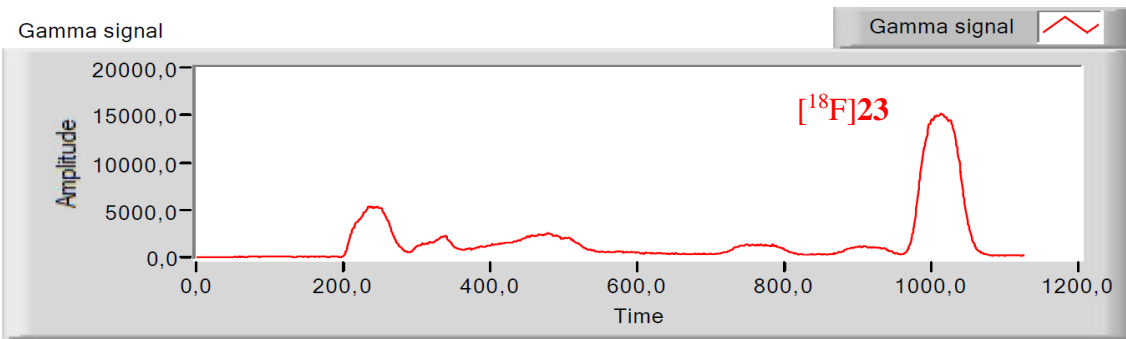


Figure S45. Preparative HPLC chromatogram of automated synthesis, rt: 16.5 min.



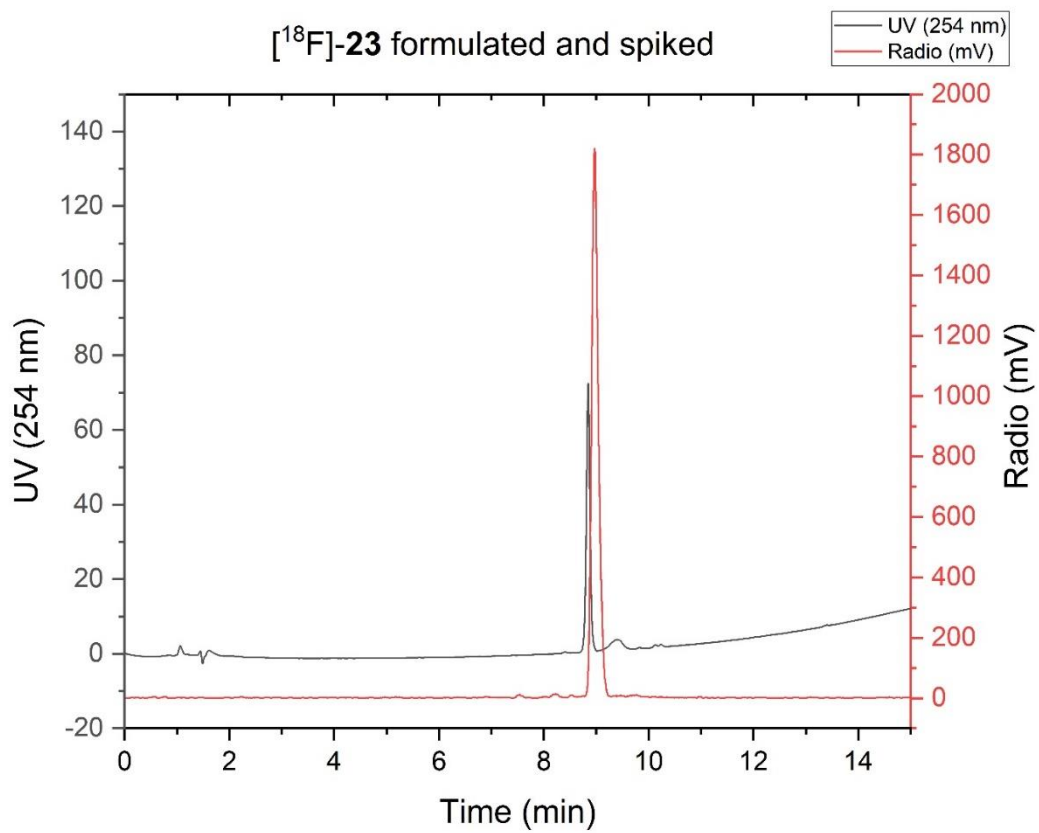


Figure S46. Analytical HPLC of formulated product [¹⁸F]23, spiked with ¹⁹F-reference.

[¹⁸F]2-Fluoro-4-(1,2,4,5-tetrazin-3-yl)-2-fluoroethyl-benzoate (29)

The precursor (31) and reference compound (29) were synthesized according to *Scheme S7*. Manual radiosynthesis: The synthesis was performed according to the general procedure for manual labeling. Synthesis specific details:

Table S19. Details for [¹⁸F]29 synthesis.

Original procedure (not existing)	
Preconditioning of QMA	-
Elution of QMA	-
Reaction solvent and precursor concentration	-
Reaction time and temperature	-
Derived conditions (4A)	
Preconditioning of QMA	K ₃ PO ₄ (0.5M, 10 mL)
Elution of QMA	Bu ₄ NOMs (20 μmol), MeOH
Reaction solvent and precursor concentration	tBuOH/DMSO, 86:14 (1 mL), 1.4 mg (3.1 μmol)
Reaction time and temperature	100 °C, 5 min

Automated synthesis: Synthesis was performed on a Scansys research module (Scansys Laboratorieteknik) reaction conditions from Manual radiosynthesis (4A) were used. Reaction was quenched with 2 mL 0.1% TFA in H₂O. Purification using semipreparative HPLC, with a C-18 column (Luna® 5μm C18(2) 100Å, 250 x 10 mm) used an isocratic method (45% MeCN with 0.1% TFA in H₂O (v/v), 3.0 mL/min, rt: 18.5 min. Fraction was collected in 60 mL H₂O and applied to a Sep-Pak C18 Plus and subsequently formulated by eluting with 1 mL EtOH into 9 mL sterile water for injection. Analytical HPLC for manual and automated synthesis according to the general procedure. UV detection at 254 nm, rt (radio): 9.25 min, TLC eluent: n-heptane/EtOAc, 50:50, rf: 0.5. RCY: 5.2±2.8%, A_m: 96.3 ± 5.8 MBq/μmol.

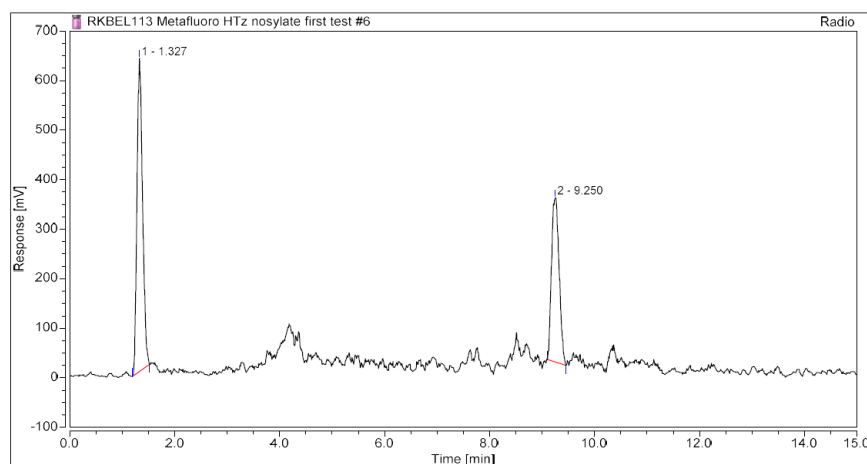


Figure S47. Analytical HPLC chromatogram of crude product, rt: 9.25 min

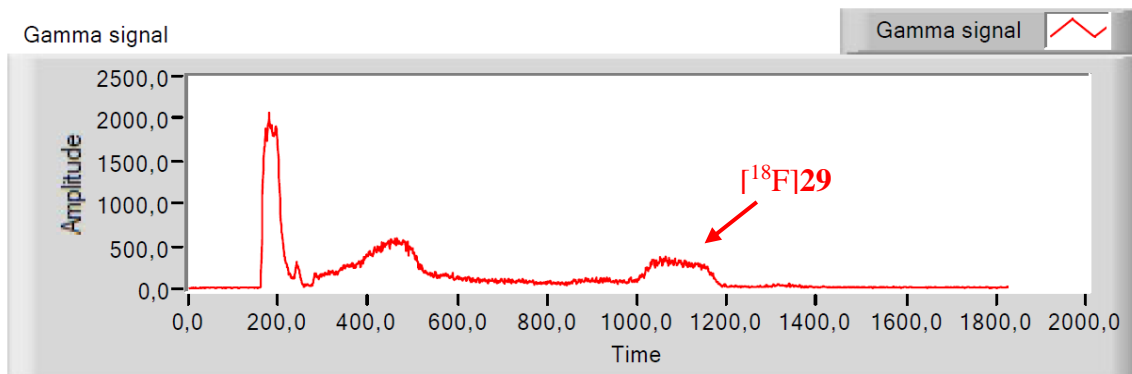


Figure S48. Preparative HPLC chromatogram of automated synthesis, rt: 18.5 min.

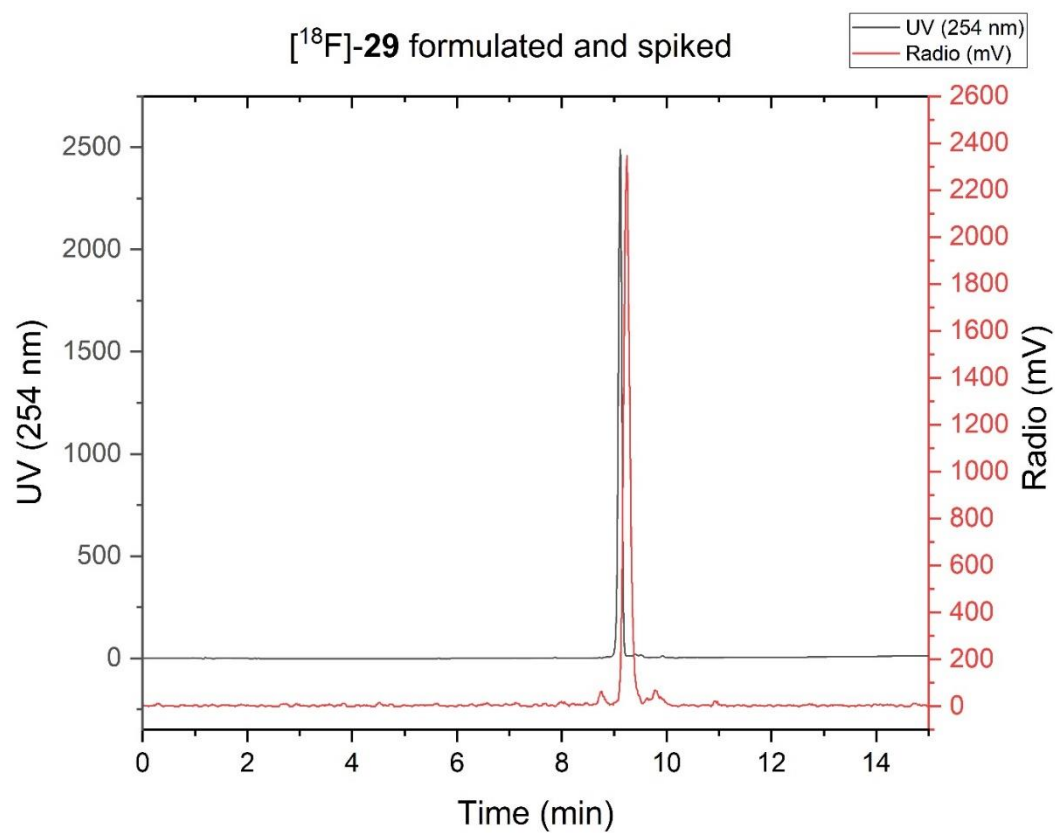


Figure S49. Analytical HPLC of formulated product [¹⁸F]29, spiked with ¹⁹F-reference.

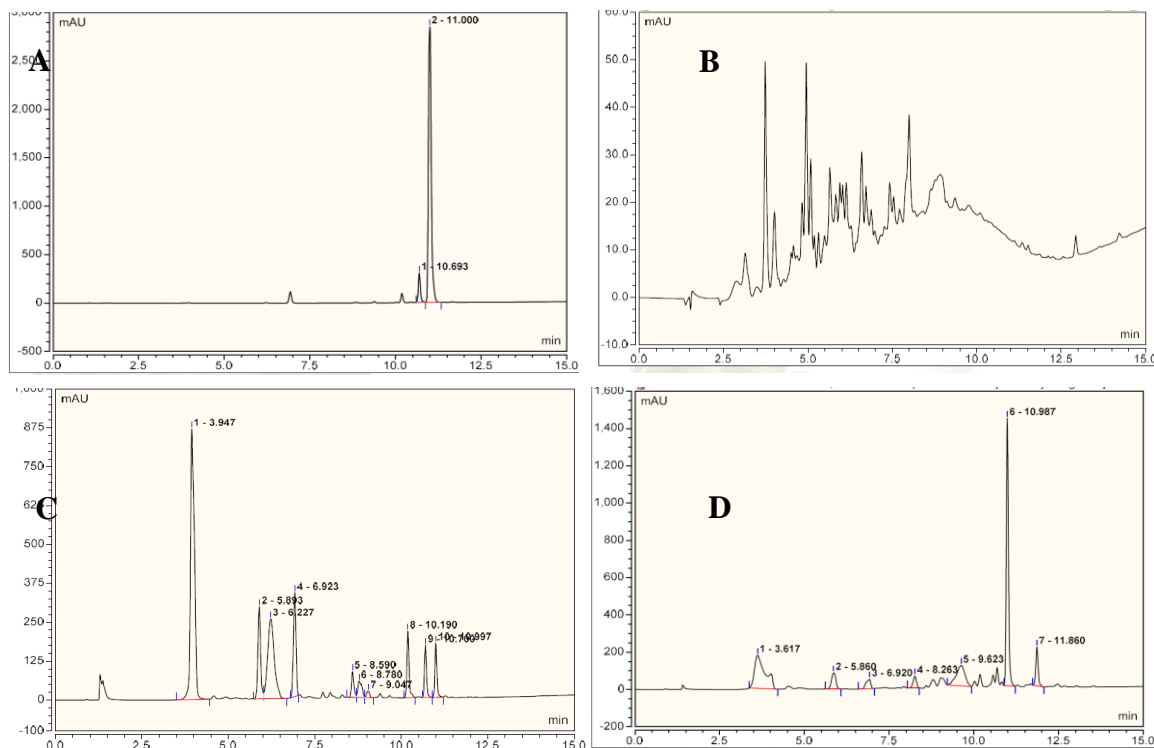


Figure S50. UV-trace of analytical HPLC to compare how different reaction conditions influence the amount of remaining precursor **9**. A) Precursor **24** as reference, rt: 11.00 min. B) Conditions from Li et. al. C) Conditions **4A** with DMSO and D) Conditions **4A** with tBuOH/MeCN as solvent.

Leaving group screening for tetrazine labeling

The manual tetrazine labeling optimization to obtain the pRCY was performed according to the general procedure for manual radiolabeling reactions. For the labeling of [^{18}F]**23** we used the OM's precursor (**24**), OT's precursor (**25**) and the ON's precursor (**26**). For the labeling of [^{18}F]**29** we used the OT's precursor (**31**) and the ON's precursor (**32**). All reactions were carried out at 100 °C, the results are presented in *Table S20*.

Table S20 Results from manual radiolabeling reactions to obtain the ^{18}F -radiolabelled tetrazines [^{18}F]**23** and [^{18}F]**29**.

Target product	Precursor	Preconditioning	Elution	Solvent	pRCY
[^{18}F] 23	24	PO_4^{3-}	Bu_4NOMs	tBuOH/MeCN	1.8%
[^{18}F] 23	25	PO_4^{3-}	Bu_4NOMs	tBuOH/MeCN	4.5%
[^{18}F] 23	26	PO_4^{3-}	Bu_4NOMs	tBuOH/MeCN	25.8±3.8% ^a
[^{18}F] 23	26	PO_4^{3-}	Bu_4NOMs	tBuOH/DMSO	23.6%
[^{18}F] 23	26	CO_3^{2-}	Bu_4NOMs	tBuOH/MeCN	0%
[^{18}F] 23	26	PO_4^{3-}	Et_4NHCO_3	tBuOH/MeCN	0%
[^{18}F] 23	26	CO_3^{2-}	$\text{Bu}_4\text{NH}_2\text{PO}_4$	tBuOH/MeCN	0%
[^{18}F] 23	26	CO_3^{2-}	Et_4NHCO_3	MeCN	0% ^b
[^{18}F] 29	31	PO_4^{3-}	Bu_4NOMs	tBuOH/DMSO	4.6%
[^{18}F] 29	32	PO_4^{3-}	Bu_4NOMs	tBuOH/DMSO	11.5±3.5% ^a
[^{18}F] 29	32	CO_3^{2-}	Et_4NHCO_3	MeCN	0% ^b

^aReaction performed in triplicates, ^b Conditions from Li et al. Reaction time: 15 min, reaction temperature: 85°C, precursor amount: 9 μmol .

Click kinetics of synthesized Tz references towards TCOs

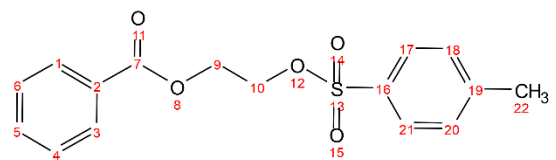
Reaction kinetics of the synthesized tetrazines **23** and **29** were determined by pseudo-first order measurements in MeCN at $25.0 \pm 0.1^\circ\text{C}$ in a SX20 stopped flow photometer (Applied Photophysics).¹¹ The pseudo first order rate constant was determined by linearization of the decay curve followed by linear fitting. The second order rate constant was calculated from the pseudo-first order rate constant, results are presented in *Table S21*.

Table S21. Measured click kinetics of tetrazine reference compounds towards TCO by stop flow measurements.

Compound	Measured k_2 ($\text{M}^{-1}\text{s}^{-1}$) in MeCN 25°C
[¹⁹ F] 23	682
[¹⁹ F] 29	2676

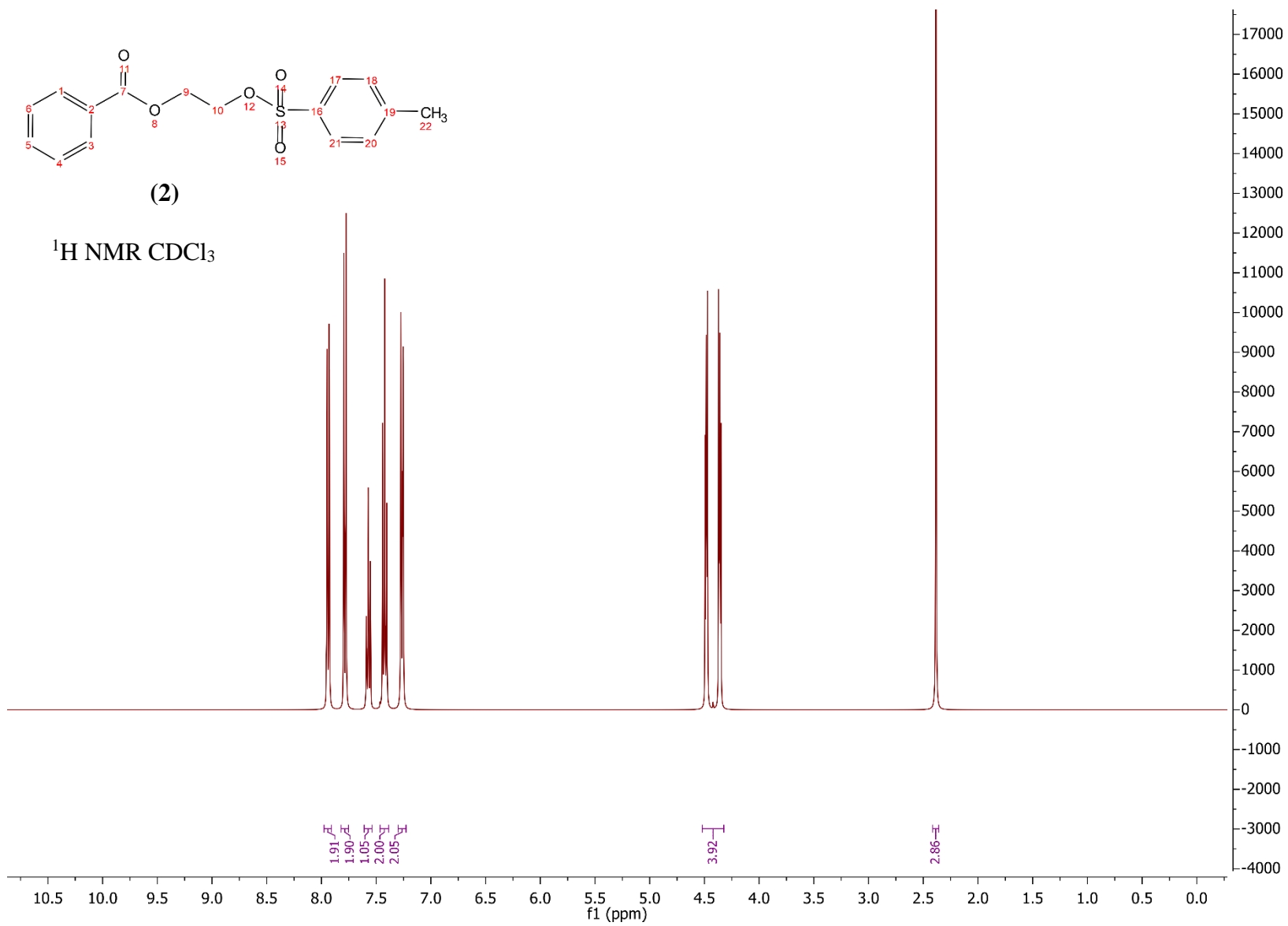
NMR spectra

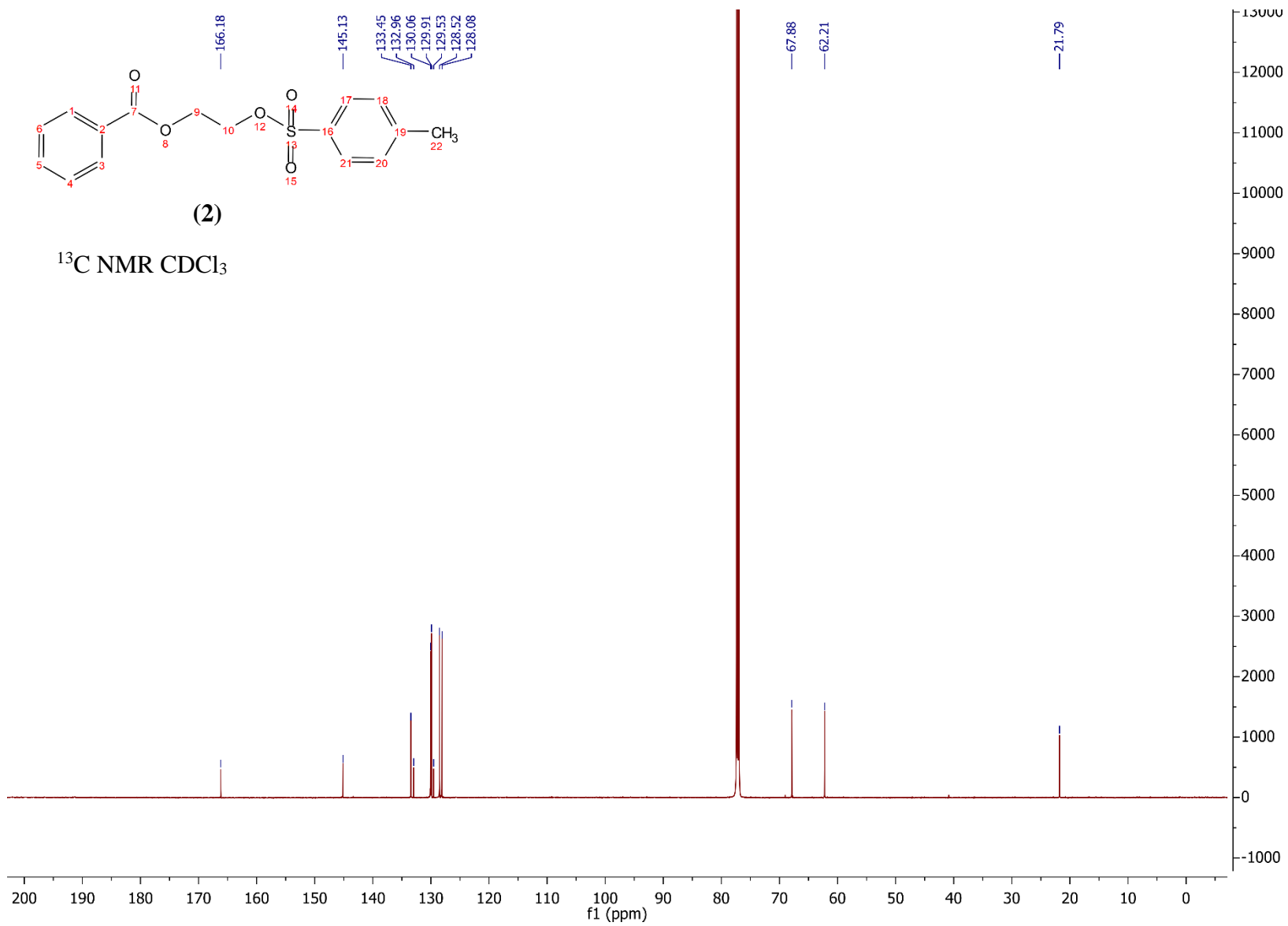
The ¹H, ¹³C and ¹⁹F (when relevant) NMRs of the synthesized compounds can be found below.

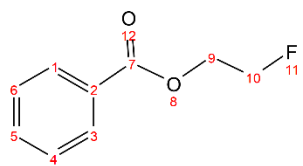


(2)

$^1\text{H NMR CDCl}_3$

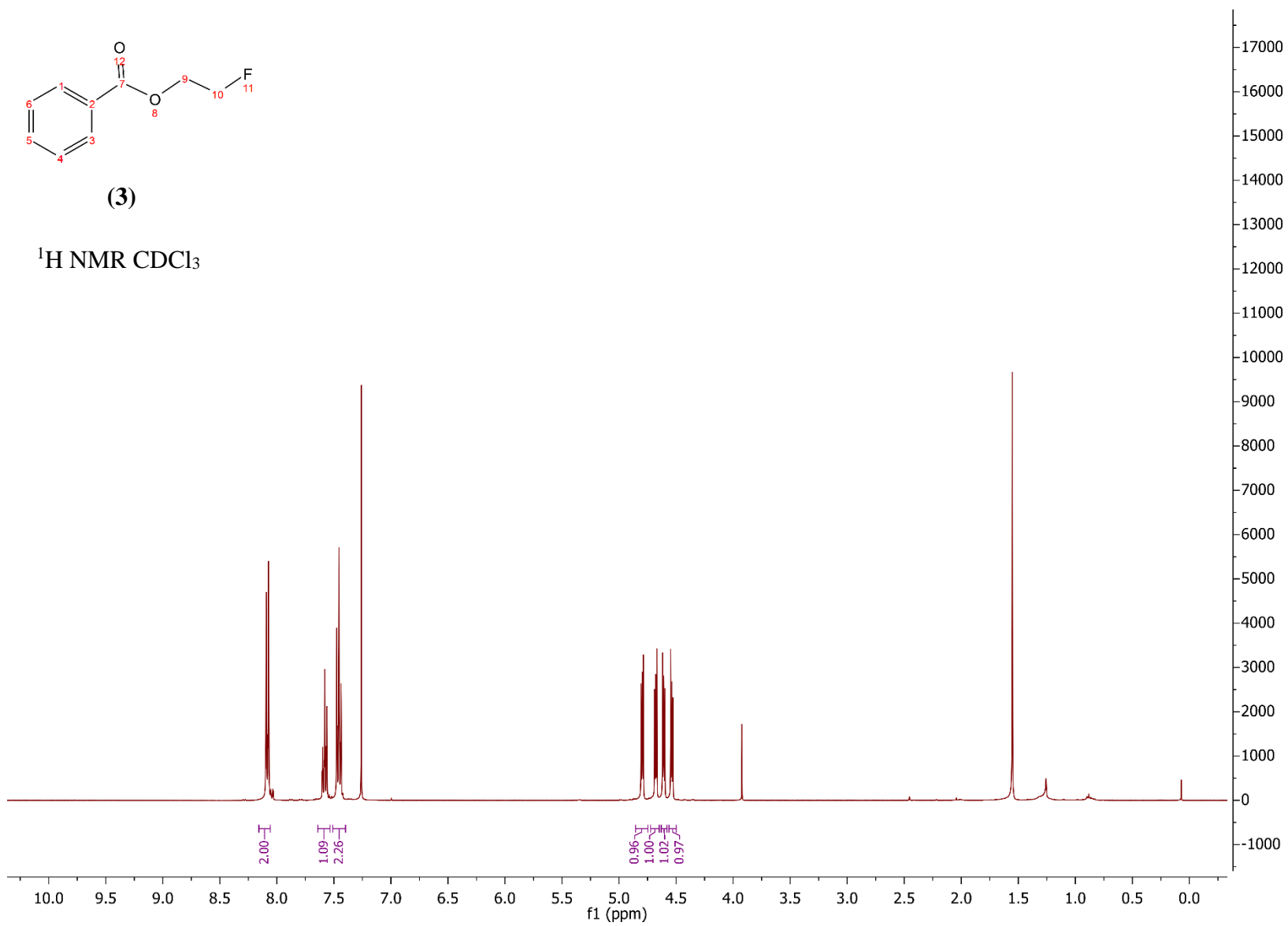


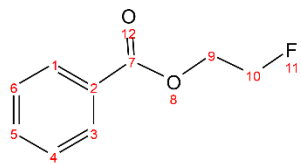




(3)

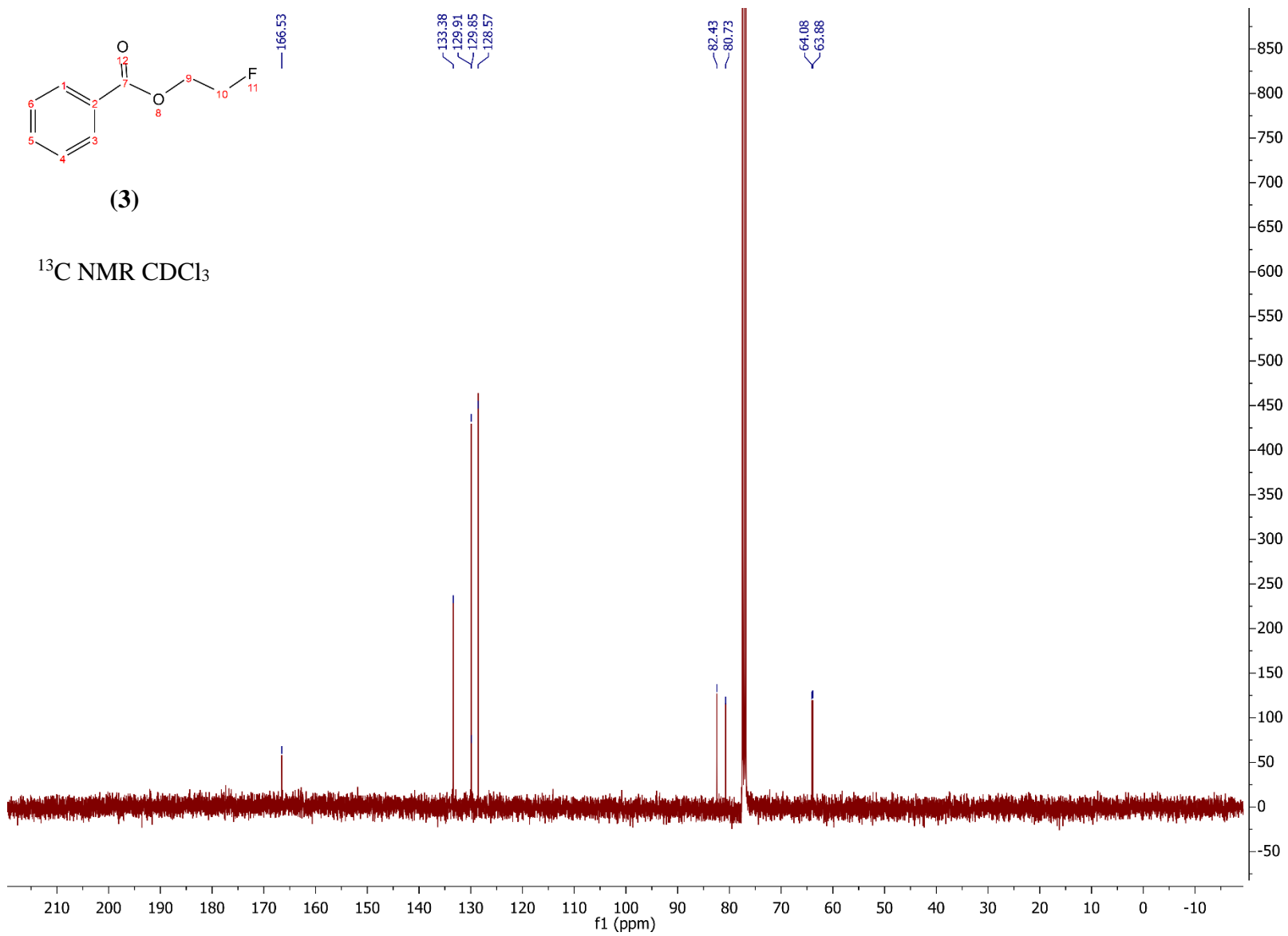
¹H NMR CDCl₃

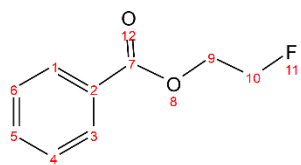




(3)

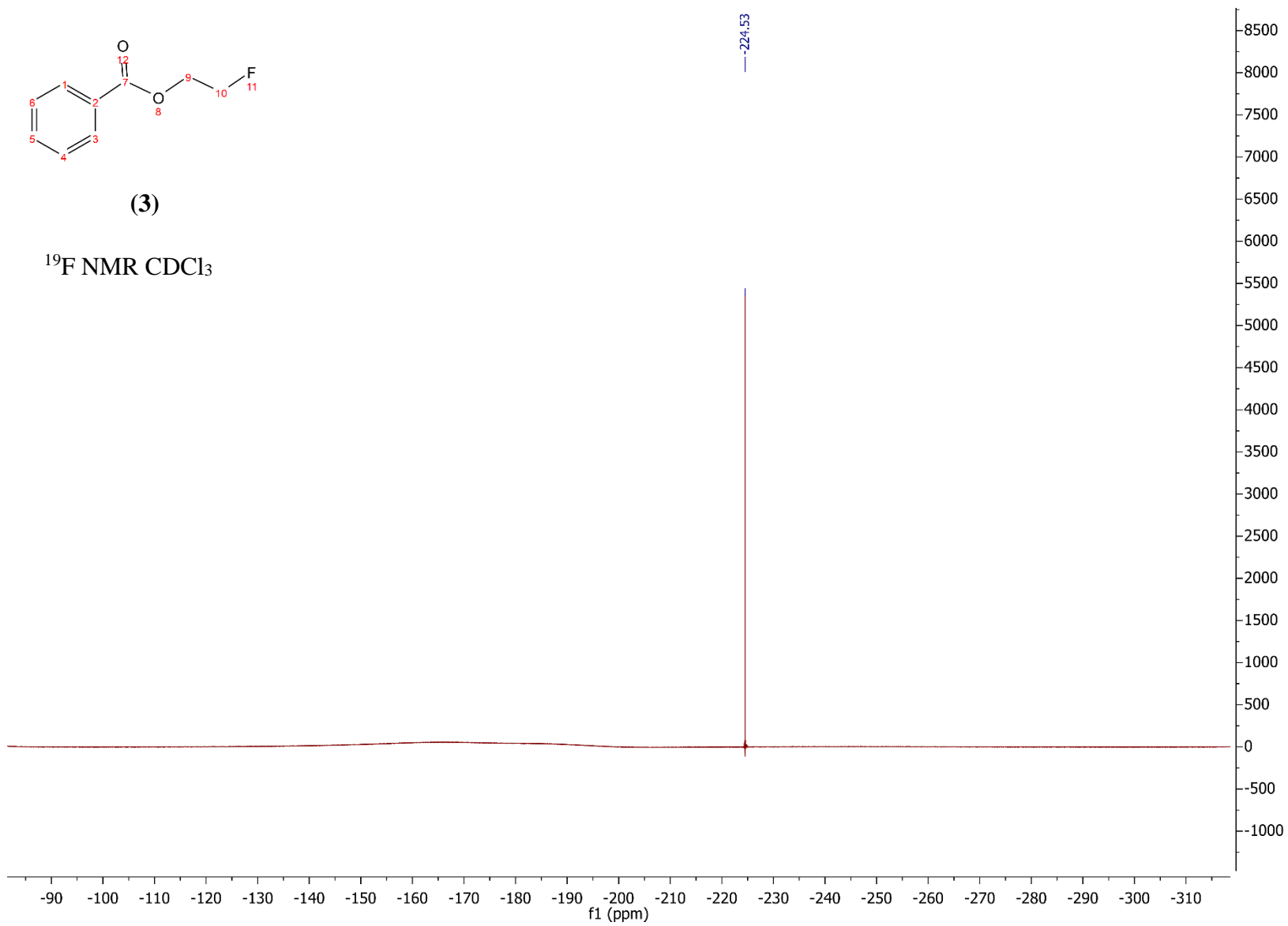
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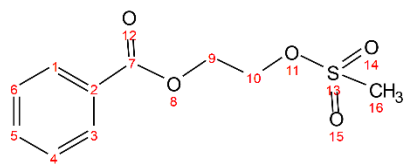




(3)

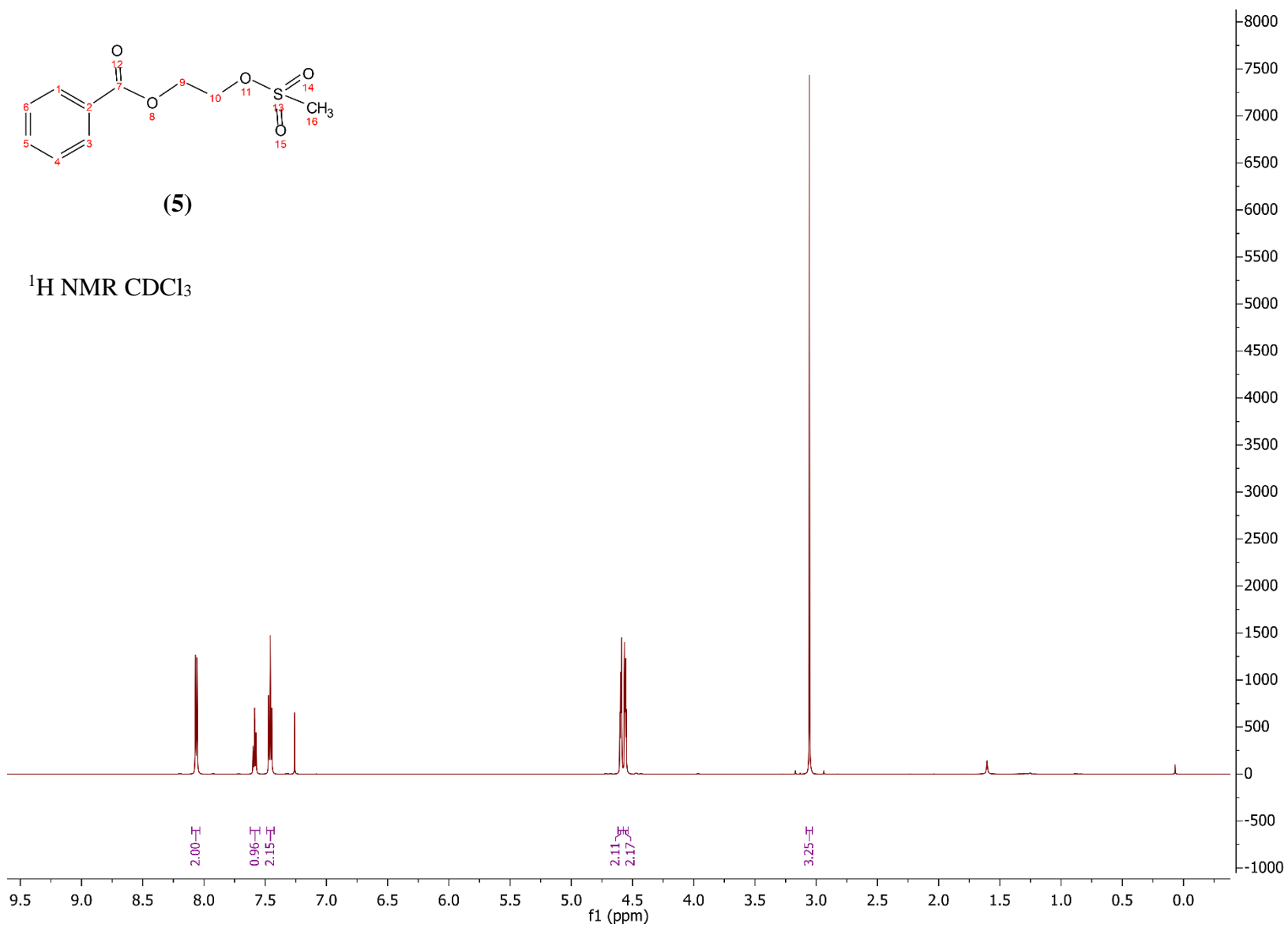
^{19}F NMR CDCl_3

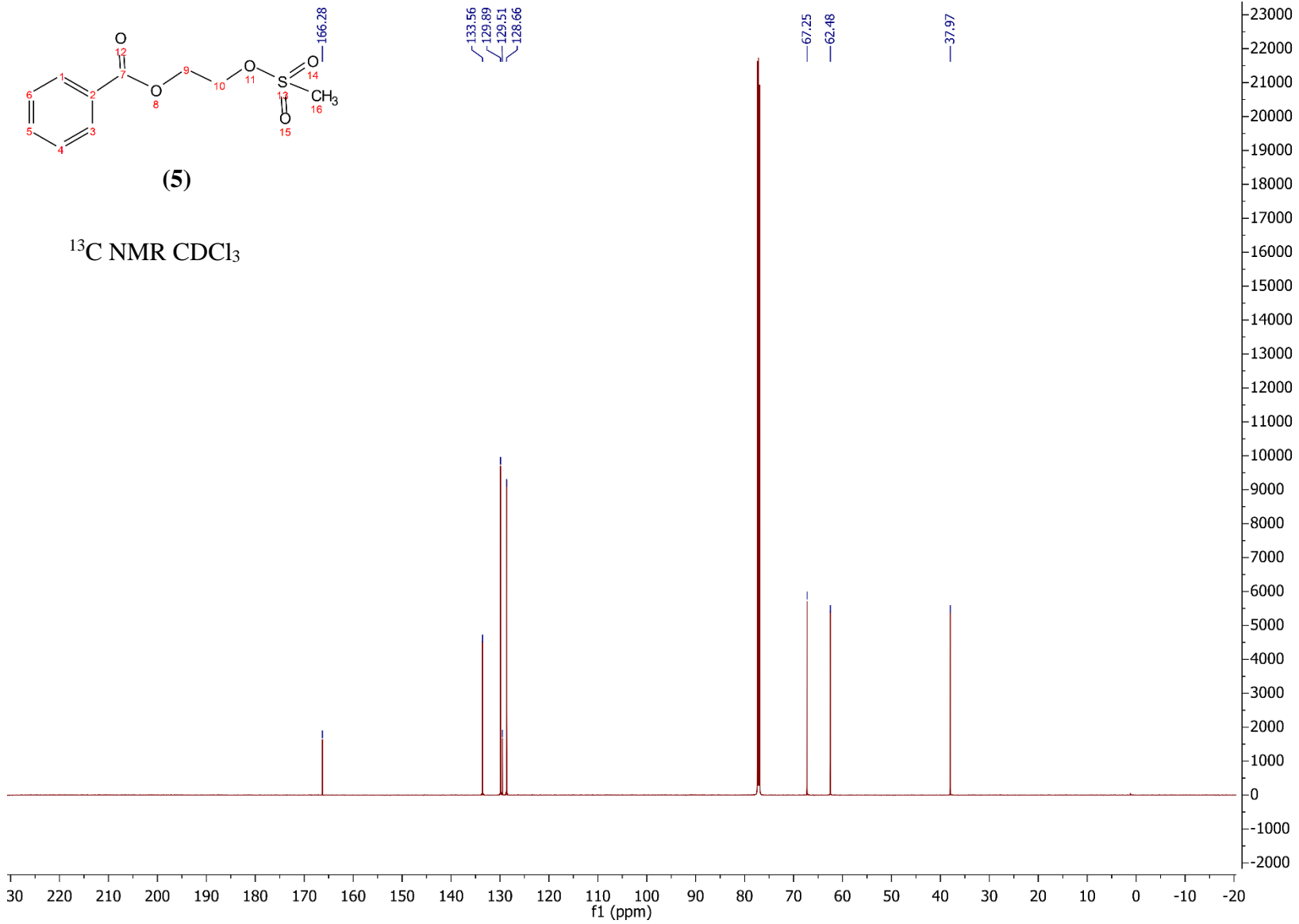


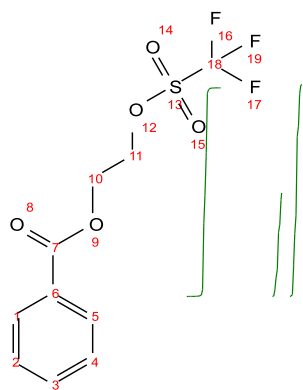


(5)

$^1\text{H NMR CDCl}_3$

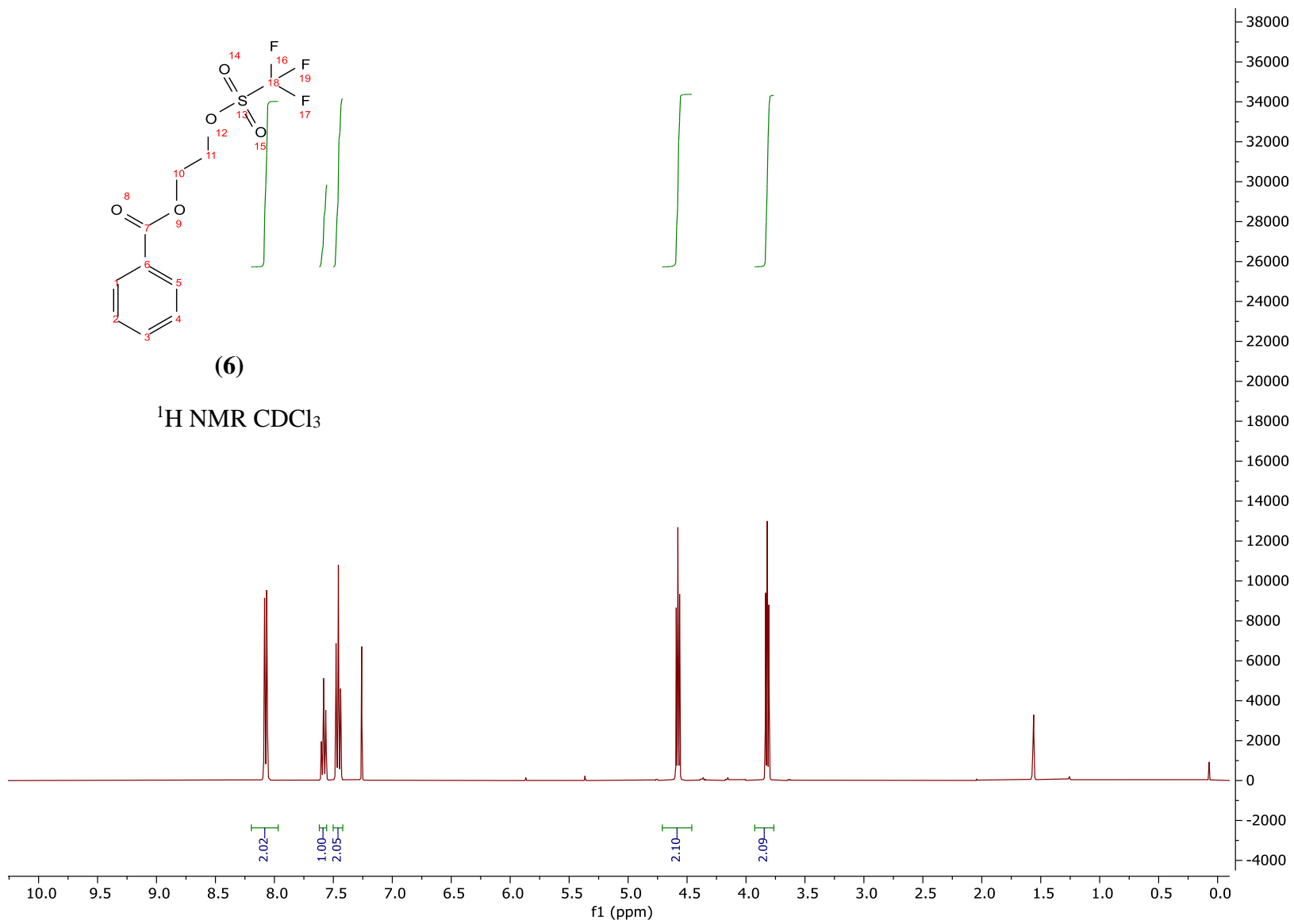


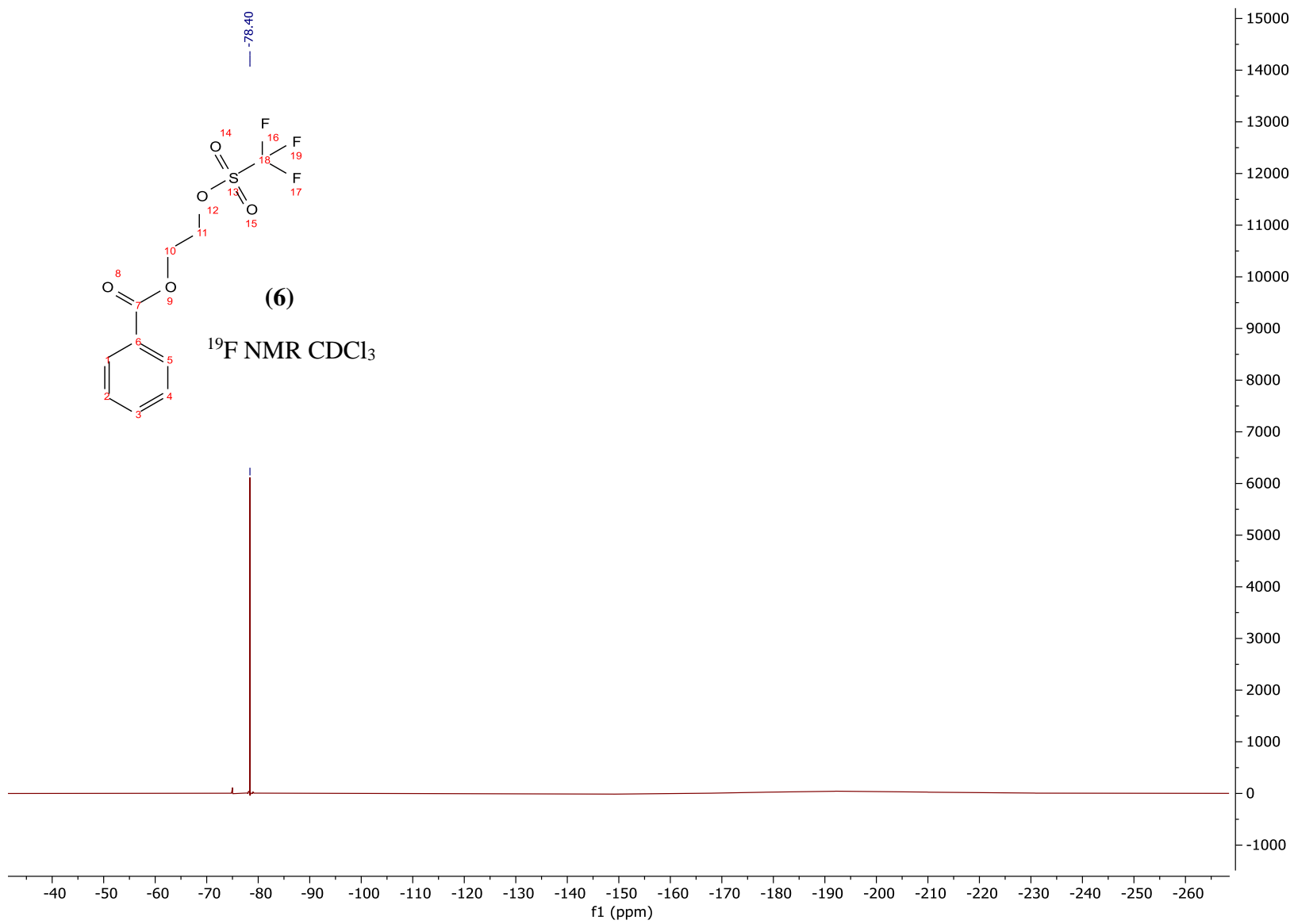


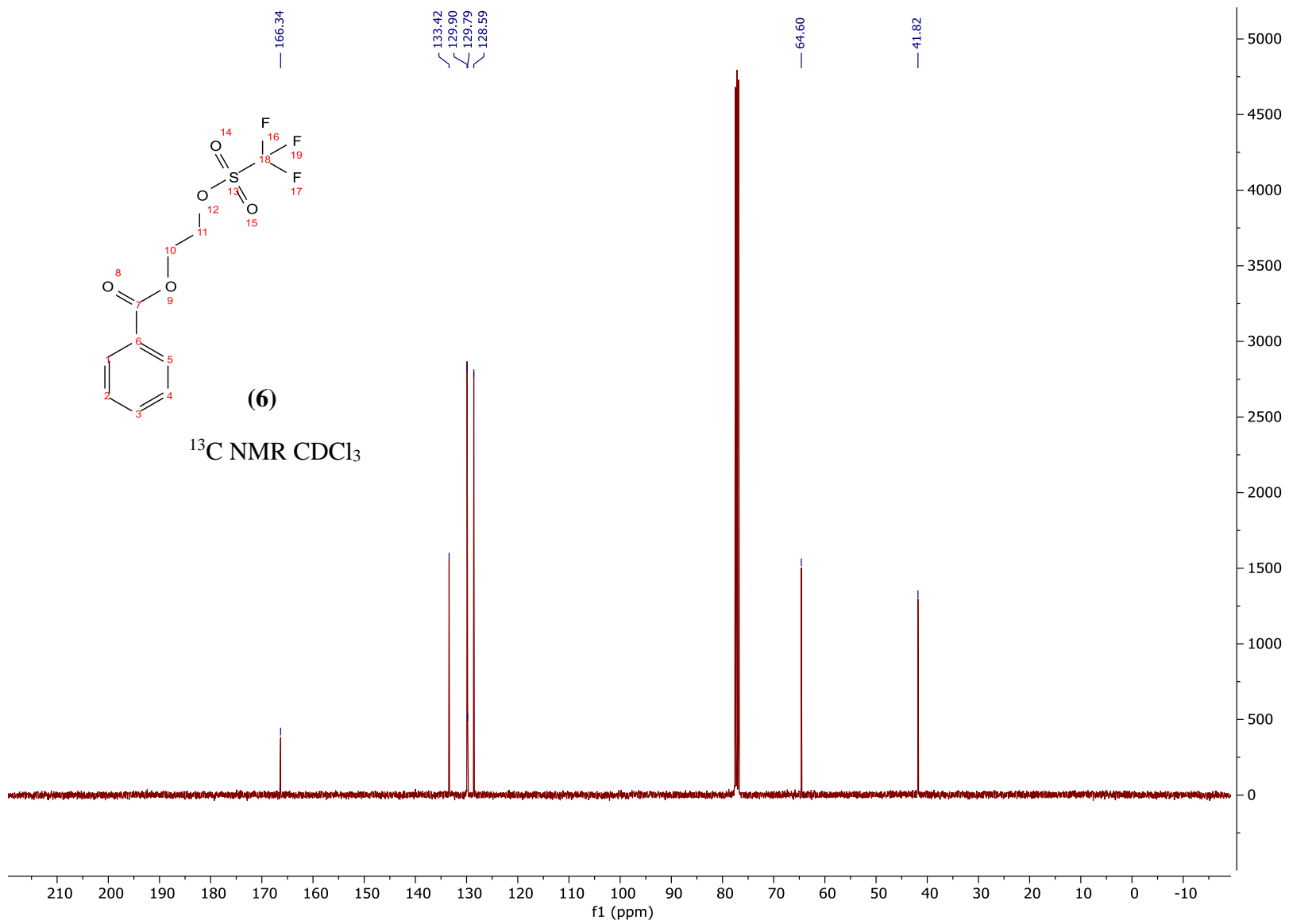


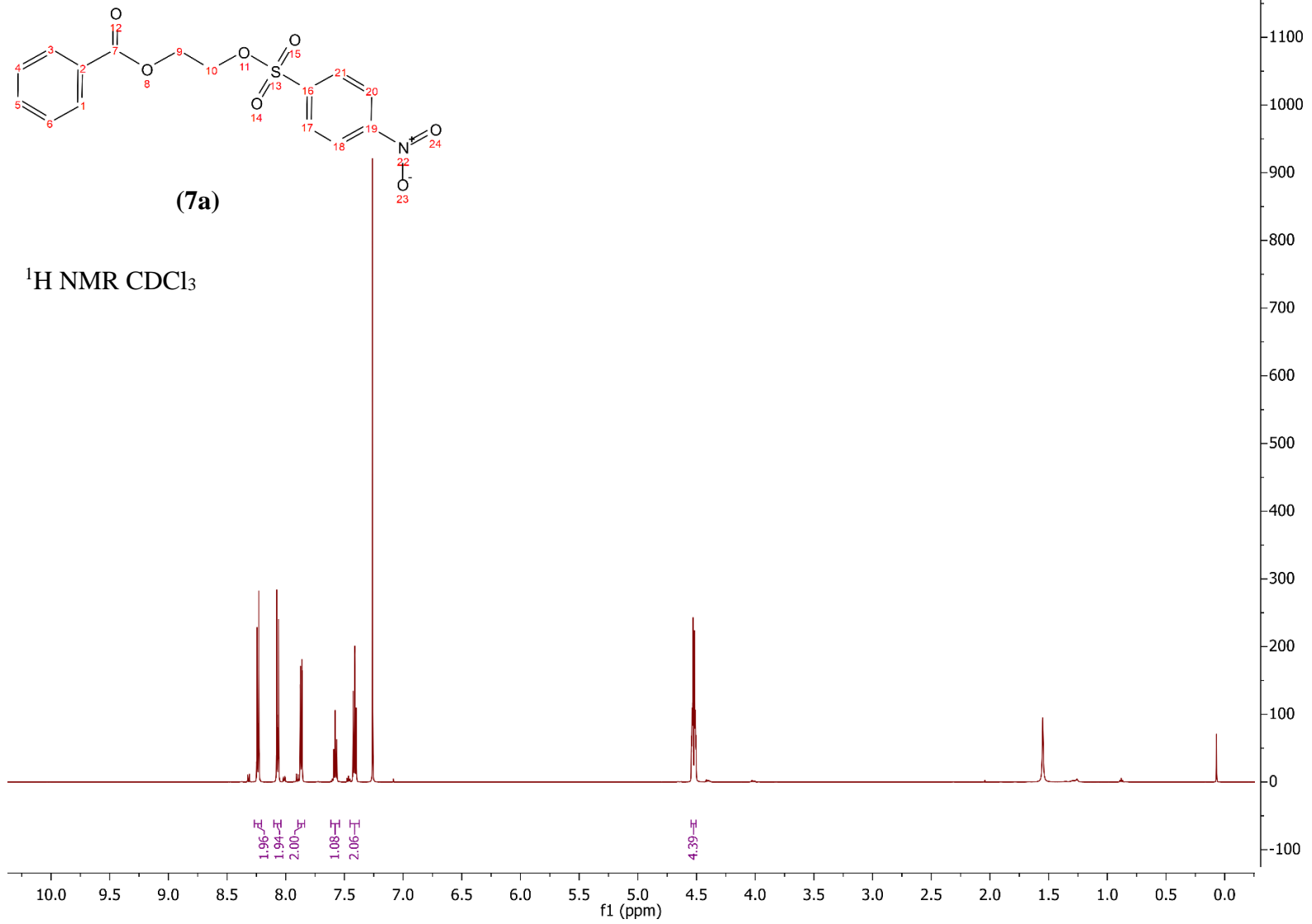
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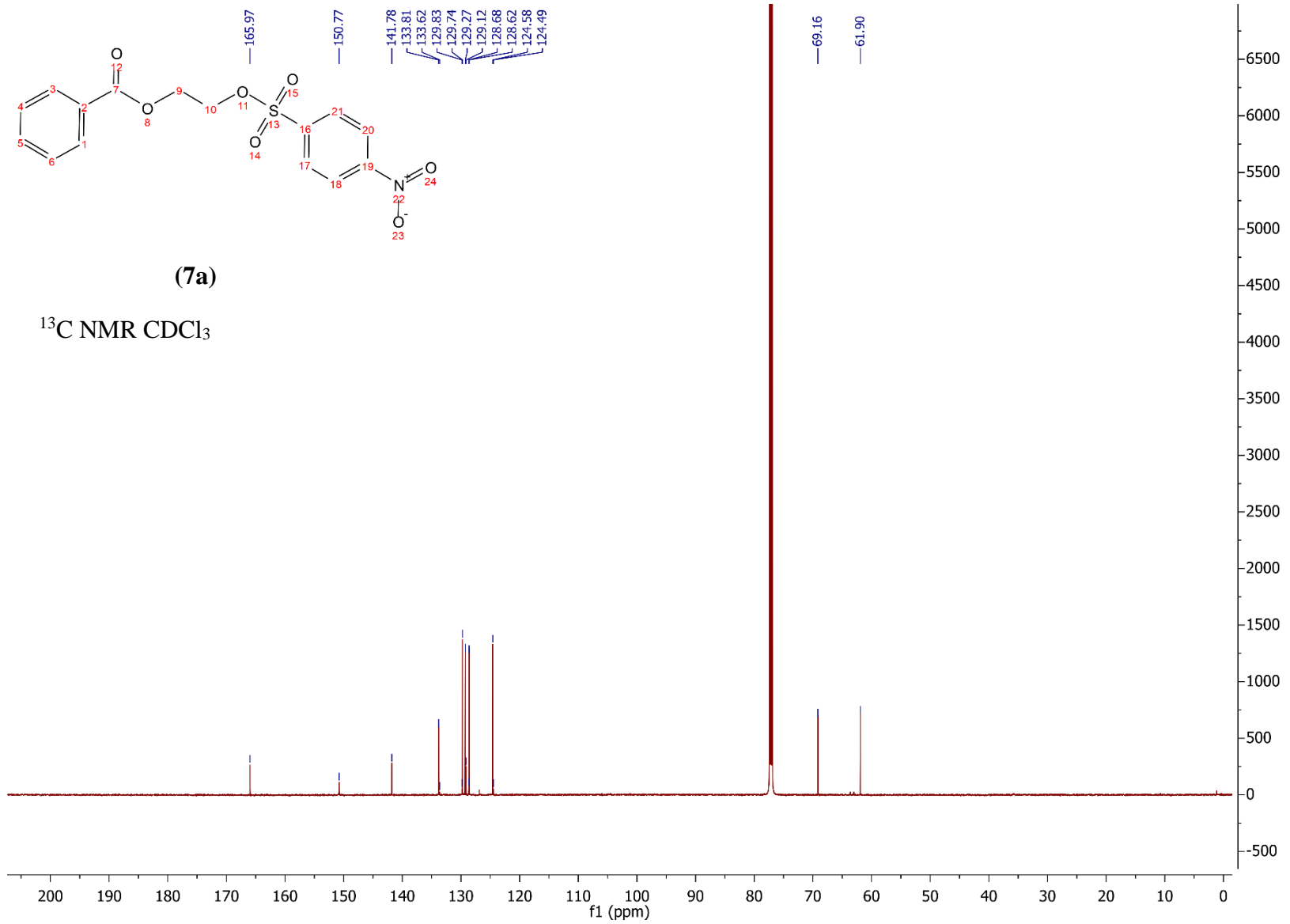
$^1\text{H NMR CDCl}_3$

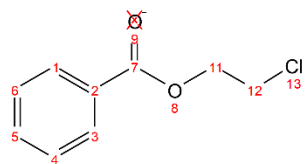






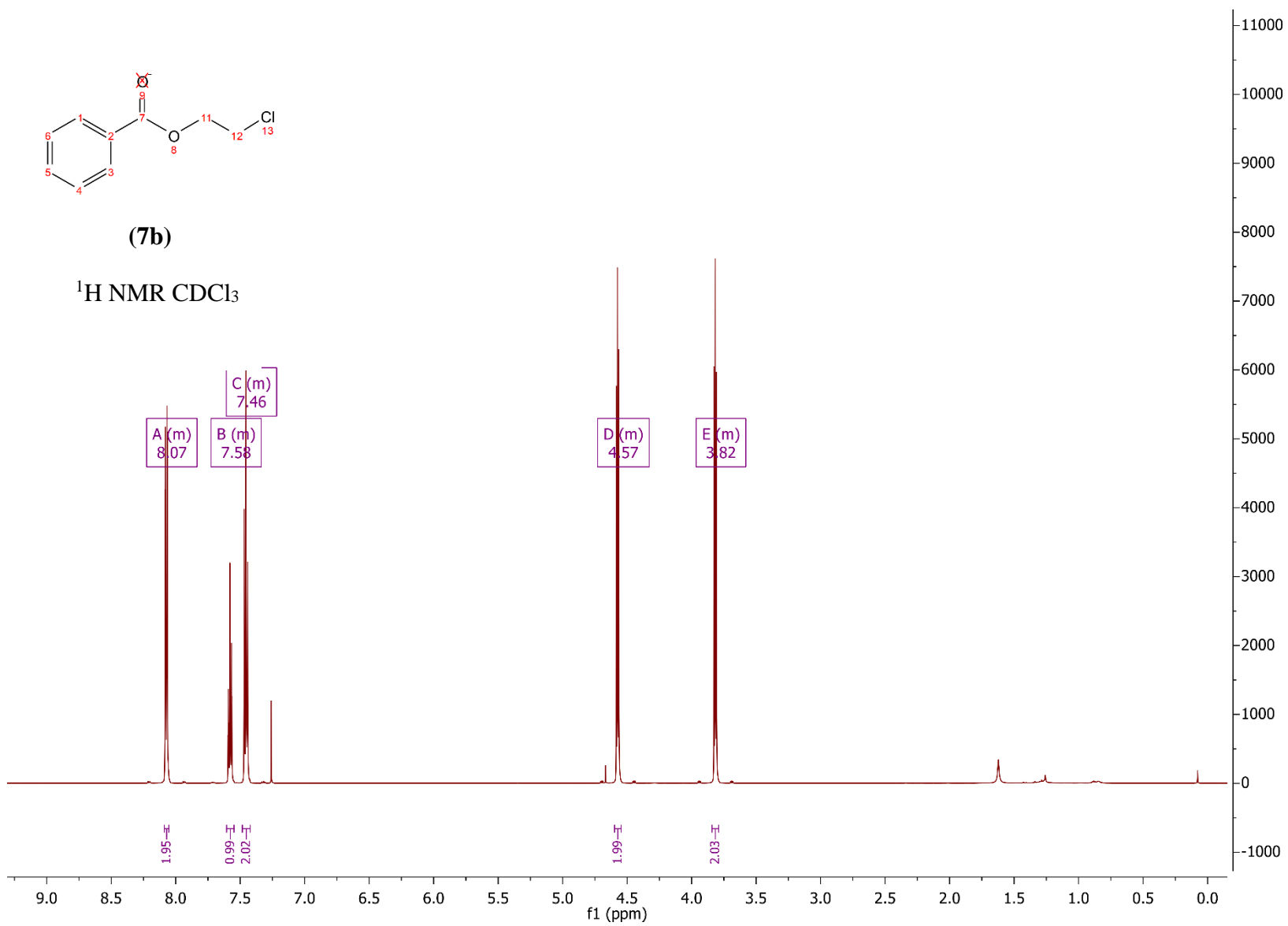


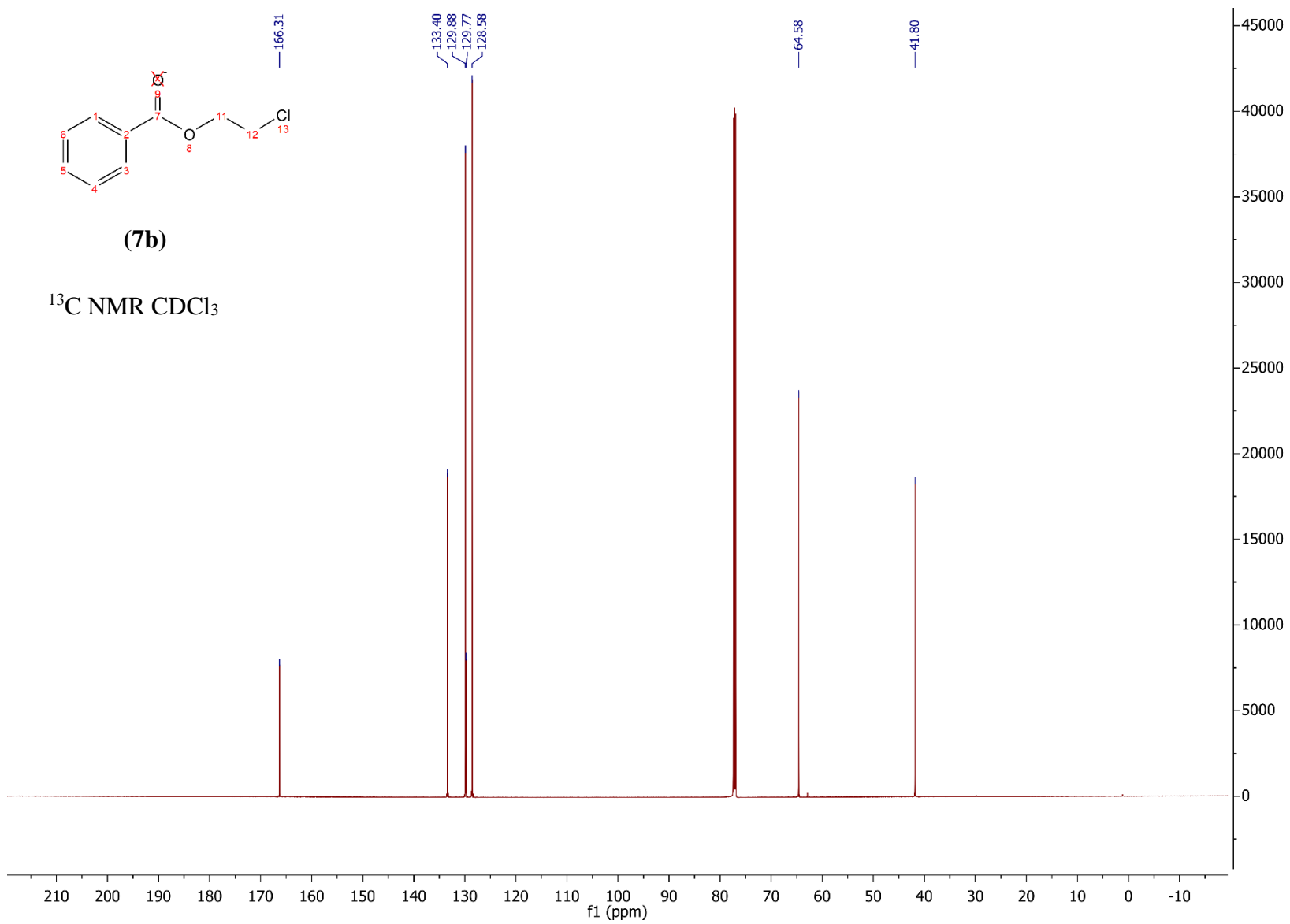


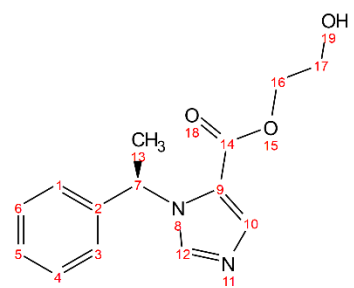


(7b)

$^1\text{H NMR CDCl}_3$

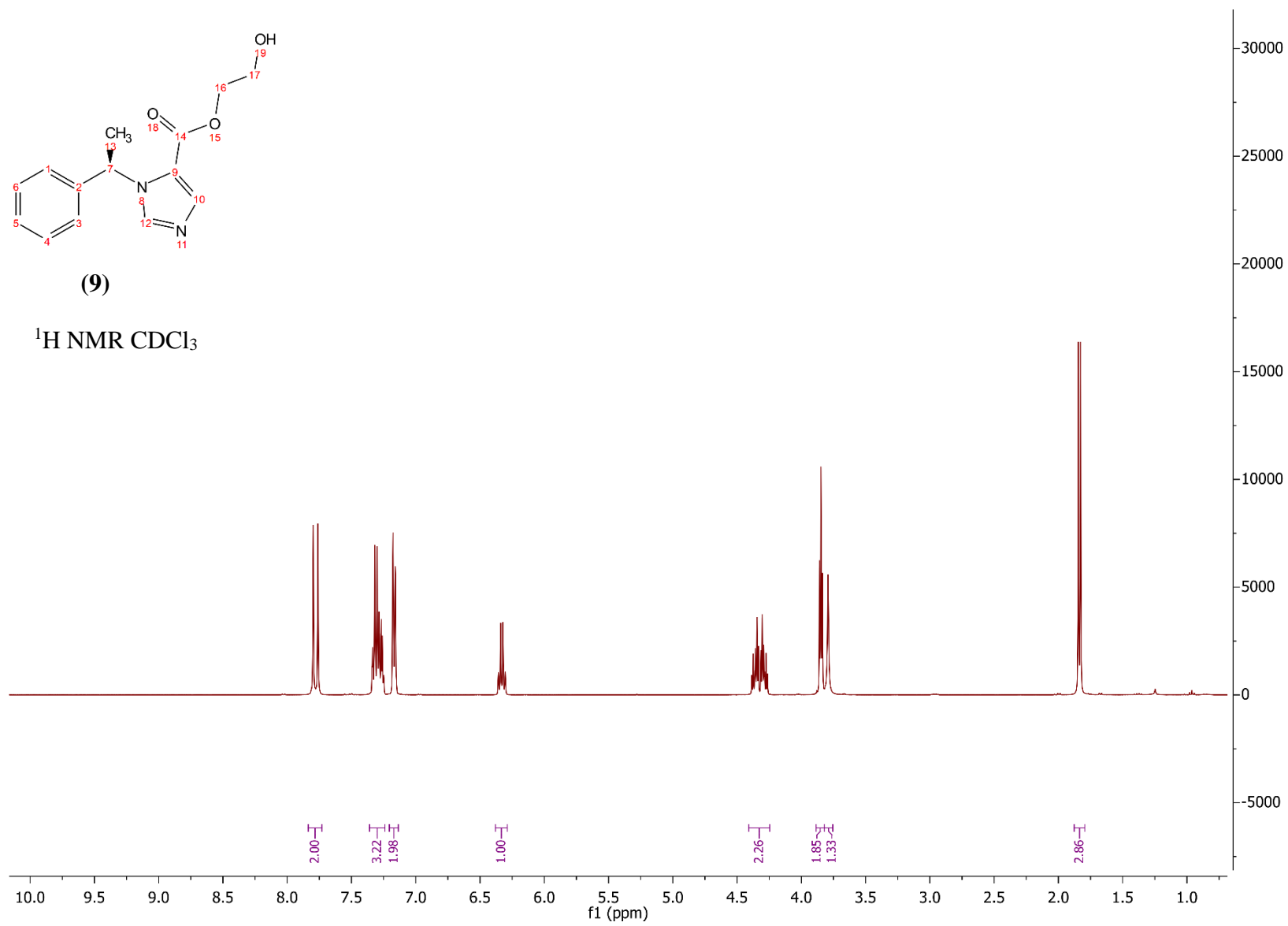


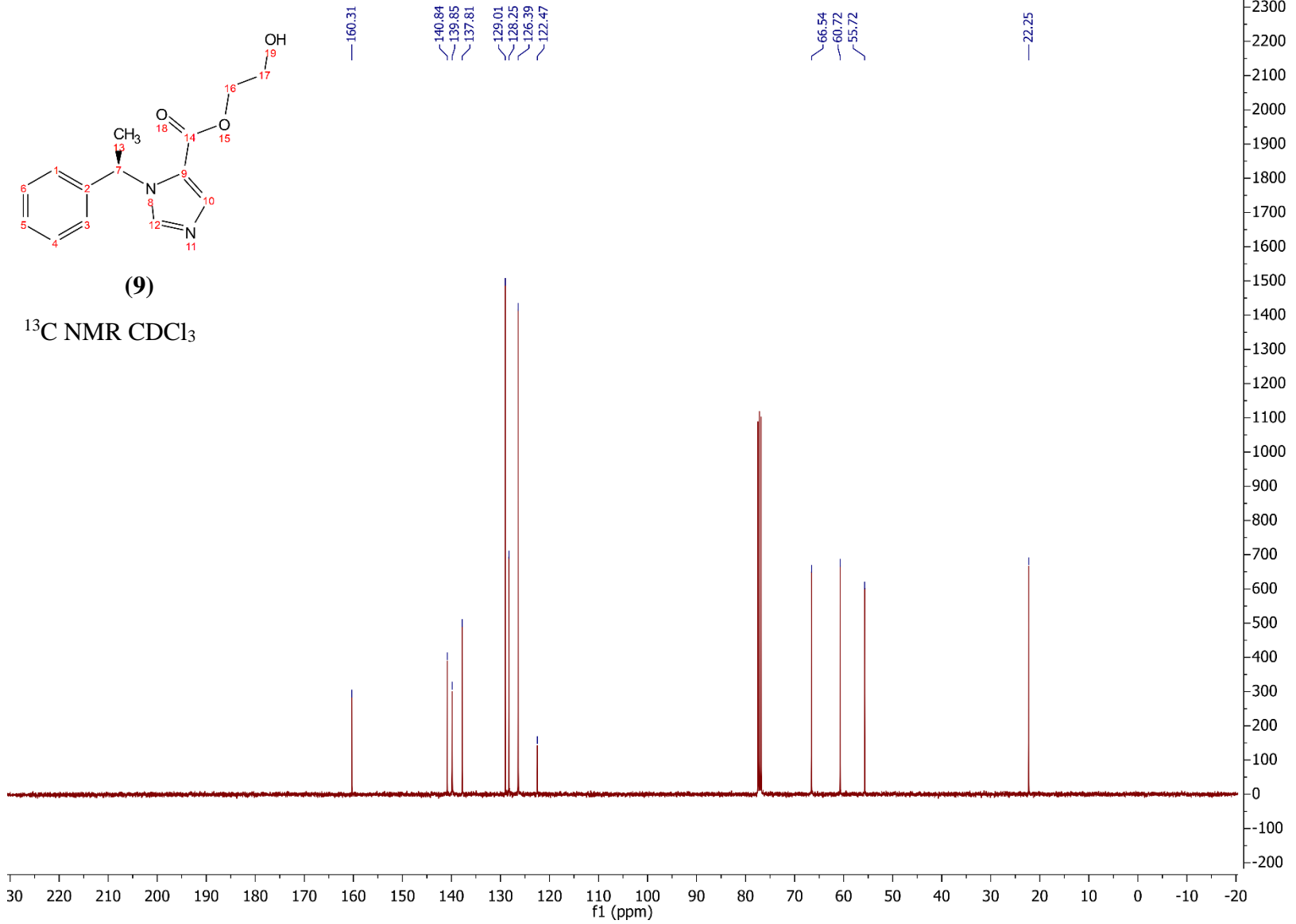


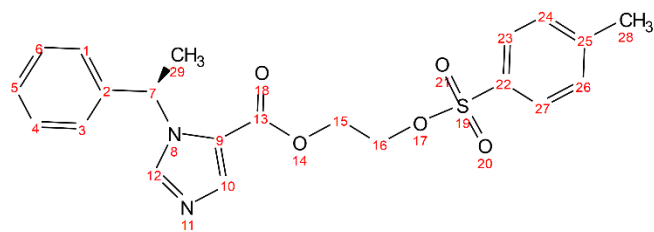


(9)

$^1\text{H NMR CDCl}_3$

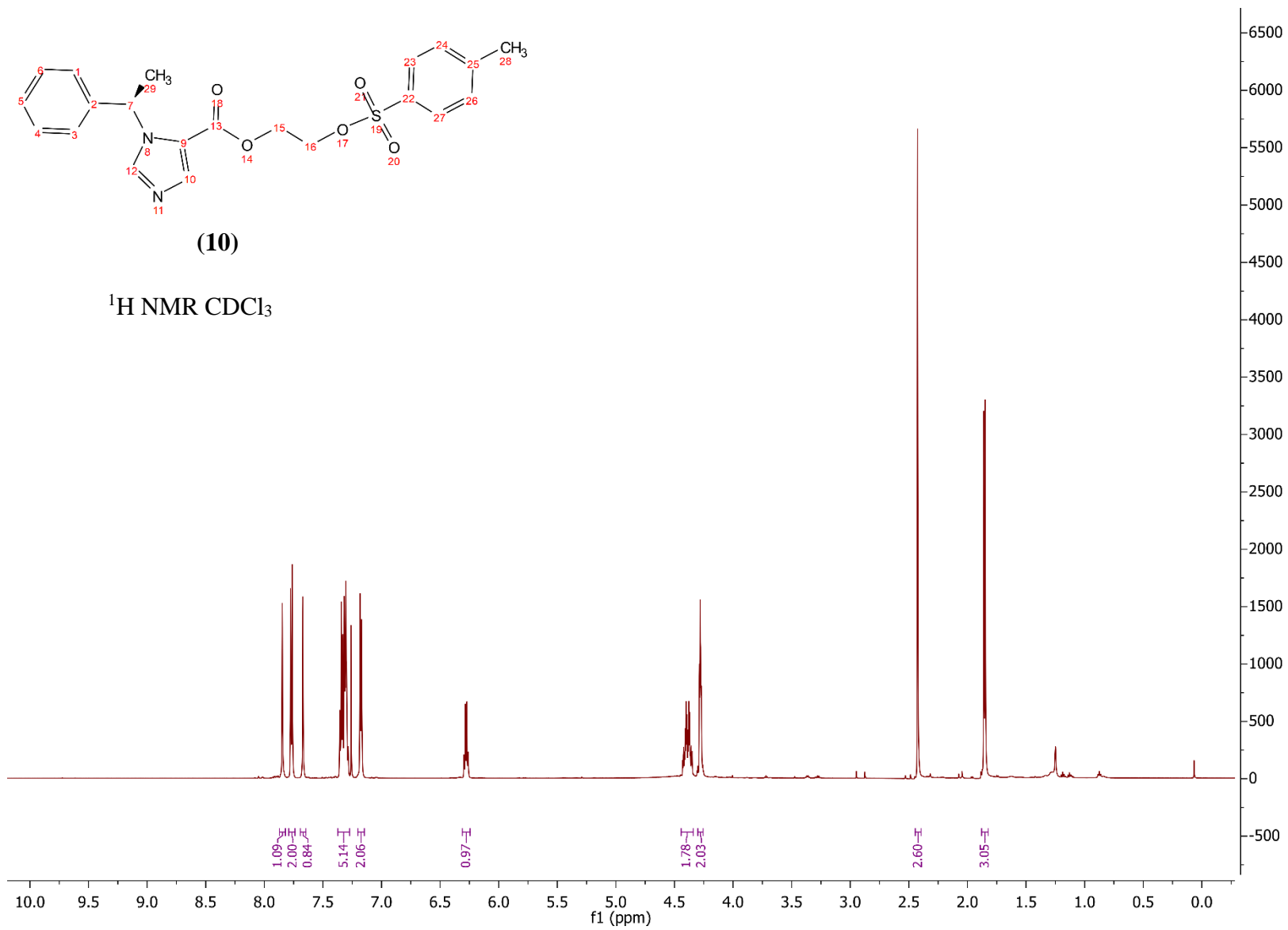


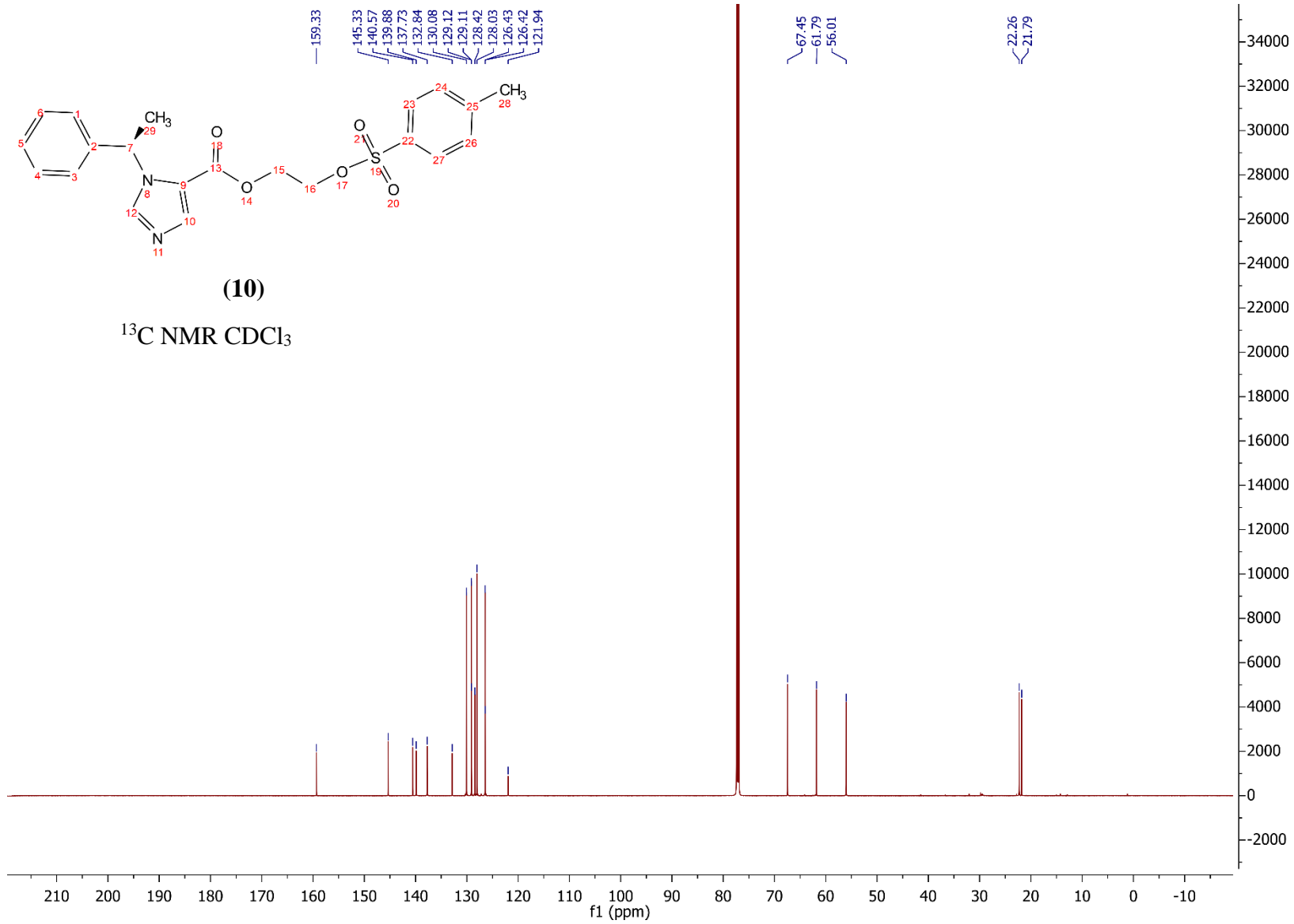


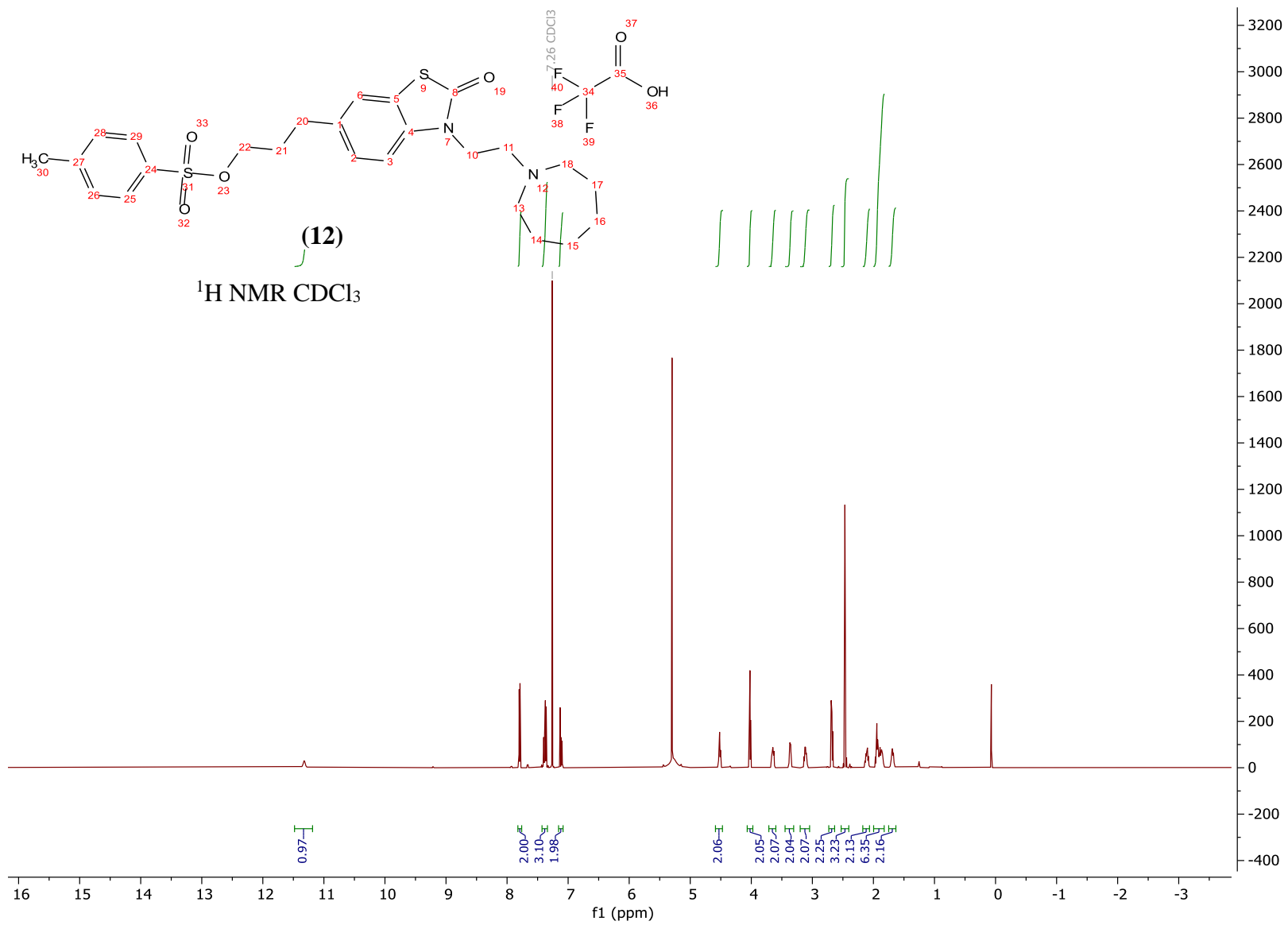


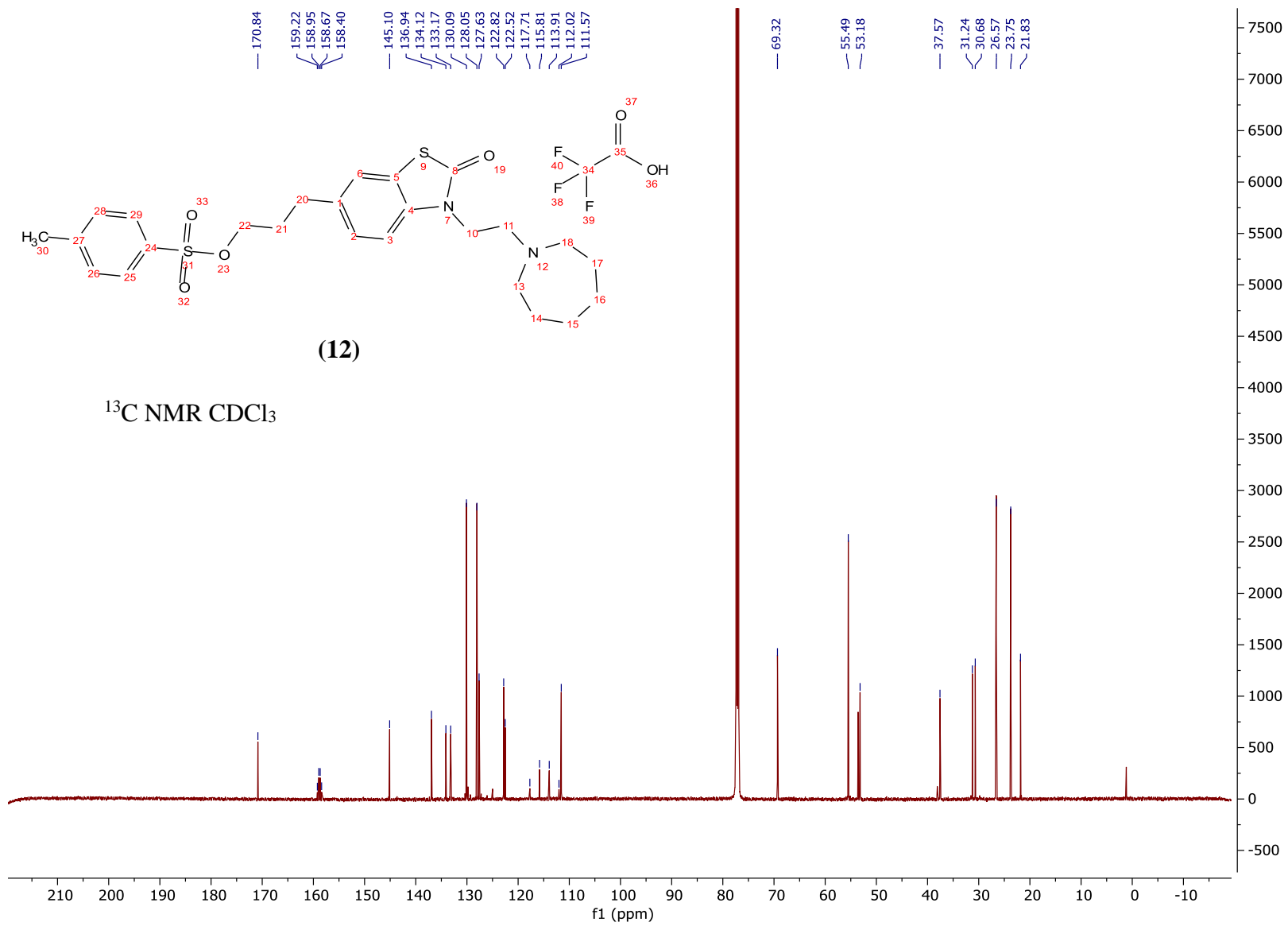
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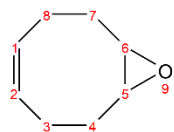
^1H NMR CDCl_3





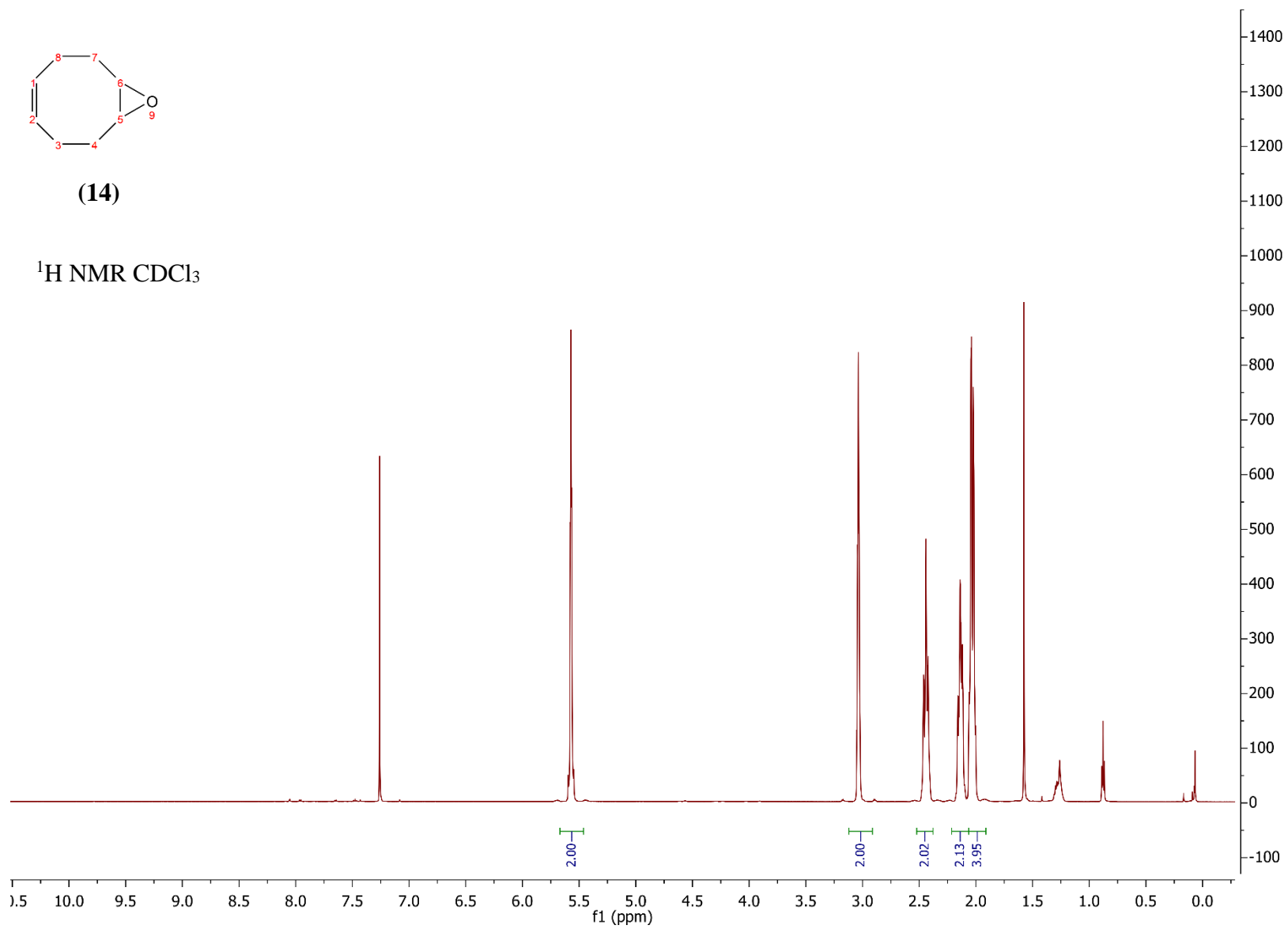


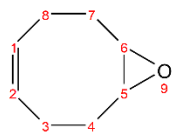




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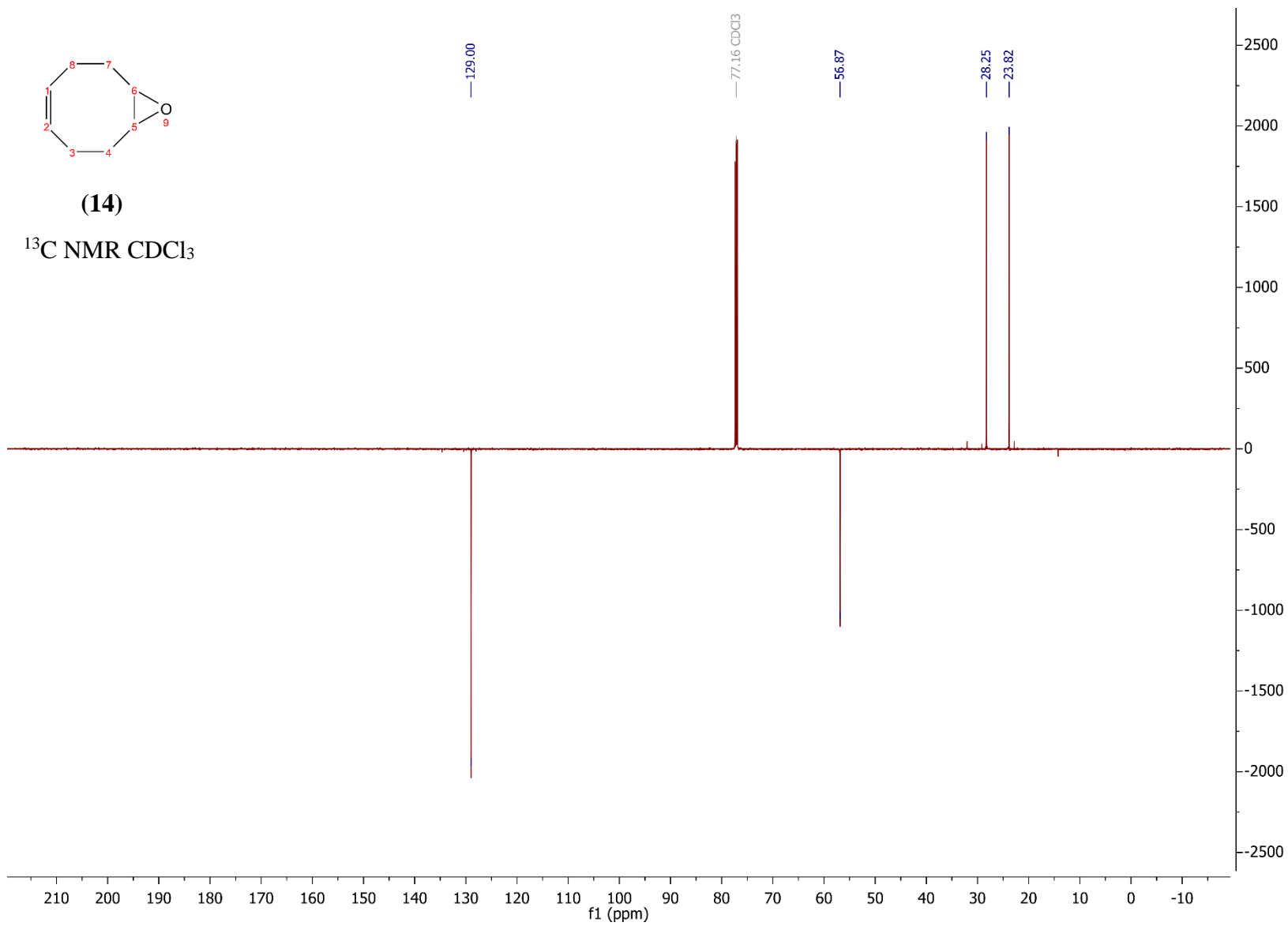
$^1\text{H NMR CDCl}_3$

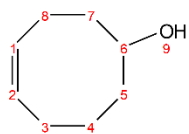




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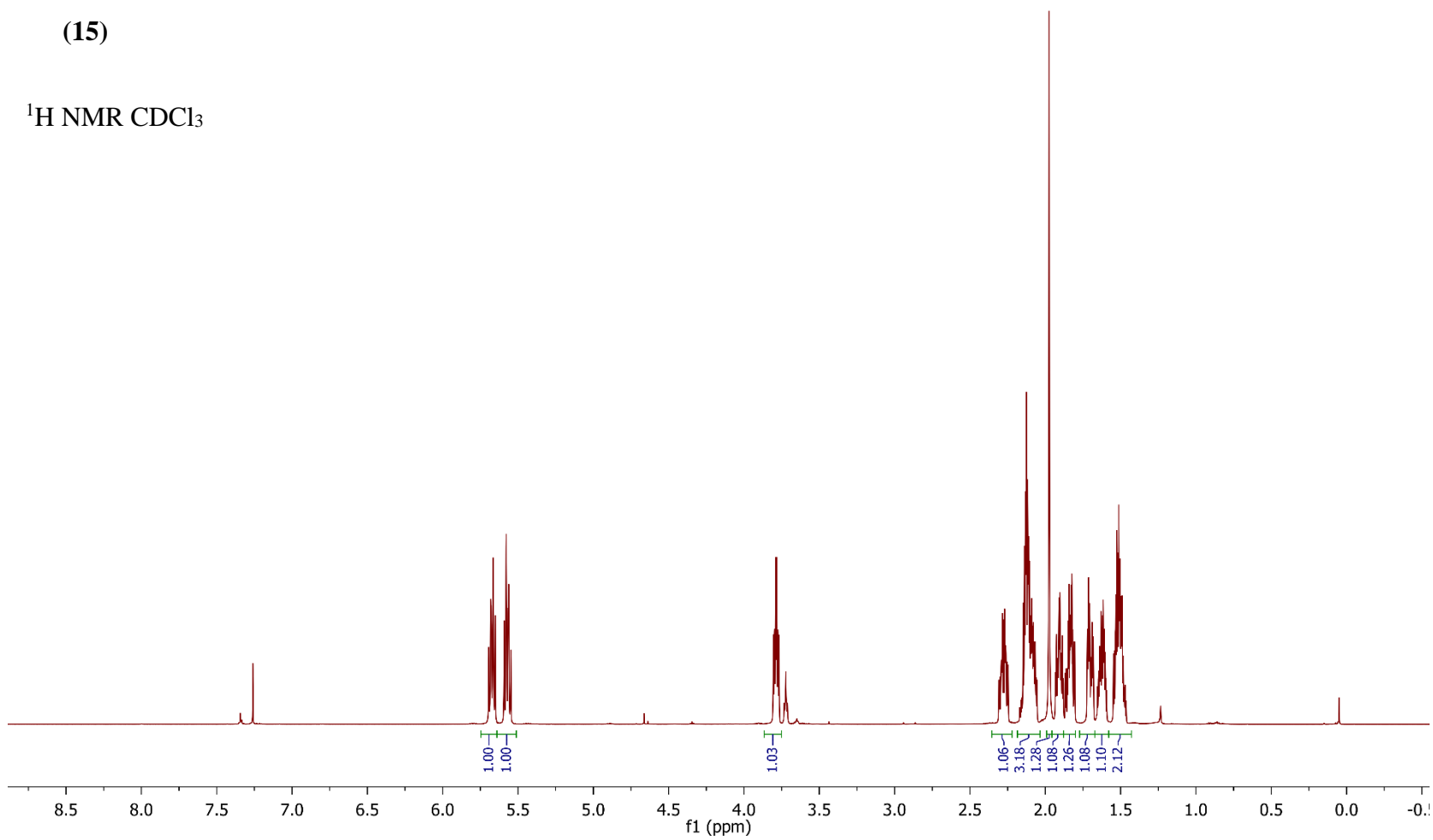
^{13}C NMR CDCl_3

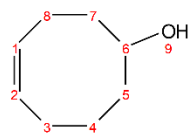




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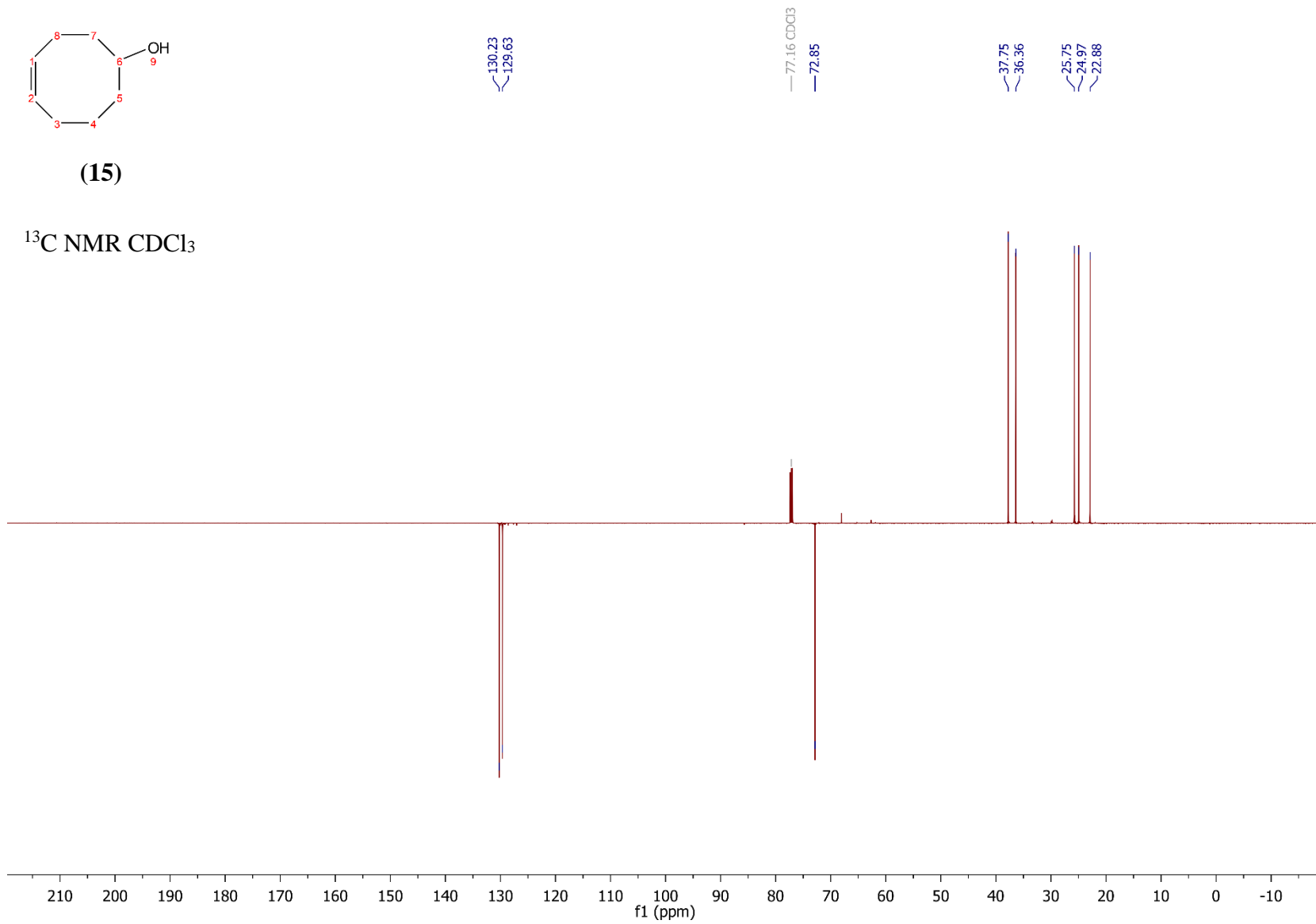
^1H NMR CDCl_3

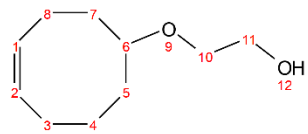




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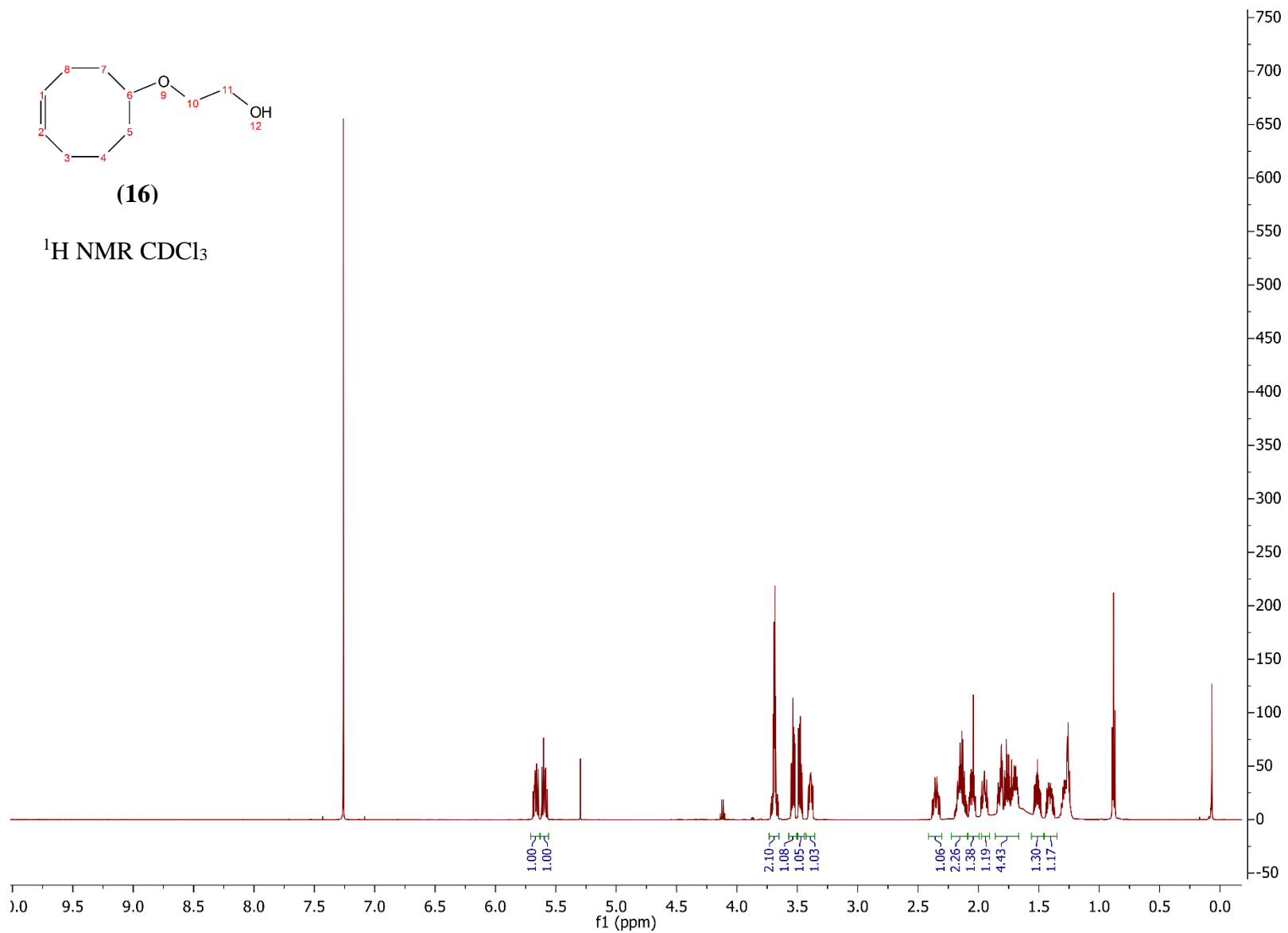
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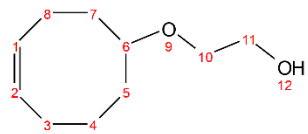




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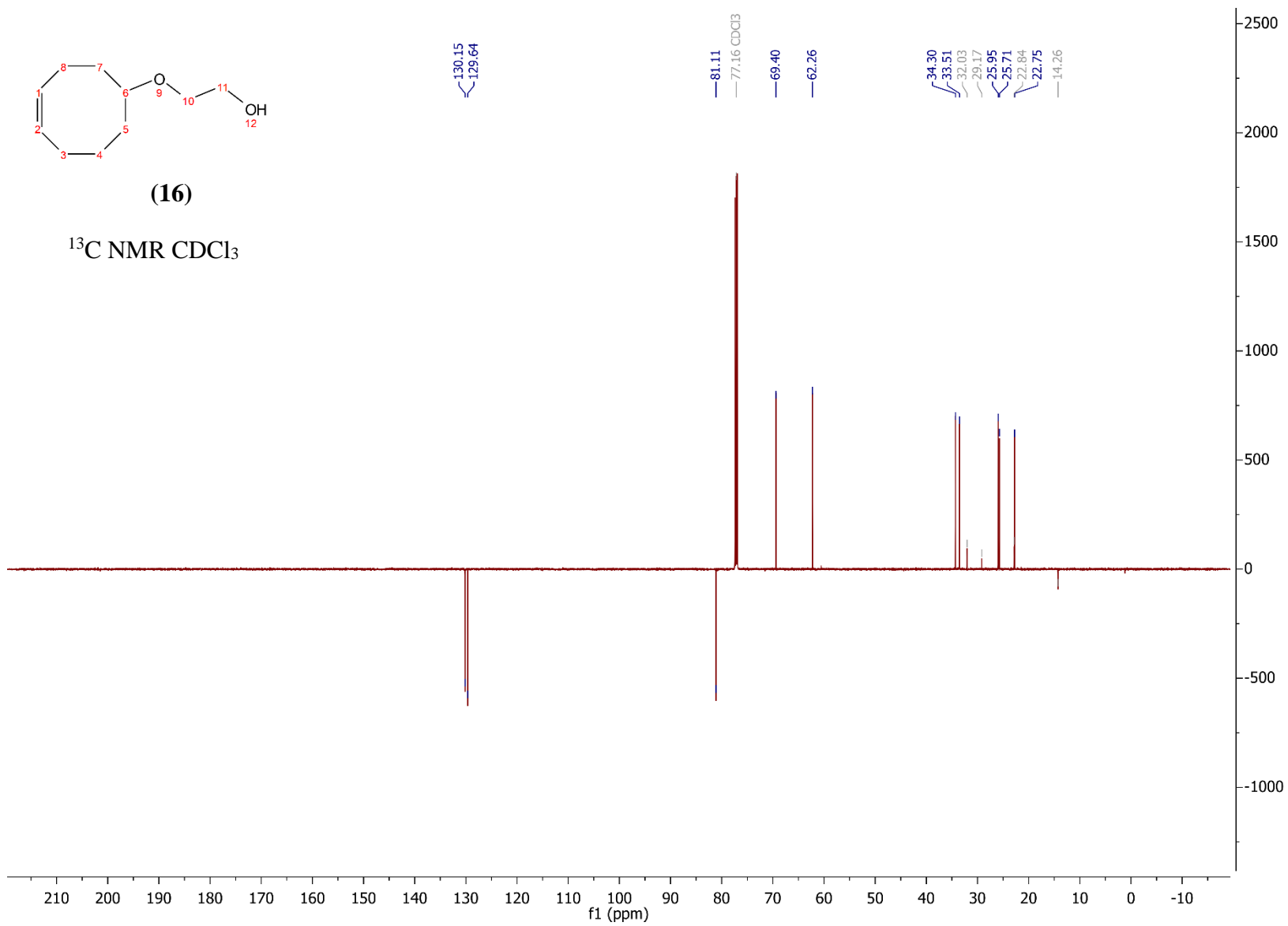
$^1\text{H NMR CDCl}_3$

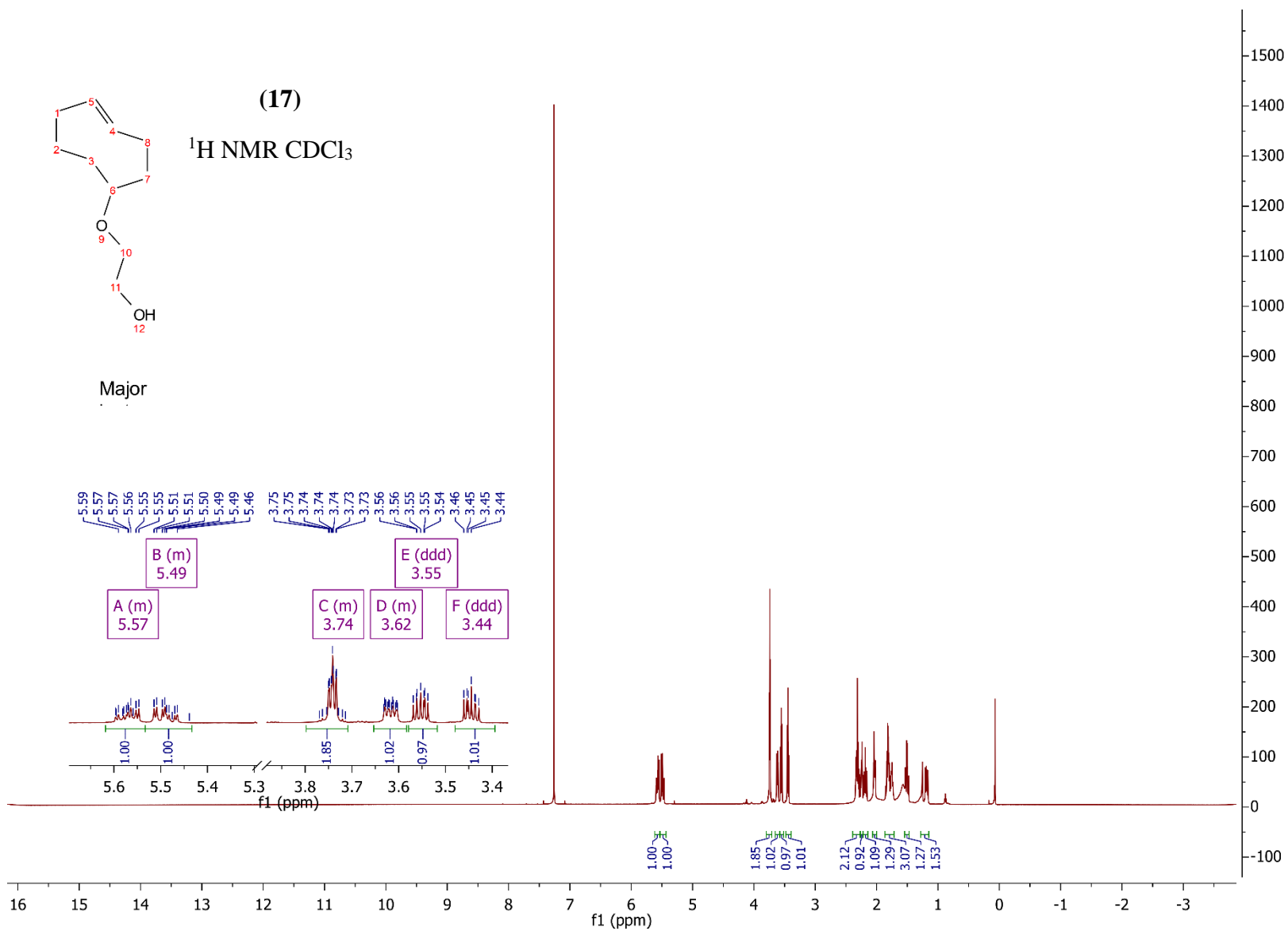




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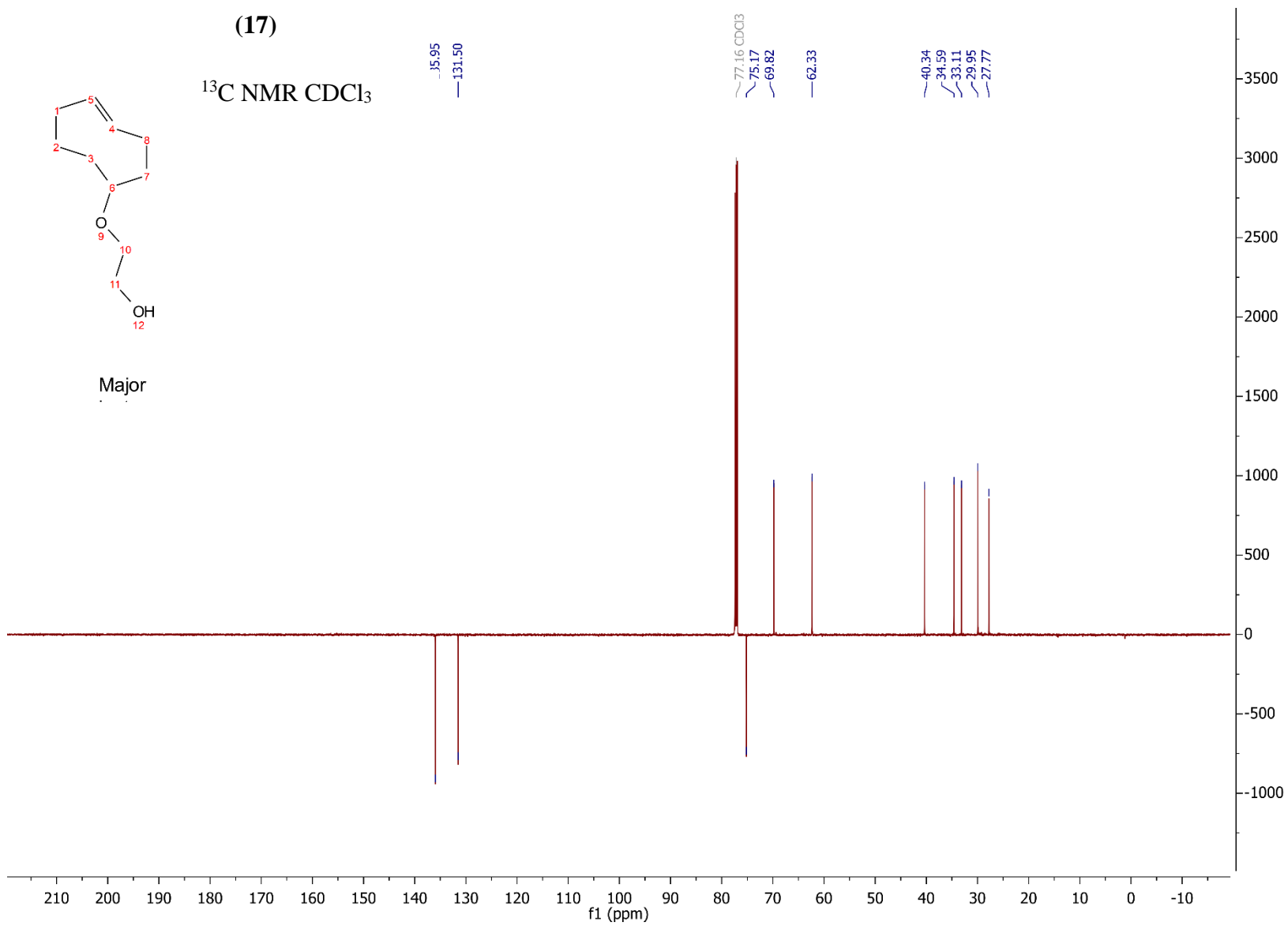
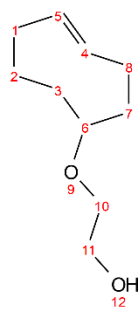
^{13}C NMR CDCl_3

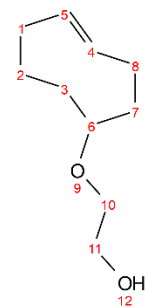




(17)

^{13}C NMR CDCl_3

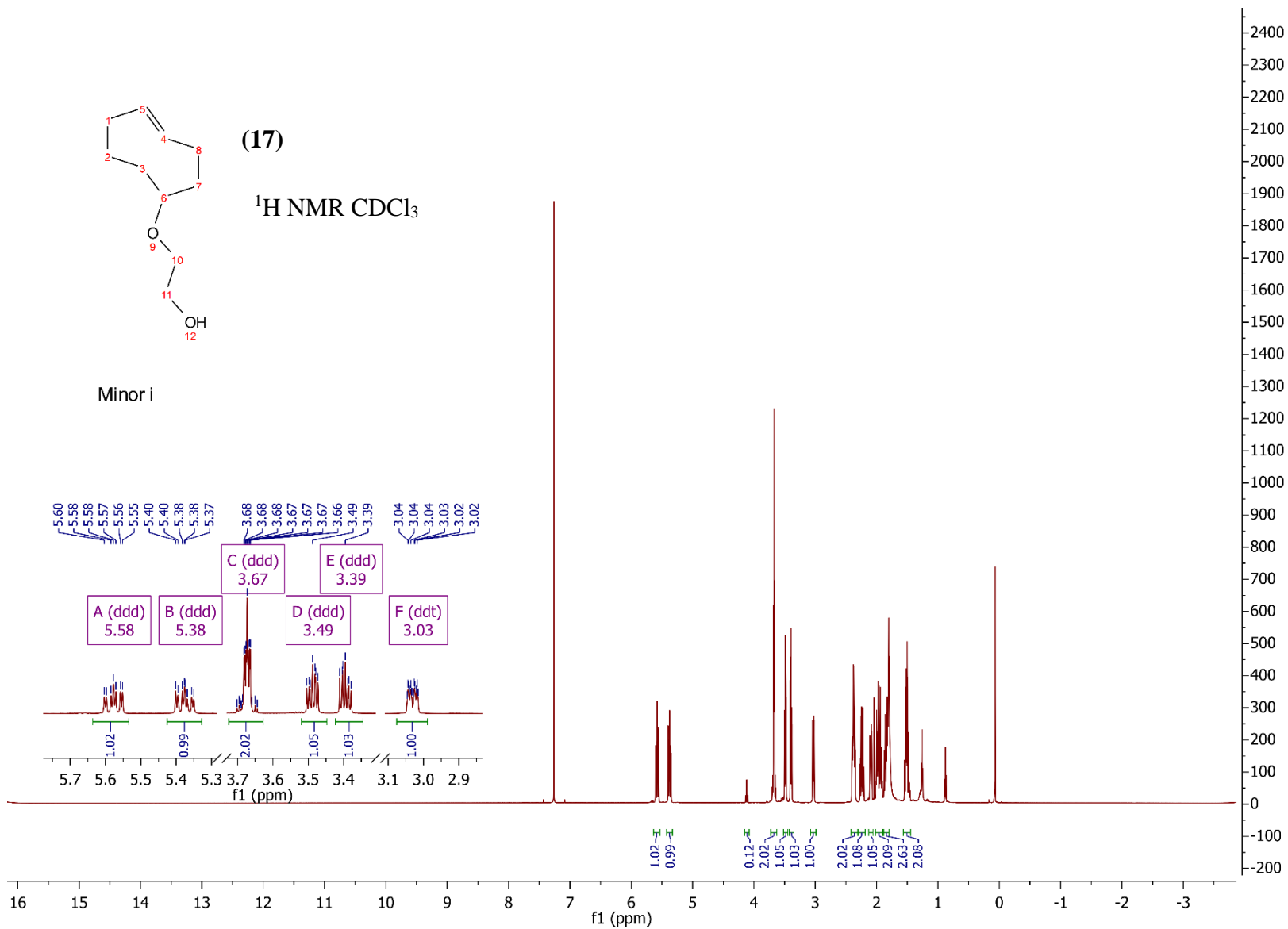


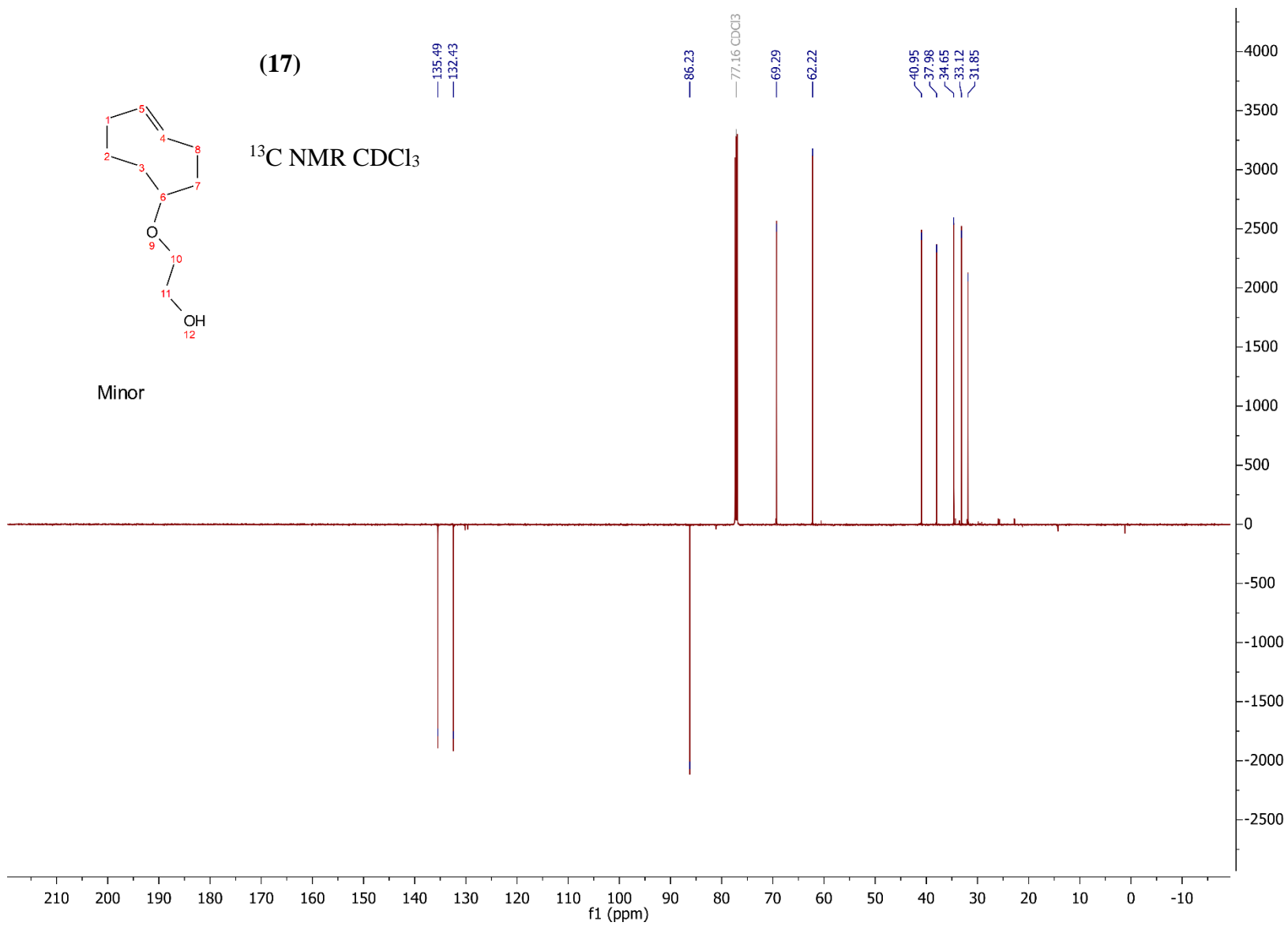


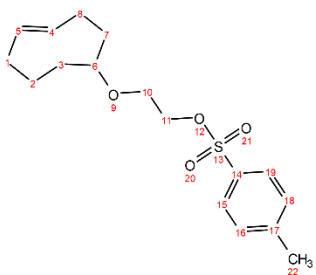
(17)

¹H NMR CDCl₃

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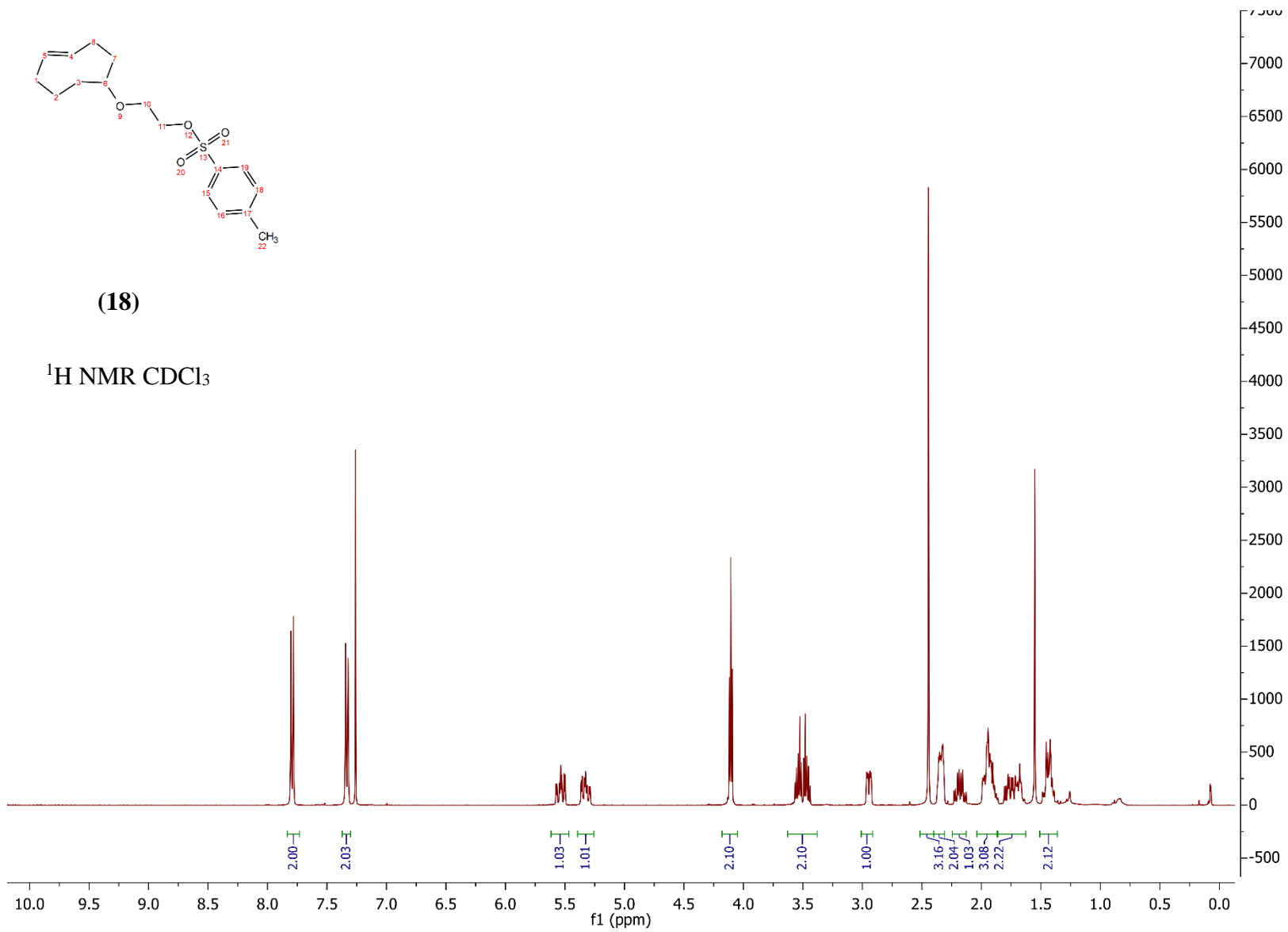


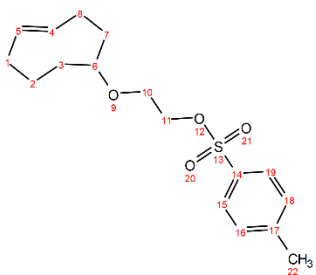




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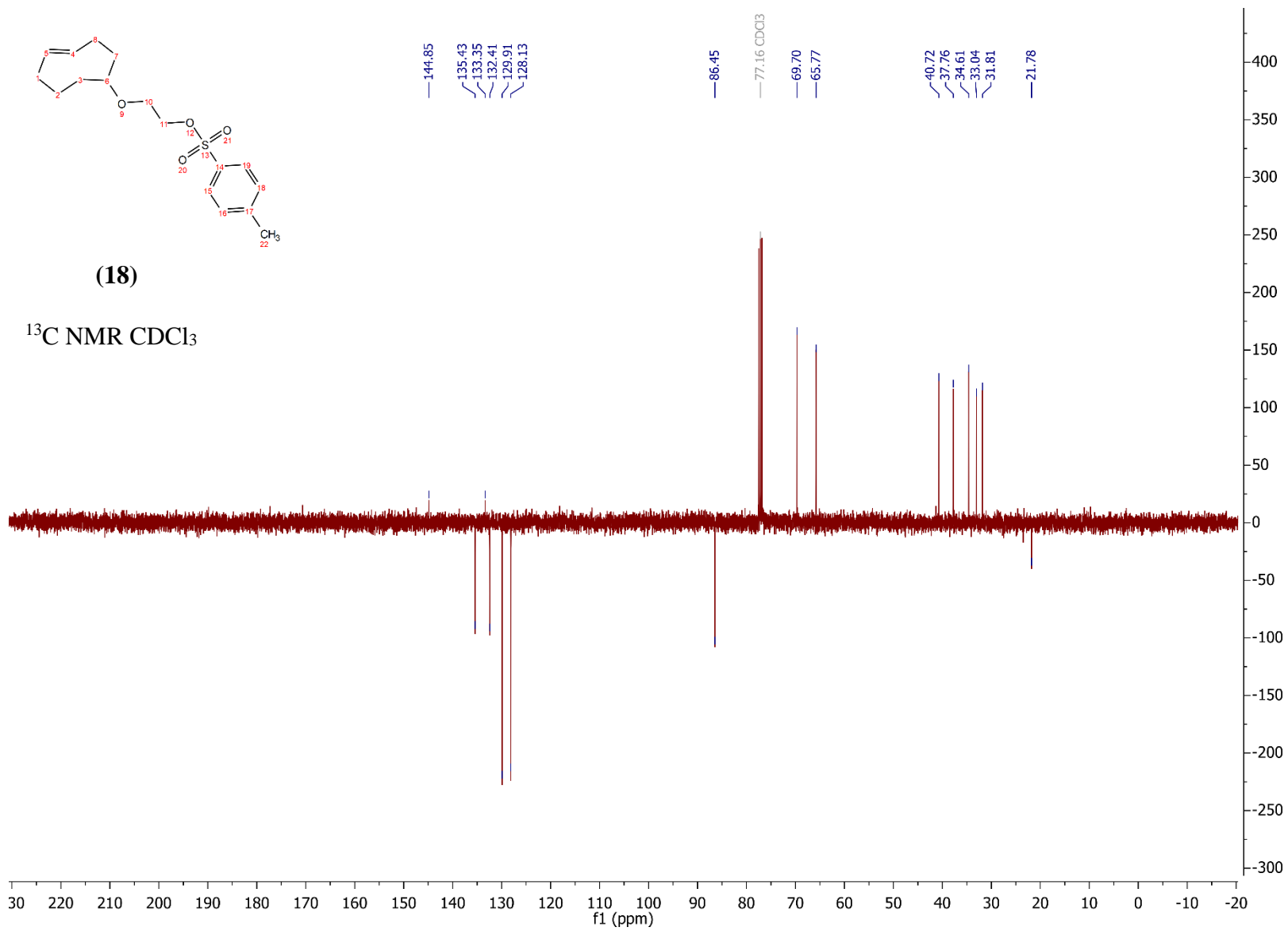
^1H NMR CDCl_3

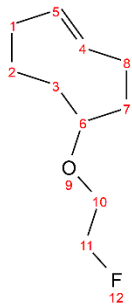




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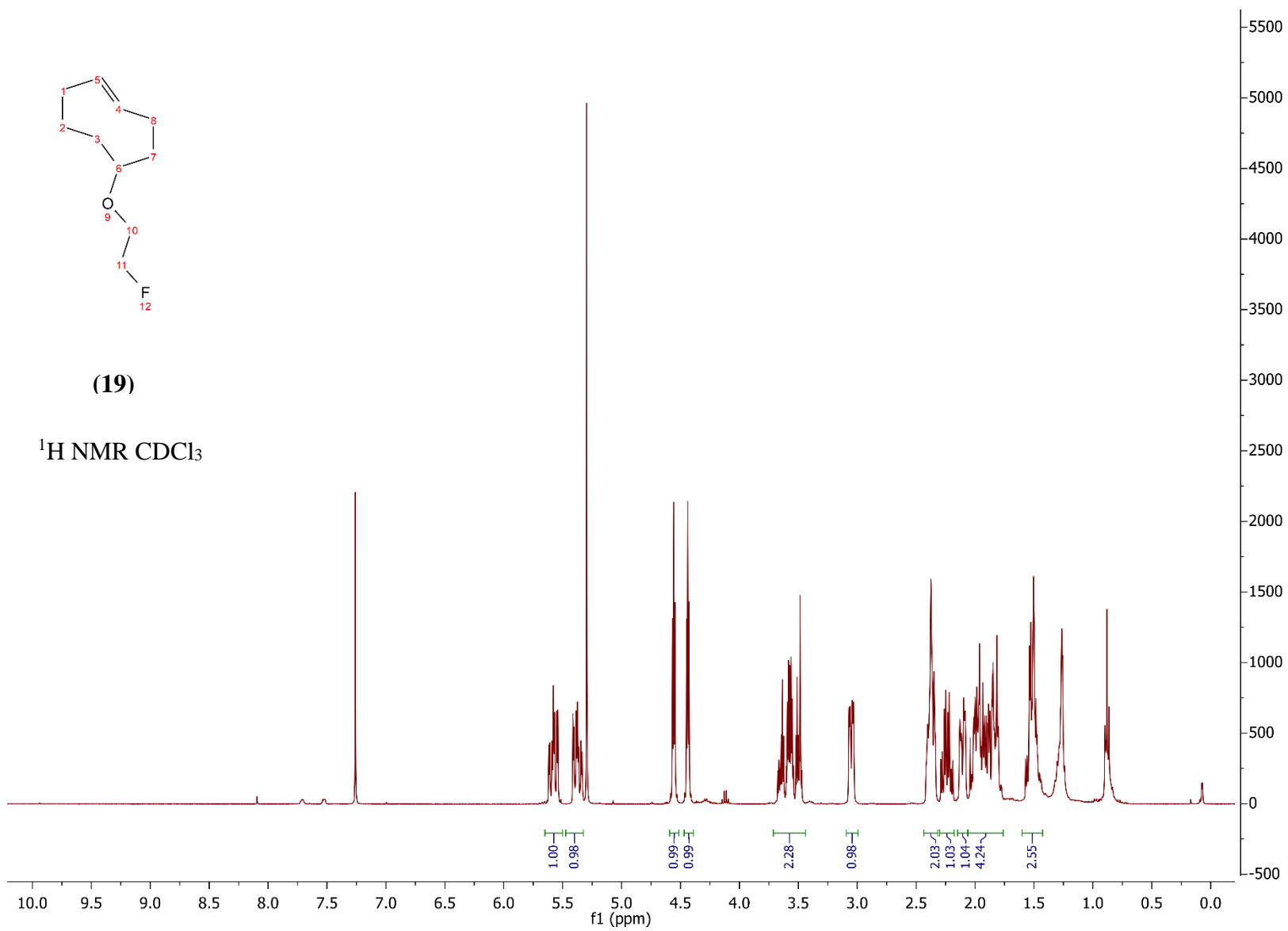
^{13}C NMR CDCl_3

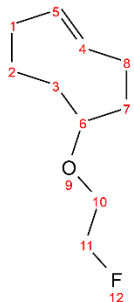




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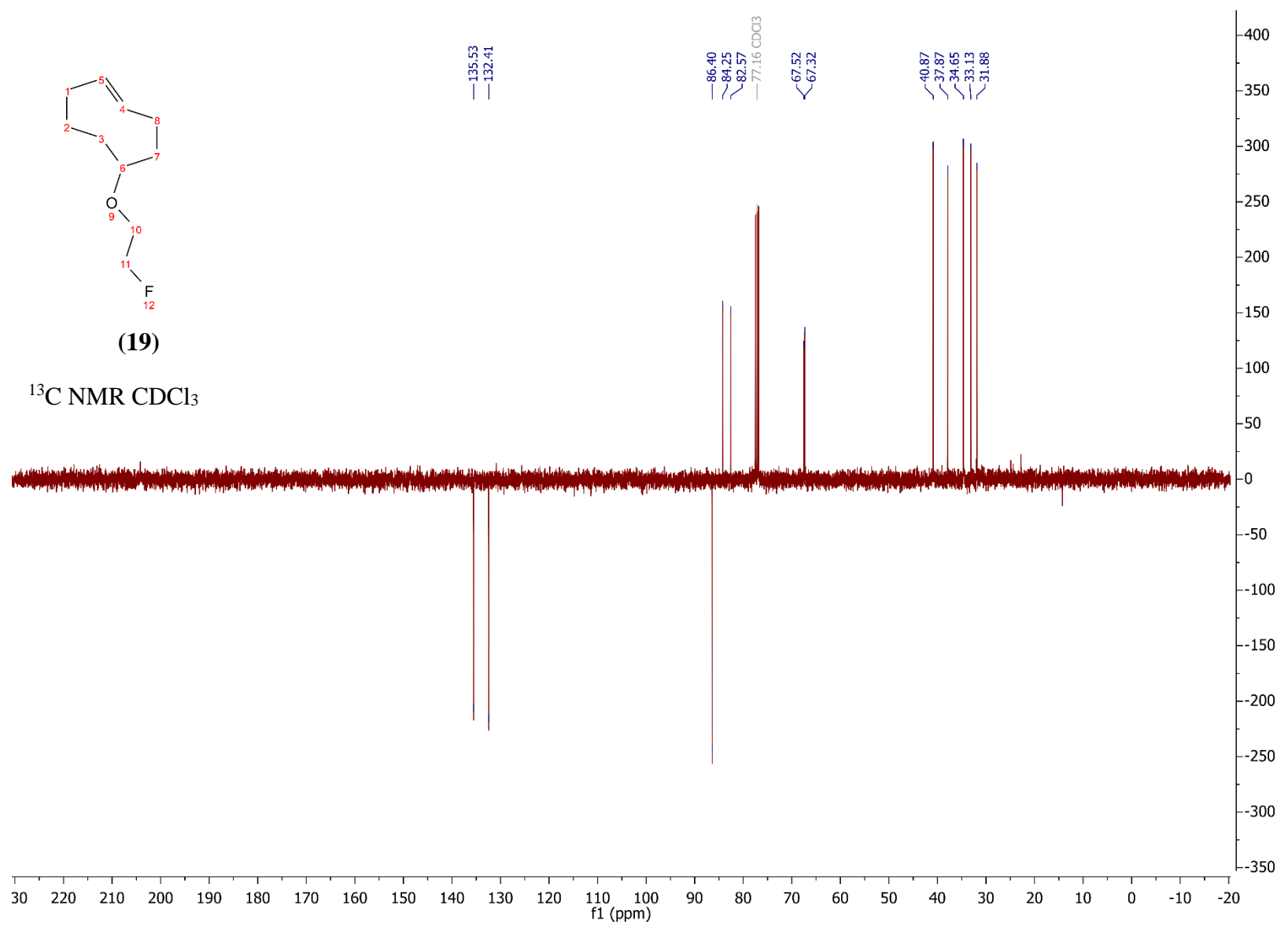
¹H NMR CDCl₃

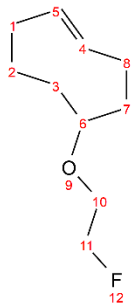




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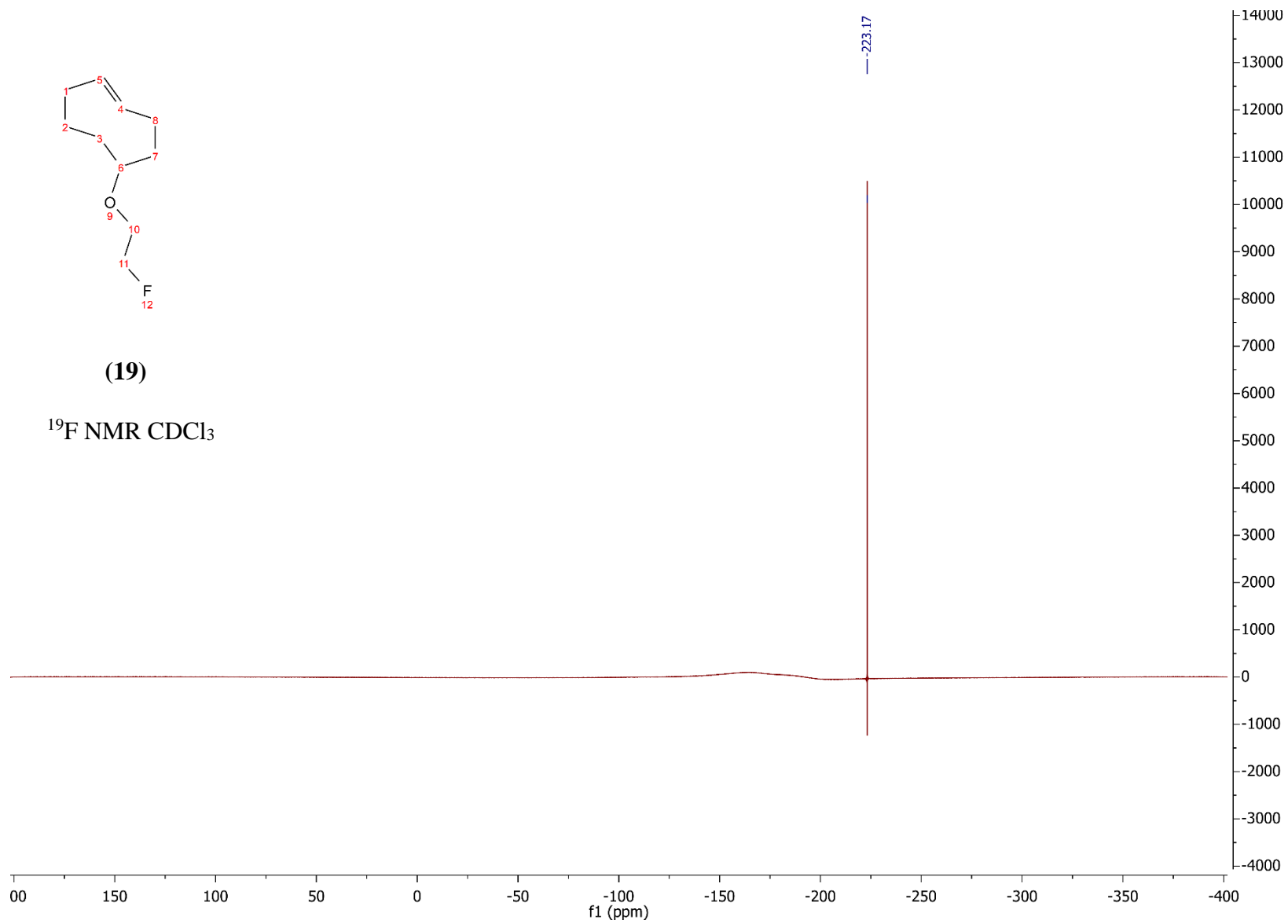
¹³C NMR CDCl₃

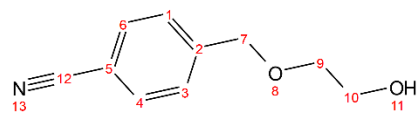




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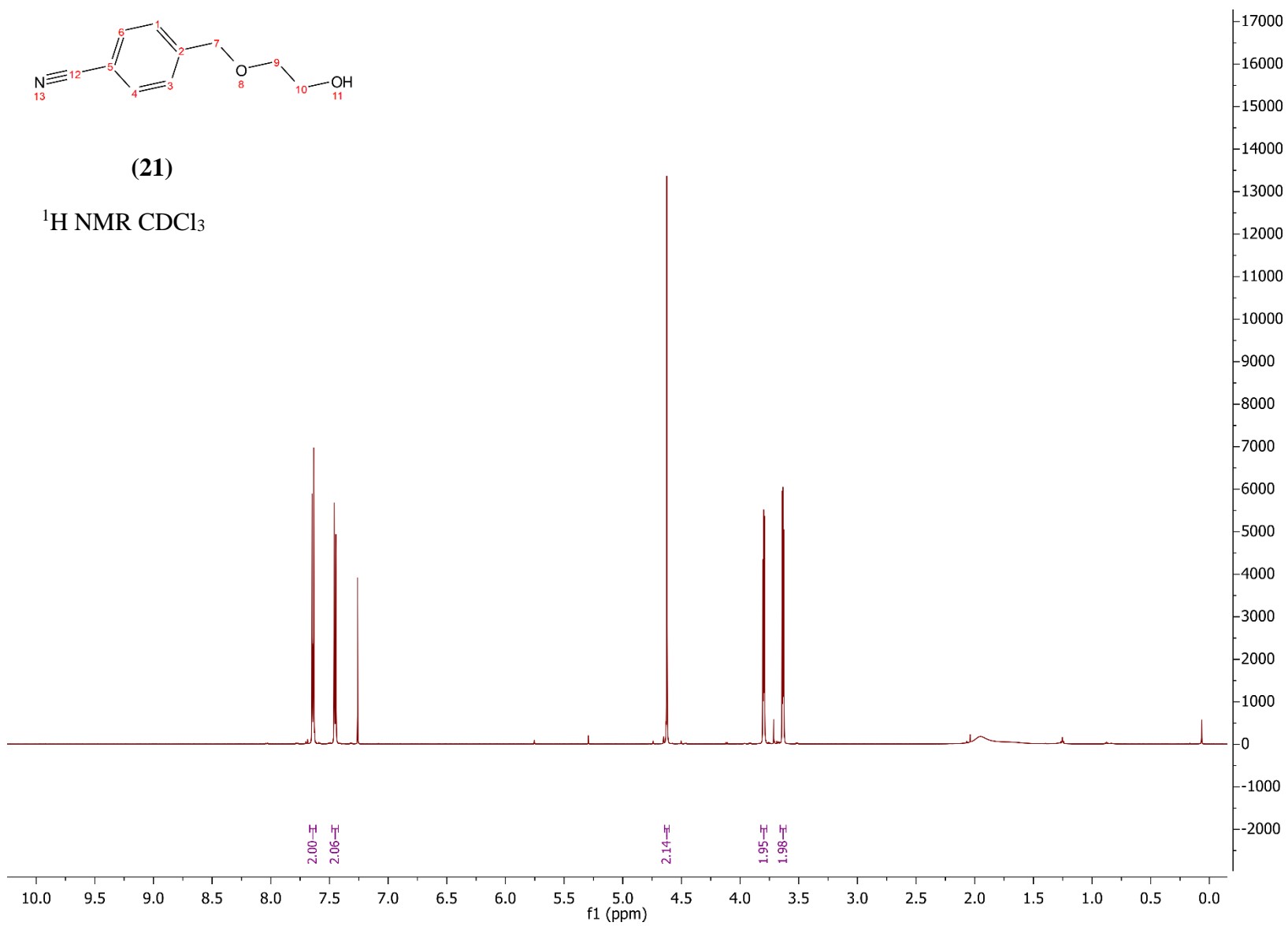
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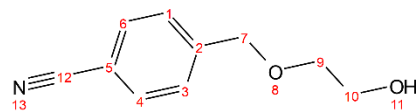




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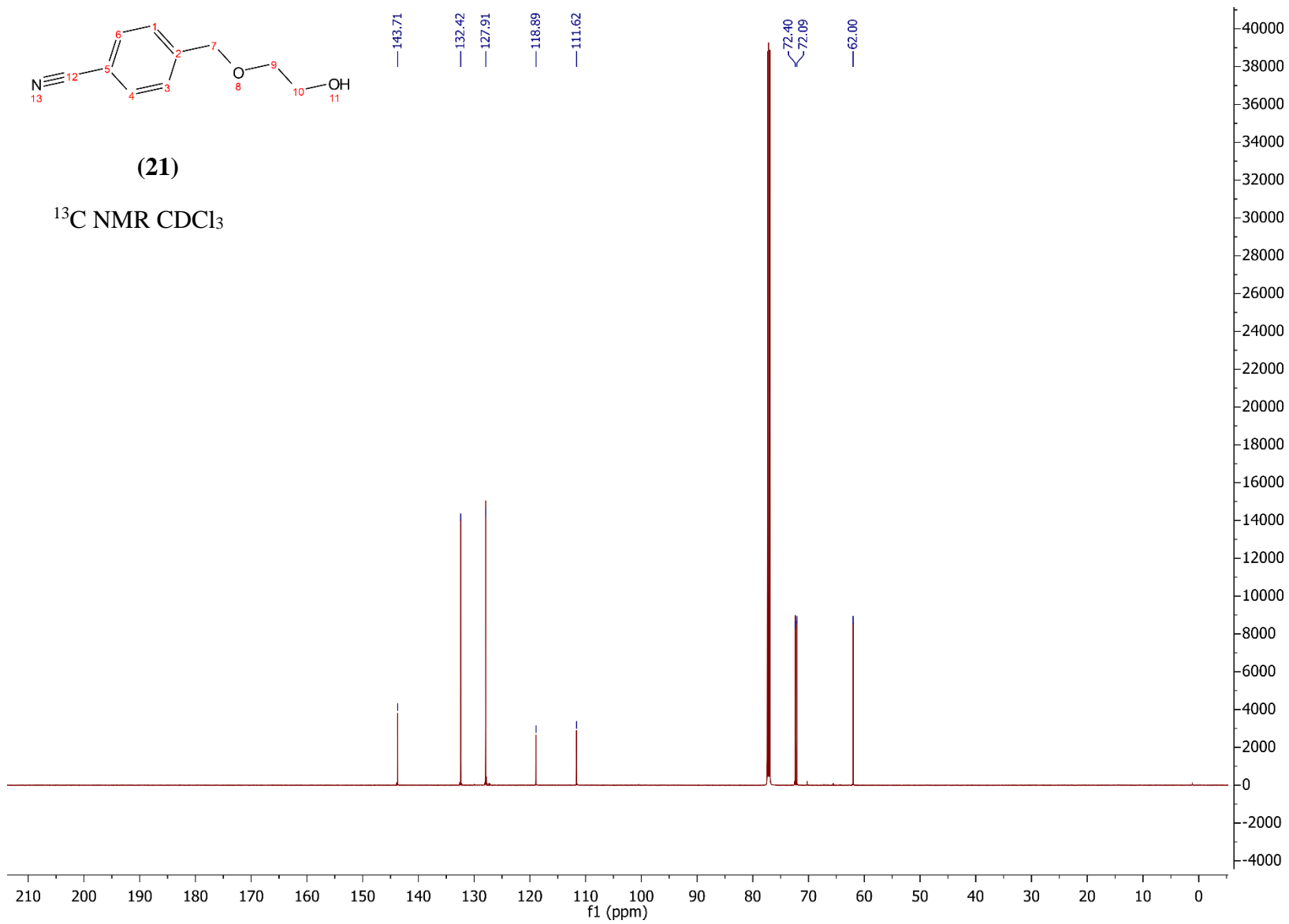
$^1\text{H NMR CDCl}_3$

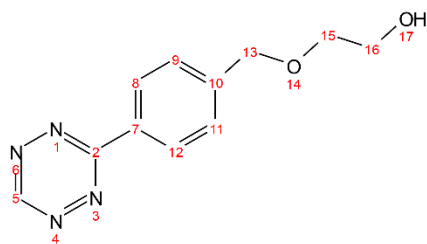




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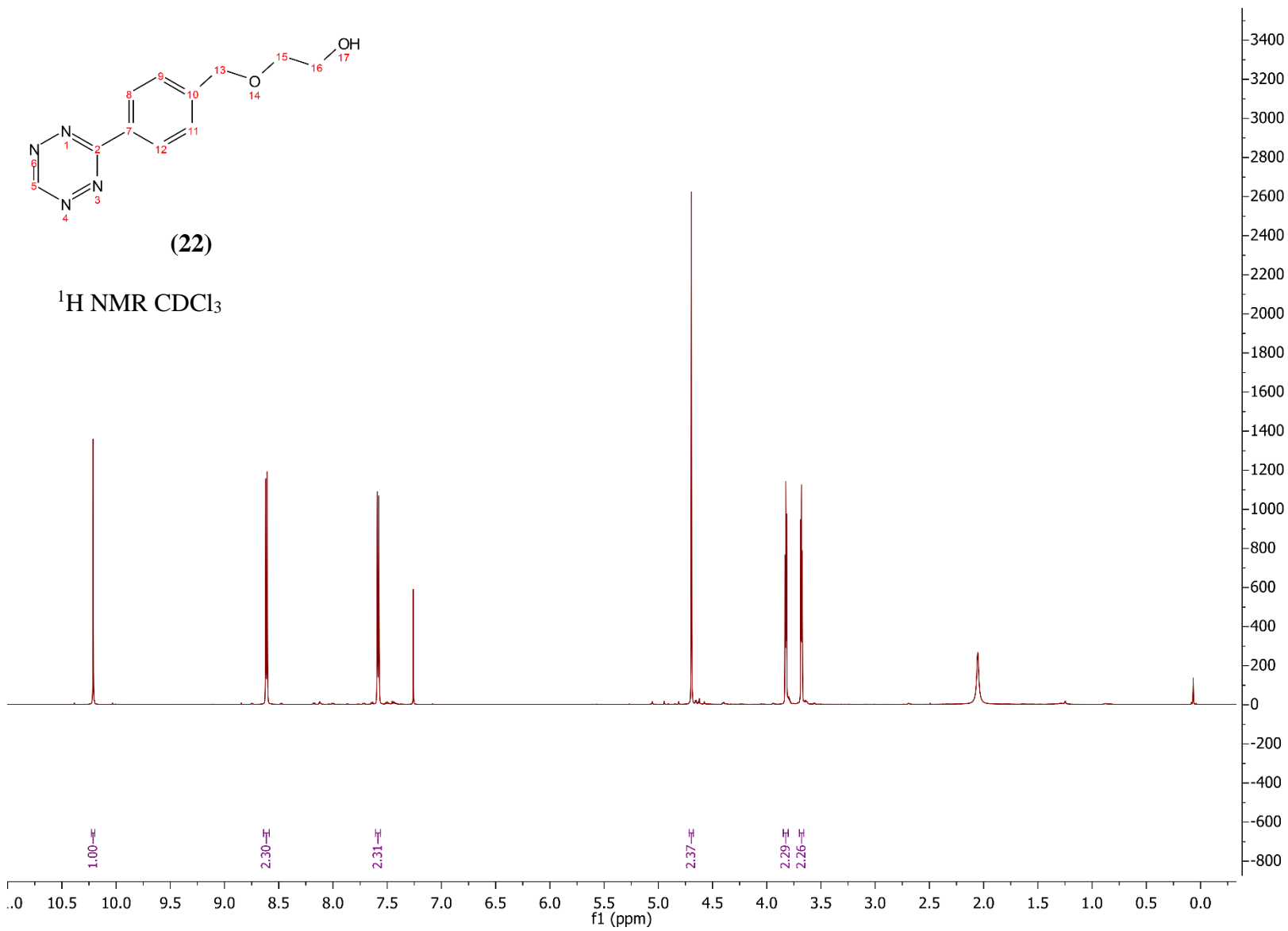
¹³C NMR CDCl₃

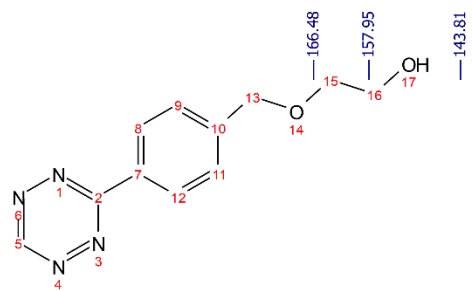




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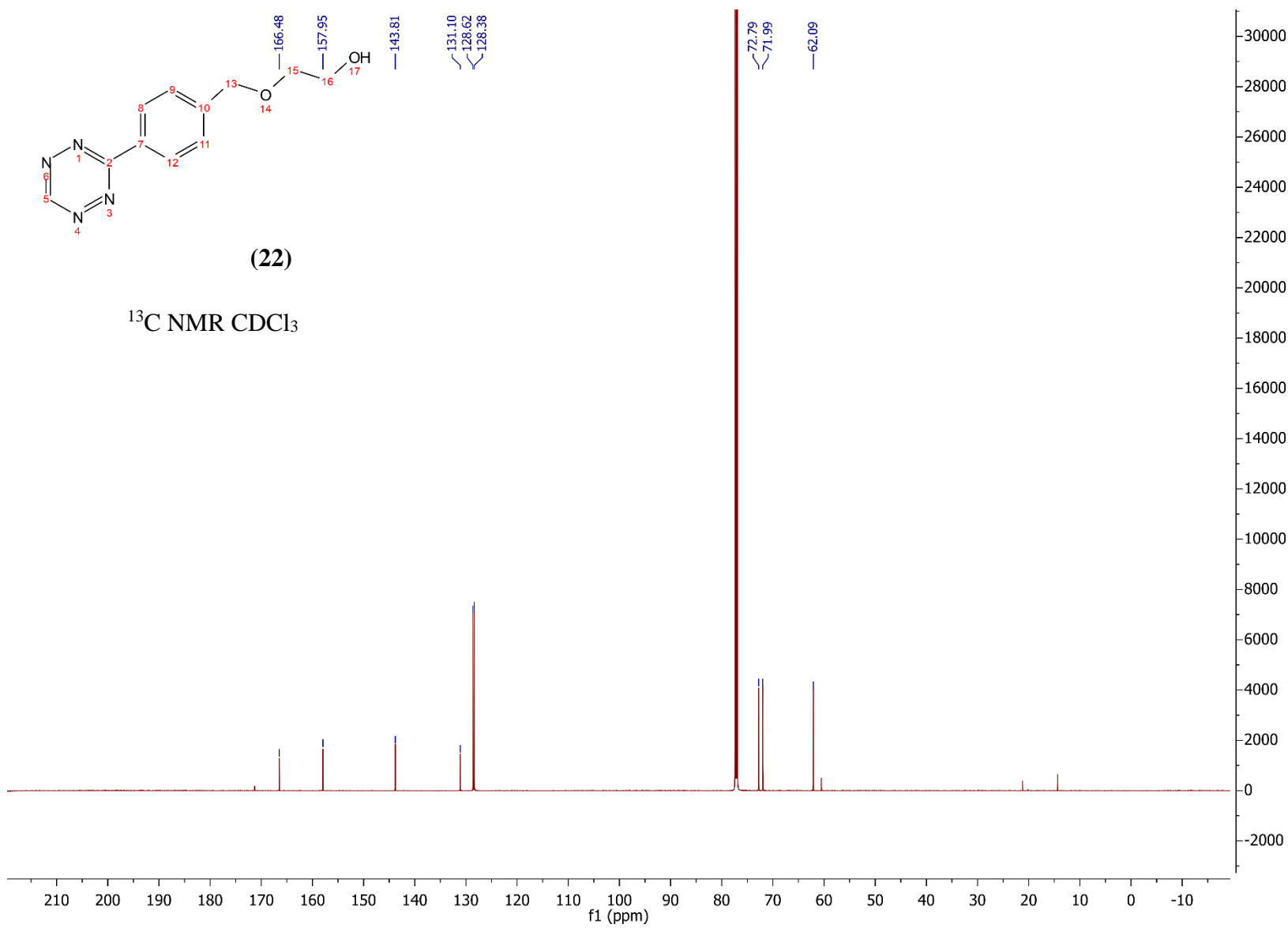
¹H NMR CDCl₃

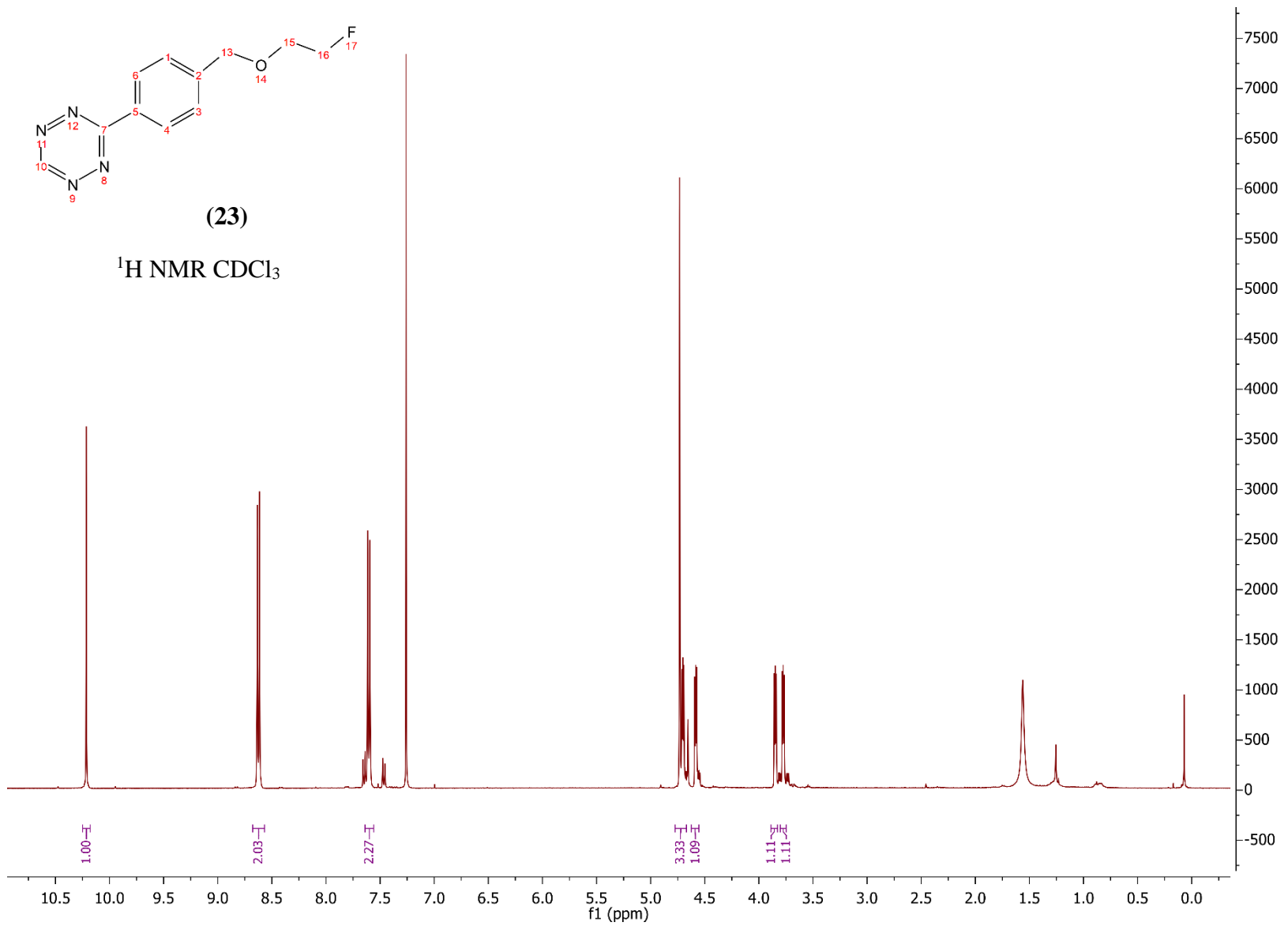


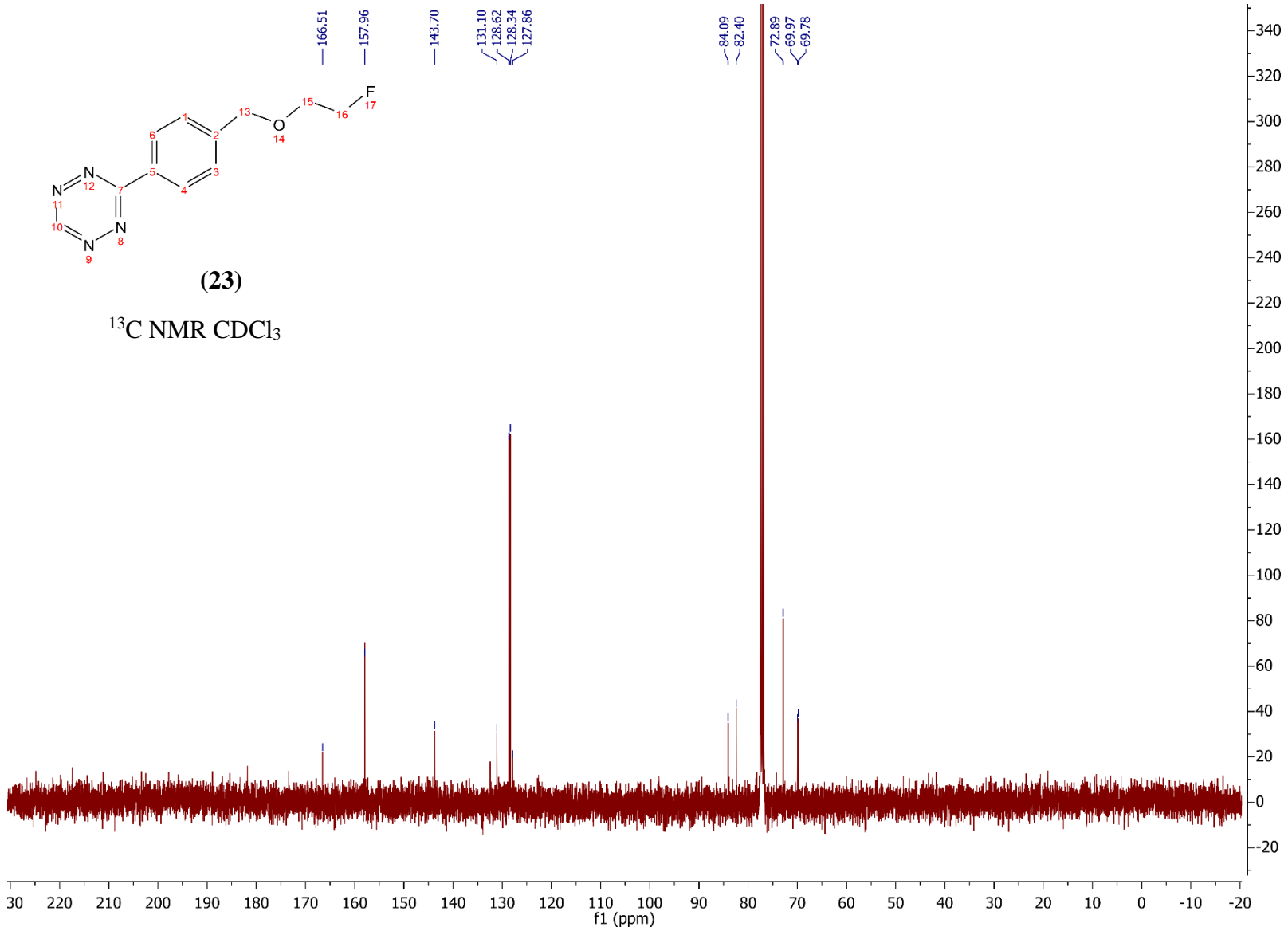


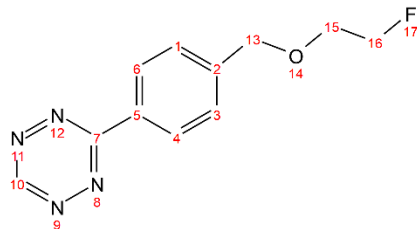
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^{13}C NMR CDCl_3



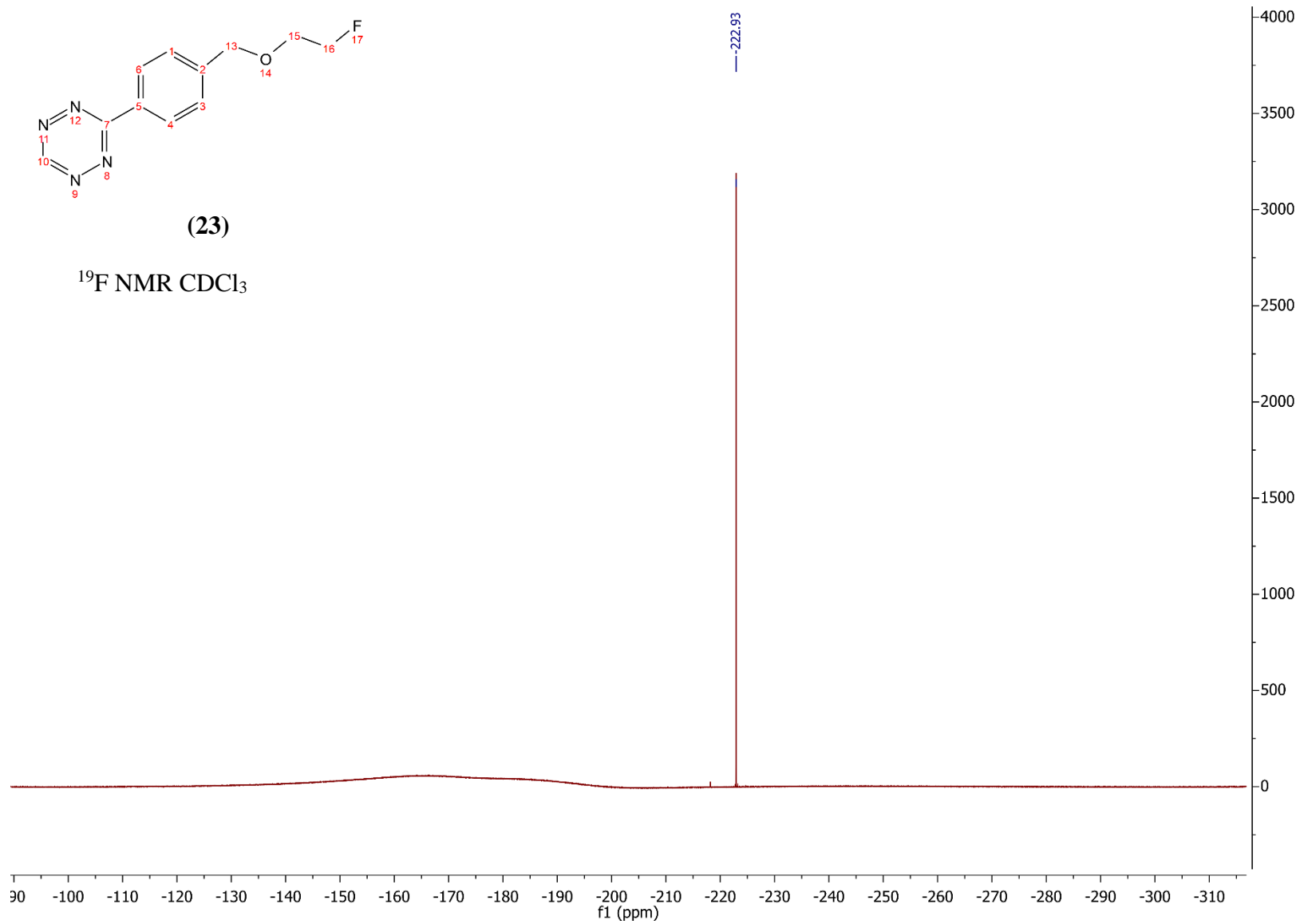


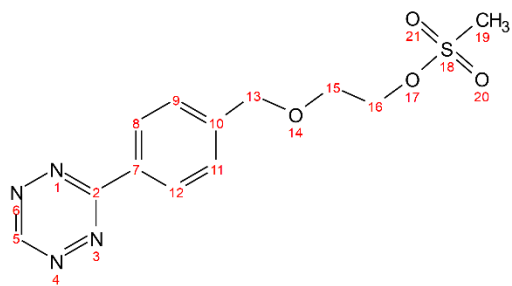




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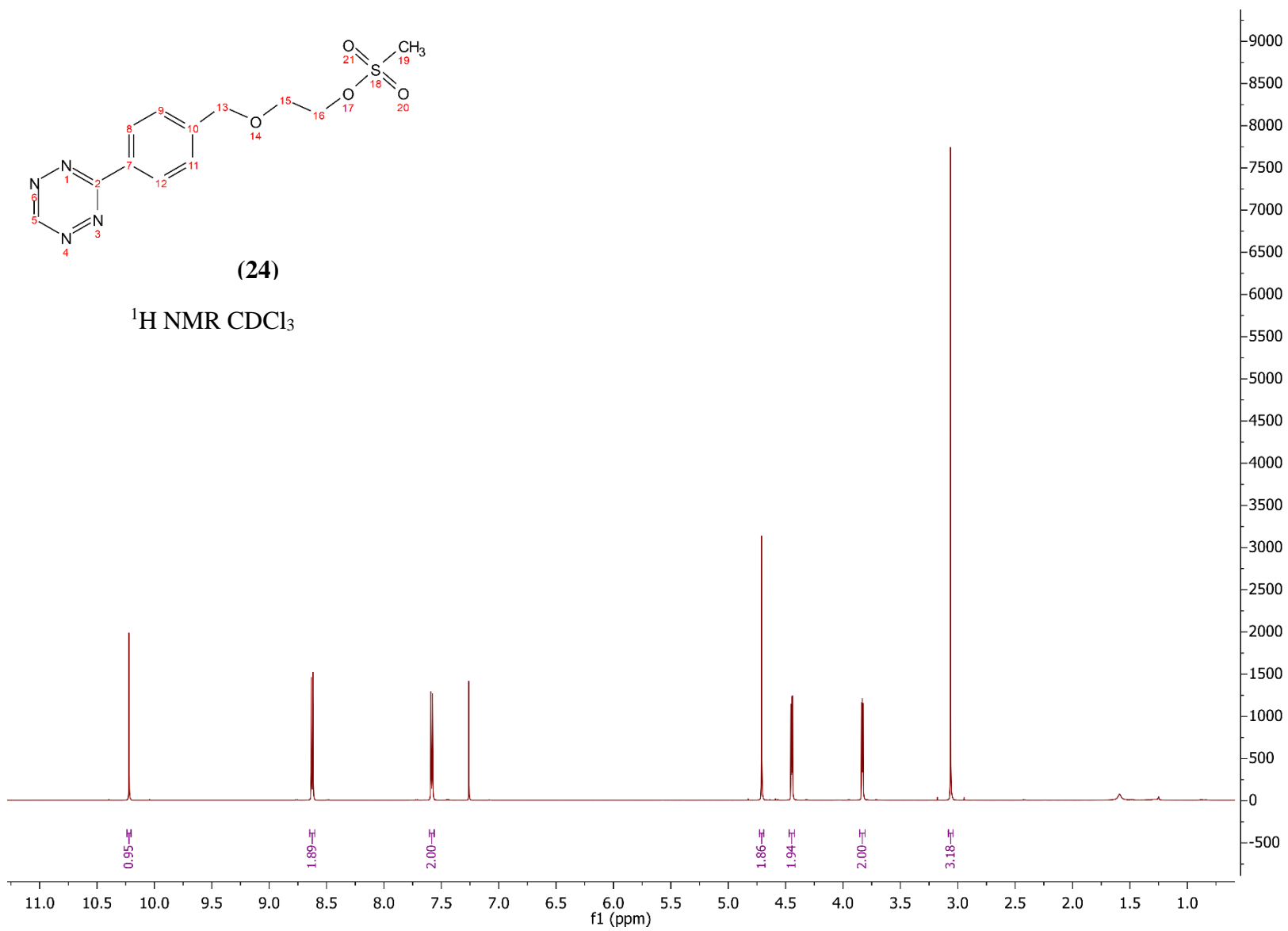
^{19}F NMR CDCl_3

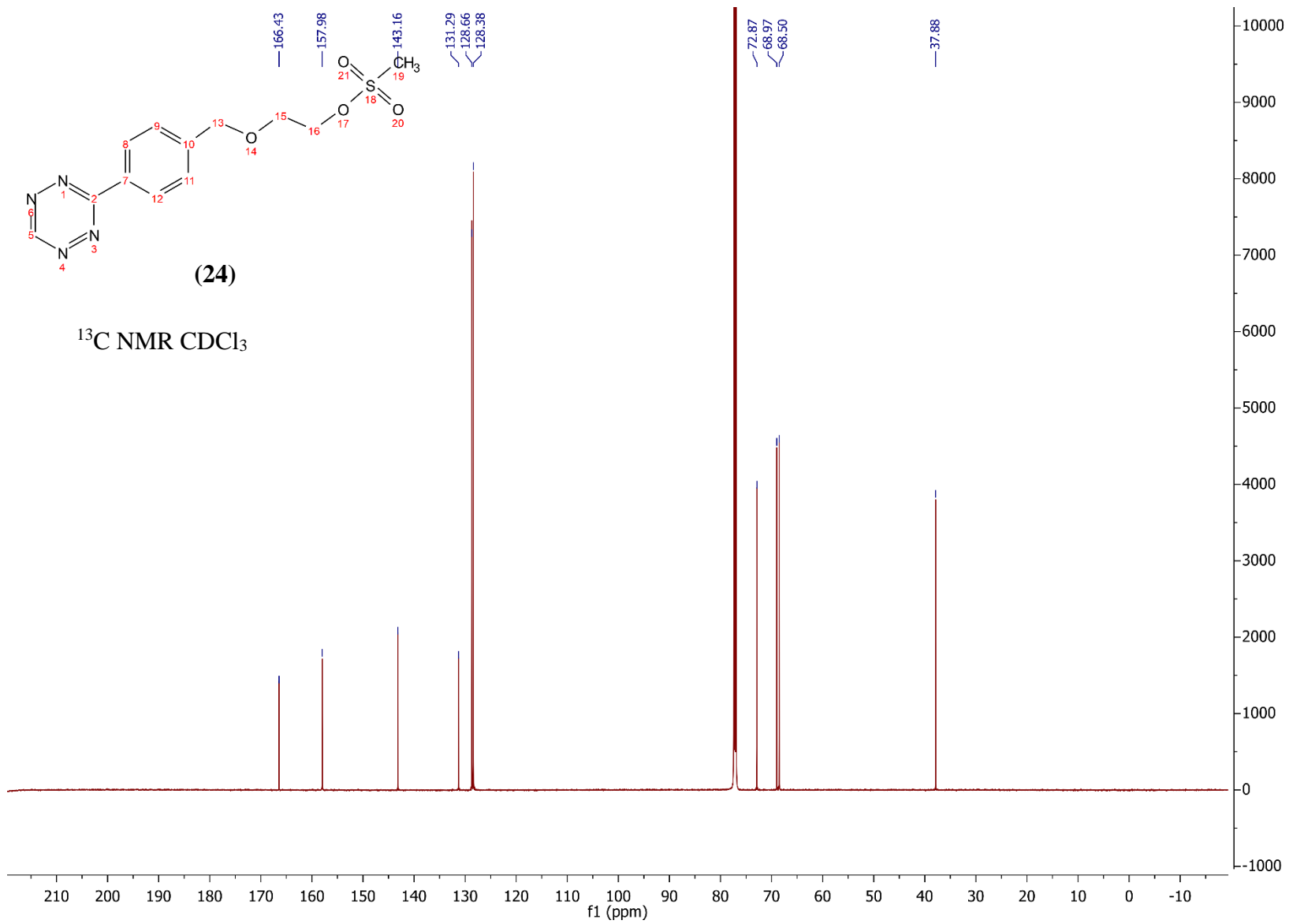


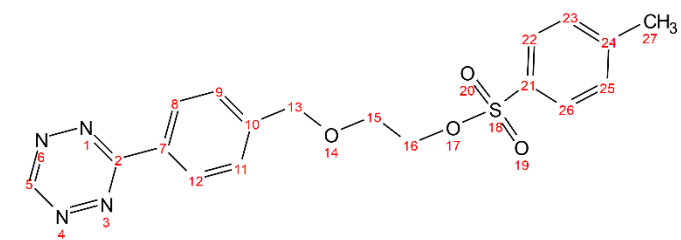


(24)

$^1\text{H NMR CDCl}_3$

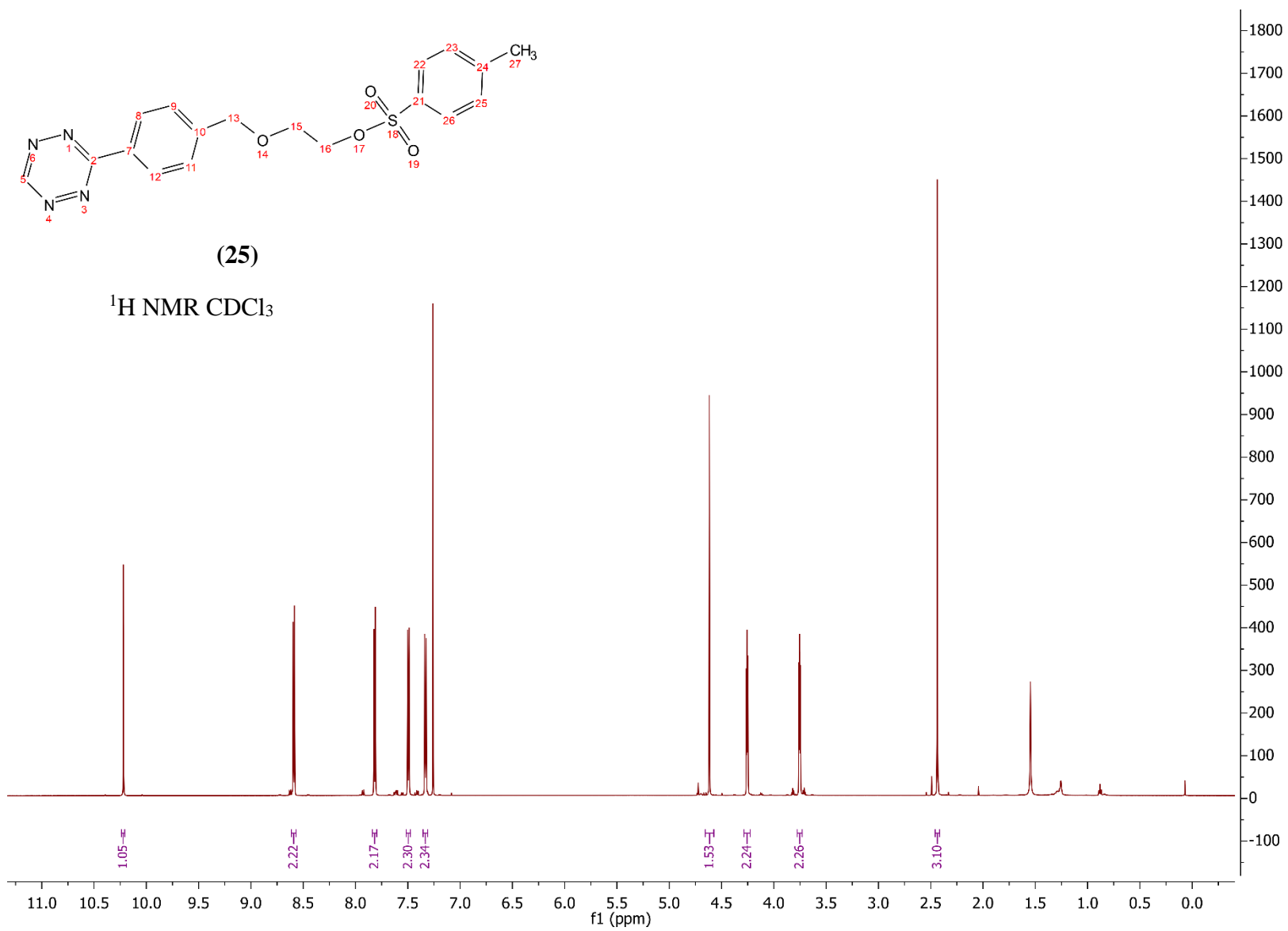


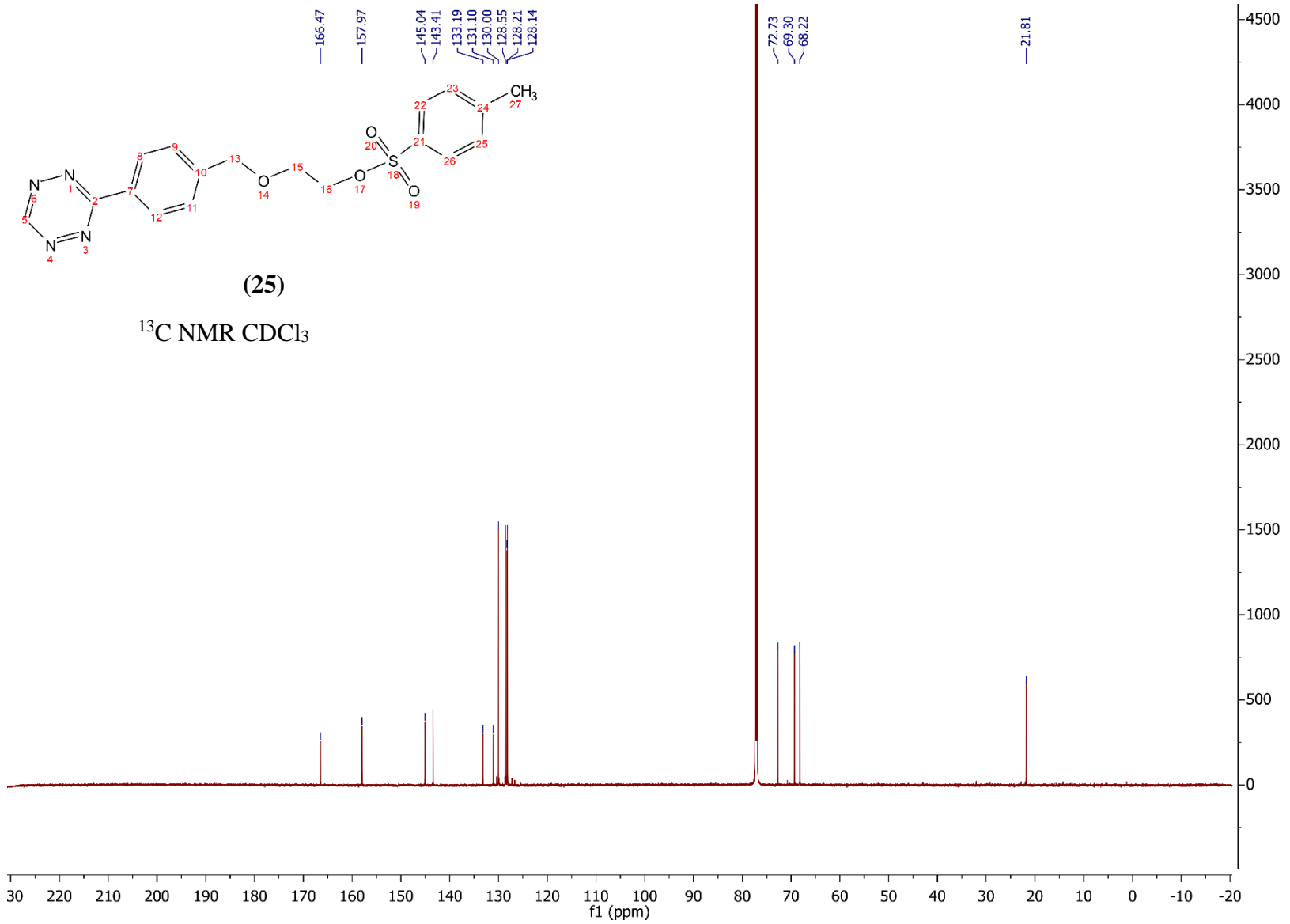


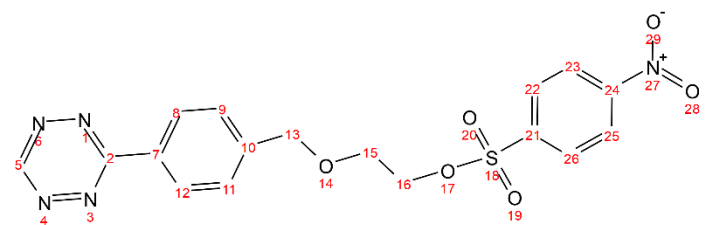


(25)

$^1\text{H NMR CDCl}_3$

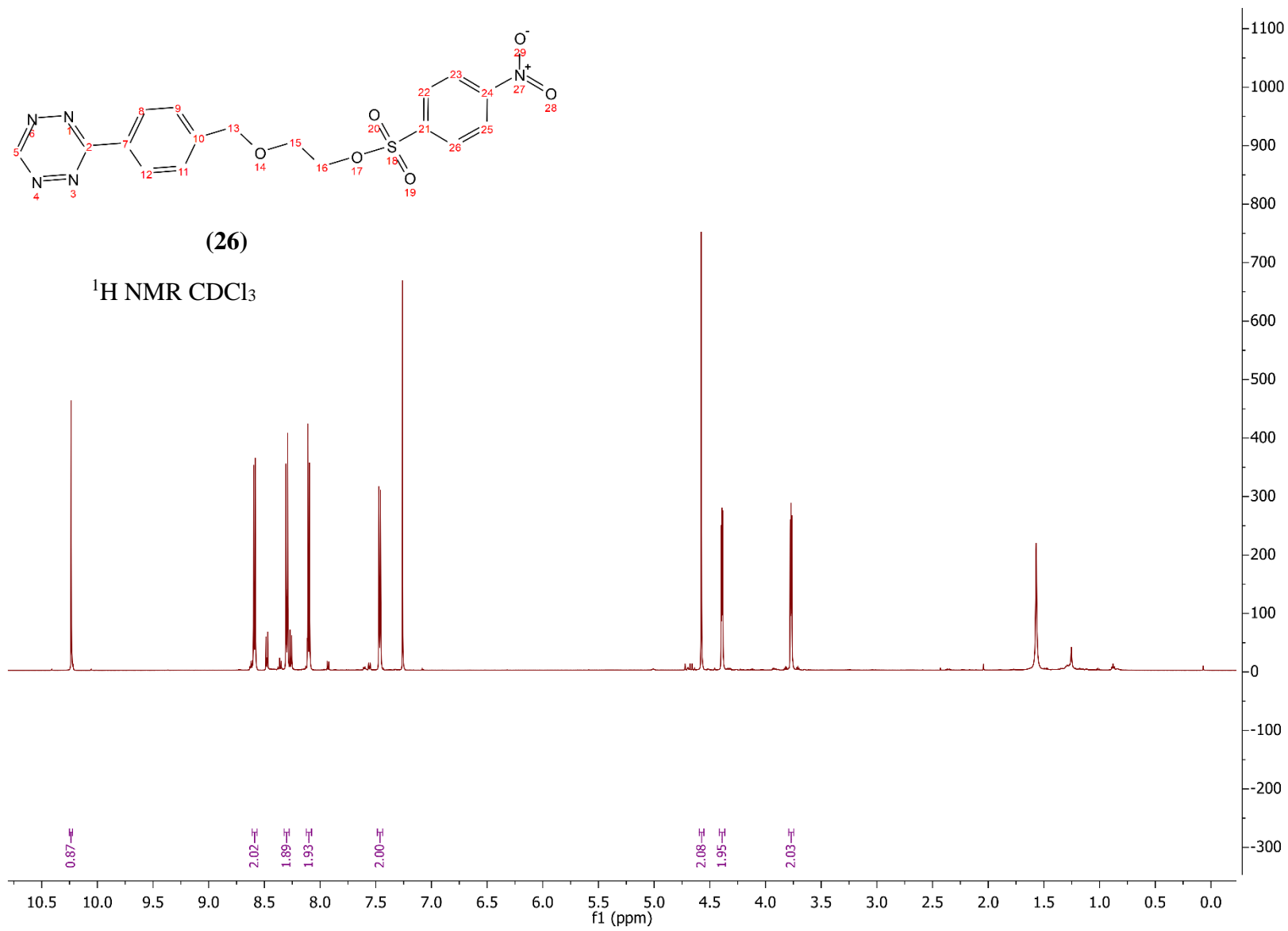


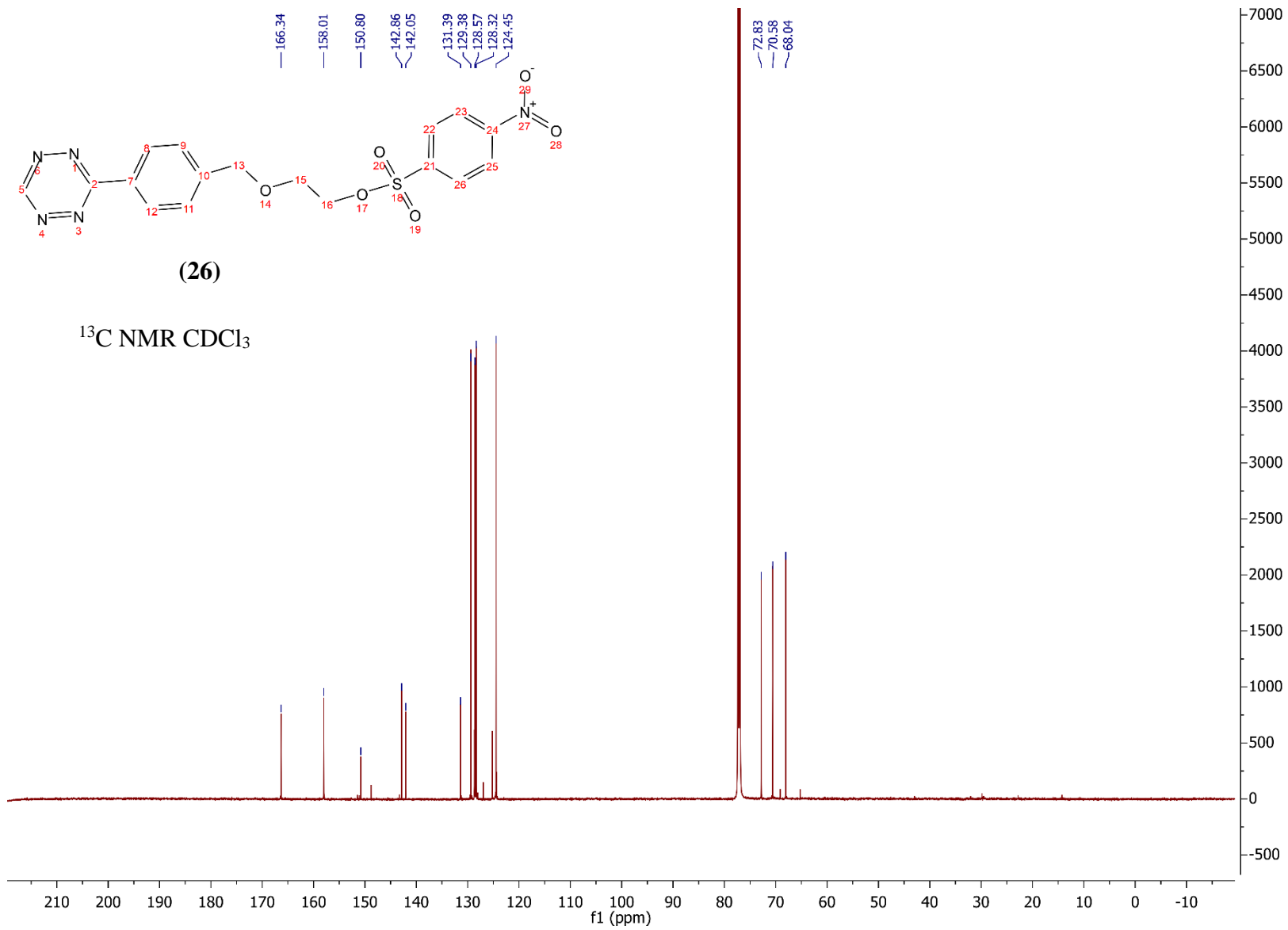


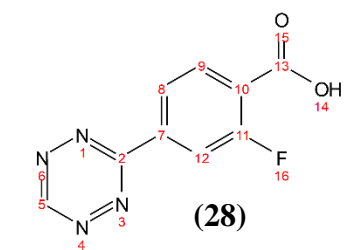


(26)

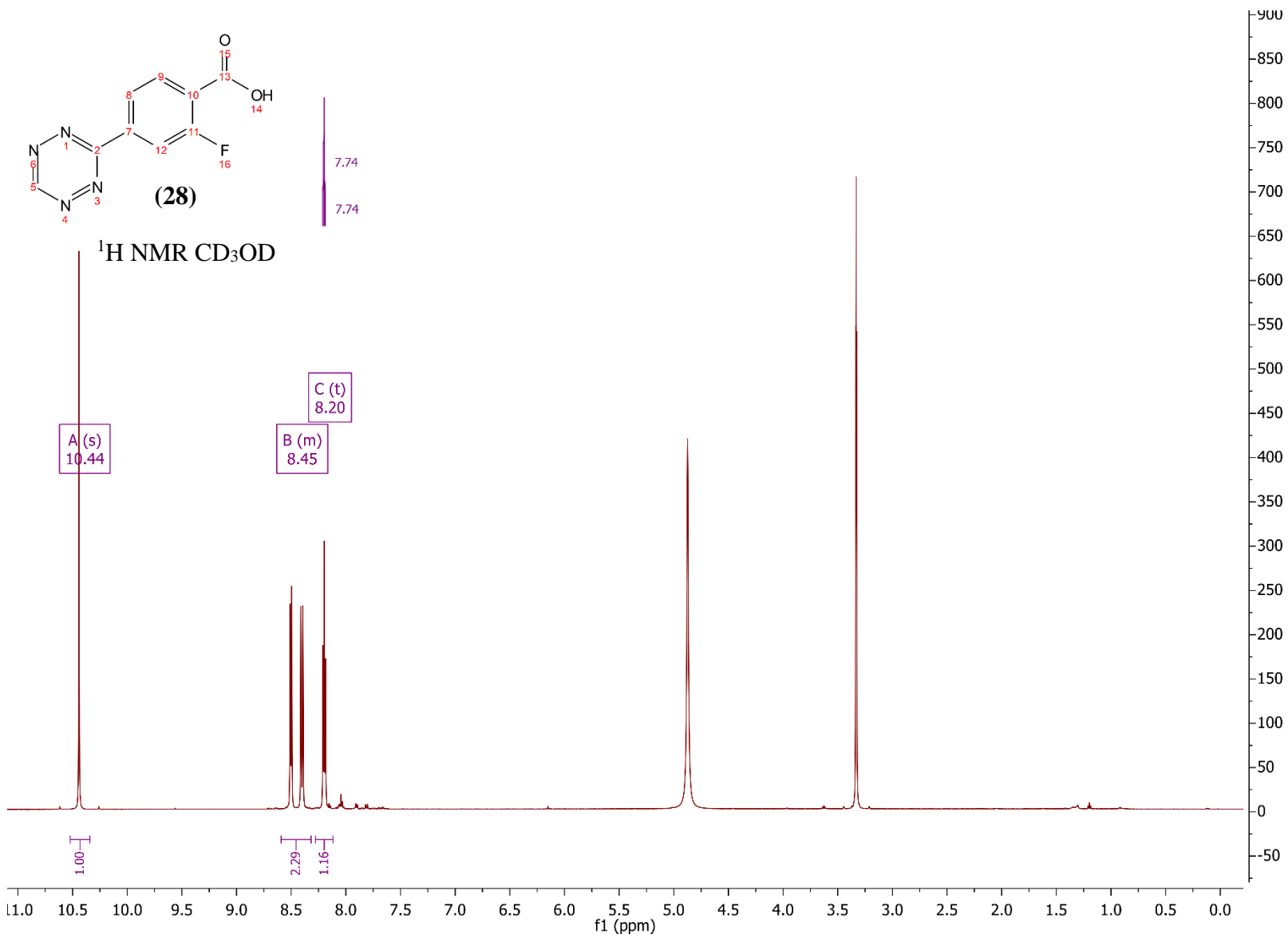
$^1\text{H NMR CDCl}_3$

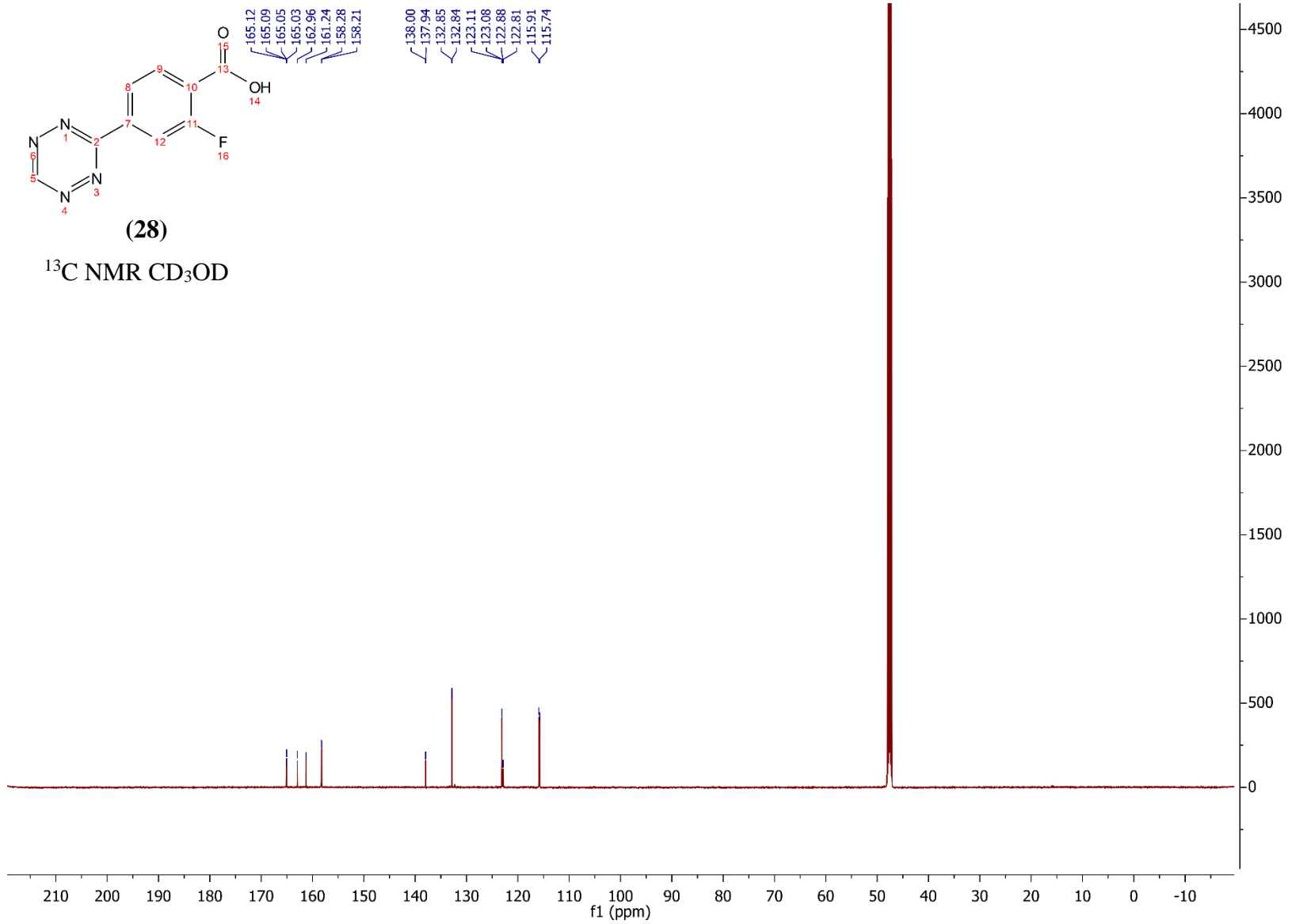


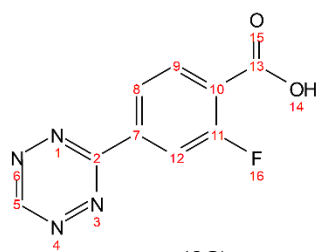




$^1\text{H NMR CD}_3\text{OD}$

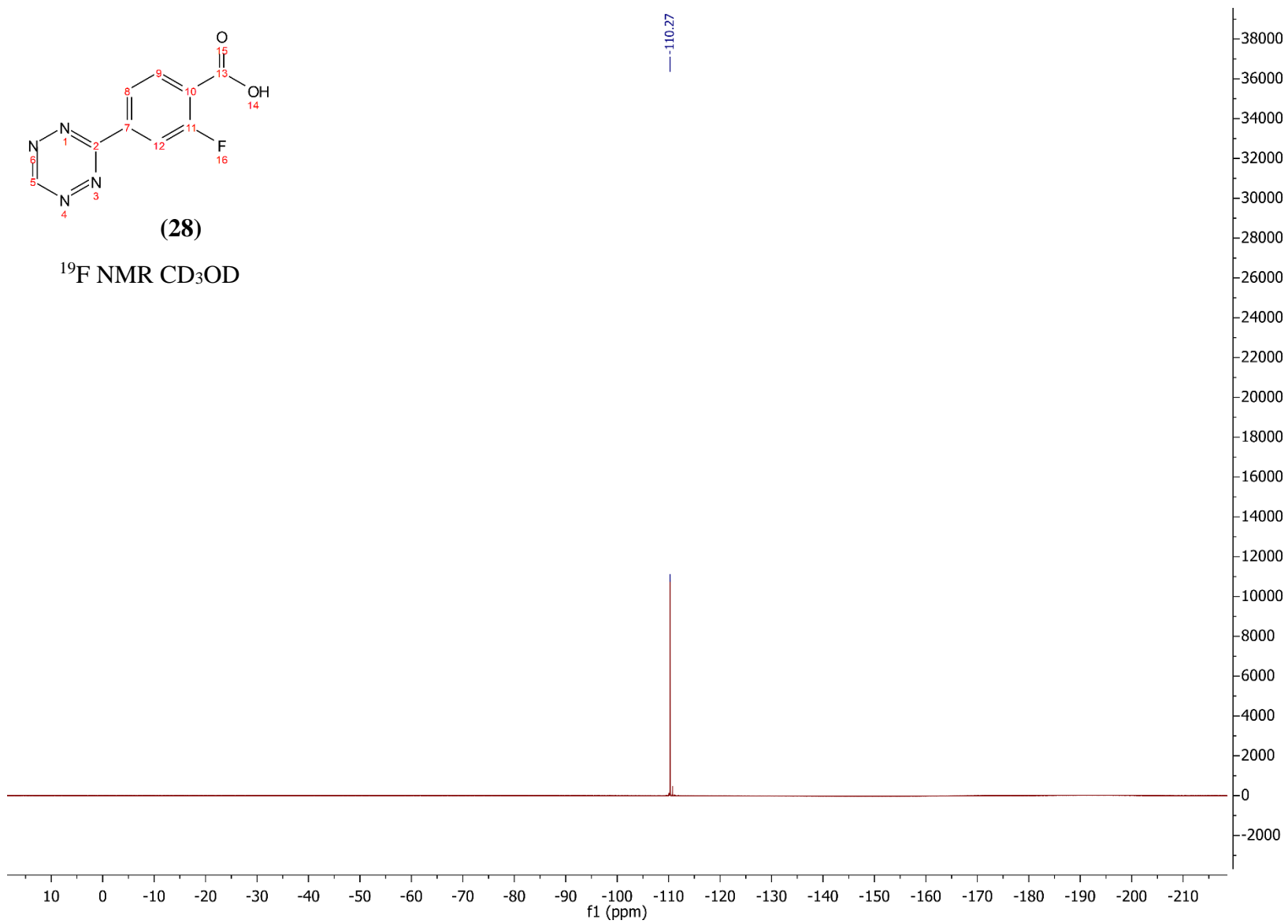


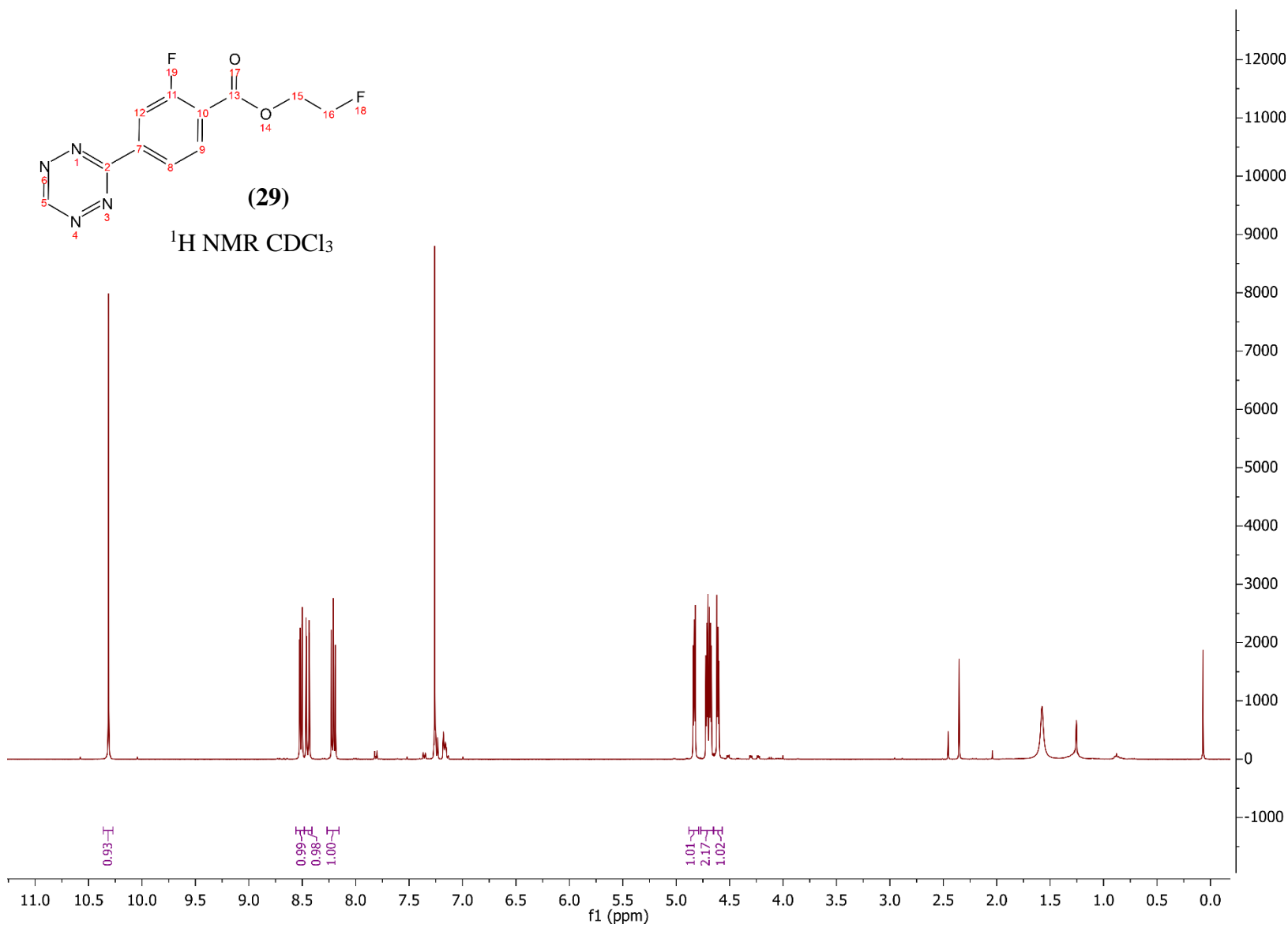
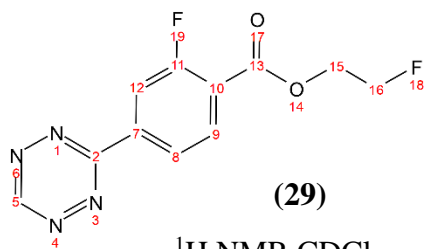


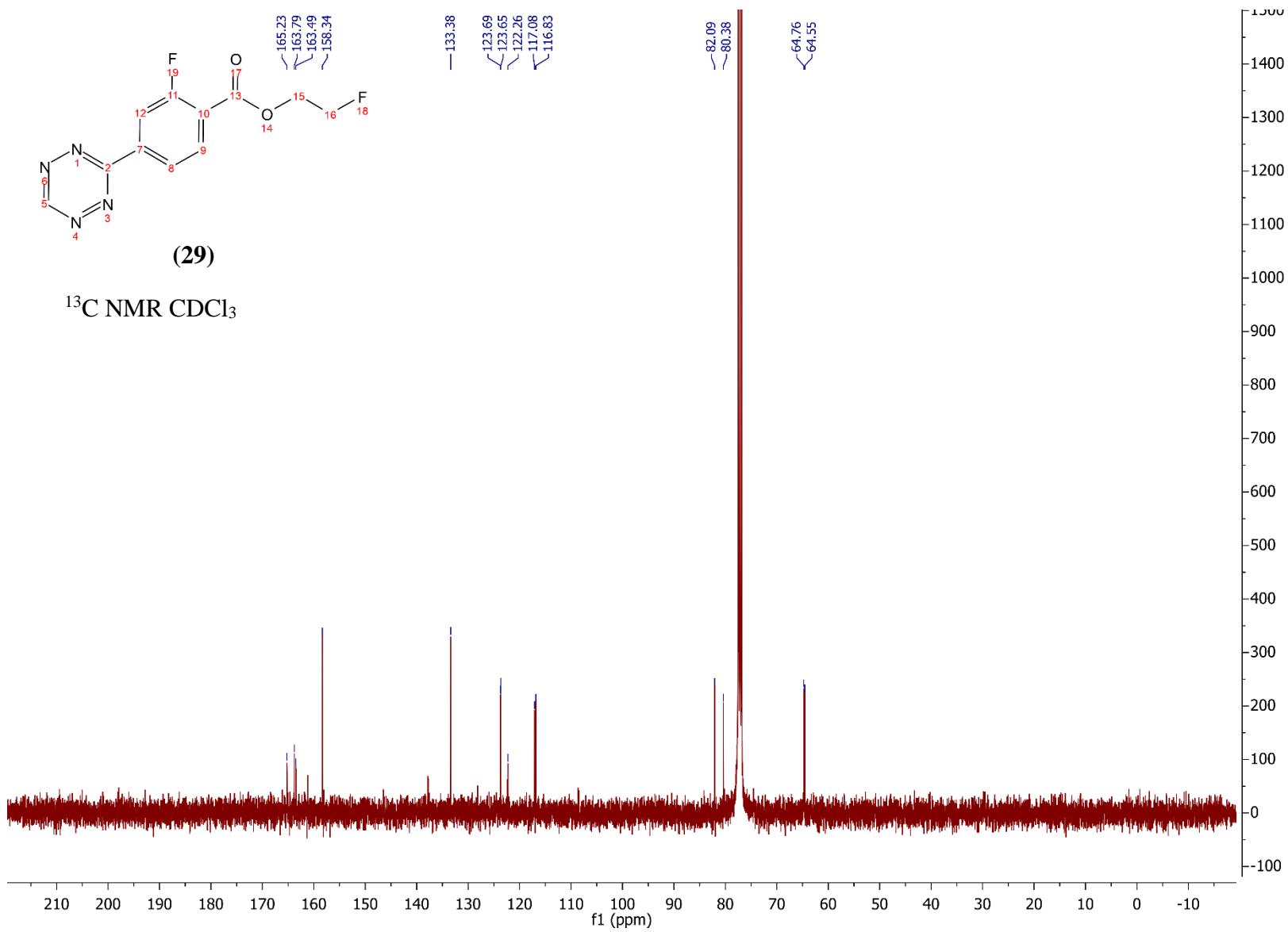


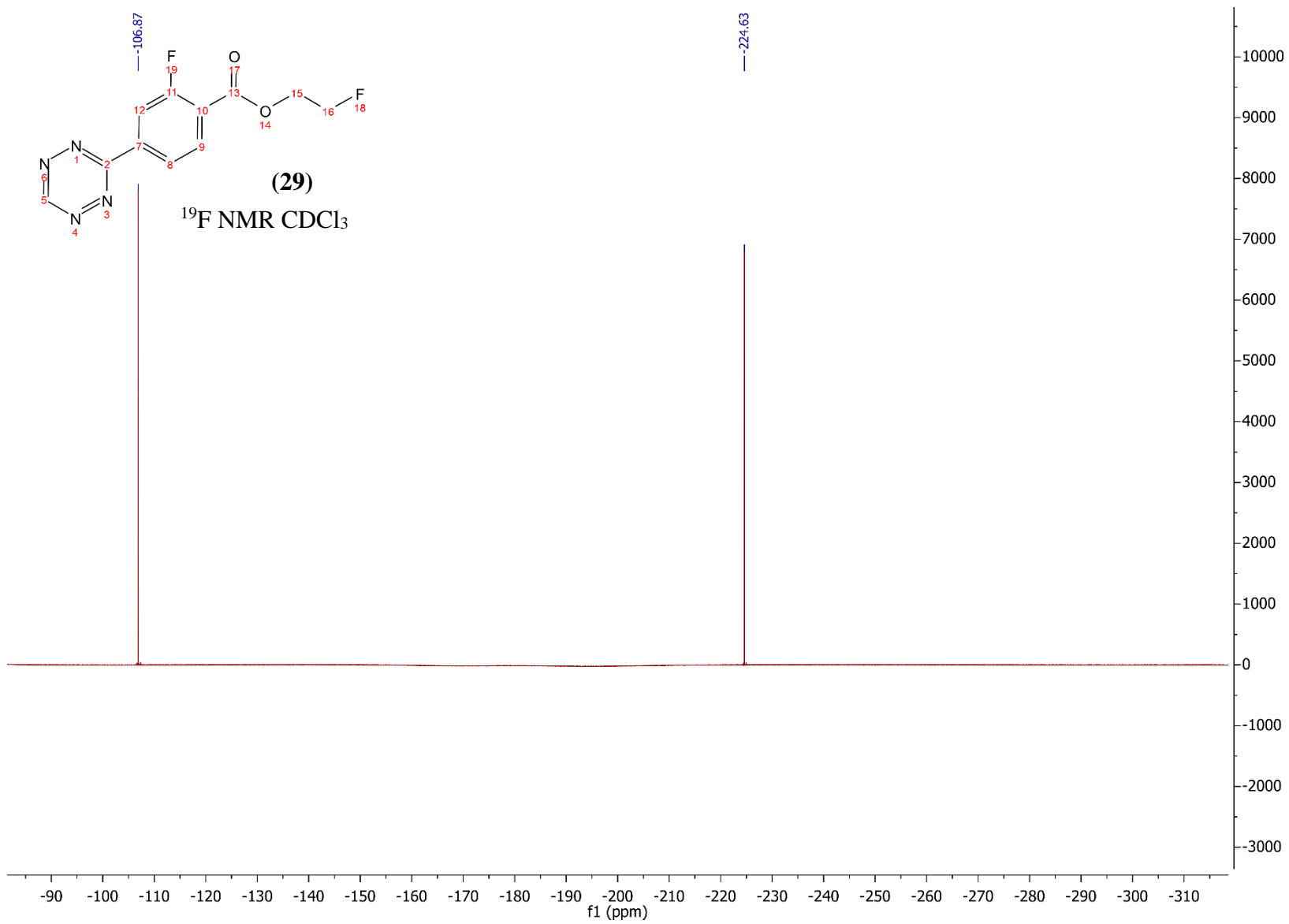
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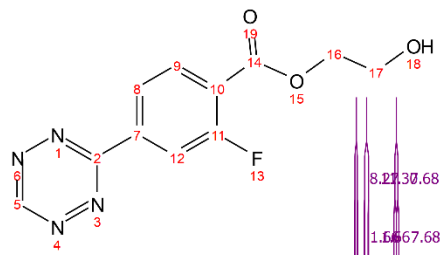
^{19}F NMR CD_3OD





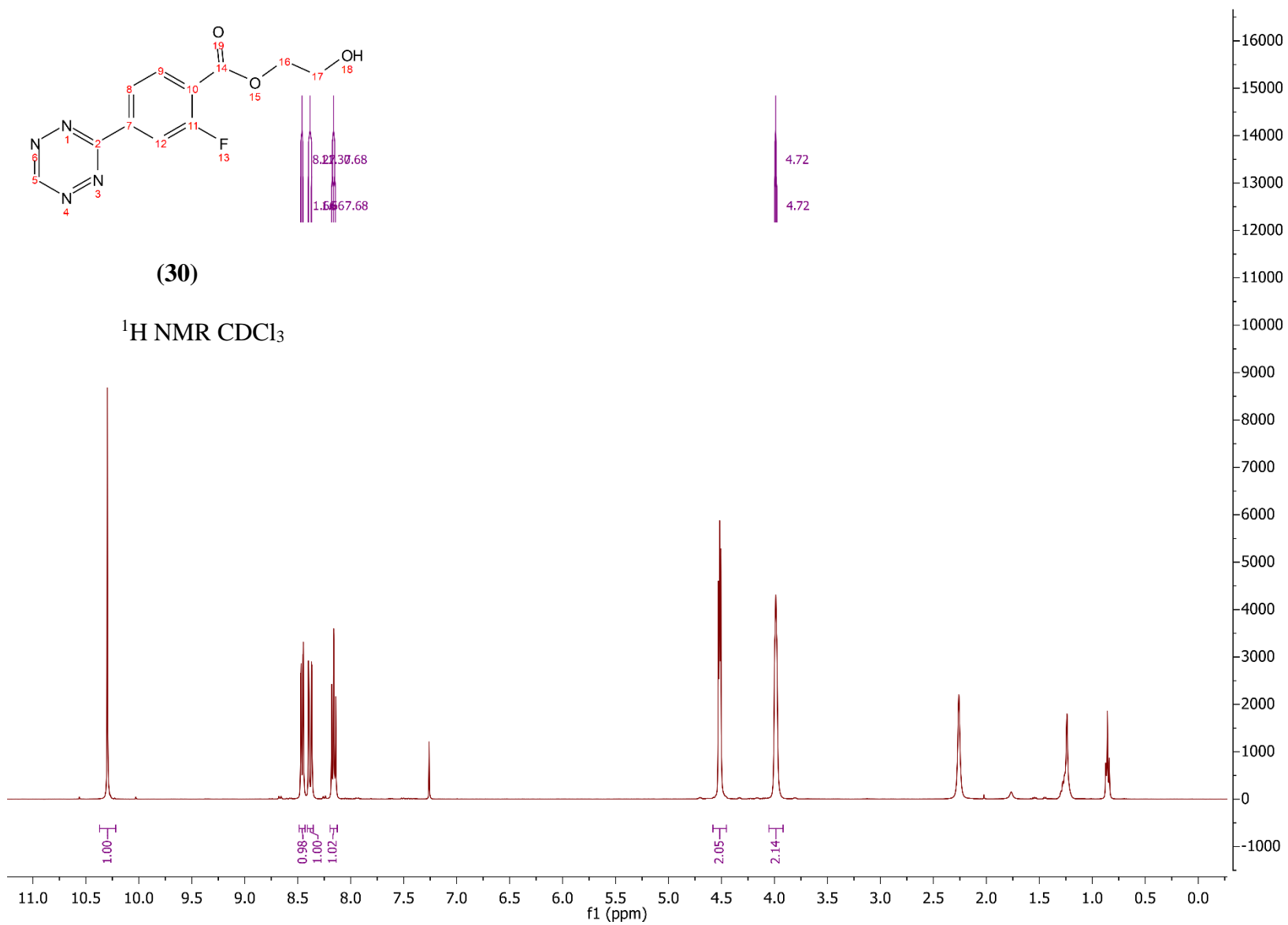


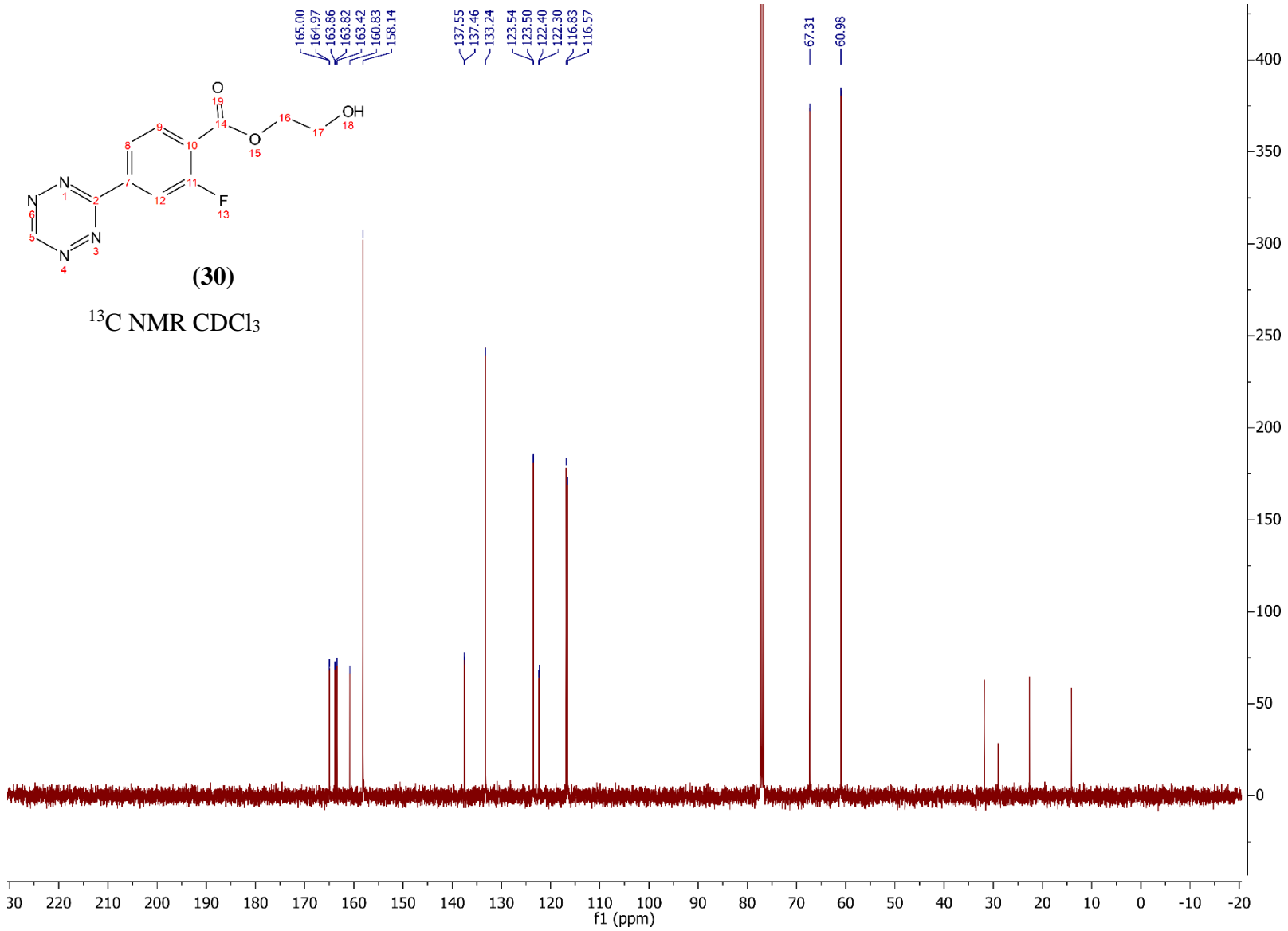


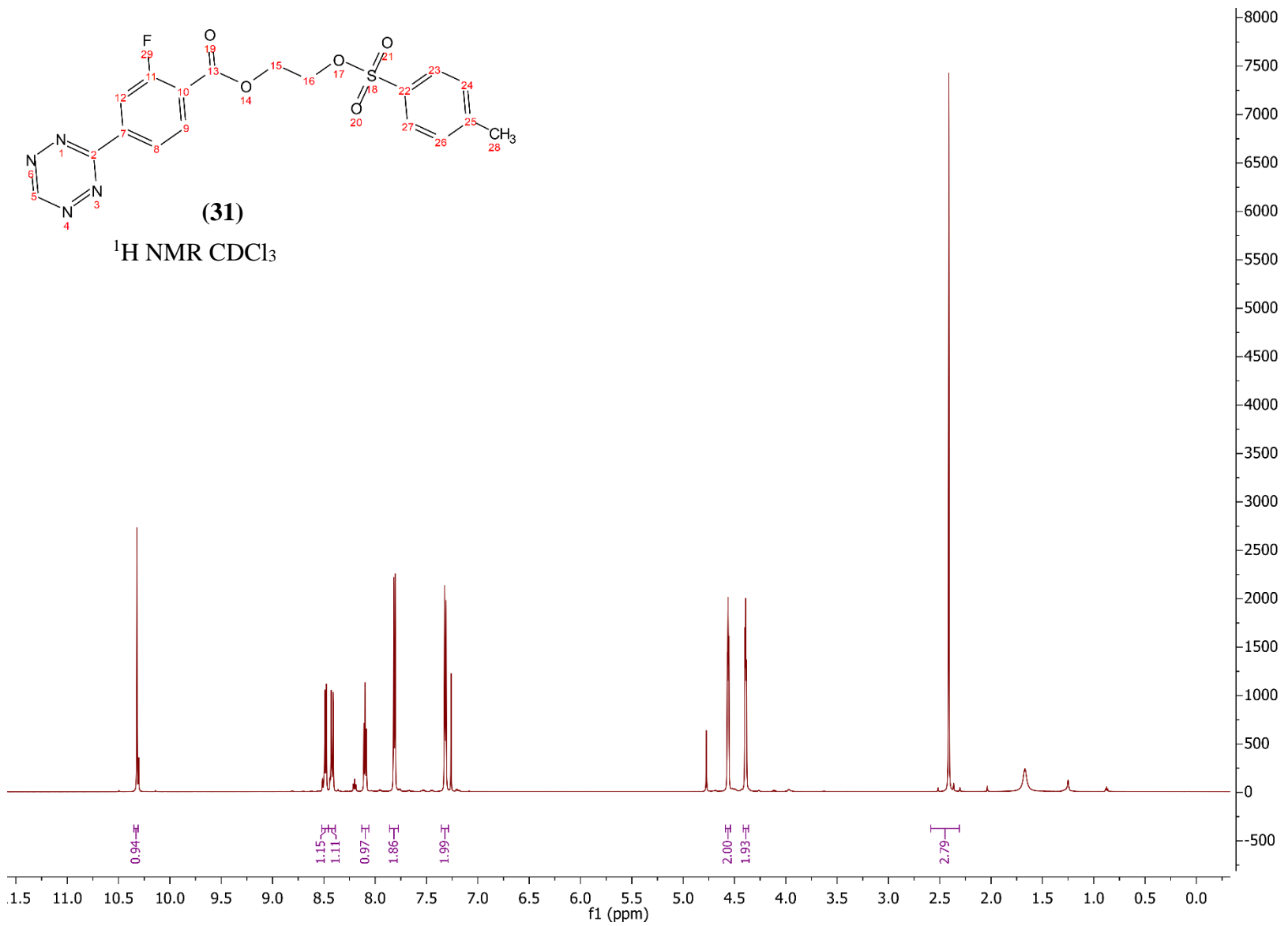


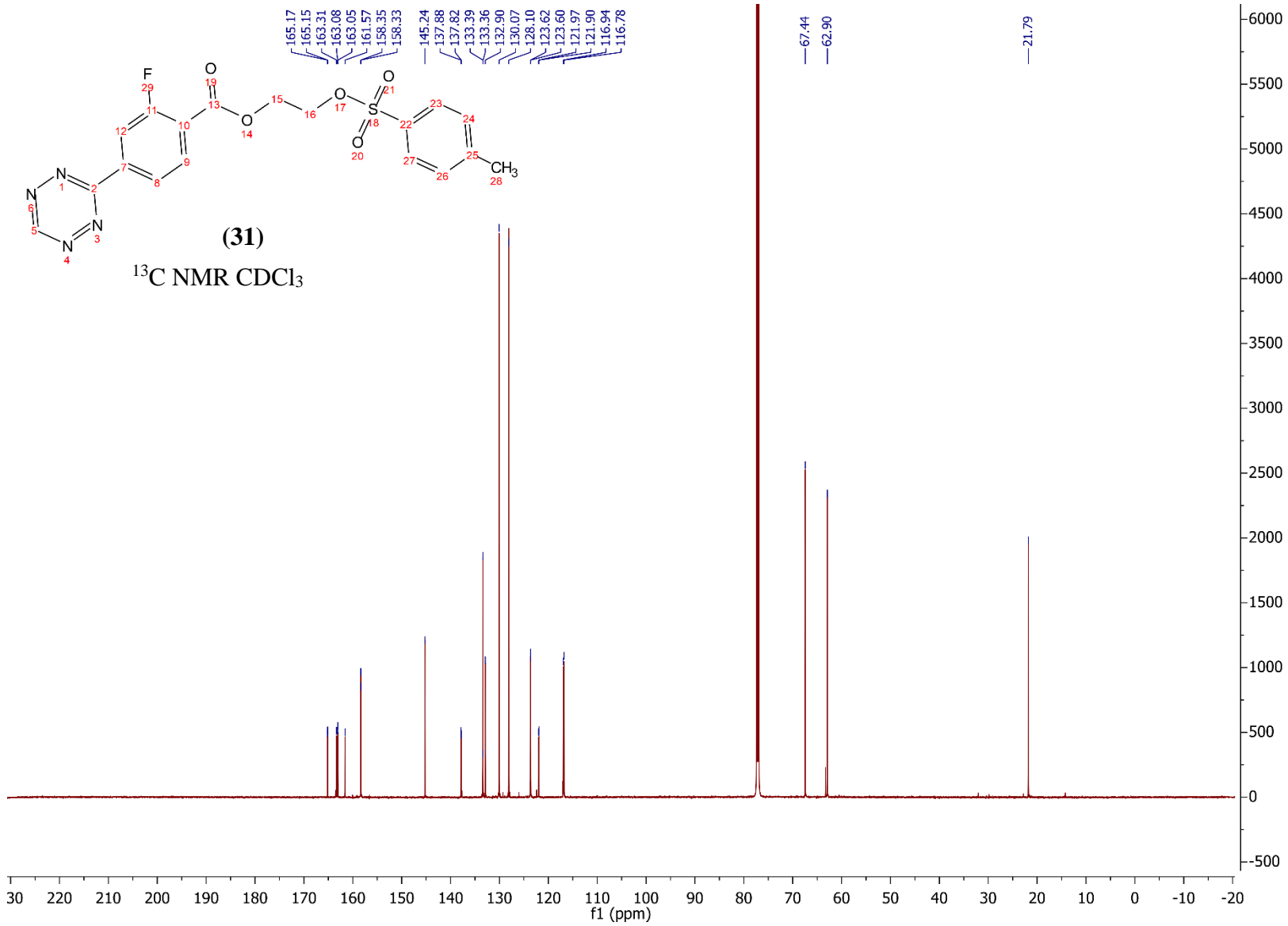
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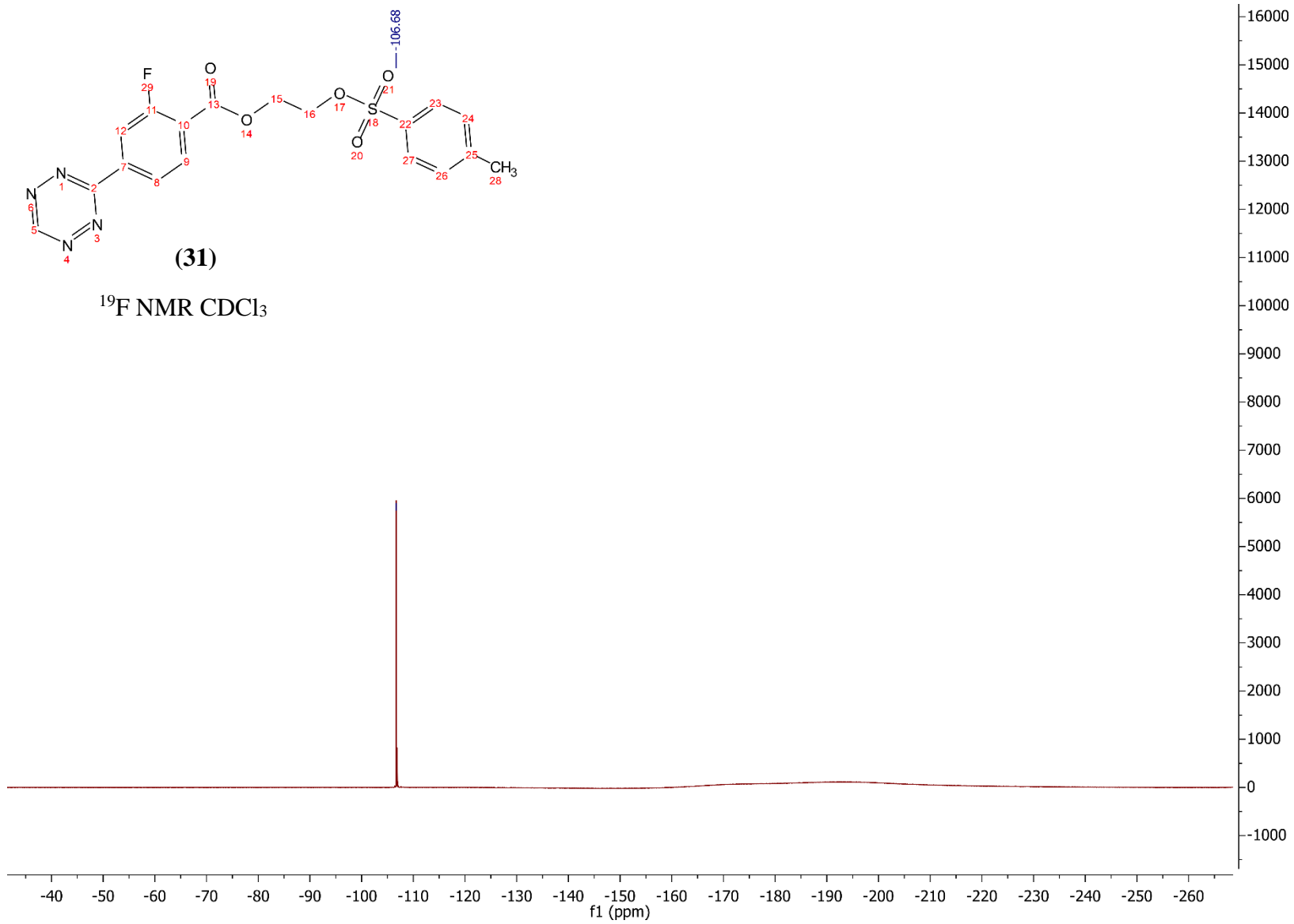
¹H NMR CDCl₃

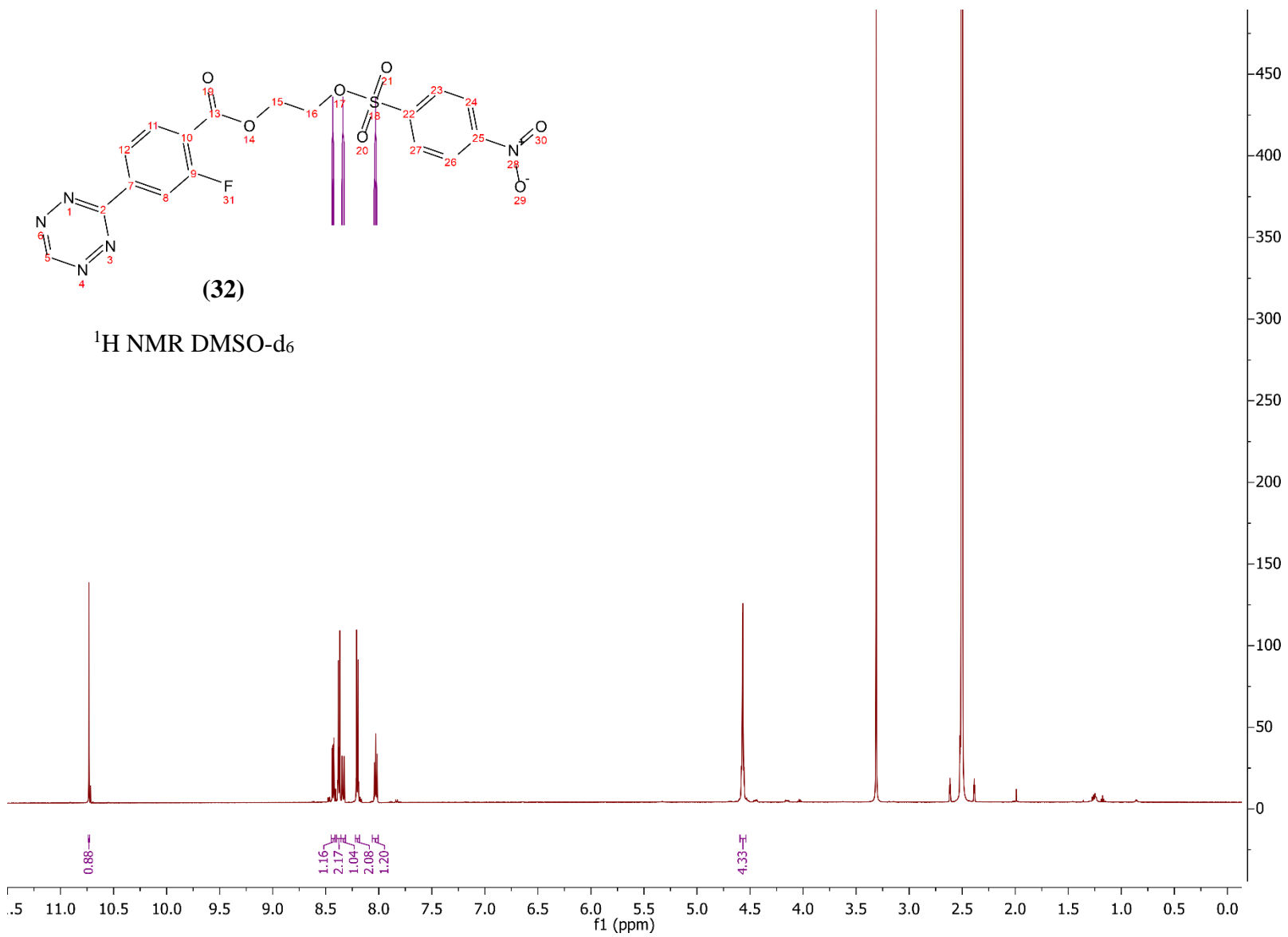


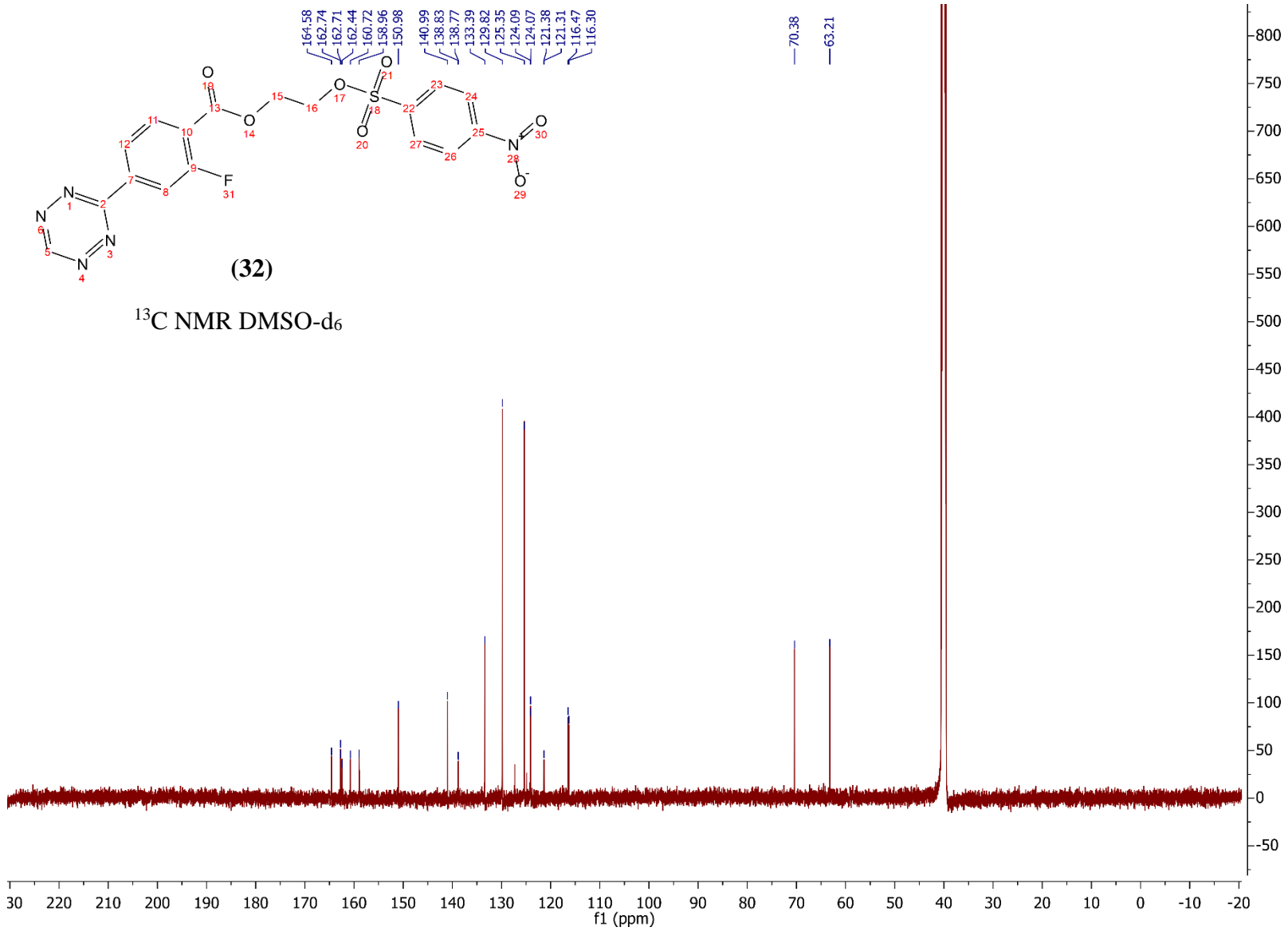


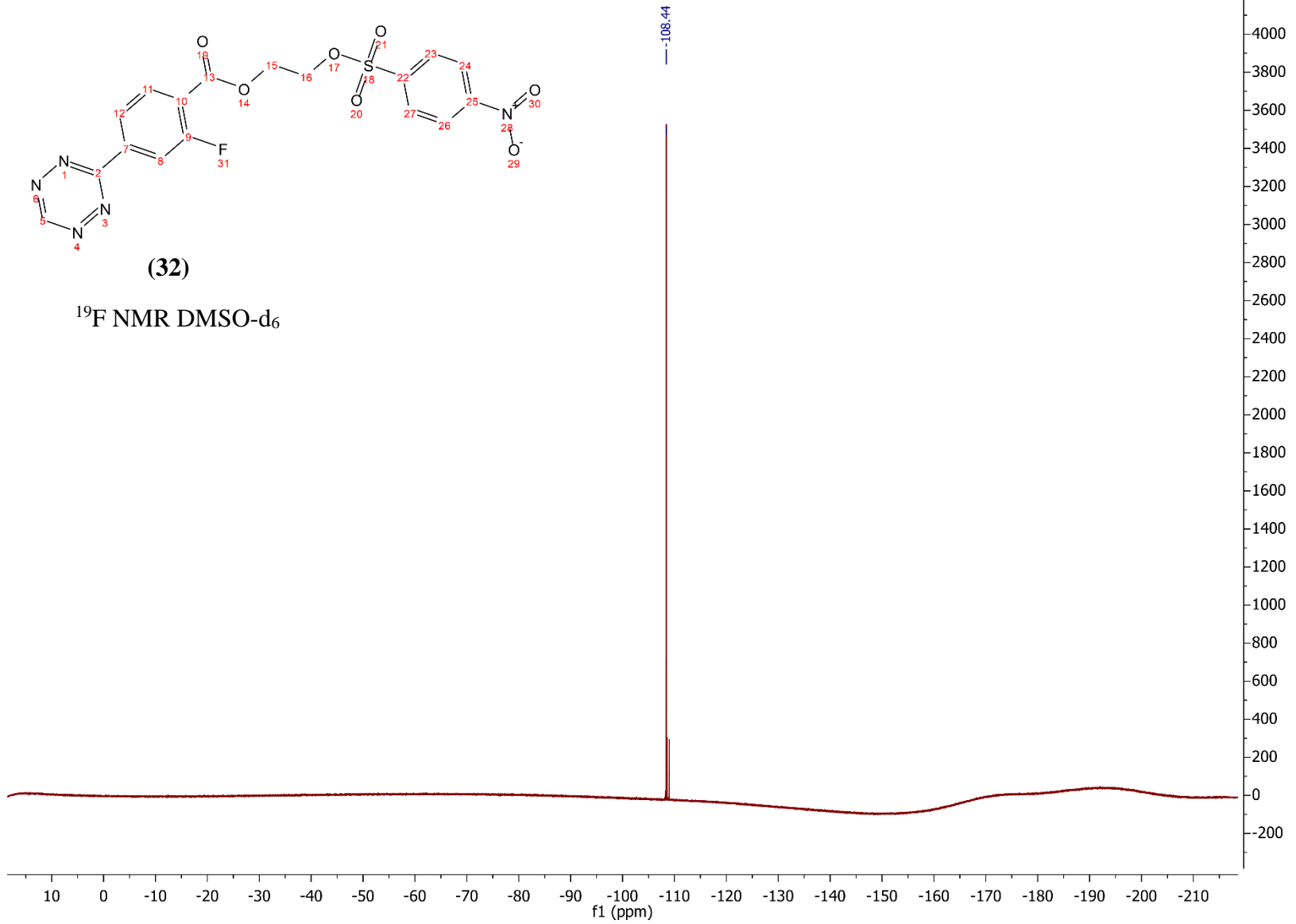












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