Electronic Supplementary Information

Radiosynthesis and Evaluation of PET Ligand [^{18}F]FS1P1 for Imaging Sphingosine-1-Phosphate Receptor 1

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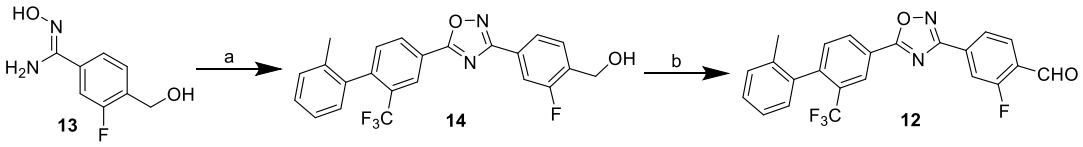
Content

1. Synthesis of compound 12



Scheme S1. Reagents and conditions: (a) **2**, EDCI, HOBt, DMF, RT to 120 °C; (b) Dess-Martin reagent, DCM, 0 °C-RT, 42% for 2 steps.

To a round-bottom flask equipped with a stir bar was added acid **2** (280 mg, 1.0 mmol), HOBt (135 mg, 1.0 mmol), EDCI (287 mg, 1.5 mmol), and DMF (10 mL). The reaction was stirred for 0.5 h followed by adding amidoxime **13** (220 mg 1.2 mmol). Then, the reaction mixture was stirred at 120 °C for 2 h and monitored by TLC. After reaction finished, the reaction mixture was diluted with water and extracted with ethyl acetate. The ethyl acetate layer was washed with saturated brine, and dried over anhydrous $MgSO_4$. After filtration and concentration, the crude residue was used directly for next step without further purification.

The crude residue was dissolved in dichloromethane (10 mL). Dess-Martin reagent (508 mg, 1.0 mmol) was added to the reaction solution at 0 °C. Then, the reaction mixture was stirred at room temperature and monitored by TLC. After accomplishment, the reaction was diluted with dichloromethane and water, the separated dichloromethane layer was washed with saturated brine and dried over anhydrous $MgSO_4$. After filtering and concentrated in vacuum, the crude residue was purified on a silica gel column to afford **12** (180 mg, yield 42%).

2. ^{1}H NMR and ^{13}C NMR spectra for new compounds

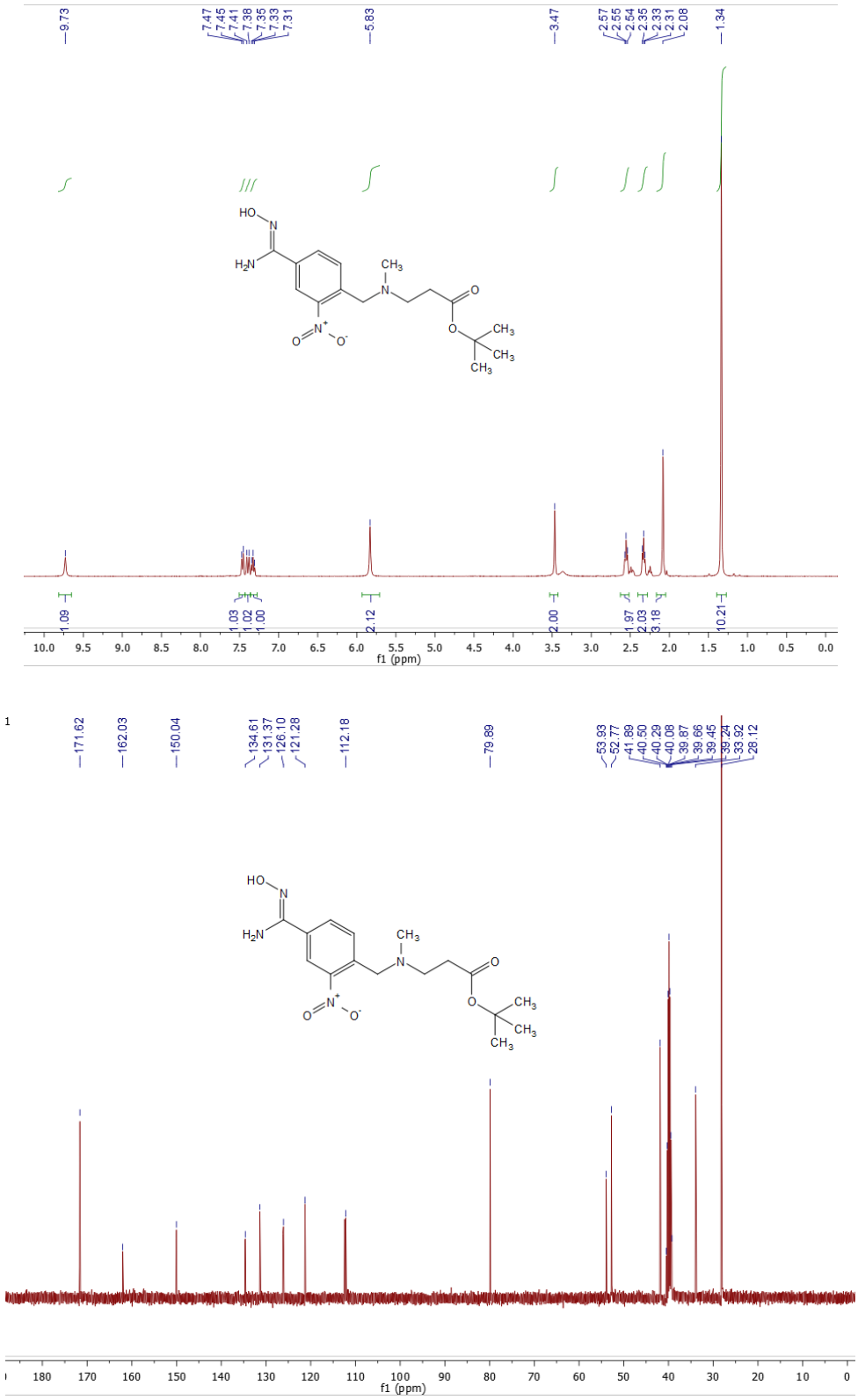


Figure S1. ^{1}H NMR (top) and ^{13}C NMR (bottom) of **4**.

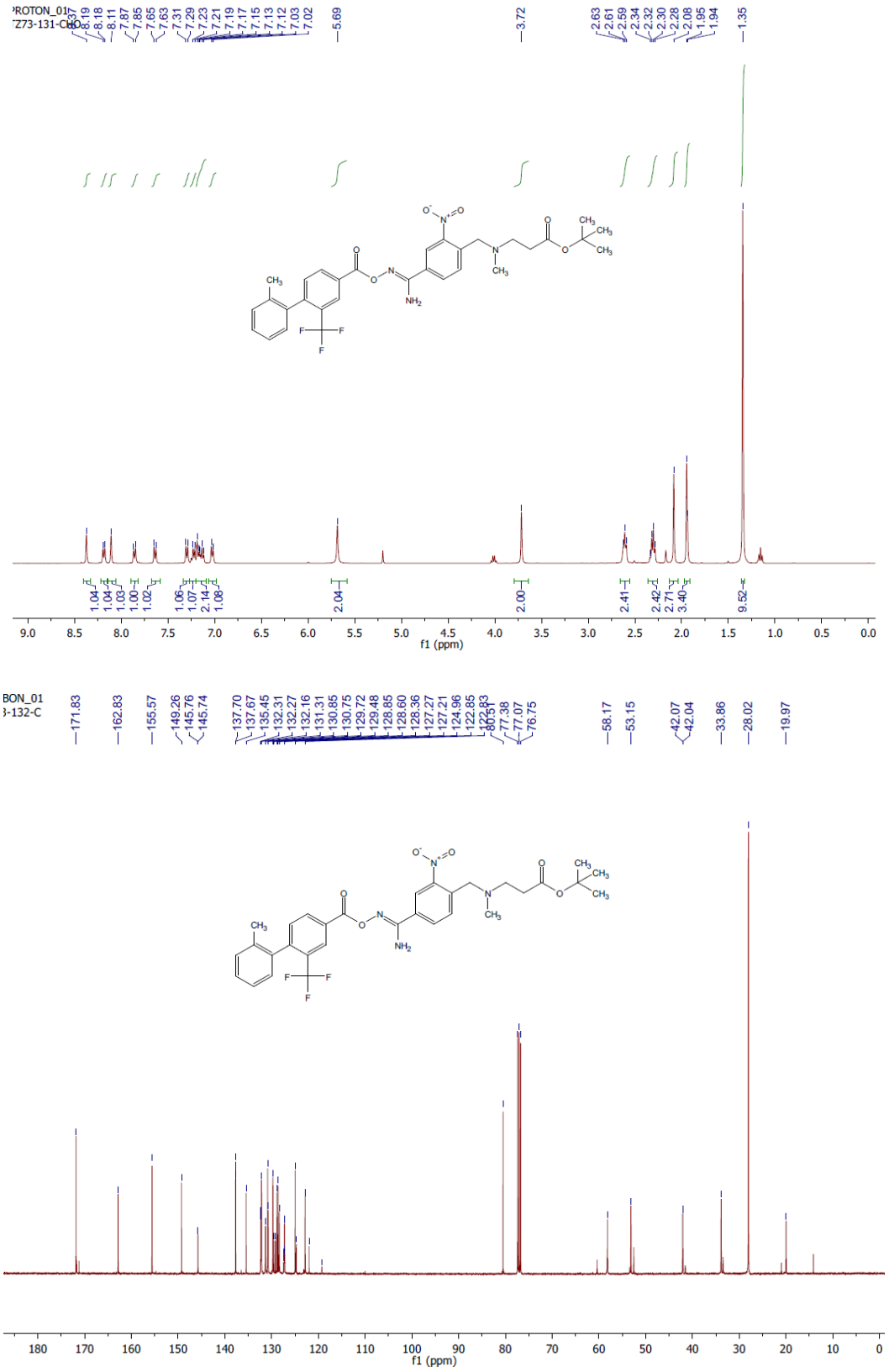


Figure S2. ^{1}H NMR (top) and ^{13}C NMR (bottom) of **5**.

Figure S3. ^{1}H NMR (top) and ^{13}C NMR (bottom) of **6**.

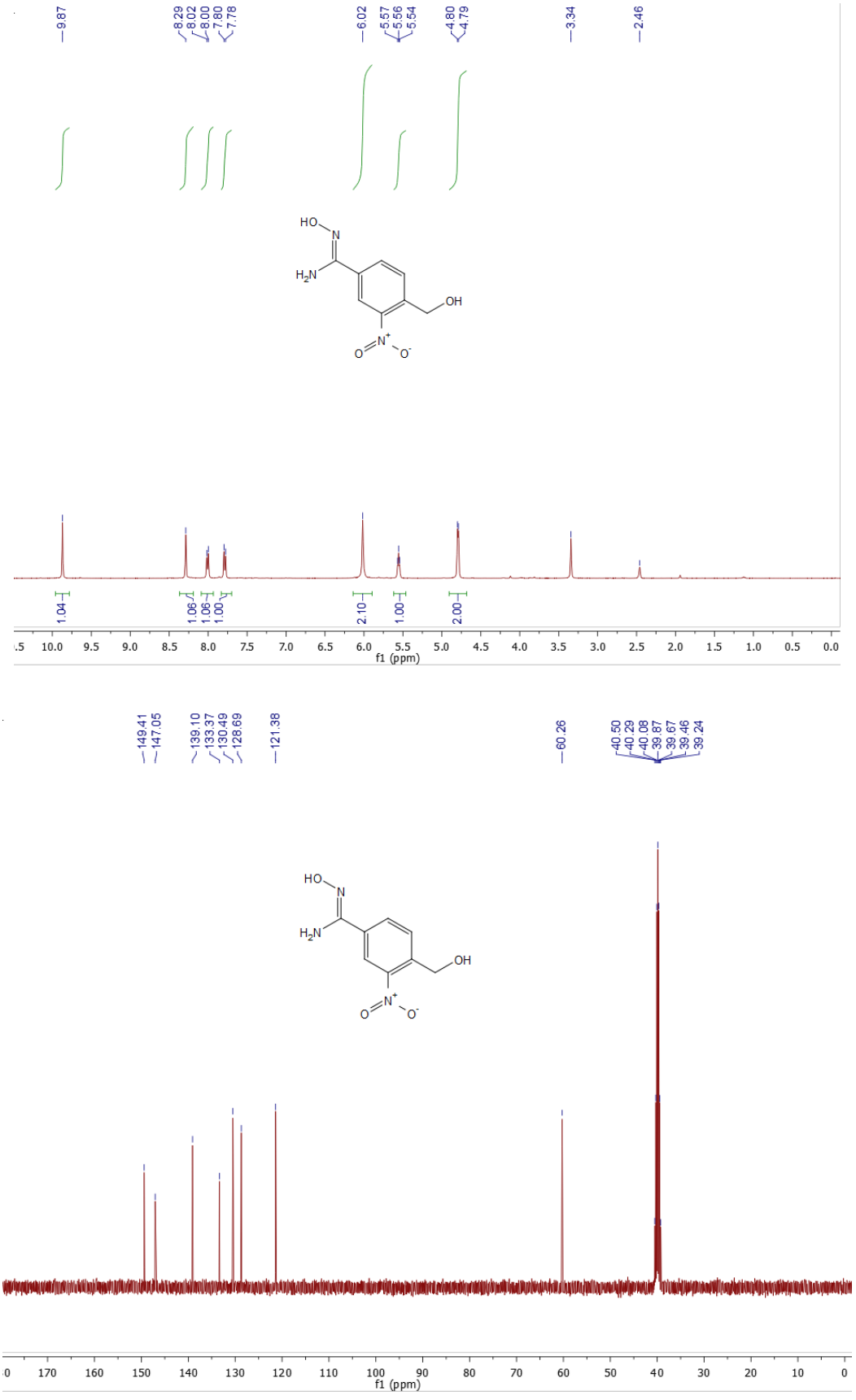


Figure S4. ^{1}H NMR (top) and ^{13}C NMR (bottom) of **7**.

Figure S5. ^{1}H NMR (top) and ^{13}C NMR (bottom) of **8**.

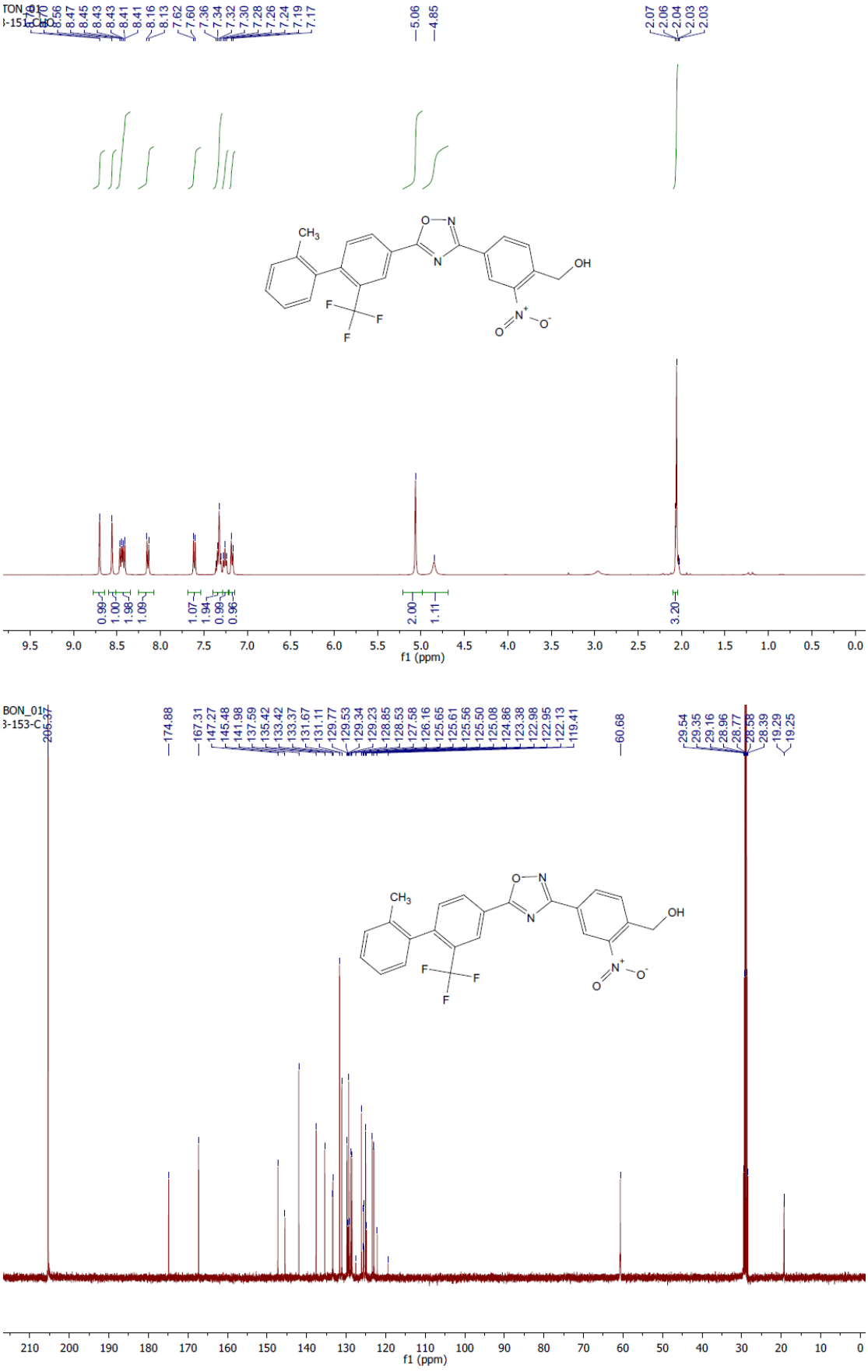


Figure S6. ^{1}H NMR (top) and ^{13}C NMR (bottom) of **9**.

Figure S7. ^{1}H NMR (top) and ^{13}C NMR (bottom) of **10**.

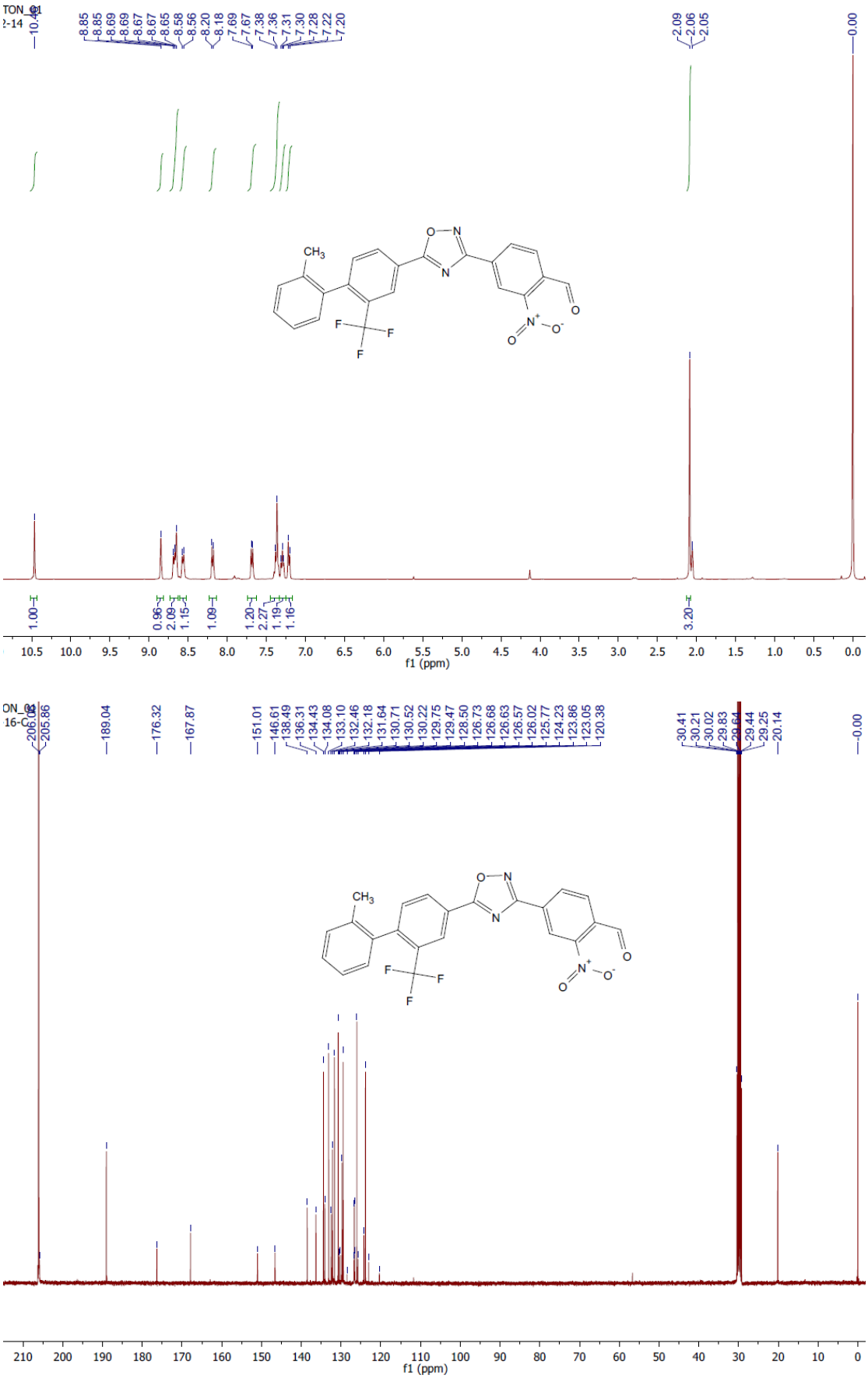


Figure S8. ^{1}H NMR (top) and ^{13}C NMR (bottom) of **11**.

Figure S9. ^{1}H NMR (top) and ^{13}C NMR (bottom) of **12**.

3. Radiochemistry HPLC chromatograms

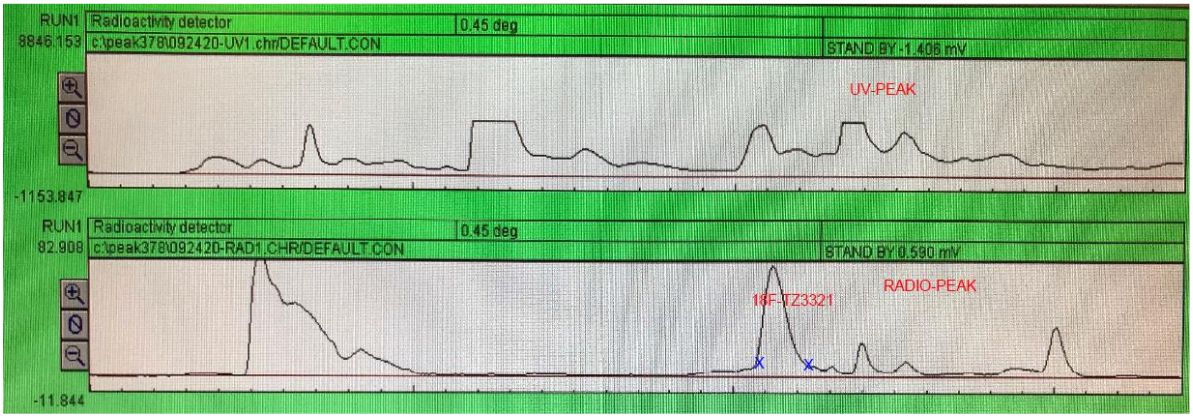


Figure S10. Semi-preparative HPLC chromatogram of the reaction solution [^{18}F]**FS1P1**.

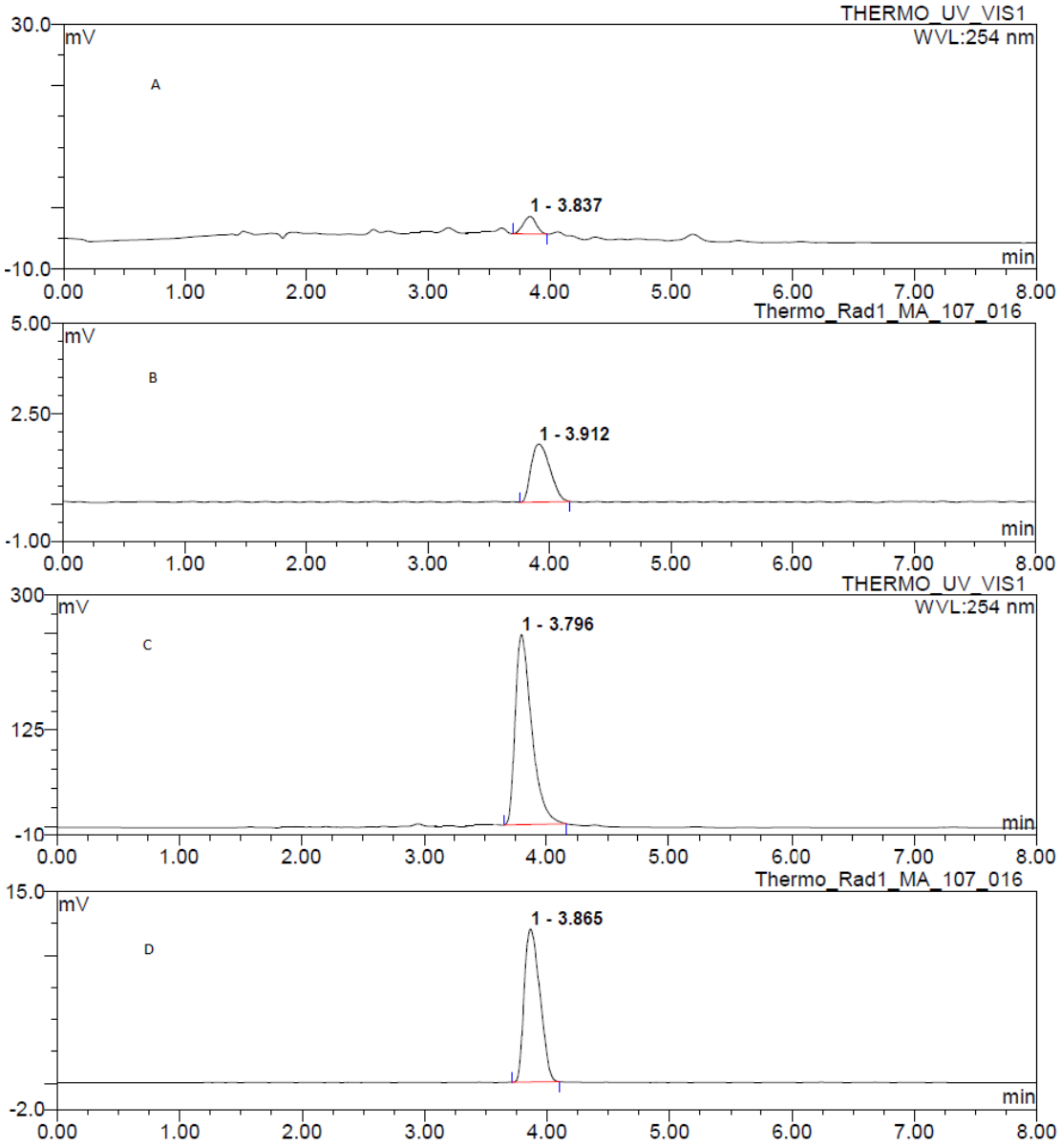


Figure S11. Typical analytical HPLC trace of formulated [^{18}F]**FS1P1**. Panel **A** shows UV trace for [^{18}F]**FS1P1** with 10% ethanol in 0.9% saline; panel **B**: [^{18}F]**FS1P1** radiochemical trace; panel **C**: UV trace for co-injection of [^{18}F]**FS1P1** and **CS1P1**; panel **D**: radiochemical trace for co-injection of [^{18}F]**FS1P1** and **CS1P1**. Analytical HPLC conditions: Phenomenex SB-C18, 250 × 4.6 mm, mobile phase 75% acetonitrile in 0.1 M ammonium formate, pH 4.5, flow rate 1.5 mL/min, detection wavelength 254 nm.

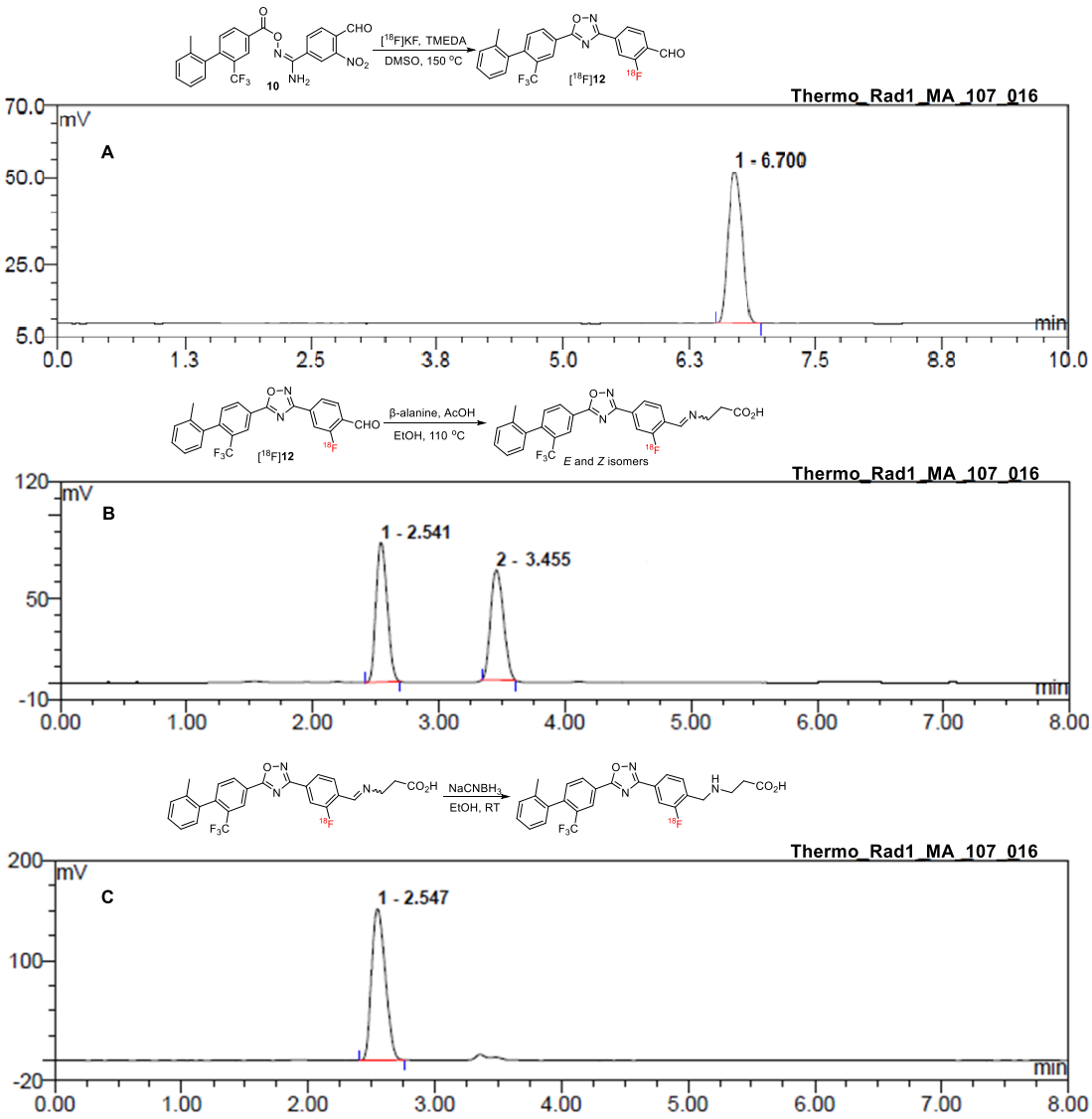


Figure S12. Typical analytical HPLC trace of [^{18}F]-intermediates. Panel **A** shows radiochemical trace for [^{18}F]**12** (step 1); Analytical HPLC conditions: Agilent SB-C18 column, 250 × 4.6 mm, mobile phase 90% acetonitrile in 0.1 M ammonium formate, pH 4.5, flow rate 1.5 mL/min; panel **B**: [^{18}F]imine radiochemical trace (step 2); panel **C**: radiochemical trace of [^{18}F]amino acid (step 3), Analytical HPLC conditions: Phenomenex SB-C18, 250 × 4.6 mm, mobile phase 75% acetonitrile in 0.1 M ammonium formate, pH 4.5, flow rate 1.5 mL/min.