

# Antioxidant activity, DFT-calculation, and docking of 5-amino-*N*-(3-di(per)fluoroalkyl-2-iodo-*n*-propyl)-1,2,3-triazole-4-carboxamides

Ivanna Danyliuk<sup>a\*</sup>, Sergiy Kemsykyi<sup>a</sup>, Lesya Saliyeva<sup>b</sup>, Nataliia Slyvka<sup>b</sup>, Dmytro Mel'nyk<sup>c</sup>,  
Oksana Mel'nyk<sup>c</sup>, Victor Dorokhov<sup>a</sup> and Mykhailo Vovk<sup>a</sup>

<sup>a</sup> *Institute of Organic Chemistry, National Academy of Sciences of Ukraine, 5 Academician Kukhar Str., Kyiv 02660, Ukraine, e-mail: [ivannayu@ukr.net](mailto:ivannayu@ukr.net)* \* Corresponding author. Tel.: +380-68-729-20-47. (I. Danyliuk)

<sup>b</sup> *Lesya Ukrainka Volyn National University, 13 Voli Avenue, Lutsk 43025, Ukraine*

<sup>c</sup> *Ivano-Frankivsk National Medical University, 2 Halytska St., Ivano-Frankivsk 76000, Ukraine*

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## Synthesis and spectra characteristics of compounds 4a-e

*General procedure for the synthesis of compounds 4a-e.* A solution of 5-amino-*N*-(3-di(per)fluoroalkyl-2-iodo-*n*-propyl)-1,2,3-triazole-4-carboxamides **3a-r** (1 mmol) in acetic acid (AcOH) (5 mL) was added dropwise over 15 min to a solution of *t*-BuONO (1.5 mmol) in AcOH (5 mL) at room temperature for 12 h. The solvent was evaporated, water was added (20 mL) and the mixture was extracted with dichloromethane (DCM) (3 x 15 mL). The organic layers were collected, dried over anhydrous MgSO<sub>4</sub> and filtered, the solvent was removed and the residue was purified by column chromatography on silica gel (with a 35:1 chloroform-methanol mixture as an eluent).

*Chemical characterization of N-(4,4-difluoro-2-iodopentyl)-1-phenyl-1H-1,2,3-triazole-4-carboxamide (4a).* White solid, mp 117-119°C; yield 81%. <sup>1</sup>H-NMR (302 MHz, CDCl<sub>3</sub>): δ 1.69 (t, 3H, *J* = 18.4 Hz, CF<sub>2</sub>CH<sub>3</sub>), 2.62-2.75 (m, 2H, CH<sub>2</sub>CF<sub>2</sub>), 3.73-3.82 (m, 1H, CH<sub>2</sub>NH), 3.96-4.04 (m, 1H, CH<sub>2</sub>NH), 4.44-4.52 (m, 1H, CH-I), 7.50-7.65 (m, 4H, Ar-H + NH), 7.74-7.76 (m, 2H, Ar-H), 8.51 (m, 1H, 1H<sub>triazole</sub>). <sup>13</sup>C-NMR (151 MHz, CDCl<sub>3</sub>): δ CF<sub>2</sub> signals are not assigned, 22.17, 23.88 (t, *J* = 27.2 Hz), 46.23 (t, *J* = 25.7 Hz), 47.30, 120.75, 123.68, 129.50, 129.97, 136.50, 143.33, 159.91. <sup>19</sup>F-NMR (188 MHz, CDCl<sub>3</sub>): δ - 86.44 to - 88.07 (m, 1F), - 89.63 to - 91.30 (m, 1F). IR (KBr, cm<sup>-1</sup>): 1662 (C=O), 3303-3373 (N-H). HRMS-ESI (m/z): [M+H]<sup>+</sup> calcd for C<sub>14</sub>H<sub>16</sub>F<sub>2</sub>IN<sub>4</sub>O<sup>+</sup>, 421.0331; found 421.0332.

*Chemical characterization of N-(4,4,5,5,6,6,7,7,7-nonafluoro-2-iodoheptyl)-1-phenyl-1H-1,2,3-triazole-4-carboxamide (4b).* White solid, mp 165-167°C; yield 90%. <sup>1</sup>H-NMR (302 MHz, CDCl<sub>3</sub>): δ 2.81-2.99 (m, 2H, CH<sub>2</sub>CF<sub>2</sub>), 3.80-3.89 (m, 1H, CH<sub>2</sub>NH), 3.94-4.04 (m, 1H, CH<sub>2</sub>NH), 4.49-4.59 (m, 1H, CH-I), 7.48-7.60 (m, 3H, Ar-H + NH), 7.71-7.77 (m, 3H, Ar-H), 8.54 (m, 1H, 1H<sub>triazole</sub>). <sup>13</sup>C-NMR (76 MHz, CDCl<sub>3</sub>): δ CF<sub>3</sub>(CF<sub>2</sub>)<sub>3</sub> signals are not assigned, 17.18, 39.01 (t, *J* = 21.3 Hz), 47.39, 120.86, 123.90, 129.68, 130.10, 136.55, 143.20, 160.12. <sup>19</sup>F-NMR (188 MHz, CDCl<sub>3</sub>): δ - 80.75 to - 80.84 (m, 3F), - 112.82 to - 113.51 (m, 2F), - 124.11 to - 124.28 (m, 2F), - 125.61 to - 125.75 (m, 2F). IR (KBr, cm<sup>-1</sup>): 1659 (C=O), 3333 (N-H). HRMS-ESI (m/z): [M+H]<sup>+</sup> calcd for C<sub>16</sub>H<sub>13</sub>F<sub>9</sub>IN<sub>4</sub>O<sup>+</sup>, 574.9985; found 574.9996.

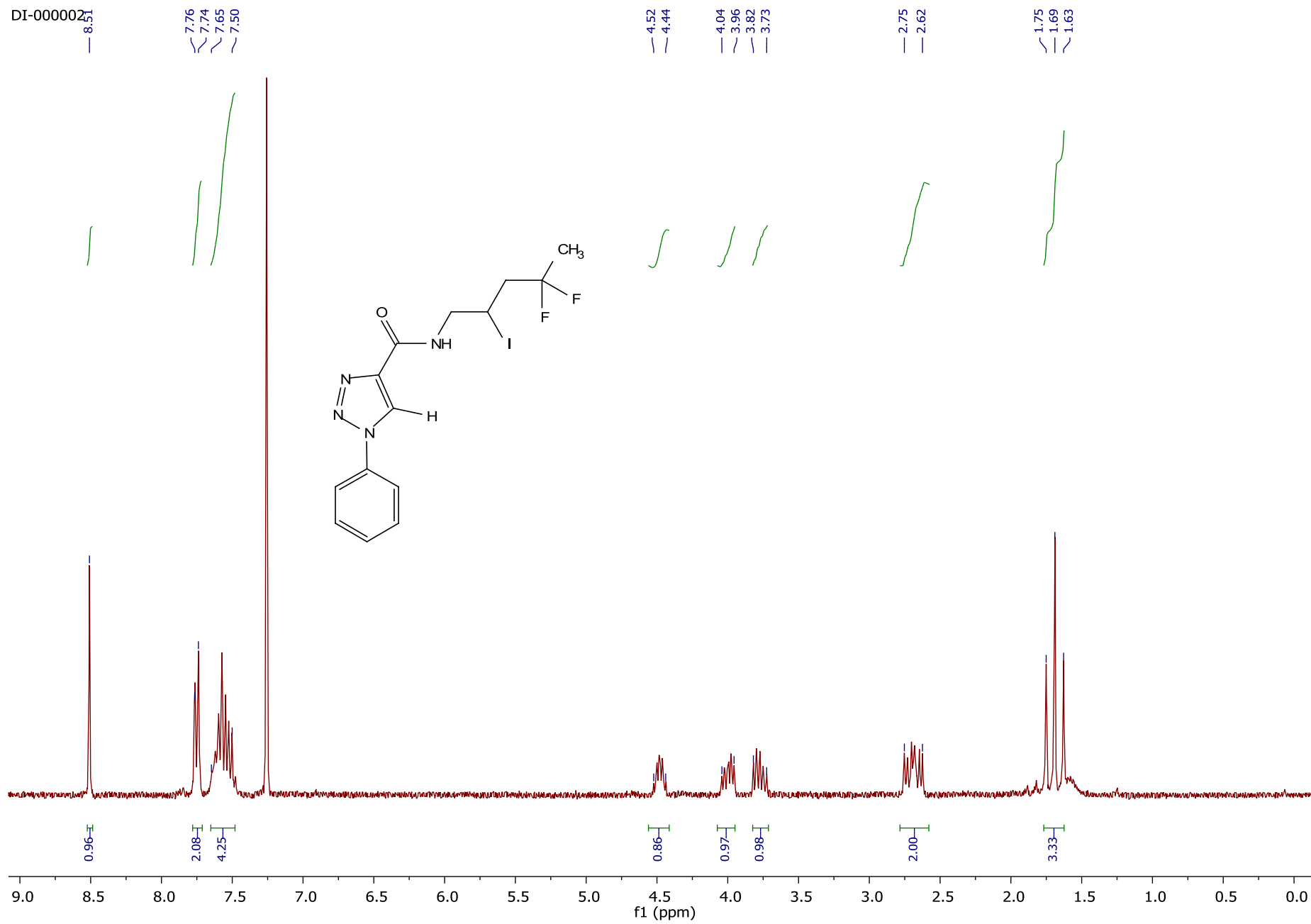
*Chemical characterization of N-(4,4-difluoro-2-iodopentyl)-1-(4-methoxyphenyl)-1H-1,2,3-triazole-4-carboxamide (4c).* White solid, mp 145-147°C; yield 93%. <sup>1</sup>H-NMR (302 MHz, CDCl<sub>3</sub>): δ 1.68 (t, 3H, *J* = 18.1 Hz, CF<sub>2</sub>CH<sub>3</sub>), 2.62-2.75 (m, 2H, CH<sub>2</sub>CF<sub>2</sub>), 3.72-3.81 (m, 1H, CH<sub>2</sub>NH), 3.88 (s, 3H, OCH<sub>3</sub>), 3.94-4.03 (m, 1H, CH<sub>2</sub>NH), 4.43-4.52 (m, 1H, CH-I), 7.04 (d, 2H, *J* = 9.1 Hz, Ar-H); 7.63-7.66 (m, 3H, Ar-H + NH), 8.42 (m, 1H, 1H<sub>triazole</sub>). <sup>13</sup>C-NMR (126 MHz, CDCl<sub>3</sub>): δ 21.66, 23.35 (t, *J* = 27.7 Hz), 45.71

(t,  $J = 25.4$  Hz), 46.83, 55.16, 114.47, 121.86, 122.58 (t,  $J = 241.3$  Hz,  $\text{CF}_3$ ), 123.25, 129.36, 142.64, 159.53, 159.85.  $^{19}\text{F}$ -NMR (188 MHz,  $\text{CDCl}_3$ ):  $\delta$  - 86.48 to - 88.03 (m, 1F); - 89.57 to - 91.24 (m, 1F). IR (KBr,  $\text{cm}^{-1}$ ): 1662 (C=O), 3293 (N-H). HRMS-ESI ( $m/z$ ):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{15}\text{H}_{18}\text{F}_2\text{IN}_4\text{O}_2^+$ , 451.0437; found 451.0440.

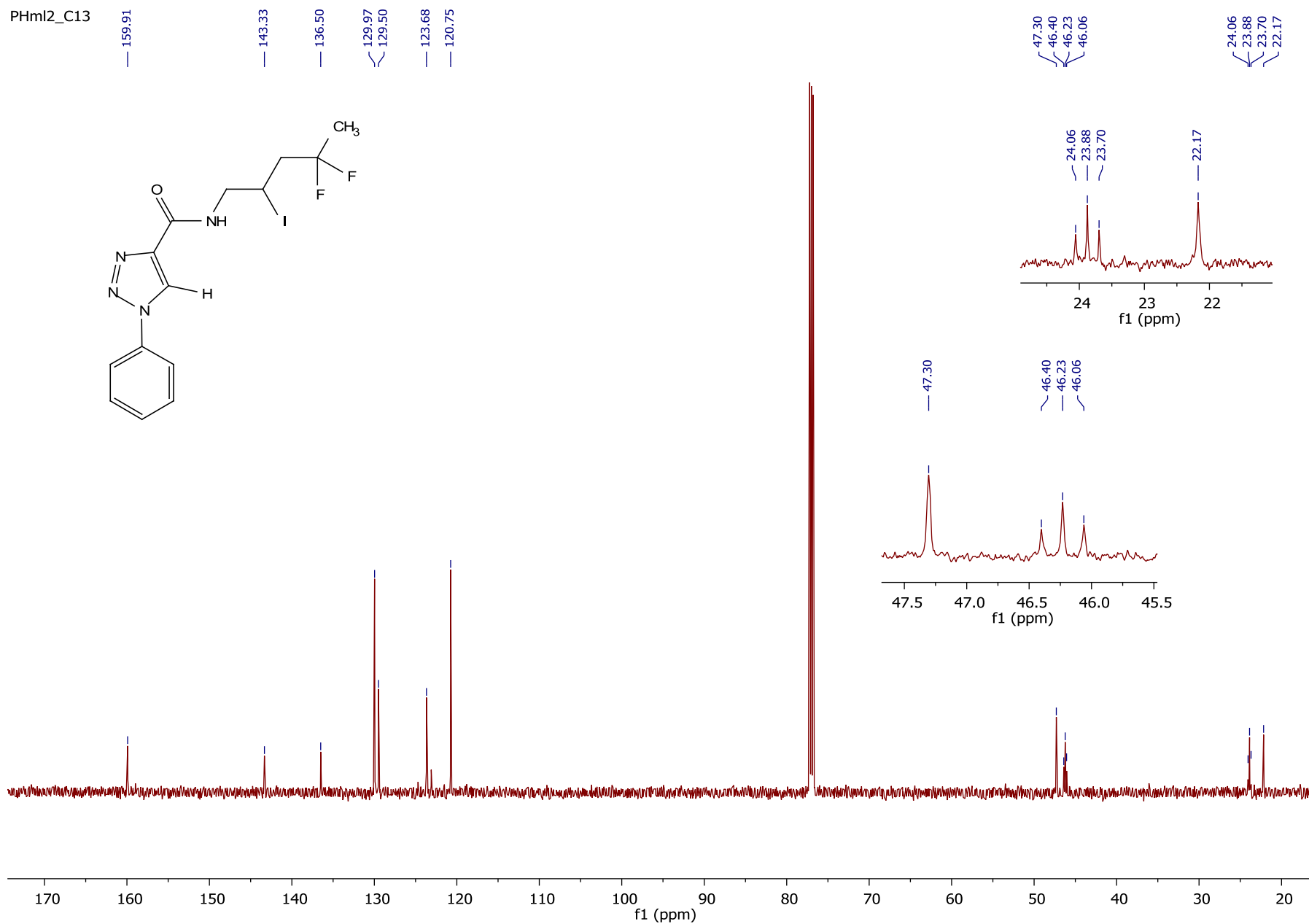
*Chemical characterization of N-(4,4-difluoro-2-iodopentyl)-1-(4-fluorophenyl)-1H-1,2,3-triazole-4-carboxamide (4d).* White solid, mp 133-135°C; yield 85%.  $^1\text{H}$ -NMR (302 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.69 (t, 3H,  $J = 19.6$  Hz,  $\text{CF}_2\text{CH}_3$ ), 2.62-2.75 (m, 2H,  $\text{CH}_2\text{CF}_2$ ), 3.72-3.82 (m, 1H,  $\text{CH}_2\text{NH}$ ), 3.95-4.04 (m, 1H,  $\text{CH}_2\text{NH}$ ), 4.44-4.52 (m, 1H, CH-I), 7.24-7.29 (m, 2H, Ar-H), 7.59-7.64 (m, 1H, NH), 7.71-7.76 (m, 2H, Ar-H), 8.47 (m, 1H,  $1\text{H}_{\text{triazole}}$ ).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{CDCl}_3$ ):  $\delta$  22.14, 23.89 (t,  $J = 27.2$  Hz), 46.24 (t,  $J = 25.7$  Hz), 47.29, 117.00 (d,  $J = 24.2$  Hz), 122.81 (d,  $J = 9.1$  Hz), 123.12 (t,  $J = 240.8$  Hz,  $\text{CF}_3$ ), 123.89, 132.74 (d,  $J = 3.02$  Hz), 143.42, 159.81, 162.84 (d,  $J = 250.7$  Hz).  $^{19}\text{F}$ -NMR (188 MHz,  $\text{CDCl}_3$ ):  $\delta$  - 86.50 to - 88.16 (m, 1F); - 89.82 to - 91.40 (m, 1F); - 110.67 (s, 1F). IR (KBr,  $\text{cm}^{-1}$ ): 1660 (C=O), 3309-3355 (N-H). HRMS-ESI ( $m/z$ ):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{14}\text{H}_{15}\text{F}_3\text{IN}_4\text{O}^+$ , 439.0237; found 439.0239.

*Chemical characterization of 1-(4-fluorophenyl)-N-(4,4,5,5,6,6,7,7,7-nonafluoro-2-iodoheptyl)-1H-1,2,3-triazole-4-carboxamide (4e).* White solid, mp 158-160°C; yield 87%.  $^1\text{H}$ -NMR (302 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.83-2.97 (m, 2H,  $\text{CH}_2\text{CF}_2$ ), 3.78-3.88 (m, 1H,  $\text{CH}_2\text{NH}$ ), 3.94-4.03 (m, 1H,  $\text{CH}_2\text{NH}$ ), 4.48-4.57 (m, 1H, CH-I), 7.24-7.30 (m, 2H, Ar-H), 7.63-7.67 (m, 1H, NH), 7.71-7.76 (m, 2H, Ar-H), 8.48 (m, 1H,  $1\text{H}_{\text{triazole}}$ ).  $^{13}\text{C}$ -NMR (151 MHz,  $\text{CDCl}_3$ ):  $\delta$   $\text{CF}_3(\text{CF}_2)_3$  signals are not assigned, 17.03, 38.94 (t,  $J = 21.1$  Hz), 47.29, 117.03 (d,  $J = 24.2$  Hz), 122.82 (d,  $J = 9.0$  Hz), 123.97, 132.70 (d,  $J = 3.0$  Hz), 143.23, 159.89, 162.89 (d,  $J = 250.7$  Hz).  $^{19}\text{F}$ -NMR (188 MHz,  $\text{CDCl}_3$ ):  $\delta$  - 80.86 to - 80.97 (m, 3F); - 110.54 (s, 1F); - 112.89 to -113.69 (m, 2F); - 124.21 to -124.44 (m, 2F); - 125.69 to -125.93 (m, 2F). IR (KBr,  $\text{cm}^{-1}$ ): 1656 (C=O), 3339 (N-H). HRMS-ESI ( $m/z$ ):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{16}\text{H}_{12}\text{F}_{10}\text{IN}_4\text{O}^+$ , 592.9890; found 592.9893.

Figure S1. <sup>1</sup>H NMR spectrum (302 MHz, CDCl<sub>3</sub>) of compound **4a**



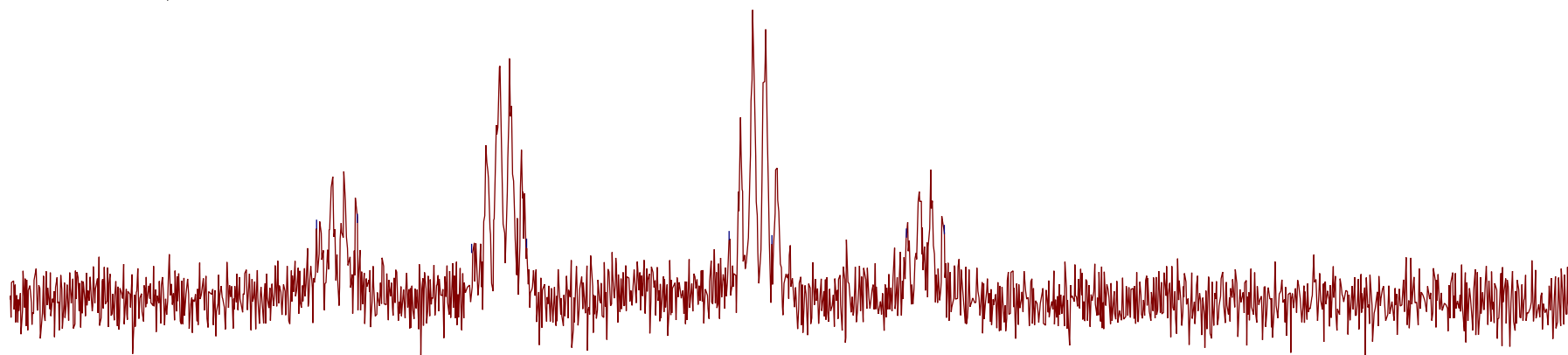
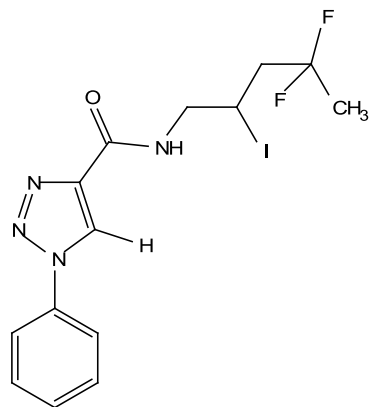
**Figure S2.**  $^{13}\text{C}$  NMR spectrum (151 MHz,  $\text{CDCl}_3$ ) of compound **4a**



**Figure S3.**  $^{19}\text{F}$  NMR spectrum (188 MHz,  $\text{CDCl}_3$ ) of compound **4a**

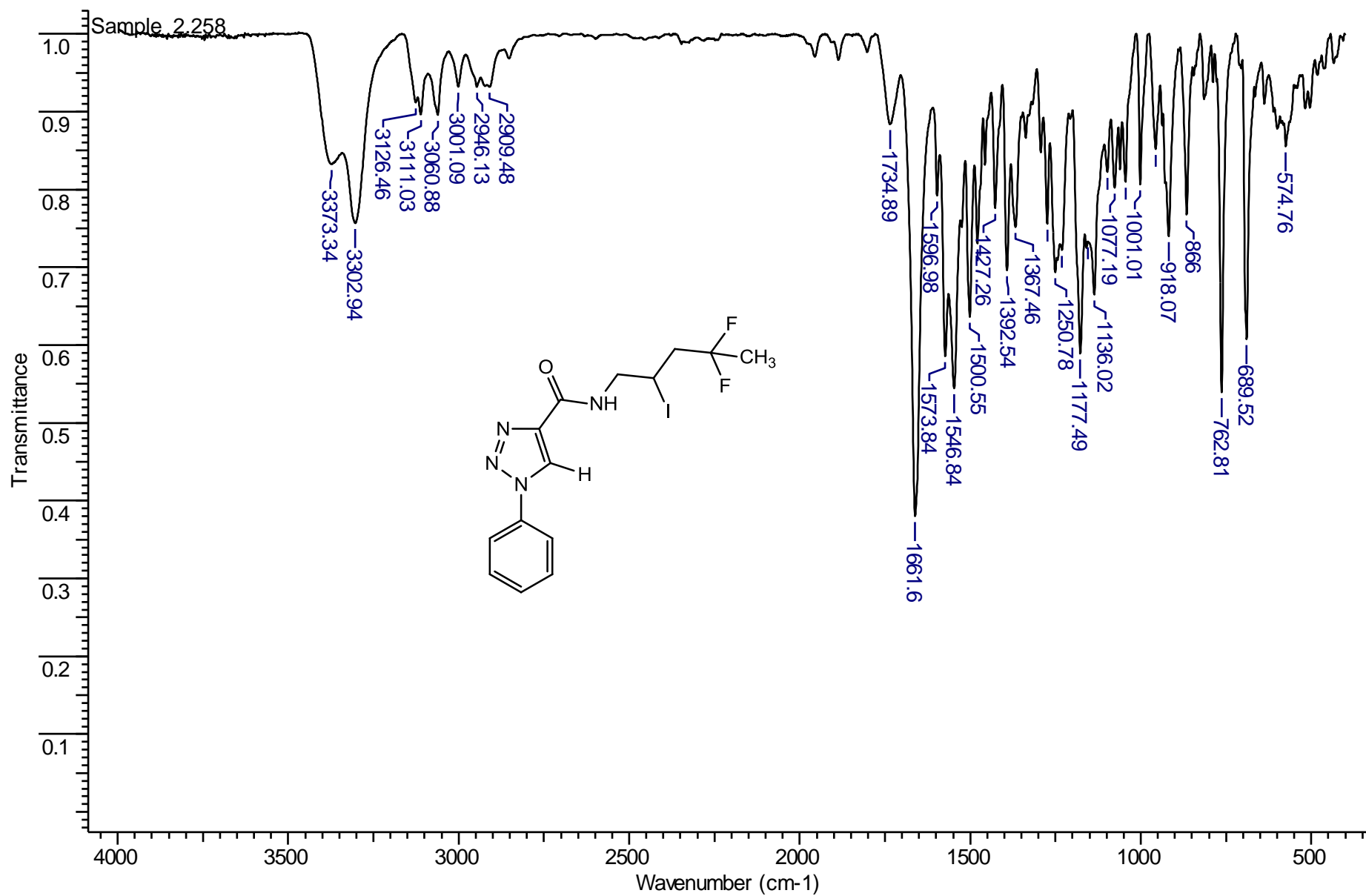
DI-240190-19f  
Frequency 188.13  
Solvent  $\text{cdcl}_3$   
Temp. 25.0  
2024-12-09T13:16:54

-86.44    -86.76    -87.64    -88.07    -89.63    -89.97    -91.01    -91.30



-84.5 -85.0 -85.5 -86.0 -86.5 -87.0 -87.5 -88.0 -88.5 -89.0 -89.5 -90.0 -90.5 -91.0 -91.5 -92.0 -92.5 -93.0 -93.5 -94.0 -94.5 -95.0 -95.5 -96.0  
f1 (ppm)

Figure S4. IR spectrum of compound 4a





**Figure S5.**  $^1\text{H}$  NMR spectrum (302 MHz,  $\text{CDCl}_3$ ) of compound **4b**

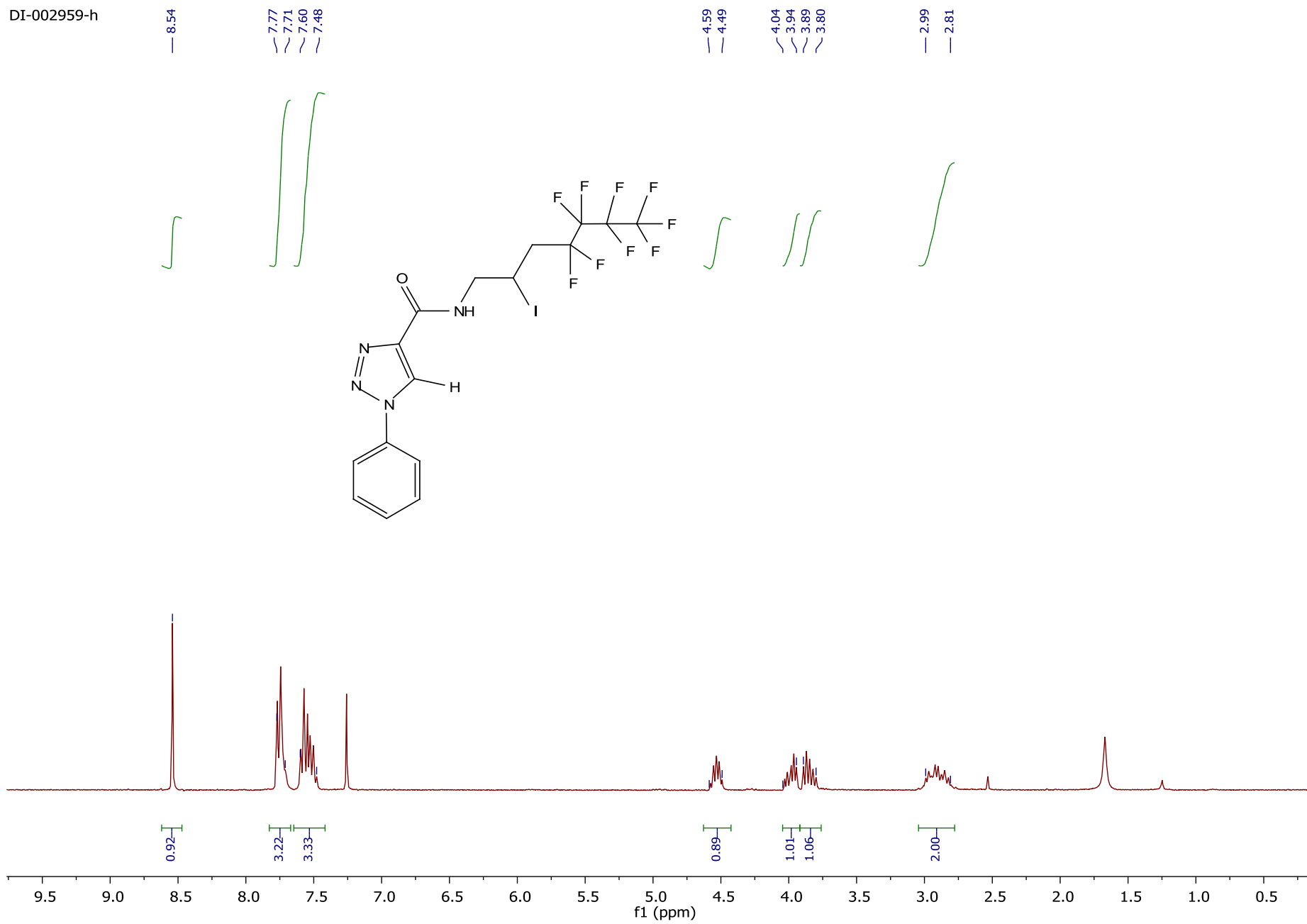


Figure S6.  $^{13}\text{C}$  NMR spectrum (76 MHz,  $\text{CDCl}_3$ ) of compound **4b**

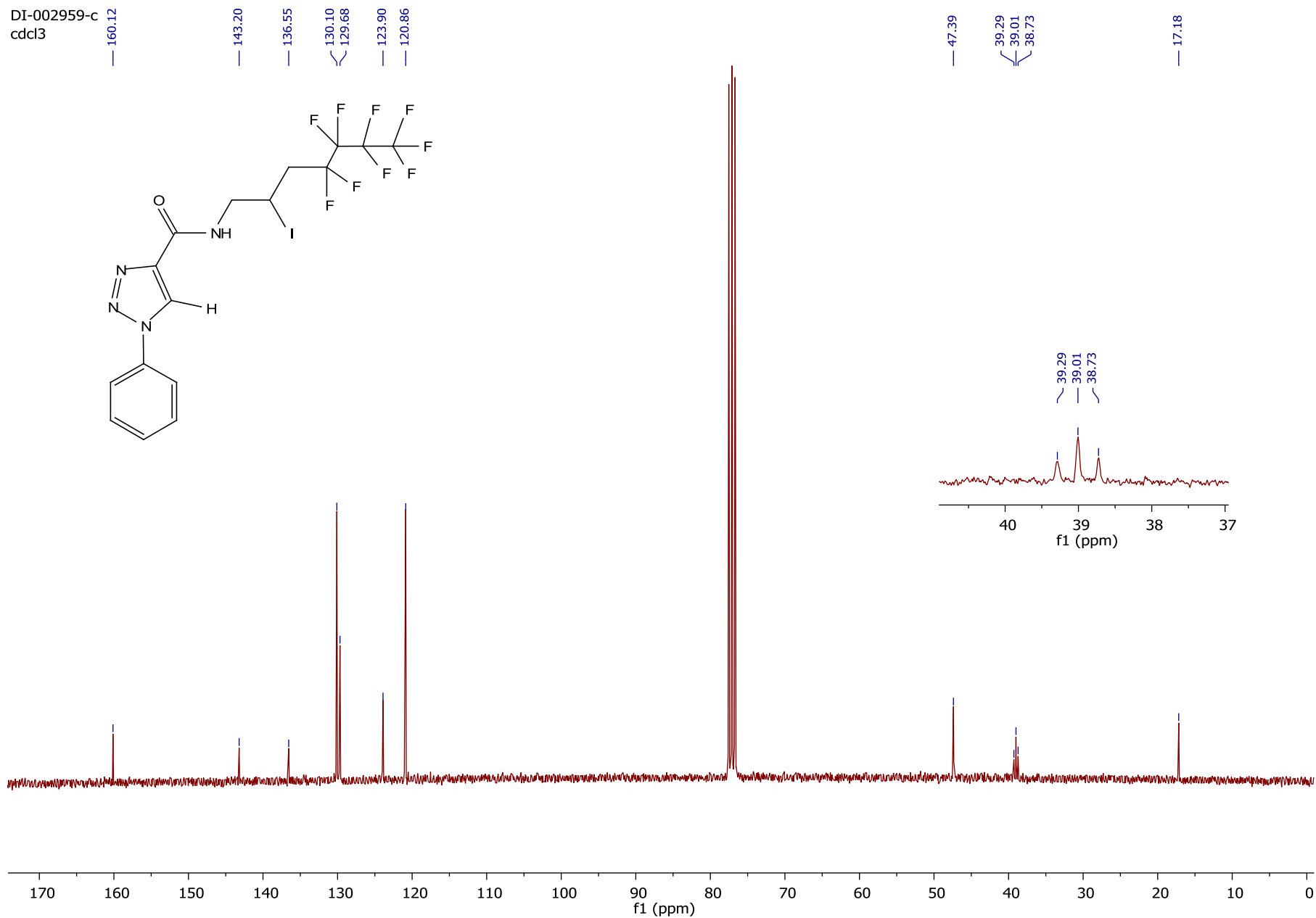


Figure S7. <sup>19</sup>F NMR spectrum (188 MHz, CDC<sub>3</sub>) of compound **4b**

DI-002959-19f  
F19 cdcl3

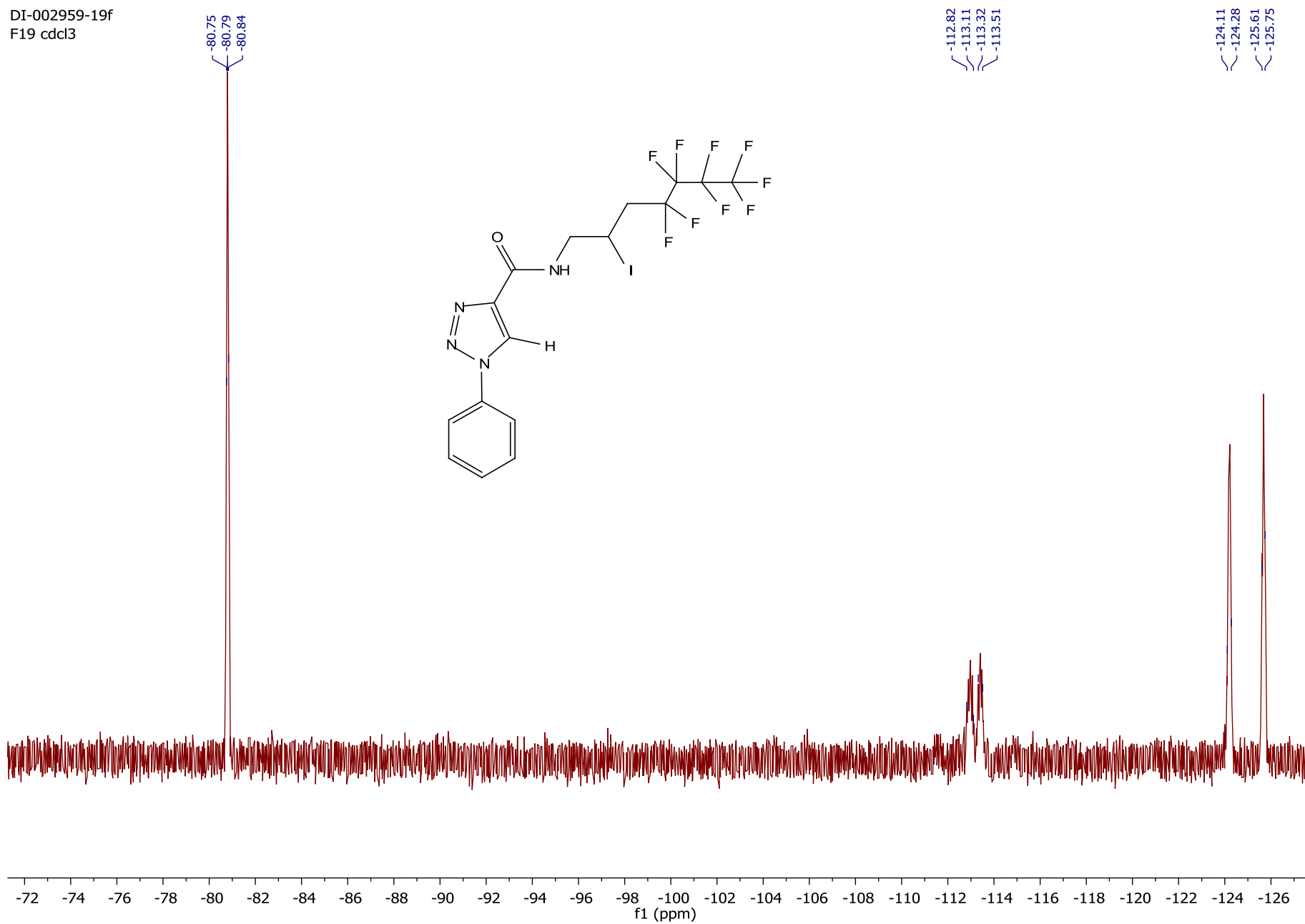


Figure S8. IR spectrum of compound 4b

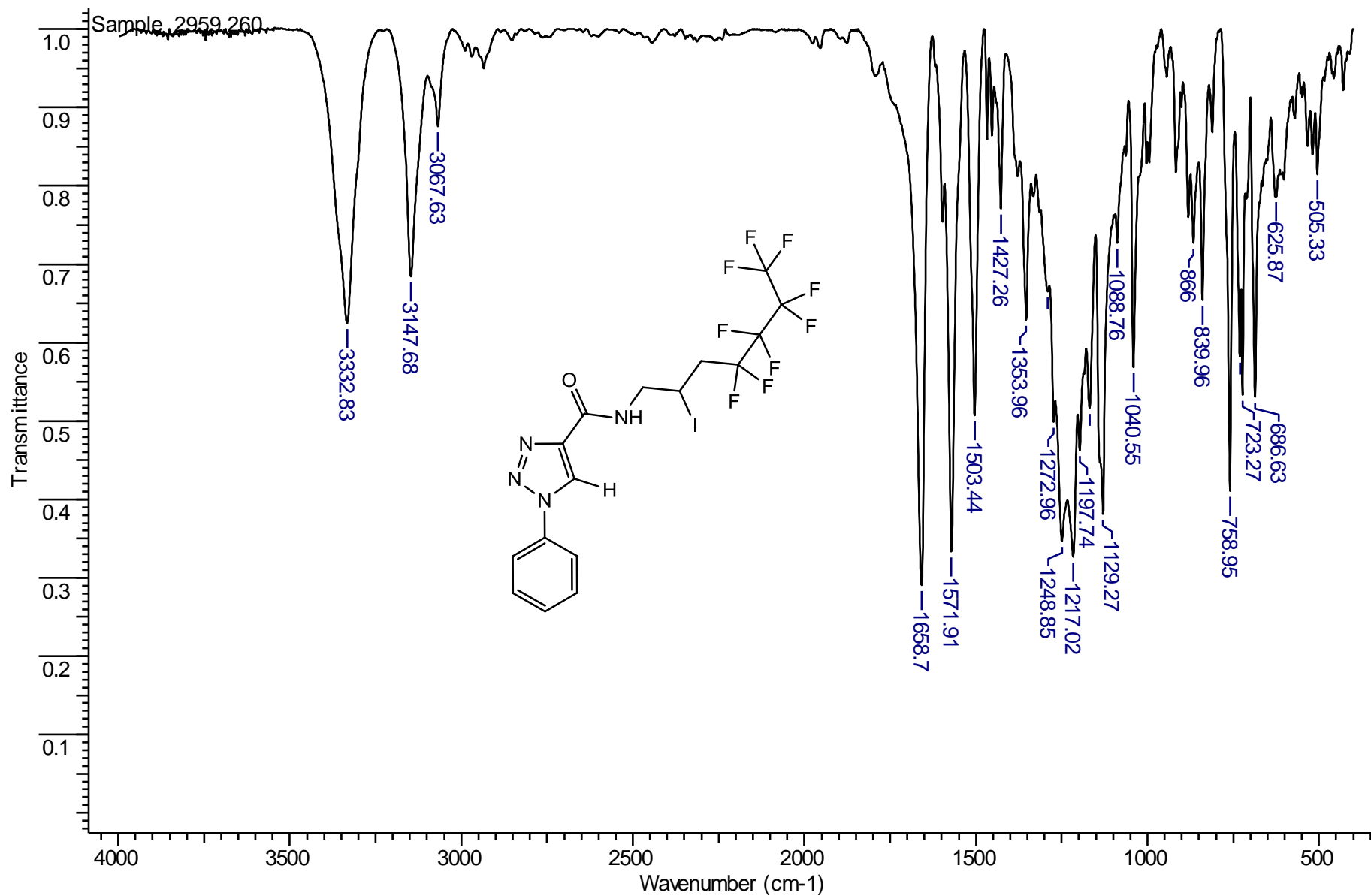


Figure S9 <sup>1</sup>H NMR spectrum (302 MHz, CDCl<sub>3</sub>) of compound 4c

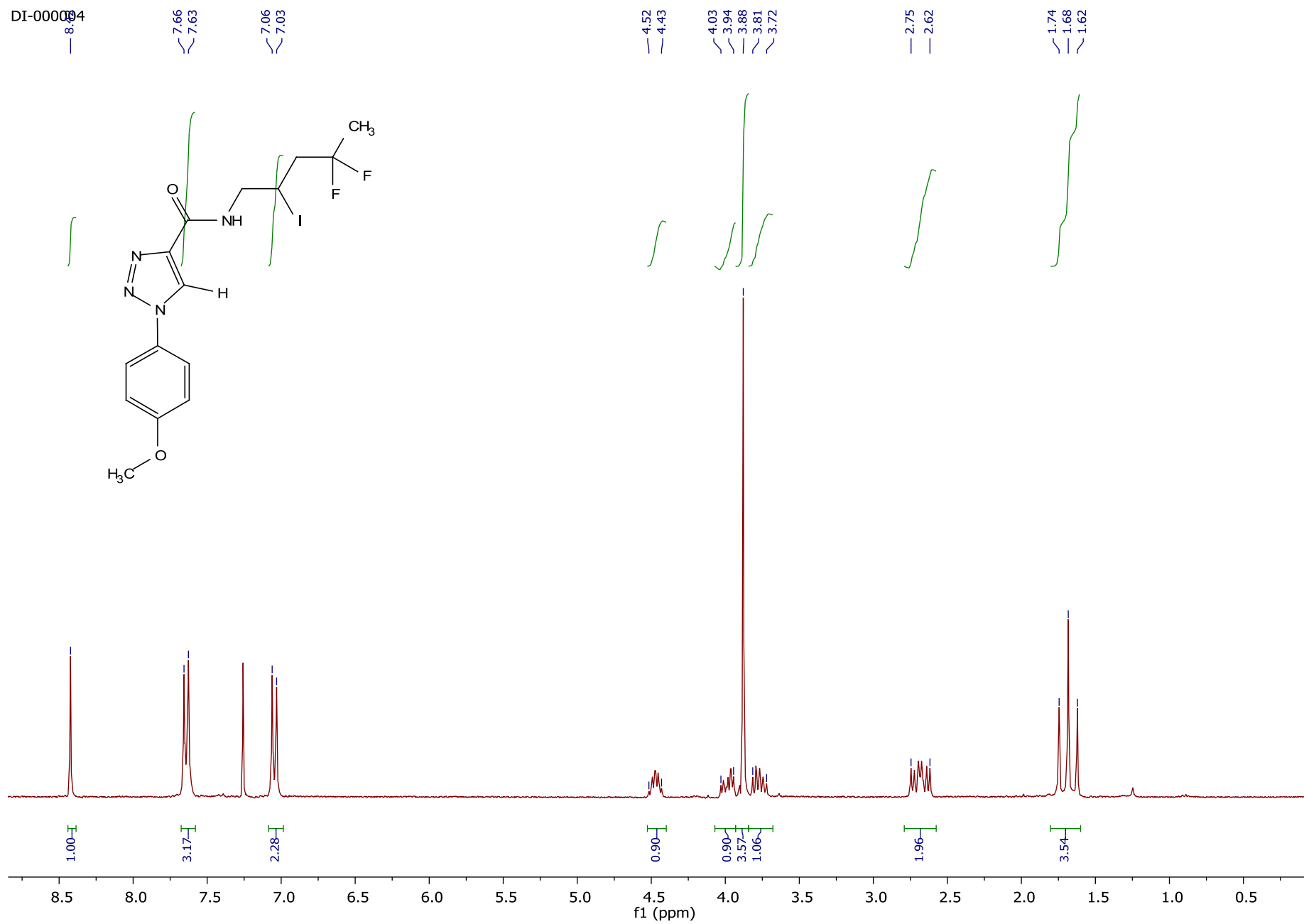
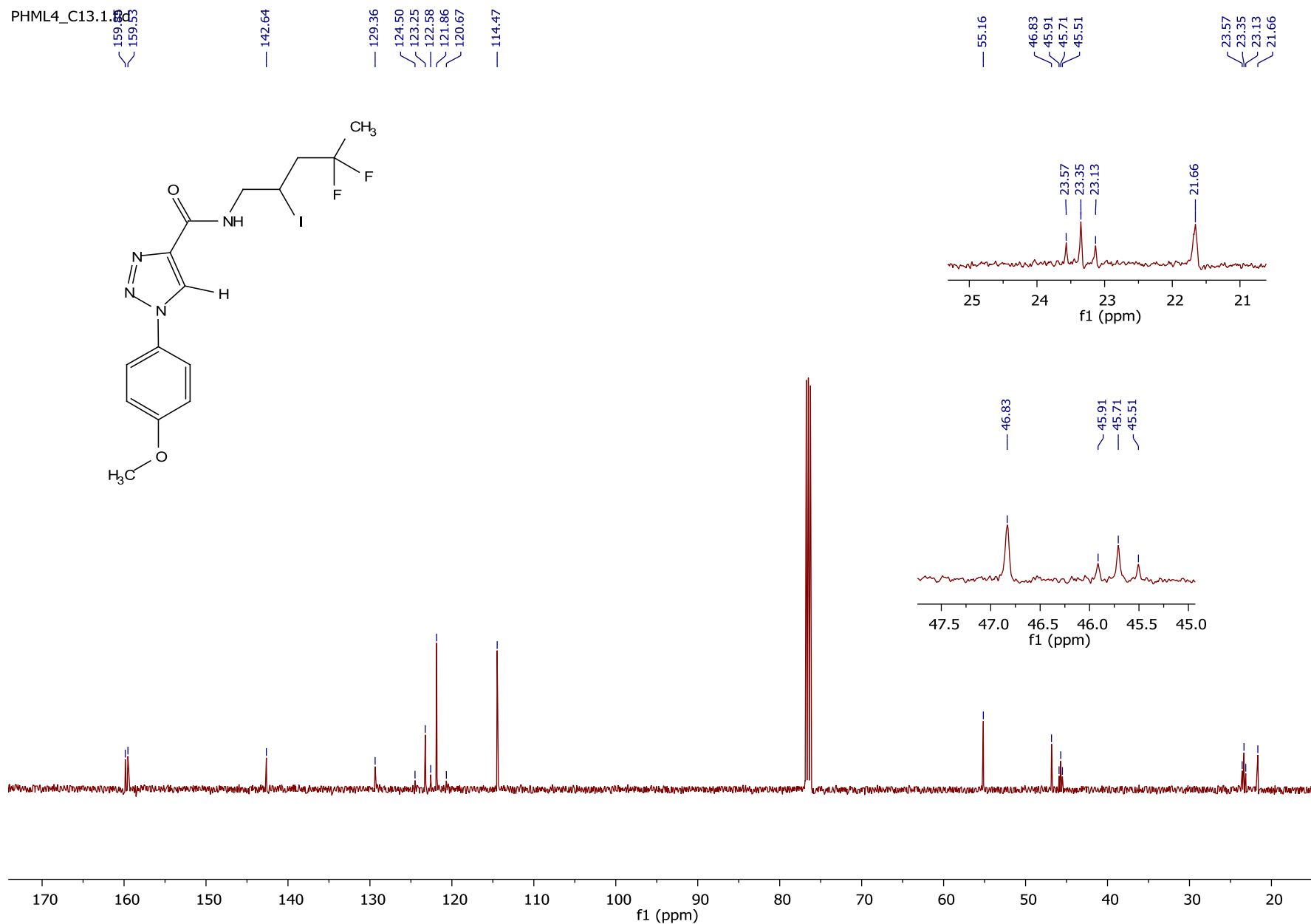


Figure S10.  $^{13}\text{C}$  NMR spectrum (126 MHz,  $\text{CDCl}_3$ ) of compound 4c



**Figure S11.**  $^{19}\text{F}$  NMR spectrum (188 MHz,  $\text{CDCl}_3$ ) of compound **4c**

DI-000004-19f  
F19 cdcl3

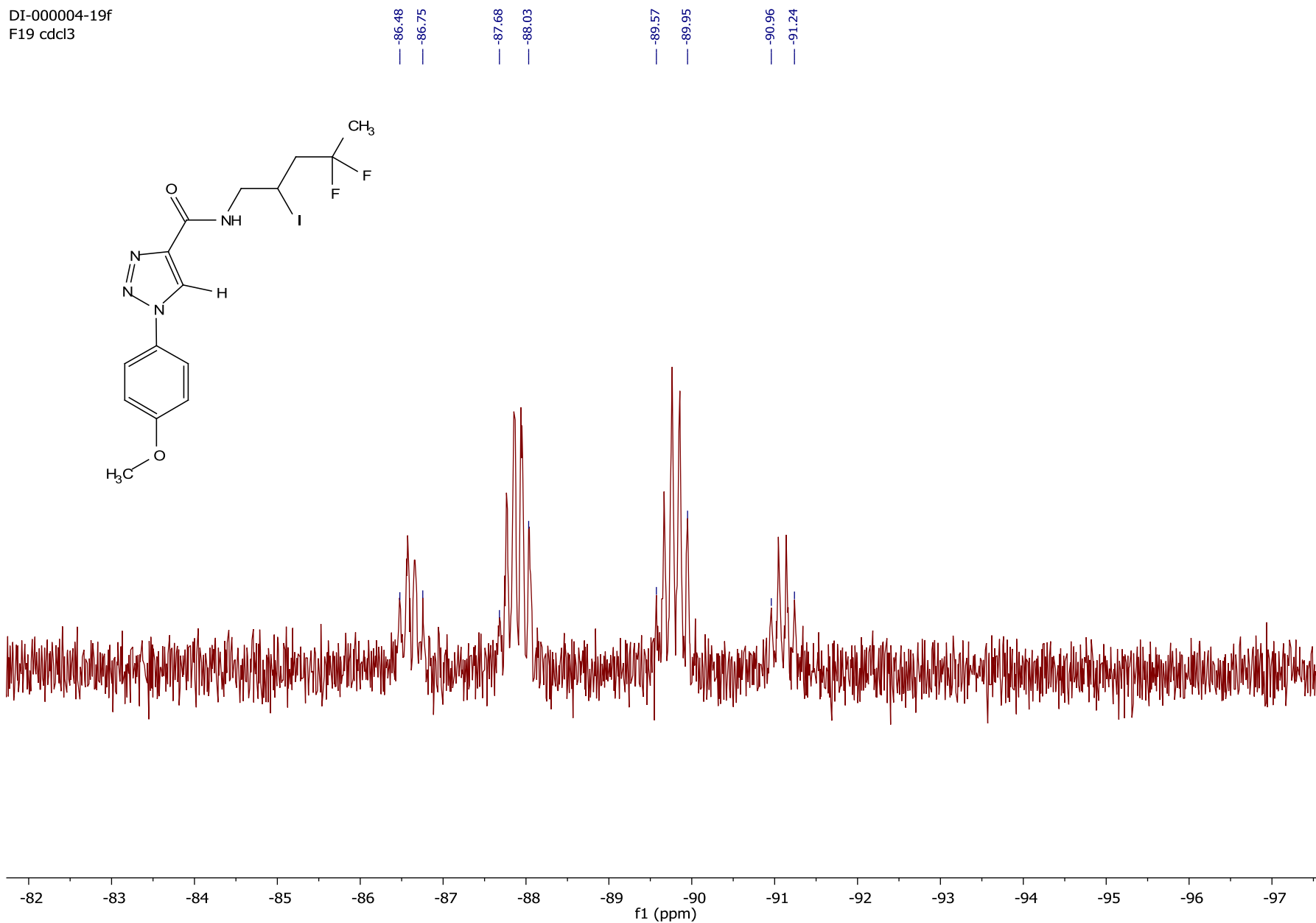


Figure S12. IR spectrum of compound 4c

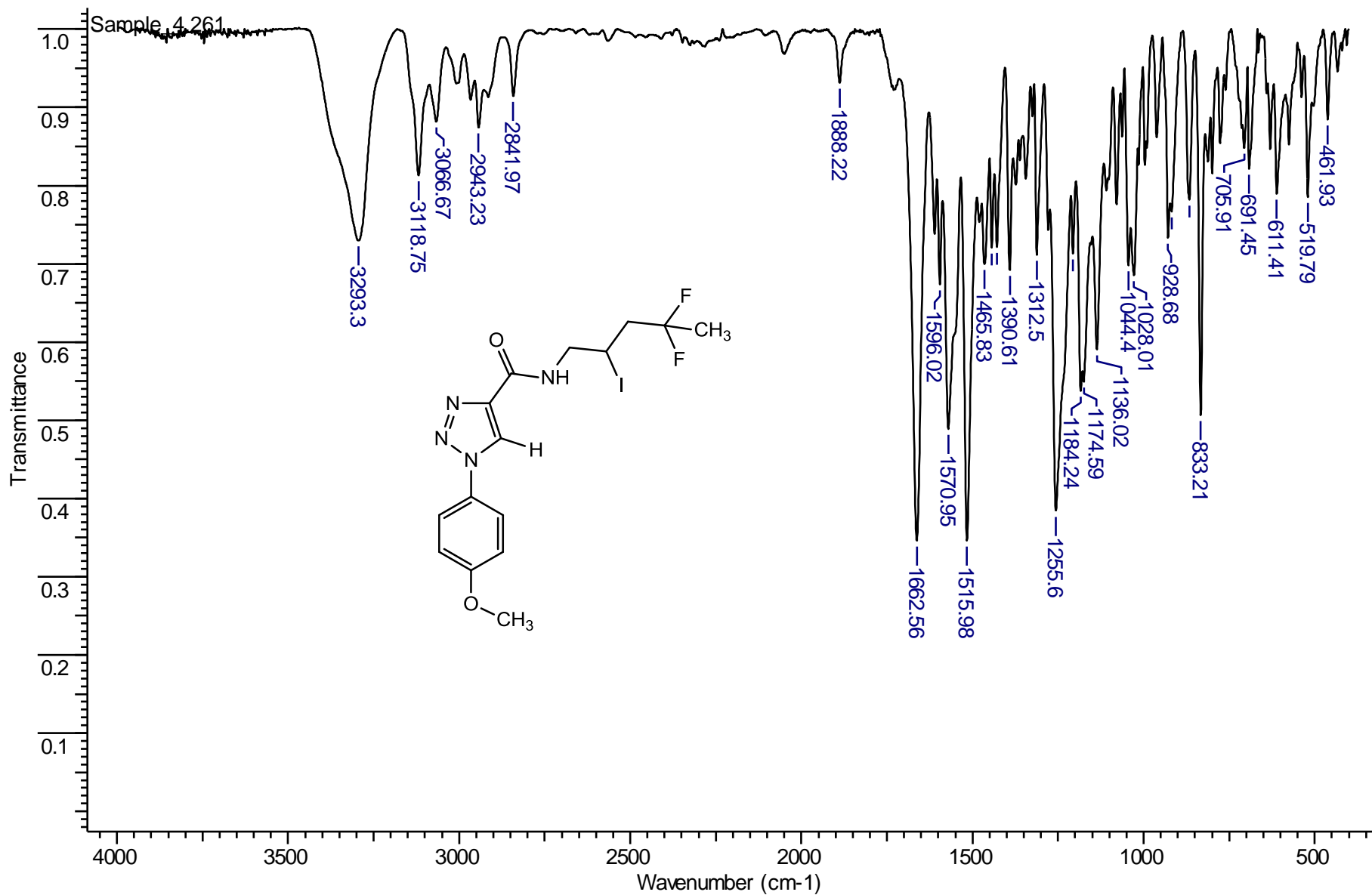




Figure S13. <sup>1</sup>H NMR spectrum (302 MHz, CDCl<sub>3</sub>) of compound **4d**

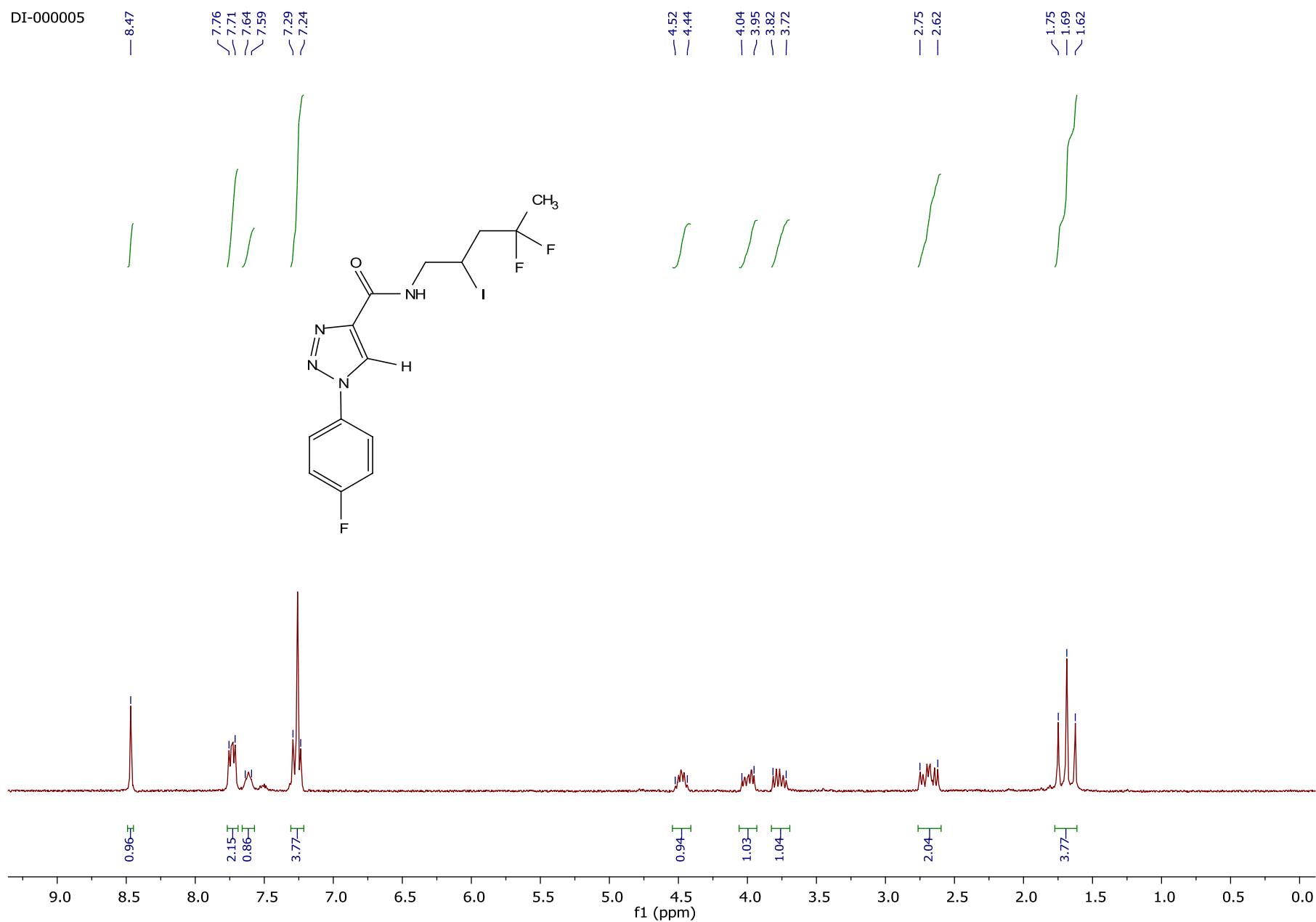


Figure S14. <sup>13</sup>C NMR spectrum (151 MHz, CDCl<sub>3</sub>) of compound **4d**

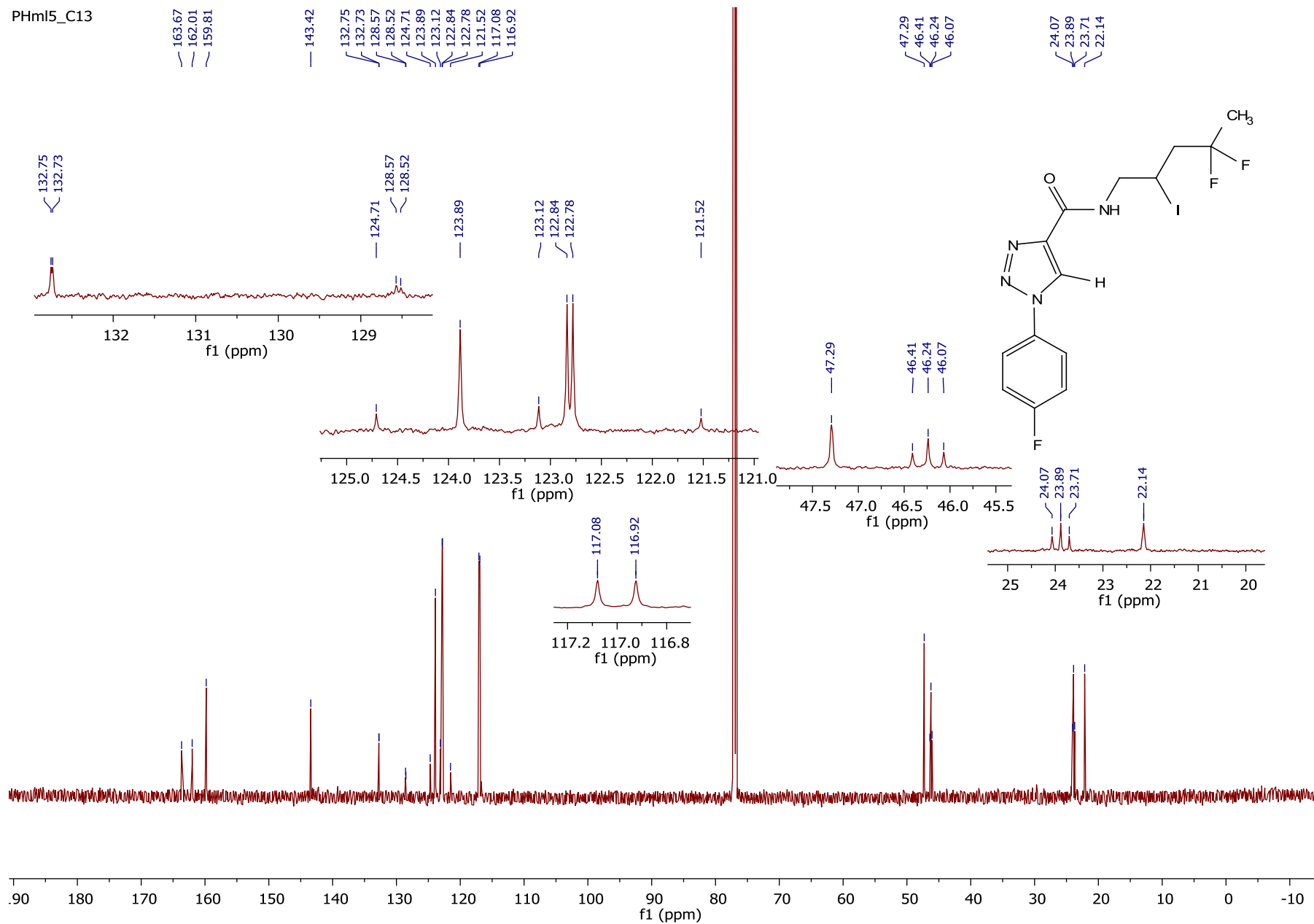
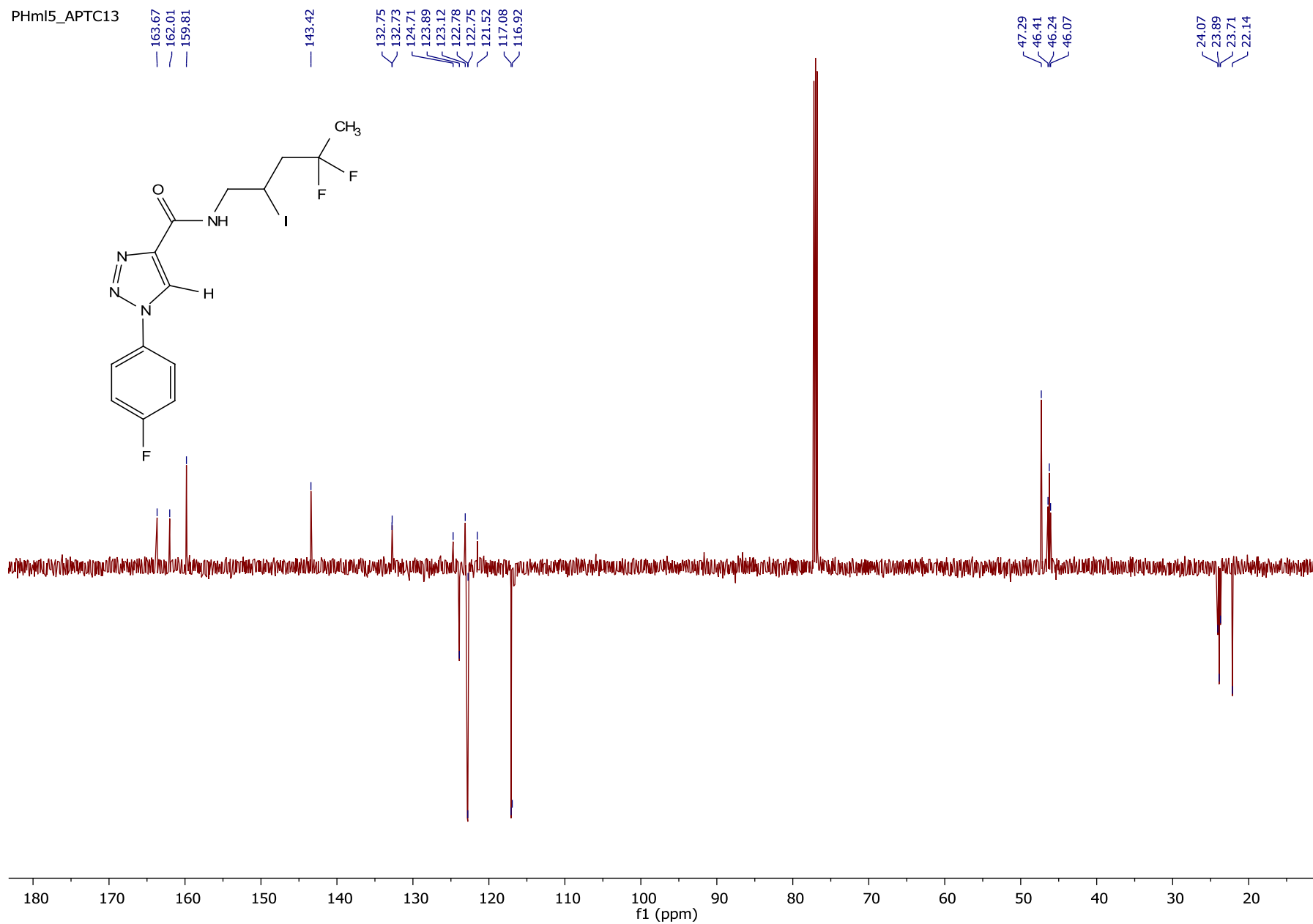


Figure S15. <sup>13</sup>C/APT NMR spectrum (151 MHz, CDCl<sub>3</sub>) of compound 4d



**Figure S16.**  $^{19}\text{F}$  NMR spectrum (188 MHz,  $\text{CDCl}_3$ ) of compound **4d**

DI-000005-19f  
F19 cdcl3

-86.50  
-86.77  
-87.77  
-88.16  
  
-89.82  
-90.10  
-91.11  
-91.40

-110.67

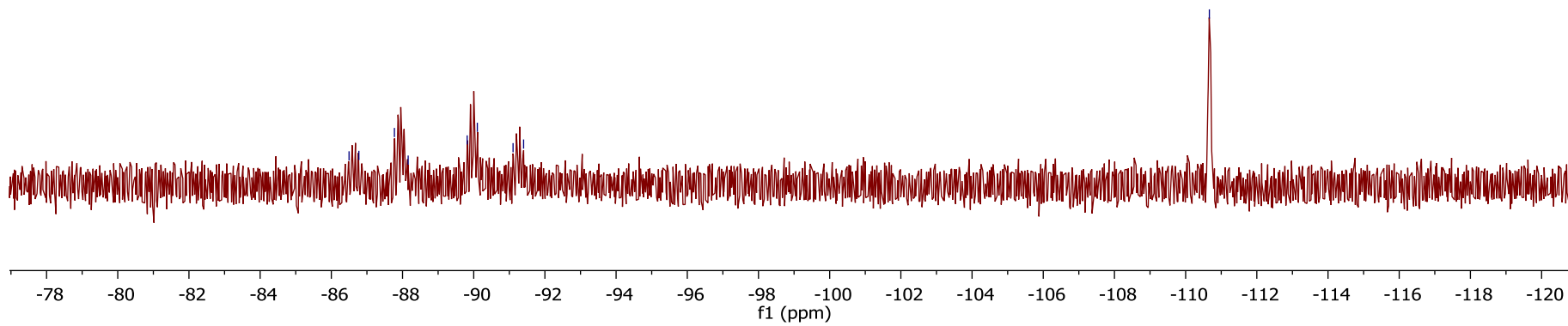
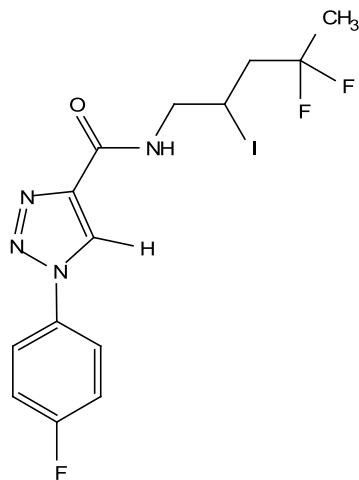


Figure S17. IR spectrum of compound 4d

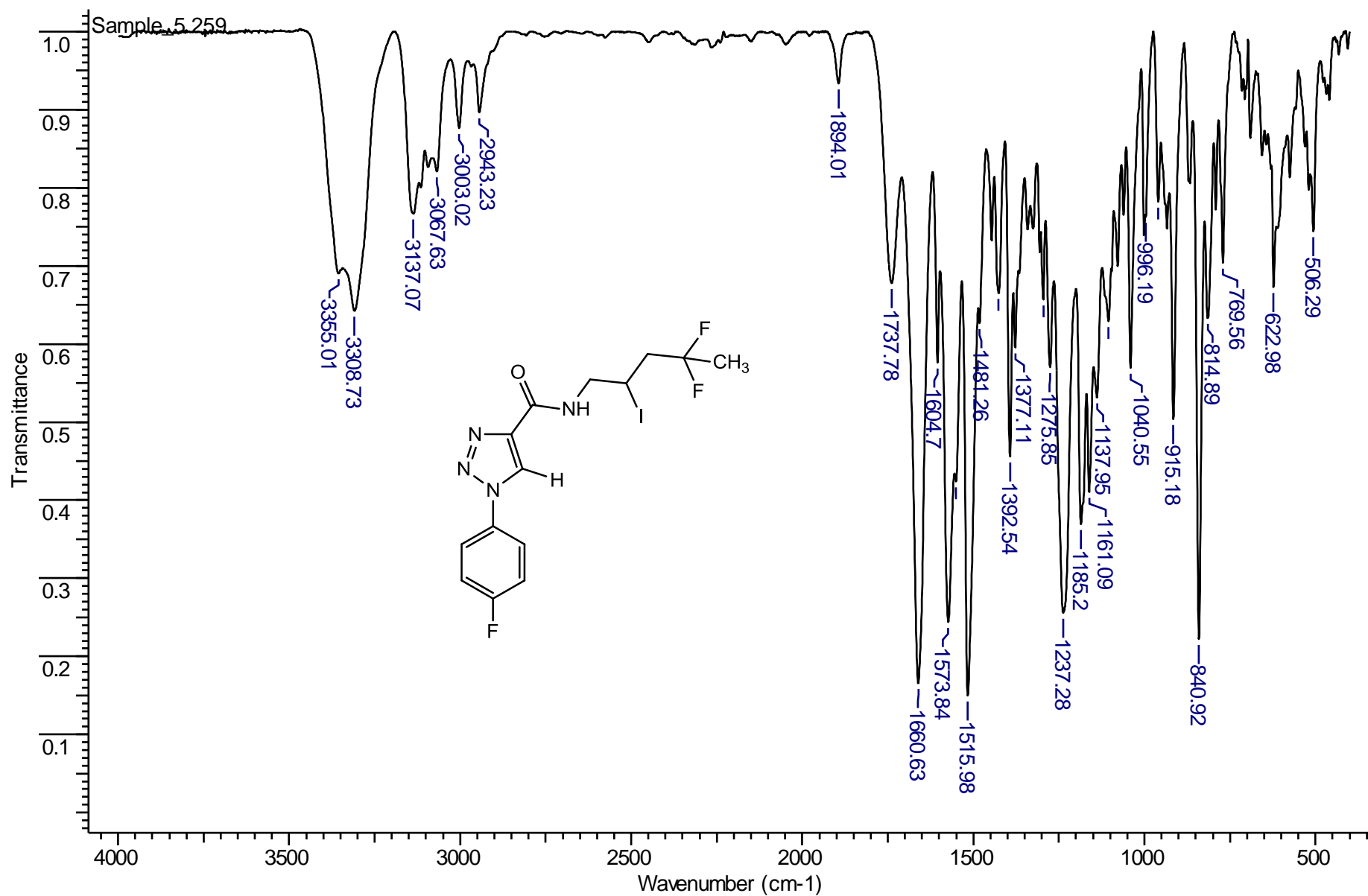
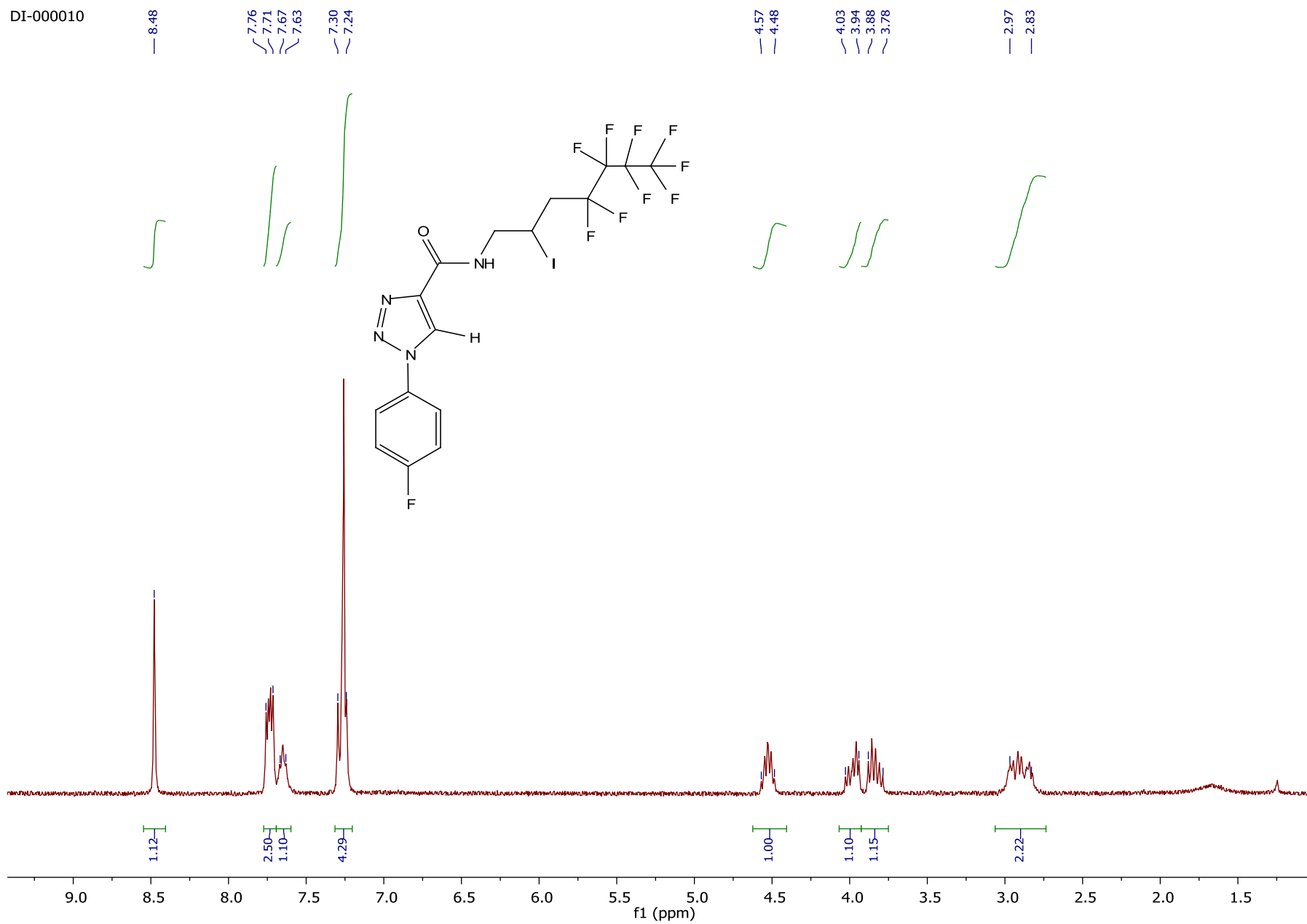
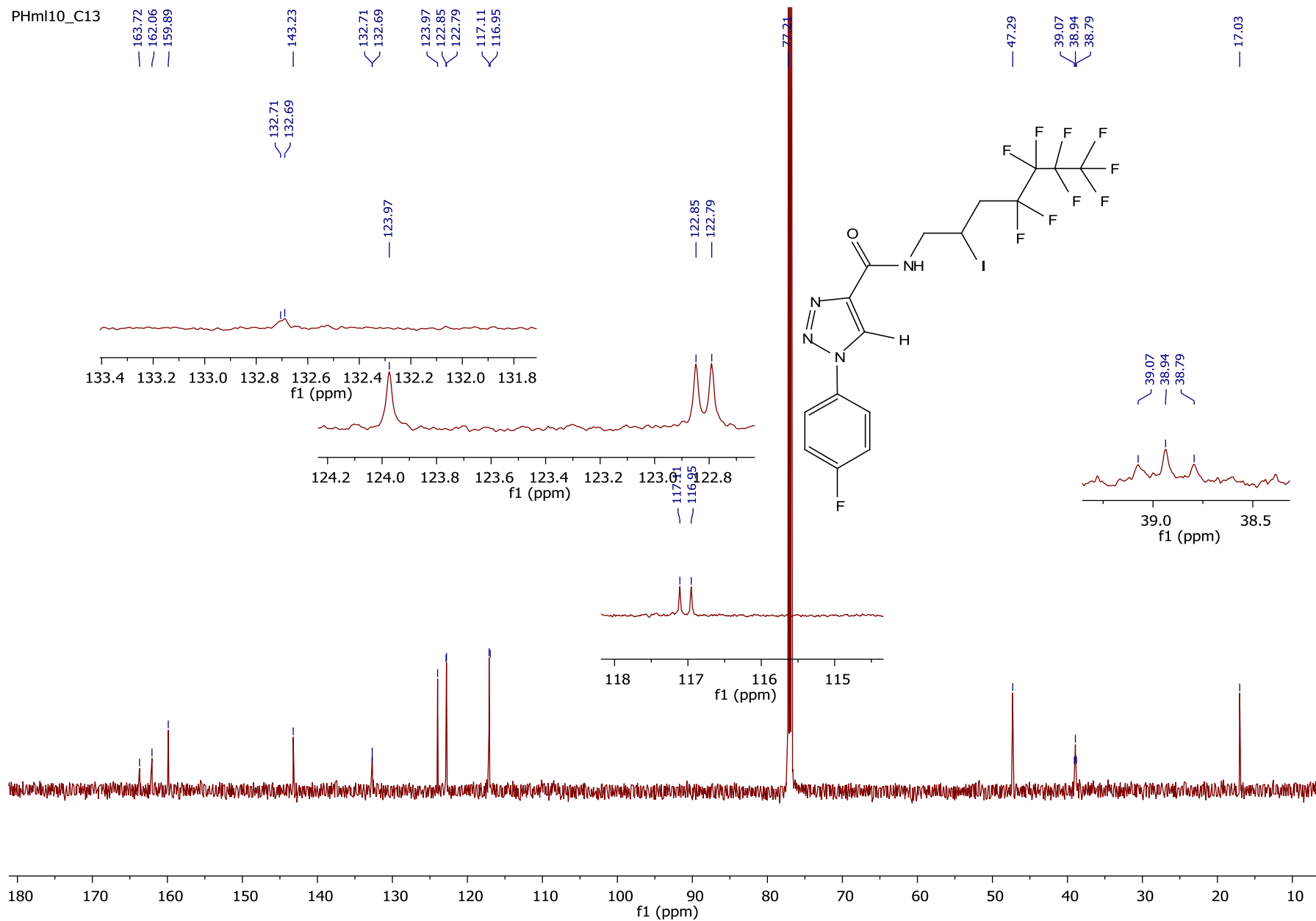


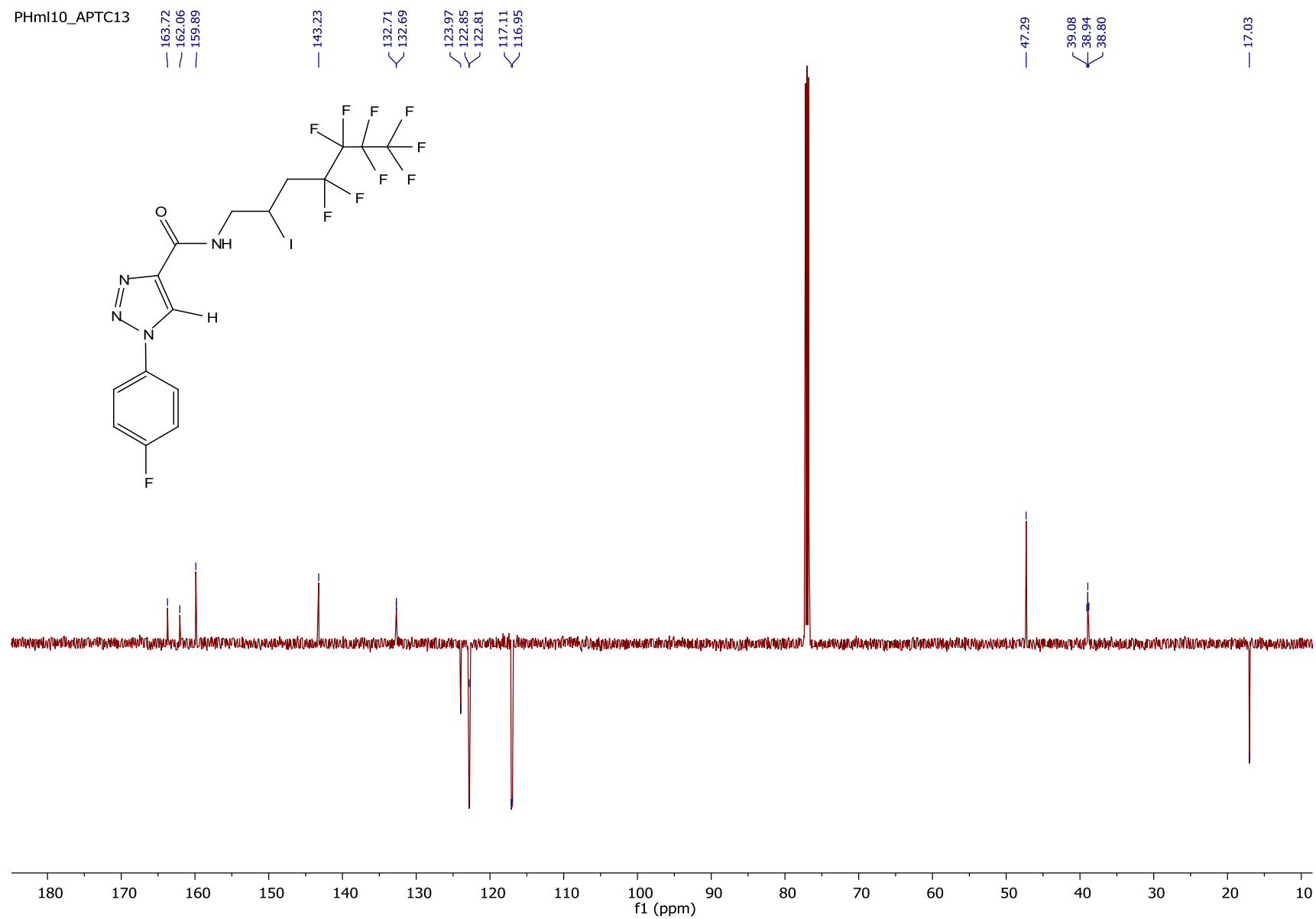
Figure S18. <sup>1</sup>H NMR spectrum (302 MHz, CDCl<sub>3</sub>) of compound **4e**



**Figure S19.**  $^{13}\text{C}$  NMR spectrum (151 MHz,  $\text{CDCl}_3$ ) of compound **4e**



**Figure S20.**  $^{13}\text{C}/\text{APT}$  NMR spectrum (151 MHz,  $\text{CDCl}_3$ ) of compound **4e**





**Figure S21.**  $^{19}\text{F}$  NMR spectrum (188 MHz,  $\text{CDCl}_3$ ) of compound **4e**

DI-000010-19f  
F19 cdcl3

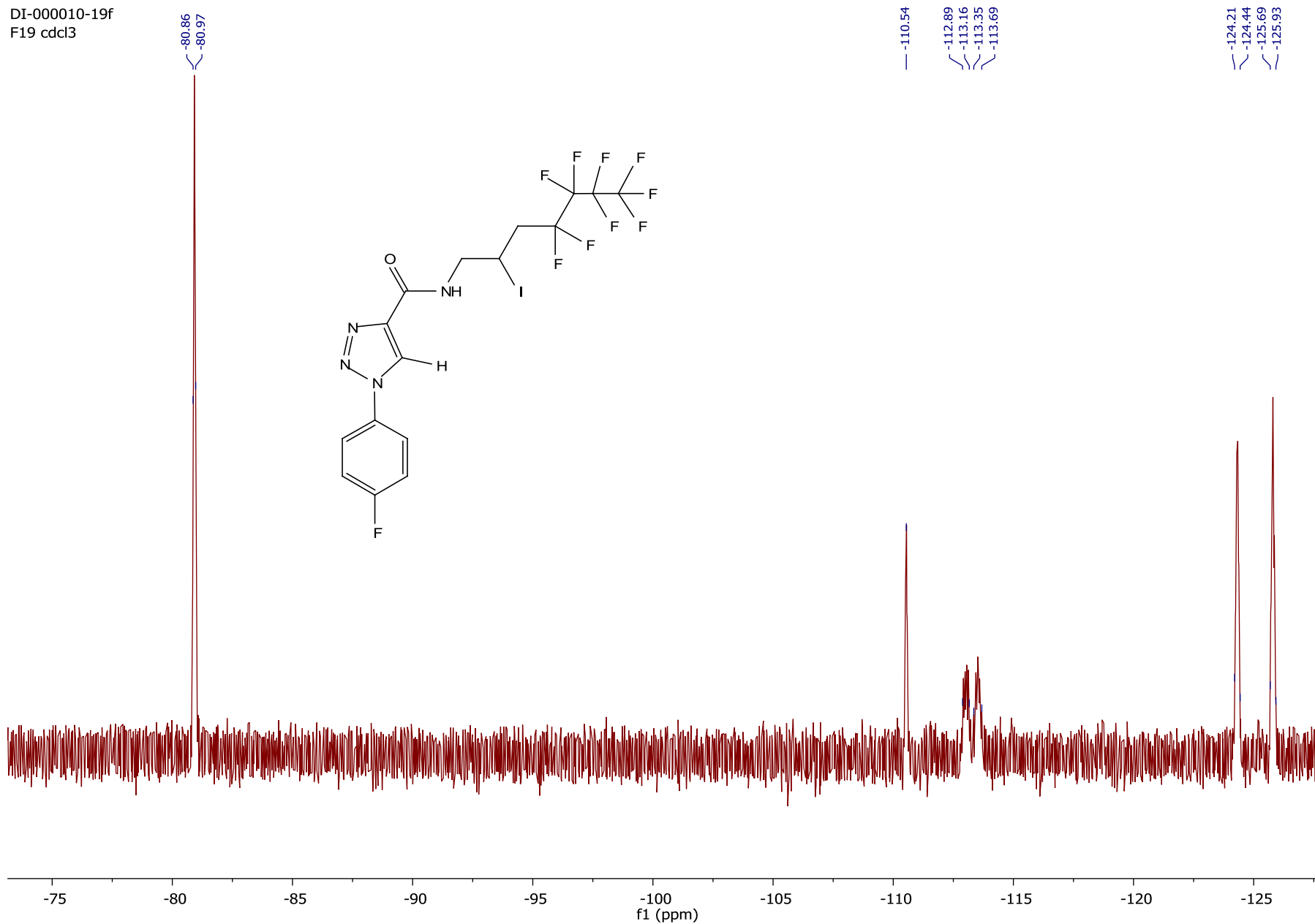


Figure S22. IR spectrum of compound 4e

