

SUPPLEMENTARY INFORMATION

Development of CXCR4 modulators based on the lead compound RB-108

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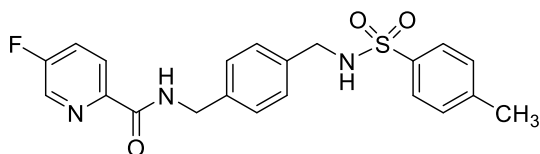
Section A:

Spectroscopic data of compounds **Ia-b**, **IIa-c**, and **IIIa-o**.

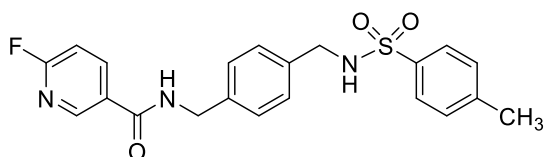
Section B:

¹H and ¹³C NMR Spectra of compounds **Ia-b**, **IIa-c**, and **IIIa-o**.

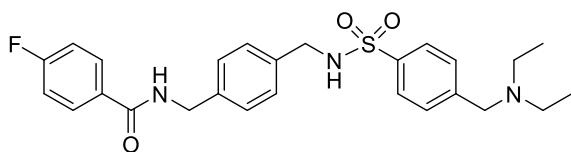
Section A: Spectroscopic data of compounds **Ia-b**, **IIa-c**, and **IIIa-o**.



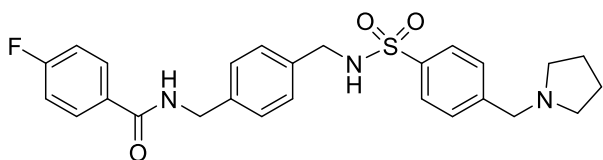
5-Fluoro-N-(4-(((4-methylphenyl)sulfonamido)methyl)benzyl)picolinamide (Ia). White solid, yield 75%, m.p. 133-135 °C. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 9.29 (t, $J = 6.4$ Hz, 1H), 8.65 (d, $J = 2.8$ Hz, 1H), 8.11 (dd, $J = 8.8, 4.7$ Hz, 1H), 8.02 (t, $J = 6.4$ Hz, 1H), 7.88 – 7.93 (m, 1H), 7.67 (d, $J = 8.2$ Hz, 2H), 7.36 (d, $J = 8.2$ Hz, 2H), 7.23 (d, $J = 8.2$ Hz, 2H), 7.16 (d, $J = 8.1$ Hz, 2H), 4.43 (d, $J = 6.4$ Hz, 2H), 3.89 (d, $J = 6.3$ Hz, 2H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 162.88, 161.92, 159.36, 146.70, 142.50, 138.37, 137.74, 136.92, 136.67, 136.10, 129.53, 127.51, 127.23, 126.48, 124.51, 124.33, 124.15, 124.09, 45.88, 42.15, 20.90. HRMS calcd for $\text{C}_{21}\text{H}_{21}\text{O}_3\text{N}_3\text{SF}$ 414.12822 $[\text{M} + \text{H}]^+$, found 414.12812.



6-Fluoro-N-(4-(((4-methylphenyl)sulfonamido)methyl)benzyl)nicotinamide (Ib). White solid, yield 60%, m.p. 186-188 °C. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 9.24 (t, $J = 5.9$ Hz, 1H), 8.73 (d, $J = 1.9$ Hz, 1H), 8.42 (td, $J = 8.2, 2.5$ Hz, 1H), 8.04 (t, $J = 6.3$ Hz, 1H), 7.68 (d, $J = 8.2$ Hz, 2H), 7.38 (d, $J = 7.9$ Hz, 2H), 7.31 (dd, $J = 8.6, 2.7$ Hz, 1H), 7.25 (d, $J = 7.9$ Hz, 2H), 7.19 (d, $J = 7.8$ Hz, 2H), 4.45 (d, $J = 5.9$ Hz, 2H), 3.91 (d, $J = 6.2$ Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 165.37, 163.53, 162.98, 147.42, 147.26, 142.52, 141.43, 141.34, 138.05, 137.76, 136.31, 129.55, 128.54, 127.56, 127.20, 126.49, 109.59, 109.21, 45.84, 42.38, 20.91. HRMS calcd for $\text{C}_{21}\text{H}_{21}\text{O}_3\text{N}_3\text{SF}$ 414.12822 $[\text{M} + \text{H}]^+$, found 414.12820.

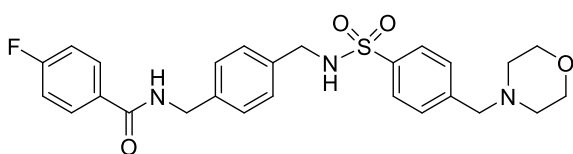


N-(4-(((4-((diethylamino)methyl)phenyl)sulfonamido)methyl)benzyl)-4-fluorobenzamide (IIa). White solid, yield 84%, m.p. 143-145 °C. ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 9.03 (t, $J = 6.0$ Hz, 1H), 8.06 (t, $J = 6.3$ Hz, 1H), 7.92 – 7.98 (m, 2H), 7.73 (d, $J = 8.3$ Hz, 2H), 7.49 (d, $J = 8.2$ Hz, 2H), 7.30 (t, $J = 8.9$ Hz, 2H), 7.21 (d, $J = 8.2$ Hz, 2H), 7.15 (d, $J = 8.1$ Hz, 2H), 4.42 (d, $J = 6.0$ Hz, 2H), 3.95 (d, $J = 6.2$ Hz, 2H), 2.45 (q, $J = 7.1$ Hz, 4H), 0.97 (t, $J = 7.1$ Hz, 6H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 165.03, 164.68, 163.03, 145.13, 138.97, 138.49, 136.17, 130.78, 130.76, 129.88, 129.82, 128.84, 127.61, 127.52, 127.09, 127.03, 126.37, 115.27, 115.12, 56.38, 46.32, 45.86, 42.36, 11.66. HRMS calcd for $\text{C}_{26}\text{H}_{31}\text{O}_3\text{N}_3\text{SF}$ 484.2065 $[\text{M} + \text{H}]^+$, found 484.2084.



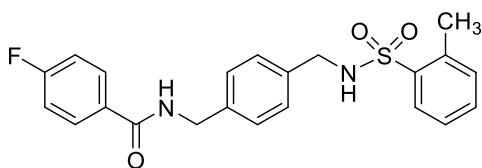
***N*-(4-(((4-(pyrrolidin-1-ylmethyl)phenyl)sulfonamido)methyl)benzyl)-4-fluorobenzamide (IIb).**

White solid, yield 77%, m.p. 151-153 °C. ¹H NMR (600 MHz, DMSO-*d*₆) δ 9.04 (t, *J* = 6.0 Hz, 1H), 8.07 (t, *J* = 6.3 Hz, 1H), 7.94 – 7.96 (m, 2H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.30 (t, *J* = 8.8 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 4.42 (d, *J* = 5.9 Hz, 2H), 3.94 (d, *J* = 6.0 Hz, 2H), 3.62 (s, 2H), 2.42 (s, 2H), 1.68 – 1.71 (m, 4H). ¹³C NMR (150 MHz, DMSO-*d*₆) δ 165.04, 164.68, 163.03, 144.30, 130.79, 130.77, 139.07, 138.49, 136.14, 129.88, 129.82, 128.88, 127.54, 127.10, 126.44, 115.28, 115.13, 58.94, 53.48, 45.87, 42.36, 23.14. HRMS calcd for C₂₆H₂₉O₃N₃SF 482.1908 [M + H]⁺, found 482.1930.



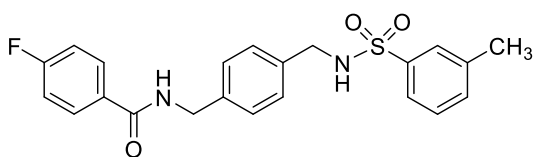
***N*-(4-(((4-(morpholinomethyl)phenyl)sulfonamido)methyl)benzyl)-4-fluorobenzamide (IIc).**

White solid, yield 78%, m.p. 165-167 °C. ¹H NMR (600 MHz, DMSO-*d*₆) δ 9.04 (t, *J* = 6.0 Hz, 1H), 8.08 (t, *J* = 6.3 Hz, 1H), 7.94 – 7.96 (m, 2H), 7.74 (d, *J* = 8.2 Hz, 2H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.30 (t, *J* = 8.8 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 4.42 (d, *J* = 5.9 Hz, 2H), 3.94 (d, *J* = 6.2 Hz, 2H), 3.58 (t, *J* = 4.6 Hz, 4H), 3.52 (s, 2H), 2.35 (s, 4H). ¹³C NMR (150 MHz, DMSO-*d*₆) δ 165.05, 164.68, 163.03, 142.71, 139.34, 138.50, 136.13, 130.78, 130.76, 129.88, 129.82, 129.31, 127.53, 127.41, 127.40, 127.10, 126.46, 115.28, 115.13, 66.15, 61.66, 53.12, 45.86, 42.36. HRMS calcd for C₂₆H₂₉O₄N₃SF 498.1857 [M + H]⁺, found 498.1871.

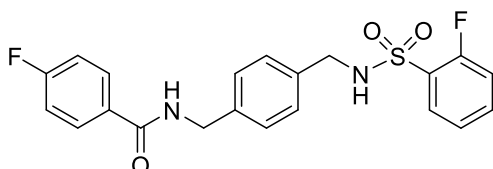


4-Fluoro-*N*-(4-(((2-methylphenyl)sulfonamido)methyl)benzyl)benzamide (IIIa).

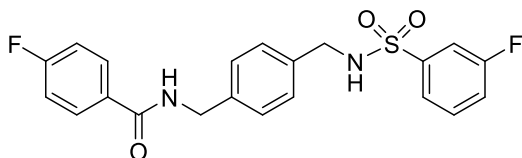
White solid, yield 75%, m.p. 144-146 °C. ¹H NMR (600 MHz, DMSO-*d*₆) δ 9.04 (t, *J* = 6.0 Hz, 1H), 8.19 (d, *J* = 5.6 Hz, 1H), 7.94 – 7.97 (m, 2H), 7.80 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.47 (td, *J* = 7.5, 1.4 Hz, 1H), 7.29 – 7.36 (m, 4H), 7.18 (dd, *J* = 8.1, 34.8 Hz, 4H), 4.42 (d, *J* = 5.9 Hz, 2H), 3.97 (d, *J* = 4.9 Hz, 2H), 2.55 (s, 3H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 165.11, 165.06, 162.63, 138.89, 138.47, 136.43, 136.39, 132.43, 132.32, 130.81, 130.78, 129.91, 129.82, 128.32, 127.47, 127.09, 126.16, 115.34, 115.13, 45.60, 42.37, 19.82. HRMS calcd for C₂₂H₂₂O₃N₂SF 413.13297 [M + H]⁺, found 413.13310.



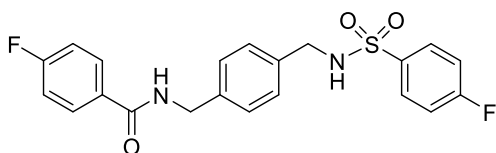
4-Fluoro-N-(4-(((3-methylphenyl)sulfonamido)methyl)benzyl)benzamide (IIIb). White solid, yield 79%, m.p. 171-173 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.05 (t, *J* = 6.0 Hz, 1H), 8.07 (s, 1H), 7.94 – 7.97 (m, 2H), 7.59 (d, *J* = 5.6 Hz, 2H), 7.40 – 7.47 (m, 2H), 7.31 (t, *J* = 8.8 Hz, 2H), 7.20 (dd, *J* = 19.2, 8.0 Hz, 4H), 4.43 (d, *J* = 6.0 Hz, 2H), 3.94 (s, 2H), 2.36 (s, 3H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 165.07, 165.04, 162.60, 140.59, 138.76, 138.49, 136.13, 132.84, 130.79, 130.77, 129.88, 129.79, 128.97, 127.54, 127.10, 126.70, 123.56, 115.30, 115.08, 45.88, 42.35, 20.81. HRMS calcd for C₂₂H₂₂O₃N₂SF 413.13297 [M + H]⁺, found 413.13233.



4-Fluoro-N-(4-(((2-fluorophenyl)sulfonamido)methyl)benzyl)benzamide (IIIc). White solid, yield 88%, m.p. 133-135 °C. ¹H NMR (600 MHz, DMSO-*d*₆) δ 9.04 (t, *J* = 6.0 Hz, 1H), 8.47 (s, 1H), 7.94 – 7.98 (m, 2H), 7.73 – 7.76 (m, 1H), 7.60 – 7.64 (m, 1H), 7.29 – 7.37 (m, 4H), 7.18 (dd, *J* = 8.2, 18.0 Hz, 4H), 4.41 (d, *J* = 6.0 Hz, 2H), 4.08 (s, 2H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 165.11, 165.06, 162.64, 159.33, 156.81, 138.50, 136.09, 135.07, 134.98, 130.81, 130.78, 129.91, 129.82, 129.52, 128.84, 128.70, 127.44, 127.10, 124.76, 124.73, 117.21, 117.00, 115.35, 115.13, 45.69, 42.36. HRMS calcd for C₂₁H₁₉O₃N₂SF₂ 417.10790 [M + H]⁺, found 417.10751.

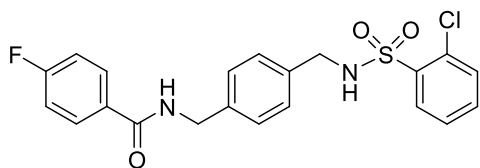


4-Fluoro-N-(4-(((3-fluorophenyl)sulfonamido)methyl)benzyl)benzamide (IIIId). White solid, yield 82%, m.p. 164-166 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.05 (t, *J* = 6.0 Hz, 1H), 8.27 (t, *J* = 6.3 Hz, 1H), 7.93 – 7.98 (m, 2H), 7.59 – 7.65 (m, 2H), 7.54 – 7.57 (m, 1H), 7.45 – 7.50 (m, 1H), 7.28 – 7.34 (m, 2H), 7.20 (dd, *J* = 19.6, 8.2 Hz, 4H), 4.42 (d, *J* = 6.0 Hz, 2H), 3.98 (d, *J* = 6.2 Hz, 2H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 165.07, 162.94, 162.65, 160.48, 142.88, 142.81, 138.66, 135.87, 131.64, 131.56, 130.80, 130.77, 129.93, 129.84, 127.64, 127.17, 119.59, 119.37, 115.38, 115.16, 113.63, 113.39, 109.58, 45.93, 42.37. HRMS calcd for C₂₁H₁₉O₃N₂SF₂ 417.10790 [M + H]⁺, found 417.10812.

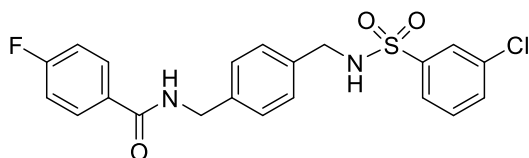


4-Fluoro-N-(4-(((4-fluorophenyl)sulfonamido)methyl)benzyl)benzamide (IIIe). White solid, yield 80%, m.p. 170-172 °C. ¹H NMR (600 MHz, DMSO-*d*₆) δ 9.05 (t, *J* = 6.0 Hz, 1H), 8.17 (s, 1H), 7.94 – 7.97 (m, 2H), 7.82 – 7.85 (m, 2H), 7.38 – 7.42 (m, 2H), 7.28 – 7.32 (m, 2H), 7.20 (dd, *J* = 8.1, 31.2 Hz, 4H), 4.42 (d, *J* = 5.9 Hz, 2H), 3.95 (s, 2H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 165.27, 165.10, 165.07, 162.77, 162.63, 138.60, 137.11, 137.08, 135.94, 130.79, 130.77, 129.91, 129.82, 129.51,

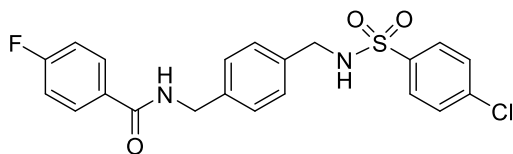
129.42, 127.60, 127.15, 116.37, 116.15, 115.33, 115.11, 45.90, 42.38. HRMS calcd for $C_{21}H_{19}O_3N_2SF_2$ 417.10790 $[M + H]^+$, found 417.10765.



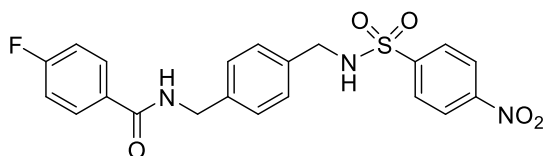
4-Fluoro-N-(4-((2-chlorophenyl)sulfonamido)methyl)benzyl)benzamide (III f). White solid, yield 77%, m.p. 128-130 °C. 1H NMR (600 MHz, DMSO- d_6) δ 9.03 (t, $J = 6.0$ Hz, 1H), 8.42 (t, $J = 6.0$ Hz, 1H), 7.94 – 7.97 (m, 2H), 7.90 (dd, $J = 7.8, 1.6$ Hz, 1H), 7.53 – 7.59 (m, 2H), 7.44 – 7.47 (m, 1H), 7.29 – 7.32 (m, 2H), 7.17 (dd, $J = 13.5, 8.1$ Hz, 4H), 4.40 (d, $J = 6.0$ Hz, 2H), 4.06 (d, $J = 5.7$ Hz, 2H). ^{13}C NMR (100 MHz, DMSO- d_6) δ 165.11, 165.05, 162.64, 138.49, 138.25, 136.08, 133.75, 131.62, 130.81, 130.78, 130.58, 130.31, 129.91, 129.82, 127.51, 127.47, 127.04, 115.35, 115.14, 45.79, 42.35. HRMS calcd for $C_{21}H_{19}O_3N_2SFCl$ 433.07835 $[M + H]^+$, found 433.07837.



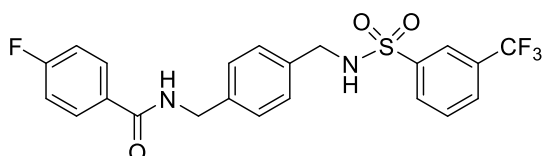
4-Fluoro-N-(4-((3-chlorophenyl)sulfonamido)methyl)benzyl)benzamide (III g). White solid, yield 80%, m.p. 160-162 °C. 1H NMR (600 MHz, DMSO- d_6) δ 9.04 (t, $J = 6.0$ Hz, 1H), 8.29 (s, 1H), 7.94 – 7.97 (m, 2H), 7.72 – 7.74 (m, 2H), 7.66 – 7.68 (m, 1H), 7.58 (t, $J = 7.9$ Hz, 1H), 7.29 – 7.32 (m, 2H), 7.19 (dd, $J = 7.9, 28.8$ Hz, 4H), 4.42 (d, $J = 6.0$ Hz, 2H), 3.99 (s, 2H). ^{13}C NMR (100 MHz, DMSO- d_6) δ 165.48, 163.05, 143.08, 139.08, 136.19, 134.15, 132.66, 131.63, 131.23, 131.20, 130.33, 130.24, 128.06, 127.58, 126.52, 125.57, 115.76, 115.55, 46.35, 42.79. HRMS calcd for $C_{21}H_{19}O_3N_2SCl$ 433.07835 $[M + H]^+$, found 433.07849.



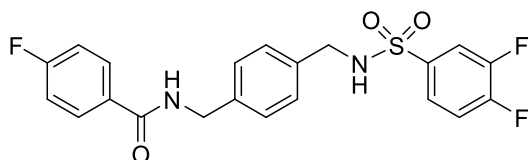
4-Fluoro-N-(4-((4-chlorophenyl)sulfonamido)methyl)benzyl)benzamide (III h). White solid, yield 82%, m.p. 169-171 °C. 1H NMR (600 MHz, DMSO- d_6) δ 9.05 (t, $J = 6.0$ Hz, 1H), 8.23 (s, 1H), 7.94 – 7.97 (m, 2H), 7.76 – 7.79 (m, 2H), 7.63 – 7.65 (m, 2H), 7.28 – 7.32 (m, 2H), 7.20 (dd, $J = 8.1, 30.6$ Hz, 4H), 4.43 (d, $J = 6.0$ Hz, 2H), 3.96 (s, 2H). ^{13}C NMR (100 MHz, DMSO- d_6) δ 165.06, 139.57, 138.63, 137.15, 135.88, 130.79, 130.76, 129.91, 129.82, 129.27, 128.42, 127.60, 127.15, 115.32, 115.10, 45.89, 42.37. HRMS calcd for $C_{21}H_{19}O_3N_2SFCl$ 433.07835 $[M + H]^+$, found 433.07809.



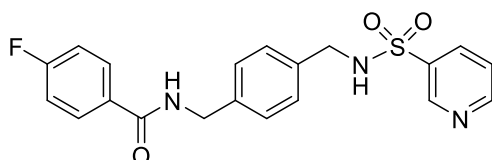
4-Fluoro-N-(4-(((4-nitrophenyl)sulfonamido)methyl)benzyl)benzamide (IIIi). White solid, yield 60%, m.p. 186-188 °C. ^1H NMR (400 MHz, DMSO- d_6) δ 9.05 (t, J = 6.0 Hz, 1H), 8.53 (s, 1H), 8.35 – 8.39 (m, 2H), 7.99 – 8.02 (m, 2H), 7.93 – 7.96 (m, 2H), 7.28 – 7.33 (m, 2H), 7.19 (dd, J = 18.4, 8.1 Hz, 4H), 4.40 (d, J = 5.9 Hz, 2H), 4.02 (s, 2H). ^{13}C NMR (100 MHz, DMSO- d_6) δ 165.06, 162.63, 149.43, 146.32, 138.74, 135.63, 130.77, 130.74, 129.90, 129.81, 128.04, 127.66, 127.15, 124.48, 115.32, 115.11, 45.93, 42.34. HRMS calcd for $\text{C}_{21}\text{H}_{19}\text{O}_5\text{N}_3\text{SF}$ 444.10240 $[\text{M} + \text{H}]^+$, found 444.10239.



4-Fluoro-N-(4-(((3-(trifluoromethyl)phenyl)sulfonamido)methyl)benzyl)benzamide (IIIj). White solid, yield 65%, m.p. 170-172 °C. ^1H NMR (400 MHz, DMSO- d_6) δ 9.04 (t, J = 6.0 Hz, 1H), 8.40 (t, J = 5.8 Hz, 1H), 7.93 – 8.04 (m, 5H), 7.78 (t, J = 7.8 Hz, 1H), 7.31 (t, J = 8.9 Hz, 2H), 7.16 (dd, J = 17.2, 7.6 Hz, 4H), 4.39 (d, J = 5.9 Hz, 2H), 4.02 (d, J = 5.2 Hz, 2H). ^{13}C NMR (100 MHz, DMSO- d_6) δ 165.03, 162.62, 142.06, 138.64, 135.57, 130.78, 130.75, 130.71, 130.48, 129.89, 129.86, 129.80, 129.53, 128.97, 128.93, 127.62, 127.14, 124.77, 123.00, 122.96, 115.32, 115.10, 45.92, 42.32. HRMS calcd for $\text{C}_{22}\text{H}_{19}\text{O}_3\text{N}_2\text{SF}_4$ 467.10470 $[\text{M} + \text{H}]^+$, found 467.10488.

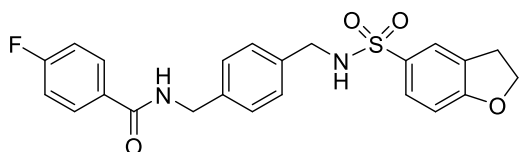


4-Fluoro-N-(4-(((3,4-difluorophenyl)sulfonamido)methyl)benzyl)benzamide (IIIk). White solid, yield 70%, m.p. 165-167 °C. ^1H NMR (400 MHz, DMSO- d_6) δ 9.06 (t, J = 6.0 Hz, 1H), 8.29 (s, 1H), 7.93 – 7.97 (m, 2H), 7.77 – 7.81 (m, 1H), 7.62 – 7.66 (m, 2H), 7.30 (t, J = 8.9 Hz, 2H), 7.20 (dd, J = 22.4, 8.0 Hz, 4H), 4.42 (d, J = 5.9 Hz, 2H), 4.00 (s, 2H). ^{13}C NMR (100 MHz, DMSO- d_6) δ 165.08, 162.65, 150.44, 138.71, 137.97, 135.75, 130.80, 130.77, 129.93, 129.84, 127.69, 127.18, 124.38, 124.34, 124.30, 124.26, 118.68, 118.50, 116.48, 116.29, 115.36, 115.15, 45.95, 42.37. HRMS calcd for $\text{C}_{21}\text{H}_{18}\text{O}_3\text{N}_2\text{SF}_3$ 435.09847 $[\text{M} + \text{H}]^+$, found 435.09855.

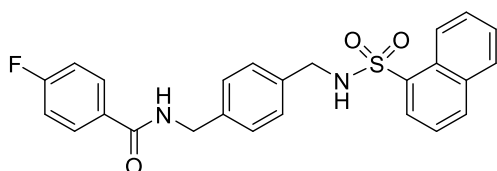


4-Fluoro-N-(4-(((pyridine-3-sulfonamido)methyl)benzyl)benzamide (IIIl). White solid, yield 50%, m.p. 165-167 °C. ^1H NMR (400 MHz, DMSO- d_6) δ 9.05 (t, J = 6.0 Hz, 1H), 8.91 (d, J = 2.5 Hz, 1H), 8.75 (dd, J = 4.8, 1.4 Hz, 1H), 8.40 (t, J = 6.0 Hz, 1H), 8.08 – 8.11 (m, 1H), 7.93 – 7.97 (m, 2H), 7.56 (dd, J = 8.0, 4.9 Hz, 1H), 7.28 – 7.34 (m, 2H), 7.18 (d, J = 17.6, 8.1 Hz, 4H), 4.41 (d, J = 5.9 Hz, 2H),

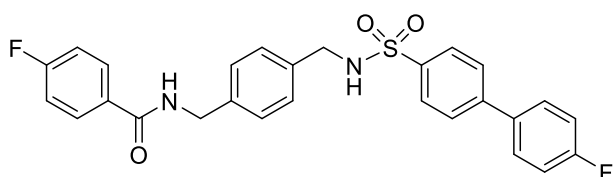
4.02 (d, $J = 5.7$ Hz, 2H). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 165.10, 165.05, 162.62, 152.80, 146.97, 138.64, 137.17, 135.68, 134.39, 130.79, 130.76, 129.90, 129.81, 127.62, 127.16, 124.14, 115.34, 115.12, 45.87, 42.34. HRMS calcd for $\text{C}_{20}\text{H}_{19}\text{O}_3\text{N}_3\text{SF}$ 400.11257 $[\text{M} + \text{H}]^+$, found 400.11220.



4-Fluoro-N-(4-(((2,3-dihydrobenzofuran)-5-sulfonamido)methyl)benzyl)benzamide (III m). White solid, yield 79%, m.p. 215-217 °C. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 9.06 (t, $J = 6.0$ Hz, 1H), 7.93 – 7.98 (m, 2H), 7.90 (t, $J = 6.4$ Hz, 1H), 7.60 (m, 1H), 7.55 (dd, $J = 8.4, 2.1$ Hz, 1H), 7.28 – 7.34 (m, 2H), 7.20 (dd, $J = 19.2, 8.2$ Hz, 4H), 6.90 (d, $J = 8.4$ Hz, 1H), 4.62 (t, $J = 8.8$ Hz, 2H), 4.43 (d, $J = 5.9$ Hz, 2H), 3.89 (d, $J = 6.3$ Hz, 2H), 3.22 (t, $J = 8.8$ Hz, 2H). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 165.09, 165.06, 162.77, 162.62, 138.46, 136.22, 132.22, 129.90, 129.81, 128.63, 127.77, 127.58, 127.07, 123.95, 115.33, 115.11, 108.94, 72.09, 45.90, 42.36, 28.46. HRMS calcd for $\text{C}_{23}\text{H}_{22}\text{O}_4\text{N}_2\text{SF}$ 441.12788 $[\text{M} + \text{H}]^+$, found 441.12788.

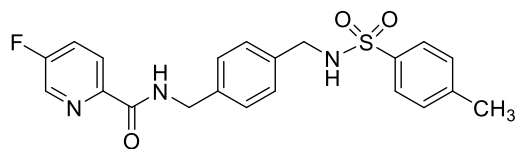


4-Fluoro-N-(4-((naphthalene-1-sulfonamido)methyl)benzyl)benzamide (III n). White solid, yield 72%, m.p. 143-145 °C. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 9.01 (t, $J = 6.0$ Hz, 1H), 8.67 (d, $J = 8.0$ Hz, 1H), 8.49 (s, 1H), 8.18 (d, $J = 8.3$ Hz, 1H), 8.10 (dd, $J = 7.4, 1.3$ Hz, 1H), 8.06 (d, $J = 8.0$ Hz, 1H), 7.93 – 7.97 (m, 2H), 7.58 – 7.73 (m, 3H), 7.28 – 7.33 (m, 2H), 7.15 (dd, $J = 17.4, 8.2$ Hz, 4H), 4.38 (d, $J = 6.0$ Hz, 2H), 3.99 (s, 2H). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 165.07, 165.01, 162.59, 138.39, 136.16, 135.75, 133.81, 133.58, 130.79, 130.76, 129.87, 129.78, 128.86, 128.34, 127.73, 127.49, 127.37, 126.96, 126.75, 124.72, 124.44, 115.29, 115.07, 45.68, 42.31. HRMS calcd for $\text{C}_{25}\text{H}_{22}\text{O}_3\text{N}_2\text{SF}$ 449.13297 $[\text{M} + \text{H}]^+$, found 449.13243.

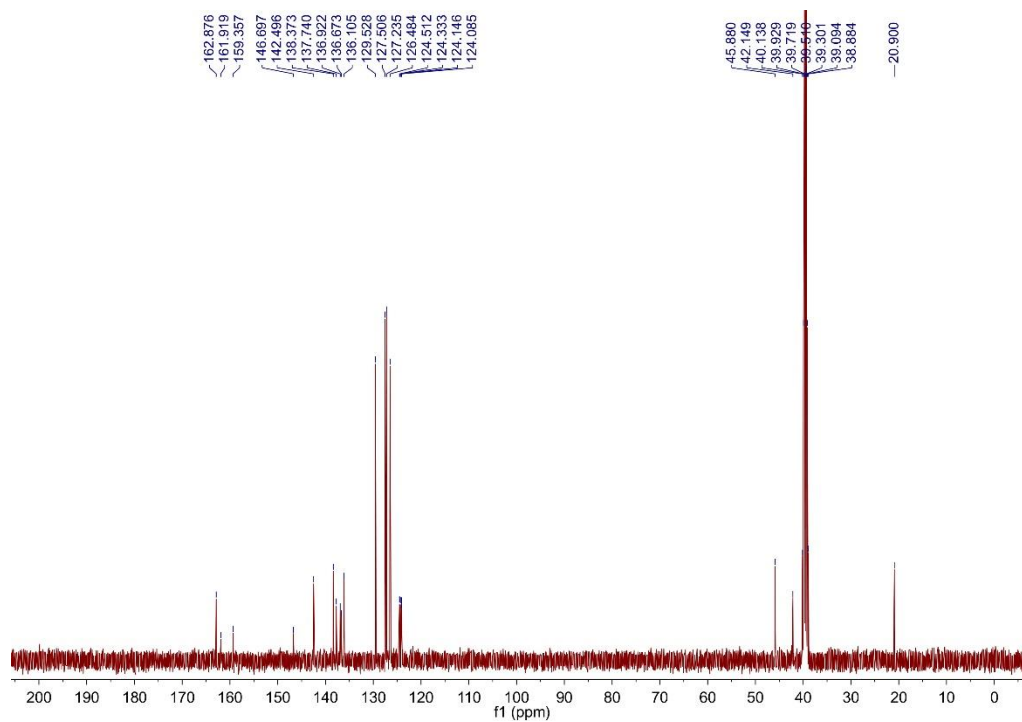
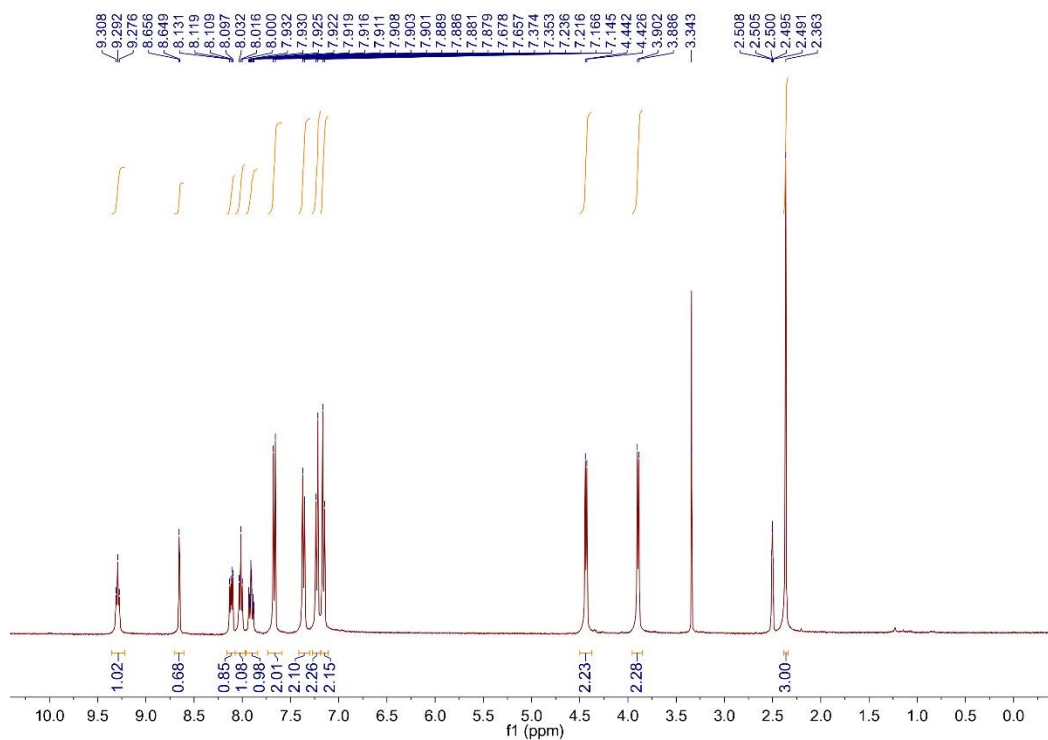


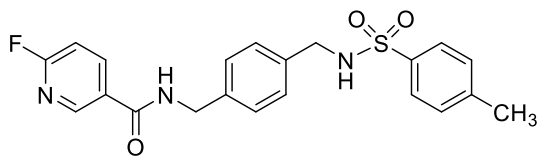
4-Fluoro-N-(4-(((4'-fluoro-[1,1'-biphenyl])-4-sulfonamido)methyl)benzyl)benzamide (III o). White solid, yield 77%, m.p. 189-191 °C. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 9.05 (t, $J = 6.0$ Hz, 1H), 8.18 (t, $J = 6.0$ Hz, 1H), 7.93 – 7.96 (m, 2H), 7.86 (s, 4H), 7.78 – 7.81 (m, 2H), 7.28 – 7.37 (m, 4H), 7.22 (dd, $J = 13.2, 8.4$ Hz, 4H), 4.42 (d, $J = 5.9$ Hz, 2H), 3.97 (d, $J = 5.2$ Hz, 2H). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 165.06, 163.64, 162.61, 161.19, 142.78, 139.39, 138.56, 136.10, 135.05, 135.02, 130.78, 130.76, 129.89, 129.80, 129.24, 129.16, 127.58, 127.33, 127.16, 127.14, 116.07, 115.85, 115.32, 115.10, 45.91, 42.37. HRMS calcd for $\text{C}_{27}\text{H}_{23}\text{O}_3\text{N}_2\text{SF}_2$ 493.13920 $[\text{M} + \text{H}]^+$, found 493.13953.

Section B: ^1H and ^{13}C NMR Spectra of compounds **Ia-b**, **IIa-c**, and **IIIa-o**.

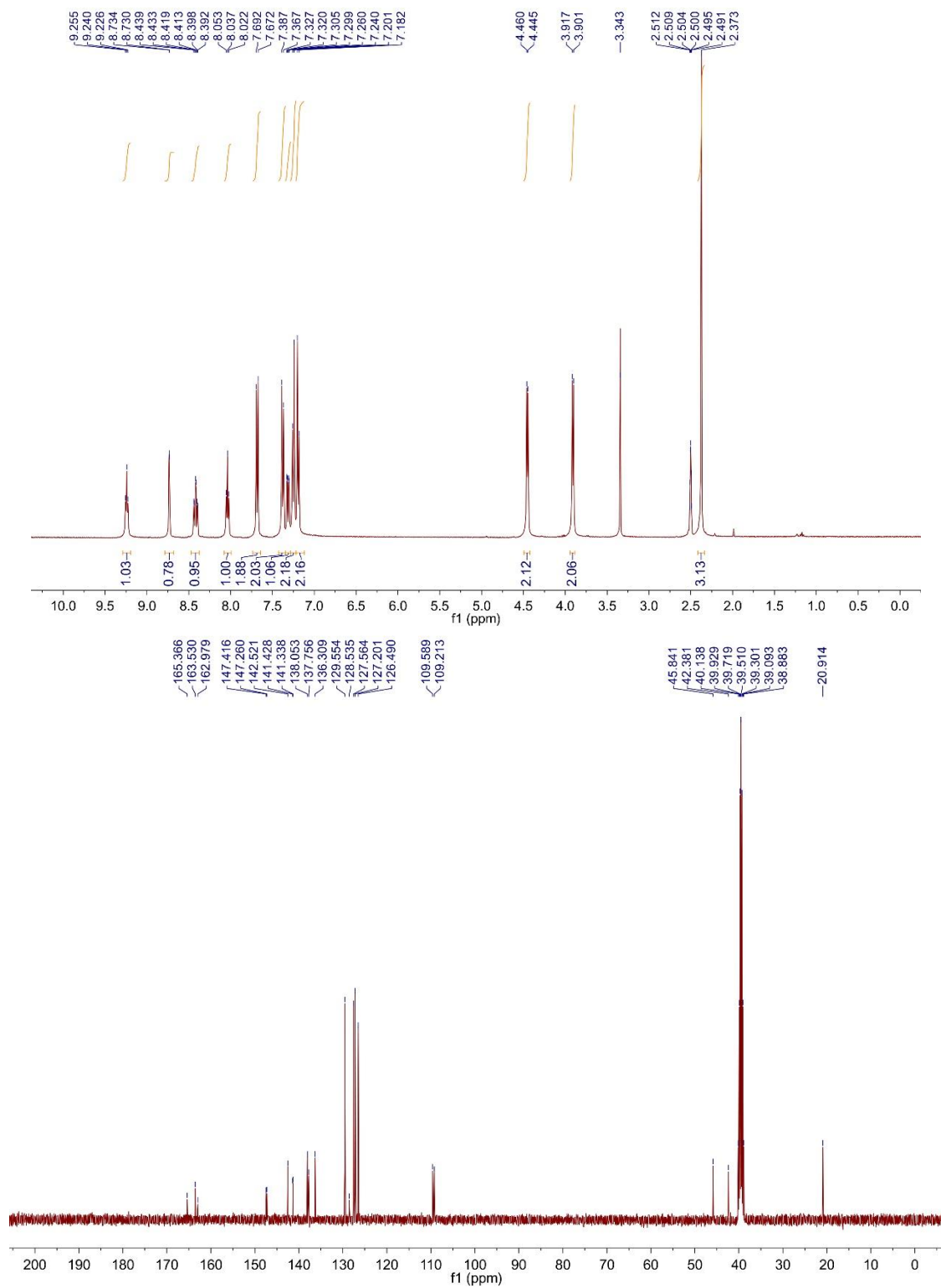


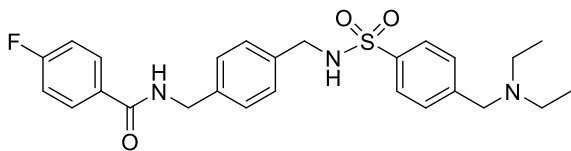
5-Fluoro-N-(4-(((4-methylphenyl)sulfonamido)methyl)benzyl)picolinamide (Ia).



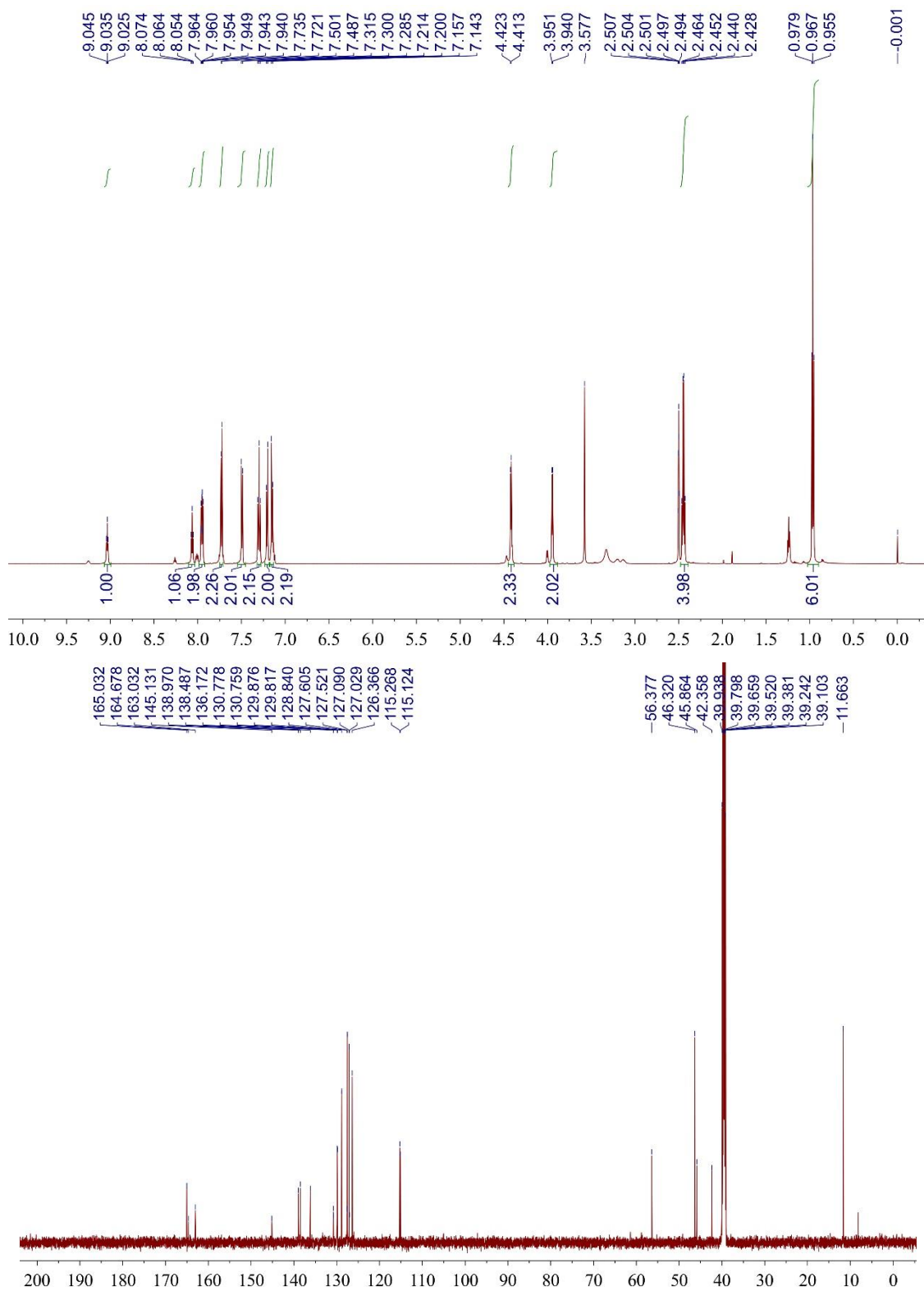


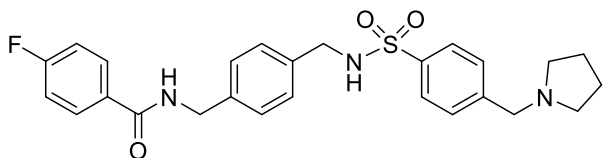
6-Fluoro-N-(4-(((4-methylphenyl)sulfonamido)methyl)benzyl)nicotinamide (Ib).



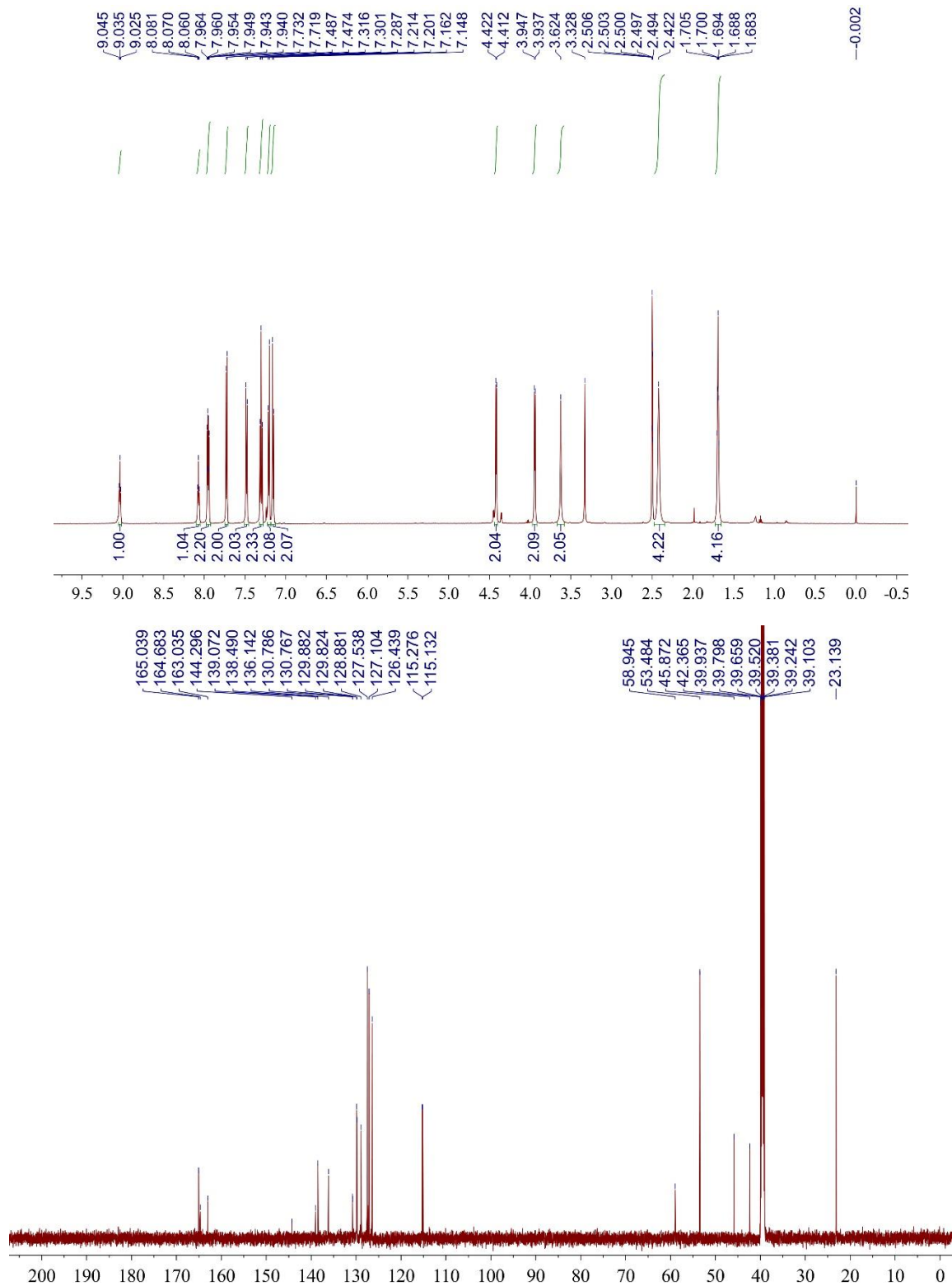


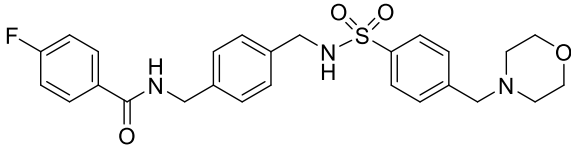
N-(4-(((4-((diethylamino)methyl)phenyl)sulfonamido)methyl)benzyl)-4-fluorobenzamide (IIa).



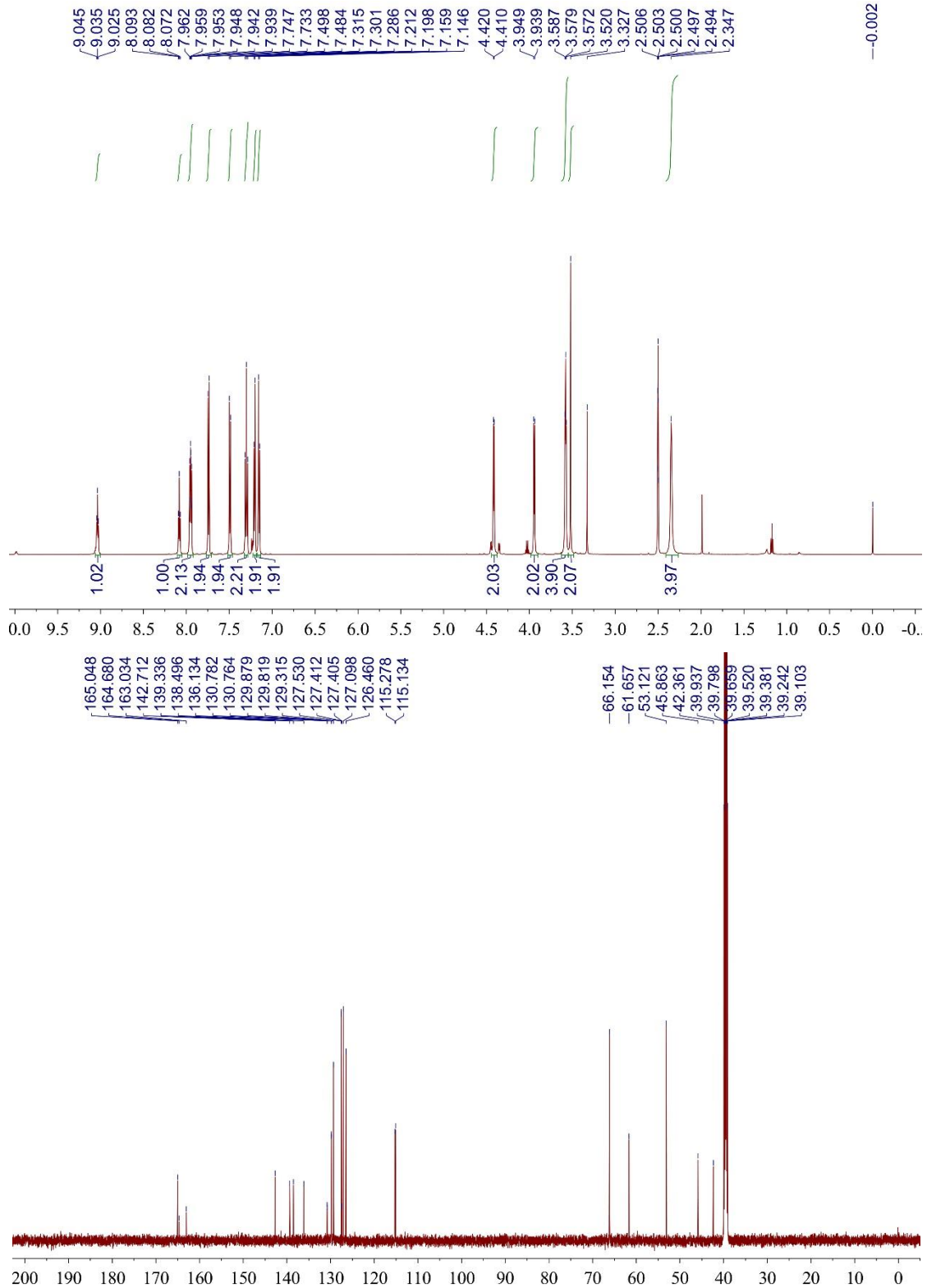


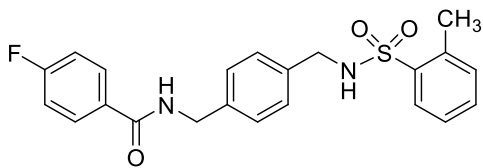
4-Fluoro-N-(4-(((4-(pyrrolidin-1-ylmethyl)phenyl)sulfonamido)methyl)benzyl)benzamide (IIb).



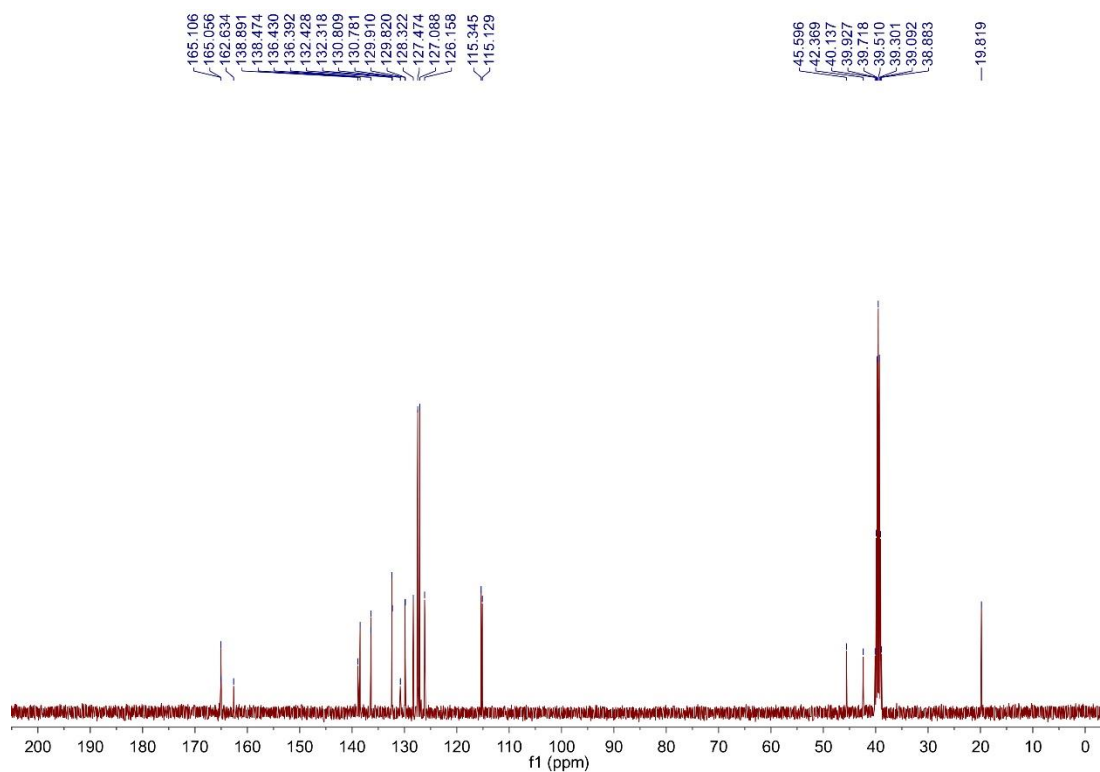
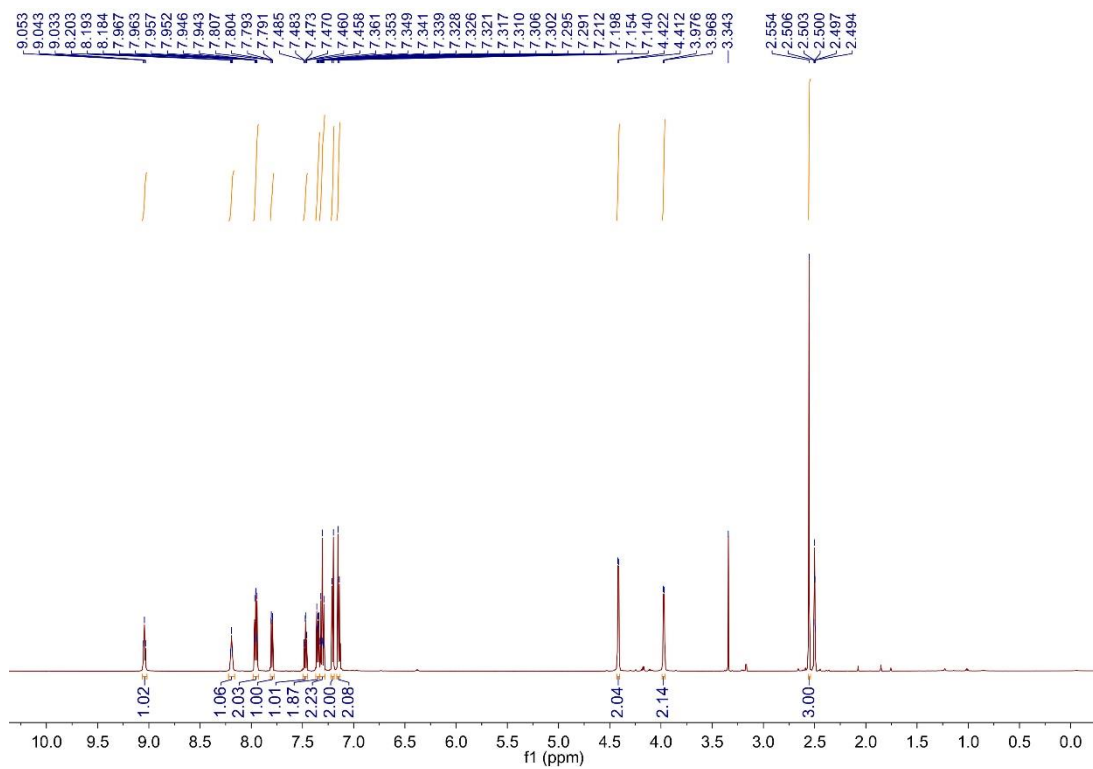


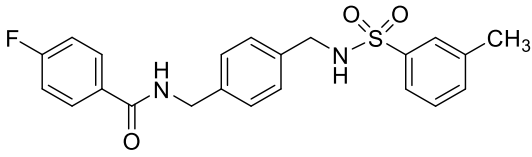
4-Fluoro-N-(4-(((4-(morpholinomethyl)phenyl)sulfonamido)methyl)benzyl)benzamide (IIc).



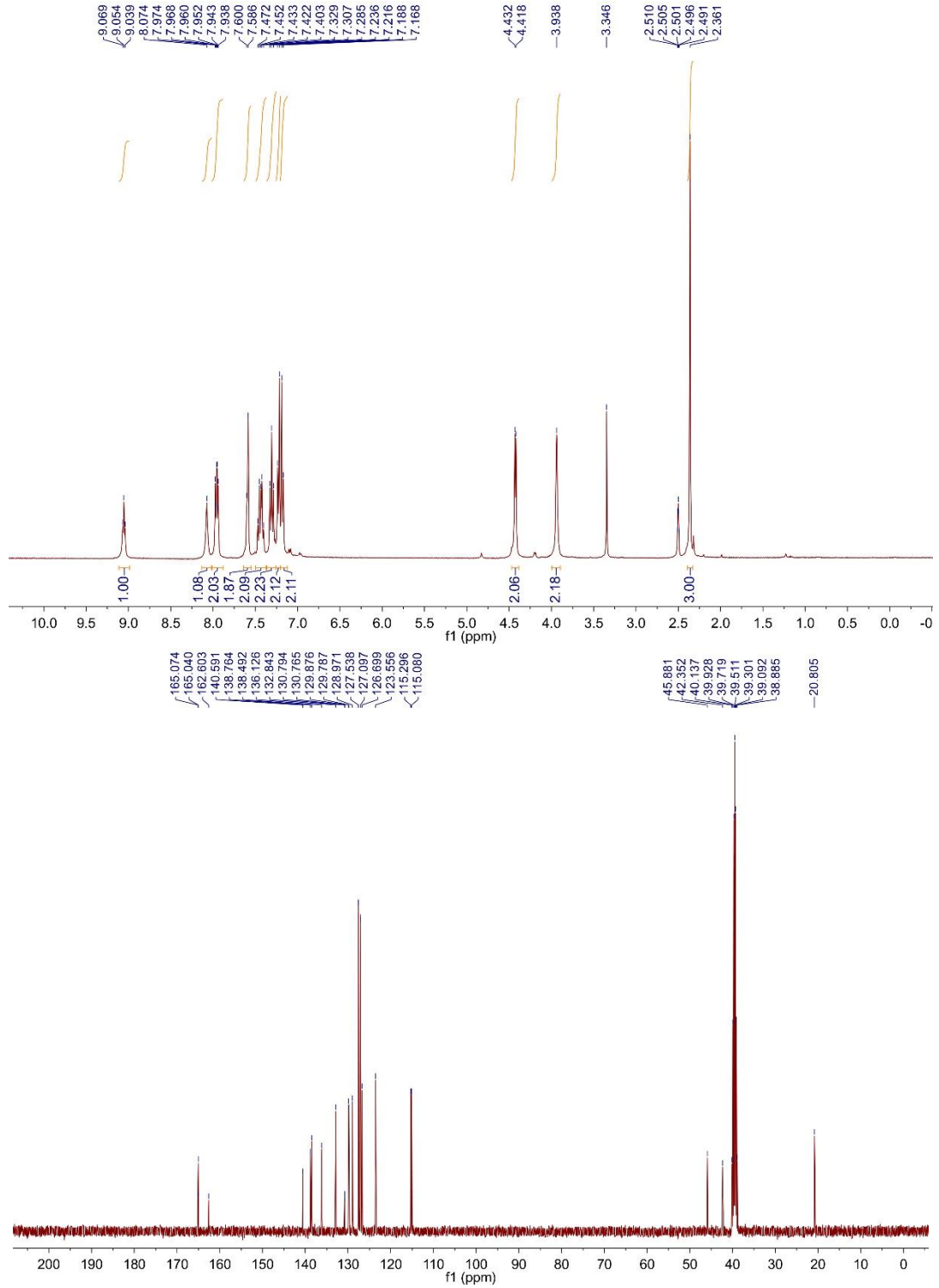


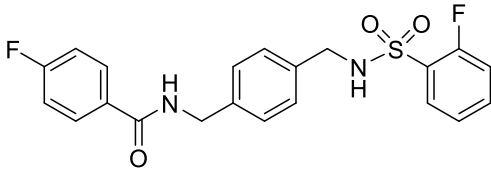
4-Fluoro-N-(4-(((2-methylphenyl)sulfonamido)methyl)benzyl)benzamide (IIIa).



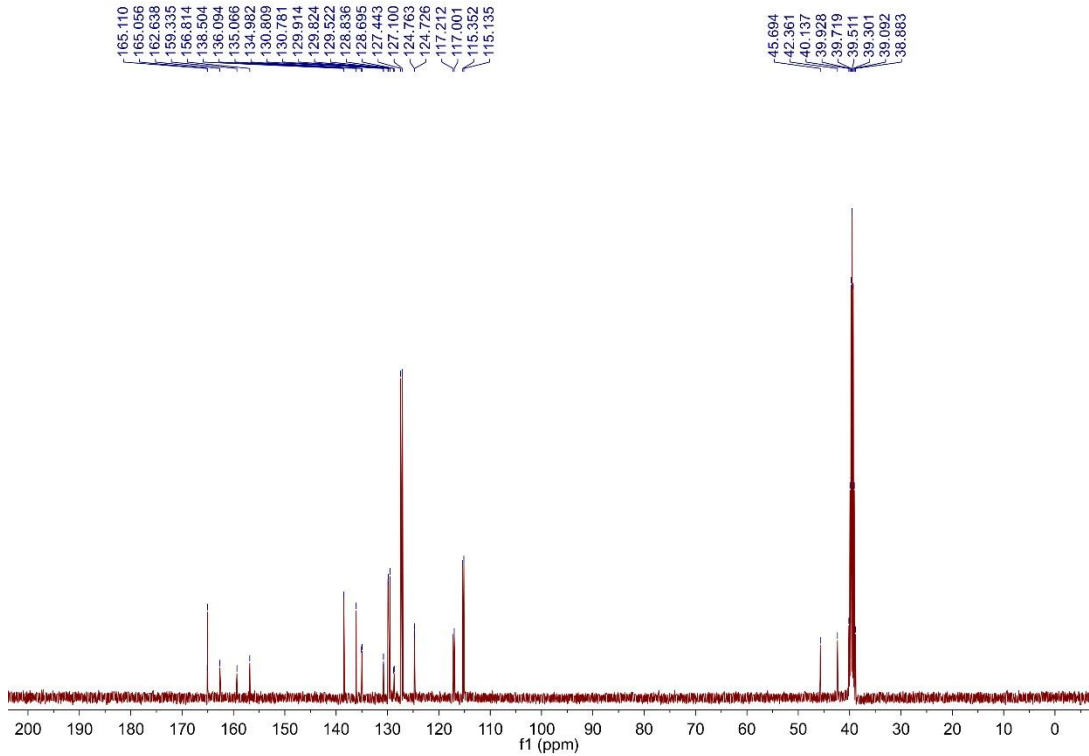
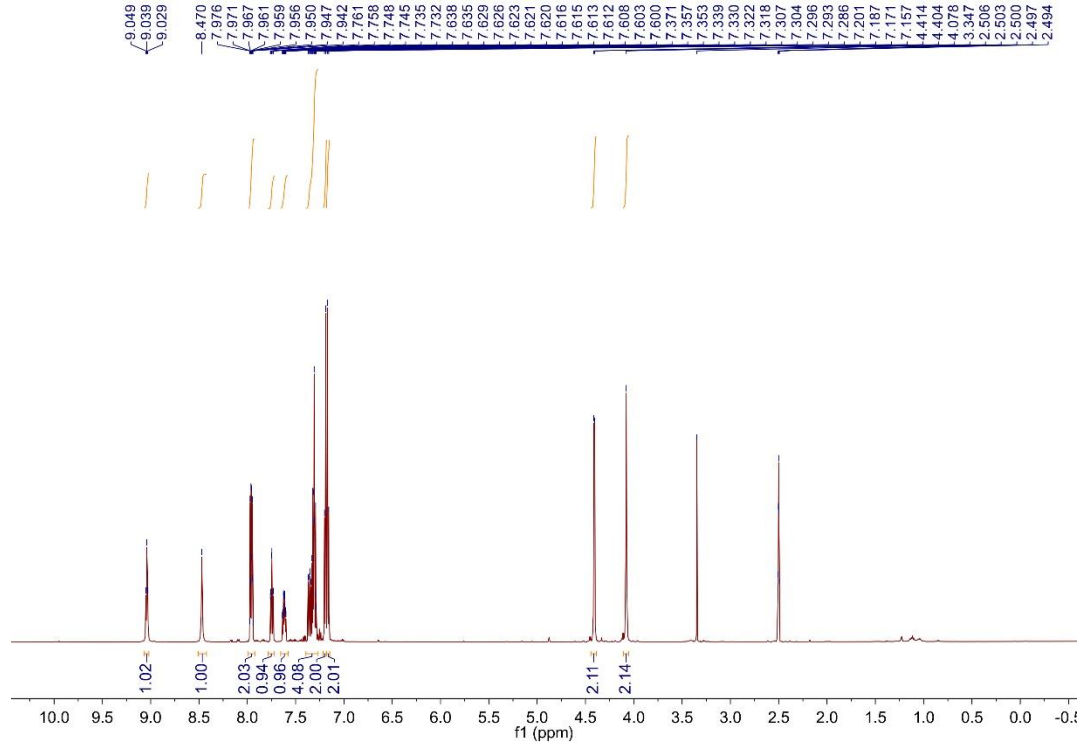


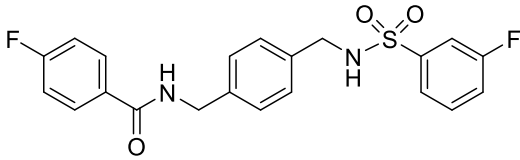
4-Fluoro-N-(4-(((3-methylphenyl)sulfonamido)methyl)benzyl)benzamide (IIIb).



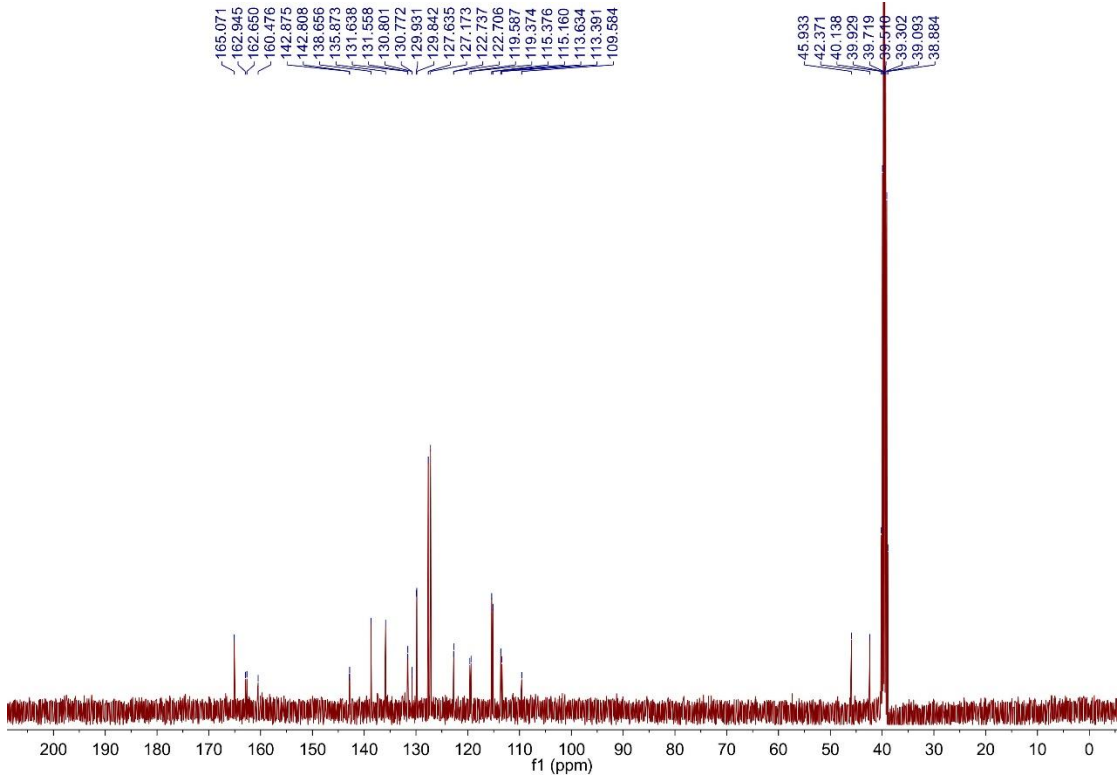
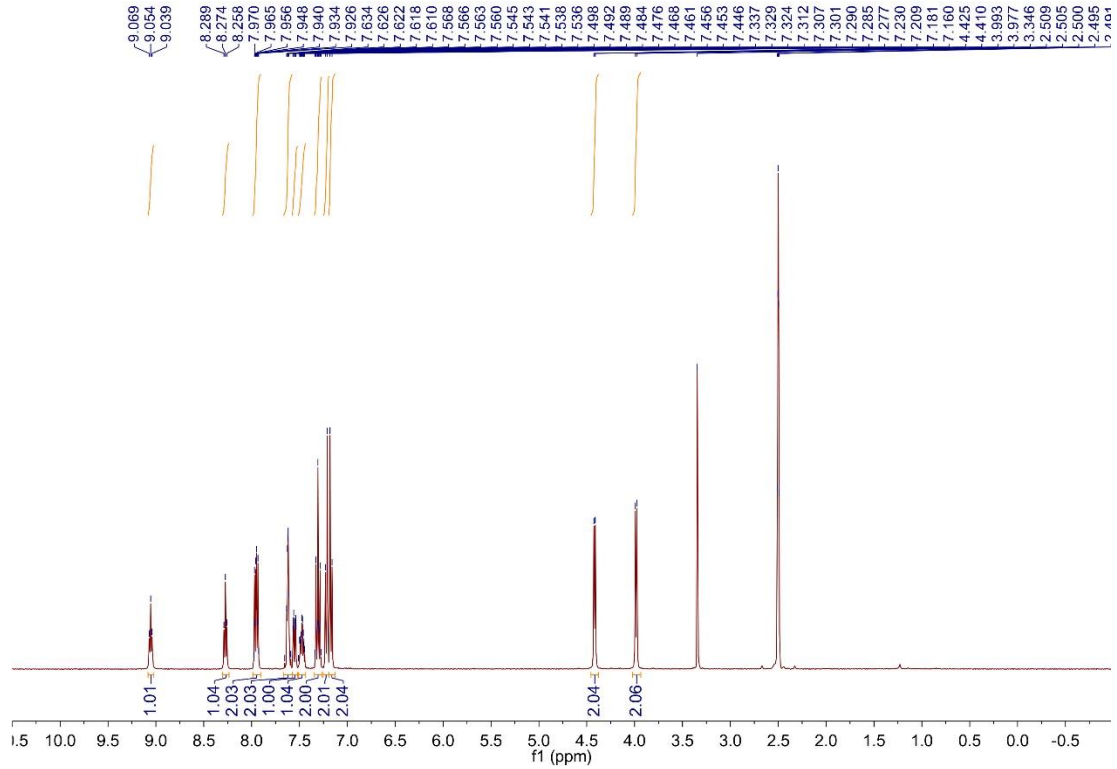


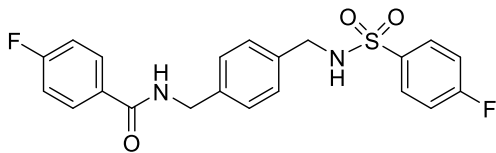
4-Fluoro-N-(4-(((2-fluorophenyl)sulfonamido)methyl)benzyl)benzamide (IIIc).



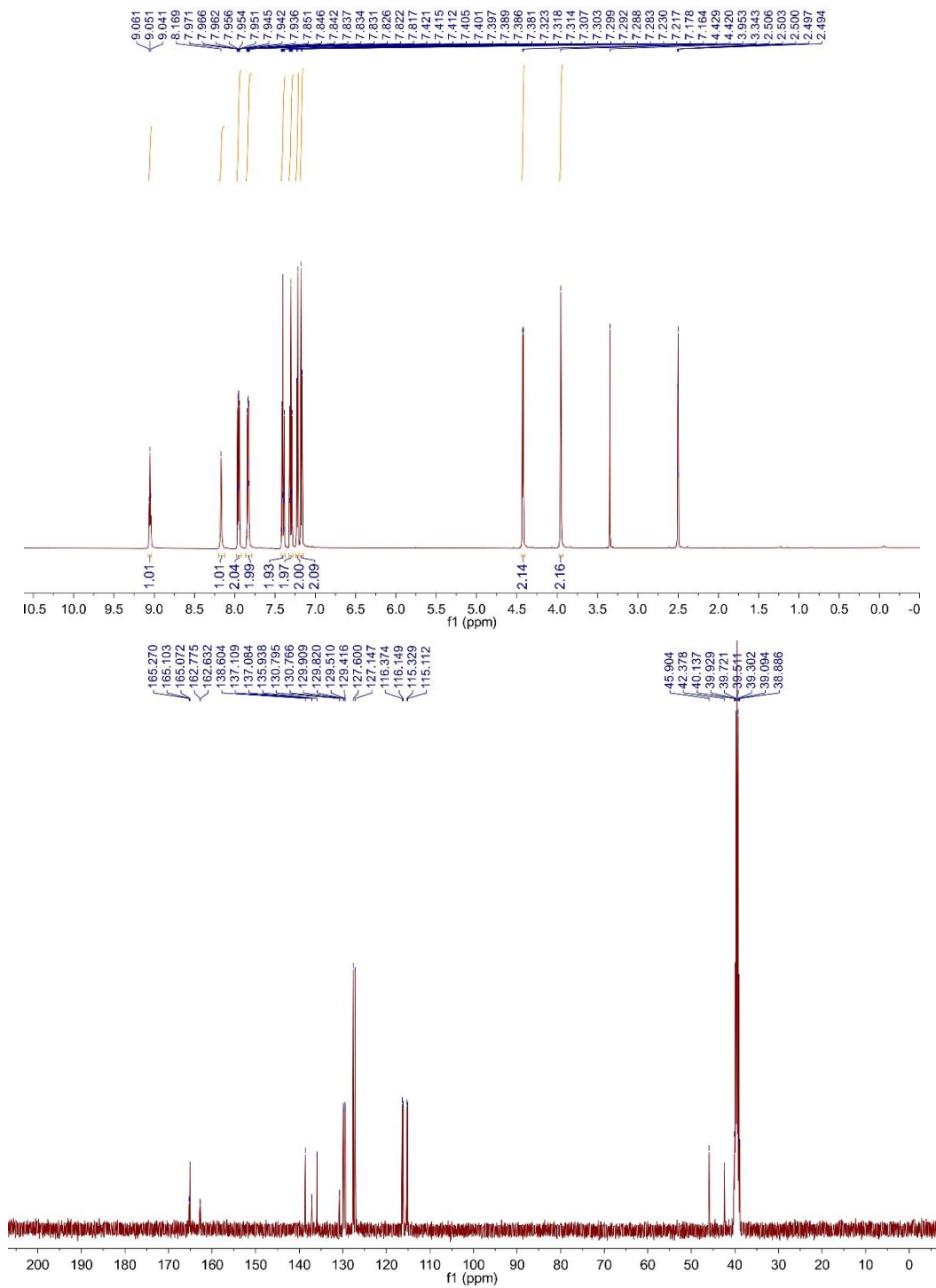


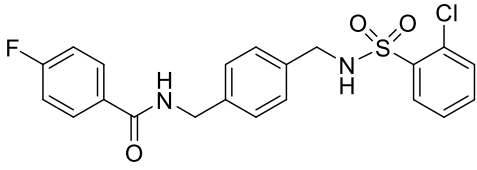
4-Fluoro-N-(4-(((3-fluorophenyl)sulfonamido)methyl)benzyl)benzamide (III d).



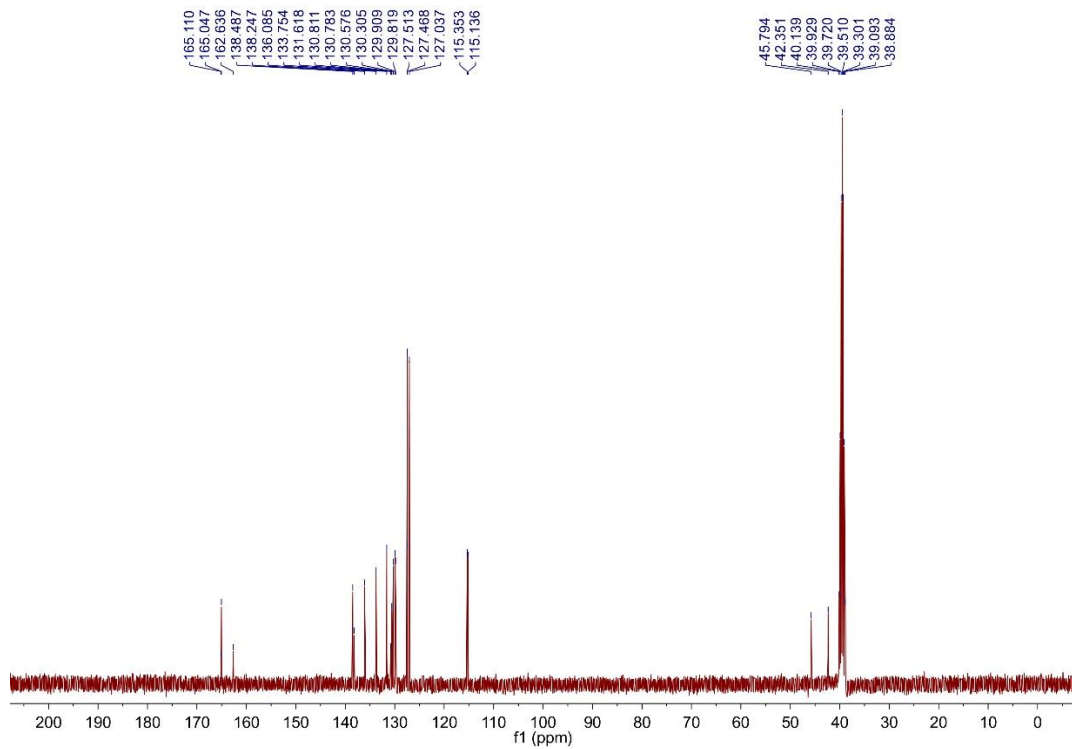
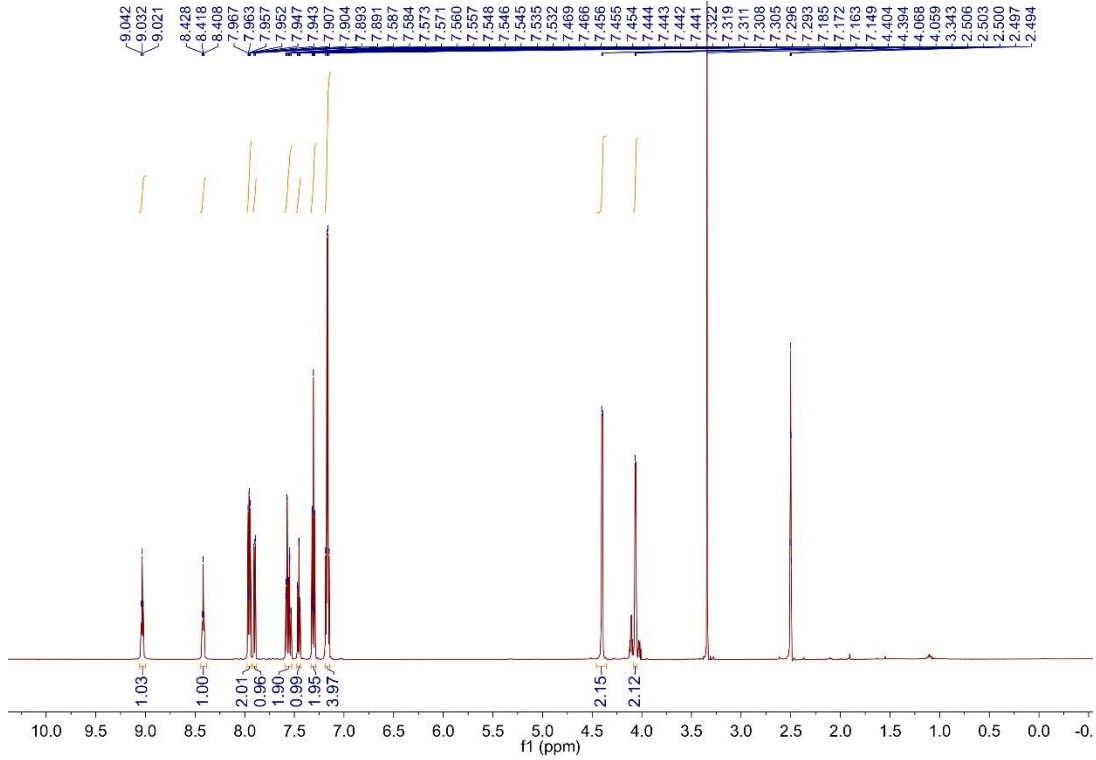


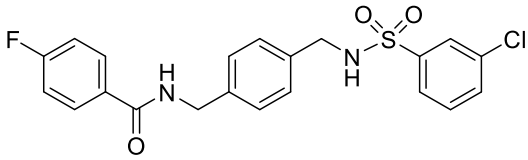
4-Fluoro-N-(4-((4-fluorophenyl)sulfonamido)methyl)benzyl)benzamide (IIIe).



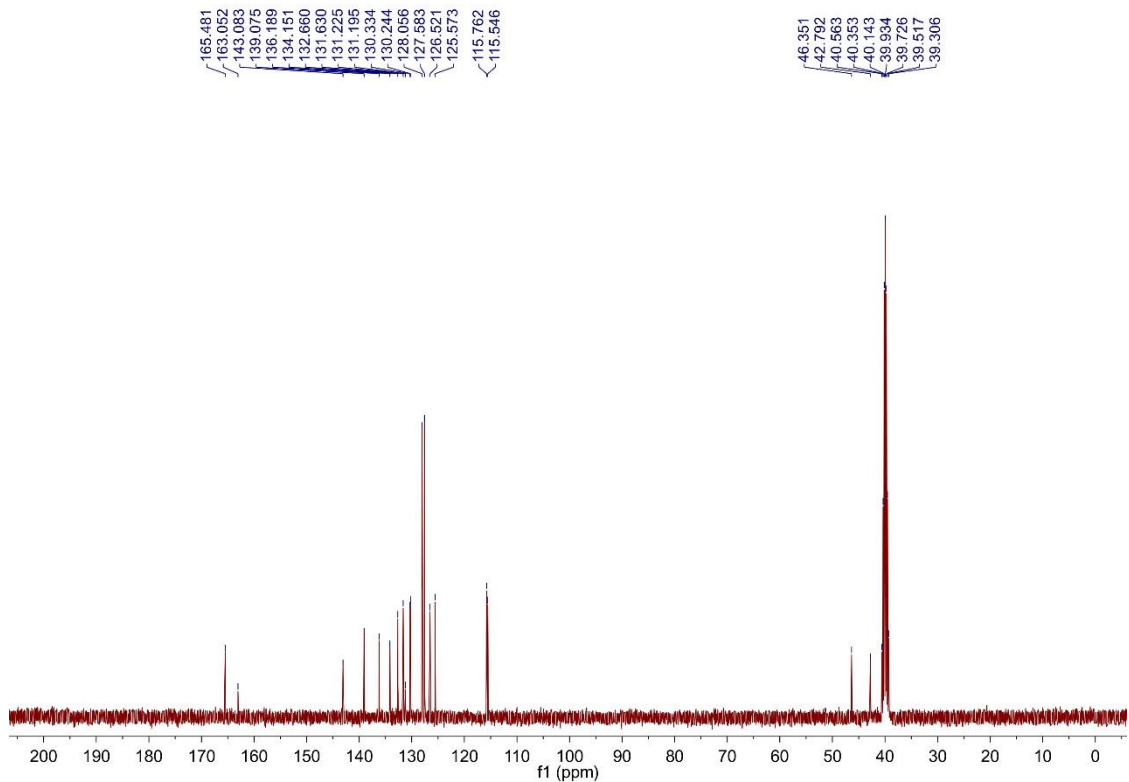
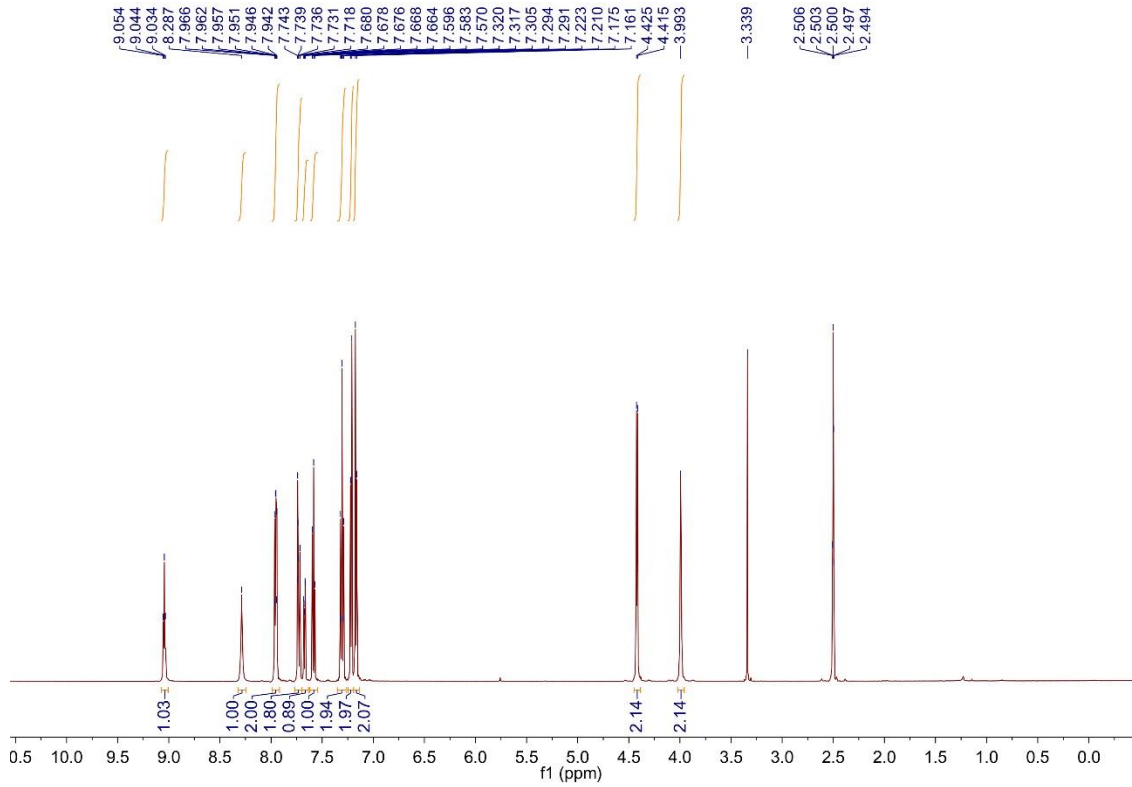


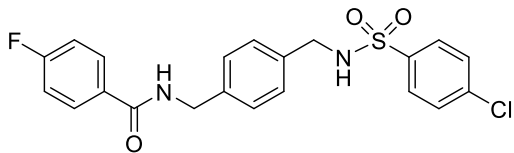
4-Fluoro-N-(4-(((2-chlorophenyl)sulfonamido)methyl)benzyl)benzamide (III f).



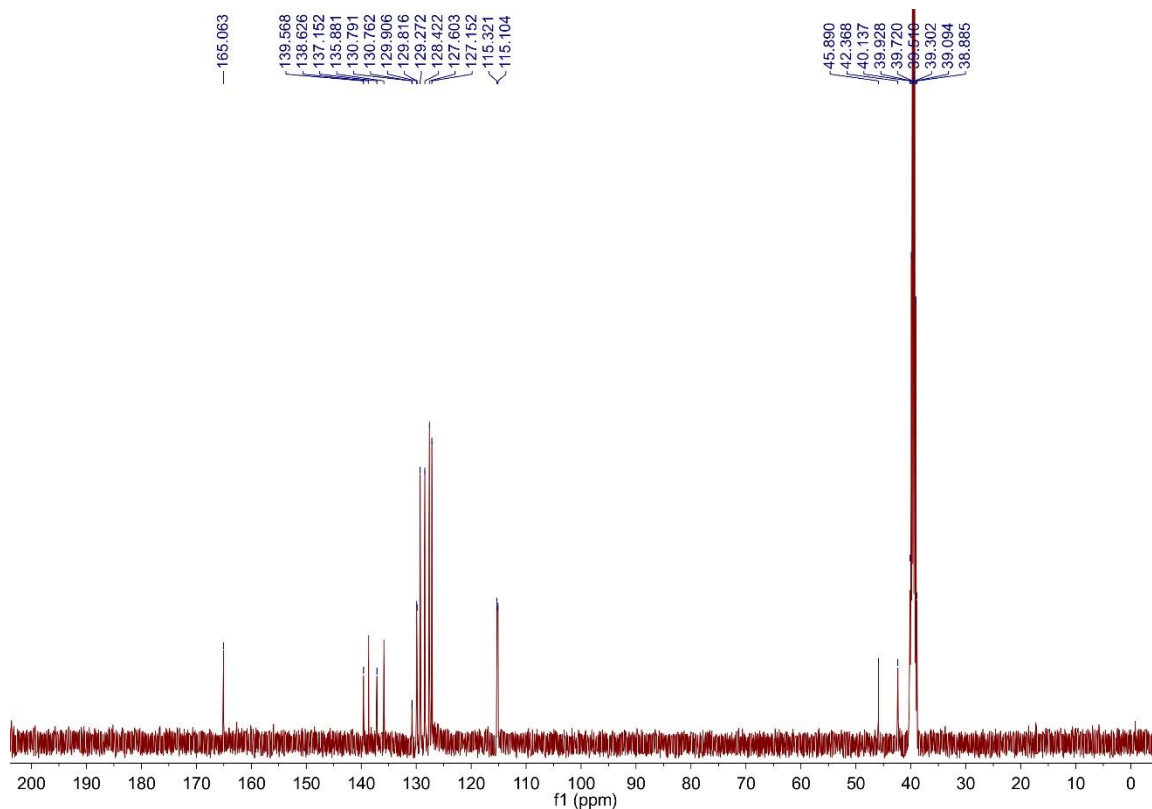
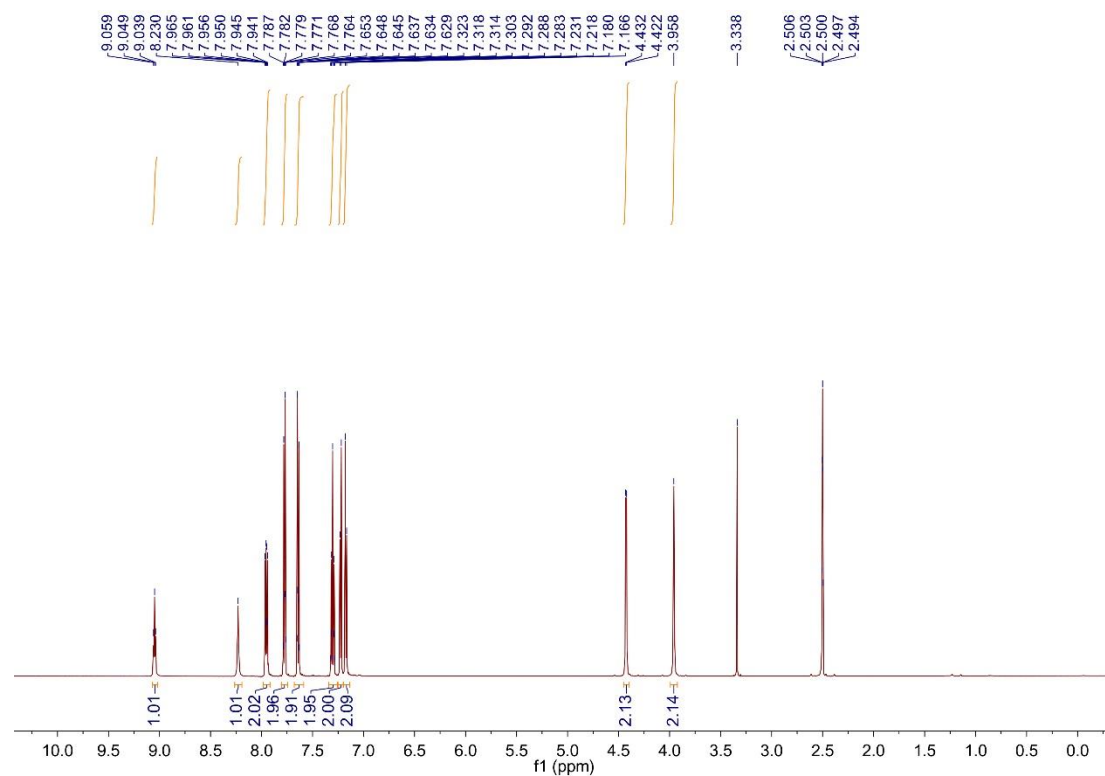


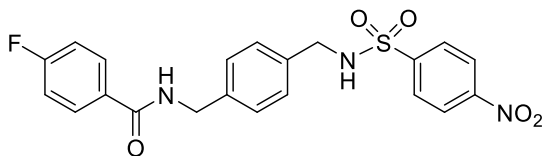
4-Fluoro-N-(4-(((3-chlorophenyl)sulfonamido)methyl)benzyl)benzamide (IIIg).



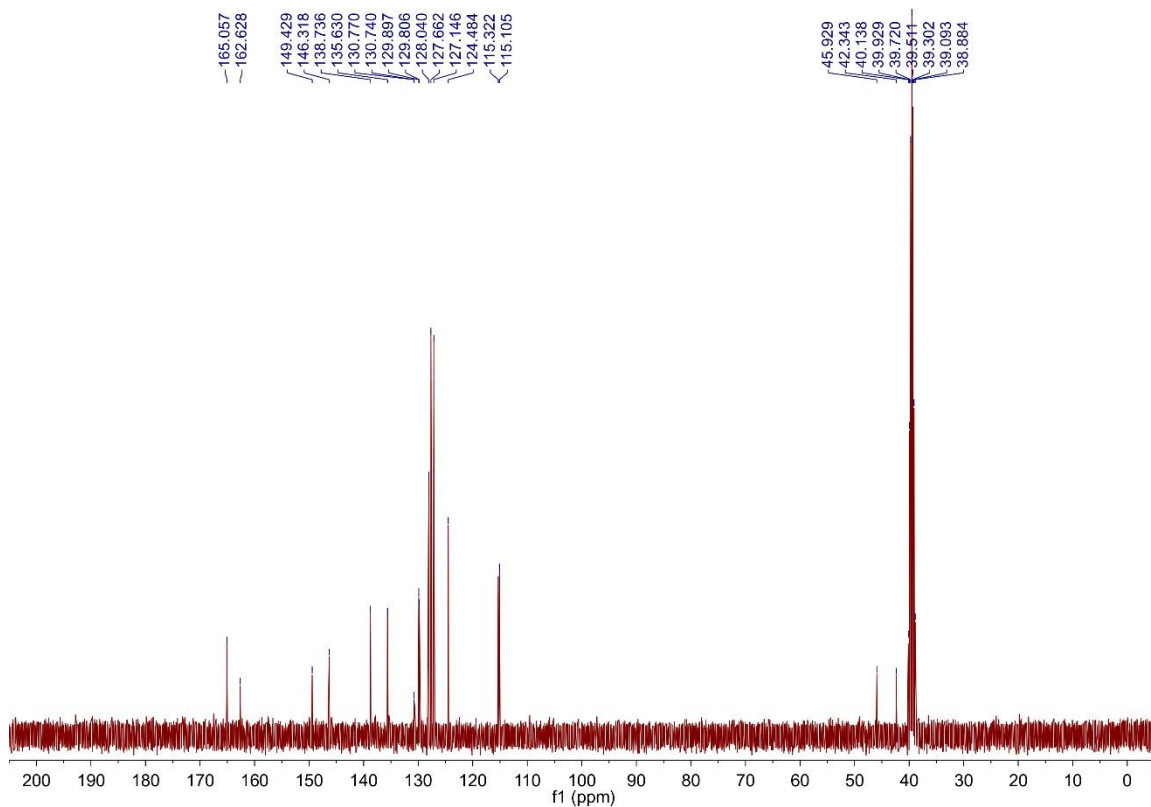
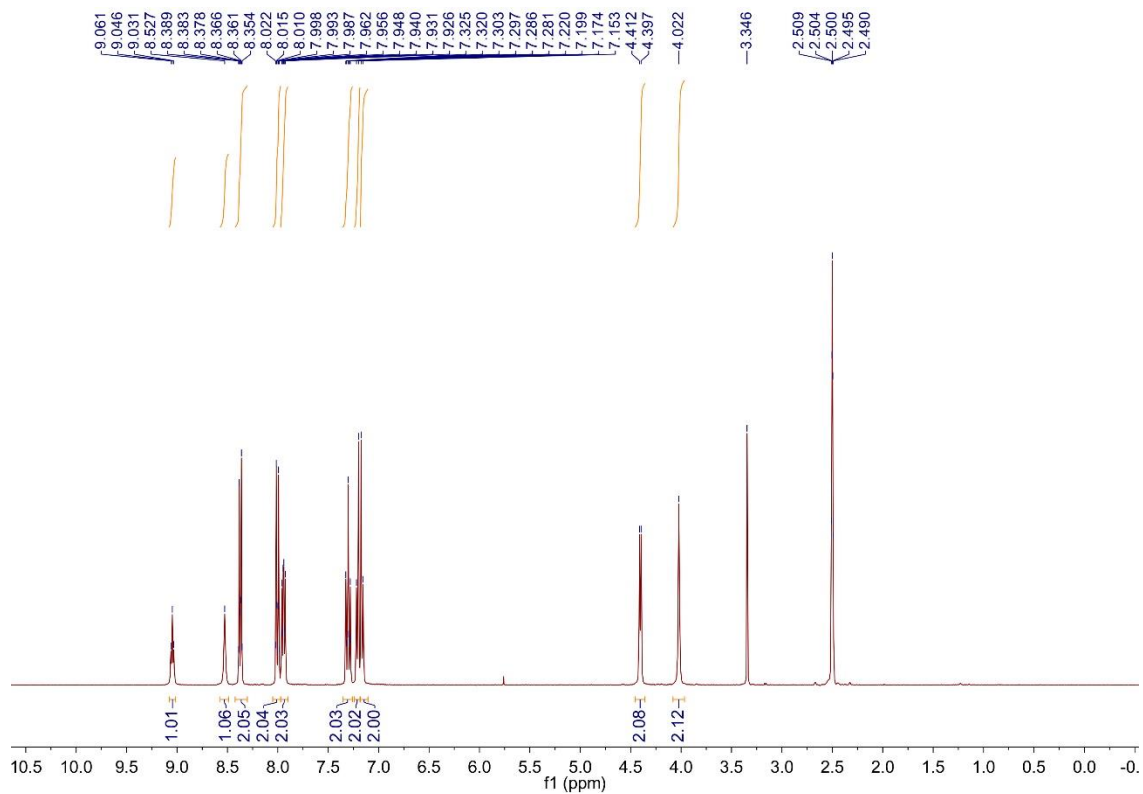


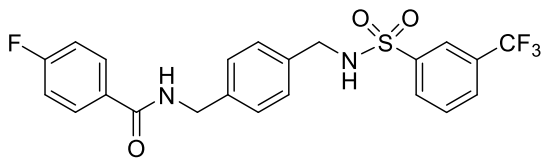
4-Fluoro-N-(4-(((4-chlorophenyl)sulfonamido)methyl)benzyl)benzamide (IIIh).



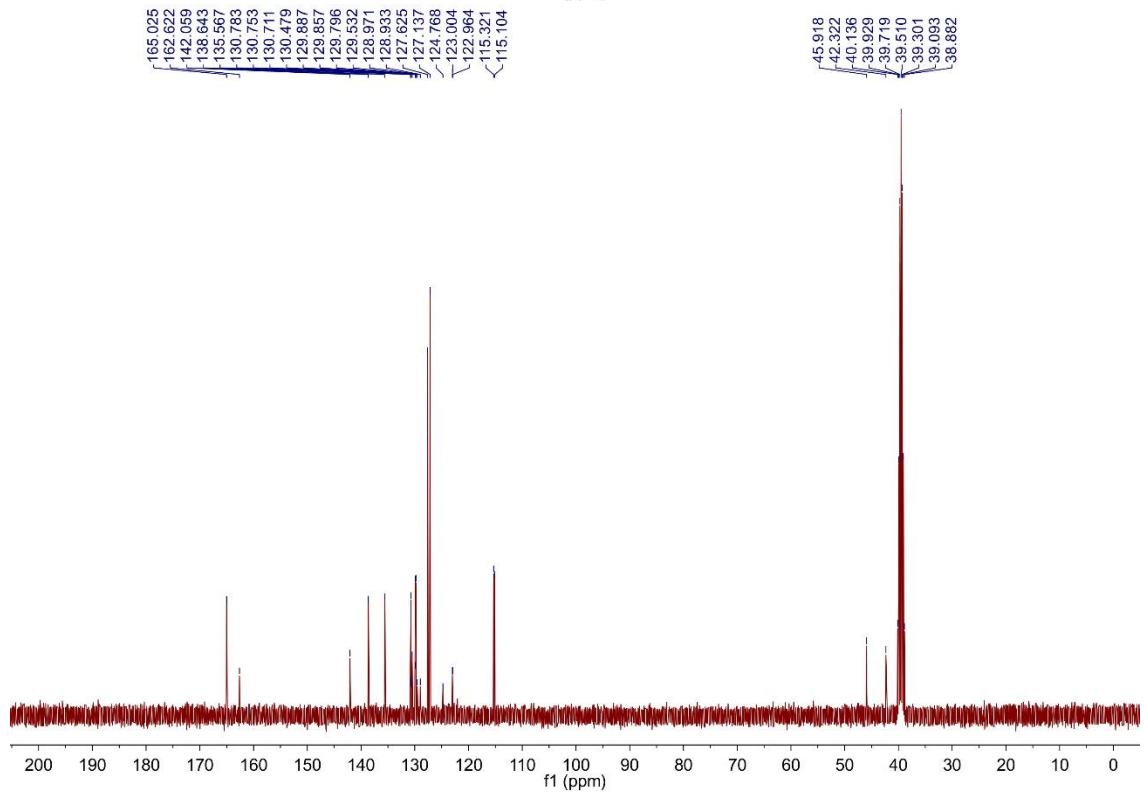
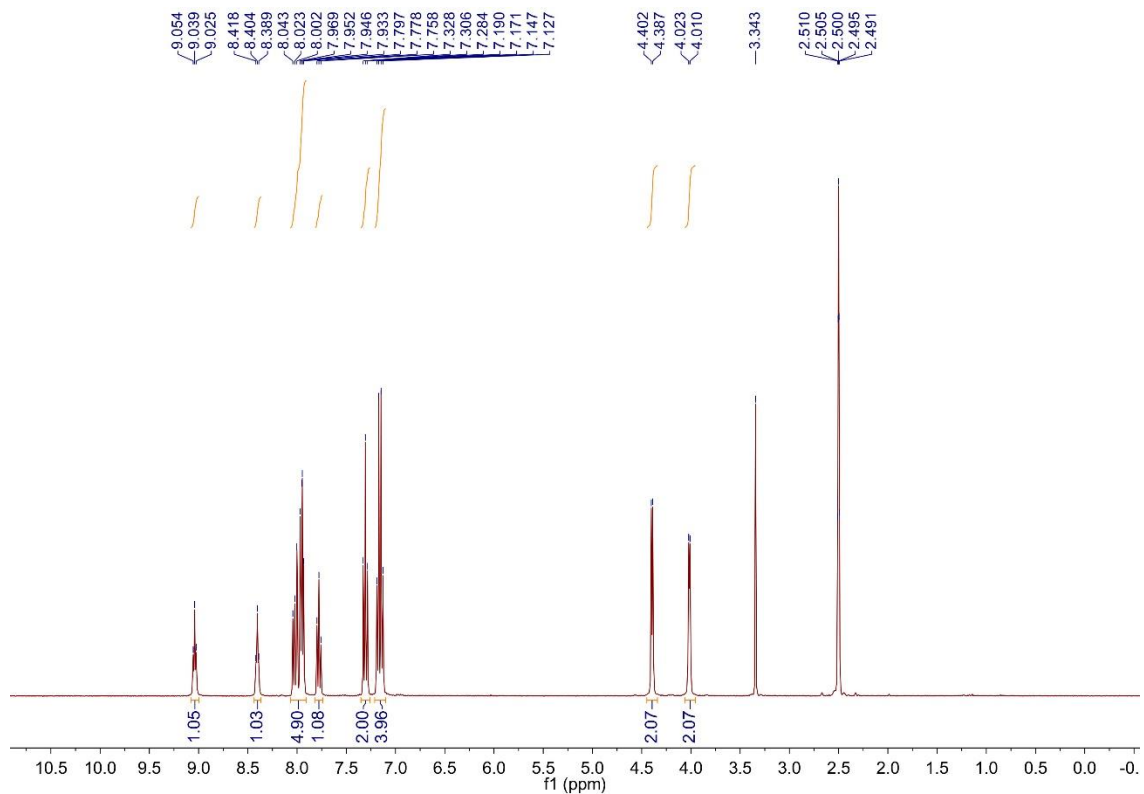


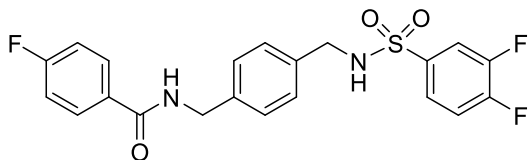
4-Fluoro-N-(4-(((4-nitrophenyl)sulfonamido)methyl)benzyl)benzamide (IIIi).



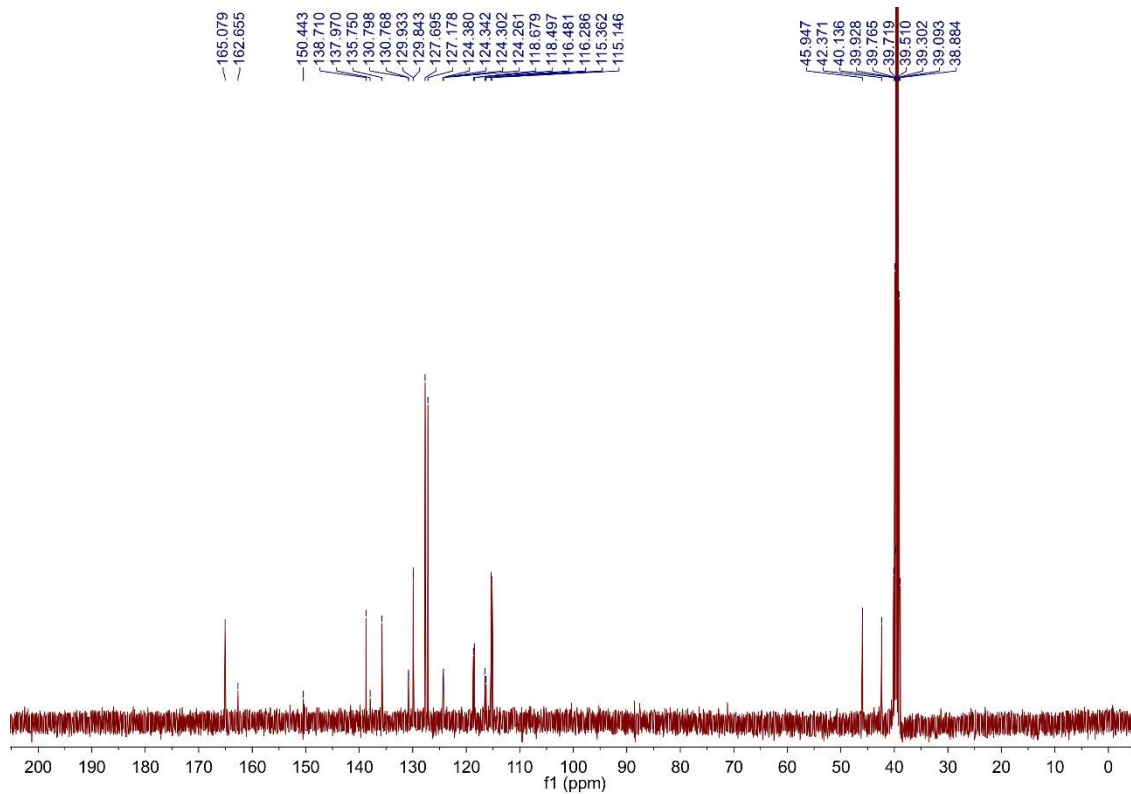
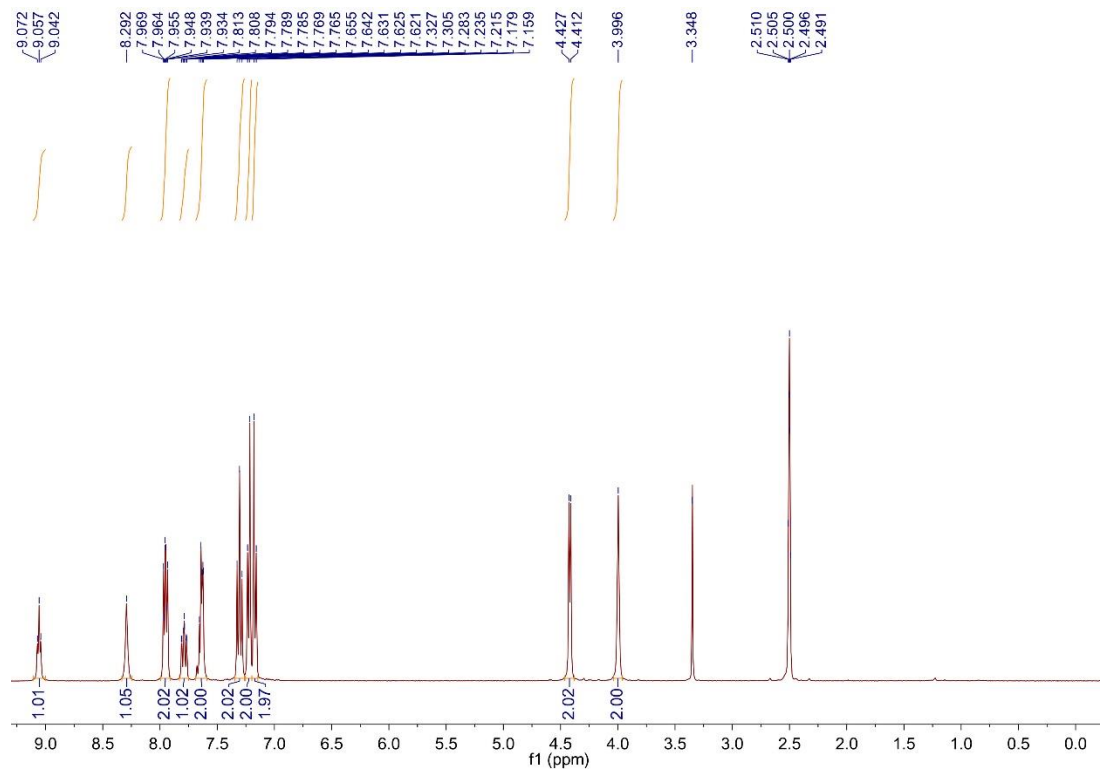


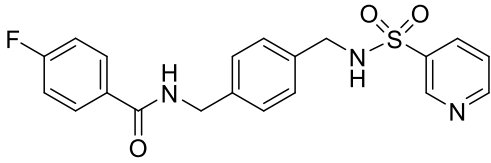
4-Fluoro-N-(4-(((3-(trifluoromethyl)phenyl)sulfonamido)methyl)benzyl)benzamide (IIIj).



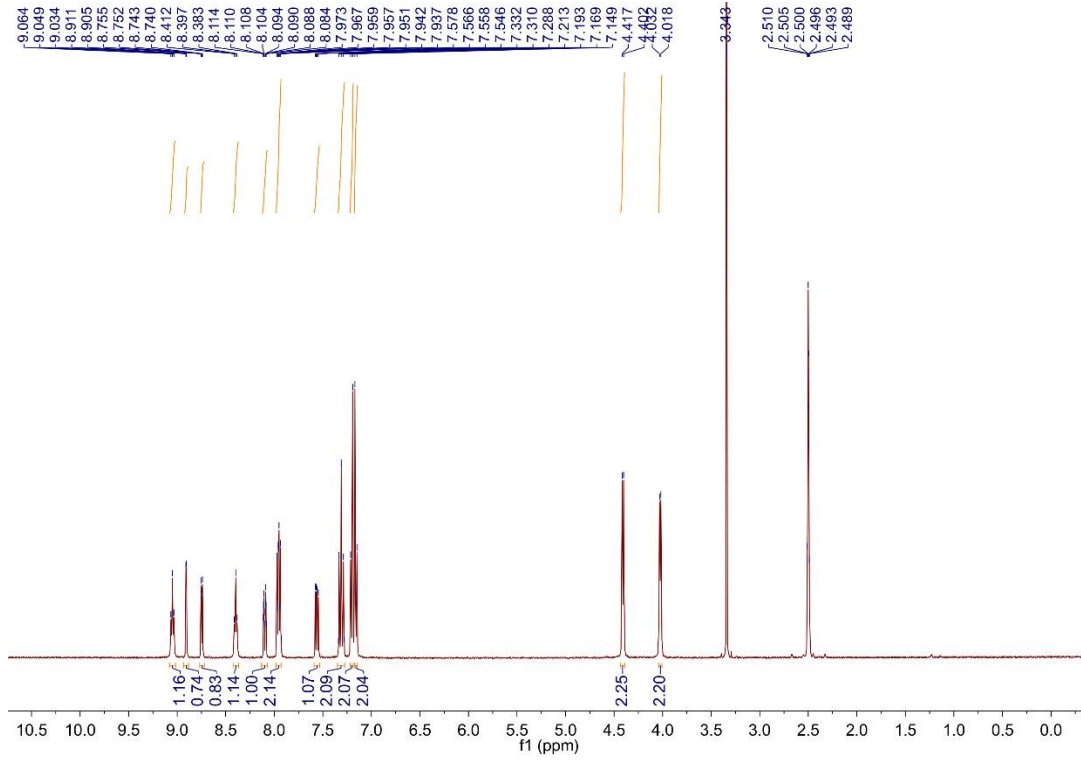


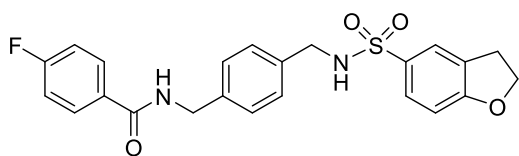
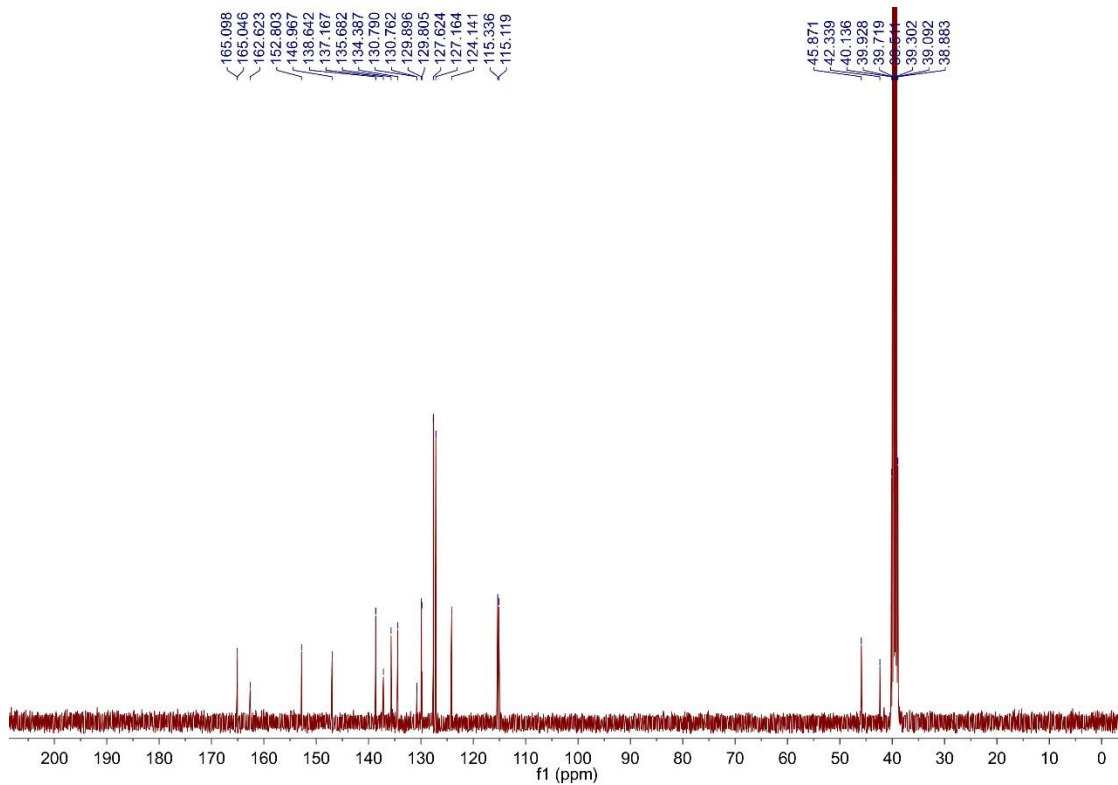
4-Fluoro-N-(4-(((3,4-difluorophenyl)sulfonamido)methyl)benzyl)benzamide (IIIk).



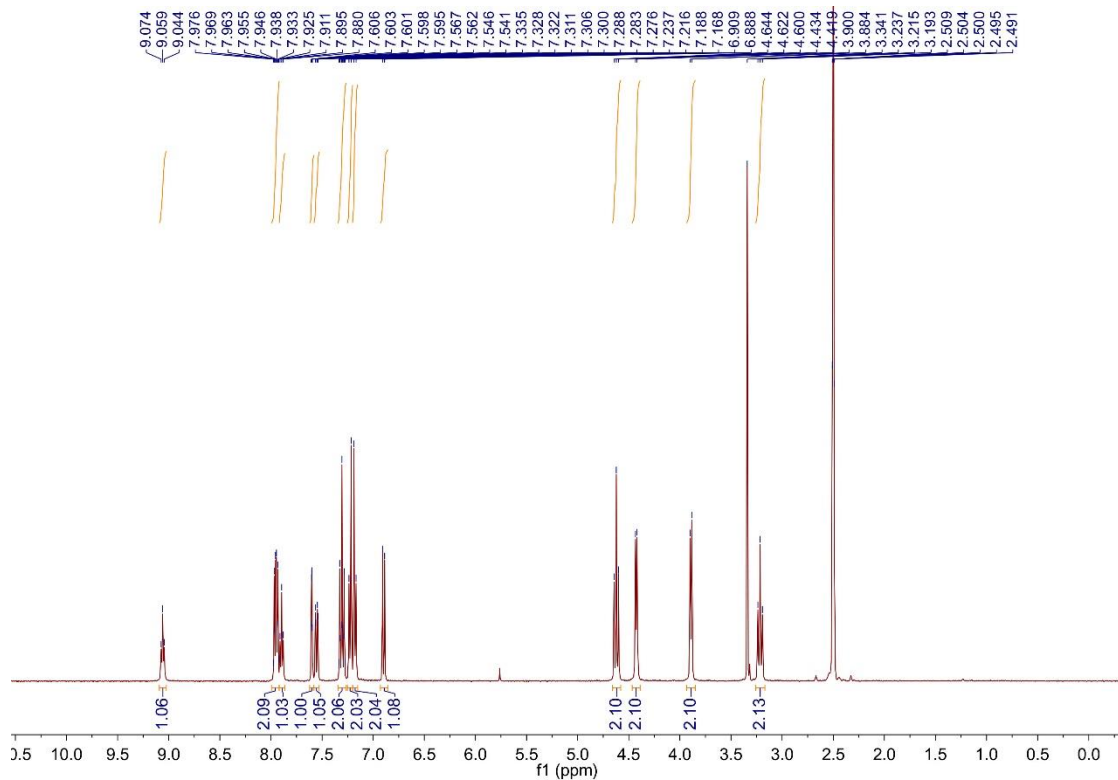


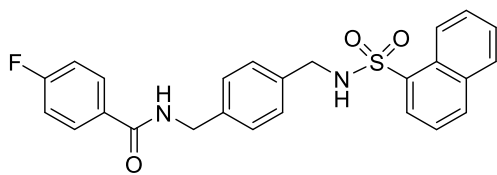
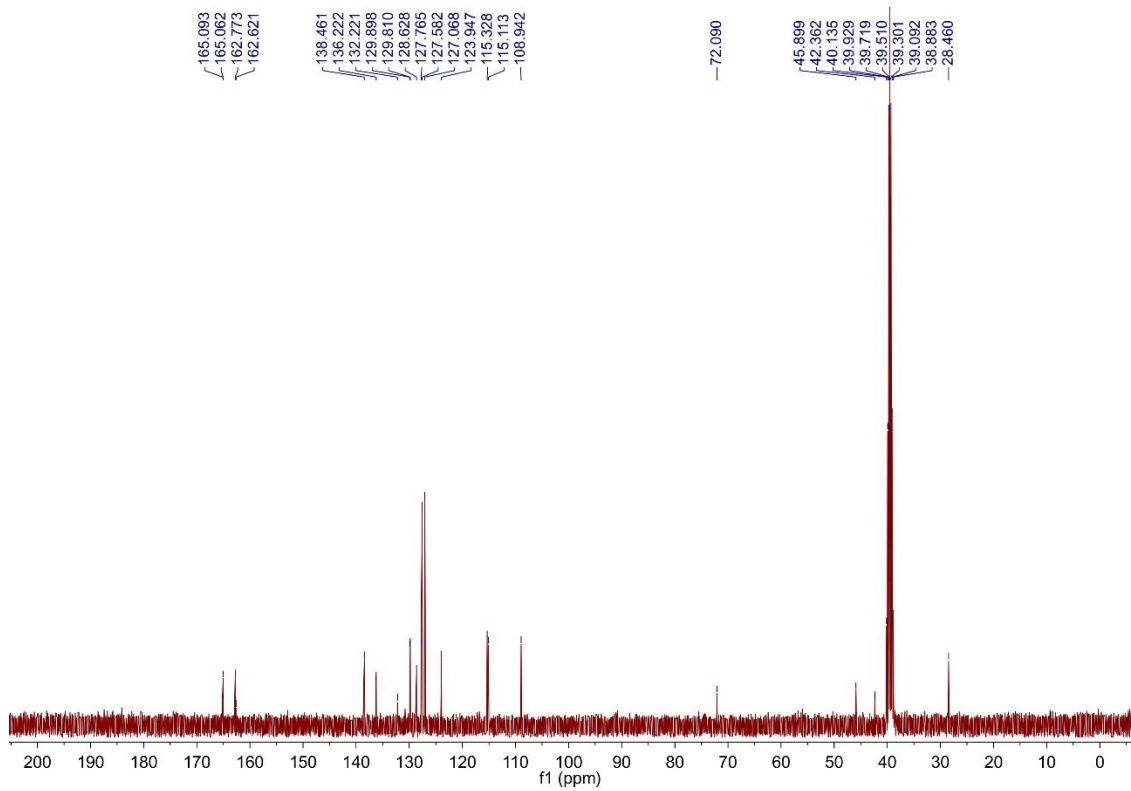
4-Fluoro-N-(4-((pyridine-3-sulfonamido)methyl)benzyl)benzamide (III).



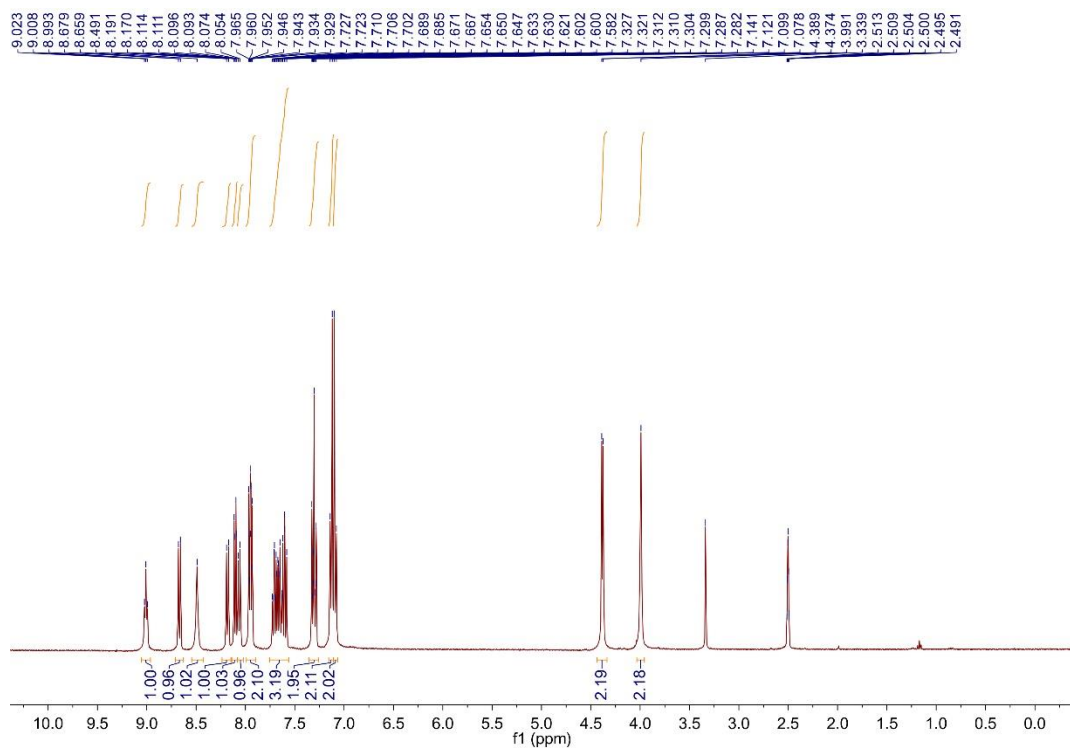


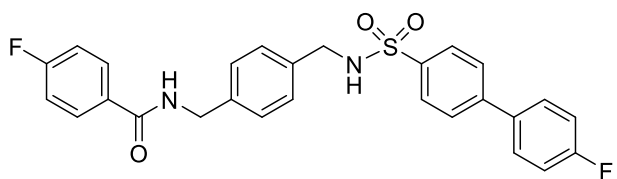
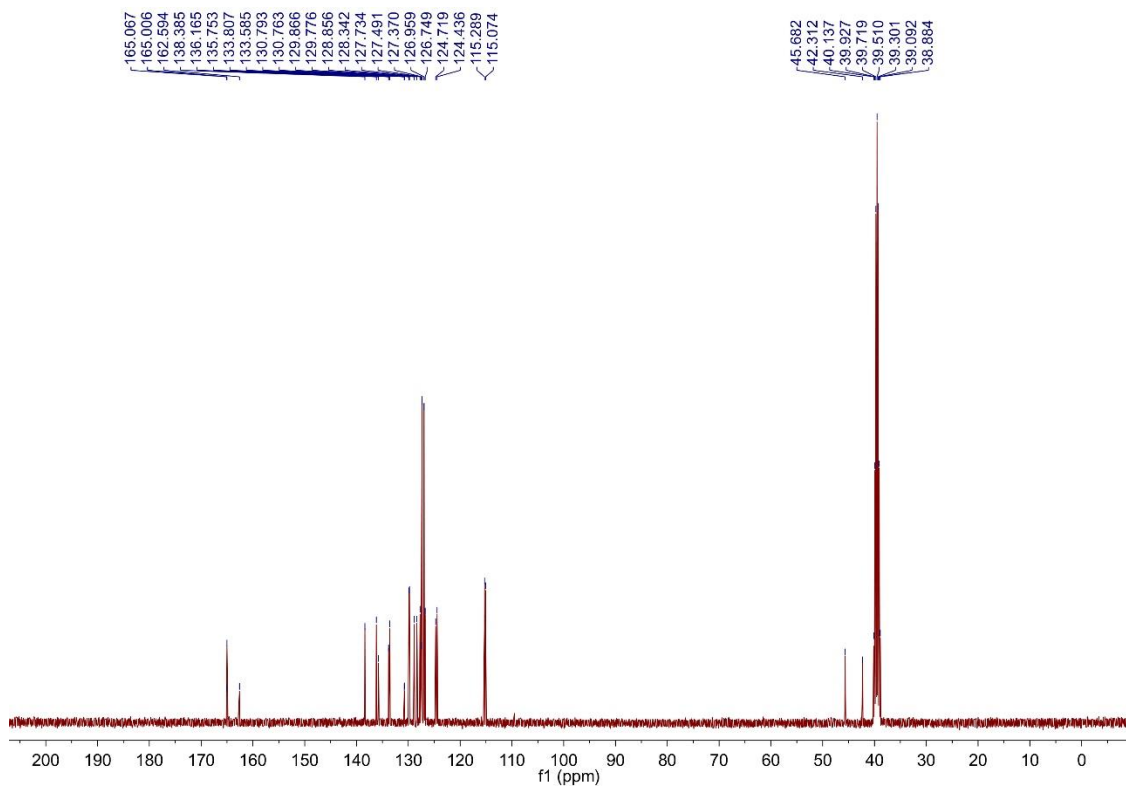
4-Fluoro-N-(4-(((2,3-dihydrobenzofuran)-5-sulfonamido)methyl)benzyl)benzamide (IIIb).





4-Fluoro-N-(4-((naphthalene-1-sulfonamido)methyl)benzyl)benzamide (IIIh).





4-Fluoro-N-(4-(((4'-fluoro-[1,1'-biphenyl])-4-sulfonamido)methyl)benzyl)benzamide (IIIo).

