Supplementary Materials: Synthesis and fungicidal activity of novel pyrroloindole scaffolds and their derivatives

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Abstract: The key scaffold of pyrroloindole ring is a very important structure, which is isolated from plants and fungi with a variety of medical and fungicidal activities. In the paper, a series of pyrroloindole analogues were synthesized from indole-3-acetonitrile and screened for their antifungal activities against plant pathogenic fungi. Compounds **a2** and **a15** exhibited potent antifungal activities with a minimum inhibitory concentration of 15.63 μg/mL against 6 kinds of fungi, and can be used as a novel antifungal agent for further development.

Key words: pyrroloindole; antifungal activities;plant pathogenic fungi; fluorobenzene

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1. Spectroscopic Data

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(3-chloropyridin-4-yl)methanone(a1)

White solid, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 8.65 (s, 1H), 8.57 (d, *J* = 4.8 Hz, 1H), 7.30 – 6.89 (m, 11H), 6.72 (dt, *J* = 14.8, 7.5 Hz, 1H), 6.17 (d, *J* = 7.8 Hz, 1H), 5.97 (d, *J* = 10.1 Hz, 1H), 4.57 (dd, *J* = 49.8, 16.5 Hz, 2H), 3.42 – 3.02 (m, 4H), 2.40 – 2.20 (m, 2H). ^{13}C-NMR (100 MHz, Acetone - d_6), δ: 164.58 (C), 161.79 (d, *J* = 242.7 Hz, C), 161.68 (d, *J* = 242.3 Hz, C), 150.66 (C), 149.58 (CH), 148.58 (CH), 143.54 (C), 135.17 (d, *J* = 2.5 Hz, C), 133.74 (d, *J* = 3.1 Hz, C), 131.71 (d, *J* = 7.9 Hz, 2CH), 131.29 (C), 128.61 (d, *J* = 6.3 Hz, 2CH), 128.57 (CH), 127.12 (C) 123.49 (CH), 121.83 (CH), 117.64 (CH), 114.77 (d, *J* = 19.8 Hz, 2CH), 114.56 (d, *J* = 19.6 Hz, 2CH), 105.94 (CH), 81.88 (CH), 57.25 (CH_2), 48.53 (C), 47.24 (CH_2), 43.38 (CH_2), 38.15 (CH_2). MS(ESI(+)) calcd for $C_{30}H_{24}ClF_2N_3O^+$ $[M+H]^+$: 516.16; found: 516.16.

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(5-chloropyrazin-2-yl)methanone(a2)

Yellow oil, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 8.73 (t, *J* = 1.2 Hz, 1H), 8.69 – 8.66 (m, 1H), 7.16 – 7.11 (m, 1H), 7.08 – 7.02 (m, 3H), 6.99 – 6.92 (m, 6H), 6.71 (td, *J* = 7.4, 1.0 Hz, 1H), 6.16 (d, *J* = 7.8 Hz, 1H), 6.02 (s, 1H), 4.53 (q, *J* = 16.3 Hz, 2H), 3.93 (ddd, *J* = 11.5, 7.1, 1.2 Hz, 1H), 3.46 – 3.39 (m, 1H), 3.21 (d, *J* = 13.4 Hz, 1H), 3.03 (d, *J* = 13.5 Hz, 1H), 2.34 – 2.25 (m, 2H). ^{13}C-NMR (100 MHz, Acetone - d_6), δ: 164.69 (C), 161.79 (d, *J* = 242.1 Hz, C), 161.70 (d, *J* = 241.8 Hz, C), 150.57 (C), 147.71 (C), 145.02 (C), 142.49 (CH), 141.50 (CH), 135.28 (d, *J* = 2.6 Hz, C), 133.84 (d, *J* = 2.9 Hz, C), 131.71 (d, *J* = 8.0 Hz, 2CH), 131.55 (C), 128.70 (d, *J* = 8.0 Hz, 2CH), 128.55 (CH), 123.48 (CH), 117.66 (CH), 114.73 (d, *J* = 18.0 Hz, 2CH), 114.55 (d, *J* = 22.0 Hz, 2CH), 106.21 (CH), 82.83 (CH), 56.5 1 (CH_2), 48.80 (C), 48.63 (CH_2), 43.51 (CH_2), 37.98 (CH_2). MS(ESI(+)) calcd for $C_{29}H_{23}ClF_2N_4O^+$ $[M+H]^+$: 517.15; found: 517.15.

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(6-chloropyridin-2-yl)methanone(a3)

Yellow oil, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 8.00 – 7.94 (m, 1H), 7.71 (dd, *J* = 7. 6, 0.8 Hz, 1H), 7.57 – 7.54 (m, 1H), 7.15 – 7.12 (m, 1H), 7.01 – 6.90 (m, 8H), 6.77 – 6.68 (m, 2H), 6.14 (d, *J* = 7.8 Hz, 1H), 6.01 (s, 1H), 4.53 (q, *J* = 16.3 Hz, 2H), 3.86 (ddd, *J* = 11.5, 7.1, 1.1 Hz, 1H), 3.48 – 3.39 (m, 1H), 3.21 (d, *J* = 13.4 Hz, 1H), 3.04 (t, *J* = 8.7 Hz, 1H), 2.28 (ddd, *J* = 9.6, 8.7, 5.1 Hz, 2H). ^{13}C-NMR (100 MHz, Acetone - d_6), δ: 165.81 (C), 161.78 (d, *J* = 243.8 Hz, 2CH), 161.68 (d, *J* = 243.2 Hz, 2CH), 154.49 (C), 150.60 (C), 149. 33 (C), 140.38 (C), 135.33 (d, *J* = 2.8 Hz, C), 133.91 (d, *J* = 2.9 Hz, C), 131.70 (d, *J* = 7.6 Hz, 2CH), 131.59 (CH), 128.67 (d, *J* = 8.6 Hz, 2CH), 128.52 (CH), 125.77 (CH), 123.47 (CH), 122.82 (CH), 117.55 (CH), 114.75 (d, *J* = 21.0 Hz, 2CH), 114.54 (d, *J* = 21.0 Hz, 2CH), 1 06.155 (CH), 82.75 (CH), 56.48 (CH_2), 48.77 (C), 48.72 (CH_2), 43.56 (CH_2), 38.05 (CH_2). MS (ESI(+)) calcd for $C_{30}H_{24}ClF_2N_3O^+$ $[M+H]^+$: 516.16; found: 516.16.

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(pyrazin-2-yl)methanone(a4)

Yellow oil, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 8.90 (s, 1H), 8.69 (d, *J* = 2.4 Hz, 1H), 8.62 – 8.59 (m, 1H), 7.14 (d, *J* = 7.3 Hz, 1H), 7.06 – 6.91 (m, 10H), 6.16 (d, *J* = 7.9 Hz, 1H), 6.03 (s, 1H), 4.54 (q, *J* = 16.3 Hz, 2H), 3.94 – 3.88 (m, 1H), 3.42 (dt, *J* = 13.8, 6.6 Hz, 1H), 3.22 (d, *J* = 13.4 Hz, 1H), 3.03 (d, *J* = 13.5 Hz, 1H), 2.29 (dd, *J* = 10.7, 4.6 Hz, 2H). ^{13}C-NMR (100 MHz, Acetone - d_6), δ: 166.42 (C), 162.59 (d, *J* = 242.7 Hz, C), 162.48 (d, *J* = 242.2 Hz, C), 151.42 (C), 150.23 (CH), 146.69 (C), 146.20 (CH), 143.54 (CH), 136.10 (d, *J* = 2.7 Hz, C), 134.68 (d, *J* = 2.9 Hz, C), 132.50 (d, *J* = 7.8 Hz, 2CH), 132.39 (C), 129.46 (d, *J* = 7.7 Hz, 2CH), 129.32 (CH), 124.27 (CH), 118.38 (CH), 115.55 (d, *J* = 21.5 Hz, 2CH), 115.33 (d, *J* = 21.3 Hz, 2CH), 106.95 (CH), 83.56 (CH), 57.28 (CH_2), 49.57 (C), 49.39 (CH_2), 44.35 (CH_2), 38.89 (CH_2). MS(ESI(+)) calcd for $C_{29}H_{24}F_2N_4O^+$ $[M+H]^+$: 483.19; found: 483.19.

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(4-methoxyphenyl)methanone(a5)

White solid, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 7.52 (d, *J* = 7.7 Hz, 2H), 7.17 (d, *J* = 7.2 Hz, 1H), 6.99 (ddd, *J* = 18.0, 8.3, 3.3 Hz, 11H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.19 – 6.07

(m, 2H), 4.52 (dd, *J* = 69.9, 16.3 Hz, 2H), 3.87 (s, 3H), 3.69 (d, *J* = 7.3 Hz, 1H), 3.42 (d, *J* = 3.8 Hz, 1H), 3.25 (d, *J* = 13.4 Hz, 1H), 3.06 (d, *J* = 13.4 Hz, 1H), 2.34 – 2.18 (m, 2H). ^{13}C-NMR (100 MHz, Acetone - d_6), δ: 169.54 (C), 161.74 (d, *J* = 242.4 Hz, C), 161.58 (d, *J* = 242.1 Hz, C), 161.33 (C), 150.84 (C), 135.34 (d, *J* = 2.9 Hz, C), 134.02 (d, *J* = 3.2 Hz, C), 131.64 (d, *J* = 7.9 Hz, 2CH), 131.49 (C), 129.69 (2CH), 128.45 (d, *J* = 7.0 Hz, 2CH), 128.45 (CH), 123.47 (CH), 117.28 (CH), 114.66 (d, *J* = 21.4 Hz, 2CH), 114.45 (d, *J* = 21.5 Hz, 2CH), 113.24 (2CH), 105.83 (CH), 82.02 (CH), 56.51 (CH_2), 54.85 (CH_3), 49.44 (C), 48.12 (CH_2), 43.65 (CH_2), 38.23 (CH_2). MS(ESI(+)) calcd for $C_{32}H_{28}F_2N_2O_2^+$ $[M+H]^+$: 511.2; found: 511.2.

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(naphthalen-1-yl)methanone(a6)

White solid, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 7.91 (d, *J* = 8.3 Hz, 2H), 7.63 (d, *J* = 8.3 Hz, 1H), 7.52 – 7.41 (m, 3H), 7.31 (d, *J* = 6.9 Hz, 1H), 7.14 – 7.08 (m, 3H), 7.06 – 6.92 (m, 7H), 6.69 – 6.63 (m, 1H), 6.23 – 6.13 (m, 2H), 4.65 (t, *J* = 21.4 Hz, 2H), 3.21 (d, *J* = 13.4 Hz, 1H), 3.16 – 2.99 (m, 3H), 2.14 (dd, *J* = 6.1, 1.8 Hz, 2H). ^{13}C-NMR (100 MHz, Acetone - d_6), δ: 169.14 (C), 161.85 (d, *J* = 241.2 Hz, C), 161.76 (d, *J* = 240.7 Hz, C), 150.85 (C), 135.60 (C), 135.23 (d, *J* = 2.9 Hz, C), 133.96 (d, *J* = 3.1 Hz, C), 133.56 (C), 131.88 (d, *J* = 8.0 Hz, 2CH), 131.76 (C), 129.42 (CH), 129.13 (C), 128.72 (d, *J* = 8.2 Hz, 2CH), 128.56 (CH), 128.44 (CH), 126.90 (CH), 126.39 (CH), 125.21 (CH), 124.86 (CH), 123.99 (CH), 123.52 (CH), 117.50 (CH), 114.85 (d, *J* = 22.4 Hz, 2CH), 114.63 (d, *J* = 21.8 Hz, 2CH), 105.85 (CH), 81.91 (CH), 57.16 (CH_2), 48.76 (C), 48.03 (CH_2), 43.56 (CH_2), 38.17 (CH_2). MS(ESI(+)) calcd for $C_{35}H_{28}F_2N_2O^+$ $[M+H]^+$: 531.22; found: 531.22.

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(2-fluoropyridin-3-yl)methanone(a7)

Yellow oil, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 8.31 (d, *J* = 4.1 Hz, 1H), 7.94 (t, *J* = 8.3 Hz, 1H), 7.45 – 7.37 (m, 1H), 7.15 (d, *J* = 7.3 Hz, 1H), 7.06 – 6.90 (m, 9H), 6.70 (t, *J* = 7.4 Hz, 1H), 6.14 (d, *J* = 7.9 Hz, 1H), 5.98 (s, 1H), 4.52 (q, *J* = 16.4 Hz, 2H), 3.47 (dd, *J* = 11.2, 5.8 Hz, 1H), 3.32 – 3.19 (m, 2H), 3.05 (d, *J* = 13.4 Hz, 1H), 2.29 (dt, *J* = 11.3, 4.7 Hz, 2H). ^{13}C-NMR (100 MHz, Acetone - d_6), δ: 163.93 (d, *J* = 4.2 Hz, C), 161.81 (d, *J* = 241.6 Hz, C), 161.70 (d, *J* = 242.2 Hz, C), 158.85 (d, *J* = 236.8 Hz, C), 150.75 (CH), 149.09 (d, *J* = 15.1 Hz, CH), 140.49 (d, *J* = 3.8 Hz, C), 135.25 (d, *J* = 2.7 Hz, C), 133.86 (d, *J* = 2.8 Hz, C), 131.66 (d, *J* = 7.9 Hz, 2CH), 131.31 (CH), 128.56 (d, *J* = 7.7 Hz, 2CH), 128.60 (CH), 123.53 (CH), 122.11 (CH), 122.09 (d, *J* = 4.2 Hz, C), 119.74 (CH), 117.62 (C), 114.76 (d, *J* = 22.3 Hz, 2CH), 114.54 (d, *J* = 21.9 Hz, 2CH), 106.04 (CH), 82.27 (CH), 57.12 (C), 48.66 (CH_2), 47.83 (CH_2), 43.66 (CH_2), 38.05 (CH_2). MS(ESI(+)) calcd for $C_{30}H_{24}F_3N_3O^+$ $[M+H]^+$: 500.19; found: 500.19.

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(6-methylpyridin-3-yl)methanone(a8)

Yellow oil, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 8.54 (s, 1H), 7.73 (d, *J* = 7.7 Hz, 1H), 7.26 (d, *J* = 7.9 Hz, 1H), 7.13 (d, *J* = 7.1 Hz, 1H), 7.04 – 6.90 (m, 9H), 6.70 (t, *J* = 7.4 Hz, 1H), 6.14 (d, *J* = 7.8 Hz, 1H), 6.06 (s, 1H), 4.50 (dd, *J* = 46.0, 16.5 Hz, 2H), 3.62 (dd, *J* = 15.8, 8.9 Hz, 1H), 3.41 (d, *J* = 6.2 Hz, 1H), 3.23 (d, *J* = 13.4 Hz, 1H), 3.03 (d, *J* = 13.3 Hz, 1H), 2.51 (s, 3H), 2.31 – 2.22 (m, 2H). ^{13}C-NMR (100 MHz, Acetone - d_6), δ: 167.97 (C), 161.79 (d, *J* = 242.6 Hz, C), 161.65 (d, *J* = 242.2 Hz, C), 160.27 (C), 150.80 (C), 148.06 (CH), 135.40 (C), 135.34 (d, *J* = 3.1 Hz, C), 133.96 (d, *J* = 2.8 Hz, C), 131.67 (d, *J* = 7.8 Hz, 2CH), 131.43 (CH), 129.31 (CH), 128.55 (C), 128.51 (d, *J* = 7.4 Hz, 2CH), 123.54 (CH), 122.29 (CH), 117.42 (CH), 114.74 (d, *J* = 21.7 Hz, 2CH), 114.51 (d, *J* = 22.8 Hz, 2CH), 105.93 (CH), 82.27 (CH), 56.71 (CH_2), 49.17 (C), 48.39 (CH_2), 43.69 (CH_2), 38.28 (CH_2), 23.65 (CH_3). MS(ESI(+)) calcd for $C_{31}H_{27}F_2N_3O^+$ $[M+H]^+$: 496.21; found: 496.21.

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(pyridin-2-yl)methanone(a9)

Yellow oil, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 8.56 (d, *J* = 4.4 Hz, 1H), 7.90 (td, *J* = 7.7, 1.1 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.45 (dd, *J* = 6.8, 5.5 Hz, 1H), 7.13 (d, *J* = 7.3 Hz, 1H), 7.07 – 6.91 (m, 10H), 6.12 (d, *J* = 7.9 Hz, 1H), 6.03 (s, 1H), 4.60 (d, *J* = 16.3 Hz, 1H), 4.48 (d, *J* = 16.3 Hz, 1H), 3.90 (dd, *J* = 11.5, 6.9 Hz, 1H), 3.42 (td, *J* = 11.4, 5.7

Hz, 1H), 3.22 (d, *J* = 13.4 Hz, 1H), 3.03 (d, *J* = 13.4 Hz, 1H), 2.25 (dd, *J* = 14.1, 5.4 Hz, 2H). ^{13}C-NMR NMR (100 MHz, Acetone - d_6), δ: 167.41 (C), 161.78 (d, *J* = 242.1 Hz, C), 161.66 (d, *J* = 242.0 Hz, C)，154.36 (C), 150.73 (C), 148.09 (CH), 137.14 (CH), 136.94 (C), 135.41 (d, *J* = 2.6 Hz, C), 134.00 (d, *J* = 3.1 Hz, C), 131.71 (d, *J* = 7.6 Hz, 2CH), 128.67 (d, *J* = 7.8 Hz, 2CH), 128.46 (CH), 125.05 (CH), 123.89 (CH), 123.45 (CH), 117.44 (CH), 11 4.73 (d, *J* = 21.3 Hz, 2CH), 114.52 (d, *J* = 21.1 Hz, 2CH), 106.05 (CH), 82.63 (CH), 56.45 (CH_2), 48.71 (C), 47.10 (CH_2), 43.65 (CH_2), 38.21 (CH_2). MS(ESI(+)) calcd for $C_{30}H_{25}F_2N_3O^+$ $[M+H]^+$: 482.20; found: 482.20.

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(2-chloropyridin-4-yl)methanone(a10)

White solid, ^{1}H-NMR (400 MHz, Acetone - d6), δ: 8.46 (d, *J* = 5.0 Hz, 1H), 7.50 – 7.35 (m, 2H), 7.15 (d, *J* = 7.3 Hz, 1H), 7.05 – 6.91 (m, 9H), 6.71 (t, *J* = 7.4 Hz, 1H), 6.17 (d, *J* = 7.9 Hz, 1H), 5.98 (s, 1H), 4.52 (dd, *J* = 39.4, 16.5 Hz, 2H), 3.61 – 3.51 (m, 1H), 3.43 – 3.32 (m, 1H), 3.24 (d, *J* = 13.4 Hz, 1H), 3.04 (d, *J* = 13.4 Hz, 1H), 2.30 (dd, *J* = 9.4, 5.0 Hz, 2H).^{13}C-NMR (100 MHz, Acetone - d6) δ: 166.27 (C), 161.77 (d, *J* = 242.6 Hz, C), 161.65 (d, *J* = 242.3 Hz, C), 151.27 (CH), 150.68 (C), 150.26 (C), 147.26 (C), 135.31 (d, *J* = 2.9 Hz, C), 133.81 (d, *J* = 3.2 Hz, C), 131.61 (d, *J* = 7.9 Hz, 2CH), 131.24 (C), 128.55 (CH), 128.48 (d, *J* = 7.9 Hz, 2CH), 123.49 (CH), 122.06 (CH), 120.64 (CH), 117.52 (CH), 114.73 (d, *J* = 21.5 Hz, 2CH), 114.50 (d, *J* = 21.2 Hz, 2CH), 105.95 (CH), 82.38 (CH), 56.83 (CH_2), 48.67 (C), 48.35 (CH_2), 43.51 (CH_2), 38.10 (CH_2). MS(ESI(+)) calcd for $C_{30}H_{24}ClF_2N_3O^+$ $[M+H]^+$: 516.16; found: 516.16.

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(5-methylpyrazin-2-yl)methanone(a11)

Yellow solid, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 8.78 (s, 1H), 8.49 (s, 1H), 7.14 (d, *J* = 7.3 Hz, 1H), 7.05 – 6.92 (m, 10H), 6.14 (d, *J* = 7.9 Hz, 1H), 6.04 (s, 1H), 4.53 (dd, *J* = 36.9, 16.3 Hz, 2H), 3.92 (dd, *J* = 11.4, 6.8 Hz, 1H), 3.16 – 3.08 (m, 2H), 2.57 (s, 3H), 2. 48 (s, 1H), 2.28 (dd, *J* = 12.5, 5.6 Hz, 2H).^{13}C-NMR (100 MHz, Acetone - d_6), δ: 165.90 (C), 161.74 (d, *J* = 242.5 Hz, C), 161.62 (d, *J* = 242.3 Hz, C), 155.49 (C), 150.57 (C), 146.36 (C), 144.30 (CH), 142.23 (CH), 135.26 (d, *J* = 2.9 Hz, C), 133.86 (d, *J* = 3.2 Hz, C), 131.55 (CH),131.67 (d, *J* = 7.9 Hz, 2CH), 128.61 (d, *J* = 7.9 Hz, 2CH), 128.47 (C), 123.45 (CH), 1 17.52 (CH), 114.71 (d, *J* = 21.6 Hz, 2CH), 114.49 (d, *J* = 22.1 Hz, 2CH), 106.07 (CH), 82.6 4 (CH), 56.36 (C), 48.66 (CH_2), 48.60 (CH_2), 43.46 (CH_2), 38.01 (CH_2), 20.76 (CH_3). MS(ESI (+)) calcd for $C_{30}H_{26}F_2N_4O^+$ $[M+H]^+$: 497.21; found: 497.21.

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(pyridin-4-yl)methanone(a12)

White solid, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 8.64 (d, *J* = 5.4 Hz, 2H), 7.38 (d, *J* = 5.5 Hz, 2H), 7.13 (d, *J* = 7.3 Hz, 1H), 6.97 (ddt, *J* = 20.5, 17.7, 5.7 Hz, 9H), 6.70 (t, *J* = 7.4 Hz, 1H), 6.15 (d, *J* = 7.8 Hz, 1H), 6.00 (s, 1H), 4.51 (dd, *J* = 39.1, 16.4 Hz, 2H), 3.5 9 – 3.49 (m, 1H), 3.35 (td, *J* = 10.8, 6.8 Hz, 1H), 3.23 (d, *J* = 13.4 Hz, 1H), 3.03 (d, *J* = 13.4 Hz, 1H), 2.35 – 2.24 (m, 2H). ^{13}C-NMR (100 MHz, Acetone - d_6), δ: 167.79 (C), 161.7 9 (d, *J* = 241.2 Hz, C), 161.67 (d, *J* = 240.9 Hz, C), 150.74 (2CH), 150.10 (C), 143.74 (C), 135.34 (d, *J* = 2.9 Hz, C), 133.91 (d, *J* = 3.2 Hz, C), 131.71 (d, *J* = 7.9 Hz, 2CH), 131.36 (C), 128.58 (d, *J* = 7.7 Hz, 2CH), 128.47 (CH), 123.54 (CH), 121.46 (2CH), 117.52 (CH), 11 4.88 (d, *J* =21.3 Hz, 2CH), 114.64 (d, *J* = 21.1 Hz, 2CH), 105.99 (CH), 82.33 (CH), 56.85 (CH_2), 48.87 (C), 48.47 (CH_2), 43.63 (CH_2), 38.15 (CH_2). MS(ESI(+)) calcd for $C_{30}H_{25}F_2N_3O^+$ [$M+H]^+$: 482.20; found: 482.20.

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(2-chloropyridin-3-yl)methanone(a13)

White solid, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 8.44 (dd, *J* = 4.7, 1.9 Hz, 1H), 7.72 (s, 1H), 7.47 (dd, *J* = 7.3, 4.9 Hz, 1H), 7.16 (dd, *J* = 7.3, 0.6 Hz, 1H), 7.06 – 6.90 (m, 9H), 6.71 – 6.63 (m, 1H), 6.16 (d, *J* = 7.6 Hz, 1H), 5.96 (s, 1H), 4.58 (dd, *J* = 55.3, 16.3 Hz, 2 H), 3.33 (ddd, *J* = 10.9, 6.5, 1.8 Hz, 1H), 3.21 (dd, *J* = 37.5, 13.3 Hz, 2H), 3.05 (d, *J* = 13. 4 Hz, 1H), 2.34 – 2.23 (m, 2H). ^{13}C-NMR (100 MHz, Acetone - d_6), δ: 165.36 (C), 163.02 (d, *J* = 241.1 Hz, C), 160.61 (d, *J* = 240.8 Hz, C), 150.76 (C), 150.22 (CH), 146.36 (C), 137. 16 (CH), 135.29 (d, *J* = 2.9 Hz, C), 133.81 (d, *J* = 3.1 Hz, C), 133.07 (C), 131.79 (d, *J* = 7.9

Hz, 2CH), 131.38 (CH), 128.71 (d, *J* = 7.9 Hz, 2CH), 128.60 (C), 123.51 (CH), 123.21 (CH), 117.62 (CH), 114.90 (d, *J* = 19.8 Hz, 2CH), 114.71 (d, *J* = 21.2 Hz, 2CH), 105.94 (CH), 8 1.94 (CH), 57.32 (CH_2), 48.56 (C), 47.44 (CH_2), 43.53 (CH_2), 38.26 (CH_2). MS(ESI(+)) calcd for $C_{30}H_{24}ClF_2N_3O^+$ $[M+H]^+$: 516.16; found: 516.16.

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(6-chloropyridin-3-yl)methanone(a14)

Yellow solid, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 8.49 (s, 1H), 7.93 (d, *J* = 8.1 Hz, 1 H), 7.51 (d, *J* = 8.2 Hz, 1H), 7.28 – 6.83 (m, 11H), 6.71 (t, *J* = 7.4 Hz, 1H), 6.16 (d, *J* = 7.8 Hz, 1H), 6.04 (s, 1H), 4.51 (dd, *J* = 42.1, 16.5 Hz, 2H), 3.71 – 3.61 (m, 1H), 3.45 (dt, *J* = 17.0, 8.4 Hz, 1H), 3.23 (d, *J* = 13.4 Hz, 1H), 3.04 (d, *J* = 13.4 Hz, 1H), 2.38 – 2.24 (m, 2H). ^{13}C-NMR (100 MHz, Acetone - d_6), δ: 166.61 (C), 161.77 (d, *J* = 242.6 Hz, C), 161. 62 (d, *J* = 242.3 Hz, C), 152.22 (C), 150.72 (C), 148.80 (C), 138.48 (CH), 135.31 (d, *J* = 2. 6 Hz, C), 133.86 (d, *J* = 3.1 Hz, C), 131.62 (d, *J* = 7.9 Hz, 2CH), 131.45 (C), 131.29 (CH), 128.54 (CH), 128.46 (d, *J* = 8.0 Hz, 2CH), 123.85 (CH), 123.50 (CH), 117.46 (CH), 114.71 (d, *J* = 21.6 Hz, 2CH), 114.48 (d, *J* = 22.4 Hz, 2CH), 105.93 (CH), 82.31 (CH), 56.71 (CH_2), 49.03 (C), 48.33 (CH_2), 43.57 (CH_2), 38.12 (CH_2). MS(ESI(+)) calcd for $C_{30}H_{24}ClF_2N_3O^+$ $[M+H]^+$: 516.16; found: 516.16.

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(5,6-dichloropyridin-3-yl)methanone(a15)

White solid, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 8.43 (d, *J* = 1.9 Hz, 1H), 8.06 (d, *J* = 1.9 Hz, 1H), 7.14 (d, *J* = 7.3 Hz, 1H), 7.03 – 6.92 (m, 9H), 6.71 (t, *J* = 7.4 Hz, 1H), 6.1 7 (d, *J* = 7.9 Hz, 1H), 6.02 (s, 1H), 4.50 (dd, *J* = 42.6, 16.5 Hz, 2H), 3.73 – 3.66 (m, 1H), 3.46 (td, *J* = 10.8, 6.7 Hz, 1H), 3.23 (d, *J* = 13.4 Hz, 1H), 3.02 (d, *J* = 13.4 Hz, 1H), 2.34 – 2.26 (m, 2H). ^{13}C-NMR (100 MHz, Acetone - d_6), δ: 165.29 (C), 161.81 (d, *J* = 242.5 Hz, C), 161.67 (d, *J* = 242.3 Hz, C), 150.74 (C), 149.47 (C), 146.38 (CH), 138.08 (C), 135.36 (d, *J* = 2.4 Hz, C), 133.84 (d, *J* = 2.5 Hz, C), 132.91 (C), 131.66 (d, *J* = 7.9 Hz, 2CH), 131.62 (CH), 131.28 (C), 129.71 (CH), 128.54 (d, *J* = 8.6 Hz, 2CH), 123.54 (CH), 117.55 (CH), 114.7 7 (d, *J* = 21.8 Hz, 2CH), 114.55 (d, *J* = 23.3 Hz, 2CH), 106.00 (CH), 82.45 (CH), 56.84 (C H$_2$), 48.99 (C), 48.39 (CH_2), 43.64 (CH_2), 38.22 (CH_2). MS(ESI(+)) calcd for $C_{30}H_{23}Cl_2F_2N_3O^+$ [M+H]+: 550.12; found: 550.12.

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(5-methylpyridin-3-yl)methanone(a16)

Yellow solid, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 8.46 (d, *J* = 9.7 Hz, 2H), 7.62 (s, 1 H), 7.14 (d, *J* = 7.2 Hz, 1H), 7.08 – 6.90 (m, 9H), 6.70 (t, *J* = 7.3 Hz, 1H), 6.16 (d, *J* = 7. 8 Hz, 1H), 6.05 (s, 1H), 4.51 (dd, *J* = 49.1, 16.5 Hz, 2H), 3.63 – 3.54 (m, 1H), 3.40 (dt, *J* = 17.1, 8.4 Hz, 1H), 3.23 (d, *J* = 13.4 Hz, 1H), 3.04 (d, *J* = 13.4 Hz, 1H), 2.33 (d, *J* = 11. 6 Hz, 3H), 2.30 – 2.22 (m, 2H). ^{13}C NMR (100 MHz, Acetone - d_6), δ: 167.88 (C), 161.76 (d, *J* = 242.6 Hz, C), 161.52 (d, *J* = 242.3 Hz, C), 151.42 (CH), 150.76 (C), 145.61 (CH), 13 5.40 (d, *J* = 3.1 Hz, C), 135.08 (C), 133.91 (d, *J* = 3.2 Hz, C), 132.77 (CH), 131.64 (d, *J* = 7.9 Hz, 2CH), 131.60 (C), 131.38 (C), 128.52 (CH), 128.48 (d, *J* = 7.2 Hz, 2CH), 123.49 (C H), 117.39 (CH), 114.70 (d, *J* = 21.5 Hz, 2CH), 114.48 (d, *J* = 23.1 Hz, 2CH), 105.87 (CH), 82.17 (CH), 56.67 (CH_2), 49.03 (C), 48.30 (CH_2), 43.58 (CH_2), 38.18 (CH_2), 17.24 (CH_3). MS (ESI(+)) calcd for $C_{31}H_{27}F_2N_3O^+$ $[M+H]^+$: 496.21; found: 496.21.

(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)(pyridin-3-yl)methanone(a17)

Brown oil, ^{1}H-NMR (600 MHz, $CDCl_3$), δ: 8.63 (s, 2H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.29 (dd, *J* = 7.6, 4.9 Hz, 1H), 7.03 (td, *J* = 7.7, 1.2 Hz, 1H), 6.94 – 6.78 (m, 9H), 6.70 (t, *J* = 7.3 Hz, 1H), 6.17 (d, *J* = 7.8 Hz, 1H), 5.96 (s, 1H), 4.52 (d, *J* = 16.3 Hz, 1H), 4.38 (d, *J* = 16.3 Hz, 1H), 3.53 (dd, *J* = 10.8, 7.4 Hz, 1H), 3.37 (td, *J* = 11.5, 5.4 Hz, 1H), 3.10 (d, *J* = 13.5 Hz, 1H), 2.86 (d, *J* = 13.5 Hz, 1H), 2.21 (dd, *J* = 12.2, 5.3 Hz, 1H), 2.09 (td, *J* = 12.1, 7.5 Hz, 1H). ^{13}C-NMR (150 MHz, $CDCl_3$), δ: 168.08 (C), 161.87 (d, *J* = 245.0 Hz, C), 161.7 9 (d, *J* = 244.5 Hz, C), 151.37 (CH), 150.61 (CH), 148.43 (C), 135.30 (C), 134.45 (d, *J* = 3. 4 Hz, C), 132.72 (d, *J* = 3.2 Hz, C), 131.70 (CH), 131.34 (d, *J* = 7.8 Hz, 2CH), 130.55 (C), 128.97 (CH), 128.28 (d, *J* = 7.7 Hz, 2CH), 123.48 (CH), 123.25 (CH), 117.65 (CH), 115.11 (

d, J = 21.1 Hz, 2CH), 114.90 (d, J = 21.2 Hz, 2CH), 106.27 (CH), 82.31 (CH), 56.68 (CH_2), 49.34 (C), 48.67 (CH_2), 44.25 (CH_2), 38.37 (CH_2). MS(ESI(+)) calcd for $C_{30}H_{25}F_2N_3O^+$ $[M+H]^+$: 482.20; found: 482.20.

(2-aminopyridin-3-yl)(3a,8-bis(4-fluorobenzyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indol-1(2H)-yl)methanone(a18)

White solid, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 8.03 (dd, J = 4.8, 1.6 Hz, 1H), 7.46 (d, J = 5.5 Hz, 1H), 7.14 (d, J = 7.2 Hz, 1H), 7.05 – 6.87 (m, 9H), 6.70 (t, J = 7.4 Hz, 1H), 6.56 (dd, J = 7.4, 4.9 Hz, 1H), 6.08 (dd, J = 36.5, 26.1 Hz, 4H), 4.43 (t, J = 21.1 Hz, 2H), 3.67 (s, 1H), 3.48 – 3.17 (m, 2H), 3.04 (d, J = 13.4 Hz, 1H), 2.34 – 2.19 (m, 2H). ^{13}C NMR (100 MHz, Acetone - d_6) δ: 169.11 (C), 161.77 (d, J = 242.7 Hz, C), 161.15 (d, J = 242.4 Hz, C), 157.98 (C), 150.84 (CH), 150.16 (C), 136.77 (CH), 135.22 (d, J = 2.9 Hz, C), 133.93 (d, J = 3.2 Hz, C), 131.62 (d, J = 7.9 Hz, 2CH), 131.43 (C), 128.48 (CH), 128.44 (d, J = 8.8 Hz, 2CH), 123.51 (CH), 117.43 (CH), 114.68 (d, J = 21.6 Hz, 2CH), 114.44 (d, J = 21.3 Hz, 2CH), 112.69 (CH), 111.71 (C), 105.87 (CH), 82.12 (CH), 70.40 (CH_2), 56.75 (C), 48.17 (CH_2), 43.66 (CH_2), 38.37 (CH_2). MS(ESI(+)) calcd for $C_{30}H_{26}F_2N_4O^+$ $[M+H]^+$: 497.21; found: 497.21.

2-(3a,8-bis(4-fluorobenzyl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-1-carbonyl)benzaldehyde(a19)

Brown solid, ^{1}H-NMR (400 MHz, Acetone - d_6), δ: 8.45 (dd, J = 4.7, 1.5 Hz, 1H), 7.73 (s, 1H), 7.47 (dd, J = 7.1, 5.1 Hz, 1H), 7.17 (d, J = 7.3 Hz, 1H), 6.96 (ddd, J = 45.0, 25.2, 17.9 Hz, 10H), 6.70 (t, J = 7.4 Hz, 1H), 6.17 (d, J = 7.6 Hz, 1H), 5.96 (s, 1H), 4.58 (dd, J = 54.6, 16.4 Hz, 2H), 3.36 – 3.02 (m, 4H), 2.37 – 2.25 (m, 2H). ^{13}C-NMR (100 MHz, Acetone - d_6), δ: 197.05 (C), 165.34 (C), 161.79 (d, J = 242.7 Hz, C), 161.68 (d, J = 242.3 Hz, C), 150.73 (C), 150.31 (C) 150.18 (C), 145.33 (C), 137.11 (CH), 135.27 (d, J = 2.9 Hz, C), 133.78 (d, J = 3.0 Hz, C), 133.04 (CH), 131.70 (d, J = 7.8 Hz, 2CH), 131.34 (CH), 128.63 (d, J = 7.9 Hz, 2CH), 128.54 (CH), 123.46 (CH), 123.15 (CH), 117.56 (CH), 114.74 (d, J = 19.1 Hz, 2CH), 114.53 (d, J = 18.8 Hz, 2CH), 105.89 (CH), 81.88 (CH), 57.25 (CH_2), 48.49 (C), 47.36 (CH_2), 43.45 (CH_2), 38.17 (CH_2). MS(ESI(+)) calcd for $C_{32}H_{26}F_2N_2O_2^+$ $[M+H]^+$: 509.20; found: 509.20.

2. ^{1}H- and ^{13}C-NMR Spectra

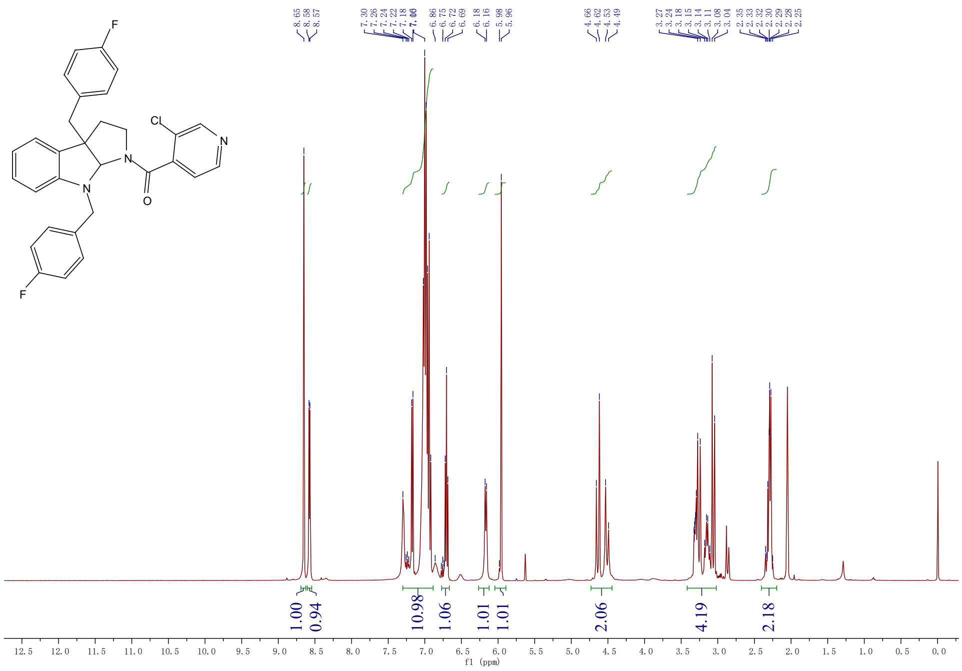

Figure 1. [1]H-NMR spectroscopic data for compound **a1**.

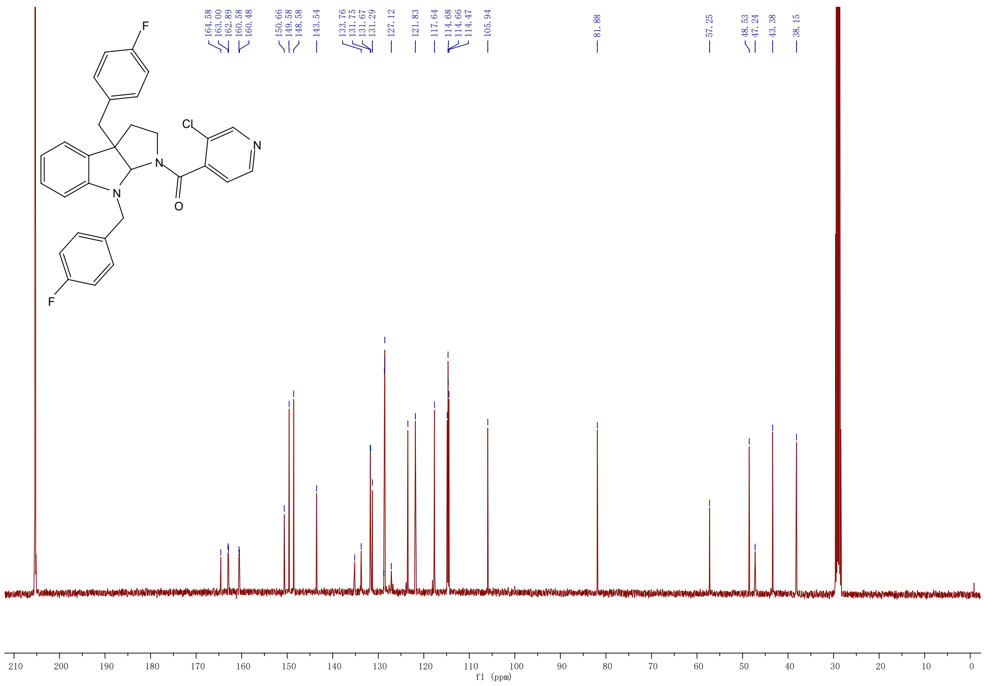

Figure 2. [13]C-NMR spectroscopic data for compound **a1**

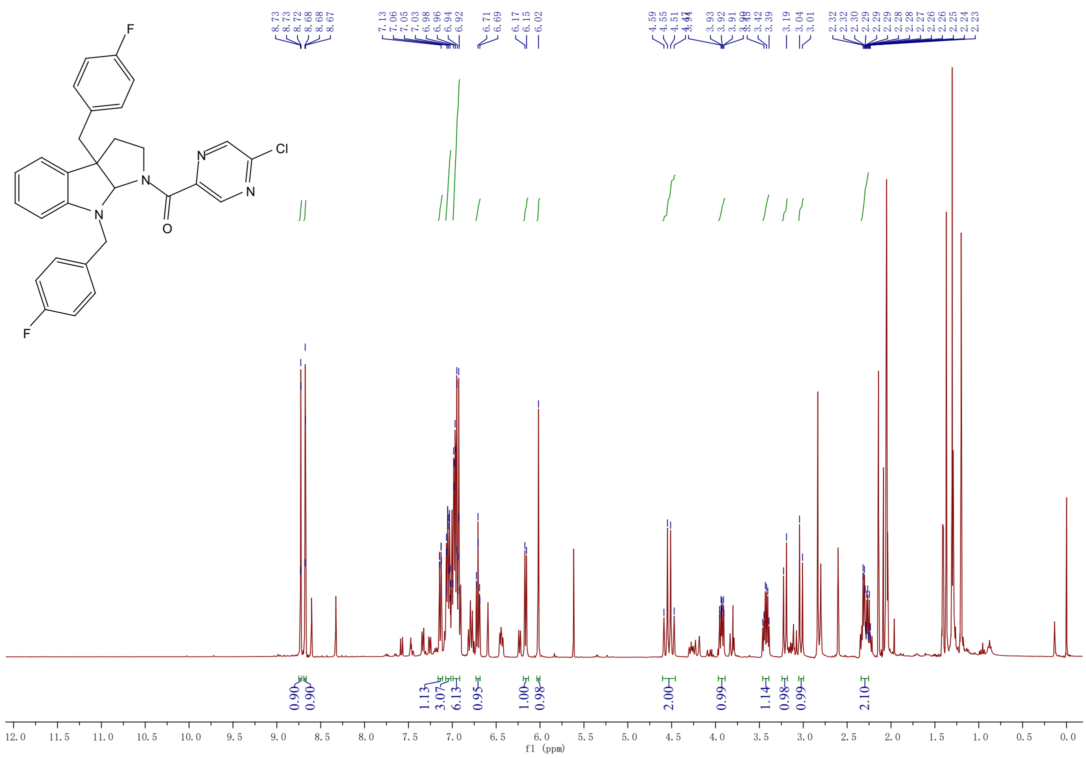

Figure 3. [1]H-NMR spectroscopic data for compound **a2**.

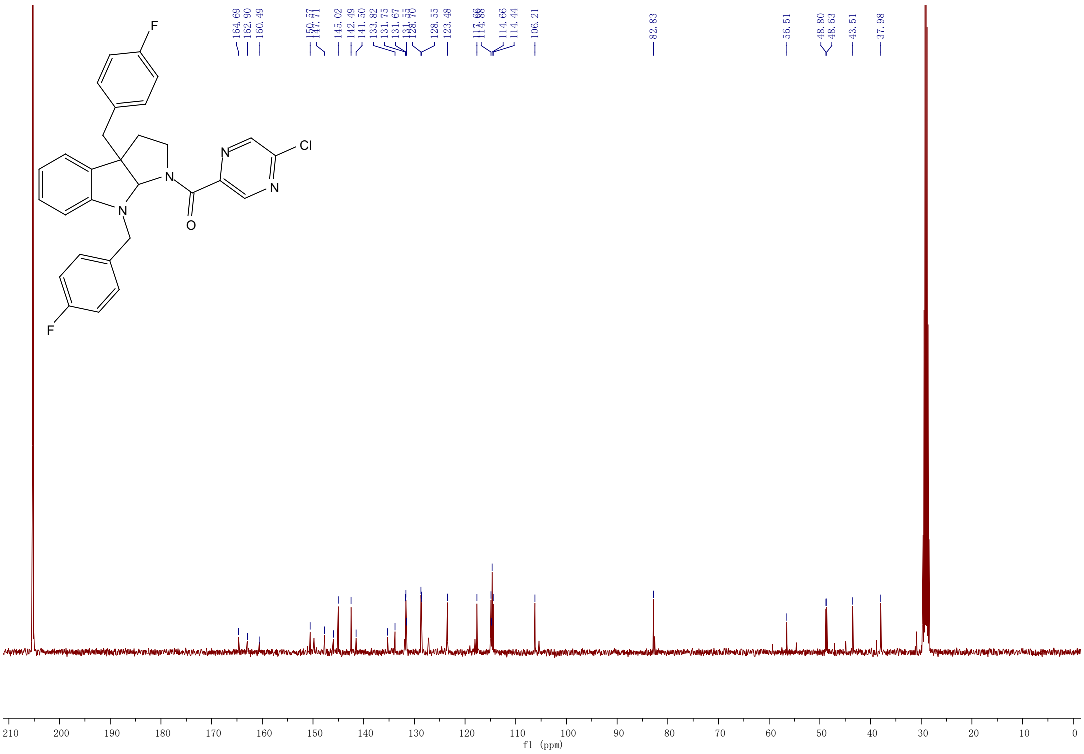

Figure 4. [13]C-NMR spectroscopic data for compound **a2**

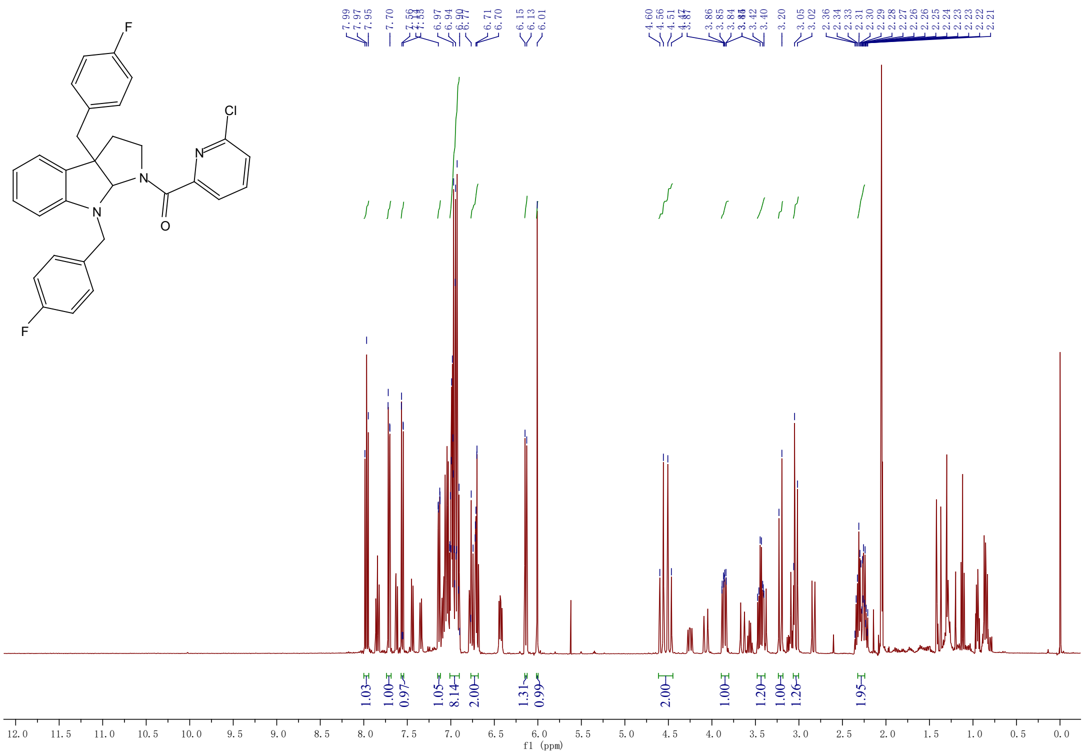

Figure 5. [1]H-NMR spectroscopic data for compound **a3**.

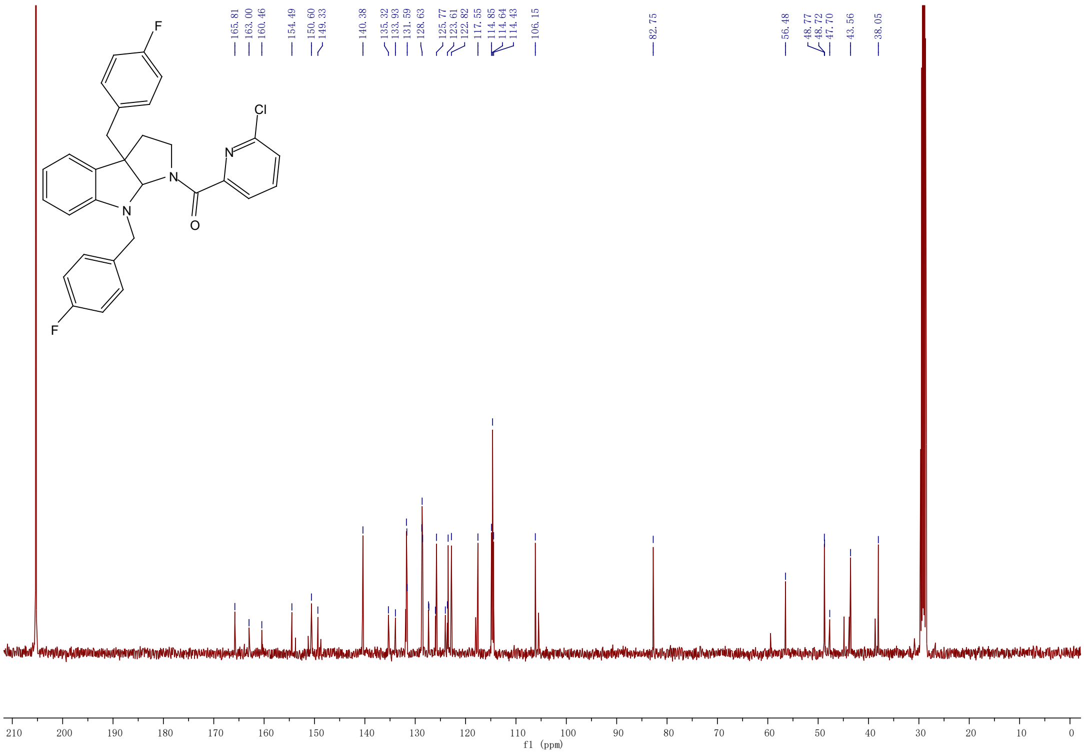

Figure 6. ^{13}C-NMR spectroscopic data for compound **a3**

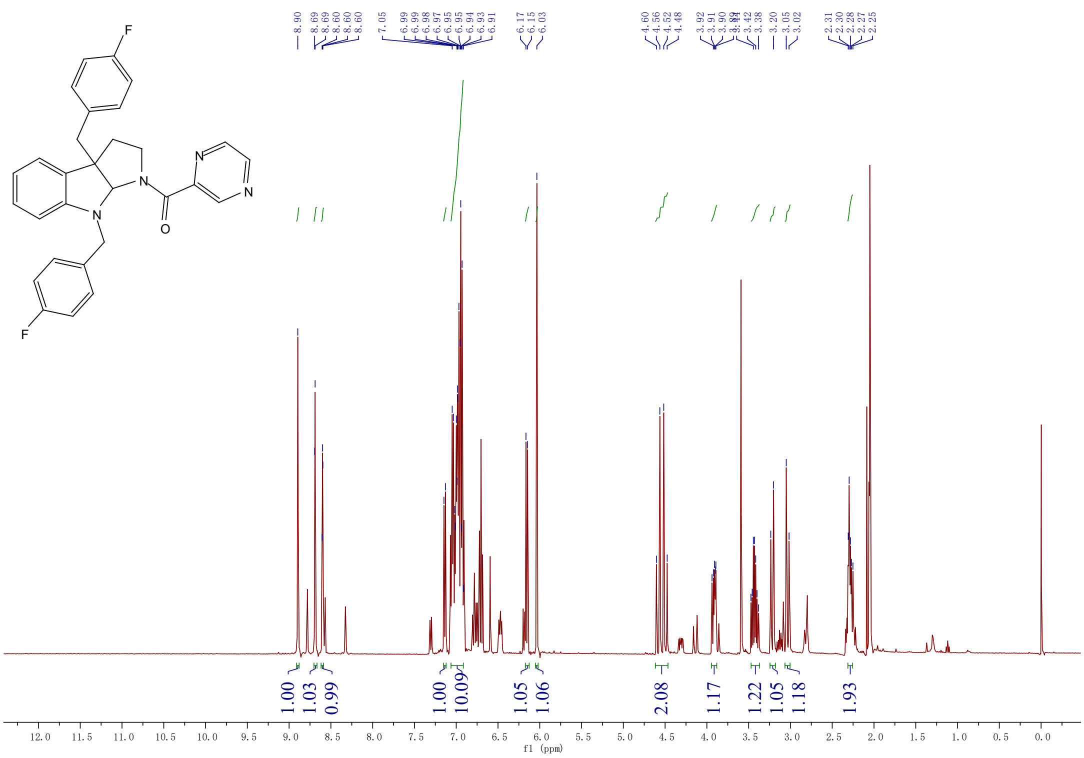

Figure 7. ^{1}H-NMR spectroscopic data for compound **a4**.

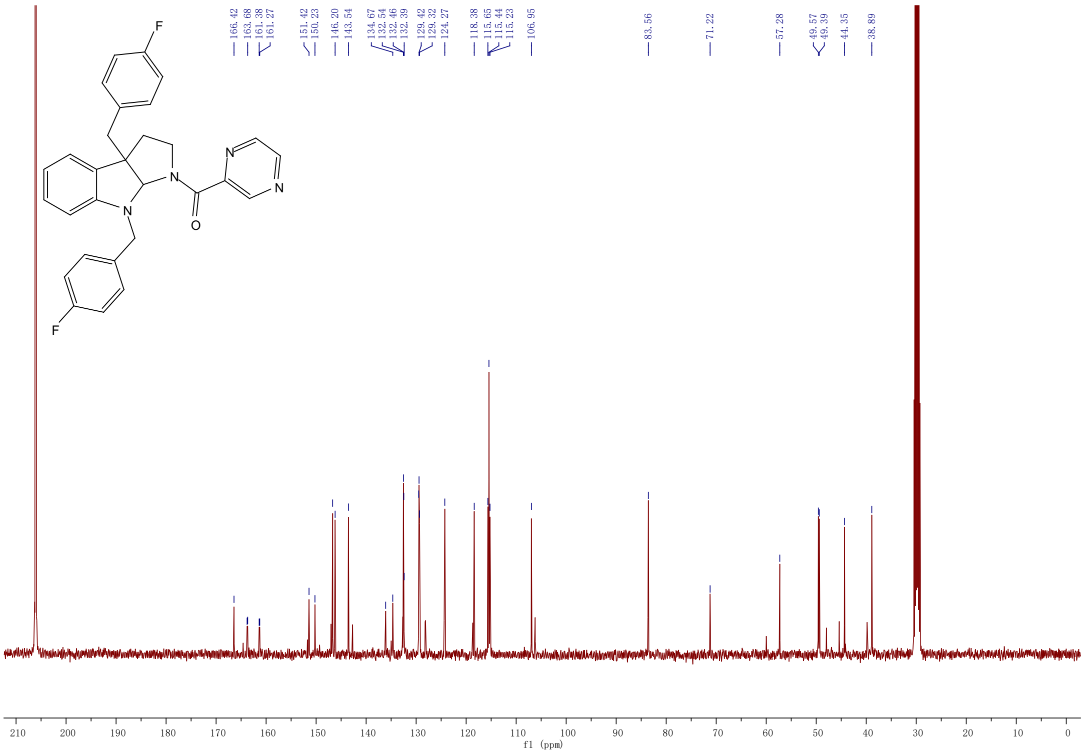

Figure 8. ^{13}C-NMR spectroscopic data for compound **a4**.

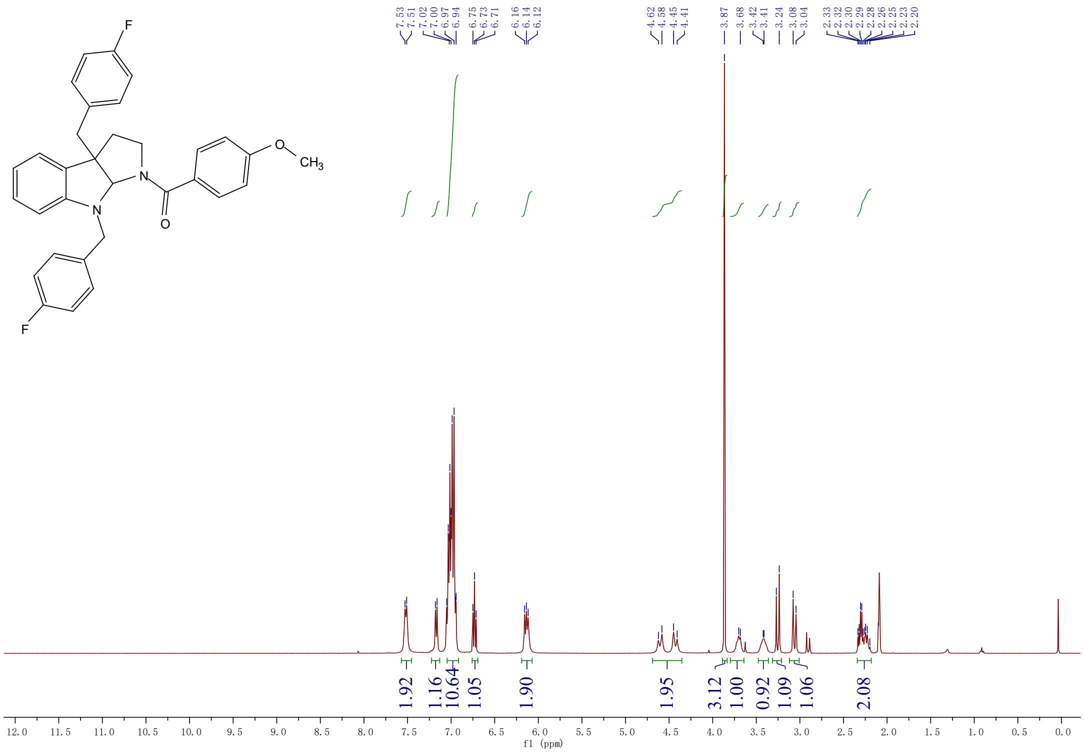

Figure 9. ^{1}H-NMR spectroscopic data for compound **a5**.

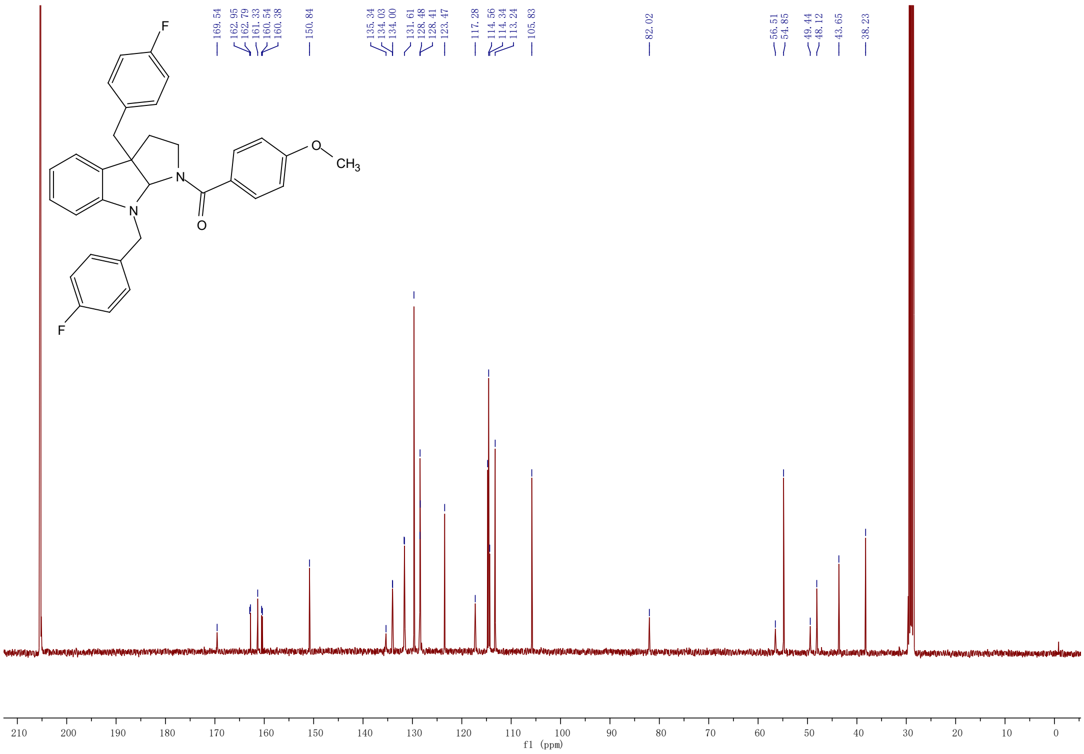

Figure 10. ^{13}C-NMR spectroscopic data for compound **a5**.

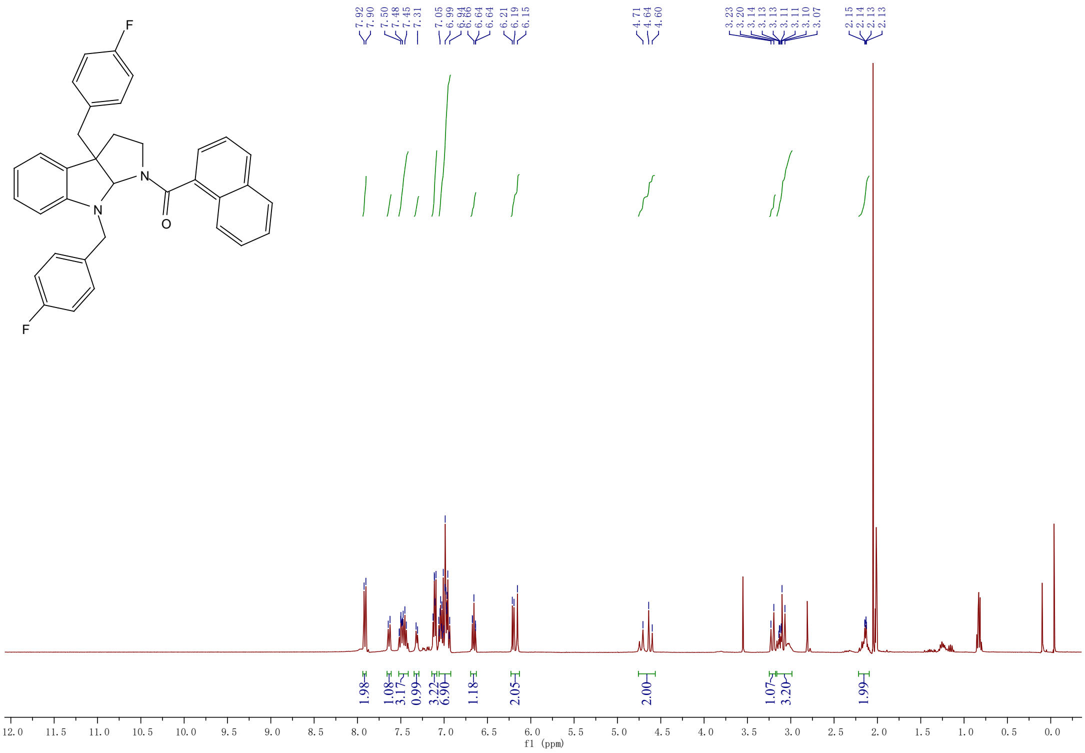

Figure 11. ^{1}H-NMR spectroscopic data for compound **a6**.

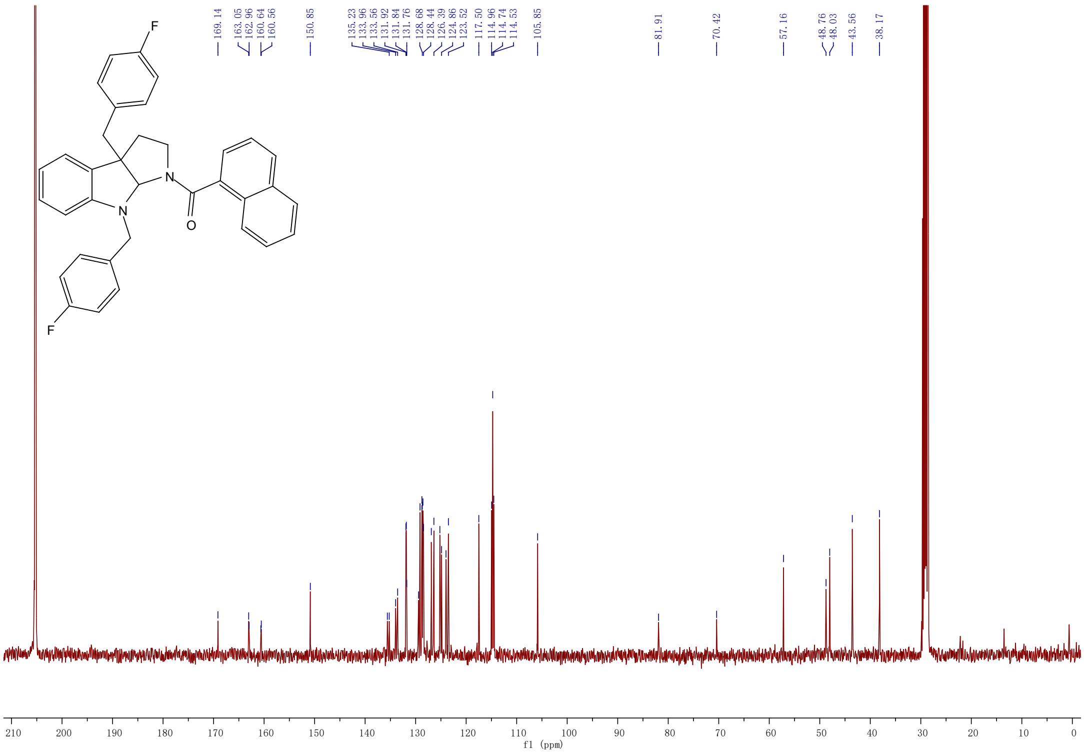

Figure 12. ^{13}C-NMR spectroscopic data for compound **a6**.

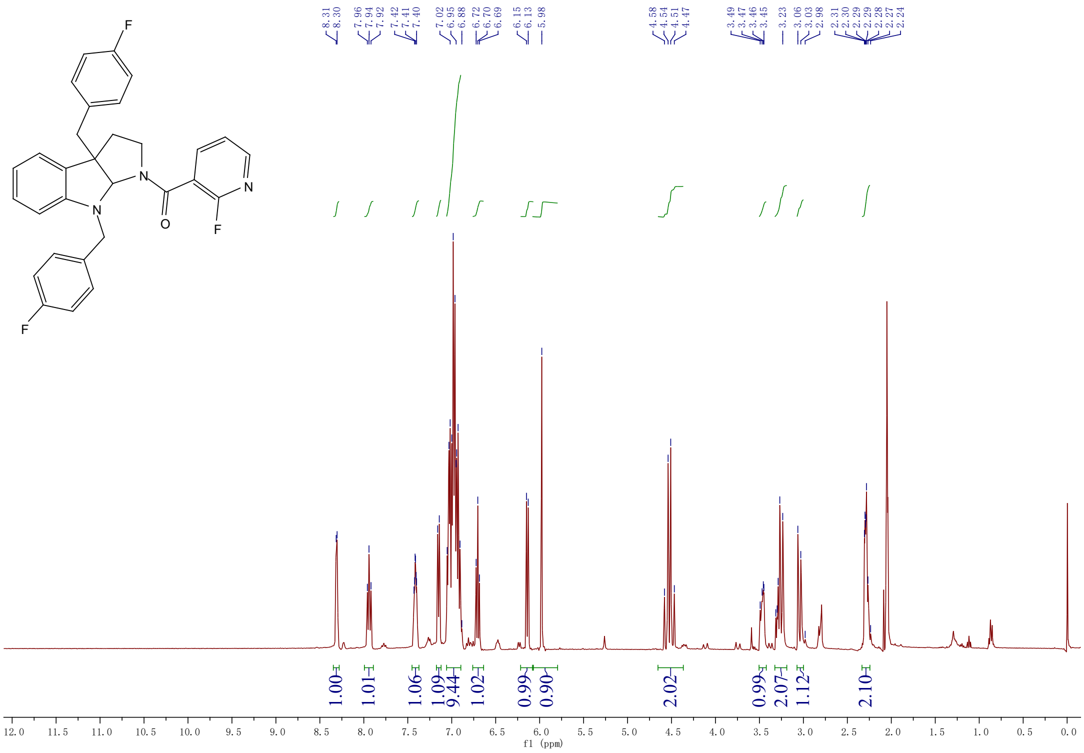

Figure 13. ^{1}H-NMR spectroscopic data for compound **a7**.

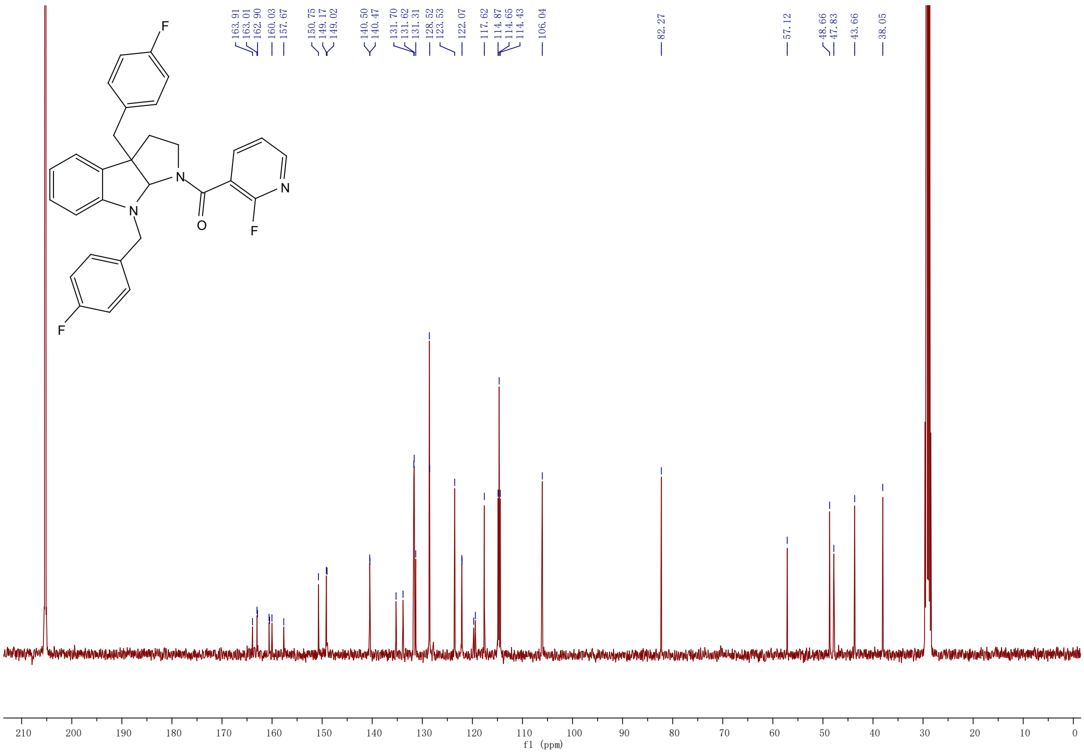

Figure 14. ^{13}C-NMR spectroscopic data for compound **a7**.

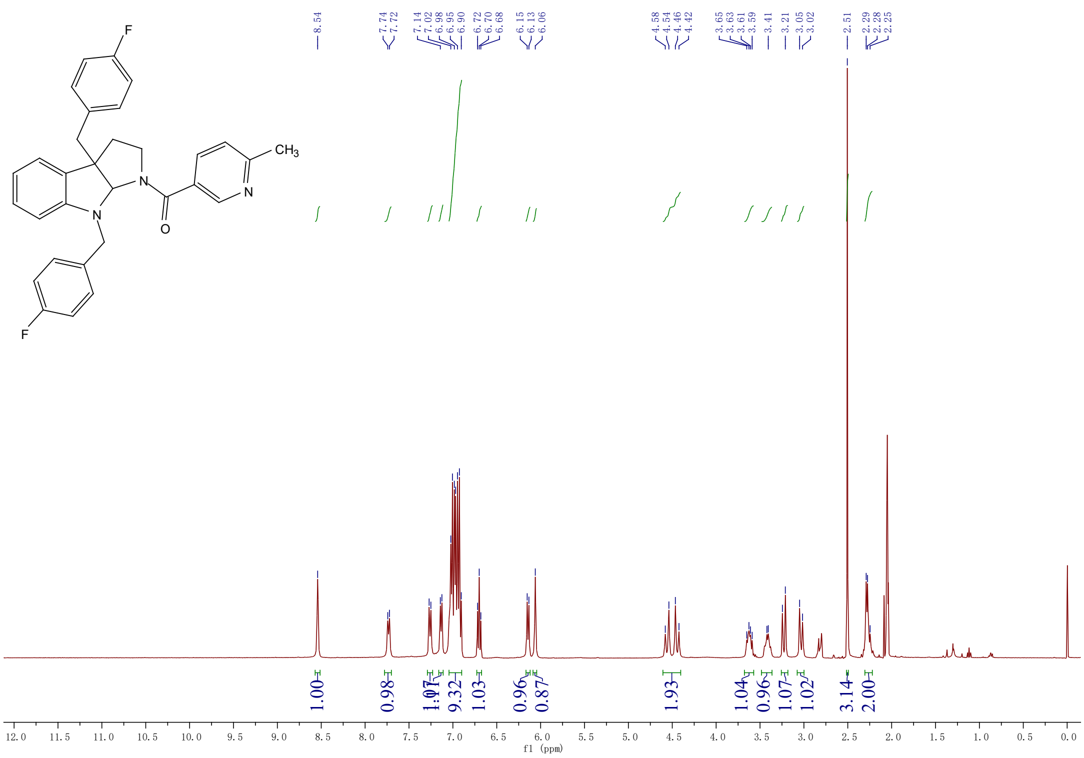

Figure 15. ^{1}H-NMR spectroscopic data for compound **a8**.

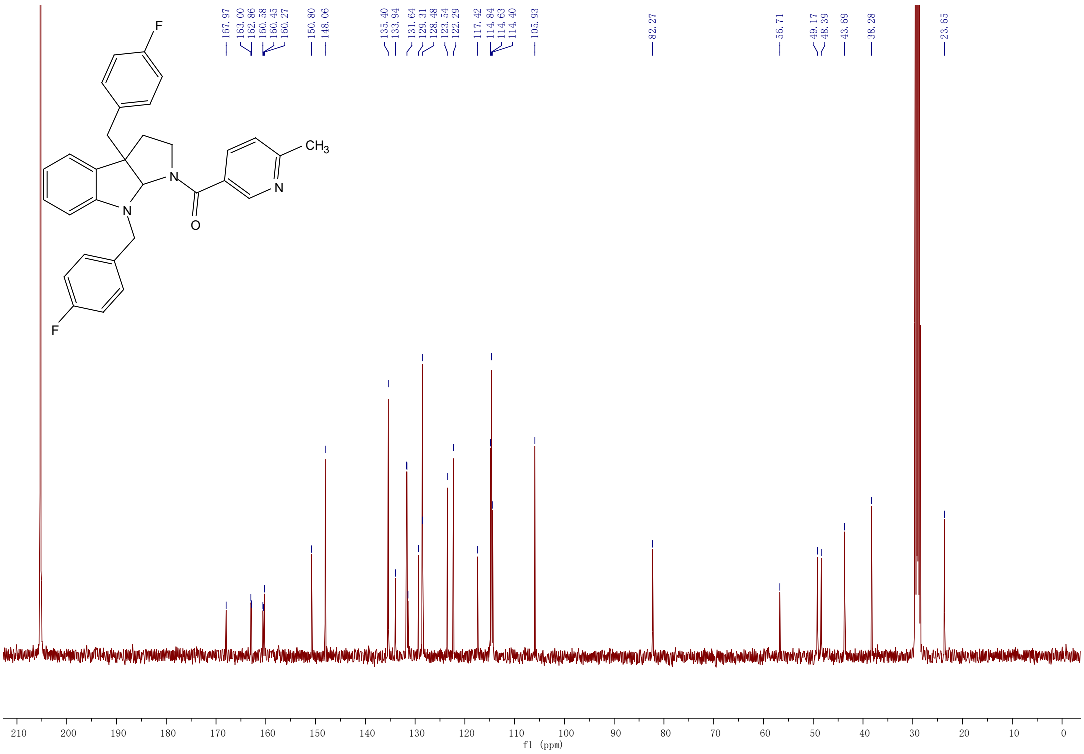

Figure 16. ^{13}C-NMR spectroscopic data for compound **a8**.

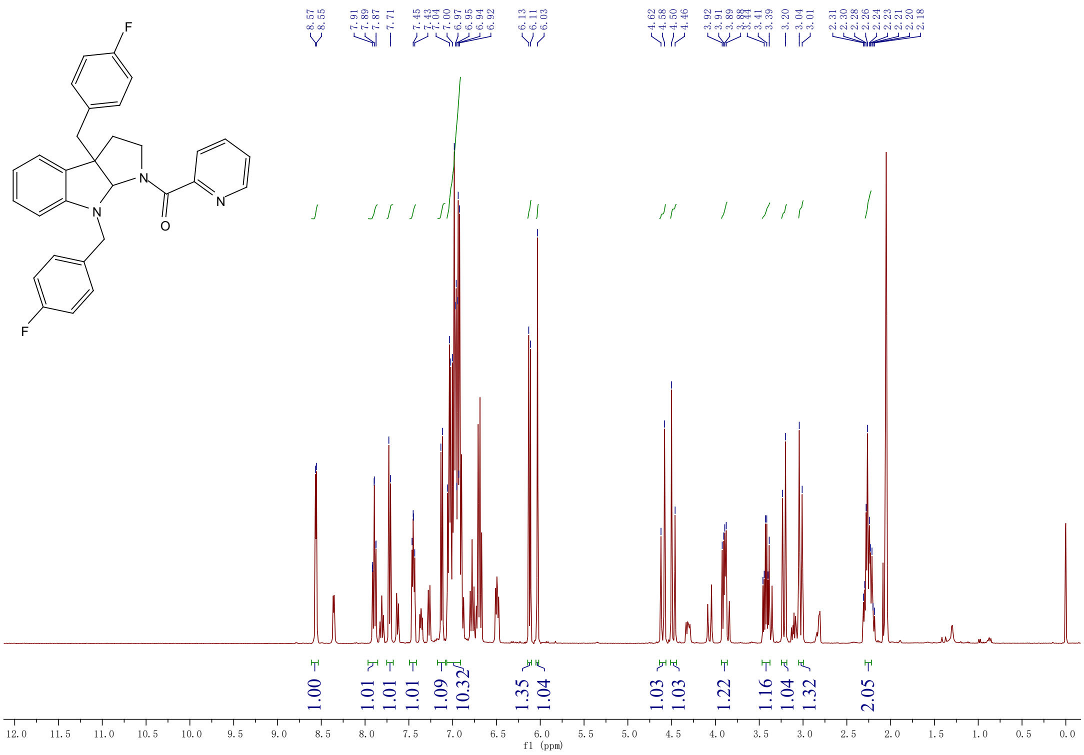

Figure 17. ^{1}H-NMR spectroscopic data for compound **a9**.

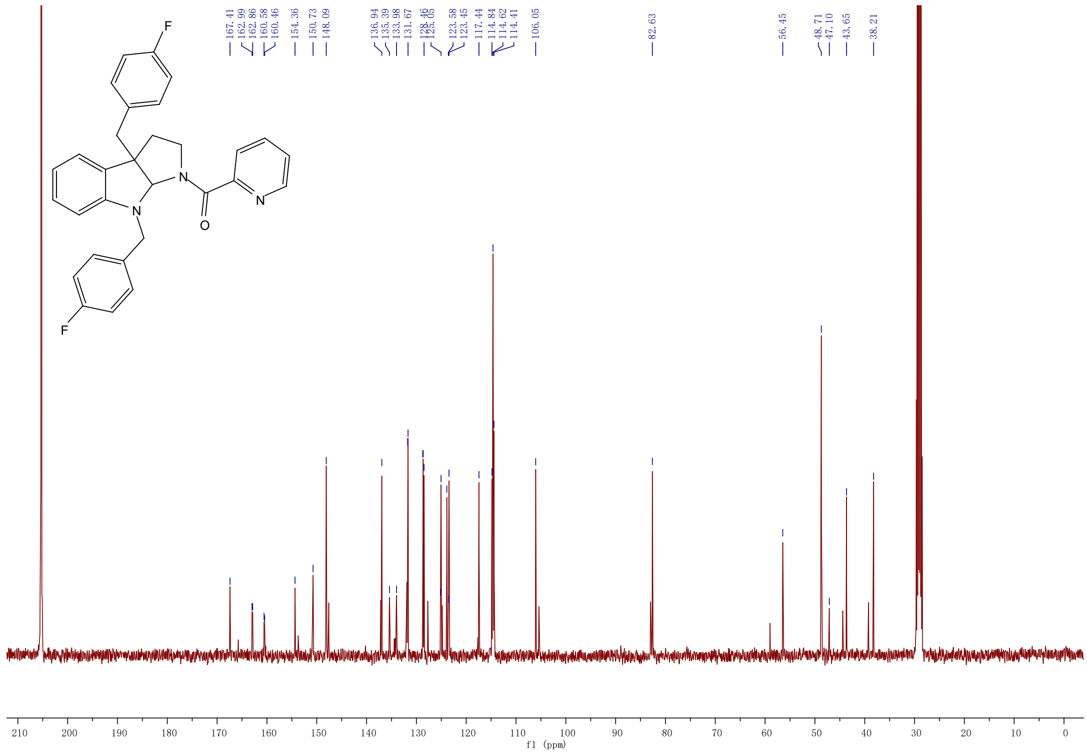

Figure 18. [13]C-NMR spectroscopic data for compound **a9**.

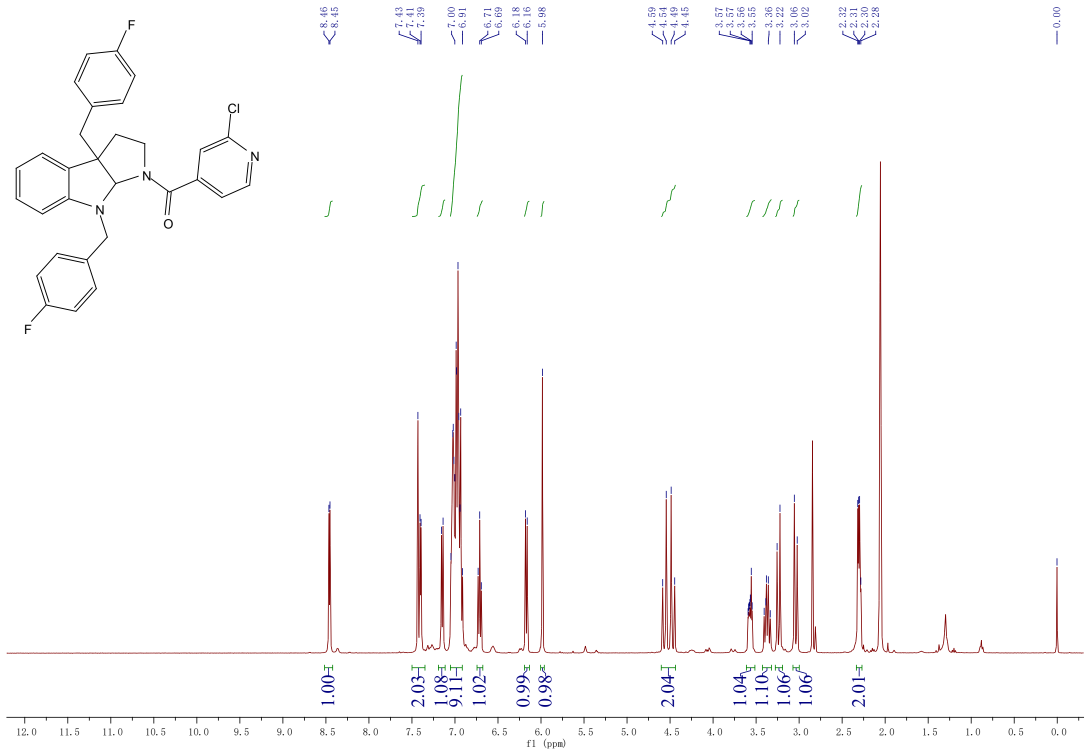

Figure 19. [1]H-NMR spectroscopic data for compound **a10**.

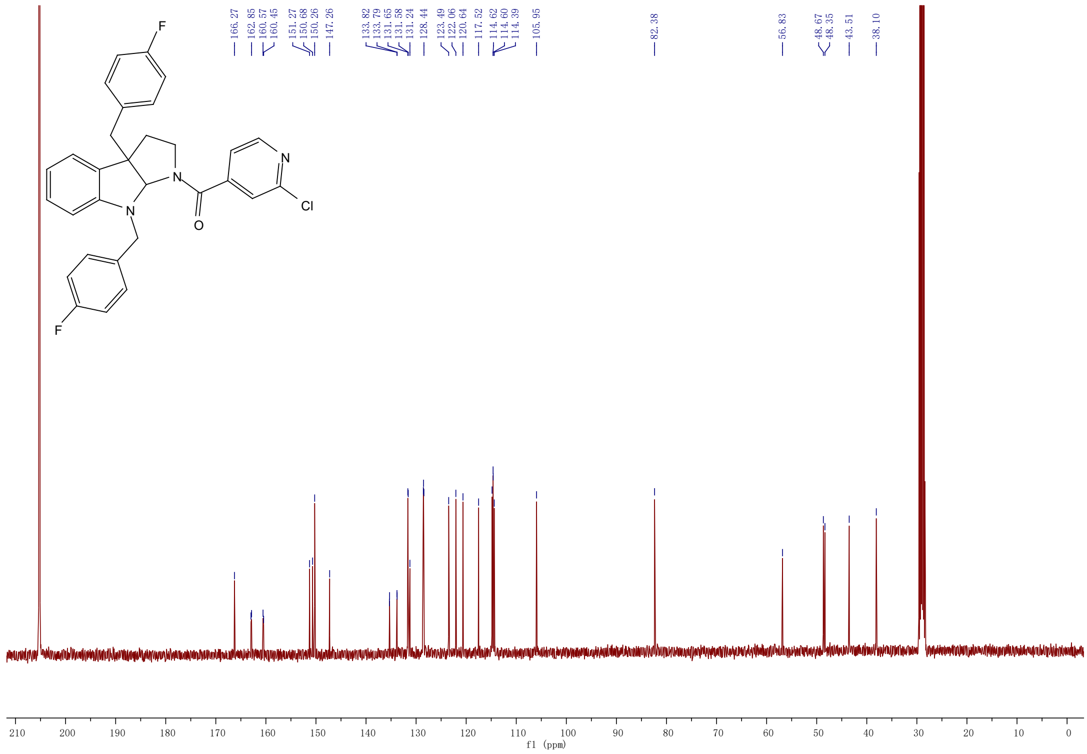

Figure 20. ^{13}C-NMR spectroscopic data for compound **a10**.

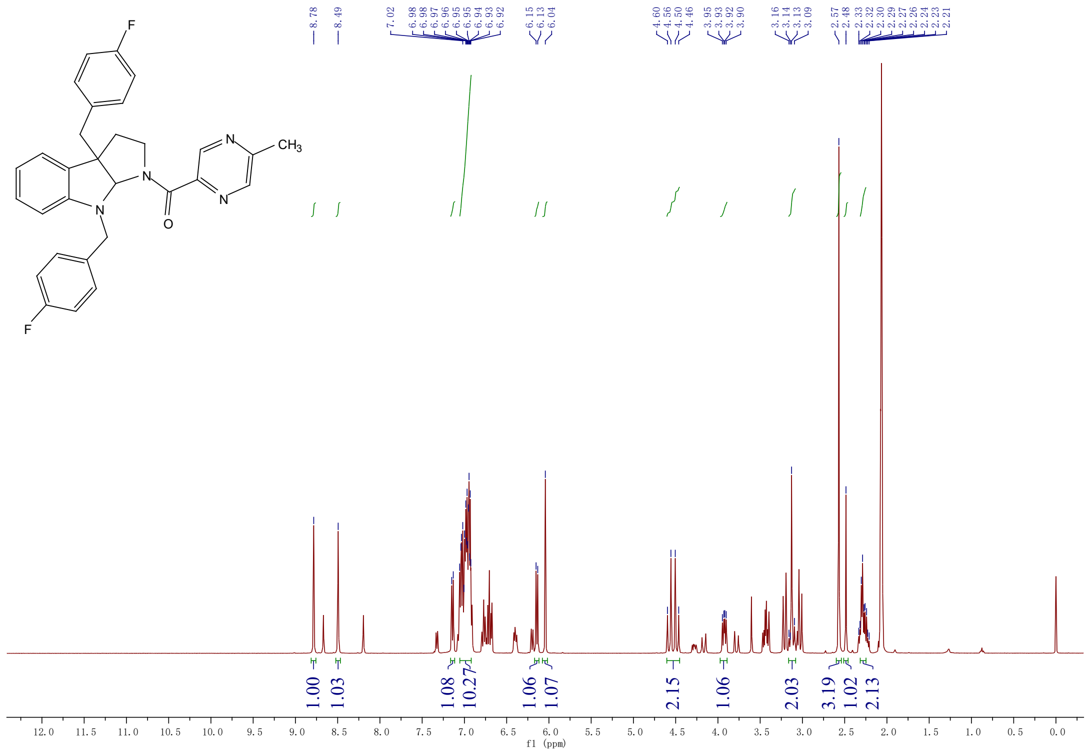

Figure 21. ^{1}H-NMR spectroscopic data for compound **a11**.

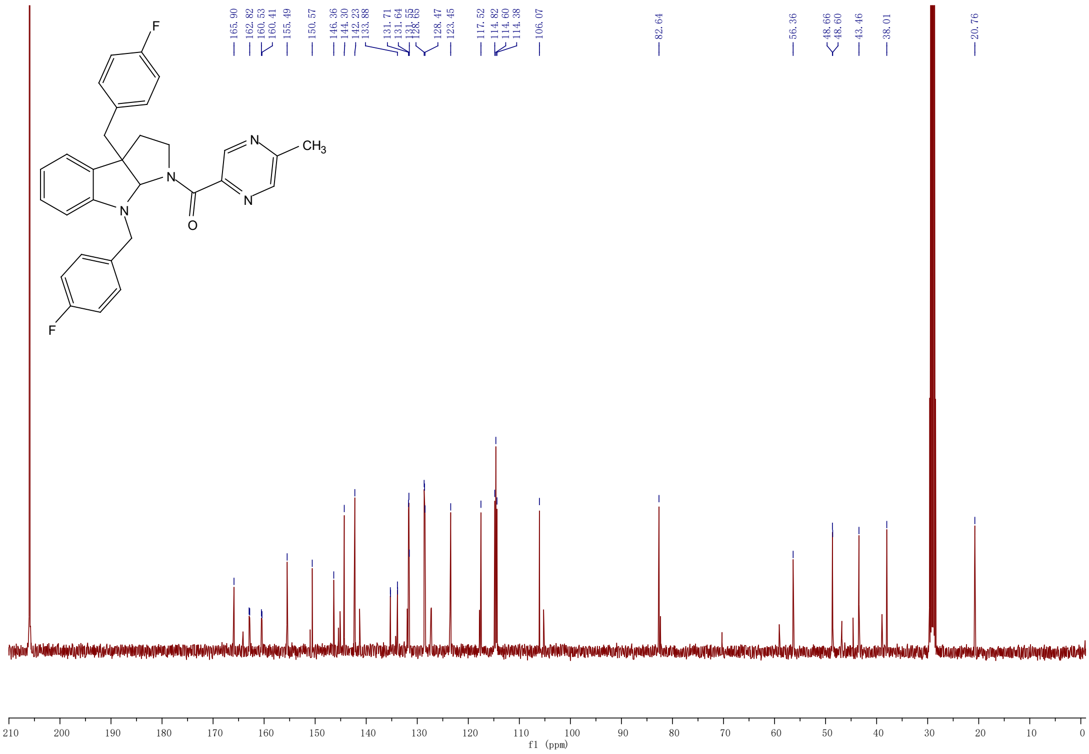

Figure 22. [13]C-NMR spectroscopic data for compound **a11**.

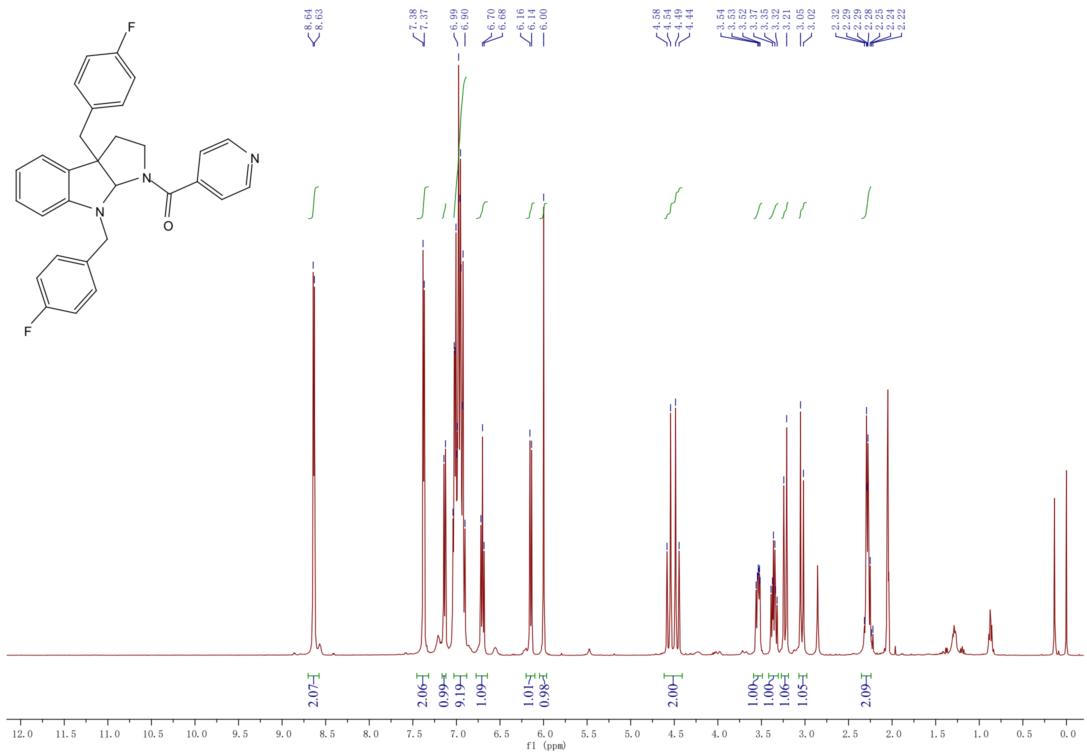

Figure 23. [1]H-NMR spectroscopic data for compound **a12**.

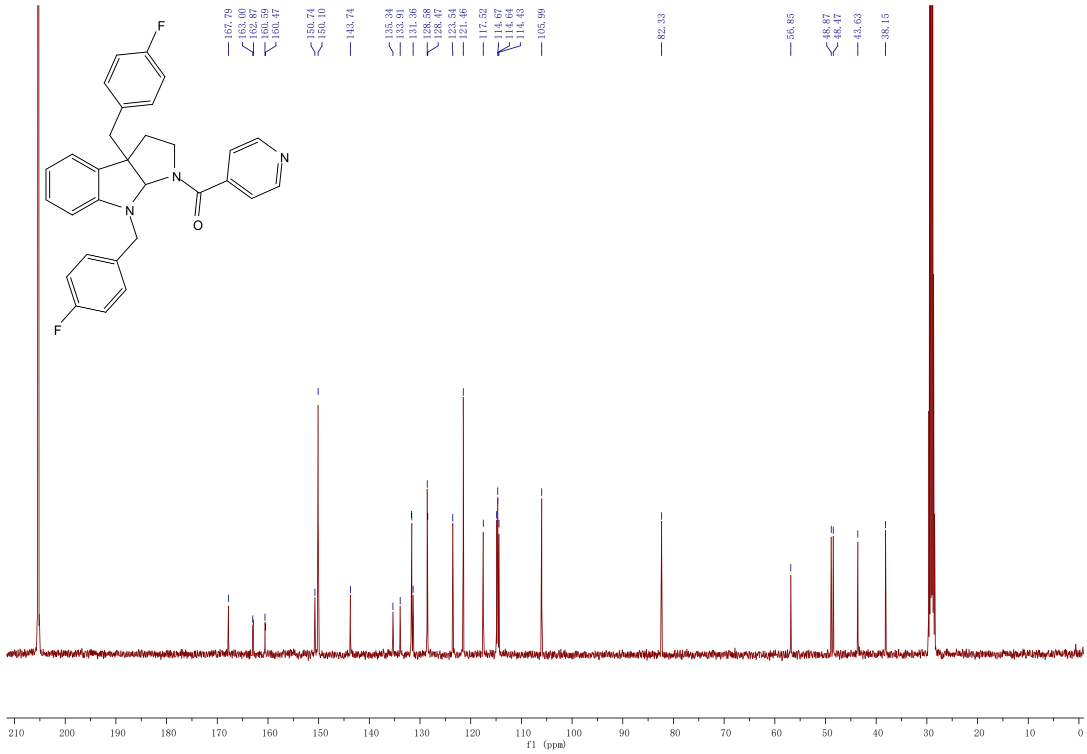

Figure 24. [13]C-NMR spectroscopic data for compound **a12**.

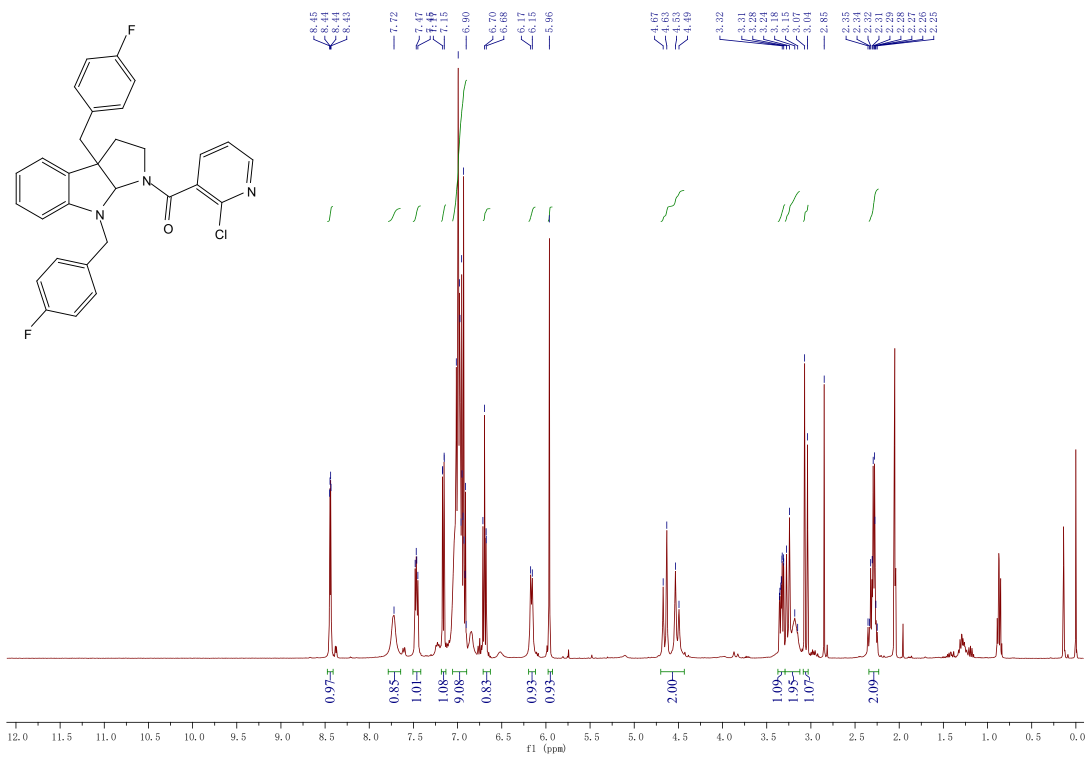

Figure 25. [1]H-NMR spectroscopic data for compound **a13**.

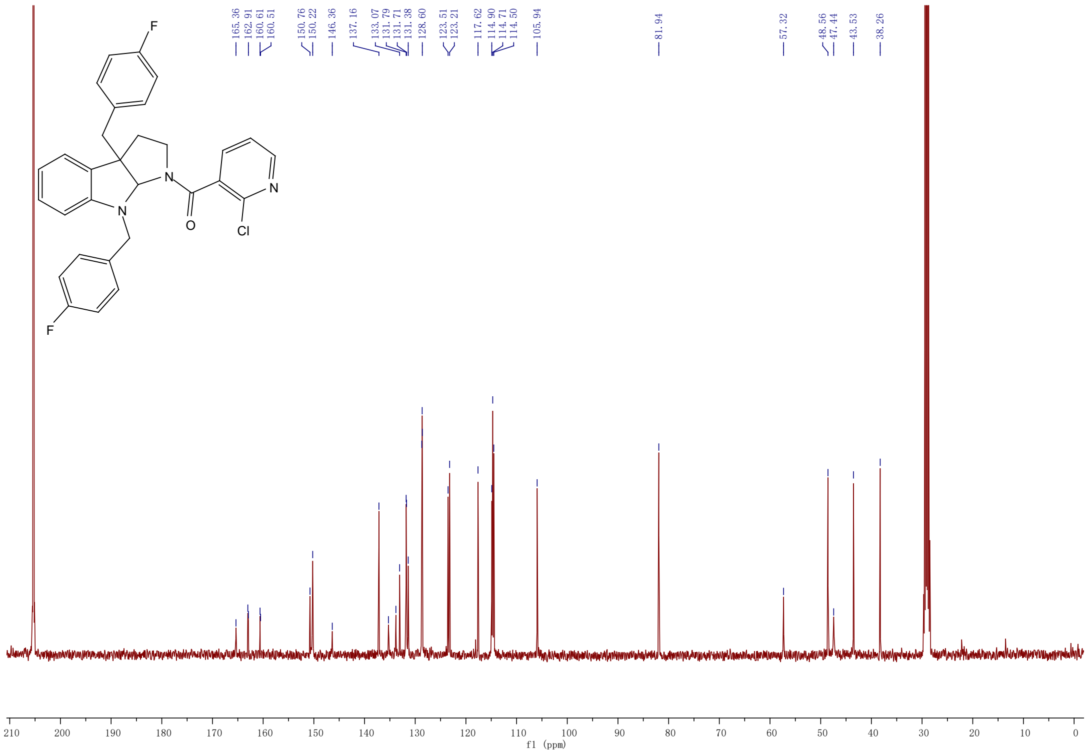

Figure 26. ^{13}C-NMR spectroscopic data for compound **a13**.

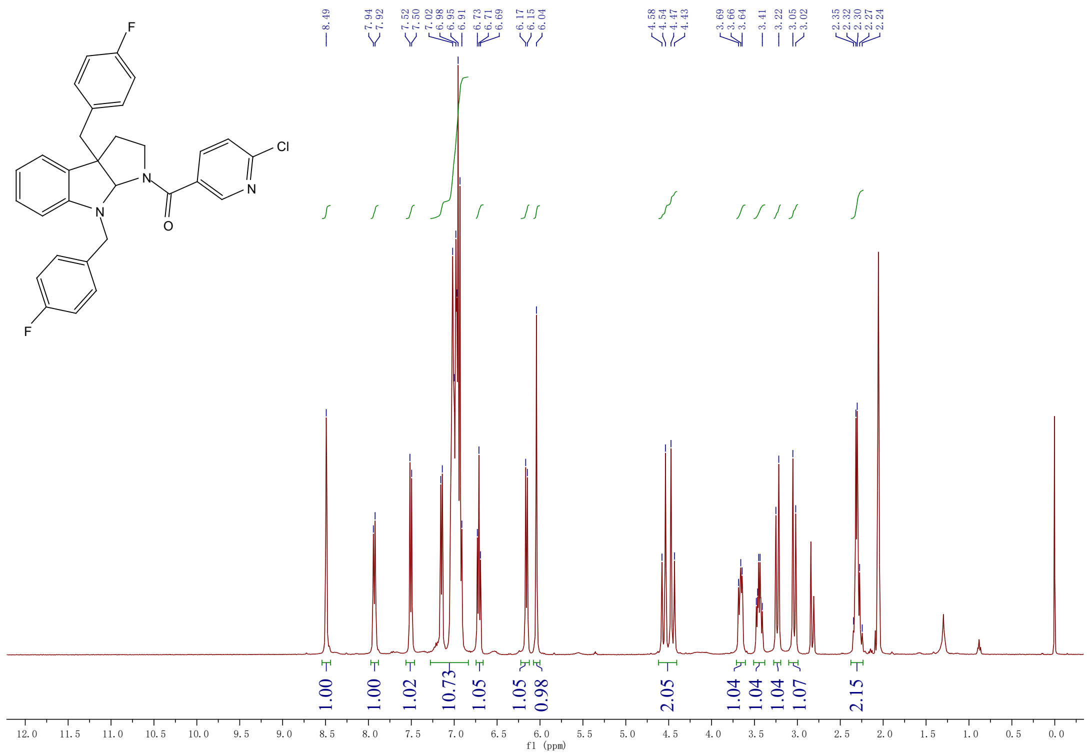

Figure 27. ^{1}H-NMR spectroscopic data for compound **a14**.

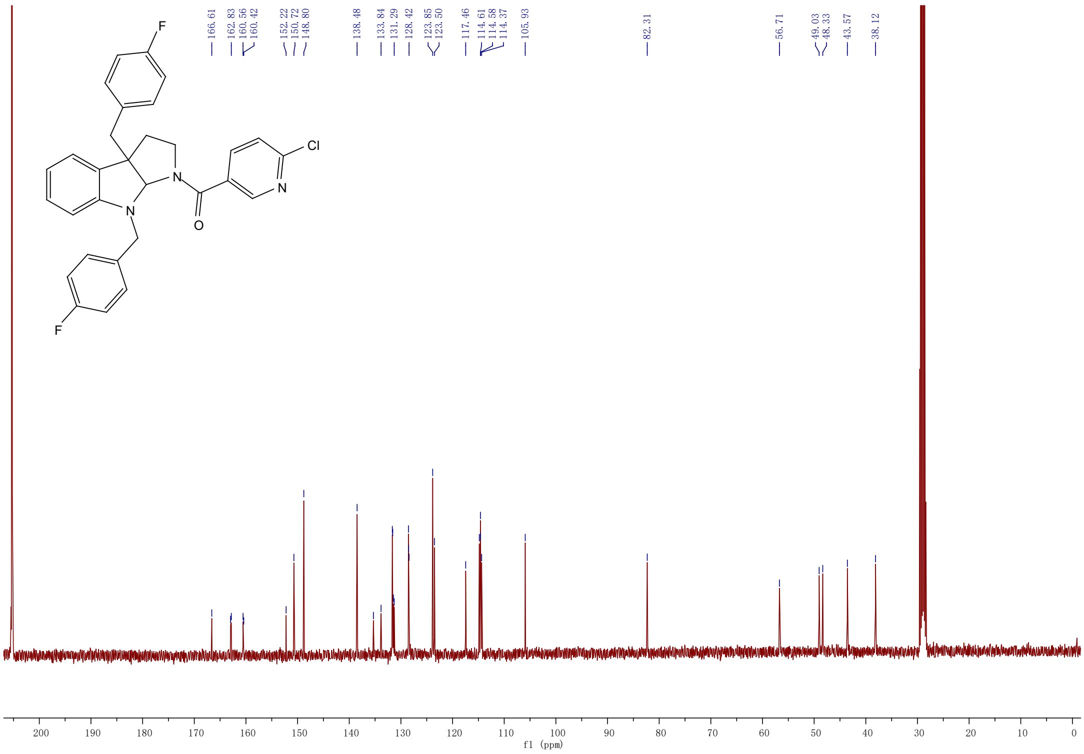

Figure 28. ^{13}C-NMR spectroscopic data for compound **a14**.

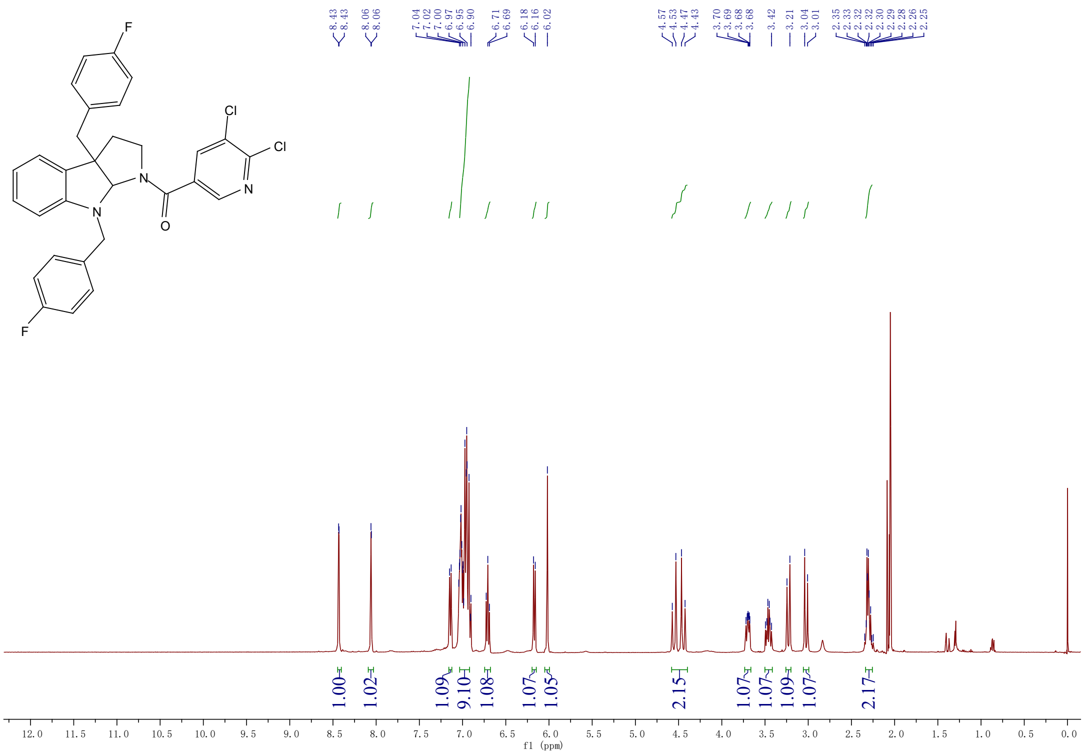

Figure 29. ^{1}H-NMR spectroscopic data for compound **a15**.

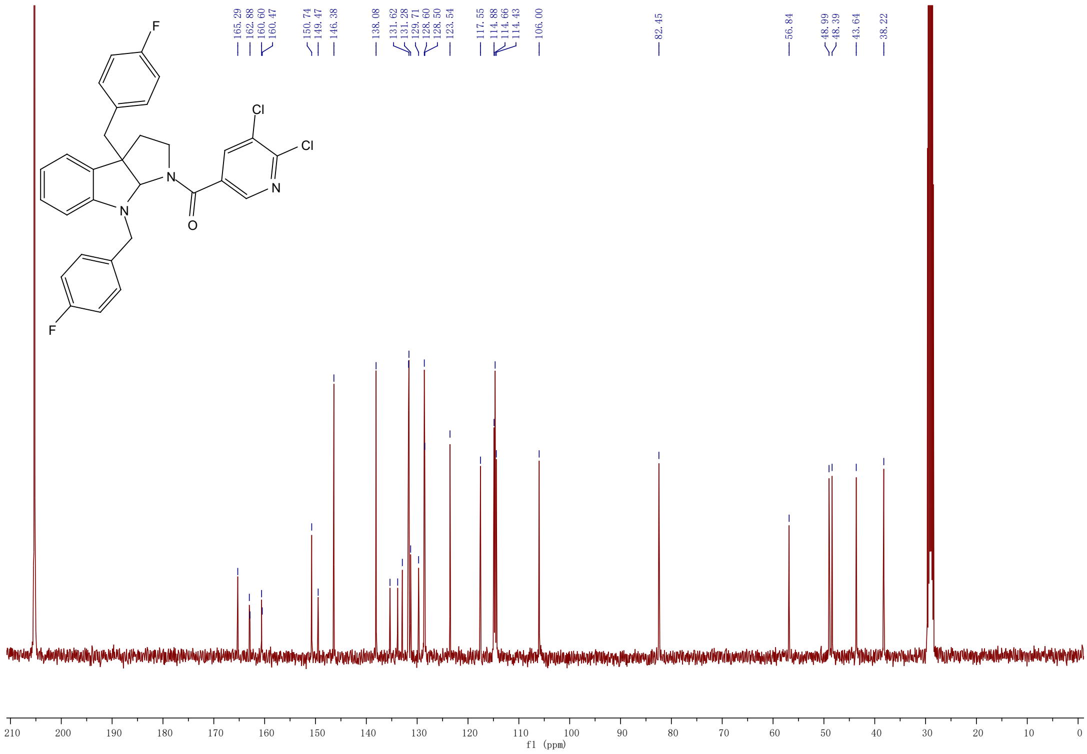

Figure 30. ^{13}C-NMR spectroscopic data for compound **a15**.

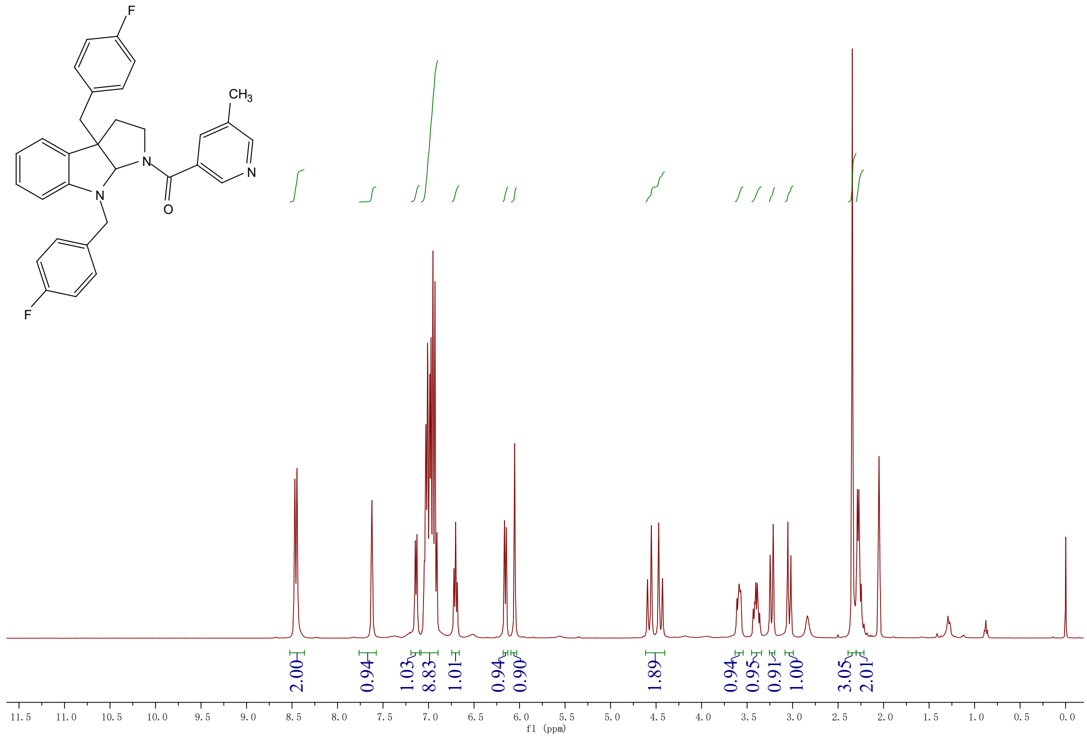

Figure 31. ^{1}H-NMR spectroscopic data for compound **a16**.

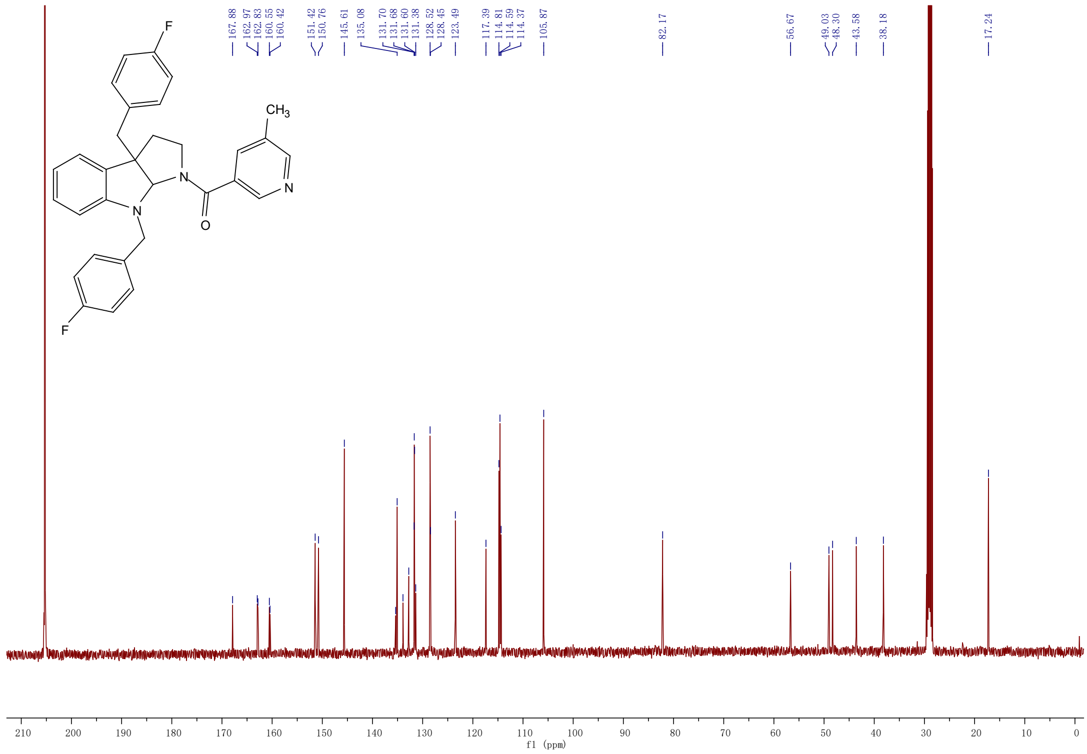

Figure 32. [13]C-NMR spectroscopic data for compound **a16**.

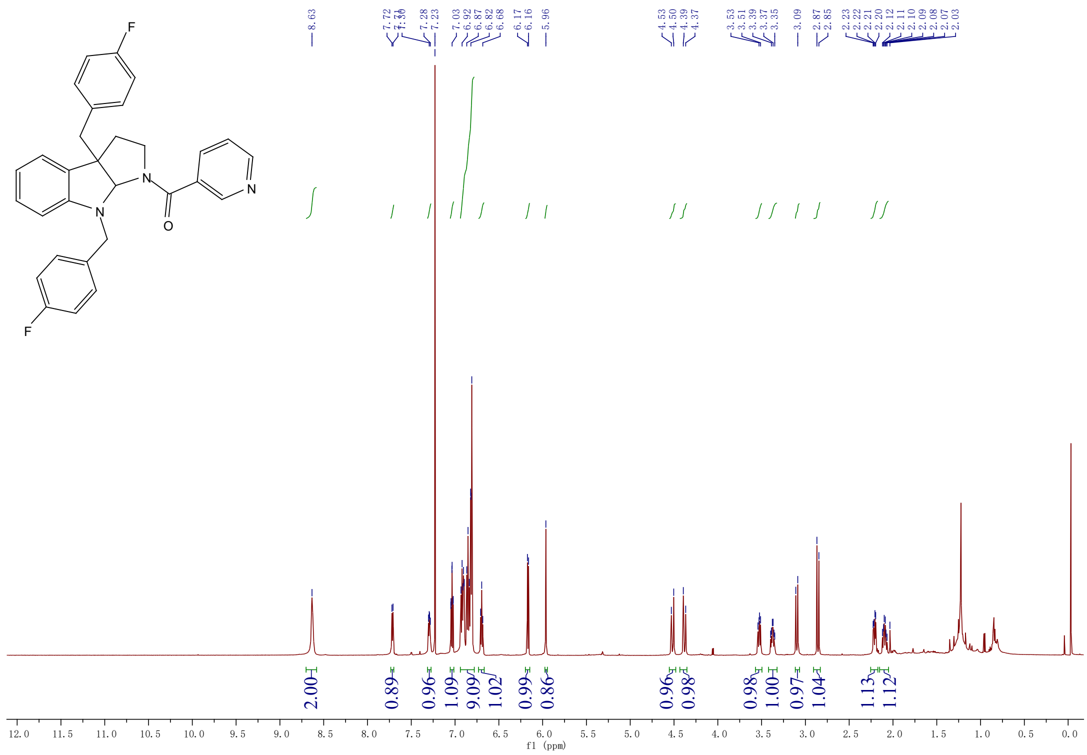

Figure 33. [1]H-NMR spectroscopic data for compound **a17**.

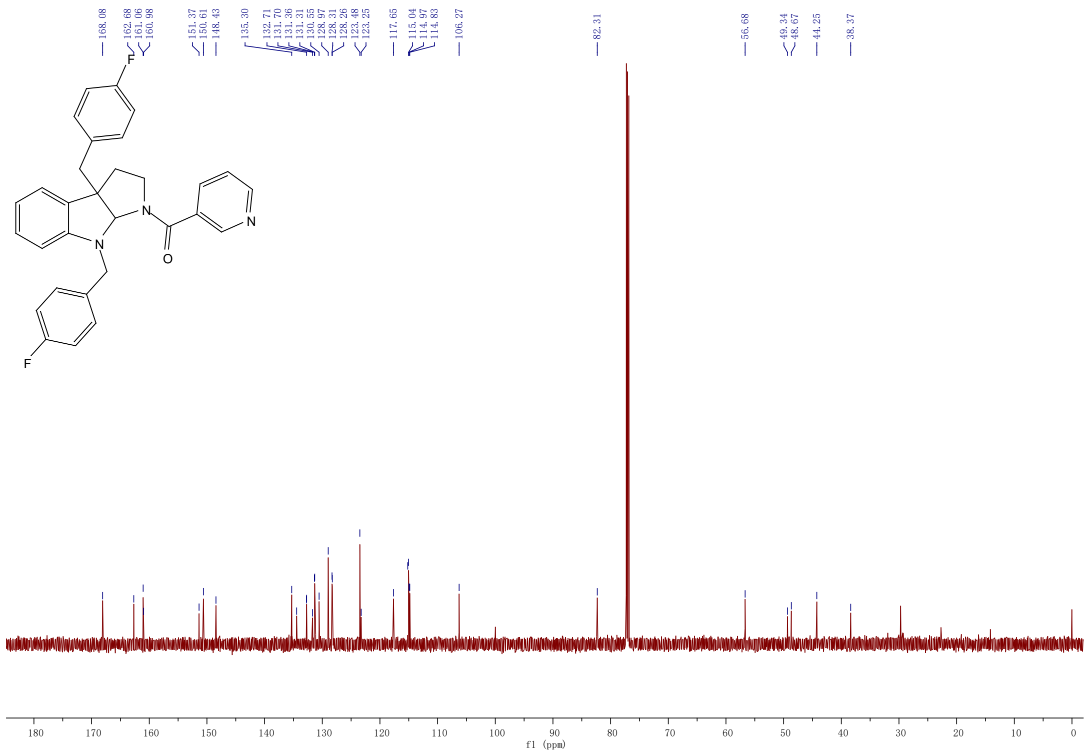

Figure 34. ^{13}C-NMR spectroscopic data for compound **a17**.

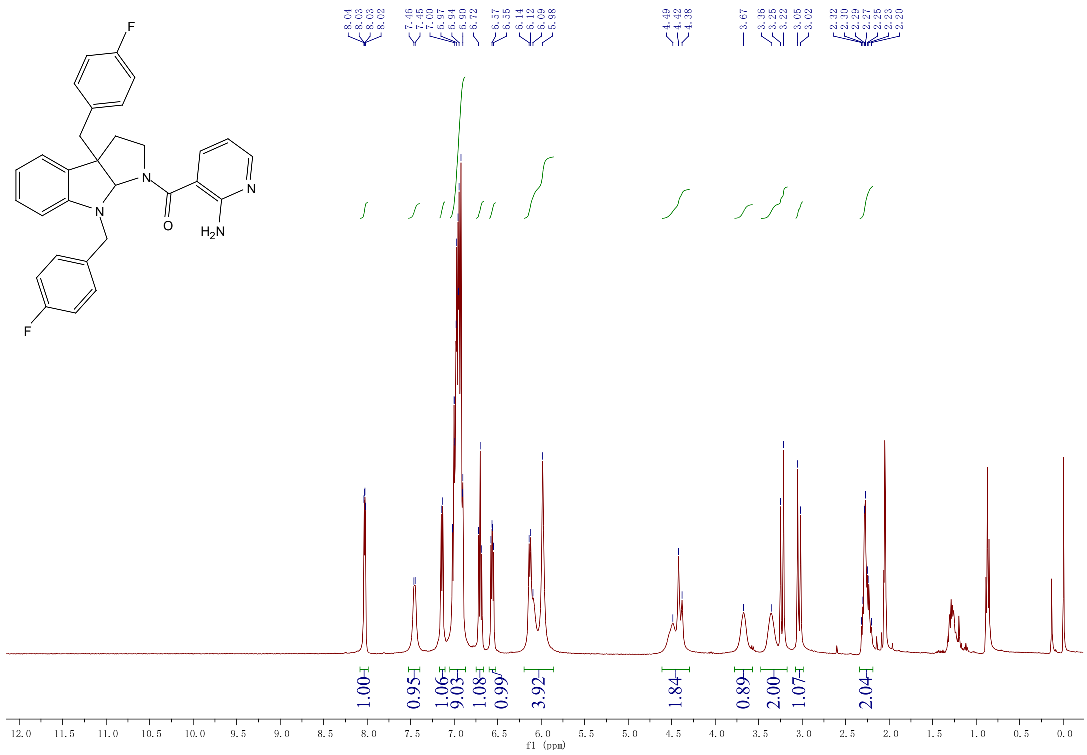

Figure 35. ^{1}H-NMR spectroscopic data for compound **a18**.

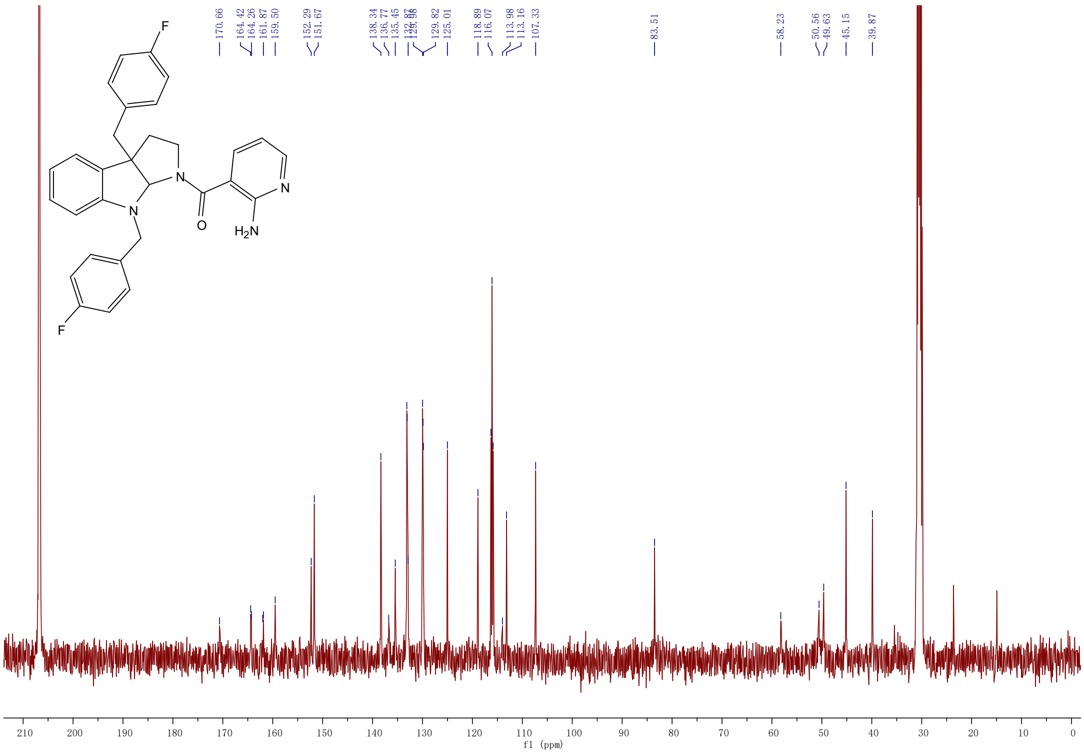

Figure 36. ^{13}C-NMR spectroscopic data for compound **a18**.

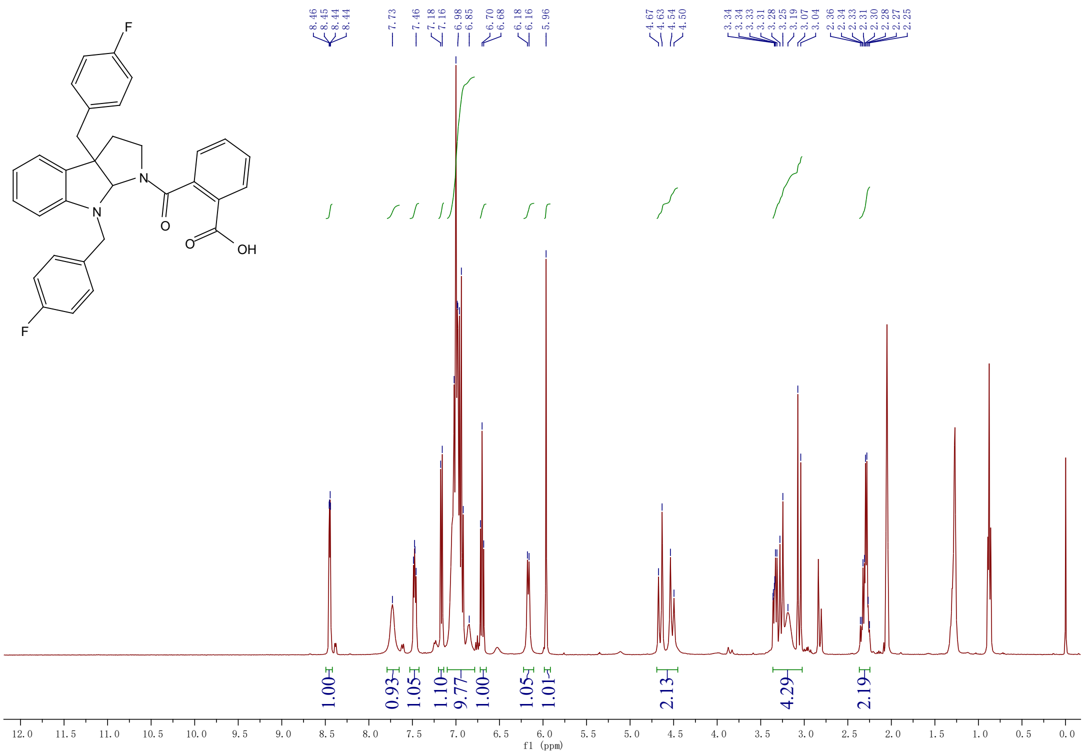

Figure 37. ^{1}H-NMR spectroscopic data for compound **a19**.

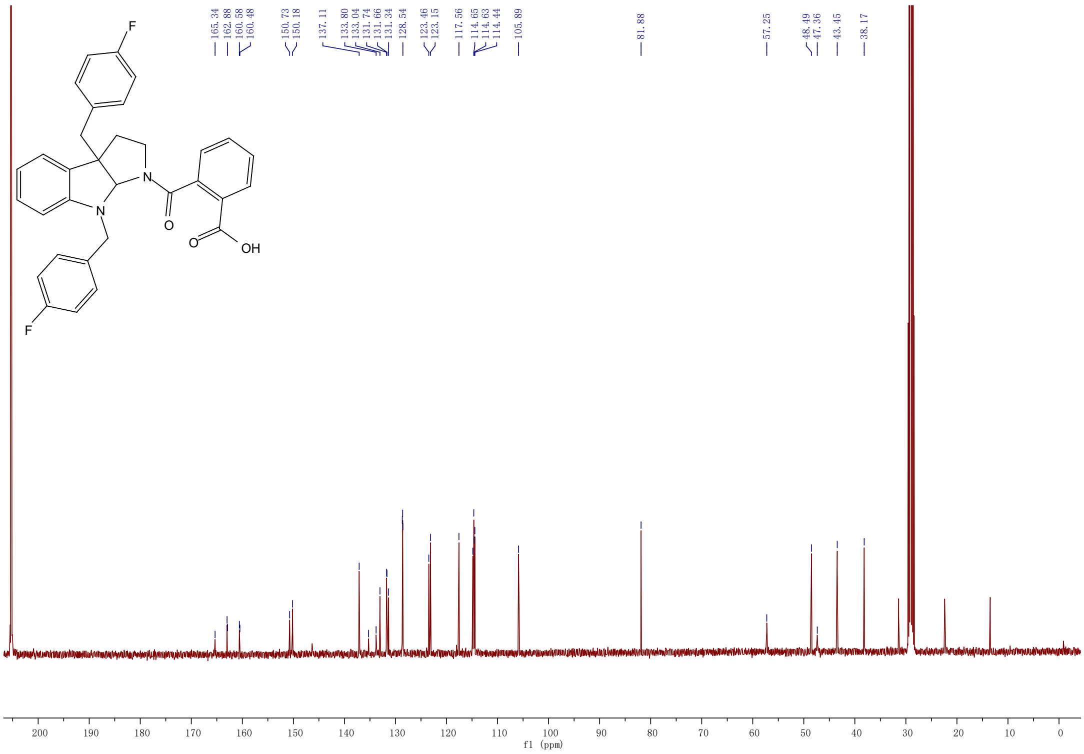

Figure 38. ^{13}C-NMR spectroscopic data for compound **a19**.