

Supplementary material

Part 1: The chemical characterization data of **A1–A6**, **B1–B10**, **C1–C9** and **D1–D7**, as well as some representative original spectrums (NMR, MS, HPLC), were shown as follows.

(3*E*,5*E*)-3,5-bis((1*H*-pyrrol-2-yl)methylene)piperidin-4-one (**A1**)

Orange powder, 54.32% yield, mp 265.5-267.5 °C. ¹H NMR (500 MHz, DMSO-*d*₆) δ: 11.439 (s, 2H, Ar-H¹×2), 7.520 (s, 2H, Ar-H⁵×2), 7.073 (s, 2H, Ar-CH=C×2), 6.401 (s, 2H, Ar-H³×2), 6.269 (s, 2H, Ar-H⁴×2), 3.873 (s, 4H, NH-CH₂×2), 2.607 (s, 1H, CH₂-NH-CH₂). ESI-MS *m/z*: 254.03 (M+H)⁺, calcd for C₁₅H₁₅N₃O: 253.12. HPLC purity: 95.18%.

(3*E*,5*E*)-3,5-bis(furan-2-ylmethylene)piperidin-4-one (**A2**)

Yellowish brown powder, 83.27% yield, mp 136.7-138.6 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.943 (d, *J* = 5.0 Hz, 2H, Ar-H⁵×2), 7.792 (s, 2H, Ar-CH=C×2), 7.352 (d, *J* = 3.0 Hz, 2H, Ar-H³×2), 6.889 (d, *J* = 3.0 Hz, 2H, Ar-H⁴×2), 4.234 (s, 4H, N-CH₂×2), 1.833 (s, 1H, -NH). ESI-MS *m/z*: 256.12 (M+H)⁺, calcd for C₁₅H₁₃NO₃: 255.09. HPLC purity: 97.25%.

(3*E*,5*E*)-3,5-bis(thiophen-2-ylmethylene)piperidin-4-one (**A3**)

Yellow powder, 76.39% yield, mp 205.4-208.7 °C. ¹H NMR (500 MHz, DMSO-*d*₆) δ: 7.907 (d, *J* = 5.0 Hz, 2H, Ar-H⁵×2), 7.785 (s, 2H, Ar-CH=C×2), 7.559 (s, 2H, Ar-H³×2), 7.259 (d, *J* = 4.0 Hz, 2H, Ar-H⁴×2), 4.002 (s, 4H, N-CH₂×2), 1.237 (s, 1H, -NH). ESI-MS *m/z*: 287.76 (M+H)⁺, calcd for C₁₅H₁₃NOS₂: 287.04. HPLC purity: 100%.

(3*E*,5*E*)-3,5-bis((5-methyl-1*H*-pyrrol-2-yl)methylene)piperidin-4-one (**A4**)

Orange yellow powder, 62.55% yield, mp 191.6-193.0 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.743 (s, 2H, Ar-CH=C×2), 6.829 (s, 2H, Ar-H¹×2), 6.424 (d, *J* = 3.5 Hz, 2H, Ar-H³×2), 6.261 (s, 2H, Ar-H⁴×2), 4.072 (s, 4H, NH-CH₂×2), 3.744 (s, 6H, -CH₃×2), 1.860 (s, 1H, CH₂-NH-CH₂). ESI-MS *m/z*: 282.04 (M+H)⁺, calcd for C₁₇H₁₉N₃O: 281.15.

HPLC purity: 100%.

(3E,5E)-3,5-bis((5-methylfuran-2-yl)methylene)piperidin-4-one (A5)

Orange powder, 87.35% yield, mp 137.8-139.2 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.412 (s, 2H, Ar-CH=C×2), 6.551 (d, *J* = 3.0 Hz, 2H, Ar-H³×2), 6.115 (d, *J* = 3.0 Hz, 2H, Ar-H⁴×2), 4.229 (s, 4H, N-CH₂×2), 2.356 (s, 6H, -CH₃×2), 1.849 (s, 1H, -NH). ESI-MS *m/z*: 284.11 (M+H)⁺, calcd for C₁₇H₁₇NO₃: 283.12. HPLC purity: 100%.

(3E,5E)-3,5-bis((5-methylthiophen-2-yl)methylene)piperidin-4-one (A6)

Orange yellow powder, 77.14% yield, mp 197.3-198.7 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.835 (s, 2H, Ar-CH=C×2), 7.136 (d, *J* = 3.0 Hz, 2H, Ar-H³×2), 6.804 (d, *J* = 2.5 Hz, 2H, Ar-H⁴×2), 4.121 (s, 4H, N-CH₂×2), 2.542 (s, 6H, -CH₃×2), 1.745 (s, 1H, -NH). ESI-MS *m/z*: 315.85 (M+H)⁺, calcd for C₁₇H₁₇NOS₂: 315.08. HPLC purity: 97.56%.

(3E,5E)-3,5-bis(3-fluorobenzylidene)piperidin-4-one (B1)

Light yellow powder, 84.7% yield, mp 139.0-140.5 °C. ¹H-NMR (500MHz, CDCl₃), δ: 7.987 (s, 2H, Ar-CH=C×2), 7.678 (d, *J* = 8.0 Hz, 2H, Ar-H⁶×2), 7.390 (t, *J* = 8.0 Hz, 2H, Ar-H⁵×2), 7.296 (d, *J* = 8.0 Hz, 2H, Ar-H⁴×2), 7.245 (d, *J* = 7.5 Hz, 2H, Ar-H²×2), 3.977 (s, 4H, N-CH₂×2), 1.745 (s, 1H, -NH). ESI-MS *m/z*: 312.21 (M+H)⁺, calcd for C₁₉H₁₅F₂NO: 311.11. HPLC purity: 98.86%.

(3E,5E)-3,5-bis(4-fluorobenzylidene)piperidin-4-one (B2)

Light yellow powder, 89.3% yield, mp 169.0-170.5 °C. ¹H-NMR (500MHz, CDCl₃), δ: 7.785 (s, 2H, Ar-CH=C×2), 7.396 (d, *J* = 8.0 Hz, 4H, Ar-H²×2, Ar-H⁶×2), 7.125 (d, *J* = 8.5 Hz, 4H, Ar-H³×2, Ar-H⁵×2), 3.972 (s, 4H, N-CH₂×2), 1.766 (s, 1H, -NH). ESI-MS *m/z*: 312.20 (M+H)⁺, calcd for C₁₉H₁₅F₂NO: 311.11. HPLC purity: 100%.

(3E,5E)-3,5-bis(2-chlorobenzylidene)piperidin-4-one (B3)

Light yellow powder, 68.66% yield, mp 112.3-113.4 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.965 (s, 2H, Ar-CH=C×2), 7.459 (t, *J* = 3.0 Hz, 2H, Ar-H³×2), 7.285 (d, *J* = 5.5 Hz,

2H, Ar-H⁵×2), 7.214 (t, $J = 3.0$ Hz, 2H, Ar-H⁶×2), 7.194 (d, $J = 4.0$ Hz, 2H, Ar-H⁴×2), 3.999 (d, $J = 2.0$ Hz, 4H, N-CH₂×2), 2.048 (s, 1H, -NH). ESI-MS m/z : 344.08 (M+H)⁺, calcd for C₁₉H₁₅Cl₂NO: 343.05. HPLC purity: 100%.

(3E,5E)-3,5-bis(2-bromobenzylidene)piperidin-4-one (B4)

Yellow powder, 76.34% yield, mp 147.4-149.6 °C. ¹H NMR (500 MHz, CDCl₃) δ : 7.906 (s, 2H, Ar-CH=C×2), 7.649 (dd, $J_1 = 1.5$ Hz, $J_2 = 10.0$ Hz, 2H, Ar-H³×2), 7.340 (dt, $J_1 = 1.5$ Hz, $J_2 = 9.0$ Hz, 2H, Ar-H⁵×2), 7.228 (dd, $J_1 = 2.0$ Hz, $J_2 = 10.0$ Hz, 2H, Ar-H⁶×2), 7.206 (dd, $J_1 = 3.0$ Hz, $J_2 = 9.5$ Hz, 2H, Ar-H⁴×2), 3.982 (d, $J = 2.5$ Hz, 4H, N-CH₂×2), 1.734 (s, 1H, -NH). ESI-MS m/z : 431.99 (M+H)⁺, calcd for C₁₉H₁₅Br₂NO: 430.95. HPLC purity: 100%.

(3E,5E)-3,5-bis(2-methoxybenzylidene)piperidin-4-one (B5)

Yellow powder, 83.58% yield, mp 157.2-159.6 °C. ¹H NMR (500 MHz, CDCl₃) δ : 8.006 (s, 2H, Ar-CH=C×2), 7.336 (t, $J = 7.5$ Hz, 2H, Ar-H⁴×2), 7.162 (d, $J = 7.5$ Hz, 2H, Ar-H⁶×2), 6.964 (t, $J = 7.5$ Hz, 2H, Ar-H⁵×2), 6.915 (d, $J = 8.5$ Hz, 2H, Ar-H³×2), 4.028 (s, 4H, N-CH₂×2), 3.856 (s, 6H, -OCH₃×2), 1.734 (s, 1H, -NH). ESI-MS m/z : 335.75 (M+H)⁺, calcd for C₂₁H₂₁NO₃: 335.15. HPLC purity: 100%.

(3E,5E)-3,5-bis(4-chlorobenzylidene)piperidin-4-one (B6)

Light yellow powder, 72.88% yield, mp 191.3-193.7 °C. ¹H NMR (500 MHz, CDCl₃) δ : 7.734 (s, 2H, Ar-CH=C×2), 7.390 (d, $J = 10.5$ Hz, 4H, Ar-H²×2, Ar-H⁶×2), 7.308 (d, $J = 10.5$ Hz, 4H, Ar-H³×2, Ar-H⁵×2), 4.115 (d, $J = 2.5$ Hz, 4H, N-CH₂×2), 3.856 (s, 6H, -OCH₃×2), 1.685 (s, 1H, -NH). ESI-MS m/z : 344.08 (M+H)⁺, calcd for C₁₉H₁₅Cl₂NO: 343.05. HPLC purity: 95.43%.

(3E,5E)-3,5-bis(3-bromobenzylidene)piperidin-4-one (B7)

White powder, 69.60% yield, mp 120.6-124.6 °C. ¹H NMR (500 MHz, CDCl₃) δ : 8.020 (s, 2H, Ar-CH=C×2), 7.516 (s, 2H, Ar-H²×2), 7.420 (d, $J = 7.5$ Hz, 2H, Ar-H⁶×2), 7.360 (d, $J = 7.5$ Hz, 2H, Ar-H⁴×2), 7.192 (t, $J = 8.5$ Hz, 2H, Ar-H⁵×2), 4.120 (s, 4H, N-

CH₂×2), 1.622 (s, 1H, -NH). ESI-MS m/z: 431.99 (M+H)⁺, calcd for C₁₉H₁₅Br₂NO: 430.95. HPLC purity: 96.25%.

(3E,5E)-3,5-bis(4-bromobenzylidene)piperidin-4-one (B8)

Light yellow powder, 58.05% yield, mp 206.7-208.7 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.711 (s, 2H, Ar-CH=C×2), 7.548 (d, *J* = 8.0 Hz, 4H, Ar-H²×2, Ar-H⁶×2), 7.240 (d, *J* = 8.5 Hz, 4H, Ar-H³×2, Ar-H⁵×2), 4.105 (s, 4H, N-CH₂×2), 1.676 (s, 1H, -NH). ESI-MS m/z: 431.99 (M+H)⁺, calcd for C₁₉H₁₅Br₂NO: 430.95. HPLC purity: 100%.

(3E,5E)-3,5-bis(3-methoxybenzylidene)piperidin-4-one (B9)

Light yellow powder, 54.25% yield, mp 164.5-167.2 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.781 (s, 2H, Ar-CH=C×2), 7.636 (t, *J* = 8.5 Hz, 2H, Ar-H⁵×2), 7.122 (d, *J* = 8.0 Hz, 2H, Ar-H⁶×2), 7.062 (s, 2H, Ar-H²×2), 6.915 (d, *J* = 8.5 Hz, 2H, Ar-H³×2), 4.018 (s, 4H, N-CH₂×2), 3.841 (s, 6H, -OCH₃×2), 1.619 (s, 1H, -NH). ESI-MS m/z: 335.75 (M+H)⁺, calcd for C₂₁H₂₁NO₃: 335.15. HPLC purity: 97.03%.

(3E,5E)-3,5-bis(4-methoxybenzylidene)piperidin-4-one (B10)

Light yellow powder, 77.22% yield, mp >300 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.792 (s, 2H, Ar-CH=C×2), 7.373 (d, *J* = 8.0 Hz, 4H, Ar-H²×2, Ar-H⁶×2), 6.951 (d, *J* = 8.5 Hz, 4H, Ar-H³×2, Ar-H⁵×2), 4.128 (s, 4H, N-CH₂×2), 3.852 (s, 6H, -OCH₃×2), 1.704 (s, 1H, -NH). ESI-MS m/z: 335.75 (M+H)⁺, calcd for C₂₁H₂₁NO₃: 335.15. HPLC purity: 100%.

(3E,5E)-3,5-bis(2,5-difluorobenzylidene)piperidin-4-one (C1)

Light yellow powder, 37.35% yield, mp 195.2-197.2 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.911 (s, 2H, Ar-CH=C×2), 7.180 (d, *J* = 8.5 Hz, 2H, Ar-H³×2), 7.036 (d, *J* = 8.5 Hz, 2H, Ar-H⁴×2), 7.064 (s, 2H, Ar-H⁶×2), 3.991 (s, 4H, N-CH₂×2), 1.681 (s, 1H, -NH). ESI-MS m/z: 347.75 (M+H)⁺, calcd for C₁₉H₁₃F₄NO: 347.09. HPLC purity: 100%.

(3E,5E)-3,5-bis(2-fluoro-4-methoxybenzylidene)piperidin-4-one (C2)

Light yellow powder, 53.32% yield, mp 145.8-147.2 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.836 (s, 2H, Ar-CH=C×2), 7.203 (t, *J* = 10.5 Hz, 2H, Ar-H⁶×2), 6.728 (d, *J*₁ = 3.0 Hz, *J*₂ = 10.5 Hz, 2H, Ar-H³×2), 6.964 (t, *J*₁ = 3.0 Hz, *J*₂ = 10.0 Hz, 2H, Ar-H⁵×2), 4.031 (s, 4H, N-CH₂×2), 3.839 (s, 6H, -OCH₃×2), 1.753 (s, 1H, -NH). ESI-MS *m/z*: 371.78 (M+H)⁺, calcd for C₂₁H₁₉F₂NO₃: 371.13. HPLC purity: 100%.

(3*E*,5*E*)-3,5-bis(2-fluoro-6-methoxybenzylidene)piperidin-4-one (C3)

Light yellow powder, 73.22% yield, mp 165.5-167.5 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.792 (s, 2H, Ar-CH=C×2), 6.927 (d, *J* = 7.5 Hz, 2H, Ar-H⁴×2), 6.706 (d, *J* = 7.5 Hz, 2H, Ar-H³×2), 6.622 (d, *J* = 7.0 Hz, 2H, Ar-H⁵×2), 4.019 (s, 4H, N-CH₂×2), 3.754 (s, 6H, -OCH₃×2), 1.627 (s, 1H, -NH). ESI-MS *m/z*: 371.78 (M+H)⁺, calcd for C₂₁H₁₉F₂NO₃: 371.13. HPLC purity: 100%.

(3*E*,5*E*)-3,5-bis(2-bromo-5-methoxybenzylidene)piperidin-4-one (C4)

Yellow powder, 71.33% yield, mp 174.0-176.5 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.850 (s, 2H, Ar-CH=C×2), 7.522 (d, *J* = 11.0 Hz, 2H, Ar-H³×2), 6.782 (d, *J* = 11.0 Hz, 2H, Ar-H⁴×2), 6.730 (d, *J* = 3.0 Hz, 2H, Ar-H⁶×2), 3.998 (s, 4H, N-CH₂×2), 3.806 (s, 6H, -OCH₃×2), 1.703 (s, 1H, -NH). ESI-MS *m/z*: 492.03 (M+H)⁺, calcd for C₂₁H₁₉Br₂NO₃: 490.97. HPLC purity: 97.61%.

(3*E*,5*E*)-3,5-bis(2-bromo-6-fluorobenzylidene)piperidin-4-one (C5)

Light yellow powder, 69.35% yield, mp 172.2-173.3 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.558 (s, 2H, Ar-CH=C×2), 7.451 (d, *J* = 8.0 Hz, 2H, Ar-H³×2), 7.162 (q, *J* = 8.0 Hz, 2H, Ar-H⁴×2), 7.098 (t, *J* = 8.5 Hz, 2H, Ar-H⁵×2), 3.744 (s, 4H, N-CH₂×2), 1.721 (s, 1H, -NH). ESI-MS *m/z*: 468.00 (M+H)⁺, calcd for C₁₉H₁₃Br₂F₂NO: 466.93. HPLC purity: 97.35%.

(3*E*,5*E*)-3,5-bis(2-bromo-5-fluorobenzylidene)piperidin-4-one (C6)

White powder, 79.25% yield, mp 135.8-137.6 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.816 (s, 2H, Ar-CH=C×2), 7.481 (d, *J* = 7.5 Hz, 2H, Ar-H³×2), 7.014 (d, *J* = 7.5 Hz, 2H, Ar-H⁴×2), 6.864 (s, 2H, Ar-H⁶×2), 3.971 (s, 4H, N-CH₂×2), 1.622 (s, 1H, -NH). ESI-MS

m/z: 468.00 (M+H)⁺, calcd for C₁₉H₁₃Br₂F₂NO: 466.93. HPLC purity: 100%.

(3E,5E)-3,5-bis(2-bromo-5-chlorobenzylidene)piperidin-4-one (C7)

White powder, 43.82% yield, mp 129.2-130.0 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.879 (s, 2H, Ar-CH=C×2), 7.460 (d, *J* = 8.5 Hz, 2H, Ar-H³×2), 7.133 (d, *J* = 7.5 Hz, 2H, Ar-H⁴×2), 7.055 (s, 2H, Ar-H⁶×2), 3.970 (s, 4H, N-CH₂×2), 1.657 (s, 1H, -NH). ESI-MS m/z: 499.91 (M+H)⁺, calcd for C₁₉H₁₃Br₂Cl₂NO: 498.87. HPLC purity: 100%.

(3E,5E)-3,5-bis(2,5-dibromobenzylidene)piperidin-4-one (C8)

Yellow powder, 51.69% yield, mp 219.8-221.4 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.787 (s, 2H, Ar-CH=C×2), 7.509 (t, *J* = 8.0 Hz, 2H, Ar-H⁶×2), 7.343 (d, *J* = 8.0 Hz, 2H, Ar-H³×2), 7.325 (s, 2H, Ar-H⁴×2), 3.977 (s, 4H, N-CH₂×2), 1.723 (s, 1H, -NH). ESI-MS m/z: 587.82 (M+H)⁺, calcd for C₁₉H₁₃Br₄NO: 586.77. HPLC purity: 99.17%.

(3E,5E)-3,5-bis(2,6-dichlorobenzylidene)piperidin-4-one (C9)

Light yellow powder, 84.74% yield, mp 183.8-184.6 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.640 (s, 2H, Ar-CH=C×2), 7.357 (d, *J* = 8.0 Hz, 4H, Ar-H³×2, Ar-H⁵×2), 7.228 (t, *J* = 8.0 Hz, 2H, Ar-H⁴×2), 3.674 (s, 4H, N-CH₂×2), 1.610 (s, 1H, -NH). ESI-MS m/z: 412.00 (M+H)⁺, calcd for C₁₉H₁₃Cl₄NO: 410.98. HPLC purity: 97.52%.

(3E,5E)-3,5-bis((5-bromo-1H-indol-3-yl)methylene)piperidin-4-one (D1)

White powder, 39.13% yield, mp 201.0-203.0 °C. ¹H NMR (500 MHz, DMSO-d₆) δ: 10.032 (s, 2H, Ar-NH³×2), 8.361 (s, 2H, Ar-H²×2), 8.223 (s, 2H, Ar-CH=C×2), 7.501 (d, *J* = 10.5 Hz, 2H, Ar-H⁵×2), 7.415 (d, *J* = 2.5 Hz, 2H, Ar-H⁴×2), 7.393 (d, *J* = 2.5 Hz, 2H, Ar-H⁷×2), 4.052 (s, 4H, N-CH₂×2), 1.708 (s, 1H, -NH). ESI-MS m/z: 510.01 (M+H)⁺, calcd for C₂₃H₁₇Br₂N₃O: 508.97. HPLC purity: 96.18%.

(3E,5E)-3,5-bis((E)-3-(2-methoxyphenyl)allylidene)piperidin-4-one (D2)

Orange powder, 72.35% yield, mp 134.9-136.8 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.530 (dd, *J*₁ = 2.0 Hz, *J*₂ = 10.0 Hz, 2H, Ar-H⁶×2), 7.472 (d, *J* = 15.0 Hz, 2H, Ar-CH=CH-CH×2), 7.343 (d, *J* = 19.0 Hz, 2H, Ar-CH=CH-CH×2), 7.287 (dt, *J*₁ = 2.0 Hz,

$J_2 = 11.0$ Hz, 2H, Ar-H⁴×2), 7.343 (dd, $J_1 = 15.0$ Hz, $J_2 = 19.0$ Hz, 2H, Ar-CH=CH-CH×2), 6.956 (t, $J = 9.0$ Hz, 2H, Ar-H⁵×2), 6.896 (d, $J = 10.0$ Hz, 2H, Ar-H³×2), 4.035 (d, $J = 1.0$ Hz, 4H, N-CH₂×2), 3.883 (s, 6H, -OCH₃×2), 1.824 (s, 1H, -NH). ESI-MS m/z : 388.28 (M+H)⁺, calcd for C₂₅H₂₅NO₃: 387.18. HPLC purity: 100%.

(3E,5E)-3,5-bis((E)-3-(4-bromophenyl)allylidene)piperidin-4-one (D3)

Yellow powder, 67.35% yield, mp 211.3-213.7 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.471 (dd, $J_1 = 4.5$ Hz, $J_2 = 10.5$ Hz, 4H, Ar-H²×2, Ar-H⁶×2), 7.425 (d, $J = 15.0$ Hz, 2H, Ar-CH=CH-CH×2), 7.340 (dd, $J_1 = 1.5$ Hz, $J_2 = 9.0$ Hz, 4H, Ar-H³×2, Ar-H⁵×2), 6.920 (d, $J = 19.0$ Hz, 2H, Ar-CH=CH-CH×2), 6.853 (dd, $J_1 = 15.0$ Hz, $J_2 = 19.0$ Hz, 2H, Ar-CH=CH-CH×2), 4.110 (d, $J = 2.5$ Hz, 4H, N-CH₂×2), 1.633 (s, 1H, -NH). ESI-MS m/z : 484.08 (M+H)⁺, calcd for C₂₃H₁₉Br₂NO: 482.98. HPLC purity: 100%.

(3E,5E)-3,5-bis(naphthalen-2-ylmethylene)piperidin-4-one (D4)

Yellow powder, 39.17% yield, mp 206.2-208.3 °C. ¹H NMR (500 MHz, DMSO-d₆) δ: 8.101 (s, 2H, H²×2), 7.959-8.101 (m, 4H, H³×2, H⁶×2), 7.941 (t, $J = 9.0$ Hz, 2H, H⁷×2), 7.769 (s, 2H, Ar-CH=C×2), 7.660 (d, $J = 8.5$ Hz, 2H, H⁸×2), 7.562-7.585 (m, 4H, H⁴×2, H⁵×2), 4.027 (s, 4H, N-CH₂×2), 1.740 (s, 1H, -NH). ESI-MS m/z : 375.92 (M+H)⁺, calcd for C₂₇H₂₁NO: 375.16. HPLC purity: 95.99%.

(3E,5E)-3,5-bis(4-(diphenylamino)benzylidene)piperidin-4-one (D5)

Orange yellow powder, 41.05% yield, mp 126.5-128.4 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.678 (d, $J = 8.5$ Hz, 4H, Ar-H²×2, Ar-H⁶×2), 7.356 (s, 2H, Ar-CH=C×2), 7.341 (t, $J = 8.0$ Hz, 8H, Ar'-H³×4, Ar'-H⁵×4), 7.175 (d, $J = 6.5$ Hz, 8H, Ar'-H²×4, Ar'-H⁶×4), 7.168 (d, $J = 7.5$ Hz, 2H, Ar'-H⁴×2), 6.964 (t, $J = 8.5$ Hz, 4H, Ar-H³×2, Ar-H⁵×2), 3.722 (d, $J = 7.0$ Hz, 4H, N-CH₂×2), 1.681 (s, 1H, -NH). ESI-MS m/z : 610.42 (M+H)⁺, calcd for C₄₃H₃₅N₃O: 609.28. HPLC purity: 100%.

(3E,5E)-3,5-bis(4-(2-(dimethylamino)ethoxy)benzylidene)piperidin-4-one (D6)

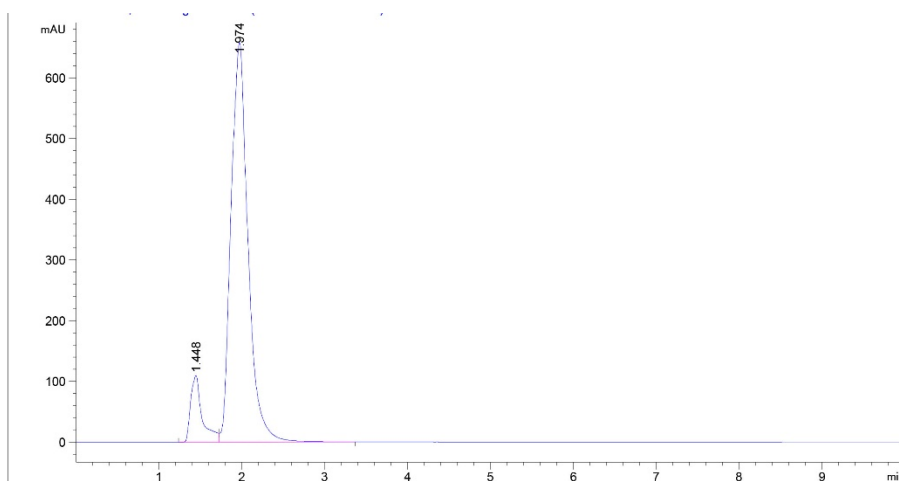
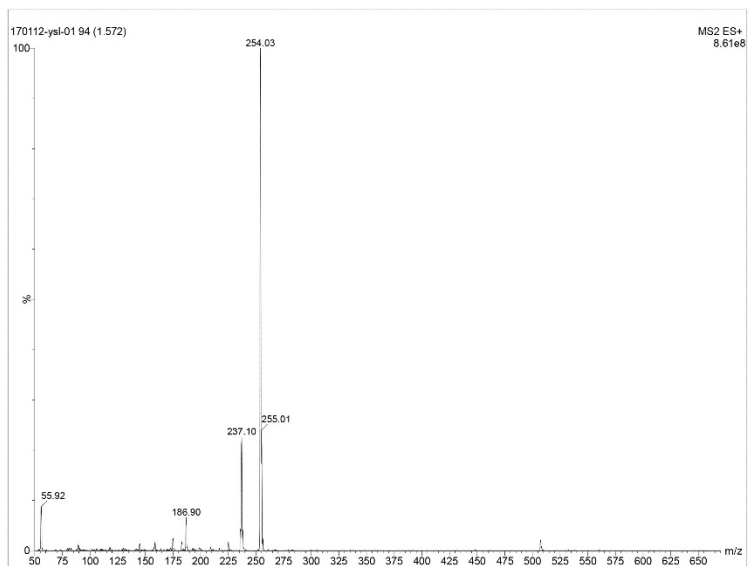
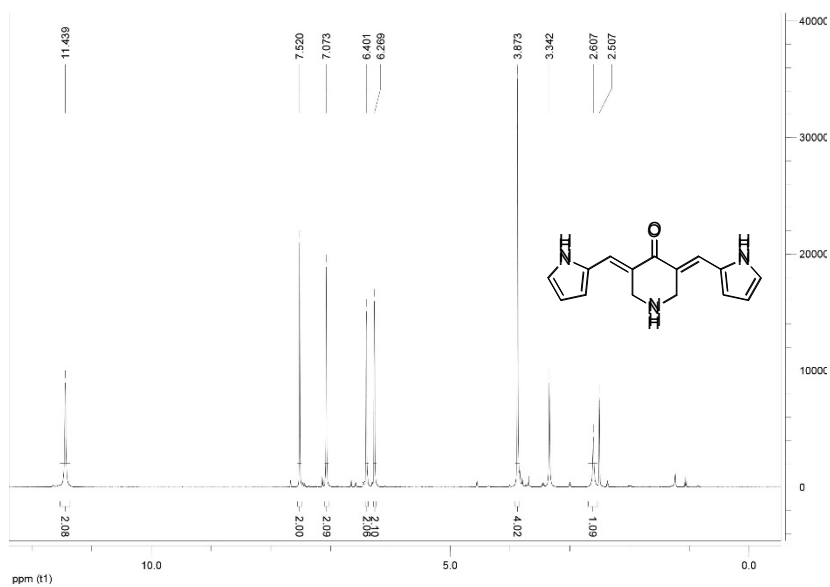
Orange yellow powder, 44.48% yield, mp 111.8-113.2 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.758 (s, 2H, Ar-CH=C×2), 7.346 (d, $J = 8.0$ Hz, 4H, Ar-H²×2, Ar-H⁶×2), 6.937 (d,

$J = 8.0$ Hz, 4H, Ar-H³×2, Ar-H⁵×2), 4.146 (s, 4H, N-CH₂×2), 4.059 (t, $J = 6.0$ Hz, 4H, -OCH₂CH₂N-×2), 2.463 (t, $J = 7.0$ Hz, 4H, -OCH₂CH₂N-×2), 2.623 (s, 12H, -NCH₃×4), 1.975 (t, $J = 6.5$ Hz, 1H, -NH). ESI-MS m/z : 450.41 (M+H)⁺, calcd for C₂₇H₃₅N₃O₃: 449.27. HPLC purity: 99.36%.

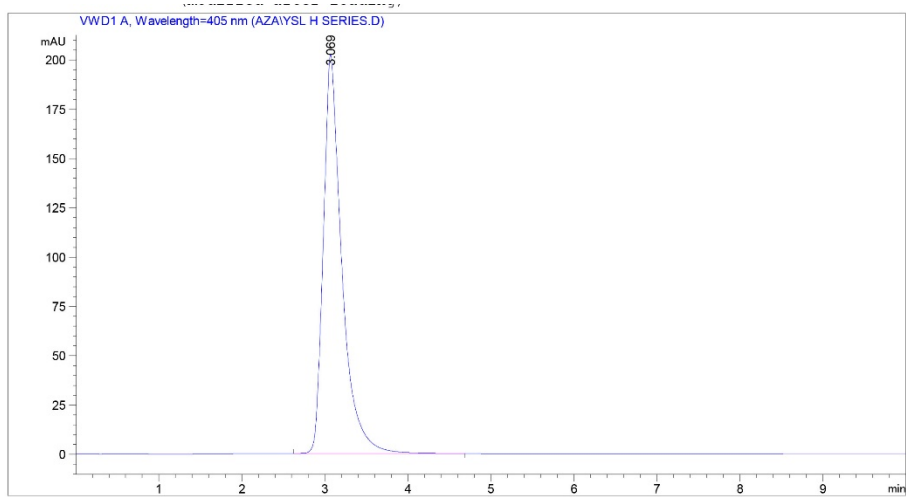
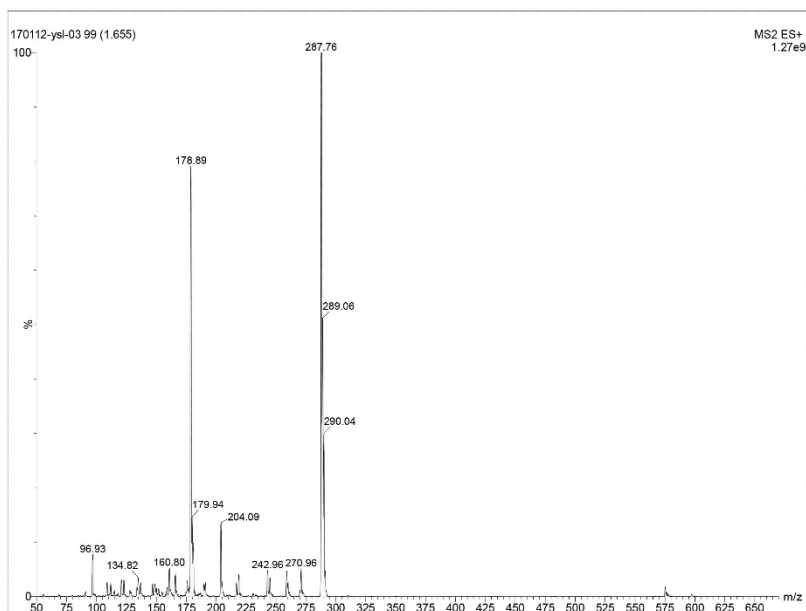
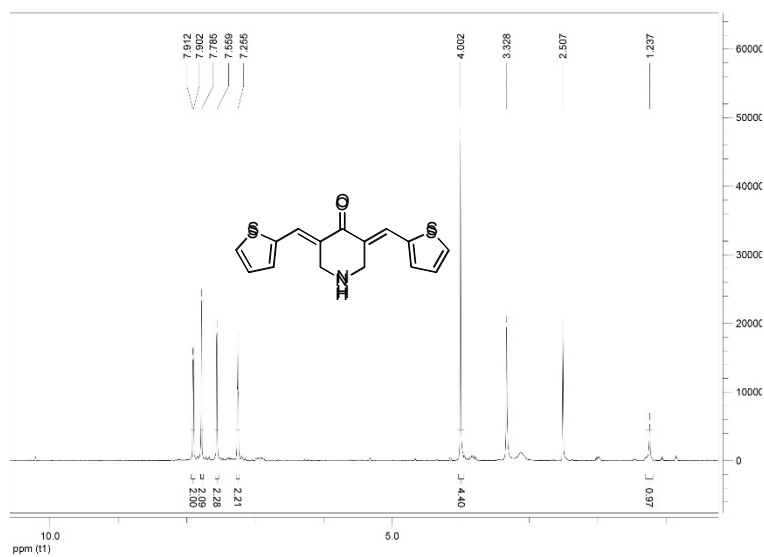
(3E,5E)-3,5-bis(4-(dibutylamino)benzylidene)piperidin-4-one (D7)

Purple powder, 37.80% yield, mp 148.8-151.5 °C. ¹H NMR (500 MHz, DMSO-d₆) δ : 7.463 (s, 2H, Ar-CH=C×2), 7.302 (d, $J = 11.0$ Hz, 4H, Ar-H²×2, Ar-H⁶×2), 6.689 (d, $J = 11.0$ Hz, 2H, Ar-H³×2, Ar-H⁵×2), 3.972 (s, 4H, NH-CH₂×2), 3.320 (t, $J = 9.5$ Hz, 8H, -NCH₂CH₂CH₂×4), 1.536 (s, 1H, -NH), 1.516 (t, $J = 8.0$ Hz, 8H, -NCH₂CH₂CH₂×4), 1.330 (q, $J = 9.5$ Hz, 8H, -NCH₂CH₂CH₂×4), 0.924 (t, $J = 8.5$ Hz, 12H, -CH₃×4). ESI-MS m/z : 530.56 (M+H)⁺, calcd for C₃₅H₅₁N₃O: 529.40. HPLC purity: 100%.

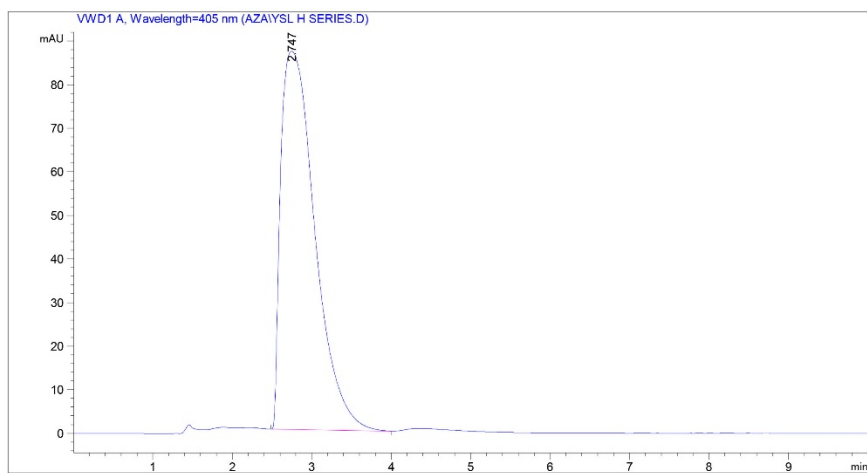
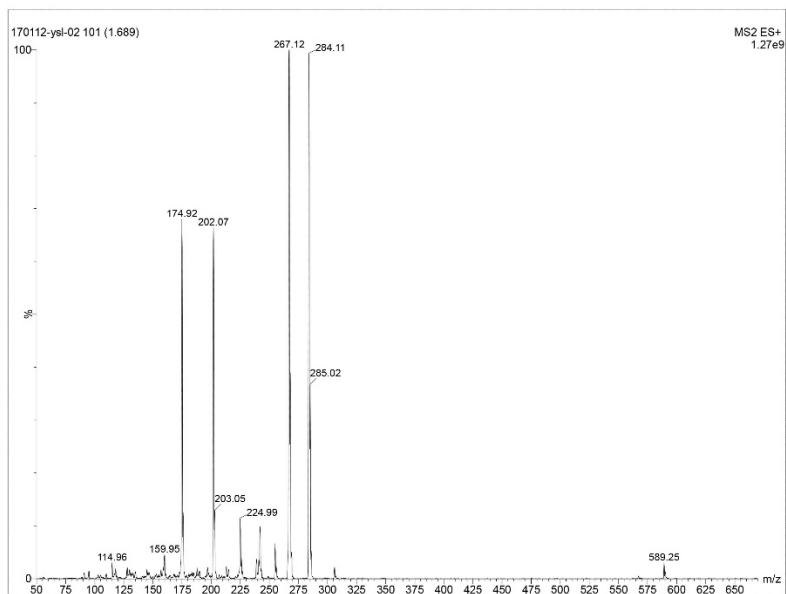
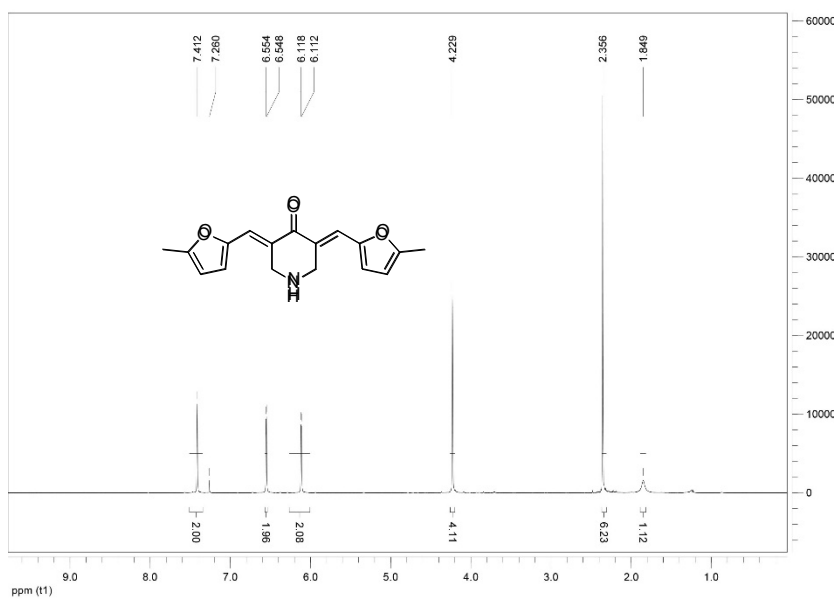
The original spectrums (NMR, MS, HPLC) of A1



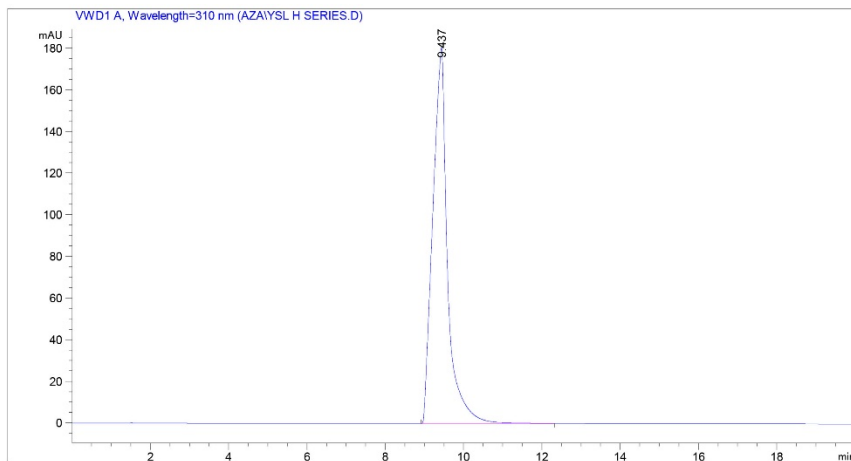
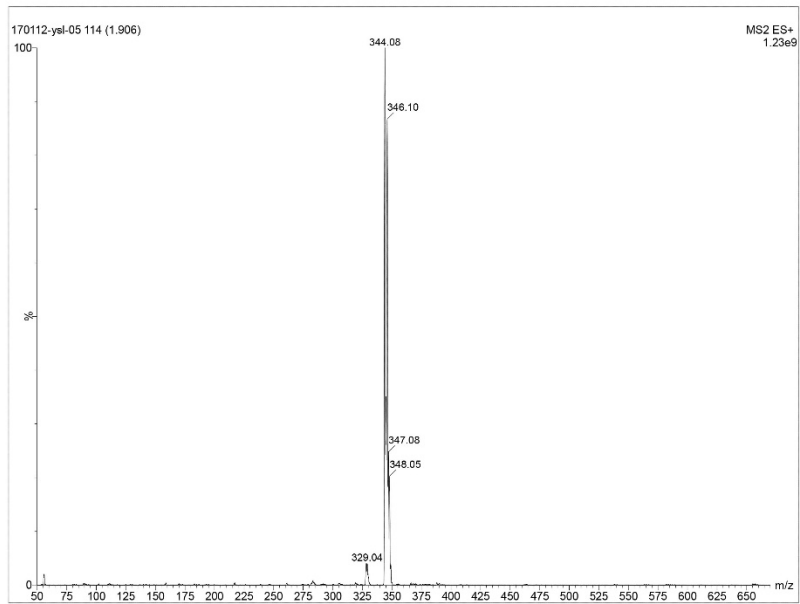
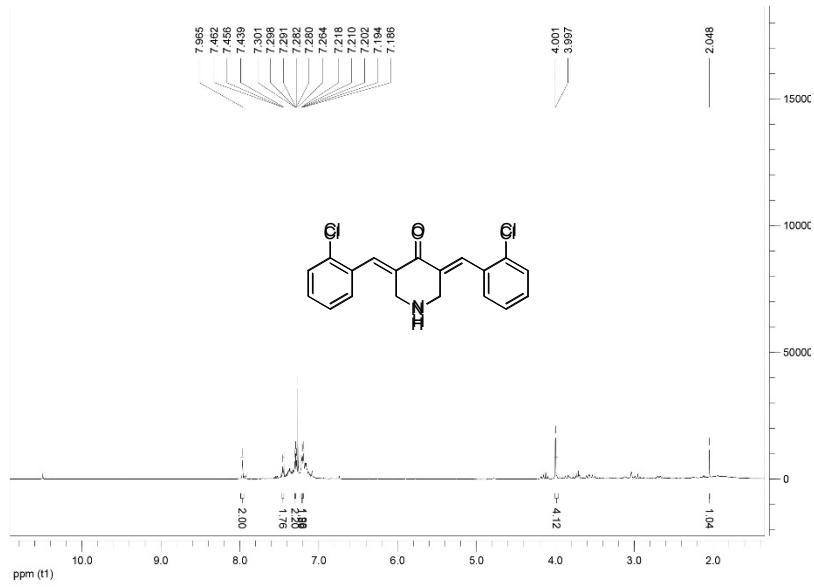
The original spectrums (NMR, MS, HPLC) of A3



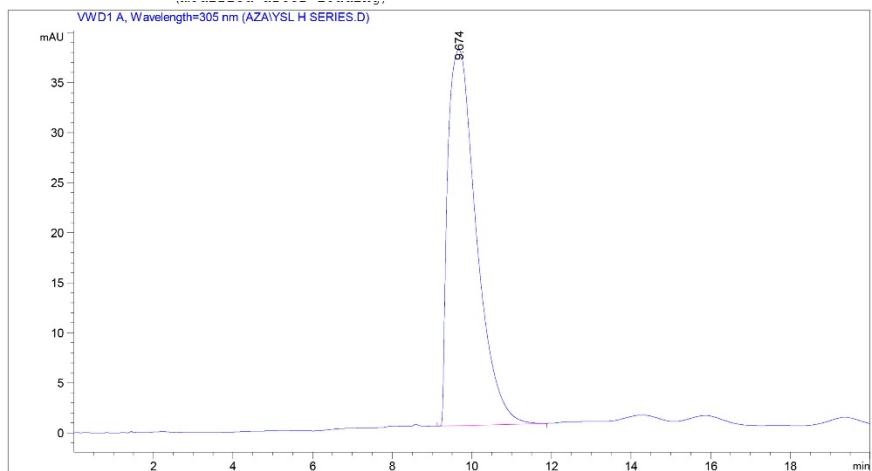
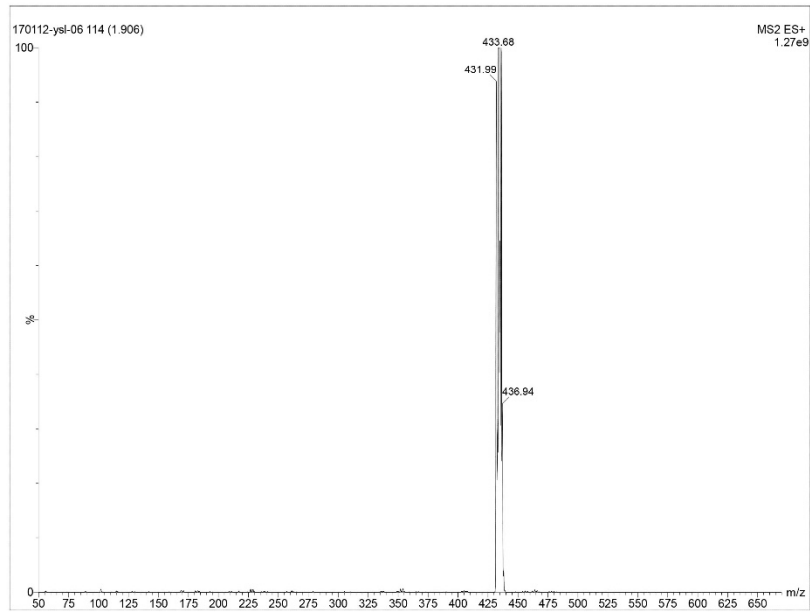
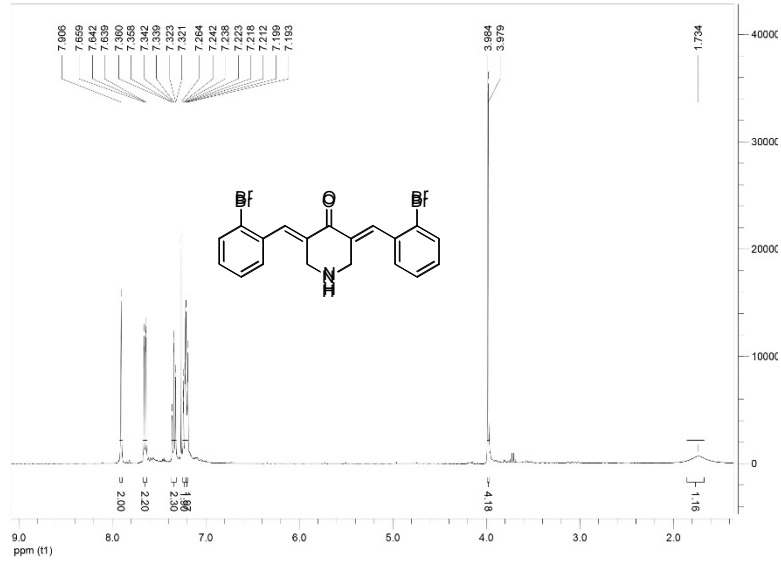
The original spectrums (NMR, MS, HPLC) of A5



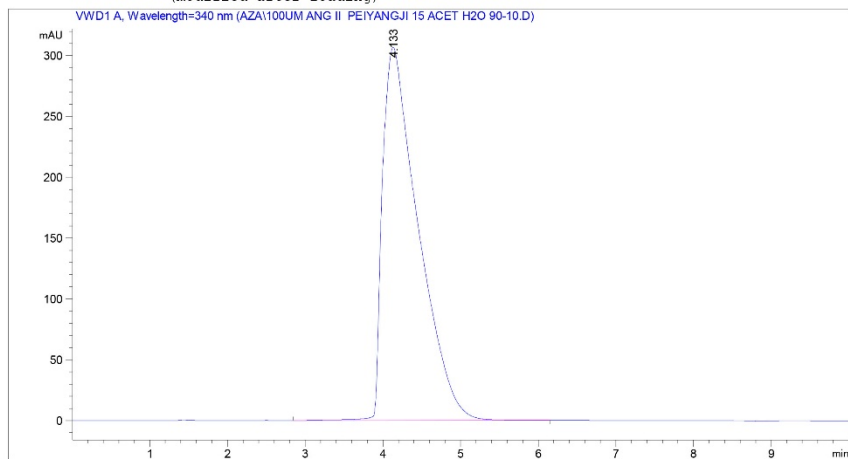
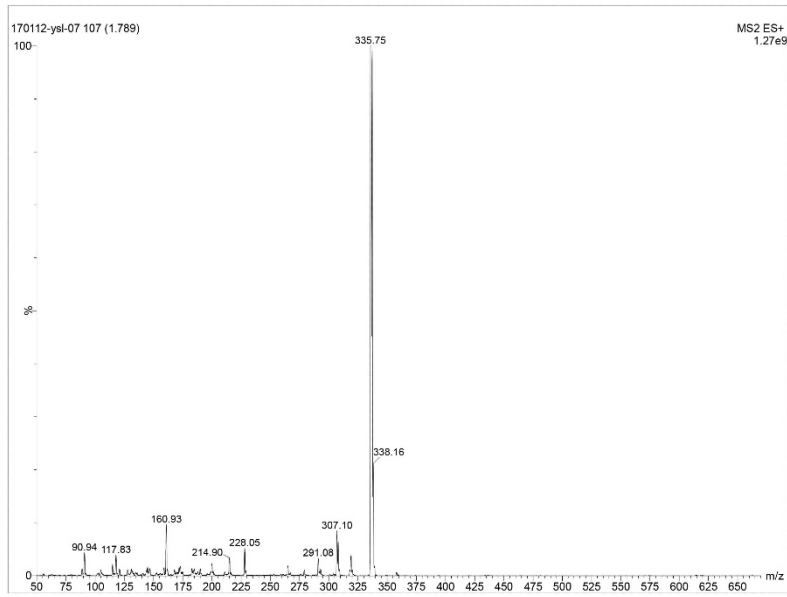
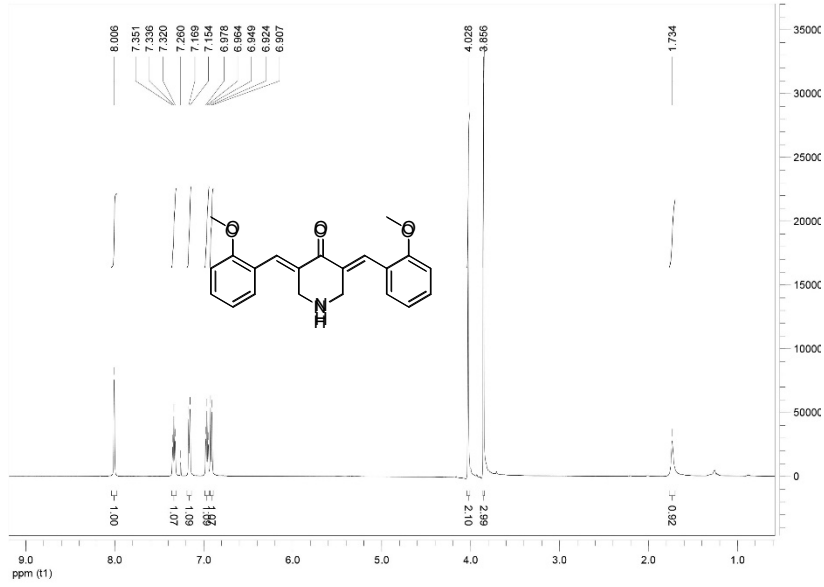
The original spectrums (NMR, MS, HPLC) of **B3**



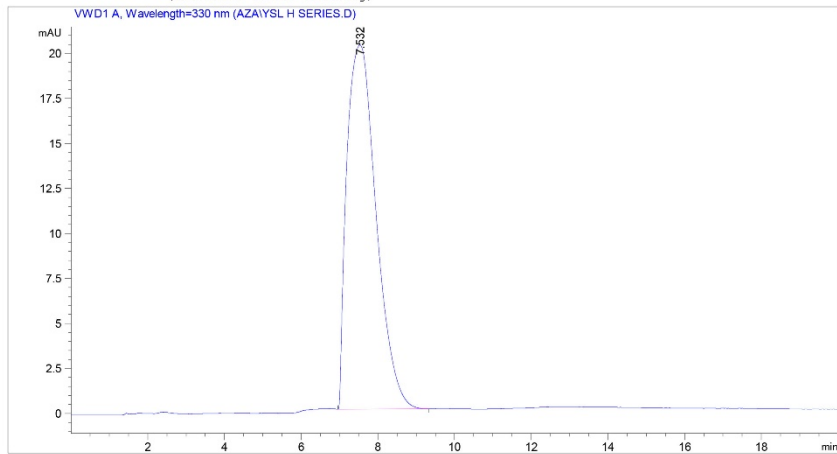
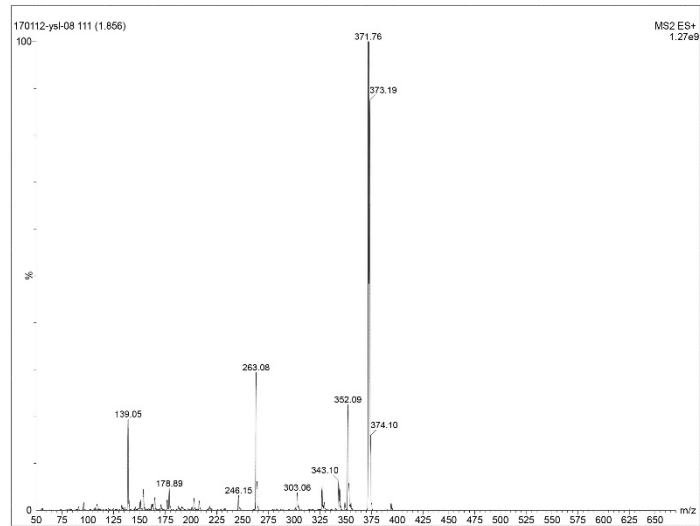
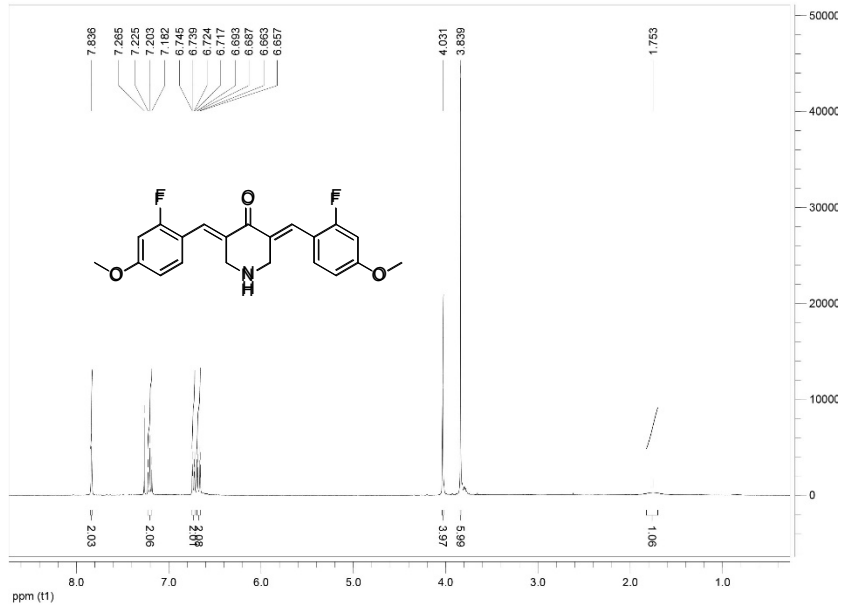
The original spectrums (NMR, MS, HPLC) of **B4**



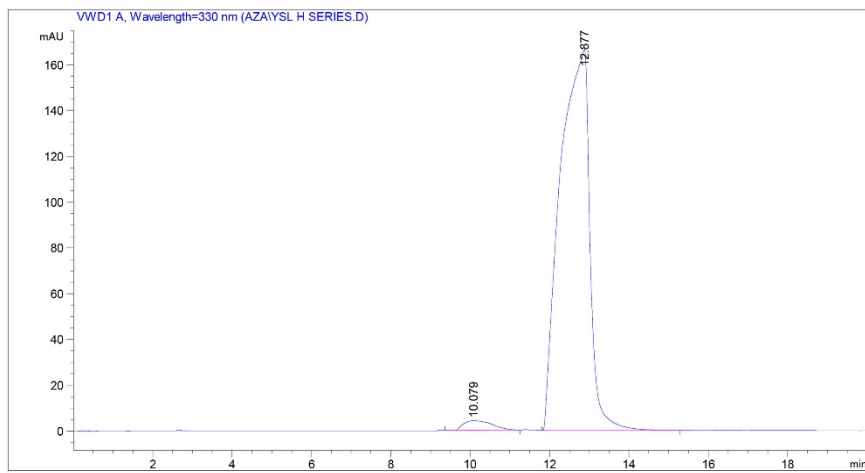
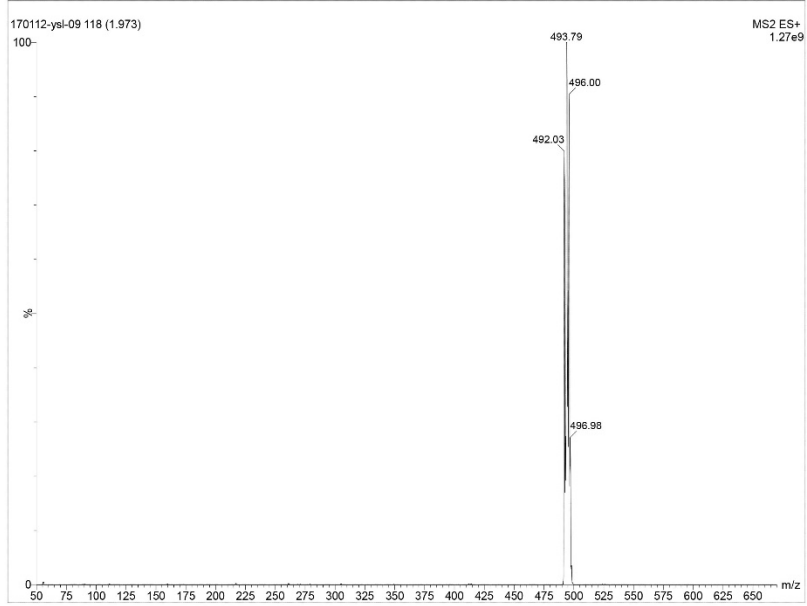
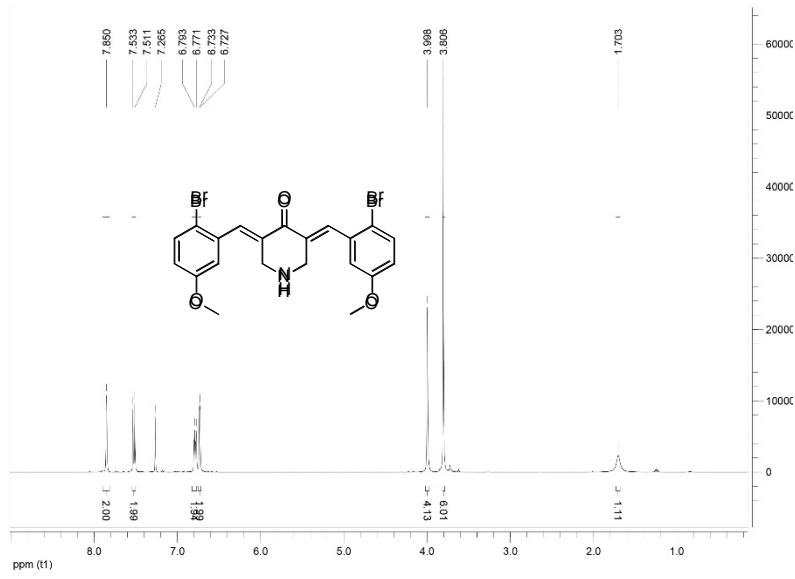
The original spectrums (NMR, MS, HPLC) of **B5**



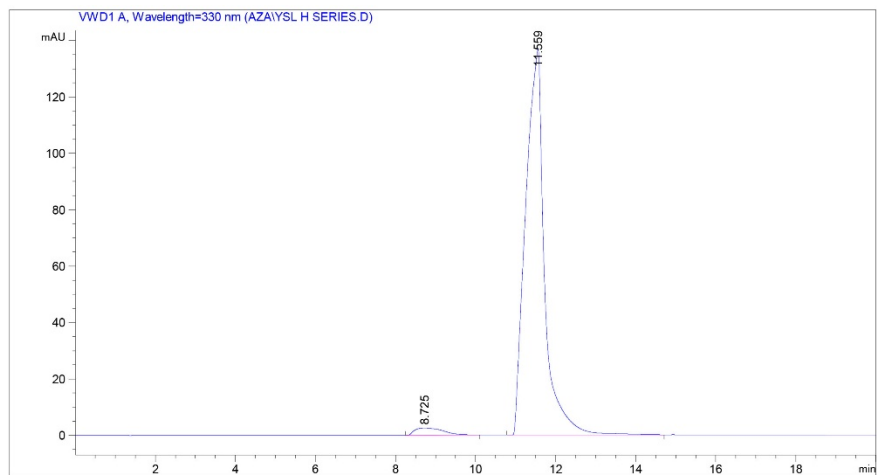
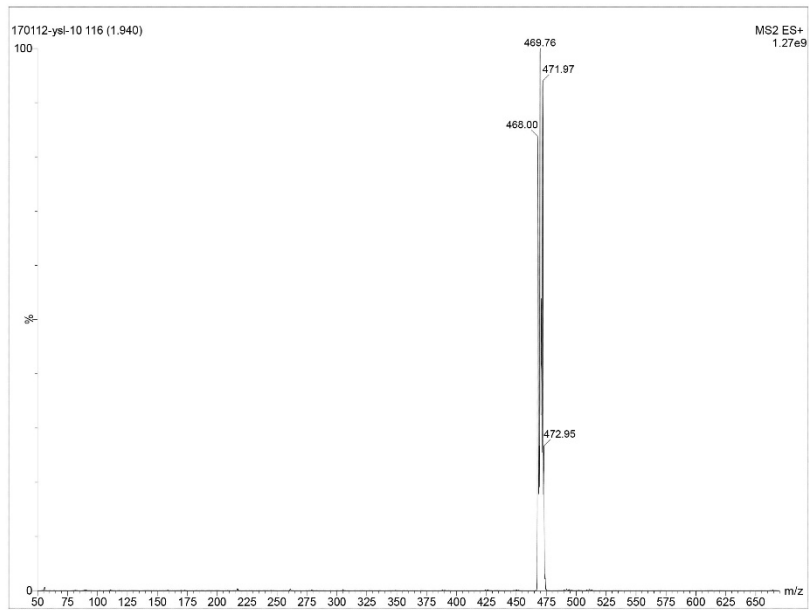
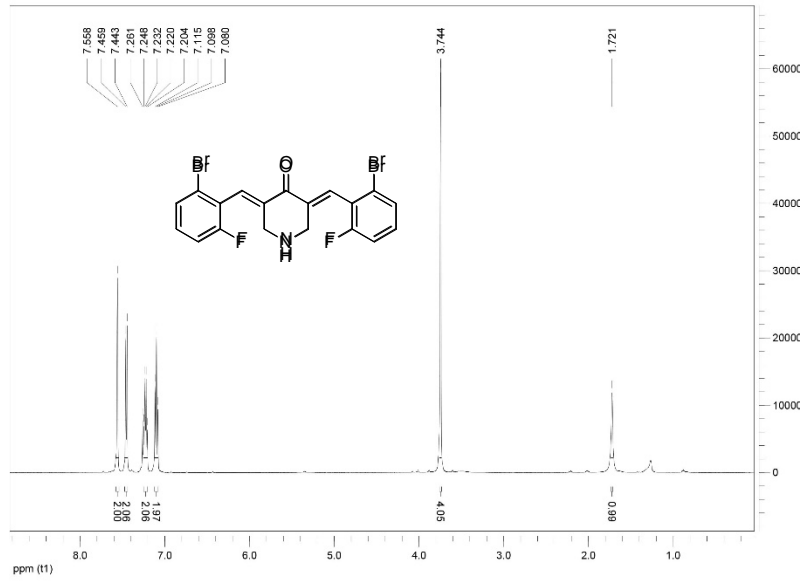
The original spectrums (NMR, MS, HPLC) of **C2**



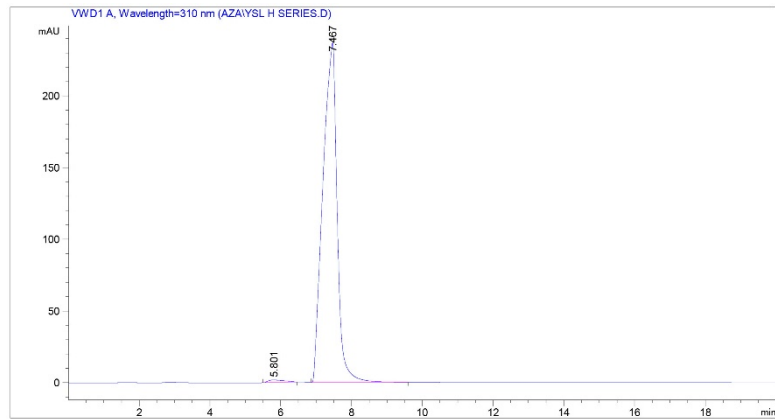
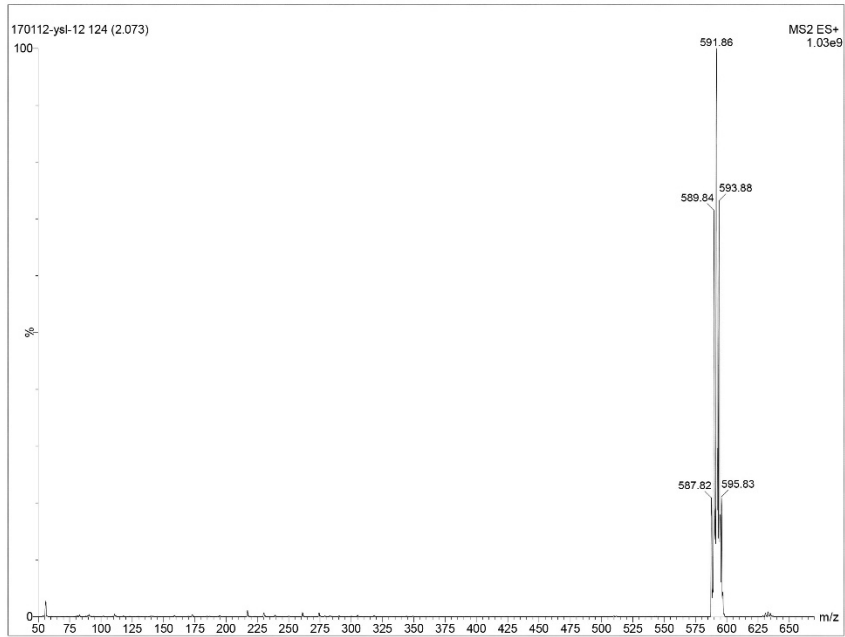
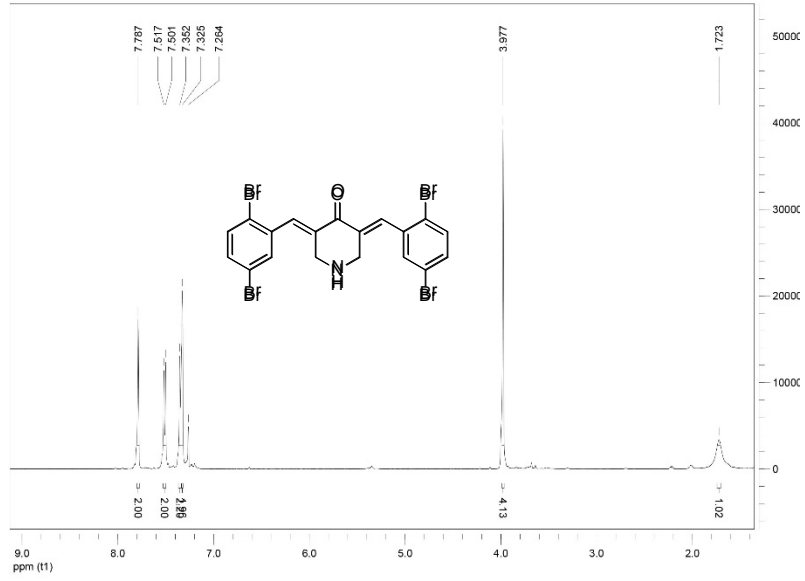
The original spectrums (NMR, MS, HPLC) of C4



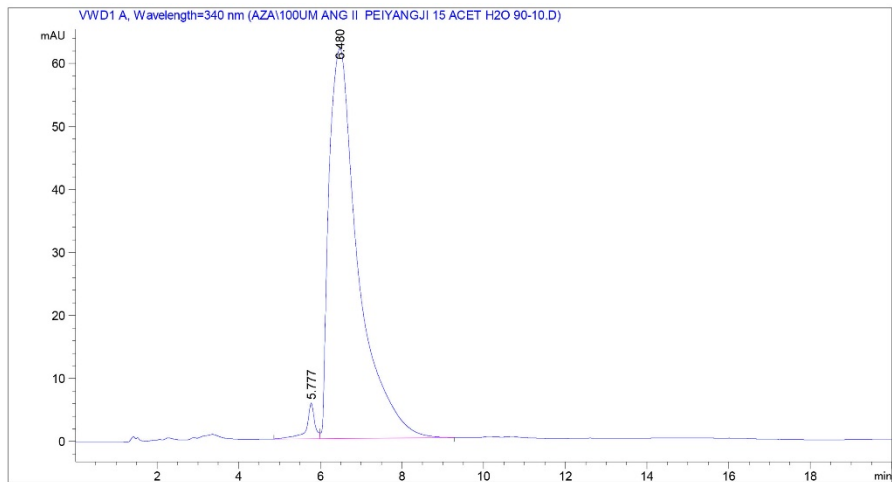
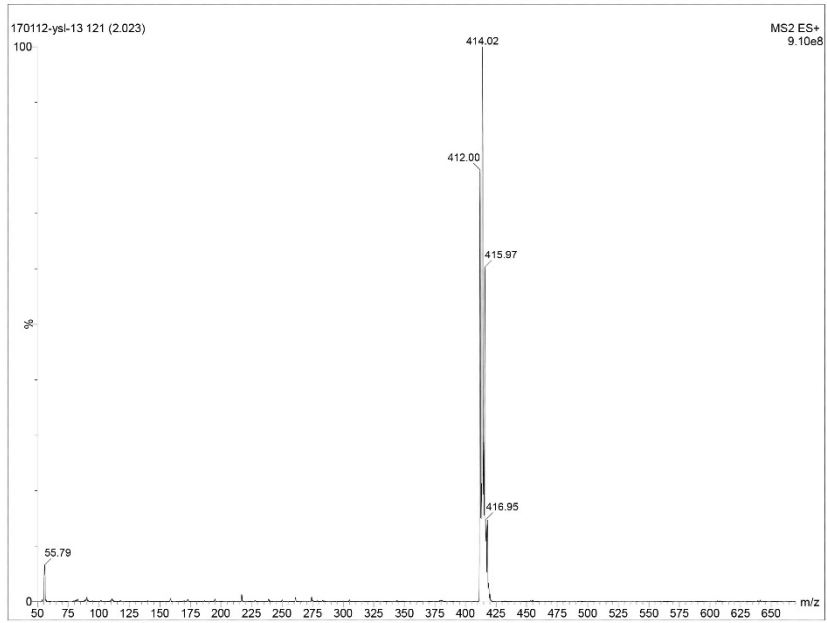
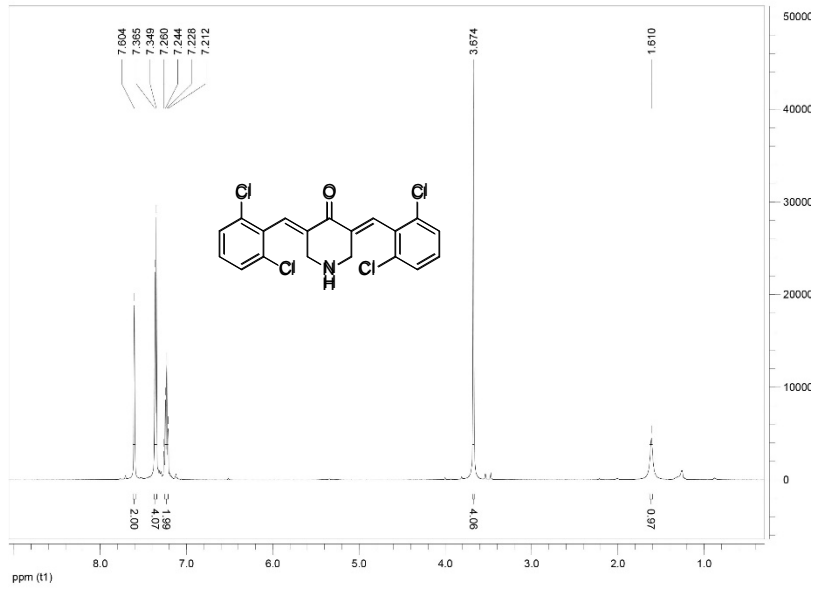
The original spectrums (NMR, MS, HPLC) of **C5**



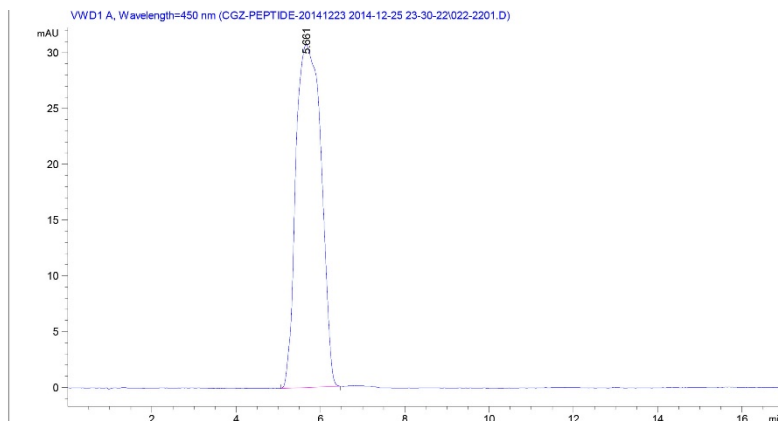
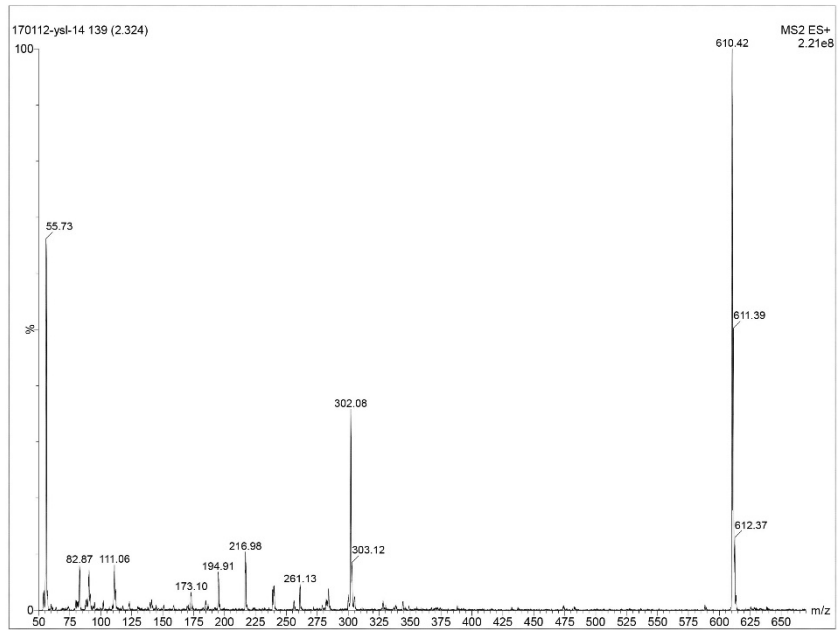
The original spectrums (NMR, MS, HPLC) of C8



The original spectrums (NMR, MS, HPLC) of **C9**



The original spectrums (NMR, MS, HPLC) of **D5**



Part 2: Other than **D6**, the binding affinity between others active compounds, **B1**, **B2**, **B4** (IC_{50} less than $10 \mu\text{M}$ in kinase assay), and $IKK\beta$ was measured by SPR. The results was as shown below.

