Supplementary information

Curcumin derivatives with 1,5-diaryl-3-oxo-1,4-pentadiene: a novel dual-function lead showing anticancer and MDR reversal effects

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Synthesis of intermediates A, B, C, D, E

The synthetic method of intermediates A-E was reported in our previous study[16]. The compounds were recrystallized from chloroform-ethanol (A); ethanol (B); methanol (C); and methanol-chloroform (D) and (E). The melting points (°C) and yields (%) of A-E were as follows: A: 245-247, 78%; B: 217-220, 70%; C: 207-210, 84%; D: 223-224, 79%; E: 221-227, 66%.

3,5-Bis(2-bromo-4,5-dimethoxybenzylidene)-4-piperidone (A)： Lemon yellow powder; UV λmax (log ε) 211 (4.74), 256 (4.12), 366 (4.09) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.77 (s, 2H, NH.HCl), 7.90 (s, 2H), 7.36 (s, 2H), 7.00 (s, 2H), 4.46 (d, *J* = 1.1 Hz, 4H), 3.85 (s, 6H), 3.82 (s, 6H). IR υ_{max}/cm^{-1}: 2928 (N-H), 1661 (C=O), 1689 (C=C), 1267 (C-O), 1066 (C-N), 589 (C-Br).

3,5-Bis(2-fluorobenzylidene)-4-piperidone (B): Pale yellow crystal; UV λmax (log ε) 206 (4.43), 275 (4.32) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.08 (s, 2H, NH.HCl), 7.90 (s, 2H), 7.60 - 7.49 (m, 4H), 7.41 - 7.35 (m, 4H), 4.37 (s, 4H). IR υ_{max}/cm^{-1}: 2926 (N-H), 1667 (C=O), 1608 (C=C), 1205 (C-F), 1098 (C-N).

3,5-Bis(4-fluorobenzylidene)-4-piperidone (C): Pale yellow crystal; UV λmax (log ε) 204 (4.75), 230 (4.28), 326 (4.35) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.19 (s, 2H), 7.86 (s, 2H), 7.64 - 7.59 (m, 4H), 7.41 - 7.34 (m, 4H), 4.45 (d, *J* = 1.4 Hz, 4H). IR υ_{max}/cm^{-1}: 2874 (N-H), 1657 (C=O), 1598 (C=C), 1154 (C-F), 1070 (C-N).

3,5-Bis(3-bromobenzylidene)-4-piperidone (D): Pale yellow crystal; UV λ_{max} (log *ε*) 207 (4.83), 236 (3.98), 316 (3.99) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.85 (s, 2H), 7.84 (s, 2H), 7.78 - 7.77 (m, 2H), 7.71 - 7.68 (m, 2H), 7.54 - 7.47 (m, 4H), 4.47 (d, *J* = 1.7 Hz, 4H). IR υ_{max}/cm^{-1}: 2911 (N-H), 1679 (C=O), 1610 (C=C), 1073 (C-N), 532 (C-Br).

3,5-Bis(4-trifluoromethylbenzylidene)-4-piperidone (E): Light yellow crystals; UV λ_{max} (log ε) 205 (4.43), 226 (4.24), 314 (4.46) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.84 (d, *J* = 8.3 Hz, 4H), 7.78 - 7.69 (m, 6H), 4.20 (d, *J* = 1.7 Hz, 4H). IR υ_{max}/cm^{-1}: 2838 (N-H), 1656 (C=O), 1502 (C=C), 1067 (C-F), 1013 (C-N).

General synthetic methods of of 1a-1e, 2a-2e, 3a-3e, 4a-4e, 5a-5e

A, B, C, D, E (1 mmol) with potassium carbonate (5 mmol) respectively was put into acetonitrile (10 mL), and heated at 65-80 ℃ until the solid was dissolved. Then 4-nitrobenzyl bromide, 4-cyanobenzyl bromide, 4-trifluoromethylbenzyl bromide, 3-fluorobenzyl bromide or 3,5-ditrifluoromethylbenzyl bromide (1 mmol) solved in a little amount of acetonitrile alternatively was added to the mixture, followed by stirring for about 30 min-1 h at 80 ℃, inspected by TLC (petroleum ether/acetone: 4:1). After the reaction, acetonitrile was removed under vaccum. To the residue was added 2 mL acetone and 4 mL 1 mol/L HCl to produce the precipitate. Then the solid was collected. At last, the target compounds ware recrystalized from methanol-chloroform or acetone (**1a-1e and 2a-2e**), or methanol (**3a-3e and 4a-4e**), or ethanol or chloroform (**5a-5e**). The melting points (°C) and yields (%) of **1a-1e, 2a-2e, 3a-3e, 4a-4e, 5a-5e** were as follows: **1a**: 209-212, 49%; **1b**: 199-202, 67%; **1c**: 170-173, 78%; **1d**: 187-190, 52%; **1e**: 194-198, 48%; **2a**: 170-173, 65%; **2b**: 167-171, 66%; **2c**: 122-125, 54%; **2d**: 179-182, 50%; **2e**: 167-170, 67%; **3a**: 188-191, 47%; **3b**: 174-176, 47%; **3c**: 177-179, 42%; **3d**: 167-168, 55%, **3e**: 149-152, 66%; **4a**: 181-184, 54%; **4b**: 179-183, 82%; **4c**: 180-182, 45%; **4d**: 189-192, 71%; **4e**: 161-164, 35%; **5a**: 171-173, 25%; **5b**: 167-169, 42%; **5c**: 198-200, 38%; **5d**: 193-195, 44%; **5e**: 142-145, 35%.

*(3E,5E)-3,5-bis(2-bromo-4,5-dimethoxybenzylidene)-1-(4-nitrophenyl)piperidin-4-ne (**1a**):* Yellow powder; UV λ_{max} (log ε) 212 (4.70), 262 (4.41), 368 (4.21) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.16 (d, *J* = 8.7 Hz, 2H), 7.89 (s, 2H), 7.77 (d, *J* = 6.3 Hz, 2H), 7.33 (s, 2H), 6.87 (s, 2H), 4.37 (s, 6H), 3.84 (s, 6H), 3.78 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 190.2 (C=O), 150.8 (2C), 147.9 (4C), 138.1, 132.0, 130.0 (2C), 125.1 (2C), 123.8 (2C), 123.5 (2C), 116.7 (2C), 116.0 (2C), 115.9 (2C), 113.4 (2C), 56.5, 56.1 (2C), 56.0 (2C), 50.9 (2C). IR υ_{max}/cm^{-1}: 1668.4 (C=O), 1586.0 (C=C), 1501.2 (N-O), 1347.7 (N-O), 1247.1 (C-O), 1047.6 (C-N), 583.5 (C-Br). HRMS calculated for $C_{30}H_{28}Br_2N_2O_7$ [M+H]: 687.0342/ [M+H+2, ^{79}Br]: 689.0330/[M+H+4, ^{81}Br]: 691.0311; found: 688.0243/686.0263/690.0222.

*4-((3E,5E)-3,5-bis(2-bromo-4,5-dimethoxybenzylidene)-4-oxopiperidin-1-yl)benzonitrile (**1b**):* Pale yellow powder; UV λmax (log ε) 212 (4.68), 256 (4.18); 369 (4.07); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.87 (s, 2H), 7.79 – 7.73 (m, 4H), 7.31 (s, 2H), 6.84 (s, 2H), 4.47 (d, *J* = 23.2 Hz, 6H), 3.82 (s, 6H), 3.76 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 190.2 (C=O), 150.9 (2C), 147.9 (4C), 138.9, 132.4 (2C), 132.1 (2C), 129.7 (2C), 124.9 (2C), 118.3, 116.8 (2C), 116.1 (2C), 113.4 (2C), 112.1, 56.7, 56.2 (2C), 56.1 (2C), 50.4 (2C). IR υ_{max}/cm^{-1}: 2231.1 (CN), 1669.6 (C=O), 1586.4 (C=C), 1247.0

(C-O), 1048.1 (C-N), 563.5 (C-Br). HRMS calculated for $C_{31}H_{28}Br_2N_2O_5$ [M+H]: 667.0354/[M+H+2, ^{79}Br]: 669.0347/[M+H+4, ^{81}Br]: 671.0325; found: 668.0345/666.0365/70.0324.

(3E,5E)-3,5-bis(2-bromo-4,5-dimethoxybenzylidene)-1-(4-(trifluoromethyl)phenyl)piperidin-4-one ***(1c)****:* Dark yellow powder; UV λ_{max} (log ε) 211 (4.62), 261 (3.89), 369 (4.21) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.93 (s, 2H), 7.79 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 8.2 Hz, 2H), 7.34 (s, 2H), 6.88 (s, 2H), 4.51 (d, *J* = 27.3 Hz, 6H), 3.84 (s, 6H), 3.78 (s, 6H).^{13}C NMR (101 MHz, DMSO-d_6) δ 190.2 (C=O), 150.9 (2C), 147.9 (4C), 139.0, 132.1 (2C), 129.4 (q, *J* = 31.4 Hz, aryl C), 128.0 (2C), 125.4 (q, *J* = 3.8 Hz, aryl C, 2C), 123.9 (q, *J* = 271.0 Hz, CF_3), 116.7 (2C), 116.1 (2C), 115.9 (2C), 113.4 (2C), 56.5, 56.1 (2C), 56.0 (2C), 50.3 (2C). IR υ_{max}/cm^{-1}: 1671.0 (C=O), 1587.0 (C=C), 1246.5 (C-O), 1163.5 (C-F), 1066.4 (C-N), 581.2 (C-Br). HRMS calculated for $C_{31}H_{28}Br_2F_3NO_5$ [M+H]: 710.0319/ [M+H+2, ^{79}Br]: 712.0318/[M+H+4, ^{81}Br]: 714.0290; found: 711.0266/709.0286/713.0245.

(3E,5E)-3,5-bis(2-bromo-4,5-dimethoxybenzylidene)-1-(3-fluorophenyl)piperidin-4-one ***(1d)****:* Dark yellow powder; UV λmax (log ε) 257 (4.18), 369 (4.18) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.90 (s, 2H), 7.43 – 7.36 (m, 3H), 7.34 (s, 2H), 7.23 – 7.19 (m, 1H), 6.89 (s, 2H), 4.44 (s, 6H), 3.84 (s, 6H), 3.81 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 190.8 (C=O), 161.9 (d, *J*=243.3), 154.5 (2C), 150.8 (2C), 148.6, 147.9 (4C), 130.6 (d, *J* = 26.8 Hz), 127.9, 125.2 (d, *J* = 75.3 Hz), 119.3, 116.7, 116.1 (2C), 116.0, 113.3 (2C), 110.5 (2C), 56.5, 56.2 (2C), 55.9 (2C), 50.7 (2C). IR υ_{max}/cm^{-1}: 1671.7 (C=O), 1588.2 (C=C), 1246.6 (C-O), 1164.9 (C-F), 1046.9 (C-N), 583.7 (C-Br). HRMS calculated for $C_{30}H_{28}Br_2FNO_5$ [M+H]: 660.0406/[M+H+2, ^{79}Br]: 662.0409/[M+H+4, ^{81}Br]: 664.0378; found: 661.0298/659.0318/663.0277.

(3E,5E)-1-(3,5-bis(trifluoromethyl)phenyl)-3,5-bis(2-bromo-4,5-dimethoxybenzylidene)piperidin-4-one ***(1e)****:* Dark yellow powder; UV λ_{max} (log ε) 261 (3.93), 378 (3.74) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.93 (s, 3H), 7.72 (s, 2H), 7.28 (s, 2H), 6.85 (s, 2H), 3.91 (s, 2H), 3.82 (s, 10H), 3.74 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 186.2 (C=O), 150.2 (2C), 147.8 (2C), 140.9, 134.8 (2C), 133.2 (2C), 130.0 (q, *J* = 32.6, 2C), 129.7 (unresolved septet, *J* = 2.9 Hz), 125.9 (2C), 123.3 (q, *J* = 271.5, 2C), 121.0 (2C), 116.1 (2C), 115.8 (2C), 113.4 (2C), 58.0, 56.0 (2C), 55.6 (2C), 52.6 (2C). IR υ_{max}/cm^{-1}: 1670.4 (C=O), 1592.0 (C=C), 1266.9 (C-O), 1158.6 (C-F), 1084.9 (C-N), 581.2 (C-Br). HRMS calculated for $C_{32}H_{27}Br_2F_6NO_5$ [M+H]: 778.0236/ [M+H+2, ^{79}Br]: 780.0224/ [M+H+4, ^{81}Br]: 782.0206; found: 779.0140/777.0160/ 781.0119.

(3E,5E)-3,5-bis(2-fluorobenzylidene)-1-(4-nitrophenyl)piperidin-4-one ***(2a)****:* Yellow crystal; UV λ_{max} (log ε) 206 (4.79), 273 (4.29) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.07 – 8.04 (m, 2H), 7.72 (s, 2H), 7.51 – 7.37 (m, 6H), 7.31 – 7.22 (m, 4H), 3.81 (d, *J* = 12.8 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 186.1 (C=O), 160.3 (d, *J*=247.8, 2C), 146.6, 146.0, 135.0 (d, *J*=0.8 Hz, 2C),131.6 (d, *J* = 8.7 Hz, 2C), 130.8 (d, *J*=2.2 Hz, 2C), 129.6 (2C), 127.8 (d, *J*=4.4 Hz, 2C), 124.6 (d, *J* = 3.6 Hz, 2C), 123.3 (2C), 122.1 (d, *J* = 12.9 Hz, 2C), 115.7 (d, *J*=21.7 Hz, 2C), 58.8, 53.5 (2C). IR υ_{max}/cm^{-1}: 1674.0 (C=O), 1618.8 (C=C), 1509.3 (N-O), 1340.2 (N-O), 1206.3 (C-F), 1097.1 (C-N). HRMS calculated for $C_{26}H_{20}F_2N_2O_3$ [M+H]: 447.1591; found: 446.1442.

4-((3E,5E)-3,5-bis(2-fluorobenzylidene)-4-oxopiperidin-1-yl)benzonitrile ***(2b)****:* Pale yellow crystal; UV λ_{max} (log ε) 229 (4.83), 275 (4.02), 306 (4.05) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72 (s, 2H), 7.67 – 7.64 (m, 2H), 7.49-7.44 (m, 2H), 7.41-7.36 (m, 4H), 7.32 – 7.23 (m, 4H), 3.77 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 186.1 (C=O), 160.3 (d, *J*=247.8, 2C), 143.7 (2C), 135.1, 132.0 (2C), 131.6 (d, *J* = 8.7 Hz, 2C), 130.7 (d, *J*=2.2 Hz, 2C), 129.4 (2C), 127.8 (d, *J*=4.4 Hz, 2C), 124.6 (d, *J* = 3.5 Hz, 2C), 122.1 (d, *J* = 12.9 Hz, 2C), 118.7, 115.8 (d, *J*=21.6 Hz, 2C), 109.8, 59.1, 53.4 (2C). IR υ_{max}/cm^{-1}: 2227.4 (CN), 1675.6 (C=O), 1621.8 (C=C), 1205.6 (C-F), 1097.4 (C-N). HRMS calculated for $C_{27}H_{20}F_2N_2O$ [M+H]: 427.1697; found: 426.1544.

(3E,5E)-3,5-bis(2-fluorobenzylidene)-1-(4-(trifluoromethyl)phenyl)piperidin-4-one ***(2c)****:* Yellow crystal; UV λ_{max} (log ε) 210 (4.58), 273 (4.32) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72 (s, 2H), 7.53 (d, *J* = 8.1 Hz, 2H), 7.47 – 7.35 (m, 6H), 7.30 – 7.20 (m, 4H), 3.77 (d, *J* = 3.9 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 186.1 (C=O), 160.3 (d, *J*=247.9, 2C), 142.6 (2C), 135.1,131.6 (d, *J* = 8.9 Hz, 2C), 130.7 (d, *J*=2.5 Hz, 2C), 129.3 (2C), 127.8 (d, *J*=4.8 Hz, 2C), 127.7 (q, *J* = 31.8 Hz, aryl C), 124.9 (q, *J* = 4.1 Hz, 2C), 124.5 (d, *J* = 3.7 Hz, 2C), 124.2 (q, *J* = 270.7 Hz, CF_3), 122.1 (d, *J* = 13.0 Hz, 2C), 115.7 (d, *J*=21.7 Hz, 2C), 59.0, 53.4 (2C). IR υ_{max}/cm^{-1}: 1671.8 (C=O), 1619.1 (C=C), 1235.2 (C-F), 1097.6 (C-N). HRMS calculated for $C_{27}H_{20}F_5NO$ [M+H]: 470.1642; found: 469.1465.

(3E,5E)-3,5-bis(2-fluorobenzylidene)-1-(3-fluorophenyl)piperidin-4-one ***(2d)****:* Pale yellow crystal; UV λ_{max} (log ε) 207 (4.81), 269 (4.19), 298 (4.15) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.95 (s, 2H), 7.57 – 7.51 (m, 2H), 7.42 – 7.25 (m, 9H), 7.13 – 7.08 (m, 1H), 4.43 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 182.1 (C=O), 162.2 (d, *J*=243.4), 160.7 (d, *J*=248.5, 2C), 133.5 (2C), 133.1 (d, *J* = 8.8 Hz, 2C), 132.8 (2C), 131.4 (d, *J*=2.0 Hz, 2C), 131.0 (d, *J* = 8.3 Hz), 129.2, 127.6, 125.3 (d, *J*=3.4 Hz, 2C), 121.8 (d, *J* = 13.2, 2C), 118.3 (d, *J* = 23.2 Hz), 116.7 (d, *J*=21.4 Hz), 116.5 (d, *J*=21.4 Hz, 2C), 56.3, 50.7 (2C). IR υ_{max}/cm^{-1}: 1669.7 (C=O), 1608.7 (C=C), 1253.9 (C-F), 1098.4 (C-N). HRMS calculated for $C_{26}H_{20}F_3NO$ [M+H]: 420.1666; found: 419.1497.

(3E,5E)-1-(3,5-bis(trifluoromethyl)phenyl)-3,5-bis(2-fluorobenzylidene) piperidin-4-one ***(2e)****:* Yellow crystal; UV λ_{max} (log ε) 207 (4.83), 274 (4.30) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.28 (s, 2H), 8.06 (s, 1H), 7.92 (s, 2H), 7.57 – 7.52 (m, 4H), 7.45-7.41 (m, 4H), 7.36 – 7.26 (m, 4H), 4.47 (d, *J* = 59.0 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 181.9 (C=O), 160.3 (d, *J*=248.7, 2C), 143.5 (2C), 136.1, 132.5 (d, *J* = 8.1 Hz, 2C), 132.0 (2C), 130.1 (2C), 130.9 (d, *J*=1.8 Hz, 2C), 130.3 (q, *J* = 32.9, 2C), 124.7 (d, *J*=3.4 Hz, 2C), 123.0 (q, *J* = 271.8, 2C), 122.5, 121.3 (d, *J* = 13.2 Hz, 2C), 116.0 (d, *J*=21.4 Hz, 2C), 56.0, 51.1 (2C). IR υ_{max}/cm^{-1}: 1679.4 (C=O), 1608.7 (C=C), 1279.1 (C-F), 1099.9 (C-N). HRMS calculated for $C_{30}H_{19}F_{12}NO$ [M+H]: 538.1510; found: 537.1339.

*(3E,5E)-3,5-bis(4-fluorobenzylidene)-1-(4-nitrobenzyl)piperidin-4-one (**3a**):* Yellow powder; UV λ_{max} (log ε) 204 (4.63), 224 (4.43), 324 (4.32) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.16 – 8.08 (m, 2H), 7.89 (s, 2H), 7.83 (d, *J* = 8.5 Hz, 2H), 7.56 – 7.53 (m, 4H), 7.35 – 7.29 (m, 4H), 4.53 (d, *J* = 24.9 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 188.0 (C=O), 162.8 (d, *J*=248.5, 2C), 147.8 (2C), 138.9, 133.0 (d, *J* = 8.6 Hz, 4C), 132.4 (2C), 130.1 (d, *J*=3.1 Hz, 2C), 126.8, 123.4 (4C), 115.9 (d, *J*=21.6 Hz, 4C), 56.0, 50.6 (2C).IR υ_{max}/cm^{-1}: 1664.1 (C=O), 1594.7 (C=C), 1507.7 (N-O), 1351.2 (N-O), 1156.9 (C-F), 1106.2 (C-N). HRMS calculated for $C_{26}H_{20}F_2N_2O_3$ [M+H]: 447.1569; found: 446.1442.

*4-(((3E,5E)-3,5-bis(4-fluorobenzylidene)-4-oxopiperidin-1-yl)methyl)benzonitrile (**3b**):* Pale yellow powder; UV λ_{max} (log ε) 203 (4.55), 230 (4.48), 325 (4.22) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.89 (s, 2H), 7.78 – 7.73 (m, 4H), 7.55 – 7.51 (m, 4H), 7.36 – 7.30 (m, 4H), 4.49 (d, *J* = 7.6 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 186.6 (C=O), 162.8 (d, *J*=248.5, 2C), 138.9 (2C), 133.0 (d, *J* = 8.7 Hz, 4C), 132.4 (4C), 132.0 (2C), 130.1 (d, *J*=3.0 Hz, 2C), 118.2 (2C), 115.9 (d, *J*=21.7 Hz, 4C), 111.9, 56.3, 50.4 (2C). IR υ_{max}/cm^{-1}: 2235.5 (CN), 1667.0 (C=O), 1596.4 (C=C), 1159.5 (C-F), 1108.0 (C-N). HRMS calculated for $C_{27}H_{20}F_2N_2O$ [M+H]: 427.1668; found: 426.1544.

*(3E,5E)-3,5-bis(4-fluorobenzylidene)-1-(4-(trifluoromethyl)benzyl)piperidin-4-one (**3c**):* Yellow powder; UV λ_{max} (log ε) 208 (4.65), 228 (4.43), 325 (4.40) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.92 (s, 2H), 7.76 (d, *J* = 7.9 Hz, 2H), 7.61 (d, *J* = 7.9 Hz, 2H), 7.52 (dd, *J* = 7.9, 5.7 Hz, 4H), 7.31 (t, *J* = 8.5 Hz, 4H), 4.52 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 182.0 (C=O), 162.8 (d, *J*=248.4, 2C), 139.3 (2C), 133.0 (d, *J* = 8.7 Hz, 4C), 132.9 (2C), 132.0 (2C), 130.1 (d, *J*=3.1 Hz, 2C), 130.0 (q, *J* = 32.3 Hz, aryl C), 126.5, 125.3 (q, *J* = 3.6 Hz, aryl C, 2C), 123.8 (q, *J* = 271.0 Hz, CF_3), 115.9 (d, *J*=21.7 Hz, 4C), 55.8, 50.0 (2C). IR υ_{max}/cm^{-1}: 1664.7 (C=O), 1594.7 (C=C), 1158.5 (C-F), 1113.9 (C-N). HRMS calculated for $C_{27}H_{20}F_5NO$ [M+H]: 470.1637; found: 469.1465.

*(3E,5E)-1-(3-fluorobenzyl)-3,5-bis(4-fluorobenzylidene)piperidin-4-one (**3d**):* Yellow powder; UV λ_{max} (log ε) 204 (4.58), 228 (4.27), 324 (4.29) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.91 (s, 2H), 7.57 – 7.54 (m, 4H), 7.38 – 7.32 (m, 7H), 7.20 – 7.15 (m, 2H), 4.47 (d, *J* = 25.0 Hz, 6H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 179.0 (C=O), 162.8 (d, *J*=248.3), 161.8 (d, *J*=243.5, 2C), 138.9 (2C), 133.0 (d, *J* = 8.6 Hz, 4C), 132.9 (d, *J*=4.7 Hz), 132.8 (2C), 130.6 (d, *J* = 9.3 Hz), 127.2 (2C), 119.2, 115.9 (d, *J*=21.6 Hz, 4C), 115.8, 114.8 (d, *J* = 21.7 Hz), 56.6, 50.8 (2C). IR υ_{max}/cm^{-1}: 1667.5 (C=O), 1596.1 (C=C), 1157.4 (C-F), 1105.1 (C-N). HRMS calculated for $C_{26}H_{20}F_3NO$ [M+H]: 420.1695; found: 419.1497.

*(3E,5E)-1-(3,5-bis(trifluoromethyl)benzyl)-3,5-bis(4-fluorobenzylidene)piperidin-4-one (**3e**):* Pale yellow powder; UV λ_{max} (log ε) 204 (4.78), 228 (4.23), 324 (4.20) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.36 (s, 2H), 8.07 (s, 1H), 7.89 (s, 2H), 7.58 (dd, *J* = 8.7, 5.5 Hz, 4H), 7.34 – 7.26 (m, 4H), 4.59 (d, *J* = 32.8 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 181.9 (C=O), 162.8 (d, *J*=248.5, 2C), 138.5 (2C), 133.1 (d, *J* = 8.6 Hz, 4C), 132.4 (2C), 130.4, 130.2 (q, *J* = 32.9, 2C), 130.1 (d, *J*=3.1 Hz, 2C), 124.4 (2C), 123.1, 123.0 (q, *J* = 271.5, CF_3, 2C), 115.9 (d, *J*=21.7 Hz, 4C), 56.2, 51.0 (2C). IR υ_{max}/cm^{-1}: 1678.0 (C=O), 1597.2 (C=C), 1162.8 (C-F), 1106.2 (C-N). HRMS calculated for $C_{28}H_{19}F_8NO$ [M+H]: 538.1496; found: 537.1339.

*(3E,5E)-3,5-bis(3-bromobenzylidene)-1-(4-nitrophenyl) piperidin-4-one (**4a**):* Yellow crystal; UV λ_{max} (log ε) 207 (4.75), 240 (4.27), 316 (4.31) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.14 (dd, *J* = 9.0, 2.0 Hz, 2H), 7.84 (d, *J* = 9.5 Hz, 4H), 7.66 – 7.62 (m, 4H), 7.47 – 7.41 (m, 4H), 4.54 (d, *J* = 30.7 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 182.0 (C=O), 147.8 (2C), 145.0, 138.4, 135.8 (2C), 132.6 (2C), 132.4 (2C), 130.8 (2C), 130.0 (2C), 129.3 (2C), 123.8 (2C), 123.5 (2C), 122.1 (2C), 56.2, 50.5 (2C). IR υ_{max}/cm^{-1}: 1676.5 (C=O), 1606.4 (C=C), 1518.9 (N-O), 1351.1 (N-O), 1074.4 (C-N), 531.8 (C-Br). HRMS calculated for $C_{26}H_{20}Br_2N_2O_3$ [M+H]: 566.9920/ [M+H+2, ^{79}Br]: 568.9910/[M+H+4, ^{81}Br]: 570.9886; found: 567.9820/565.9841/569.9800.

*4-((3E,5E)-3,5-bis(3-bromobenzylidene)-4-oxopiperidin-1-yl)benzonitrile (**4b**):* Pale yellow crystal; UV λ_{max} (log ε) 204 (4.67), 235 (4.41), 320 (4.13) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.86 (s, 2H), 7.77 (s, 4H), 7.67 – 7.65 (m, 4H), 7.46 – 7.41 (m, 4H), 4.50 (d, *J* = 18.8 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 181.8 (C=O), 138.5, 135.8 (2C), 132.6 (2C), 132.5 (4C), 132.4 (2C), 132.0 (2C), 130.8 (2C), 129.3 (2C), 122.1 (4C), 118.2, 112.0, 56.3, 50.2 (2C). IR υ_{max}/cm^{-1}: 2234.7 (CN), 1674.2 (C=O), 1602.4 (C=C), 1073.1 (C-N), 569.5 (C-Br). HRMS calculated for $C_{27}H_{20}Br_2N_2O$ [M+H]: 547.0025/ [M+H+2, ^{79}Br]: 549.0018/[M+H+4, ^{81}Br]: 550.9992; found: 547.9922/545.9942/549.9901.

*(3E,5E)-3,5-bis(3-bromobenzylidene)-1-(4-(trifluoromethyl) phenyl)piperidin-4-one (**4c**):* Yellow crystal; UV λ_{max} (log ε) 209 (4.69), 233 (4.13), 319 (4.24) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.88 (s, 2H), 7.78 (d, *J* = 7.9 Hz, 2H), 7.69 – 7.60 (m, 6H), 7.47 – 7.39 (m, 4H), 4.50 (d, *J* = 16.8 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 182.0 (C=O), 138.7 (2C), 135.8 (2C), 132.6 (4C), 131.4, 130.8 (2C), 129.6 (q, *J* = 32.1 Hz, aryl C), 129.2 (2C), 125.3 (q, *J* = 3.6 Hz, aryl C, 2C), 123.8 (q, *J* = 271.1 Hz, CF_3), 123.8 (2C), 123.5 (2C), 122.1 (2C), 56.2, 50.1 (2C). IR υ_{max}/cm^{-1}: 1667.2 (C=O), 1601.4 (C=C), 1187.0 (C-F), 1076.7 (C-N), 528.4 (C-Br). HRMS calculated for $C_{27}H_{20}Br_2F_3NO$ [M+H]: 589.9962/[M+H+2, ^{79}Br]: 591.9962/[M+H+4, ^{81}Br]: 593.9928; found: 590.9843/588.9864/592.9823.

*(3E,5E)-3,5-bis(3-bromobenzylidene)-1-(3-fluorophenyl) piperidin-4-one (**4d**):* Yellow crystal; UV λ_{max} (log ε) 207 (4.60), 237 (4.09), 317 (4.13) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.87 (s, 2H), 7.69 – 7.66 (m, 4H), 7.48 – 7.36 (m, 7H), 7.19 – 7.16 (m, 1H), 4.47 (d, *J* = 15.0 Hz, 6H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 182.4 (C=O), 161.8 (d, *J*=243.6), 135.9 (2C), 132.6 (4C), 132.5 (2C), 132.0 (2C), 130.8 (2C), 130.6 (d, *J* = 8.4 Hz), 130.0 (d, *J*=3.9 Hz), 129.4 (2C), 129.0, 122.1 (2C), 122.0, 117.8, 56.9, 50.0 (2C). IR $_{max}$/cm^{-1}: 1669.2 (C=O), 1605.0 (C=C), 1190.0 (C-F), 1076.5 (C-N), 679.1 (C-Br). HRMS calculated for $C_{26}H_{20}Br_2FNO$ [M+H]: 539.9991/[M+H+2, ^{79}Br]: 541.9992/[M+H+4, ^{81}Br]: 543.9958; found: 540.9875/538.9896/542.9855.

*(3E,5E)-1-(3,5-bis(trifluoromethyl)phenyl)-3,5-bis(3-bromo benzylidene)piperidin-4-one (**4e**):* Yellow crystal; UV λ_{max} (log ε) 205 (4.78), 247 (4.08), 316 (4.13) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.33 (s, 2H), 8.09 (s, 1H), 7.85 (s, 2H), 7.70 – 7.65 (m, 4H), 7.49 – 7.40 (m, 4H), 4.56 (d, *J* = 34.9 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 192.1 (C=O), 138.1 (2C), 137.1, 135.8 (2C), 132.7 (2C), 132.6 (2C), 132.0 (2C), 131.4 (2C), 130.8 (2C), 130.3 (q, *J* = 32.9 Hz, 2C), 129.2 (2C), 128.2 (2C), 123.0 (q, *J* = 271.5 Hz, CF_3, 2C), 122.4, 122.1 (2C), 56.2, 50.1 (2C). IR υ_{max}/cm^{-1}: 1676.7 (C=O), 1608.3 (C=C), 1181.9 (C-F), 1075.0 (C-N), 529.5 (C-Br). HRMS calculated for $C_{28}H_{19}Br_2F_6NO$ [M+H]: 657.9839/[M+H+2, ^{79}Br]: 659.9843/[M+H+4, ^{81}Br]: 661.9807; found: 658.9717/656.9738/660.9697.

*(3E,5E)-1-(4-nitrophenyl)-3,5-bis(4-(trifluoromethyl)benzyli dene)piperidin-4-one (**5a**):* Yellow crystal; UV λ_{max} (log ε) 205 (4.71), 227 (4.43), 313 (4.69) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.09 – 8.06 (m, 2H), 7.95 (s, 2H), 7.82 – 7.74 (m, 6H), 7.66 (d, *J* = 8.2 Hz, 4H), 4.46 (d, *J* = 14.5 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 182.5 (C=O), 147.6 (2C), 138.3, 137.6 (2C), 132.2, 130.9 (6C), 129.6 (d, *J*=31.8 Hz, 2C), 125.5 (q, *J* = 3.8 Hz, 4C), 125.3 (2C), 123.9 (q, *J* = 270.9, Hz, CF_3, 2C), 123.4 (2C), 55.7, 50.4 (2C). IR υ_{max}/cm^{-1}: 1681.6 (C=O), 1610.8 (C=C), 1541.2 (N-O), 1317.8 (N-O), 1067.2 (C-F), 1013.3 (C-N). HRMS calculated for $C_{28}H_{20}F_6N_2O_3$ [M+H]: 547.1493; found: 546.1378.

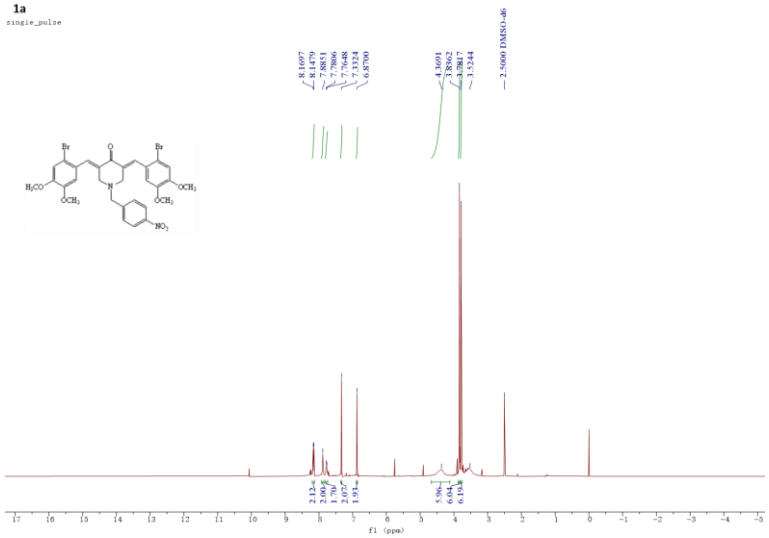
*4-((3E,5E)-4-oxo-3,5-bis(4-(trifluoromethyl)benzylidene) piperidin-1-yl) benzonitrile (**5b**):* Pale yellow crystal; UV λ_{max} (log ε) 204 (4.57), 229 (4.53), 314 (4.53) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.76 (d, *J* = 8.3 Hz, 4H), 7.70 (s, 2H), 7.64 – 7.62 (m, 6H), 7.40 (d, *J* = 8.4 Hz, 2H), 3.86 (s, 4H), 3.80 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 186.6 (C=O), 143.6 (2C), 138.4 (d, *J*=1.4 Hz, 2C), 135.5 (2C), 133.9, 132.1 (2C), 130.8 (4C), 129.5 (2C), 129.0 (d, *J*=31.8 Hz, 2C), 125.3 (q, *J* = 3.8 Hz, 4C), 123.4 (q, *J* = 269.5, Hz, CF_3, 2C), 118.6, 109.9, 59.1, 53.4 (2C). IR υ_{max}/cm^{-1}: 2224.8 (CN), 1679.2 (C=O), 1613.3 (C=C), 1065.5 (C-F), 1014.3 (C-N). HRMS calculated for $C_{29}H_{20}F_6N_2O$ [M+H]: 527.1606; found: 526.1480.

*(3E,5E)-3,5-bis(4-(trifluoromethyl)benzylidene)-1-(4-(trifluoromethyl)phenyl)piperidin-4-one (**5c**):* Pale yellow crystal; UV λ_{max} (log ε) 206 (4.72), 295 (4.50) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.76 – 7.71 (m, 6H), 7.63 (d, *J* = 8.5 Hz, 4H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 2H), 3.86 (s, 4H), 3.79 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 186.8 (C=O), 142.4, 142.5, 138.5 (d, *J*=1.4 Hz, 2C), 135.5 (2C), 134.1, 130.8 (4C), 129.4 (2C),128.9 (d, *J*=31.7 Hz, 2C), 127.8 (d, *J*=31.5 Hz), 125.3 (q, *J* = 3.9 Hz, 4C), 124.9 (q, *J* = 3.9 Hz, 2C), 124.1 (q, *J* = 270.5, Hz, CF_3), 124.0 (q, *J* = 270.4, Hz, CF_3, 2C), 58.9, 53.1 (2C). IR υ_{max}/cm^{-1}: 1671.1 (C=O), 1615.5 (C=C), 1066.0 (C-F), 1015.8 (C-N). HRMS calculated for $C_{29}H_{20}F_9NO$ [M+H]: 570.1533; found: 569.1401.

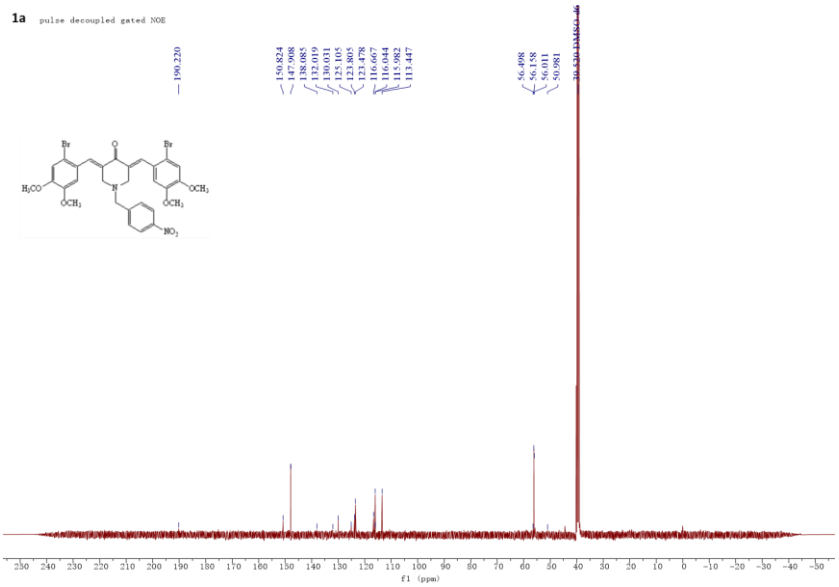
*(3E,5E)-1-(3-fluorophenyl)-3,5-bis(4-(trifluoromethyl)benzyli dene)piperidin-4-one (**5d**):* Yellow crystal; UV λ_{max} (log ε) 206 (4.79), 227 (4.35), 315 (4.65) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.94 (s, 2H), 7.79 (d, *J* = 8.3 Hz, 4H), 7.64 (d, *J* = 8.3 Hz, 4H), 7.32 – 7.23 (m, 3H), 7.09 – 7.04 (m, 1H), 4.40 (d, *J* = 37.8 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 182.2 (C=O), 161.7 (d, *J*=243.5), 138.4 (2C), 137.6 (2C), 131.2 (2C), 131.0 (d, *J* = 6.9 Hz), 130.9 (4C), 130.6 (d, *J*=8.1 Hz), 130.0 (d, *J*=2.8 Hz), 129.6 (q, *J*=31.9 Hz, 2C), 129.2 (d, *J* = 10.3 Hz), 127.1, 125.5 (q, *J* = 3.8 Hz, 4C), 123.9 (q, *J* = 270.8, Hz, CF_3, 2C), 116.0 (d, *J* = 21.4 Hz), 56.4, 50.3 (2C). IR υ_{max}/cm^{-1}: 1673.9 (C=O), 1614.0 (C=C), 1117.9 (C-F), 1014.0 (C-N). HRMS calculated for $C_{28}H_{20}F_7NO$ [M+H]: 520.1603; found: 519.1433.

*(3E,5E)-1-(3,5-bis(trifluoromethyl)phenyl)-3,5-bis(4-(trifluoromethyl)benzylidene)piperidin-4-one (**5e**):* Yellow crystal; UV λ_{max} (log ε) 205 (4.76), 226 (4.36), 313 (4.63) nm; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.27 (s, 2H), 7.97 (d, *J* = 22.6 Hz, 3H), 7.81 – 7.68 (m, 8H), 4.49 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 182.4 (C=O), 137.9, 137.6 (2C), 132.1 (2C), 130.9 (4C), 130.2 (d, *J*=32.9 Hz, 2C), 130.1 (2C), 129.6 (q, *J* = 31.9 Hz, 2C), 125.4 (q, *J* = 3.7 Hz, aryl C, 6C), 123.9 (q, *J* = 270.7, Hz, CF_3, 2C), 123.0 (q, *J* = 272.9, Hz, CF_3, 2C), 122.9, 56.2, 50.9 (2C). IR υ_{max}/cm^{-1}: 1685.1 (C=O), 1612.8 (C=C), 1067.2 (C-F), 1017.1 (C-N). HRMS calculated for $C_{30}H_{19}F_{12}NO$ [M+H]: 638.1422; found: 637.1275.

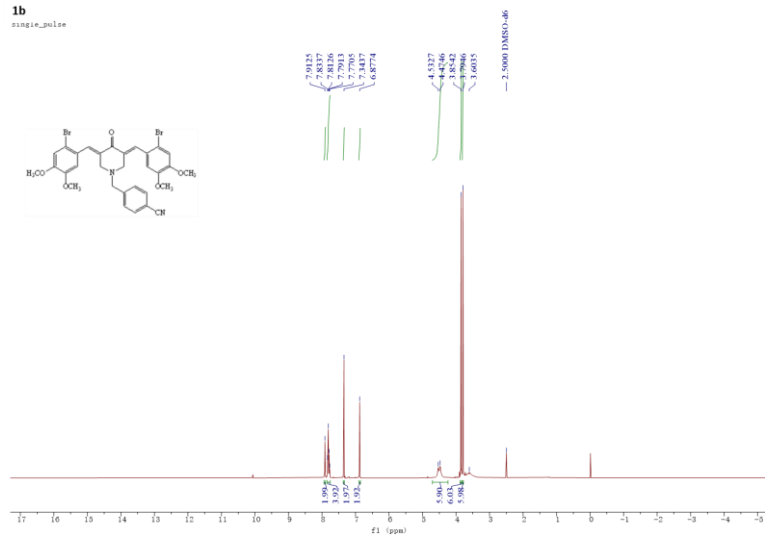
*^{1}H NMR of (3E,5E)-3,5-bis(2-bromo-4,5-dimethoxybenzylidene)-1-(4-nitrophenyl)piperidin-4-ne (**1a**)*



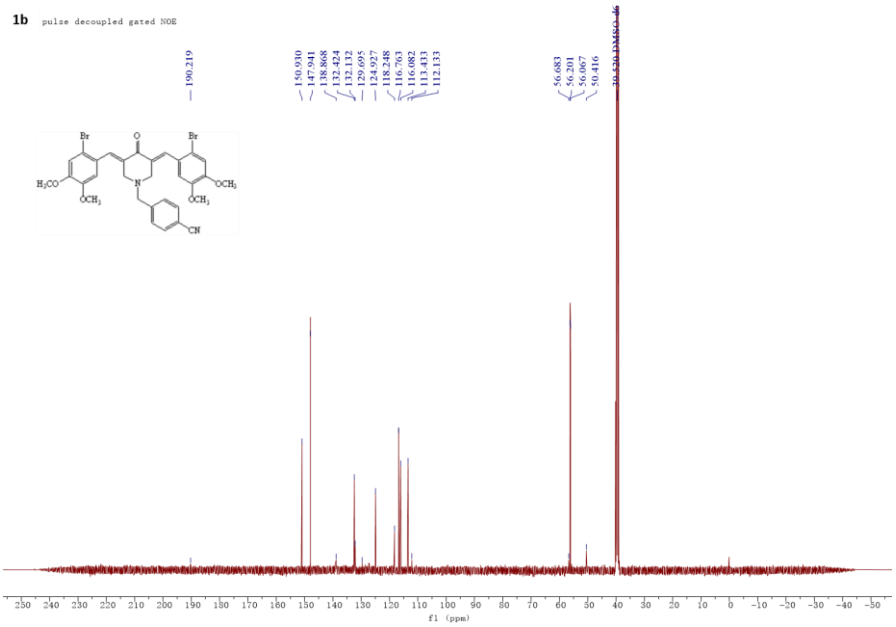
*^{13}C NMR of (3E,5E)-3,5-bis(2-bromo-4,5-dimethoxybenzylidene)-1-(4-nitrophenyl)piperidin-4-ne (**1a**)*



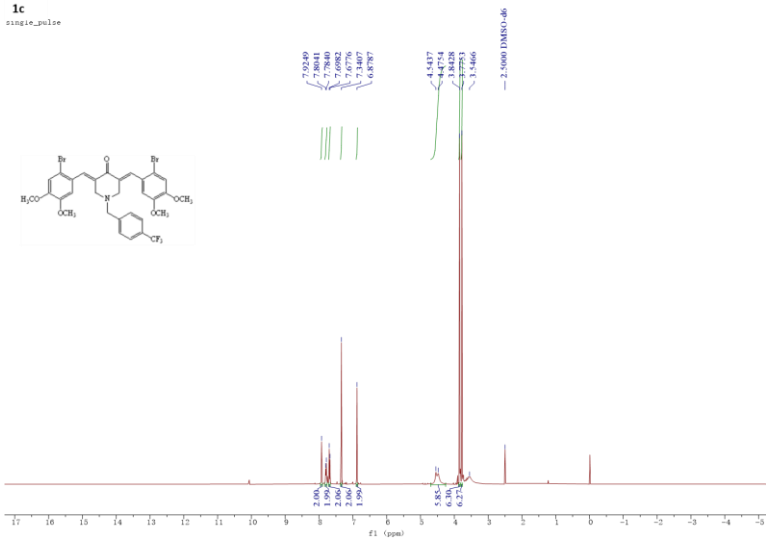
*^{1}H NMR of 4-((3E,5E)-3,5-bis(2-bromo-4,5-dimethoxybenzylidene)-4-oxopiperidin-1-yl)benzonitrile (**1b**)*



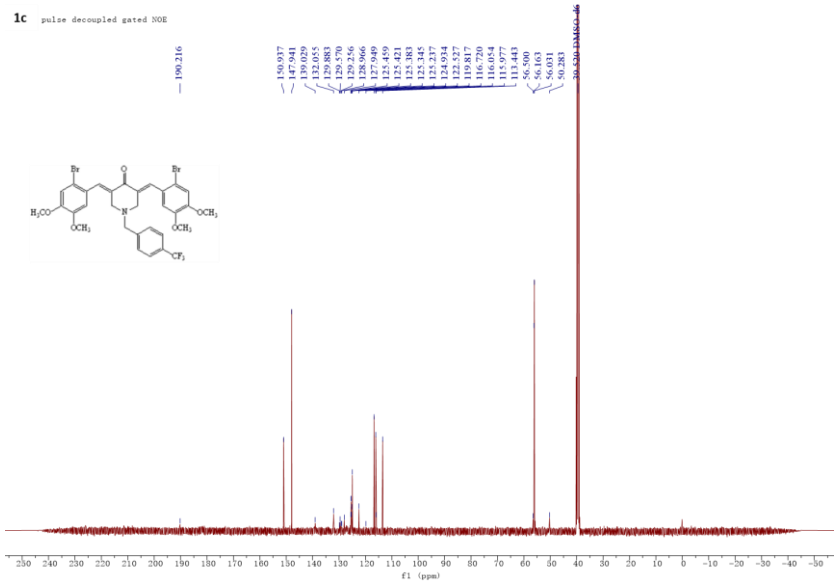
*^{13}C NMR of 4-((3E,5E)-3,5-bis(2-bromo-4,5-dimethoxybenzylidene)-4-oxopiperidin-1-yl)benzonitrile (**1b**)*



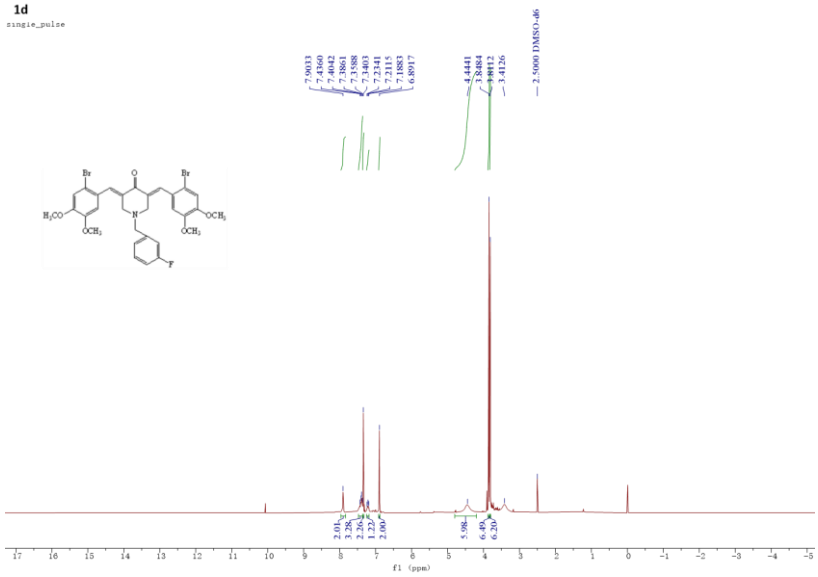
*[1]H NMR of (3E,5E)-3,5-bis(2-bromo-4,5-dimethoxybenzylidene)-1-(4-(trifluoromethyl)phenyl)piperidin-4-one (**1c**)*



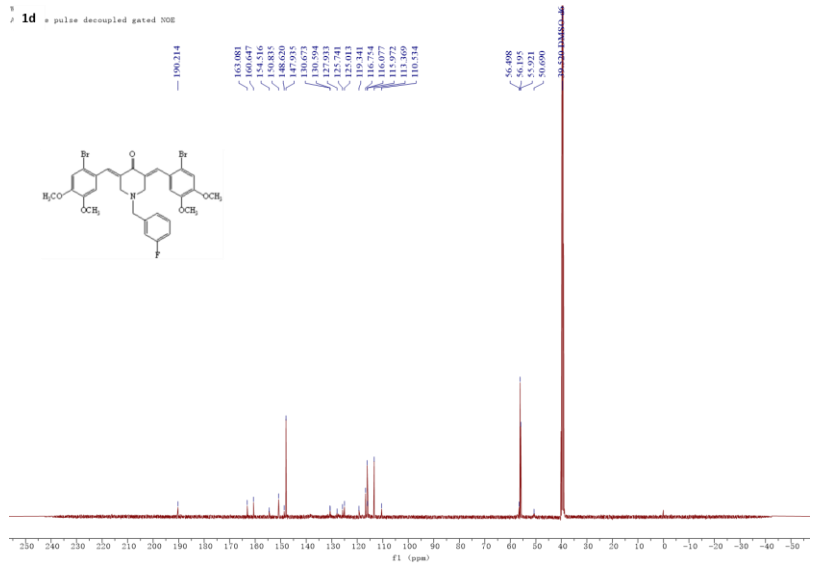
*[13]C NMR of (3E,5E)-3,5-bis(2-bromo-4,5-dimethoxybenzylidene)-1-(4-(trifluoromethyl)phenyl)piperidin-4-one (**1c**)*



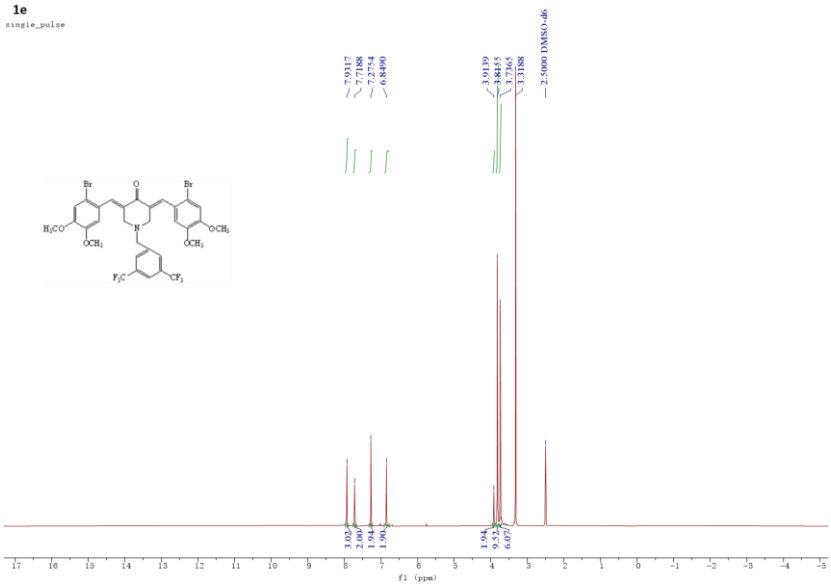
*[1]H NMR of (3E,5E)-3,5-bis(2-bromo-4,5-dimethoxybenzylidene)-1-(3-fluorophenyl)piperidin-4-one (**1d**)*



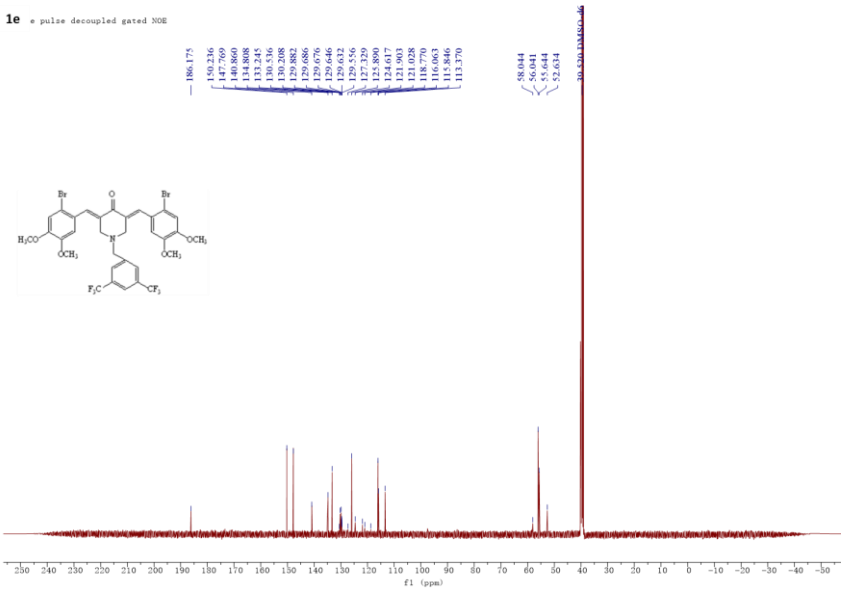
*^{13}C NMR of (3E,5E)-3,5-bis(2-bromo-4,5-dimethoxybenzylidene)-1-(3-fluorophenyl)piperidin-4-one (**1d**)*



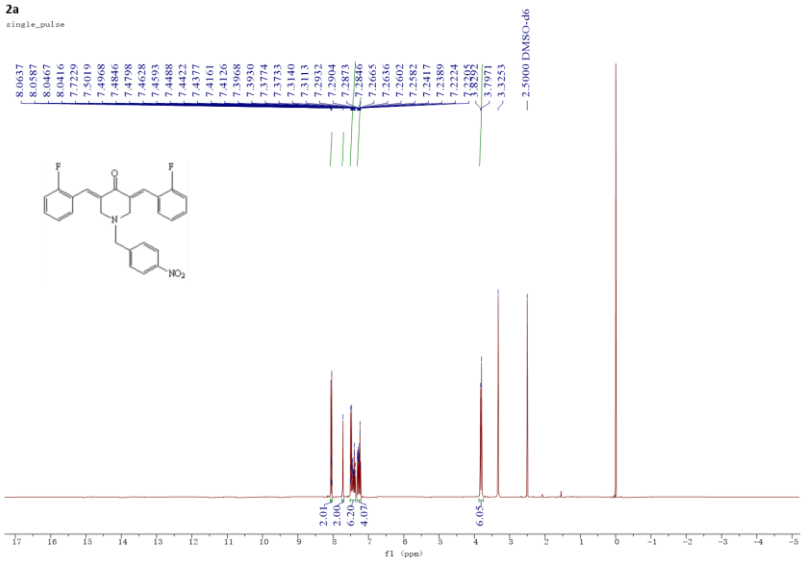
*^{1}H NMR of (3E,5E)-1-(3,5-bis(trifluoromethyl)phenyl)-3,5-bis(2-bromo-4,5-dimethoxybenzylidene)piperidin-4-one (**1e**)*



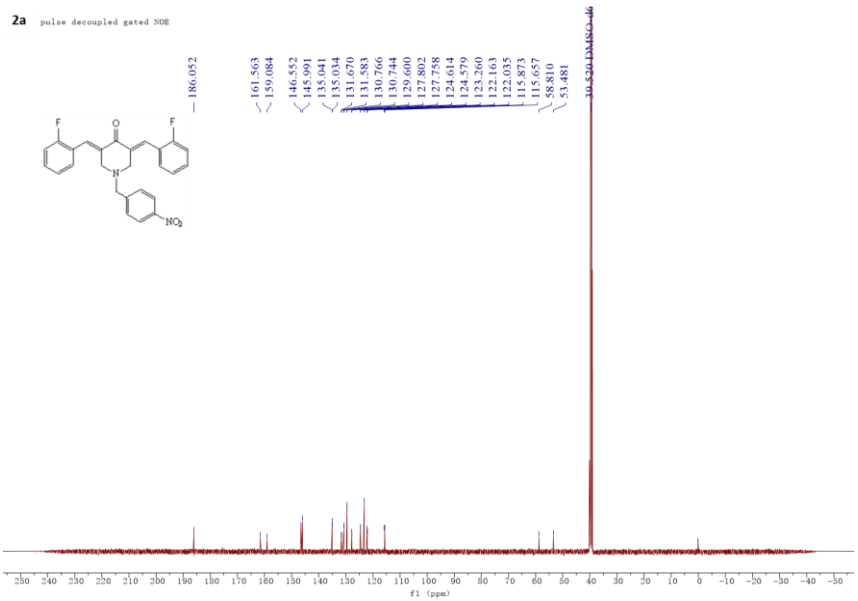
*^{13}C NMR of (3E,5E)-1-(3,5-bis(trifluoromethyl)phenyl)-3,5-bis(2-bromo-4,5-dimethoxybenzylidene)piperidin-4-one (**1e**)*



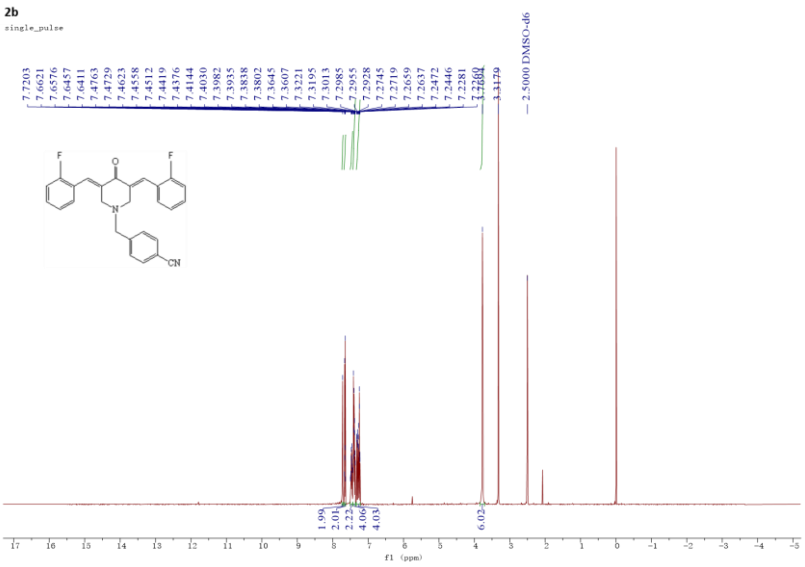
*[1]H NMR of (3E,5E)-3,5-bis(2-fluorobenzylidene)-1-(4-nitrophenyl) piperidin-4-one (**2a**)*



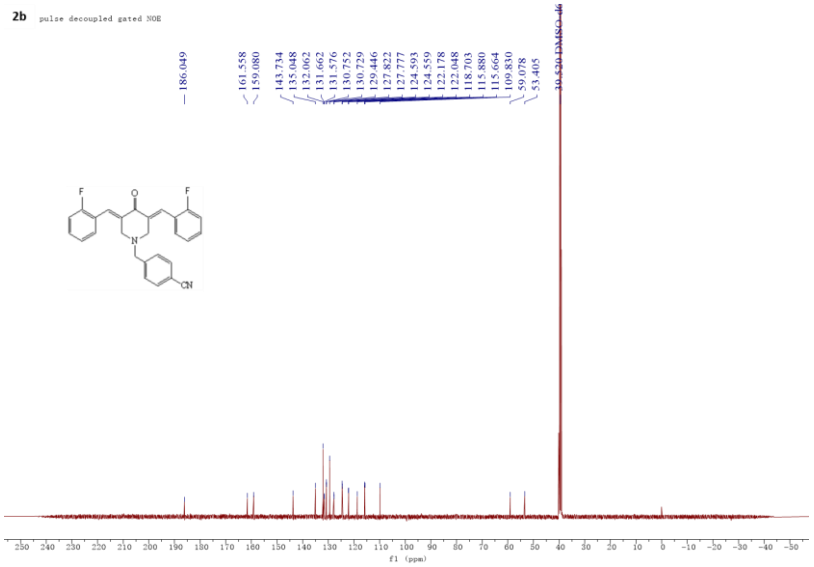
*[13]C NMR of (3E,5E)-3,5-bis(2-fluorobenzylidene)-1-(4-nitrophenyl) piperidin-4-one (**2a**)*



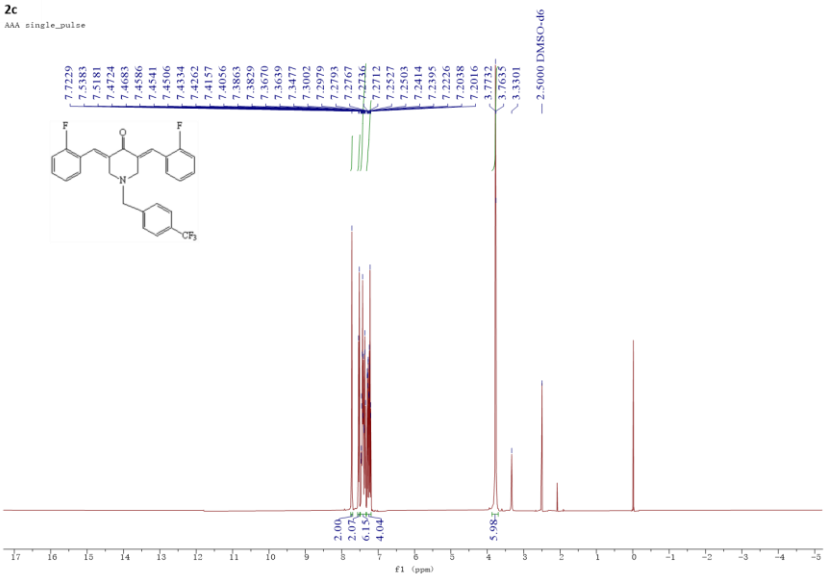
*[1]H NMR of 4-((3E,5E)-3,5-bis(2-fluorobenzylidene)-4-oxopiperidin-1-yl)benzonitrile (**2b**)*



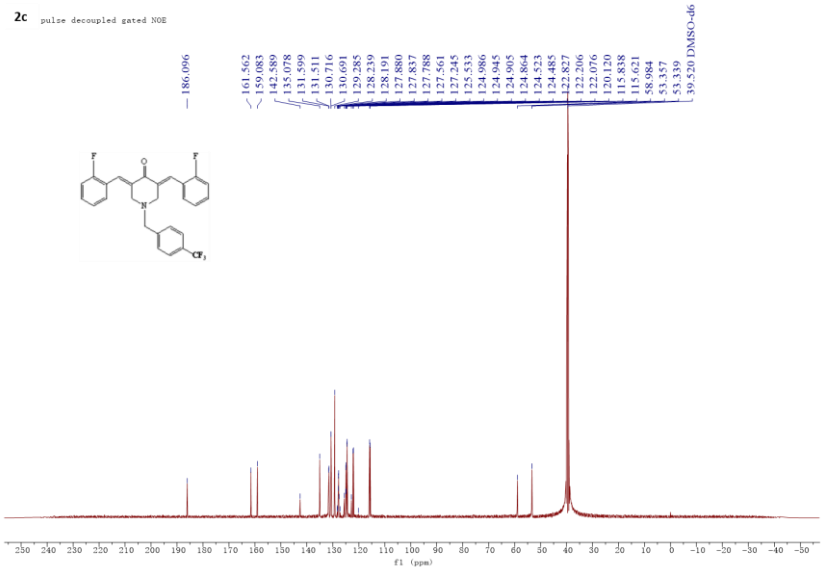
*[13]C NMR of 4-((3E,5E)-3,5-bis(2-fluorobenzylidene)-4-oxopiperidin-1-yl)benzonitrile (**2b**)*



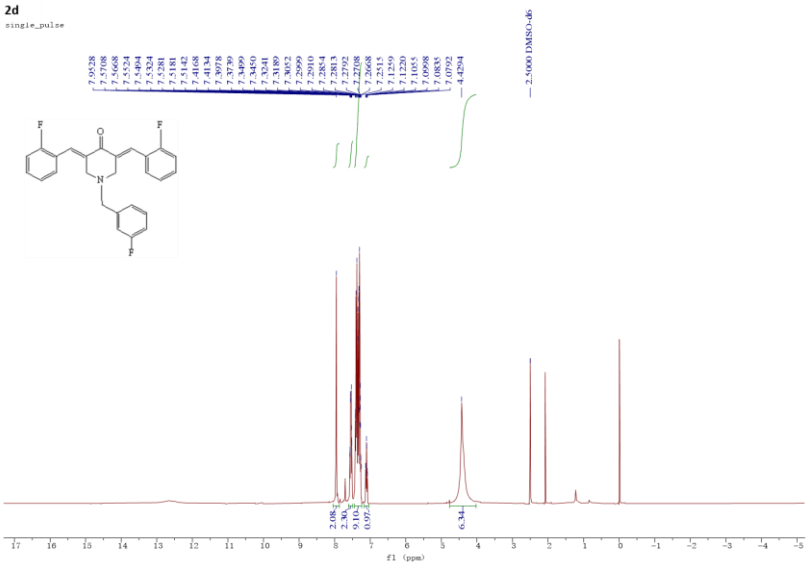
*[1]H NMR of (3E,5E)-3,5-bis(2-fluorobenzylidene)-1-(4-(trifluoromethyl) phenyl)piperidin-4-one (**2c**)*



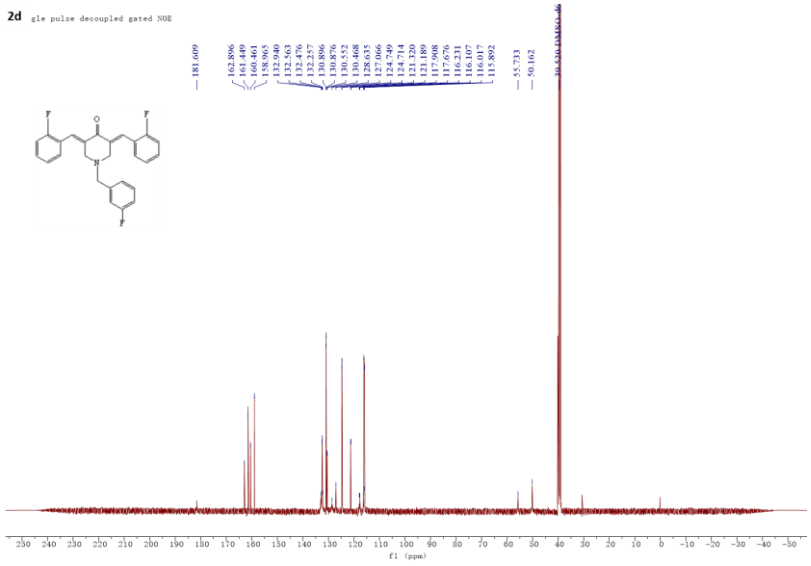
*^{13}C NMR of (3E,5E)-3,5-bis(2-fluorobenzylidene)-1-(4-(trifluoromethyl) phenyl)piperidin-4-one (**2c**)*



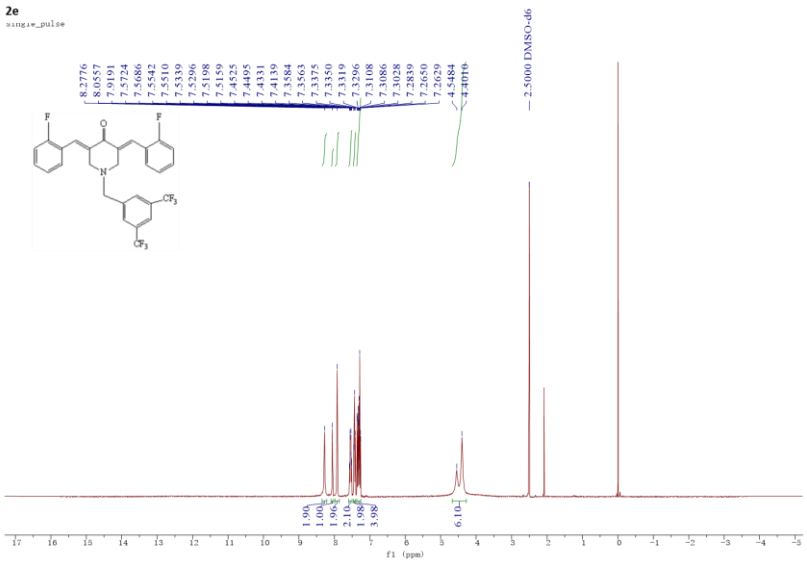
*^{1}H NMR of (3E,5E)-3,5-bis(2-fluorobenzylidene)-1-(3-fluorophenyl) piperidin-4-one (**2d**)*



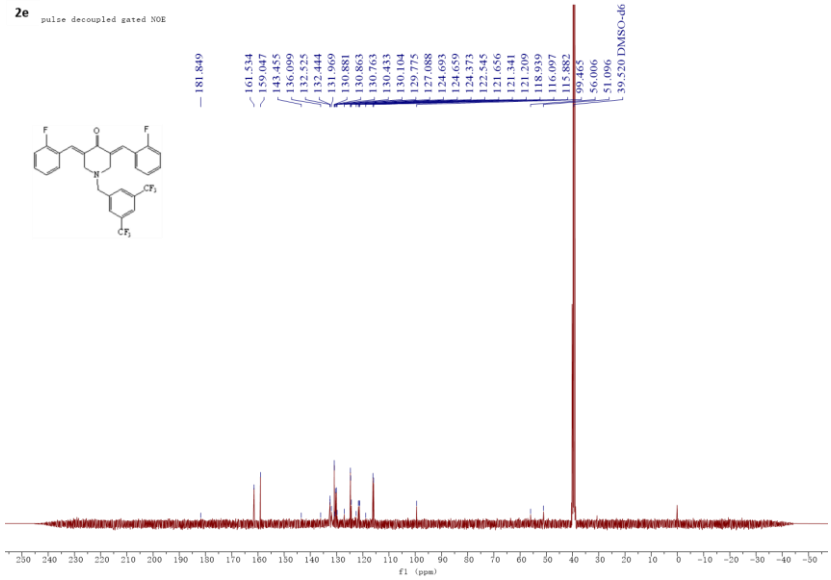
*^{13}C NMR of (3E,5E)-3,5-bis(2-fluorobenzylidene)-1-(3-fluorophenyl) piperidin-4-one (**2d**)*



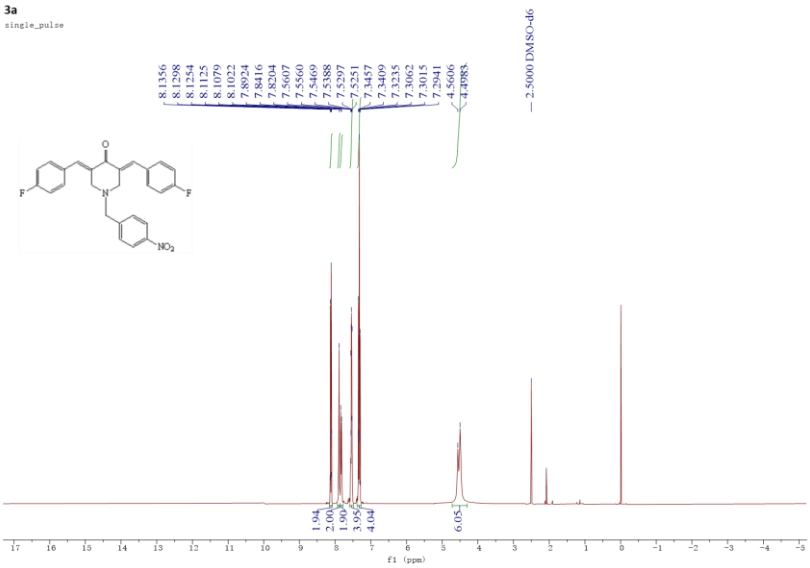
*^{1}H NMR of (3E,5E)-1-(3,5-bis(trifluoromethyl)phenyl)-3,5-bis(2-fluoro benzylidene) piperidin-4-one (**2e**)*



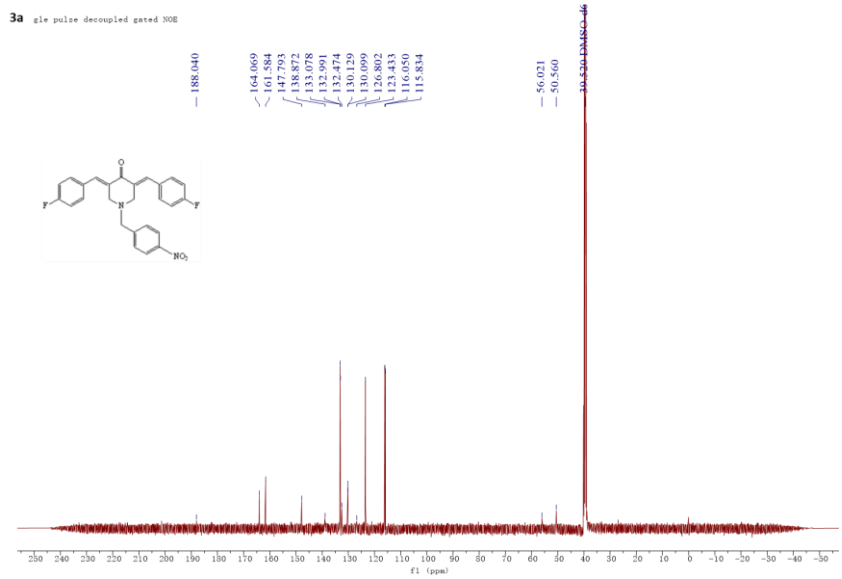
*^{13}C NMR of (3E,5E)-1-(3,5-bis(trifluoromethyl)phenyl)-3,5-bis(2-fluoro benzylidene) piperidin-4-one (**2e**)*



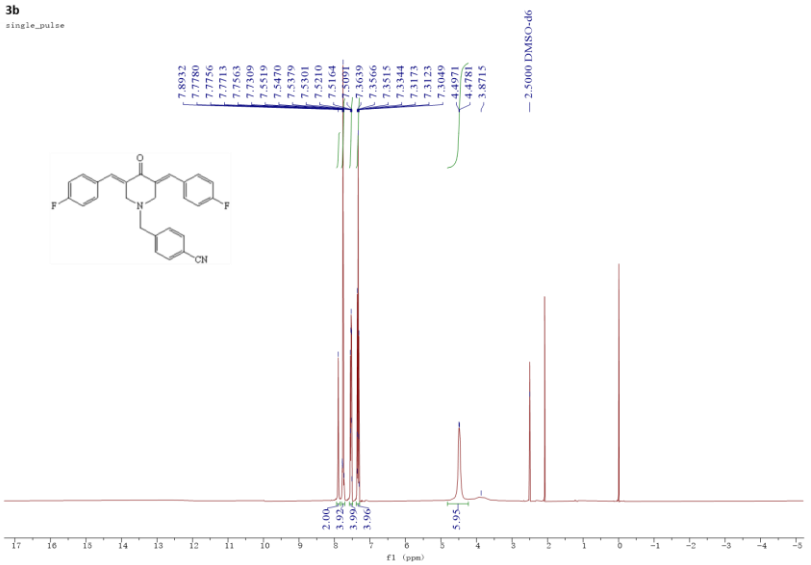
*^{1}H NMR of (3E,5E)-3,5-bis(4-fluorobenzylidene)-1-(4-nitrobenzyl) piperidin-4-one (**3a**)*



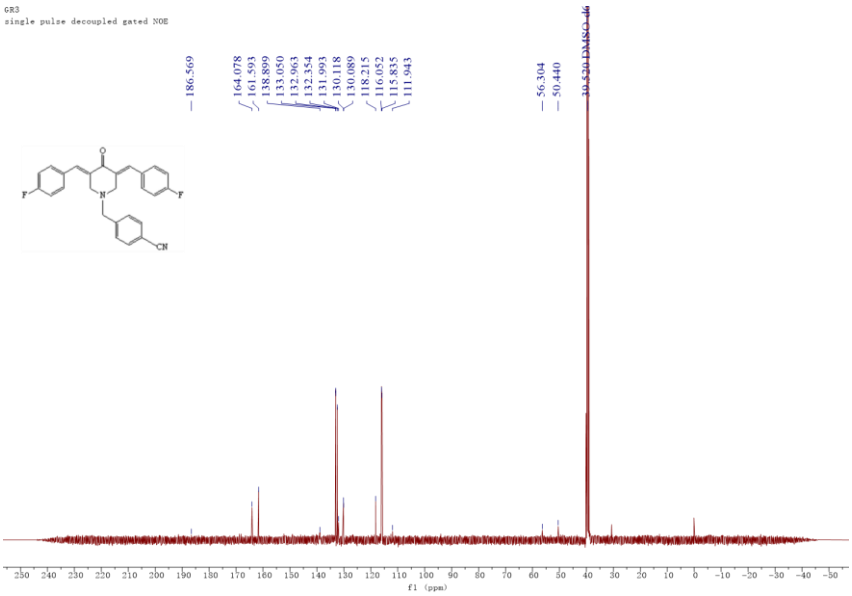
*^{13}C NMR of (3E,5E)-3,5-bis(4-fluorobenzylidene)-1-(4-nitrobenzyl) piperidin-4-one (**3a**)*



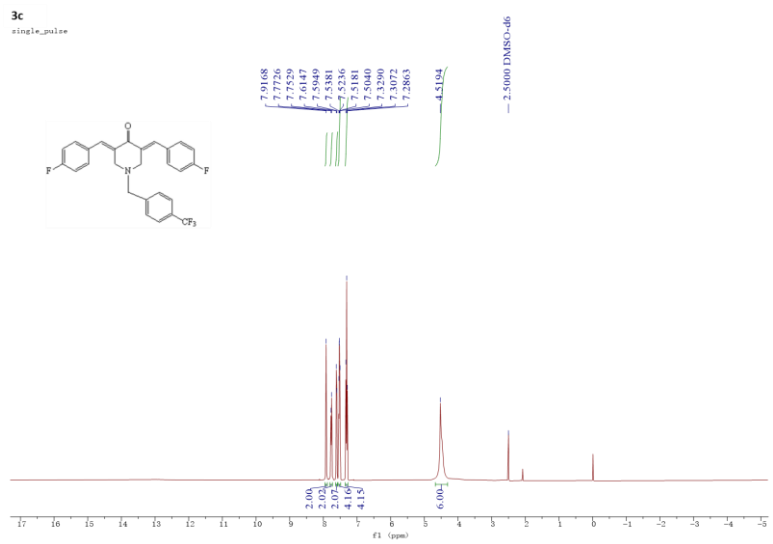
*^{1}H NMR of 4-(((3E,5E)-3,5-bis(4-fluorobenzylidene)-4-oxopiperidin-1-yl) methyl)benzonitrile (**3b**)*



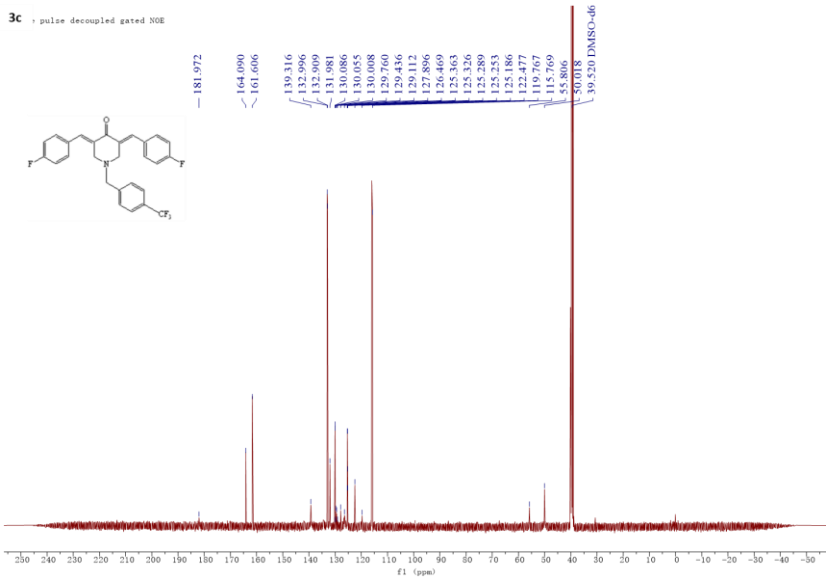
*^{13}C NMR of 4-(((3E,5E)-3,5-bis(4-fluorobenzylidene)-4-oxopiperidin-1-yl) methyl)benzonitrile (**3b**)*



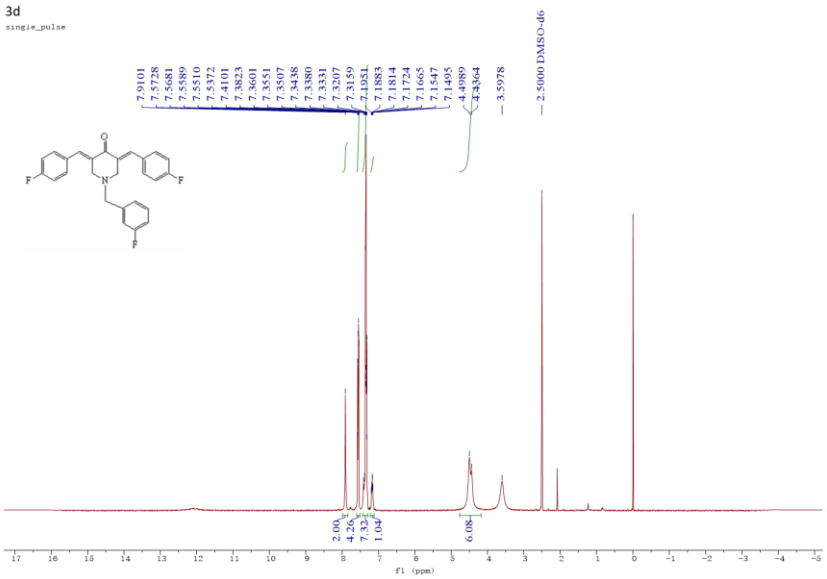
*[1]H NMR of (3E,5E)-3,5-bis(4-fluorobenzylidene)-1-(4-(trifluoromethyl) benzyl)piperidin-4-one (**3c**)*



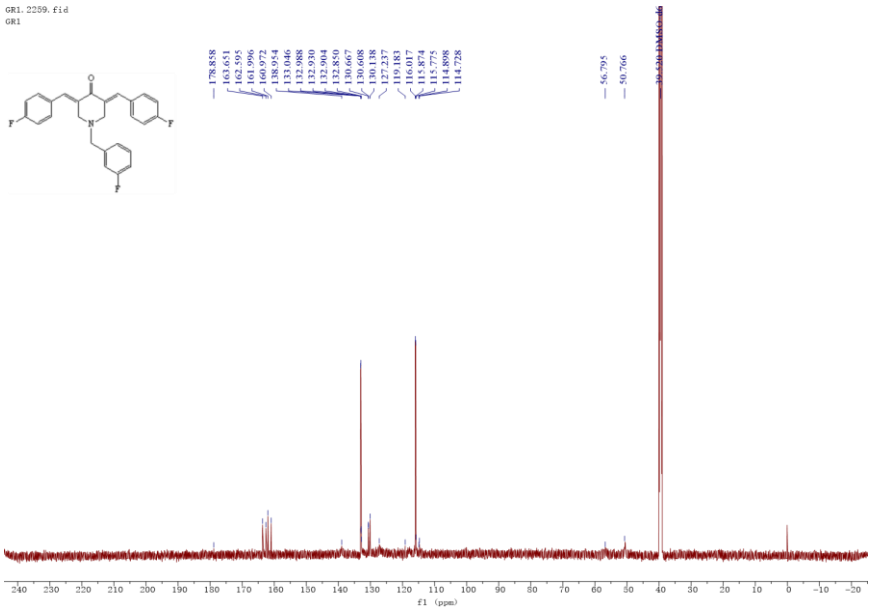
*[13]C NMR of (3E,5E)-3,5-bis(4-fluorobenzylidene)-1-(4-(trifluoromethyl) benzyl)piperidin-4-one (**3c**)*



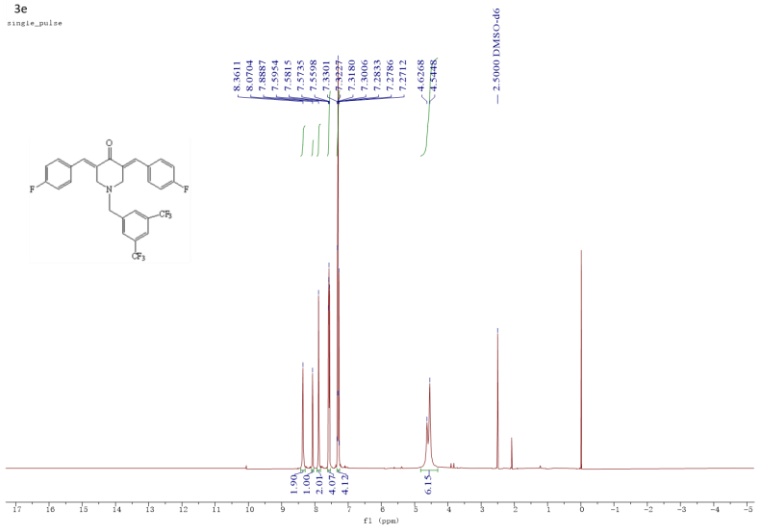
*[1]H NMR of (3E,5E)-1-(3-fluorobenzyl)-3,5-bis(4-fluorobenzylidene) piperidin-4-one (**3d**):*



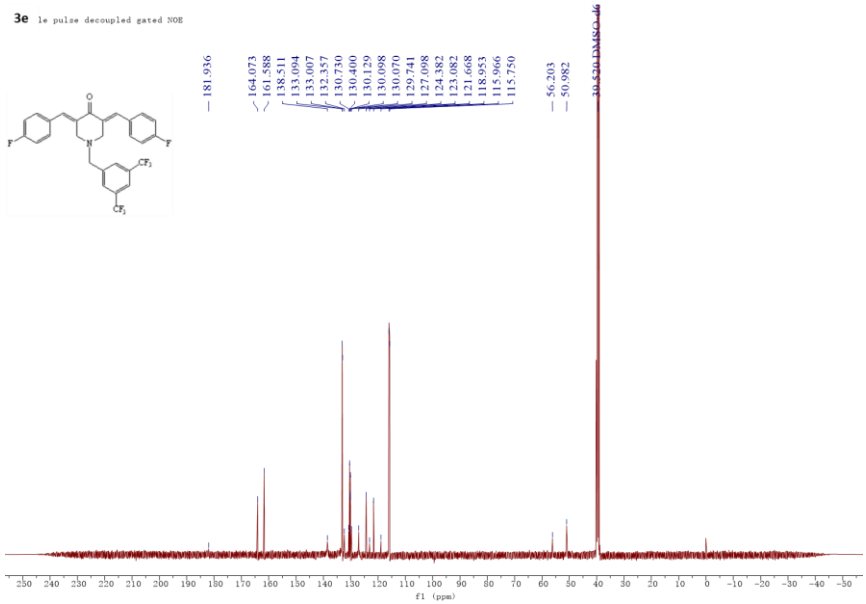
*^{13}C NMR of (3E,5E)-1-(3-fluorobenzyl)-3,5-bis(4-fluorobenzylidene) piperidin-4-one (**3d**):*



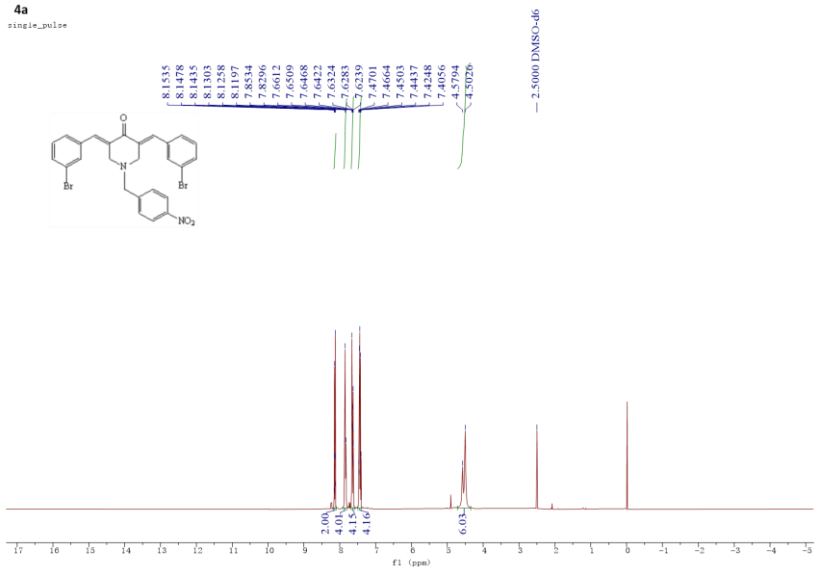
*^{1}H NMR of (3E,5E)-1-(3,5-bis(trifluoromethyl)benzyl)-3,5-bis(4-fluoro benzylidene)piperidin-4-one (**3e**):*



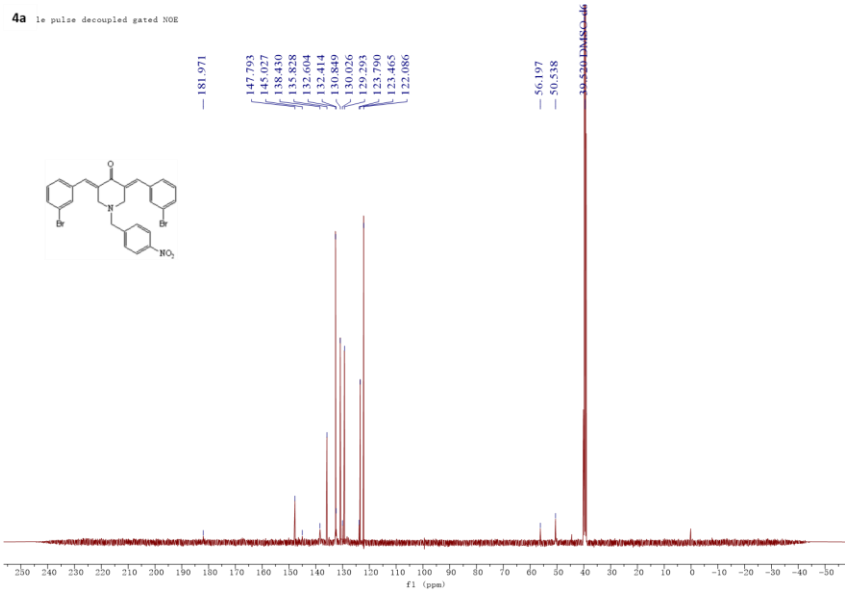
*^{13}C NMR of (3E,5E)-1-(3,5-bis(trifluoromethyl)benzyl)-3,5-bis(4-fluoro benzylidene)piperidin-4-one (**3e**):*



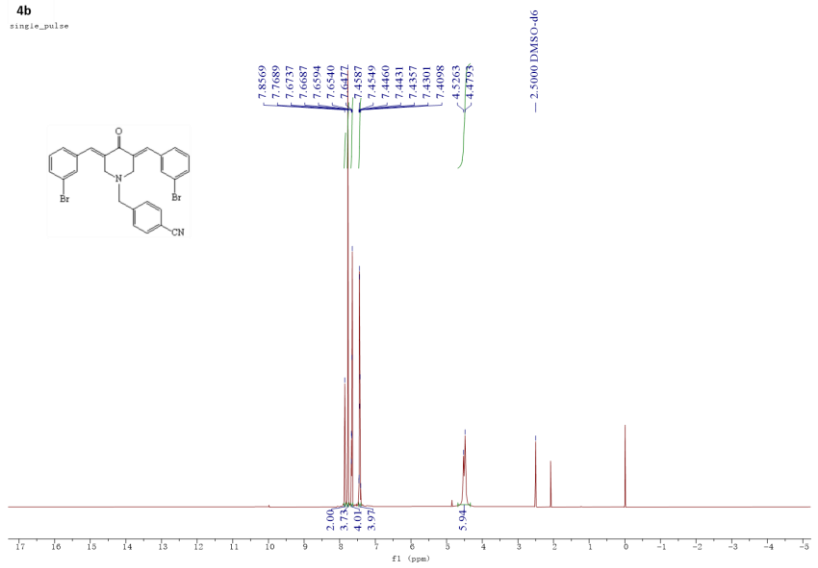
*^{1}H NMR of (3E,5E)-3,5-bis(3-bromobenzylidene)-1-(4-nitrophenyl) piperidin-4-one (**4a**)*



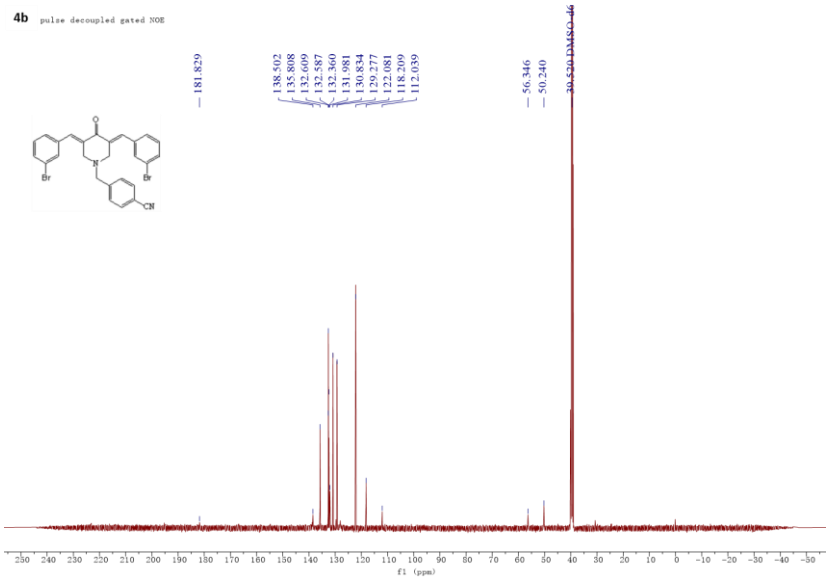
*^{13}C NMR of (3E,5E)-3,5-bis(3-bromobenzylidene)-1-(4-nitrophenyl) piperidin-4-one (**4a**)*



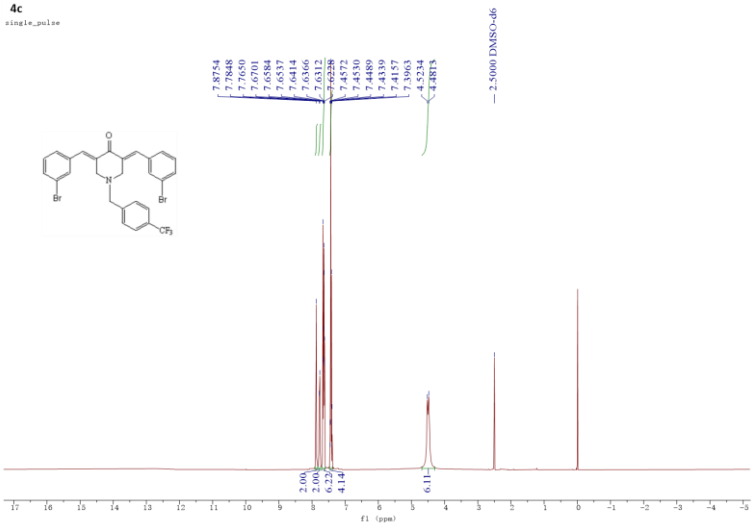
*^{1}H NMR of 4-((3E,5E)-3,5-bis(3-bromobenzylidene)-4-oxopiperidin-1-yl)benzonitrile (**4b**)*



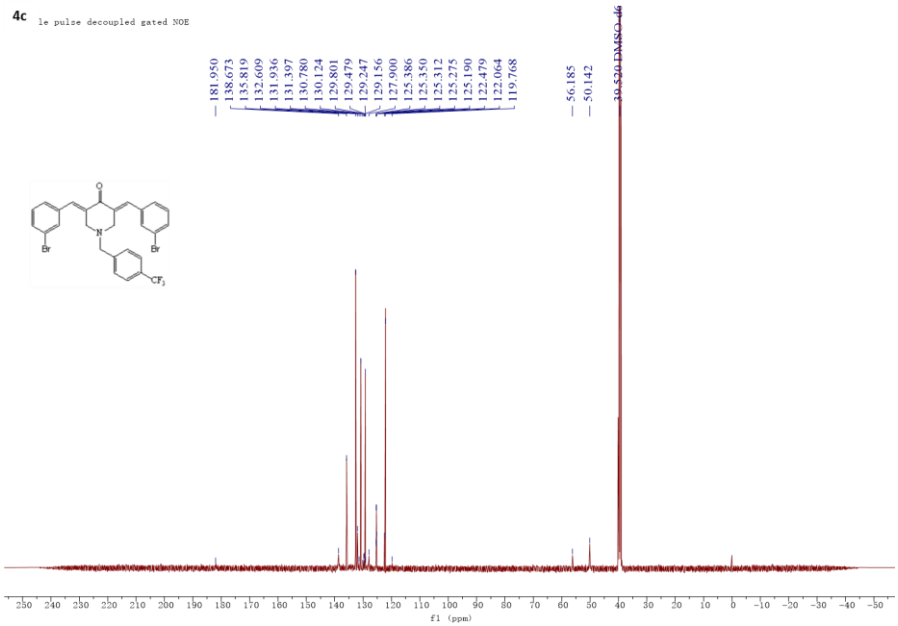
*^{13}C NMR of 4-((3E,5E)-3,5-bis(3-bromobenzylidene)-4-oxopiperidin-1-yl)benzonitrile (**4b**)*



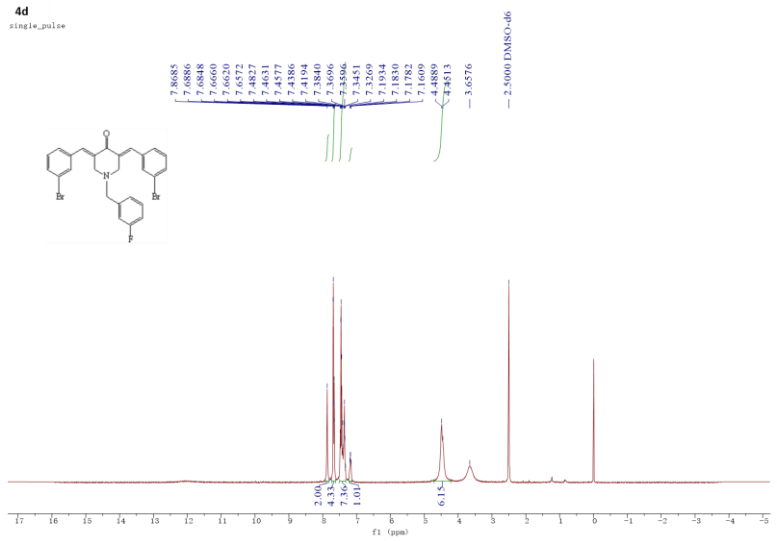
*^{1}H NMR of (3E,5E)-3,5-bis(3-bromobenzylidene)-1-(4-(trifluoromethyl) phenyl)piperidin-4-one (**4c**)*



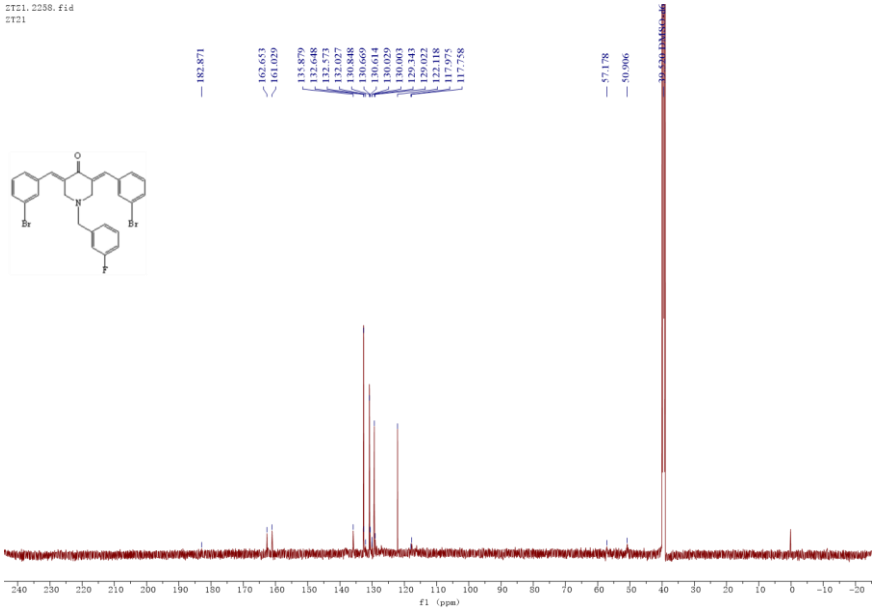
*^{13}C NMR of (3E,5E)-3,5-bis(3-bromobenzylidene)-1-(4-(trifluoromethyl) phenyl)piperidin-4-one (**4c**)*



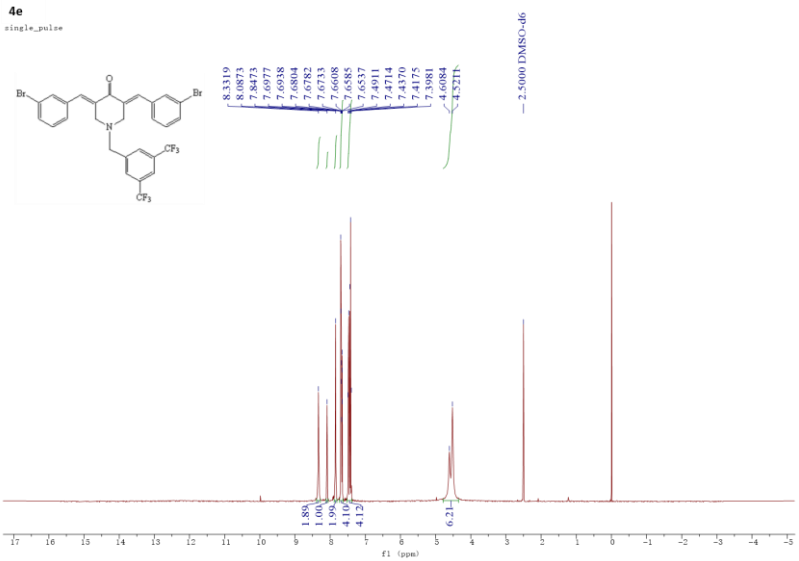
*[1]H NMR of (3E,5E)-3,5-bis(3-bromobenzylidene)-1-(3-fluorophenyl) piperidin-4-one (**4d**)*



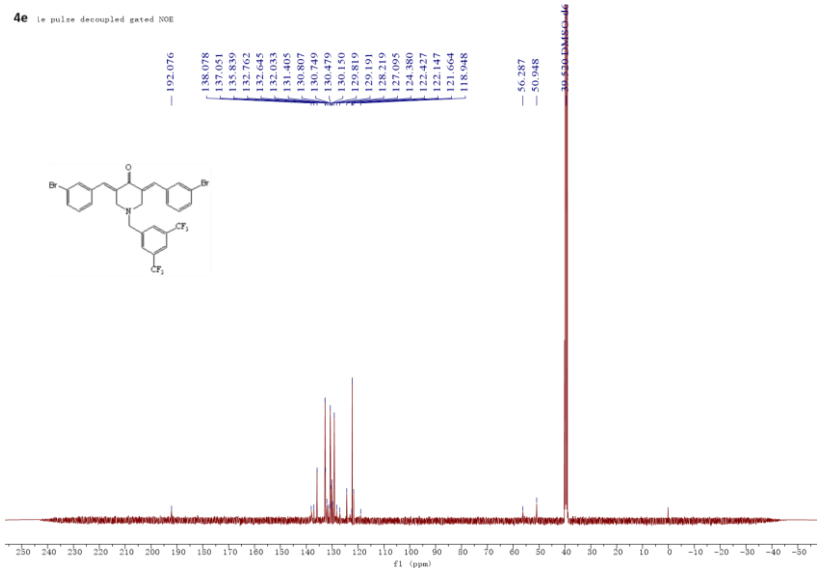
*[13]C NMR of (3E,5E)-3,5-bis(3-bromobenzylidene)-1-(3-fluorophenyl) piperidin-4-one (**4d**)*



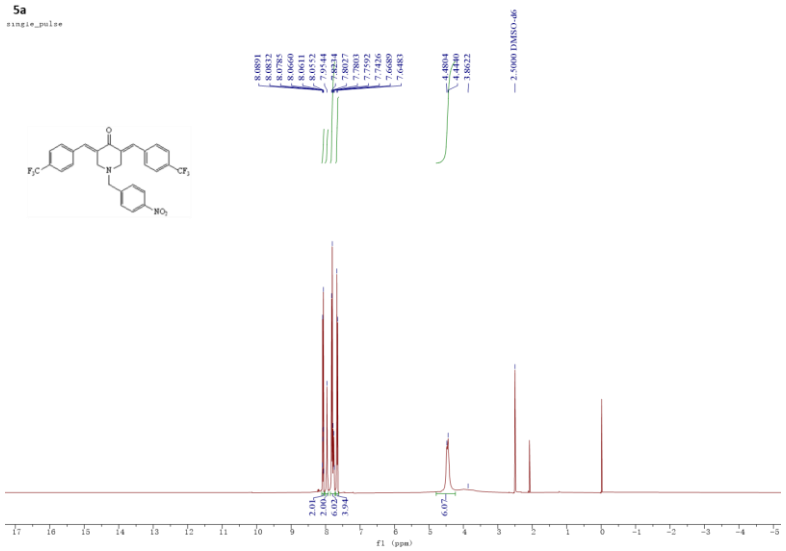
*[1]H NMR of (3E,5E)-1-(3,5-bis(trifluoromethyl)phenyl)-3,5-bis(3-bromo benzylidene)piperidin-4-one (**4e**)*



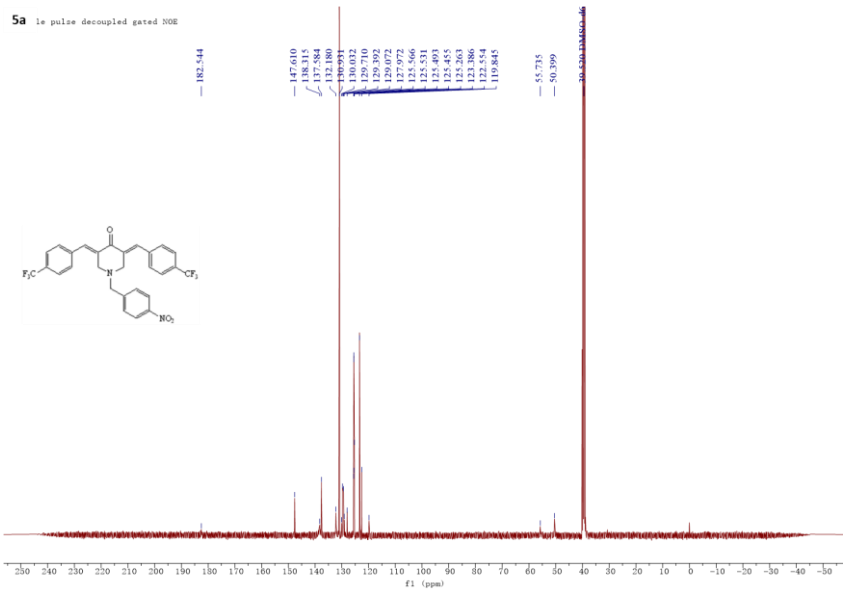
*^{13}C NMR of (3E,5E)-1-(3,5-bis(trifluoromethyl)phenyl)-3,5-bis(3-bromo benzylidene)piperidin-4-one (**4e**)*



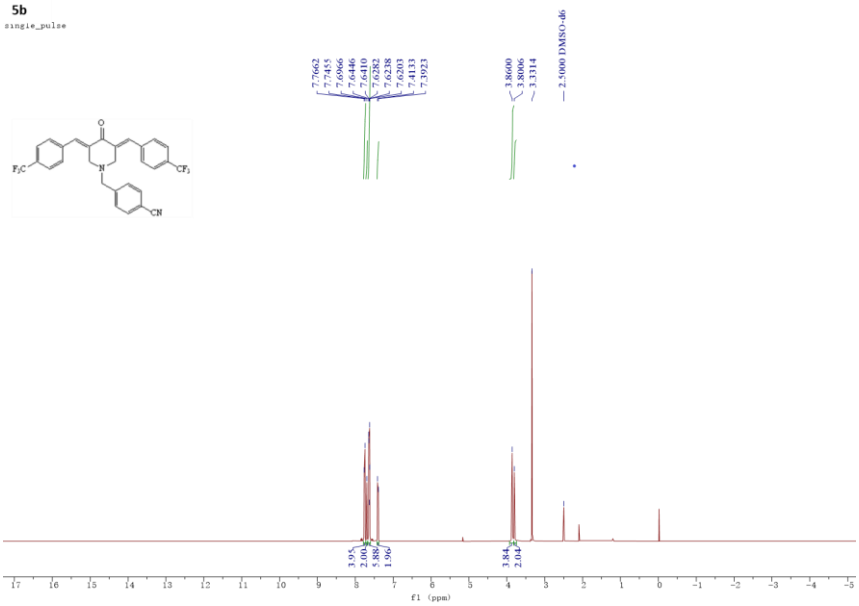
*^{1}H NMR of (3E,5E)-1-(4-nitrophenyl)-3,5-bis(4-(trifluoromethyl)benzyli dene)piperidin-4-one (**5a**)*



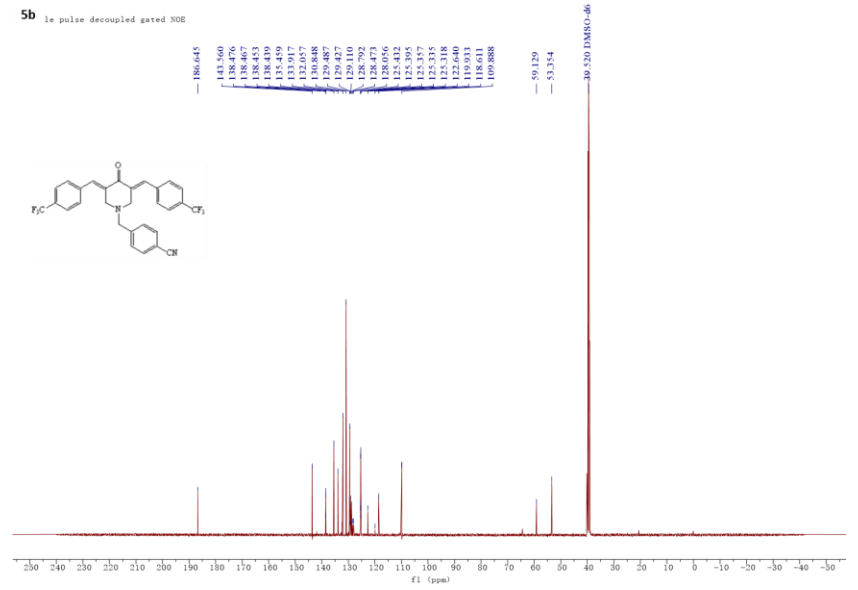
*^{13}C NMR of (3E,5E)-1-(4-nitrophenyl)-3,5-bis(4-(trifluoromethyl)benzyli dene)piperidin-4-one (**5a**)*



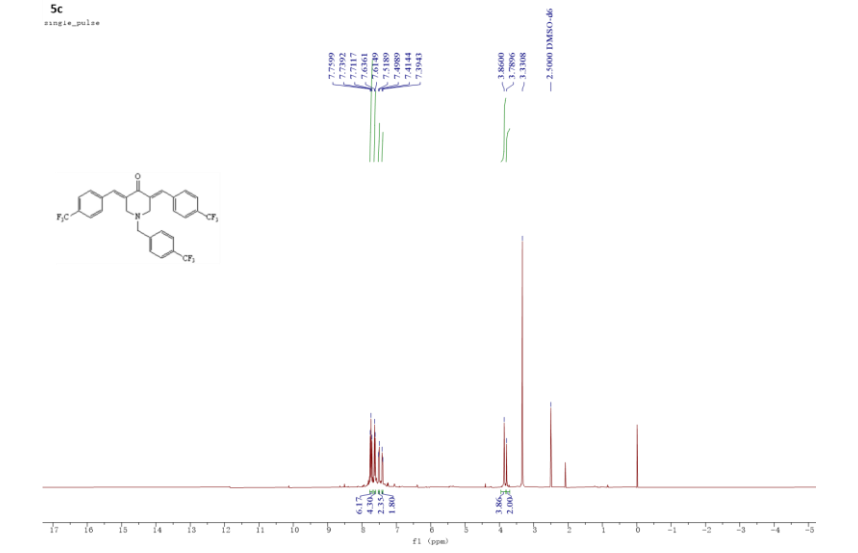
*^{1}H NMR of 4-((3E,5E)-4-oxo-3,5-bis(4-(trifluoromethyl)benzylidene) piperidin-1-yl) benzonitrile (**5b**)*



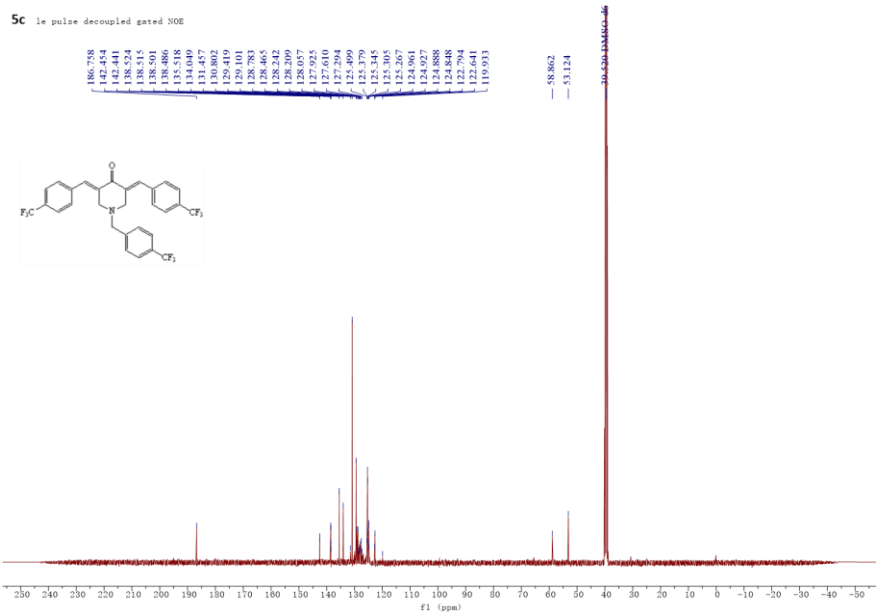
*^{13}C NMR of 4-((3E,5E)-4-oxo-3,5-bis(4-(trifluoromethyl)benzylidene) piperidin-1-yl) benzonitrile (**5b**)*



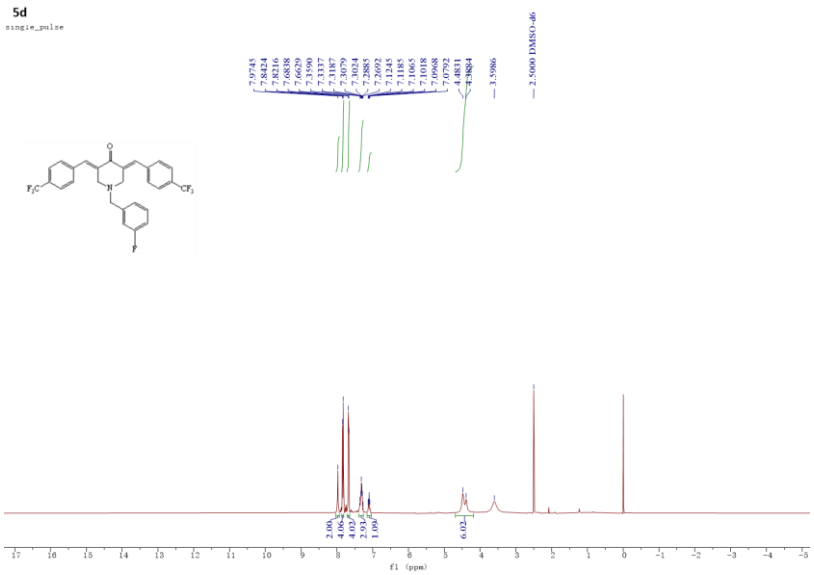
*^{1}H NMR of (3E,5E)-3,5-bis(4-(trifluoromethyl)benzylidene)-1-(4-(trifluoro methyl)phenyl)piperidin-4-one (**5c**)*



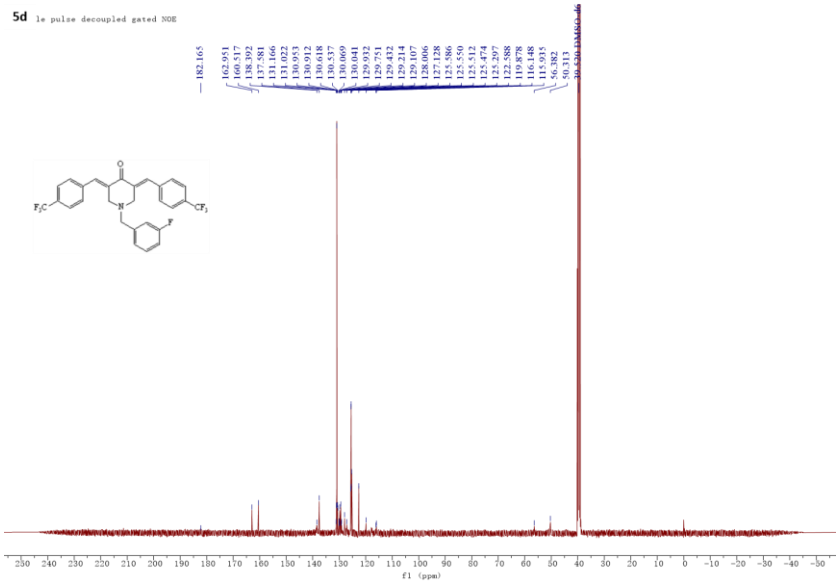
*^{13}C NMR of (3E,5E)-3,5-bis(4-(trifluoromethyl)benzylidene)-1-(4-(trifluoro methyl)phenyl)piperidin-4-one (**5c**)*



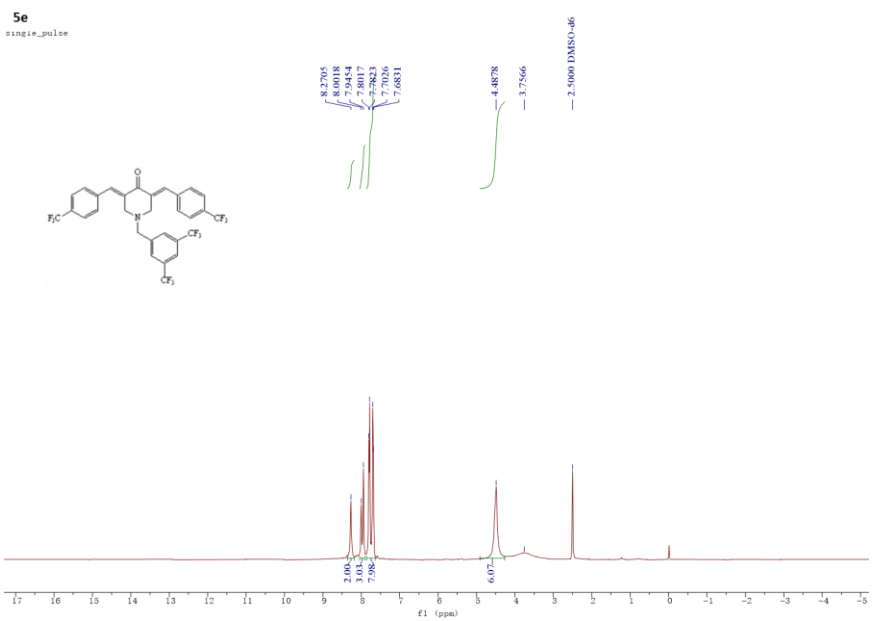
*^{1}H NMR of (3E,5E)-1-(3-fluorophenyl)-3,5-bis(4-(trifluoromethyl)benzyli dene)piperidin-4-one (**5d**)*



*^{13}C NMR of (3E,5E)-1-(3-fluorophenyl)-3,5-bis(4-(trifluoromethyl)benzyli dene)piperidin-4-one (**5d**)*



*^{1}H NMR of (3E,5E)-1-(3,5-bis(trifluoromethyl)phenyl)-3,5-bis(4-(trifluoro methyl)benzylidene)piperidin-4-one (**5e**)*



*^{13}C NMR of (3E,5E)-1-(3,5-bis(trifluoromethyl)phenyl)-3,5-bis(4-(trifluoro methyl)benzylidene)piperidin-4-one (**5e**)*