Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

L-Cysteine functionalized magnetic nanoparticles (LCMNP): a novel magnetically separable organocatalyst for one-pot synthesis of 2-amino-*4H*-chromene-3-carbonitriles in water

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Outline

1. **Experimental**
2. **Spectral data for synthesized compounds**
3. **Copy of ^{1}H NMR, ^{13}C NMR and IR of synthesized compounds**
4. **Figure 1S: A comparison between the FT-IR spectra of Fe_3O_4, Fe_3O_4@SiO_2, VMNP, L-cysteine and LCMNP material**

1. Experimental

1.1. General

1.2. General Procedure for the synthesis of L-cystein-modified magnetic nanoparticles (LCMNPs)

1.2.1. Preparation of Fe_3O_4 nanoparticles

Magnetic nanoparticles were prepared *via* co-precipitation of Fe (III) and Fe (II) ions in the presence of sodium hydroxide. In a canonical flask, a mixture of $FeCl_2.2H_2O$ (16 mmol, 2.6 g) and $FeCl_3.6H_2O$ (30 mmol, 8.1 g) was dissolved in 100 mL of deionized water. Then, the pH of this solution was increased to 11 by adding a 3 M solution of NaOH as drop wise (in a period of 5 minute) at 40 °C. Subsequently, the temperature of mixture was enhanced to 80 °C and the solution was stirred for 20 minute in this temperature. The magnetic nanoparticles as a dark solid were isolated from the solution by magnetic separation and washed with deionized water until pH 7 reached.

1.2.2. Preparation of $Fe_3O_4@SiO_2$ nanoparticles

$Fe_3O_4@SiO_2$ nanoparticles were prepared based on the literature with some modification: to a mixture of 125 mL of heptanes, 25 mL of i-PrOH, 20 mL of PEG-300, and 10 mL of water, 2 g of Fe_3O_4 was added. Then the mixture was stired by mechanical stirrer under N_2 gas for 30 minutes. 20 mL of tetraethyl orthosilicate (TEOS) was added to the mixture next and then the solution was stirred for 12 h at 30 °C. After the specified time, 10 mL of ammonia was added and the solution was stirred continuously for another 12 h. The precipitation was washed with ethanol (3 x 10) and collected by external magnetic field. The desired product was dried under vacuum overnight.

1.2.3. Synthesis of vinyl magnetic nanoparticle (VMNP)

In a three-necked flask (100 mL) containing 70 mL of dry chloroform, 10 g of Fe_3O_4 was charged. Then trimethoxy(vinyl)silane (3.54 g, 0.02 mol) was added to the reaction mixture drop-wise over a period of 5 min at room temperature. When the addition was completed, the mixture was stirred for 12 h at the refluxing temperature of chloroform. Then, the reaction mixture was filtered and the obtained solid was dried in a vacuum at 50 °C to obtain a vinyl MNP (VMNP) substrate.

1.2.4. Synthesis of L-cystein magnetic nanoparticles (LCMNPs) catalyst

For the synthesis of LCMNPs catalyst, 0.5 g of *L*-cystein was added in to a prepared solution containing 5g of VMNP in 30 mL chloroform in the presence of AIBN (1.0 mmol). Subsequently, the mixture was stirred for 12h at refluxing temperature of chloroform. The resulting precipitate was filtered through a celite pad, washed with water, dried in vacuum to afford the LCMNPs catalyst.

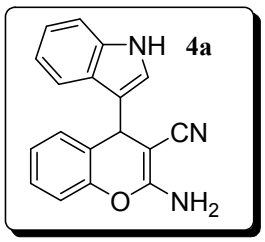
1.3. General Procedure for the synthesis of compounds

A mixture of nucleophile (indole, *N,N*-dimethylbenzenamine, malonitrile, TMSCN) (1.0 mmol), salicylaldehyde (1.0 mmol) and malonitrile (1.0 mmol) in presence of L-cysteine magnetic nanoparticles (LCMNPs) (0.05 g, 8.5 mol %) as catalyst in round bottom flask was stirred at 80 °C in water as a green solvent for appropriate time (Table 1). After completion of the reaction, as indicated by TLC, The catalyst was recovered magnetically by attaching a general magnet to the exterior of the reactor vessel and the reaction mixture was filtered and the remaining washed with warm ethanol (3 x 5 mL). All the

isolated products gave satisfactory spectral and physical data. The isolated catalyst could be recycled, see Supplementary data for details.

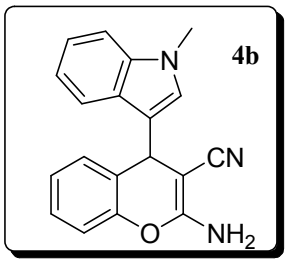
2. Spectral data for synthesized compounds:

1. ***2-amino-4-(1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4a)**



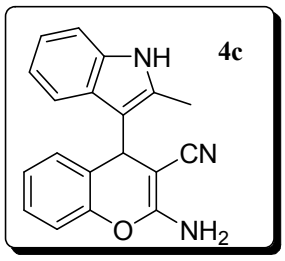
Yellow crystal (yield: 90%, 0.25 g); Mp: 321-325 ^{o}C. IR (KBr): 3888, 3440, 3379, 3348, 3201, 3055, 2923, 2854, 2360, 2206, 1620, 1566, 1481, 1388, 1334, 1249, 1226, 1157, 1095, 1064, 894, 871, 748, 586, 478, 423 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO/TMS) δ (ppm): 5.45 (s, 1H), 6.24-6.37 (m, 3H), 6.80-7.24 (m, 7H), 7.49 (s, 1H), 10.86 (s, 1H). ^{13}C-NMR (62.5 MHz, DMSO/TMS) δ (ppm): 30.6, 70.7, 89.6, 111.6, 116.1, 116.4, 117.9, 118.5, 120.9, 122.8, 123.7, 124.6, 127.5, 129.2, 136.6, 149.6, 156.9, 159.3; MS (m/z): 287 (M+). Anal. Calcd for $C_{18}H_{13}N_3O$: C, 75.25; H, 4.56; N, 14.63. Found: C, 76.05; H, 4.61; N, 14.75.

2. ***2-amino-4-(1-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4b)**



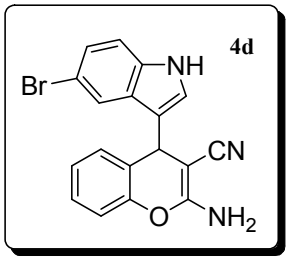
Yellow crystal (yield: 91%, 0.27 g); Mp: 240-243 ^{o}C. IR (KBr): 3440, 3332, 3240, 2923, 2214, 1620, 1566, 1473, 1396, 1326, 1249, 1226, 1157, 1056, 802, 748, 424 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 3.63 (s, 3H), 5.46 (s, 1H), 6.16-6.38 (m, 2H), 6.69-7.29 (m, 9H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 30.2, 32.1, 70.7, 89.6, 109.4, 114.9, 116.1, 117.3, 118.5, 119.0, 120.8, 123.7, 124.7, 126.9, 127.7, 129.1, 136.8, 149.6, 159.3; MS (m/z): 301 (M+). Anal. Calcd for $C_{19}H_{15}N_3O$: C, 75.73; H, 5.02; N, 13.94. Found: C, 75.81; H, 5.16; N, 14.01.

3. ***2-amino-4-(2-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4c)**

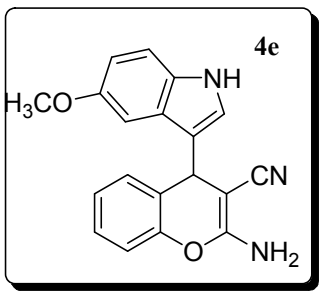


Orange crystal (yield: 88%, 0.26 g); Mp: 315-316 ^{o}C. IR (KBr): 3471, 3394, 3155, 2476, 2198, 1635, 1604, 1558, 1496, 1468, 1396, 1326, 1288, 1203, 1172, 1033, 740 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 3.31 (s, 3H), 5.45 (s, 1H), 6.41 (s, 2H), 6.79-6.82 (m, 1H), 6.91 (s, 2H), 7.05 (d, 2H, *J* = 7.5 Hz), 7.10-7.24 (m, 3H), 10.87 (s, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 11.41, 29.3, 70.9, 89.3, 110.6, 113.5, 116.2, 117.1, 118.5, 120.2, 123.7, 124.3, 126.3, 127.5, 129.2, 135.2, 149.2, 156.9, 159.2; MS (m/z): 301 (M+). Anal. Calcd for $C_{19}H_{15}N_3O$: C, 75.73; H, 5.02; N, 13.94. Found: C, 75.09; H, 5.16; N, 14.05.

4. ***2-amino-4-(5-bromo-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4d)**



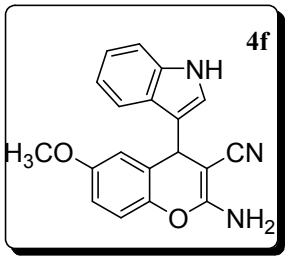
Yellow crystal (yield: 78%, 0.28 g); Mp: 260-262 ^{o}C. IR (KBr): 3440, 3340, 3147, 2206, 1635, 1566, 1473, 1396, 1334, 1249, 1218, 1072, 763 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 5.24 (s, 1H), 6.10-6.20 (m, 3H), 6.73-7.00 (m, 5H), 7.18-7.27 (m, 2H), 10.99 (s, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 35.5, 50.3, 76.0, 94.7, 116.4, 118.9, 121.4, 123.2, 125.8, 128.6, 129.1, 129.8, 132.9, 134.3, 140.5, 154.9, 162.1, 164.6; MS (m/z): 365 (M+). Anal. Calcd for $C_{18}H_{12}BrN_3O$: C, 59.03; H, 3.30; N, 11.47. Found: C, 60.10; H, 3.36; N, 11.56.



5. ***2-amino-4-(5-methoxy-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4e)**

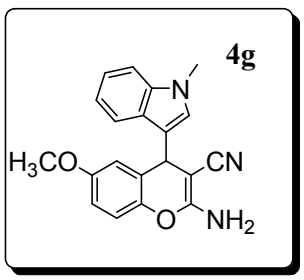
Yellow crystal (yield: 92%, 0.28 g); Mp: 192-194 ^{o}C. IR (KBr): 3433, 3340, 2923, 2854, 2183, 1651, 1573, 1481, 1396, 1257, 1203, 1172, 1041, 756 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 3.91, (s, 3H), 4.70 (s, 1H), 6.43-6.50 (m, 2H), 6.58 (s, 2H), 6.75-6.86 (m, 3H), 6.91-7.00 (m, 3H), 10.53 (s, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 32.3, 55.0, 56.1, 100.8, 110.4, 112.1, 115.6, 118.5, 120.8, 123.5, 123.7, 124.3, 125.5, 127.7, 129.2, 131.9, 148.4, 152.6, 160.1; MS (m/z): 317 (M+). Anal. Calcd fsor $C_{19}H_{15}N_3O_2$: C, 71.91; H, 4.76; N, 13.24. Found: C, 72.05; H, 4.86; N, 13.34.

6. ***2-amino-4-(1H-indol-3-yl)-6-methoxy-4H-chromene-3-carbonitrile*** **(4f)**



Orange crystal (yield: 86%, 0.26 g); Mp: 198-200 ^{o}C. IR (KBr): 3386, 3348, 3247, 2900, 2206, 1620, 1573, 1473, 1411, 1319, 1249, 1172, 1056, 972, 856, 786 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 3.86 (s, 3H), 5.35 (s, 1H), 6.20-6.80 (m, 5H), 6.94-7.01 (m, 3H), 7.16-7.34 (m, 1H), 7.48 (s, 1H), 10.86 (s, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 25.3, 55.1, 69.2, 78.4, 90.2, 100.8, 111.3, 113.6, 115.5, 116.4, 117.8, 120.7, 125.1, 127.5, 134.3, 136.4, 150.4, 156.3, 159.3; MS (m/z): 317 (M+). Anal. Calcd for $C_{19}H_{15}N_3O_2$: C, 71.91; H, 4.76; N, 13.24. Found: C, 72.06; H, 4.79; N, 13.32.

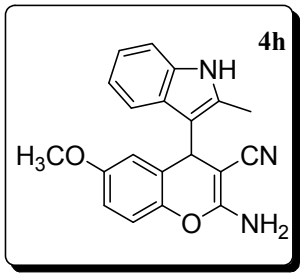
7. ***2-amino-6-methoxy-4-(1-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4g)**



Yellow crystal (yield: 88%, 0.28 g); Mp: 290-293 ^{o}C. IR (KBr): 3448, 3371, 3301, 3178, 2931, 2839, 2198, 1627, 1558, 1481, 1396, 1326, 1203, 1172, 1126, 1072, 1033, 964, 833, 794, 740 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm):

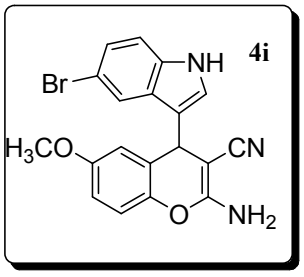
3.66 (s, 6H), 5.38 (s, 1H), 6.23 (s, 1H), 6.39 (s, 1H), 6.55 (d, 1H, *J* = 6.0 Hz), 6.64 (s, 1H), 6.85-6.88 (m, 1H), 7.04 (s, 2H), 7.28 (d, 2H, *J* = 7.0 Hz), 7.371 (s, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 29.7, 32.2, 55.2, 70.7, 89.8, 100.9, 109.7, 110.4, 116.7, 117.6, 118.5, 121.0, 125.2, 126.8, 129.7, 136.9, 150.3, 156.8, 158.5, 159.3; MS (m/z): 331 (M+). Anal. Calcd for $C_{20}H_{17}N_3O_2$: C, 72.49; H, 5.17; N, 12.68. Found: C, 72.53; H, 5.26; N, 12.71.

8. ***2-amino-6-methoxy-4-(2-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4h)**



Yellow crystal (yield: 87%, 0.28 g); Mp: > 326 °C (dec). IR (KBr): 3471, 3394, 3155, 2476, 2198, 1635, 1604, 1558, 1496, 1468, 1396, 1326, 1288, 1203, 1172, 1033, 740 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 2.45 (s, 3H), 3.68 (s, 3H), 5.35 (s, 1H), 6.41 (s, 2H), 6.51-6.55 (m, 1H), 6.62 (s, 1H), 7.76-6.82 (m, 1H), 6.89-6.93 (m, 2H), 7.17-7.20 (m 2H), 10.87 (s, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 11.37, 28.8, 55.1, 70.9, 89.4, 100.5, 100.6, 113.6, 116.2, 117.1, 118.5, 120.2, 126.3, 129.8, 131.4, 135.2, 149.8, 156.9, 158.4, 159.1; MS (m/z): 331 (M+). Anal. Calcd for $C_{20}H_{17}N_3O_2$: C, 72.49; H, 5.17; N, 12.68. Found: C, 72.56; H, 5.26; N, 12.77.

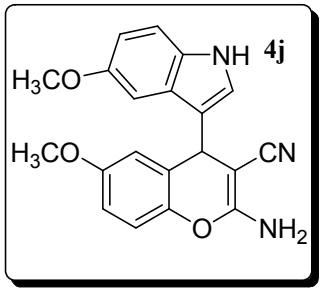
9. ***2-amino-4-(5-bromo-1H-indol-3-yl)-6-methoxy-4H-chromene-3-carbonitrile*** **(4i)**



Orange crystal (yield: 83%, 0.32 g); > 326 °C (dec). IR (KBr): 3425, 3355, 3240, 2846, 2198, 1604, 1558, 1496, 1404, 1195, 1172, 1033, 786 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 3.70 (s, 3H), 5.39 (s, 1H), 6.28 (s, 1H), 6.47-6.52 (m, 1H), 6.62-6.63 (m, 1H), 7.01 (s, 3H), 7.24-7.70 (m, 3H), 11.17

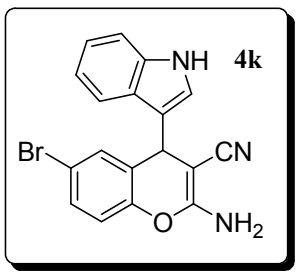
(s, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 21.9, 55.2, 71.6, 89.1, 96.5, 101.2, 110.1, 113.7, 116.1, 120.3, 121.5, 124.3, 129.4, 135.2, 138.5, 141.2, 146.4, 150.1, 158.7; MS (m/z): 395 (M+). Anal. Calcd for $C_{19}H_{14}BrN_3O_2$: C, 57.59; H, 3.56; N, 10.60. Found: C, 57.64; H, 3.67; N, 11.01.

10. ***2-amino-6-methoxy-4-(5-methoxy-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4j)**



Yellow crystal (yield: 91%, 0.31 g); Mp: 198-200 ^{o}C. IR (KBr): 3463, 3348, 3224, 2831, 2198, 1620, 1589, 1558, 1496, 1481, 1388, 1288, 1195, 1172, 1118, 1056, 794 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 3.39 (s, 3H), 3.64 (s, 3H), 5.34 (s, 1H), 6.19-6.72 (m, 7H), 7.07-7.14 (m, 1H), 7.41 (s, 1H), 10.65 (s, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 29.9, 54.9, 55.1, 70.7, 89.8, 100.8, 110.1, 110.3, 112.1, 116.7, 117.9, 123.4, 125.2, 129.8, 131.8, 150.4, 152.6, 156.8, 158.5, 159.3; MS (m/z): 347 (M+). Anal. Calcd for $C_{20}H_{17}N_3O_3$: C, 69.15; H, 4.93; N, 12.10. Found: C, 69.25; H, 5.06; N, 12.14.

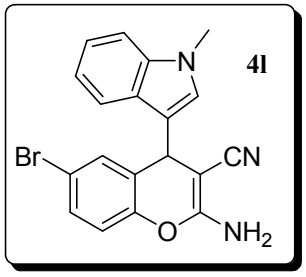
11. ***2-amino-6-bromo-4-(1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4k)**



Orange crystal (yield: 88%, 0.31 g); Mp: > 325^{o}C (dec). IR (KBr): 3448, 3386, 3247, 2900, 2206, 160, 1573, 1473, 1411, 1319, 1249, 1172, 1056, 972, 856, 786 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 5.46 (s, 1H), 6.26 (s, 2H), 6.44 (s, 2H), 6.81 (t, 1H, J = 7.5 Hz), 6.97 (t, 1H, J = 7.0 Hz),

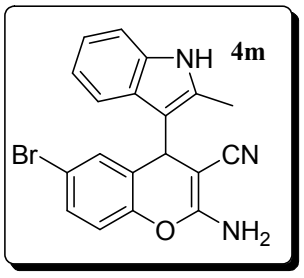
7.17 (d, 1H, *J* = 8.0 Hz), 7.26-7.27 (m, 1H), 7.30-7.31 (m, 1H), 7.55-7.56 (m, 1H), 10.95 (s, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 30.5, 88.8, 111.8, 115.0, 116.2, 117.3, 117.9, 118.5, 118.6, 121.0, 123.1, 127.1, 130.3, 131.4, 136.6, 148.9, 156.9, 159.3; MS (m/z): 365 (M+). Anal. Calcd for $C_{18}H_{12}BrN_3O$: C, 59.03; H, 3.30;; N, 11.47. Found: C, 59.14; H, 3.38; N, 11.51.

12. ***2-amino-6-bromo-4-(1-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4l)**



Orange crystal (yield: 94%, 0.34 g); Mp: 301-304 ^{o}C. IR (KBr): 3371, 3456, 2923, 2206, 1627, 1558, 1473, 1396, 1326, 1249, 740 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 3.69 (s, 3H), 5.50 (s, 1H), 6.29 (s, 1H), 6.47 (s, 1H), 6.77 (s, 2H), 6.84-6.90 (m, 2H), 7.06-7.09 (m, 2H), 7.24-7.33 (m, 2H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 30.2, 32.1, 70.7, 89.6, 109.4, 114.9, 116.1, 118.1, 118.5, 119.0, 120.8, 123.7, 124.7, 126.9, 127.5, 129.1, 130.6, 156.8, 159.3; MS (m/z): 379 (M+). Anal. Calcd for $C_{19}H_{14}BrN_3O$: C, 60.02; H, 3.71; N, 11.05. Found: C, 60.13; H, 3.89; N, 11.67.

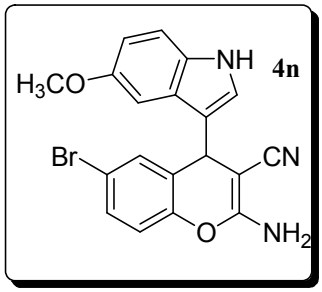
13. ***2-amino-6-bromo-4-(2-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4m)**



Orange crystal (yield: 90%, 0.34 g); 336-338 ^{o}C. IR (KBr): 3448, 3363, 3332, 3147, 2715, 2206, 1627, 1558, 1473, 1396, 1249, 1226, 1188, 1149, 1072, 817, 740 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 2.45 (s, 3H), 5.49 (s, 1H), 6.50 (s, 2H), 6.82 (t, 1H, *J* = 7.0 Hz), 6.94 (t, 1H, *J* = 7.0 Hz), 7.05-7.09 (m, 2H), 7.20-7.24 (m, 2H), 7.29-7.34 (m, 1H). ^{13}C-NMR (62.5 MHz, DMSO-

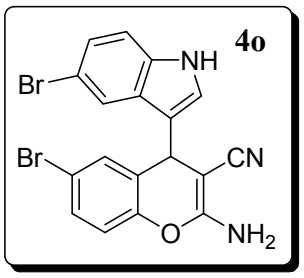
d_6/TMS) δ (ppm): 11.3, 29.2, 71.1, 88.7, 110.8, 113.0, 115.0, 116.0, 116.8, 118.8, 120.4, 126.8, 130.4, 131.3, 131.8, 135.2, 148.5, 156.9, 159.2; MS (m/z): 379 (M+). Anal. Calcd for $C_{19}H_{14}BrN_3O$: C, 60.02; H, 3.71; N, 11.05. Found: C, 60.15; H, 3.76; N, 11.19.

14. ***2-amino-6-bromo-4-(5-methoxy-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4n)**



Orange crystal (yield: 93%, 0.36 g); Mp: > 330 °C (dec). IR (KBr): 3332, 3193, 2399, 2206, 1620, 1558, 1473, 1396, 1326, 1249, 1180, 1056, 918, 624 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 3.59 (s, 3H), 5.43 (s, 1H), 6.27 (s, 2H), 6.44 (s, 2H), 6.70 (s, 1H), 7.08 (d, 1H, *J* = 8.5 Hz), 7.18 (d, 1H, *J* = 8.7 Hz), 7.29-7.31 (m, 1H), 7.46-7.47 (m, 1H), 10.78 (s, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 30.4, 55.0, 70.8, 88.8, 100.4, 110.4, 112.3, 115.0, 116.3, 117.0, 118.5, 123.7, 125.1, 127.2, 131.7, 149.0, 152.7, 156.8, 159.4; MS (m/z): 395 (M+). Anal. Calcd for $C_{19}H_{14}BrN_3O_2$: C, 57.59; H, 3.56; N, 10.60. Found: C, 58.06; H, 3.86; N, 10.74.

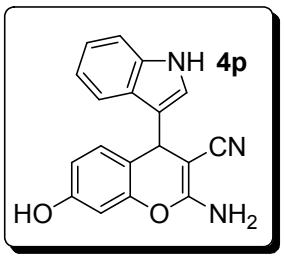
15. ***2-amino-6-bromo-4-(5-bromo-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4o)**



Yellow crystal (yield: 88%, 0.39 g); Mp: > 390°C (dec). IR (KBr): 3348, 3209, 2854, 2206, 1612, 1542, 1473, 1388, 1049 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 5.47 (s, 1H), 6.33 (s, 1H), 6.49 (s, 1H), 7.07-7.13 (m, 2H), 7.26-7.36 (m, 4H), 7.57-7.58 (m, 1H), 11.18 (s, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 35.4, 76.1, 93.9, 116.6, 119.1, 120.4, 122.6, 123.9, 125.5, 128.8, 130.1, 132.2, 135.8, 136.5, 140.5, 154.2, 162.1, 164,7; MS (m/z): 442

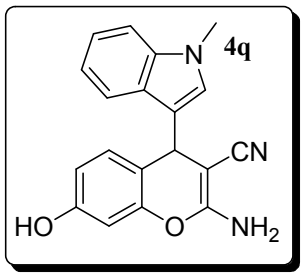
(M+). Anal. Calcd for $C_{18}H_{11}Br_2N_3O$: C, 48.57; H, 2.49; N, 9.44. Found: C, 48.55; H, 2.56; N, 10.01.

16. ***2-amino-7-hydroxy-4-(1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4p)**



Orange crystal (yield: 86%, 0.25 g); Mp: > 269 ^oC (dec). IR (KBr): 3348, 3217, 2854, 2206, 1620, 1512, 1473, 1404, 1257, 1188, 840, 794, 416 cm^{-1}. ^1H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 5.29 (s, 1H), 6.17 (s, 1H), 6.32 (s, 1H), 6.43 (s, 1H), 6.77 (s, 2H), 6.92 (d, 2H, *J* = 7.5 Hz), 7.23-7.29 (m, 2H), 7.37 (s, 1H), 7.46 (s, 1H), 10.83 (s, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 25.6, 70.6, 89.9, 100.8, 111.5, 113.8, 115.0, 116.6, 118.3, 120.8, 124.9, 125.9, 129.7, 153.1, 156.6, 159.2, 161.9, 166.1 ; MS (m/z): 303 (M+). Anal. Calcd for $C_{18}H_{13}N_3O_2$: C, 71.28; H, 4.32; N, 13.85. Found: C, 71.45; H, 4.46; N, 13.99.

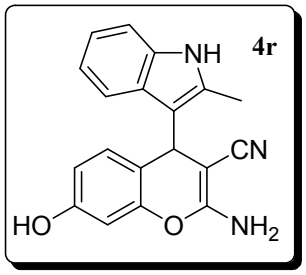
17. ***2-amino-7-hydroxy-4-(1-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4q)**



Yellow crystal (yield: 89%, 0.27 g); Mp: > 326 ^oC (dec). IR (KBr): 3448, 3348, 2923, 2615, 2206, 1620, 1566, 1473, 1396, 1326, 1249, 1195, 1064, 748, 424 cm^{-1}. ^1H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 3.66, (s, 3H), 5.34 (s, 1H), 6.20 (s, 2H), 6.37-6.41 (m, 2H), 6.46-6.47 (m, 1H), 6.86 (t, 1H, *J* = 7.5 Hz), 6.95-7.06 (m, 2H), 7.27 (s, 1H), 7.31 (s, 1H), 7.36 (s, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 29.7, 32.2, 70.7, 90.0, 102.3, 109.7, 11.5, 115.1, 116.5, 117.8, 118.5, 121.1, 125.3, 126.7, 129.7, 136.9, 150.2, 156.6, 159.3; MS (m/z):

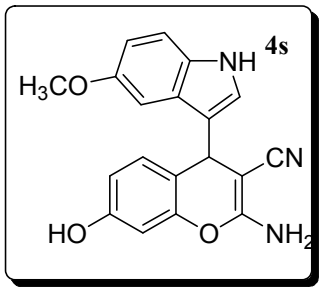
317 (M+). Anal. Calcd for $C_{19}H_{15}N_3O_2$: C, 71.91; H, 4.76; N, 13.24. Found: C, 71.75; H, 7.96; N, 13.10.

18. ***2-amino-7-hydroxy-4-(2-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4r)**



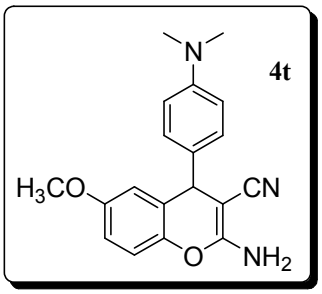
Orange crystal (yield: 84%, 0.26 g); Mp: > 269 °C (dec). IR (KBr): 3433, 3386, 3332, 3232, 2846, 2221, 1620, 1573, 1473, 1404, 1249, 1188, 1056, 856, 779, 748 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 2.43, (s, 3H), 5.29 (s, 1H), 6.40 (s, 4H), 6.79-6.87 (m, 3H), 7.17 (s, 2H), 9.54 (s, 1H), 10.84 (s, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 11.3, 28.8, 70.9, 89.7, 102.1, 110.6, 111.7, 113.8, 114.6, 116.3, 118.5, 120.2, 126.5, 129.8, 131.3, 135.2, 149.7, 156.6, 159.1; MS (m/z): 317 (M+). Anal. Calcd for $C_{19}H_{15}N_3O_2$: C, 71.91; H, 4.76; N, 13.24. Found: C, 72.07; H, 4.76; N, 13.46.

19. ***2-amino-7-hydroxy-4-(5-methoxy-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4s)**



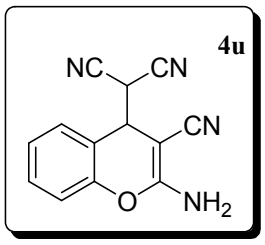
Orange crystal (yield: 90%, 0.29 g); Mp: 225-227 °C. IR (KBr): 3749, 3394, 3247, 2923, 2206, 1620, 1566, 1473, 1396, 1172 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 3.58, (s, 3H), 5.27 (s, 1H), 6.19 (s, 1H), 6.33 (s, 1H), 6.44 (s, 1H), 6.53 (s, 1H), 6.63 (s, 2H), 6.70 (s, 1H), 7.01 (s, 1H), 7.17 (d, 1H, J = 3.5 Hz), 7.38 (s, 1H), 10.65 (s, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 34.2, 54.9, 67.0, 89.9, 91.0, 100.8, 102.1, 111.7, 115.1, 116.2, 123.5, 125.3, 126.4, 129.8, 131.8, 150.3, 152.5, 156.8, 159.2; MS (m/z): 333 (M+). Anal. Calcd for $C_{19}H_{15}N_3O_3$: C, 68.46; H, 4.54; N, 12.61. Found: C, 68.55; H, 4.66; N, 12.74.

20. ***2-amino-4-(4-(dimethylamino)phenyl)-6-methoxy-4H-chromene-3-carbonitrile*** **(4t)**



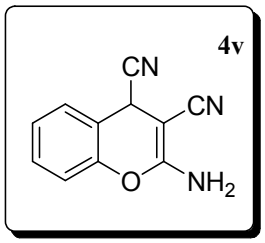
Yellow crystal (yield: 83%, 0.26 g); Mp: > 301 ^{o}C (dec). IR (KBr): 3448, 3355, 3232, 2839, 2198, 1635, 1604, 1558, 1512, 1404, 1296, 1172, 1118, 1033, 786 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 3.34 (s, 6H), 3.68 (s, 3H), 4.80 (s, 1H), 6.28 (s, 1H), 6.46-6.51 (m, 2H), 6.64-6.81 (m, 4H), 7.02 (s, 2H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 21.8, 30.5, 34.2, 55.1, 85.7, 101.3, 109.6, 110.0, 111.0, 113.5, 116.5, 129.4, 129.6, 131.8, 134.7, 141.4, 150.9, 152.5, 159.3; MS (m/z): 321 (M+). Anal. Calcd for $C_{19}H_{19}N_3O_2$: C, 71.01; H, 5.96; N, 13.08. Found: C, 71.05; H, 6.06; N, 13.64.

21. ***2-(2-amino-3-cyano-4H-chromen-4-yl)malononitrile*** **(4u)**



Yellow crystal (yield: 88%, 0.20 g); Mp: > 332 ^{o}C (dec). IR (KBr): 3386, 3348, 3178, 2893, 2198, 1641, 1558, 1604, 1488, 1411, 1350, 1272, 1234, 1072, 756 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 3.30 (s, 1H), 4.90 (s, 1H), 6.65 (s, 1H), 7.04 (s, 1H), 7.19 (s, 2H), 7.39-7.40 (m, 2H). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 30.3, 34.6, 83.6, 113.3, 116.2, 116.7, 117.7, 124.0, 128.9, 130.0, 151.5, 156.8, 160.3; MS (m/z): 321 (M+). Anal. Calcd for $C_{19}H_{19}N_3O_2$: C, 71.01; H, 5.96; N, 13.08. Found: C, 71.10; H, 6.03; N, 13.29.

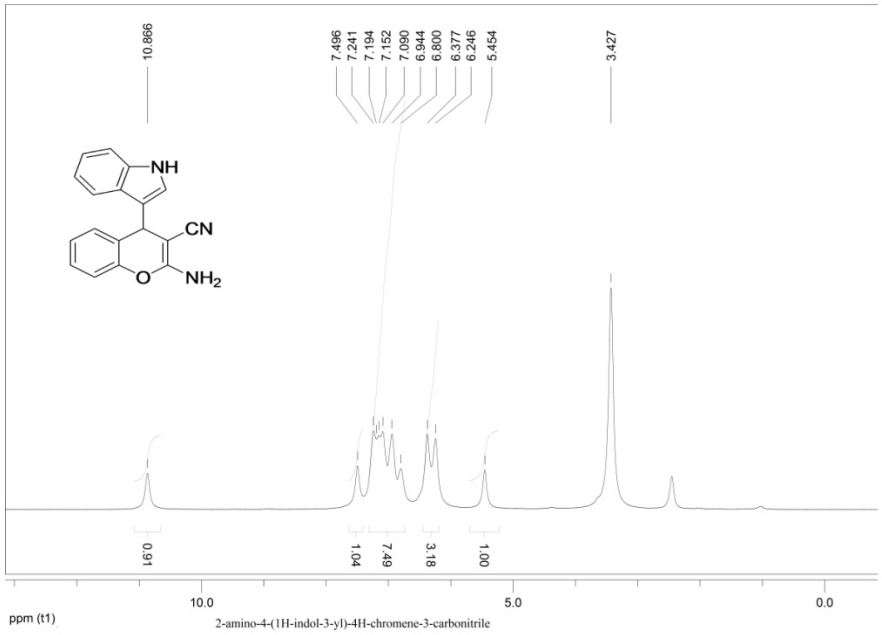
22. ***2-amino-4H-chromene-3,4-dicarbonitrile*** **(4v)**

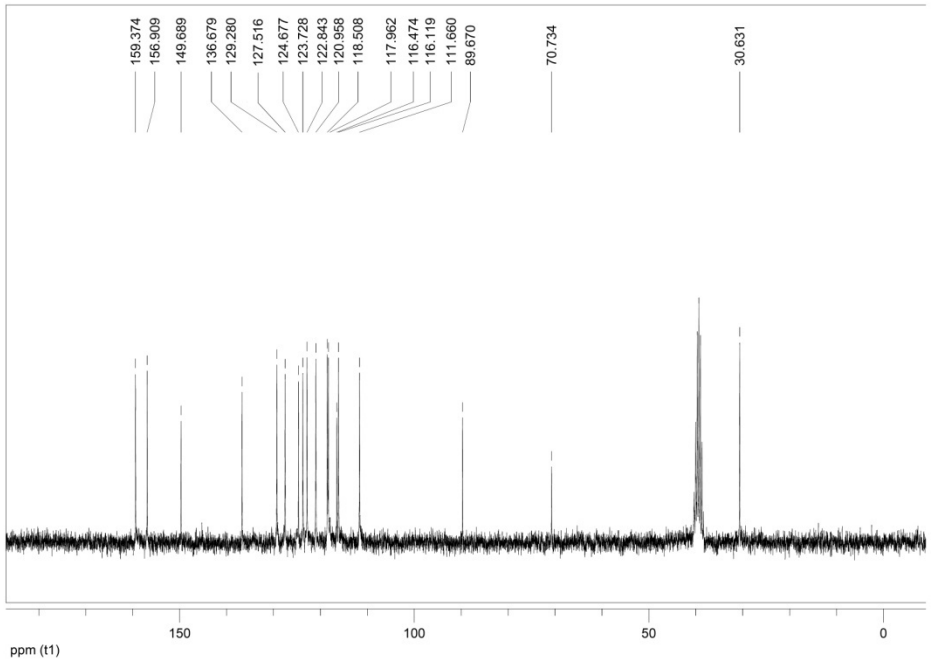


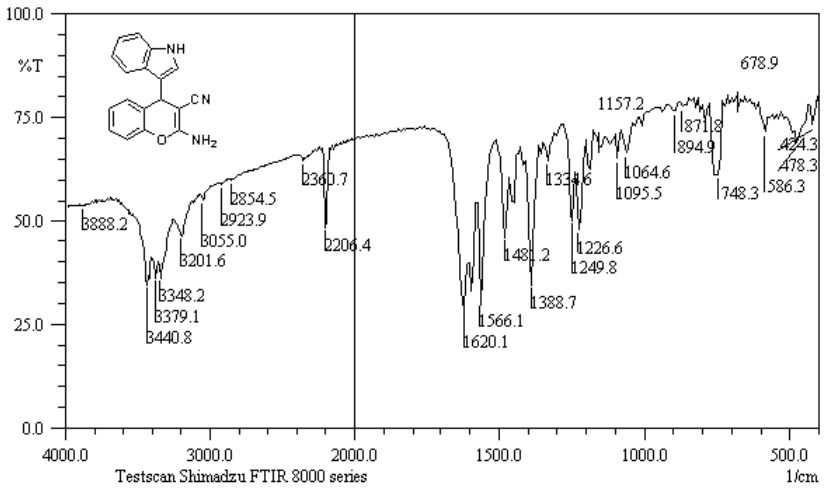
Yellow crystal (yield: 90%, 0.17 g); Mp: > 312 ^{o}C (dec). IR (KBr): 3386, 3348, 3178, 2893, 2198, 1641, 1558, 1604, 1488, 1411, 1350, 1272, 1234, 1072, 756 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d$_6$/TMS) δ (ppm): 3.30 (s, 1H), 4.90 (s, 1H), 6.65 (s, 1H), 7.04 (s, 1H), 7.19 (s, 2H), 7.39-7.40 (m, 2H). ^{13}C-NMR (62.5 MHz, DMSO-d$_6$/TMS) δ (ppm): 25.4, 85.4, 115.0, 116.6, 117.4, 119.1, 121.1, 124.6, 125.2, 134.6, 160.1; MS (m/z): 197 (M+). Anal. Calcd for $C_{11}H_7N_3O$: C, 67.00; H, 3.58; N, 21.31. Found: C, 67.07; H, 3.66; N, 21.39.

3. Copy of ^{1}H NMR, ^{13}C NMR and IR of synthesized compounds

1. ***2-amino-4-(1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4a)**

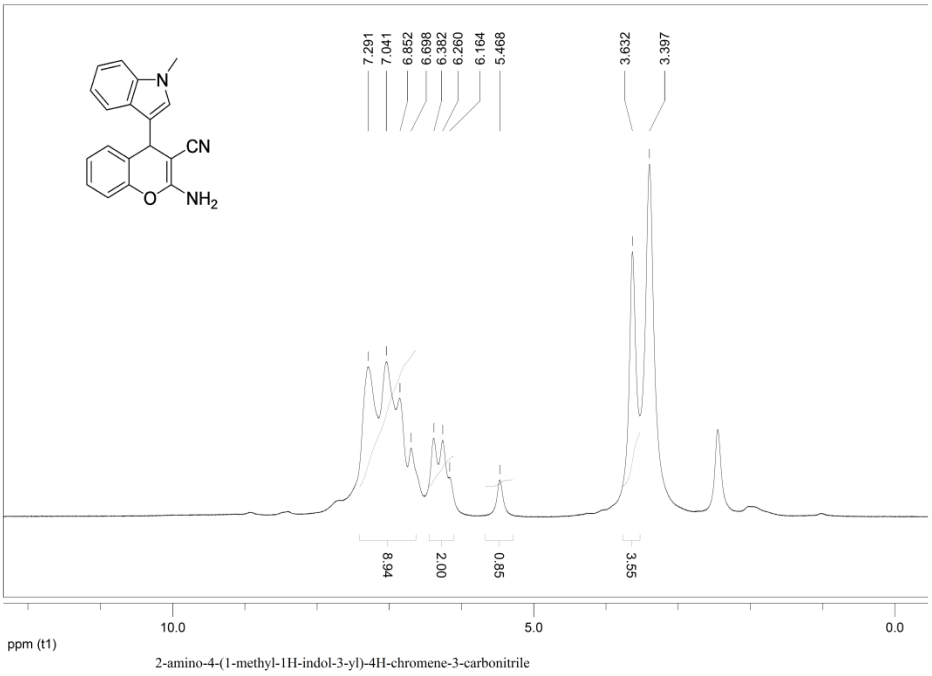

10.866
7.496
7.241
7.194
7.152
7.090
6.944
6.800
6.377
6.246
5.454
3.427
NH
CN
O
NH2
0.91
1.04
7.49
3.18
1.00
10.0
5.0
0.0
ppm (t1)
2-amino-4-(1H-indol-3-yl)-4H-chromene-3-carbonitrile

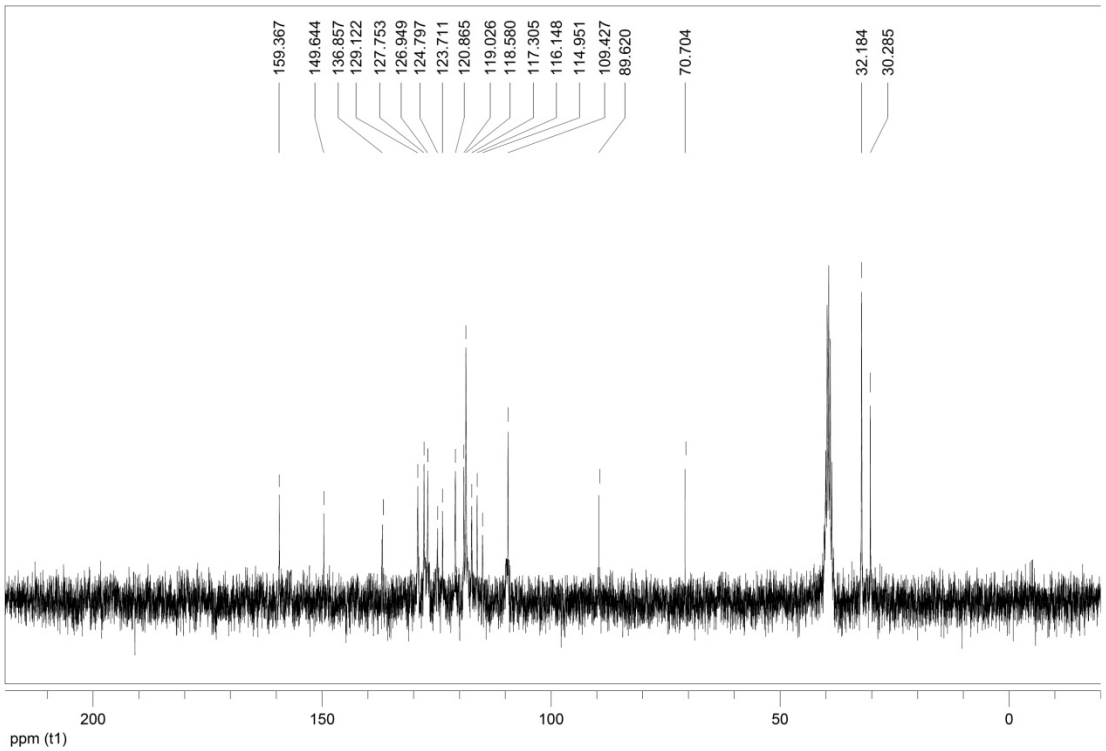

159.374
156.909
149.689
136.679
129.280
127.516
124.677
123.728
122.843
120.958
118.508
117.962
116.474
116.119
111.660
89.670
70.734
30.631
150
100
50
0
ppm (t1)

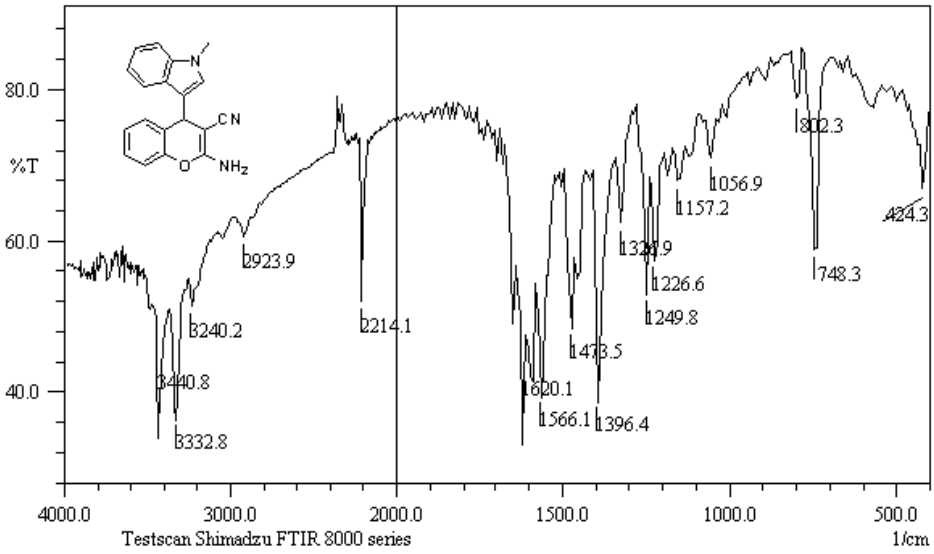


2-amino-4-(1H-indol-3-yl)-4H-chromene-3-carbonitrile

2. *2-amino-4-(1-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile* (4b)

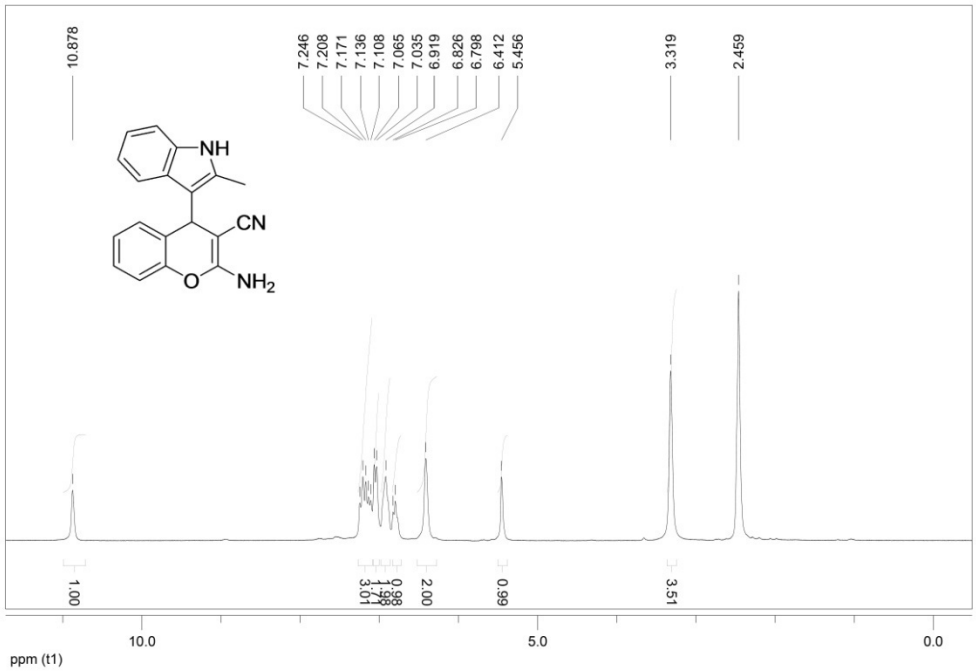




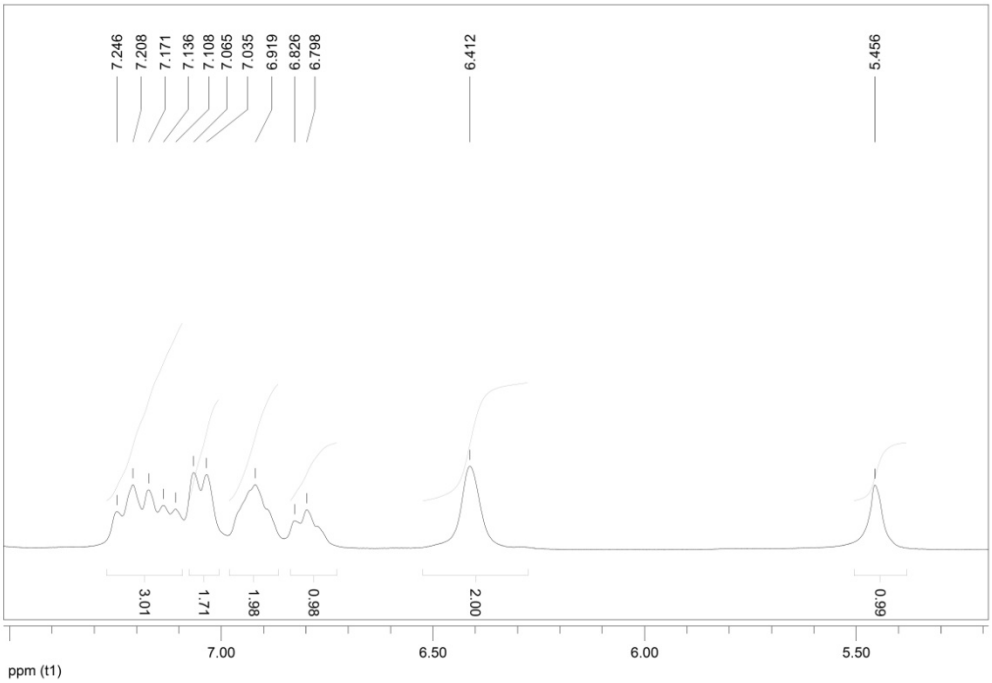


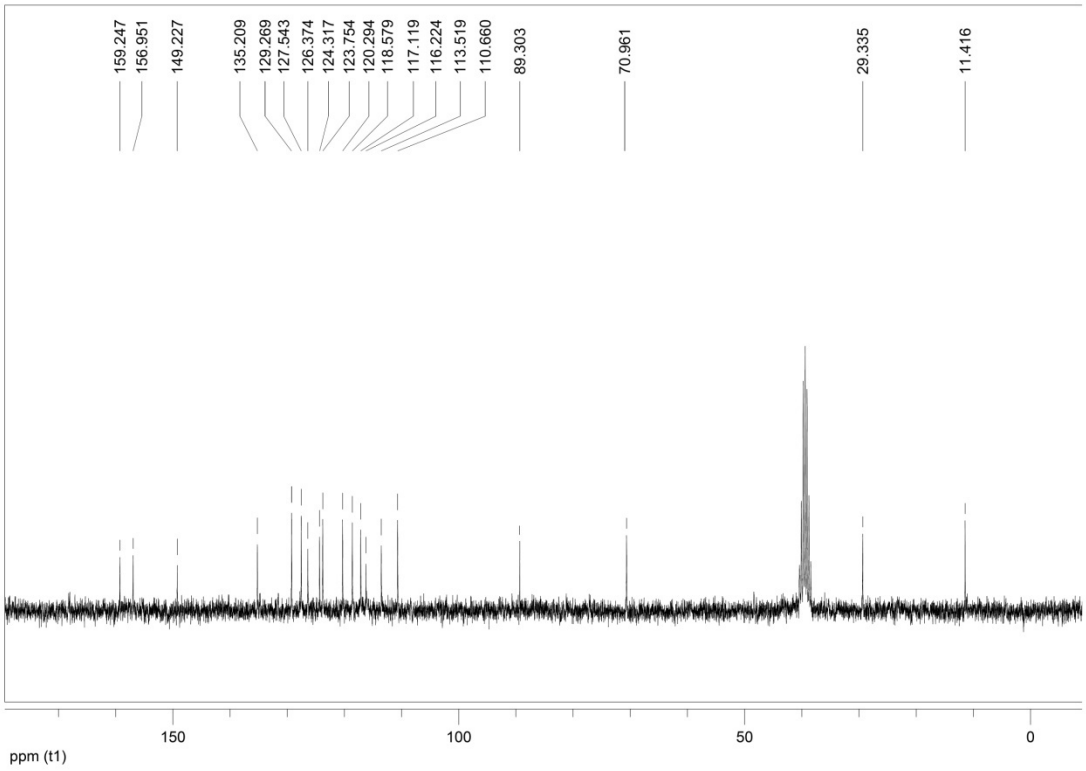
2-amino-4-(1-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile

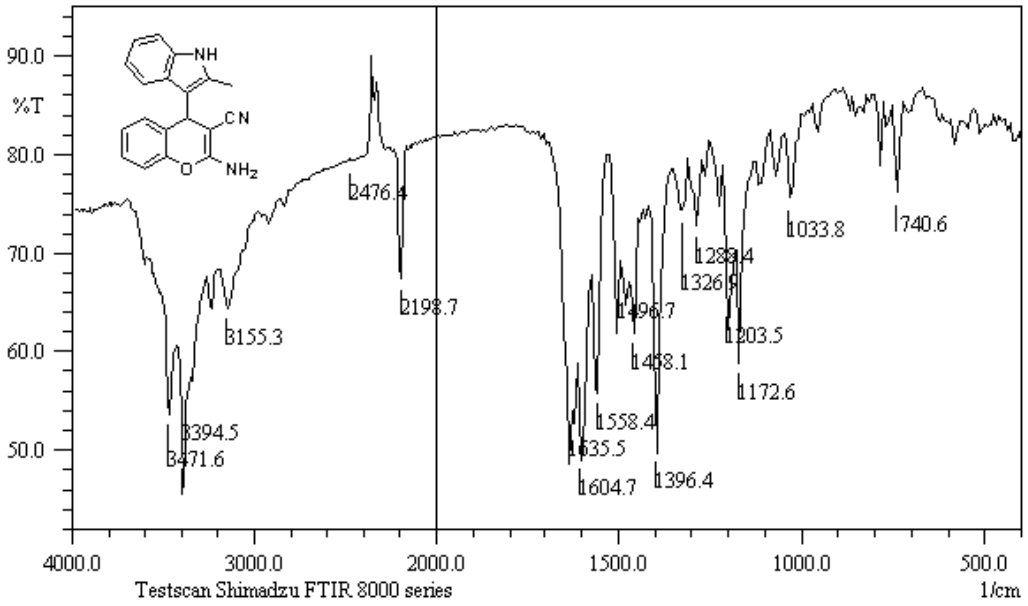
3. ***2-amino-4-(2-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4c)**



2-amino-4-(2-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile

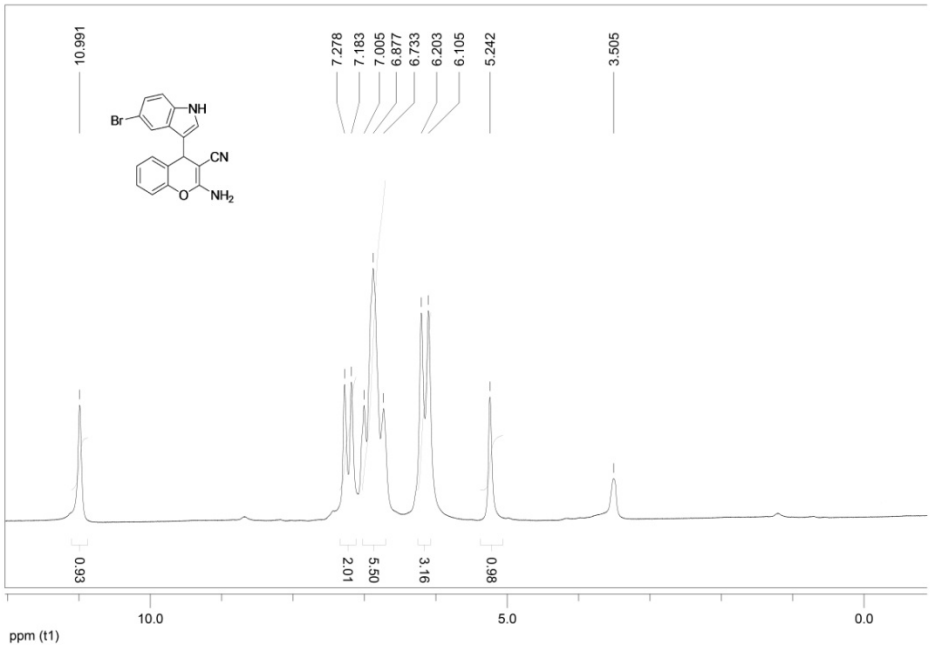




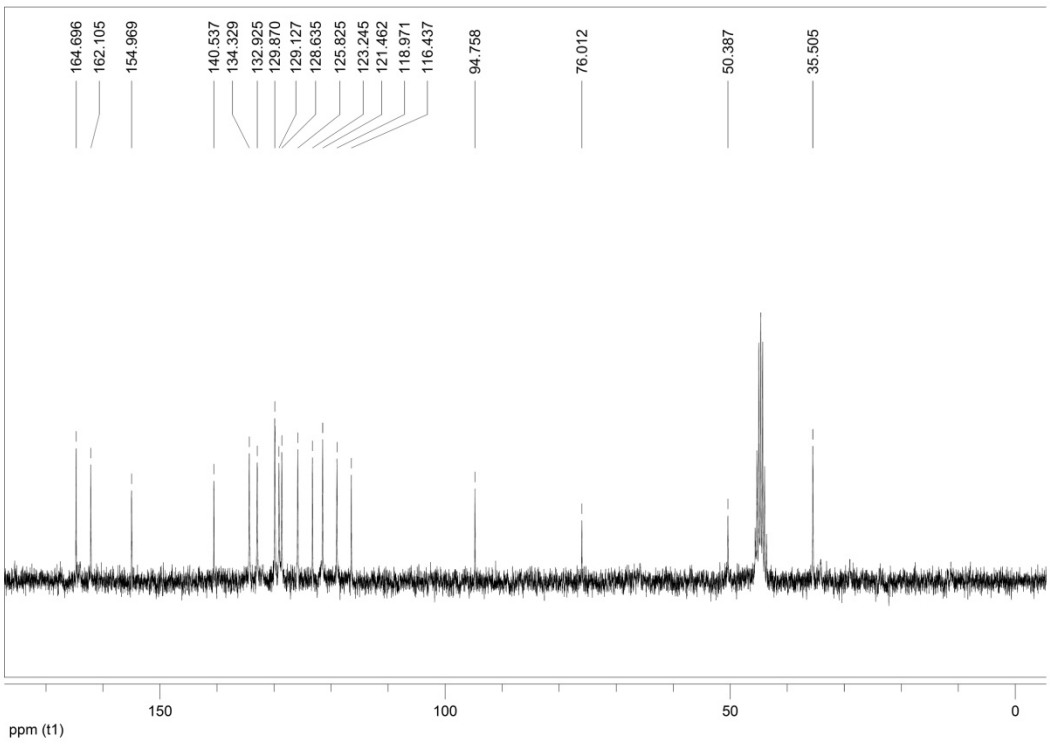


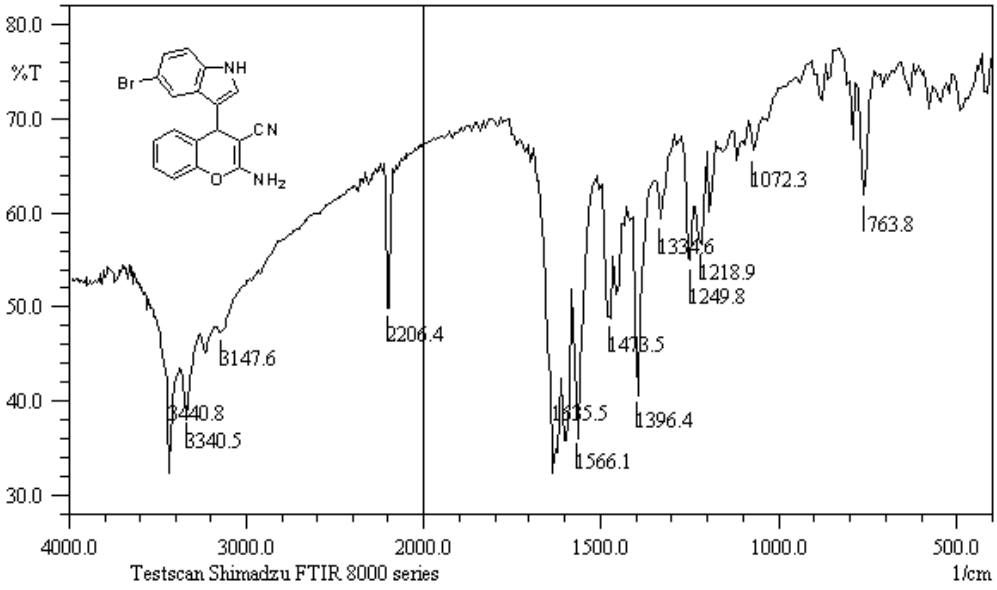
2-amino-4-(2-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile

4. ***2-amino-4-(5-bromo-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4d)**



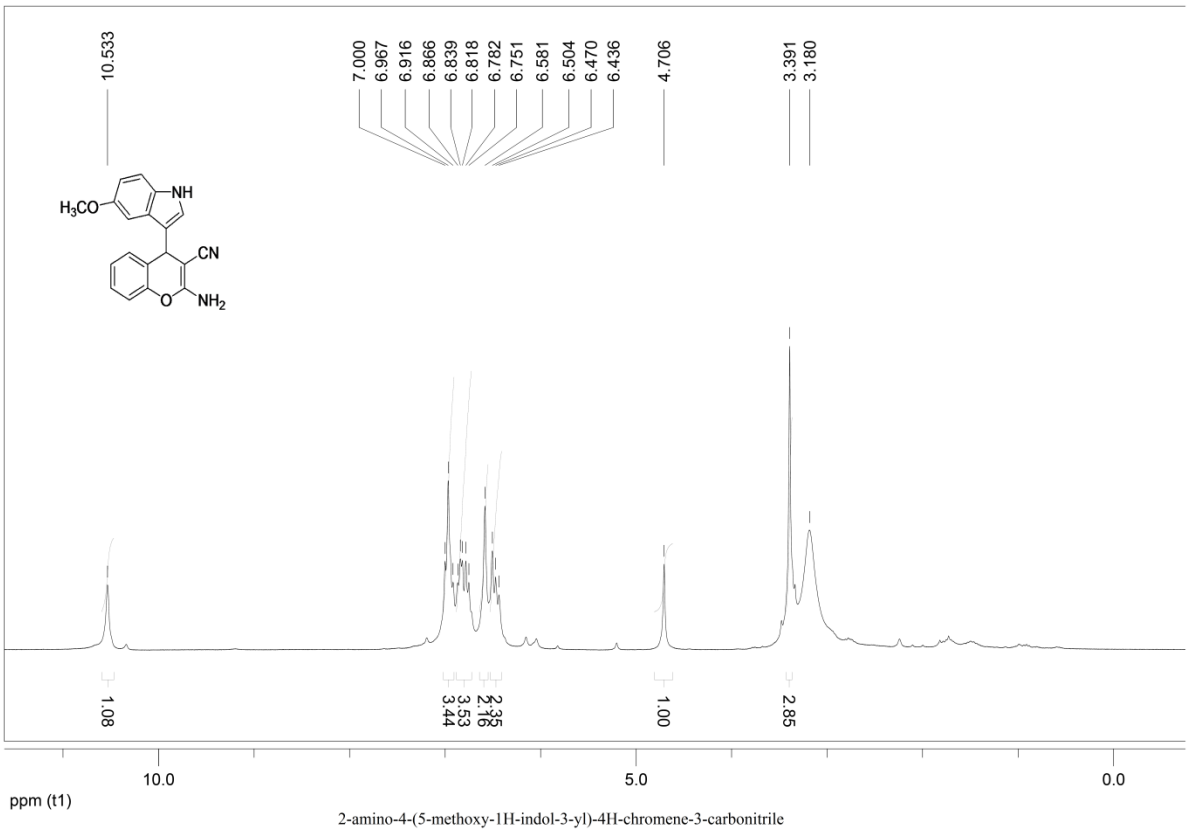
2-amino-4-(5-bromo-1H-indol-3-yl)-4H-chromene-3-carbonitrile



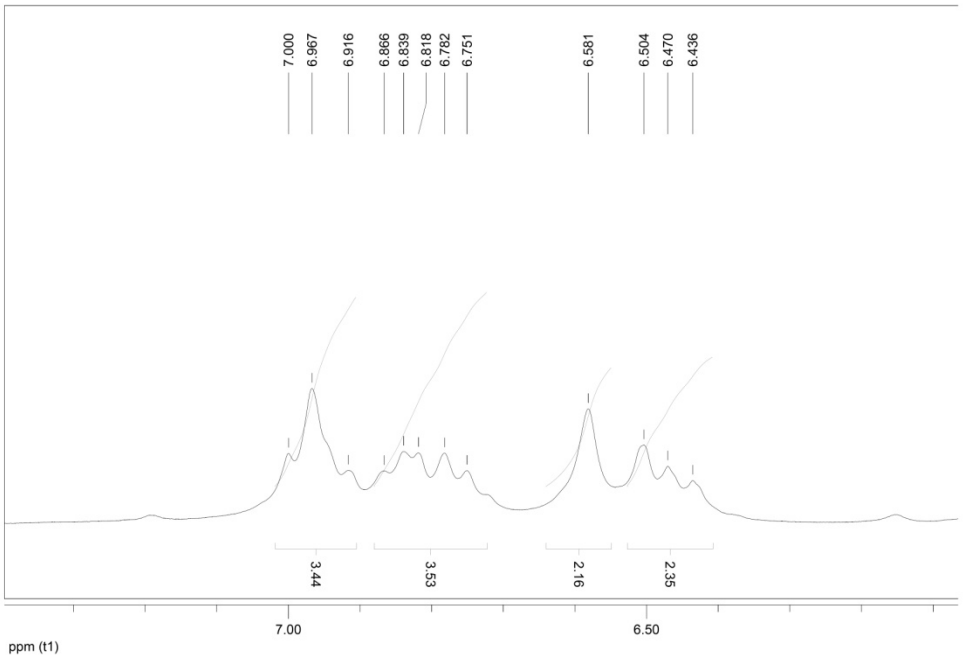


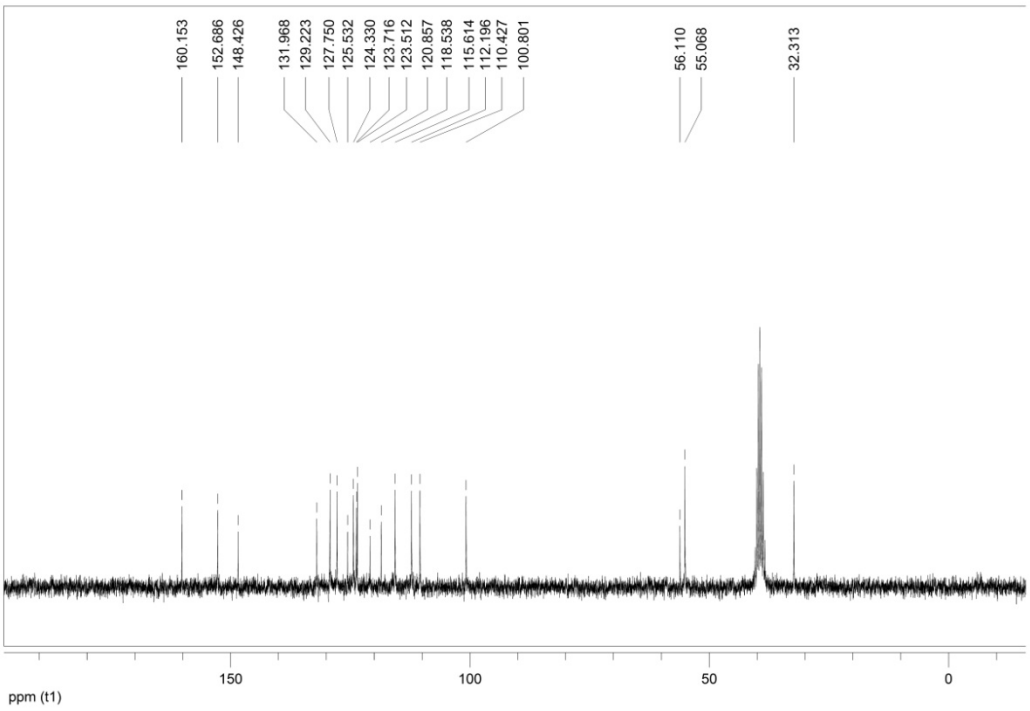
2-amino-4-(5-bromo-1H-indol-3-yl)-4H-chromene-3-carbonitrile

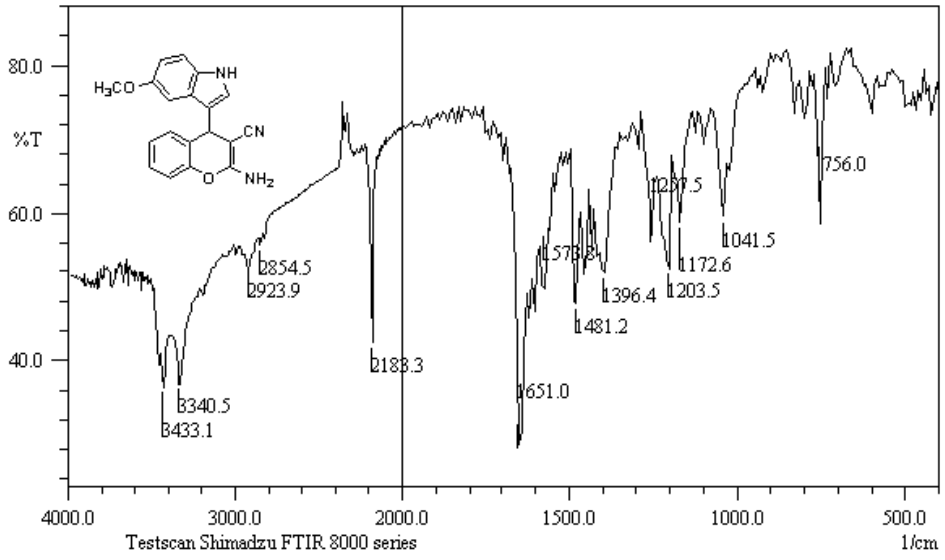
5. ***2-amino-4-(5-methoxy-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4e)**



2-amino-4-(5-methoxy-1H-indol-3-yl)-4H-chromene-3-carbonitrile

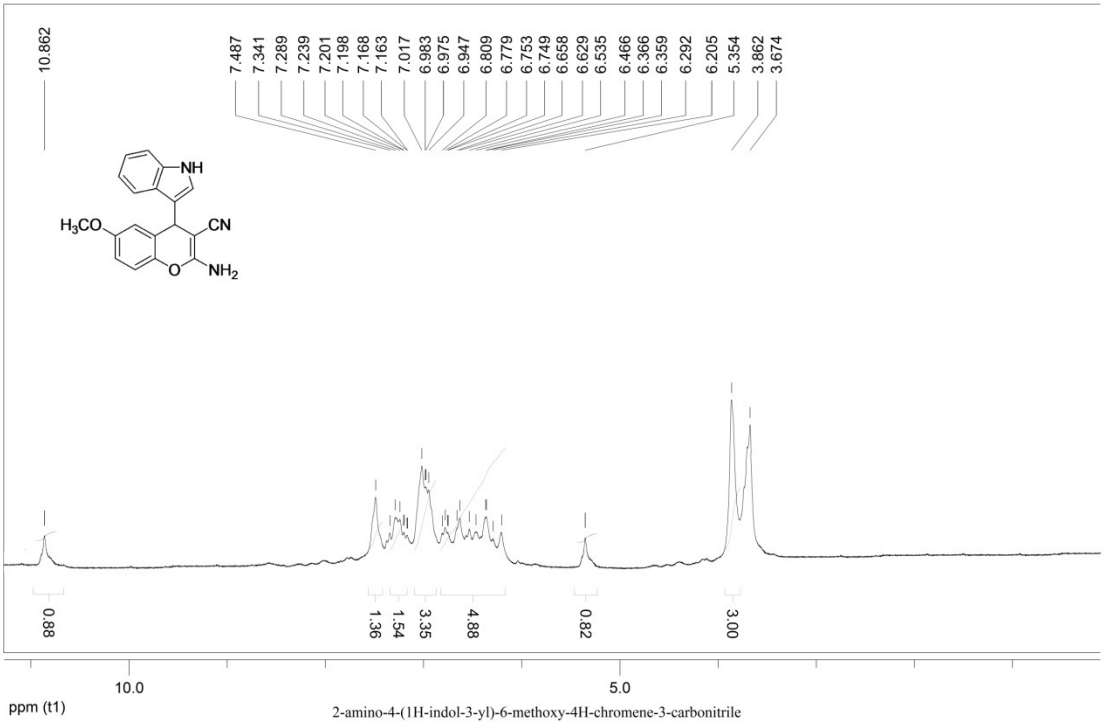

7.000
6.967
6.916
6.866
6.839
6.818
6.782
6.751
6.581
6.504
6.470
6.436
3.44
3.53
2.16
2.35
7.00
6.50
ppm (t1)


160.153
152.686
148.426
131.968
129.223
127.750
125.532
124.330
123.716
123.512
120.857
118.538
115.614
112.196
110.427
100.801
56.110
55.068
32.313
150
100
50
0
ppm (t1)

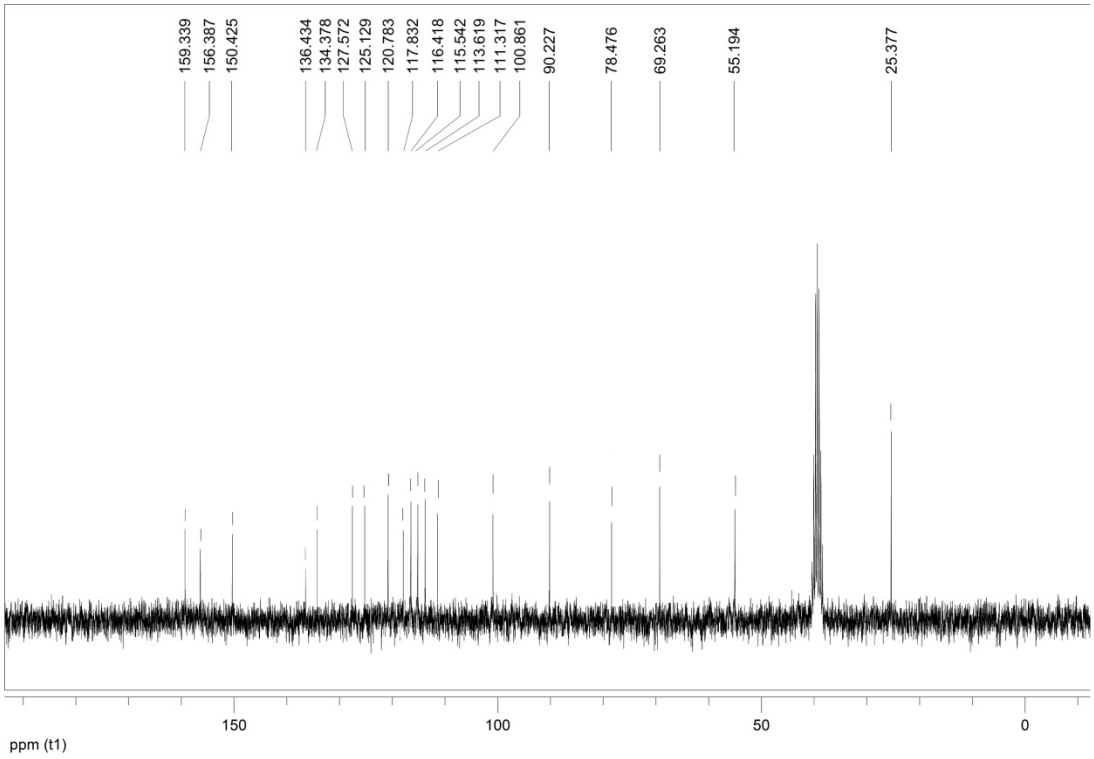


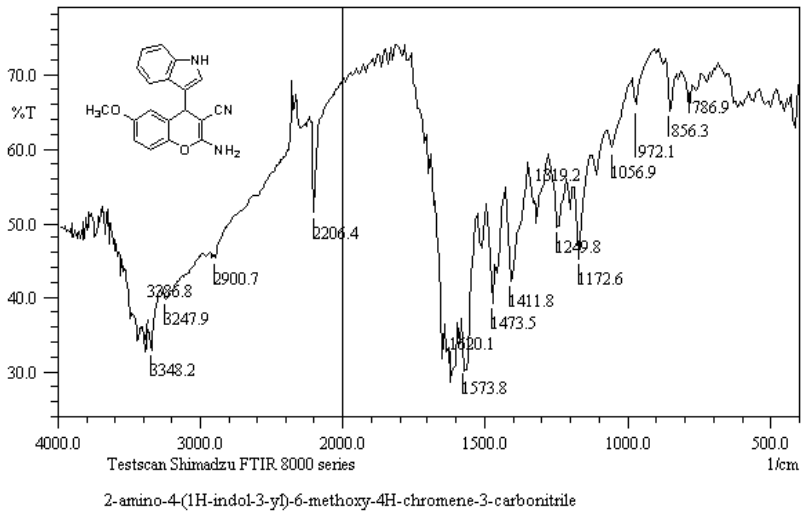
2-amino-4-(5-methoxy-1H-indol-3-yl)-4H-chromene-3-carbonitrile

6. *2-amino-4-(1H-indol-3-yl)-6-methoxy-4H-chromene-3-carbonitrile* (4f)



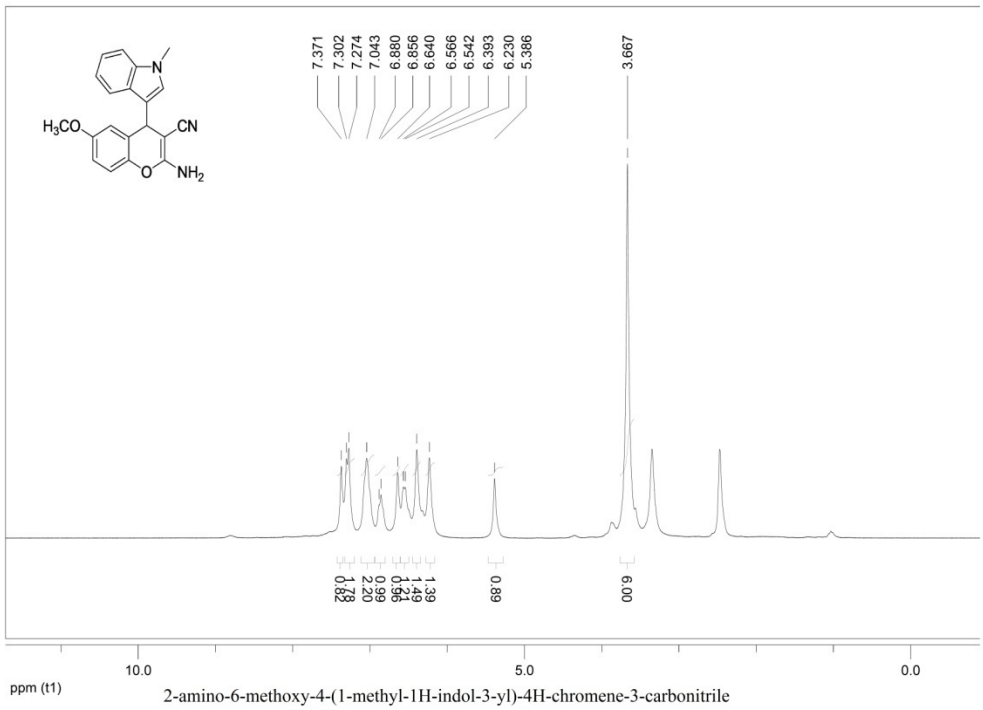
2-amino-4-(1H-indol-3-yl)-6-methoxy-4H-chromene-3-carbonitrile



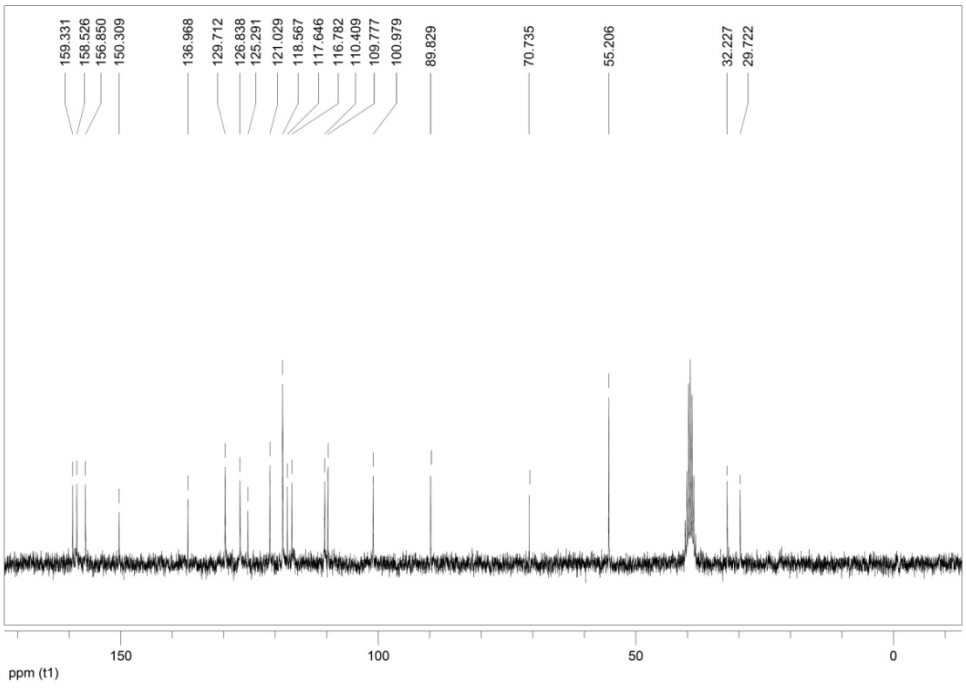


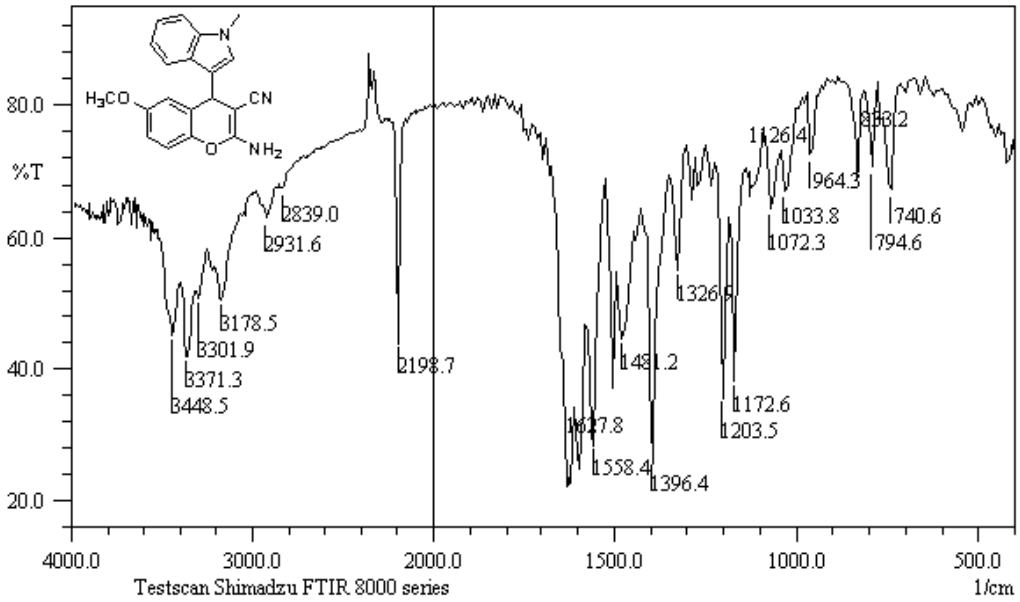
2-amino-4-(1H-indol-3-yl)-6-methoxy-4H-chromene-3-carbonitrile

7. ***2-amino-6-methoxy-4-(1-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4g)**



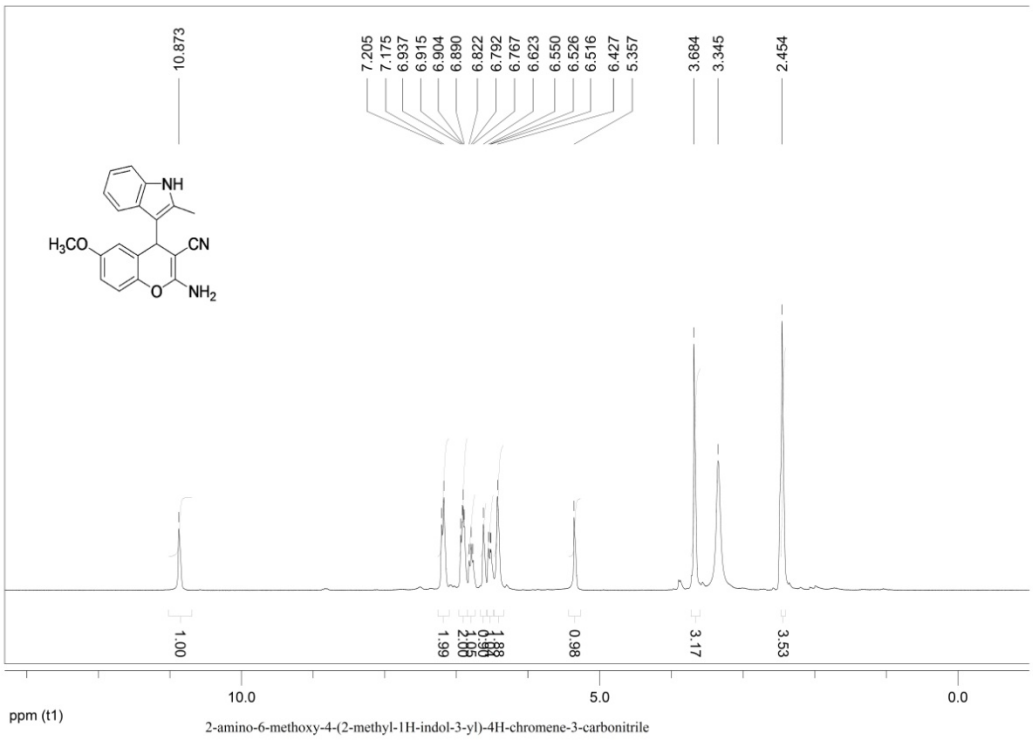
2-amino-6-methoxy-4-(1-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile



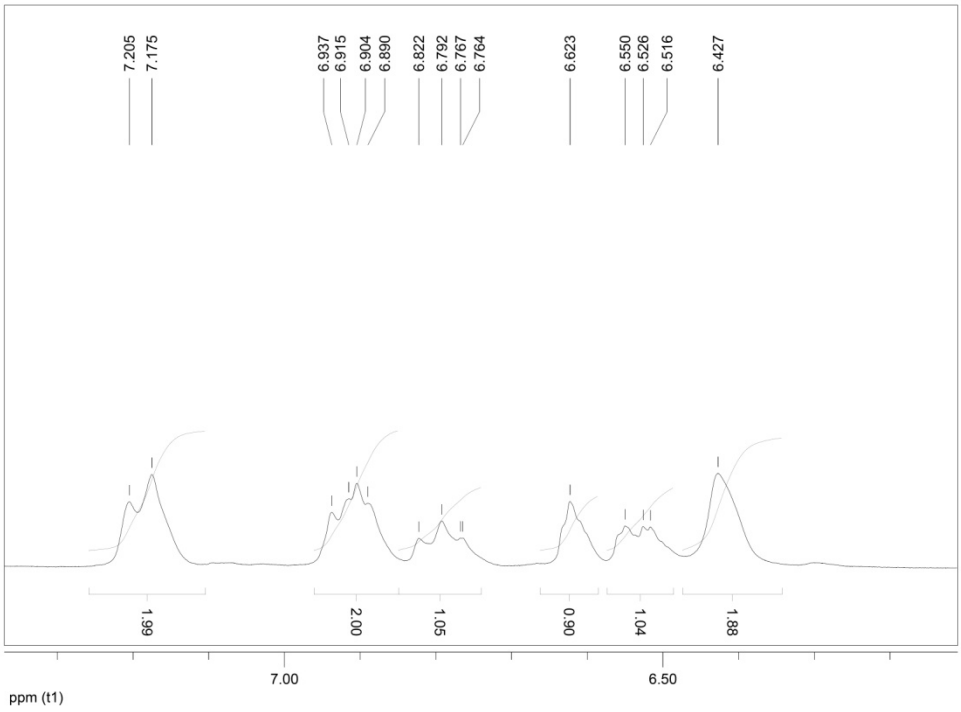


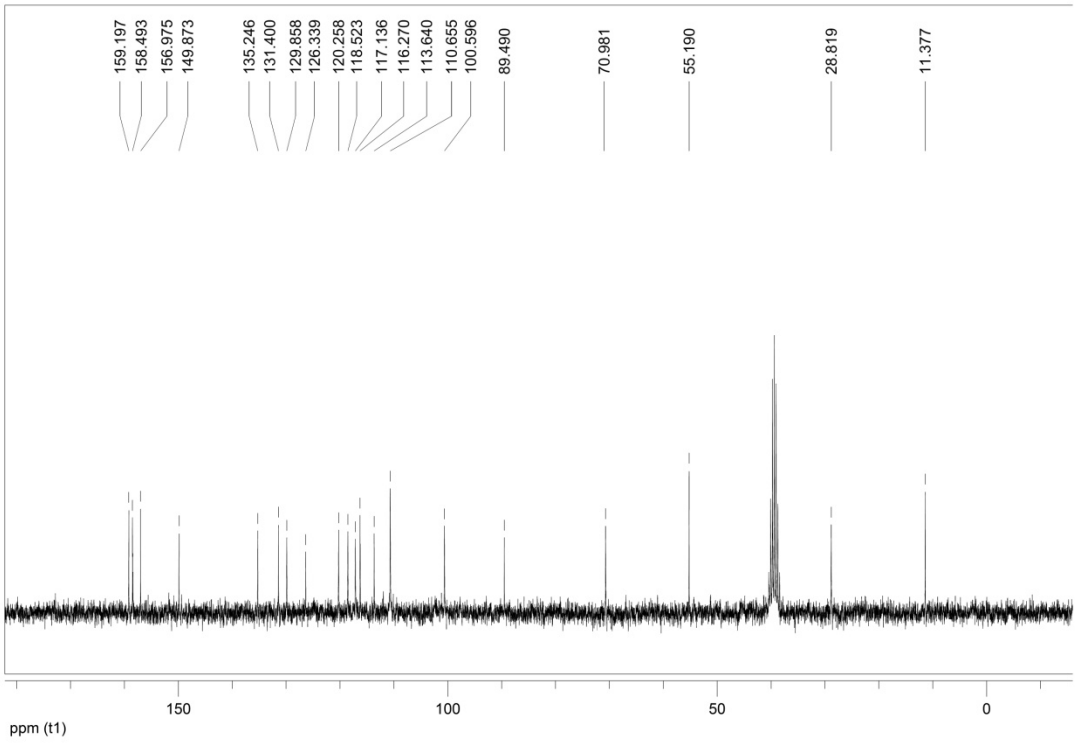
2-amino-6-methoxy-4-(1-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile

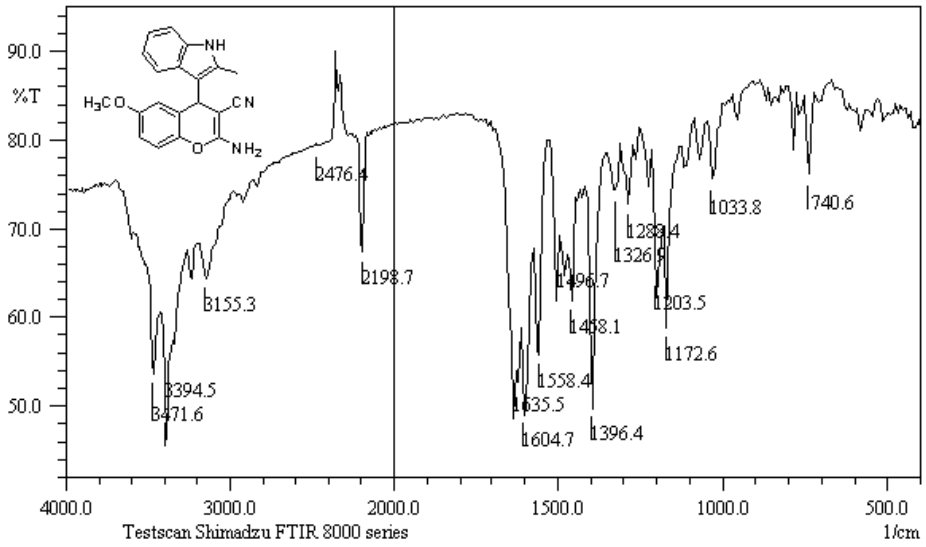
8. ***2-amino-6-methoxy-4-(2-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4h)**



2-amino-6-methoxy-4-(2-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile

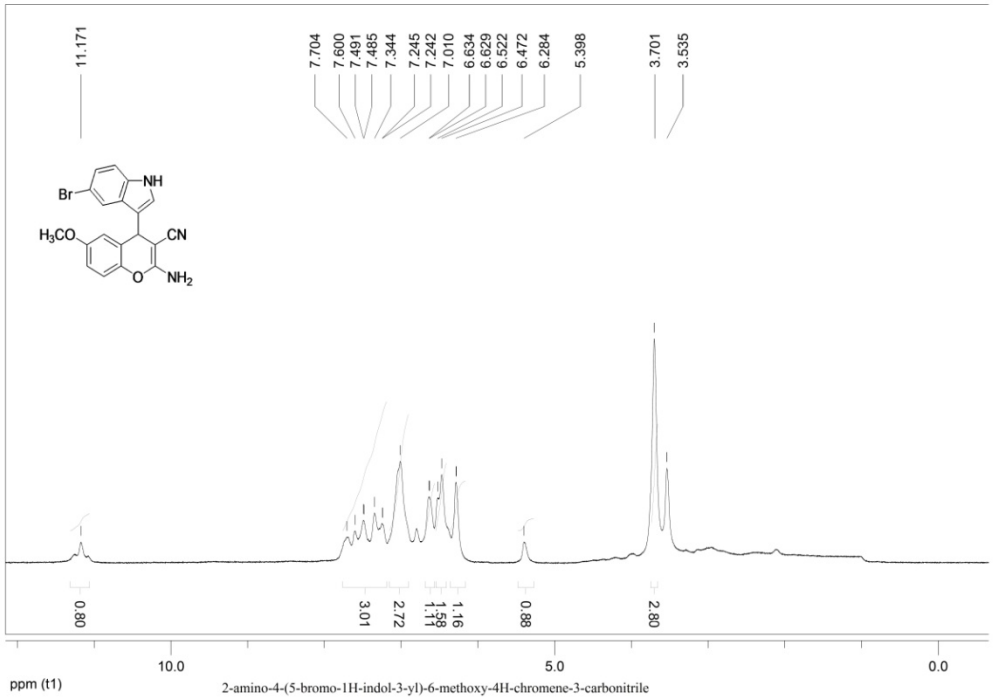

7.205
7.175
6.937
6.915
6.904
6.890
6.822
6.792
6.767
6.764
6.623
6.550
6.526
6.516
6.427
1.99
2.00
1.05
0.90
1.04
1.88
7.00
6.50
ppm (t1)

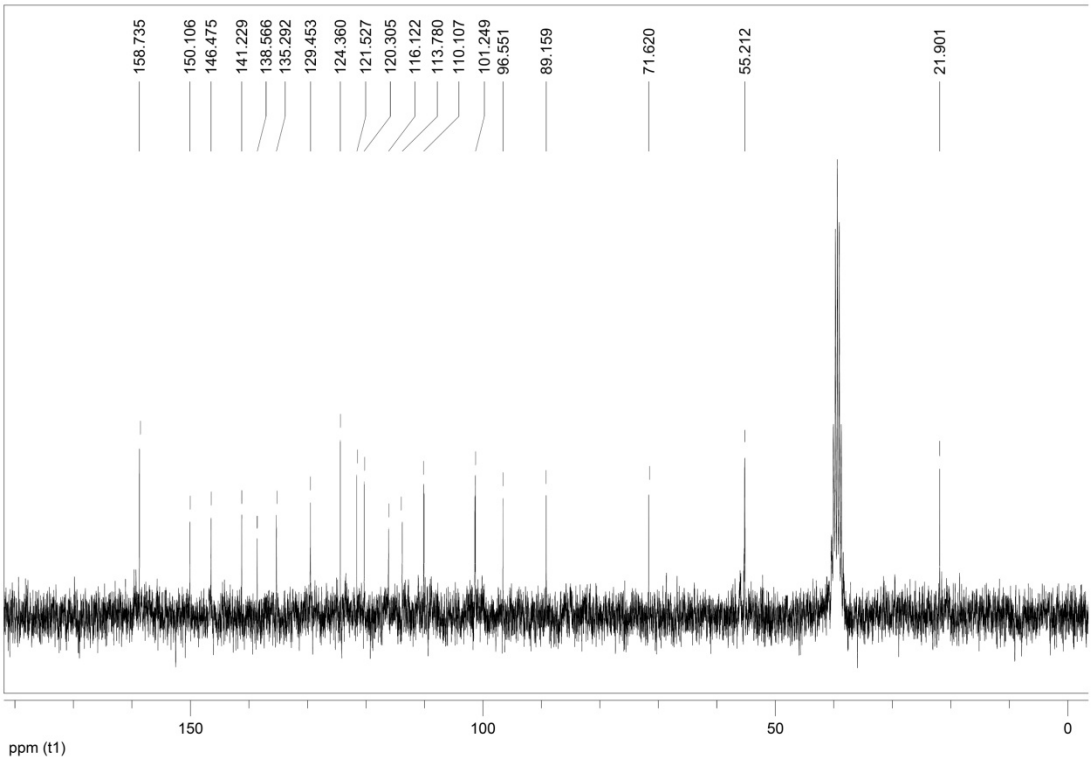

159.197
158.493
156.975
149.873
135.246
131.400
129.858
126.339
120.258
118.523
117.136
116.270
113.640
110.655
100.596
89.490
70.981
55.190
28.819
11.377
150
100
50
0
ppm (t1)

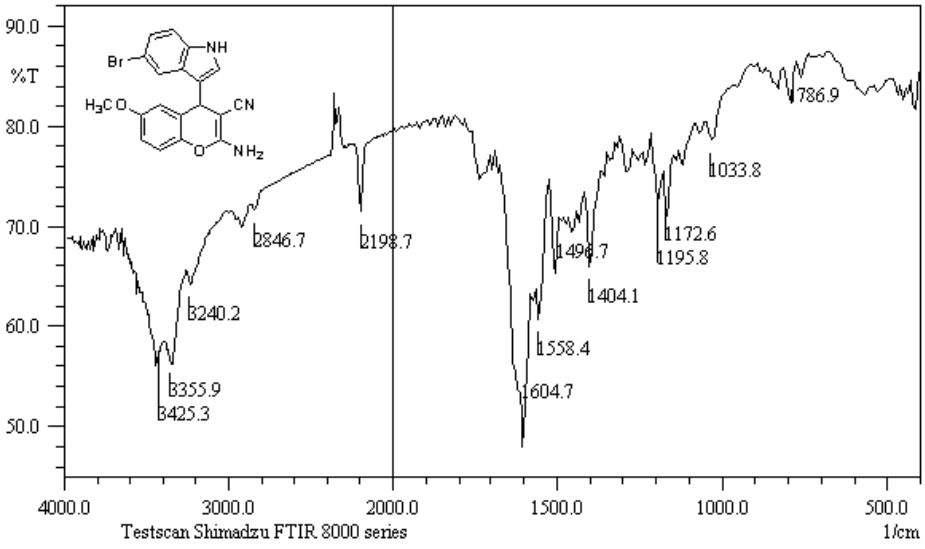


2-amino-6-methoxy-4-(2-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile

9. ***2-amino-4-(5-bromo-1H-indol-3-yl)-6-methoxy-4H-chromene-3-carbonitrile*** **(4i)**

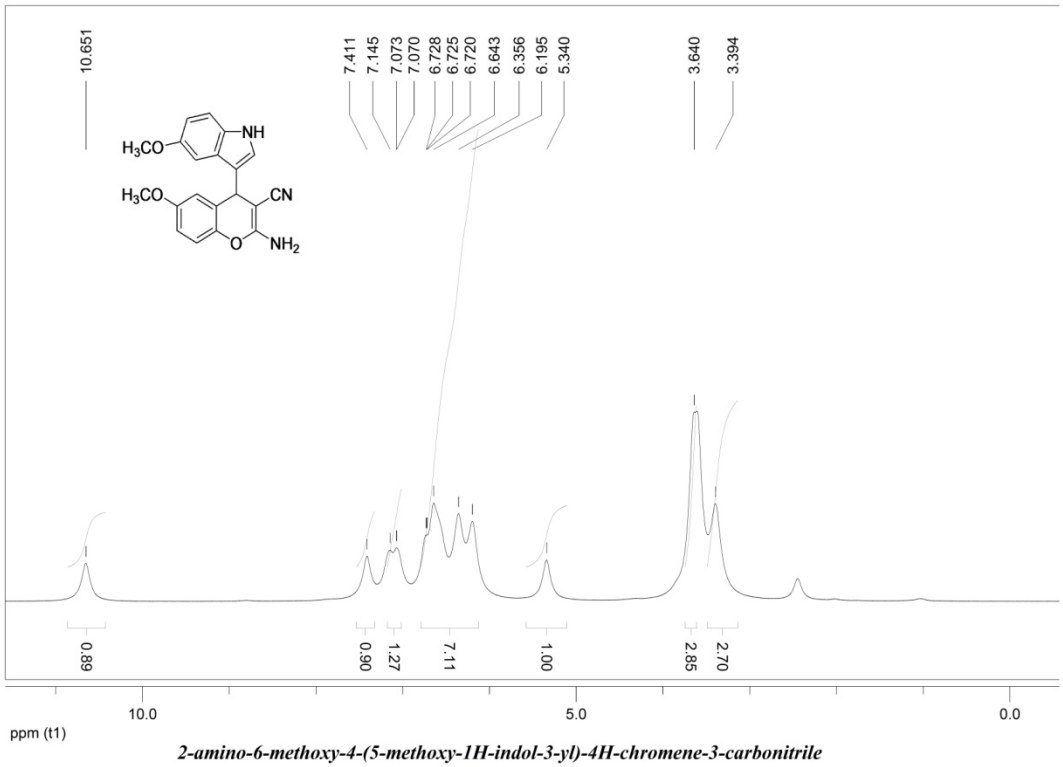




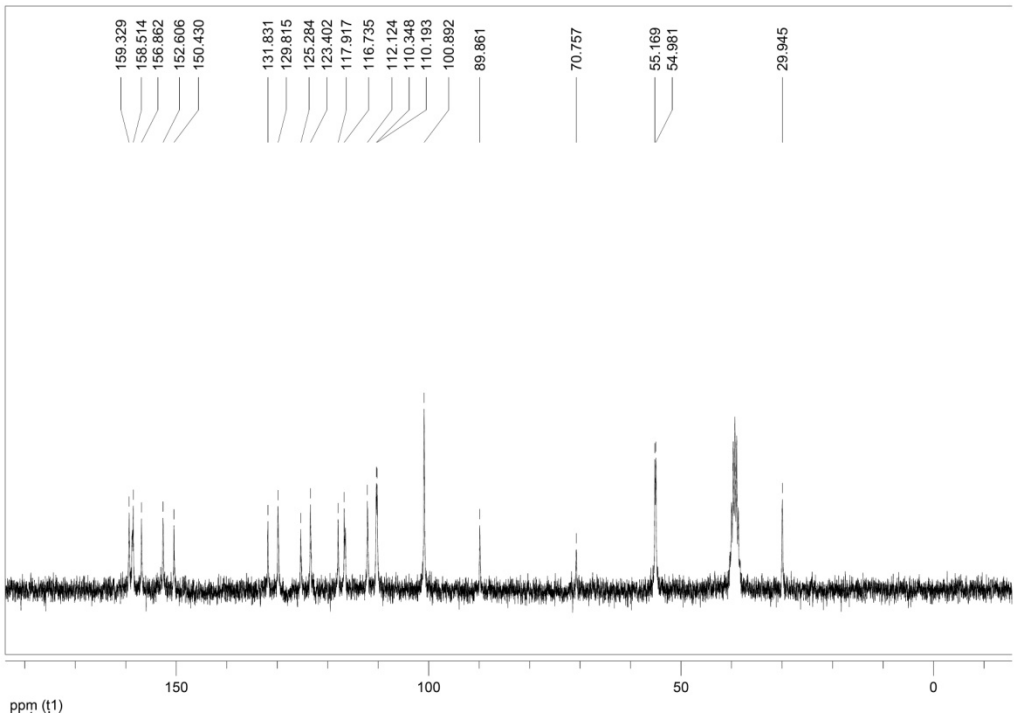


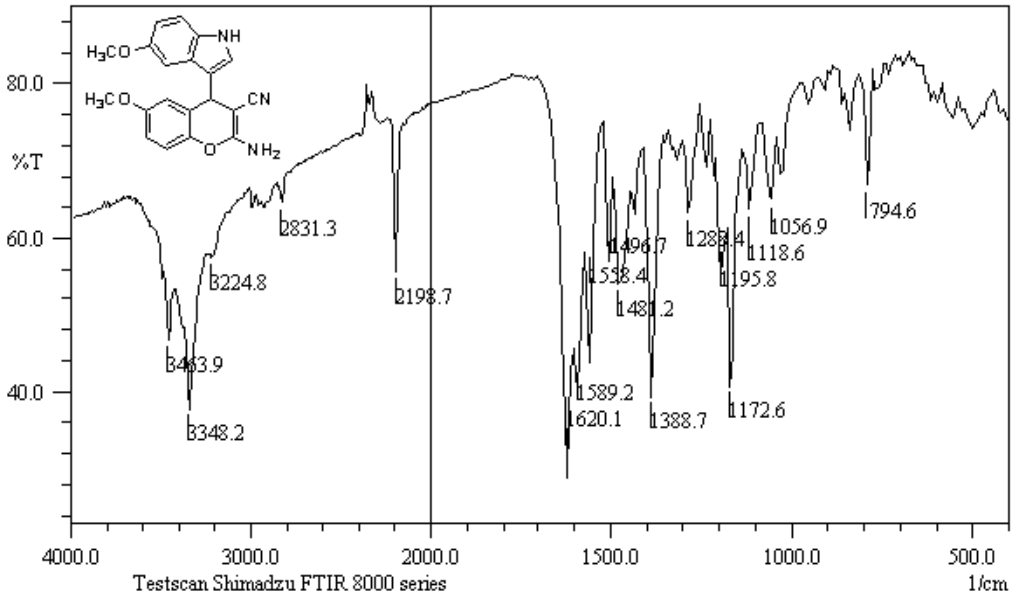
2-amino-4-(5-bromo-1H-indol-3-yl)-6-methoxy-4H-chromene-3-carbonitrile

10. ***2-amino-6-methoxy-4-(5-methoxy-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4j)**



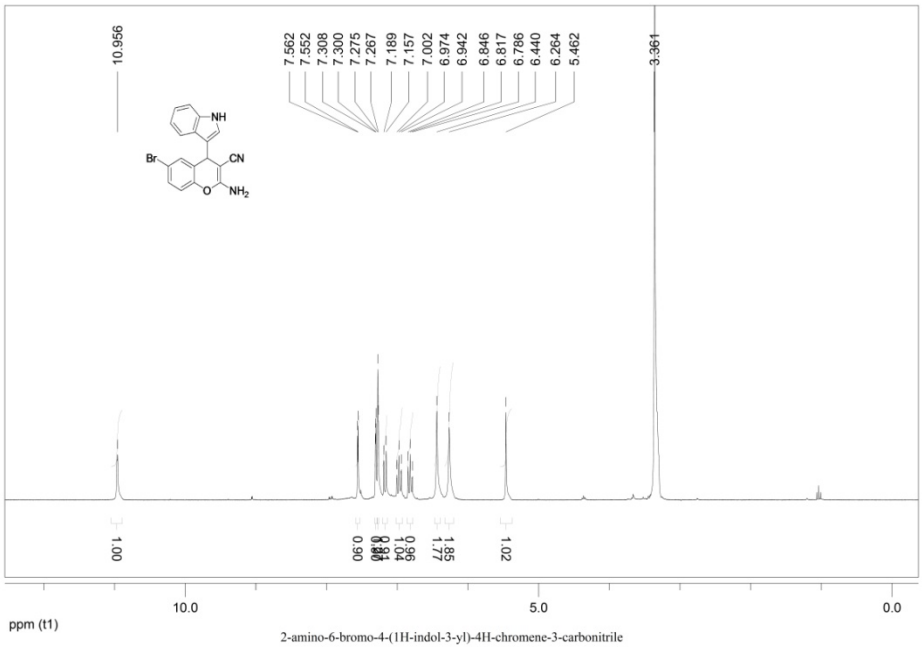
2-amino-6-methoxy-4-(5-methoxy-1H-indol-3-yl)-4H-chromene-3-carbonitrile

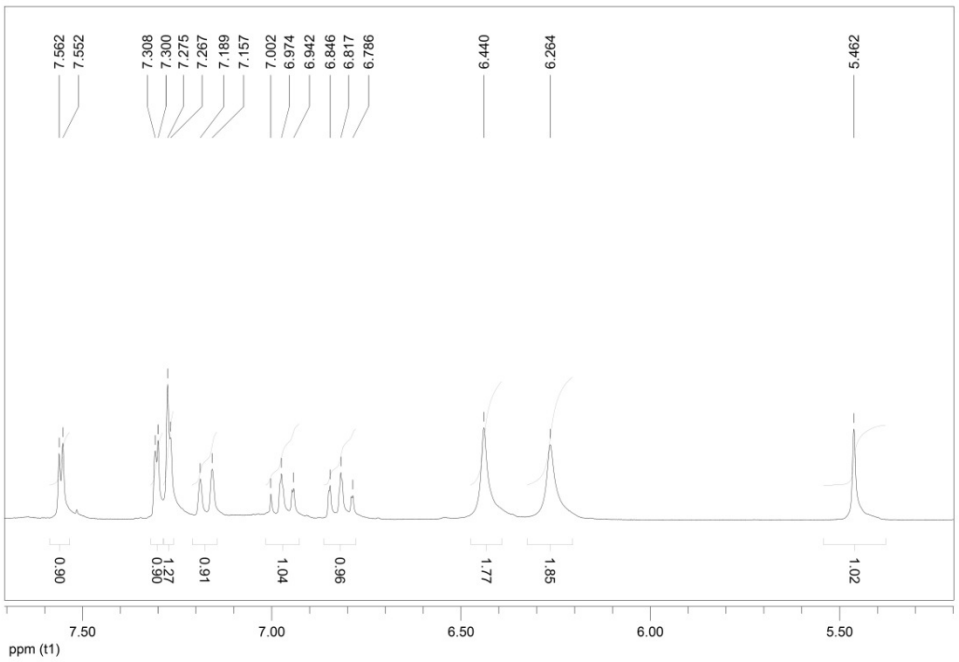


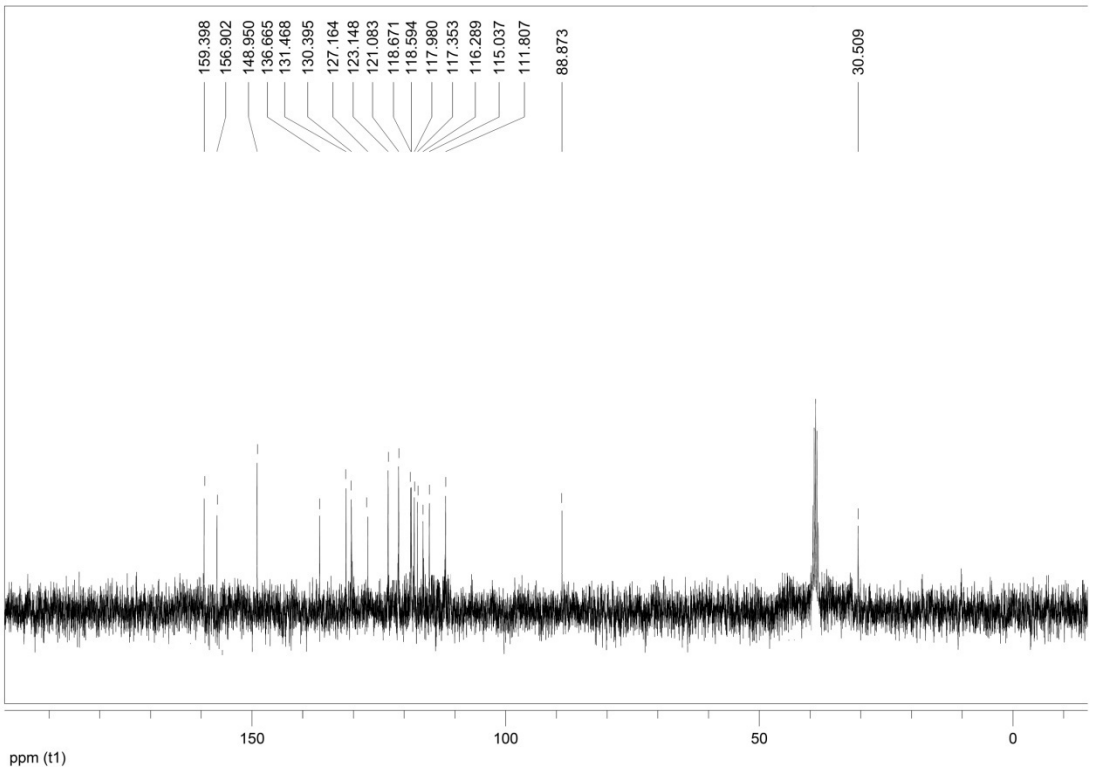


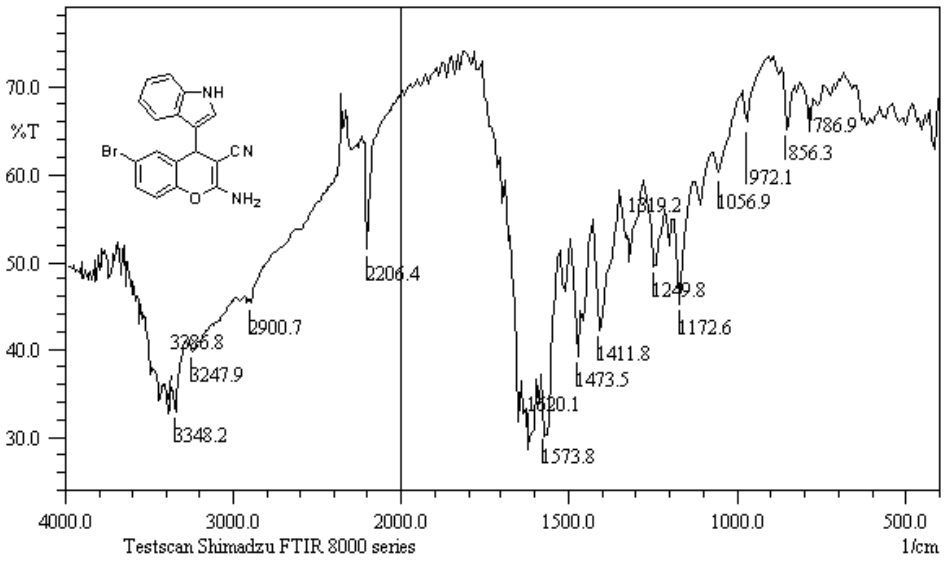
2-amino-6-methoxy-4-(5-methoxy-1H-indol-3-yl)-4H-chromene-3-carbonitrile

11. ***2-amino-6-bromo-4-(1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4k)**



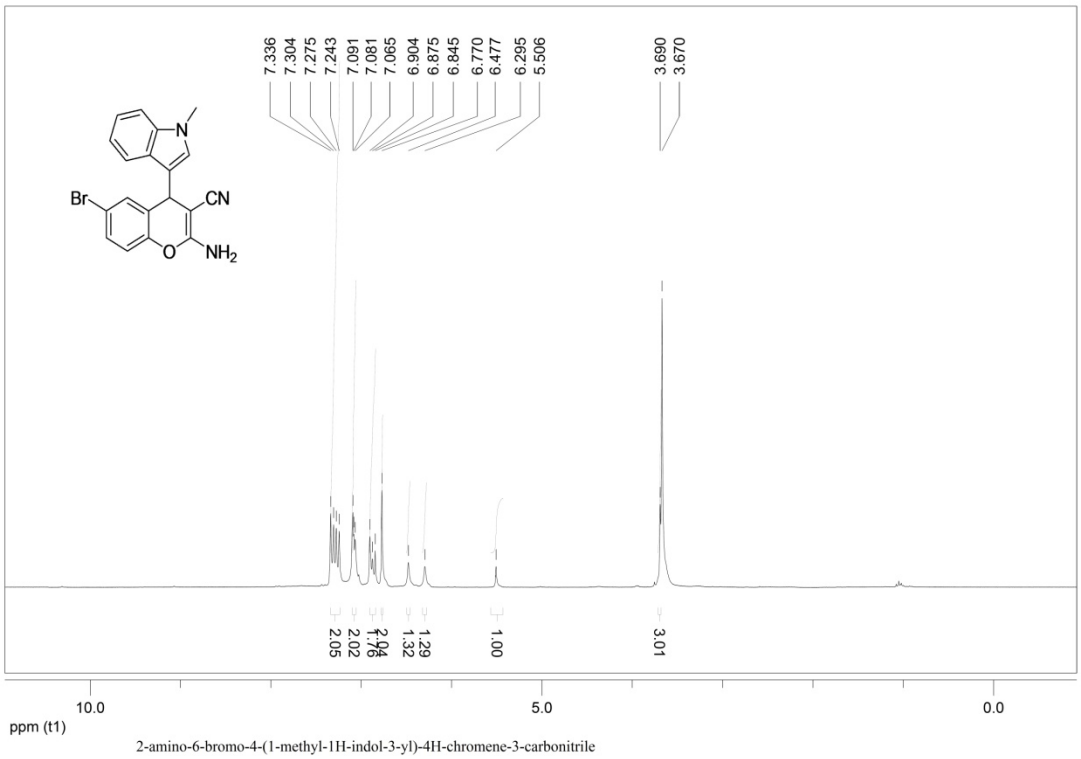

7.562
7.552
7.308
7.300
7.275
7.267
7.189
7.157
7.002
6.974
6.942
6.846
6.817
6.786
6.440
6.264
5.462
0.90
0.90
1.27
0.91
1.04
0.96
1.77
1.85
1.02
7.50
7.00
6.50
6.00
5.50
ppm (t1)


159.398
156.902
148.950
136.665
131.468
130.395
127.164
123.148
121.083
118.671
118.594
117.980
117.353
116.289
115.037
111.807
88.873
30.509
150
100
50
0
ppm (t1)

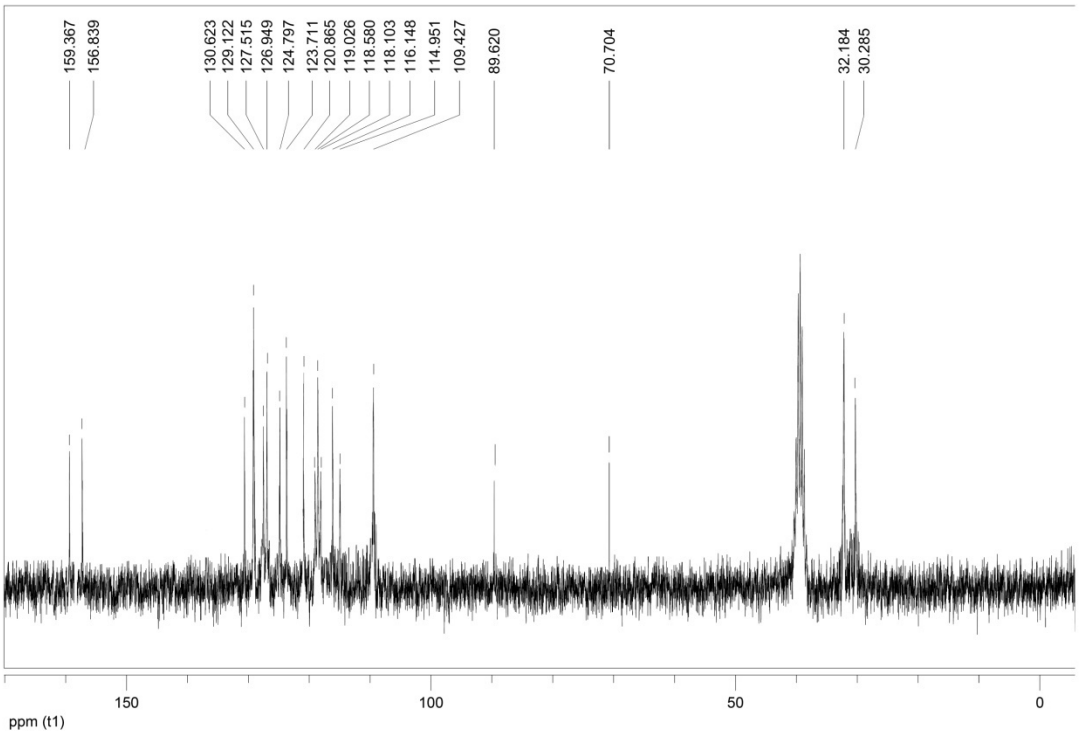


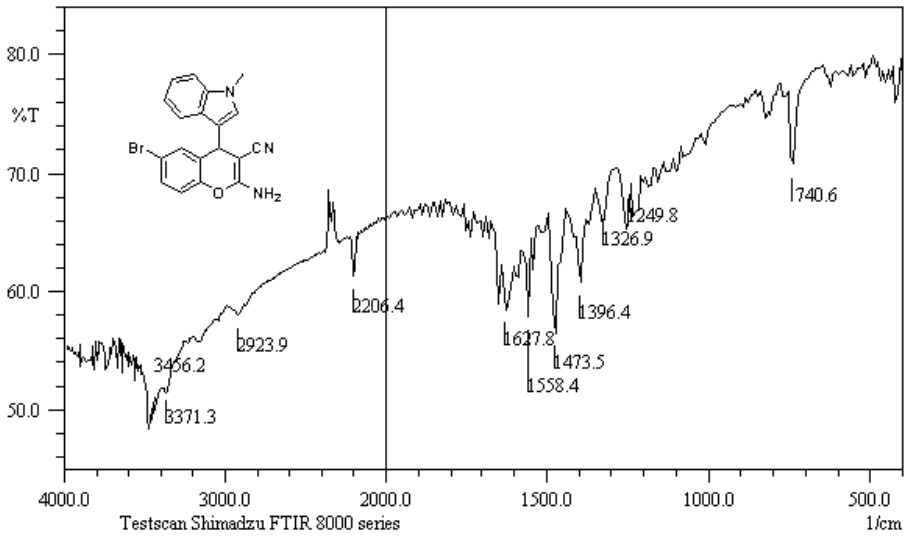
2-amino-6-bromo-4-(1H-indol-3-yl)-4H-chromene-3-carbonitrile

12. ***2-amino-6-bromo-4-(1-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4l)**



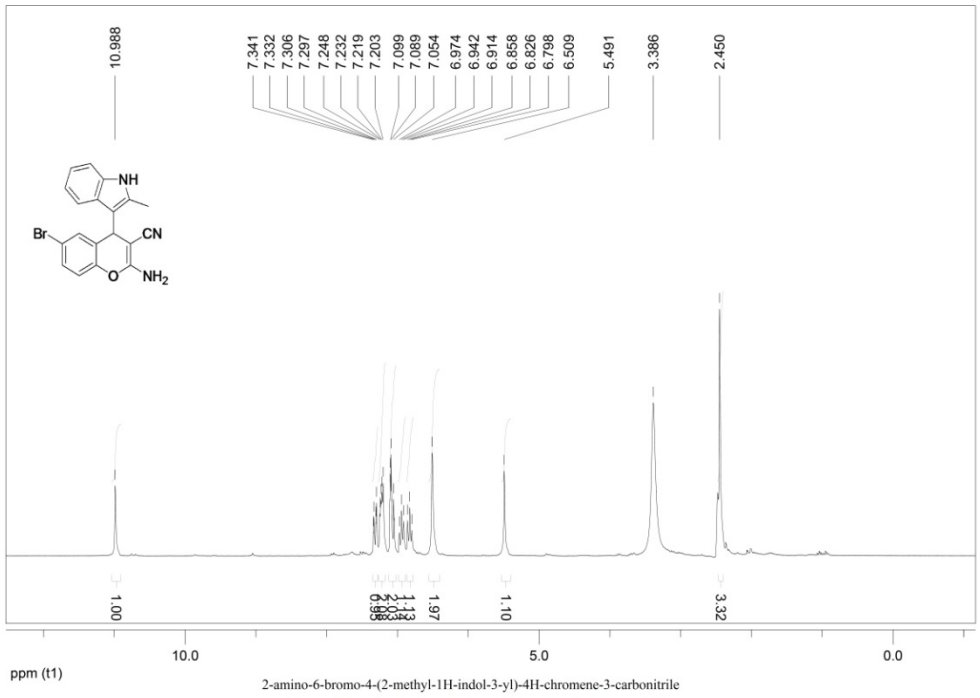
2-amino-6-bromo-4-(1-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile

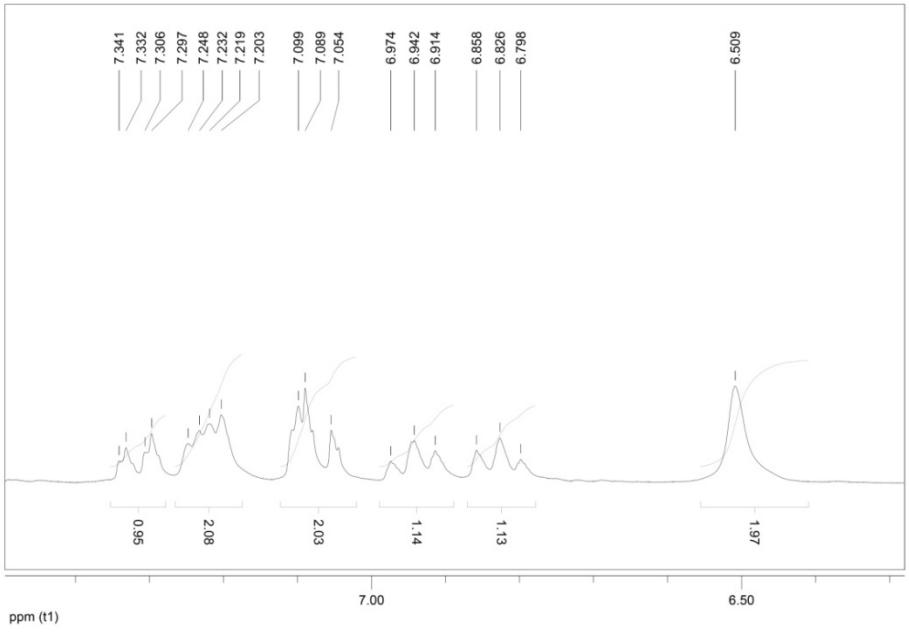


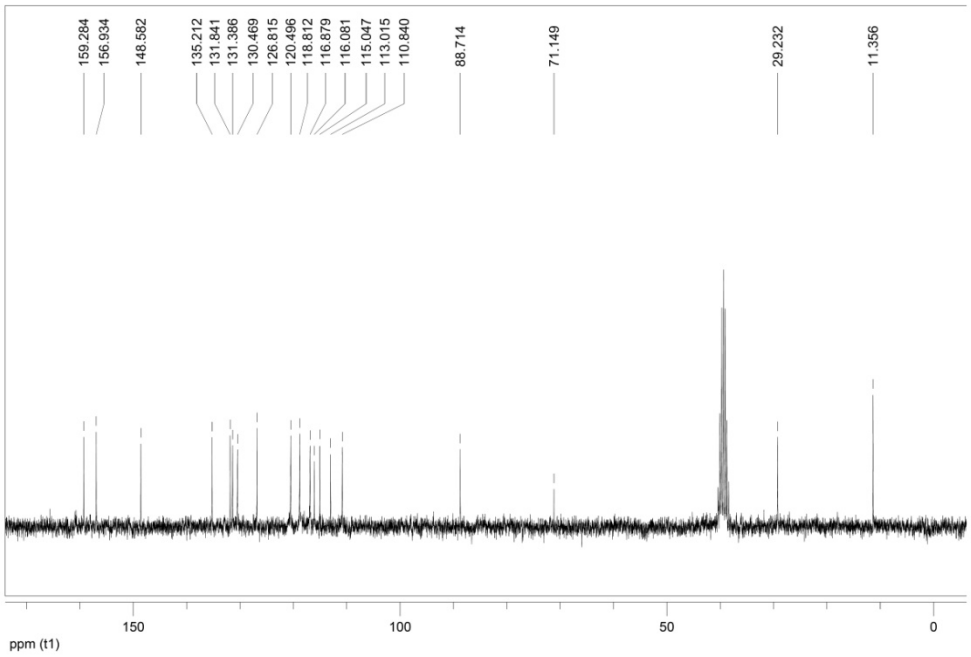


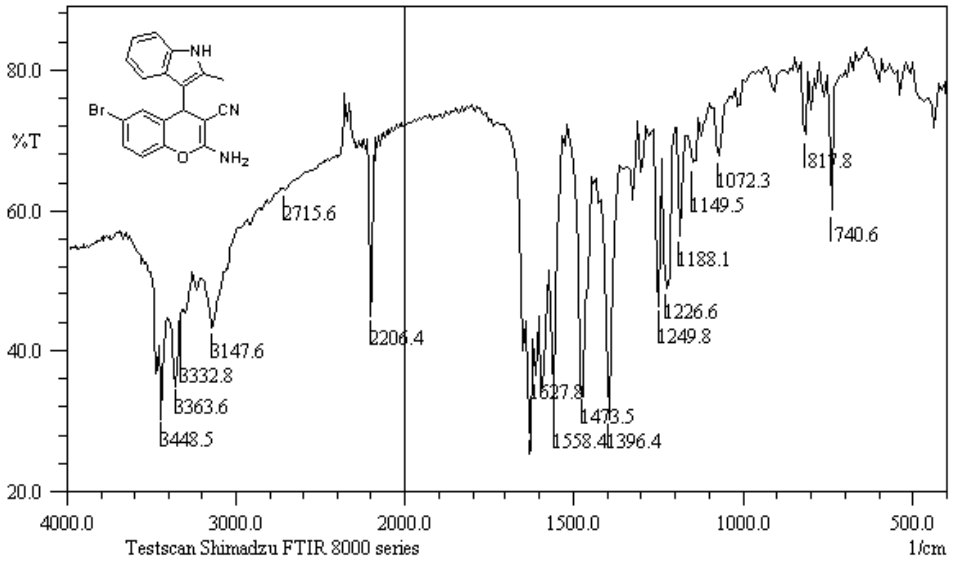
2-amino-6-bromo-4-(1-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile

13. ***2-amino-6-bromo-4-(2-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4m)**



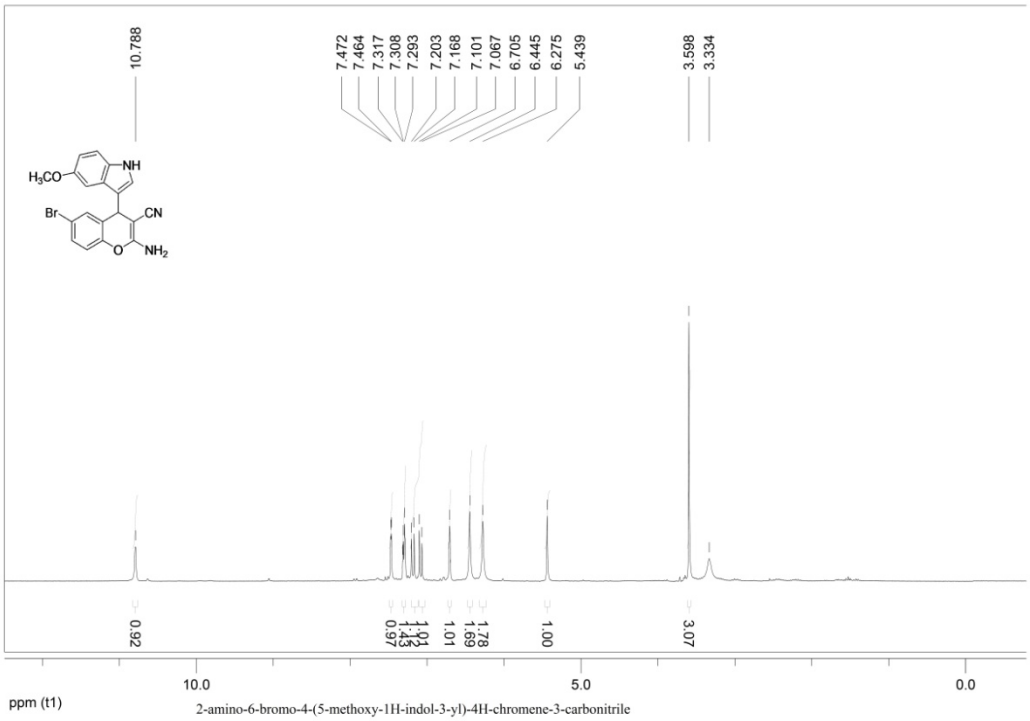


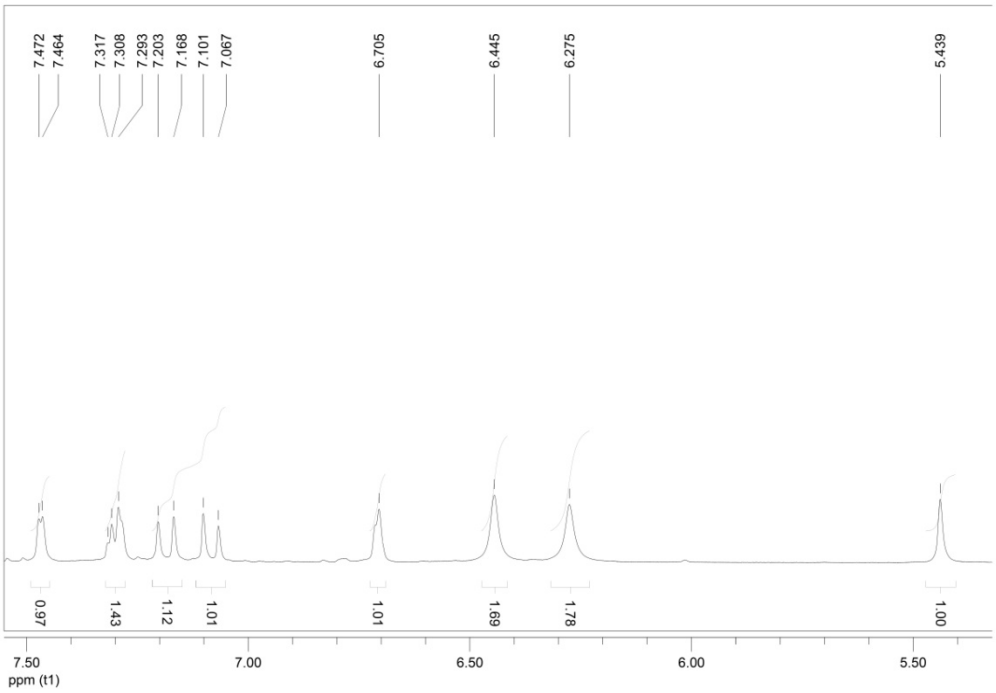


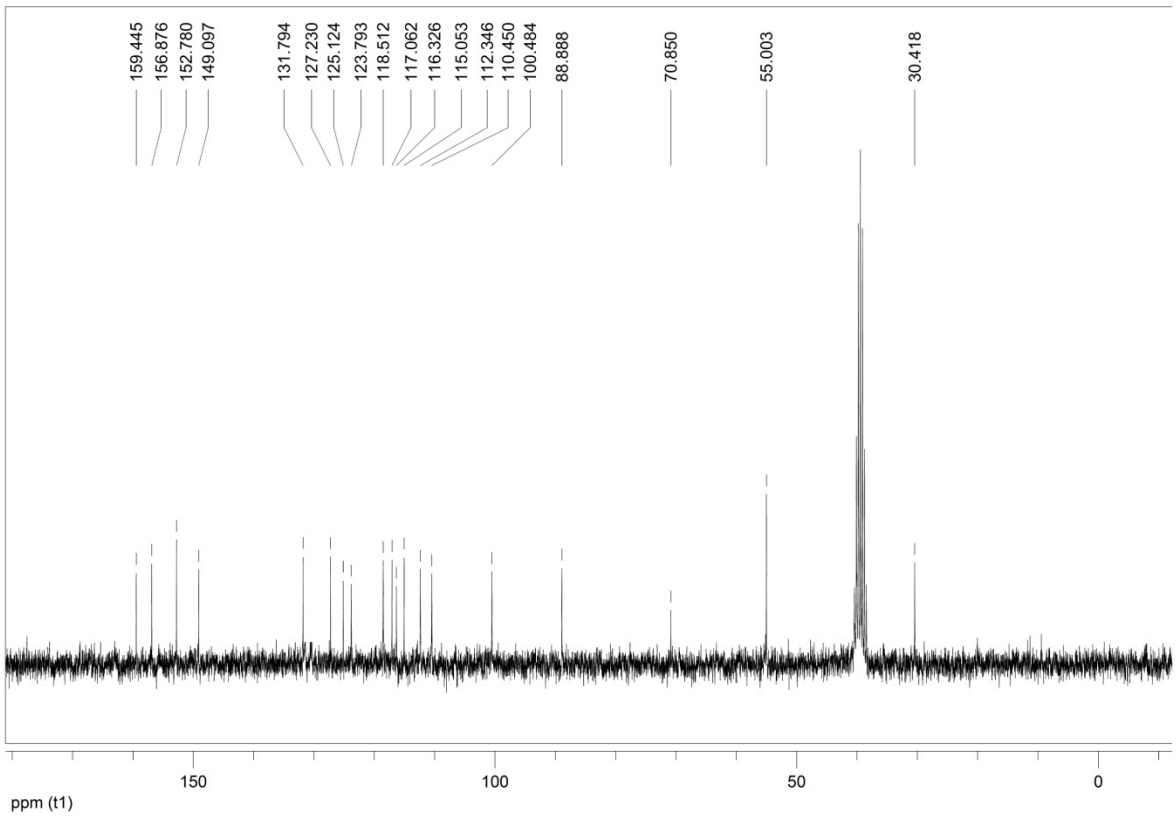


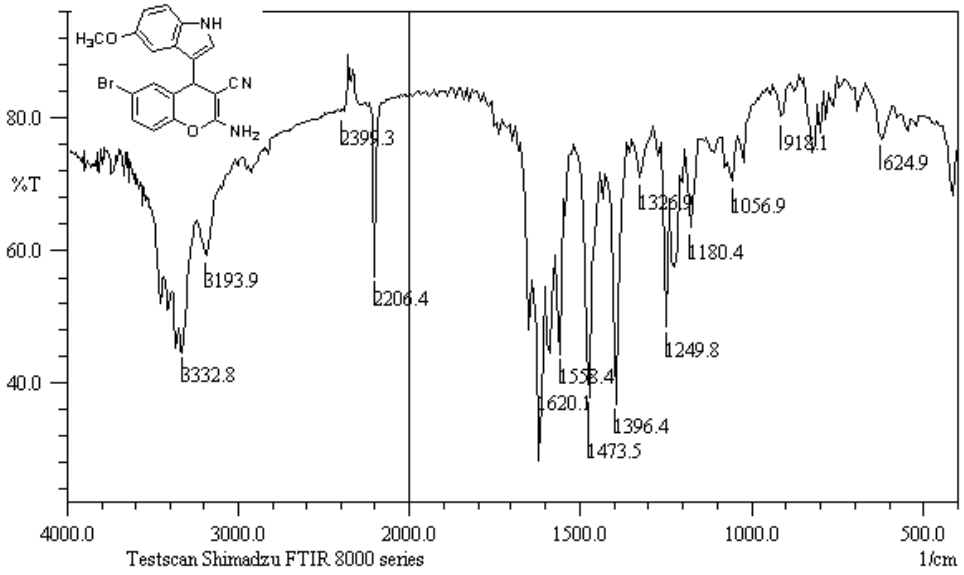
2-amino-6-bromo-4-(2-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile

14. ***2-amino-6-bromo-4-(5-methoxy-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4n)**



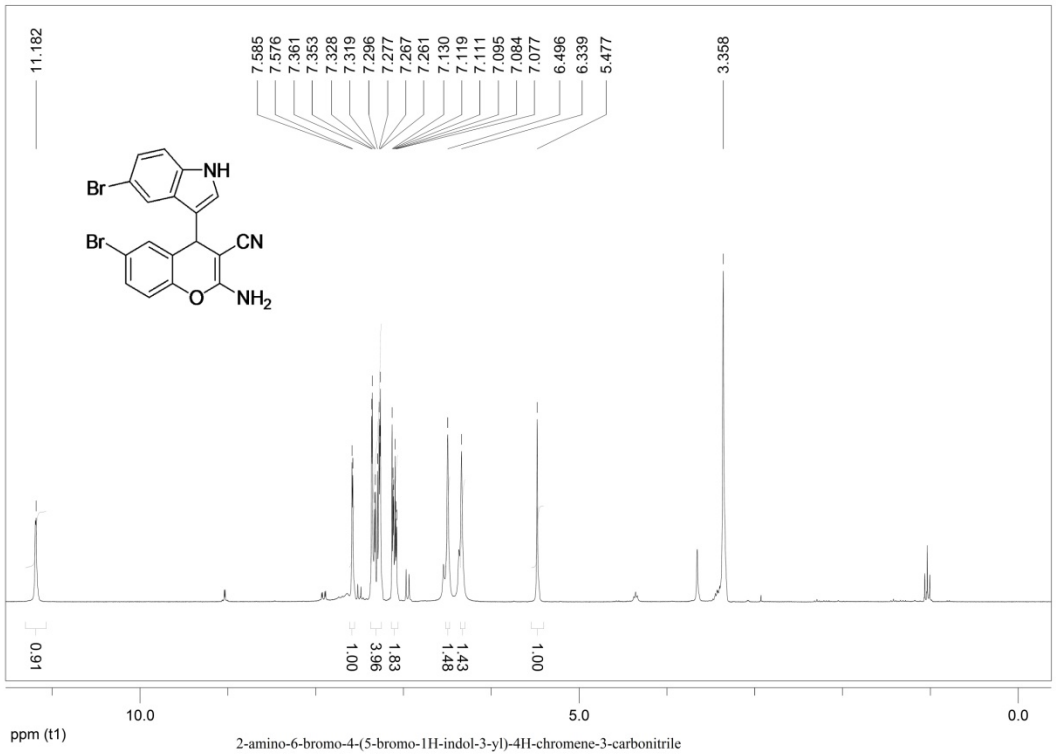


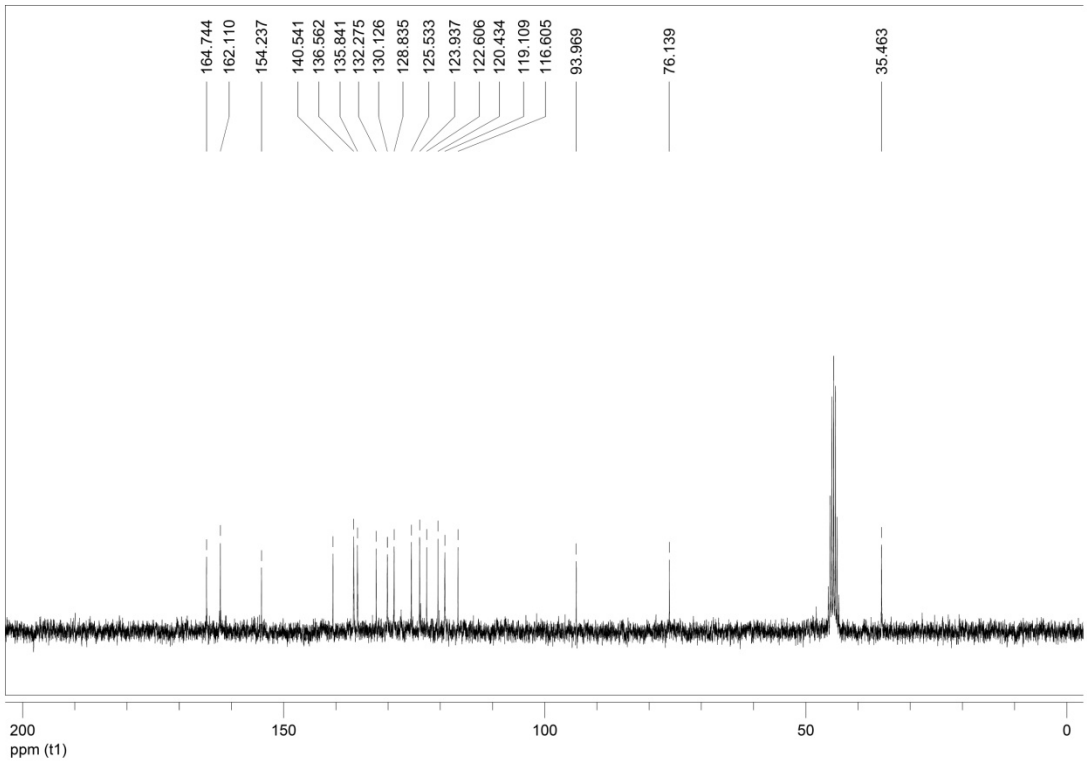


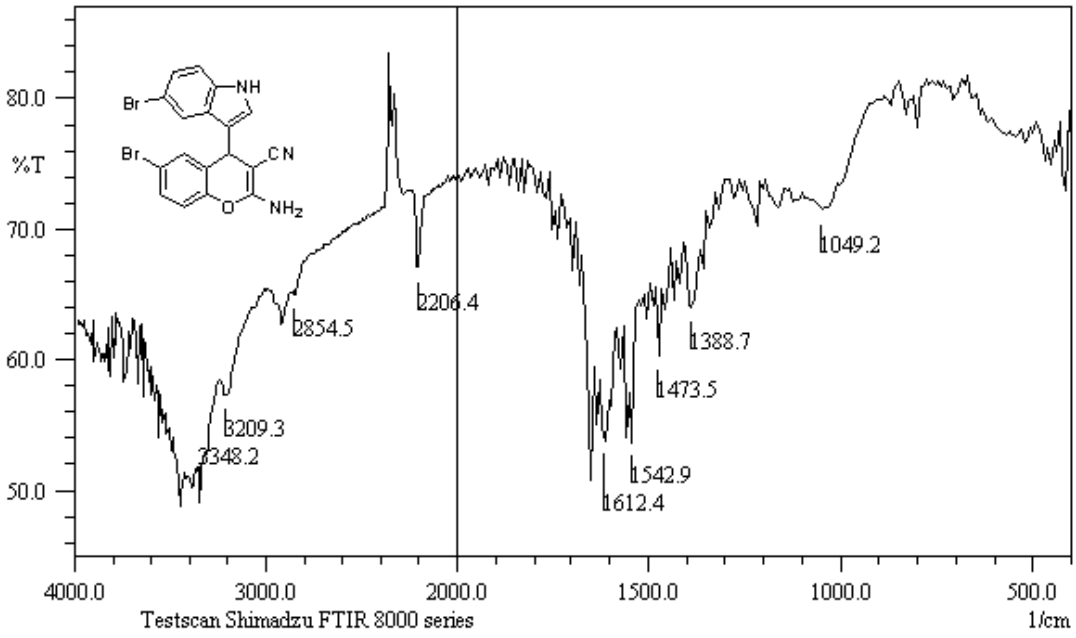


2-amino-6-bromo-4-(5-methoxy-1H-indol-3-yl)-4H-chromene-3-carbonitrile

15. ***2-amino-6-bromo-4-(5-bromo-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4o)**

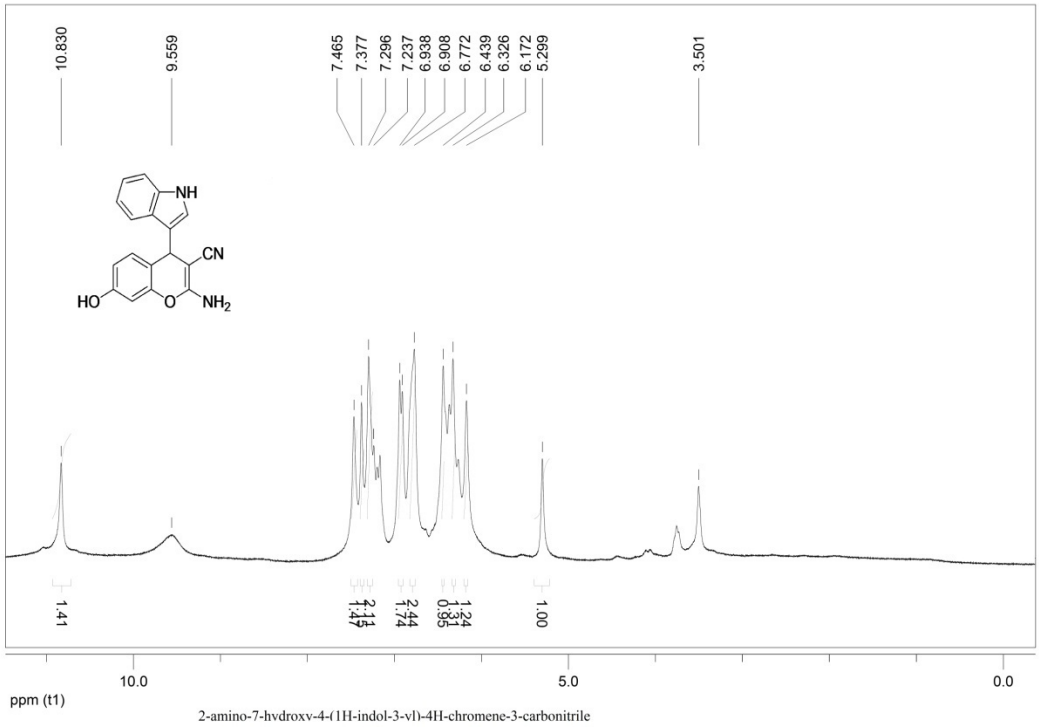




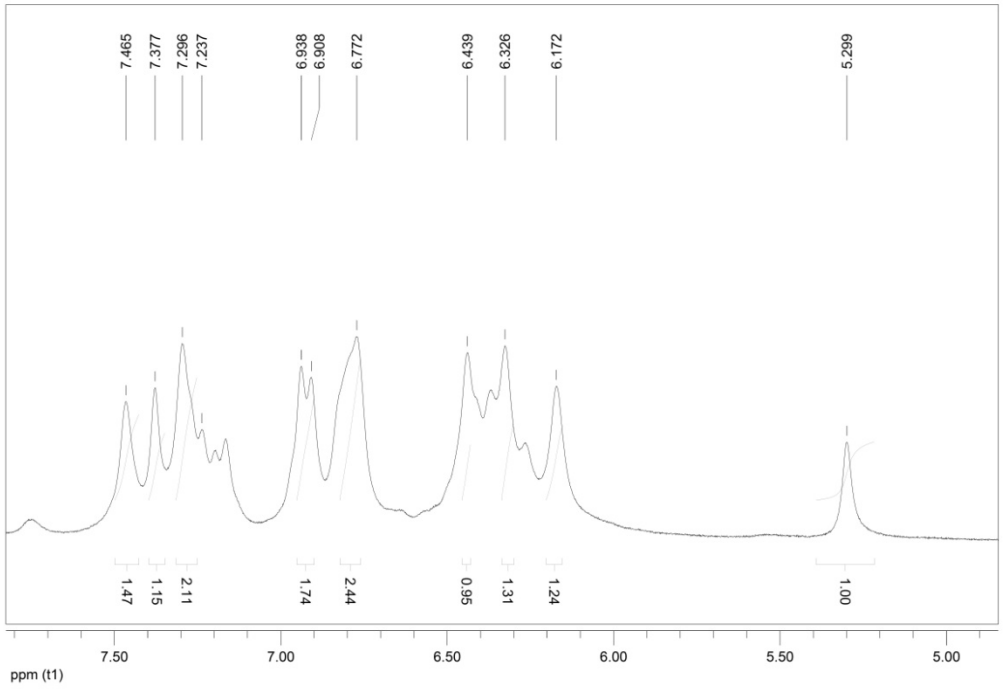


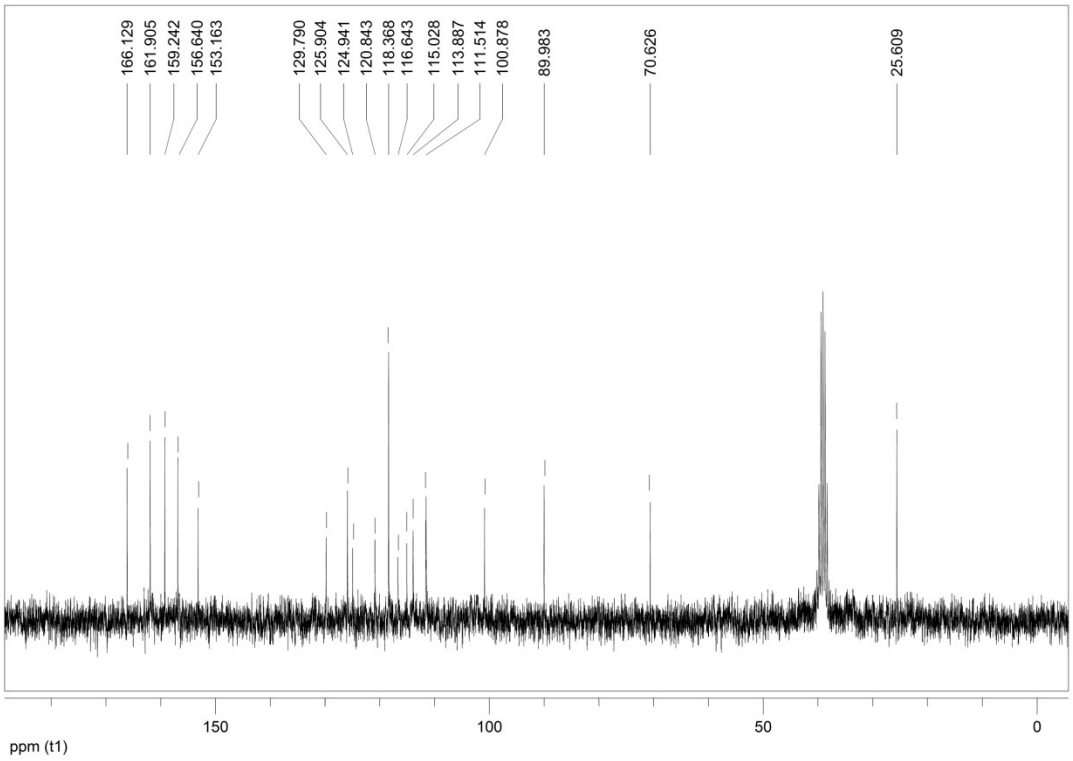
2-amino-6-bromo-4-(5-bromo-1H-indol-3-yl)-4H-chromene-3-carbonitrile

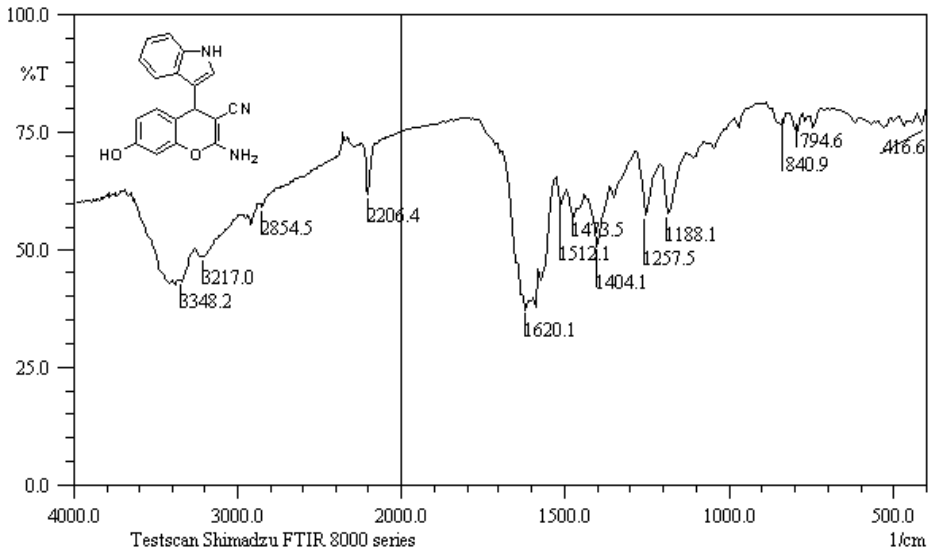
16. ***2-amino-7-hydroxy-4-(1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4p)**



2-amino-7-hydroxy-4-(1H-indol-3-yl)-4H-chromene-3-carbonitrile

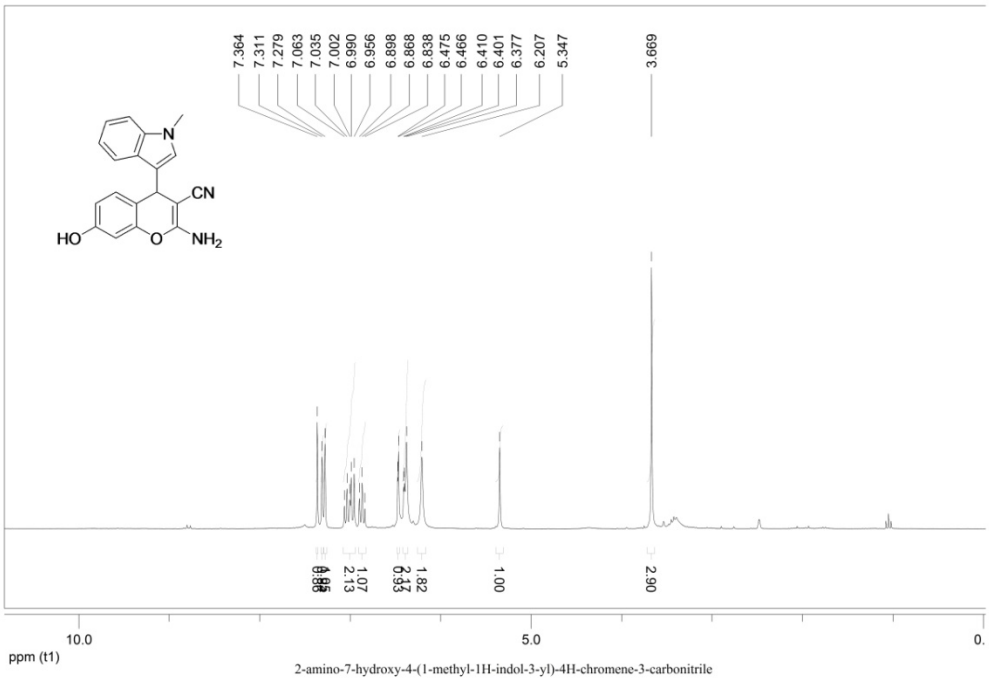

7.465
7.377
7.296
7.237
6.938
6.908
6.772
6.439
6.326
6.172
5.299
1.47
1.15
2.11
1.74
2.44
0.95
1.31
1.24
1.00
7.50
7.00
6.50
6.00
5.50
5.00
ppm (t1)


166.129
161.905
159.242
156.640
153.163
129.790
125.904
124.941
120.843
118.368
116.643
115.028
113.887
111.514
100.878
89.983
70.626
25.609
150
100
50
0
ppm (t1)

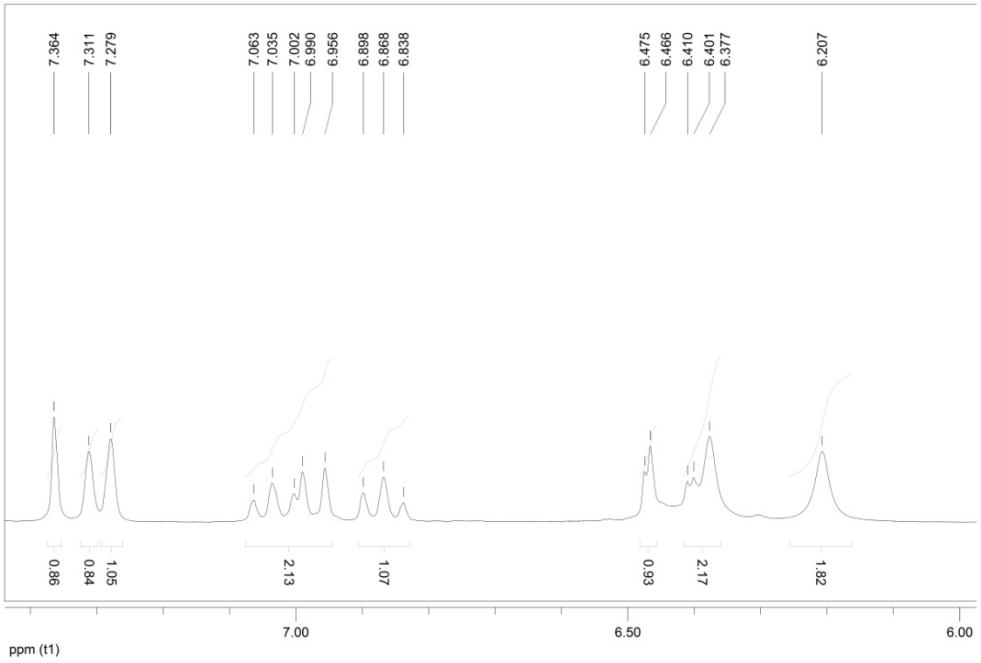


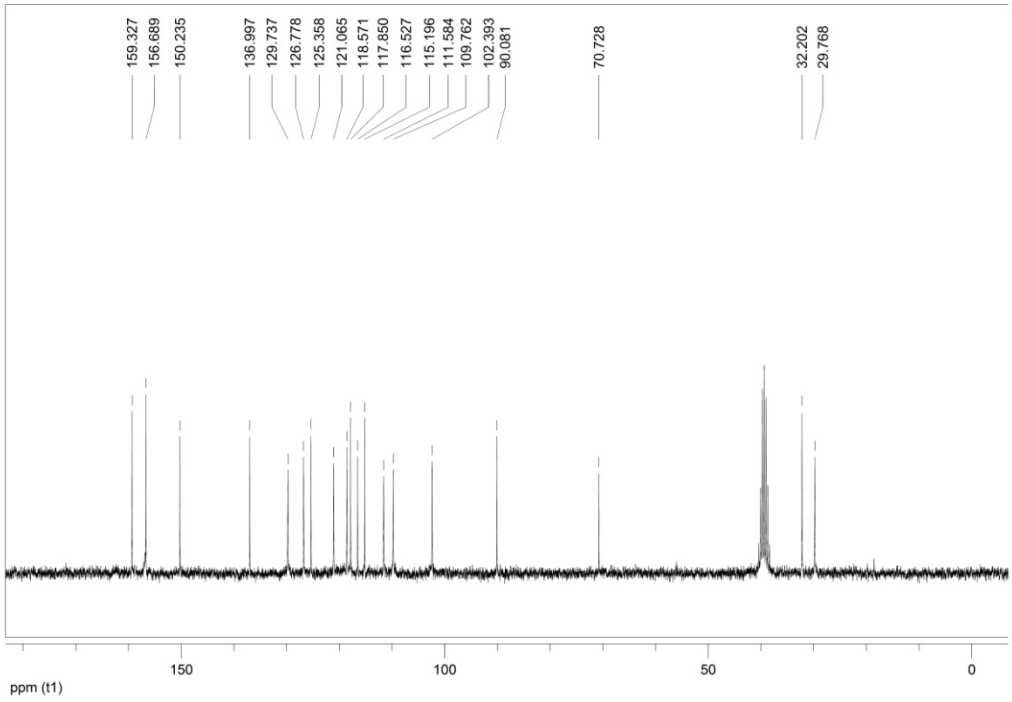
2-amino-7-hydroxy-4-(1H-indol-3-yl)-4H-chromene-3-carbonitrile

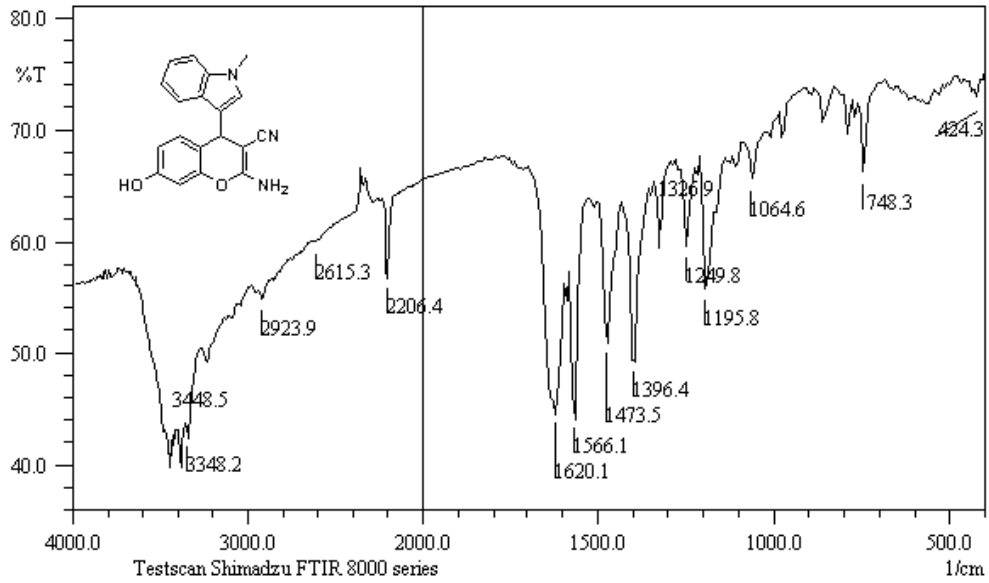
17. ***2-amino-7-hydroxy-4-(1-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4q)**



2-amino-7-hydroxy-4-(1-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile

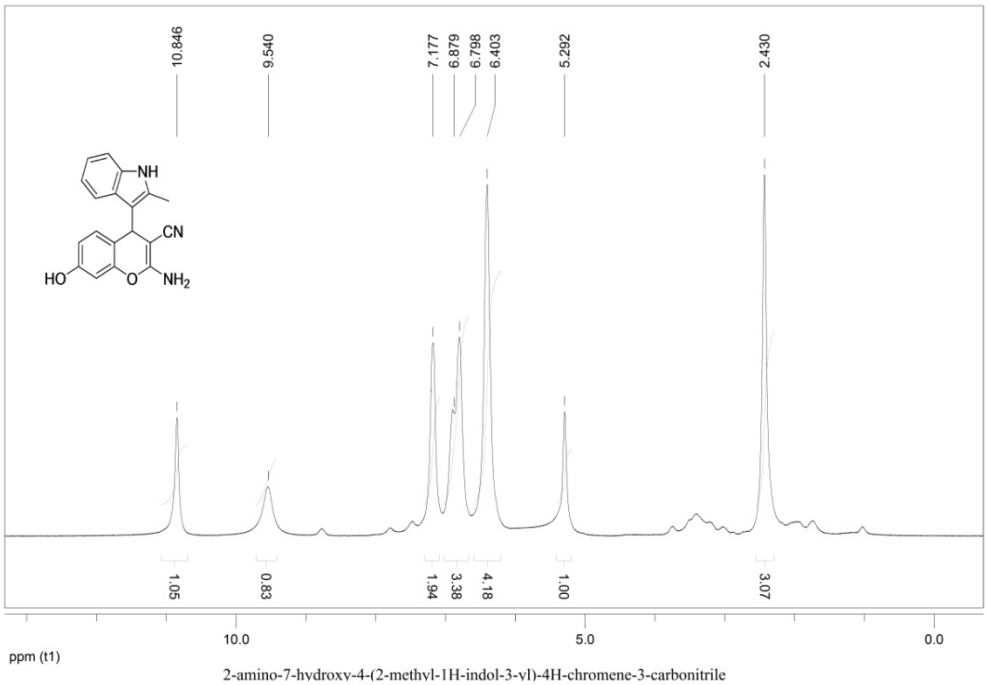

7.364
7.311
7.279
7.063
7.035
7.002
6.990
6.956
6.898
6.868
6.838
6.475
6.466
6.410
6.401
6.377
6.207
0.86
0.84
1.05
2.13
1.07
0.93
2.17
1.82
7.00
6.50
6.00
ppm (t1)


159.327
156.689
150.235
136.997
129.737
126.778
125.358
121.065
118.571
117.850
116.527
115.196
111.584
109.762
102.393
90.081
70.728
32.202
29.768
150
100
50
0
ppm (t1)

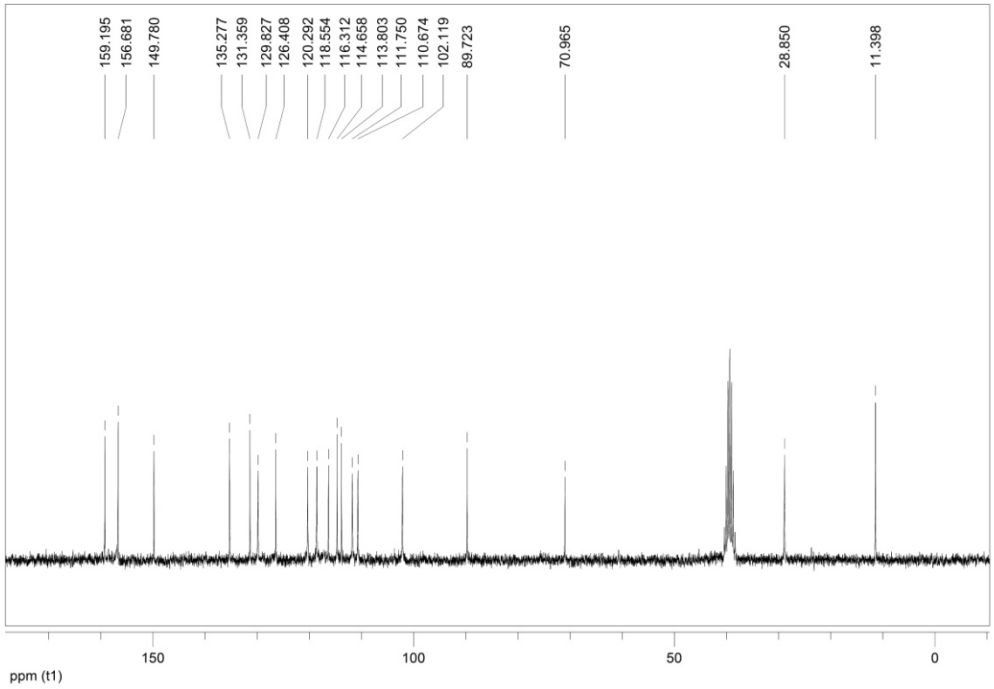


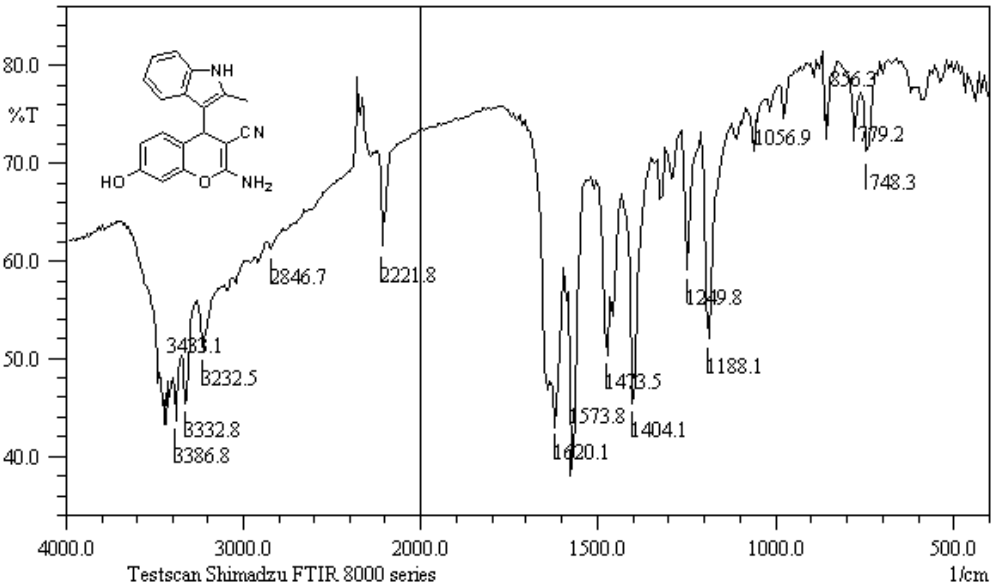
2-amino-7-hydroxy-4-(1-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile

18. ***2-amino-7-hydroxy-4-(2-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4r)**



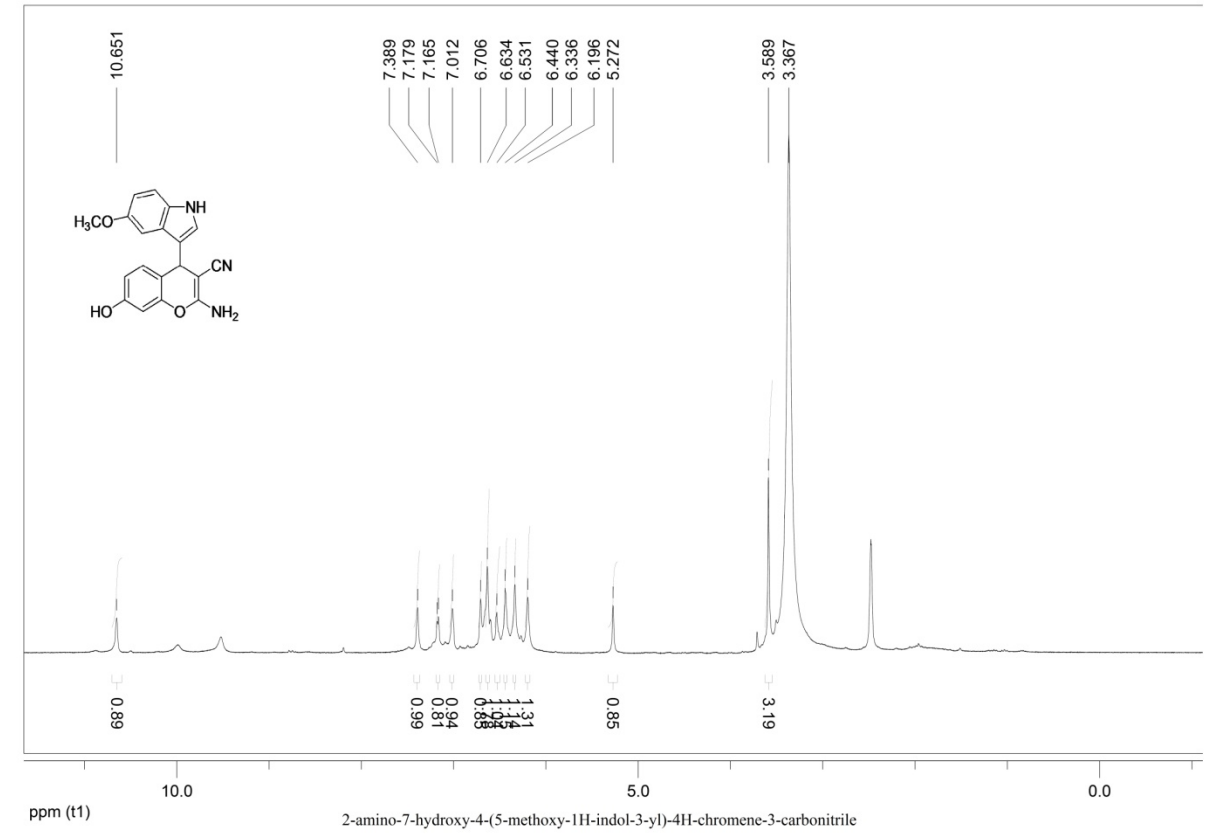
2-amino-7-hydroxy-4-(2-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile

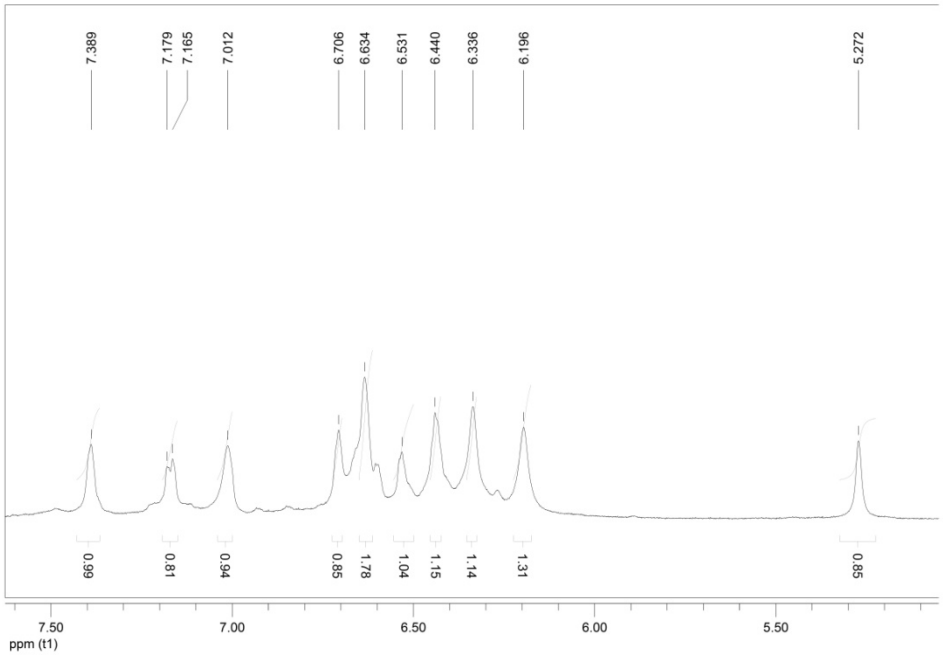


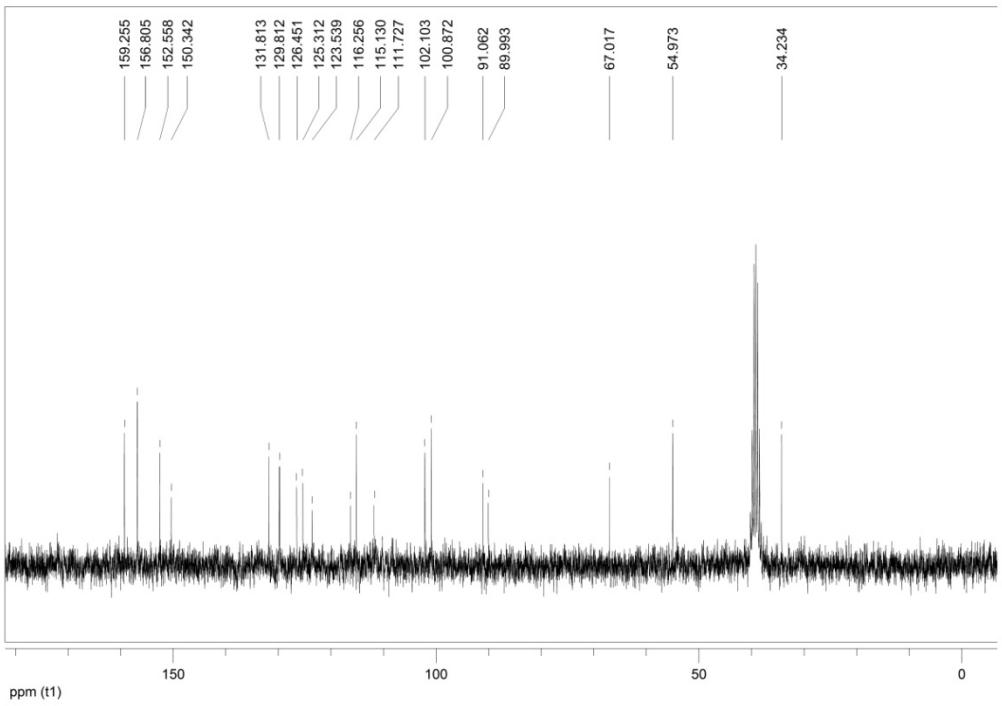


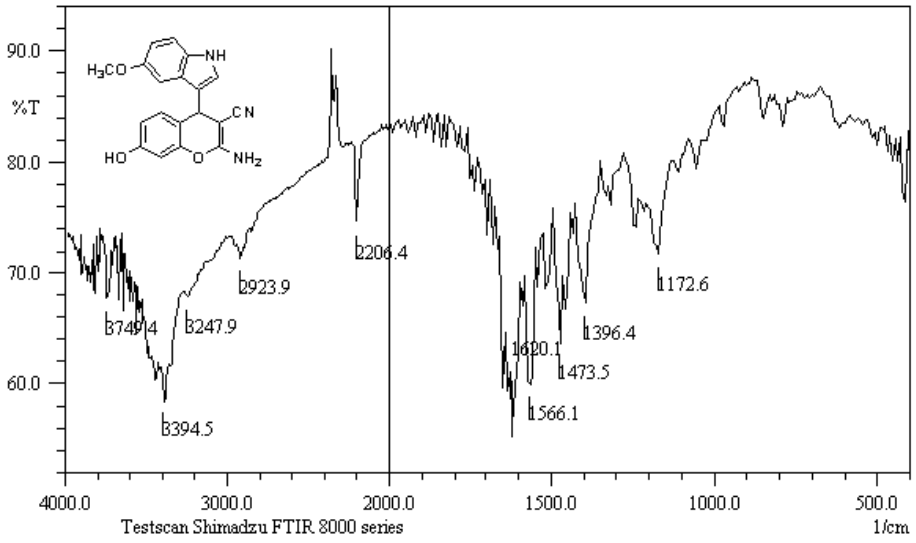
2-amino-7-hydroxy-4-(2-methyl-1H-indol-3-yl)-4H-chromene-3-carbonitrile

19. ***2-amino-7-hydroxy-4-(5-methoxy-1H-indol-3-yl)-4H-chromene-3-carbonitrile*** **(4s)**



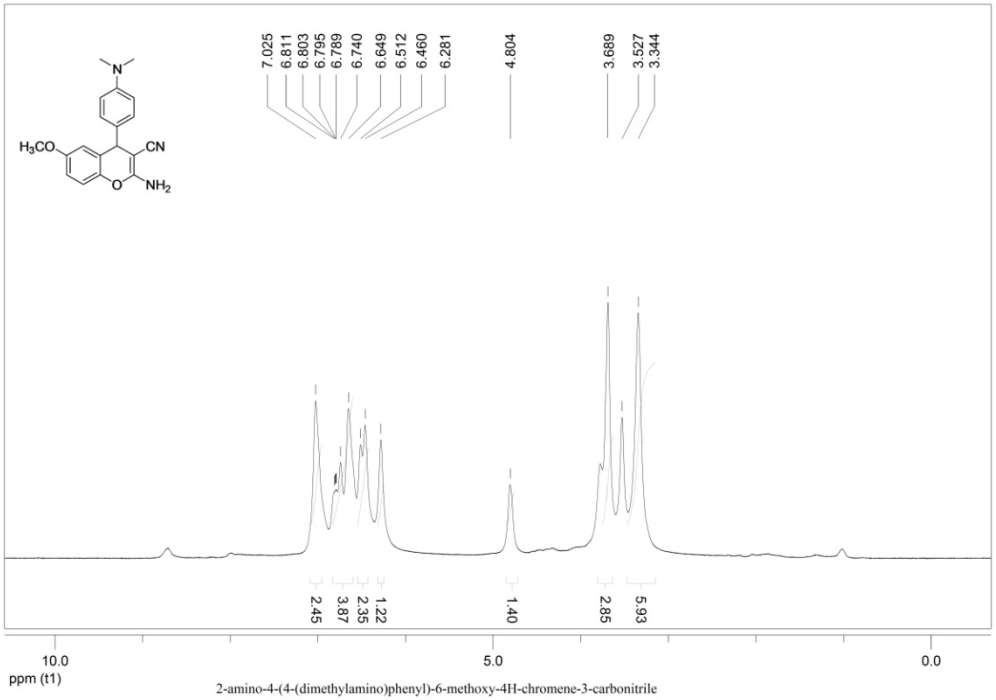


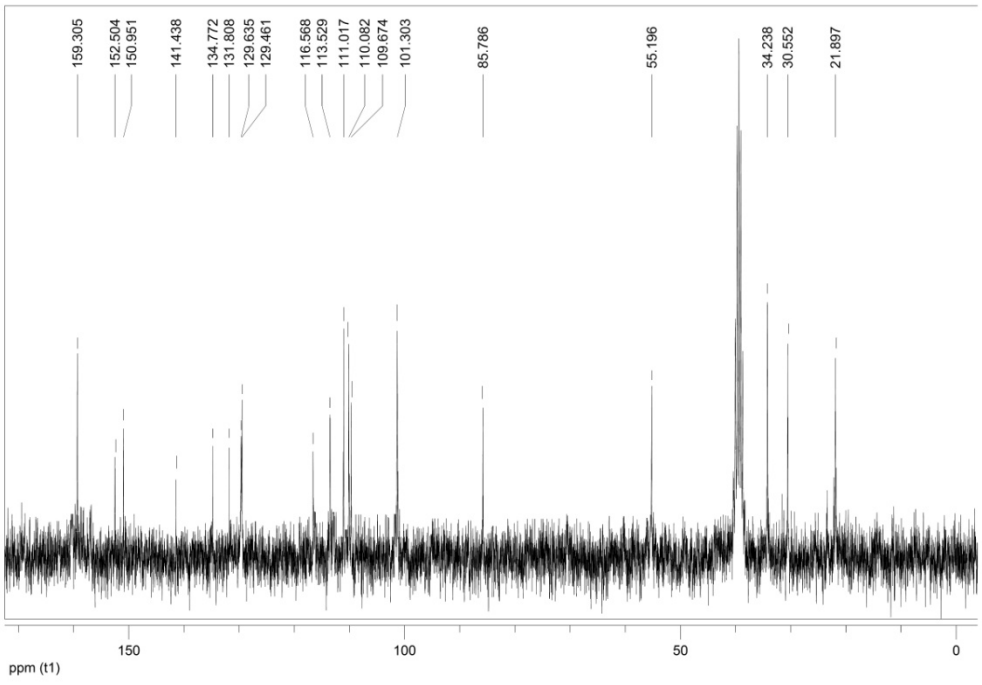


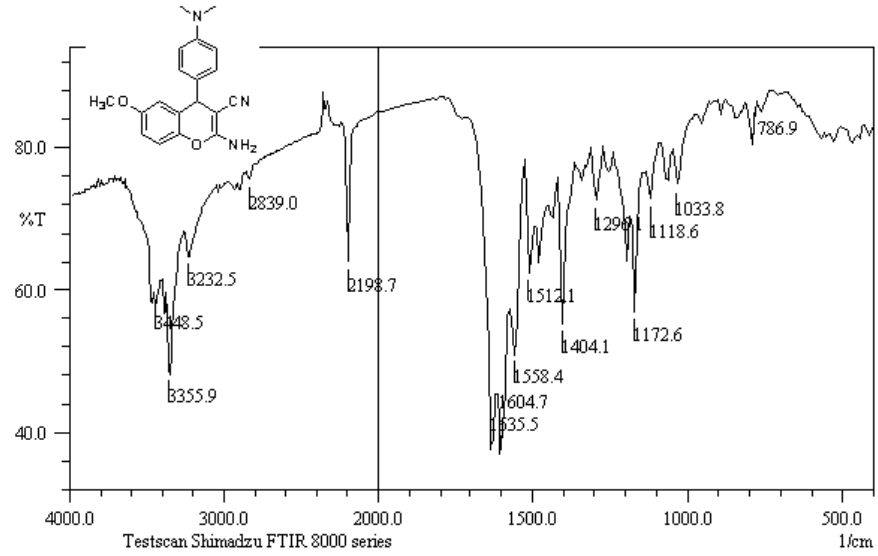


2-amino-7-hydroxy-4-(5-methoxy-1H-indol-3-yl)-4H-chromene-3-carbonitrile

20. ***2-amino-4-(4-(dimethylamino)phenyl)-6-methoxy-4H-chromene-3-carbonitrile*** **(4t)**

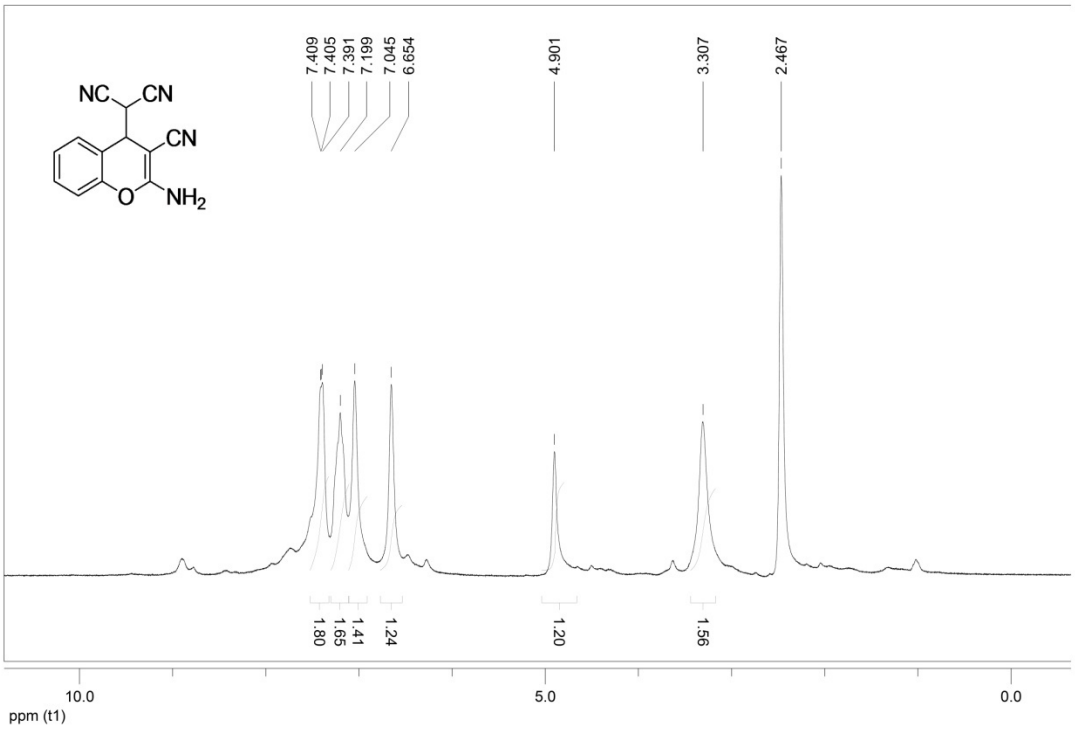

7.025
6.811
6.803
6.795
6.789
6.740
6.649
6.512
6.460
6.281
4.804
3.689
3.527
3.344
2.45
3.87
2.35
1.22
1.40
2.85
5.93
10.0
5.0
0.0
ppm (t1)
2-amino-4-(4-(dimethylamino)phenyl)-6-methoxy-4H-chromene-3-carbonitrile

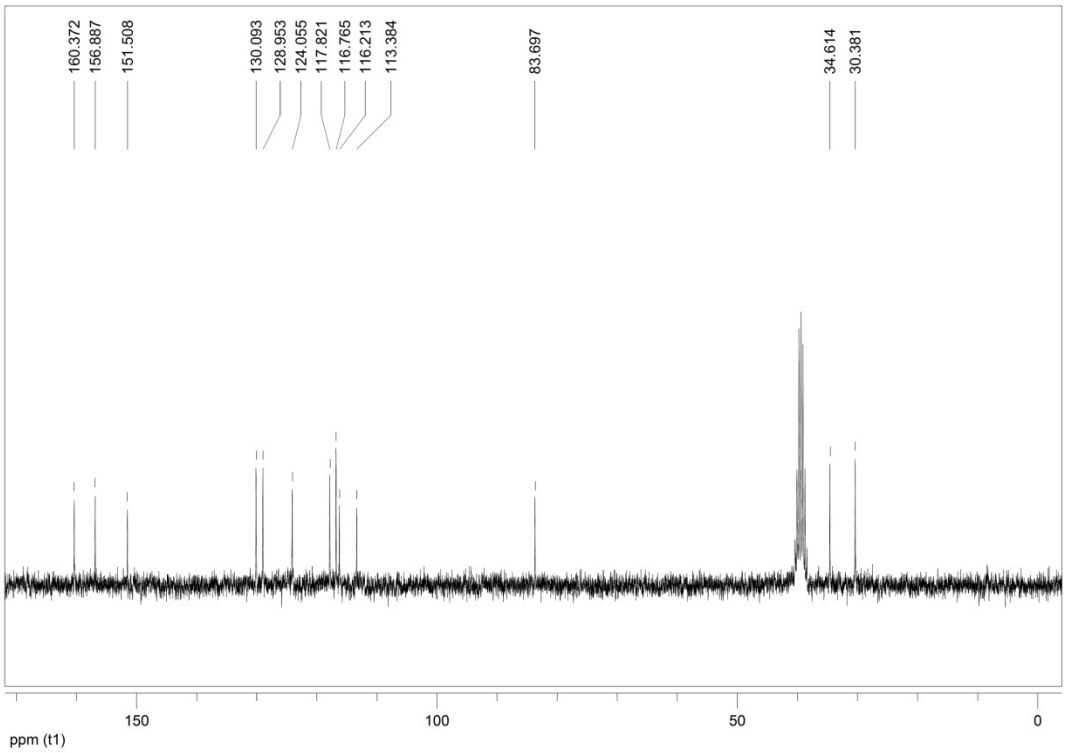

159.305
152.504
150.951
141.438
134.772
131.808
129.635
129.461
116.568
113.529
111.017
110.082
109.674
101.303
85.786
55.196
34.238
30.552
21.897
150
100
50
0
ppm (t1)

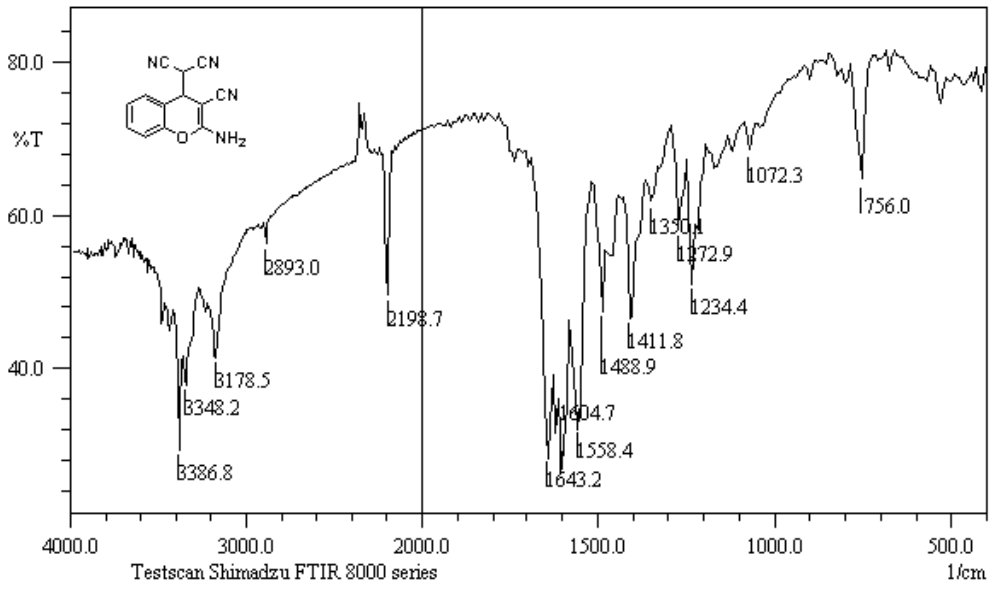


2-amino-4-(4-(dimethylamino)phenyl)-6-methoxy-4H-chromene-3-carbonitrile

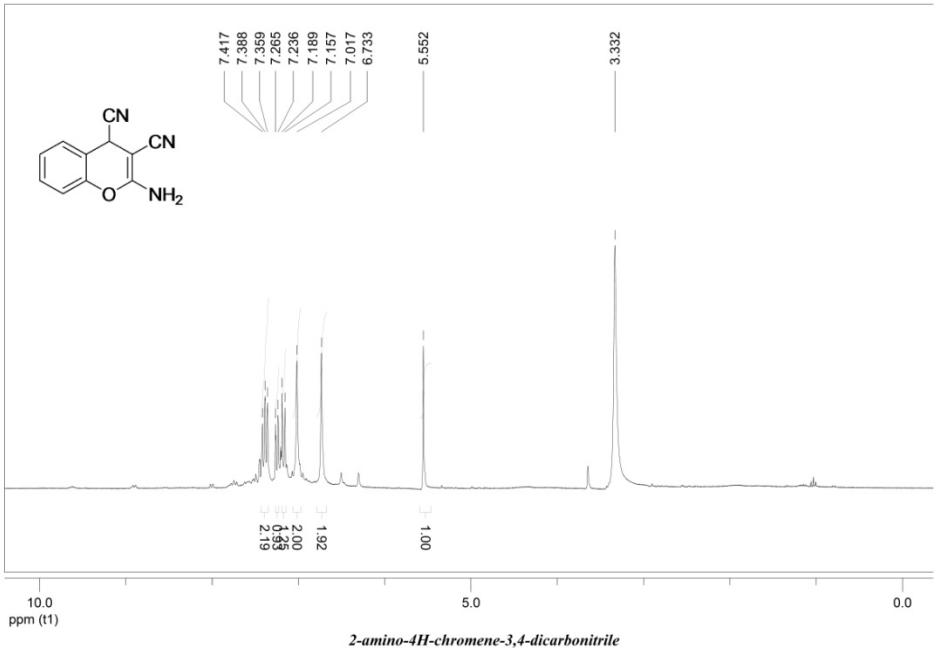
21. 2-(2-amino-3-cyano-4H-chromen-4-yl)malononitrile (4u)



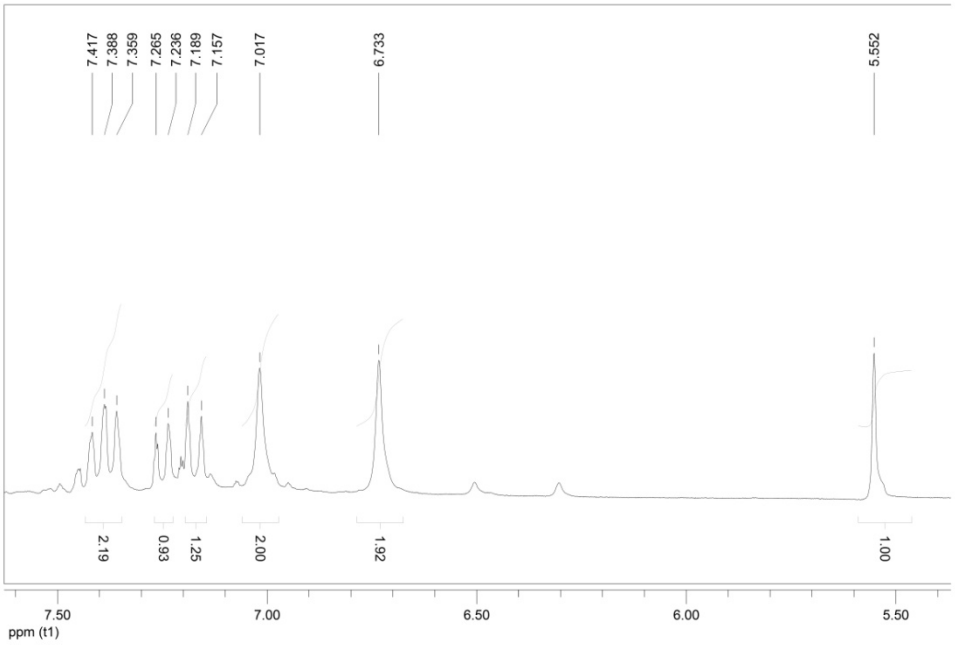

160.372
156.887
151.508
130.093
128.953
124.055
117.821
116.765
116.213
113.384
83.697
34.614
30.381
150
100
50
0
ppm (t1)

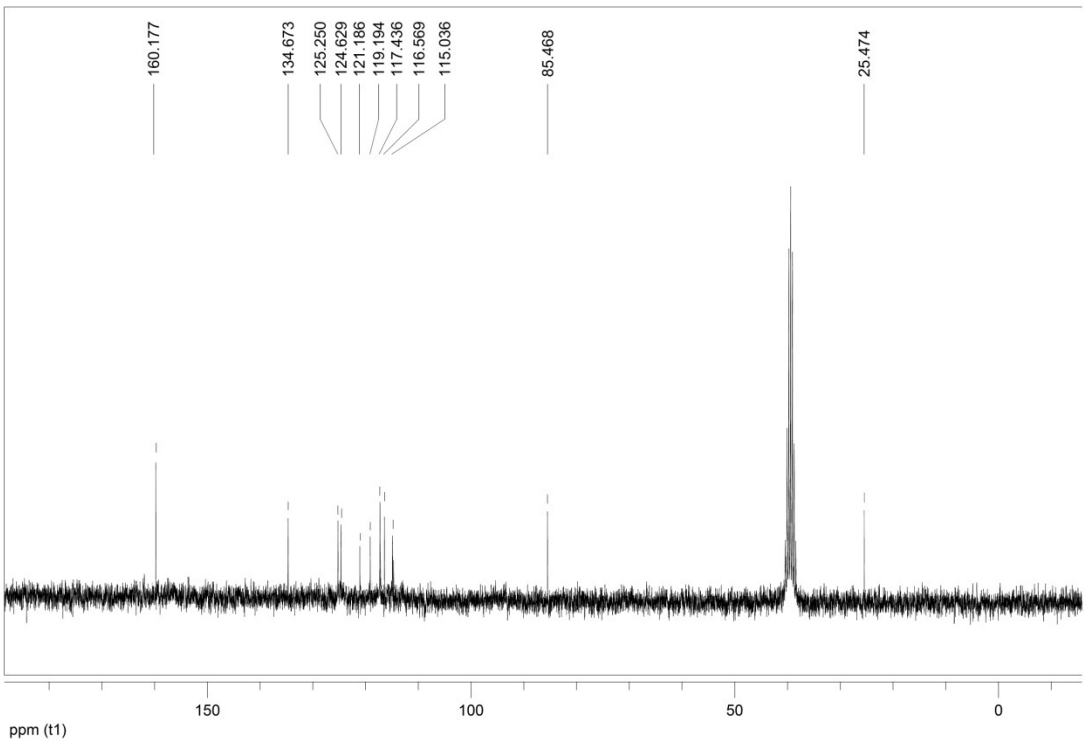

NC
CN
CN
O
NH2
80.0
%T
60.0
40.0
3386.8
3348.2
3178.5
2893.0
2198.7
1643.2
1604.7
1558.4
1488.9
1411.8
1350.4
1272.9
1234.4
1072.3
756.0
4000.0
3000.0
2000.0
1500.0
1000.0
500.0
Testscan Shimadzu FTIR 8000 series
1/cm

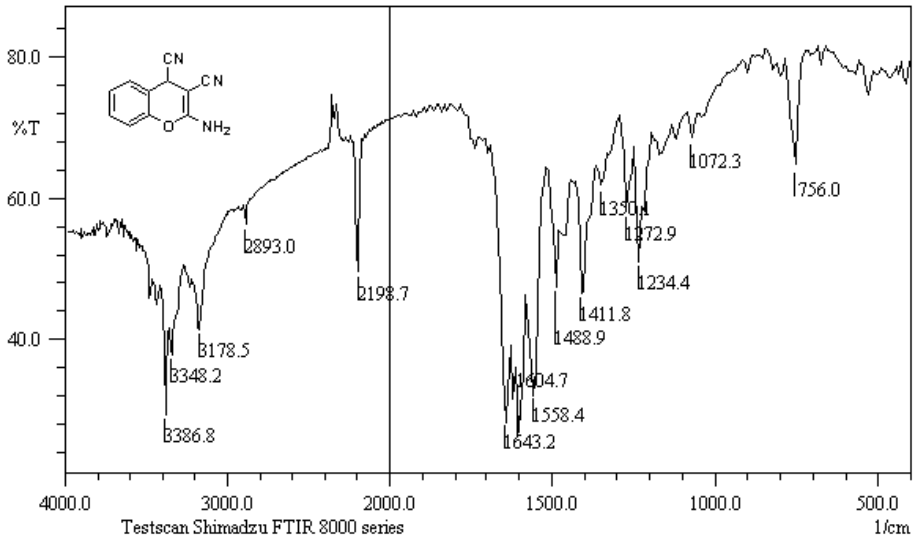
22. *2-amino-4H-chromene-3,4-dicarbonitrile* (4v)



2-amino-4H-chromene-3,4-dicarbonitrile







2-amino-4H-chromene-3,4-dicarbonitrile

Figure 1S: A comparison between the FT-IR spectra of Fe_3O_4, Fe_3O_4@SiO_2, VMNP, L-cysteine and LCMNP material