Supporting Information

Green Chemistry Oriented Multi-Component Strategy to Hybrid Heterocycle

Balakrishnan Rajarathinam, Kandhasamy Kumaravel and Gnanasambandam Vasuki*

Department of Chemistry, Pondicherry University,

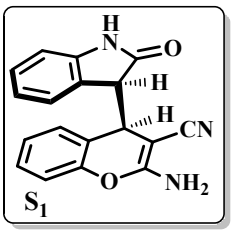
R.V. Nagar, Kalapet, Puducherry-605 014, Tel: +91-413265498, Fax: +91-413-2656740,

E-mail: vasukig@gmail.com

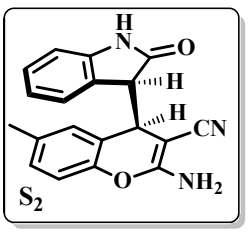
General procedure

To a stirred aqueous mixture of oxindole **2** (3 mmol) respective 2–hydroxybenzaldehyde **1** (3 mmol) and malononitrile **3** (3 mmol) were added successively in 25 mL water at ambient temperature under an open atmosphere with vigorous stirring for appropriate time. The precipitated solid was filtered, washed with water and then 5 mL of ethyl acetate/hexane mixture (2:8). The product **S_9** obtained was pure by TLC and spectral techniques.

2-amino-4-(2-oxoindolin-3-yl)-4*H*-chromene-3-carbonitrile S_1: Yellow solid (isolated as a 64:36 mixture of diastereomers), yield 92%; mp = 230 ºC; IR (KBr): ν_{max} = 3459, 3333, 2924, 2853, 2195, 2185, 1703, 1643, 1617, 1577 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 10.41 (s, ≈ 1H + 1H), 7.68-6.43 (m, ≈ 8H + 8H), 7.01 (s, ≈ 2H + 2H), 4.24 (d, J = 2.8 Hz, ≈ 1H + 1H), 3.62 (d, J = 2.4 Hz, 1H + 1H), ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 176.7, 176.1, 162.1, 161.9, 149.7, 149.3, 143.5, 142.9, 128.7, 128.5, 128.3, 128.1, 128.0, 127.6, 126.8, 126.6,124.7, 124.2, 123.7, 123.5, 122.3, 121.4, 121.2, 121.0, 120.2, 120.0, 119.7, 118.8, 115.8, 115.6, 109.2, 109.1, 53.2, 52.8, 52.4, 50.2, 37.2, 36.6 ppm; HR-MS m/z: calcd for $C_{18}H_{13}N_3O_2$[M+Na]+: 326.0905; found: 326.0906.

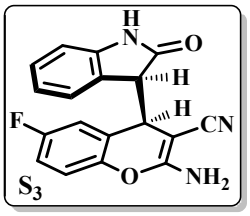


2-amino-6-methyl-4-(2-oxoindolin-3-yl)-4*H*-chromene-3-carbonitrile S_2: White solid (isolated as a 60:40 mixture of diastereomers), yield 83%; mp = 228

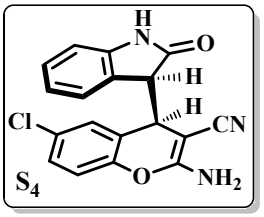


ºC; IR (KBr): ν_{max} = 3411, 3301, 3177, 2924, 2180, 1700, 1657, 1617, 1586 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 10.43 (s, ≈ 1H + 1H), 7.18-6.42 (m, ≈ 7H + 7H), 7.02 (s, ≈ 2H + 2H), 4.19 (d, J = 2.4 Hz, ≈ 1H + 1H), 3.61 (d, J = 2.0 Hz, ≈ 1H + 1H), 2.15 (s, ≈ 3H + 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 176.7, 176.1, 162.1, 162.1, 147.6, 147.3, 143.5, 142.9,133.7, 133.0, 129.1, 128.9, 128.4, 128.0, 127.8, 126.8, 126.7, 123.7, 123.5, 121.1, 120.9, 120.3, 120.2, 119.4, 115.5, 115.3, 109.2, 109.1, 53.2, 52.7, 52.2, 50.1, 37.2, 36.6, 20.3, 20.3 ppm; HR-MS m/z: calcd for $C_{19}H_{15}N_3O_2$[M+Na]+: 340.1062; found: 340.1063.

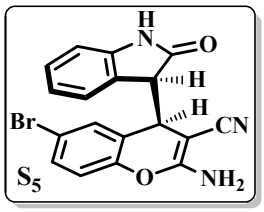
2-amino-6-fluoro-4-(2-oxoindolin-3-yl)-4*H*-chromene-3-carbonitrile S_3: White solid (isolated as a 76:24 mixture of diastereomers), yield 85%; mp = 229 ºC; IR (KBr): ν_{max} = 3457, 3336, 3211, 3082, 2923, 2198, 1708, 1663, 1611, 1589 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 10.49 (s, ≈ 1H + 1H), 7.20-6.47 (m, ≈ 7H + 7H), 7.09 (s, ≈ 2H + 2H), 4.26 (d, J = 3.2 Hz, ≈ 1H + 1H), 3.67 (d, J = 3.2 Hz, ≈ 1H + 1H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 176.6, 175.9, 162.1, 161.9, 159.0, 156.6, 146.0, 145.7, 145.7, 143.5, 142.9, 128.1, 126.6, 126.4, 123.8, 123.5, 123.2, 121.7, 121.7, 121.3, 121.0, 120.0, 117.5, 117.5, 117.3, 117.2, 115.4, 115.1, 114.5, 114.3, 113.9, 113.6, 109.3, 109.1, 52.7, 52,6, 51,5, 49.7, 37.3, 36.7 ppm; HR-MS m/z: calcd for $C_{18}H_{12}FN_3O_2$[M+Na]+: 344.0811; found: 344.0813.



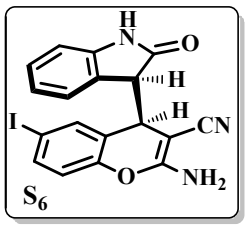
2-amino-6-chloro-4-(2-oxoindolin-3-yl)-4*H*-chromene-3-carbonitrile S_4: Pale pink solid (isolated as a 63:37 mixture of diastereomers), yield 84%; mp = 230 ºC; IR (KBr): ν_{max} = 3453, 3409, 3285, 3195, 2932, 2198, 2186, 1707, 1655, 1617, 1576 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 10.51 (s, ≈ 1H + 1H), 7.20-6.47 (m, ≈ 7H + 7H), 7.09 (s, ≈ 2H + 2H), 4.25 (d, J = 2.4 Hz, ≈ 1H + 1H), 3.67 (s, ≈ 1H + 1H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 176.6, 175.9, 161.9, 161.8, 148.5, 148.3, 143.5, 142.9, 128.5, 128.3, 128.2, 128.1, 127.9, 127.6, 127.3, 126.6, 126.4, 123.9, 123.6, 123.4, 122.1, 121.3, 121.1, 119.9, 119.8, 117.7, 117.5, 109.3, 109.2, 52.7, 51.7, 50.1, 37.0, 36.5 ppm; HR-MS m/z: calcd for $C_{18}H_{12}ClN_3O_2$[M+Na]+: 360.0515; found: 360.0517.



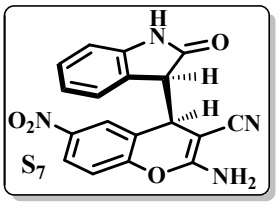
2-amino-6-bromo-4-(2-oxoindolin-3-yl)-4*H*-chromene-3-carbonitrile S_5: Pale yellow solid (isolated as a 60:40 mixture of diastereomers), yield 87%; mp = 232 ºC; IR (KBr): ν_{max} = 3428, 3342, 3196, 2924, 2184, 1701, 1661, 1645, 1615, 1572 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 10.51 (s, ≈ 1H + 1H), 7.47-6.56 (m, ≈ 7H + 7H), 7.08 (s, ≈ 2H + 2H), 4.26 (d, J = 2.8 Hz, ≈ 1H + 1H), 3.66 (d, J = 2.8 Hz, ≈ 1H+ 1H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 176.5, 175.9, 161.8, 161.7, 148.9, 148.8, 143.5, 142.9, 131.4, 131.2, 130.8, 128.2, 126.6, 126.4, 123.9, 123.8, 123.6, 122.6, 121.3, 121.1, 119.9, 119.8, 118.0, 117.8, 116.0, 115.6, 109.2, 109.2, 52.7, 52.7, 51.7, 50.2, 36.9, 36.4 ppm; HR-MS m/z: calcd for $C_{18}H_{12}BrN_3O_2$[M+Na]+: 404.0010; found: 404.0012.



2-amino-6-iodo-4-(2-oxoindolin-3-yl)-4*H*-chromene-3-carbonitrile S_6: Pale pink solid (isolated as a 50:50 mixture of diastereomers), yield 80%; mp = 227 ºC; IR (KBr): ν_{max} = 3445, 3192, 2923, 2185, 1701, 1644, 1615, 1567 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 10.50 (s, 1H), 10.35 (s, 1H) 7.60-6.58 (m, ≈ 7H + 7H), 6.87 (s, ≈ 2H + 2H), 4.29 (d, J = 2.0 Hz, 1H), 4.23 (d, J = 2.4 Hz, 1H) 3.67 (d, J = 1.2 Hz, 1H), 3.65 (d, J = 1.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 176.5, 175.9, 161.8, 161.7, 149.5, 149.4, 143.5, 142.9, 137.2, 136.9, 136.6, 136.1, 128.1, 126.7, 126.5, 123.9, 123.6, 122.8, 121.2, 121.0, 119.9, 119.8, 118.2, 118.0, 88.0, 87.7, 52.7, 52.7, 51.8, 50.4, 36.6, 36.3 ppm; HR-MS m/z: calcd for $C_{18}H_{12}BrN_3O_2$[M+Na]+: 451.9871; found: 451.8772.

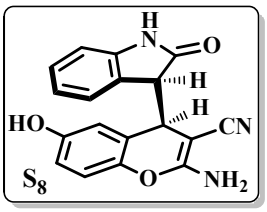


2-amino-6-nitro-4-(2-oxoindolin-3-yl)-4*H*-chromene-3-carbonitrile S_7: Yellow solid (isolated as a 64:36 mixture of diastereomers), yield 82%; mp = 242 ºC; IR (KBr): ν_{max} = 3337, 3203, 2924, 2852, 2199, 1702, 1663, 1650, 1619, 1581, 1524 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 10.53 (s, ≈ 1H + 1H) 8.16-6.62 (m, ≈ 7H + 7H), 7.22 (s, ≈ 2H + 2H), 4.40 (d, J = 2.8 Hz, 1H), 3.73 (d, J = 2.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 176.5, 175.9, 161.4, 161.3, 154.2, 143.5, 143.4, 143.3, 142.9, 128.4, 128.3, 126.4, 126.3, 124.5, 124.3, 124.3, 124.1, 124.0, 123.8, 122.5, 121.8, 121.4, 121.3,

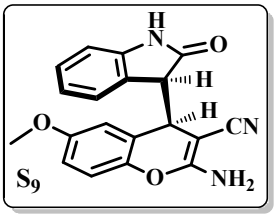


119.6, 119.4, 117.3, 117.0, 109.4, 109.3, 52.9, 52.6, 51.5, 50.6, 37.0, 36.6 ppm; HR-MS m/z: calcd for $C_{18}H_{12}N_4O_4$[M+Na]+: 371.0756; found: 371.0758.

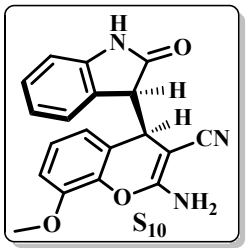
2-amino-6-hydroxy-4-(2-oxoindolin-3-yl)-4*H*-chromene-3-carbonitrile S_8: Pale brown solid (isolated as a 77:23 mixture of diastereomers), yield 78%; mp = 218 ºC; IR (KBr): ν_{max} = 3475, 3357, 3240, 2185, 1692, 1645, 1606, 1585 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 10.40 (s, ≈ 1H + 1H), 9.43 (s, ≈ 1H + 1H), 7.15-6.43 (m, ≈ 7H + 7H), 6.54 (s, ≈ 2H + 2H),4.21 (d, J = 2.8 Hz, ≈ 1H + 1H), 4.15 (s, ≈ 1H + 1H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 176.6, 176.2, 162.4, 162.2, 154.0, 153.5, 143.5, 143.0, 142.6, 142.1, 128.0, 128.9, 126.8, 126.7, 123.6, 123.6, 122.3, 121.8, 121.0, 120.6, 120.4, 116.6, 116.3, 115.5, 115.2, 113.5, 113.3, 109.2, 109.2, 53.2, 52.7, 52.2, 49.6, 37.4, 36.8 ppm; HR-MS m/z: calcd for $C_{18}H_{13}N_3O_3$[M+Na]+: 342.0854; found: 342.0856.



2-amino-6-methoxy-4-(2-oxoindolin-3-yl)-4*H*-chromene-3-carbonitrile S_9: Pale pink solid (isolated as a 98:02 mixture of diastereomers), yield 81%; mp = 236 ºC; IR (KBr): ν_{max} = 3444, 3338, 3212, 2925, 2190, 1683, 1643, 1618, 1586 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 10.57 (s, ≈ 1H + 1H), 7.37-6.44 (m, ≈ 7H + 7H), 7.01 (s, ≈ 2H + 2H), 4.22 (d, J = 2.8 Hz, ≈ 1H + 1H), 3.73 (d, J = 2.8 Hz, ≈ 1H + 1H), 3.64 (s, ≈ 3H + 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 176.9, 176.1, 162.1, 155.2, 143.2, 142.9, 128.2, 128.0, 126.6, 123.7, 121.2, 121.0, 116.7, 116.4, 113.9, 112.0, 109.1, 55.2, 54.6, 52.8, 52.6, 51.9, 37.5, 37.0 ppm; HR-MS m/z: calcd for $C_{19}H_{15}N_3O_3$[M+Na]+: 356.1011; found: 356.1012.

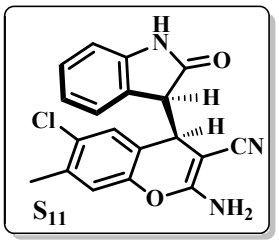


2-amino-8-methoxy-4-(2-oxoindolin-3-yl)-4*H*-chromene-3-carbonitrile S_{10}: White solid (isolated as a 82:18 mixture of diastereomers), yield 78%; mp = 233 ºC; IR (KBr): ν_{max} = 3443, 3338, 3212, 2925, 2190, 1683, 1643, 1618, 1586 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 10.41 (s, ≈ 1H + 1H), 7.17-6.60 (m, ≈ 7H + 7H), 7.09 (s, ≈ 2H + 2H), 4.23 (d, J = 2.8 Hz, 1H + 1H), 3.67 (s, ≈ 3H + 3H), 3.63 (d, J = 2.8 Hz 1H + 1H) ppm; ^{13}C NMR (100

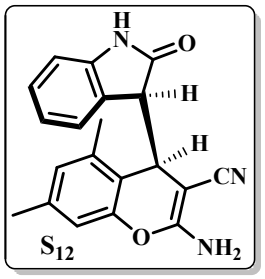


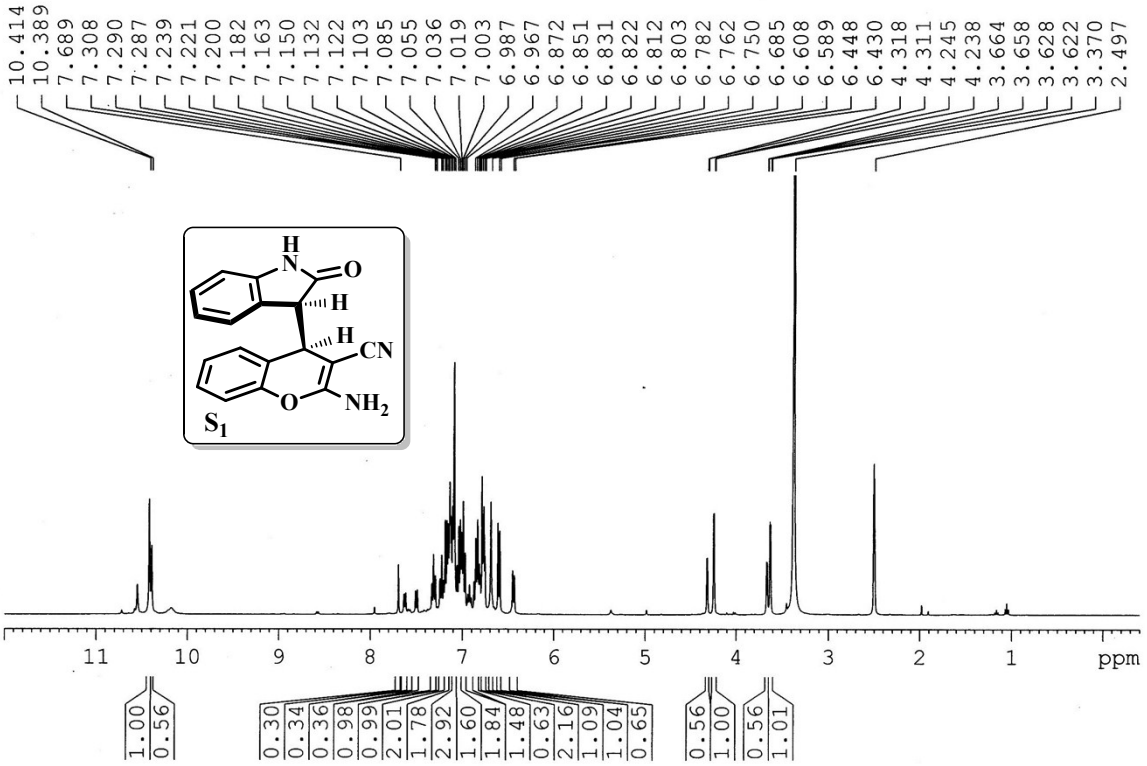
MHz, DMSO-d_6): δ = 176.6, 176.1, 162.0, 146.9, 146.7, 143.5, 143.0, 139.1, 138.7, 128.0, 126.9, 126.7, 124.4, 124.0, 123.6, 123,5, 122.3, 121.2, 121.0, 120.6, 120.2, 120.1, 119.2, 118.8, 111.2, 109,2, 109,1, 55.7, 55.5, 53.1, 52.7, 52.4, 50.2, 37.2, 36.7 ppm; HR-MS m/z: calcd for $C_{19}H_{15}N_3O_3$[M+Na]+: 356.1011; found: 356.1012.

2-amino-7-chloro-6-methyl-4-(2-oxoindolin-3-yl)-4*H*-chromene-3-carbonitrile S_{11}: Yellow solid (isolated as a 56:44 mixture of diastereomers), yield 89%; mp = 238 ºC; IR (KBr): ν_{max} = 3444, 3334, 3190, 2923, 2207, 2193, 1706, 1643, 1619, 1567 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.50 (s, ≈ 1H + 1H), 7.58-6.61 (m, ≈ 6H + 6H), 7.18 (s, ≈ 2H + 2H), 4.28 (s, ≈ 1H + 1H), 3.68 (s, ≈ 1H + 1H), 2.29 (s, ≈ 3H + 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 176.4, 176.0, 163.8, 162.5, 154.2, 153.9, 142.9, 141.9, 121.1, 120.0, 119.9, 118.9, 117.0, 116.9, 116.1, 113.5, 64.3, 64.0, 51.5, 47.5, 38.1, 38.0 ppm; HR-MS m/z: calcd for $C_{19}H_{14}ClN_3O_2$[M+Na]+: 374.0672; found: 374.0673.

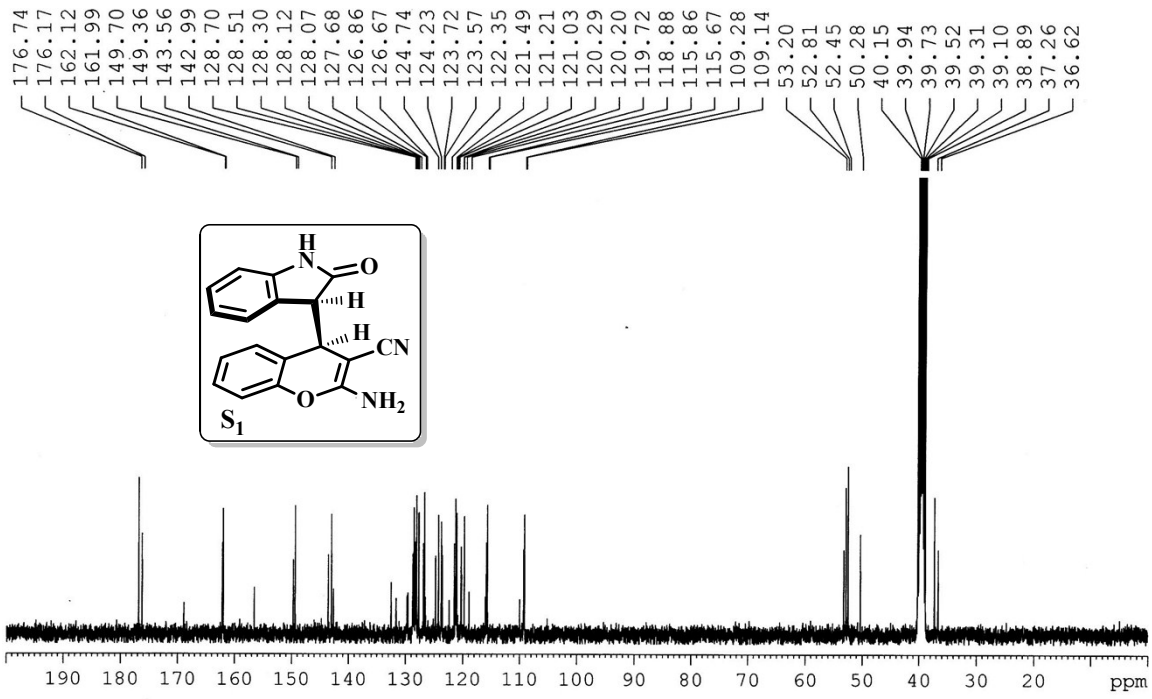


2-amino-5,7-dimethyl-4-(2-oxoindolin-3-yl)-4*H*-chromene-3-carbonitrile S_{12}: White solid (isolated as a 94:06 mixture of diastereomers), yield 86%; mp = 228 ºC; IR (KBr): ν_{max} = 3450, 3240, 3181, 3158, 2923, 2188, 1620, 1606, 1572 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.52 (s, ≈ 1H + 1H), 7.40-6.33 (m, ≈ 6H + 6H), 6.55 (s, ≈ 2H + 2H), 4.25 (d, J = 2.4 Hz, ≈ 1H + 1H), 3.52 (s, ≈ 1H + 1H), 2.40 (s, ≈ 3H + 3H), 2.30 (s, ≈ 3H + 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 176.4, 172.6, 150.2, 143.7, 137.8, 135.7, 127.9, 127.6, 126.8, 123.6, 124.8, 120.1, 118.4, 113.9, 109.2 51.5, 50.0, 34.6, 20.5, 18.0 ppm; HR-MS m/z: calcd for $C_{20}H_{17}N_3O_2$[M+Na]+: 354.1218; found: 354.1220.

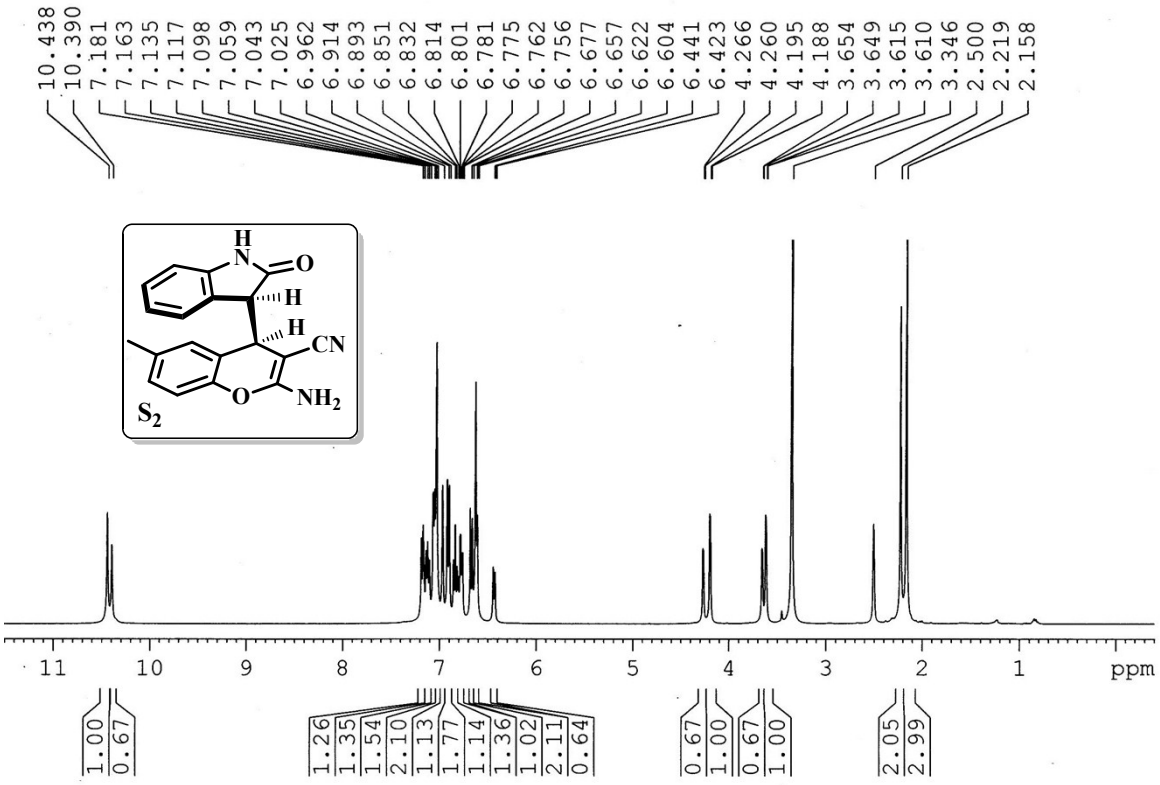




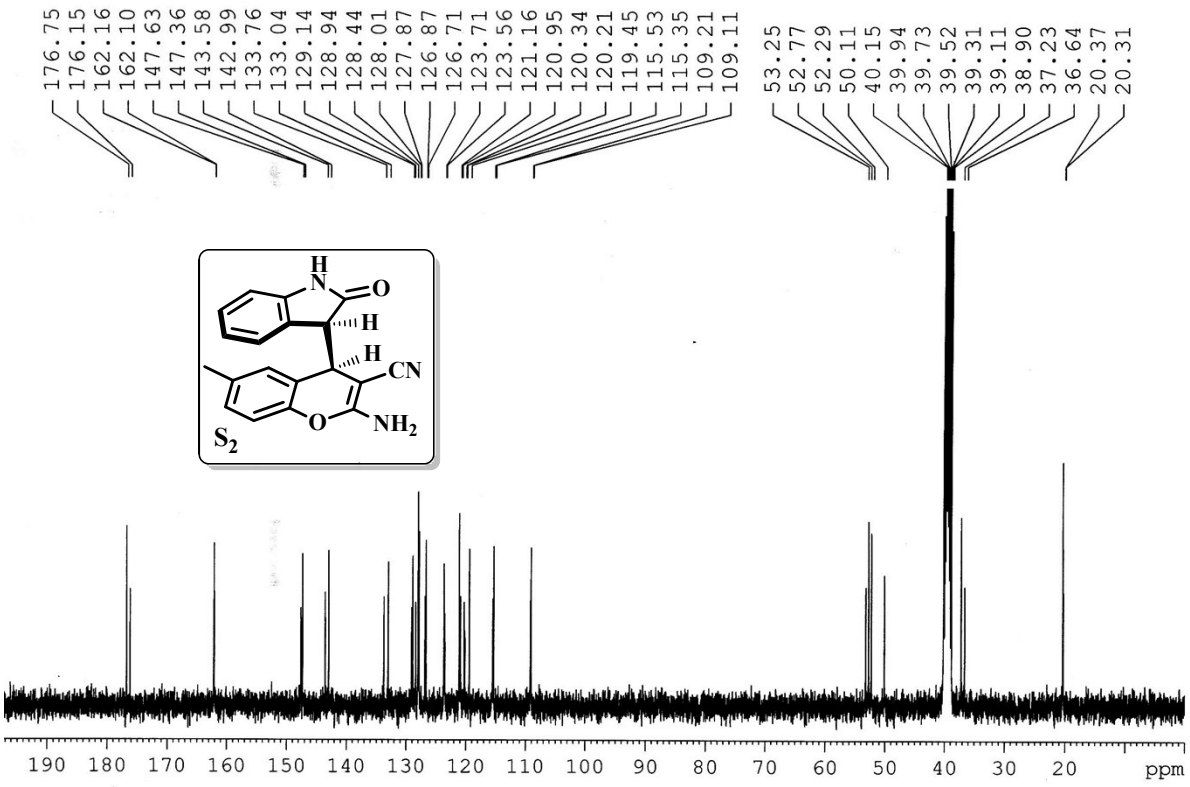
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound S_1



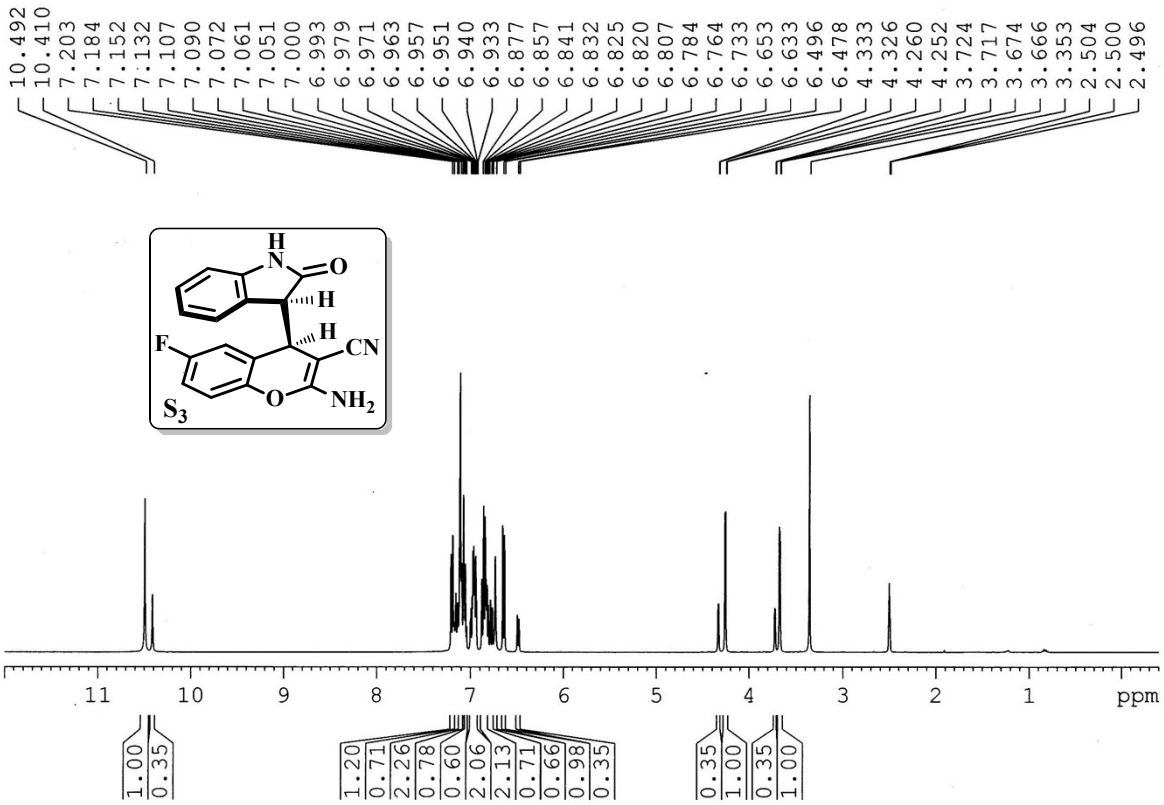
^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound S_1



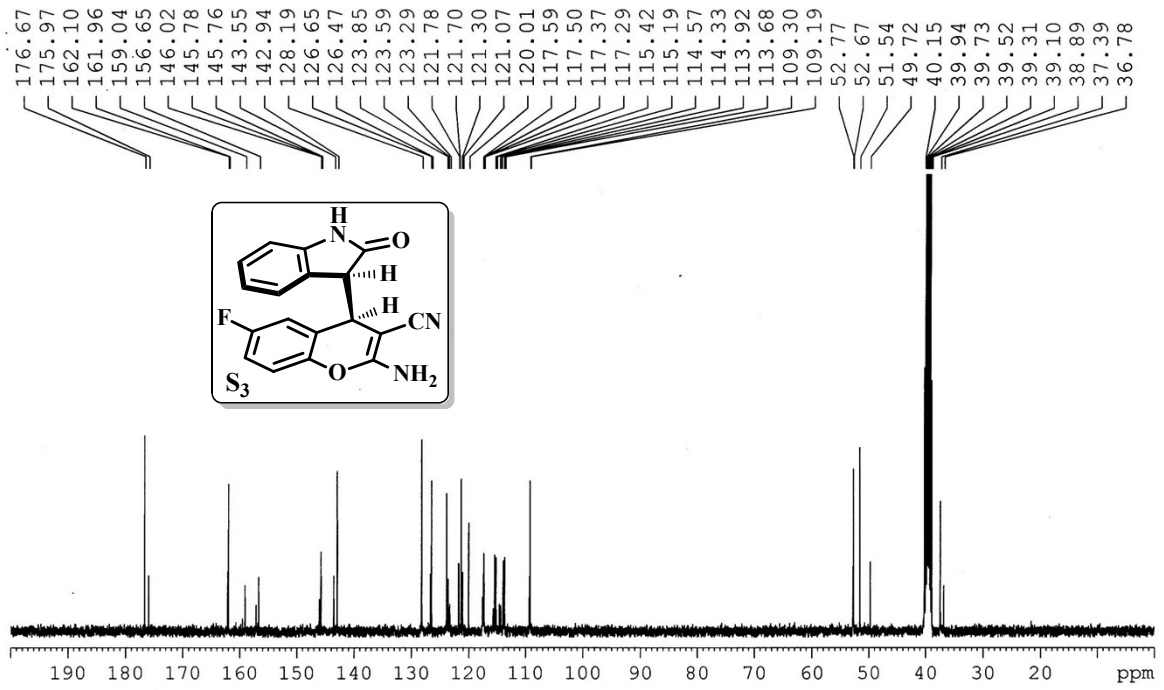
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound S_2



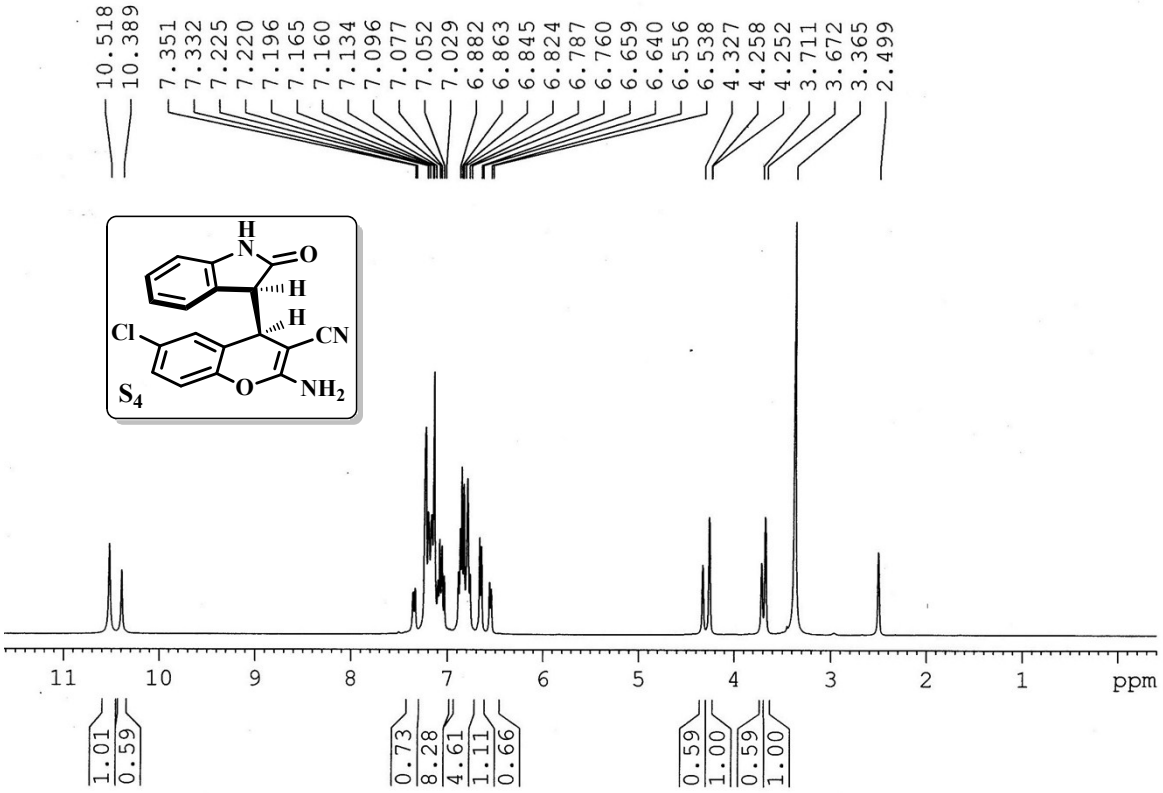
^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound S_2



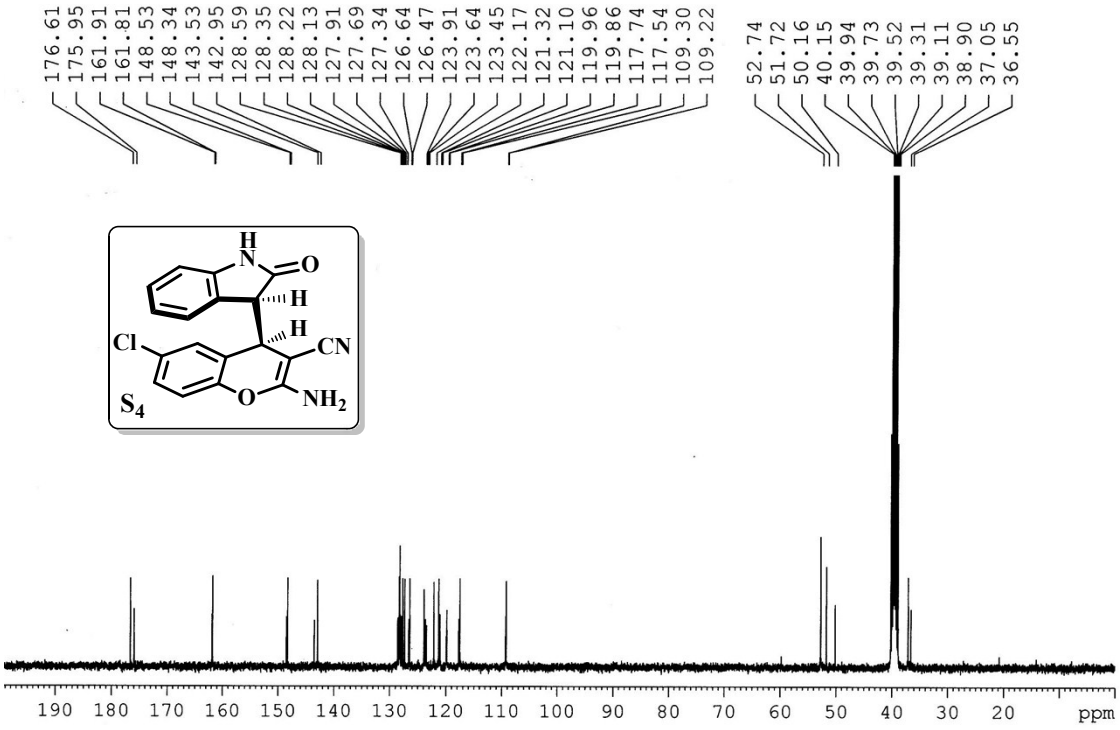
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound S_3



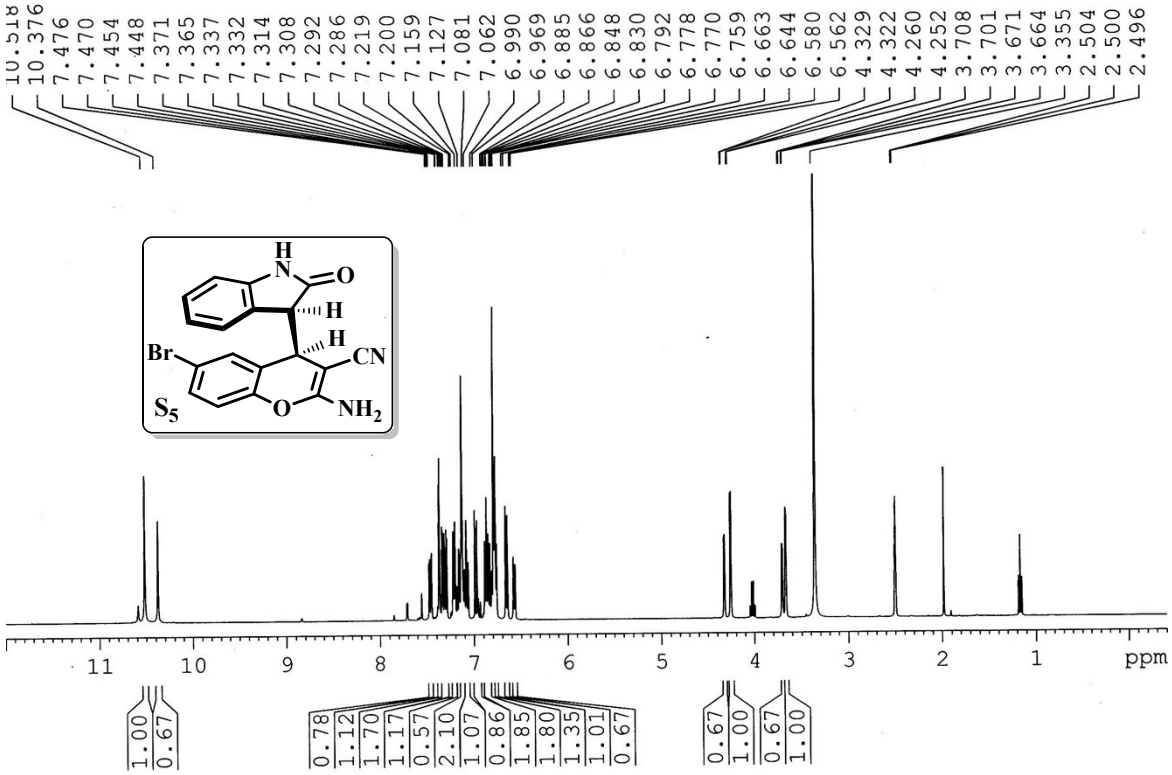
^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound S_3



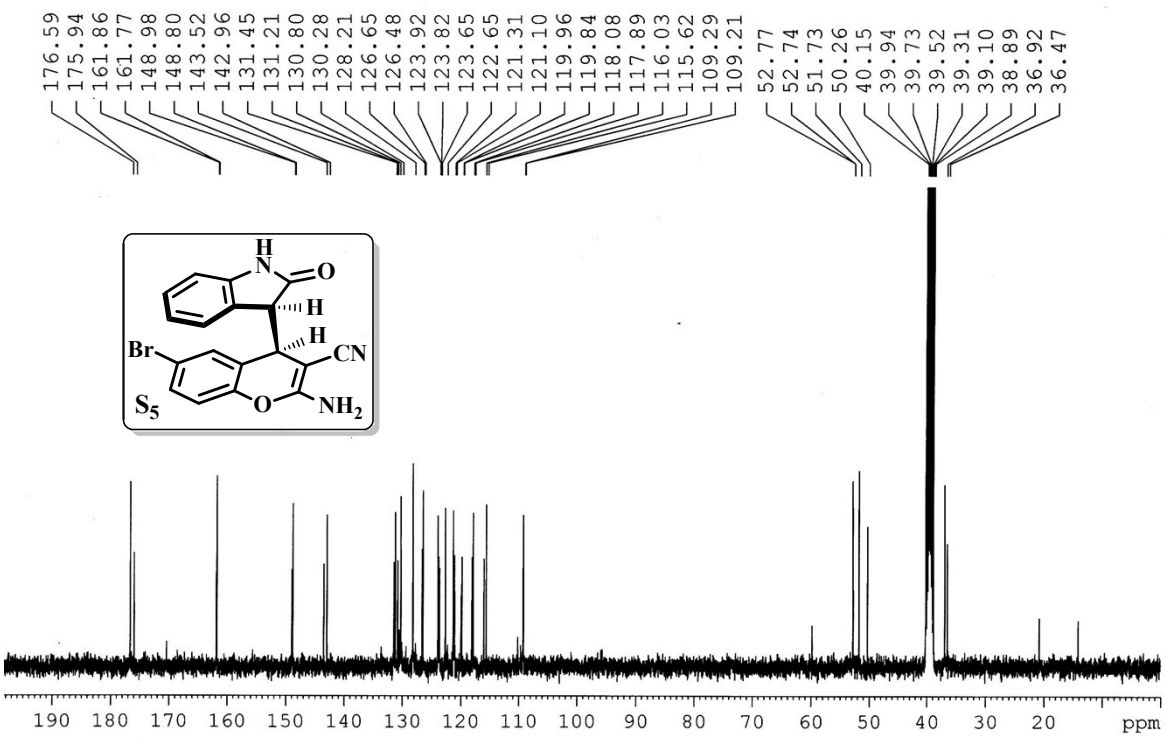
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound S_4



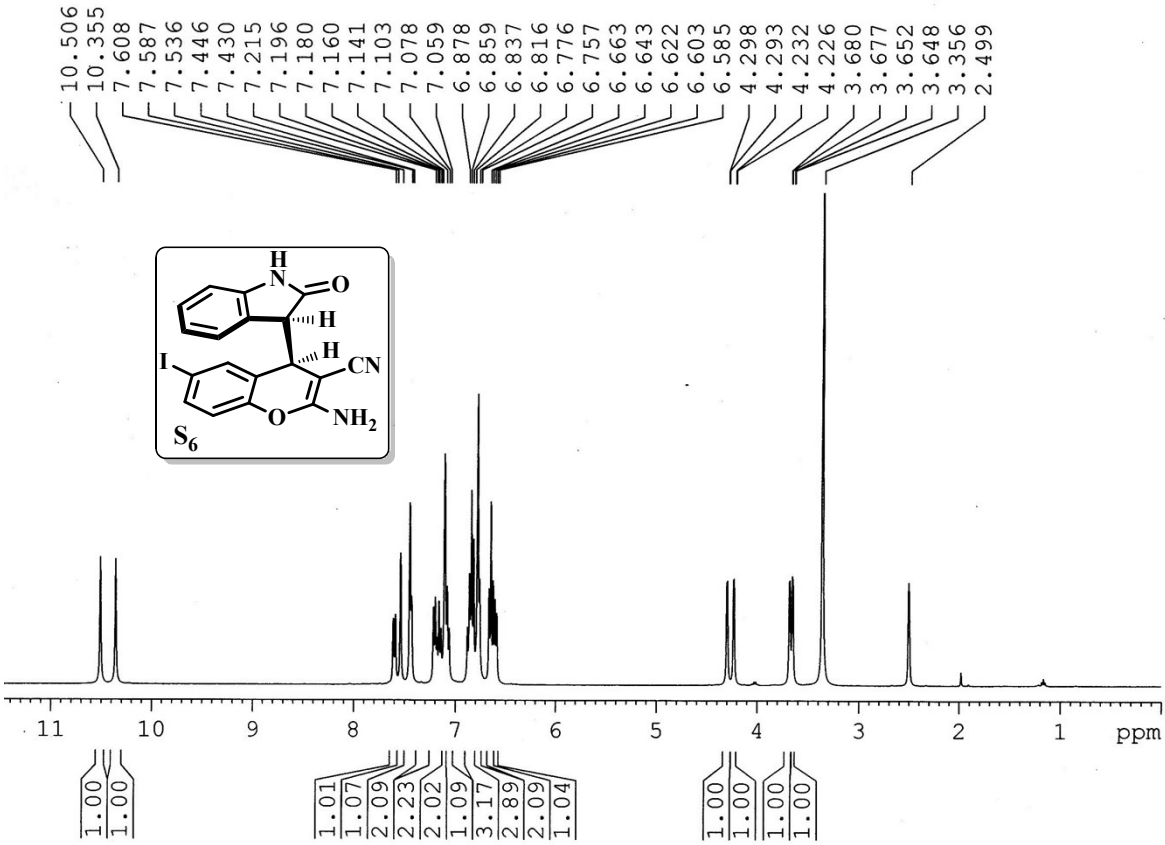
^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound S_4



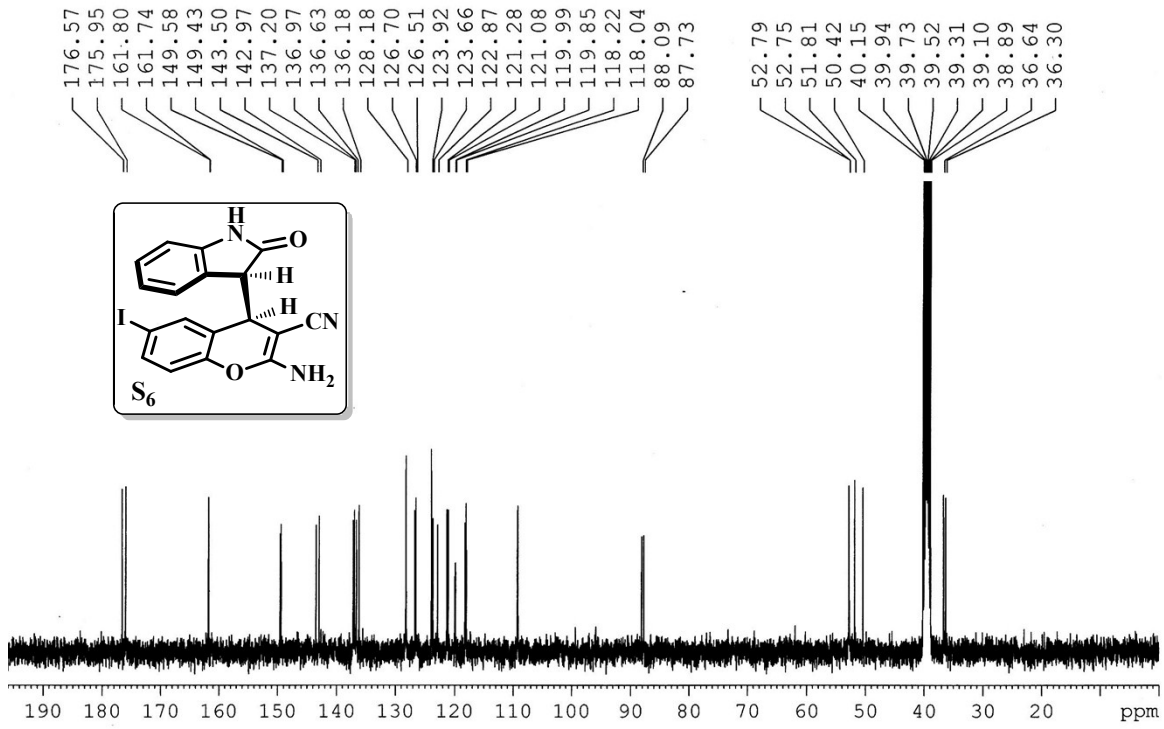
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound S_5



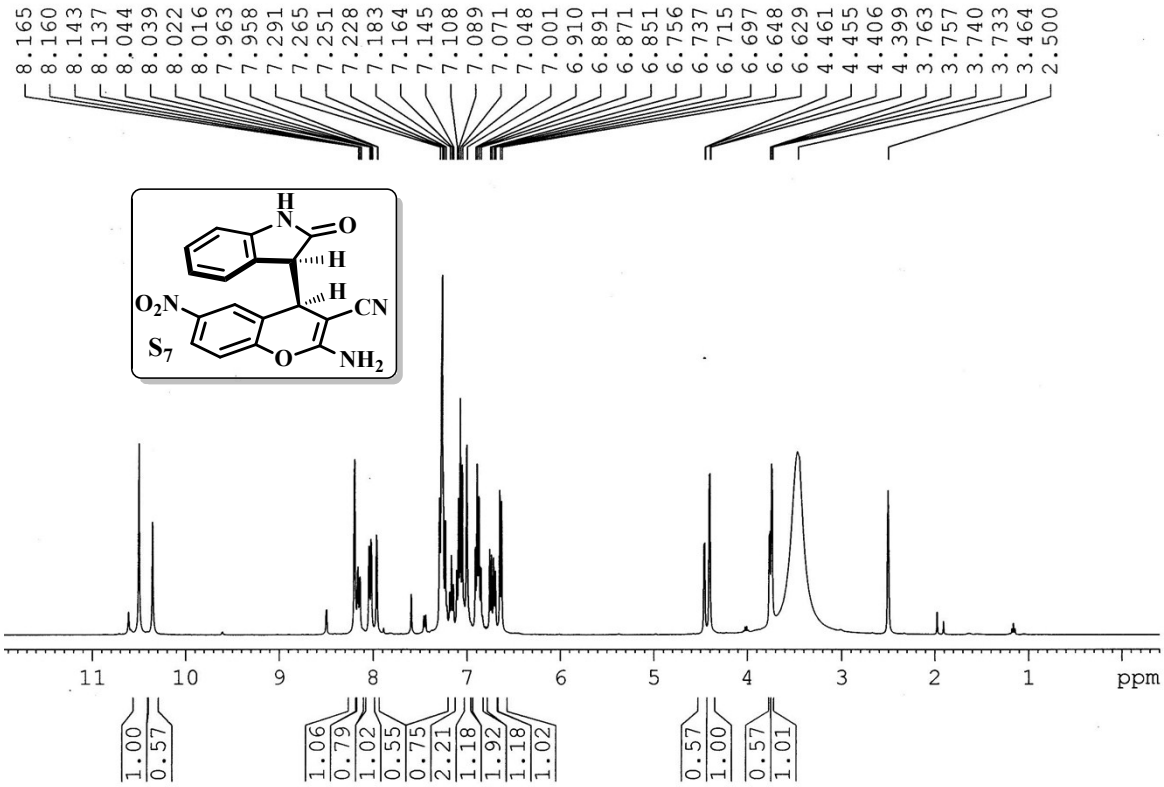
^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound S_5



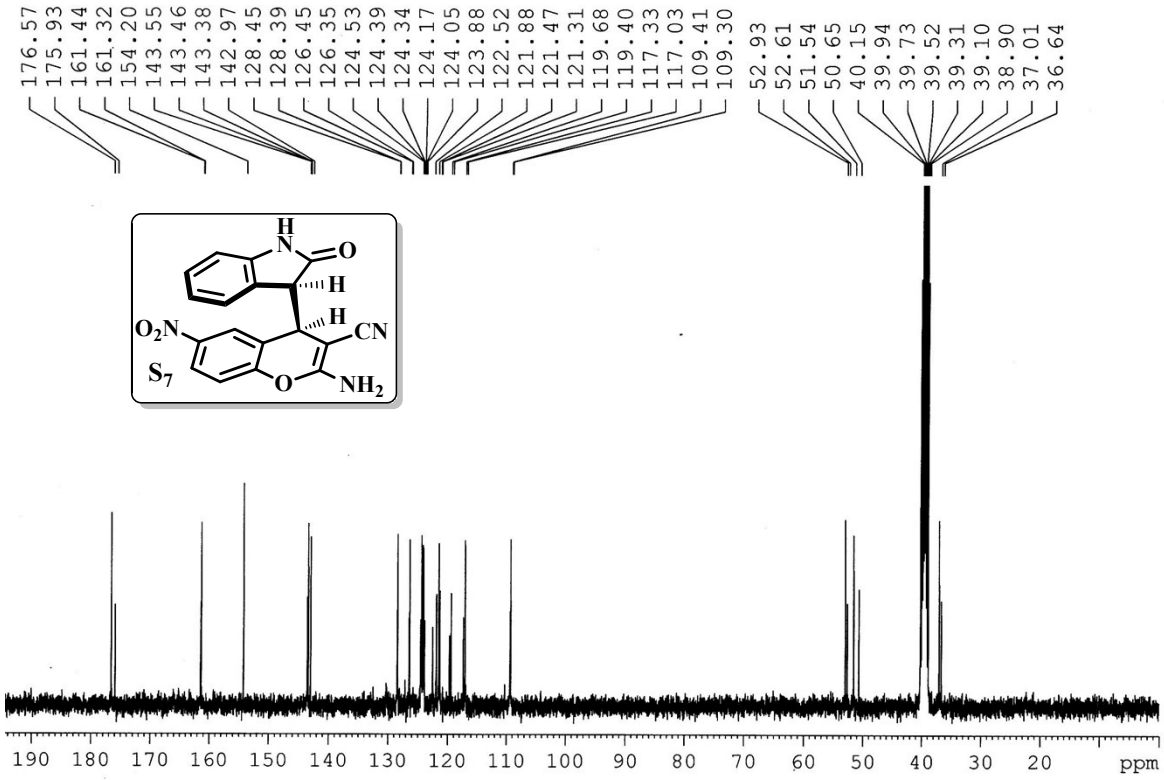
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound S_6



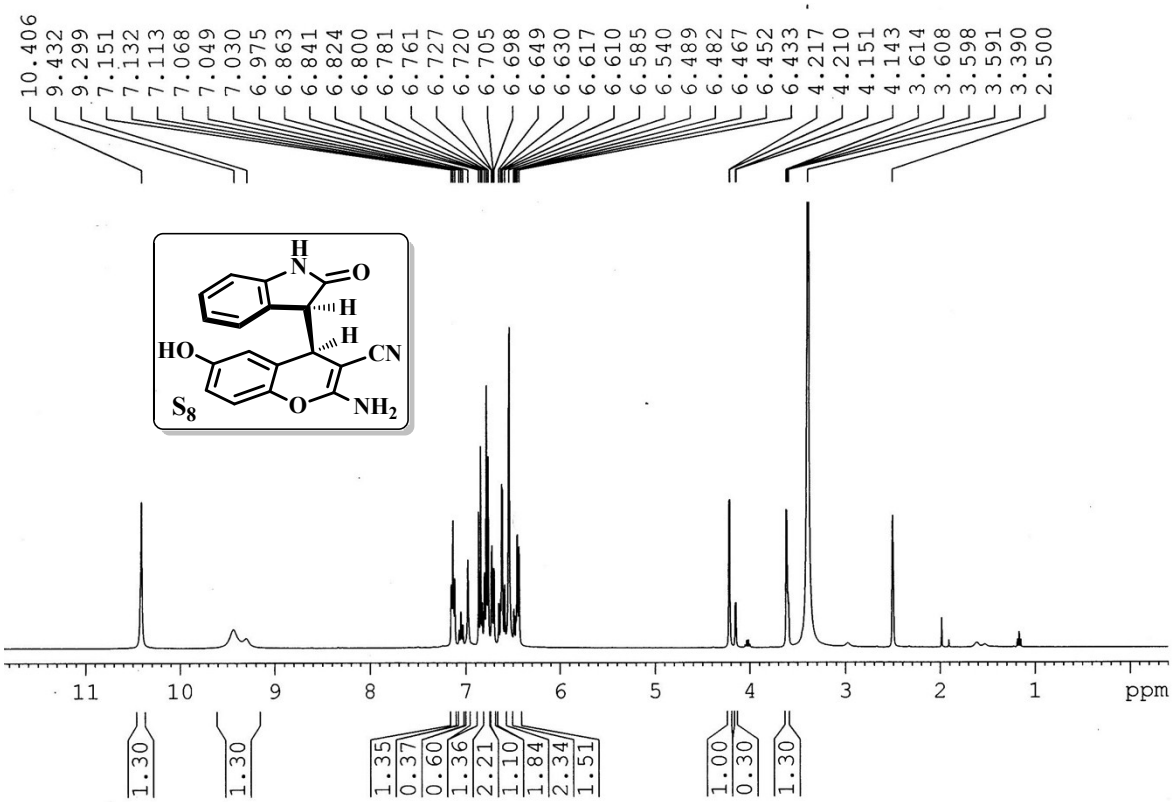
^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound S_6



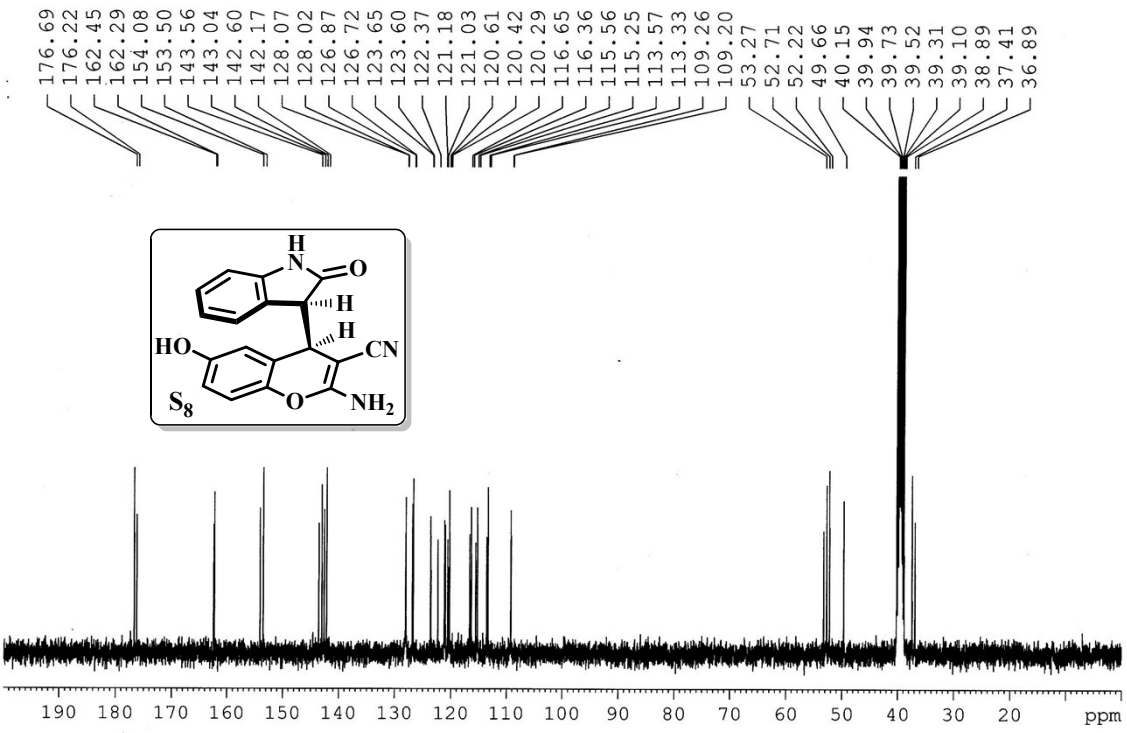
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound S_7



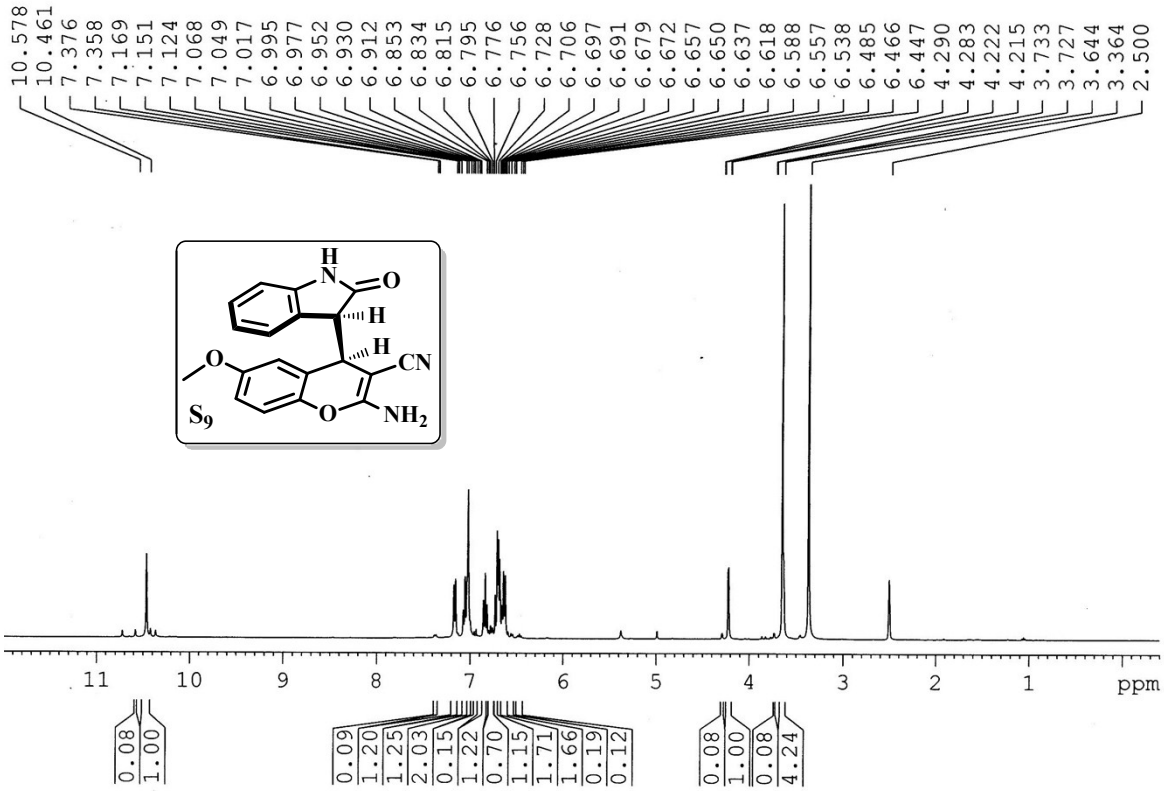
^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound S_7



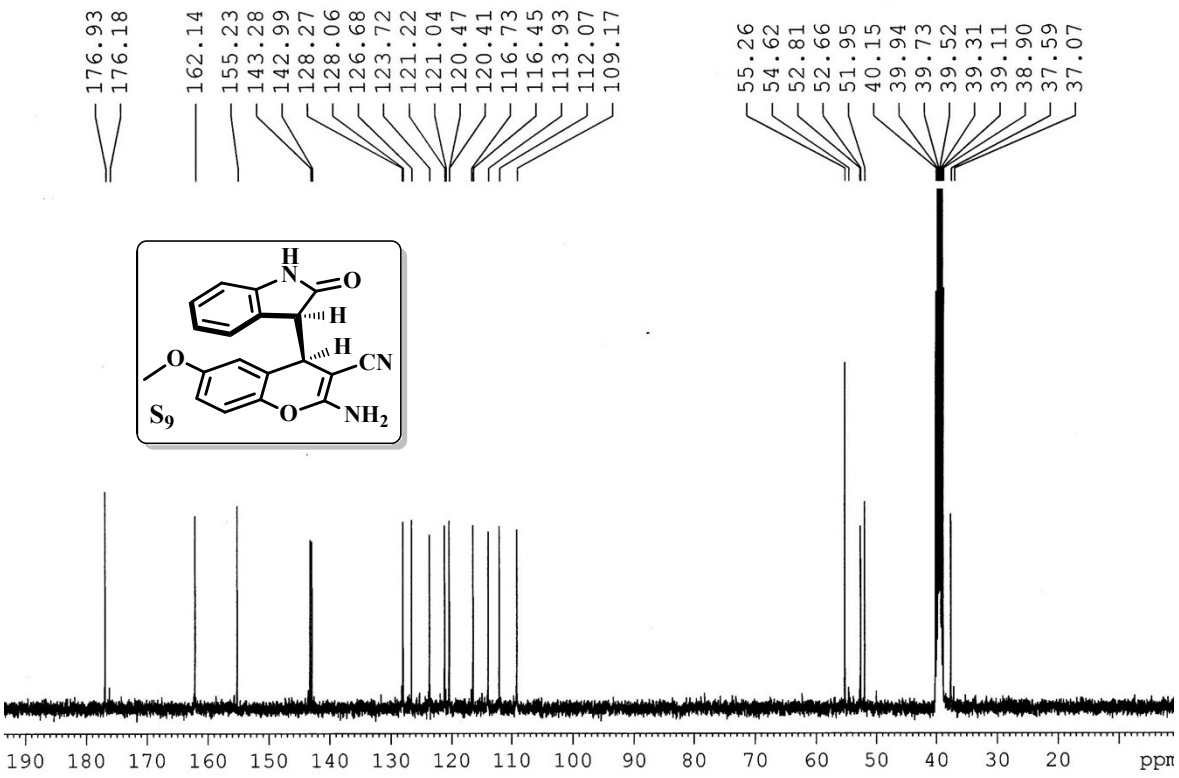
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound S_8



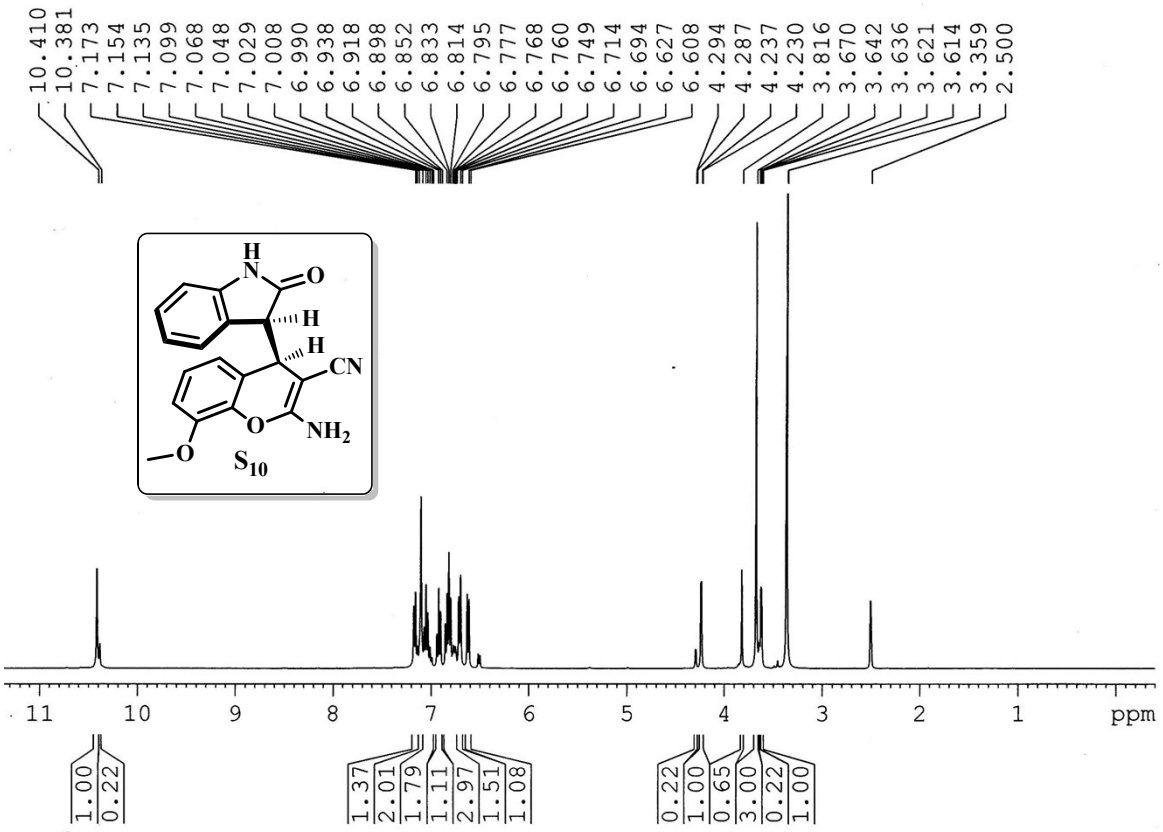
^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound S_8



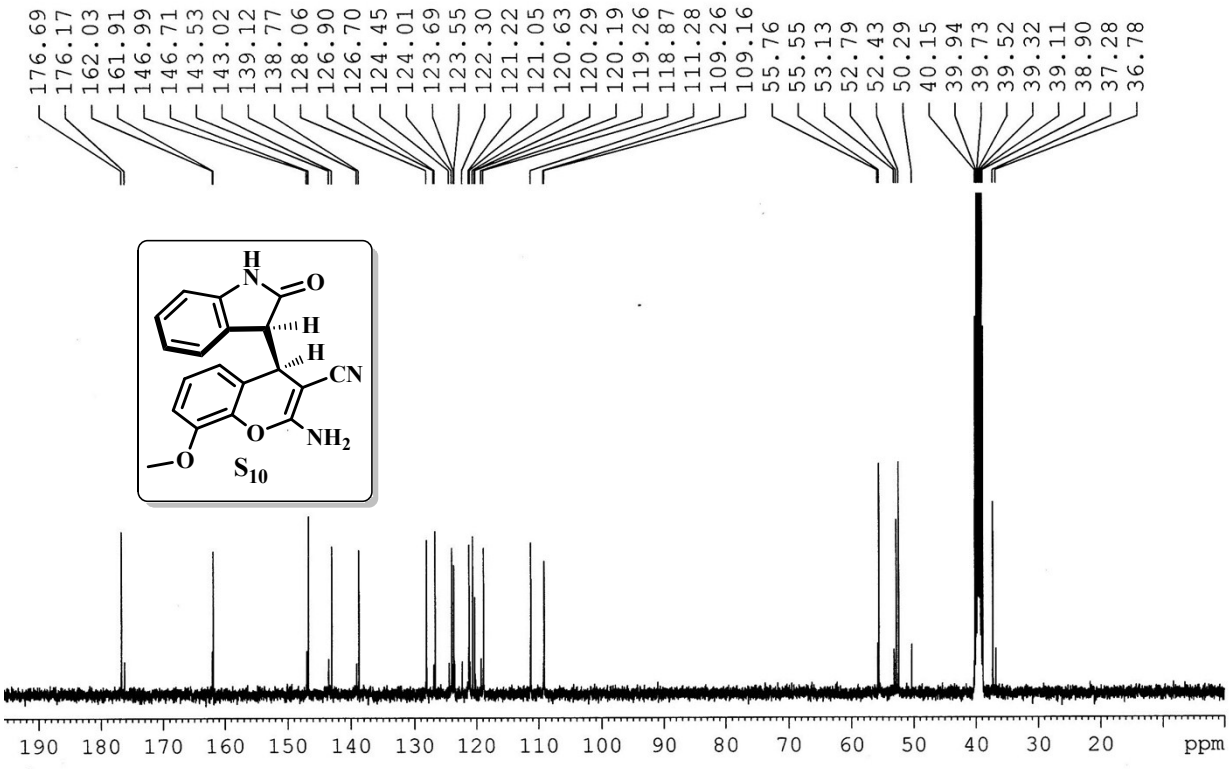
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound S_9



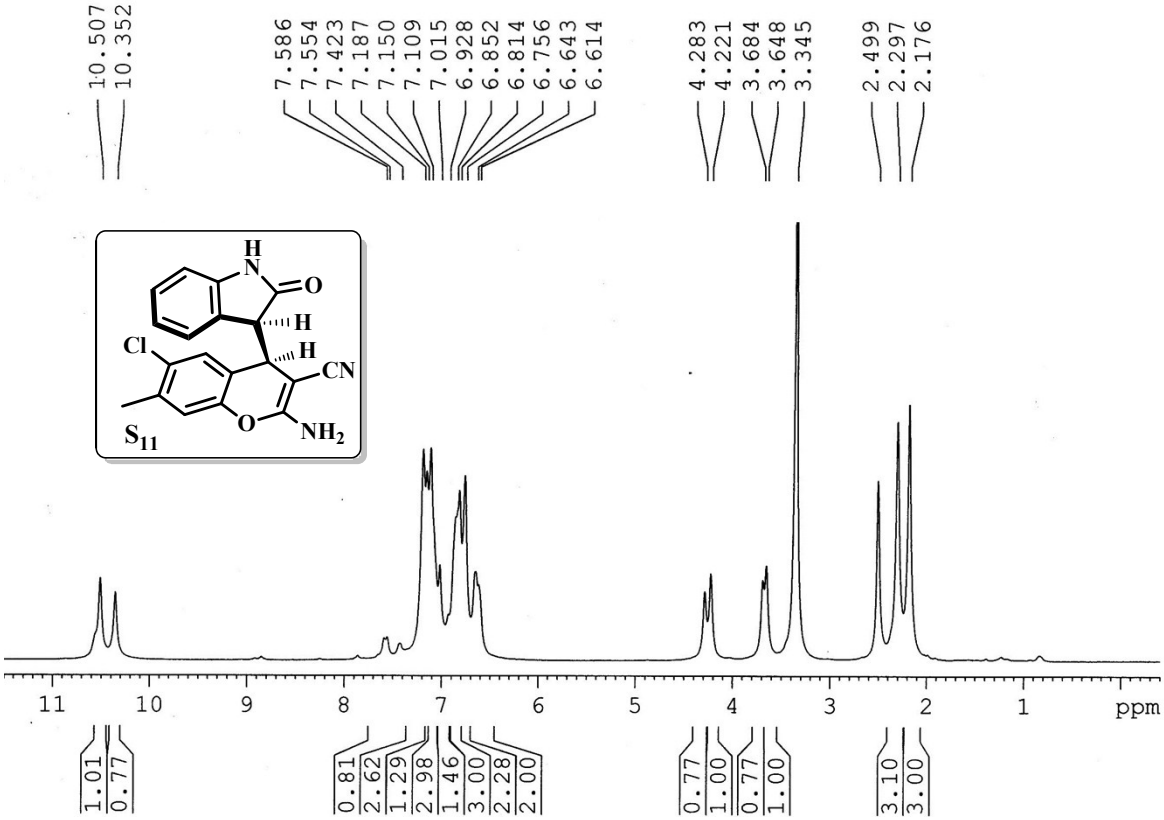
^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound S_9



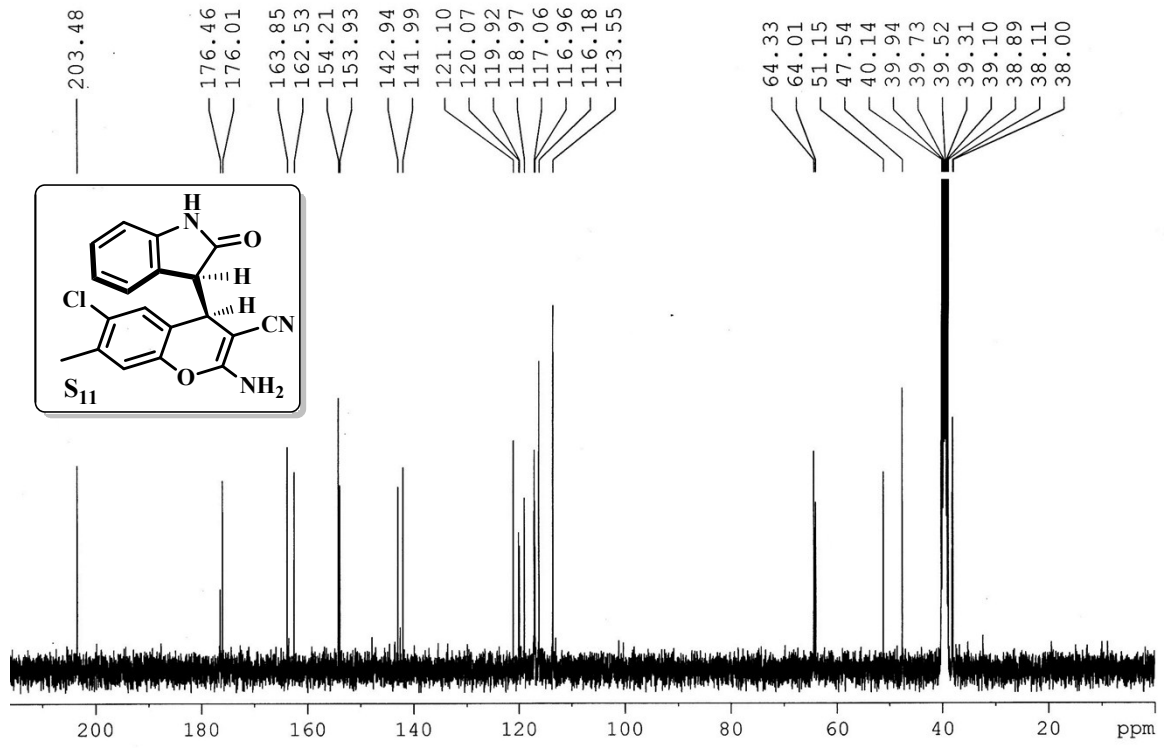
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound S_{10}



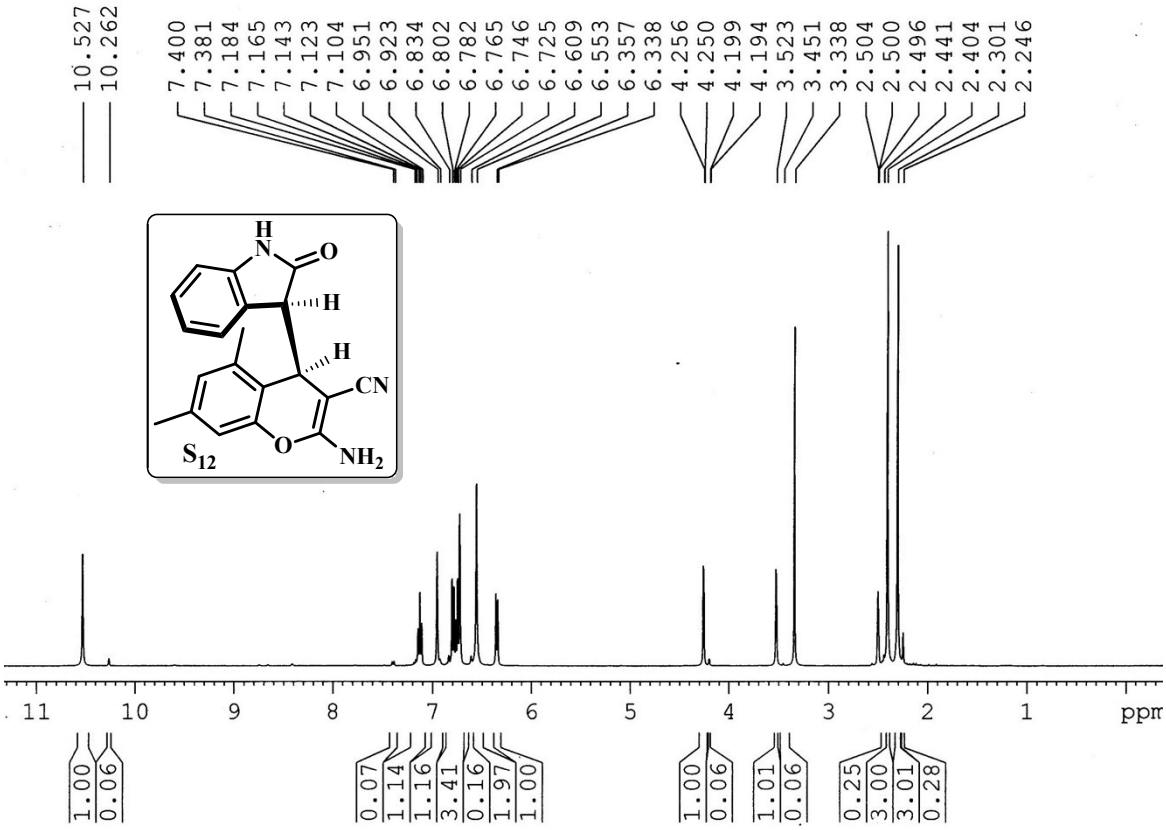
^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound S_{10}



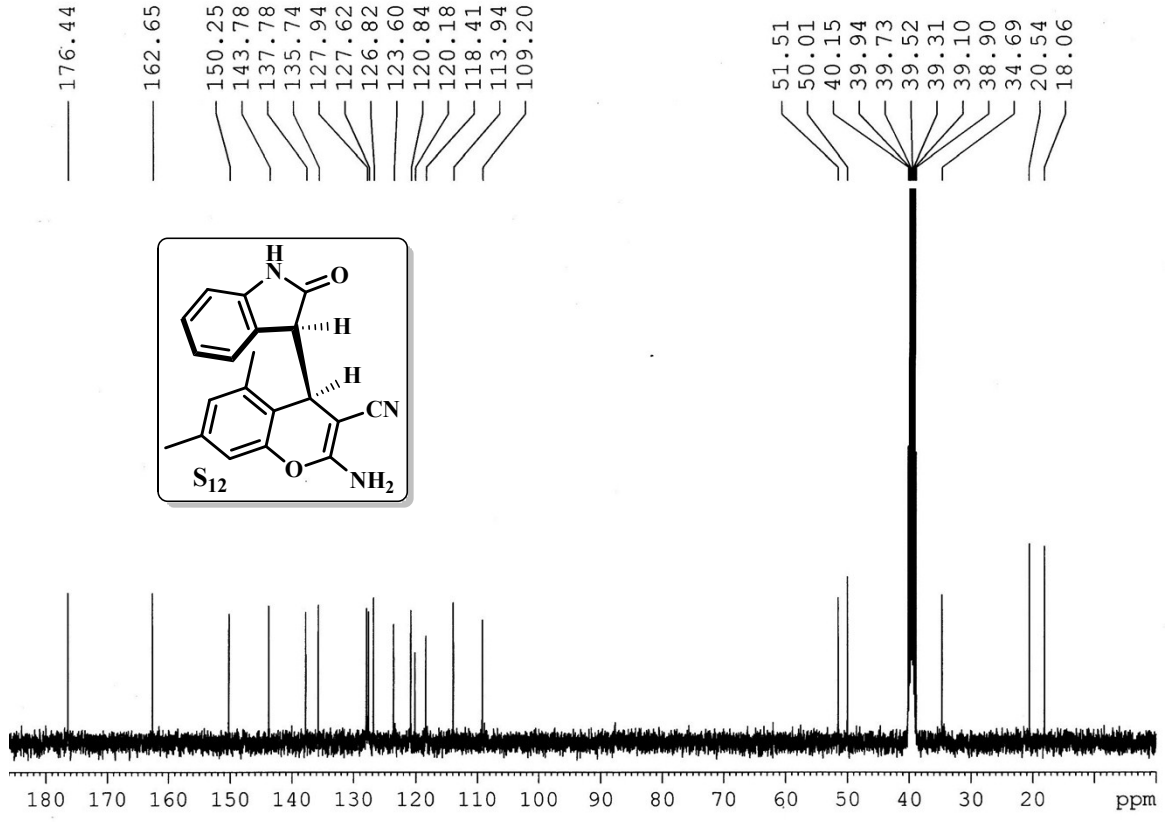
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound S_{11}



^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound S_{11}



^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound S_{12}



^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound S_{12}