Supporting Information

An acid-catalyzed 1,4-addition isocyanide-based multicomponent reaction in neat water

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General Experimental

^{1}H and ^{13}C NMR were recorded on a Bruker 400 spectrometer. ^{1}H NMR data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constant (Hz), relative intensity. ^{13}C NMR data are reported as follows: chemical shift in ppm (δ). LC/MS analyses were performed on a Shimadzu-2020 LC-MS instrument using the following conditions: Shim-pack VP-ODS C18 column (reverse phase, 150 x 4.6 mm); a linear gradient from 10% water and 90% acetonitrile to 75% acetonitrile and 25% water over 6.0 min; flow rate of 0.5 mL/min; UV photodiode array detection from 200 to 400 nm. High-resolution mass spectra (HRMS) were recorded on Thermo Scientific Exactive Plus System. The products were purified by Biotage Isolera™ Spektra Systems and hexane/EtOAc solvent systems. All reagents and solvents were obtained from commercial sources and used without further purification.

General procedures for compound 5.

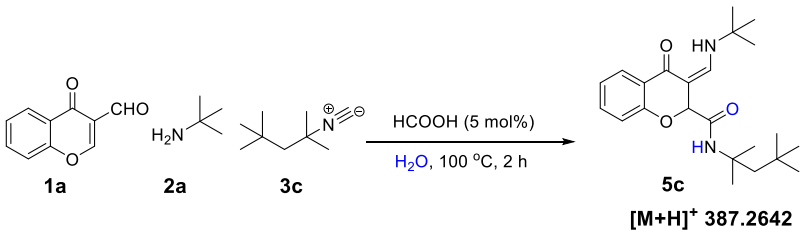
The solution of formic acid (5 mol%, aqueous soultion) was added to a mixture of aldehyde (0.3 mmol), amine (0.3 mmol) and isocyanide (0.3 mmol). Then this system was stirred in water (2.0 mL) at 100 ℃ for 2 h and then monitored by TLC. When the reaction was completed, the reaction mixture was diluted with EtOAc (15.0 mL), washed with sat. $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$ and concentrated. The residue was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) to afford the relative targeted product **5**.

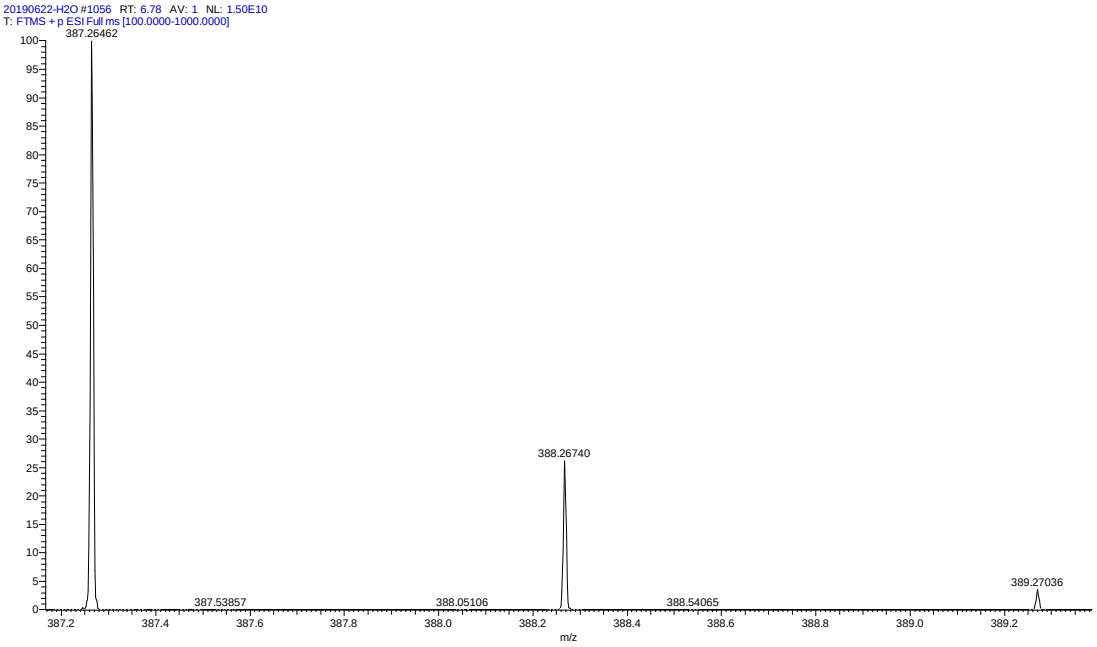
General procedure for compound 11

The solution of formic acid (5 mol%, aqueous soultion) was added to a mixture of chromone-3-carboxaldehyde **1a** (0.2 mmol), 2-methylpropan-2-amine **2a** (0.2 mmol), 1,1,3,3-tetramethylbutyl isocyanide **3c** (0.2 mmol). Then this system was stirred in water (1.5 mL) at 100 ℃ for 2 h and then monitored by TLC. When the reaction was completed, the reaction mixture was concentrated under reduced pressure. In a solution of this residue in dichloromethane (DCM) (3.0 mL), [bis(trifluoroacetoxy)iodo]benzene (PIFA, 0.2 mmol) and trifluoroacetic acid (TFA, 0.2 mmol) were added and stirred at room temperature for 6 h. When the reaction was completed, the reaction mixture was diluted with EtOAc (15.0 mL), washed with sat.

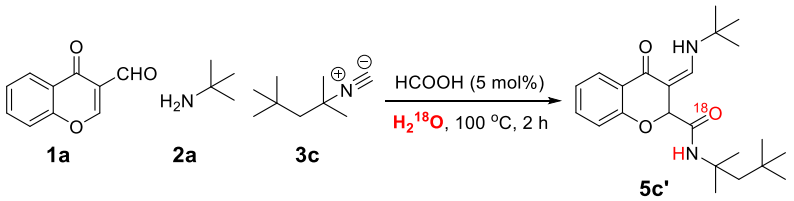
Na_2CO_3 and brine. The organic layer was dried over $MgSO_4$ and concentrated. The residue was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) to afford the product **11**.

Control experiments



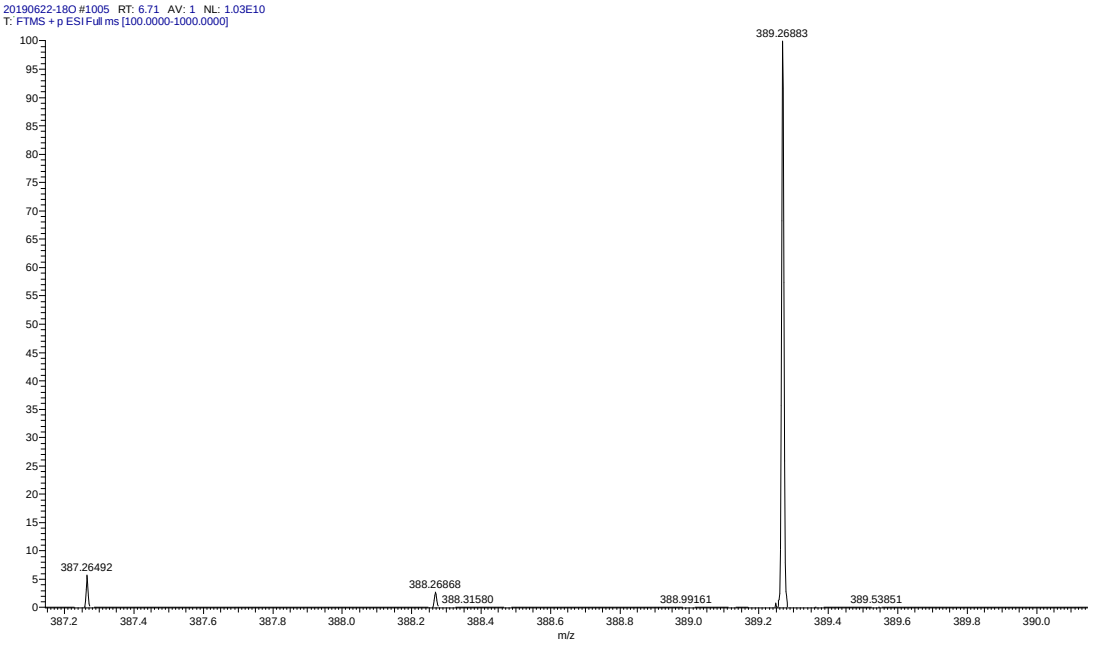


m/z	Intensity	Relative
121.02840	24675974.0	0.14
174.05490	101199264.0	0.58
230.11754	34497744.0	0.20
331.20160	30973452.0	0.18
385.24933	39078452.0	0.22
387.26462	17416132608.0	100.00
388.26730	4454016000.0	25.57
389.27026	619520576.0	3.56
390.27338	55054208.0	0.32



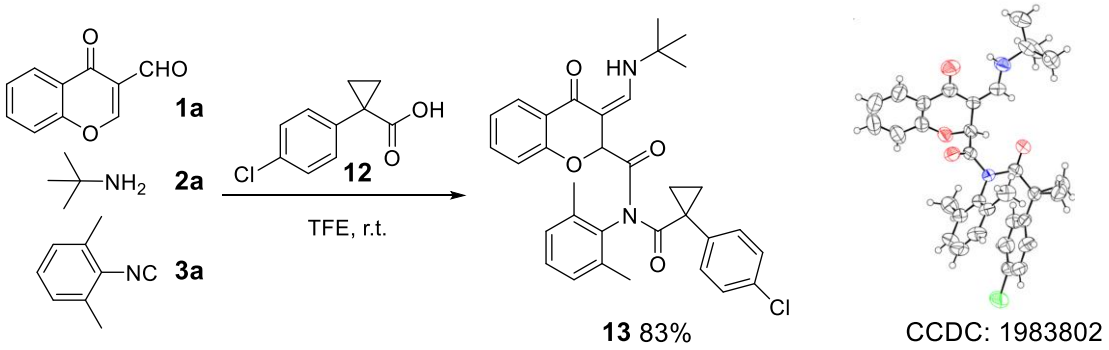
1a **2a** **3c** **5c'**

$[M+H]^+$ 389.2685



m/z	Intensity	Relative
387.26495	751660544.0	5.87
388.26874	348332512.0	2.72
388.47635	3765759.8	0.03
389.00110	3907922.0	0.03
389.26883	12809865216.0	100.00
389.54413	4167084.3	0.03
390.05676	3746140.0	0.03
390.27167	3424700672.0	26.73
391.27271	3780219136.0	29.51

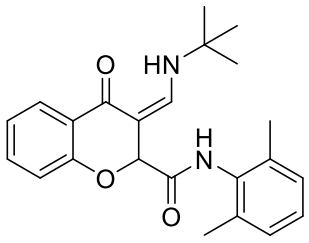
Acylatation of compound 5a



A solution of chromone-3-carboxaldehyde **1a** (0.3 mmol), 2-methylpropan-2-amine **2a** (0.3 mmol), 2-isocyano-1,3-dimethylbenzene **3a** (0.3 mmol) and 1-(4-chlorophenyl)cyclopropane-1-carboxylic acid **12** (0.3 mmol) was stirred in 2,2,2-trifluoroethanol (TFE, 2.0 mL) for 2 h. The reaction mixture was monitored by TLC. When the reaction was completed, the solvent was removed under reduced pressure. Then the reaction mixture was diluted with EtOAc (15.0 mL), washed with sat. $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$ and concentrated. The residue was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) to afford product **13** with 83% yield.

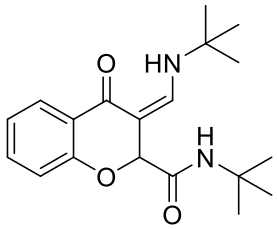
NMR Characterization Data and Figures of Products

(Z)-3-((tert-butylamino)methylene)-N-(2,6-dimethylphenyl)-4-oxochromane-2-carboxamide



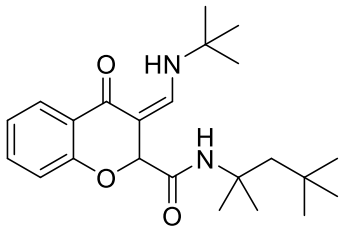
5a, 94 mg, light green solid, 83% (EA/Hex = 20%, Rf = 0.3), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.85 (d, *J* = 13.1 Hz, 1H), 7.93 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.67 (s, 1H), 7.47 – 7.35 (m, 2H), 7.16 – 6.96 (m, 5H), 5.50 (s, 1H), 2.04 (s, 6H), 1.34 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.81, 168.96, 156.42, 149.08, 135.33, 133.67, 132.83, 128.19, 127.56, 126.62, 123.66, 122.63, 116.53, 95.50, 78.55, 52.91, 29.99, 18.14. HRMS (ESI) m/z calcd for $C_{23}H_{27}N_2O_3^+$ $(M+H)^+$ 379.2016, found 379.2012.

(Z)-N-(tert-butyl)-3-((tert-butylamino)methylene)-4-oxochromane-2-carboxamide



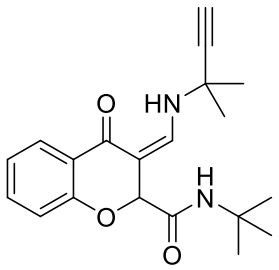
5b, 87 mg, light yellow solid, 88% (EA/Hex = 20%, Rf = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.74 (d, *J* = 12.6 Hz, 1H), 7.87 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.41 – 7.33 (m, 1H), 7.29 (d, *J* = 13.3 Hz, 1H), 7.10 – 7.02 (m, 1H), 6.93 (d, *J* = 8.2 Hz, 1H), 6.31 (s, 1H), 5.17 (s, 1H), 1.33 (s, 9H), 1.31 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.35, 168.87, 156.52, 148.57, 133.41, 126.48, 123.78, 122.34, 116.42, 95.96, 78.52, 52.79, 51.20, 29.99, 28.58. HRMS (ESI) m/z calcd for $C_{19}H_{27}N_2O_3^+$ $(M+H)^+$ 331.2016, found 331.2019.

(Z)-3-((tert-butylamino)methylene)-4-oxo-N-(2,4,4-trimethylpentan-2-yl)chromane-2-carboxamide



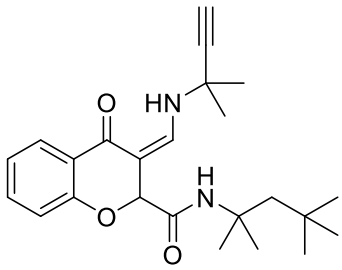
5c, 80 mg, light yellow solid, 70% (EA/Hex = 20%, Rf = 0.30), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.81 (d, *J* = 13.2 Hz, 1H), 7.96 (d, *J* = 2.5 Hz, 1H), 7.43 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.34 (d, *J* = 13.4 Hz, 1H), 6.82 (d, *J* = 8.7 Hz, 1H), 6.31 (s, 1H), 5.14 (s, 1H), 1.38 (s, 2H), 1.34 (s, 9H), 0.91 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.55, 168.22, 155.36, 149.27, 135.90, 129.19, 125.21, 118.35, 114.92, 95.25, 78.51, 55.29, 51.94, 31.38, 29.96, 29.12, 28.69. HRMS (ESI) m/z calcd for $C_{23}H_{35}N_2O_3^+$ $(M+H)^+$ 387.2642, found 387.2646.

(Z)-N-(tert-butyl)-3-(((2-methylbut-3-yn-2-yl)amino)methylene)-4-oxochromane-2-carboxamide



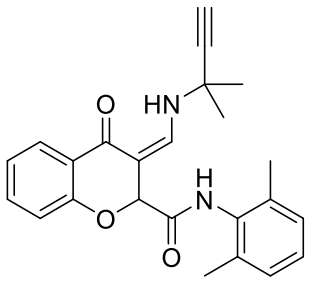
5d, 88 mg, light yellow solid, 86% (EA/Hex = 20%, Rf = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.64 (d, *J* = 12.7 Hz, 1H), 7.87 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.55 (dd, *J* = 12.6, 0.8 Hz, 1H), 7.39 (ddd, *J* = 8.2, 7.3, 1.8 Hz, 1H), 7.11 – 7.02 (m, 1H), 6.95 (dd, *J* = 8.2, 0.8 Hz, 1H), 6.30 (s, 1H), 5.19 (d, *J* = 0.8 Hz, 1H), 2.49 (s, 1H), 1.60 (d, *J* = 1.3 Hz, 6H), 1.32 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.34, 168.43, 156.81, 148.72, 133.79, 126.61, 123.56, 122.39, 116.61, 97.23, 84.85, 78.54, 73.21, 51.25, 31.26, 30.99, 28.60. HRMS (ESI) m/z calcd for $C_{20}H_{25}N_2O_3^+$ $(M+H)^+$ 341.1860, found 341.1857.

(Z)-3-(((2-methylbut-3-yn-2-yl)amino)methylene)-4-oxo-N-(2,4,4-trimethylpentan-2-yl)chromane-2-carboxamide



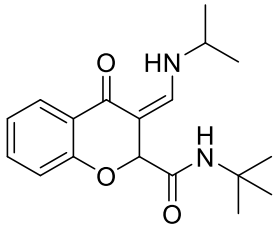
5e, 94 mg, light yellow solid, 79% (EA/Hex = 20%, Rf = 0.25),^{1}H NMR (400 MHz, $CDCl_3$) δ 10.66 (d, *J* = 12.5 Hz, 1H), 7.90 – 7.80 (m, 1H), 7.56 (dd, *J* = 12.7, 0.7 Hz, 1H), 7.38 (ddd, *J* = 8.2, 7.3, 1.8 Hz, 1H), 7.09 – 7.00 (m, 1H), 6.93 (dd, *J* = 8.2, 0.7 Hz, 1H), 6.34 (s, 1H), 5.16 (d, *J* = 0.7 Hz, 1H), 2.49 (s, 1H), 1.59 (d, *J* = 3.0 Hz, 5H), 1.36 (d, *J* = 7.7 Hz, 6H), 0.89 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.17, 168.26, 156.76, 148.96, 133.78, 126.61, 123.48, 122.35, 116.57, 96.98, 84.87, 78.51, 73.23, 55.19, 51.95, 51.17, 31.36, 29.14, 28.68. HRMS (ESI) m/z calcd for $C_{24}H_{33}N_2O_3^+$ $(M+H)^+$ 397.2486, found 397.2502.

(Z)-N-(2,6-dimethylphenyl)-3-(((2-methylbut-3-yn-2-yl)amino)methylene)-4-oxochromane-2-carboxamide



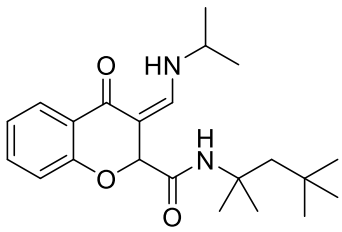
5f, 67 mg, light yellow solid, 57% (EA/Hex = 30%, Rf = 0.35), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.75 (d, *J* = 12.5 Hz, 1H), 7.93 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.73 – 7.56 (m, 2H), 7.42 (ddd, *J* = 8.2, 7.4, 1.7 Hz, 1H), 7.10 – 6.99 (m, 5H), 5.52 (s, 1H), 2.50 (s, 1H), 2.04 (s, 6H), 1.60 (d, *J* = 1.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.81, 168.53, 156.71, 149.25, 135.36, 134.06, 132.84, 128.18, 127.56, 126.75, 123.45, 122.68, 116.74, 96.75, 84.81, 78.54, 73.33, 51.23, 31.10, 18.19. HRMS (ESI) m/z calcd for $C_{24}H_{25}N_2O_3^+$ $(M+H)^+$ 389.1860, found 389.1861.

(Z)-N-(tert-butyl)-3-((isopropylamino)methylene)-4-oxochromane-2-carboxamide



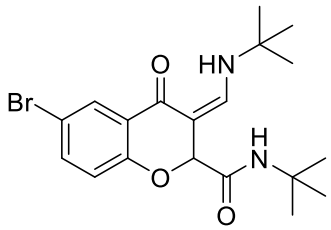
5g, 65 mg, light yellow solid, 69% (EA/Hex = 20%, Rf = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.41 (s, 1H), 7.87 (d, *J* = 6.6 Hz, 1H), 7.36 (dd, *J* = 11.3, 4.1 Hz, 1H), 7.18 (d, *J* = 13.0 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.93 (d, *J* = 8.2 Hz, 1H), 6.30 (s, 1H), 5.15 (s, 1H), 3.53 (dt, *J* = 13.2, 6.5 Hz, 1H), 1.30 (dd, *J* = 5.4, 4.7 Hz, 9H), 1.27 (d, *J* = 6.5 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.33, 168.93, 156.50, 150.76, 133.46, 126.53, 122.34, 116.39, 95.90, 78.29, 51.23, 50.60, 28.60, 23.77, 23.57. HRMS (ESI) m/z calcd for $C_{18}H_{25}N_2O_3^+$ $(M+H)^+$ 317.1860, found 317.1861.

(Z)-3-((isopropylamino)methylene)-4-oxo-N-(2,4,4-trimethylpentan-2-yl)chromane-2-carboxamide



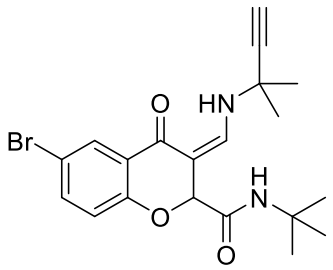
5h, 66 mg, light yellow solid, 60% (EA/Hex = 25%, Rf = 0.30), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.43 (d, *J* = 7.4 Hz, 1H), 7.93 – 7.78 (m, 1H), 7.36 (ddd, *J* = 8.6, 7.4, 1.7 Hz, 1H), 7.20 (d, *J* = 13.0 Hz, 1H), 7.04 (ddd, *J* = 7.4, 4.4, 0.8 Hz, 1H), 6.92 (dd, *J* = 8.2, 0.4 Hz, 1H), 6.35 (s, 1H), 5.12 (s, 1H), 3.52 (td, *J* = 13.3, 6.6 Hz, 1H), 1.65 (d, *J* = 18.8 Hz, 2H), 1.35 (d, *J* = 3.8 Hz, 6H), 1.27 (dd, *J* = 6.5, 0.8 Hz, 6H), 0.87 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.26, 168.81, 156.46, 151.06, 133.46, 126.53, 123.59, 122.31, 116.36, 95.63, 78.30, 55.17, 51.81, 50.64, 31.53, 31.33, 29.21, 28.74, 23.82, 23.54. HRMS (ESI) m/z calcd for $C_{22}H_{33}N_2O_3^+$ $(M+H)^+$ 373.2486, found 373.2486.

(Z)-6-bromo-N-(tert-butyl)-3-((tert-butylamino)methylene)-4-oxochromane-2-carboxamide



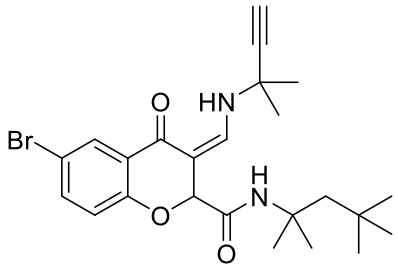
5i, 72 mg, light green solid, 59% (EA/Hex = 20%, Rf = 0.25),^{1}H NMR (400 MHz, $CDCl_3$) δ 10.78 (d, *J* = 12.6 Hz, 1H), 7.97 (d, *J* = 2.5 Hz, 1H), 7.44 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.31 (d, *J* = 13.4 Hz, 1H), 6.83 (d, *J* = 8.6 Hz, 1H), 6.25 (s, 1H), 5.17 (s, 1H), 1.33 (s, 9H), 1.32 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.66, 168.44, 155.39, 149.04, 135.93, 129.21, 118.38, 114.98, 95.48, 78.53, 53.03, 51.34, 29.94, 28.59. HRMS (ESI) m/z calcd for $C_{19}H_{26}BrN_2O_3^+$ $(M+H)^+$ 409.1121, found 409.1131.

(Z)-6-bromo-N-(tert-butyl)-3-(((2-methylbut-3-yn-2-yl)amino)methylene)-4-oxochromane-2-carboxamide



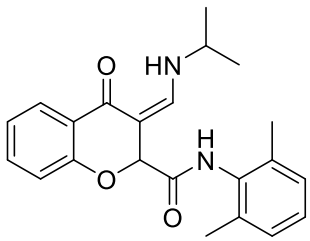
5j, 92 mg, light yellow solid, 74% (EA/Hex = 20%, Rf = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.67 (d, *J* = 12.5 Hz, 1H), 7.96 (d, *J* = 2.5 Hz, 1H), 7.58 (d, *J* = 12.7 Hz, 1H), 7.49 – 7.43 (m, 1H), 6.85 (d, *J* = 8.7 Hz, 1H), 6.24 (s, 1H), 5.19 (s, 1H), 2.50 (d, *J* = 0.5 Hz, 1H), 1.60 (s, 6H), 1.33 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.74, 168.02, 155.68, 149.24, 136.32, 129.31, 125.04, 118.58, 115.03, 96.67, 84.58, 78.56, 73.50, 51.40, 31.24, 30.97, 28.63. HRMS (ESI) m/z calcd for $C_{20}H_{24}BrN_2O_3^+$ $(M+H)^+$ 419.0965, found 419.0997.

(Z)-6-bromo-3-(((2-methylbut-3-yn-2-yl)amino)methylene)-4-oxo-N-(2,4,4-trimethylpentan-2-yl)chromane-2-carboxamide



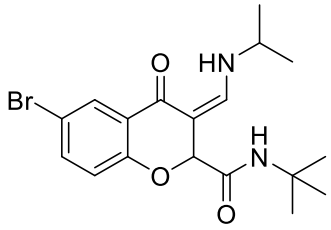
5k, 112 mg, light yellow solid, 80% (EA/Hex = 30%, Rf = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.70 (d, *J* = 12.7 Hz, 1H), 7.96 (d, *J* = 2.5 Hz, 1H), 7.60 (d, *J* = 12.7 Hz, 1H), 7.46 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.84 (d, *J* = 8.7 Hz, 1H), 6.30 (s, 1H), 5.17 (s, 1H), 2.51 (s, 1H), 1.67 (s, 2H), 1.60 (d, *J* = 2.5 Hz, 6H), 1.38 (d, *J* = 9.0 Hz, 6H), 0.91 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.87, 167.83, 155.65, 149.47, 137.28, 136.30, 129.30, 128.80, 124.96, 119.73, 118.55, 114.98, 96.44, 78.54, 73.52, 55.35, 52.47, 52.01, 31.60, 30.99, 29.68, 29.11. HRMS (ESI) m/z calcd for $C_{24}H_{31}BrN_2O_3^+$ $(M+H)^+$ 475,1591, found 475.1595.

(Z)-N-(2,6-dimethylphenyl)-3-((isopropylamino)methylene)-4-oxochromane-2-carboxamide



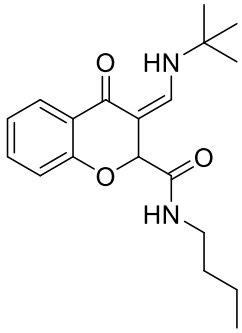
5l, 78 mg, white solid, 71% (EA/Hex = 30%, Rf = 0.25),^{1}H NMR (400 MHz, $CDCl_3$) δ 10.44 (d, *J* = 11.7 Hz, 1H), 7.93 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.66 (s, 1H), 7.40 (ddd, *J* = 8.3, 7.4, 1.1 Hz, 1H), 7.26 (dd, *J* = 13.6, 6.8 Hz, 2H), 7.13 – 7.02 (m, 4H), 5.48 (s, 1H), 3.53 (dq, *J* = 13.3, 6.7 Hz, 1H), 2.03 (s, 6H), 1.28 (dd, *J* = 6.5, 3.7 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.02, 168.94, 156.47, 151.15, 135.31, 133.75, 132.80, 128.19, 127.55, 126.68, 123.61, 122.64, 116.56, 95.52, 78.44, 50.74, 23.72, 23.62, 18.12. HRMS (ESI) m/z calcd for $C_{22}H_{25}N_2O_3^+$ $(M+H)^+$ 365.1860, found 365.1865.

(Z)-6-bromo-N-(tert-butyl)-3-((isopropylamino)methylene)-4-oxochromane-2-carboxamide



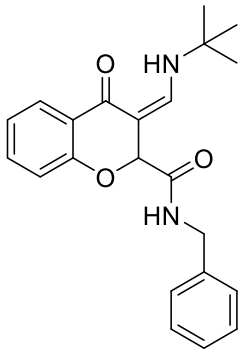
5m, 82 mg, white solid, 69% (EA/Hex = 20%, Rf = 0.35),^{1}H NMR (400 MHz, $CDCl_3$) δ 10.45 (d, *J* = 21.3 Hz, 1H), 7.96 (d, *J* = 2.5 Hz, 1H), 7.44 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.23 (d, *J* = 13.4 Hz, 1H), 6.82 (d, *J* = 8.7 Hz, 1H), 6.30 (s, 1H), 5.12 (d, *J* = 0.4 Hz, 1H), 3.54 (td, *J* = 13.3, 6.6 Hz, 1H), 1.36 (d, *J* = 5.6 Hz, 6H), 1.28 (d, *J* = 6.5 Hz, 6H), 0.90 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$) δ 178.50, 169.19, 156.22, 152.30, 136.82, 130.09, 125.97, 119.20, 115.80, 96.05, 79.19, 56.19, 52.74, 51.64, 32.44, 32.23, 30.06, 29.61, 24.61, 24.37. HRMS (ESI) m/z calcd for $C_{18}H_{24}BrN_2O_3^+$ $(M+H)^+$ 395.0965, found 395.0961.

(Z)-N-butyl-3-((tert-butylamino)methylene)-4-oxochromane-2-carboxamide



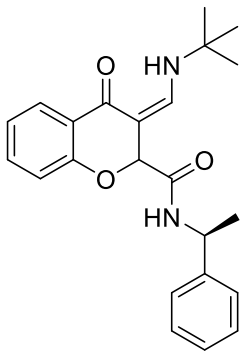
5n, 35mg, yellow solid, 36% (EA/Hex = 20%, Rf = 0.3), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.78 (d, J = 13.7 Hz, 1H), 7.87 (d, J = 7.8 Hz, 1H), 7.40 – 7.28 (m, 2H), 7.05 (t, J = 7.5 Hz, 1H), 6.94 (d, J = 8.2 Hz, 1H), 6.42 (s, 1H), 5.28 (s, 1H), 3.25 (ddd, J = 29.6, 13.4, 6.8 Hz, 2H), 1.48 – 1.43 (m, 2H), 1.25 (s, 9H), 1.20 (d, J = 7.2 Hz, 2H), 0.84 (dd, J = 8.0, 6.7 Hz, 3H). 13C NMR (101 MHz, $CDCl_3$) δ 179.02, 169.97, 156.48, 148.86, 133.48, 126.50, 123.58, 122.34, 116.35, 95.58, 52.82, 38.99, 31.46, 29.98, 29.66, 29.39, 19.81, 13.62. HRMS (ESI) m/z calcd for $C_{19}H_{27}N_2O_3^+$ $(M+H)^+$ 331.2016, found 331.2014.

(Z)-N-benzyl-3-((tert-butylamino)methylene)-4-oxochromane-2-carboxamide



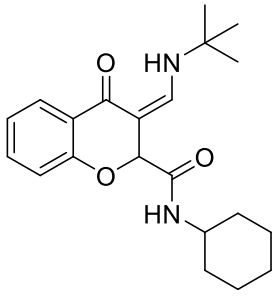
5o, 45 mg, yellow solid, 42% (EA/Hex = 20%, Rf = 0.3), ^{1}H NMR (400 MHz, $cdcl_3$) δ 10.78 (d, *J* = 13.5 Hz, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.40 – 7.24 (m, 6H), 7.11 (d, *J* = 6.8 Hz, 1H), 7.06 (t, *J* = 7.4 Hz, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.78 (s, 1H), 5.36 (s, 1H), 4.57 – 4.38 (m, 2H), 1.33 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.09, 156.44, 148.83, 137.69, 133.57, 128.66, 127.45, 1127.28, 126.53, 123.99, 122.43, 116.50, 95.49, 52.86, 43.06, 29.53. HRMS (ESI) m/z calcd for $C_{22}H_{25}N_2O_3^+$ $(M+H)^+$ 365.1860, found 365.1859.

(Z)-3-((tert-butylamino)methylene)-4-oxo-N-((S)-1-phenylethyl)chromane-2-carboxamide



5p (*dr* =1:1), 62mg, yellow solid, 55% (EA/Hex = 20%, Rf = 0.3), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.79 (d, J = 12.9 Hz, 1H), 10.70 (d, J = 12.4 Hz, 1H), 7.99 (d, J = 7.7 Hz, 1H), 7.90 – 7.86 (m, 1H), 7.67 (s, 1H), 7.54 (s, 1H), 7.45 (d, J = 8.5 Hz, 1H), 7.42 (s, 1H), 7.33 (d, J = 7.1 Hz, 4H), 7.28 (s, 2H), 7.22 (d, J = 7.7 Hz, 2H), 7.19 – 7.14 (m, 3H), 7.05 (dd, J = 17.2, 7.7 Hz, 2H), 6.96 – 6.91 (m, 1H), 5.29 (d, J = 14.8 Hz, 2H), 5.07 – 4.99 (m, 2H), 1.46 (s, 3H), 1.34 (s, 3H), 1.23 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.17, 179.02, 169.28, 168.94, 158.21, 156.45, 154.77, 149.06, 148.34, 134.22, 133.44, 128.84, 128.54, 128.40, 128.38, 127.49, 126.11, 126.05, 125.61, 125.47, 125.43, 124.02, 123.87, 122.38, 117.32, 116.52, 116.46, 78.42, 78.22, 52.81, 52.48, 48.76, 48.53, 29.99, 29.45, 22.00, 21.87. HRMS (ESI) m/z calcd for $C_{23}H_{27}N_2O_3^+$ $(M+H)^+$ 379.2016, found 379.2015.

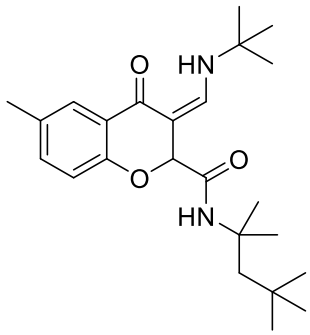
(Z)-3-((tert-butylamino)methylene)-N-cyclohexyl-4-oxochromane-2-carboxamide



5q, 41mg, yellow solid, 39% (EA/Hex = 20%, Rf = 0.3), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.76 (d, *J* = 13.2 Hz, 1H), 8.18 (s, 1H), 7.37 (dd, *J* = 17.8, 8.6 Hz, 2H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 6.32 (d, *J* = 6.8 Hz, 1H), 5.26 (s, 1H), 3.70 (d, *J* = 12.7 Hz, 1H), 1.75 – 1.65 (m, 3H), 1.59 – 1.48 (m, 3H), 1.33 (s, 9H), 1.20 – 1.10 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.19, 169.02, 155.50, 134.11, 133.73, 133.14, 126.49, 125.72, 125.17, 122.35, 118.20, 116.34, 96.20, 52.55, 48.15, 29.90, 29.54,

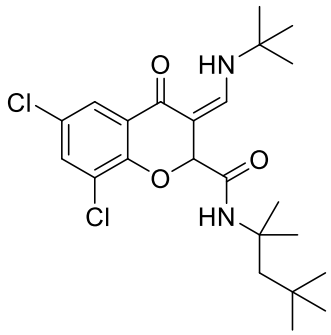
25.38, 24.54. HRMS (ESI) m/z calcd for $C_{21}H_{29}N_2O_3^+$ $(M+H)^+$ 357.2173, found 357.2177.

(Z)-3-((tert-butylamino)methylene)-6-methyl-4-oxo-N-(2,4,4-trimethylpentan-2-yl)chromane-2-carboxamide



5r, 95 mg, yellow solid, 79% (EA/Hex = 20%, Rf = 0.3), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.76 (d, *J* = 13.2 Hz, 1H), 7.65 (s, 1H), 7.30 (d, *J* = 13.4 Hz, 1H), 7.16 (d, *J* = 8.3 Hz, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 6.37 (s, 1H), 5.10 (d, *J* = 0.9 Hz, 1H), 2.29 (s, 3H), 1.66 (s, 2H), 1.36 (d, *J* = 7.9 Hz, 6H), 1.33 (d, *J* = 1.7 Hz, 9H), 0.89 (d, *J* = 1.4 Hz, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.47, 168.79, 154.42, 148.70, 134.18, 131.67, 126.42, 123.31, 116.14, 95.88, 78.42, 55.12, 52.73, 51.92, 31.54, 31.48, 31.35, 29.99, 29.14, 28.78, 28.67, 20.57. HRMS (ESI) m/z calcd for $C_{24}H_{37}N_2O_3^+$ $(M+H)^+$ 401.2799, found 401.2800.

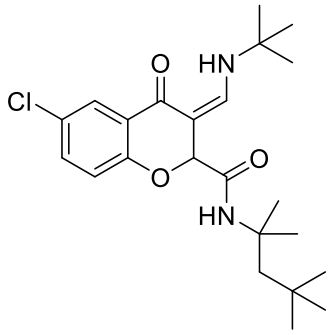
(Z)-3-((tert-butylamino)methylene)-6,8-dichloro-4-oxo-N-(2,4,4-trimethylpentan-2-yl)chromane-2-carboxamide



5s, 113 mg, yellow solid, 83% (EA/Hex = 20%, Rf = 0.3), ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (d, *J* = 2.9 Hz, 1H), 7.73 (d, *J* = 1.2 Hz, 1H), 7.49 (d, *J* = 3.3 Hz, 1H), 7.41 (s, 1H), 7.34 (d, *J* = 5.1 Hz, 1H), 5.18 (s, 1H), 1.67 (s, 2H) 1.46 (s, 6H), 1.36 (s,

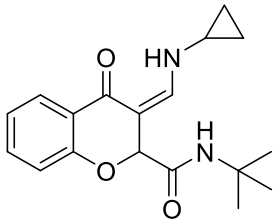
9H), 1.00 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.12, 167.96, 156.12, 150.34, 133.93, 132.41, 129.13, 124.82, 123.17, 78.80, 51.21, 31.75, 31.43, 29.92, 29.35. HRMS (ESI) m/z calcd for $C_{23}H_{33}Cl_2N_2O_3^+$ $(M+H)^+$ 455.1863, found 455.1863.

(Z)-3-((tert-butylamino)methylene)-6-chloro-4-oxo-N-(2,4,4-trimethylpentan-2-yl)chromane-2-carboxamide



5t, 89mg, yellow solid, 71% (EA/Hex = 20%, Rf = 0.3), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.83 (d, *J* = 12.7 Hz, 1H), 7.84 (s, 1H), 7.34 (dd, *J* = 17.9, 11.1 Hz, 2H), 6.89 (d, *J* = 8.2 Hz, 1H), 6.34 (s, 1H), 5.17 (s, 1H), 1.70 (s, 2H), 1.40 (d, *J* = 6.9 Hz, 6H), 1.36 (s, 9H), 0.93 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.75, 168.31, 154.93, 149.31, 133.10, 127.72, 126.18, 124.86, 118.01, 95.38, 78.58, 55.32, 53.07, 51.98, 31.62, 31.42, 30.00, 29.16, 28.73. HRMS (ESI) m/z calcd for $C_{23}H_{34}ClN_2O_3^+$ $(M+H)^+$ 421.2252, found 421.2250.

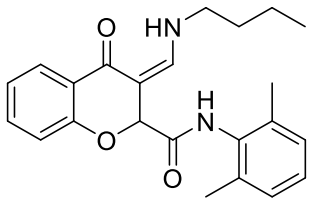
(Z)-N-(tert-butyl)-3-((cyclopropylamino)methylene)-4-oxochromane-2-carboxamide



5u, 44 mg, light green solid, 47% (EA/Hex = 30%, Rf = 0.35), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 (d, *J* = 12.3 Hz, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.42 – 7.35 (m, 1H), 7.20 (s, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 6.28 (s, 1H), 5.14 (s, 1H), 2.82 (s, 1H), 1.30 (s, 9H), 0.77 – 0.73 (m, 2H), 0.71 (dd, *J* = 4.8, 3.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.18, 156.97, 153.18, 134.06, 127.08, 123.87,

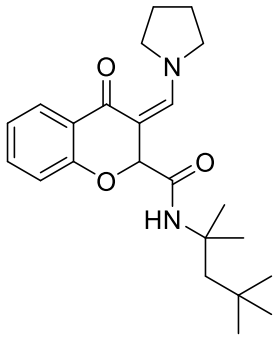
122.72, 116.81, 97.28, 78.70, 51.62, 29.78, 28.96, 6.93. HRMS (ESI) m/z calcd for $C_{18}H_{23}N_2O_3^+$ $(M+H)^+$ 315.1703, found 315.1701.

(Z)-3-((butylamino)methylene)-N-(2,6-dimethylphenyl)-4-oxochromane-2-carboxamide



5v, 24 mg, white solid, 21% (EA/Hex = 30%, Rf = 0.3), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.45 (d, *J* = 12.7 Hz, 1H), 7.94 (d, *J* = 7.9 Hz, 1H), 7.65 (s, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.22 (d, *J* = 13.1 Hz, 1H), 7.08 (dd, *J* = 14.9, 7.5 Hz, 2H), 7.02 (d, *J* = 7.8 Hz, 2H), 5.47 (s, 1H), 3.29 (dd, *J* = 13.2, 6.6 Hz, 2H), 2.03 (s, 6H), 1.38 (dd, *J* = 15.0, 7.6 Hz, 2H), 1.24 (t, *J* = 6.7 Hz, 2H), 0.91 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.55, 155.51, 153.31, 151.26, 133.67, 126.59, 124.00, 122.54, 116.79, 96.79, 71.38, 62.59, 49.21, 32.85, 30.00, 19.66, 13.59. HRMS (ESI) m/z calcd for $C_{23}H_{27}N_2O_3^+$ $(M+H)^+$ 379.2016, found 379.2021.

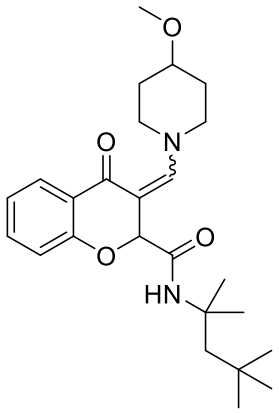
(Z)-4-oxo-3-(pyrrolidin-1-ylmethylene)-N-(2,4,4-trimethylpentan-2-yl)chromane-2-carboxamide



5w, 72 mg, light green solid, 63% (EA/Hex = 40%, Rf = 0.2), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.95 (d, *J* = 7.6 Hz, 1H), 7.42 – 7.34 (m, 1H), 7.06 – 6.98 (m, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 6.08 (s, 1H), 5.77 (s, 1H), 3.86 (s, 2H), 3.53 (s, 2H), 1.96 (s, 2H), 1.21 (s, 6H), 0.97 (d, *J* = 12.2 Hz, 2H), 0.84 (d, *J* = 13.2 Hz, 2H), 0.76 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.30, 169.90, 156.82, 146.98, 133.64, 127.89,

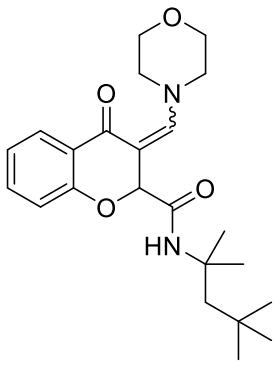
122.10, 116.02, 75.67, 55.11, 51.27, 31.37, 31.14, 29.66, 29.35, 28.84. HRMS (ESI) m/z calcd for $C_{23}H_{33}N_2O_3^+$ $(M+H)^+$ 385.2486, found 385.2486.

3-((4-methoxypiperidin-1-yl)methylene)-4-oxo-N-(2,4,4-trimethylpentan-2-yl)chromane-2-carboxamide



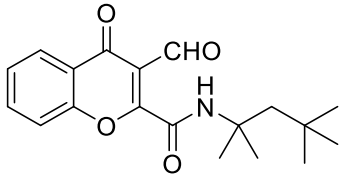
5x, 84 mg, light green solid, 66% (EA/Hex = 40%, Rf = 0.2), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.5 Hz, 1H), 7.82 (s, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 1H), 6.10 (s, 1H), 5.77 (s, 1H), 3.87 – 3.68 (m, 2H), 3.59 – 3.41 (m, 3H), 3.35 (s, 3H), 1.94 (dd, *J* = 16.1, 9.7 Hz, 2H), 1.75 (d, *J* = 11.4 Hz, 2H), 1.24 (s, 2H), 1.23 (d, *J* = 8.4 Hz, 6H), 0.77 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.83, 169.39, 149.65, 133.75, 127.83, 122.17, 116.11, 97.40, 75.90, 73.92, 55.78, 55.18, 51.21, 31.49, 31.39, 31.30, 31.21, 31.13, 30.71, 29.67, 29.36, 28.87, 28.78. HRMS (ESI) m/z calcd for $C_{25}H_{37}N_2O_4^+$ $(M+H)^+$ 429.2478, found 429.2477.

3-(morpholinomethylene)-4-oxo-N-(2,4,4-trimethylpentan-2-yl)chromane-2-carboxamide



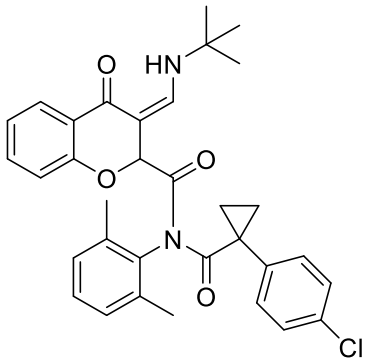
5y, 69 mg, light green solid, 58% (EA/Hex = 40%, Rf = 0.2), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.7 Hz, 1H), 7.76 (s, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.93 (d, *J* = 8.2 Hz, 1H), 6.10 (s, 1H), 5.76 (s, 1H), 3.86 – 3.74 (m, 6H), 3.49 (dd, *J* = 8.5, 5.1 Hz, 2H), 1.24 (s, 2H), 1.22 (s, 6H), 0.76 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.92, 169.34, 157.19, 149.62, 134.02, 127.94, 123.17, 122.30, 116.08, 98.14, 75.74, 66.53, 55.24, 51.53, 51.23, 31.49, 31.38, 31.13, 29.38, 28.84. HRMS (ESI) m/z calcd for $C_{23}H_{33}N_2O_4^+$ $(M+H)^+$ 401.2435, found 401.2330.

3-formyl-4-oxo-N-(2,4,4-trimethylpentan-2-yl)-4H-chromene-2-carboxamide



11, 28 mg, white solid, 42% (EA/Hex = 25%, Rf = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.36 (s, 1H), 8.34 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.83 (ddd, *J* = 8.7, 7.3, 1.7 Hz, 1H), 7.59 (td, *J* = 7.7, 1.0 Hz, 1H), 7.51 – 7.43 (m, 1H), 2.11 (s, 2H), 1.70 (s, 6H), 0.86 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.96, 175.76, 156.73, 155.59, 146.04, 135.85, 127.52, 126.42, 124.62, 121.18, 118.24, 66.59, 54.62, 31.66, 30.72, 29.35. HRMS (ESI) m/z calcd for $C_{23}H_{27}N_2O_3^+$ $(M+H)^+$ 330.1700, found 330.1705.

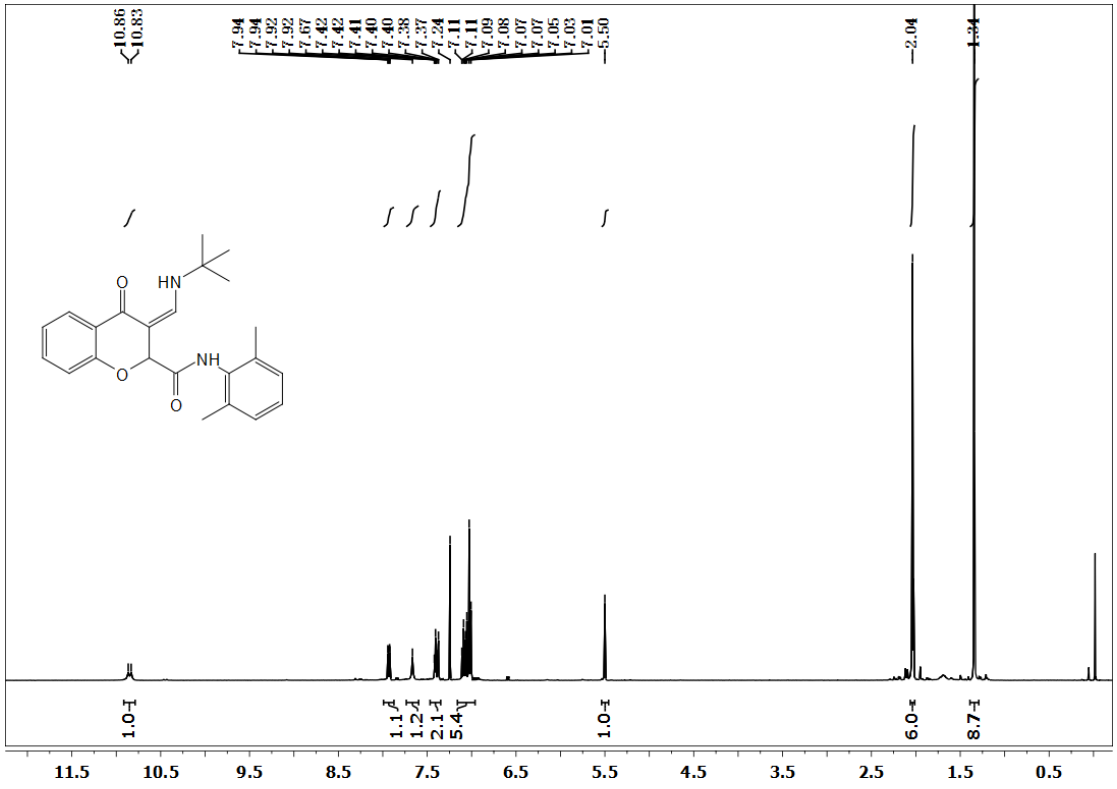
(Z)-3-((tert-butylamino)methylene)-N-(1-(4-chlorophenyl)cyclopropane-1-carbonyl)-N-(2,6-dimethylphenyl)-4-oxochromane-2-carboxamide

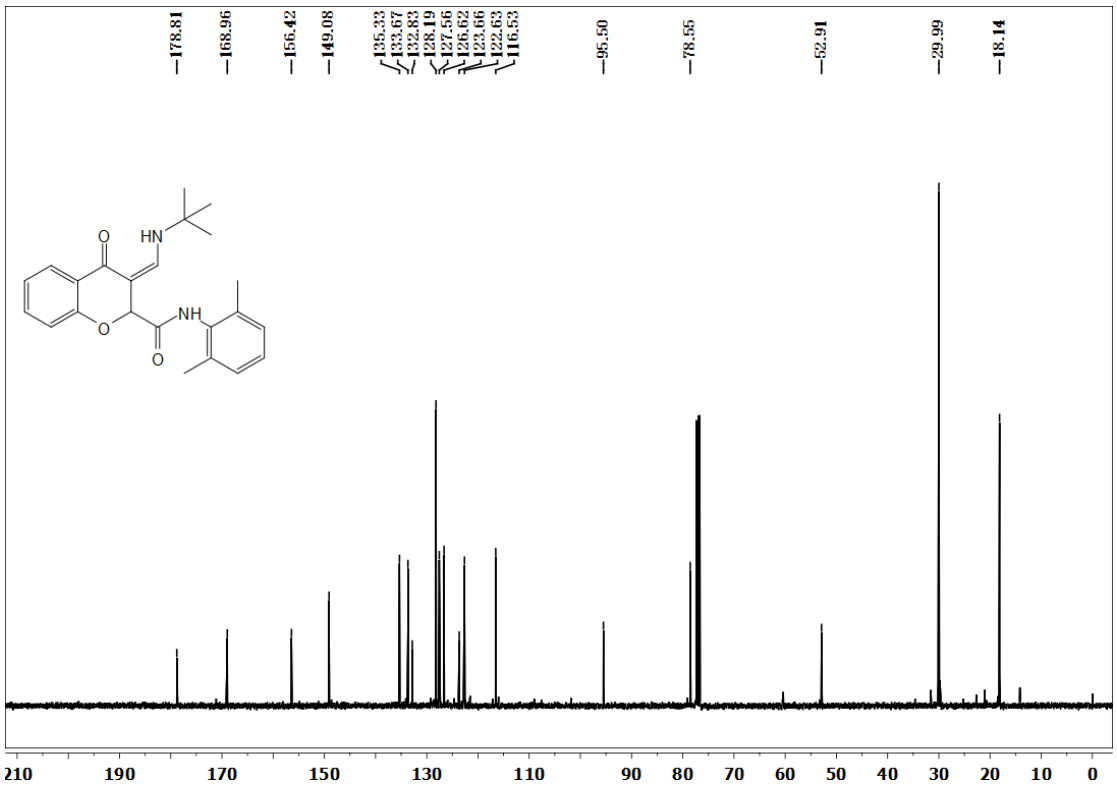


13, 139 mg, light green solid, 83% (EA/Hex = 20%, Rf = 0.3), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.45 (d, *J* = 13.4 Hz, 1H), 7.75 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.32 (ddd, *J* = 8.2, 7.3, 1.8 Hz, 1H), 7.07 – 6.95 (m, 2H), 6.97 – 6.87 (m, 4H), 6.68 (d, *J* = 7.3 Hz, 1H),

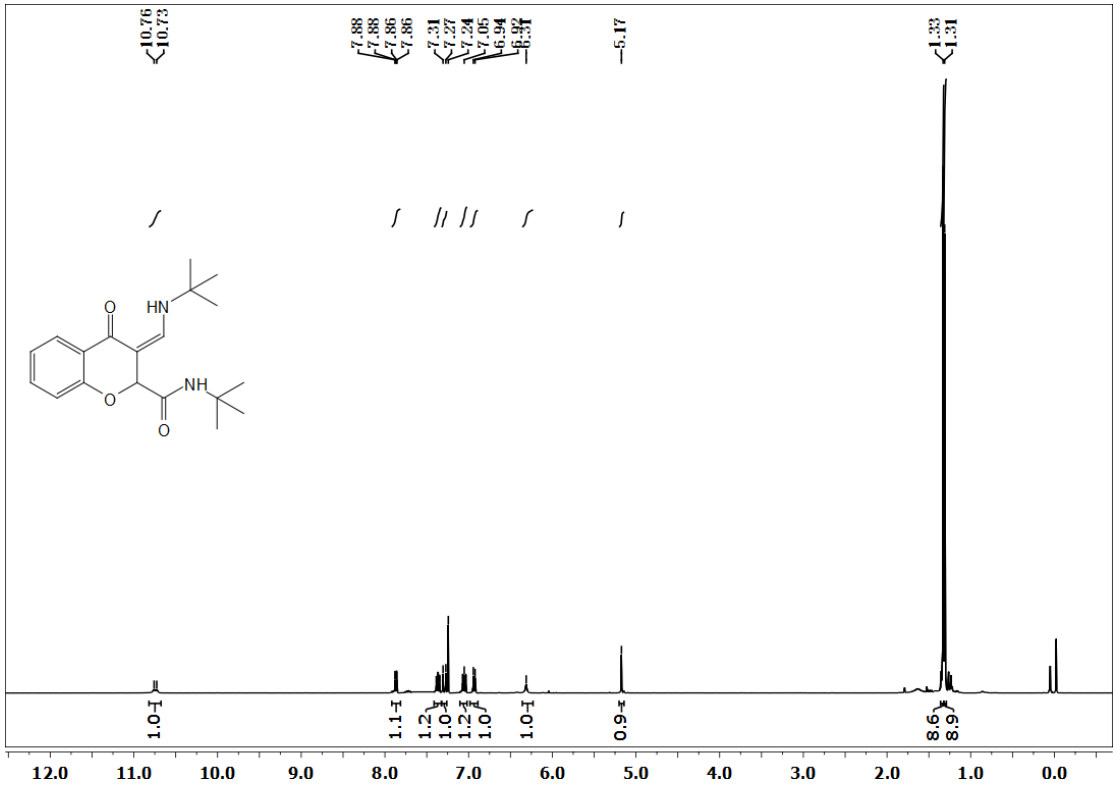
6.62 (d, *J* = 8.3 Hz, 2H), 6.05 (s, 1H), 1.92 (s, 2H), 1.91 – 1.82 (m, 1H), 1.55 – 1.49 (m, 1H), 1.37 (s, 9H), 1.23 – 1.13 (m, 1H), 0.82 (ddd, *J* = 9.4, 7.2, 3.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.52, 177.01, 158.74, 148.86, 137.36, 136.73, 136.61, 135.01, 133.93, 132.67, 130.79, 128.82, 128.46, 127.97, 125.93, 123.13, 121.35, 117.04, 95.91, 79.48, 52.80, 32.33, 30.09, 18.26, 18.06, 17.71. HRMS (ESI) m/z calcd for $C_{33}H_{34}ClN_2O_4^+$ $(M+H)^+$ 557.2202, found 557.2201.

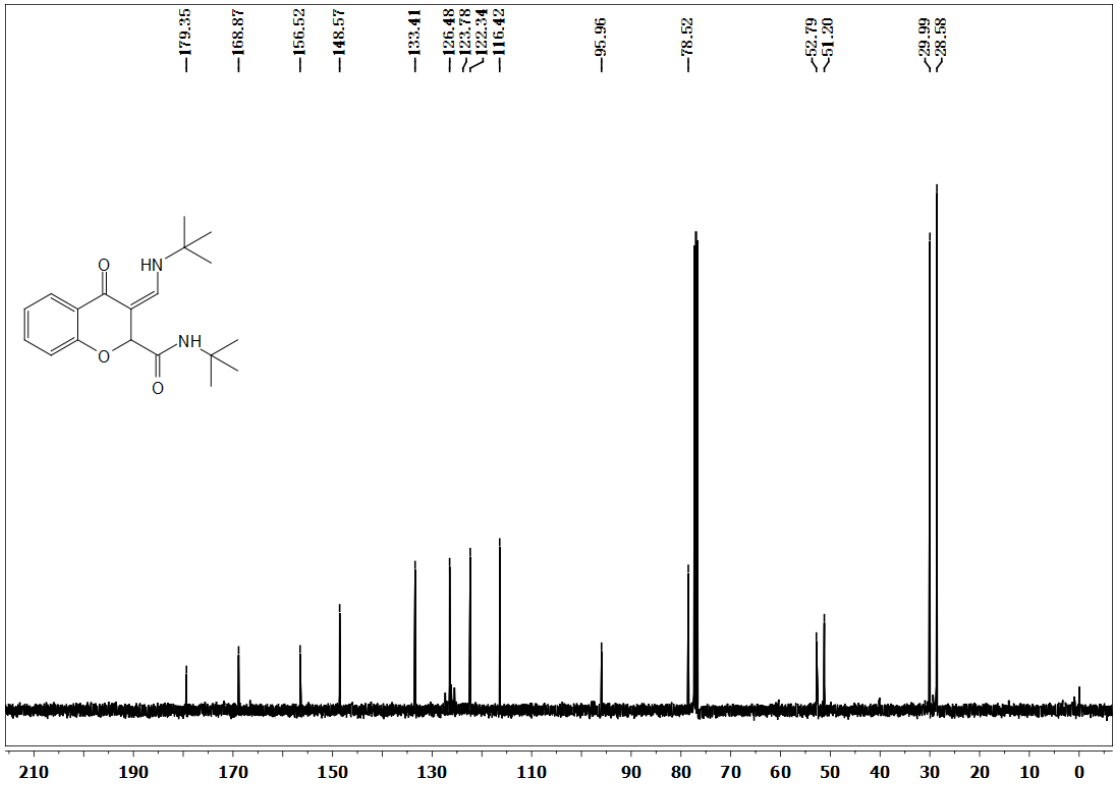
^{1}H NMR and ^{13}C NMR spectrum of **5a**



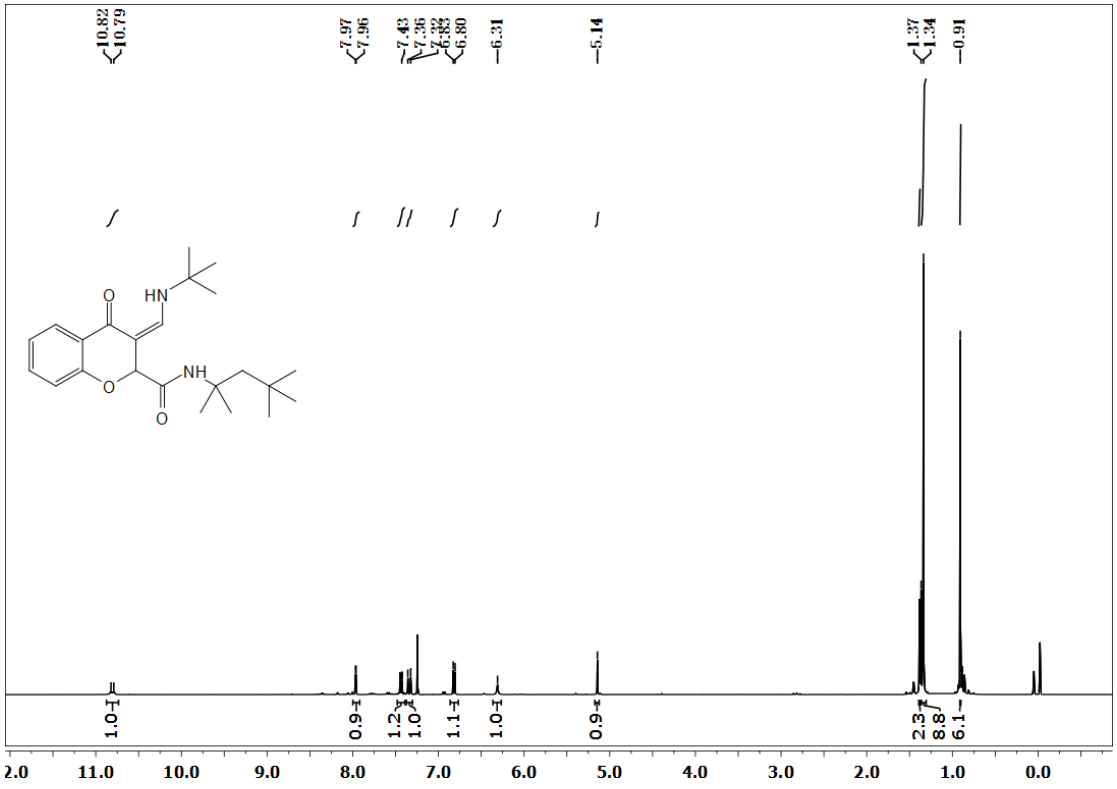


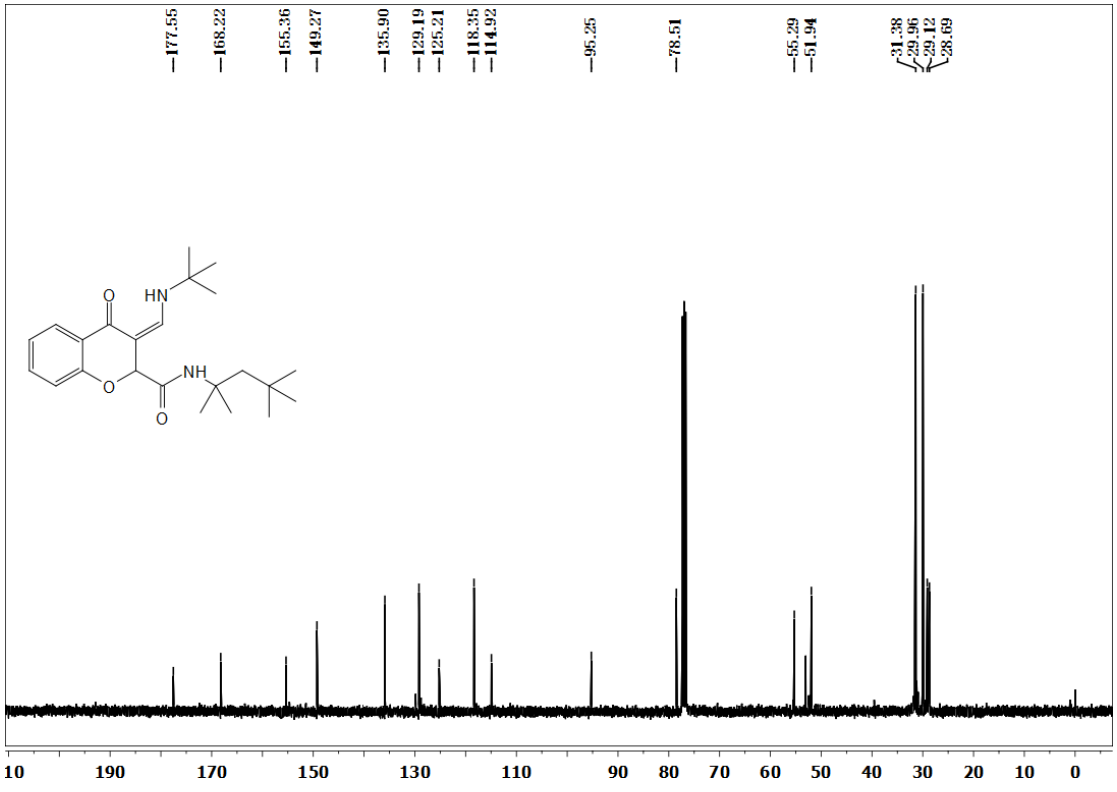
^{1}H NMR and ^{13}C NMR spectrum of **5b**



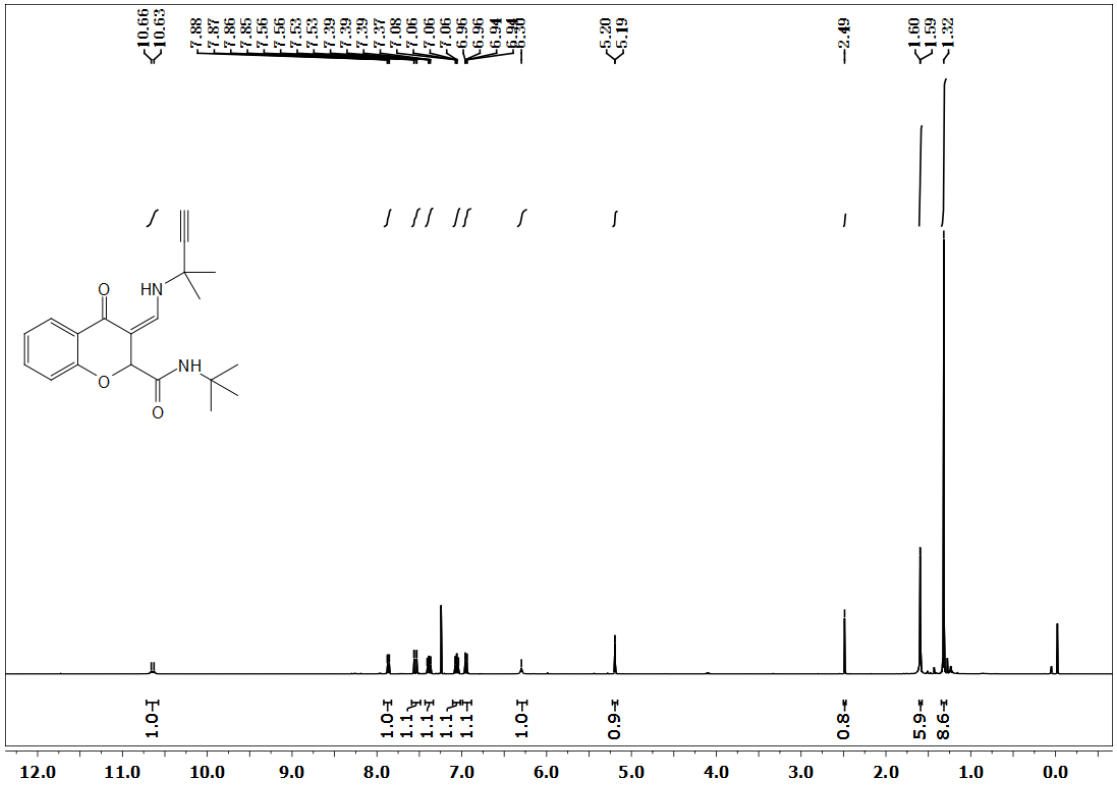


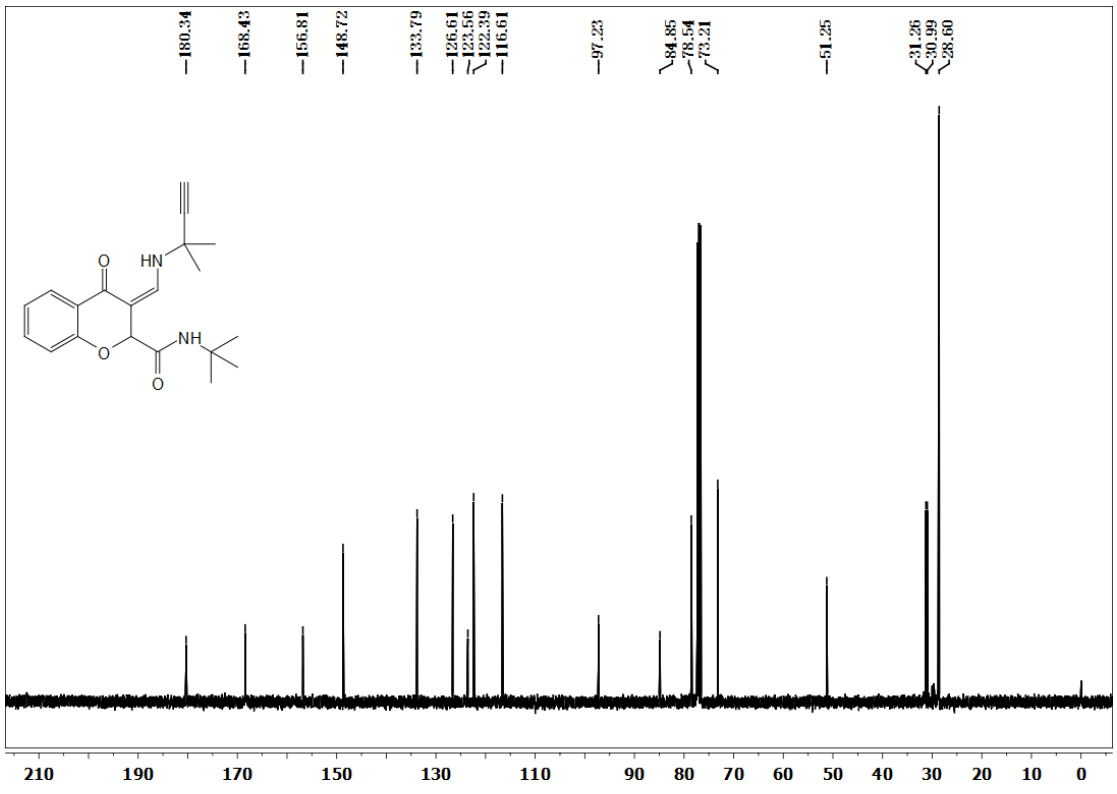
^{1}H NMR and ^{13}C NMR spectrum of **5c**



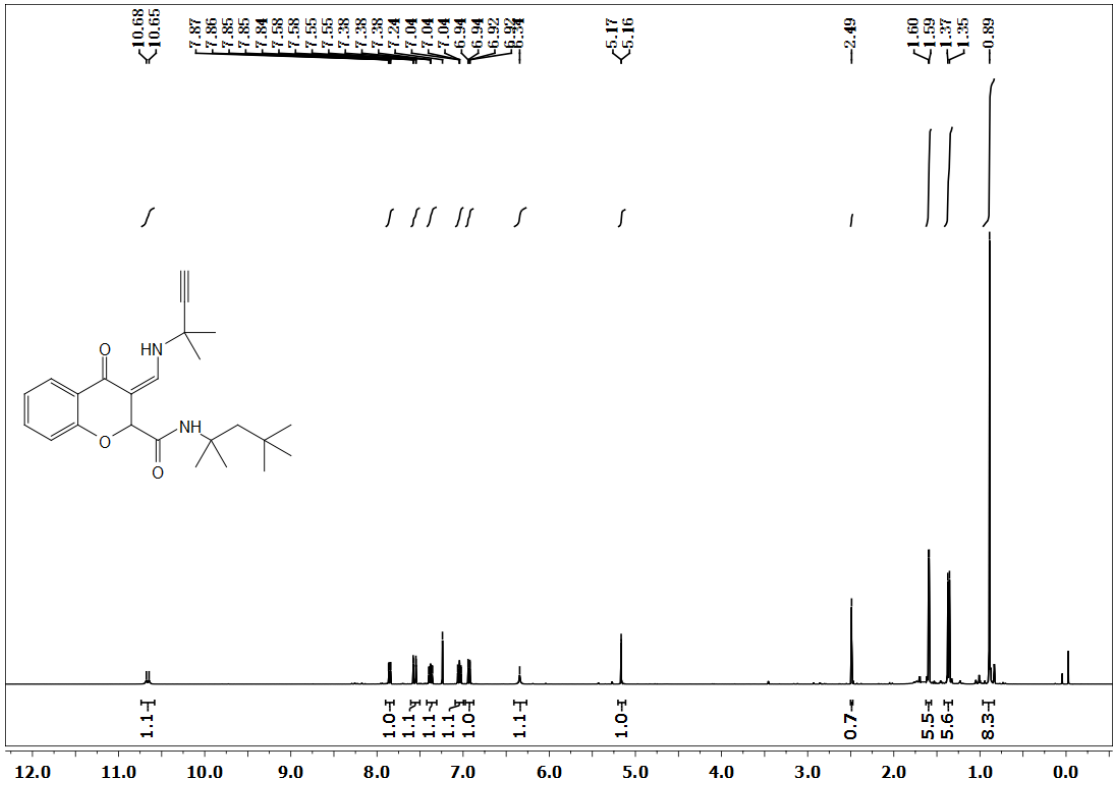


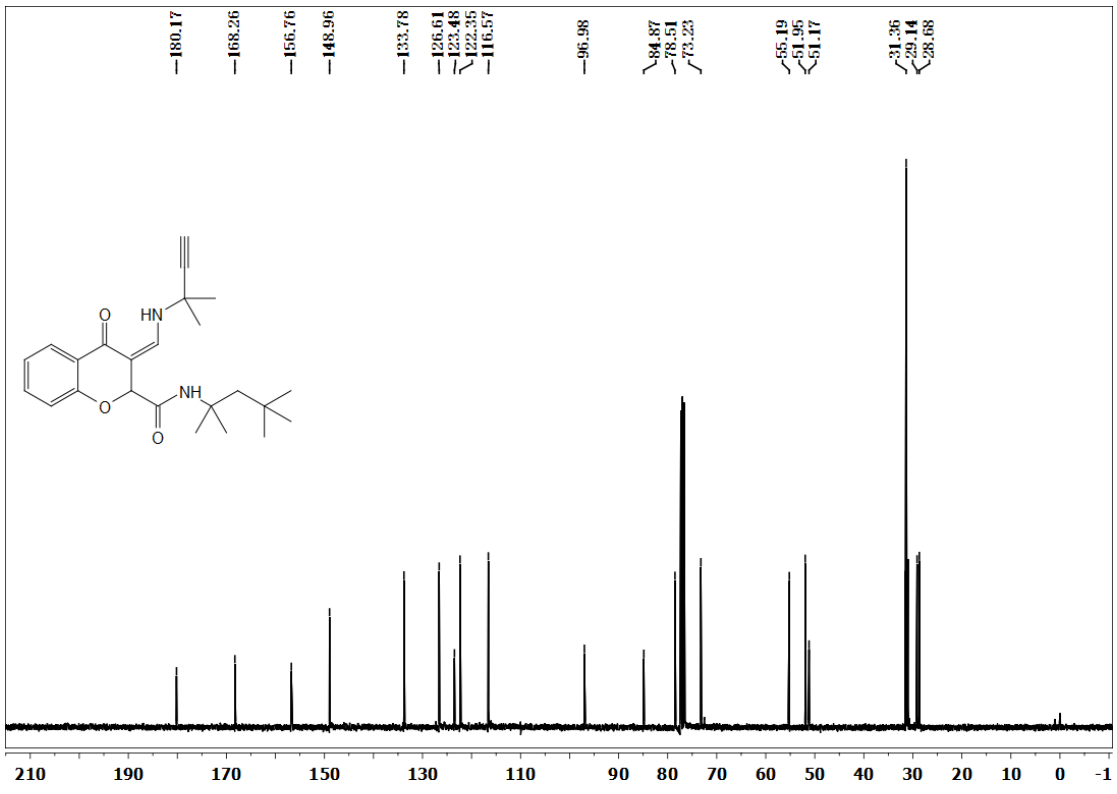
^{1}H NMR and ^{13}C NMR spectrum of **5d**



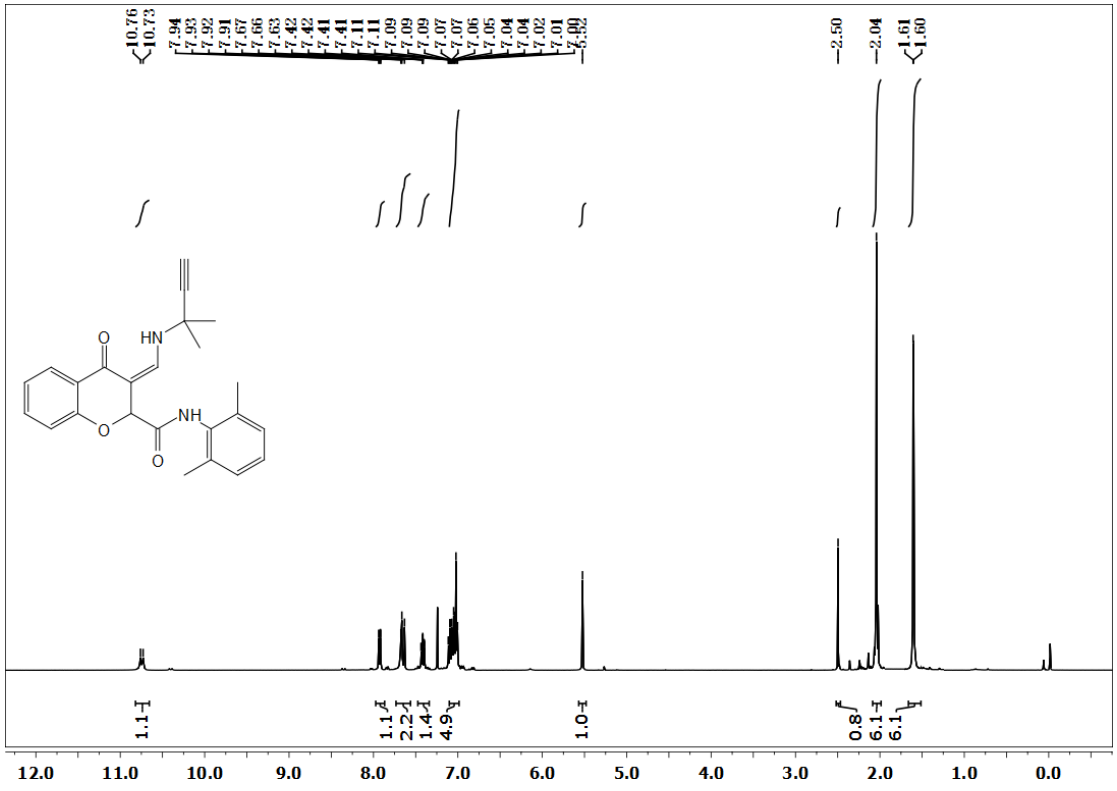


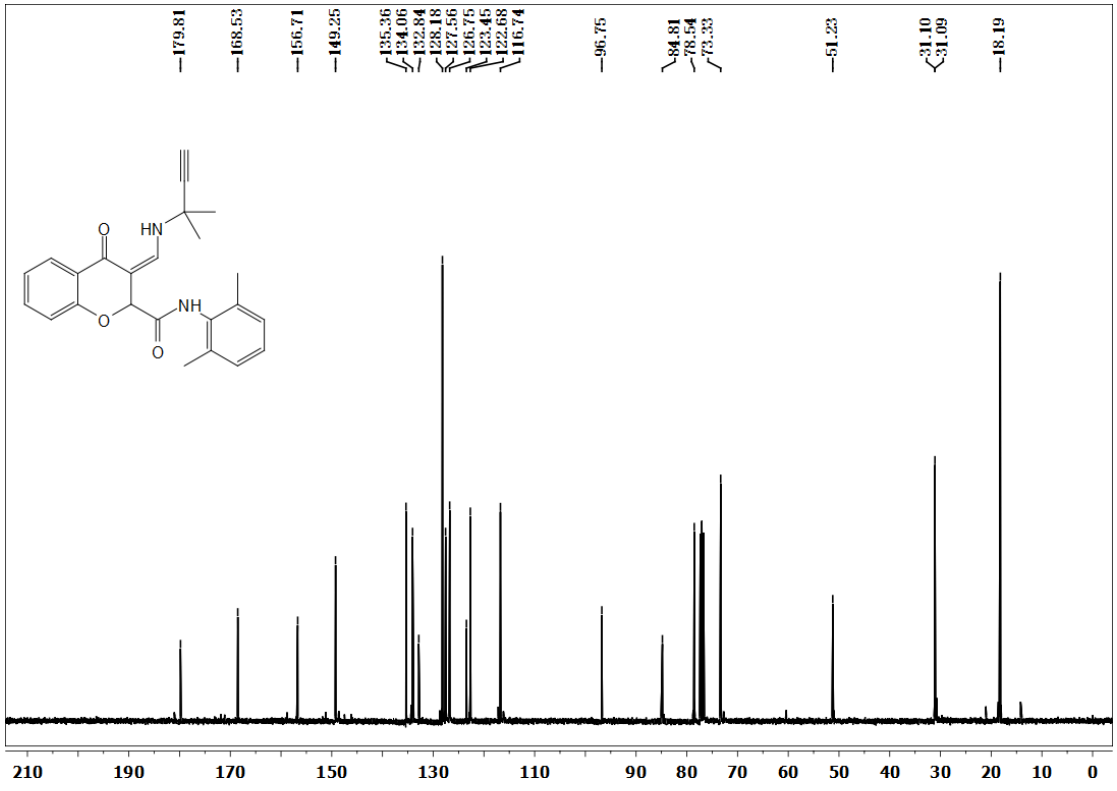
^{1}H NMR and ^{13}C NMR spectrum of **5e**



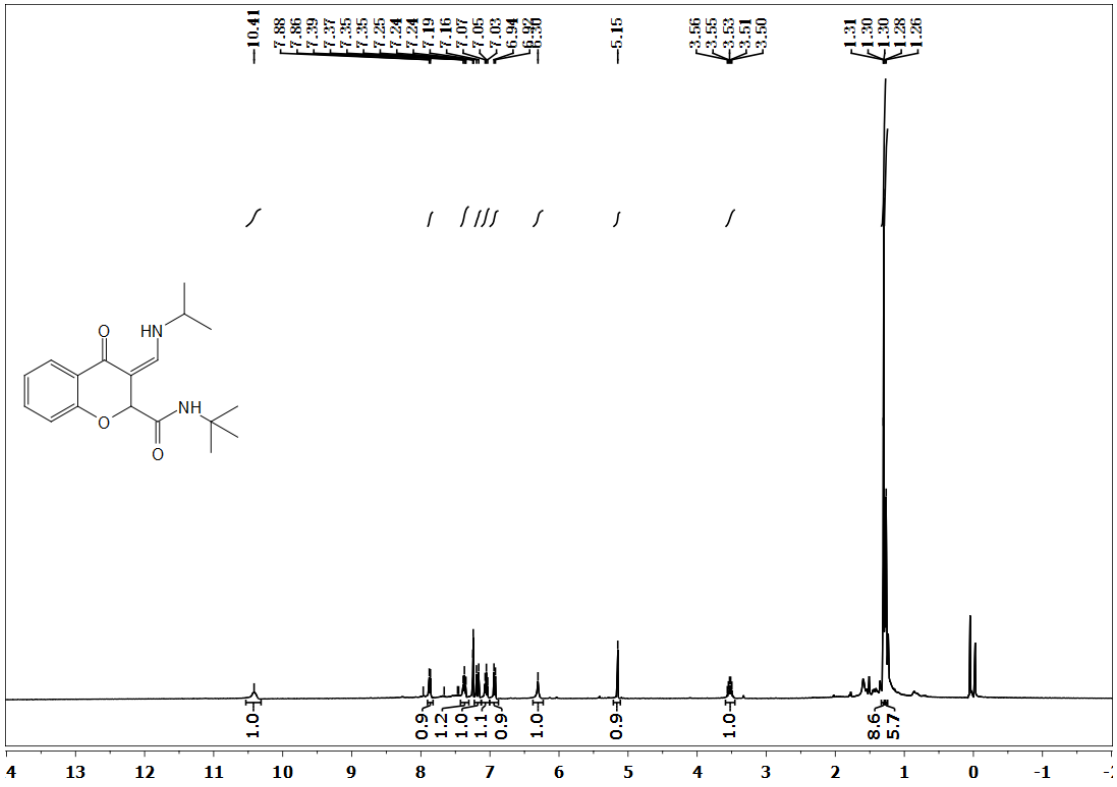


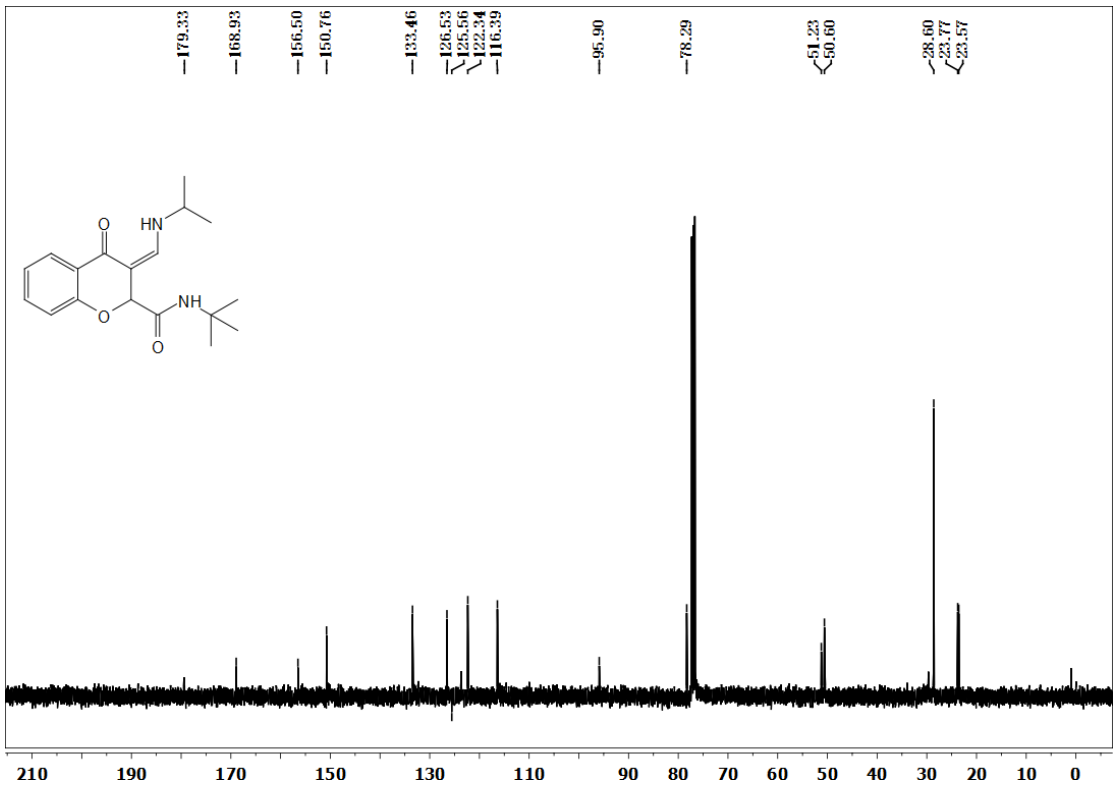
^{1}H NMR and ^{13}C NMR spectrum of **5f**



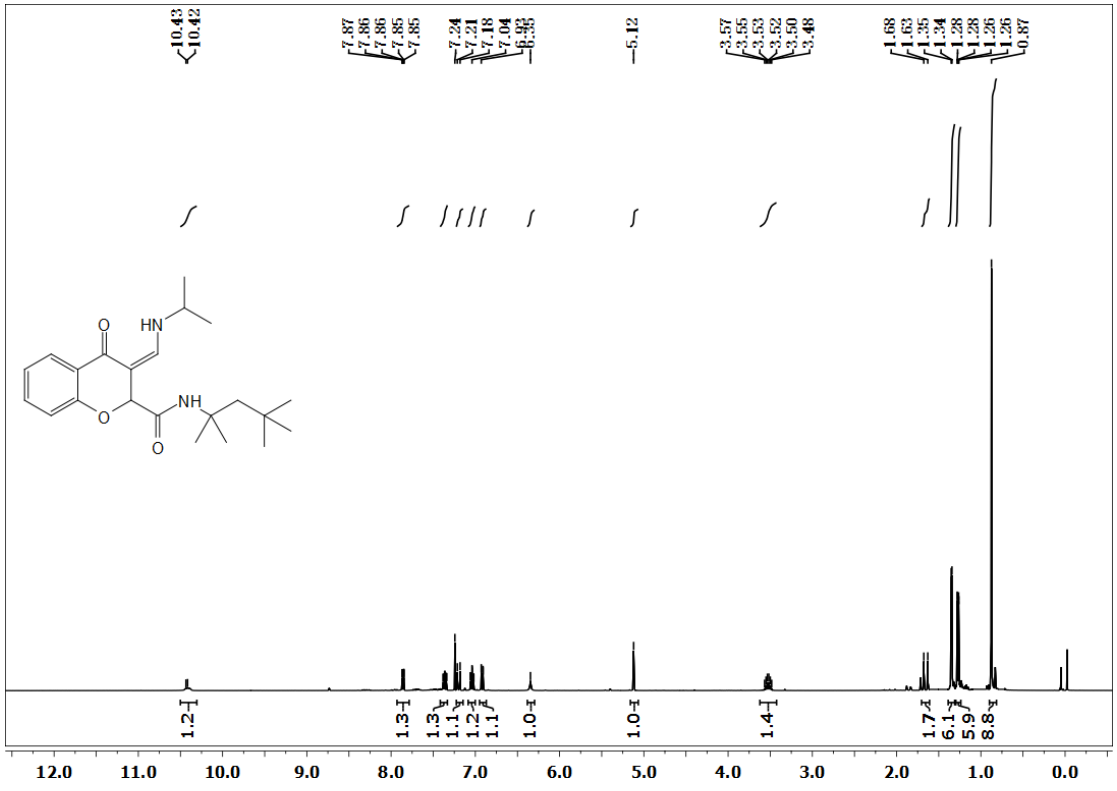


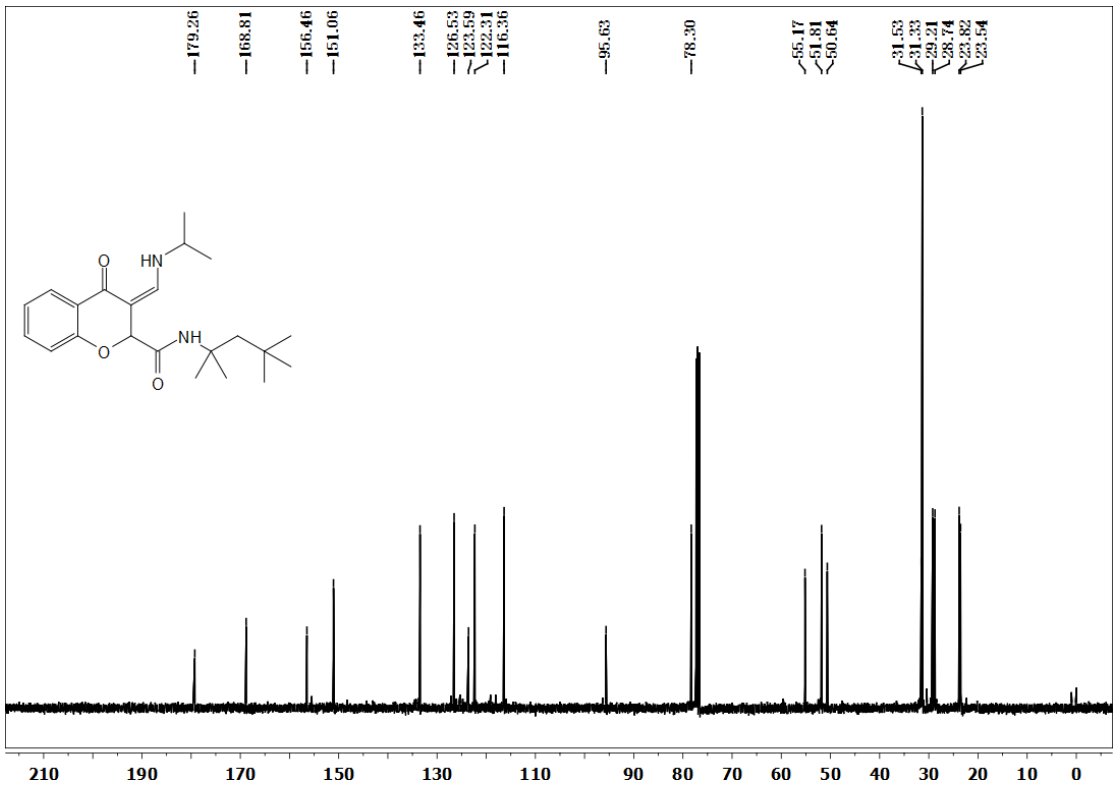
^{1}H NMR and ^{13}C NMR spectrum of **5g**



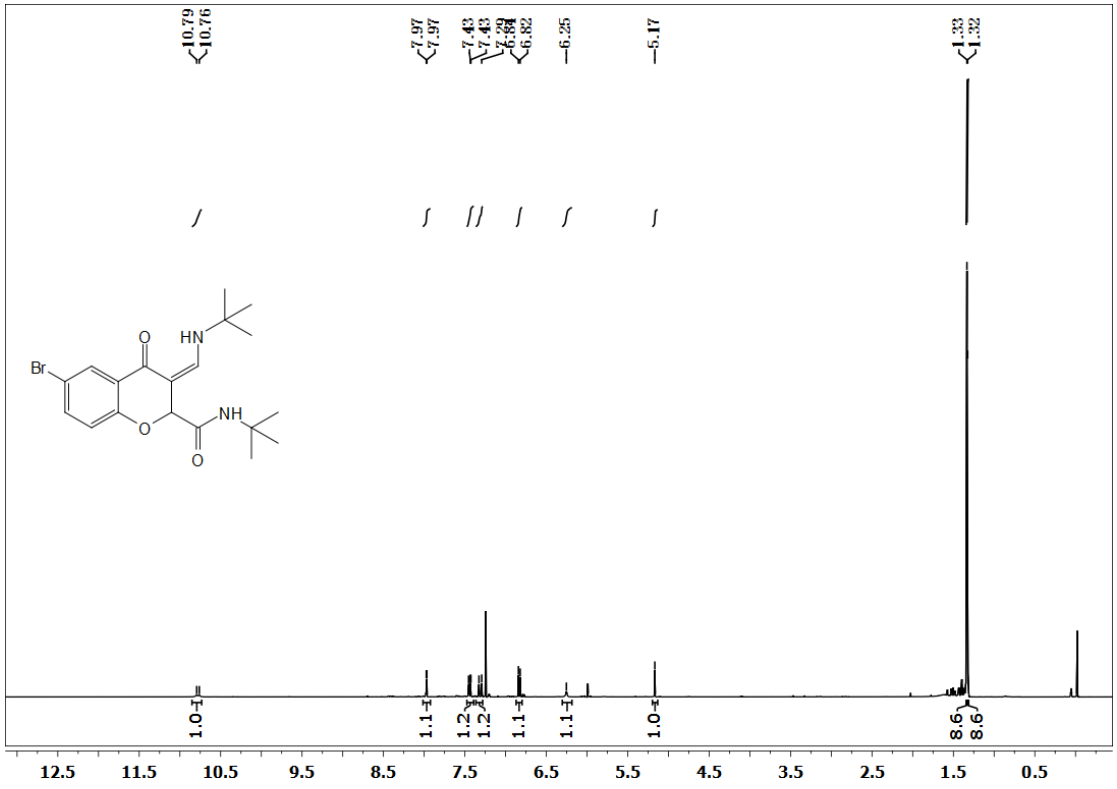


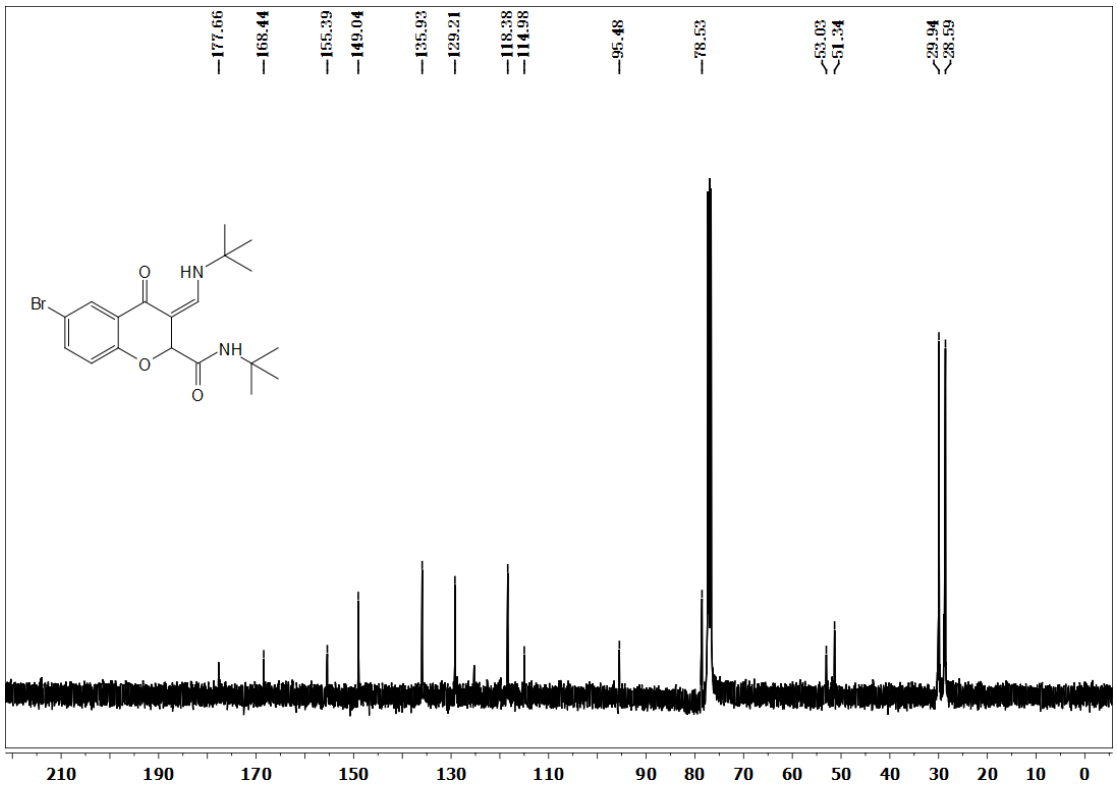
^{1}H NMR and ^{13}C NMR spectrum of **5h**



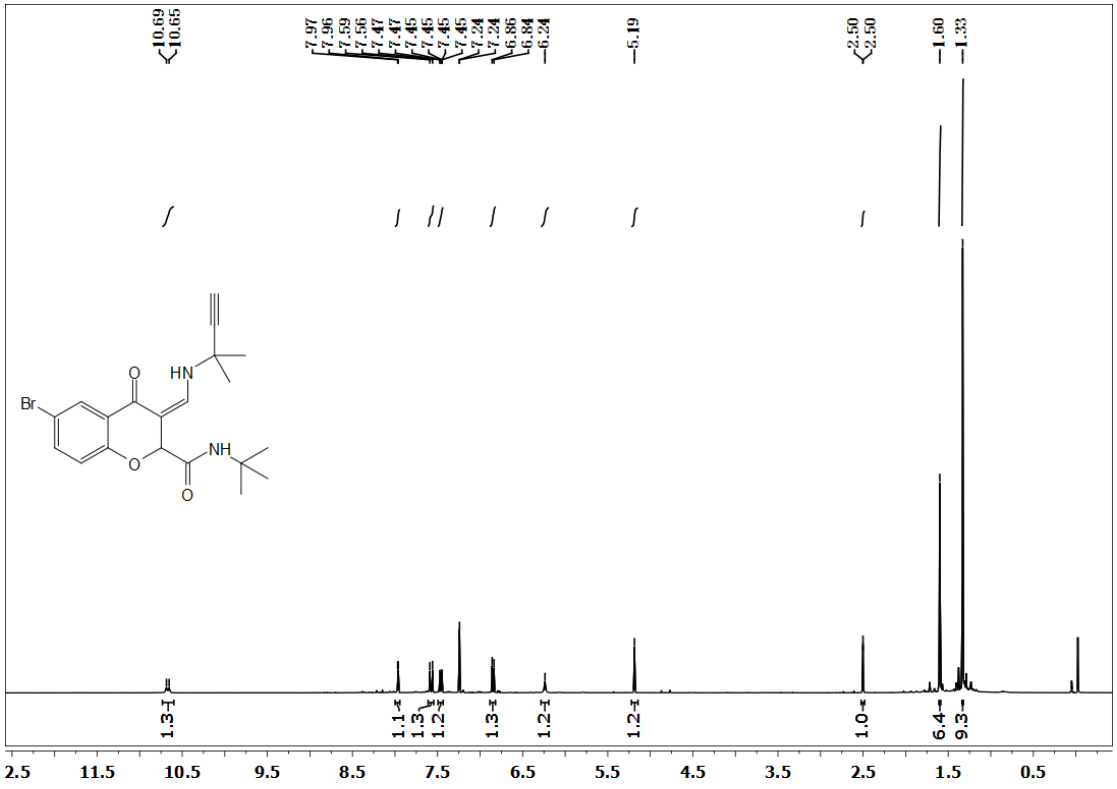


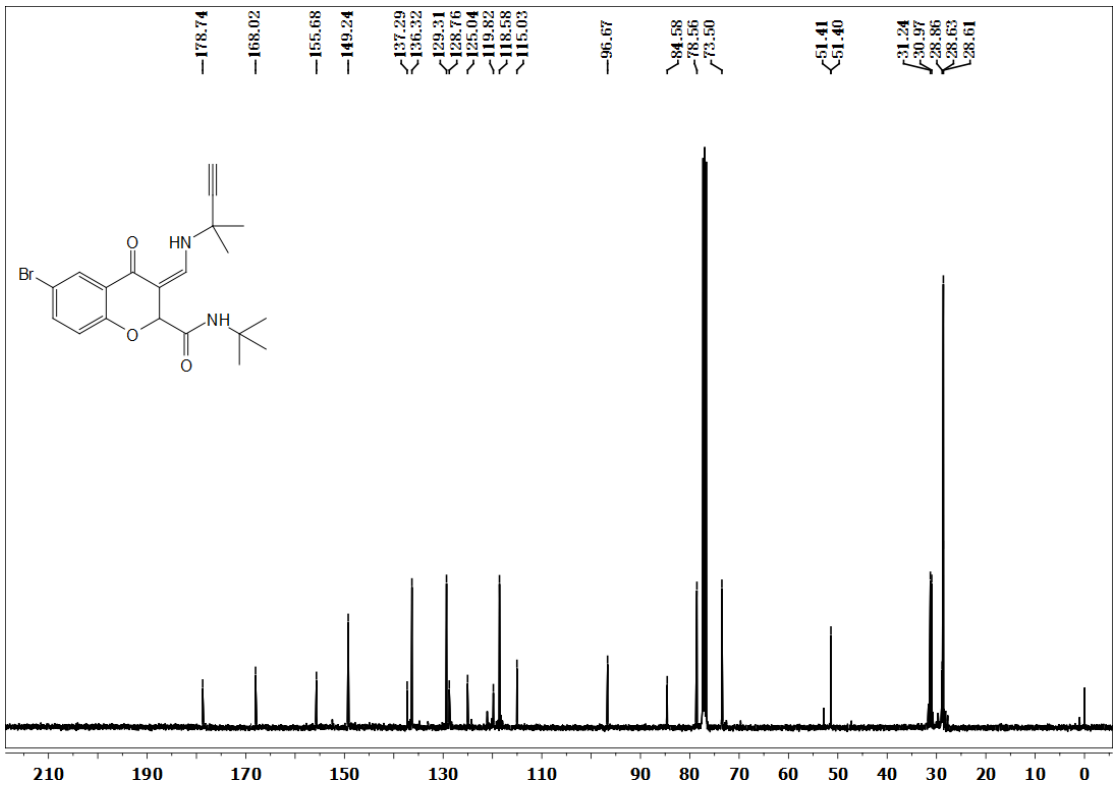
^{1}H NMR and ^{13}C NMR spectrum of **5i**



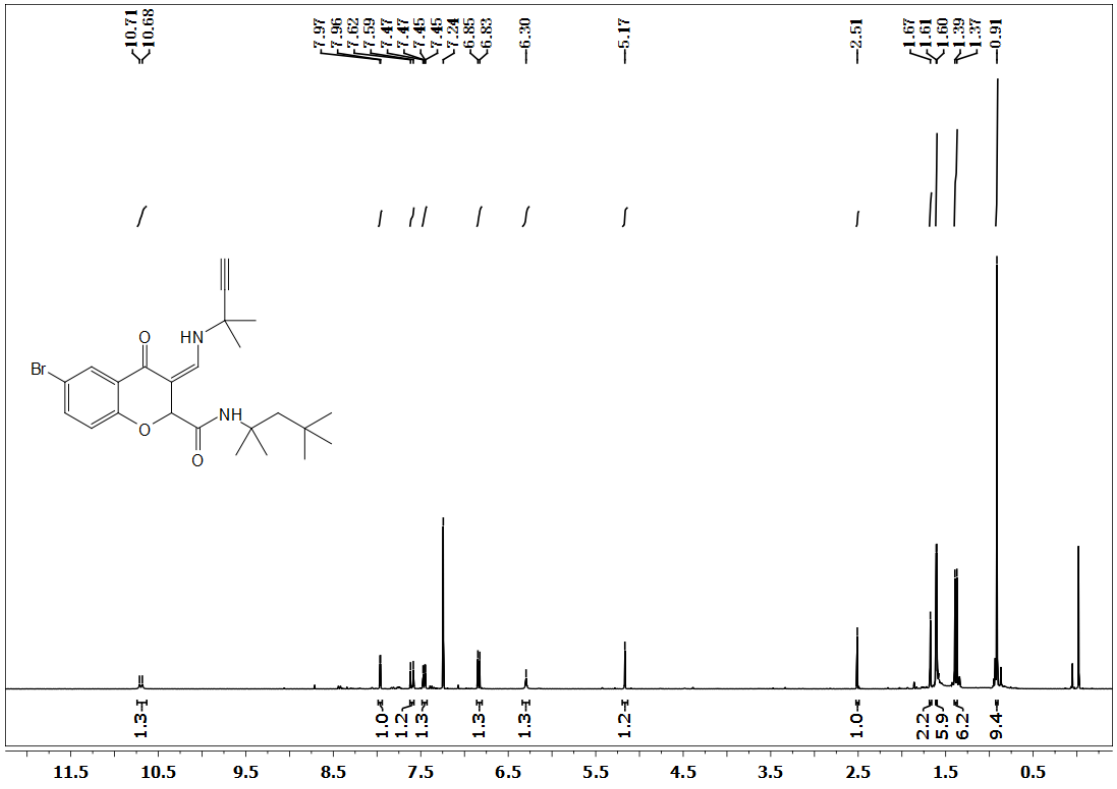


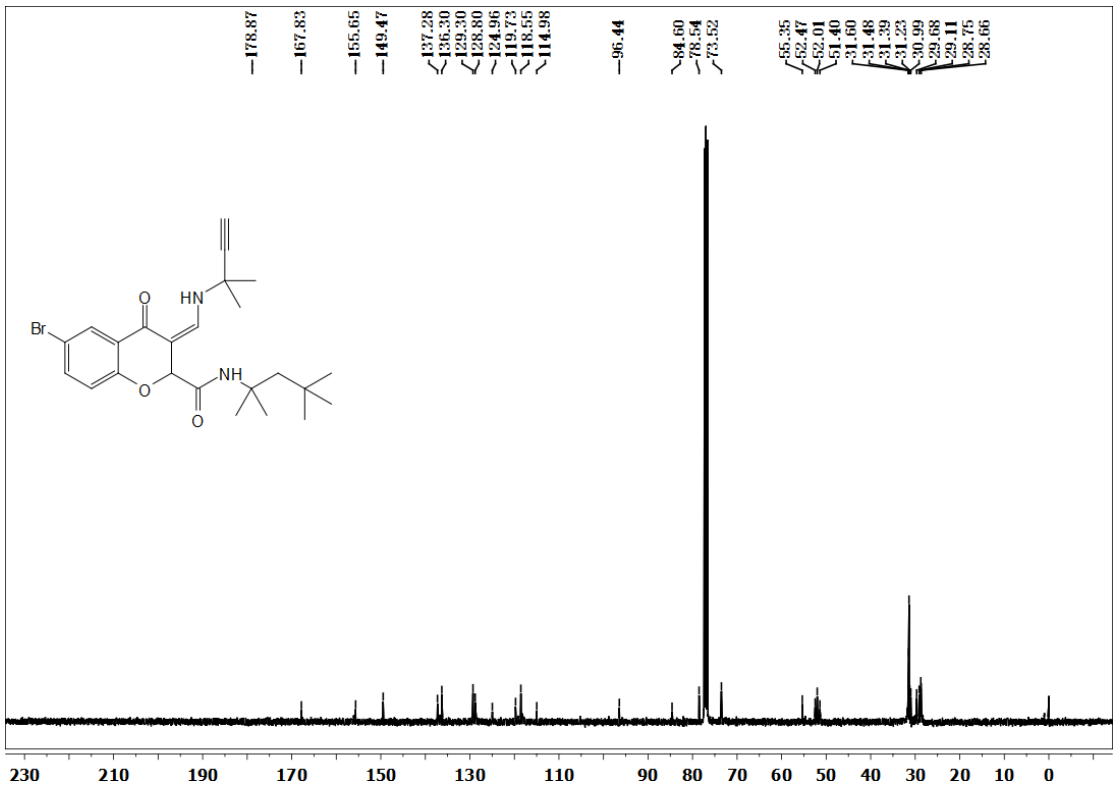
^{1}H NMR and ^{13}C NMR spectrum of **5j**



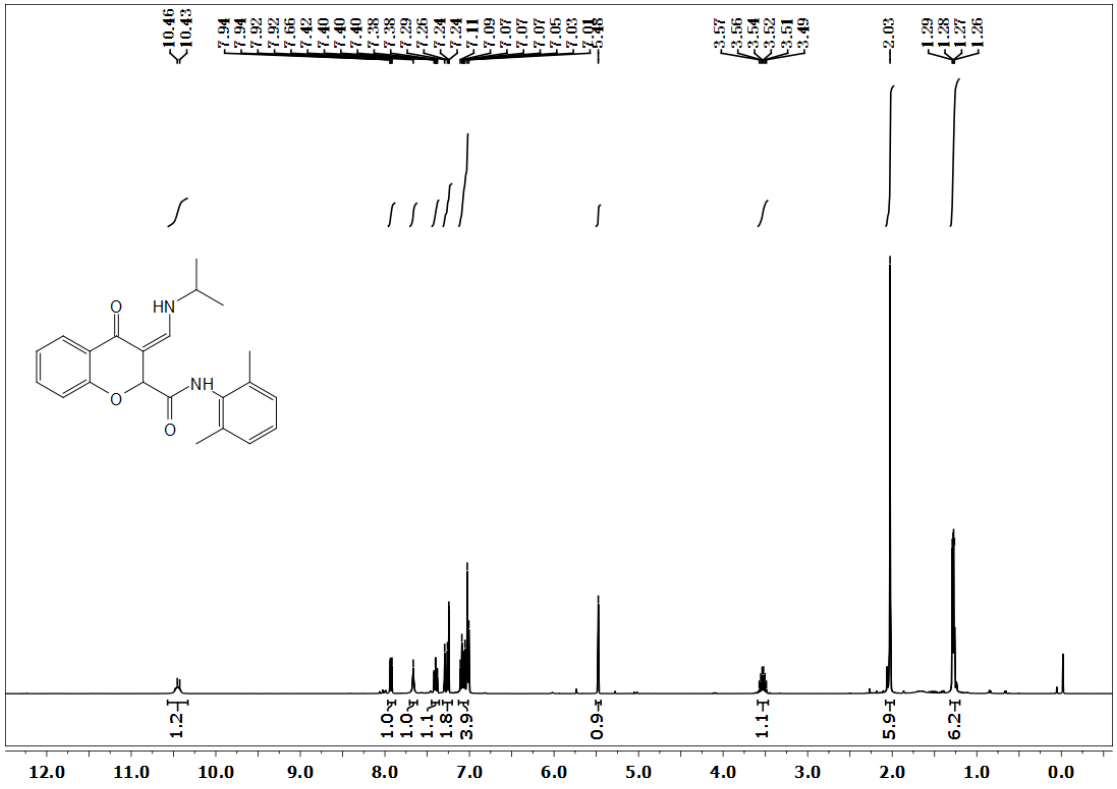


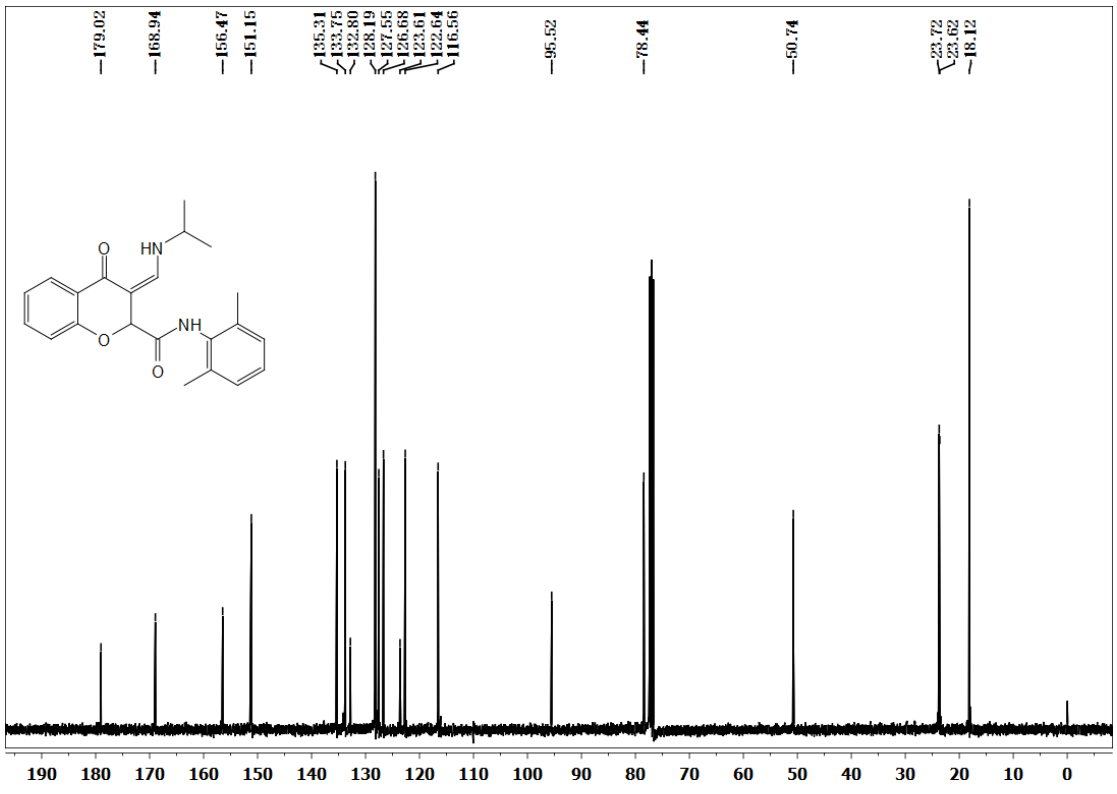
^{1}H NMR and ^{13}C NMR spectrum of **5k**



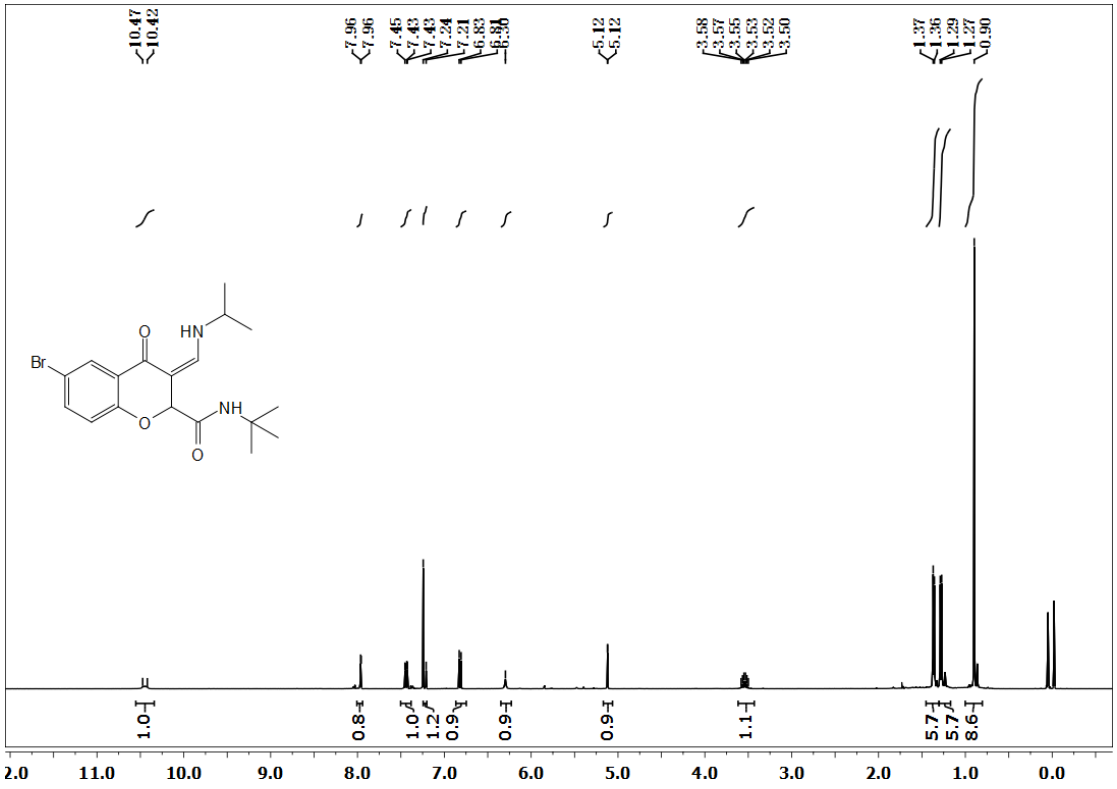


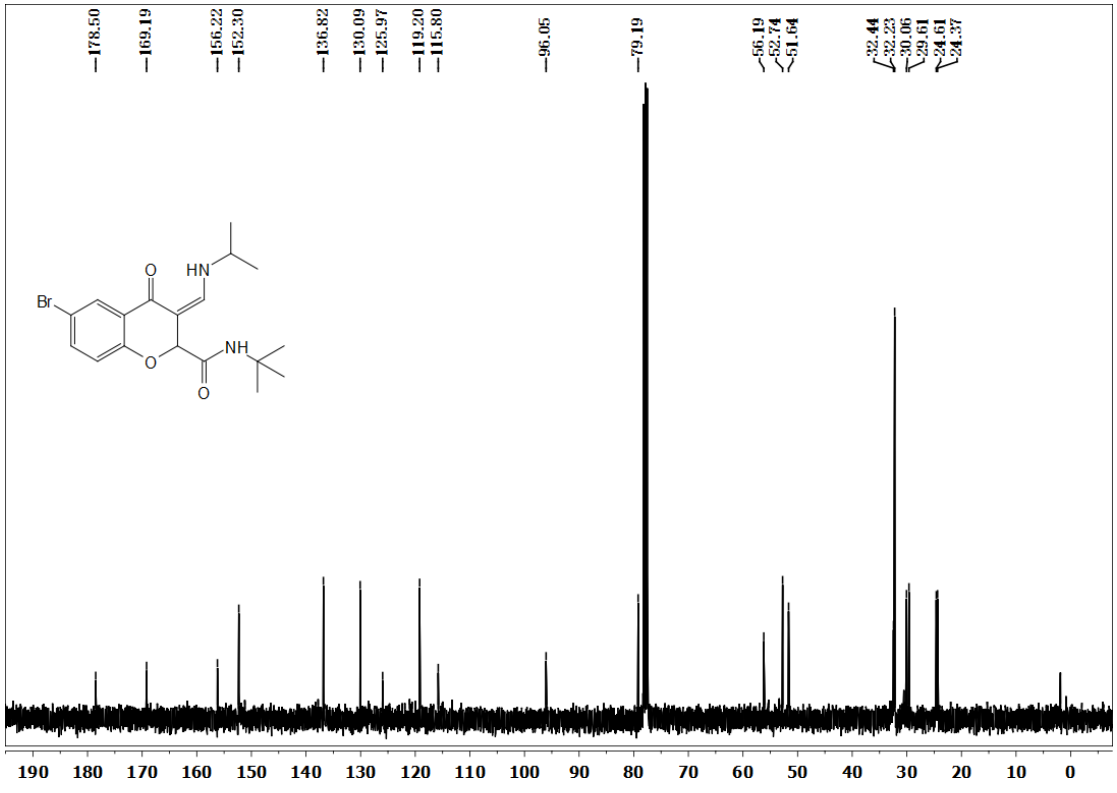
^{1}H NMR and ^{13}C NMR spectrum of **5l**



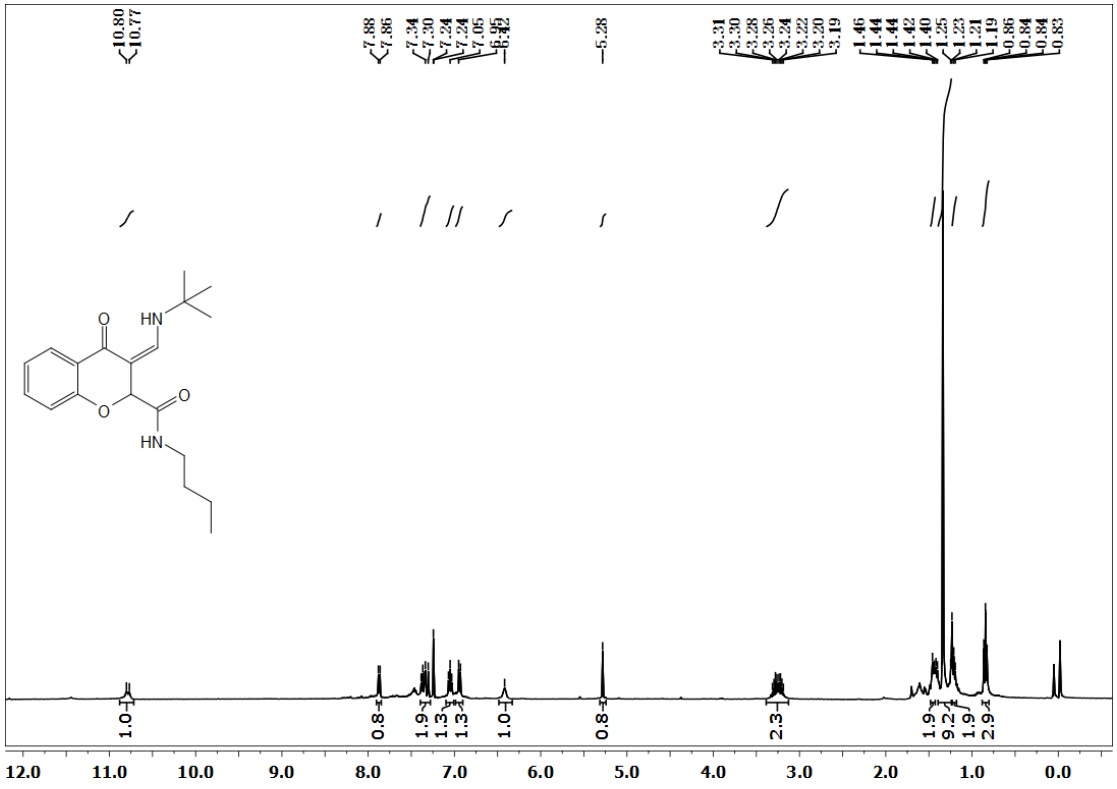


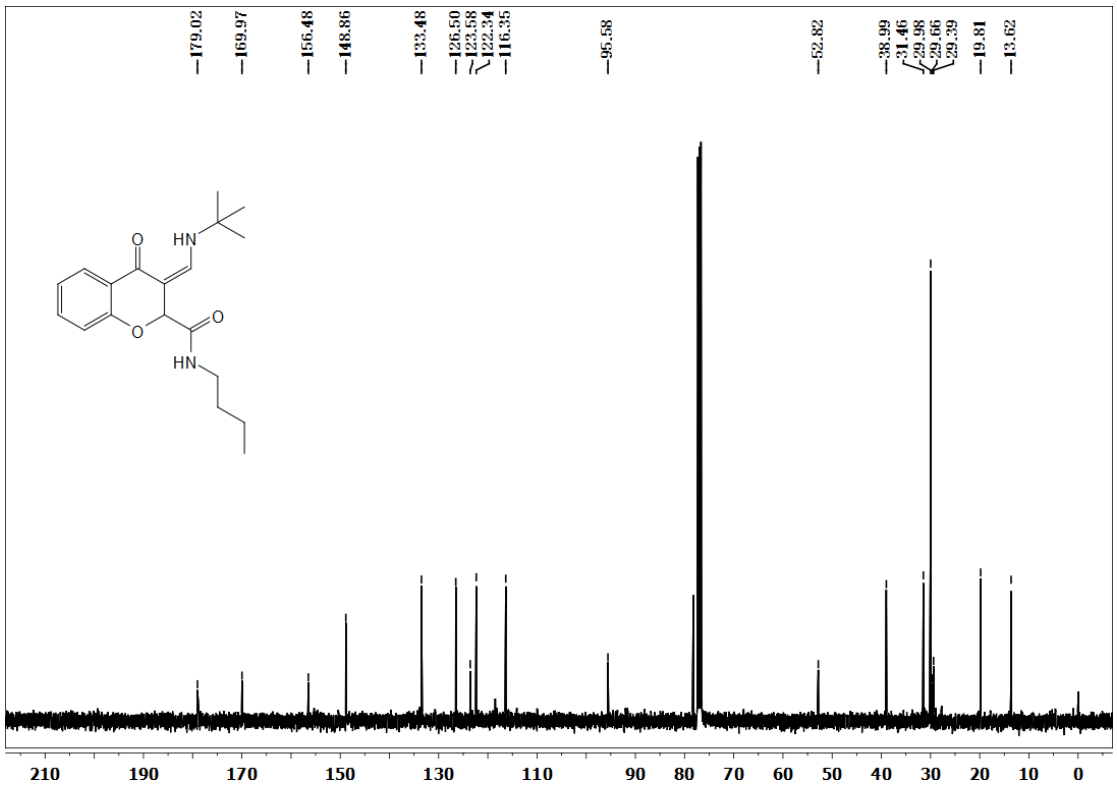
^{1}H NMR and ^{13}C NMR spectrum of **5m**



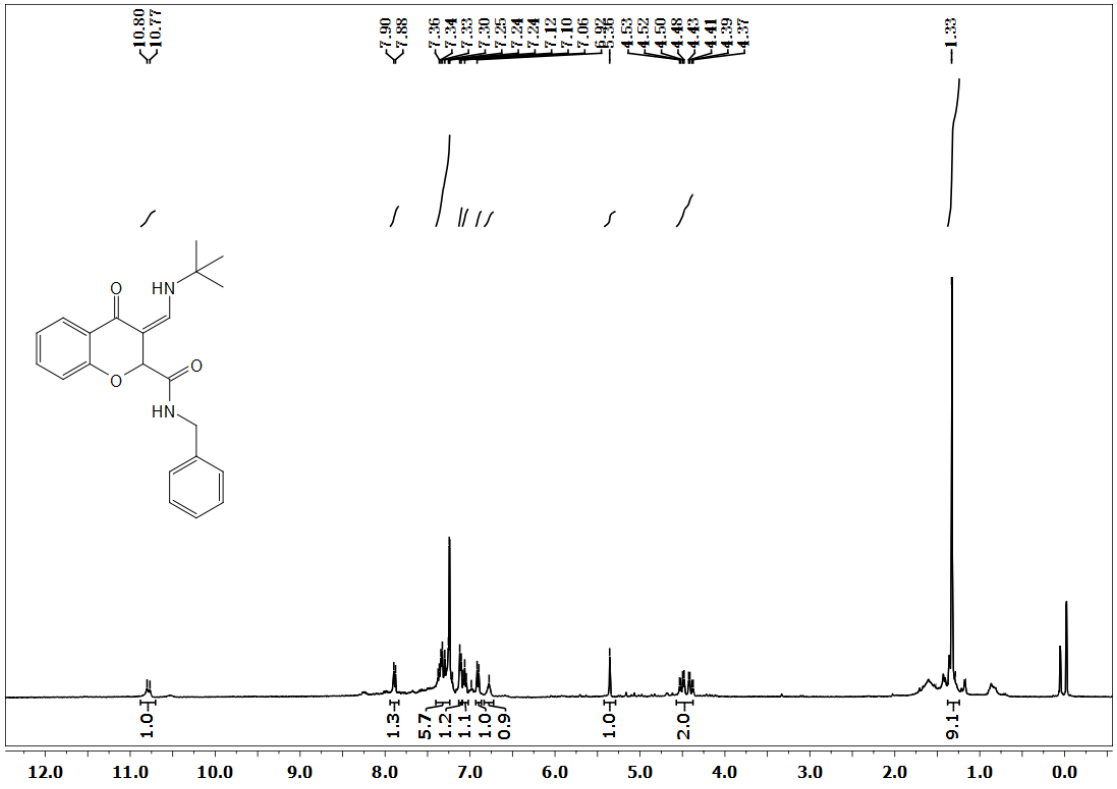


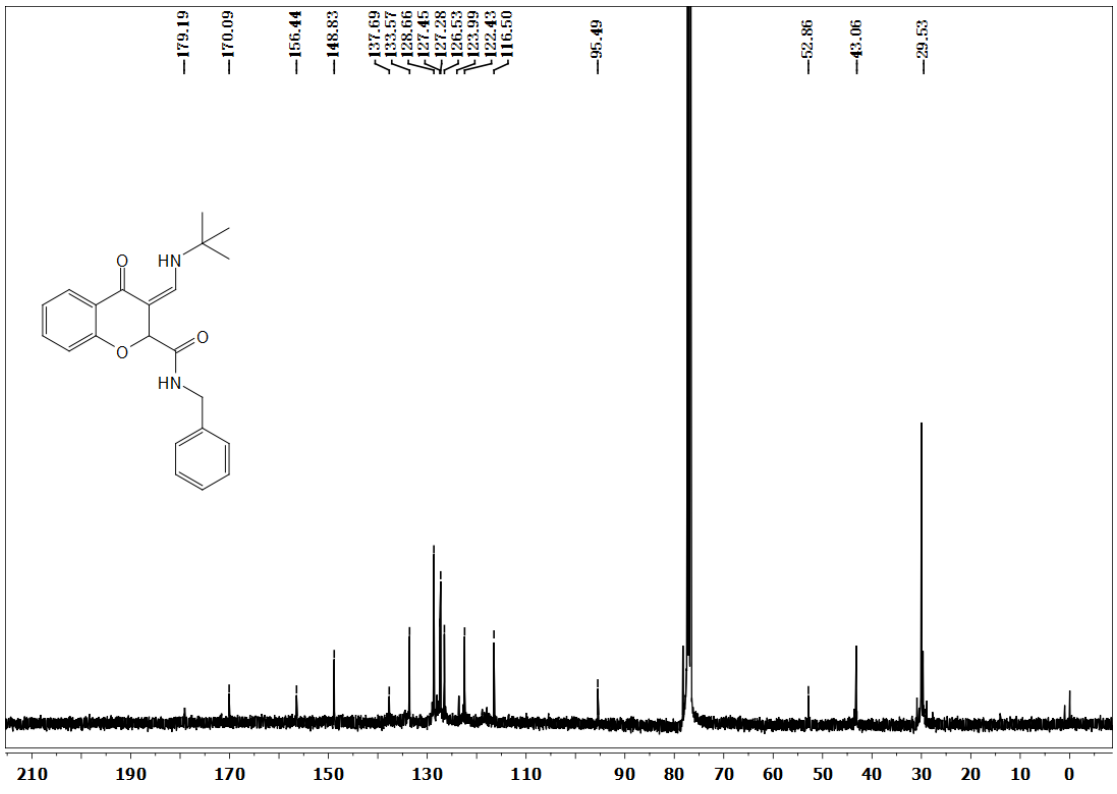
^{1}H NMR and ^{13}C NMR spectrum of **5n**



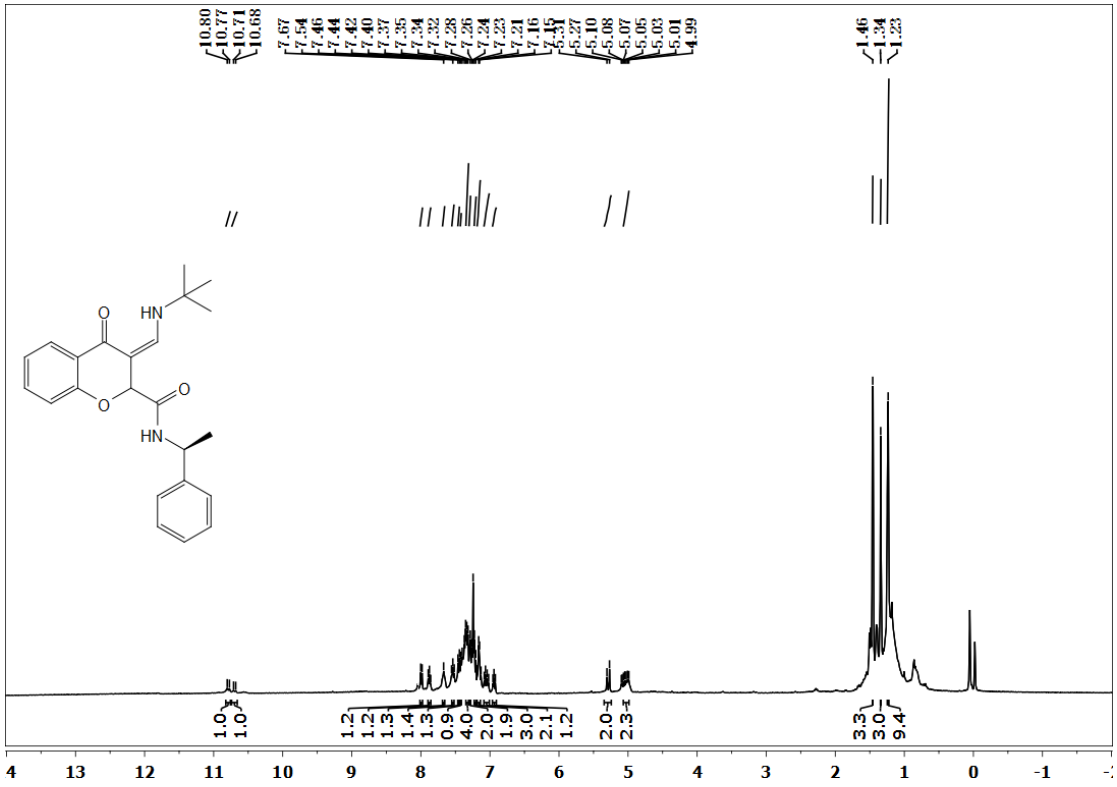


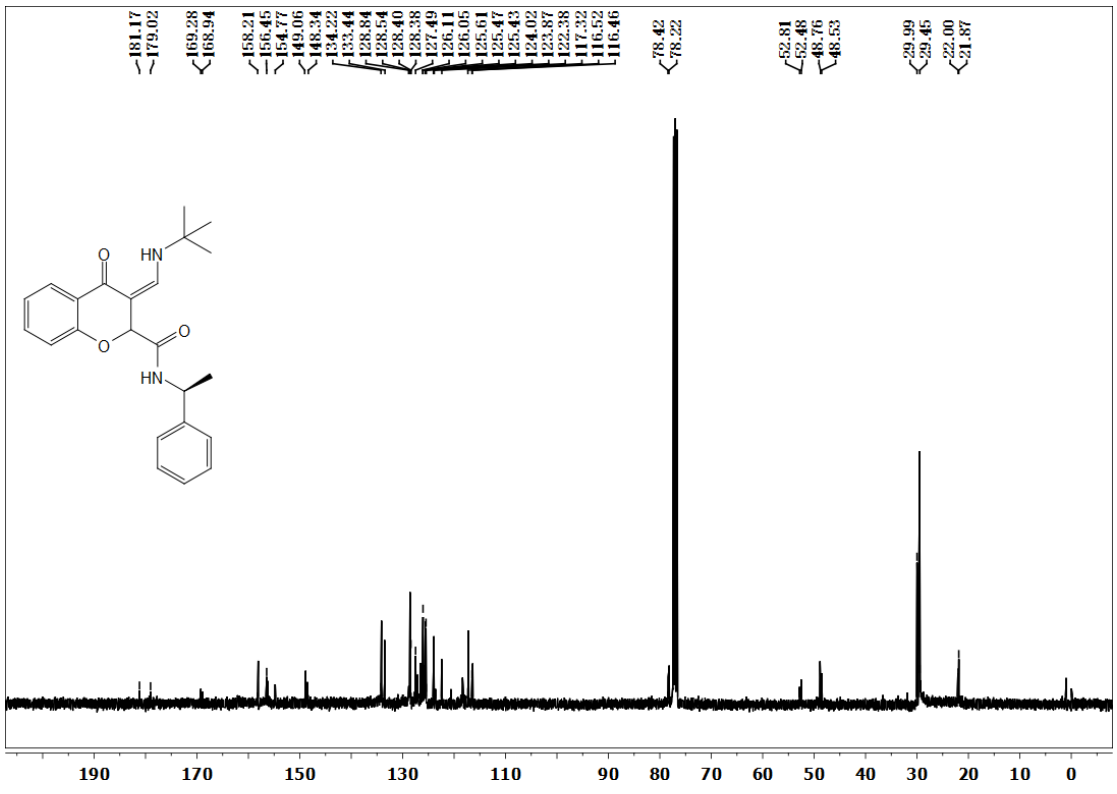
^{1}H NMR and ^{13}C NMR spectrum of **5o**



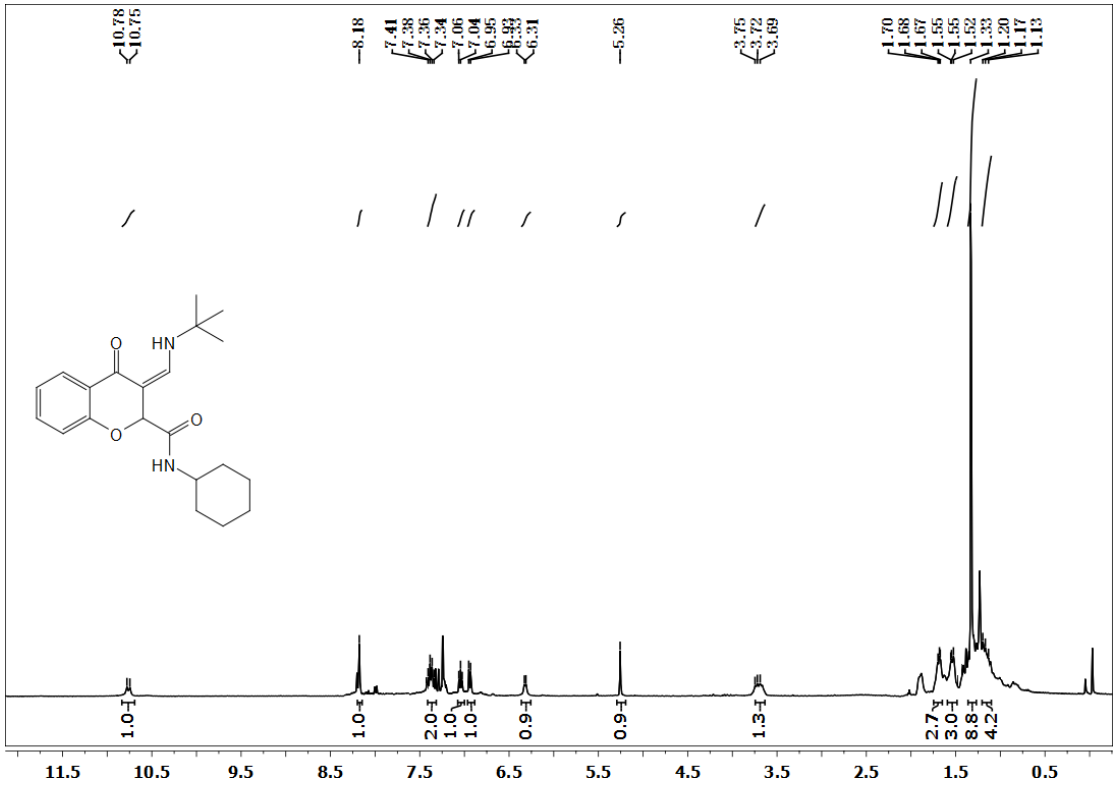


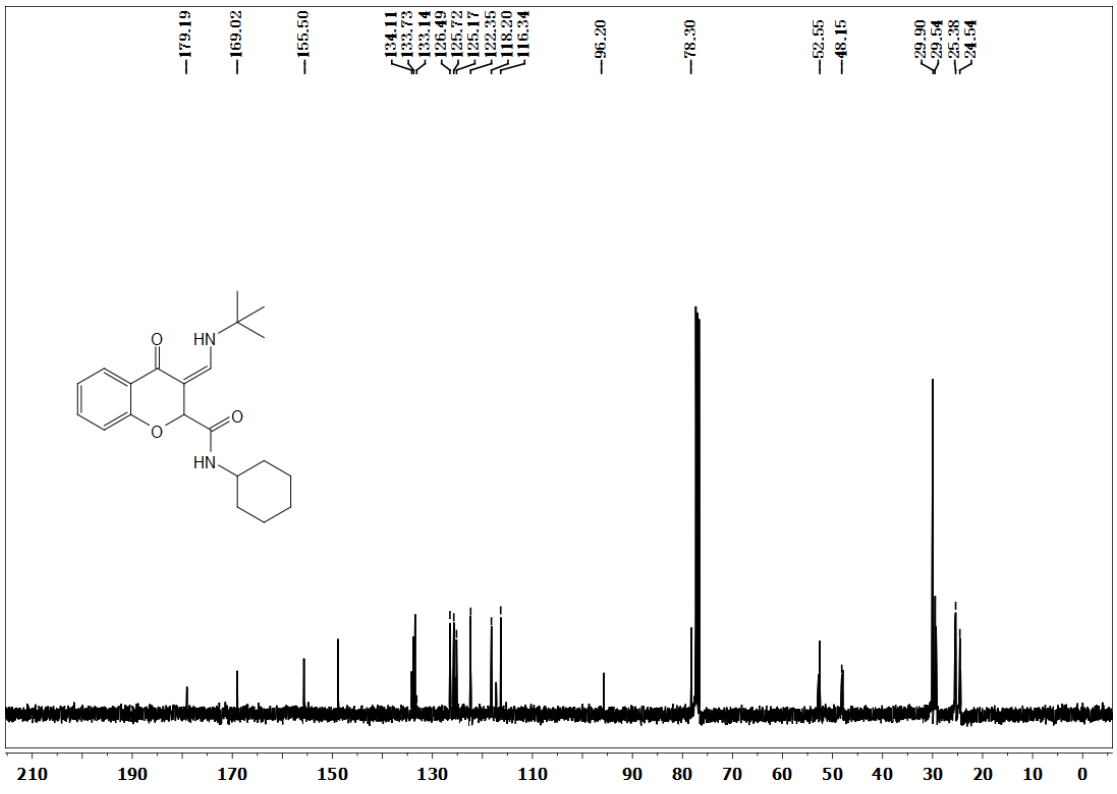
^{1}H NMR and ^{13}C NMR spectrum of **5p**



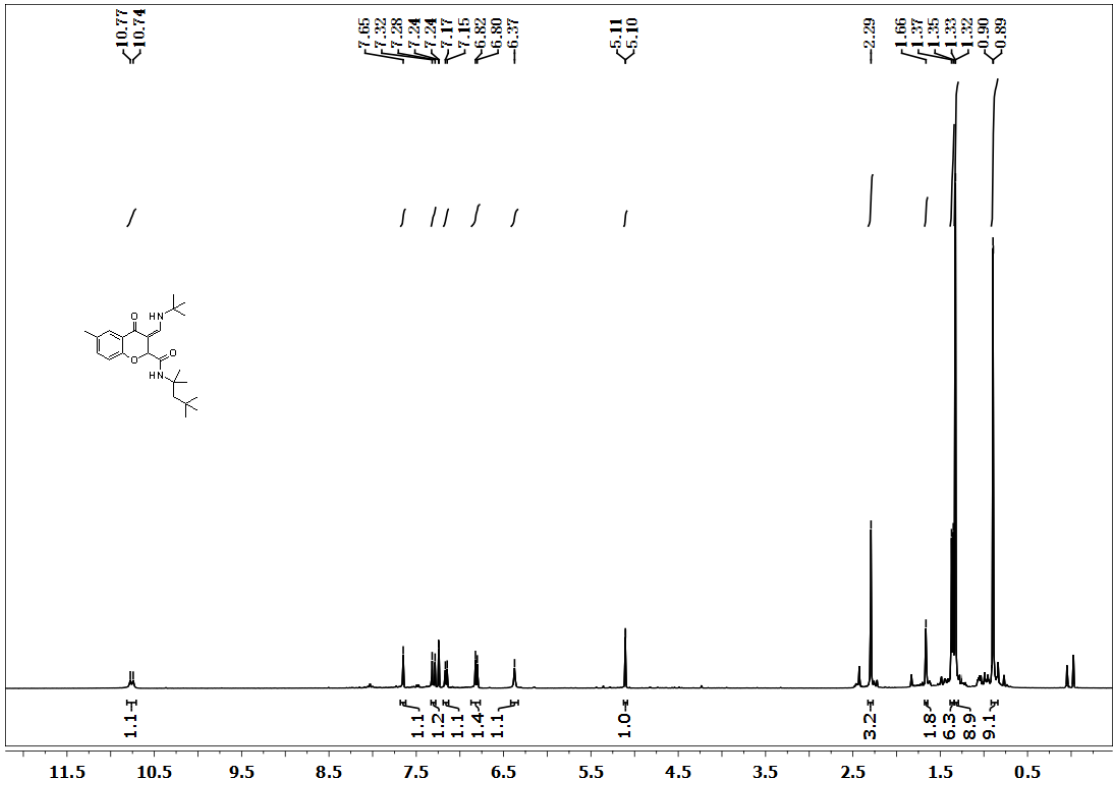


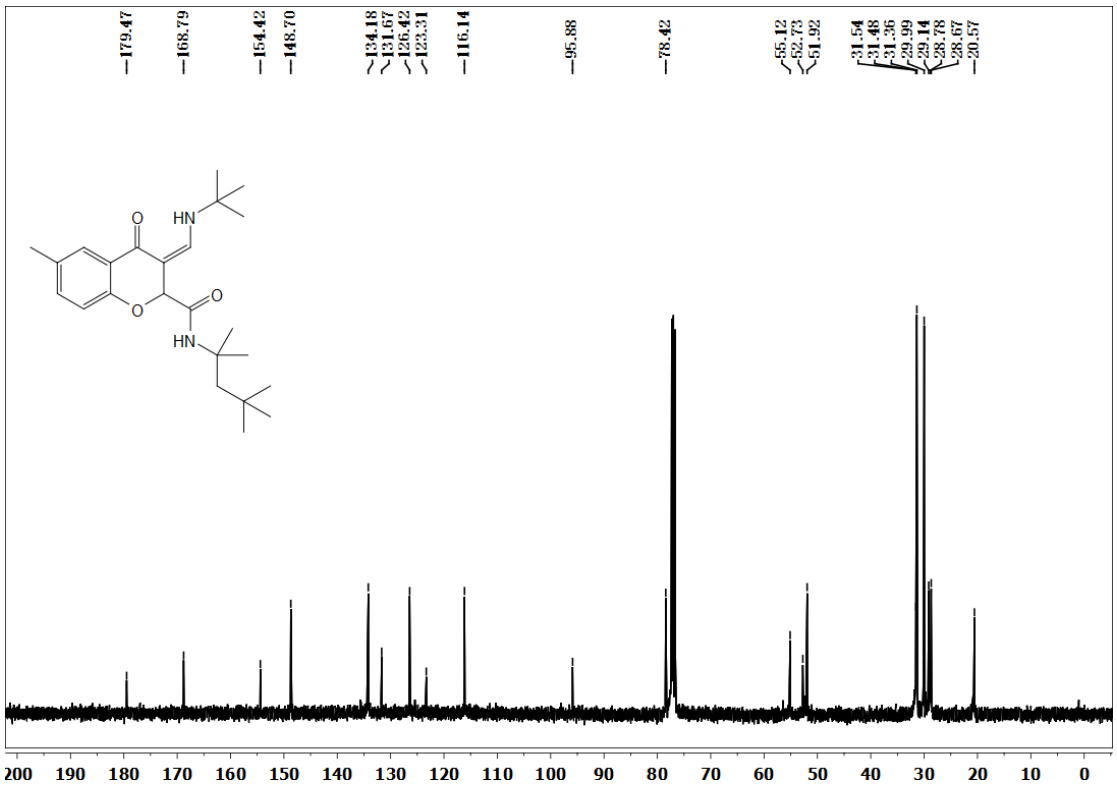
^{1}H NMR and ^{13}C NMR spectrum of **5q**



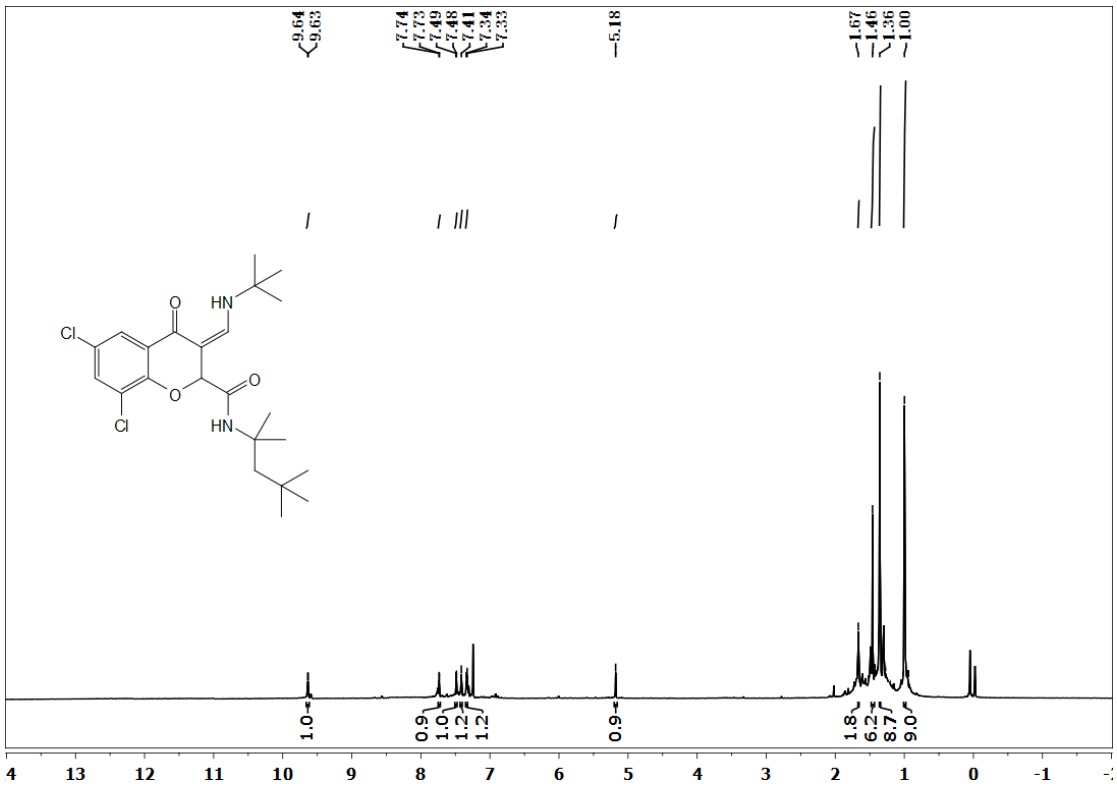


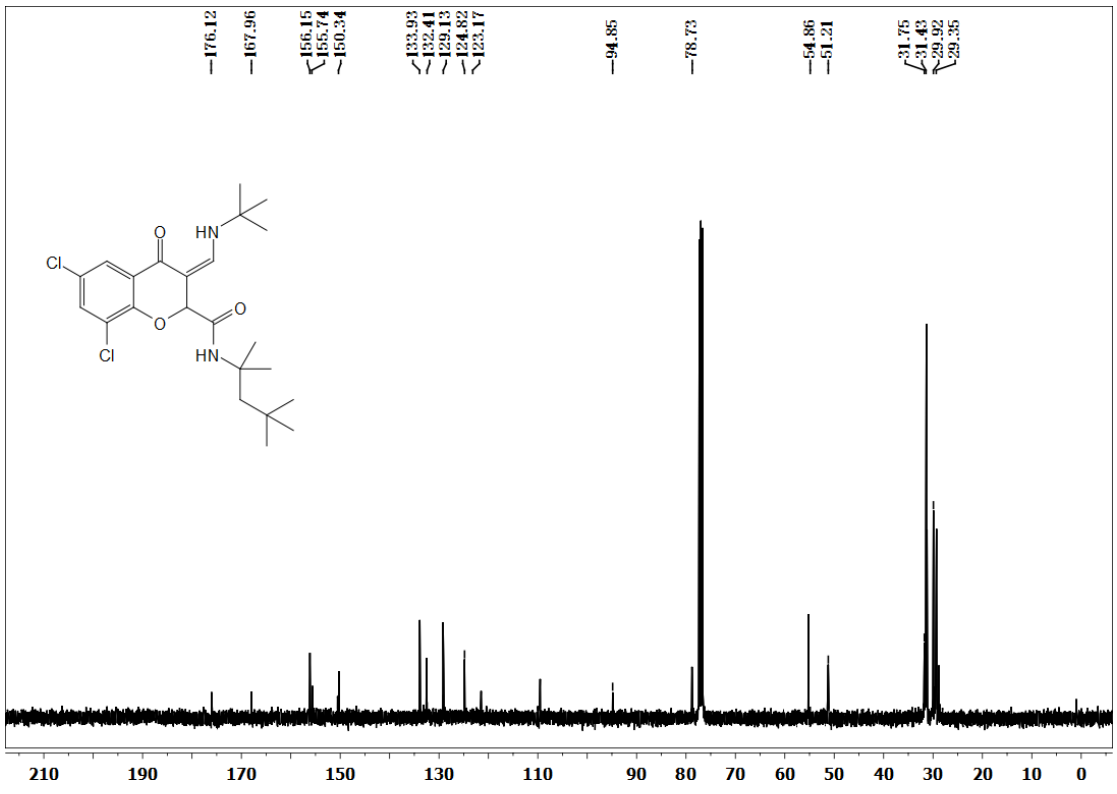
^{1}H NMR and ^{13}C NMR spectrum of **5r**



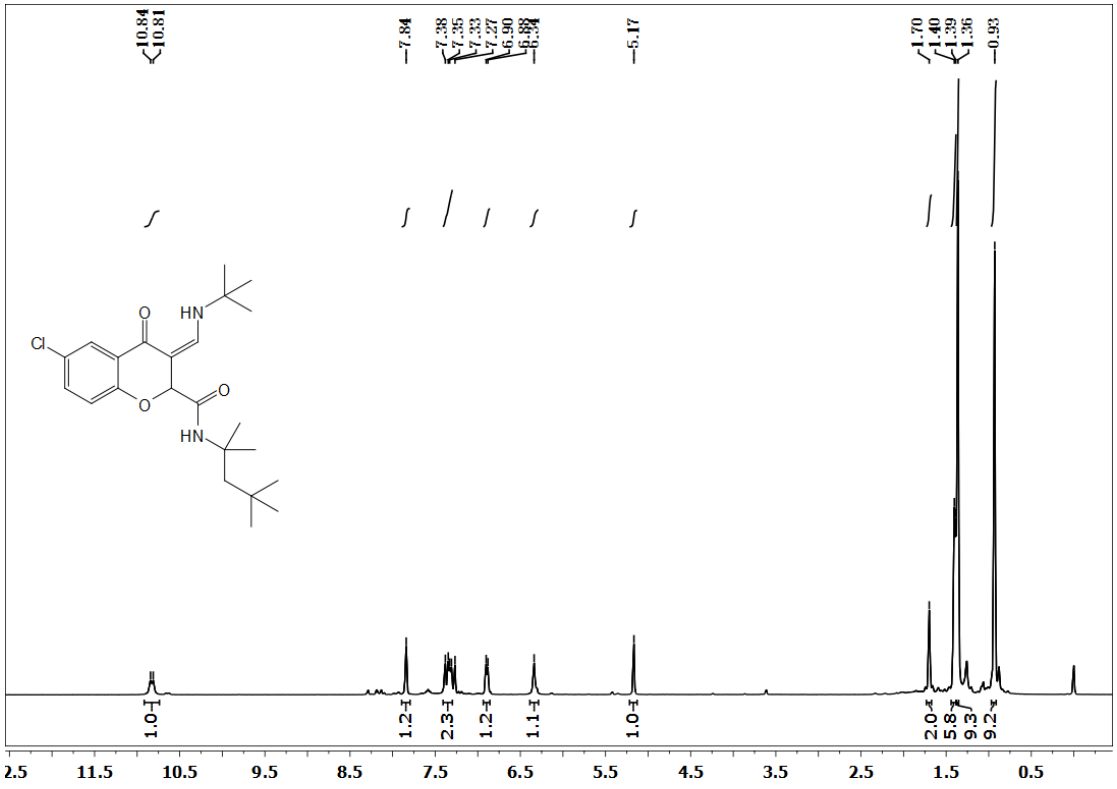


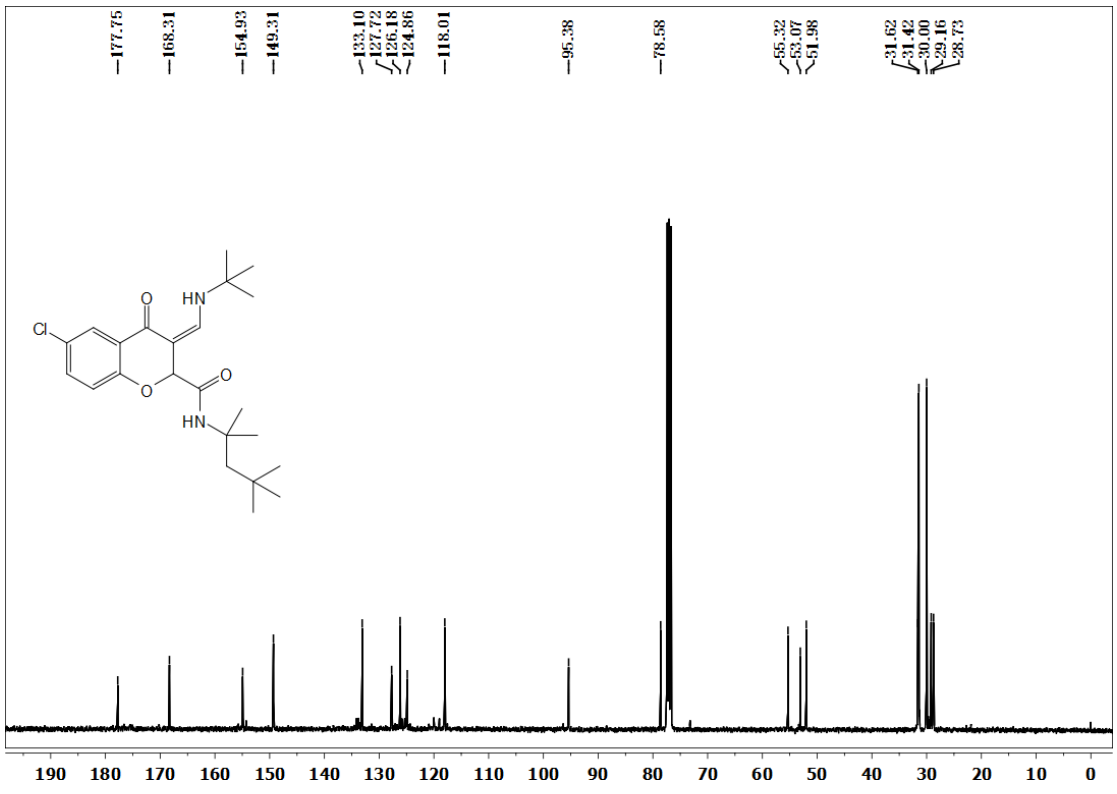
^{1}H NMR and ^{13}C NMR spectrum of **5s**



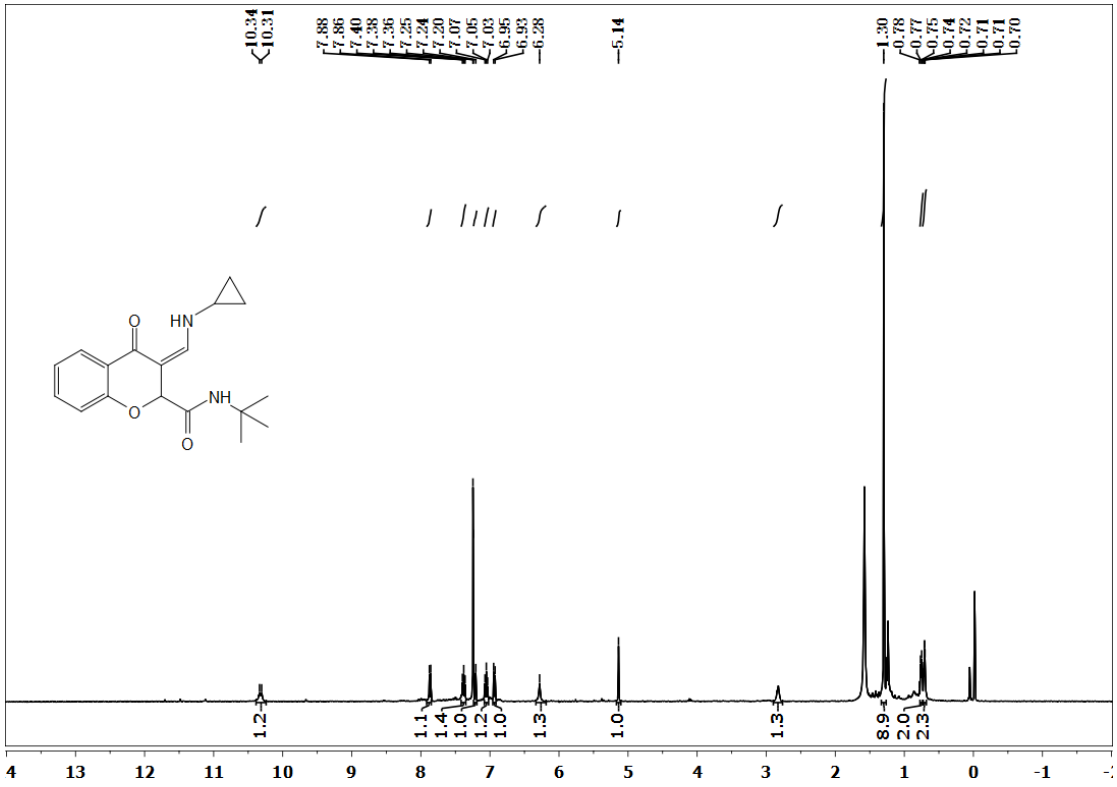


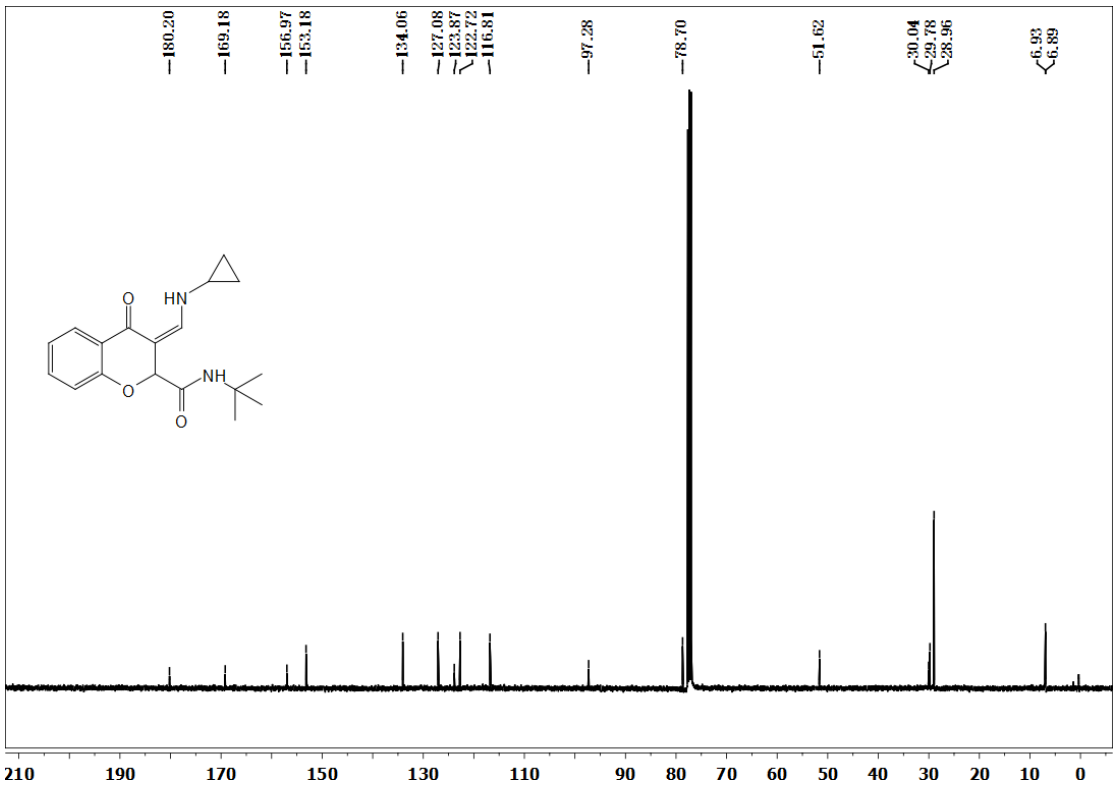
^{1}H NMR and ^{13}C NMR spectrum of **5t**



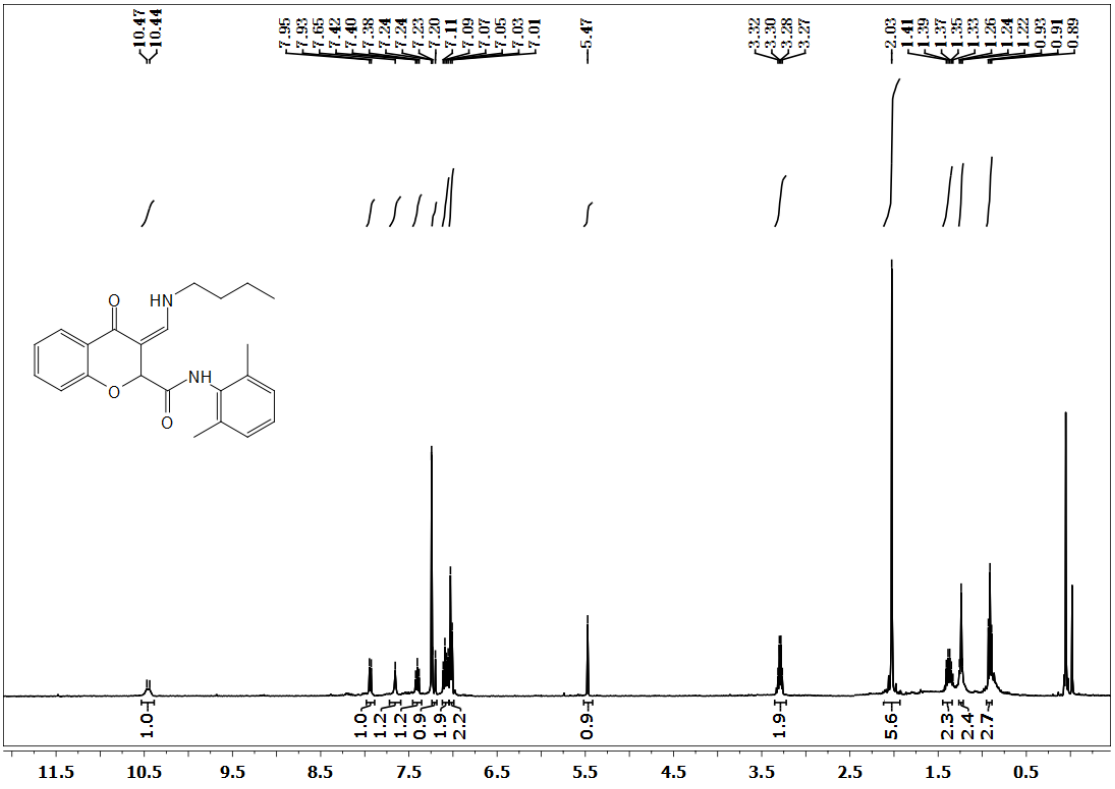


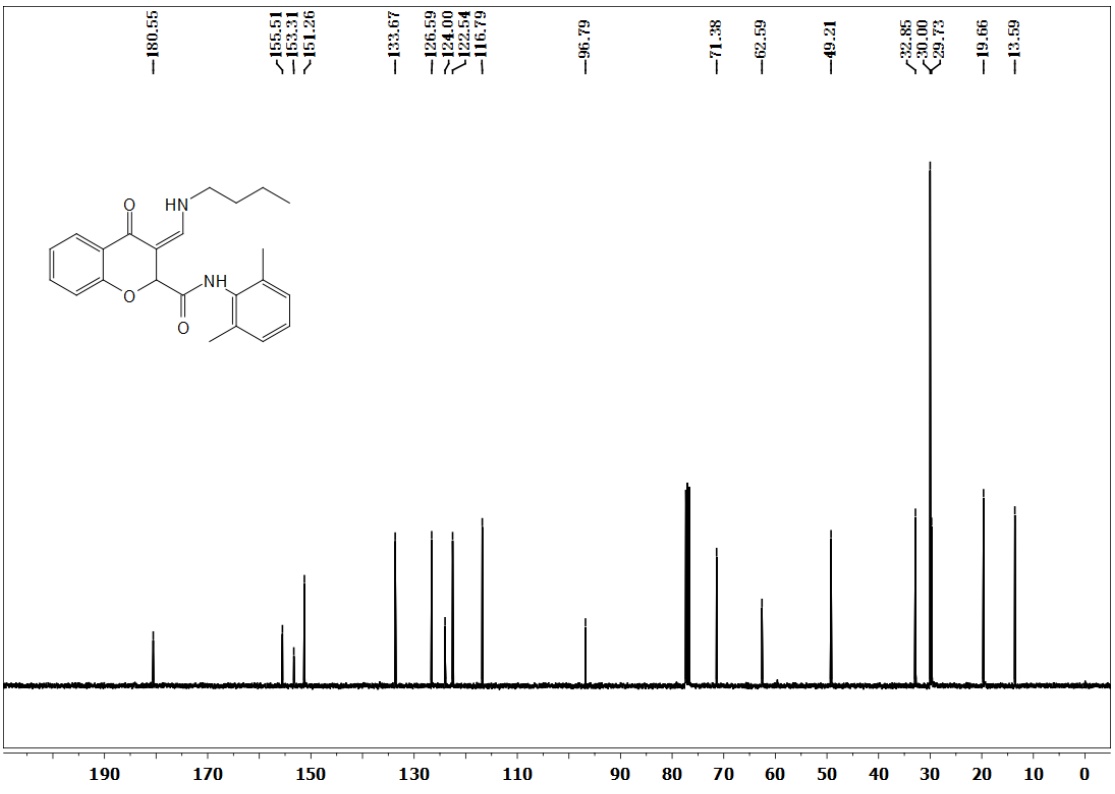
^{1}H NMR and ^{13}C NMR spectrum of **5u**



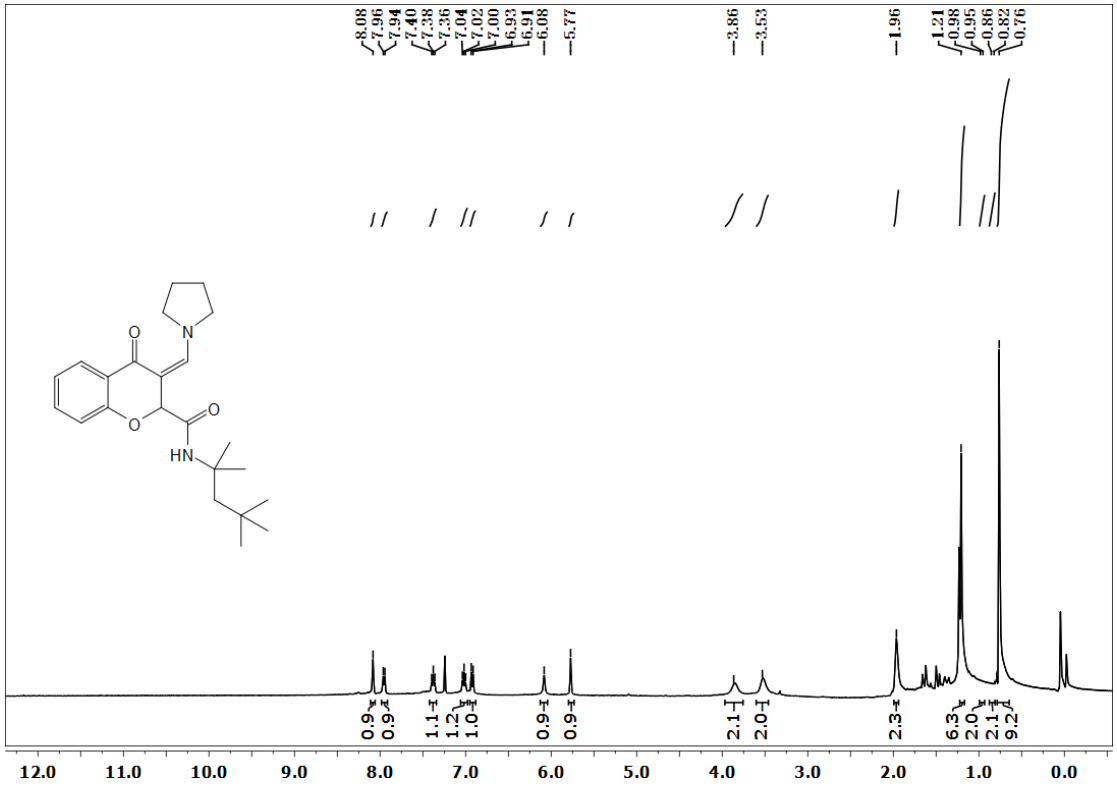


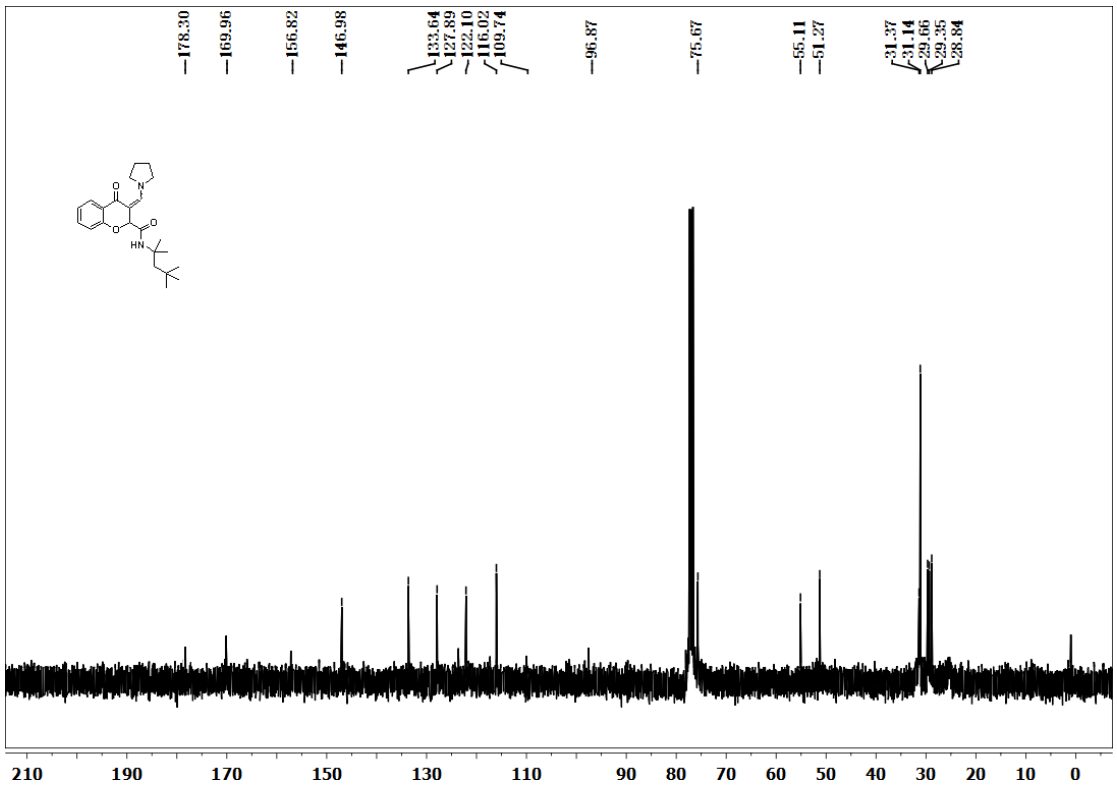
^{1}H NMR and ^{13}C NMR spectrum of **5v**



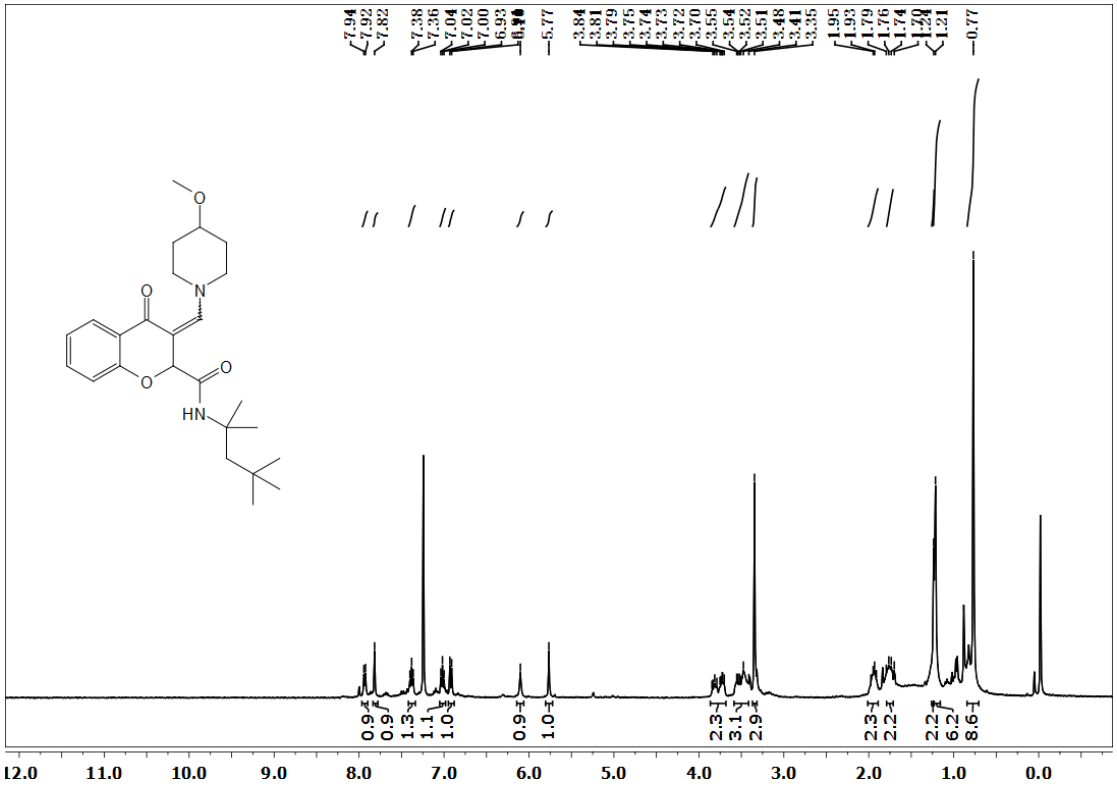


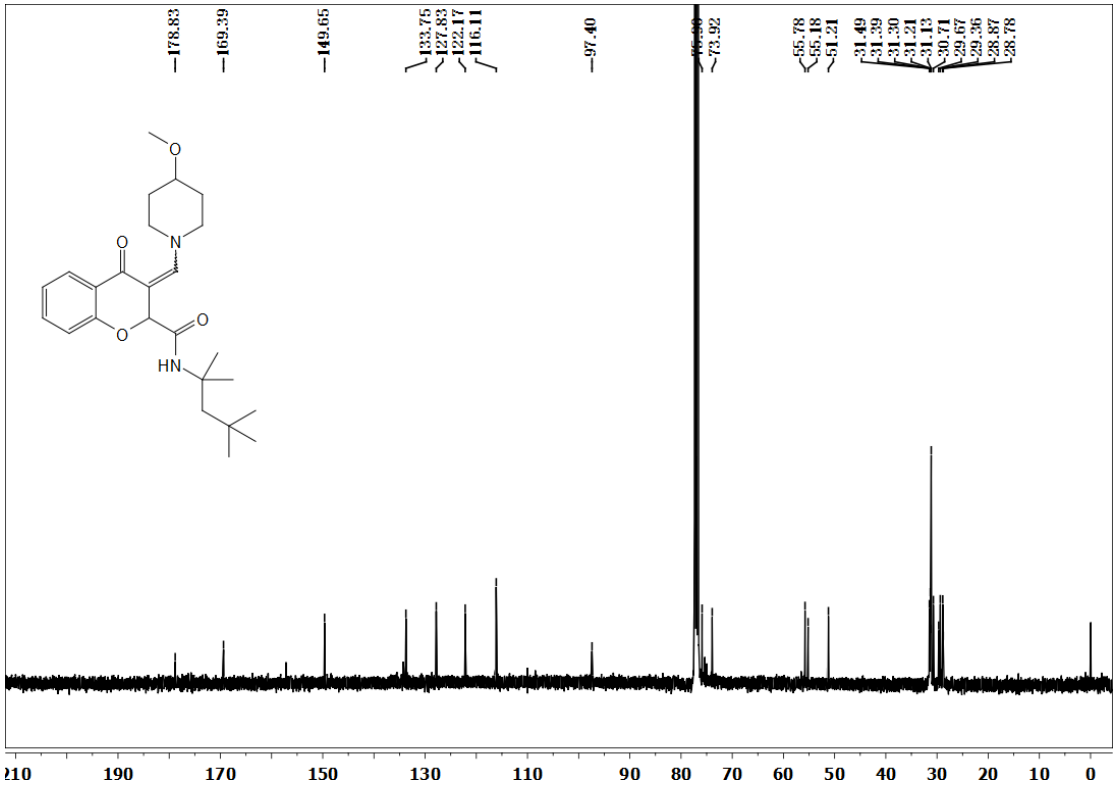
^{1}H NMR and ^{13}C NMR spectrum of **5w**



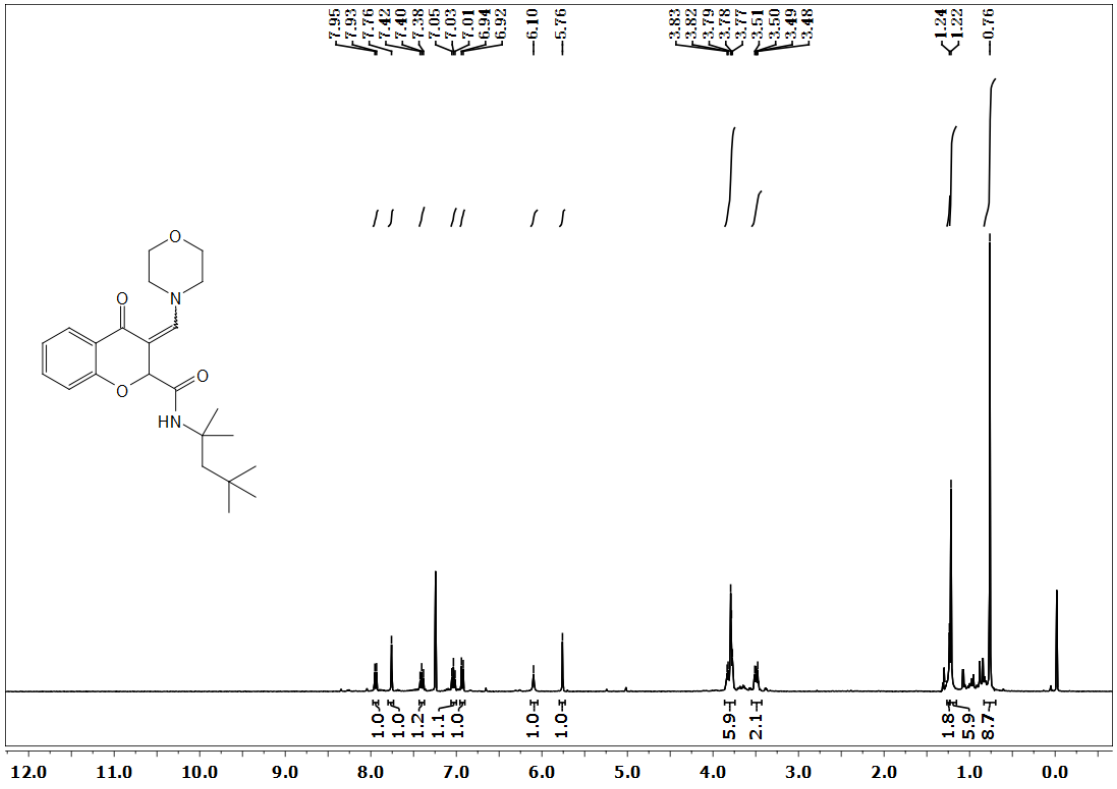


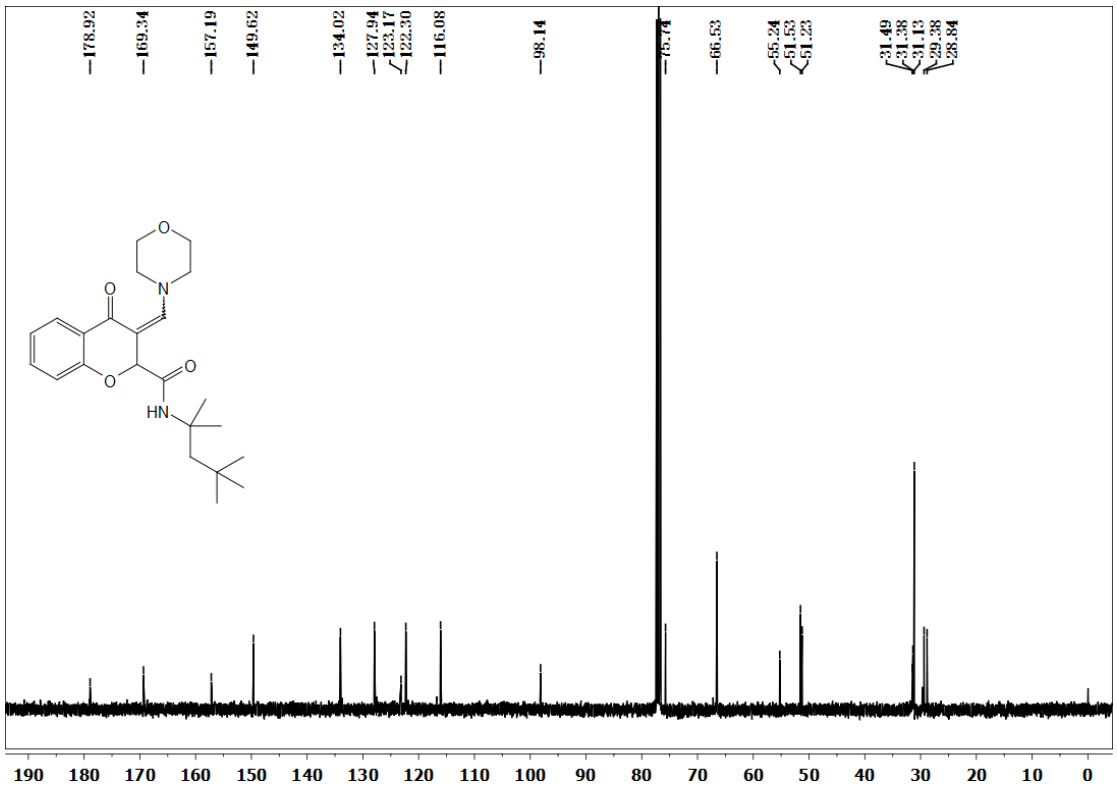
^{1}H NMR and ^{13}C NMR spectrum of **5x**



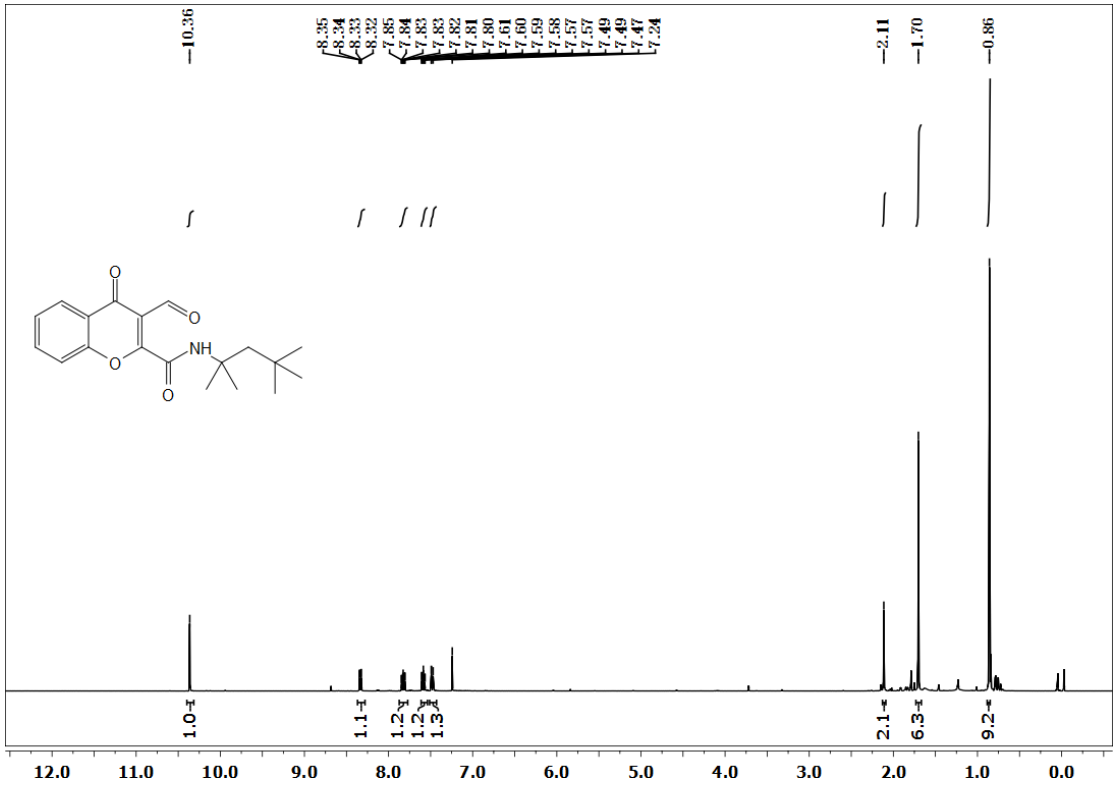


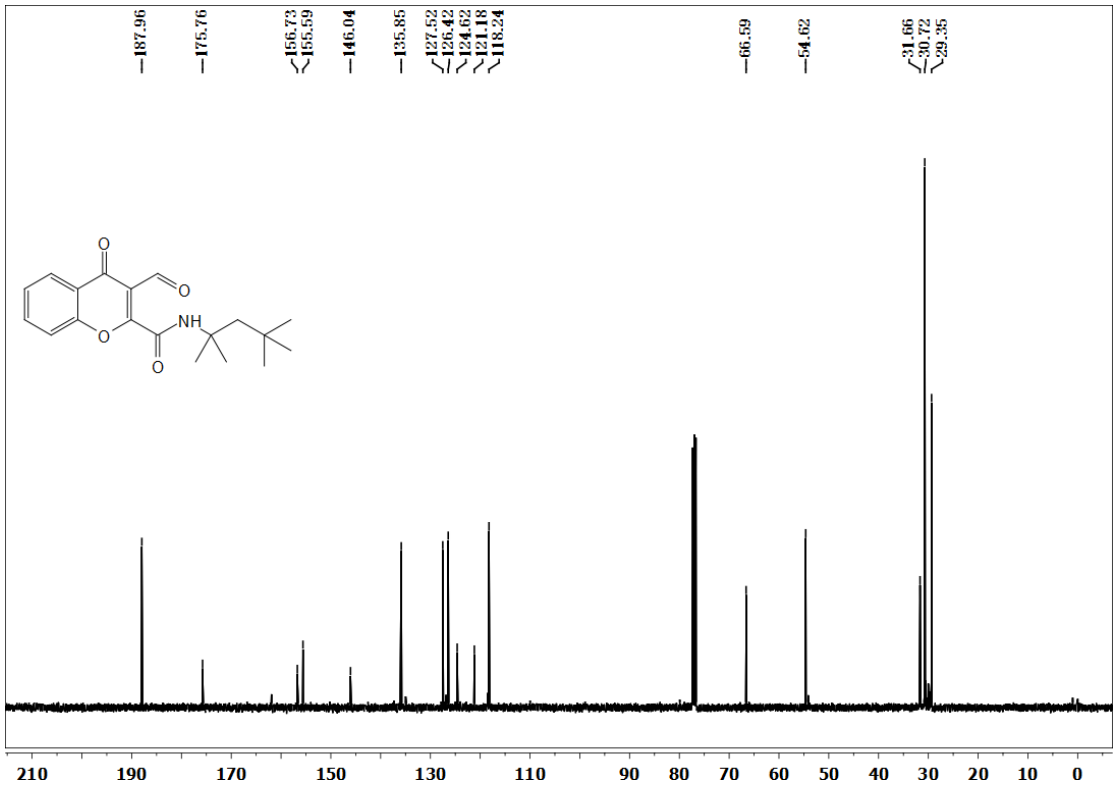
^{1}H NMR and ^{13}C NMR spectrum of **5y**



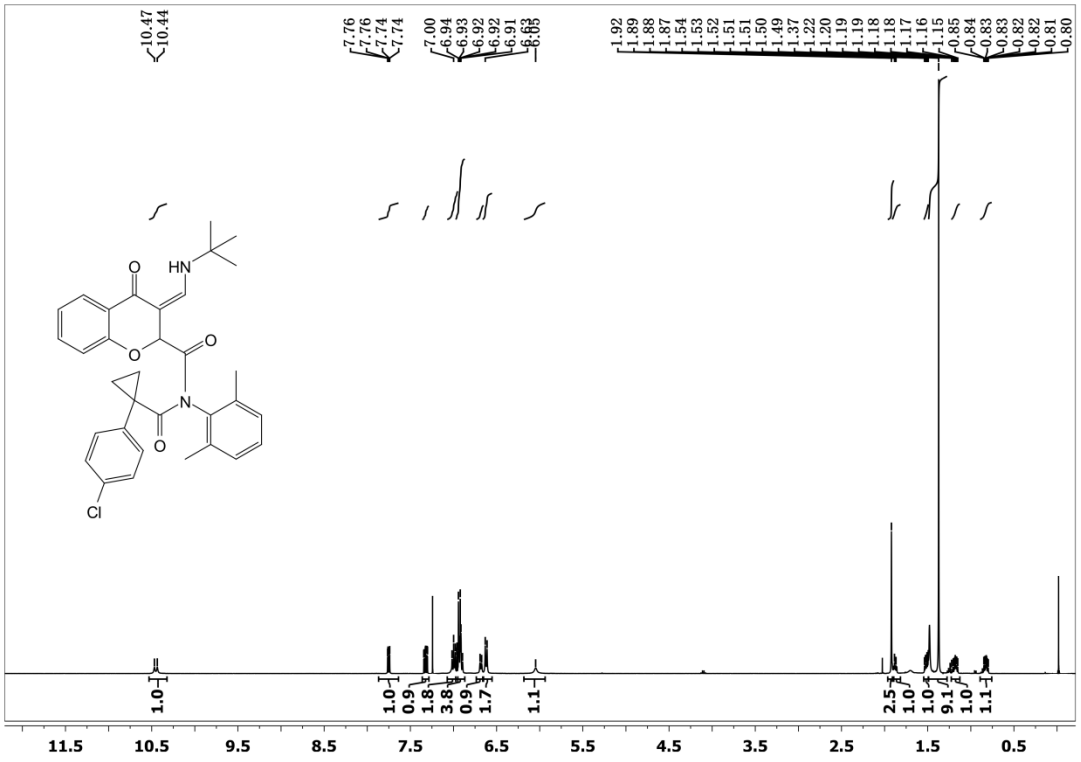


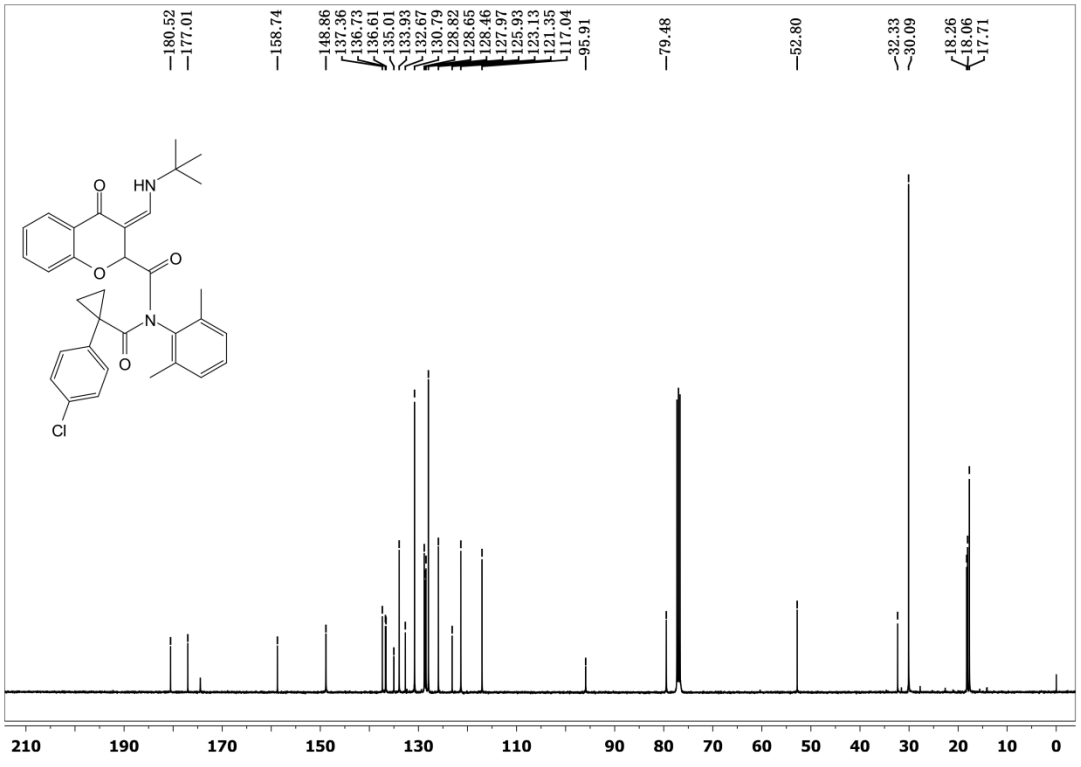
^{1}H NMR and ^{13}C NMR spectrum of **11**





^{1}H NMR and ^{13}C NMR spectrum of **13**





checkCIF/PLATON report

Structure factors have been supplied for datablock(s) A

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: A

```
Bond precision:  C-C = 0.0060 A          Wavelength=0.71073

Cell:           a=10.3143(11)    b=13.9869(12)       c=20.0442(9)
                alpha=90         beta=99.155(18)     gamma=90
Temperature:    296 K

                Calculated                Reported
Volume          2854.8(4)                 2854.8(4)
Space group     P 21/c                    P 1 21/c 1
Hall group      -P 2ybc                   -P 2ybc
Moiety formula  C33 H33 Cl N2 O4          C33 H33 Cl N2 O4
Sum formula     C33 H33 Cl N2 O4          C33 H33 Cl N2 O4
Mr              557.06                    557.09
Dx,g cm-3       1.296                     1.296
Z               4                         4
Mu (mm-1)       0.175                     0.175
F000            1176.0                    1177.1
F000'           1177.09
h,k,lmax        12,16,23                  12,16,23
Nref            5029                      5020
Tmin,Tmax       0.952,0.966               0.952,0.966
Tmin'           0.952

Correction method= # Reported T Limits: Tmin=0.952 Tmax=0.966
AbsCorr = NONE

Data completeness= 0.998          Theta(max)= 25.000

R(reflections)= 0.0607( 2297)     wR2(reflections)= 0.1398( 5020)

S = 1.110                 Npar= 361
```

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

```
ABSTY03_ALERT_1_C  The _exptl_absorpt_correction_type has been given as none.
           However values have been given for Tmin and Tmax. Remove
           these if an absorption correction has not been applied.
  From the CIF: _exptl_absorpt_correction_T_min   0.952
  From the CIF: _exptl_absorpt_correction_T_max   0.966
PLAT026_ALERT_3_C Ratio Observed / Unique Reflections (too) Low ..        46% Check
PLAT230_ALERT_2_C Hirshfeld Test Diff for    C21      --C29      .        5.3 s.u.
PLAT241_ALERT_2_C High   'MainMol' Ueq as Compared to Neighbors of         C9 Check
PLAT241_ALERT_2_C High   'MainMol' Ueq as Compared to Neighbors of        C26 Check
PLAT242_ALERT_2_C Low    'MainMol' Ueq as Compared to Neighbors of         C1 Check
PLAT242_ALERT_2_C Low    'MainMol' Ueq as Compared to Neighbors of        C30 Check
PLAT334_ALERT_2_C Small Aver. Benzene C-C Dist C23      -C28            1.37 Ang.
PLAT340_ALERT_3_C Low Bond Precision on  C-C Bonds ..............    0.00597 Ang.
PLAT905_ALERT_3_C Negative K value in the Analysis of Variance ...    -1.909 Report
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L=    0.595         9 Report
PLAT978_ALERT_2_C Number C-C Bonds with Positive Residual Density.         0 Info
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Alert level G

```
PLAT066_ALERT_1_G Predicted and Reported Tmin&Tmax Range Identical         ? Check
PLAT073_ALERT_1_G H-atoms ref, but _hydrogen_treatment Reported as     constr Check
PLAT380_ALERT_4_G Incorrectly? Oriented X(sp2)-Methyl Moiety .....       C13 Check
PLAT380_ALERT_4_G Incorrectly? Oriented X(sp2)-Methyl Moiety .....       C18 Check
PLAT793_ALERT_4_G Model has Chirality at C20         (Centro SPGR)         S Verify
PLAT883_ALERT_1_G No Info/Value for _atom_sites_solution_primary .     Please Do !
PLAT933_ALERT_2_G Number of OMIT Records in Embedded .res File ...         5 Note
PLAT960_ALERT_3_G Number of Intensities with I  <   - 2*sig(I) ...        17 Check
PLAT983_ALERT_1_G The Cl-f"=    0.1603 Deviates from  IT-Value =      0.1585Check
```

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   0 ALERT level A = Most likely a serious problem - resolve or explain
   0 ALERT level B = A potentially serious problem, consider carefully
  12 ALERT level C = Check. Ensure it is not caused by an omission or oversight
   9 ALERT level G = General information/check it is not something unexpected

   5 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   8 ALERT type 2 Indicator that the structure model may be wrong or deficient
   5 ALERT type 3 Indicator that the structure quality may be low
   3 ALERT type 4 Improvement, methodology, query or suggestion
   0 ALERT type 5 Informative message, check
```

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica, Journal of Applied Crystallography, Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 17/03/2019; check.def file version of 04/03/2019

Datablock A - ellipsoid plot