A new route to substituted furocoumarins via copper-catalyzed cyclization utilizing ketoximes

Tuong A. To, Yen H. Vo, Anh T. Nguyen, Anh N. Q. Phan, Thanh Truong, Nam T. S. Phan*

Faculty of Chemical Engineering, HCMC University of Technology, VNU-HCM,
268 Ly Thuong Kiet, District 10, Ho Chi Minh City, Viet Nam

*Email: ptsnam@hcmut.edu.vn

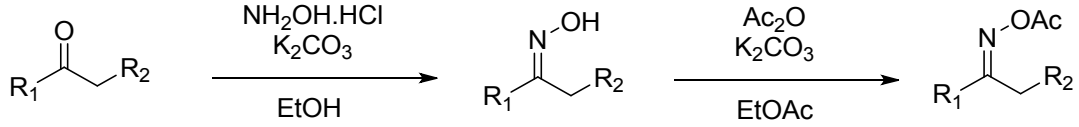
Ph: (+84 8) 38647256 ext. 5681 Fx: (+84 8) 38637504

Supporting information

Materials and instrumentation

All reagents and starting materials were obtained commercially from Sigma-Aldrich, Acros and Merck, and were used as received without any further purification unless otherwise noted. Gas chromatographic (GC) analyses were performed using a Shimadzu GC 2010-Plus equipped with a flame ionization detector (FID) and an SPB-5 column (length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.25 μm). The temperature program for GC analysis held samples at 160 ^{o}C for 1 min; heated them from 160 to 280 ^{o}C at 40 ^{o}C/min; held them at 280 ^{o}C for 8 min. Inlet and detector temperatures were set constant at 280 ^{o}C. The GC yield was calculated using diphenyl ether as the internal standard. GC-MS analyses were analyzed on a Shimadzu GCMS-QP2010Ultra with a ZB-5MS column (length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.25 μm). The temperature program for GC-MS analysis held samples at 50 ^{o}C for 2 min; heated samples from 50 to 280^{o}C at 10 ^{o}C/min and held them at 280 ^{o}C for 10 min. Inlet temperature was set constant at 280 ^{o}C. MS spectra were compared with the spectra gathered in the NIST library. The ^{1}H NMR and ^{13}C NMR were recorded on Bruker AV 500 spectrometers using residual solvent peak as a reference. FT-IR spectra were recorded on a Bruker Tensor 27 and samples were prepared as KBr plates. HR-MS spectra were recorded by an Agilent HPLC 1200 Series coupled to Bruker micrOTOF-QII.

General procedure to prepare oxime aceates



The mixture of ketones (22 mmol), K_2CO_3 (3.036 g, 22 mmol), hydroxylamine hydrochloride (2.290 g, 33 mmol) and ethanol (10 mL) were magnetically stirred at 60 ^oC for 1 h. The reaction mixture was cooled to room temperature, quenched with H_2O then organic components were extracted with ethyl acetate (3 x 20 mL) and washed with brine (3 x 20 mL) then neutralized by HCl 1 M. The organic layers were dried over anhydrous Na_2SO_4 and concentrated under vacuum to obtain the crude oximes which were used directly on the next step without purification.

The crude oximes and K_2CO_3 (3.036 g, 22 mmol) were added to the mixture of anhydride acetic (4.2 mL, 44.4 mmol) and ethyl acetate (20 mL), then stirred at room temperature for 1 h. The next work-up procedure was conducted similarly to that of previous step. Solid crude oxime acetates were further purified by recrystallization in ethyl acetate and hexane and liquid crude oxime were further purified by silica gel column chromatography using hexane and ethyl acetate as eluent.

General procedure to synthesize furo[3,2,c]coumarins

In a typical experiment, a solution of $CuBr_2$ (1 mol%) in toluene (1 mL) were added to a 8 mL screw-capped vial containing 4-hydroxycoumarin (0.2 mmol, 32.4 mg), propiophenone oxime acetate (0.3 mmol, 57.3 mg) and diphenyl ether (0.2 mmol, 34.0 mg) as internal standard. The mixture was stirred at 120 °C for 1 h under an argon atmosphere. The GC yield of product were monitored by withdrawing aliquots from the reaction mixture, quenching with brine (1 mL), extracting with ethyl acetate (3 x 1 mL), drying over anhydrous Na_2SO_4 and being analyzed by GC with reference to diphenyl ether. After the completion of the reaction, the mixture was cooled to room temperature. Resulting solution was quenched with distilled water (5 mL), extracted by dichloromethane (3 x 5 mL), dried over anhydrous Na_2SO_4 prior to the removal of solvent under vacuum. The crude product was purified by silica gel column chromatography using hexane and dichloromethane (1.5:1, v/v) as eluent. The product identity was further confirmed by ^{1}H NMR, ^{13}C NMR, FT-IR and HR-MS.

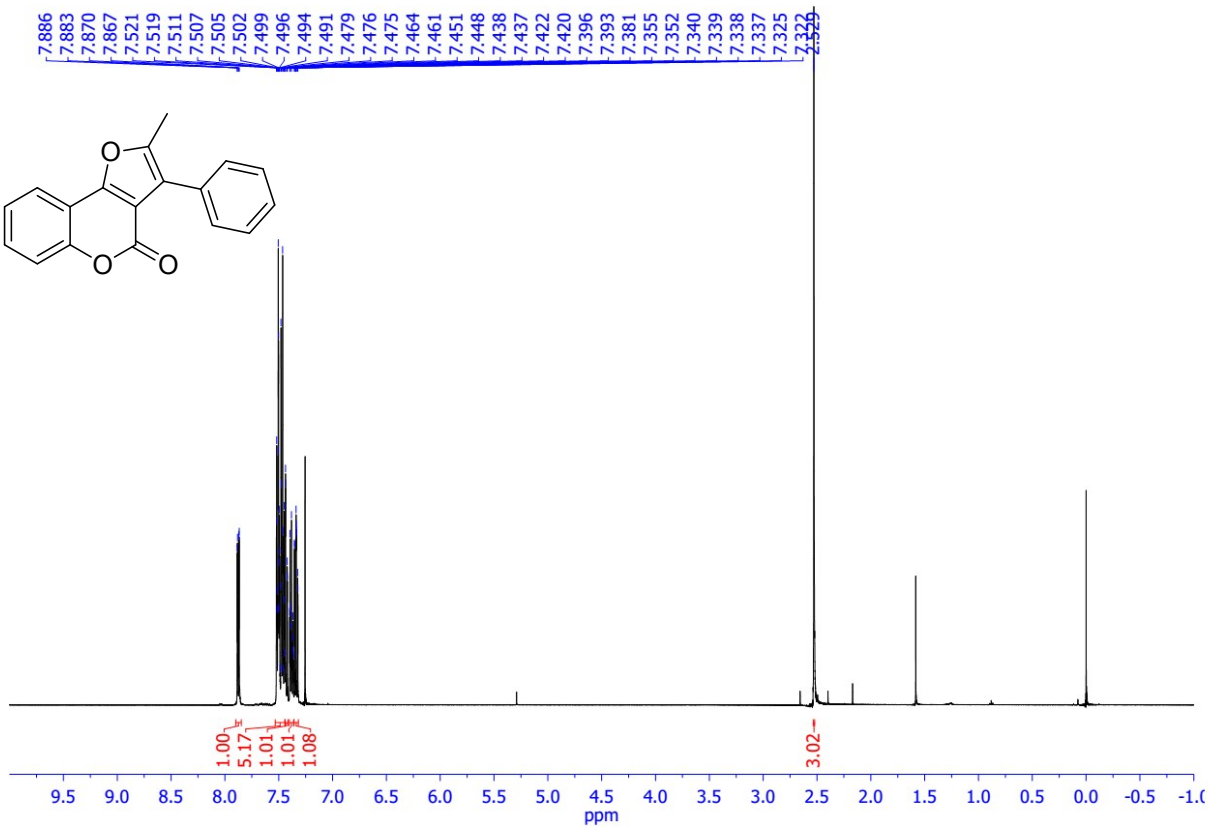


Fig.S1. ^{1}H-NMR spectra of 2-methyl-3-phenyl-4H-furo[3,2-c]chromen-4-one (**3aa**)

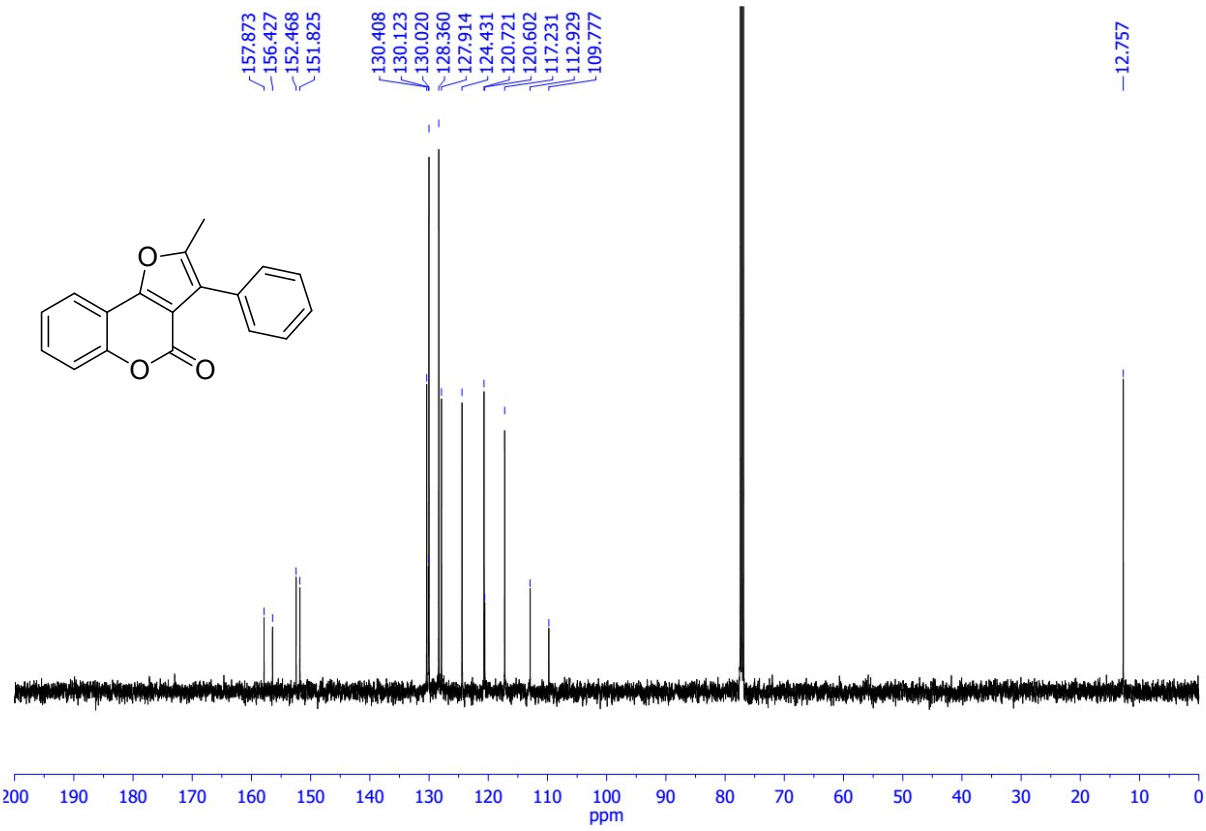


Fig.S2. ^{13}C-NMR spectra of 2-methyl-3-phenyl-4H-furo[3,2-c]chromen-4-one (**3aa**)

Characterization Data for 2-methyl-3-phenyl-4H-furo[3,2-c]chromen-4-one (3aa)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1,v/v) as eluent: white solid, 81% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (dd, J = 8.0, 1.5 Hz, 1H), 7.53 – 7.44 (m, 5H), 7.43 (dd, J = 8.5, 1.0 Hz, 1H), 7.40 – 7.36 (m, 1H), 7.34 (ddd, J = 8.0, 7.5, 1.0 Hz, 1H), 2.53 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 157.9, 156.4, 152.5, 151.8, 130.4, 130.1, 130.0, 128.4, 127.9, 124.4, 120.7, 120.6, 117.2, 112.9, 109.8, 12.8. FT-IR ν (cm^{-1}) 1734, 1626, 1589, 1500, 1443, 1318, 1082, 963. HR-MS (ESI) m/z ([M+Na]$^+$), calcd for $C_{18}H_{12}Na_1O_3$ 299.0679, found 299.0692.

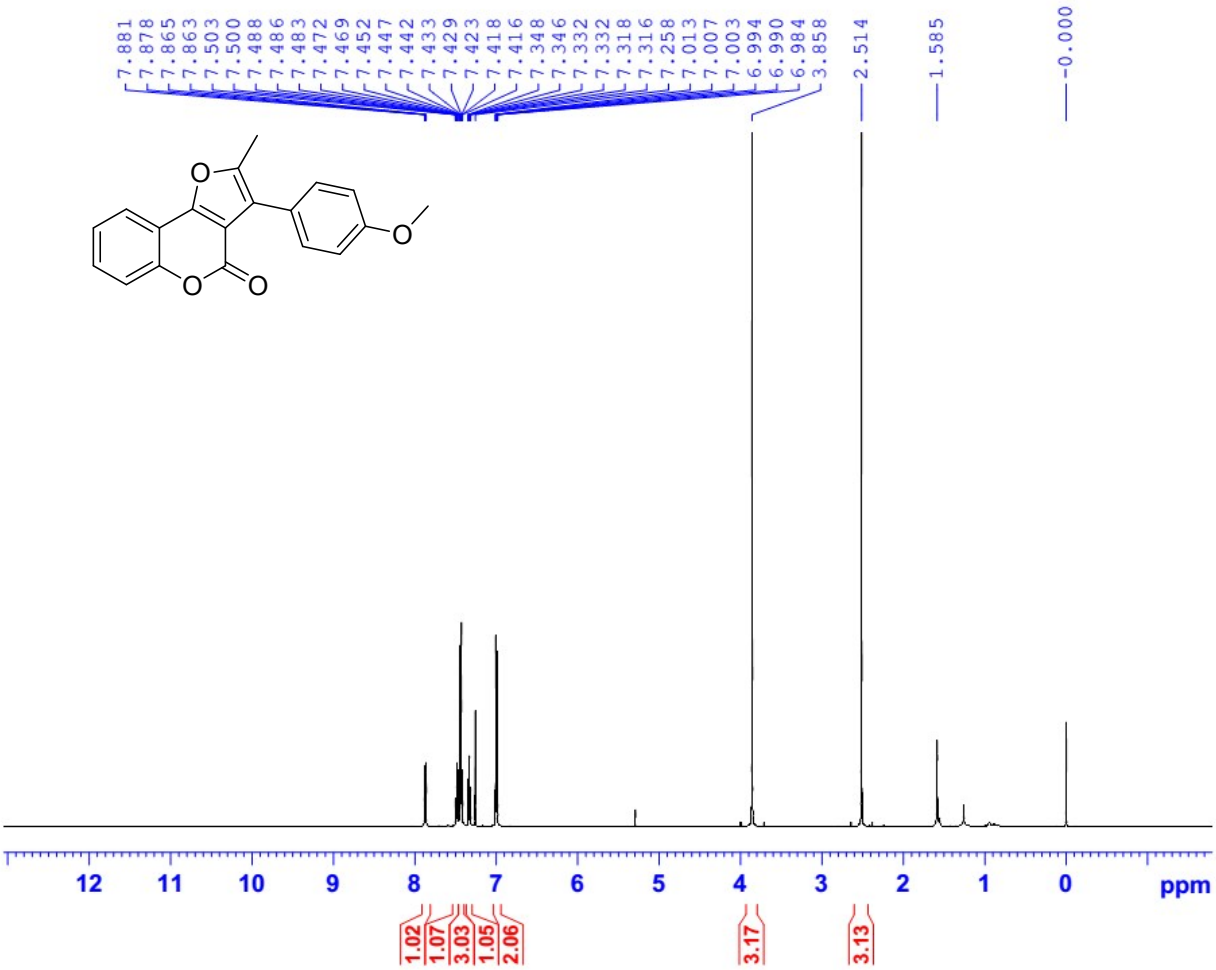


Fig.S3. ^{1}H-NMR spectra of 3-(4-methoxyphenyl)-2-methyl-4H-furo[3,2-c]chromen-4-one **(3ab)**

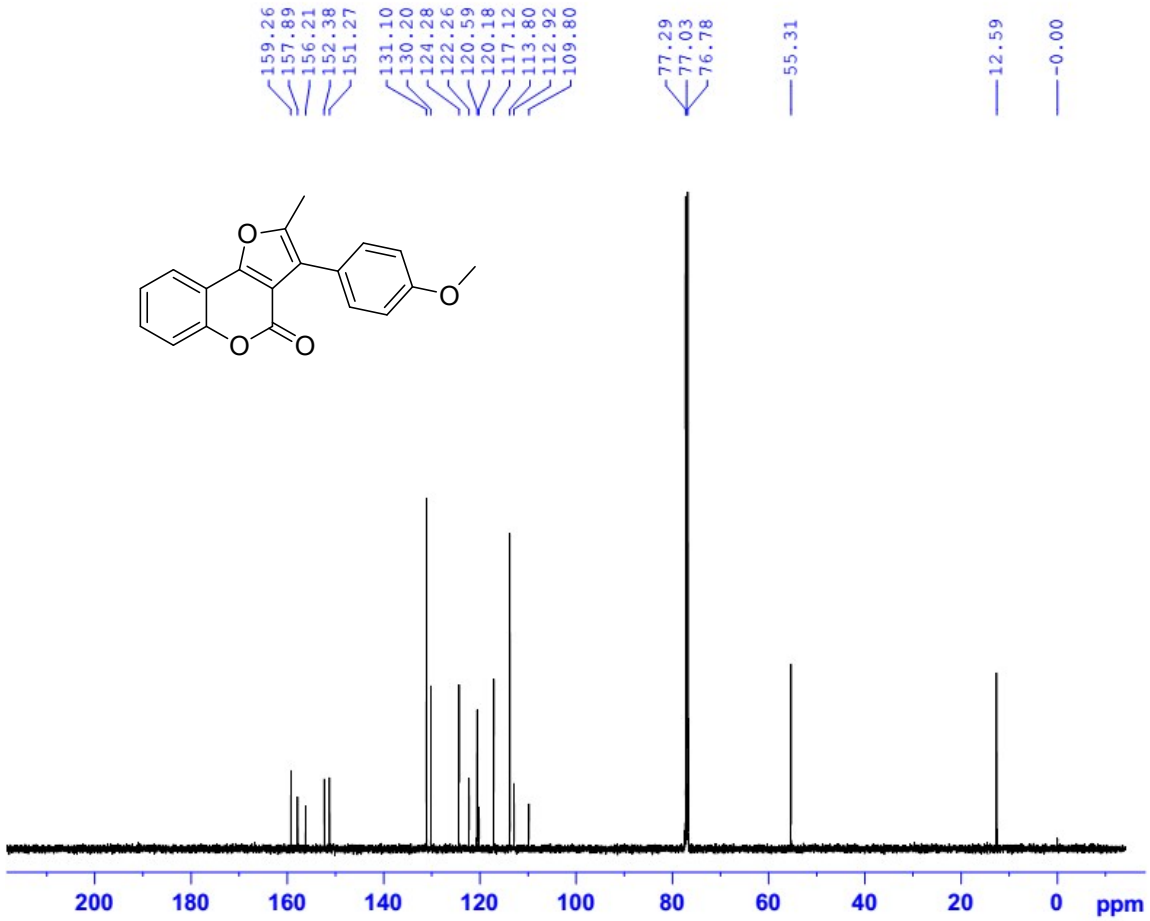


Fig.S4. ^{13}C-NMR spectra of 3-(4-methoxyphenyl)-2-methyl-4H-furo[3,2-c]chromen-4-one **(3ab)**

Characterization Data for 3-(4-methoxyphenyl)-2-methyl-4H-furo[3,2-c]chromen-4-one (3ab)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1, v/v) as eluent: white solid, 79% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (dd, J = 8.0, 1.5 Hz, 1H), 7.51 – 7.46 (m, 1H), 7.46 – 7.40 (m, 3H), 7.00 (m, 1H), 3.86 (s, 3H), 2.51 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 157.9, 156.2, 152.4, 151.3, 131.1, 130.2, 124.3, 122.3, 120.6, 120.2, 117.1, 113.8, 112.9, 109.8, 55.3, 12.6. FT-IR ν (cm^{-1}) 1740, 1630, 1595, 1515, 1436, 1382, 1289, 1251, 1175, 1067, 946, 838, 755. HR-MS (ESI) m/z ($[M+Na]^+$), calcd for $C_{19}H_{14}Na_1O4$ 329.0784, found 329.0791.

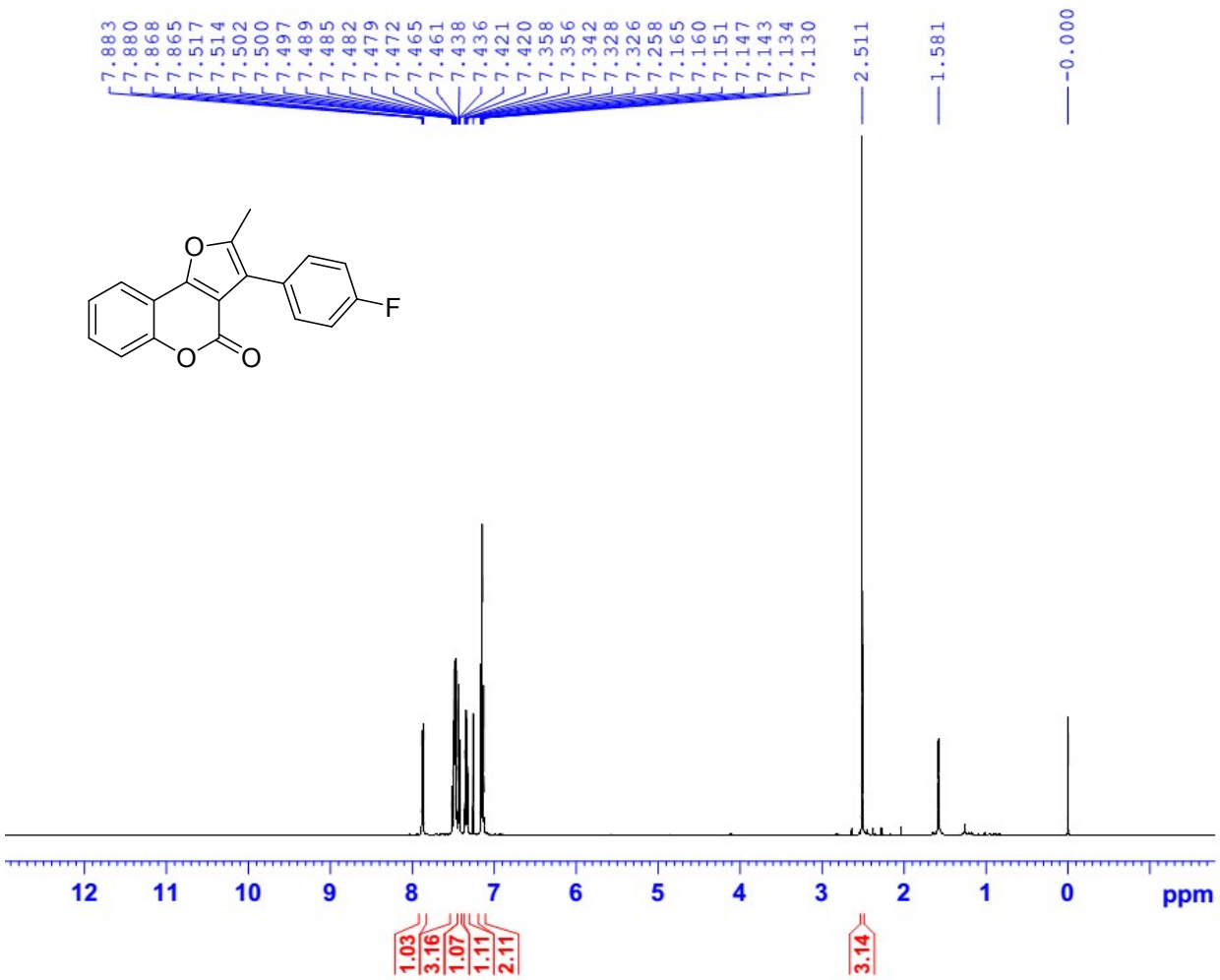


Fig.S5. [1]H-NMR spectra of 3-(4-fluorophenyl)-2-methyl-4H-furo[3,2-c]chromen-4-one **(3ac)**

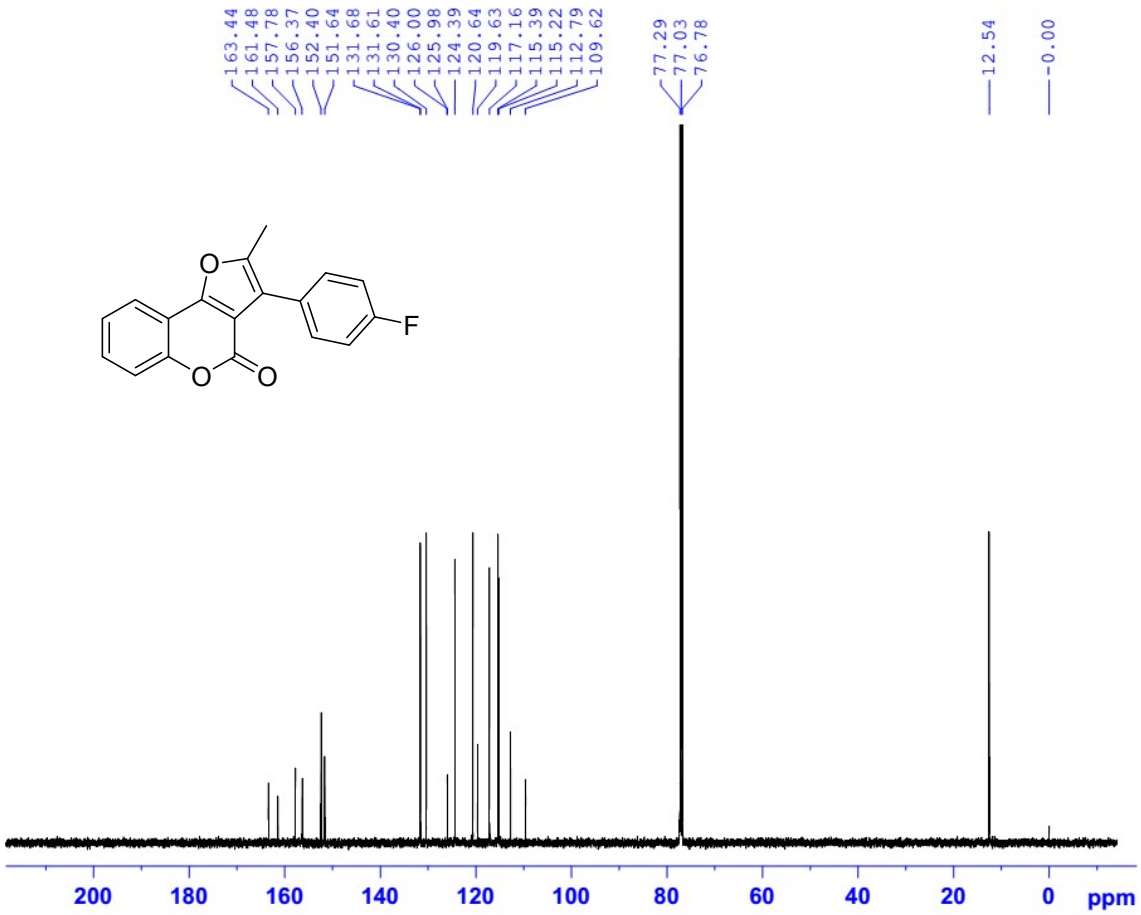


Fig.S6. ^{13}C-NMR spectra of 3-(4-fluorophenyl)-2-methyl-4H-furo[3,2-c]chromen-4-one **(3ac)**

Characterization Data for 3-(4-fluorophenyl)-2-methyl-4H-furo[3,2-c]chromen-4-one (3ac)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1,v/v) as eluent: white solid, 89% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (dd, J = 7.5, 1.5 Hz, 1H), 7.53 – 7.45 (m, 3H), 7.43 (dd, J = 8.5, 1.0 Hz, 1H), 7.34 (td, J = 8.0, 1.0 Hz, 1H), 7.15 (tt, J = 8.0, 2.0 Hz, 1H), 2.51 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.4 (d, J = 250 Hz), 157.8, 156.4, 152.4, 151.6, 131.6 (d, J = 9 Hz), 130.4, 126.0 (d, J = 2 Hz), 124.4, 120.6, 119.6, 117.2, 115.4, 115.3 (d, J = 21 Hz), 112.8, 109.6, 12.5. FT-IR ν (cm^{-1}) 1731, 1627, 1594, 1510, 1383, 1224, 1157, 1073, 844, 757. HR-MS (ESI) m/z ([M+Na]$^+$), calcd for $C_{18}H_{11}F_1Na_1O_3$ 317.0584, found 317.0592.

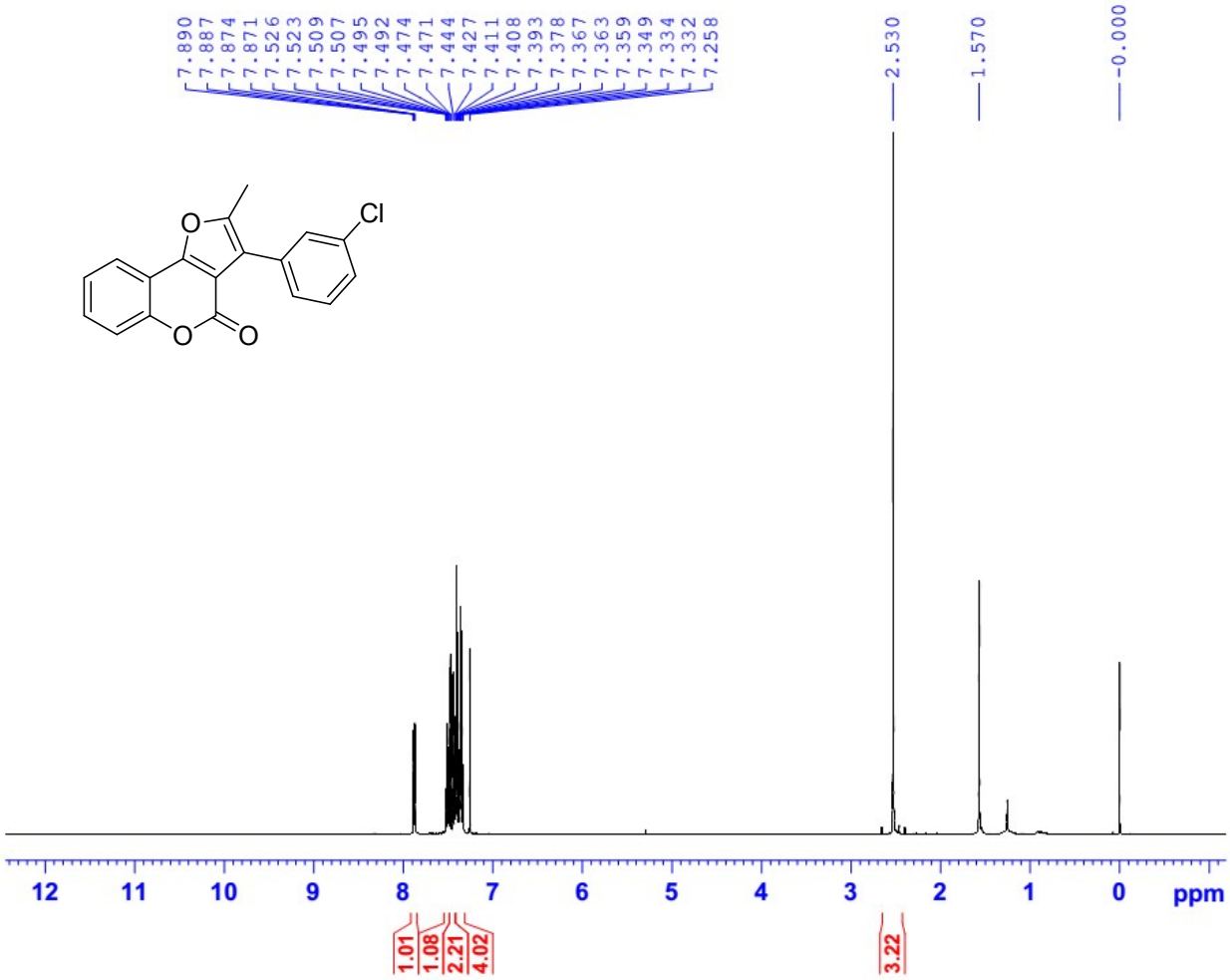


Fig.S7. ^{1}H-NMR spectra of 3-(3-chlorophenyl)-2-methyl-4H-furo[3,2-c]chromen-4-one **(3ad)**

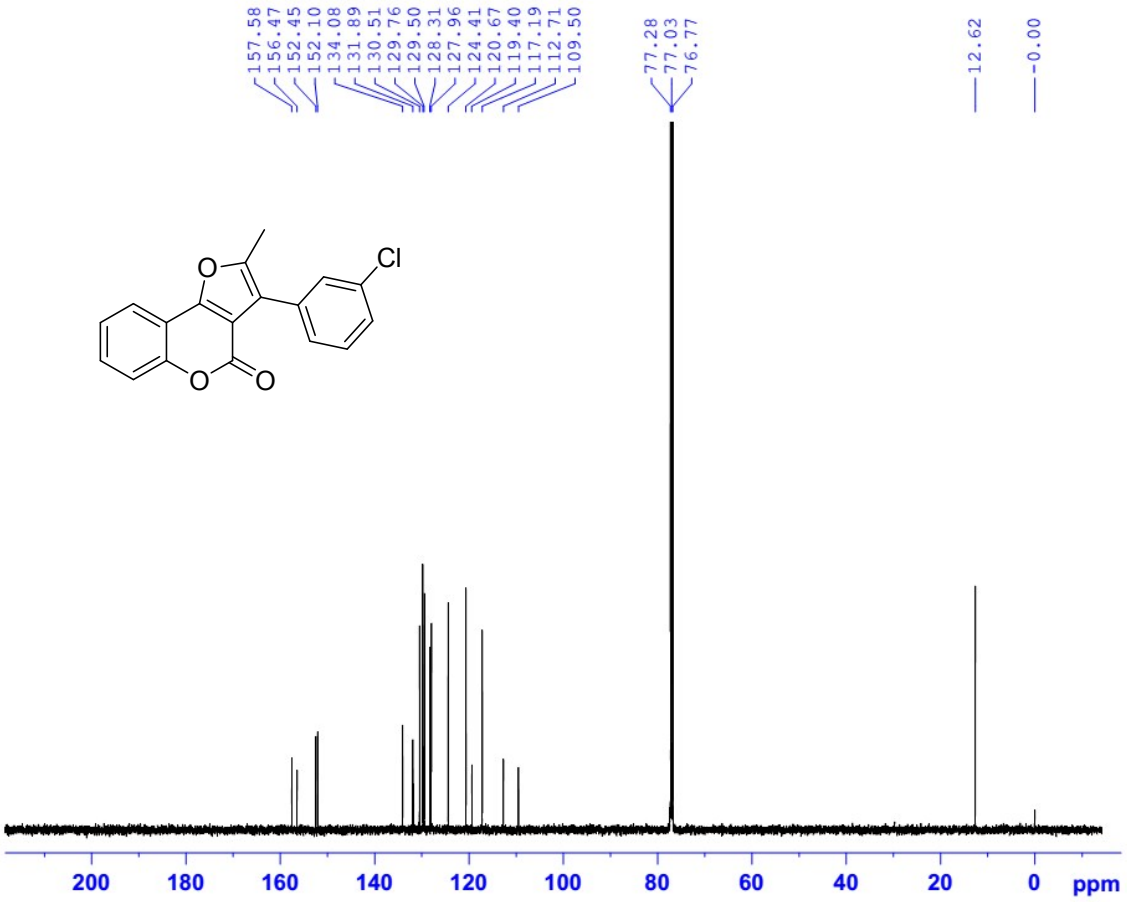


Fig.S8. ^{13}C-NMR spectra of 3-(3-chlorophenyl)-2-methyl-4H-furo[3,2-c]chromen-4-one **(3ad)**

Characterization Data for 3-(3-chlorophenyl)-2-methyl-4H-furo[3,2-c]chromen-4-one (3ad)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1,v/v) as eluent: white solid, 60% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (dd, J = 8.0, 1.5 Hz, 1H), 7.51 (td, J = 8.0, 1.5 Hz, 1H), 7.48 – 7.42 (m, *2*H), 7.42 – 7.33 (m, *4*H), 2.53 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.6, 156.5, 152.4, 152.1, 134.1, 131.9, 130.5, 129.8, 129.5, 128.3, 128.0, 124.4, 120.7, 119.4, 117.2, 112.7, 109.5, 12.6. FT-IR ν (cm^{-1}) 1722, 1630, 1586, 1500, 1381, 1064, 957, 896, 778, 752, 691. HR-MS (ESI) m/z ([M+Na]$^+$), calcd for $C_{18}H_{11}Cl_1Na_1O_3$ 333.0289, found 333.0293.

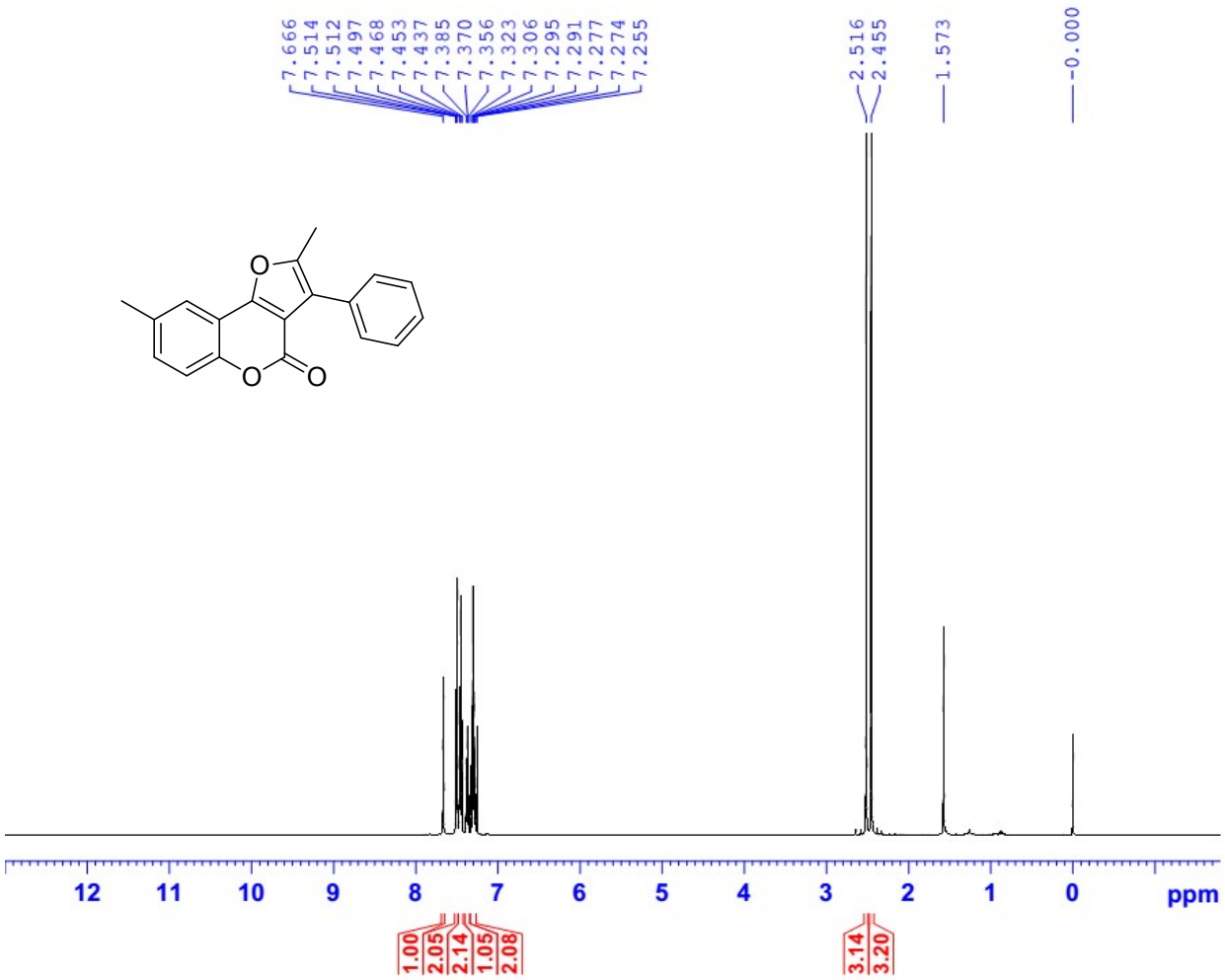


Fig.S9. ^{1}H-NMR spectra of 2,8-dimethyl-3-phenyl-4H-furo[3,2-c]chromen-4-one **(3ba)**

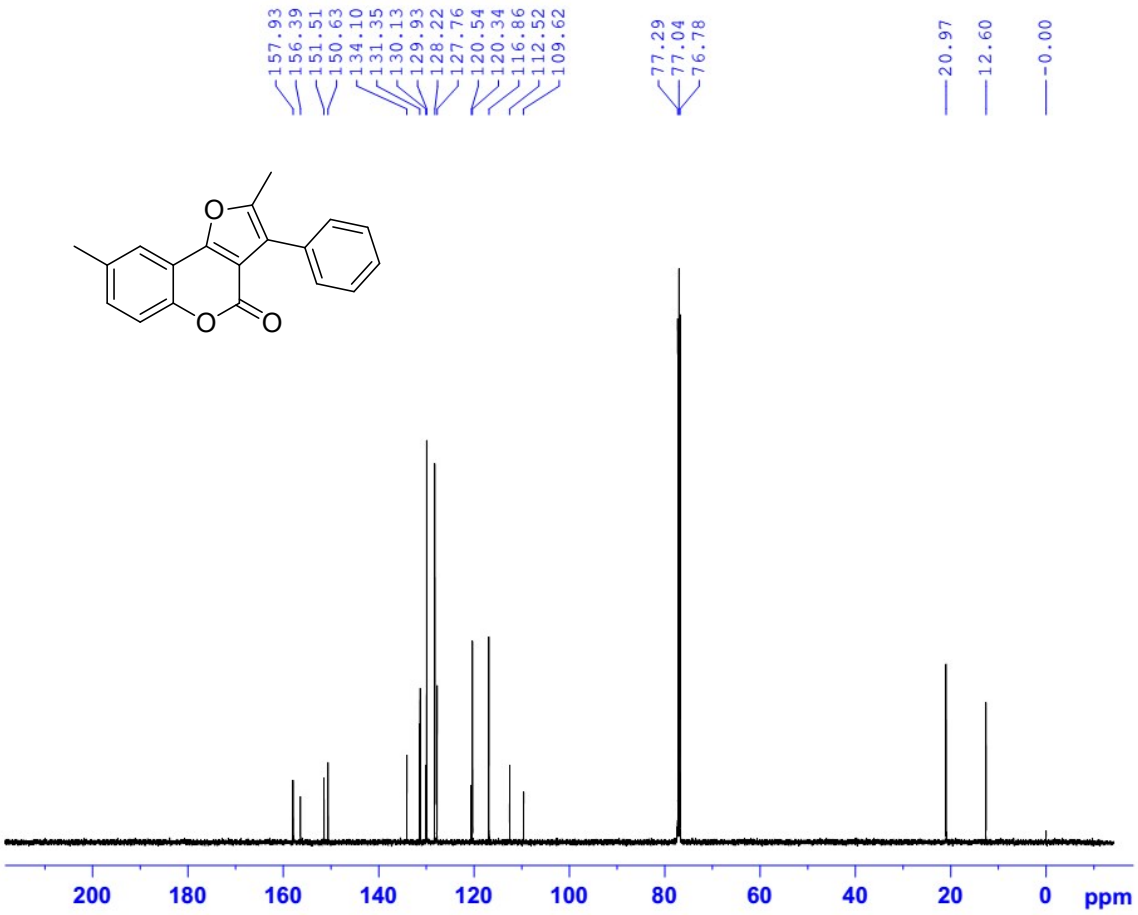


Fig.S10. ^{13}C-NMR spectra of 2,8-dimethyl-3-phenyl-4H-furo[3,2-c]chromen-4-one **(3ba)**

Characterization Data for 2,8-dimethyl-3-phenyl-4H-furo[3,2-c]chromen-4-one (3ba)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1,v/v) as eluent: white solid, 80% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.51 (d, J = 8.5, 1.0 Hz, 1H), 7.45 (t, J = 8.0 Hz, 1H), 7.33 – 7.27 (m, 2H), 2.52 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.9, 156.4, 151.5, 150.6, 134.1, 131.4, 130.1, 129.9, 128.2, 127.8, 120.5, 120.3, 116.9, 112.5, 109.6, 20.97, 12.6. FT-IR ν (cm^{-1}) 1726, 1630, 1566, 1499, 1443, 1363, 1083, 821, 787, 753, 700. HR-MS (ESI) m/z ([M+Na]$^{+}$), calcd for $C_{19}H_{14}Na_1O_3$ 313.0835, found 313.0839

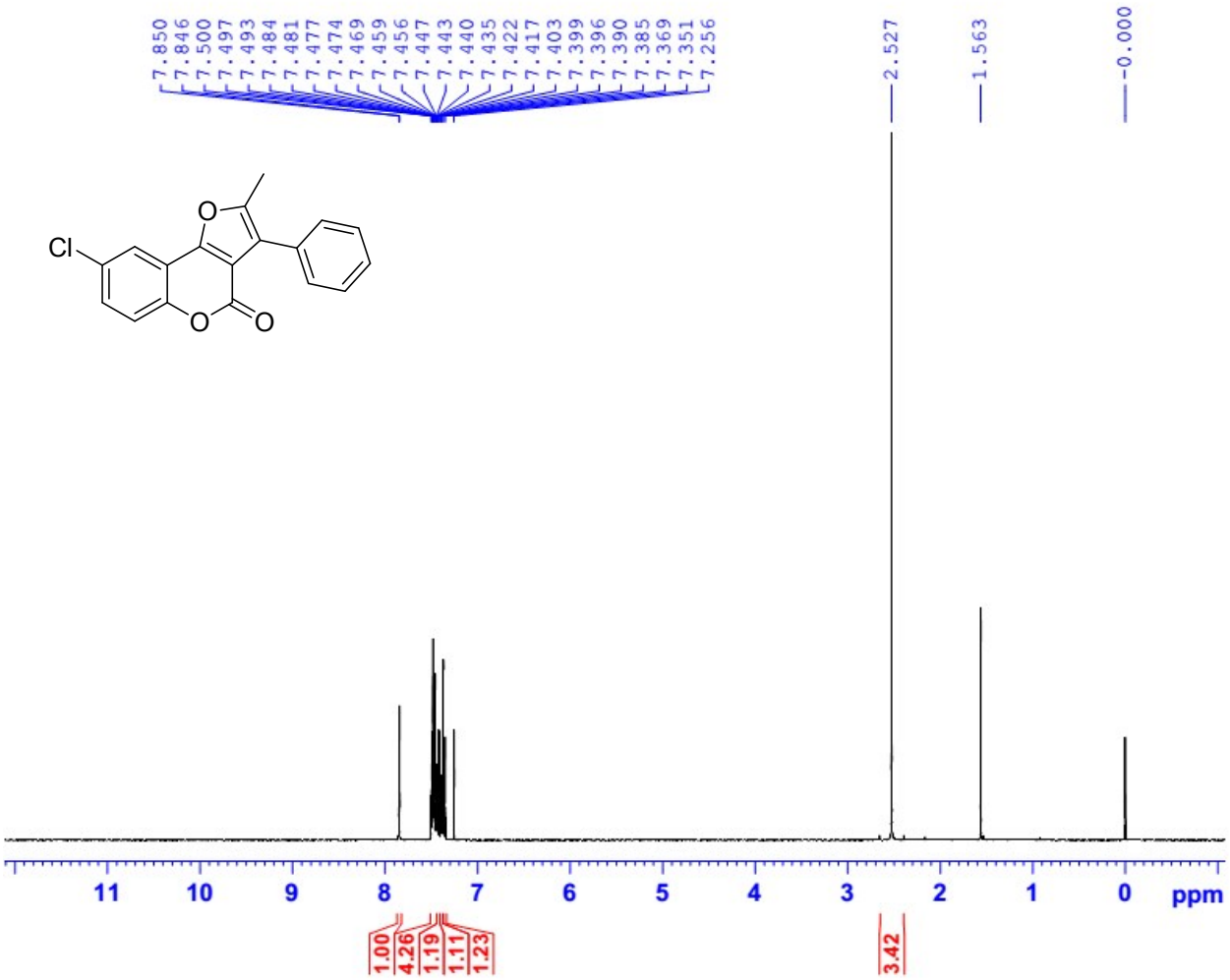


Fig.S11. ^{1}H-NMR spectra of 8-chloro-2-methyl-3-phenyl-4H-furo[3,2-c]chromen-4-one **(3ca)**

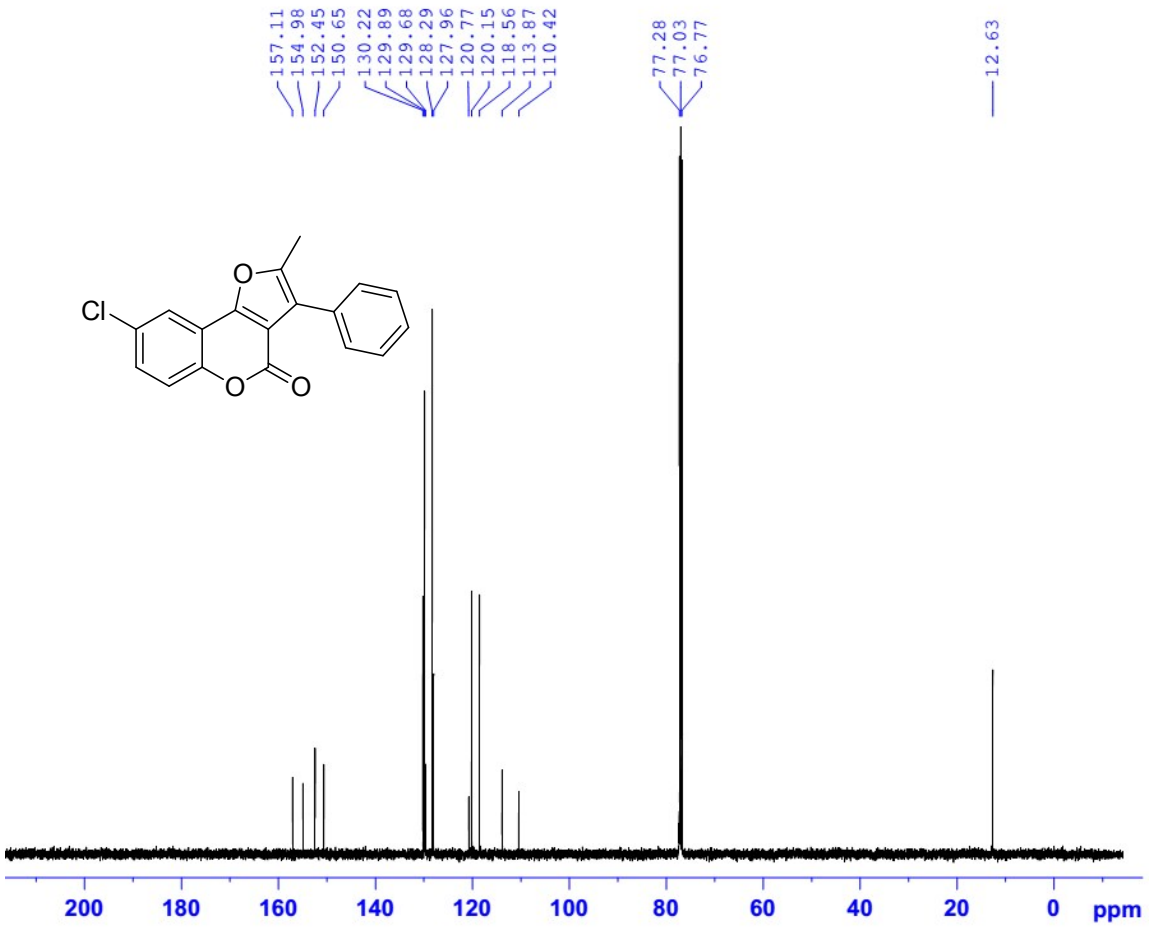


Fig.S12. ^{13}C-NMR spectra of 8-chloro-2-methyl-3-phenyl-4H-furo[3,2-c]chromen-4-one **(3ca)**

Characterization Data for 8-chloro-2-methyl-3-phenyl-4H-furo[3,2-c]chromen-4-one (3ca)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1,v/v) as eluent: white solid, 75% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 2.0 Hz, 1H), 7.51 – 7.45 (m, 4H), 7.43 (dd, J = 8.0, 2.0 Hz, 1H), 7.39 (td, J = 7.0, 2.0 Hz, 1H), 7.36 (d, J = 7.0 Hz, 1H), 2.53 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1, 155.0, 152.4, 150.6, 130.2, 129.9, 129.7, 128.3, 128.0, 120.8, 120.2, 118.6, 113.9, 110.4, 12.6. FT-IR ν (cm^{-1}) 1762, 1589, 1554, 1504, 1446, 1419, 1361, 1114, 1056, 964, 817, 756, 696. HR-MS (ESI) m/z ([M+Na]$^+$), calcd for $C_{18}H_{11}Cl_1Na_1O_3$ 333.0289, found 333.0295.

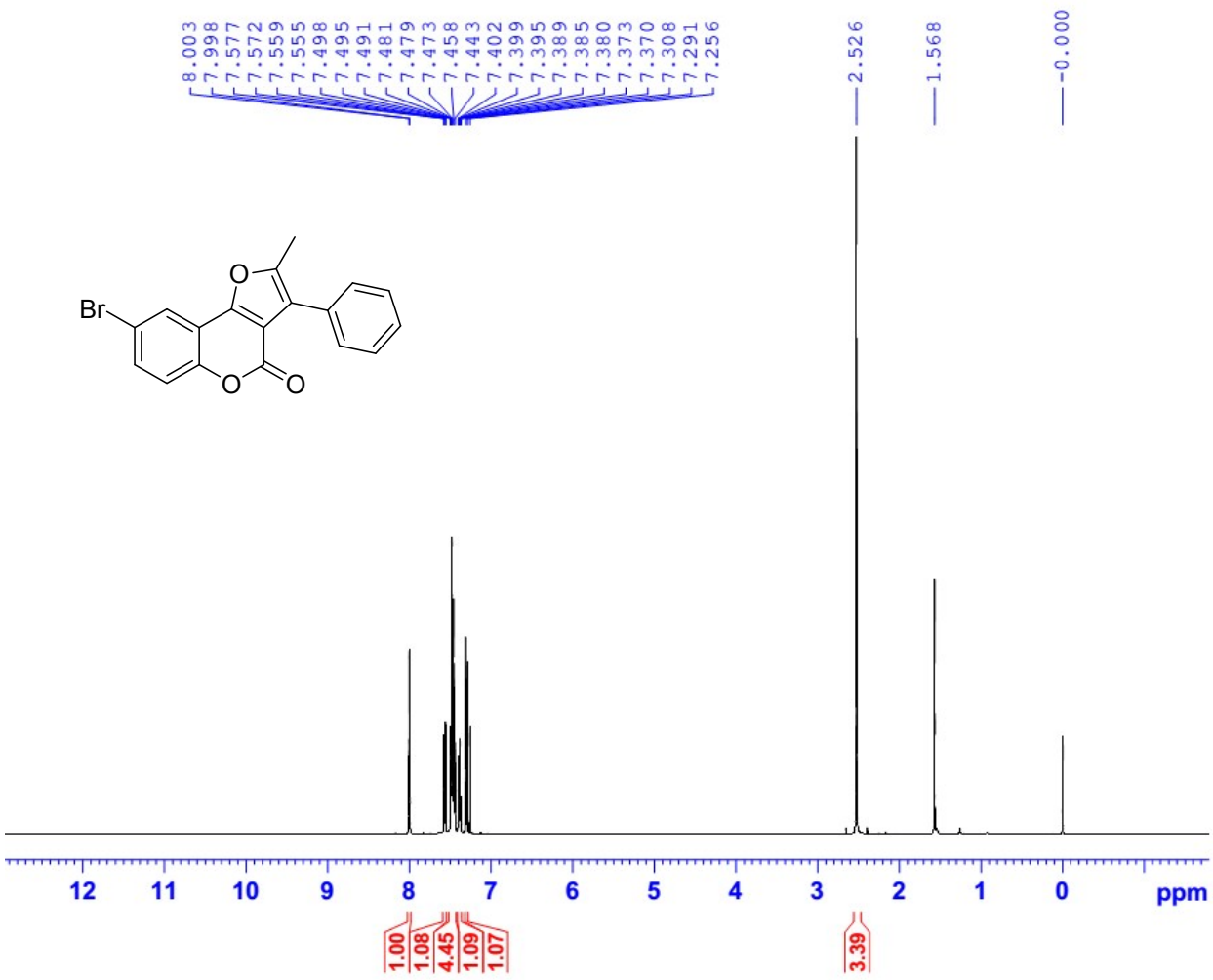


Fig.S13. ^{1}H-NMR spectra of 8-bromo-2-methyl-3-phenyl-4H-furo[3,2-c]chromen-4-one **(3da)**

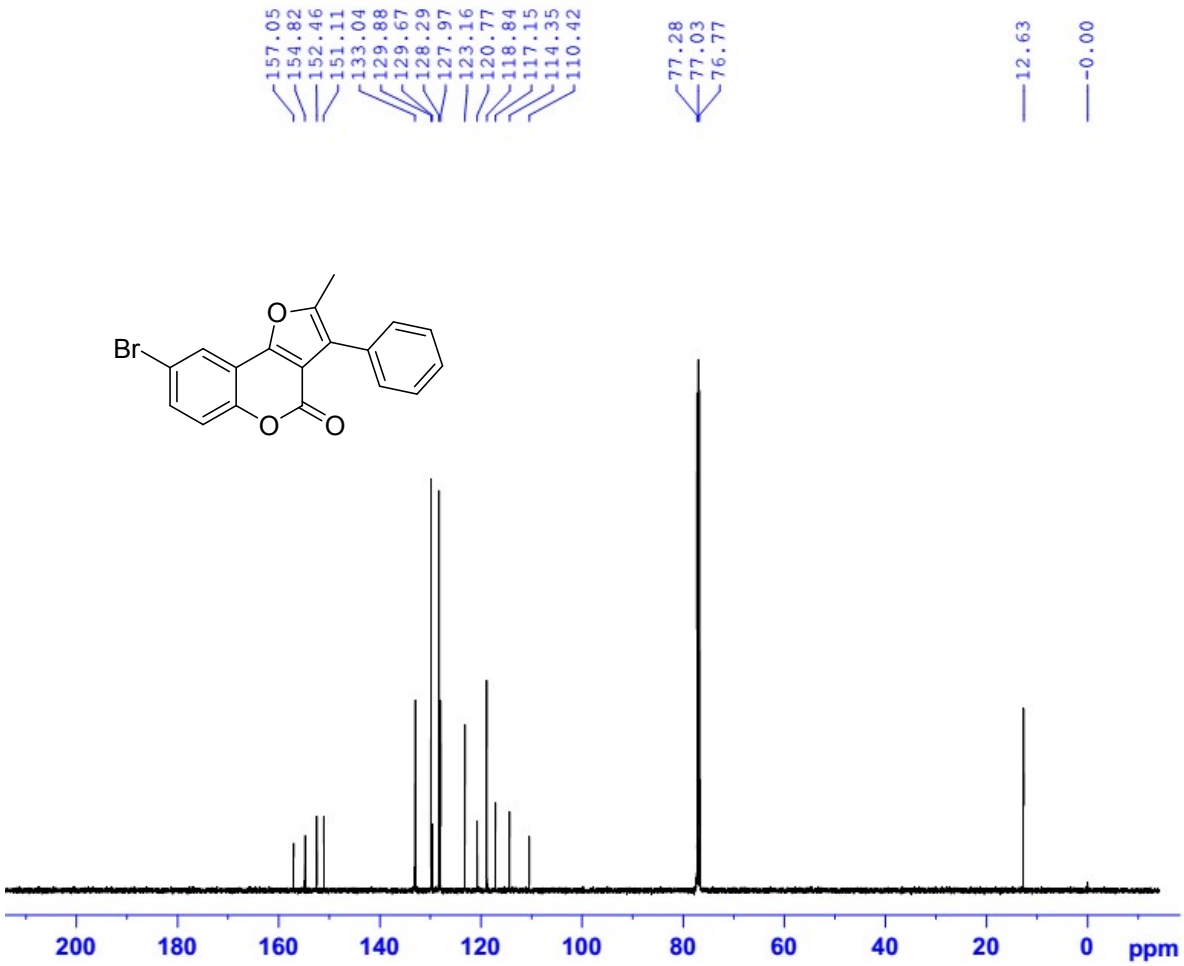


Fig.S14. ^{13}C-NMR spectra of 8-bromo-2-methyl-3-phenyl-4H-furo[3,2-c]chromen-4-one **(3da)**

Characterization Data for 8-bromo-2-methyl-3-phenyl-4H-furo[3,2-c]chromen-4-one (3da)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1,v/v) as eluent: white solid, 70% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 2.0 Hz, 1H), 7.56 (dd, J = 8.5, 2.0 Hz, 1H), 7.51 – 7.43 (m, 4H), 7.39 (tt, J = 7.0, 2.0 Hz, 1H), 7.30 (d, J = 8.5 Hz, 1H), 2.53 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.0, 154.8, 152.5, 151.1, 133.0, 129.9, 129.7, 128.3, 128.0, 123.2, 120.8, 118.8, 117.2, 114.4, 110.4, 12.6. FT-IR ν (cm^{-1}) 1751, 1631, 1589, 1554, 1504, 1353, 1114, 1087, 1056, 964, 829, 756, 698. HR-MS (ESI) m/z ([M+Na]$^+$), calcd for $C_{18}H_{11}Br_1Na_1O_3$ 376.9784, found 376.9793.

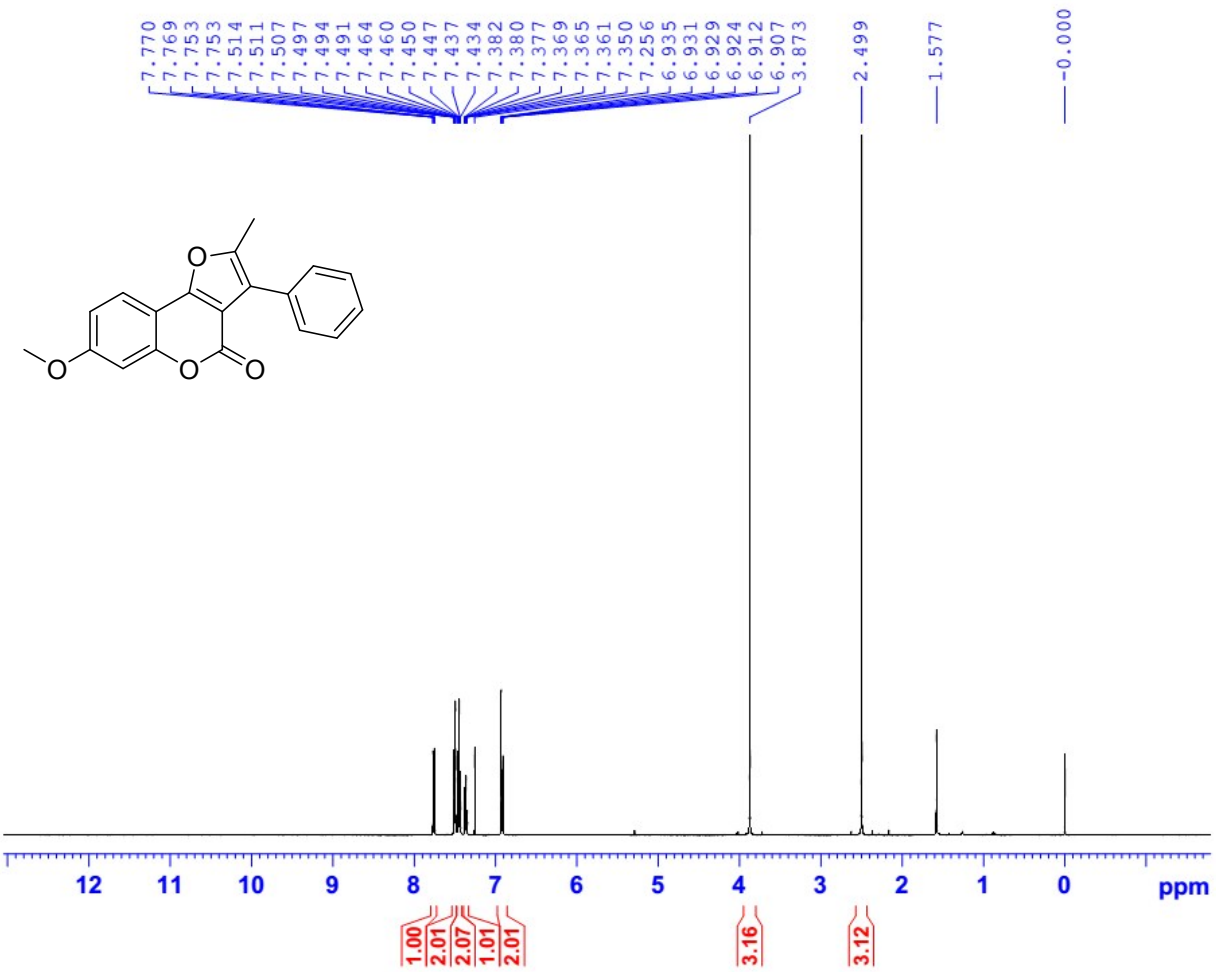


Fig.S15. ^{1}H-NMR spectra of 7-methoxy-2-methyl-3-phenyl-4H-furo[3,2-c]chromen-4-one **(3ea)**

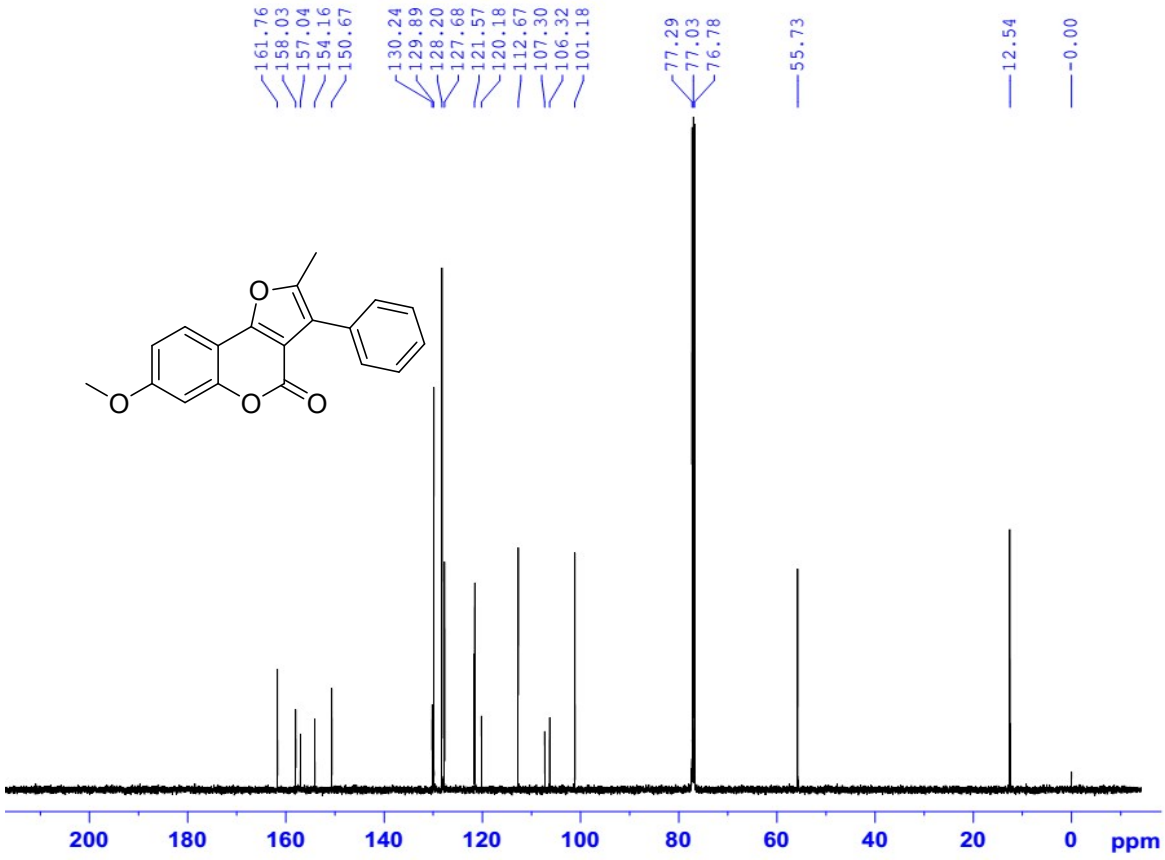


Fig.S16. ^{13}C-NMR spectra of 7-methoxy-2-methyl-3-phenyl-4H-furo[3,2-c]chromen-4-one **(3ea)**

Characterization Data for 7-methoxy-2-methyl-3-phenyl-4H-furo[3,2-c]chromen-4-one (3ea)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1,v/v) as eluent: white solid, 81% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (dd, J = 8.0, 0.5 Hz, 1H), 7.50 (dt, J = 8.5, 1.5 Hz, 2H), 7.45 (td, J = 7.0, 1.5 Hz, 2H), 7.36 (tt, J = 7.0, 1.5 Hz, 1H), 6.94 – 6.90 (m, 2H), 3.87 (s, 3H), 2.50 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 158.0, 157.0, 154.2, 150.7, 130.2, 129.9, 128.2, 127.7, 121.6, 120.2, 112.7, 107.3, 106.3, 101.18, 55.7, 12.5. FT-IR ν (cm^{-1}) 1725, 1630, 1594, 1505, 1457, 1380, 1280, 1158, 1110, 970, 752, 696. HR-MS (ESI) m/z ([M+Na]$^+$), calcd for $C_{19}H_{14}Na_1O_4$ 329.0784, found 329.0789.

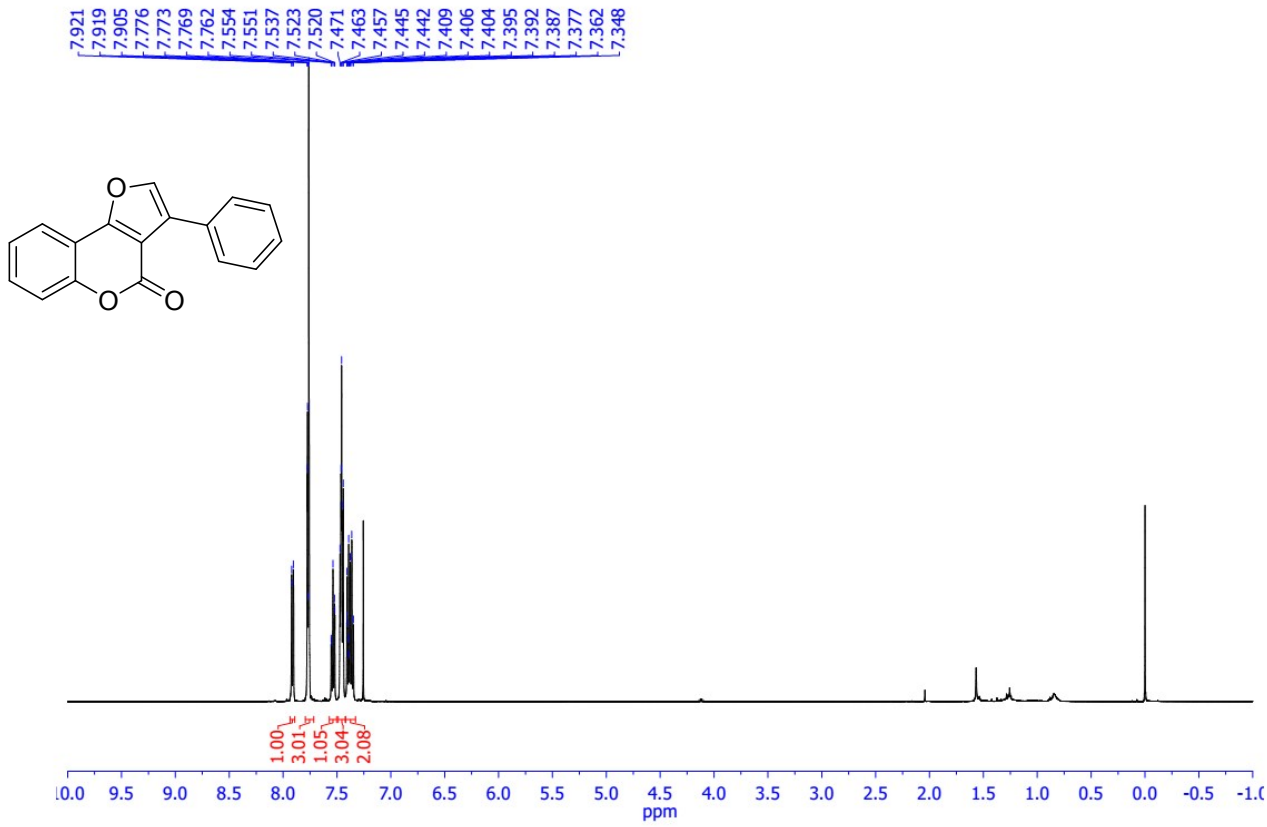


Fig.S17. ^{1}H-NMR spectra of 3-phenyl-4H-furo[3,2-c]chromen-4-one **(3ae)**

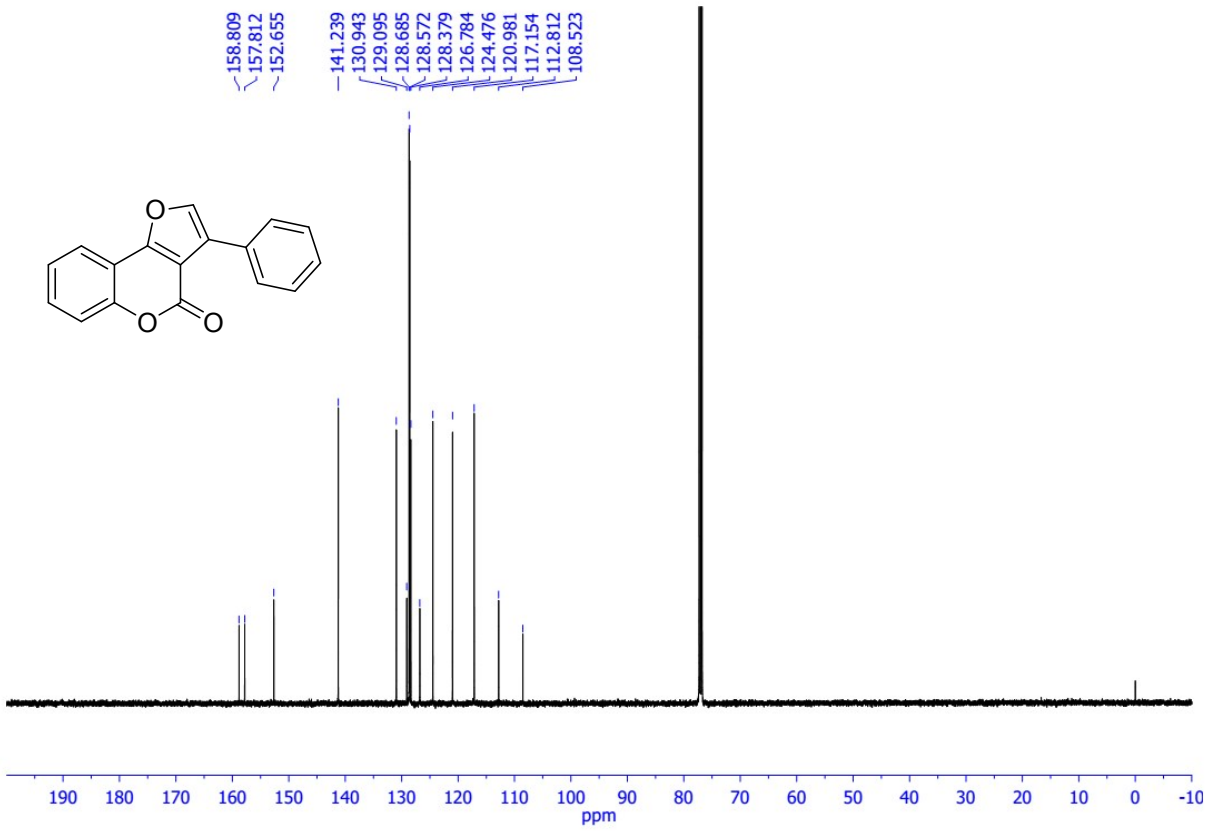


Fig.S18. ^{13}C-NMR spectra of 3-phenyl-4H-furo[3,2-c]chromen-4-one **(3ae)**

Characterization Data for 3-phenyl-4H-furo[3,2-c]chromen-4-one (3ae)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1,v/v) as eluent: white solid, 77% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (dd, J = 8.0, 1.0 Hz, 1H), 7.79 – 7.72 (m, 3H), 7.57 – 7.50 (m, 1H), 7.49 – 7.42 (m, 3H), 7.42 – 7.33 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 158.8, 157.8, 152.6, 141.2, 130.9, 129.1, 128.7, 128.6, 128.4, 126.8, 124.5, 121.0, 117.2, 112.8, 108.5. FT-IR ν(cm^{-1}) 1741, 1628, 1493, 1100, 1072, 1043, 965, 753, 694. HR-MS (ESI) m/z ([M+Na]$^{+}$), calcd for $C_{17}H_{10}Na_1O_3$ 285.0522, found 285.0525.

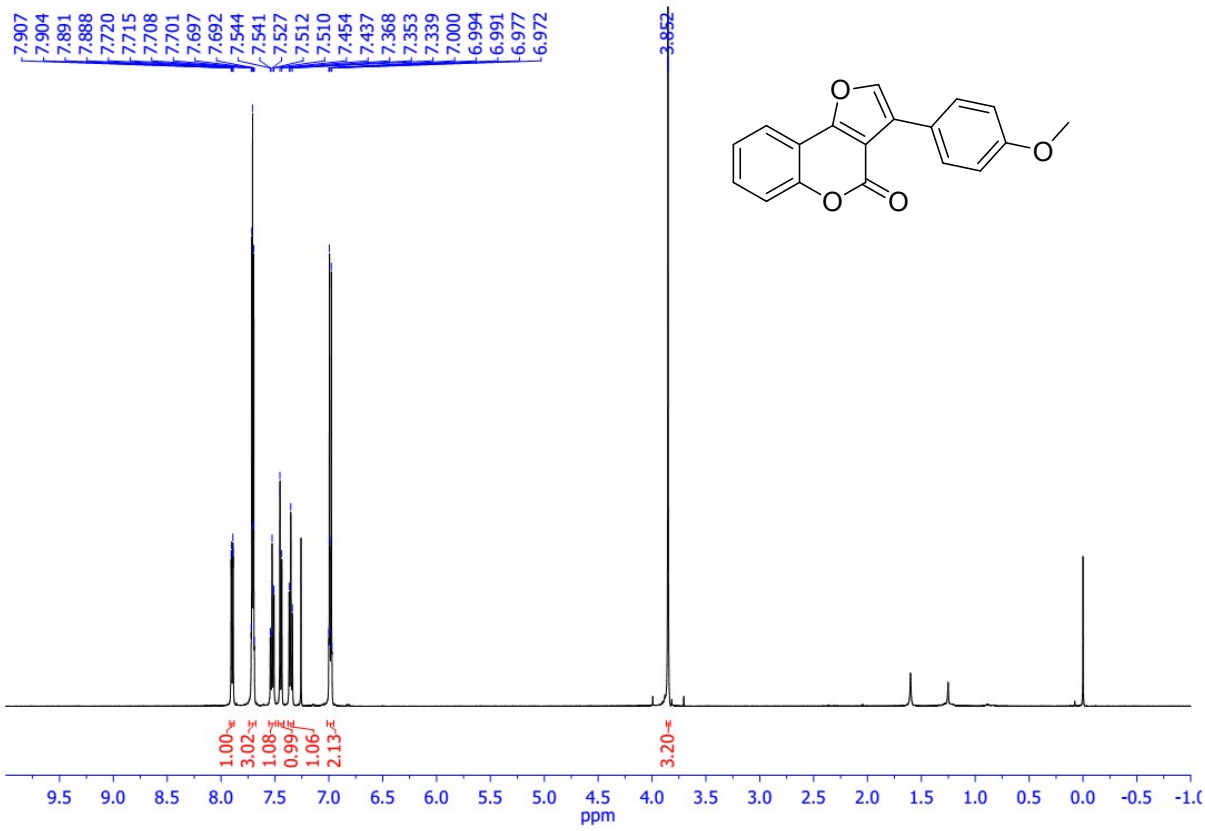


Fig.S19. ^{1}H-NMR spectra of 3-(4-methoxyphenyl)-4H-furo[3,2-c]chromen-4-one **(3af)**

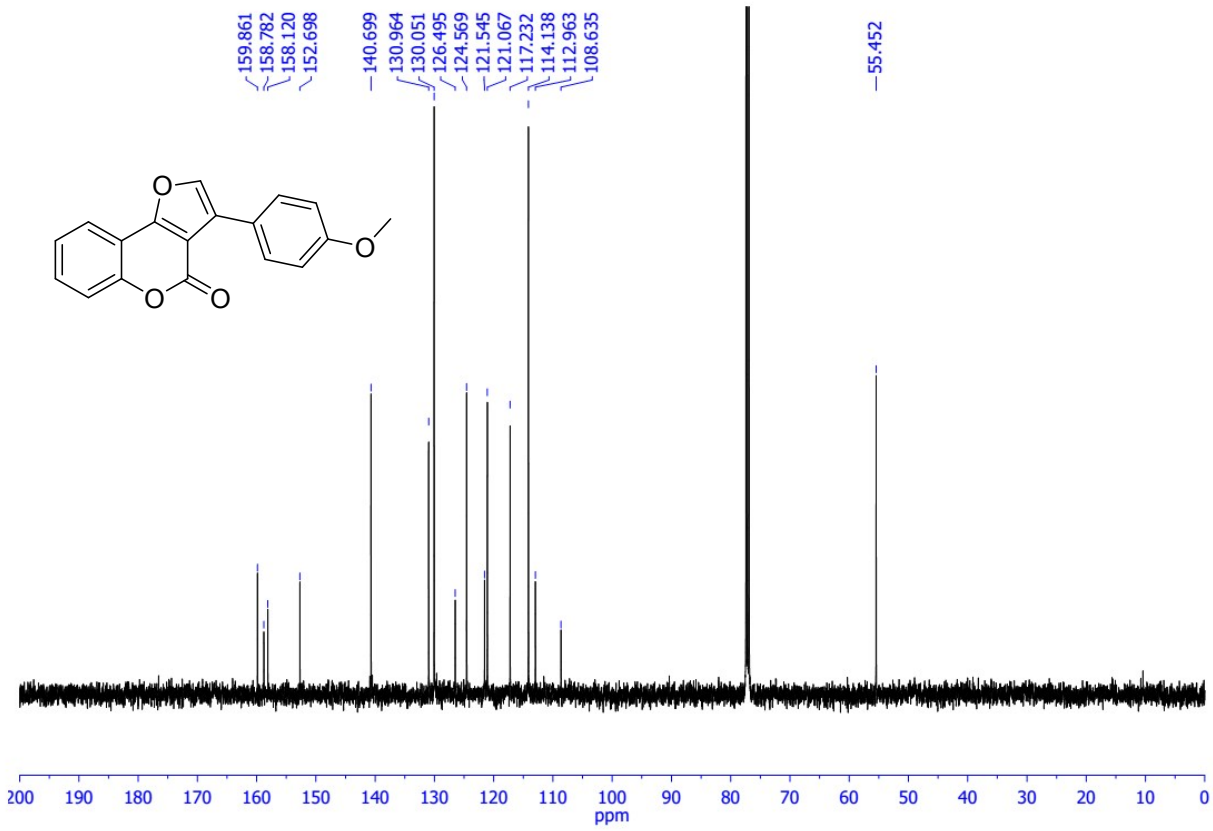


Fig.S20. ^{13}C-NMR spectra of 3-(4-methoxyphenyl)-4H-furo[3,2-c]chromen-4-one **(3af)**

Characterization Data for 3-phenyl-4H-furo[3,2-c]chromen-4-one (3af)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1,v/v) as eluent: white solid, 57% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (dd, J = 8.0, 1.5 Hz, 1H), 7.74 – 7.68 (m, 3H), 7.56 – 7.49 (m, 1H), 7.45 (d, J = 8.5 Hz, 1H), 7.35 (t, J = 7.5 Hz, 1H), 7.02 – 6.95 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.9, 158.8, 158.1, 152.7, 140.7, 131.0, 130.0, 126.5, 124.6, 121.6, 121.1, 117.2, 114.1, 113.0, 108.6, 55.4. FT-IR ν (cm^{-1}) 1730, 1627, 1543, 1501, 1243, 1101, 1076, 967, 833, 798, 759. HR-MS (ESI) m/z ([M+Na]$^{+}$), calcd for $C_{18}H_{12}Na_1O_4$ 315.0628, found 315.0630.

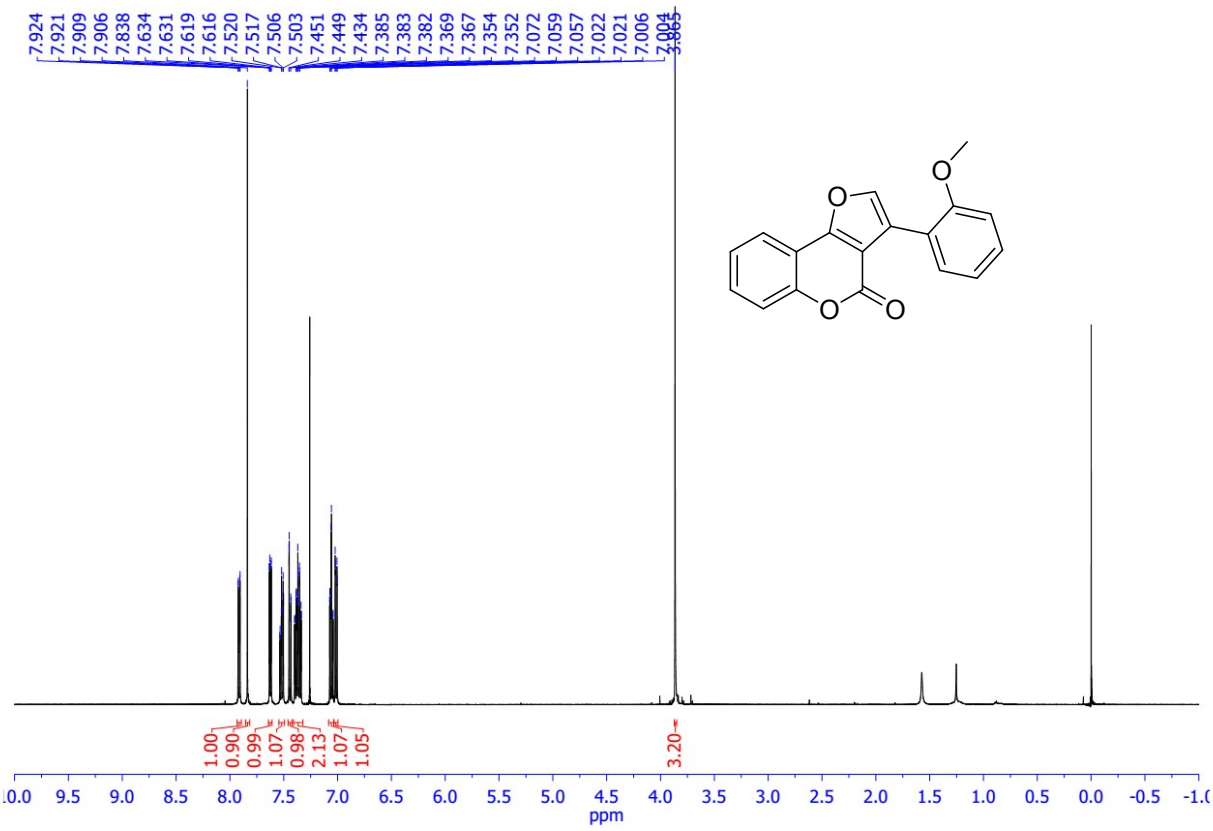


Fig.S21. ^{1}H-NMR spectra of 3-(2-methoxyphenyl)-4H-furo[3,2-c]chromen-4-one **(3ag)**

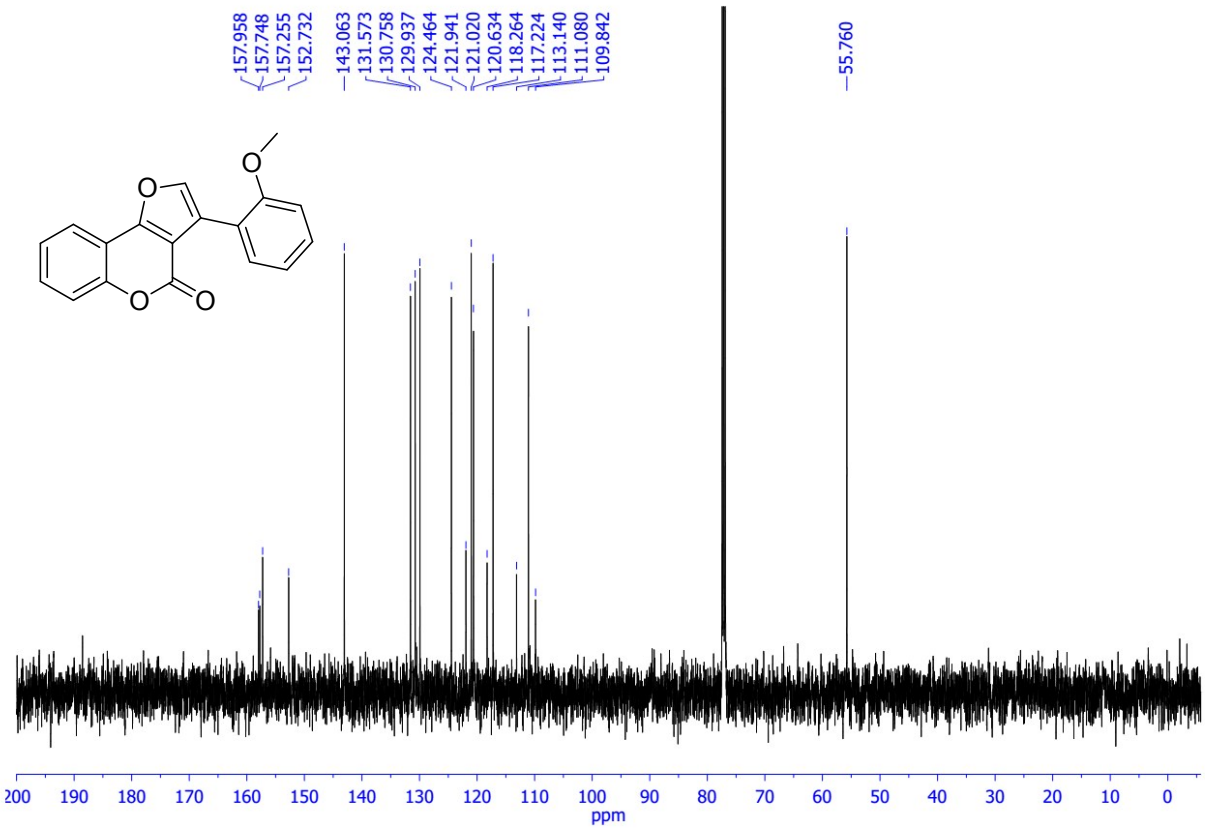


Fig.S22. ^{13}C-NMR spectra of 3-(2-methoxyphenyl)-4H-furo[3,2-c]chromen-4-one **(3ag)**

Characterization Data for 3-(2-methoxyphenyl)-4H-furo[3,2-c]chromen-4-one (3ag)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1,v/v) as eluent: white solid, 49% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (dd, J = 8.0, 1.5 Hz, 1H), 7.84 (s, 1H), 7.62 (dd, J = 7.5, 1.5 Hz, 1H), 7.55 – 7.49 (m, 1H), 7.44 (dd, J = 8.5, 1.0 Hz, 1H), 7.41 – 7.32 (m, 2H), 7.06 (td, J = 7.5, 1.0 Hz, 1H), 7.01 (dd, J = 8.5, 1.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 158.0, 157.8, 157.2, 152.7, 143.1, 131.6, 130.8, 130.0, 124.5, 121.9, 121.0, 120.6, 118.3, 117.2, 113.1, 111.1, 109.8, 55.8. FT-IR ν (cm^{-1}) 1748, 1628, 1573, 1498, 1245, 1021, 964, 739. HR-MS (ESI) m/z ($[M+Na]^+$), calcd for $C_{18}H_{12}Na_1O_4$ 315.0628, found 315.0630.

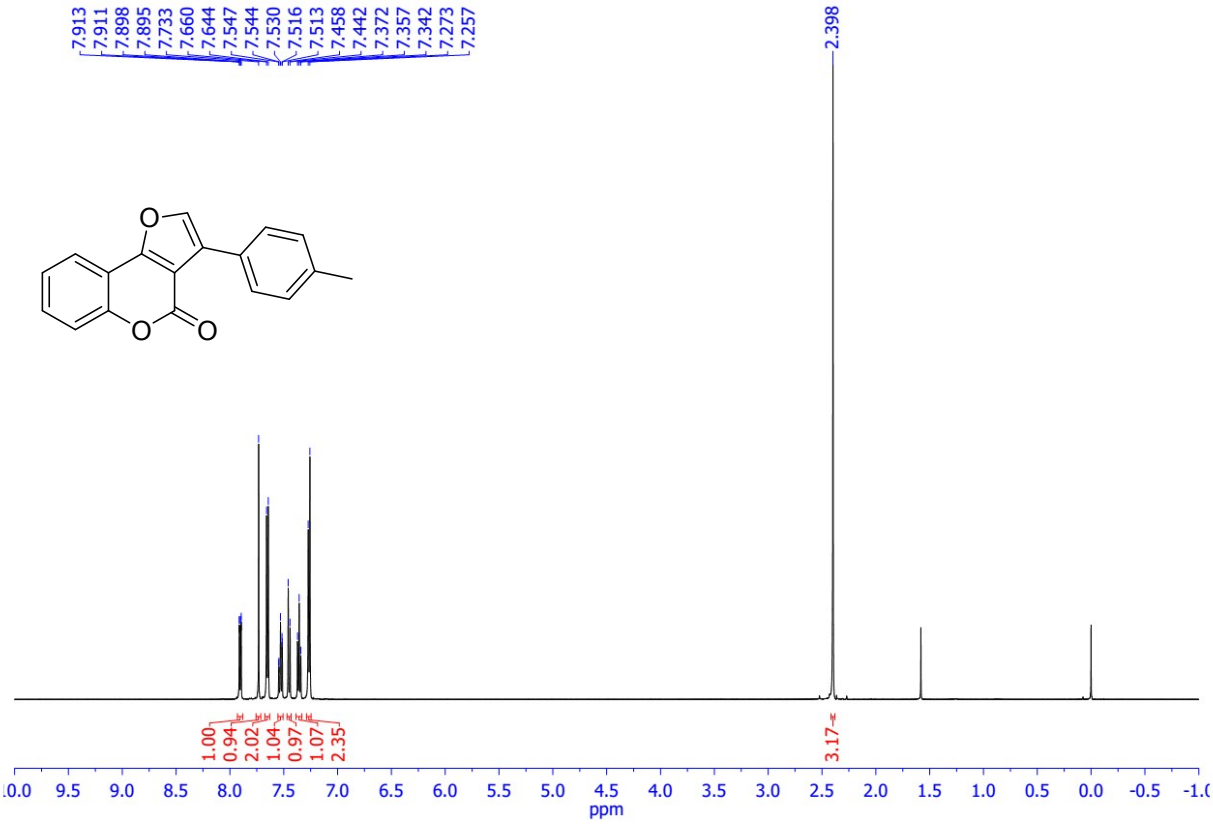


Fig.S23. ^{1}H-NMR spectra of 3-(p-tolyl)-4H-furo[3,2-c]chromen-4-one **(3ah)**

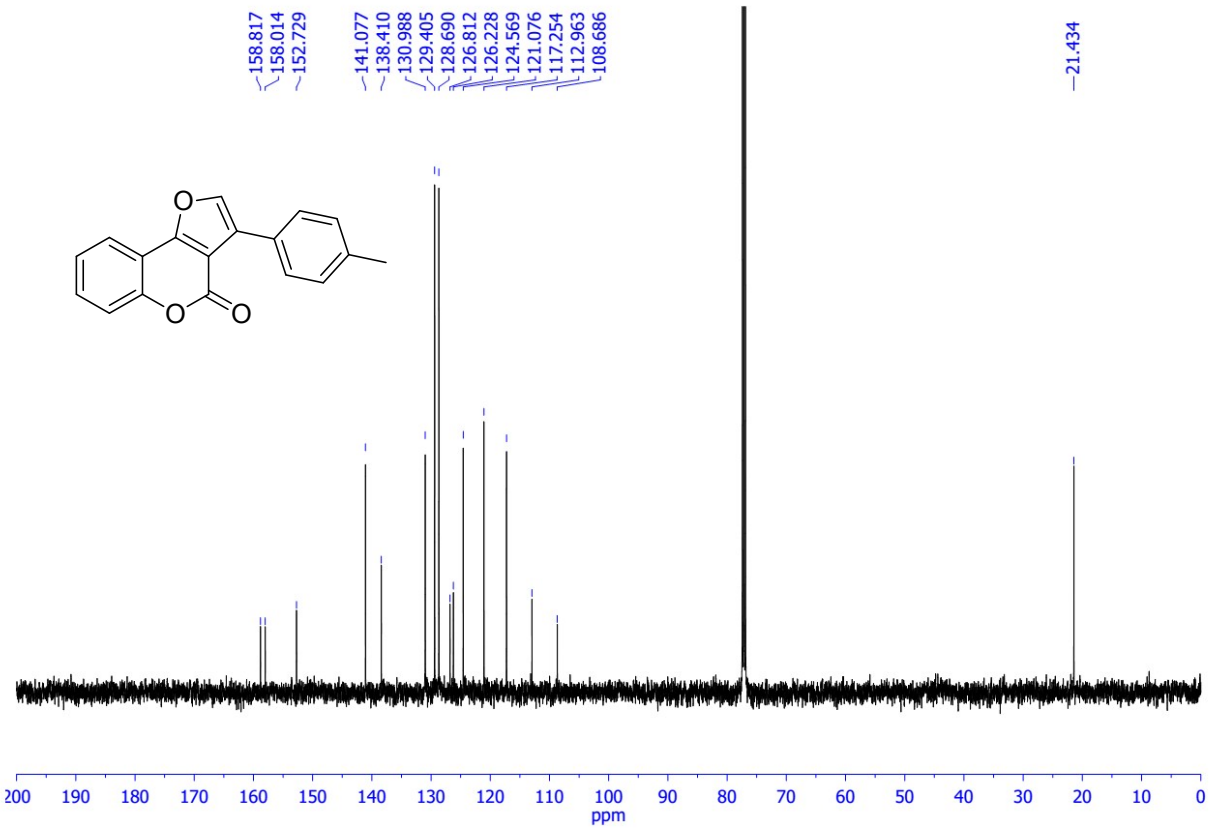


Fig.S24. ^{13}C-NMR spectra of 3-(p-tolyl)-4H-furo[3,2-c]chromen-4-one **(3ah)**

Characterization Data for 3-(p-tolyl)-4H-furo[3,2-c]chromen-4-one (3ah)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1,v/v) as eluent: white solid, 76% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.73 (s, 1H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.55 – 7.51 (m, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR (125 MHz,) δ = 158.8, 158.0, 152.7, 141.1, 138.4, 130.9, 129.4, 128.7, 126.8, 126.2, 124.6, 121.1, 117.3, 112.9, 108.7, 21.4. FT-IR ν (cm^{-1}) 1731, 1624, 1498, 1441, 1116, 1038, 969, 760. HR-MS (ESI) m/z ($[M+Na]^+$), calcd for $C_{18}H_{12}Na_1O_3$299.0679, found 299.0679.

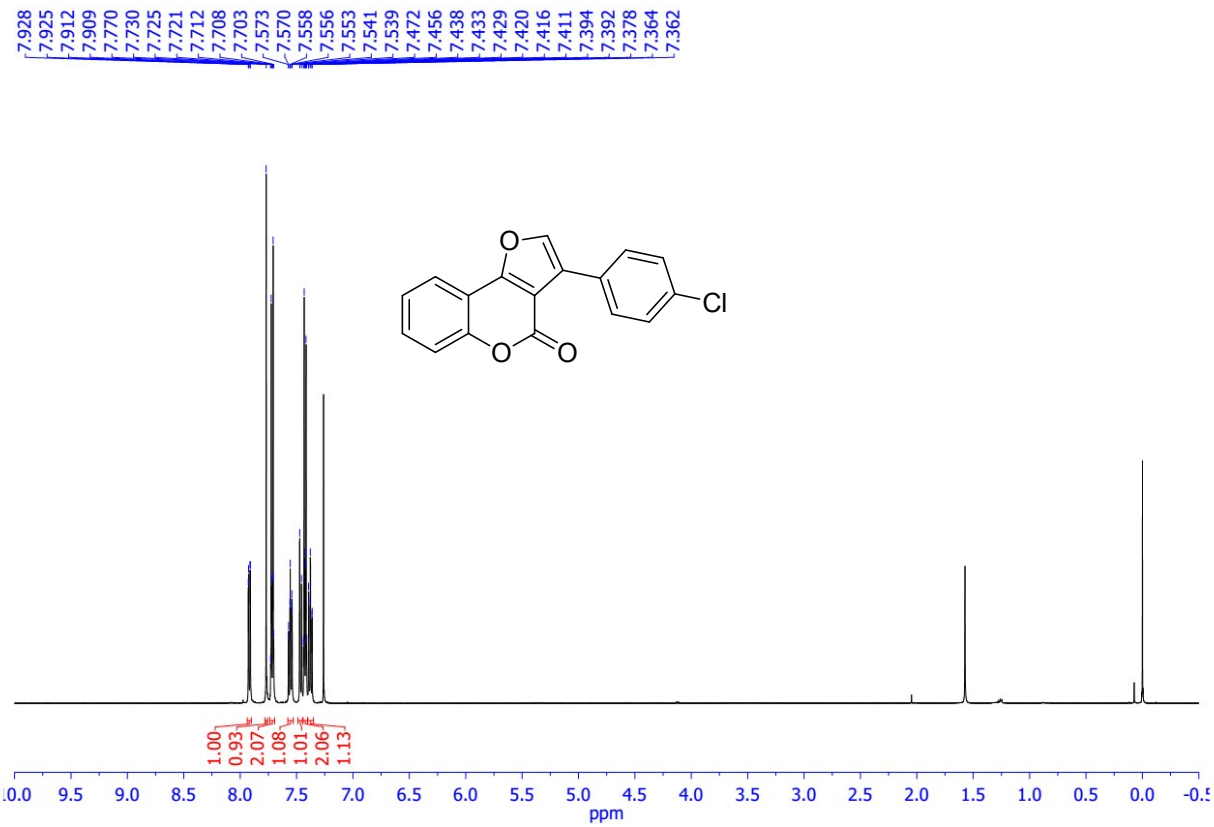


Fig.S25. ^{1}H-NMR spectra of 3-(4-chlorophenyl)-4H-furo[3,2-c]chromen-4-one **(3ai)**

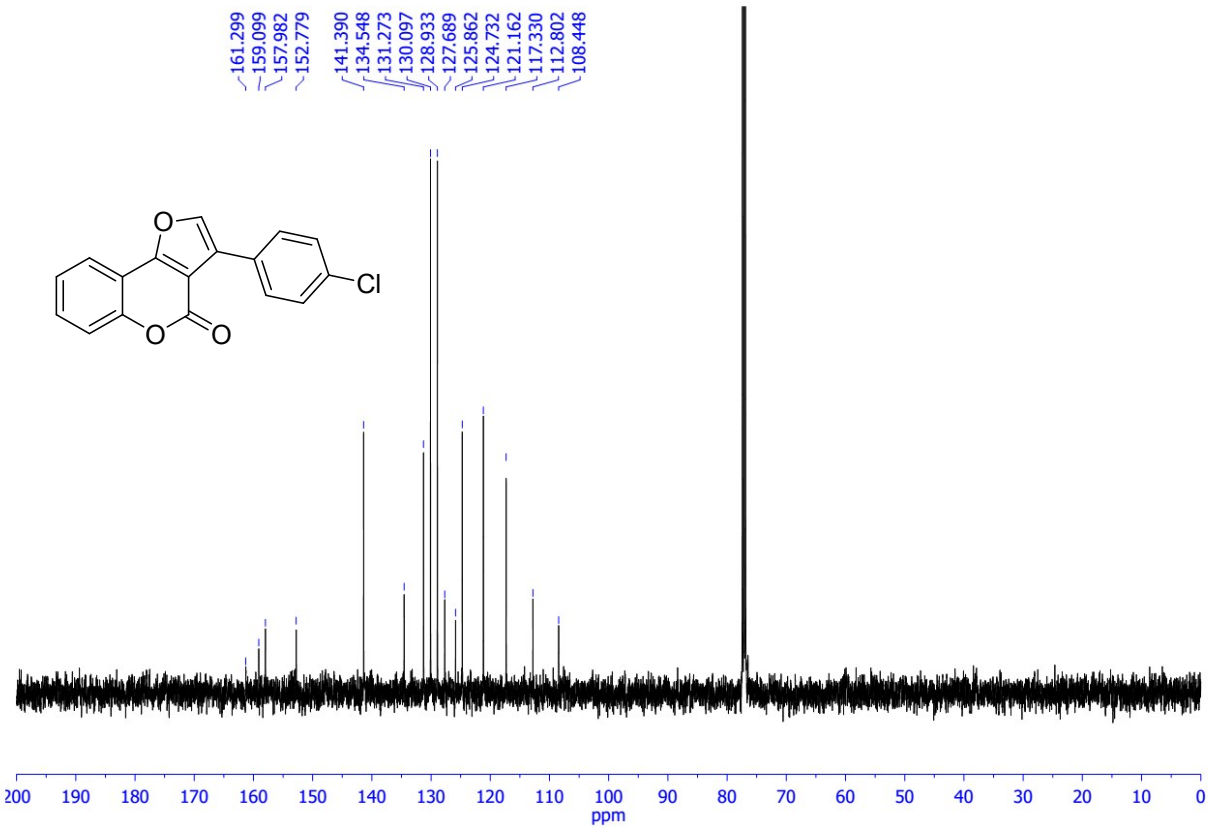


Fig.S26. ^{13}C-NMR spectra of 3-(4-chlorophenyl)-4H-furo[3,2-c]chromen-4-one **(3ai)**

Characterization Data for 3-(4-chlorophenyl)-4H-furo[3,2-c]chromen-4-one (3ai)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1,v/v) as eluent: white solid, 79% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (dd, J = 8.0, 1.5 Hz, 1H), 7.77 (s, 1H), 7.74 – 7.69 (m, 2H), 7.56 (ddd, J = 8.5, 7.5, 1.5 Hz, 1H), 7.46 (d, J = 8.0 Hz, 1H), 7.44 – 7.40 (m, 2H), 7.40 – 7.35 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 161.3, 159.1, 158.0, 152.8, 141.4, 134.6, 131.3, 130.1, 128.9, 127.7, 125.9, 124.7, 121.2, 117.3, 112.8, 108.4. FT-IR ν(cm^{-1}) 1744, 1629, 1543, 1485, 1394, 1091, 1070, 1048, 969, 924, 889, 826, 775, 751, 505. HR-MS (ESI) m/z ([M+Na]$^{+}$), calcd for $C_{17}H_9Cl_1Na_1O_3$ 319.0138, found 319.0131.

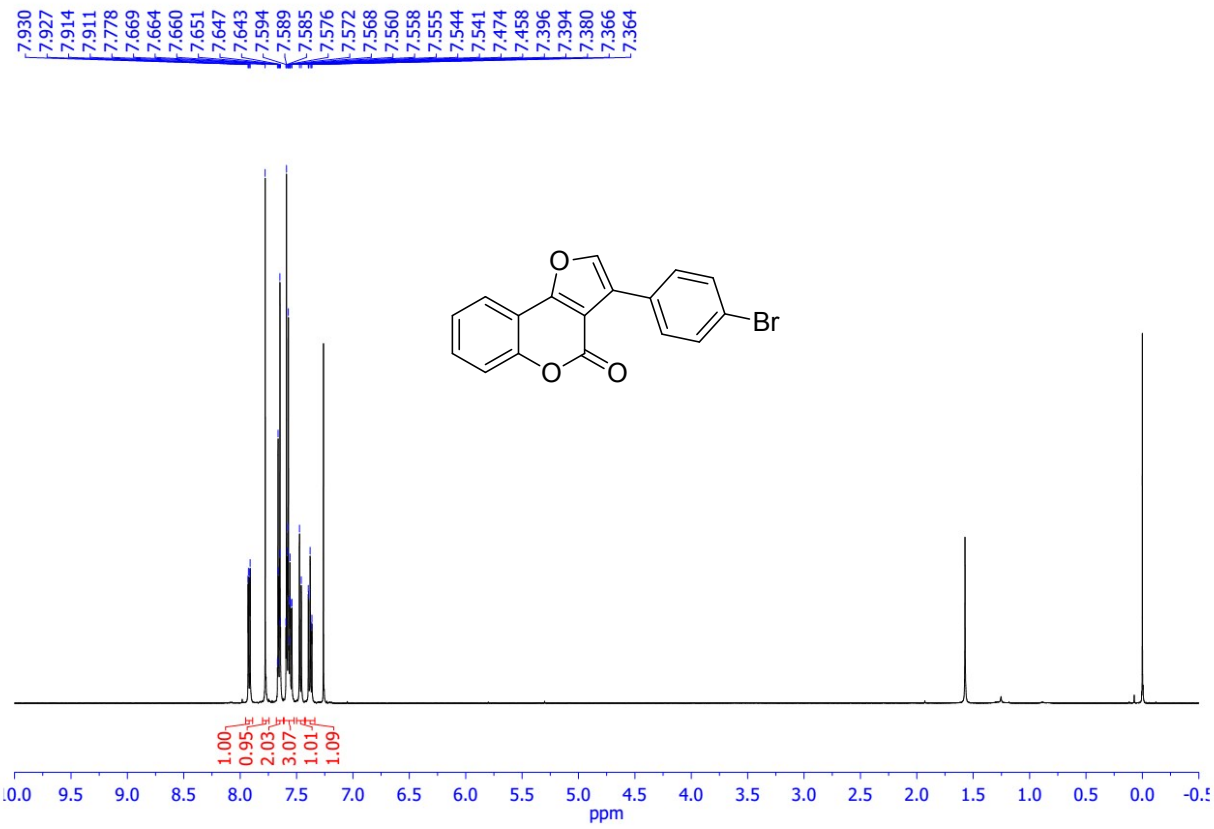


Fig.S27. [1]H-NMR spectra of 3-(4-bromophenyl)-4H-furo[3,2-c]chromen-4-one **(3aj)**

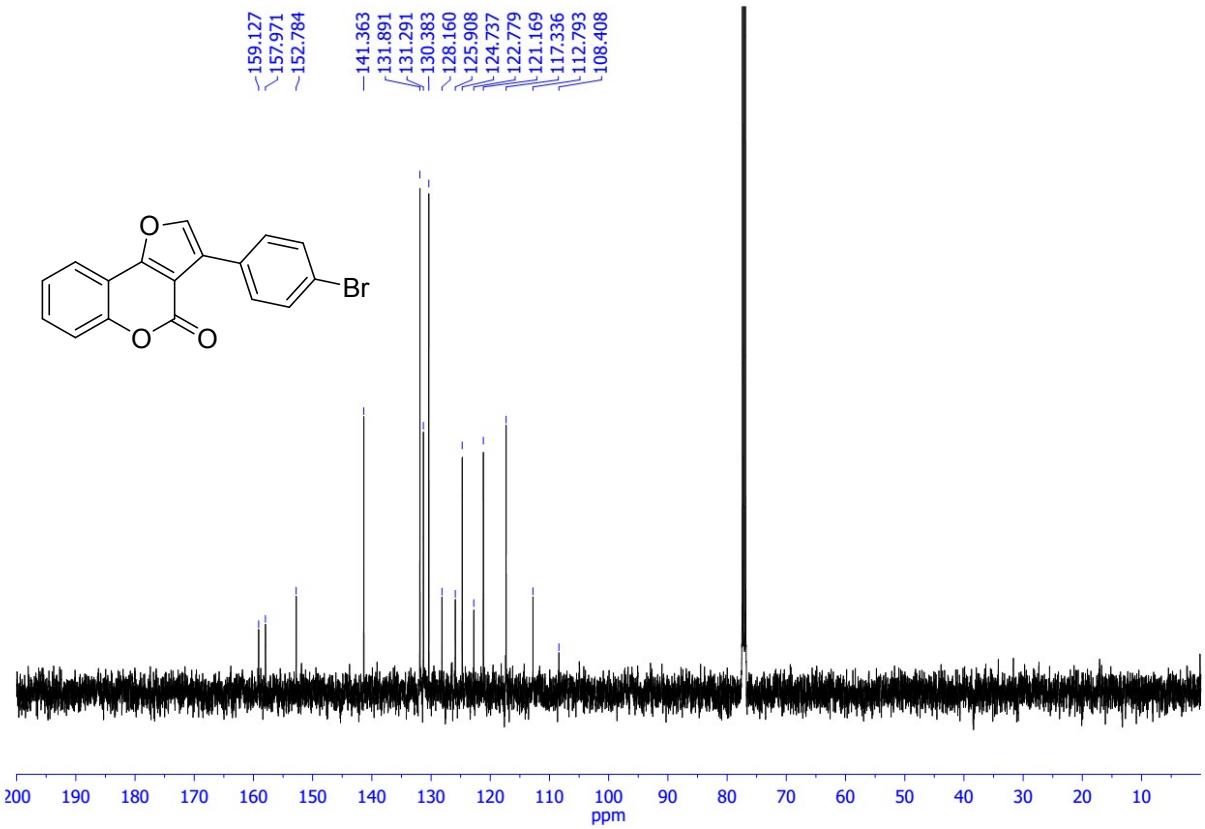


Fig.S28. ^{13}C-NMR spectra of 3-(4-bromophenyl)-4H-furo[3,2-c]chromen-4-one **(3aj)**

Characterization Data for 3-(4-bromophenyl)-4H-furo[3,2-c]chromen-4-one (3aj)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1,v/v) as eluent: white solid, 66% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (dd, J = 8.0, 1.5 Hz, 1H), 7.78 (s, 1H), 7.68 – 7.62 (m, 2H), 7.61 – 7.52 (m, 3H), 7.47 (d, J = 8.0 Hz, 1H), 7.42 – 7.34 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.1, 158.0, 152.8, 141.4, 131.9, 131.3, 130.4, 128.2, 125.9, 124.7, 122.8, 121.2, 117.3, 112.8, 108.4. FT-IR ν (cm^{-1}) 1746, 1628, 1541, 1482, 1101, 1070, 1047, 968, 924, 824, 776, 748, 519. HR-MS (ESI) m/z ($[M+Na]^+$), calcd for $C_{17}H_9Br_1Na_1O_3$ 362.9627, found 362.9622.

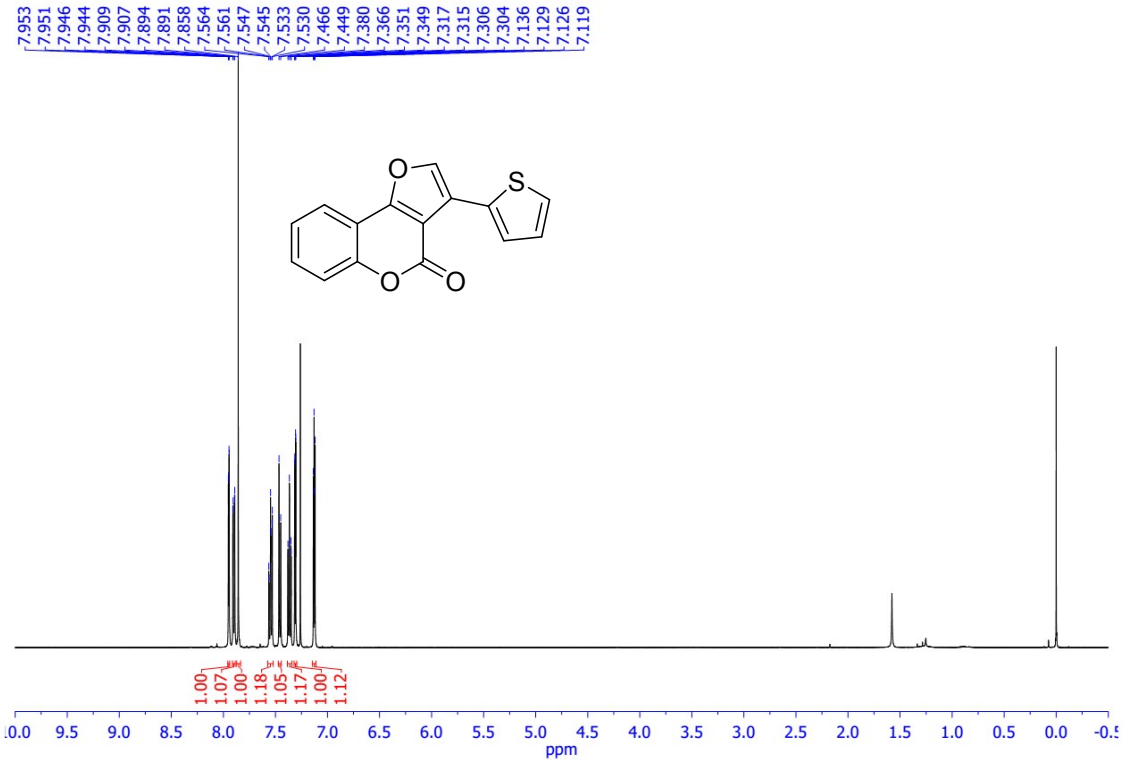


Fig.S29. ^{1}H-NMR spectra of 3-(thiophen-2-yl)-4H-furo[3,2-c]chromen-4-one (**3ak)**

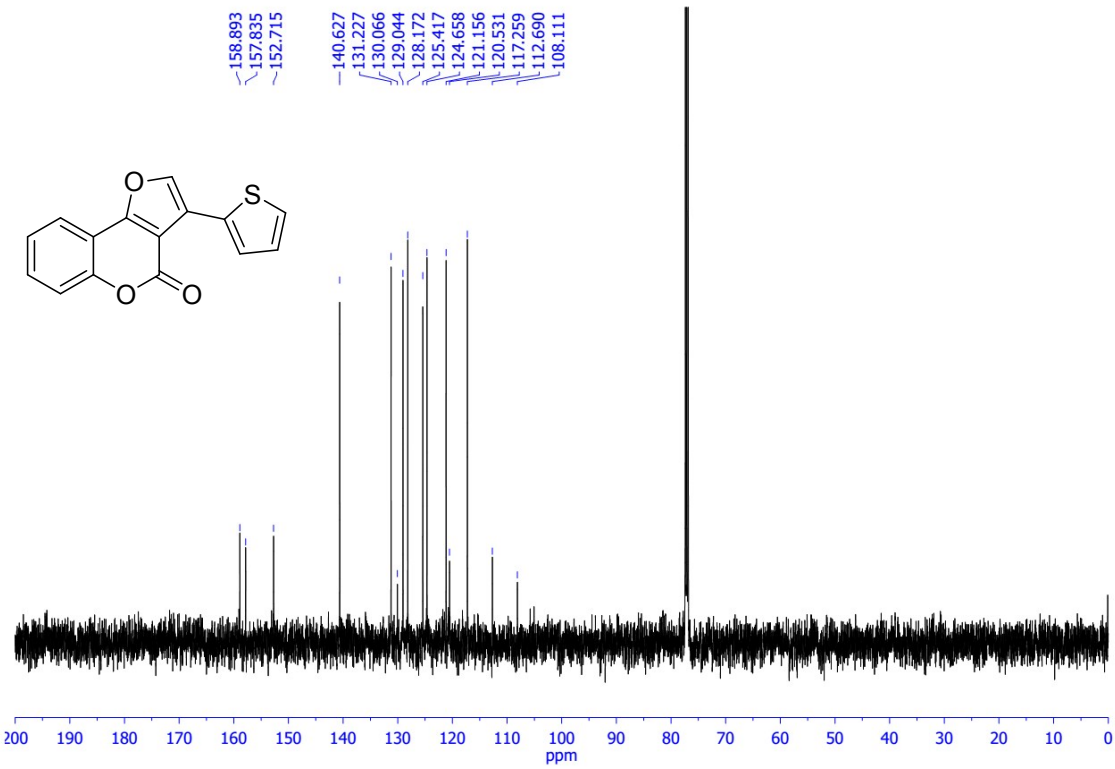


Fig.S30. ^{13}C-NMR spectra of 3-(thiophen-2-yl)-4H-furo[3,2-c]chromen-4-one (**3ak)**

Characterization Data for 3-(thiophen-2-yl)-4H-furo[3,2-c]chromen-4-on (3ak)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1,v/v) as eluent: white solid, 86% yield. ^{1}H NMR (500 MHz,) δ 7.95 (dd, *J* = 3.5, 1.0 Hz, 1H), 7.90 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.86 (s, 1H), 7.57 – 7.52 (m, 1H), 7.46 (d, *J* = 8.5 Hz, 1H), 7.38 – 7.34 (m, 1H), 7.31 (dd, *J* = 5.0, 1.0 Hz, 1H), 7.13 (dd, *J* = 5.0, 3.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 158.9, 157.8, 152.7, 140.6, 131.2, 130.1, 129.0, 128.2, 125.4, 124.7, 121.2, 120.5, 117.3, 112.7, 108.1. FT-IR ν (cm^{-1}) 1736, 1626, 1495, 1417, 1319, 1203, 1109, 1030, 1009, 955, 901, 846, 754, 705. HR-MS (ESI) m/z ([M+Na]$^+$), calcd for $C_{15}H_8S_1Na_1O_3$ 291.0086, found 291.0093.

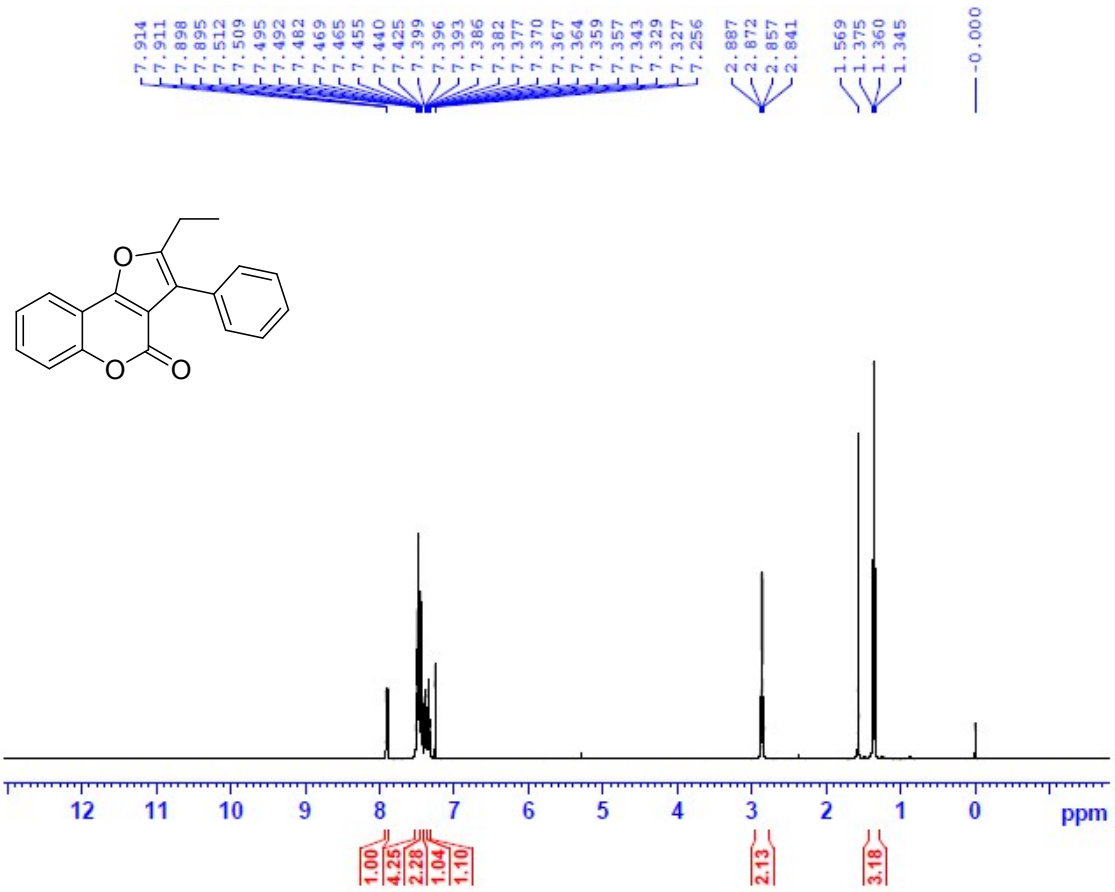


Fig.S31. ^{1}H-NMR spectra of 2-ethyl-3-phenyl-4H-furo[3,2-c]chromen-4-one (**3al)**

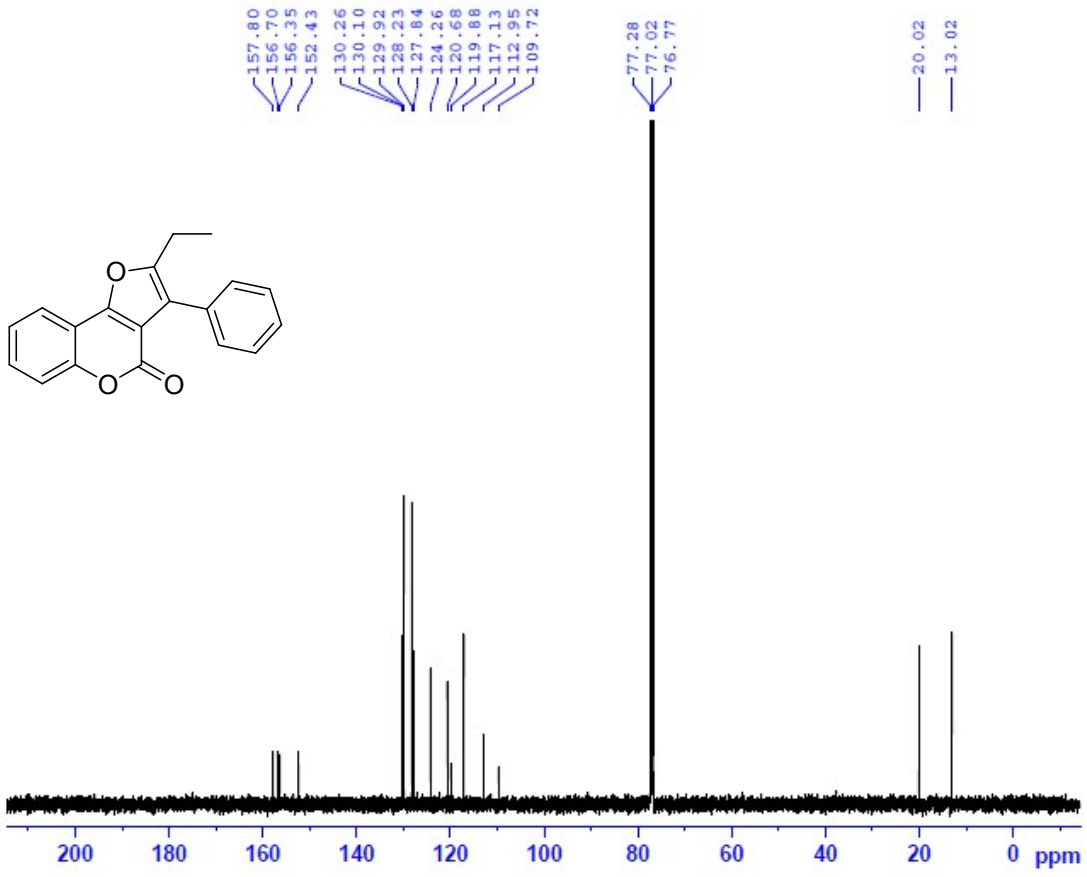


Fig.S32. ^{13}C-NMR spectra of 2-ethyl-3-phenyl-4H-furo[3,2-c]chromen-4-one (**3al)**

Characterization Data for 2-ethyl-3-phenyl-4H-furo[3,2-c]chromen-4-one (3al)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1, v/v) as eluent: white solid, 73% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.9 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.51 – 7.46 (m, 4H), 7.44 – 7.43 (d, *J* = 7.5 Hz, 2H), 7.40 – 7.38 (m, 3H), 7.37 – 7.33 (m, 1H), 2.89 – 2.84 (m, 2H), 1.38 – 1.35 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 157.8, 156.7, 156.4, 152.4, 130.3, 130.1, 129.9, 128.2, 127.8, 124.3, 120.7, 119.9, 117.1, 113.0, 109.7, 20.0, 13.0. FT-IR ν(cm^{-1}) 2977, 1731, 1630, 1501, 1450, 1085, 1059, 960, 752, 704. HR-MS (ESI) m/z ([M+Na]$^+$), calcd for $C_{19}H_{14}Na_1O_3$ 313.0835, found 313.0838.

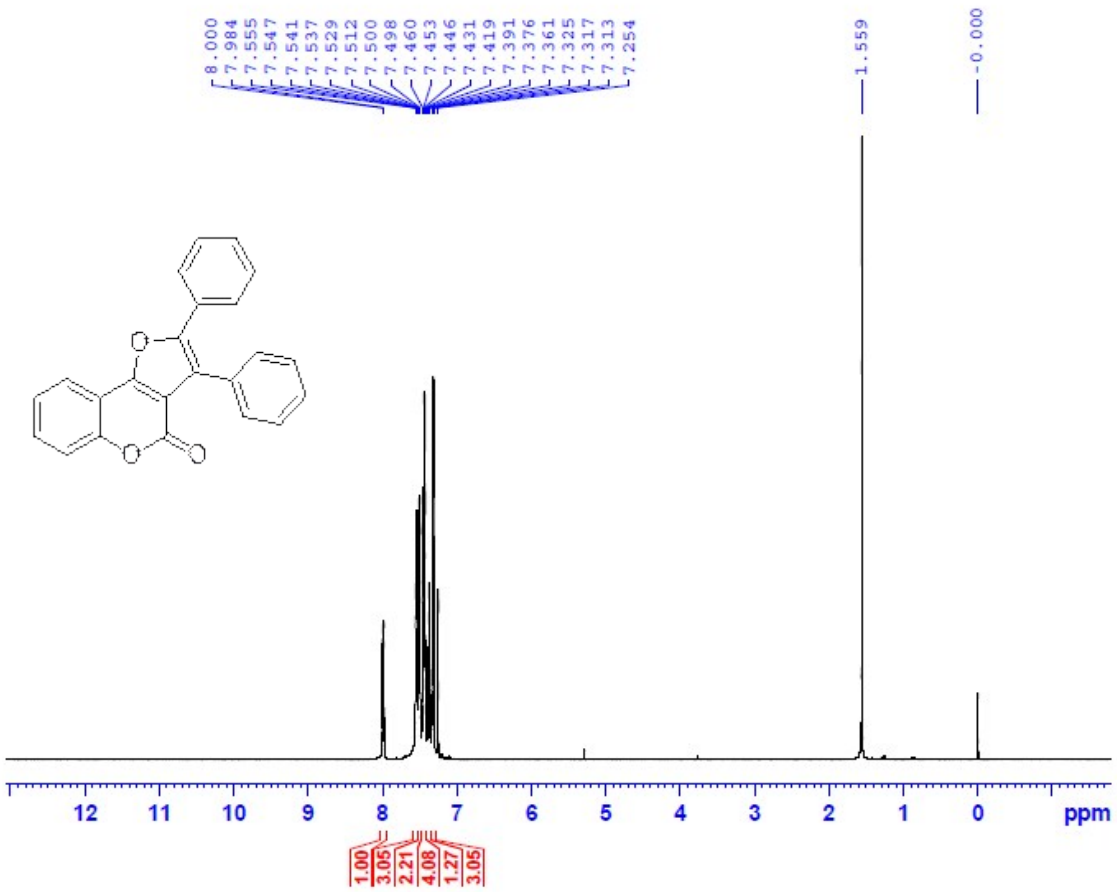


Fig.S33. ^{1}H-NMR spectra of 2,3-diphenyl-4H-furo[3,2-c]chromen-4-one (**3am**)

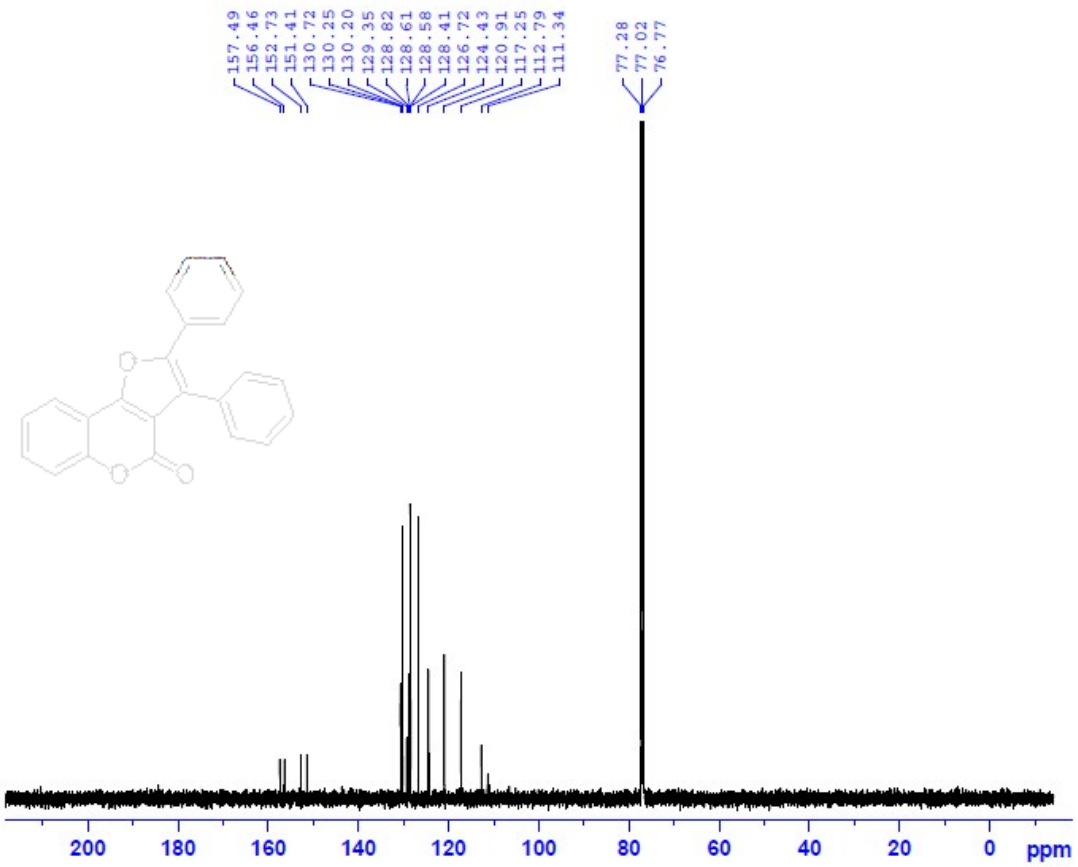


Fig.S34. ^{13}C-NMR spectra of 2,3-diphenyl-4H-furo[3,2-c]chromen-4-one (**3am**)

Characterization Data for 2,3-diphenyl-4H-furo[3,2-c]chromen-4-one (**3am**)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1, v/v) as eluent: white solid, 77% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.99 (d, *J* = 8.0 Hz, 1H), 7.56 – 7.53 (m, 3H), 7.51 (dd, *J* = 7.0, 1.0 Hz, 2H), 7.46 – 7.42 (m, 4H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.34 - 7.30 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 157.5, 156.5, 152.7, 151.4, 130.7, 130.3, 130.2, 129.4, 128.8, 128.6, 128.6, 128.4, 126.7, 124.4, 120.9, 117.3, 112.8, 111.3. FT-IR ν (cm^{-1}) 1736, 1626, 1502, 1096, 965, 772, 744, 696. HR-MS (ESI) m/z ($[M+Na]^+$), calcd for $C_{23}H_{11}Na_1O_3$ 361.0835, found 361.0840.

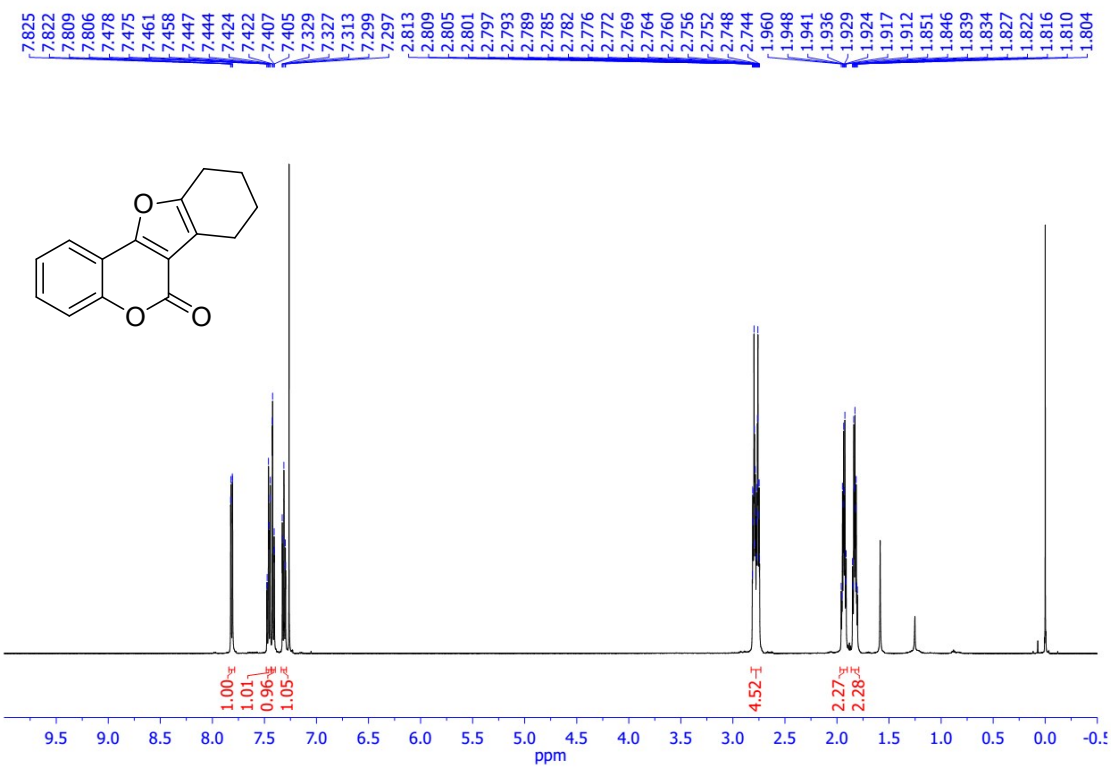


Fig.S35. ^{1}H-NMR spectra of 7,8,9,10-tetrahydro-6H-benzofuro[3,2-c]chromen-6-one (**3an**)

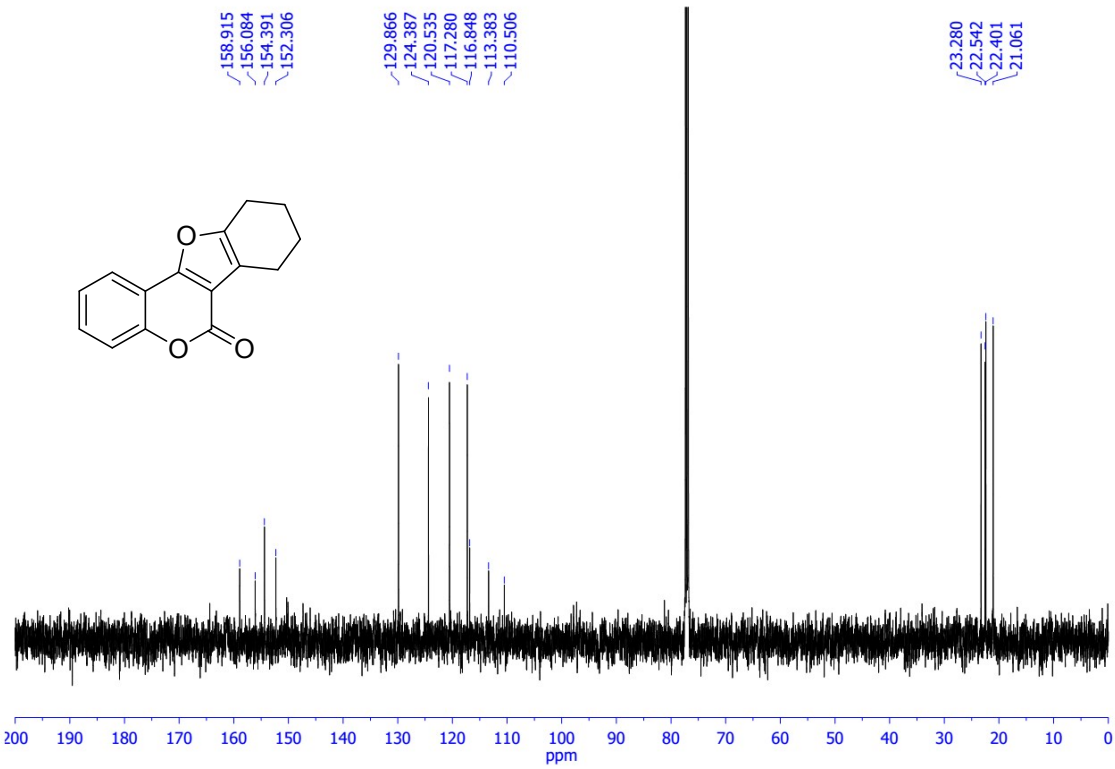


Fig.S36. ^{13}C-NMR spectra of 7,8,9,10-tetrahydro-6H-benzofuro[3,2-c]chromen-6-one (**3an**)

Characterization Data for 7,8,9,10-tetrahydro-6H-benzofuro[3,2-c]chromen-6-one (3an)

Prepared as shown in the general experimental procedure and was purified by silica gel column chromatography using hexane/dichloromethane (1.5:1, v/v) as eluent: white solid, 75% yield. ^{1}H NMR (500 MHz,) δ 7.82 (dd, J = 8.0, 1.5 Hz, 1H), 7.48 – 7.44 (m, 1H), 7.41 (dd, J = 8.5, 1.0 Hz, 1H), 7.34 – 7.29 (m, 1H), 2.82 – 2.73 (m, 4H), 1.97 – 1.90 (m, 2H), 1.86 – 1.79 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 158.91, 156.08, 154.39, 152.31, 129.87, 124.39, 120.53, 117.28, 116.85, 113.38, 110.51, 23.28, 22.54, 22.40, 21.06. FT-IR ν (cm^{-1}) 2936, 1727, 1618, 1500, 1439, 1382, 1078, 1030, 973, 762. HR-MS (ESI) m/z ([M+Na]$^+$), calcd for $C_{15}H_{12}Na_1O_3$ 263.0679, found 263.0677.