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Supporting Information

Diversity-Oriented Synthesis of Natural-Product-like Libraries Containing a 3-Methylbenzofuran Moiety for the Discovery of New Chemical Elicitors

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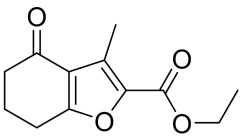
1. General Information: Unless otherwise noted, all commercial materials were used without further purification. Solvents obtained from Aladdin were used directly without further purification, and solvents obtained from other corporations were used after purification directed by *Purification of Laboratory Chemicals, 6th Ed*. Nuclear magnetic resonance (NMR) spectra were recorded with Bruker AVANCE 400MHz. ^{1}H and ^{13}C chemical shifts are reported in ppm downfield of tetramethylsilane and referenced to residual solvent peak ($CHCl_3$ = 7.26 (^{1}H NMR), DMSO = 2.50 (^{1}H NMR), $CDCl_3$ = 77.16 (^{13}C NMR) unless otherwise noted. Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad resonance. High resolution mass spectra for new compounds were recorded at mass spectrometry facilities, Zhejiang University. X-ray diffractions were recorded at x-ray facilities, Zhejiang University. HRMS were obtained using ESI ionization.

2. General procedure

General procedure for the synthesis of compound 3

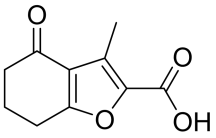
1, 3-cyclohexanedone (20 g, 0.178 mol) was added to a solution of KOH (10 g, 0.178 mol) in water (240 mL). After **5** min, ethyl 2-chloroacetoacetate (29.35 g, 0.178 mol) in MeOH (60 mL) was added. The mixture was stirred at room temperature for 5 days. After being acidified by 4 N HCl (300 mL), the solution was extracted by ethyl acetate (3 × 250 mL). The combined extracts were washed with brine (300 mL) and dried (Na_2SO_4), and the solvent was evaporated under vacuum to give the furan ester **1** (25.7 g, 65%). Without further purification, compound **1** (20 g, 0.09 mol) was dissolved in methanol (84 mL) and water (32 mL) and treated with KOH (35.4 g, 0.56 mol). After stirring overnight at room temperature, the reaction mixture was diluted with water (160 mL), acidified with 6 N HCl, and extracted with ethyl acetate (3 × 250 mL). The extract was washed with brine (250 mL), dried (Na_2SO_4), and the solvent was evaporated under vacuum to give the furan acid **2** (15.73 g, 90%). Without further purification, the furan acid **2** (10 g, 0.052 mol) in diethylene glycol (80 mL) was treated with Cu powder (3.27 g, 0.052 mol) and dry pyridine (8.23 g, 0.104 mol) and heated at 170-175 °C for 10 h. The mixture was cooled to room temperature, diluted with ice water (150 mL), acidified (4 N HCl, 100 mL), and extracted with ether (3 × 100 mL). The combined ether extracts were washed with water (100 mL) and saturated aqueous $NaHCO_3$ solution (150 mL), dried (Na_2SO_4), and evaporated to give pale yellow crystals **3** (6.6 g, 85%).

Ethyl 3-methyl-4-oxo-4,5,6,7-tetrahydrobenzofuran-2-carboxylate (1)



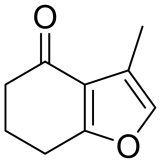
White solid. Yield: 65%. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.38 (q, *J* = 7.1 Hz, 2H), 2.94 (t, *J* = 6.3 Hz, 2H), 2.60 – 2.46 (m, 5H), 2.20 (p, *J* = 6.4 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H).

3-methyl-4-oxo-4,5,6,7-tetrahydrobenzofuran-2-carboxylic acid (2)



White solid. Yield: 90%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.91 (t, J = 6.2 Hz, 2H), 2.44 (m, 5H), 2.08 (p, J = 6.4 Hz, 2H).

3-methyl-6,7-dihydrobenzofuran-4(5*H*)-one (3)



Yellowish solid. Yield: 85%. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.11 – 6.98 (m, 1H), 2.83 (t, J = 6.3 Hz, 2H), 2.47 (dd, J = 7.2, 5.8 Hz, 2H), 2.26 – 2.06 (m, 5H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 195.70, 167.40, 138.90, 120.41, 119.07, 38.29, 23.63, 22.75, 9.07.

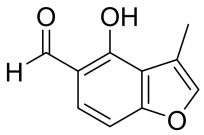
General procedure for the synthesis of compounds 7, 8, 9

To a solution of **3** (2.1g, 14 mmol) in dry toluene (150 mL) was added NaH (2.47g, 61.7 mmol, 60%) at 0 °C, and the mixture was stirred for 30 min. Into the reaction mixture was added a solution of ethyl formate (3.42 g, 46.2 mmol) in dry toluene (20 mL) over a period of 30 min at 0 °C. The mixture was stirred at 0 °C for 1 h and allowed to warm to room temperature and stirred at room temperature for 8 h. Water (100 mL) was added to the mixture at 0 °C and acidified by 2 N HCl. The organic layer was separated, the aqueous layer was extracted with ether, and the combined organic extracts were washed with brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a crude product **4**. Without further purification, the product **4** (2.0 g) in dry toluene (20 mL) was treated with 2,3-Dichloro-5,6-dicyano-l,4- benzoquinone (DDQ) (3.06 g, 13.5 mmol), and the mixture was heated under reflux for 6 h. The reaction mixture was allowed to cool to room temperature and filtered. The solids were washed with toluene and the filtrate was evaporated in vacuo. The residue, purified by column chromatography, gave the corresponding product **7** (1.48 g, 75%, 2 steps).

To a stirred solution of sodium hydride (2.8 g, 70 mmol, 60% dispersion in mineral oil) in dry DME (100 mL) under N_2 was added a solution of **3** (2.1g, 14 mmol) in dry DME (20 mL) at 0 °C, and the mixture was stirred at 0 °C for 30 min. Into the reaction mixture was added a solution of ethyl acetate (3.69 g, 42 mmol) in dry DME (20 mL) over a period of 30 min at 0 °C. The mixture was heated slowly to reflux over 30 min and heated at reflux for 3 h. After the mixture had cooled, water (40 mL) and saturated NH_4Cl solution (120 mL) were added dropwise, and the aqueous layer was extracted with ethyl acetate (3 × 80 mL). The combined organic layers were washed with brine and dried over Na_2SO_4, and evaporation of the solvent gave the crude product **5**. Without further purification, the product **5** in dry toluene (60 mL) was treated with DDQ (3.06 g, 13.5 mmol) and the mixture was heated under reflux for 6 h. The reaction mixture was allowed to cool to room temperature and filtered. The solids were washed with toluene and the filtrate was evaporated in vacuo. Purification by column chromatography gave the corresponding product **8** (1.87 g, 70%, 2 steps).

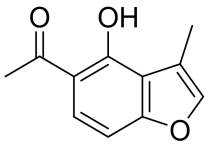
The target compound **9** was prepared by following the same procedure as for **8**. Reaction of tetrahydrobenzofuran **3** (2.1g, 14 mmol) with dimethyl carbonate (6.3 g, 70 mmol) in DME (150 mL) afforded **6** as white solid. The product **6** (2.0 g) was treated with DDQ in dry toluene (60 mL) to give compound **9** (2.16 g, 75%, 2 steps).

4-hydroxy-3-methylbenzofuran-5-carbaldehyde (7)



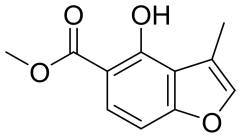
Yellowish solid. Yield: 75%. m.p. 55.1-56.2 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.97 (s, 1H), 9.87 (s, 1H), 7.37 (d, *J* = 8.6 Hz, 1H), 7.31 (q, *J* = 1.4 Hz, 1H), 7.04 (d, *J* = 8.6 Hz, 1H), 2.41 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 195.98, 161.03, 159.49, 141.21, 129.73, 117.71, 117.00, 115.28, 104.85, 9.46. HRMS (EI) *m/z*: 176.0471 (M^{+}); calc. for $C_{10}H_8O_3$: 176.0473.

1-(4-hydroxy-3-methylbenzofuran-5-yl)ethan-1-one (8)



Yellowish solid. Yield: 70%. m.p. 61.7-62.4 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.28 (s, 1H), 7.58 (d, *J* = 8.8 Hz, 1H), 7.28 (q, *J* = 1.4 Hz, 1H), 6.93 (d, *J* = 8.9 Hz, 1H), 2.63 (s, 3H), 2.41 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 204.10, 160.50, 160.42, 140.79, 126.97, 117.87, 117.26, 114.05, 103.71, 26.93, 9.57. HRMS (EI) *m/z*: 190.0630 (M^{+}); calc. for $C_{11}H_{10}O_3$: 190.0630.

methyl 4-hydroxy-3-methylbenzofuran-5-carboxylate (9)



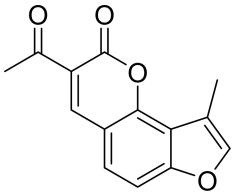
White solid. Yield: 75%. m.p. 71.1-72.1 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.43 (s, 1H), 7.71 (d, *J* = 8.8 Hz, 1H), 7.28 (q, *J* = 1.4 Hz, 1H), 6.93 (d, *J* = 8.8 Hz, 1H), 3.95 (s, 3H), 2.41 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.28, 160.21, 159.02, 140.65, 125.86, 117.59, 116.87, 105.68, 103.85, 52.10, 9.59. HRMS (EI) *m/z*: 206.0576 (M^{+}); calc. for $C_{11}H_{10}O_4$: 206.0579.

General procedure for the synthesis of angular 3-methylfuranocoumarins

A solution of **7** (200 mg, 1.12 mmol), ethyl acetoacetate (146 mg, 1.12 mmol) and 2d piperidine in dry EtOH (10 mL**)** was heated at reflux for 4 h. The product precipitated quantitatively from the solution as it was formed. The precipitate was filtered and washed with ethanol to afford pure **10a** as a white solid in 90% yield.

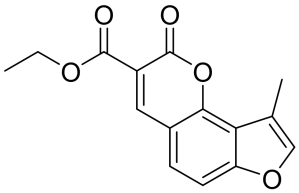
Target compounds **10b-10h** were prepared by following the same procedure as for **10a**.

3-acetyl-9-methyl-*2H*-furo[2,3-*h*]chromen-2-one (10a)



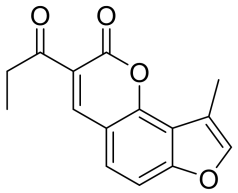
Yellow solid. Yield: 90%. m.p. 185.0-185.7 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.55 (s, 1H), 7.47 – 7.36 (m, 2H), 7.33 (d, *J* = 8.6 Hz, 1H), 2.67 (s, 3H), 2.46 (d, *J* = 1.3 Hz, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 194.55, 158.46, 158.24, 150.55, 147.86, 141.68, 124.99, 120.29, 116.14, 115.13, 111.87, 108.82, 29.59, 8.47. HRMS (EI) *m/z*: 242.0581 (M $^{+}$); calc. for $C_{14}H_{10}O_4$: 242.0579.

ethyl 9-methyl-2-oxo-*2H*-furo[2,3-*h*]chromene-3-carboxylate (10b)



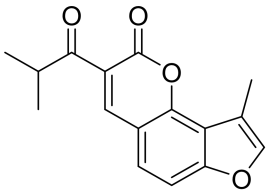
White solid. Yield: 92%. m.p. 129.2-129.7 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.63 (s, 1H), 7.51 – 7.33 (m, 3H), 4.42 (q, *J* = 7.1 Hz, 2H), 2.51 (d, *J* = 1.4 Hz, 3H), 1.43 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.37, 159.37, 156.53, 151.35, 149.89, 142.64, 125.27, 117.18, 116.16, 114.93, 112.43, 109.58, 61.76, 14.27, 9.51. HRMS (EI) *m/z*: 272.0686 (M $^{+}$); calc. for $C_{15}H_{12}O_5$: 272.0685.

9-methyl-3-propionyl-*2H*-furo[2,3-*h*]chromen-2-one (10c)



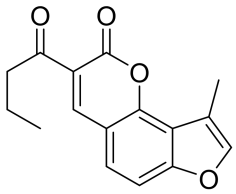
Yellowish solid. Yield: 82%. m.p. 165.8-166.4 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.64 (s, 1H), 7.52 – 7.45 (m, 2H), 7.41 (d, *J* = 8.6 Hz, 1H), 3.19 (q, *J* = 7.2 Hz, 2H), 2.54 (d, *J* = 1.4 Hz, 3H), 1.20 (t, *J* = 7.2 Hz, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.63, 159.40, 159.14, 151.45, 148.82, 142.66, 125.94, 121.30, 117.15, 116.15, 112.97, 109.79, 36.00, 9.53, 8.00. HRMS (EI) *m/z*: 256.0736 (M $^{+}$); calc. for $C_{15}H_{12}O_4$: 256.0736.

3-isobutyryl-9-methyl-*2H*-furo[2,3-*h*]chromen-2-one (10d)



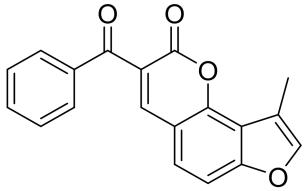
Yellowish solid. Yield: 84%. m.p. 152.7-154.0 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.59 (s, 1H), 7.52 – 7.44 (m, 2H), 7.40 (d, *J* = 8.6 Hz, 1H), 3.90 (hept, *J* = 6.8 Hz, 1H), 2.54 (d, *J* = 1.4 Hz, 3H), 1.21 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 202.41, 159.33, 158.82, 151.40, 149.21, 142.66, 125.77, 121.37, 117.14, 116.13, 113.06, 109.73, 38.42, 18.33, 9.50. HRMS (EI) *m/z*: 270.0895 (M^+); calc. for $C_{16}H_{14}O_4$: 270.0892.

3-butyryl-9-methyl-*2H*-furo[2,3-*h*]chromen-2-one (10e)



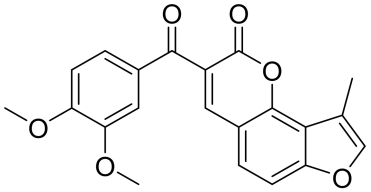
Yellowish solid. Yield: 86%. m.p. 157.7-159.3 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.62 (s, 1H), 7.52 – 7.44 (m, 2H), 7.41 (d, *J* = 8.5 Hz, 1H), 3.13 (t, *J* = 7.2 Hz, 2H), 2.54 (d, *J* = 1.4 Hz, 3H), 1.74 (h, *J* = 7.4 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.14, 159.39, 159.11, 151.46, 148.80, 142.66, 125.92, 121.53, 117.16, 116.16, 112.99, 109.78, 44.40, 17.44, 13.81, 9.52. HRMS (EI) *m/z*: 270.0891 (M^+); calc. for $C_{16}H_{14}O_4$: 270.0892.

3-benzoyl-9-methyl-*2H*-furo[2,3-*h*]chromen-2-one (10f)



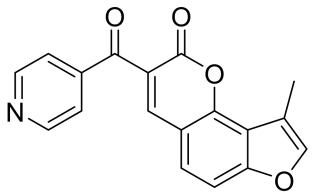
Yellowish solid. Yield: 85%. m.p. 215.5-216.2 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.55 (s, 1H), 8.03 – 7.87 (m, 3H), 7.81 – 7.65 (m, 2H), 7.67 – 7.50 (m, 3H), 2.45 (d, *J* = 1.3 Hz, 3H).
^{13}C NMR (101 MHz, DMSO-d_6) δ 191.78, 158.10, 157.80, 149.96, 147.11, 143.50, 136.32, 133.63, 129.46, 128.62, 125.84, 123.31, 116.28, 114.93, 112.91, 109.24, 9.15. HRMS (EI) *m/z*: 304.0737 (M^+); calc. for $C_{19}H_{12}O_4$: 304.0736.

3-(3,4-dimethoxybenzoyl)-9-methyl-*2H*-furo[2,3-*h*]chromen-2-one (10g)



White solid. Yield: 83%. m.p. 238.2-239.5 °C.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 (s, 1H), 7.57 (d, *J* = 2.0 Hz, 1H), 7.51 – 7.38 (m, 4H), 6.89 (d, *J* = 8.4 Hz, 1H), 3.96 (d, *J* = 1.6 Hz, 6H), 2.58 – 2.53 (m, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 190.43, 158.86, 158.49, 153.98, 150.68, 149.22, 146.26, 142.66, 129.40, 125.41, 124.83, 124.32, 117.43, 116.10, 112.78, 111.14, 109.90, 109.57, 56.15, 56.09, 9.58. HRMS (EI) *m/z*: 364.0951 (M^+); calc. for $C_{21}H_{16}O_6$: 364.0947.

3-isonicotinoyl-9-methyl-*2H*-furo[2,3-*h*]chromen-2-one (10h)



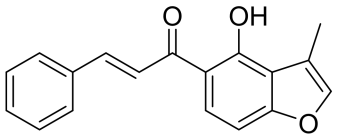
Yellow solid. Yield: 87%. m.p. 250.2-252.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.85 – 8.79 (m, 2H), 8.44 (s, 1H), 7.69 – 7.62 (m, 2H), 7.55 – 7.43 (m, 3H), 2.55 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 191.35, 159.61, 158.28, 151.54, 150.24, 149.62, 143.75, 142.97, 125.58, 122.09, 121.79, 117.55, 116.20, 112.74, 110.11, 9.51. HRMS (EI) *m/z*: 305.0693 (M^{+}); calc. for $C_{18}H_{11}NO_4$: 305.0688.

General procedure for the synthesis of angular 3-methylfuranochalcones

NaH (2 mmol, 60% dispersion in mineral oil) was added in portions to a solution of **8** (1 mmol) in dry THF (5 mL), under N_2 and with vigorous stirring. After being stirred for **15** min, a solution of the corresponding benzaldehyde (1 mmol) in dry THF (3 mL) was added dropwise over 5 min, and the reaction mixture was stirred at room temperature for 2 h. Water (10 mL) was added to quench the reaction. The pH of the mixture was adjusted at 1 by adding 2 N HCl. The product was precipitated as a colorful solid in aqueous solution. After filtration, the crude product was recrystallized from EtOH to afford the pure product as a colorful solid.

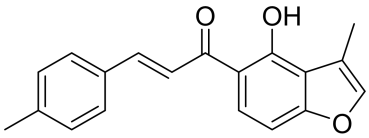
Using this procedure, target compounds **11b**-**11ab** were obtained. An additional amount of product can be obtained from the mother liquors. To this end, the solvent was evaporated in vacuo and the residue was purified by column chromatography.

(*E*)-1-(4-hydroxy-3-methylbenzofuran-5-yl)-3-phenylprop-2-en-1-one (11a)



Yellow solid. Yield: 82%. m.p. 192.0-193.0 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.97 (s, 1H), 7.91 (d, *J* = 15.5 Hz, 1H), 7.78 (dd, *J* = 9.1, 1.5 Hz, 1H), 7.70 – 7.60 (m, 3H), 7.46 – 7.39 (m, 3H), 7.29 (t, *J* = 1.4 Hz, 1H), 6.99 (dd, *J* = 8.9, 1.1 Hz, 1H), 2.44 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 192.29, 160.95, 159.46, 143.53, 139.76, 133.73, 129.66, 127.96, 127.53, 124.95, 119.71, 117.08, 116.28, 113.18, 102.72, 8.60. HRMS (EI) *m/z*: 278.0949 (M^{+}); calc. for $C_{18}H_{14}O_3$: 278.0943.

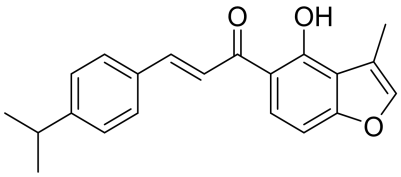
(*E*)-1-(4-hydroxy-3-methylbenzofuran-5-yl)-3-(*p*-tolyl)prop-2-en-1-one (11b)



Orange solid. Yield: 85%. m.p. 115.8-116.9 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 14.03 (s, 1H), 7.91 (d, *J* = 15.4 Hz, 1H), 7.80 (d, *J* = 8.9 Hz, 1H), 7.64 (d, *J* = 15.5 Hz, 1H), 7.60 – 7.54 (m, 2H), 7.30 (q, *J* = 1.4 Hz, 1H), 7.23 (s, 1H), 6.99 (d, *J* = 8.9 Hz, 1H), 2.44 (d, *J* = 1.4 Hz, 3H), 2.41

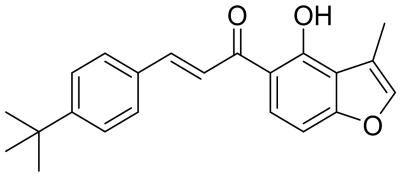
(s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.44, 161.97, 160.46, 144.70, 141.34, 140.77, 132.06, 129.77, 128.63, 125.99, 119.69, 118.12, 117.33, 114.27, 103.69, 21.59, 9.65. HRMS (EI) *m/z*: 292.1098 (M^+); calc. for $C_{19}H_{16}O_3$: 292.1099.

(*E*)-1-(4-hydroxy-3-methylbenzofuran-5-yl)-3-(4-isopropylphenyl)prop-2-en-1-one (11c)



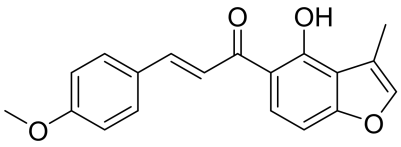
Brown solid. Yield: 87%. m.p. 97.1-98.8 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 14.04 (s, 1H), 7.89 (d, *J* = 15.4 Hz, 1H), 7.77 (d, *J* = 8.9 Hz, 1H), 7.66 – 7.52 (m, 3H), 7.31 – 7.25 (m, 3H), 6.97 (d, *J* = 8.9 Hz, 1H), 2.94 (hept, *J* = 6.9 Hz, 1H), 2.42 (d, *J* = 1.4 Hz, 3H), 1.27 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.40, 161.97, 160.45, 152.18, 144.69, 140.75, 132.44, 128.76, 127.14, 125.98, 119.73, 118.10, 117.32, 114.28, 103.68, 34.18, 23.79, 9.65. HRMS (EI) *m/z*: 320.1415 (M^+); calc. for $C_{21}H_{20}O_3$: 320.1412.

(*E*)-3-(4-(tert-butyl)phenyl)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (11d)



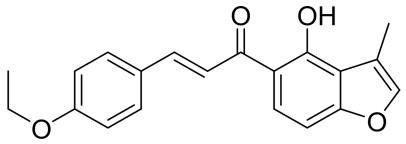
Yellow solid. Yield: 84%. m.p. 128.1-129.1 °C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 14.03 (s, 1H), 7.91 (d, *J* = 15.4 Hz, 1H), 7.79 (d, *J* = 9.0 Hz, 1H), 7.70 – 7.55 (m, 3H), 7.49 – 7.42 (m, 2H), 7.29 (t, *J* = 1.6 Hz, 1H), 6.99 (d, *J* = 8.9 Hz, 1H), 2.44 (d, *J* = 1.5 Hz, 3H), 1.35 (s, 9H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 193.12, 161.98, 160.47, 153.50, 144.75, 140.81, 140.60, 130.25, 125.94, 119.89, 118.14, 117.33, 114.21, 105.80, 103.70, 61.04, 56.25, 9.63. HRMS (EI) *m/z*: 334.1567 (M^+); calc. for $C_{22}H_{22}O_3$: 334.1569.

(*E*)-1-(4-hydroxy-3-methylbenzofuran-5-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (11e)



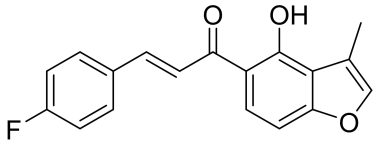
Yellow solid. Yield: 88%. m.p. 148.4-149.9 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 14.10 (s, 1H), 7.90 (d, *J* = 15.3 Hz, 1H), 7.79 (d, *J* = 8.9 Hz, 1H), 7.67 – 7.60 (m, 2H), 7.55 (d, *J* = 15.4 Hz, 1H), 7.30 (q, *J* = 1.4 Hz, 1H), 7.03 – 6.89 (m, 3H), 3.87 (s, 3H), 2.44 (d, *J* = 1.4 Hz, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.32, 161.91, 161.82, 160.38, 144.44, 140.72, 130.42, 127.51, 125.91, 118.21, 118.09, 117.31, 114.46, 114.27, 103.61, 55.44, 9.65. HRMS (EI) *m/z*: 308.1051 (M^+); calc. for $C_{19}H_{16}O_4$: 308.1049.

(*E*)-3-(4-ethoxyphenyl)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (11f)



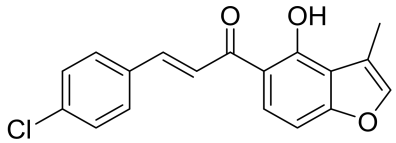
Yellow solid. Yield: 85%. m.p. 148.6-149.3 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 14.11 (s, 1H), 7.93 – 7.74 (m, 2H), 7.66 – 7.50 (m, 3H), 7.29 (t, *J* = 1.5 Hz, 1H), 7.01 – 6.89 (m, 3H), 4.09 (q, *J* = 7.0 Hz, 2H), 2.44 (d, *J* = 1.4 Hz, 3H), 1.44 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.35, 161.91, 161.27, 160.38, 144.54, 140.71, 130.44, 127.33, 125.91, 118.09, 117.32, 114.93, 114.29, 103.60, 63.70, 14.74, 9.65. HRMS (EI) *m/z*: 322.1202 (M^{+}); calc. for $C_{20}H_{18}O_4$: 322.1205.

(*E*)-3-(4-fluorophenyl)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (11g)



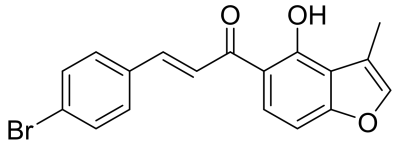
Yellow solid. Yield: 74%. m.p. 162.9-163.3 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.97 (s, 1H), 7.90 (d, *J* = 15.4 Hz, 1H), 7.80 (d, *J* = 8.9 Hz, 1H), 7.74 – 7.57 (m, 3H), 7.33 (q, *J* = 1.4 Hz, 1H), 7.22 – 7.10 (m, 2H), 7.02 (d, *J* = 8.9 Hz, 1H), 2.47 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.12, 162.01, 160.53, 143.24, 140.84, 131.05 (d, *J* = 3.3 Hz), 130.48 (d, *J* = 8.7 Hz), 125.93, 120.48 (d, *J* = 2.5 Hz), 118.15, 117.33, 116.31, 116.09, 114.17, 103.81, 9.63. HRMS (EI) *m/z*: 296.0847 (M^{+}); calc. for $C_{18}H_{13}FO_3$: 296.0849.

(*E*)-3-(4-chlorophenyl)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (11h)



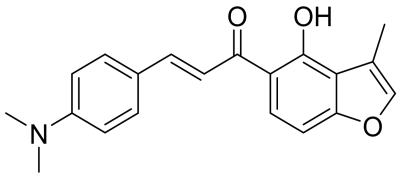
Yellow solid. Yield: 81%. m.p. 160.6-161.7 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.93 (d, *J* = 2.7 Hz, 1H), 7.96 – 7.74 (m, 2H), 7.73 – 7.55 (m, 3H), 7.53 – 7.37 (m, 2H), 7.32 (s, 1H), 7.01 (dd, *J* = 9.0, 3.1 Hz, 1H), 2.46 (d, *J* = 3.5 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 192.51, 161.54, 160.06, 142.53, 140.37, 136.10, 132.75, 129.18, 128.79, 125.42, 120.71, 117.64, 116.83, 113.66, 103.35, 9.13. HRMS (EI) *m/z*: 312.0553 (M^{+}); calc. for $C_{18}H_{13}ClO_3$: 312.0553.

(*E*)-3-(4-bromophenyl)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (11i)



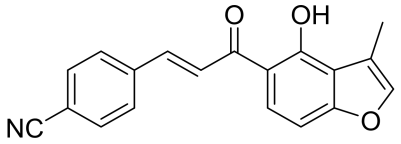
Yellow solid. Yield: 76%. m.p. 168.2-169.4 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.90 (s, 1H), 7.86 – 7.69 (m, 2H), 7.67 – 7.45 (m, 5H), 7.29 (t, *J* = 1.4 Hz, 1H), 6.98 (d, *J* = 8.9 Hz, 1H), 2.43 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 192.99, 162.05, 160.56, 143.10, 140.87, 133.66, 132.25, 129.88, 125.93, 125.00, 121.28, 118.15, 117.33, 114.15, 103.87, 9.64. HRMS (EI) *m/z*: 356.0047 (M^{+}); calc. for $C_{18}H_{13}BrO_3$: 356.0048.

(*E*)-3-(4-(dimethylamino)phenyl)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (11j)



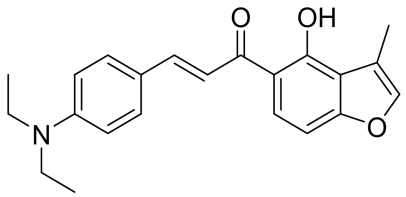
Red solid. Yield: 86%. m.p. 231.1-232.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 14.35 (s, 1H), 7.90 (d, *J* = 15.2 Hz, 1H), 7.79 (d, *J* = 8.9 Hz, 1H), 7.64 – 7.52 (m, 2H), 7.46 (d, *J* = 15.2 Hz, 1H), 7.28 (q, *J* = 1.4 Hz, 1H), 6.97 (d, *J* = 8.9 Hz, 1H), 6.75 – 6.66 (m, 2H), 3.05 (s, 6H), 2.44 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.29, 161.80, 160.18, 152.12, 145.61, 140.56, 130.68, 125.82, 122.56, 118.05, 117.30, 114.99, 114.44, 111.84, 103.33, 40.15, 9.69. HRMS (EI) *m/z*: 321.1369 (M^+); calc. for $C_{20}H_{19}NO_3$: 321.1365.

(*E*)-4-(3-(4-hydroxy-3-methylbenzofuran-5-yl)-3-oxoprop-1-en-1-yl)benzonitrile (11k)



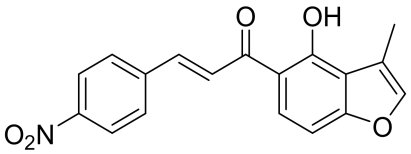
Yellow solid. Yield: 73%. m.p. 210.7-212.4 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.77 (s, 1H), 7.87 (d, *J* = 15.5 Hz, 1H), 7.82 – 7.64 (m, 6H), 7.32 (s, 1H), 7.01 (d, *J* = 8.9 Hz, 1H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 192.07, 161.07, 160.26, 141.32, 140.55, 138.58, 132.22, 128.29, 125.43, 123.64, 117.87, 117.74, 116.87, 113.62, 113.11, 103.62, 9.10. HRMS (EI) *m/z*: 303.0902 (M^+); calc. for $C_{19}H_{13}NO_3$: 303.0895.

(*E*)-3-(4-(diethylamino)phenyl)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (11l)



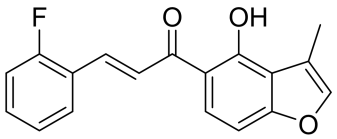
Yellow solid. Yield: 88%. m.p. 140.1-141.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 14.40 (s, 1H), 7.90 (d, *J* = 15.1 Hz, 1H), 7.80 (d, *J* = 8.9 Hz, 1H), 7.55 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 15.1 Hz, 1H), 7.30 – 7.24 (m, 1H), 6.97 (d, *J* = 8.9 Hz, 1H), 6.66 (d, *J* = 8.4 Hz, 2H), 3.42 (q, *J* = 7.1 Hz, 4H), 2.44 (d, *J* = 1.4 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.27, 161.78, 160.14, 149.88, 145.71, 140.53, 131.05, 125.78, 121.75, 118.05, 117.31, 114.49, 114.32, 111.29, 103.28, 44.56, 12.62, 9.69. HRMS (EI) *m/z*: 349.1679 (M^+); calc. for $C_{22}H_{23}NO_3$: 349.1678.

(*E*)-1-(4-hydroxy-3-methylbenzofuran-5-yl)-3-(4-nitrophenyl)prop-2-en-1-one (11m)



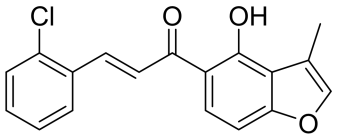
Dark red solid. Yield: 81%. m.p. 238.9-240.7 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.78 (s, 1H), 8.36 – 8.29 (m, 2H), 7.95 (d, *J* = 15.6 Hz, 1H), 7.87 – 7.78 (m, 4H), 7.35 (d, *J* = 1.5 Hz, 1H), 7.06 (d, *J* = 8.9 Hz, 1H), 2.48 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 192.93, 162.06, 160.57, 142.77, 140.85, 134.90, 133.62, 131.45, 127.96, 127.73, 126.04, 123.61, 117.34, 114.14, 103.86, 9.63. HRMS (EI) *m/z*: 323.0798 (M^+); calc. for $C_{18}H_{13}NO_5$: 323.0794.

(*E*)-3-(2-fluorophenyl)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (11n)



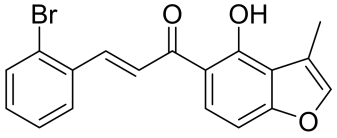
Yellow solid. Yield: 73%. m.p. 124.4-125.4 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.94 (d, *J* = 2.5 Hz, 1H), 7.99 (d, *J* = 15.7 Hz, 1H), 7.90 – 7.72 (m, 2H), 7.66 (t, *J* = 7.7 Hz, 1H), 7.41 (q, *J* = 7.0, 6.5 Hz, 1H), 7.30 (s, 1H), 7.19 (dt, *J* = 27.0, 8.8 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 192.76, 161.53, 160.04, 140.31, 136.80 (d, *J* = 1.8 Hz), 131.48 (d, *J* = 8.7 Hz), 129.52(d, *J* = 3.1 Hz), 125.55, 124.04 (d, *J* = 3.7 Hz), 122.89 (d, *J* = 11.4 Hz), 122.45, 122.34, 117.58, 115.96, 115.74, 113.69, 103.33, 9.13. HRMS (EI) *m/z*: 296.0851 (M^+); calc. for $C_{18}H_{13}FO_3$: 296.0849.

(*E*)-3-(2-chlorophenyl)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (11o)



Yellow solid. Yield: 83%. m.p. 145.1-146.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.89 (s, 1H), 8.32 (d, *J* = 15.5 Hz, 1H), 7.85 – 7.75 (m, 2H), 7.68 (d, *J* = 15.5 Hz, 1H), 7.52 – 7.44 (m, 1H), 7.41 – 7.31 (m, 3H), 7.02 (d, *J* = 8.9 Hz, 1H), 2.47 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 192.56, 161.58, 160.09, 140.38, 139.80, 135.12, 132.65, 130.82, 129.89, 127.40, 126.61, 125.55, 122.98, 117.67, 116.87, 113.68, 103.38, 9.15. HRMS (EI) *m/z*: 312.0558 (M^+); calc. for $C_{18}H_{13}ClO_3$: 312.0553.

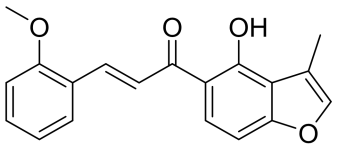
(*E*)-3-(2-bromophenyl)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (11p)



Yellow solid. Yield: 81%. m.p. 151.2-152.3 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.87 (s, 1H), 8.26 (d, *J* = 15.4 Hz, 1H), 7.78 (d, *J* = 8.7 Hz, 2H), 7.71 – 7.55 (m, 2H), 7.45 – 7.27 (m, 3H), 7.01 (d, *J* = 8.9 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 192.93, 162.06, 160.57, 142.77, 140.85, 134.90, 133.62, 131.45, 127.96, 127.73, 126.04, 123.61, 118.13, 117.34,

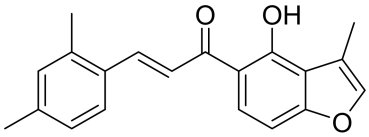
114.14, 103.86, 9.63. HRMS (EI) *m/z*: 356.0050 (M^+); calc. for $C_{18}H_{13}BrO_3$: 356.0048.

(*E*)-1-(4-hydroxy-3-methylbenzofuran-5-yl)-3-(2-methoxyphenyl)prop-2-en-1-one (11q)



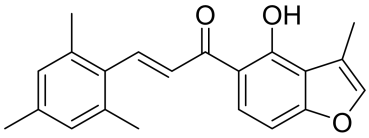
Yellow solid. Yield: 86%. m.p. 145.2-146.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 14.10 (s, 1H), 8.20 (d, *J* = 15.6 Hz, 1H), 7.84 – 7.69 (m, 2H), 7.63 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.37 (ddd, *J* = 8.6, 7.5, 1.7 Hz, 1H), 7.27 (s, 1H), 6.96 (td, *J* = 13.0, 11.9, 7.9 Hz, 3H), 3.92 (s, 3H), 2.43 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.89, 161.95, 160.39, 158.92, 140.69, 140.19, 131.97, 129.52, 126.09, 123.77, 121.37, 120.77, 118.05, 117.32, 114.38, 111.25, 103.59, 55.57, 9.66. HRMS (EI) *m/z*: 308.1051 (M^+); calc. for $C_{19}H_{16}O_4$: 308.1049.

(*E*)-3-(2,4-dimethylphenyl)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (11r)



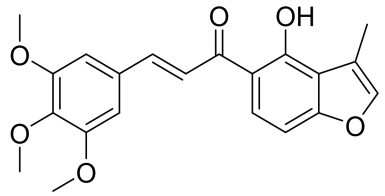
Light brown solid. Yield: 85%. m.p. 155.0-156.3 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 14.03 (s, 1H), 8.19 (d, *J* = 15.2 Hz, 1H), 7.78 (d, *J* = 8.9 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 15.3 Hz, 1H), 7.29 (q, *J* = 1.4 Hz, 1H), 7.07 (d, *J* = 7.2 Hz, 2H), 6.98 (d, *J* = 8.9 Hz, 1H), 2.47 (s, 3H), 2.44 (d, *J* = 1.4 Hz, 3H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.43, 161.96, 160.42, 142.13, 140.93, 140.73, 138.54, 131.79, 130.92, 127.19, 126.49, 125.99, 120.69, 118.08, 117.31, 114.27, 103.66, 21.40, 19.81, 9.63. HRMS (EI) *m/z*: 306.1259 (M^+); calc. for $C_{20}H_{18}O_3$: 306.1256.

(*E*)-1-(4-hydroxy-3-methylbenzofuran-5-yl)-3-mesitylprop-2-en-1-one (11s)



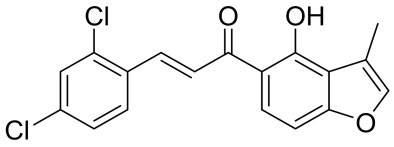
Yellow solid. Yield: 86%. m.p. 141.9-142.7 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.94 (s, 1H), 8.07 (d, *J* = 15.8 Hz, 1H), 7.67 (d, *J* = 8.9 Hz, 1H), 7.34 – 7.26 (m, 2H), 7.01 – 6.88 (m, 3H), 2.45 (d, *J* = 1.4 Hz, 3H), 2.42 (s, 6H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.50, 161.99, 160.46, 143.06, 140.79, 138.78, 137.26, 131.46, 129.37, 126.06, 125.99, 118.11, 117.33, 114.23, 103.77, 21.31, 21.12, 9.64. HRMS (EI) *m/z*: 320.1416 (M^+); calc. for $C_{21}H_{20}O_3$: 320.1412.

(*E*)-1-(4-hydroxy-3-methylbenzofuran-5-yl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (11t)



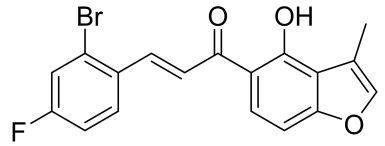
Yellow solid. Yield: 87%. m.p. 146.6-147.6 °C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 14.01 (s, 1H), 7.86 – 7.76 (m, 2H), 7.54 (d, *J* = 15.3 Hz, 1H), 7.30 (d, *J* = 1.7 Hz, 1H), 7.00 (d, *J* = 8.8 Hz, 1H), 6.88 (s, 2H), 3.94 (s, 6H), 3.92 (s, 3H), 2.44 (d, *J* = 1.5 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 193.42, 161.95, 160.44, 154.41, 144.57, 140.74, 132.02, 128.47, 125.99, 125.96, 119.86, 118.10, 117.31, 114.27, 103.68, 34.98, 31.15, 9.63. HRMS (EI) *m/z*: 368.1262 (M^+); calc. for $C_{21}H_{20}O_6$: 368.1260.

(*E*)-3-(2,4-dichlorophenyl)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (11u)



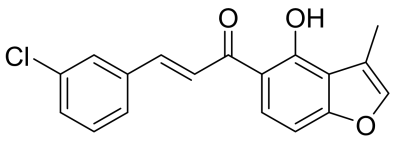
Yellow solid. Yield: 80%. m.p. 184.1-185.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.84 (s, 1H), 8.24 (d, *J* = 15.5 Hz, 1H), 7.83 – 7.59 (m, 3H), 7.51 (d, *J* = 2.1 Hz, 1H), 7.37 – 7.31 (m, 2H), 7.02 (d, *J* = 8.9 Hz, 1H), 2.47 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 192.26, 161.63, 160.15, 140.43, 138.52, 136.14, 135.69, 131.22, 129.73, 128.10, 127.09, 125.47, 123.27, 117.69, 116.86, 113.62, 103.47, 9.14. HRMS (EI) *m/z*: 346.0163 (M^+); calc. for $C_{18}H_{12}Cl_2O_3$: 346.016.

(*E*)-3-(2-bromo-4-fluorophenyl)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (11v)



Yellow solid. Yield: 82%. m.p.176.2-178.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.82 (s, 1H), 8.17 (d, *J* = 15.3 Hz, 1H), 7.75 (t, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 15.4 Hz, 1H), 7.39 (dd, *J* = 8.2, 2.5 Hz, 1H), 7.30 (s, 1H), 7.16 – 7.05 (m, 1H), 6.98 (d, *J* = 8.9 Hz, 1H), 2.43 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 192.77, 164.49, 162.09, 160.61, 141.60, 140.91, 131.30 (d, *J* = 3.5 Hz), 129.15 (d, *J* = 8.9 Hz), 126.40 (d, *J* = 9.6 Hz), 125.98, 123.41 (d, *J* = 2.07 Hz), 120.88 (d, *J* = 24.6 Hz), 118.18, 117.37, 115.35 (d, *J* = 21.6 Hz), 114.10, 103.92, 9.63. HRMS (EI) *m/z*: 373.9955 (M^+); calc. for $C_{18}H_{13}BrFO_3$: 373.9954.

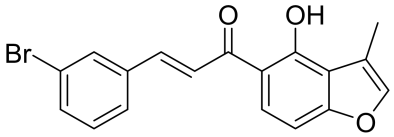
(*E*)-3-(3-chlorophenyl)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (11w)



Yellow solid. Yield: 81%. m.p. 140.9-142.5 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.86 (s,

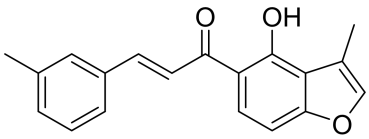
1H), 7.85 – 7.72 (m, 2H), 7.63 (t, *J* = 7.6 Hz, 2H), 7.50 (d, *J* = 7.0 Hz, 1H), 7.42 – 7.27 (m, 3H), 6.99 (d, *J* = 8.8 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 192.88, 162.05, 160.60, 142.75, 140.87, 136.59, 135.01, 130.45, 130.22, 127.92, 126.92, 125.97, 122.07, 118.13, 117.32, 114.13, 103.90, 9.60. HRMS (EI) *m/z*: 312.0554 (M^+); calc. for $C_{18}H_{13}ClO_3$: 312.0553.

(*E*)-3-(3-bromophenyl)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (11x)



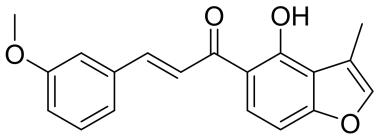
Yellow solid. Yield: 80%. m.p. 157.1-158.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.79 (s, 1H), 7.80 – 7.62 (m, 3H), 7.55 (d, *J* = 15.4 Hz, 1H), 7.51 – 7.41 (m, 2H), 7.21 (d, *J* = 7.4 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 1H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 191.81, 161.01, 159.56, 141.60, 139.83, 135.83, 132.32, 129.80, 129.44, 126.35, 124.94, 122.09, 121.03, 117.09, 116.28, 113.09, 102.87, 8.57. HRMS (EI) *m/z*: 356.0045 (M^+); calc. for $C_{18}H_{13}BrO_3$: 356.0048.

(*E*)-1-(4-hydroxy-3-methylbenzofuran-5-yl)-3-(m-tolyl)prop-2-en-1-one (11y)



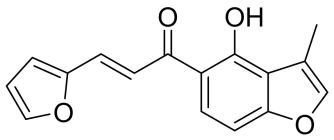
Yellow solid. Yield: 84%. m.p. 107.8-108.8 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 14.00 (s, 1H), 7.88 (d, *J* = 15.5 Hz, 1H), 7.79 (d, *J* = 8.9 Hz, 1H), 7.65 (d, *J* = 15.5 Hz, 1H), 7.46 (d, *J* = 7.7 Hz, 2H), 7.34 – 7.28 (m, 2H), 7.24 (d, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 8.9 Hz, 1H), 2.44 (d, *J* = 1.4 Hz, 3H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.38, 161.99, 160.49, 144.80, 140.78, 138.68, 134.73, 131.60, 129.11, 128.90, 126.03, 125.91, 120.52, 118.11, 117.33, 114.26, 103.73, 21.38, 9.65. HRMS (EI) *m/z*: 292.1100 (M^+); calc. for $C_{19}H_{16}O_3$: 292.1099.

(*E*)-1-(4-hydroxy-3-methylbenzofuran-5-yl)-3-(3-methoxyphenyl)prop-2-en-1-one (11z)



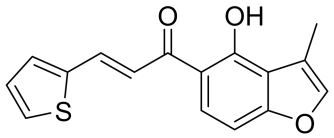
Yellow solid. Yield: 86%. m.p. 91.7-98.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 13.96 (s, 1H), 7.86 (d, *J* = 15.4 Hz, 1H), 7.77 (d, *J* = 9.0 Hz, 1H), 7.62 (d, *J* = 15.4 Hz, 1H), 7.34 (t, *J* = 7.9 Hz, 1H), 7.29 (q, *J* = 1.4 Hz, 1H), 7.27 – 7.23 (m, 1H), 7.16 (t, *J* = 2.0 Hz, 1H), 7.01 – 6.92 (m, 2H), 3.86 (s, 3H), 2.43 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.27, 162.00, 160.51, 159.95, 144.48, 140.81, 136.14, 129.99, 126.00, 121.19, 121.02, 118.11, 117.32, 116.40, 114.22, 113.61, 103.77, 55.38, 9.63. HRMS (EI) *m/z*: 308.1052 (M^+); calc. for $C_{19}H_{16}O_4$: 308.1049.

(*E*)-3-(furan-2-yl)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (11aa)



Yellow solid. Yield: 77%. m.p. 123.4-125.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 14.05 (s, 1H), 7.79 (d, *J* = 9.0 Hz, 1H), 7.68 (d, *J* = 15.1 Hz, 1H), 7.63 – 7.52 (m, 2H), 7.29 (q, *J* = 1.4 Hz, 1H), 6.98 (d, *J* = 8.9 Hz, 1H), 6.75 (d, *J* = 3.4 Hz, 1H), 6.53 (dd, *J* = 3.4, 1.8 Hz, 1H), 2.44 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 192.94, 161.93, 160.50, 151.66, 145.21, 140.75, 130.41, 126.02, 118.31, 118.06, 117.31, 116.67, 114.26, 112.81, 103.75, 9.66. HRMS (EI) *m/z*: 268.0735 (M^+); calc. for $C_{16}H_{12}O_4$: 268.0736.

(*E*)-1-(4-hydroxy-3-methylbenzofuran-5-yl)-3-(thiophen-2-yl)prop-2-en-1-one (11ab)

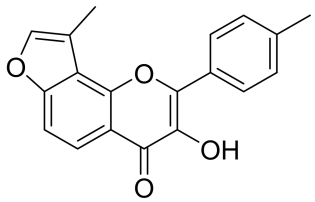


Dark red solid. Yield: 79%. m.p. 126.0-127.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 14.04 (s, 1H), 8.07 (dt, *J* = 15.1, 0.7 Hz, 1H), 7.78 (d, *J* = 8.9 Hz, 1H), 7.51 – 7.44 (m, 2H), 7.41 (dt, *J* = 3.4, 0.9 Hz, 1H), 7.32 (q, *J* = 1.4 Hz, 1H), 7.14 (dd, *J* = 5.0, 3.6 Hz, 1H), 7.02 (d, *J* = 8.9 Hz, 1H), 2.46 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 192.25, 161.45, 160.00, 140.29, 139.84, 136.55, 131.89, 128.72, 127.96, 125.39, 119.01, 117.61, 116.82,113.63, 103.27, 9.15. HRMS (EI) *m/z*: 284.0506 (M^+); calc. for $C_{16}H_{12}O_3S$: 284.0507.

General procedure for the synthesis of angular 3-methylfuranoflavonols

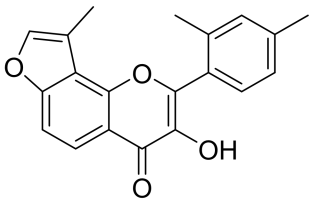
To a stirred solution of corresponding angular 3-methylfuranochalcones (1 mmol) in THF (3 mL), methanol (5 mL) and 25% aqueous sodium hydroxide solution (2 mmol) at 0 °C was added dropwise 30% aqueous H_2O_2 (2.2 mmol). The solution was sealed and stirred at 0 °C for the 1 h then stirred at room temperature for **48** h. The product precipitated from the solution as it was formed. After being acidified with 2 M HCl, the resulting flavonols were filtered from aqueous solution. The crude product was recrystallized from EtOH to afford the pure product as a colorful solid. Target compounds **12a-12j** were obtained using this procedure.

3-hydroxy-9-methyl-2-(p-tolyl)-4*H*-furo[2,3-*h*]chromen-4-one (12a)



Yellowish brown solid. Yield: 75%. m.p. 238.9-241.5 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.55 (s, 1H), 8.13 – 8.07 (m, 2H), 7.99 – 7.94 (m, 2H), 7.63 (d, *J* = 8.8 Hz, 1H), 7.39 (d, *J* = 8.2 Hz, 2H), 2.55 (d, *J* = 1.4 Hz, 3H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 172.60, 157.65, 150.23, 144.83, 143.22, 139.54, 138.75, 129.18, 128.55, 127.16, 120.90, 117.14, 116.69, 115.36, 109.93, 20.99, 9.71. HRMS (EI) *m/z*: 306.0898 (M^+); calc. for $C_{19}H_{14}O_4$: 306.0892.

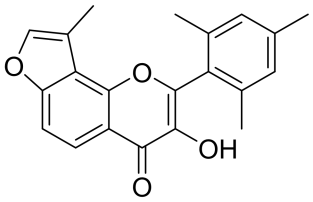
2-(2,4-dimethylphenyl)-3-hydroxy-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (12b)



Yellowish brown solid. Yield: 70%. m.p. 234.6-236.4 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.17 (d, *J* = 8.9 Hz, 1H), 7.60 – 7.38 (m, 3H), 7.23 – 7.07 (m, 2H), 6.64 (s, 1H), 2.52 – 2.29 (m, 9H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.11, 158.58, 152.05, 146.97, 142.11, 140.47, 138.37, 137.46, 131.62, 129.65, 127.25, 126.60, 121.42, 117.73, 116.52, 116.16, 110.26, 21.43, 19.96, 9.70. HRMS (EI) *m/z*: 320.1051 (M^+); calc. for $C_{20}H_{16}O_4$: 320.1049.

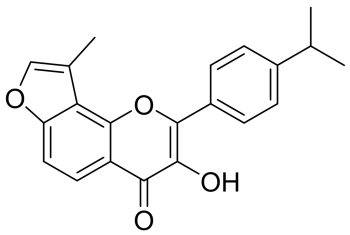
3-hydroxy-2-mesityl-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (12c)



White solid. Yield: 78%. m.p. 189.1-190.1 °C.

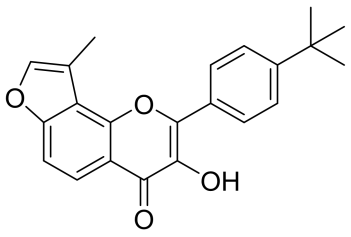
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.18 (d, *J* = 8.9 Hz, 1H), 7.53 (d, *J* = 8.9 Hz, 1H), 7.47 (p, *J* = 1.2 Hz, 1H), 7.02 (s, 2H), 6.46 (s, 1H), 2.39 – 2.34 (m, 6H), 2.27 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.03, 158.54, 152.30, 146.75, 142.07, 140.18, 137.64, 128.58, 126.58, 123.68, 121.41, 117.80, 116.73, 116.22, 110.28, 21.31, 19.72, 9.65. HRMS (EI) *m/z*: 334.1207 (M^+); calc. for $C_{21}H_{18}O_4$: 334.1205.

3-hydroxy-2-(4-isopropylphenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (12d)



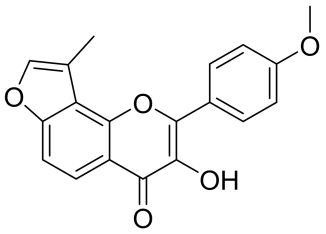
Yellowish brown solid. Yield: 72%. m.p. 249.0-251.4 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.32 – 7.99 (m, 3H), 7.47 (dd, *J* = 27.2, 9.3 Hz, 4H), 7.12 (s, 1H), 3.02 (d, *J* = 9.0 Hz, 1H), 2.66 (s, 3H), 1.32 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.38, 158.70, 151.55, 151.20, 142.18, 138.28, 128.81, 127.48, 126.88, 123.89, 121.37, 117.77, 116.76, 115.94, 110.30, 34.16, 23.82, 10.31. HRMS (EI) *m/z*: 334.1213 (M^+); calc. for $C_{21}H_{18}O_4$: 334.1205.

2-(4-(tert-butyl)phenyl)-3-hydroxy-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (12e)



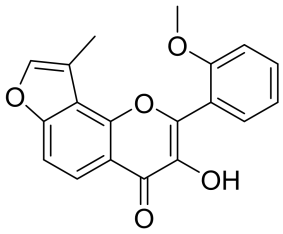
Orange solid. Yield: 59%. m.p. 167.1-168.1 °C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.21 (d, *J* = 8.1 Hz, 2H), 8.13 (d, *J* = 8.7 Hz, 1H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.55 – 7.44 (m, 2H), 7.12 (s, 1H), 2.66 (s, 3H), 1.39 (s, 9H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 158.71, 158.70, 153.43, 151.54, 151.54, 142.17, 128.43, 128.43, 127.19, 125.74, 121.37, 117.74, 115.94, 110.27, 34.95, 34.95, 31.18, 10.30. HRMS (EI) *m/z*: 348.1366 (M^+); calc. for $C_{22}H_{20}O_4$: 348.1362.

3-hydroxy-2-(4-methoxyphenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (12f)



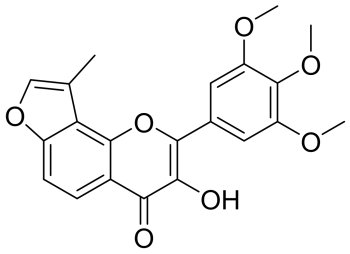
Lightgray solid. Yield: 65%. m.p. 250.7-252.8 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.45 (s, 1H), 8.16 (d, *J* = 8.5 Hz, 2H), 7.99 – 7.87 (m, 2H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.14 (d, *J* = 8.5 Hz, 2H), 3.85 (s, 3H), 2.55 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 172.39, 160.18, 157.57, 150.09, 144.90, 143.12, 138.14, 128.90, 123.62, 120.84, 117.09, 116.68, 115.33, 114.06, 109.79, 55.29, 9.77. HRMS (EI) *m/z*: 322.0851 (M^+); calc. for $C_{19}H_{14}O_5$: 322.0841.

3-hydroxy-2-(2-methoxyphenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (12g)



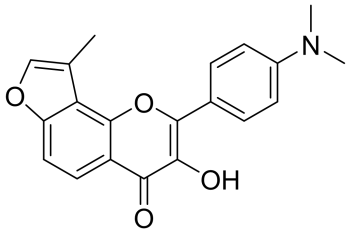
Pink solid. Yield: 70%. m.p. 238.5-240.5 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 (d, *J* = 8.8 Hz, 1H), 7.69 (d, *J* = 7.5 Hz, 1H), 7.50 (dd, *J* = 16.2, 7.5 Hz, 3H), 7.18 – 7.05 (m, 2H), 3.91 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.27, 158.46, 157.46, 152.09, 144.87, 141.93, 138.78, 131.95, 131.08, 121.37, 120.53, 119.58, 117.81, 116.53, 116.40, 111.68, 110.11, 55.69, 9.42. HRMS (EI) *m/z*: 322.0841 (M^+); calc. for $C_{19}H_{14}O_5$: 322.0841.

3-hydroxy-9-methyl-2-(3,4,5-trimethoxyphenyl)-4*H*-furo[2,3-*h*]chromen-4-one (12h)



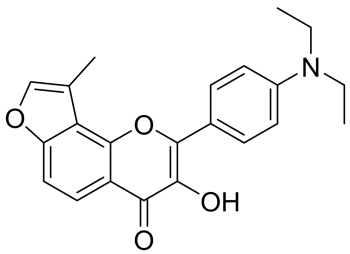
Yellow solid. Yield: 75%. m.p. 208.6-209.8 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.74 (s, 2H), 7.67 (d, *J* = 8.8 Hz, 1H), 7.50 (q, *J* = 1.3 Hz, 1H), 7.44 (d, *J* = 8.7 Hz, 1H), 4.01 (s, 6H), 3.98 (s, 3H), 2.55 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.25, 161.53, 158.43, 153.10, 150.38, 141.94, 135.71, 129.92, 116.76, 114.88, 114.47, 114.19, 109.08, 106.79, 106.75, 61.04, 56.17, 9.45. HRMS (EI) *m/z*: 382.1053 (M^{+}); calc. for $C_{21}H_{18}O_7$: 382.1053.

2-(4-(dimethylamino)phenyl)-3-hydroxy-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (12i)



Yellow solid. Yield: 65%. m.p. 277.6-279.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.16 (dd, *J* = 34.8, 8.7 Hz, 3H), 7.56 – 7.41 (m, 2H), 7.05 (s, 1H), 6.94 – 6.80 (m, 2H), 3.09 (s, 6H), 2.66 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.18, 159.03, 158.01, 152.56, 150.73, 141.53, 136.03, 128.33, 127.78, 120.80, 117.17, 115.60, 115.39, 111.77, 109.46, 40.07, 9.90. HRMS (EI) *m/z*: 335.1157 (M^{+}); calc. for $C_{20}H_{17}NO_4$: 335.1158.

2-(4-(diethylamino)phenyl)-3-hydroxy-9-methyl-4H-furo[2,3-h]chromen-4-one (12j)



Yellow solid. Yield: 67%. m.p. 253.8-254.5 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (dd, *J* = 23.0, 8.7 Hz, 3H), 7.54 – 7.42 (m, 2H), 7.02 (s, 1H), 6.80 (d, *J* = 8.7 Hz, 2H), 3.46 (q, *J* = 7.1 Hz, 4H), 2.66 (d, *J* = 1.2 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.49, 158.42, 151.12, 148.47, 146.06, 141.95, 136.71, 129.07, 124.65, 121.25, 117.63, 116.12, 111.07, 109.81, 103.60, 44.47, 12.64, 10.42. HRMS (EI) *m/z*: 363.1473 (M^{+}); calc. for $C_{22}H_{21}NO_4$: 363.1471.

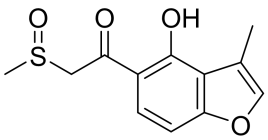
General procedure for the synthesis of angular 3-methylfuranoflavones

The mixture of dry DMSO (5.2 mL) and NaH (36.4 mmol, 60% dispersion in mineral oil) in dry toluene (60 mL) was heated under N_2 at 80 °C for 2 h. The solution was cooled to 40 °C, and to

the stirred solution was added dropwise a solution of **9** (7.2 mmol) in dry toluene (8 mL). The reaction mixture was then stirred for at 40 °C for 1 h, diluted with ether (75 mL), and quenched with a saturated solution of NH_4Cl (60 mL). The organic layer was separated, and the aqueous layer was extracted with ether (30 mL × 3). The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by column chromatography to afford **13** (95%) as a yellow solid.

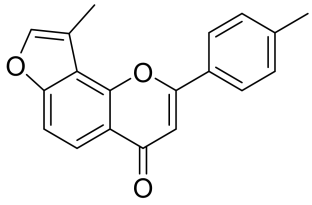
To the warm solution (40 °C) of **13** (0.42 mmol) in dry toluene (15 mL) containing a catalytic amount of piperidine (4 drops) was added dropwise a solution of substituted benzaldehyde (4.2 mmol) in dry toluene. The resulting mixture was allowed to reflux for 3 h. After the solvent was removed under reduced pressure, the residue was added 10 mL EtOH and stirred to precipitation. The resulting precipitate was filtrated, then washed with EtOH to afford pure product as a colorful solid. Products **14a-14ab** were obtained in this way, which were pure enough for most purposes.

1-(4-hydroxy-3-methylbenzofuran-5-yl)-2-(methylsulfinyl)ethan-1-one (13)



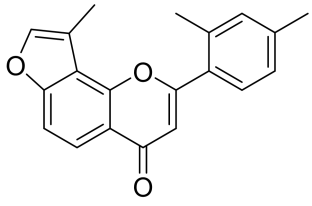
Yellow solid. Yield: 95%. m.p. 142.9-143.6 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 12.80 (s, 1H), 7.57 (d, *J* = 8.9 Hz, 1H), 7.31 (t, *J* = 1.6 Hz, 1H), 7.00 (d, *J* = 9.0 Hz, 1H), 4.45 (d, *J* = 13.9 Hz, 1H), 4.31 (d, *J* = 13.9 Hz, 1H), 2.78 (s, 3H), 2.39 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 196.19, 161.31, 161.14, 141.28, 127.18, 118.00, 117.30, 113.94, 104.80, 62.05, 39.44, 9.53.

9-methyl-2-(*p*-tolyl)-4*H*-furo[2,3-*h*]chromen-4-one (14a)



White solid. Yield: 87%. m.p. 170.1-172.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 8.8 Hz, 1H), 7.82 – 7.74 (m, 2H), 7.52 – 7.39 (m, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 6.81 (s, 1H), 2.59 (d, *J* = 1.3 Hz, 3H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.15, 162.77, 158.82, 151.89, 142.24, 142.08, 129.87, 128.98, 125.90, 121.57, 119.17, 117.73, 115.73, 110.11, 107.25, 21.53, 10.21. HRMS (EI) *m/z*: 290.0944 (M^+); calc. for $C_{19}H_{14}O_3$: 290.0943.

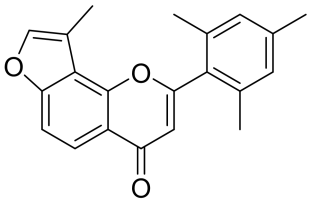
2-(2,4-dimethylphenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14b)



White solid. Yield: 89%. m.p. 200.8-201.6 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.16 (d, *J* = 8.8 Hz, 1H), 7.52 – 7.45 (m, 3H), 7.16 (d, *J* = 7.9 Hz, 2H), 6.52 (s, 1H), 2.49 (s, 3H), 2.45 (d, *J* =

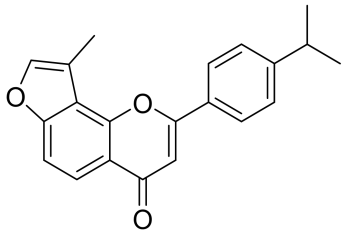
1.4 Hz, 3H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 177.57, 164.59, 158.38, 151.91, 141.74, 140.42, 135.96, 131.58, 129.52, 128.68, 126.53, 121.17, 118.53, 117.23, 115.41, 112.01, 109.73, 20.85, 19.96, 9.30. HRMS (EI) *m/z*: 304.1102 (M^+); calc. for $C_{20}H_{16}O_3$: 304.1099.

2-mesityl-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14c)



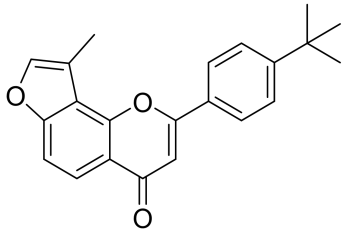
Yellowish brown solid. Yield: 83%. m.p. 215.1-216.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.17 (d, *J* = 8.8 Hz, 1H), 7.56 – 7.42 (m, 2H), 7.37 (s, 1H), 7.13 (s, 1H), 6.56 (s, 1H), 2.49 – 2.43 (m, 6H), 2.32 (d, *J* = 4.5 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.11, 165.26, 158.87, 142.19, 139.57, 134.52, 133.79, 132.62, 130.30, 130.21, 121.68, 119.06, 115.91, 112.40, 110.18, 19.92, 19.65, 19.27, 9.78. HRMS (EI) *m/z*: 318.1259 (M^+); calc. for $C_{21}H_{18}O_3$: 318.1256.

2-(4-isopropylphenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14d)



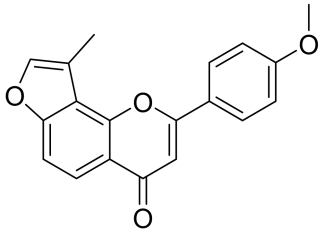
White solid. Yield: 90%. m.p. 175.2-177.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 8.8 Hz, 1H), 7.90 – 7.83 (m, 2H), 7.52 – 7.37 (m, 4H), 6.87 (s, 1H), 3.01 (hept, *J* = 6.9 Hz, 1H), 2.63 (d, *J* = 1.4 Hz, 3H), 1.31 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.23, 162.90, 158.87, 152.94, 151.98, 142.26, 129.36, 127.32, 126.13, 121.60, 119.18, 117.78, 115.76, 110.17, 107.35, 34.16, 23.75, 10.23. HRMS (EI) *m/z*: 318.1255 (M^+); calc. for $C_{21}H_{18}O_3$: 318.1256.

2-(4-(tert-butyl)phenyl)-9-methyl-4H-furo[2,3-h]chromen-4-one (14e)



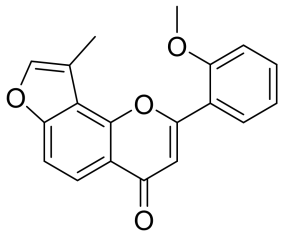
Yellowish brown solid. Yield: 80%. m.p. 238.1-239.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 8.7 Hz, 1H), 7.89 – 7.84 (m, 2H), 7.60 – 7.55 (m, 2H), 7.49 (q, *J* = 1.3 Hz, 1H), 7.46 (d, *J* = 8.7 Hz, 1H), 6.86 (s, 1H), 2.63 (d, *J* = 1.3 Hz, 3H), 1.38 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.22, 162.81, 158.87, 155.20, 151.98, 142.25, 128.99, 126.19, 125.86, 121.61, 119.22, 117.79, 115.78, 110.15, 107.41, 35.06, 31.15, 10.25. HRMS (EI) *m/z*: 332.1417 (M^+); calc. for $C_{22}H_{20}O_3$: 332.1412.

2-(4-methoxyphenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14f)



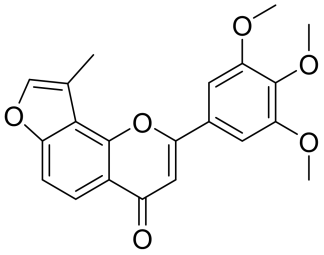
White solid. Yield: 90%. m.p. 224.0-225.5 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.11 (d, *J* = 8.7 Hz, 1H), 7.93 – 7.81 (m, 2H), 7.55 – 7.40 (m, 2H), 7.10 – 6.98 (m, 2H), 6.81 (s, 1H), 3.90 (s, 3H), 2.62 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.14, 162.75, 162.29, 158.85, 151.89, 142.25, 127.71, 124.06, 121.59, 119.05, 117.72, 115.69, 114.60, 110.12, 106.44, 55.53, 10.30. HRMS (EI) *m/z*: 306.0895 (M^{+}); calc. for $C_{19}H_{14}O_4$: 306.0892.

2-(2-methoxyphenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14g)



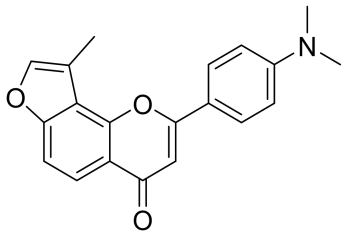
White solid. Yield: 92%. m.p. 242.7-244.8 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 8.8 Hz, 1H), 7.90 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.55 – 7.43 (m, 3H), 7.20 (s, 1H), 7.16 – 7.04 (m, 2H), 3.96 (s, 3H), 2.56 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.63, 160.32, 158.82, 157.94, 152.27, 142.10, 132.33, 128.96, 121.62, 120.95, 120.79, 119.01, 117.72, 115.87, 112.93, 111.81, 110.03, 55.65, 10.00. HRMS (EI) *m/z*: 306.0886 (M^{+}); calc. for $C_{19}H_{14}O_4$: 306.0892.

9-methyl-2-(3,4,5-trimethoxyphenyl)-4*H*-furo[2,3-*h*]chromen-4-one (14h)



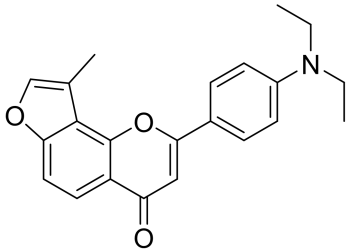
White solid. Yield: 95%. m.p. 239.1-241.9 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.11 (d, *J* = 8.8 Hz, 1H), 7.56 – 7.44 (m, 2H), 7.18 (s, 2H), 6.84 (s, 1H), 3.96 (s, 6H), 3.95 (s, 3H), 2.65 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.10, 162.24, 158.93, 153.61, 151.84, 142.43, 140.99, 126.86, 121.63, 119.07, 117.70, 115.42, 110.31, 107.37, 103.28, 61.08, 56.21, 10.17. HRMS (EI) *m/z*: 366.1109 (M^{+}); calc. for $C_{21}H_{18}O_6$: 366.1103.

2-(4-(dimethylamino)phenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14i)



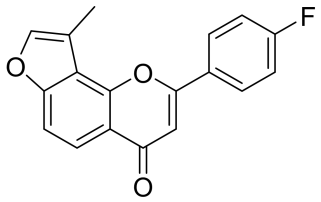
Yellow solid. Yield: 85%. m.p. 240.1-241.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 8.7 Hz, 1H), 7.77 – 7.66 (m, 2H), 7.44 (q, *J* = 1.2 Hz, 1H), 7.39 (d, *J* = 8.8 Hz, 1H), 6.71 – 6.64 (m, 3H), 3.00 (s, 6H), 2.57 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.09, 163.54, 158.63, 152.14, 151.74, 142.00, 127.28, 121.47, 119.13, 118.11, 117.63, 115.74, 111.64, 109.62, 104.45, 40.02, 10.33. HRMS (EI) *m/z*: 319.1209 (M^+); calc. for $C_{20}H_{17}NO_3$: 319.1208.

2-(4-(diethylamino)phenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14j)



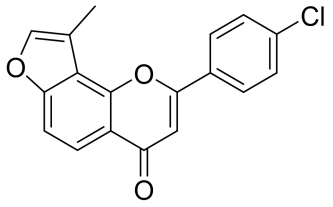
Yellow solid. Yield: 87%. m.p.198.8-199.8 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 8.7 Hz, 1H), 7.83 – 7.72 (m, 2H), 7.55 – 7.36 (m, 2H), 6.73 (d, *J* = 10.8 Hz, 3H), 3.43 (q, *J* = 7.1 Hz, 4H), 2.62 (d, *J* = 1.3 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.12, 163.67, 158.66, 151.80, 149.93, 142.00, 127.67, 121.54, 119.18, 117.66, 115.76, 111.24, 111.22, 109.62, 104.27, 44.59, 12.57, 10.37. HRMS (EI) *m/z*: 347.1522 (M^+); calc. for $C_{22}H_{21}NO_3$: 347.1521.

2-(4-fluorophenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14k)



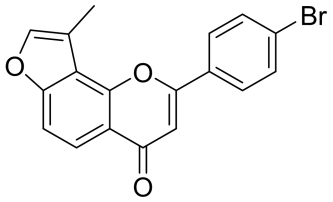
White solid. Yield: 83%. m.p. 250.1-251.1 °C,
^{1}H NMR (400 MHz, Acetone-d_6) δ 7.94 (d, *J* = 7.2 Hz, 1H), 7.83 – 7.72 (m, 2H), 7.48 – 7.37 (m, 2H), 7.26 – 7.21 (m, 2H), 6.89 (s, 1H), 3.42 (d, *J* = 1.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.04, 163.40, 161.75, 158.98, 151.93, 142.42, 128.21 (d, *J* = 8.8 Hz), 128.10 (d, *J* = 3.3 Hz), 121.65, 119.07, 117.76, 116.47 (d, *J* = 22.2 Hz), 115.63, 110.42, 107.74, 10.26. HRMS (EI) *m/z*: 294.0692 (M^+); calc. for $C_{18}H_{11}FO_3$: 294.0692.

2-(4-chlorophenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14l)



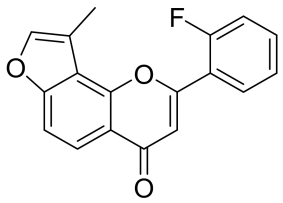
White solid. Yield: 86%. m.p. 242.8-243.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 8.8 Hz, 1H), 7.89 – 7.79 (m, 2H), 7.58 – 7.40 (m, 4H), 6.83 (s, 1H), 2.60 (d, *J* = 1.2 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.01, 161.51, 158.98, 151.91, 142.44, 137.76, 130.37, 129.54, 127.25, 121.66, 117.77, 115.63, 110.45, 108.13, 10.26. HRMS (EI) *m/z*: 310.0399 (M^{+}); calc. for $C_{18}H_{11}ClO_3$: 310.0397.

2-(4-bromophenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14m)



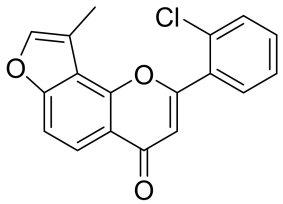
White solid. Yield: 83%. m.p. 293.1-294.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 8.8 Hz, 1H), 7.83 – 7.75 (m, 2H), 7.73 – 7.63 (m, 2H), 7.57 – 7.45 (m, 2H), 6.87 (s, 1H), 2.61 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.97, 161.61, 158.99, 151.91, 142.45, 132.51, 130.81, 127.42, 126.19, 121.65, 119.14, 117.77, 115.63, 110.49, 108.09, 10.25. HRMS (EI) *m/z*: 353.9891 (M^{+}); calc. for $C_{18}H_{11}BrO_3$: 353.9892.

2-(2-fluorophenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14n)



Light green solid. Yield: 85%. m.p. 195.1-196.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 8.7 Hz, 1H), 7.89 (td, *J* = 7.6, 1.7 Hz, 1H), 7.57 – 7.41 (m, 3H), 7.34 (td, *J* = 7.6, 1.1 Hz, 1H), 7.28 – 7.20 (m, 1H), 6.96 (s, 1H), 2.55 (d, *J* = 1.3 Hz, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.04, 159.16, 158.89, 158.26, 152.03, 142.32, 132.82 (d, *J* = 9.1 Hz), 128.69 (d, *J* = 1.7 Hz), 124.75 (d, *J* = 3.7 Hz), 121.57, 120.40 (d, *J* = 10.1 Hz), 119.03, 117.71, 117.11 (d, *J* = 22.6 Hz), 115.83, 112.64 (d, *J* = 10.7 Hz), 110.35, 9.97. HRMS (EI) *m/z*: 294.0695 (M^{+}); calc. for $C_{18}H_{11}FO_3$: 294.0692.

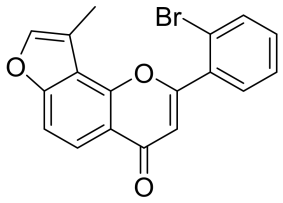
2-(2-chlorophenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14o)



White solid. Yield: 86%. m.p. 201.0-201.6 °C.

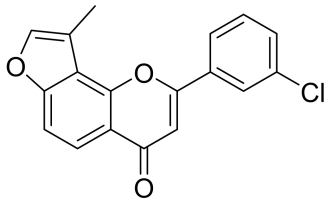
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.16 (d, *J* = 8.7 Hz, 1H), 7.67 (dd, *J* = 7.3, 2.0 Hz, 1H), 7.57 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.54 – 7.40 (m, 4H), 6.72 (s, 1H), 2.47 (d, *J* = 1.4 Hz, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.91, 161.99, 158.94, 152.36, 142.26, 132.89, 132.01, 131.80, 130.92, 130.72, 127.23, 121.61, 119.08, 117.85, 116.13, 113.39, 110.43, 9.69. HRMS (EI) *m/z*: 310.0397 (M^+); calc. for $C_{18}H_{11}ClO_3$: 310.0397.

2-(2-bromophenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14p)



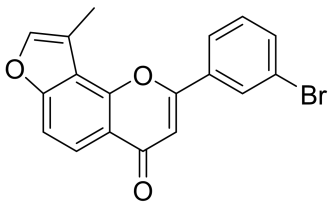
Yellowish solid. Yield: 89%. m.p. 189.3-191.0 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.16 (d, *J* = 8.7 Hz, 1H), 7.76 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.62 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.55 – 7.45 (m, 3H), 7.41 (td, *J* = 7.7, 1.8 Hz, 1H), 6.65 (s, 1H), 2.47 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.90, 163.24, 158.96, 152.34, 142.24, 134.19, 134.02, 131.90, 130.99, 127.75, 121.81, 121.62, 119.13, 117.87, 116.18, 113.26, 110.44, 9.74. HRMS (EI) *m/z*: 353.9893 (M^+); calc. for $C_{18}H_{11}BrO_3$: 353.9892.

2-(3-chlorophenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14q)



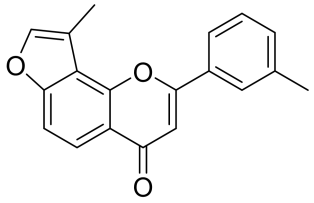
White solid. Yield: 86%. m.p. 272.1-273.1 °C.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 8.8 Hz, 1H), 7.93 (t, *J* = 1.9 Hz, 1H), 7.82 (dt, *J* = 7.4, 1.7 Hz, 1H), 7.59 – 7.46 (m, 4H), 6.90 (s, 1H), 2.64 (d, *J* = 1.3 Hz, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.98, 161.08, 159.04, 151.92, 142.50, 135.38, 133.69, 131.42, 130.49, 126.20, 124.09, 121.66, 119.19, 117.81, 115.68, 110.56, 108.56, 10.20. HRMS (EI) *m/z*: 310.0396 (M^+); calc. for $C_{18}H_{11}ClO_3$: 310.0397.

2-(3-bromophenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14r)



White solid. Yield: 89%. m.p. 239.8-239.9 °C.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 – 8.04 (m, 2H), 7.84 (dt, *J* = 7.9, 1.4 Hz, 1H), 7.68 (ddd, *J* = 8.0, 1.9, 1.0 Hz, 1H), 7.56 – 7.37 (m, 3H), 6.85 (s, 1H), 2.62 (d, *J* = 1.2 Hz, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.91, 160.88, 159.01, 151.87, 142.49, 134.30, 133.87, 130.69, 129.11, 124.49, 123.33, 121.64, 119.18, 117.79, 115.66, 110.52, 108.54, 10.16. HRMS (EI) *m/z*: 353.9891 (M^+); calc. for $C_{18}H_{11}BrO_3$: 353.9892.

9-methyl-2-(m-tolyl)-4*H*-furo[2,3-*h*]chromen-4-one (14s)

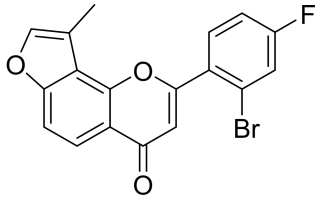


White solid. Yield: 85%. m.p. 170.8-172.0 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.11 (d, *J* = 8.8 Hz, 1H), 7.75 – 7.69 (m, 2H), 7.50 (q, *J* = 1.4 Hz, 1H), 7.46 (d, *J* = 8.8 Hz, 1H), 7.45 – 7.40 (m, 1H), 7.36 (d, *J* = 7.6 Hz, 1H), 6.86 (s, 1H), 2.62 (d, *J* = 1.3 Hz, 3H), 2.46 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.22, 162.81, 158.88, 151.97, 142.30, 138.91, 132.28, 131.79, 129.06, 126.68, 123.16, 121.60, 119.19, 117.78, 115.73, 110.22, 107.84, 21.61, 10.16. HRMS (EI) *m/z*: 290.0947 (M^+); calc. for $C_{19}H_{14}O_3$: 290.0943.

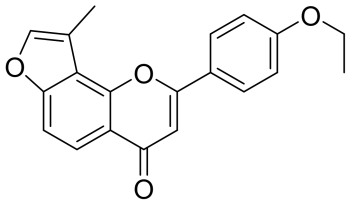
2-(2-bromo-4-fluorophenyl)-9-methyl-4H-furo[2,3-h]chromen-4-one (14t)



White solid. Yield: 83%. m.p. 207.5-208.4 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 8.8 Hz, 1H), 7.63 (dd, *J* = 8.6, 5.8 Hz, 1H), 7.55 – 7.45 (m, 3H), 7.22 (ddd, *J* = 8.5, 7.7, 2.5 Hz, 1H), 6.62 (s, 1H), 2.46 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.74, 162.26, 162.08, 158.96, 152.26, 142.31, 132.31 (d, *J* = 9.1 Hz), 130.56 (d, *J* = 3.8 Hz), 122.56 (d, *J* = 9.7 Hz), 121.60, 121.51 (d, *J* = 24.9 Hz), 119.06, 117.81, 116.07, 115.22 (d, *J* = 21.5 Hz), 113.37, 110.50, 9.74. HRMS (EI) *m/z*: 371.9795 (M^+); calc. for $C_{18}H_{10}BrFO_3$: 371.9797.

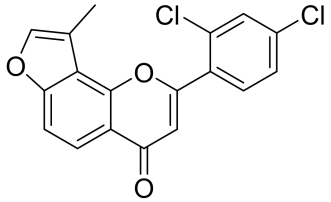
2-(4-ethoxyphenyl)-9-methyl-4H-furo[2,3-h]chromen-4-one (14u)



White solid. Yield: 85%. m.p. 217.5-219.0 °C.

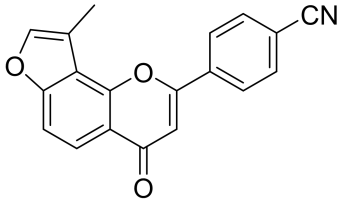
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 8.7 Hz, 1H), 7.92 – 7.72 (m, 2H), 7.48 (d, *J* = 1.6 Hz, 1H), 7.44 (d, *J* = 8.7 Hz, 1H), 7.13 – 6.91 (m, 2H), 6.77 (s, 1H), 4.11 (q, *J* = 7.0 Hz, 2H), 2.60 (d, *J* = 1.4 Hz, 3H), 1.47 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.10, 162.69, 161.67, 158.80, 151.84, 142.21, 127.63, 123.82, 121.57, 119.17, 117.70, 115.69, 115.00, 110.03, 106.39, 63.79, 14.73, 10.29. HRMS (EI) *m/z*: 320.1048 (M^+); calc. for $C_{20}H_{16}O_4$: 320.1049.

2-(2,4-dichlorophenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14v)



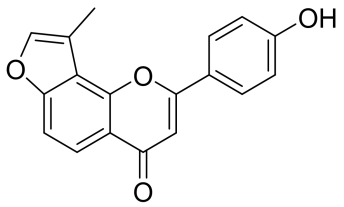
Light green solid. Yield: 87%. m.p. 220.8-222.0 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 8.8 Hz, 1H), 7.62 (d, *J* = 8.3 Hz, 1H), 7.59 (d, *J* = 2.0 Hz, 1H), 7.51 (d, *J* = 8.8 Hz, 1H), 7.48 (q, *J* = 1.3 Hz, 1H), 7.44 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.70 (s, 1H), 2.46 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.65, 160.81, 158.97, 152.28, 142.35, 137.43, 133.73, 131.42, 130.85, 130.51, 127.71, 121.62, 119.06, 117.80, 116.01, 113.53, 110.54, 9.69. HRMS (EI) *m/z*: 344.0008 (M^{+}); calc. for $C_{18}H_{10}Cl_2O_3$: 344.0007.

4-(9-methyl-4-oxo-4*H*-furo[2,3-*h*]chromen-2-yl)benzonitrile (14w)



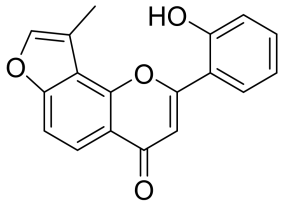
Light green solid. Yield: 80%. m.p. 333.2-334.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 (d, *J* = 8.8 Hz, 1H), 8.09 – 8.03 (m, 2H), 7.91 – 7.83 (m, 2H), 7.59 – 7.50 (m, 2H), 6.95 (s, 1H), 2.64 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 177.75, 160.22, 159.17, 151.95, 142.65, 136.12, 132.96, 126.51, 121.73, 119.27, 117.92, 117.83, 115.56, 114.89, 110.84, 109.73, 10.30. HRMS (EI) *m/z*: 301.0739 (M^{+}); calc. for $C_{19}H_{11}NO_3$: 301.0739.

2-(4-hydroxyphenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14x)



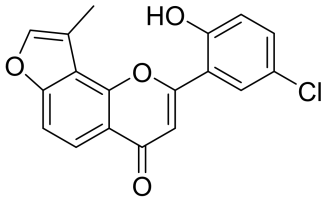
Yellowish solid. Yield: 82%. m.p. 350.1-351.1 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.34 (s, 1H), 7.98 – 7.92 (m, 2H), 7.90 (d, *J* = 9.8 Hz, 2H), 7.61 (d, *J* = 8.7 Hz, 1H), 6.96 (d, *J* = 8.3 Hz, 2H), 6.88 (s, 1H), 2.57 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 176.46, 162.49, 160.79, 157.92, 151.01, 143.34, 128.01, 121.61, 120.77, 118.58, 117.37, 115.99, 115.29, 109.97, 105.14, 9.79. HRMS (EI) *m/z*: 292.0735 (M^{+}); calc. for $C_{18}H_{12}O_4$: 292.0736.

2-(2-hydroxyphenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14y)



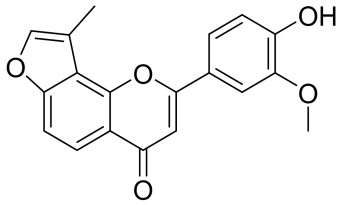
Yellowish brown solid. Yield: 80%. m.p. 236.1-237.1 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.98 (d, J = 1.6 Hz, 1H), 7.96 – 7.89 (m, 2H), 7.67 (d, J = 8.7 Hz, 1H), 7.42 (ddd, J = 8.6, 7.3, 1.7 Hz, 1H), 7.17 (s, 1H), 7.12 – 7.03 (m, 3H), 2.56 (d, J = 1.4 Hz, 3H).
^{13}C NMR (101 MHz, DMSO-d_6) δ 176.81, 160.25, 157.98, 156.47, 151.36, 143.35, 132.47, 128.21, 120.81, 119.54, 118.48, 117.76, 117.43, 117.07, 115.39, 111.33, 110.10, 9.63. HRMS (EI) *m/z*: 292.0739 (M^+); calc. for $C_{18}H_{12}O_4$: 292.0736.

2-(5-chloro-2-hydroxyphenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14z)



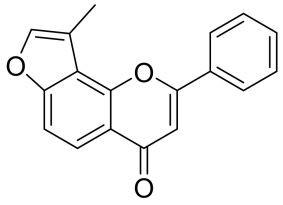
Dark red solid. Yield: 81%. m.p. 388.2-389.2 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.12 (s, 1H), 7.96 (d, J = 1.6 Hz, 1H), 7.93 – 7.85 (m, 2H), 7.64 (d, J = 8.7 Hz, 1H), 7.45 (dd, J = 8.8, 2.7 Hz, 1H), 7.18 (s, 1H), 7.09 (d, J = 8.8 Hz, 1H), 2.53 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 176.74, 158.57, 158.01, 155.39, 151.20, 143.43, 131.86, 127.47, 123.04, 120.77, 119.08, 118.81, 118.41, 117.40, 115.26, 111.72, 110.18, 9.44. HRMS (EI) *m/z*: 326.0342 (M^+); calc. for $C_{18}H_{11}ClO_4$: 326.0346.

2-(4-hydroxy-3-methoxyphenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (14aa)



Yellowish brown solid. Yield: 83%. m.p. 320.1-321.1 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.96 (s, 1H), 7.96 (d, J = 1.6 Hz, 1H), 7.90 (d, J = 8.8 Hz, 1H), 7.66 – 7.49 (m, 3H), 7.01 – 6.93 (m, 2H), 3.90 (s, 3H), 2.59 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 176.54, 162.29, 157.94, 150.97, 150.20, 147.92, 143.39, 121.86, 120.78, 119.78, 118.58, 117.38, 115.83, 115.28, 109.98, 109.60, 105.30, 55.59, 9.70. HRMS (EI) *m/z*: 322.0848 (M^+); calc. for $C_{19}H_{14}O_5$: 322.0841.

9-methyl-2-phenyl-4*H*-furo[2,3-*h*]chromen-4-one (14ab)



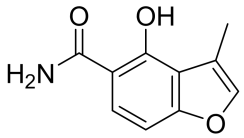
White solid. Yield: 88%. m.p. 185.5-185.7 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 8.7 Hz, 1H), 7.93 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.60 – 7.52 (m, 3H), 7.50 (d, *J* = 1.7 Hz, 1H), 7.47 (d, *J* = 8.7 Hz, 1H), 6.88 (s, 1H), 2.62 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.18, 162.64, 158.92, 151.99, 142.33, 131.87, 131.49, 129.18, 126.02, 121.62, 119.20, 117.79, 115.75, 110.29, 107.96, 10.24. HRMS (EI) *m/z*: 276.0787 (M^+); calc. for $C_{18}H_{12}O_3$: 276.0786.

General procedure for the Synthesis of angular 3-methylfuranoisoquinolinones

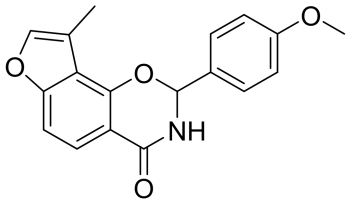
A solution of **9** (3 mmol) in methanol (15 mL) was saturated with ammonia and heated to 65 °C for 24 h in a Fisher-Porter bottle. The excess of methanol and ammonia was removed under vacuum at 40 °C to provide pure intermediate **15**. To a solution of **15** (0.42 mmol), and substituted benzaldehyde (1.26 mmol) in dry toluene (20 mL) were added followed by the catalytic amount of piperidine. The resulting mixture was allowed to reflux for 12 h. After removing the solvent under reduced pressure, the residue was purified by column chromatography to afford the product **16** as a white solid. Target compounds **16a-16i** were obtained using this procedure.

4-hydroxy-3-methylbenzofuran-5-carboxamide (15)



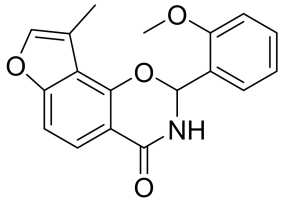
White solid. Yield: 100%. m.p. 191.5-192.5 °C. ^{1}H NMR (400 MHz, Chloroform-*d*)δ 14.32 (s, 1H), 8.40 (s, 1H), 7.87 (s, 1H), 7.75 (d, *J* = 8.8 Hz, 1H), 7.65 (q, *J* = 1.3 Hz, 1H), 7.02 (d, *J* = 8.8 Hz, 1H), 2.33 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 173.38, 158.90, 158.44, 141.19, 124.09, 117.13, 115.87, 106.98, 102.54, 9.35. HRMS (EI) *m/z*: 191.0583 (M^+); calc. for $C_{10}H_9NO_3$: 191.0582.

2-(4-methoxyphenyl)-9-methyl-2,3-dihydro-4*H*-benzofuro[5,4-*e*][1,3]oxazin-4-one (16a)



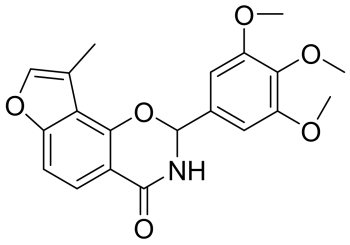
Yellowish solid. Yield: 78%. m.p. > 400 °C.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 (d, *J* = 8.7 Hz, 1H), 7.62 – 7.52 (m, 2H), 7.33 (q, *J* = 1.3 Hz, 1H), 7.19 (d, *J* = 8.6 Hz, 1H), 7.05 – 6.95 (m, 2H), 6.31 (s, 1H), 6.22 (s, 1H), 3.86 (s, 3H), 2.27 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.39, 161.02, 159.96, 153.55, 141.65, 128.31, 128.14, 124.28, 117.51, 115.98, 114.35, 111.65, 106.78, 85.66, 55.42, 9.48. HRMS (EI) *m/z*: 309.1004 (M^+); calc. for $C_{18}H_{15}NO_4$: 309.1001.

2-(2-methoxyphenyl)-9-methyl-2,3-dihydro-4*H*-benzofuro[5,4-*e*][1,3]oxazin-4-one (16b)



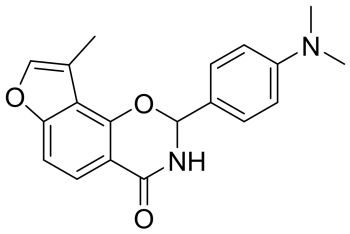
White solid. Yield: 78%. m.p. 171.0-172.7 °C.
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 8.6 Hz, 1H), 7.74 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.43 (ddd, *J* = 8.3, 7.5, 1.7 Hz, 1H), 7.35 (q, *J* = 1.3 Hz, 1H), 7.18 (d, *J* = 8.7 Hz, 1H), 7.09 (td, *J* = 7.6, 1.0 Hz, 1H), 6.98 (dd, *J* = 8.3, 1.0 Hz, 1H), 6.69 (s, 1H), 6.33 (s, 1H), 3.88 (s, 3H), 2.35 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.53, 159.86, 156.34, 153.59, 141.63, 130.88, 126.85, 124.28, 124.22, 121.01, 117.56, 115.94, 111.71, 110.71, 106.68, 81.11, 55.51, 9.54. HRMS (EI) *m/z*: 309.1003 (M^+); calc. for $C_{18}H_{15}NO_4$: 309.1001.

9-methyl-2-(3,4,5-trimethoxyphenyl)-2,3-dihydro-4*H*-benzofuro[5,4-*e*][1,3]oxazin-4-one (16c)



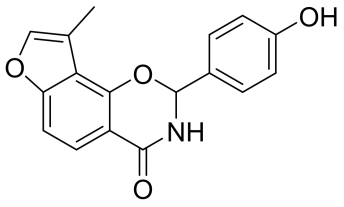
White solid. Yield: 75%. m.p. 205.3-206.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 8.7 Hz, 1H), 7.36 (q, *J* = 1.3 Hz, 1H), 7.21 (d, *J* = 8.7 Hz, 1H), 6.86 (s, 2H), 6.30 (s, 2H), 3.91 (d, *J* = 3.4 Hz, 9H), 2.32 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.37, 159.97, 153.62, 153.31, 141.80, 139.13, 131.43, 124.22, 117.52, 115.83, 111.69, 106.92, 103.70, 85.71, 60.90, 56.22, 9.54. HRMS (EI) *m/z*: 369.1220 (M^+); calc. for $C_{20}H_{19}NO_6$: 369.1212.

2-(4-(dimethylamino)phenyl)-9-methyl-2,3-dihydro-4*H*-benzofuro[5,4-*e*][1,3]oxazin-4-one (16d)



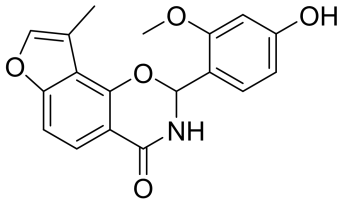
White solid. Yield: 70%. m.p. 184.5-186.7 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 8.6 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.32 (d, *J* = 1.5 Hz, 1H), 7.18 (d, *J* = 8.7 Hz, 1H), 6.80 (d, *J* = 8.2 Hz, 2H), 6.26 (d, *J* = 1.1 Hz, 1H), 5.97 (s, 1H), 3.03 (s, 6H), 2.27 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 164.05, 159.43, 153.35, 147.88, 141.04, 127.54, 123.80, 117.76, 117.01, 115.59, 111.65, 111.17, 106.12, 85.68, 39.98, 9.00. HRMS (EI) *m/z*: 322.1310 (M^+); calc. for $C_{19}H_{18}N_2O_3$: 322.1317.

2-(4-hydroxyphenyl)-9-methyl-2,3-dihydro-4*H*-benzofuro[5,4-*e*][1,3]oxazin-4-one (16e)



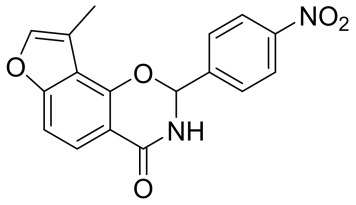
White solid. Yield: 71%. m.p. 260.1-261.1 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.72 (s, 1H), 8.80 (d, J = 2.1 Hz, 1H), 7.75 (d, J = 1.7 Hz, 1H), 7.70 (d, J = 8.6 Hz, 1H), 7.47 – 7.37 (m, 2H), 7.26 (d, J = 8.6 Hz, 1H), 6.86 – 6.78 (m, 2H), 6.39 (d, J = 1.8 Hz, 1H), 2.23 (d, J = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 163.13, 158.71, 158.41, 152.57, 142.49, 128.57, 127.22, 123.64, 116.92, 115.12, 115.07, 112.31, 105.99, 85.13, 9.11. HRMS (EI) *m/z*: 295.0842 (M $^{+}$); calc. for $C_{17}H_{13}NO_4$: 295.0845.

2-(4-hydroxy-2-methoxyphenyl)-9-methyl-2,3-dihydro-4*H*-benzofuro[5,4-*e*][1,3]oxazin-4-one (16f)



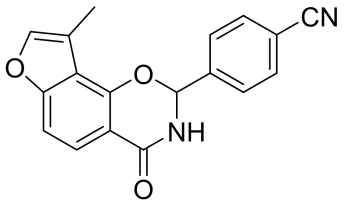
White solid. Yield: 70%. m.p. > 400 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.30 (s, 1H), 8.82 (d, J = 2.0 Hz, 1H), 7.77 (d, J = 1.6 Hz, 1H), 7.70 (d, J = 8.6 Hz, 1H), 7.27 (d, J = 8.6 Hz, 1H), 7.17 (d, J = 2.0 Hz, 1H), 7.01 (dd, J = 8.2, 2.0 Hz, 1H), 6.82 (d, J = 8.1 Hz, 1H), 6.39 (d, J = 1.8 Hz, 1H), 3.79 (s, 3H), 2.26 (d, J = 1.5 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 163.11, 158.71, 152.55, 147.62, 147.41, 142.55, 127.56, 123.65, 119.97, 116.93, 115.05, 112.35, 110.89, 106.04, 99.49, 85.18, 55.52, 9.14. HRMS (EI) *m/z*: 325.0950 (M $^{+}$); calc. for $C_{18}H_{15}NO_5$: 325.0950.

9-methyl-2-(4-nitrophenyl)-2,3-dihydro-4*H*-benzofuro[5,4-*e*][1,3]oxazin-4-one (16g)



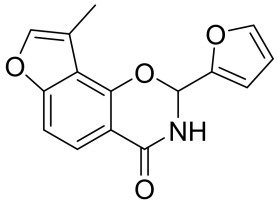
Yellowish solid. Yield: 60%. m.p. 238.9-239.9 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.14 (d, J = 2.6 Hz, 1H), 8.40 – 8.24 (m, 2H), 7.95 – 7.83 (m, 2H), 7.79 (q, J = 1.2 Hz, 1H), 7.70 (d, J = 8.6 Hz, 1H), 7.28 (d, J = 8.6 Hz, 1H), 6.74 (d, J = 2.4 Hz, 1H), 2.30 (d, J = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.39, 158.81, 151.82, 148.04, 144.11, 142.80, 128.36, 123.75, 123.63, 117.04, 115.02, 112.29, 106.52, 83.53, 9.15. HRMS (EI) *m/z*: 324.0753 (M $^{+}$); calc. for $C_{17}H_{12}N_2O_5$: 324.0746.

4-(9-methyl-4-oxo-3,4-dihydro-2*H*-benzofuro[5,4-*e*][1,3]oxazin-2-yl)benzonitrile (16h)



Yellowish solid. Yield: 62%. m.p. 258.2-261.0 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.13 – 9.05 (m, 1H), 7.96 (d, J = 8.0 Hz, 2H), 7.79 (d, J = 7.0 Hz, 3H), 7.69 (d, J = 8.6 Hz, 1H), 7.28 (d, J = 8.6 Hz, 1H), 6.68 (d, J = 2.3 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.48, 158.79, 151.90, 142.79, 142.23, 132.62, 127.88, 123.63, 118.36, 117.01, 115.01, 112.27, 112.15, 106.49, 83.77, 9.15. HRMS (EI) *m/z*: 304.0845 (M^+); calc. for $C_{18}H_{12}N_2O_3$: 304.0848.

2-(furan-2-yl)-9-methyl-2,3-dihydro-4*H*-benzofuro[5,4-*e*][1,3]oxazin-4-one (16i)

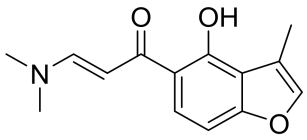


Yellow solid. Yield: 60%. m.p. 175.0-176.0 °C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.87 (d, J = 8.6 Hz, 1H), 7.50 (d, J = 1.7 Hz, 1H), 7.33 (d, J = 1.6 Hz, 1H), 7.18 (d, J = 8.7 Hz, 1H), 6.64 (d, J = 3.4 Hz, 1H), 6.54 (s, 1H), 6.48 – 6.41 (m, 2H), 2.33 (d, J = 1.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.76, 159.98, 152.58, 148.87, 143.93, 141.75, 140.75, 124.14, 115.98, 111.63, 110.76, 110.40, 106.99, 79.17, 9.42. HRMS (EI) *m/z*: 269.0687 (M^+); calc. for $C_{15}H_{11}NO_4$: 269.0688.

General procedure for the synthesis of angular 3-methylfuranoisoflavones

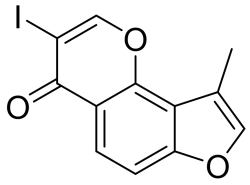
A solution of **8** (1 mmol) and *N,N*-dimethylformamide dimethyl acetal (3.5 mmol) in DMF (10 mmol) was heated to 70-75 °C for 4 h. To the cooled reaction mixture was added saturated brine (20 mL), and a green product was precipitated from the solution. The reaction mixture was filtered, and a green precipitation of **17** (99 %) was obtained. A solution of **17** in $CHCl_3$ (15 mL) was added I_2 (3 mmol, 3 equiv.), and the mixture was stirred at room temperature for 12 h. The reaction was quenched by adding 10 mL 5% aqueous $NaHSO_3$, and the aqueous layer was extracted with $CHCl_3$ (3 × 10 mL). The combined organic layer was washed with 5% aqueous $NaHCO_3$, dried over Na_2SO_4. Evaporation of the solvent gave a residue, which was purified by column chromatography to afford the product **18** (90 %). A mixture of Na_2CO_3 (0.212 g, 2 mmol), $Pd(OAc)_2$ (2 mg, 1 mol %), PEG 10000 (3.5 g), and methanol (3 mL) was heated to 50 °C with stirring. Then **18** (1 mmol) and arylboronic acid (1.5 mmol) was added to the solution, and the mixture was stirred at 50 °C for 4 h. After being cooled to room temperature, the reaction solution was diluted with H_2O (30 mL) and extracted with diethyl ether (4 × 15 mL). The collected organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by column chromatography to afford the product **19**. Target compounds **19a-19e** were obtained using this procedure.

(*E*)-3-(dimethylamino)-1-(4-hydroxy-3-methylbenzofuran-5-yl)prop-2-en-1-one (17)



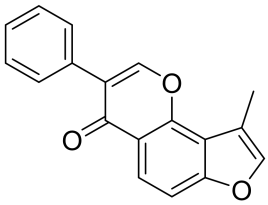
Green solid. Yield: 99%. m.p.152.7-153.5 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.09 (s, 1H), 7.86 (d, *J* = 12.0 Hz, 1H), 7.58 (d, *J* = 8.8 Hz, 1H), 7.24 (t, *J* = 1.7 Hz, 1H), 6.87 (d, *J* = 9.0 Hz, 1H), 5.75 (d, *J* = 12.0 Hz, 1H), 3.15 (s, 3H), 2.93 (s, 3H), 2.43 (d, *J* = 1.7 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 191.77, 160.91, 159.33, 154.17, 140.12, 124.83, 117.99， 117.18, 113.85, 102.41, 90.22, 45.30, 37.35, 9.73.

3-iodo-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (18)



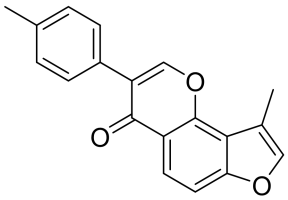
Yellow solid. Yield: 90%. m.p. 207.1-209.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.31 (s, 1H), 8.07 (d, *J* = 8.8 Hz, 1H), 7.48 – 7.38 (m, 2H), 2.40 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.95, 157.76, 155.76, 151.00, 141.52, 121.49, 116.53, 116.12, 114.99, 110.12, 86.80, 8.61. HRMS (EI) *m/z*: 325.9436 (M^+); calc. for $C_{12}H_7IO_3$: 325.9440.

9-methyl-3-phenyl-4*H*-furo[2,3-*h*]chromen-4-one (19a)



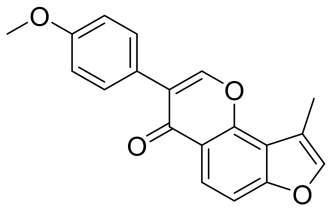
White solid. Yield: 65%. m.p. 159.1-160.3 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.22 (d, *J* = 8.8 Hz, 1H), 8.10 (s, 1H), 7.65 – 7.57 (m, 2H), 7.53 – 7.43 (m, 4H), 7.43 – 7.37 (m, 1H), 2.52 (d, *J* = 1.5 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 175.98, 158.73, 152.16, 152.10, 142.22, 131.90, 129.06, 128.49, 128.21, 125.77, 122.31, 119.86, 117.61, 116.05, 110.40, 9.70. HRMS (EI) *m/z*: 276.0789 (M^+); calc. for $C_{18}H_{12}O_3$: 276.0786.

9-methyl-3-(*p*-tolyl)-4*H*-furo[2,3-*h*]chromen-4-one (19b)



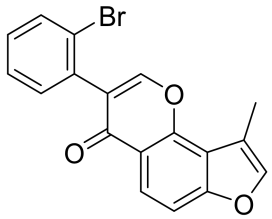
White solid. Yield: 67%. m.p. 120.0-121.2 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.20 (d, *J* = 8.8 Hz, 1H), 8.06 (s, 1H), 7.53 – 7.44 (m, 4H), 7.28 – 7.24 (m, 2H), 2.50 (d, *J* = 1.4 Hz, 3H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.04, 158.62, 152.03, 151.85, 142.14, 138.02, 129.17, 128.90, 128.87, 125.59, 122.25, 119.79, 117.53, 116.02, 110.24, 21.26, 9.66. HRMS (EI) *m/z*: 290.0938 (M^+); calc. for $C_{19}H_{14}O_3$: 290.0943.

3-(4-methoxyphenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (19c)



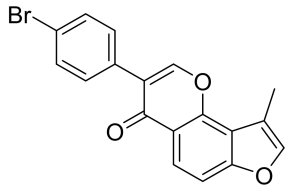
Light green solid. Yield: 70%. m.p. 133.1-134.1 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.21 (d, *J* = 8.8 Hz, 1H), 8.07 (s, 1H), 7.57 – 7.45 (m, 4H), 7.02 – 6.95 (m, 2H), 3.85 (s, 3H), 2.52 (d, *J* = 1.3 Hz, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.22, 159.63, 158.67, 152.10, 151.60, 142.15, 130.21, 125.33, 124.17, 122.30, 119.80, 117.57, 116.06, 113.98, 110.29, 55.34, 9.69. HRMS (EI) *m/z*: 306.0896 (M $^{+}$); calc. for $C_{19}H_{14}O_4$: 306.0892.

3-(2-bromophenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (19d)



White solid. Yield: 61%. m.p. 159.8-161.6 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.21 (d, *J* = 8.8 Hz, 1H), 8.02 (s, 1H), 7.70 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.57 – 7.45 (m, 2H), 7.43 – 7.32 (m, 2H), 7.31 – 7.26 (m, 1H), 2.53 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.74, 158.35, 152.97, 151.80, 141.82, 132.55, 131.79, 129.54, 126.91, 125.77, 124.37, 121.87, 119.30, 117.26, 115.60, 110.02, 9.22. HRMS (EI) *m/z*: 353.9894 (M $^{+}$); calc. for $C_{18}H_{11}BrO_3$: 353.9892.

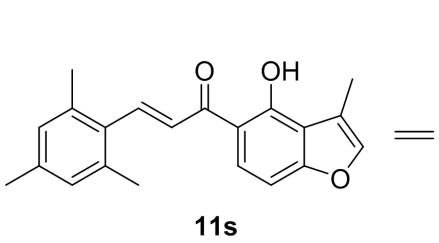
3-(4-bromophenyl)-9-methyl-4*H*-furo[2,3-*h*]chromen-4-one (19e)



White solid. Yield: 59%. m.p. 184.7-185.8 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.20 (d, *J* = 8.8 Hz, 1H), 8.10 (s, 1H), 7.61 – 7.54 (m, 2H), 7.54 – 7.44 (m, 4H), 2.51 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 175.65, 158.79, 152.07, 152.05, 142.33, 131.66, 130.83, 130.60, 124.74, 122.46, 122.23, 119.72, 117.63, 116.02, 110.56, 9.68. HRMS (EI) *m/z*: 353.9894 (M $^{+}$); calc. for $C_{18}H_{11}BrO_3$: 353.9892.

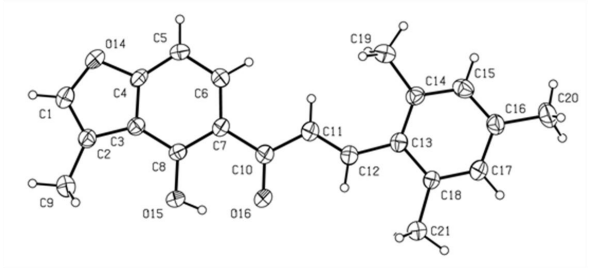
Determination of the configuration of 11s, 12c, 14h and 16a.

X-ray crystal data of 11s:



11s

=



Bond precision: C-C = 0.0064 A
Wavelength=0.71073

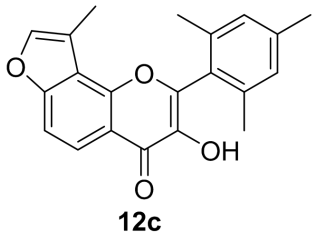
Cell:	a=7.2229(10)	alpha=90
	b=14.6972(14)	beta=97.746(11)
	c=15.7705(17)	gamma=90

Temperature: 293 K

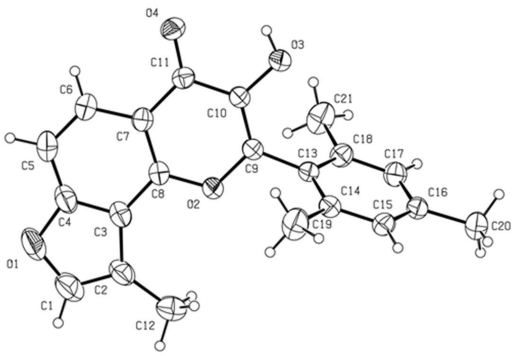
	Calculated	**Reported**
Volume	1658.9(3)	1658.9(3)
Space group	P 21/n	P 1 21/n 1
Hall group	-P 2yn	-P 2yn
Moiety formula	C21 H20 O3	C21 H20 O3
Sum formula	C21 H20 O3	C21 H20 O3
Mr	320.37	320.37
Dx,g cm^{-3}	1.283	1.283
Z	4	4
Mu (mm^{-1})	0.085	0.085
F000	680.0	680.0
F000’	680.33	
h,k,lmax	8,17,18	8,17,18
Nref	3034	3016
Tmin,Tmax	0.987,0.992	0.912,1.000
Tmin’	0.968	

Correction method= MULTI-SCAN
Data completeness= 0.994 Theta(max)= 25.350
R(reflections)= 0.1078(1884) wR2(reflections)= 0.2872(3016)
S = 1.169 Npar= 222

X-ray crystal data of 12c:



12c



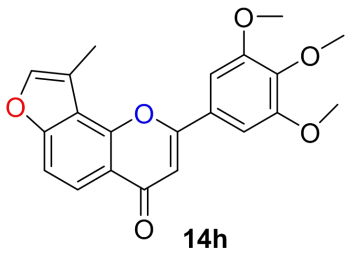
Bond precision: C-C = 0.0033 A
Wavelength= 0.71073
Cell: a=14.1228(16) alpha= 90
b=9.2810(8) beta= 114.071(14)
c=14.8338(16) gamma= 90

Temperature: 293 K

	Calculated	**Reported**
Volume	1775.2(4)	1775.3(3)
Space group	P 21/c	P 1 21/c 1
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C21 H18 O4	C21 H18 O4
Sum formula	C21 H18 O4	C21 H18 O4
Mr	334.35	334.35
Dx,g cm^{-3}	1.251	1.251
Z	4	4
Mu (mm^{-1})	0.086	0.086
F000	704.0	704.0
F000’	704.37	
h,k,lmax	17,11,17	17,11,17
Nref	3239	3236
Tmin,Tmax	0.975,0.980	0.935,1.000
Tmin’	0.975	

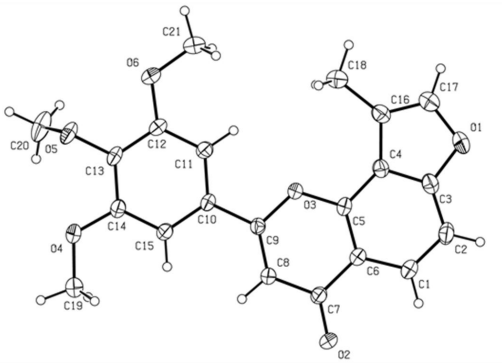
Correction method= MULTI-SCAN
Data completeness= 0.999 Theta(max)= 25.340
R(reflections)= 0.0476(2190) wR2(reflections)= 0.1400(3236)
S = 1.041 Npar= 231

X-ray crystal data of 14h:



14h

=



Bond precision: C-C = 0.0031 A

Wavelength=0.71073

Cell: a=7.8443(9) alpha=99.373(8)

b=8.5920(7) beta=104.877(10)

c=13.6376(15) gamma=99.890(8)

Temperature: 293 K

	Calculated	**Reported**
Volume	854.21(16)	854.21(15)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C21 H18 O6	C21 H18 O6
Sum formula	C21 H18 O6	C21 H18 O6
Mr	366.35	366.35
Dx,g cm^{-3}	1.424	1.424
Z	2	2
Mu (mm^{-1})	0.105	0.105
F000	384.0	384.0
F000’	384.22	
h,k,lmax	9,10,16	9,10,16
Nref	3128	3121
Tmin,Tmax	0.963,0.979	0.927,1.000
Tmin’	0.950	

Correction method= # Reported T Limits: Tmin=0.927 Tmax=1.000

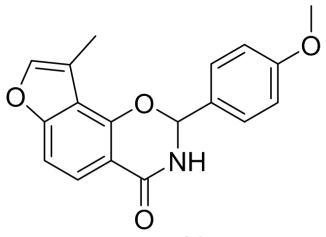
AbsCorr = MULTI-SCAN

Data completeness= 0.998 Theta(max)= 25.340

R(reflections)= 0.0467(2048) wR2(reflections)= 0.1254(3121)

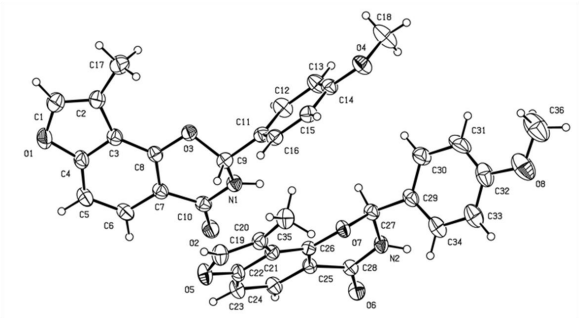
S = 1.023 Npar= 248

X-ray crystal data of 16a:



16a

=



Bond precision: C-C = 0.0044 A

Wavelength=0.71073

Cell: a=14.2605(10) alpha=90

b=12.4175(9) beta=110.920(9)

c=18.3015(14) gamma=90

Temperature: 293 K

	Calculated	**Reported**
Volume	3027.2(4)	3027.2(4)
Space group	P 21/n	P 1 21/n 1
Hall group	-P 2yn	-P 2yn
Moiety formula	C18 H15 N O4	C18 H15 N O4
Sum formula	C18 H15 N O4	C18 H15 N O4
Mr	309.31	309.31
Dx,g cm^{-3}	1.357	1.357
Z	8	8
Mu (mm^{-1})	0.097	0.097
F000	1296.0	1296.0
F000’	1296.68	
h,k,lmax	17,14,22	17,14,22
Nref	5537	5519
Tmin,Tmax	0.957,0.973	0.925,1.000

Tmin’ 0.957

Correction method= # Reported T Limits: Tmin=0.925 Tmax=1.000

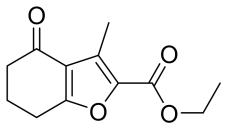
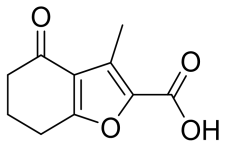
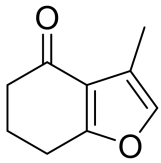
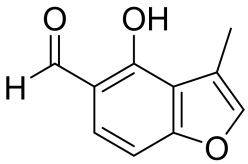
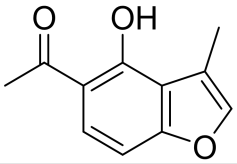
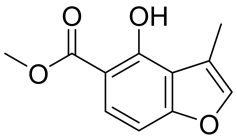
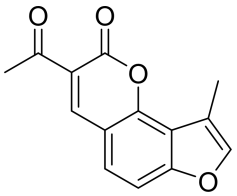
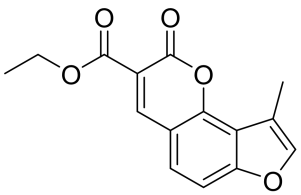
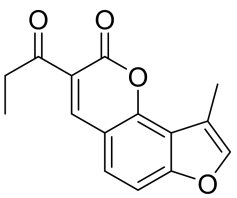
AbsCorr = MULTI-SCAN

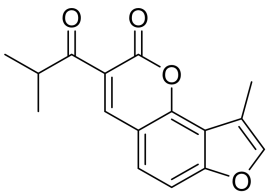
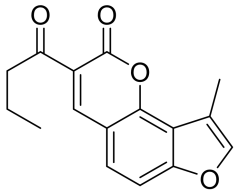
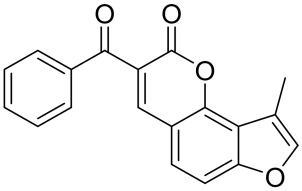
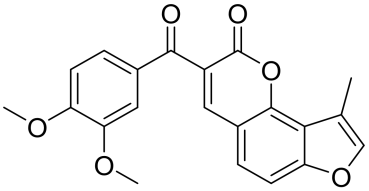
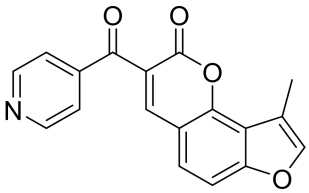
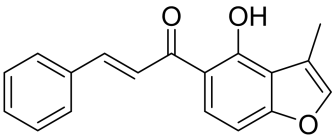
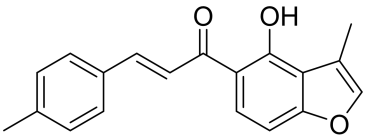
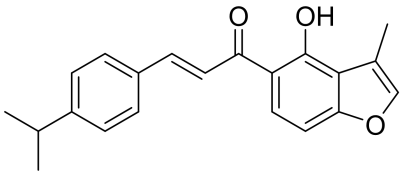
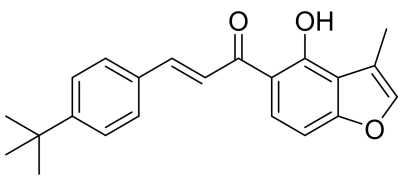
Data completeness= 0.997 Theta(max)= 25.350

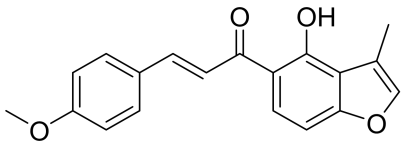
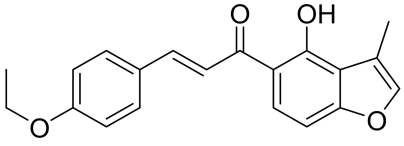
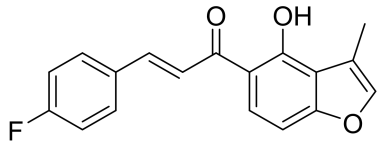
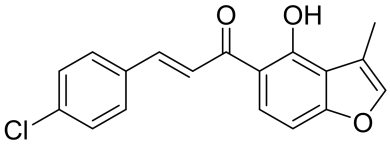
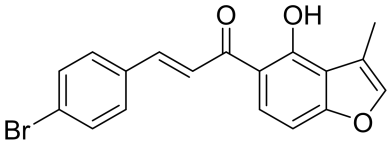
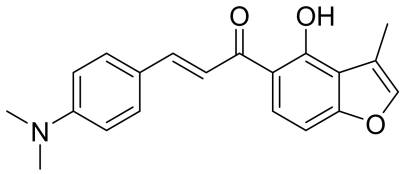
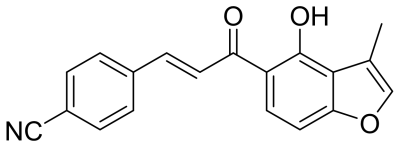
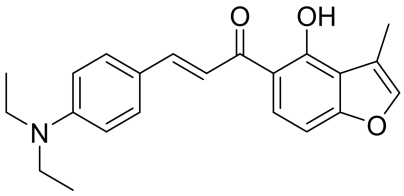
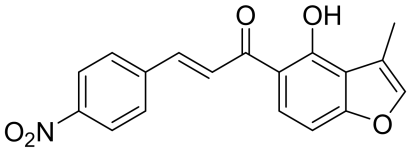
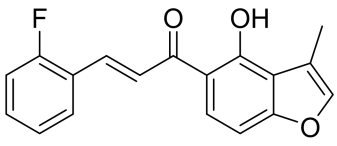
R(reflections)= 0.0584(3559) wR2(reflections)= 0.1685(5519)

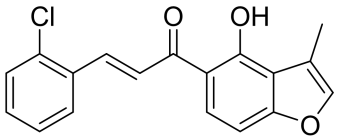
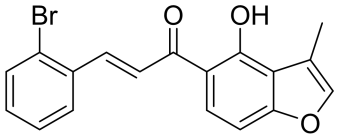
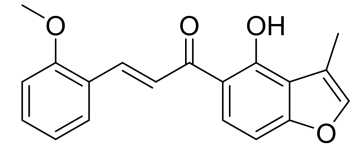
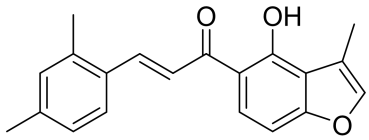
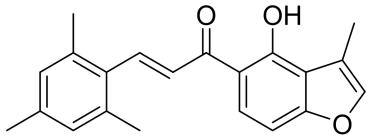
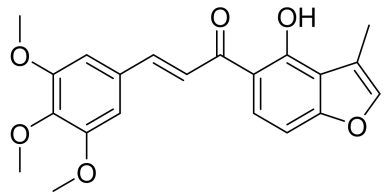
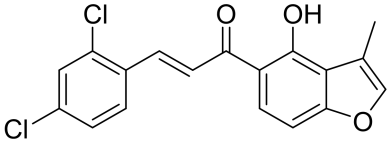
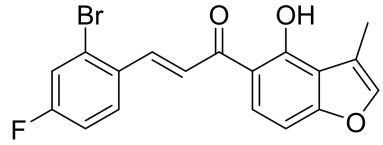
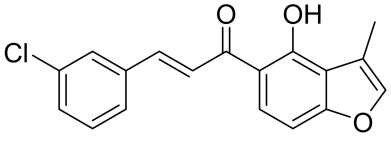
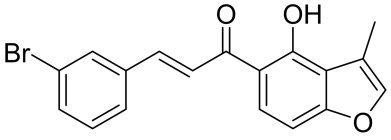
S = 1.030 Npar= 419

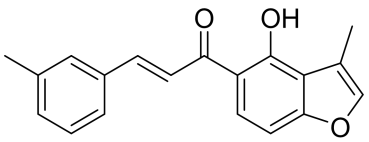
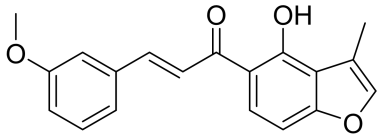
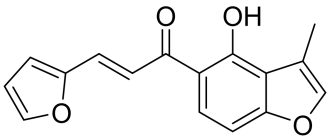
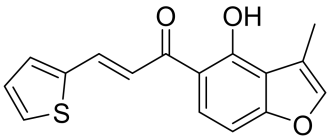
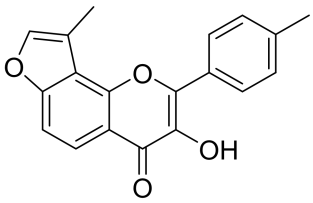
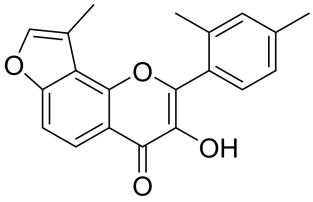
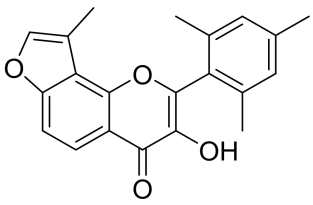
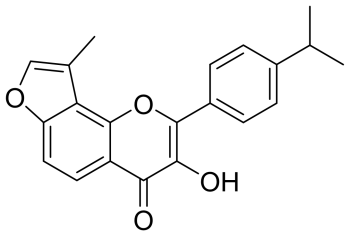
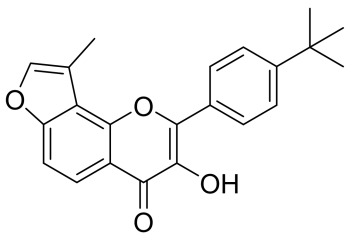
Supplementary Table 2. Relative induction of GUS activity in rice by compounds

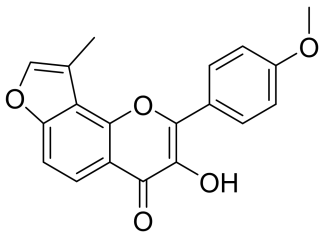
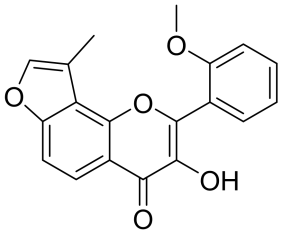
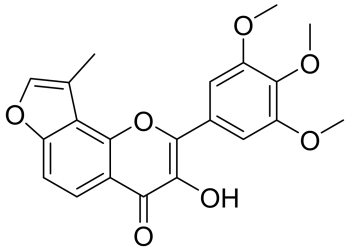
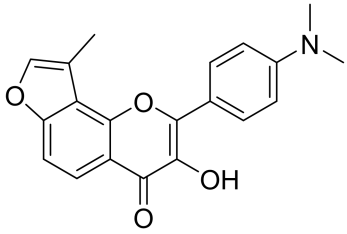
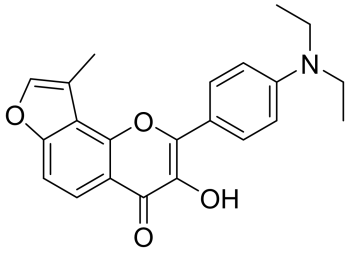
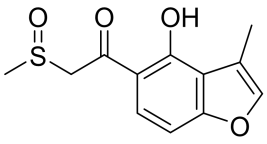
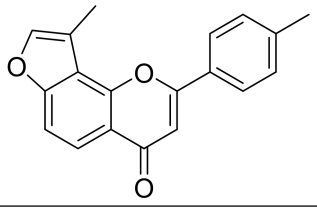
Compound	Structure	Relative induction of GUS activity[a]
1		1.09
2		0.98
3		1.68**
7		0.77
8		0.96
9		0.62
10a		0.79
10b		1.00
10c		0.90

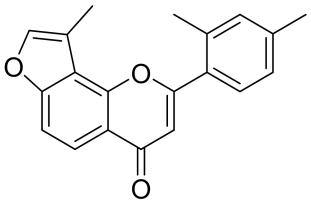
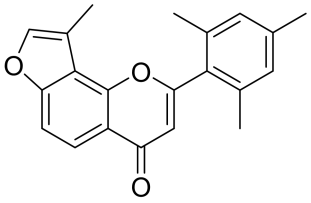
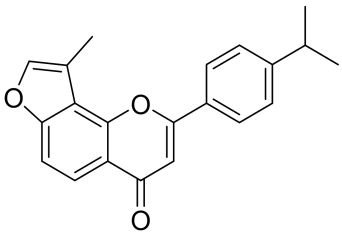
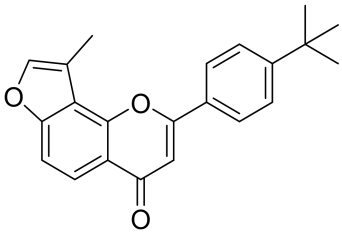
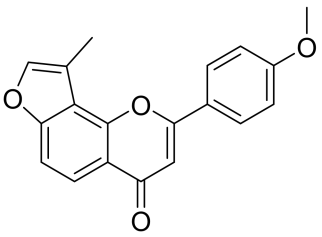
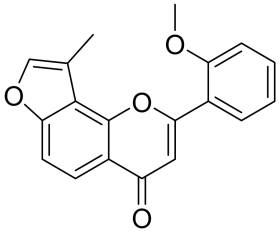
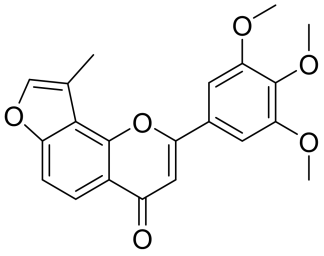
10d		1.01
10e		0.96
10f		1.24
10g		0.95
10h		1.24*
11a		1.55**
11b		1.39
11c		0.71
11d		1.83**

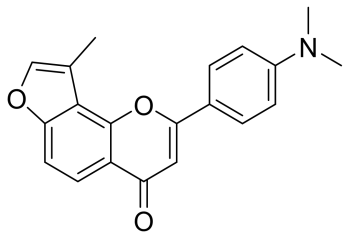
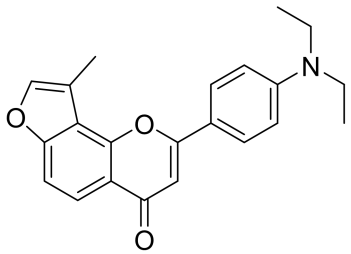
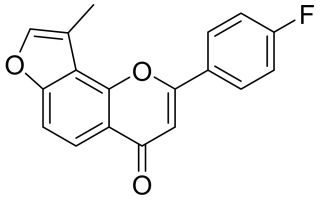
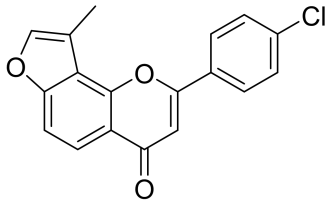
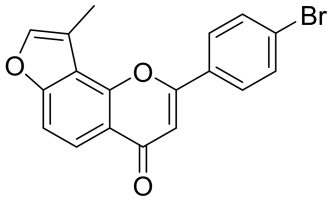
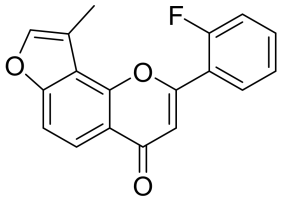
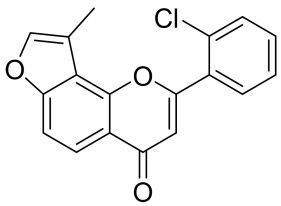
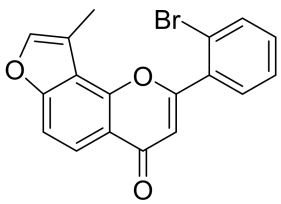
11e		1.05
11f		1.61**
11g		1.15
11h		1.53**
11i		1.15
11j		0.73*
11k		1.51**
11l		0.78
11m		1.20
11n		1.54

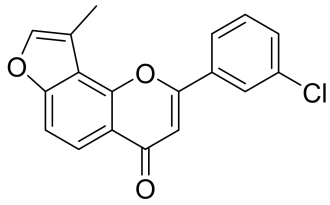
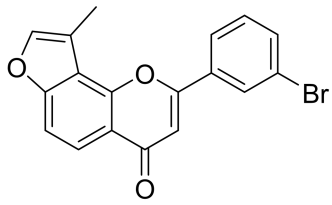
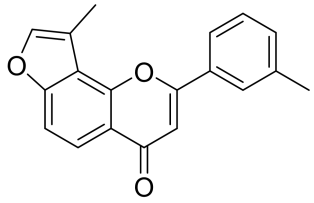
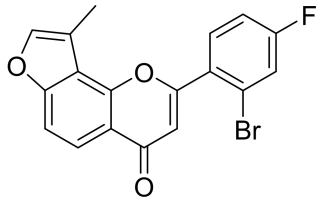
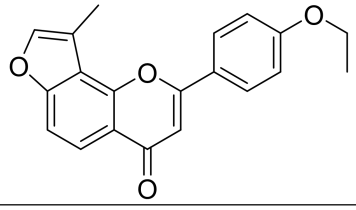
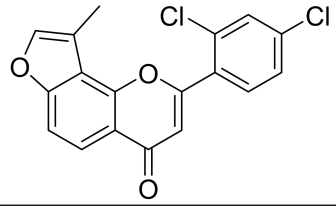
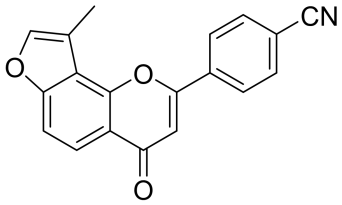
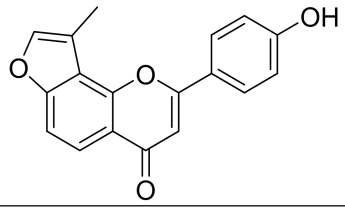
11o		1.43*
11p		0.77
11q		1.21
11r		2.11**
11s		1.33*
11t		1.18
11u		1.53*
11v		1.48**
11w		1.22
11x		1.28*

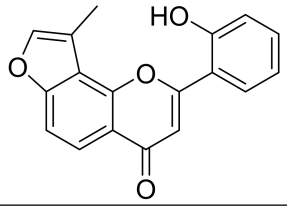
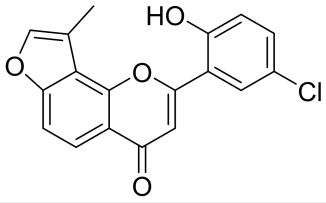
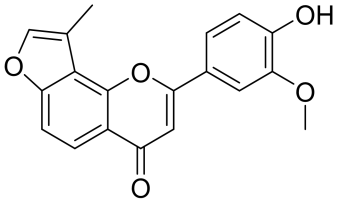
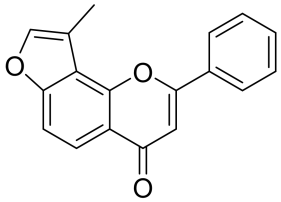
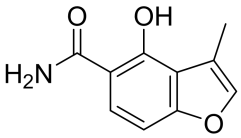
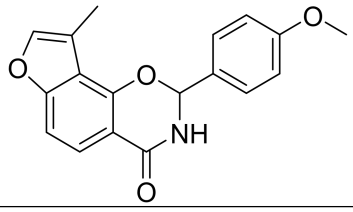
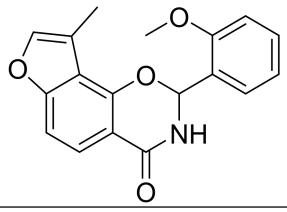
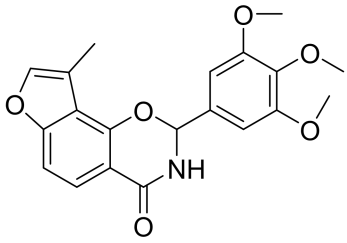
11y		1.80**
11z		1.21
11aa		1.40*
11ab		1.26
12a		1.34**
12b		1.33**
12c		1.16
12d		0.31**
12e		1.24*

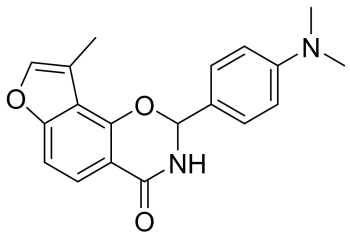
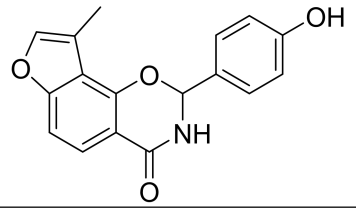
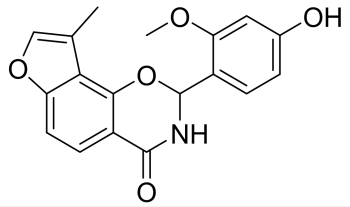
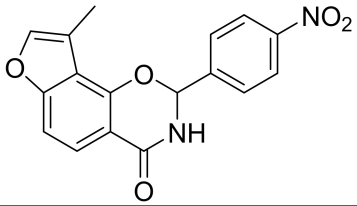
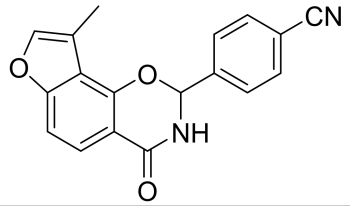
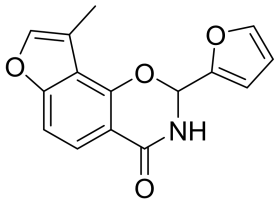
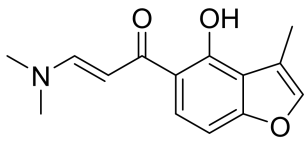
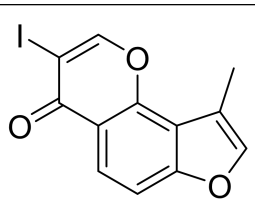
12f		1.05
12g		1.56**
12h		1.18
12i		1.12
12j		0.95
13		1.10
14a		0.85

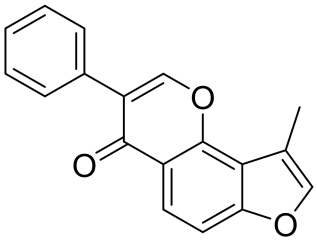
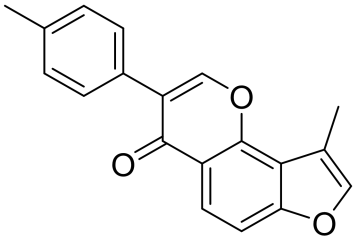
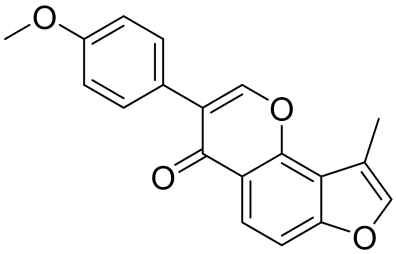
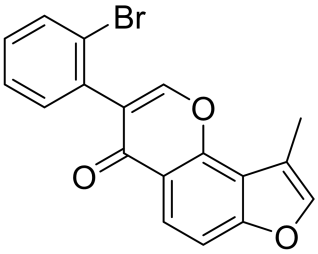
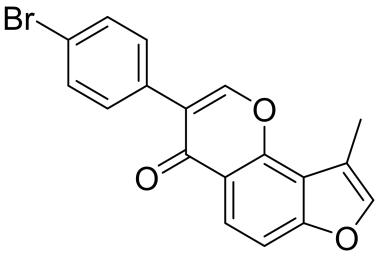
14b		1.20
14c		0.86
14d		0.79
14e		1.05
14f		1.11
14g		0.94
14h		1.01

14i		1.38
14j		1.04
14k		0.99
14l		1.13
14m		1.23
14n		0.97
14o		1.12
14p		0.90

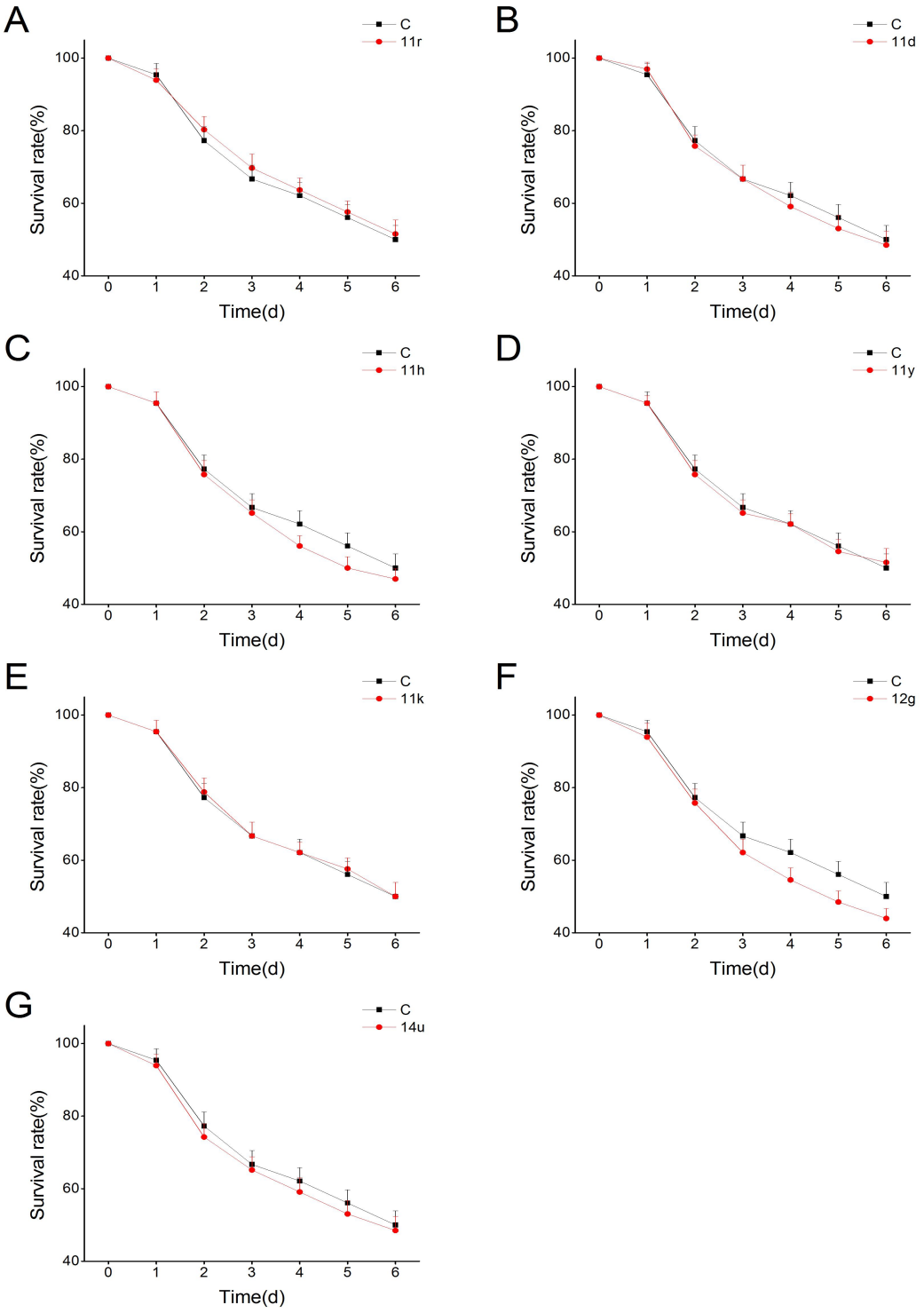
14q		1.58*
14r		1.51*
14s		1.40**
14t		1.38
14u		1.61**
14v		0.85
14w		1.34
14x		1.21

14y		1.48
14z		1.21
14aa		1.39
14ab		1.11
15		0.81
16a		0.78
16b		0.63**
16c		0.72*

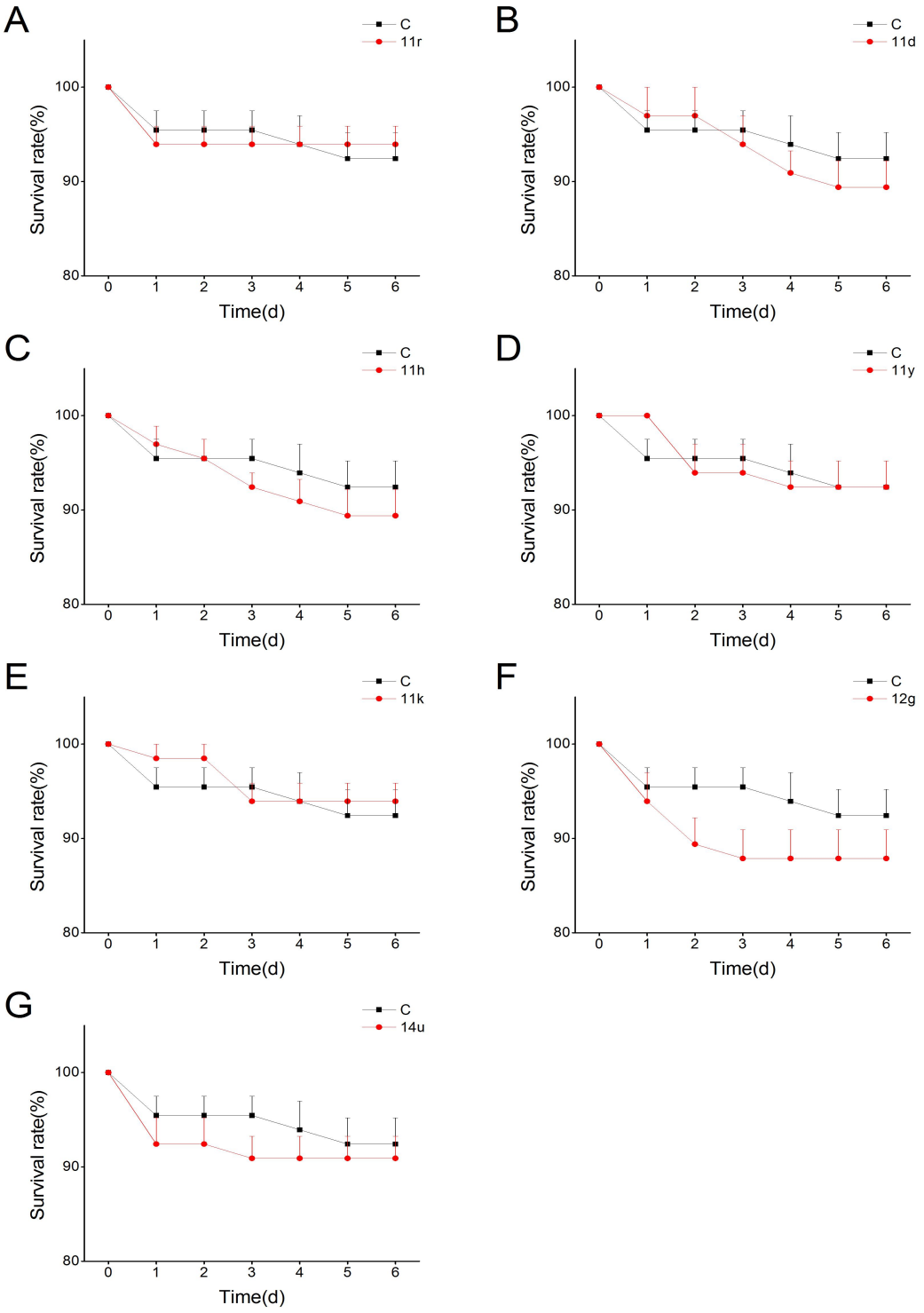
16d		0.98
16e		1.05
16f		1.13
16g		1.09
16h		1.15
16i		1.05
17		1.03
18		1.15

19a		0.99
19b		1.10
19c		1.05
19d		1.26
19e		1.21

[a] GUS activity level induced by the tested compound (5 mg L^{-1}) divided by the level induced by the control 48 h after treatment. Asterisks indicate significant differences between treatments and controls (*P <0.05, **P <0.01, Student's *t*-tests).



Supplementary Figure 1. Mean survival rate of *Nilaparvata lugens* nymphs (+SE, n = 6) fed on artificial diet that contained one of the compounds at a concentration of 20 $mg \cdot L^{-1}$ versus control groups fed on artificial diet only (C), 1-6 days after exposure. Asterisks indicate significant differences between compound treatments and controls at each time point (*P <0.05, **P <0.01, Student's t-tests).



Supplementary Figure 2. Mean survival rates of *Nilaparvata lugens* nymphs (+SE, n = 6) that had been sprayed with one of the compounds at a concentration of 20 mg·L^{-1} before being placed onto the plants versus mean survival rates of control groups, *Nilaparvata lugens* nymphs (+SE, n = 6) that had been sprayed with water only (C), 1-6 days after exposure. Asterisks indicate significant differences between treatments and controls at each time point (*P <0.05, **P <0.01, Student's t-tests).

Supplementary Table 3. Physicochemical properties used in PCA

Parameter	Description
ncarb	Count of C atoms
noxy	Count of O atoms
nta	Number of all atoms
naccr	Number of H-bond acceptors
ndonr	Number of H-bond donors
nrot	Number of rotatable bonds
MR	molar refractivity
phi	Kier molecular flexibility index
logP	LogP value based on the Crippen method
Rnc	Relative negative charge
Rpc	Relative positive charge
Tac	total of absolute charges
MSA	Molecular surface areas
ASA	Solvent-accessible surface areas
TPSA	Topological polarity surface area
RASA	Relative hydrophobic surface area
RNCS	Relative negative charge surface area
RPCS	Relative positive charge surface area
Tv	T total size index / weighted by atomic van der Waals volumes
ExactMolWt	The molecule's exact molecular weight.

Supplementary Table 4. Standard deviation and contribution of each principal component to variance

	PC1	PC2	PC3	PC4
Standard deviation	3.069	2.174	1.409	1.079
Proportion of Variance	47.090	23.636	9.930	5.823
Cumulative Proportion	47.090	70.725	80.655	86.478

Supplementary Table 5. Component loadings for PCA of library with established reference sets.

Parameter	PC1	PC2	PC3	PC4
ncarb	0.278694	0.204098	0.034114	-0.09093
noxy	0.102058	-0.26252	0.41624	-0.16286
nta	0.308028	0.051155	-0.13287	0.063423
naccr	0.180855	-0.29115	0.150677	-0.17505
ndonr	0.118171	-0.31097	-0.07951	0.333389
nrot	0.249186	-0.06009	-0.23868	0.419103
MR	0.268119	0.139421	-0.01984	-0.23901
phi	0.273069	-0.02007	-0.23564	0.349455
logP	0.105534	0.364543	0.145314	-0.13737
Rnc	-0.25322	0.202375	-0.06671	0.18875
Rpc	-0.20499	-0.00379	0.002526	0.395879
Tac	0.257715	-0.23353	0.156331	-0.10675
MSA	0.315255	0.062188	-0.11946	0.040557
ASA	0.311852	0.10732	-0.0627	0.013854
TPSA	0.145033	-0.37596	0.134846	0.033038
RASA	0.015512	0.38268	-0.2084	-0.17809
RNCS	0.058956	0.223944	0.544719	0.26623
RPCS	0.072118	0.250695	0.479067	0.341396
Tv	0.244553	0.18365	0.081461	0.092353
ExactMolWt	0.302859	0.059881	-0.05768	-0.10622

Supplementary Table 6. SMILES codes of 40 top-selling brand name drugs.

1	**Lipitor**	CC(C)C1=C(C(=C(N1CC[C@H](C[C@H](CC(=O)O)O)O)C2=CC=C(C=C2)F)C3=CC=CC=C3)C(=O)NC4=CC=CC=C4
2	**Nexium**	CC1=CN=C(C(=C1OC)C)CS(=O)C2=NC3=C(N2)C=C(C=C3)OC
3	**Prevacid**	CC1=C(C=CN=C1CS(=O)C2=NC3=CC=CC=C3N2)OCC(F)(F)F
4	**Flonase**	CCC(=O)O[C@@]1([C@@H](C[C@@H]2[C@@]1(C[C@@H]([C@]3([C@H]2C[C@@H](C4=CC(=O)C=C[C@@]43C)F)F)O)C)C)C(=O)SCF
5	**Serevent**	C1=CC=C(C=C1)CCCCOCCCCCCNCC(C2=CC(=C(C=C2)O)CO)O
6	**Singulair**	CC(C)(C1=CC=CC=C1CC[C@H](C2=CC=CC(=C2)\C=C\C3=NC4=C(C=CC(=C4)Cl)C=C3)SCC5(CC5)CC(=O)O)O
7	**Effexor**	CN(C)CC(C1=CC=C(C=C1)OC)C2(CCCCC2)O
8	**Plavix**	COC(=O)[C@H](C1=CC=CC=C1Cl)N2CCC3=C(C2)C=CS3
9	**Zocor**	CCC(C)(C)C(=O)O[C@H]1C[C@H](C=C2[C@H]1[C@H]([C@H](C=C2)C)CC[C@@H]3C[C@H](CC(=O)O3)O)C
10	**Norvasc**	CCOC(=O)C1=C(NC(=C(C1C2=CC=CC=C2Cl)C(=O)OC)C)COCCN
11	**Lexapro**	CN(C)CCC[C@@]1(C2=C(CO1)C=C(C=C2)C#N)C3=CC=C(C=C3)F
12	**Seroquel**	C1CN(CCN1CCOCCO)C2=NC3=CC=CC=C3SC4=CC=CC=C42
13	**Protonix**	COC1=C(C(=NC=C1)CS(=O)C2=NC3=C(N2)C=C(C=C3)OC(F)F)OC
14	**Ambien**	CC1=CC=C(C=C1)C2=C(N3C=C(C=CC3=N2)C)CC(=O)N(C)C
15	**Actos**	CCC1=CN=C(C=C1)CCOC2=CC=C(C=C2)CC3C(=O)NC(=O)S3
16	**Zoloft**	CN[C@H]1CC[C@H](C2=CC=CC=C12)C3=CC(=C(C=C3)Cl)Cl
17	**Wellbutrin**	CC(C(=O)C1=CC(=CC=C1)Cl)NC(C)(C)C
18	**Avandia**	CN(CCOC1=CC=C(C=C1)C[C@H]2C(=O)NC(=O)S2)C3=CC=CC=N3
19	**Risperdal**	CC1=C(C(=O)N2CCCCC2=N1)CCN3CCC(CC3)C4=NOC5=C4C=CC(=C5)F
20	**Zyprexa**	CC1=CC2=C(NC3=CC=CC=C3N=C2S1)N4CCN(CC4)C
21	**Topamax**	CC1(O[C@@H]2CO[C@@]3([C@H]([C@@H]2O1)OC(O3)(C)C)COS(=O)(=O)N)C
22	**Toprol**	CC(C)NCC(COC1=CC=C(C=C1)CCOC)O
23	**Zetia**	C1=CC(=CC=C1[C@@H]2[C@H](C(=O)N2C3=CC=C(C=C3)F)CC[C@@H](C4=CC=C(C=C4)F)O)O
24	**Fosamax**	C(CC(O)(P(=O)(O)O)P(=O)(O)O)CN
25	**Abilify**	C1CC(=O)NC2=C1C=CC(=C2)OCCCCN3CCN(CC3)C4=C(C(=CC=C4)Cl)Cl
26	**Levaquin**	C[C@H]1COC2=C3N1C=C(C(=O)C3=CC(=C2N4CCN(CC4)C)F)C(=O)O
27	**Lamictal**	C1=CC(=C(C(=C1)Cl)Cl)C2=C(N=C(N=N2)N)N
28	**Celebrex**	CC1=CC=C(C=C1)C2=CC(=NN2C3=CC=C(C=C3)S(=O)(=O)N)C(F)(F)F
29	**Benazepril**	CCOC(=O)[C@H](CCC1=CC=CC=C1)N[C@H]2CCC3=CC=CC=C3N(C2=O)CC(=O)O
30	**Zyrtec**	C1CN(CCN1CCOCC(=O)O)C(C2=CC=CC=C2)C3=CC=C(C=C3)Cl
31	**Coreg**	COC1=CC=CC=C1OCCNCC(COC2=CC=CC3=C2C4=CC=CC=C4N3)O
32	**Valtrex**	CC(C)[C@@H](C(=O)OCCOCN1C=NC2=C1NC(=NC2=O)N)N
33	**Adderall**	CC(CC1=CC=CC=C1)N
34	**Aciphex**	CC1=C(C=CN=C1CS(=O)C2=NC3=CC=CC=C3N2)OCCCOC
35	**Cymbalta**	CNCC[C@@H](C1=CC=CS1)OC2=CC=CC3=CC=CC=C32

36	**Crestor**	CC(C)C1=NC(=NC(=C1\C=C\[C@@H](C[C@H](CC(=O)O)O)O)C2=CC=C(C=C2)F)N(C)S(=O)(=O)C
37	**Diovan**	CCCCC(=O)N(CC1=CC=C(C=C1)C2=CC=CC=C2C3=NNN=N3)[C@@H](C(C)C)C(=O)O
38	**Tricor**	CC(C)OC(=O)C(C)(C)OC1=CC=C(C=C1)C(=O)C2=CC=C(C=C2)Cl
39	**Concerta**	COC(=O)C(C1CCCCN1)C2=CC=CC=C2
40	**Imitrex**	CNS(=O)(=O)CC1=CC2=C(C=C1)NC=C2CCN(C)C

Supplementary Table 7. SMILES codes of 20 coumarin and flavonoid natural products.

1	**allopsoralen**	O=C1OC2=CC=C3C(OC=C3)=C2C=C1
2	**angelicin**	O=C1OC2=C3C(OC=C3)=CC=C2C=C1
3	**xanthotoxol**	O=C1OC2=C(O)C3=C(C=CO3)C=C2C=C1
4	**Psoralen hydroquinone**	OC1=C2C(C=CO2)=C(O)C3=C1OC(C=C3)=O
5	**sphondin**	COC1=CC2=C(OC(C=C2)=O)C3=C1OC=C3
6	**2'-acetylangelicin**	O=C(O1)C=CC2=C1C(C=C(C(C)=O)O3)=C3C=C2
7	**glazarin**	O=C1C2=CC=C(OC(C)=O)C=C2OC(C)=C1C3=CC=CC=C3
8	**Sophoricol**	O=C1C2=C(O)C=C(O)C=C2OC=C1C3=CC=C(O)C=C3
9	**xenognosin B**	OC1=CC=C(C(C(C2=C(O)C=C(OC)C=C2)=CO3)=O)C3=C1
10	**4'-hydroxyflavone**	O=C1C2=CC=CC=C2OC(C3=CC=C(O)C=C3)=C1
11	**falvone**	O=C1C2=CC=CC=C2OC(C3=CC=CC=C3)=C1
12	**chrysin**	OC1=C2C(OC(C3=CC=CC=C3)=CC2=O)=CC(O)=C1
13	**kanjone**	O=C1C2=CC(OC)=C3C(C=CO3)=C2OC(C4=CC=CC=C4)=C1
14	**acacetin**	O=C1C=C(C2=CC=C(OC)C=C2)OC3=CC(O)=CC(O)=C31
15	**sophoretin**	OC1=CC(O)=C(C(C(O)=C(C2=CC=C(O)C(O)=C2)O3)=O)C3=C1
16	**chalcone**	O=C(C1=CC=CC=C1)/C=C/C2=CC=CC=C2
17	**alpinetin chalcone**	OC1=C(C(/C=C/C2=CC=CC=C2)=O)C(OC)=CC(O)=C1
18	**isoliquiritigenin**	OC1=CC=C(C(/C=C/C2=CC=C(O)C=C2)=O)C(O)=C1
19	**Lanceeolatin B**	O=C1C=C(C2=CC=CC=C2)OC3=C4C(OC=C4)=CC=C31
20	**karanjin**	O=C1C(OC)=C(C2=CC=CC=C2)OC3=C4C(OC=C4)=CC=C31