**MICROWAVE-ASSISTED SYNTHESIS AND ANTIFUNGAL ACTIVITIES
OF POLYSUBSTITUTED FURO[3,2-C]CHROMEN-4-ONES AND
7,8,9,10-TETRAHYDRO-6H-BENZOFURO[3,2-C]CHROMEN- 6-ONES**

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1. General Information

All materials were obtained from commercial sources and were used as received unless stated otherwise. Melting points were obtained on a WRS-1B melting point apparatus and are uncorrected. The microwave treatment was carried out in the microwave oven (WBFY-201, Gongyi Yuhua Instrument Co., Ltd) with emission frequency of 2450 MHz and maximum output power 800 W. NMR spectra were performed on a Bruker DRX-400 instrument (400 and 100 MHz for ^1H NMR and ^{13}C NMR respectively) using (TMS) as an internal stander and CDCl_3 as solvents. IR spectra were recorded on a Bruker Tensor 27, samples were prepared as KBr plates. The electron impact (EI) mass spectra were performed on a Thermo DSQ2 mass spectrometer at 70 eV. The Elemental analyses were performed on a VARIO EL cube (Elementar, Germany). For thin layer chromatography (TLC), silica gel GF/UV 254 was used.

2. Antifungal assay

The fungistatic activities of the synthesized compounds were measured according to the following procedures. Each of the test compounds was first prepared at 500 $\mu\text{g/mL}$ using Acetone as the solvent. The working solution (50 $\mu\text{g/mL}$) was obtained by diluting the stock solution (0.1 mL) with sterilized water (0.9 mL). The solutions (1 mL) were thoroughly mixed by shaking with thawed potato glucose (9 mL). The mixtures were poured into Petri dishes. After the dishes were cooled, the solidified plates were incubated with 5 mm mycelium disk and incubated in the culture tank at 25 °C. The solution of Acetone/distilled water (1 : 9 V/V) was used as the blank control. The diameter of fungus spread was measured 4—6 days later. The growth inhibition rates were calculated with the following equation: $Y = [(CK - A)/CK] \times 100\%$. Here, Y is the growth inhibition rate, CK is the control settlement radius, and A is the treatment group fungi settlement radius. The EC_{50} was calculated by the linear regression of logarithm of the concentration with probability of the corresponding growth inhibition by using professional statistical software DPS 7.05 version.

3. Characterization Data for Compounds 4a–j and 5a-e

3-Methyl-4H-furo[3,2-c]chromen-4-one(4a) White solid, m.p. 153.4—153.9 °C (lit.¹ 152—153 °C); ¹H NMR (400 MHz, CDCl₃) δ: 7.89 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.59 – 7.51 (m, 1H), 7.47 (d, *J* = 8.6 Hz, 2H), 7.38 (t, *J* = 7.5 Hz, 1H), 2.41 (d, *J* = 1.0 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ: 152.66, 141.34, 130.55, 124.48, 120.86, 120.49, 117.29, 113.19, 110.68, 77.41, 77.09, 76.77, 8.67; IR (KBr) ν: 1750 (C=O), 1632 (C=C); MS (70 eV) *m/z* (%): 200 (M⁺, 100), 171 (21), 144 (53), 115 (86).

2,3-Dimethyl-4H-furo[3,2-c]chromen-4-one(4b) White solid, m.p. 179.8—180.9 °C (lit.² 170—174 °C); ¹H NMR (400 MHz, CDCl₃) δ: 7.83 (d, *J* = 7.7 Hz, 1H), 7.53 – 7.41 (m, 2H), 7.35 (t, *J* = 7.5 Hz, 1H), 2.43 (s, 3H), 2.32 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ: 159.03, 155.68, 152.26, 150.90, 129.89, 124.34, 120.47, 117.18, 114.11, 113.14, 111.37, 11.62, 8.63; IR (KBr) ν: 2919, 1735 (C=O), 1629 (C=C); MS (70 eV) *m/z* (%): 214 (M⁺, 100), 199 (36), 115 (30).

7-Methoxy-3-methyl-4H-furo[3,2-c]chromen-4-one(4c) White solid, m.p. 154.4—154.7 °C (lit.³ 148—150 °C); ¹H NMR (400 MHz, CDCl₃) δ: 7.78 – 7.72 (m, 1H), 7.37 (s, 1H), 6.98 – 6.90 (m, 2H), 3.91 (s, 3H), 2.38 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ: 161.82, 159.15, 158.47, 154.38, 140.41, 121.80, 120.18, 112.69, 108.31, 106.60, 101.28, 55.78, 8.67; IR (KBr) ν: 2921, 1738 (C=O), 1629 (C=C); MS (70 eV) *m/z* (%): 230 (M⁺, 100), 215 (70), 187 (82), 159 (50). Anal. calcd for C₁₃H₁₀O₄: C 67.82, H 4.38; found C 67.98, H 4.51.

7-Methoxy-2,3-Dimethyl-4H-furo[3,2-c]chromen-4-one(4d) White solid, m.p. 141.2—143.3 °C; ¹H NMR (400 MHz, CDCl₃) δ: 7.72 (d, *J* = 8.4 Hz, 1H), 6.98 – 6.90 (m, 2H), 3.91 (s, 3H), 2.40 (s, 3H), 2.29 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ: 161.37, 159.34, 156.42, 153.97, 149.82, 121.42, 113.68, 112.54, 108.99, 106.63, 101.27, 55.75, 11.52, 8.63; IR (KBr) ν: 1749 (C=O), 1634 (C=C); MS (70 eV) *m/z* (%): 244 (M⁺, 100), 229 (55), 201 (47), 159 (35), 63 (33). Anal. calcd for C₁₄H₁₂O₄: C 68.85, H 4.95; found C 68.79, H 5.07.

7-Ethoxy-3-methyl-4H-furo[3,2-c]chromen-4-one(4e) White solid, m.p. 157.8 -158.4 °C; ¹H NMR (400 MHz, CDCl₃) δ: 7.75 (d, *J* = 9.4 Hz, 1H), 7.37 (s, 1H), 6.93 (d, *J* = 7.3 Hz, 2H), 4.13 (q, *J* = 7.0 Hz, 2H), 2.38 (s, 3H), 1.50 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ: 161.22, 159.23, 158.55 (s), 154.39, 140.36, 121.77, 120.16, 113.06, 108.23, 106.45, 101.74, 64.13, 14.67, 8.68; IR (KBr) ν: 2930, 1742 (C=O), 1631 (C=C); MS (70 eV) *m/z* (%): 244 (M⁺, 66), 216 (100), 160 (55), 77 (46). Anal. calcd for C₁₄H₁₂O₄: C 68.85, H 4.95; found C 68.92, H 5.03.

7-Ethoxy-2,3-Dimethyl-4H-furo[3,2-c]chromen-4-one(4f) White solid, m.p. 146.3—148.1 °C; ¹H NMR (400 MHz, CDCl₃) δ: 7.73 (d, *J* = 8.4 Hz, 1H), 6.93 (d, *J* = 9.0 Hz, 2H), 4.13 (q, *J* = 7.0 Hz, 2H), 2.41 (s, 3H), 2.30 (s, 3H), 1.50 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ: 160.77, 159.40, 156.51, 153.99, 149.74, 121.39, 113.67 (s), 112.93 (s), 108.93 (s), 106.50 (s), 101.74 (s), 64.08 (s), 14.69 (s), 11.53 (s), 8.65 (s); IR (KBr) ν: 2922, 1737 (C=O), 1630 (C=C); MS (70 eV) *m/z* (%): 258 (M⁺, 100), 230 (86), 215 (60), 159 (36), 115 (25). Anal. calcd for C₁₅H₁₄O₄: C 69.76, H 5.46; found C 69.61, H 5.57.

7-Isopropoxy-3-methyl-4H-furo[3,2-c]chromen-4-one(4g) White solid, m.p. 102.2—102.9 °C (lit.³ 85—87 °C); ¹H NMR (400 MHz, CDCl₃) δ: 7.75 (d, *J* = 8.6 Hz, 1H), 7.37 (d, *J* = 1.2 Hz, 1H), 6.96 – 6.88 (m, 2H), 4.65 (dt, *J* = 12.1, 6.1 Hz, 1H), 2.38 (d, *J* = 1.1 Hz, 3H), 1.43 (d, *J* = 6.1 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ: 160.23, 159.27, 158.60, 154.43, 140.33, 121.82, 120.15, 113.96, 108.18, 106.28, 102.77, 100.00, 70.66, 21.87, 8.68; IR (KBr) ν: 2926, 1741 (C=O), 1621 (C=C); MS (70 eV) *m/z* (%): 258 (M⁺, 56), 216 (100), 160 (14). Anal. calcd for C₁₅H₁₄O₄: C 69.76, H 5.46; found C 69.64, H 5.62.

7-Isopropoxy-2,3-Dimethyl-4H-furo[3,2-c]chromen-4-one(4h) White solid, m.p. 111.8—113.0 °C; ¹H NMR (400 MHz, CDCl₃) δ: 7.71 (d, *J* = 8.7 Hz, 1H), 6.98 – 6.86 (m, 2H), 4.64 (dt, *J* = 12.1, 6.0 Hz, 1H), 2.40 (s, 3H), 2.29 (s, 3H), 1.42 (d, *J* = 6.0 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ: 159.75, 159.41, 156.53, 154.02, 149.70, 121.42, 113.82, 113.66, 108.86, 106.32, 102.78, 70.59, 21.89, 11.52, 8.64; IR (KBr) ν: 2923, 1734 (C=O), 1634 (C=C); MS (70 eV) *m/z* (%): 272 (M⁺, 56), 230 (100), 215 (16). Anal. calcd for C₁₆H₁₆O₄: C 70.57, H 5.92; found C 70.68, H 6.15.

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7-Allyloxy-3-methyl-4H-furo[3,2-c]chromen-4-one(4i) White solid, m.p. 135.7—137.8 °C; ¹H NMR (400 MHz, CDCl₃) δ: 7.80 – 7.73 (m, 1H), 7.38 (s, 1H), 6.97 (dd, *J* = 4.4, 2.3 Hz, 2H), 6.10 (ddd, *J* = 22.5, 10.6, 5.3 Hz, 1H), 5.50 (dd, *J* = 17.3, 1.2 Hz, 1H), 5.39 (dd, *J* = 10.5, 1.0 Hz, 1H), 4.64 (d, *J* = 5.3 Hz, 2H), 2.38 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ: 160.73, 159.16, 158.43, 154.27, 140.43, 132.25, 121.80, 120.17, 118.60, 113.22, 108.36, 106.72, 102.17, 69.26, 8.6; IR (KBr) ν: 2930, 1741 (C=O), 1629 (C=C); MS (70 eV) *m/z* (%): 256 (M⁺, 100), 215 (70), 187 (82), 159 (50). Anal. calcd for C₁₅H₁₂O₄: C 70.31, H 4.72; found C 70.38, H 4.83.

7-Allyloxy-2,3-Dimethyl-4H-furo[3,2-c]chromen-4-one(4j) White solid, m.p. 130.6—131.4 °C; ¹H NMR (400 MHz, CDCl₃) δ: 7.73 (dd, *J* = 7.8, 1.2 Hz, 1H), 6.99 – 6.92 (m, 2H), 6.16 – 6.04 (m, 1H), 5.49 (dd, *J* = 17.3, 1.4 Hz, 1H), 5.38 (dd, *J* = 10.5, 1.3 Hz, 1H), 4.64 (dt, *J* = 5.3, 1.4 Hz, 2H), 2.41 (s, 3H), 2.30 (d, *J* = 0.6 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ: 160.31, 159.27, 156.37, 153.90, 149.83, 132.38, 121.40, 118.49, 113.71, 113.07, 109.08, 106.78, 102.20, 69.25, 11.49, 8.59; IR (KBr) ν: 2928, 1741 (C=O), 1624 (C=C); MS (70 eV) *m/z* (%): 270 (M⁺, 60), 215 (70), 187 (82), 159 (50). Anal. calcd for C₁₆H₁₄O₄: C 71.10, H 5.22; found C 70.97, H 5.31.

7,8,9,10-Tetrahydro-6H-benzofuro[3,2-c]chromen-6-one(5a) White solid, m.p. 191.5—191.6 °C (lit.⁴ 190—191 °C); ¹H NMR (400 MHz, CDCl₃) δ: 7.85 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.49 (ddd, *J* = 16.9, 11.9, 4.4 Hz, 2H), 7.41 – 7.32 (m, 1H), 2.82 (ddd, *J* = 12.7, 6.2, 1.9 Hz, 4H), 2.04 – 1.92 (m, 2H), 1.91 – 1.82 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ: 158.91, 156.03, 154.36, 152.23, 129.84, 124.37, 120.50, 117.23, 116.78, 113.31, 110.44, 23.23, 22.49, 22.35, 21.01. IR (KBr) ν: 2932, 1730 (C=O), 1628 (C=C); MS (70 eV) *m/z* (%): 240 (M⁺, 80), 212 (100), 121 (20).

3-Methoxy-7,8,9,10-Tetrahydro-6H-benzofuro[3,2-c]chromen-6-one(5b) White solid, m.p. 160.8—162.9 °C; ¹H NMR (400 MHz, CDCl₃) δ: 7.74 (d, *J* = 8.5 Hz, 1H), 6.94 (dt, *J* = 8.6, 2.3 Hz, 2H), 3.91 (s, 3H), 2.83 – 2.74 (m, 4H), 2.00 – 1.92 (m, 2H), 1.89 – 1.81 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ: 161.34, 159.19, 156.77, 153.94, 153.29, 121.44, 116.40, 112.56, 108.06, 106.81, 101.34, 55.75, 23.17, 22.47 (d, *J* = 14.9 Hz), 21.02; IR (KBr) ν: 2929, 1730 (C=O), 1628 (C=C); MS (70 eV) *m/z* (%): 270 (M⁺, 82), 242 (100), 151 (17), 115 (13). Anal. calcd for C₁₆H₁₄O₄: C 71.10, H 5.22; found C 71.16, H 5.31.

3-Ethoxy-7,8,9,10-Tetrahydro-6H-benzofuro[3,2-c]chromen-6-one(5c) White solid, m.p. 178.2—178.7 °C; ¹H NMR (400 MHz, CDCl₃) δ: 7.72 (d, *J* = 8.5 Hz, 1H), 6.96 – 6.89 (m, 2H), 4.12 (q, *J* = 7.0 Hz, 2H), 2.78 (dt, *J* = 17.6, 6.1 Hz, 4H), 1.99 – 1.80 (m, 4H), 1.50 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ: 159.76, 159.25, 156.89, 154.00, 153.17, 121.43, 116.38, 113.84, 107.93, 106.51, 102.89, 70.62, 23.16, 22.55, 22.40, 21.90, 21.03. IR (KBr) ν: 2931, 1737 (C=O), 1623 (C=C); MS (70 eV) *m/z* (%): 284 (M⁺, 100), 256 (60), 228 (80), 115 (13). Anal. calcd for C₁₇H₁₆O₄: C 71.82, H 5.67; found C 71.60, H 5.73.

3-Isopropoxy-7,8,9,10-Tetrahydro-6H-benzofuro[3,2-c]chromen-6-one(5d) White solid, m.p. 152.6—153.2 °C; ¹H NMR (400 MHz, CDCl₃) δ: 7.73 (d, *J* = 8.7 Hz, 1H), 6.97 – 6.87 (m, 2H), 4.70 – 4.59 (m, 1H), 2.79 (dt, *J* = 17.8, 6.1 Hz, 4H), 2.00 – 1.91 (m, 2H), 1.90 – 1.81 (m, 2H), 1.42 (d, *J* = 6.0 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ: 159.58, 159.16, 156.74, 153.83, 153.03, 121.30, 116.22, 113.70, 107.77, 106.33, 102.69, 99.99, 70.45, 23.02, 22.40, 22.26, 21.76, 20.88; IR (KBr) ν: 2933, 1744 (C=O), 1631 (C=C); MS (70 eV) *m/z* (%): 298 (M⁺, 35), 256 (95), 228 (100), 137 (20). Anal. calcd for C₁₈H₁₈O₄: C 72.47, H 6.08; found C 72.34, H 6.17.

3-Allyloxy-7,8,9,10-Tetrahydro-6H-benzofuro[3,2-c]chromen-6-one(5e) White solid, m.p. 119.9—121.2 °C; ¹H NMR (400 MHz, CDCl₃) δ: 7.74 (d, *J* = 8.8 Hz, 1H), 6.96 (d, *J* = 8.2 Hz, 2H), 6.10 (ddd, *J* = 22.5, 10.6, 5.3 Hz, 1H), 5.50 (dd, *J* = 17.3, 1.3 Hz, 1H), 5.39 (dd, *J* = 10.5, 1.2 Hz, 1H), 4.64 (d, *J* = 5.3 Hz, 2H), 2.85 – 2.72 (m, 4H), 2.03 – 1.91 (m, 2H), 1.90 – 1.80 (m, 2H); ¹³C NMR (101 MHz, CDCl₃) δ: 160.28, 159.18, 156.74, 153.85, 153.32, 132.37, 121.43, 118.53, 116.41, 113.11, 108.13, 106.94, 102.24, 69.26, 23.17, 22.54, 22.39, 21.02; IR (KBr) ν: 2931, 1742 (C=O), 1622 (C=C); MS (70 eV) *m/z* (%): 296 (M⁺, 50), 255 (100), 227 (40), 199 (28). Anal. calcd for C₁₈H₁₆O₄: C 72.96, H 5.44; found C 72.78, H 5.52.

4. Copies of NMR spectra

^1H NMR and ^{13}C NMR for: 3-Methyl-4H-furo[3,2-c]chromen-4-one (4a)

¹H NMR and ¹³C NMR for: 2,3-Dimethyl-4H-furo[3,2-c]chromen-4-one (4b)

^1H NMR and ^{13}C NMR for: 7-Methoxy-3-methyl-4H-furo[3,2-c]chromen-4-one (4c)

^1H NMR and ^{13}C NMR for: 7-Methoxy-2,3-Dimethyl-4H-furo[3,2-c]chromen-4-one (4d)

^1H NMR and ^{13}C NMR for: 7-Ethoxy-3-methyl-4H-furo[3,2-c]chromen-4-one (4e)

^1H NMR and ^{13}C NMR for: 7-Ethoxy-2,3-Dimethyl-4H-furo[3,2-c]chromen-4-one(4f)

^1H NMR and ^{13}C NMR for: 7-Isopropoxy-3-methyl-4H-furo[3,2-c]chromen-4-one (4g)

^1H NMR and ^{13}C NMR for: 7-Isopropoxy-2,3-Dimethyl-4H-furo[3,2-c]chromen-4-one(4h)

^1H NMR and ^{13}C NMR for: 7-Allyloxy-3-methyl-4H-furo[3,2-c]chromen-4-one (4i)

¹H NMR and ¹³C NMR for: 7-Allyloxy-2,3-Dimethyl-4H-furo[3,2-c]chromen-4-one(4j)

¹H NMR and ¹³C NMR for: 7,8,9,10-Tetrahydro-6H-benzofuro[3,2-c]chromen-6-one (5a)

¹H NMR and ¹³C NMR for:
3-Methoxy-7,8,9,10-Tetrahydro-6H-benzofuro[3,2-c]chromen-6-one (5b)

¹H NMR and ¹³C NMR for:
3-Ethoxy-7,8,9,10-Tetrahydro-6H-benzofuro[3,2-c]chromen-6-one(5c)

¹H NMR and ¹³C NMR for: 3-Isopropoxy-7,8,9,10-Tetrahydro-6H-benzofuro[3,2-c]chromen-6-one(5d)

^1H NMR and ^{13}C NMR for:
3-Allyloxy-7,8,9,10-Tetrahydro-6H-benzofuro[3,2-c]chromen-6-one(5e)

5. Mass Spectra

4a

xzc-1 #27 RT: 0.44 AV: 1 NL: 1.49E6
T: {0,0} + c EI det=380.00 Full ms [41.00-868.00]

4b

xzc-2 #37 RT: 0.62 AV: 1 NL: 1.82E6
T: {0,0} + c EI det=380.00 Full ms [41.00-868.00]

4c

xzc-4 #56 RT: 0.90 AV: 1 NL: 4.31E6
T: {0,0} + c EI det=380.00 Full ms [41.00-868.00]

4d

xzc-5 #42 RT: 0.69 AV: 1 NL: 3.80E5
T: {0,0} + c EI det=380.00 Full ms [41.00-868.00]

4e

xzc-7 #51 RT: 0.83 AV: 1 NL: 1.22E6
T: {0,0} + c EI det=380.00 Full ms [41.00-868.00]

4f

xzc-8_131225155402 #94 RT: 1.28 AV: 1 NL: 4.51E6
T: {0,0} + c EI det=380.00 Full ms [41.00-868.00]

4g

45# #176 RT: 1.50 AV: 1 NL: 6.34E8
T: + c Full ms [33.00-500.00]

4h

46# #226 RT: 1.92 AV: 1 NL: 2.61E8
T: + c Full ms [33.00-500.00]

4i

47# #230 RT: 1.95 AV: 1 NL: 3.15E8
T: + c Full ms [33.00-500.00]

4j

48# #235 RT: 1.99 AV: 1 NL: 2.36E8
T: + c Full ms [33.00-500.00]

5a

xzc-3 #26 RT: 0.47 AV: 1 NL: 3.13E6
T: {0,0} + c EI det=380.00 Full ms [41.00-868.00]

5b

xzc-6 #23 RT: 0.42 AV: 1 NL: 2.33E6
T: {0,0} + c EI det=380.00 Full ms [41.00-868.00]

5c

xzc-9 #88 RT: 1.20 AV: 1 NL: 2.36E6
T: {0,0} + c EI det=380.00 Full ms [41.00-868.00]

5d

xzc-17 #76 RT: 1.13 AV: 1 NL: 3.09E6
T: {0,0} + c EI det=370.00 Full ms [41.00-868.00]

27

5e

49# #269-289 RT: 2.28-2.45 AV: 21 SB: 52 1.39-1.65 , 2.63-2.79 NL: 8.73E6
T: + c Full ms [33.00-500.00]