

# Cytotoxicity of benzofuran-containing simplified viniferin analogues

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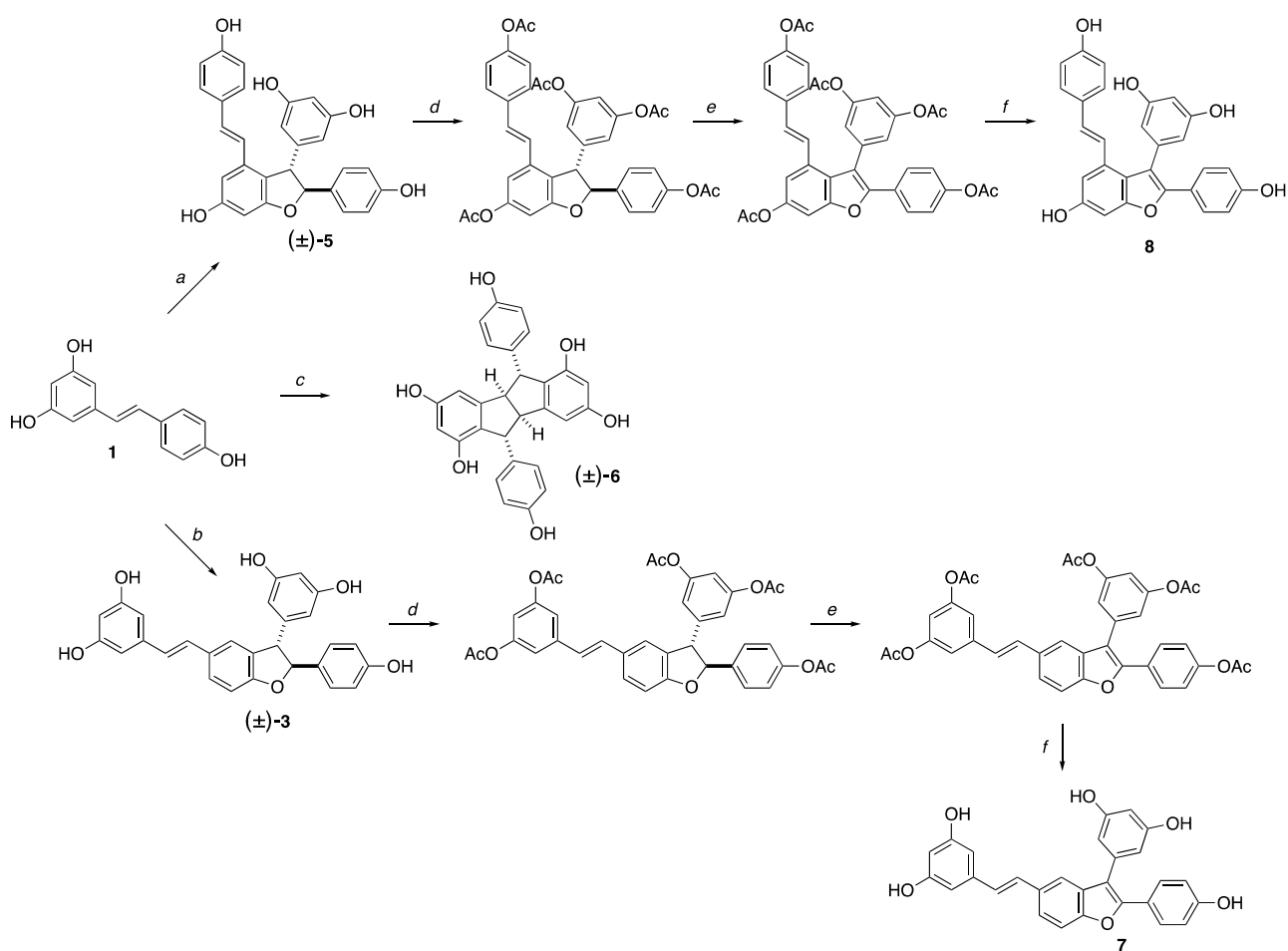
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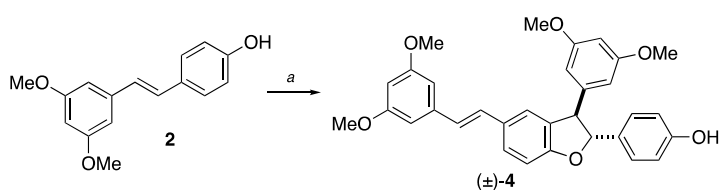
<b>Table S1.</b> Calculated physico-chemical properties	Page S2
<b>Scheme S1-S3.</b> Synthesis of compounds <b>3-9</b>	Page S3
<b>Scheme S4-S6.</b> Synthesis of compounds <b>10-13</b> and <b>15-17</b>	Page S4
<b>Scheme S7.</b> Synthesis of compound <b>14</b>	Page S5

**Table S1.** Chemicalize was used for the calculation of the physico-chemical properties for all the tested compounds, March 2024, <https://chemicalize.com/>, developed by ChemAxon.

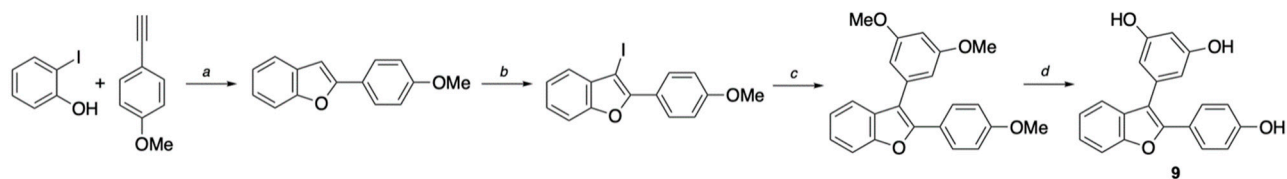
compound	Molar mass	cLogP	nHA	nHD	HLB	TPSA	VDW volume
<b>1</b>	228.08	3.40	3	3	8.66	60.69	204.56
<b>2</b>	256.11	3.69	3	1	7.91	38.69	239.77
<b>3</b>	454.14	5.96	6	5	9.36	110.38	394.53
<b>4</b>	510.20	6.54	6	1	7.29	66.38	465.54
<b>5</b>	454.48	5.96	6	5	9.36	110.38	394.32
<b>6</b>	454.48	5.31	6	6	8.93	121.38	389.5
<b>7</b>	452.46	6.17	5	5	8.81	130.41	387.01
<b>8</b>	452.46	6.17	5	5	8.81	114.29	386.91
<b>9</b>	318.33	4.44	3	3	7.45	73.83	272.54
<b>10</b>	360.37	4.91	4	4	8.89	94.06	307.92
<b>11</b>	344.37	5.13	3	3	7.21	73.83	299.59
<b>12</b>	334.33	4.13	4	4	9.14	94.06	281.19
<b>13</b>	360.36	4.91	4	4	8.89	94.06	307.96
<b>14</b>	344.37	5.13	3	3	7.21	73.83	299.36
<b>15</b>	372.42	5.42	3	1	6.30	51.83	334.71
<b>16</b>	386.45	5.57	3	0	5.83	40.83	352.03
<b>17</b>	390.44	4.72	4	0	7.17	50.06	351.54



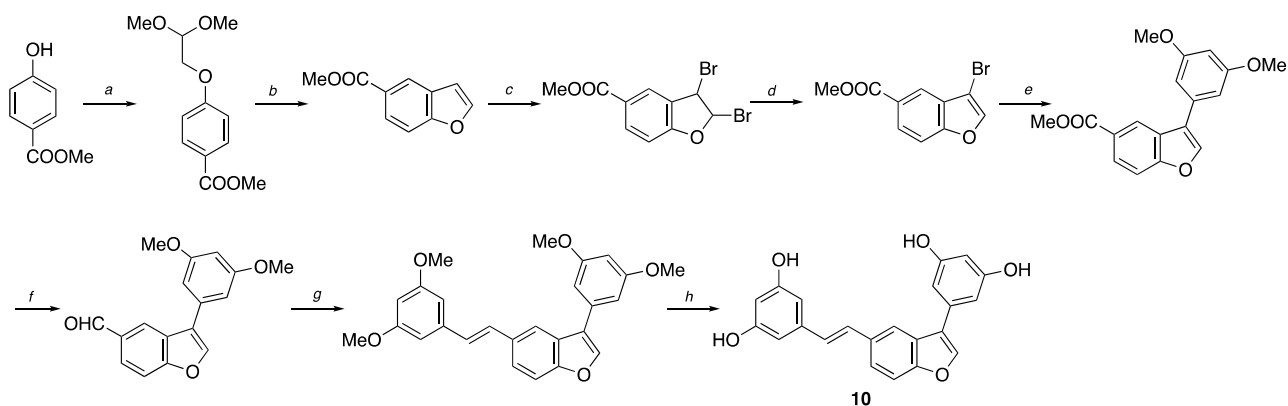
**Scheme S1.** Synthetic pathway for the obtention of **(±)-3**, **(±)-5**, **7** and **8**. *a.* FeCl<sub>3</sub>·6H<sub>2</sub>O, MeOH, rt, **15%**; *b.* i. HRP, 40 °C, acetone/citrate buffer pH 5 1:1; ii. H<sub>2</sub>O<sub>2</sub>, 40 °C, **49%** (over two steps); *c.* i. HRP, 40 °C, acetone/phosphate buffer pH 8 1:1; ii. H<sub>2</sub>O<sub>2</sub>, 40 °C, **21%** (over two steps); *d.* Ac<sub>2</sub>O, TEA, DCM/DMSO, rt, **90-92%**; *e.* DDQ, DCM, reflux, **60-84%**; *f.* KOH, MeOH, 0 °C, **55-70%**



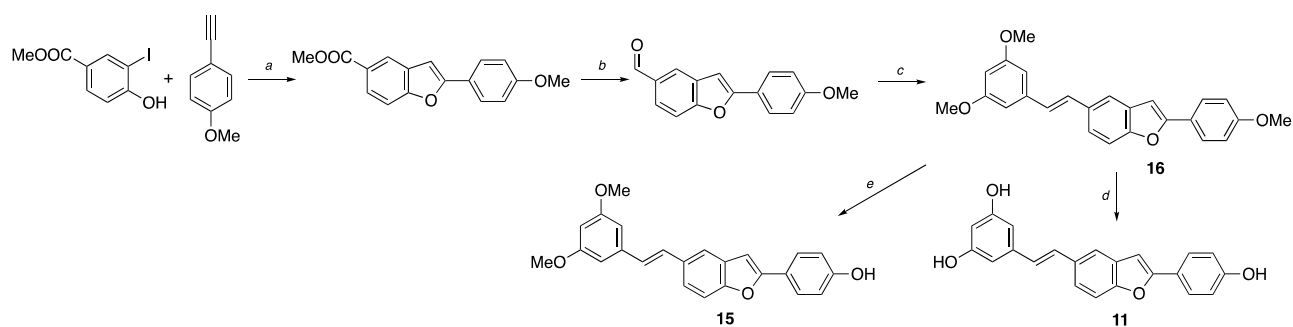
**Scheme S2.** Synthetic pathway for the obtention of **(±)-4**. *a.* i. HRP, 30 min, 40 °C, acetone/citrate buffer pH 5 1:1; ii. H<sub>2</sub>O<sub>2</sub>, 15 min, 40 °C, **60%** (over two steps)



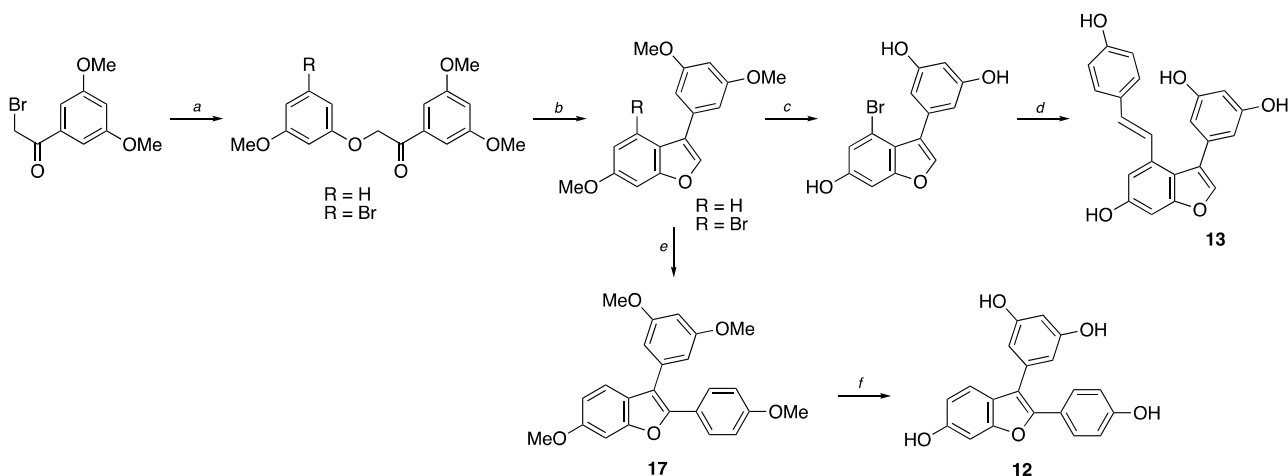
**Scheme S3.** Synthetic pathway for the obtention of **9**. *a.* CuI, PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, TEA, THF/MeCN, 100 °C, **50%**; *b.* NIS, PTSA, MeCN, rt, **74%**; *c.* 3,5-dimethoxyphenyl boronic acid, K<sub>2</sub>CO<sub>3</sub>, PdCl<sub>2</sub>(dppf), THF/H<sub>2</sub>O, 70 °C, **83%**; *d.* BBr<sub>3</sub>, DCM, 0 °C to rt, **61%**



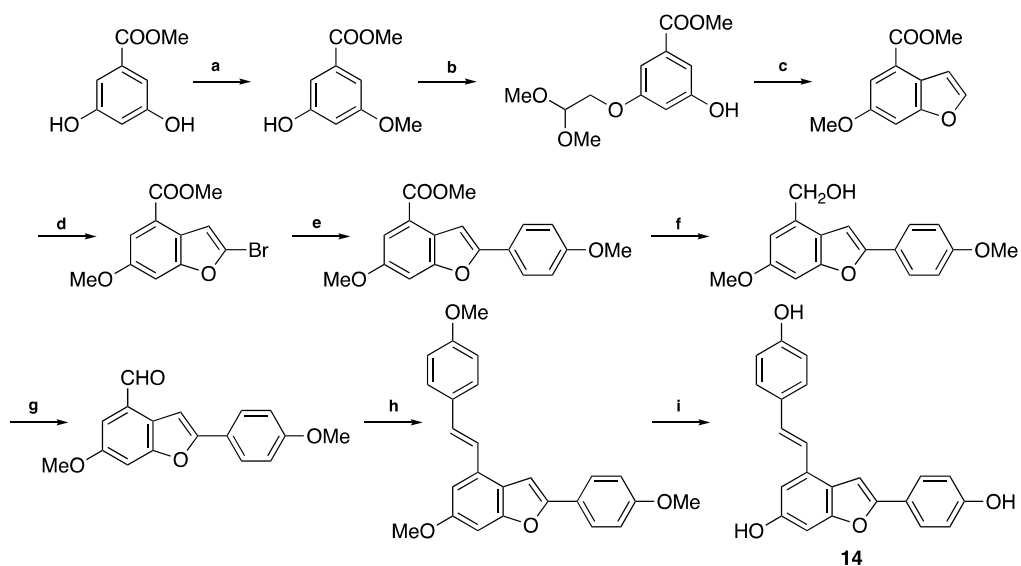
**Scheme S4.** Synthetic pathway for the obtention of **10**. *a*. 2-Br-1,1-DME, Cs<sub>2</sub>CO<sub>3</sub>, MeCN, reflux, **61%**; *b*. amberlyst-15, toluene, reflux, **51%**; *c*. Br<sub>2</sub>, DCM, 0 °C to rt, **82%**; *d*. KOH, MeOH/THF, 0 °C, **82%**; *e*. 3,5-dimethoxyphenylboronic acid, Pd(PPh<sub>3</sub>)<sub>4</sub>, Na<sub>2</sub>CO<sub>3</sub>, DME/H<sub>2</sub>O, 80 °C, **74%**; *f*. i. LiAlH<sub>4</sub>, THF, 0 °C, **97%**; ii. DMP, DCM, 0 °C to rt, **78%**; *g*. diethyl (3,5-dimethoxyphenyl)phosphonate, NaH, THF, MW, 120 °C, **80%**; *h*. BBr<sub>3</sub>, DCM, 0 °C to rt, **14%**



**Scheme S5.** Synthetic pathway for the obtention of **11**, **15** and **16**. *a*. CuI, PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, TEA, THF/MeCN, 100 °C, **62%**; *b*. LiAlH<sub>4</sub>, THF, 0 °C, **85%**; *c*. 3,5-dimethoxyphenyl phosphonate, NaH, THF, MW, 120 °C, **76%**; *d*. BBr<sub>3</sub>, DCM, 0 °C to rt, **60%**; *e*. BCl<sub>3</sub>, TBAI, DCM, 0 °C to rt, **35%**



**Scheme S6.** Synthetic pathway for the obtention of **12**, **13** and **17**. *a*. 3-methoxyphenol (R = H) or 3-Br-5-methoxyphenol (R = Br), K<sub>2</sub>CO<sub>3</sub>, acetone, reflux, **90%** (R = H) or **89%** (R = Br); *b*. Bi(OTf)<sub>3</sub>, DCM, reflux, **43%** (R = H) or **83%** (R = Br); *c*. BBr<sub>3</sub>, DCM, -78 °C to rt, **91%**; *d*. *p*-Hydroxystyrene, Pd(OAc)<sub>2</sub>, TEA, dppp, DMF, 120 °C, **80%**; *e*. 4-Br anisole, Pd(OAc)<sub>2</sub>, PCy<sub>3</sub>HBF<sub>4</sub>, K<sub>2</sub>CO<sub>3</sub>, pivalic acid, DMA, 100 °C, **80%**; *f*. BBr<sub>3</sub>, DCM, -78 °C to rt, **52%**



**Scheme S7.** Synthetic pathway for the obtainment of **14**. *a.* MeI, K<sub>2</sub>CO<sub>3</sub>, DMF, rt, **35%**; *b.* 2-Br-1,1-DME, Cs<sub>2</sub>CO<sub>3</sub>, MeCN, reflux, **67%**; *c.* amberlyst-15, PhCl, 120 °C, **63%**; *d.* NBS, 1,2-DCE/DMF, 70 °C, **80%**; *e.* 4-OMe-PBA, K<sub>2</sub>CO<sub>3</sub>, Pd(PPh<sub>3</sub>)<sub>4</sub>, 70 °C, **91%**; *f.* LiAlH<sub>4</sub>, THF, 0 °C, **89%**; *g.* DMP, DCM, **97%**; *h.* diethyl (4-OMe-Bn) phosphonate, NaH, MW, 120 °C, **54%**; *i.* BBr<sub>3</sub>, DCM, **24%**