FIGURE 1

Scheme 1

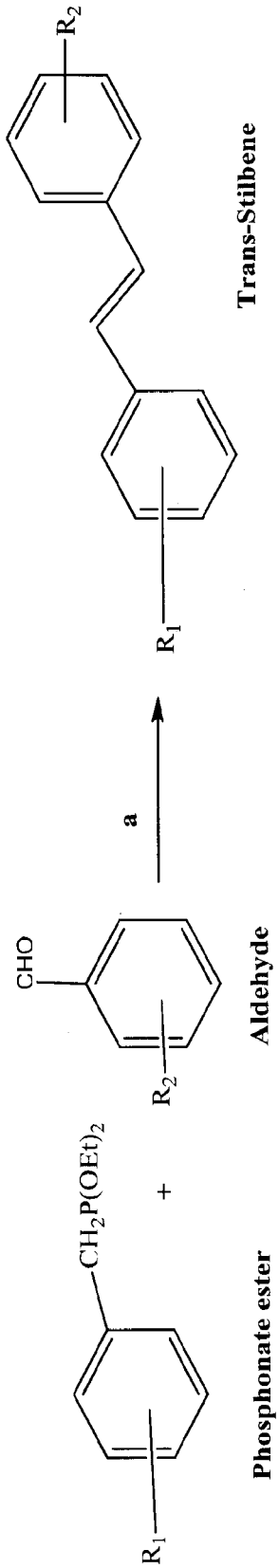


FIGURE 2

Table 1
Structures of (E)-stilbenes.[a]

Product	R_1	R_2	Reference[b]	Product	R_1	R_2	Reference[b]
1	4-OCH_3	2-F	21	29*	2-F	2,5-diF	–
2	–	2-F	21	30*	3-F	3,4-diF	–
3	–	3-F	21	31	2-F	2,6-diF	35
4	–	4-F	21	32	3-F	3-F	31
5	4-OCH_3	3-F	21	33	3-F	4-F	36
6	4-OCH_3	4-F	21	34*	3-F	2,5-diF	–
7	4-CH_3	4-F	28	35*	3-F	2,4-diF	–
8	4-CH_3	3-F	28	36*	2-F	2,4-diF	–
9	4-CH_3	2-F	28	37*	4-CH_3	2,4-diF	–
10*	2-F	2-OCH_3	–	38	4-F	2,4-diF	39
11	3-OCH_3	2-F	29	39	4-F	3,4-diF	39
12	3-OCH_3	4-F	30	40*	4-F	2,5-diF	–
13	3-OCH_3	3-F	31	41	–	2,3-diOCH_3	21
14	3-F	3,4-diOCH_3	32	42	–	2-OCH_3	21
15	4-F	3,4-diOCH_3	33	43	4-OCH_3	2,4-diOCH_3	21
16*	3-F	2,3-diOCH_3	–	44	4-OCH_3	2-Cl	21
17*	4-F	2,3-diOCH_3	–	45	4-OCH_3	3-OH	34
18*	4-F	2,5-diOCH_3	–	46	4-OCH_3	3-OCH_3, 4-OH	40
19	4-Cl	2-F	29	47	4-CH_3	3-CF_3	31
20	4-OH	2-F	34	48*	2,3-OCH_3	4-CH_3	–
21	–	2,6-diF	35	49*	3-OCH_3	2-OCH_3	–
22*	4-CH_3	3,4-diF	–	50*	3-OCH_3	2,5-diOCH_3	–
23*	4-OCH_3	2,5-diF	–	51	4-OCH_3	3-NO_2	41
24*	2-F	3,4-diF	–	52	–	3-NO_2	42
25	2-F	3-F	36	53	4-CH_3	3-NO_2	43
26*	4-OCH_3	3,4-diF	–	54*	2,3-diOCH_3	4-CF_3	–
27	2-F	2-F	37	55*	2,3-diOCH_3	4-$CH(CH_3)_2$	–
28	4-F	2-F	38	56	2,4-diOCH_3	2,5-diOCH_3	44

a Data for starred compounds is reported in the experimental section.
b Melting points and NMR data of known compounds are in agreement with the literature data.

FIGURE 3

Table 2. Activation of Nrf2 by mono-fluoro *trans* stilbenes

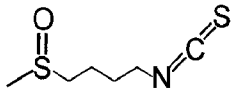
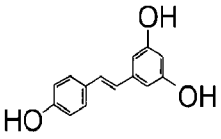
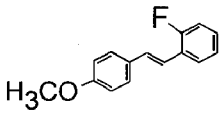
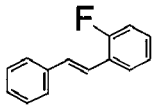
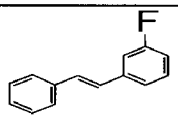
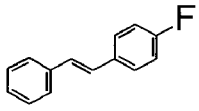
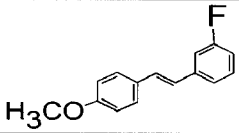
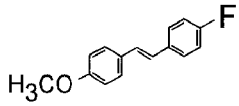
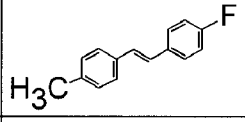
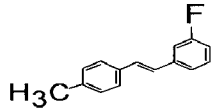
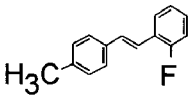
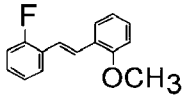
Number	Structure	EC_{50} (μM)	Fold activation
Sulforaphane		1.2 ± 0.08	12.4
Resveratrol		5.4 ± 0.5	3.2
1 (LD55)		5.4 ± 0.3	14.9
2		0.7 ± 0.1	10.7
3		3.1 ± 0.4	4.9
4		12.4 ± 0.5	4.8
5		8.9 ± 0.9	3.6
6		4.2 ± 0.4	1.7
7		1.3 ± 0.2	1.1
8		0.8 ± 0.08	4.7
9		1.4 ± 0.2	10.1
10		3.1 ± 0.2	18.4

FIGURE 3 (Cont'd)

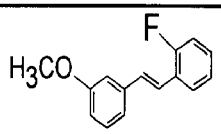
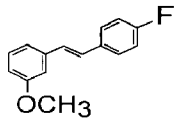
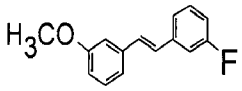
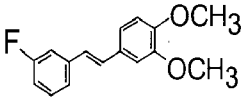
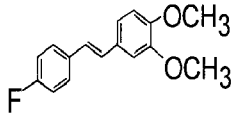
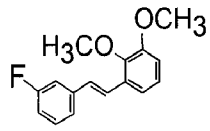
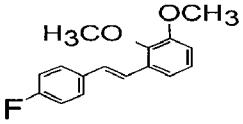
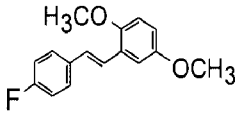
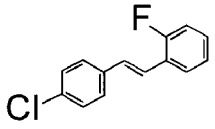
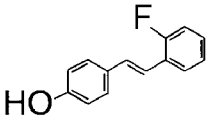
Number	Structure	EC_{50} (μM)	Fold activation
11		3.8 ± 0.2	14.4
12		6.0 ± 0.5	4.4
13		2.3 ± 0.5	15.1
14		9.5 ± 0.7	5.9
15		2.6 ± 0.5	1.6
16		1.9 ± 0.1	19.4
17		2.9 ± 0.1	16.9
18		5.1 ± 0.5	10.7
19		1.6 ± 0.2	5.3
20		11.4 ± 1.6	13.4

FIGURE 4

Table 3. Activation of Nrf2 by polyfluoro *trans* stilbenes

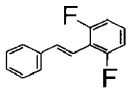
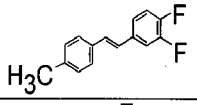
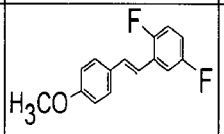
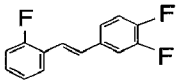
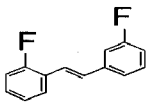
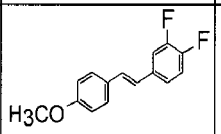
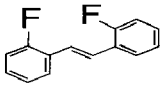
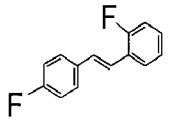
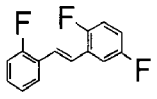
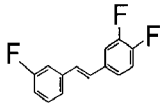
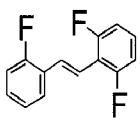
Number	Structure	EC_{50} (μM)	Fold activation
21		6.9 ± 0.1	11.4 ± 0.4
22		2.6 ± 0.18	10.2 ± 0.2
23		3.2 ± 0.5	17.0 ± 0.9
24		>15	11.5 ± 2.0[a]
25		>15	8.5 ± 0.2[a]
26		>15	4.6 ± 0.6[a]
27		4.3 ± 0.4	13.9 ± 0.9
28		3.6 ± 0.3	12.7 ± 0.4
29		5.9 ± 0.2	22.3 ± 0.5
30		5.0 ± 0.1	12.2 ± 0.8
31		1.4 ± 0.5	21.2 ± 2.0

FIGURE 4 (Cont'd)

Table 3 (Cont'd)

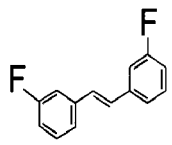
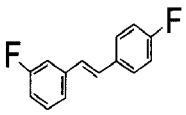
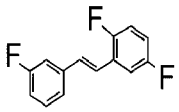
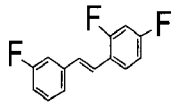
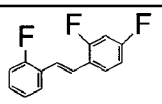
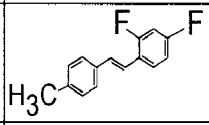
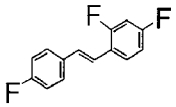
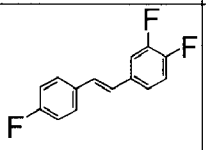
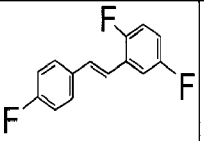
Number	Structure	EC_{50} (μM)	Fold activation
32		1.0 ± 0.12	7.0 ± 0.7
33		0.65 ± 0.12	4.5 ± 0.4
34		0.3 ± 0.02	10.7 ± 1.0
35		0.45 ± 0.01	8.2 ± 0.2
36		9.6 ± 0.14	5.0 ± 0.8
37		2.0 ± 0.07	13.5 ± 0.2
38		0.9 ± 0.08	16.8 ± 1.8
39		>15	7.0 ± 0.5[a]
40		2.9 ± 0.59	11.2 ± 0.1

FIGURE 5

Table 4. Activation of Nrf2 by non-fluoro *trans* stilbenes

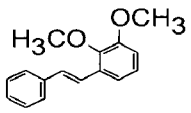
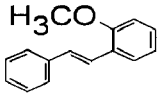
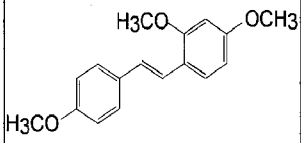
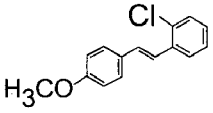
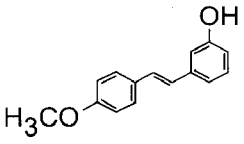
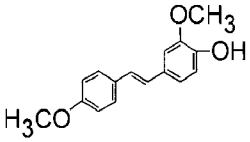
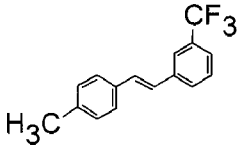
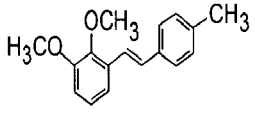
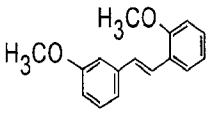
Number	Structure	EC_{50} (μM)	Fold activation
41		4.7 ± 0.7	25.4
42		4.4 ± 0.1	23.1
43		4.6 ± 0.4	15.6
44		3.1 ± 0.2	17.8
45		>15	28.1
46		3.7 ± 0.5	27.7
47		1.5 ± 0.5	19.2
48		1.1 ± 0.2	16.1
49		4.4 ± 0.2	29.2

FIGURE 5 (Cont'd)

Table 5 (Cont'd)

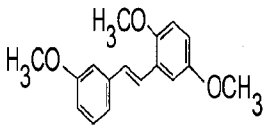
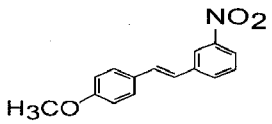
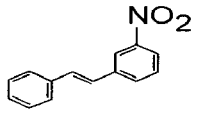
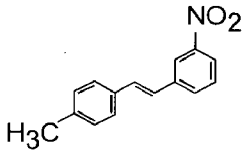
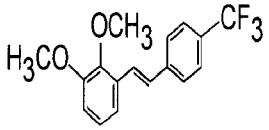
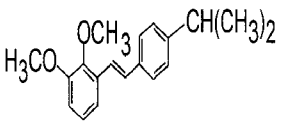
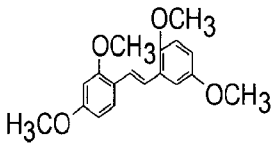
50		>15	15.7
51		3.3 ± 0.4	69.0
52		3.0 ± 0.4	18.6
53		3.7 ± 0.2	11.9
54		2.2 ± 0.1	65.5
55		2.7 ± 0.3	33.9
56		0.8 ± 0.03	12.9

FIGURE 6

EC_{50} values for inhibition of NF-κB and activation of Nrf2 by resveratrol analogues (trans stilbenes) and by curcumin analogues (dienones)

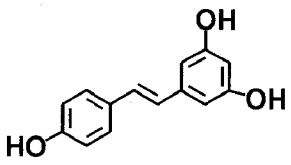
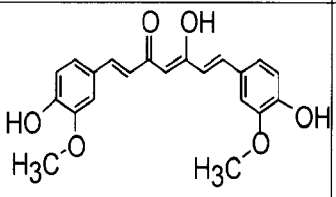
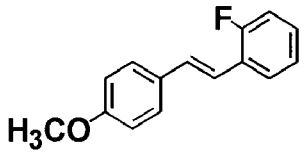
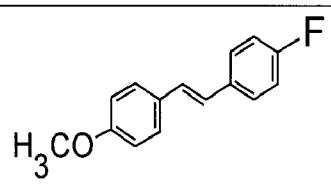
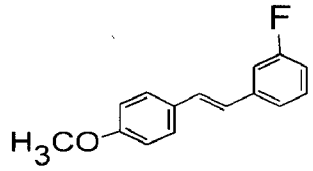
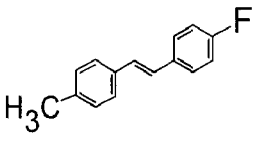
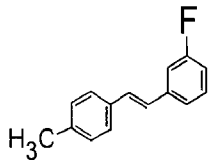
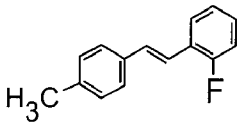
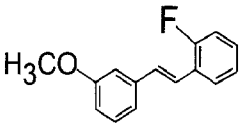
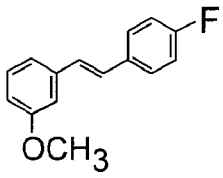
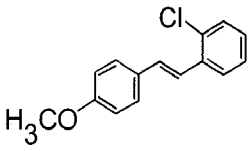
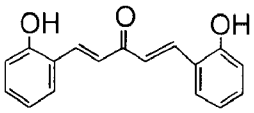
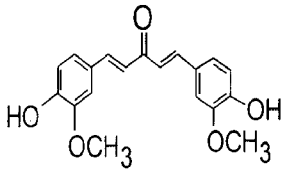
Compound	Structure	EC_{50} (μM) NFkB	EC_{50} (μM)Nrf2
Resveratrol		20 ± 3	5.4±0.5
Curcumin		8.2±0.4	21±0.02
1 (LD55)		0.15 ± 0.1	5.4±0.3
5		1.1±0.6	8.9±0.9
6		3-5	4.2±0.4
7		3-5	1.3±0.2
8		0.77±0.3	0.8±0.08

FIGURE 6 (Cont'd)

Table 6 Continued

Compound	Structure	EC_{50} (μM) NFkB	EC_{50} (μM) Nrf2
9		0.63±0.5	1.4±0.2
11		3 - 5	3.8±0.2
12		3 - 5	6.0±0.5
44		1.5±0.03	3.1±0.2
dienone analogue of curcumin		4.1±0.3	3.3±0.5
Dienone analogue		9.6±0.7	9.9±0.6