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Original article

Synthesis and biological evaluation of novel (*E*) stilbene-based antitumor agents

René Csuk*, Sabrina Albert, Bianka Siewert, Stefan Schwarz

Bereich Organische Chemie, Martin-Luther-Universität Halle-Wittenberg, Kurt-Mothes-Str. 2, D-06120 Halle (Saale), Germany

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ABSTRACT

Several new (*E*) stilbenes were synthesized by a combination of a Wittig olefination followed by Mizoroki–Heck coupling reactions. These compounds were screened for antitumor activity in a panel of 8 human cancer cell lines by a colorimetric SRB assay. Several of these compounds exhibit strong cytotoxicity. The most active compound of this series showed an average IC_{50} value of 0.03 μmol; it acts by apoptosis as shown by a dye-exclusion test, an extra acridine orange/ethidium bromide staining and DNA-laddering experiments.

1. Introduction

Stilbene-based compounds have become of particular interest to chemists because of their range of different biological activities [1,2]. Hydroxylated stilbenes, among them *trans*-resveratrol (**1**, Fig. 1) are largely present in nature and play a significant role in the prevention of coronary artery disease [3] due to its antioxidant [4,5] and anti-inflammatory properties. Resveratrol has been suggested as an anticancer agent [6] acting by the inhibition of cell proliferation [7]. The stilbene derivative tamoxifen (**2**) is currently used for the treatment of several types of breast cancer in women, and as a hormone treatment for male breast cancer. In addition, the naturally occurring *cis*-stilbene combretastatin A-4 (**3**) [8,9] from the bark of the South African tree *Combretum caffrum* showed significant antitumor activity. The same is true for several analogs of **2** [9–21]. Its derivative ombrabulin (**4**) [22] is currently in phase III clinical trials for the treatment of advanced-stage soft-tissue carcinoma. The mechanism of action for (*Z*) stilbene derivatives finally led to endothelial cell damage and subsequent necrosis [17]. For several monohydroxylated (*E*) stilbenes apoptosis in a breast cell line was induced [23].

Contrary to the findings for (*E*) resveratrol, most of (*E*) or (*Z*) configurated synthetic methylated stilbenes stop mitosis at the M phase (hence leading to polyploidic cells) whereas (*E*) resveratrol blocks cells at the S phase [24,25].

2. Results

2.1. Chemistry

In continuity of our previous investigations devoted to the synthesis of bioactive compounds, we became interested in the synthesis of stilbenes since several of them have been shown to behave as a sensitizer for anticancer drugs [26,27], cytokines [28] and radiation [29].

Although stilbenes can be obtained by a near endless list of reactions and transformations, most prominent among them are Wittig (–Horner, (Horner)–Wadsworth–Emmons) reactions [30,31], aldol-type condensations [32], as well as Negishi–Stille reactions [33] or by McMurry couplings [34]. The use of Mizoroki–Heck reactions [35–38], however, to make (*E*) configurated stilbenes seems most promising.

Several stilbenes showing antibacterial and/or antifungal activity have previously been prepared by a sequence of a Wittig olefination followed by a Mizoroki–Heck coupling [39]. We applied the same synthetic scheme (Scheme 1) for the synthesis of the cytotoxic stilbenes. Thus, Wittig reaction of suitable substituted aldehydes with methyl triphenylphoshonium iodide and ^{t}BuOK in THF gave styrenes. These styrenes were subjected to Mizoroki–Heck couplings to yield (*E*) configurated stilbenes **5**–**38**. The use of triethanolamine acting simultaneously as a base and as a solvent allows the economic synthesis of substituted (*E*) configurated stilbenes [35]. For example, **38** is characterized in its ^{19}F NMR spectrum by a signal at $\delta = -127.1$ ppm showing $J_{F,H} = 7.2$ Hz (to H-2 in *meta* position to the fluorine substituent) and 9.4 Hz

* Corresponding author. Tel.: +49 (0) 345 55 25660; fax: +49 (0) 345 55 27030.
E-mail address: rene.csuk@chemie.uni-halle.de (R. Csuk).

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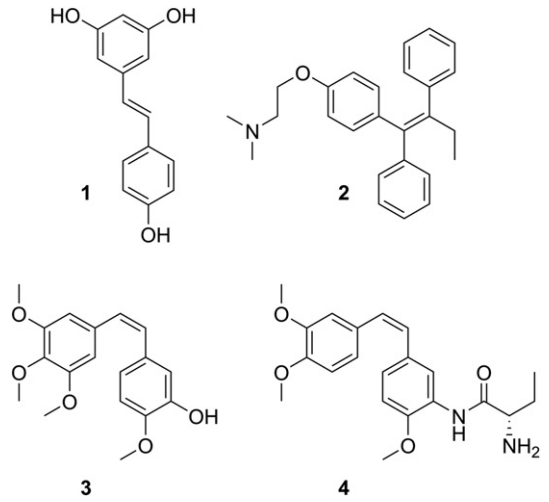


Fig. 1. Structure of resveratrol (**1**), tamoxifen (**2**), combretastatin A-4 (**3**) and ombrabulin. (**4**).

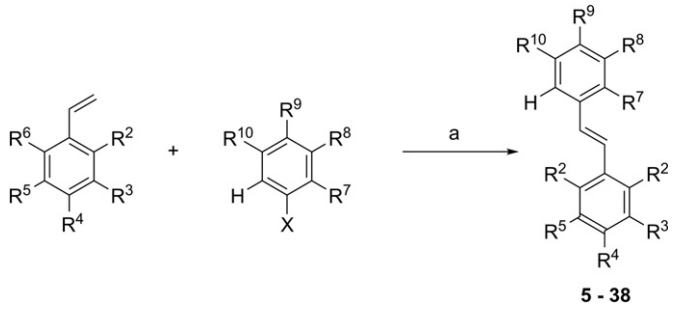
(to the adjacent proton). Carbon C-6 bearing the fluorine substituent shows a $^{1}J_{C,F} = 241.3$ Hz. The coupling constant $^{3}J = 16.6$ Hz for the alkenic protons is typical for a (*E*) configurated double bond.

2.2. Biology

Compounds **5**–**38** (and tamoxifen (**2**) as a standard) were tested for antitumor activity in a panel of 8 human cancer cell lines using a sulforhodamine B assay (SRB) [40]. The results from these tests are summarized in Table 1.

Compounds **25**, **26**, **28**, **30**, **31**, **33**, **34** and **37** showed only weak activity in the colorimetric SRB test. Also, the selectivity towards tumor cells compared to non-malignant mouse fibroblasts is low. Compound **22** was found to be inactive at all with IC_{50} values for all cell lines >30 μmol. A minimum of three methoxy groups in the molecule seems to be a prerequisite for activity.

From the comparison of activity of **9** and **10** we assumed that an extra fluorine substituent [41] led to a decreased activity. This trend, however, did not hold for compounds **6** and **7** both showing a comparable cytotoxicity. Cytotoxicity drops for the 2,4-dimethoxy analog **8** (as compared to a 2,5-dimethoxy compound **7**). In this series, a 3,5-dimethoxy substitution pattern seems to work best. Whereas dihydroxy substituted **37** showed only weak cytotoxicity, an improvement was observed for its 2,5-dimethoxy analog **36**. An even better result was observed for fluorinated **35**, but the highest cytotoxicity was found for **38** with IC_{50} values between 10 nmol and 60 nmol. Compared to tamoxifen (**3**) this reflects an improvement in cytotoxicity by factor 3. Contrary to halogenated [42] combretastatin analogs, these compounds did not show any significant antibacterial/antifungal effects.



Scheme 1. Synthesis of the stilbenes **5**–**38**: reagents and conditions: triethanolamine, Pd(II) acetate, 24 h, 100 °C.

To prove that cell death was triggered by apoptosis rather than by necrosis, an extra dye-exclusion test (trypan blue) and an acridine orange/ethidium bromide assay [43,44] as well as a DNA-laddering experiment were performed [45–47]. Thus, to determine the extent of apoptosis, trypan blue staining and counting experiments were performed (Fig. 2). The apoptotic cells have an intact cell membrane and can exclude the dye whereas necrotic cell are colored blue. The results from these experiments are summarized in Table 2.

Additional AO/EB tests support these results. In this test, green fluorescent cells were found, hence indicating an apoptotic behavior of the compounds. On principle, an AO/EB assay doesn't allow quantification of the extent of apoptosis but confirms the results from the trypan blue staining experiments. Another evidence for apoptosis is DNA laddering [45,47] as observed by gel electrophoresis. The programmed cell death is characterized by fragmentation of DNA into smaller parts of 180 bp; these can be observed as DNA laddering in gel electrophoresis.

3. Conclusions

In this study we have synthesized highly substituted (*E*) configurated stilbenes. In conclusion, these compounds are initiators of programmed cell death and several of them show high antitumor activity against a panel of 8 human cell lines. Cell death is triggered by apoptosis as shown by a dye-exclusion test, extra AO/EB assays and DNA-laddering experiments. Compound **38** shows a biological activity comparable to compretastatin A-4. Whereas compretastatins and analogs (possessing a *cis* configurated alkenic bond) possess *in vitro* a high tendency to undergo *cis*/*trans* isomerization (with accompanying decreasing loss of cytotoxicity) compound **38** was shown to be configurationally stable. Thus, as exemplified with **38** a (*Z*) configuration seems not to be a prerequisite for a high cytotoxicity. Cell death was triggered by apoptosis. It remains

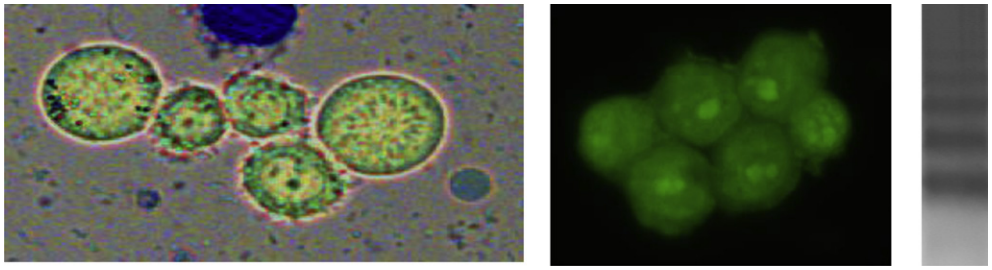


Fig. 2. Trypan blue assay (for ovarian cancer cell line A2780, left), acridine orange/ethidium bromide staining (for ovarian cancer cell line A2780, middle) and DNA laddering (for ovarian cancer cell line A2780, right) of compound **38** after treatment of the cells with IC_{50} concentrations for 24 h.

Table 1
Cytotoxicity (IC_{50} [in μmol]) for **5**–**38** (in order of decreasing cytotoxicity) and tamoxifen (**2**) in a panel of various cancer cell lines [518A2 (melanoma), A253 (head), A549 (lung), A2780 (ovarian), DLD1 (colon), 850C (anaplastic thyroid), MCF7 (mamma), LIPO (liposarcoma) and non-malignant mouse fibroblasts (NiH3T3)]. Values were obtained from SRB assays after 96 h of treatment; the values are averaged from at least 5 independent experiments; variation ±7%. Average corresponds to an averaged IC_{50} value (in μmol) including all cell lines, selectivity was calculated from the ratio of the averaged IC_{50} values for the tumor cells to the IC_{50} value for the mouse fibroblasts.

No	518A2	850C	A253	A549	A2780	DLD1	Lipo	MCF7	Average	NiH3T3	Selectivity
38	0.03	0.03	0.03	0.03	0.01	0.04	0.03	0.06	0.03	0.05	1.34
35	0.20	0.13	0.48	0.18	0.11	0.20	0.21	0.22	0.22	0.19	0.88
5	0.22	0.21	0.83	0.25	0.15	0.21	0.40	0.51	0.35	0.21	0.60
6	0.52	0.70	0.52	0.67	0.64	0.85	0.61	0.39	0.61	0.92	1.50
7	0.72	0.86	0.80	0.96	0.87	0.91	0.65	0.54	0.79	1.54	1.95
8	1.33	1.33	1.53	1.80	1.27	2.00	1.41	1.64	1.54	2.08	1.35
36	1.74	2.26	1.34	2.21	2.01	2.26	1.98	2.09	1.99	2.66	1.34
16	2.11	2.62	1.34	2.35	1.40	2.73	2.12	0.89	1.95	1.87	0.96
9	2.81	2.46	2.35	3.04	2.06	2.86	2.86	1.89	2.54	3.68	1.45
17	1.49	2.02	1.79	2.28	2.06	2.22	1.56	0.89	1.79	2.55	1.43
18	2.47	1.93	2.19	3.65	1.93	2.65	3.28	1.80	2.49	3.01	1.21
20	3.67	3.30	3.64	5.14	3.21	4.74	4.98	2.34	3.88	4.90	1.26
14	13.05	13.67	8.93	8.90	10.23	12.09	15.29	13.00	11.90	10.78	0.91
15	14.89	19.75	13.65	7.17	10.84	14.05	14.15	9.87	13.05	10.57	0.81
27	15.13	14.53	11.28	8.11	15.87	25.70	12.45	7.50	13.82	7.16	0.52
12	15.40	13.68	12.78	11.41	12.99	29.46	15.55	13.00	15.53	9.46	0.61
13	17.49	17.42	14.43	18.96	25.96	17.65	15.61	7.71	16.90	15.00	0.89
11	17.73	18.16	12.87	14.74	29.94	19.42	13.16	13.16	17.40	14.96	0.86
10	18.04	17.72	15.83	22.16	23.92	14.95	16.51	11.20	17.54	6.76	0.39
23	16.49	13.35	9.30	14.31	11.84	12.43	19.87	5.80	12.92	11.53	0.89
19	15.99	22.94	14.33	5.28	11.66	16.42	21.98	11.58	15.02	4.51	0.30
21	17.39	15.18	17.33	15.86	15.56	16.45	14.05	14.11	15.74	12.19	0.77
24	22.45	21.79	19.75	12.24	4.15	19.28	23.63	12.17	16.93	6.86	0.41
32	15.53	11.95	9.10	12.75	16.15	9.30	17.01	16.41	13.53	12.35	0.91
29	28.47	23.01	10.76	10.00	16.68	21.64	18.26	8.03	17.11	10.52	0.61
26	28.36	18.70	15.16	12.66	16.62	22.91	17.37	14.17	18.24	9.59	0.53
37	19.43	16.77	9.88	15.77	10.47	18.00	>30	10.63	14.42	21.06	1.46
25	22.03	24.76	17.25	22.46	18.89	26.83	21.28	7.25	20.09	7.45	0.37
30	25.32	22.49	16.76	21.61	28.05	16.52	26.57	9.75	20.88	19.56	0.94
28	22.92	30.17	20.74	>30	28.20	17.58	25.61	5.69	21.56	11.80	0.55
34	22.00	24.45	14.53	19.01	12.42	18.11	24.07	13.18	18.47	12.38	0.55
31	27.35	>30	21.89	17.27	15.90	24.06	>30	14.85	20.22	11.13	0.67
33	>30	>30	>30	>30	>30	25.34	>30	12.97	19.16	14.80	0.55
22	>30	>30	>30	>30	>30	>30	>30	>30	>30	24.22	0.77
Tamoxifen	7.62	11.09	8.92	9.66	7.77	4.78	8.64	7.10	8.20	7.26	0.89

subject to additional experiments whether these compounds show significant tubulin binding properties and may act as anti-angiogenic agents.

4. Experimental

4.1. General

Instrumentation, cell lines and culture conditions, SRB cytotoxicity assay and DNA fragmentation assay as described previously [48].

4.2. General procedure for the Mizoroki–Heck reactions

A mixture of the styrene (3 mmol), the halogenated benzene (3 mmol), triethanolamine (3 mmol) and Pd (II) acetate (0.03 g) was stirred under argon at 100 °C for 24 h. The reaction was cooled to 25 °C, quenched by the addition of dil. aq. hydrochloric acid (2 N, 10 ml), and extracted with ether (3 × 100 ml). The organic phases were dried (Na_2SO_4), the solvents evaporated, and the crude product was subjected to chromatography (silica gel, hexane/ethyl acetate mixtures).

4.3. (E) 3-hydroxy-3′,4,5′-trimethoxystilbene (*5*)

Following the general procedure, **5** was obtained from 3-hydroxy-4-methoxystyrene and 3,5-dimethoxyiodobenzene; yield: 58.7%; colorless solid; mp 94–96 °C (lit.: 90–91 °C [49], 89–90 °C [50]); $R_F = 0.48$ (silica gel, hexanes/ethyl acetate, 3:1); IR (KBr): ν = 3506*br*, 2999*m*, 2940*m*, 2838*m*, 1592*s*, 1511*s*, 1472*m*, 1456*m*, 1443*m*, 1427*m*, 1357*w*, 1329*w*, 1316*m*, 1293*m*, 1279*m*, 1268*s*, 1225*m*, 1198*m*, 1151*s*, 1130*m*, 1060*m*, 1027*m* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 220 (4.54), 326 (4.51) nm; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.12 (*d*, 1 H, ^4J = 1.7 Hz, C*H* (2)), 6.96 (*d*, 1H, ^3J (trans) = 16.2 Hz, CH═ (1)), 6.96 (*dd*, 1H, ^3J = 8.3 Hz, ^4J = 1.7 Hz, C*H* (6)), 6.86 (*d*, 1H, ^3J (trans) = 16.2 Hz, CH═ (2)), 6.81 (*d*, 1H, ^3J = 8.3 Hz, C*H* (5)), 6.62 (*d*, 2H, ^4J = 2.0 Hz, C*H* (2′) + C*H* (6′)), 6.35 (*t*, 1H, ^4J = 2.0 Hz, C*H* (4′)) 3.89 (*s*, 3H, OC*H*$_3$), 3.80 (*s*, 6H, OC*H*$_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.9 (C3′ + C5′, $C_{quart.}$), 146.5 (C3, $C_{quart.}$), 145.7 (C4, $C_{quart.}$), 139.6 (C1′, $C_{quart.}$), 130.9

Table 2
Apoptotic effect [in %] of derivatives on A549 cells: (±standard error, 6 experiments each); cells were treated with **5** (0.5 μM), **6** (2.5 μM), **8** (3 μM), **9** (2.5 μM), **17** (20 μM), **20** (10 μM), **35** (0.4 μM), **36** (20 μM) and **38** (0.3 μM), respectively.

Compound	**5**	**6**	**8**	**9**	**17**	**20**	**35**	**36**	**38**
Apoptosis [%]	78.0 ± 5.2	73.9 ± 4.7	74.1 ± 4.2	77.1 ± 3.2	77.7 ± 3.7	78.6 ± 4.0	64.1 ± 5.2	72.2 ± 3.3	77.3 ± 3.4

(C1, $C_{quart.}$), 128.8 (*C*H=), 127.1 (*C*H=), 119.4 (C6, *C*H), 111.9 (C2, *C*H), 110.6 (C5, *C*H), 104.4 (C2′ + C6′, *C*H), 99.7 (C4′, *C*H), 56.0 (OCH_3), 55.3 (OCH_3) ppm; MS (ESI, MeOH): *m*/*z* (%) = 285.3 (100% $[M - H]^-$), 570.8 (13% $[2M - H]^-$); analysis for $C_{17}H_{18}O_4$ (286.32): C, 71.31; H, 6.34; found: C, 71.14; H, 6.61.

4.4. (E) 4′-fluoro-3-hydroxy-3′,4,5′-trimethoxystilbene (**6**)

Following the general procedure, **6** was obtained from 3-hydroxy-4-methoxystyrene and 3,5-dimethoxy-4-fluorobromobenzene; yield: 61.6%; colorless solid; mp 179–181 °C; R_F = 0.12 (silica gel, hexanes/ethyl acetate, 8:2); IR (KBr): *ν* = 3504*br*, 2943*m*, 2844*m*, 2363*w*, 1733*w*, 1605*s*, 1519*s*, 1458*m*, 1425*m*, 1363*m*, 1334*m*, 1264*s*, 1222*m*, 1206*m*, 1163*m*, 1128*s*, 1025*m* cm^{-1}; UV–vis (methanol): λ_{max} (log *ε*) = 326 (4.30) nm; ^1H NMR (400 MHz, $CDCl_3$): *δ* = 7.06 (*d*, 1H, ^4J = 2.1 Hz, C*H* (2)), 7.05 (*d*, 1H, ^3J (trans) = 16.2 Hz, CH= (1)), 6.96 (*dd*, 1H, ^3J = 8.3 Hz, ^4J = 2.1 Hz, C*H* (6)), 6.93 (*d*, 1H, ^3J (trans) = 16.2 Hz, CH= (2)), 6.90 (*d*, 1H, ^3J = 8.3 Hz, C*H* (5)), 6.85 (*d*, 2H, $^4J_{H,F}$ = 7.3 Hz, C*H* (2′) + C*H* (6′)), 3.87 (*s*, 6H, OCH_3), 3.85 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 148.4 (*d*, $^2J_{C,F}$ = 8.9 Hz, C3′ + C5′, $C_{quart.}$), 147.3 (C4, $C_{quart.}$), 146.2 (C3, $C_{quart.}$), 141.5 (*d*, $^1J_{C,F}$ = 246.2 Hz, C4′, $C_{quart.}$), 133.6 (*d*, $^4J_{C,F}$ = 1.8 Hz, C1′, $C_{quart.}$), 130.7 (C1, $C_{quart.}$), 128.5 (*C*H=), 126.0 (*C*H=), 119.1 (C6, *C*H), 111.9 (C2, *C*H), 111.7 (C5, *C*H), 103.8 (C2′ + C6′, *C*H), 56.0 (OCH_3), 55.7 (OCH_3) ppm; ^{19}F NMR (188 MHz, $CDCl_3$): *δ* = −161.2 (*t*, $^4J_{F,H}$ = 7.3 Hz, −*F*) ppm; MS (ESI, MeOH): *m*/*z* = 303.3 (100% $[M - H]^-$), 349.0 (8% $[M + HCO_2]^-$), 606.8 (18% $[2M - H]^-$); analysis for $C_{17}H_{17}FO_4$ (304.31): C, 67.10; H, 5.63; found: C, 67.01; H, 5.82.

4.5. (E) 3-hydroxy-2′,4,5′-trimethoxystilbene (**7**)

Following the general procedure, **7** was obtained from 3-hydroxy-4-methoxystyrene and 2,5-dimethoxyiodobenzene; yield: 49.2%; off-white solid; mp 97–98 °C; R_F = 0.27 (silica gel, hexanes/ethyl acetate, 8:2); IR (KBr): *ν* = 3538*br*, 2992*w*, 2935*w*, 2834*w*, 2360*w*, 1586*w*, 1508*m*, 1492*w*, 1439*w*, 1426*w*, 1312*w*, 1286*m*, 1270*m*, 1243*w*, 1219*w*, 1195*w*, 1158*w*, 1131*w*, 1119*w*, 1047*w*, 1022*w* cm^{-1}; UV–vis (methanol): λ_{max} (log *ε*) = 233 (4.41), 314 (4.21), 362 (4.34) nm; ^1H NMR (400 MHz, $CDCl_3$): *δ* = 7.29 (*d*, 1H, ^3J (trans) = 16.6 Hz, CH= (1)), 7.20 (*d*, 1H, ^4J = 2.9 Hz, C*H* (6′)), 7.12 (*d*, 1H, ^3J (trans) = 16.6 Hz, CH= (2)), 7.10 (*d*, 1H, ^4J = 2.1 Hz, C*H* (2)), 6.98 (*dd*, 1H, ^3J = 8.3 Hz, ^4J = 2.1 Hz, C*H* (6)), 6.93 (*d*, 1H, ^3J = 8.3 Hz, C*H* (5)), 6.90 (*d*, 1H, ^3J = 8.9 Hz, C*H* (3′)), 6.74 (*dd*, 1H, ^3J = 8.9 Hz, ^4J = 2.9 Hz, C*H* (4′)), 3.85 (*s*, 3H, OCH_3), 3.82 (*s*, 3H, OCH_3), 3.77 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 154.7 (C5′, $C_{quart.}$), 152.0 (C2′, $C_{quart.}$), 148.2 (C3, $C_{quart.}$), 147.5 (C4, $C_{quart.}$), 132.1 (C1, $C_{quart.}$), 129.7 (*C*H=), 127.9 (C1′, $C_{quart.}$), 121.7 (*C*H=), 119.5 (C6, *C*H), 114.0 (C4′, *C*H), 113.1 (C2, *C*H), 113.0 (C3′ + C5, *C*H), 111.8 (C6′, *C*H), 56.4 (OCH_3), 56.1 (OCH_3), 55.7 (OCH_3) ppm; MS (ESI, MeOH): *m*/*z* = 285.2 (100% $[M - H]^-$); 570.7 (4% $[2M - H]^-$); analysis for $C_{17}H_{18}O_4$ (286.32): C, 71.31; H, 6.34; found: C, 71.22; H, 6.52.

4.6. (E) 3-hydroxy-2′,4,4′-trimethoxystilbene (**8**)

Following the general procedure, **8** was obtained from 3-hydroxy-4-methoxystyrene and 2,4-dimethoxyiodobenzene; yield: 54.7%; off-white solid; mp 139–140 °C; R_F = 0.46 (silica gel, hexanes/ethyl acetate 3:1); IR (KBr): *ν* = 3382*br*, 2990*m*, 2962*m*, 2932*m*, 2837*m*, 1604*s*, 1577*s*, 1517*s*, 1500*s*, 1460*s*, 1440*m*, 1416*m*, 1348*w*, 1323*m*, 1291*s*, 1250*s*, 1202*s*, 1157*s*, 1120*s*, 1038*s*, 1023*s* cm^{-1}; UV–vis (methanol): λ_{max} (log *ε*) = 210 (4.60), 294 (4.48), 330 (4.65) nm; ^1H NMR (400 MHz, $CDCl_3$): *δ* = 7.45 (*d*, 1H, ^3J = 8.5 Hz, C*H* (6′)), 7.23 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (1)), 7.13 (*d*, 1H, ^4J = 1.9 Hz, C*H* (2)), 6.94 (*dd*, 1H, ^3J = 8.6 Hz, ^4J = 1.9 Hz, C*H* (6)), 6.88 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (2)), 6.79 (*d*, 1H, ^3J = 8.6 Hz, C*H* (5)), 6.49 (*dd*, 1H, ^3J = 8.5 Hz, ^4J = 2.5 Hz, C*H* (5′)), 6.45 (*d*, 1H, ^4J = 2.5 Hz, C*H* (3′)), 3.88 (*s*, 3H, OCH_3), 3.85 (*s*, 3H, OCH_3), 3.81 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 160.2 (C4′, $C_{quart.}$), 157.9 (C2′, $C_{quart.}$), 145.9 (C3, $C_{quart.}$), 145.7 (C4, $C_{quart.}$), 132.2 (C1, $C_{quart.}$), 126.9 (C6′, *C*H), 126.6 (*C*H=), 121.8 (*C*H=), 119.7 (C1′, $C_{quart.}$), 118.9 (C6, *C*H), 111.7 (C2, *C*H), 110.6 (C5, *C*H), 104.9 (C5′, *C*H), 98.5 (C3′, *C*H), 55.9 (OCH_3), 55.5 (OCH_3), 55.74 (OCH_3) ppm; MS (ESI, MeOH): *m*/*z* (%) = 285.2 (100% $[M - H]^-$); 570.7 (4% $[2M - H]^-$); analysis for $C_{17}H_{18}O_4$ (286.32): C, 71.31; H, 6.34; found: C, 71.11; H, 6.52.

4.7. (E) 3,3′,4,5′-tetramethoxystilbene (**9**)

Following the general procedure, **9** was obtained from 3,4-dimethoxystyrene and 3,5-dimethoxyiodobenzene; yield: 58.8%; off-white solid; mp 72–74 °C (lit.: 66–67 °C [51], 67–68 °C [52]); R_F = 0.77 (silica gel, hexanes/ethyl acetate, 3:1); IR (KBr): *ν* = 3057*s*, 2999*s*, 2942*s*, 2833*s*, 1838*m*, 1625*w*, 1593*s*, 1575*m*, 1496*s*, 1464*s*, 1439*s*, 1419*s*, 1334*s*, 1301*m*, 1292*m*, 1272*s*, 1243*s*, 1218*s*, 1184*s*, 1161*s*, 1107*s*, 1047*s*, 1022*s* cm^{-1}; UV–vis (methanol): λ_{max} (log *ε*) = 211 (4.34), 285 (4.05), 3240 (4.09) nm; ^1H NMR (400 MHz, $CDCl_3$): *δ* = 7.04 (*d*, 1H, ^4J = 2.1 Hz, C*H* (2)), 7.02 (*dd*, 1H, ^3J = 8.1 Hz, ^4J = 2.1 Hz, C*H* (6)), 6.99 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (1)), 6.98 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (2)), 6.83 (*d*, 1H, ^3J = 8.1 Hz, C*H* (5)), 6.64 (*d*, 2H, ^4J = 2.0 Hz, C*H* (2′) + C*H* (6′)), 6.36 (*t*, 1H, ^4J = 2.0 Hz, C*H* (4′)), 3.92 (*s*, 3H, OCH_3), 3.88 (*s*, 3H, OCH_3), 3.81 (*s*, 6H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 160.9 (C3′ + C5′, $C_{quart.}$), 149.1 (C4, $C_{quart.}$), 149.0 (C3, $C_{quart.}$), 139.5 (C1′, $C_{quart.}$) 130.2 (C1, $C_{quart.}$), 128.9 (*C*H=), 126.7 (*C*H=), 120.0 (C6, *C*H), 111.2 (C5, *C*H), 108.8 (C2, *C*H), 104.3 (C2′ + C6′, *C*H), 99.7 (C4′, *C*H), 55.9 (OCH_3), 55.8 (OCH_3), 55.3 (OCH_3) ppm; MS (i.e. 70 eV): *m*/*z* (%) = 270 (100), 255 (19), 240 (16), 121 (20); analysis for $C_{18}H_{20}O_4$ (300.35): C, 71.98; H, 6.71; found: C, 71.77; H, 6.98.

4.8. (E) 4′-fluoro-3,3′,4,5′-tetramethoxystilbene (**10**)

Following the general procedure, **10** was obtained from 3,4-dimethoxystyrene and 3,5-dimethoxy-4-fluorobromobenzene; yield: 56.1%; colorless solid; mp 110–111 °C; R_F = 0.14 (silica gel, hexanes/ethyl acetate, 8:2); IR (KBr): *ν* = 3001*m*, 2961*m*, 2935*s*, 2836*m*, 1605*s*, 1521*s*, 1463*s*, 1425*s*, 1361*s*, 1336*m*, 1289*m*, 1263*s*, 1222*s*, 1198*m*, 1159*s*, 1161*s*, 1135*s*, 1024*s* cm^{-1}; UV–vis (methanol): λ_{max} (log *ε*) = 219 (4.35), 326 (4.48) nm; ^1H NMR (400 MHz, acetone-d_6): *δ* = 7.19 (*d*, 1H, ^4J = 2.1 Hz, C*H* (2)), 7.14 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (1)), 7.04 (*dd*, 1H, ^3J = 8.1 Hz, ^4J = 2.1 Hz, C*H* (6)), 7.03 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (2)), 6.93 (*d*, 2H, $^4J_{H,F}$ = 7.0 Hz, C*H* (2′) + C*H* (6′)), 6.91 (*d*, 1H, ^3J = 8.1 Hz, C*H* (5)), 3.89 (*s*, 6H, 2× OCH_3), 3.84 (*s*, 3H, OCH_3), 3.80 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, acetone-d_6): *δ* = 150.4 (C4, $C_{quart.}$), 150.3 (C3, $C_{quart.}$), 149.3 (*d*, $^2J_{C,F}$ = 7.6 Hz, C3′ + C5′, $C_{quart.}$), 142.4 (*d*, $^1J_{C,F}$ = 250.8 Hz, C4′, $C_{quart.}$), 134.3 (*d*, $^4J_{C,F}$ = 0.8 Hz, C1′, $C_{quart.}$), 131.1 (C1, $C_{quart.}$), 129.3 (*C*H=), 126.7 (*C*H=), 120.7 (C6, *C*H), 112.6 (C5, *C*H), 110.2 (C2, *C*H), 104.5 (C2′ + C6′, *C*H), 56.5 (OCH_3), 56.4 (OCH_3); ^{19}F NMR (188 MHz, acetone-d_6): *δ* = −160.5 (*t*, $^4J_{F,H}$ = 7.0 Hz, −*F*) ppm; MS (i.e., 70 eV): *m*/*z* (%) = 318 (100), 303 (20), 244 (7); analysis for $C_{18}H_{19}FO_4$ (318.34): C, 67.91; H, 6.02; found: C, 67.78; H, 6.27.

4.9. (E) 4-hydroxy-4′-fluoro-3,3′,5′-trimethoxystilbene (**11**)

Following the general procedure, **11** was obtained from 4-hydroxy-3-methoxystyrene and 3,5-dimethoxy-4-fluorobromobenzene; yield: 52.0%; off-white solid; mp 115–117 °C; R_F = 0.12 (silica gel, hexanes/ethyl acetate, 8:2); IR (KBr): *ν* = 3431*br*, 3000*w*, 2937*w*, 2841*w*, 1606*m*, 1517*s*, 1456*m*, 1428*m*, 1383*w*, 1346*m*, 1279*m*, 1259*m*, 1244*m*, 1226*m*, 1185*w*, 1160*w*, 1133*s*, 1030*w* cm^{-1}; UV–vis

(methanol): λ_{max} (log ε) = 327 (4.44) nm; ^{1}H NMR (400 MHz, CD_3CN): δ = 7.16 (*d*, 1H, ^4J = 2.1 Hz, C*H* (2)), 7.09 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (1)), 6.98 (*dd*, 1H, ^3J = 8.1 Hz, ^4J = 2.1 Hz, C*H* (6)), 6.96 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (2)), 6.86 (*d*, 2H, $^4J_{H,F}$ = 7.2 Hz, C*H* (2′) + C*H* (6′)), 6.81 (*d*, 1H, ^3J = 8.1 Hz, C*H* (5)), 3.90 (*s*, 3H, OCH_3), 3.88 (*s*, 6H, OCH_3) ppm; ^{13}C NMR (100 MHz, CD_3CN): δ = 149.4.0 (*d*, $^2J_{C,F}$ = 8.2 Hz, C5′ + C3′, $C_{quart.}$), 148.5 (C3, $C_{quart.}$), 147.2 (C4, $C_{quart.}$), 142.5 (*d*, $^1J_{C,F}$ = 251.4 Hz, C4′, $C_{quart.}$), 134.7 (*d*, $^4J_{C,F}$ = 0.8 Hz, C1′, $C_{quart.}$) 130.7 (C1, $C_{quart.}$), 129.8 (*C*H=), 126.5 (*C*H=), 121.3 (C6, *C*H), 115.9 (C5, *C*H), 110.1 (C2, *C*H), 104.7 (C2′ + C6′, *C*H), 56.5 (OCH_3), 56.4 (OCH_3) ppm; ^{19}F NMR (188 MHz, CD_3CN): δ = −161.1 (*t*, $^4J_{F,H}$ = 7.2 Hz, −*F*) ppm; MS (ESI, MeOH): *m*/*z* (%) = 303.2 (100% [M − H]$^-$); analysis for $C_{17}H_{17}FO_4$ (304.31): C, 67.10; H, 5.63; found: C, 66.86; H, 5.76.

4.10. (E) 3-methoxy-2′,4,5′-trihydroxystilbene (**12**)

Following the general procedure, **12** was obtained from 4-hydroxy-3-methoxystyrene and 2,5-dihydroxyiodobenzene: yield: 48.5%; grey solid; mp 178–179 °C; R_F = 0.62 (silica gel, hexanes/ethyl acetate, 1:1); IR (KBr): ν = 3395*br*, 2925*w*, 1607*w*, 1513*w*, 1459*w*, 1363*w*, 1297*w*, 1264*w*, 1220*w*, 1197*w*, 1121*w*, 1035*w* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 295 (4.24), 347 (4.30) nm; ^{1}H NMR (400 MHz, acetone-d_6): δ = 7.89 (*br s*, 1H, O*H*), 7.67 (*br s*, 1H, O*H*), 7.62 (*br s*, 1H, O*H*), 7.28 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (1)), 7.17 (*d*, 1H, ^4J = 1.9 Hz, C*H* (2)), 7.04 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (2)), 7.02 (*d*, 1H, ^4J = 2.9 Hz, C*H* (6′)), 6.99 (*dd*, 1H, ^3J = 8.3 Hz, ^4J = 1.9 Hz, C*H* (6)), 6.79 (*d*, 1H, ^3J = 8.3 Hz, C*H* (5)), 6.70 (*d*, 1H, ^4J = 8.8 Hz, C*H* (3′)), 6.58 (*dd*, ^3J = 8.8 Hz, ^4J = 2.9 Hz, C*H* (4′)), 3.88 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, acetone-d_6): δ = 151.2 (C5′, $C_{quart.}$), 148.5 (C3, $C_{quart.}$), 148.3 (C2′, $C_{quart.}$), 147.1 (C4, $C_{quart.}$), 130.9 (C1, $C_{quart.}$), 129.0 (*C*H=), 126.0 (C1′, $C_{quart.}$) 121.7 (*C*H=), 120.7 (C6, *C*H), 117.1 (C3′, *C*H), 115.6 (C4′ + C5, *C*H), 112.5 (C6′, *C*H), 109.8 (C2, *C*H), 56.0 (OCH_3) ppm; MS (ESI, MeOH): *m*/*z* (%) = 257.5 (100% [M − H]$^-$); 303.3 (30% [M + HCO_2]$^-$); 515.0 (81% [2M − H]$^-$); analysis for $C_{15}H_{14}O_4$ (258.27): C, 69.76; H, 5.46; found: C, 69.68; H, 5.66.

4.11. (E) 4-hydroxy-3,3′,5,5′-tetramethoxystilbene (**13**)

Following the general procedure, **13** was obtained from 3,5-dimethoxy-4-hydroxystyrene and 3,5-dimethoxyiodobenzene; yield: 57.9%; colorless solid; mp 96–98 °C; R_F = 0.29 (silica gel, hexanes/ethyl acetate, 3:1); IR (KBr): ν = 3425*br*, 2930*w*, 1593*w*, 1520*w*, 1456*w*, 1427*w*, 1361*w*, 1334*w*, 1285*w*, 1252*w*, 1208*w*, 1157*w*, 1114*w*, 1067*w* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 224 (4.40), 325 nm (4.44); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.98 (*d*, 1H, ^3J (trans) = 16.2 Hz, CH= (2)), 6.86 (*d*, 1H, ^3J (trans) = 16.2 Hz, CH= (1)), 6.73 (*s*, 2H, C*H* (2) + C*H* (6)), 6.63 (*d*, 2H, ^4J = 2.1 Hz, C*H* (2′) + C*H* (6′)), 6.42 (*t*, 1H, ^4J = 2.1 Hz, C*H* (4′)), 5.55 (*br s*, 1H, O*H*), 3.93 (*s*, 6H, OCH_3), 3.81 (*s*, 6H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.0 (C3′ + C5′, $C_{quart.}$), 147.2 (C3 + C5, $C_{quart.}$) 139.4 (C1′, $C_{quart.}$), 134.9 (C4, $C_{quart.}$), 129.3 (*C*H=), 128.7 (C1, $C_{quart.}$), 126.8 (*C*H=), 104.3 (C2′ + C6′, *C*H), 103.4 (C2 + C6, *C*H), 99.76 (C4′, *C*H), 56.3 (OCH_3), 55.3 (OCH_3) ppm; MS (ESI, MeOH): *m*/*z* (%) = 315.6 (100% [M − H]$^-$); analysis for $C_{18}H_{20}O_5$ (316.35): C, 68.34; H, 6.37; found: C, 68.17; H, 6.57.

4.12. (E) 3,5-dimethoxy-3′,4,5′-trihydroxystilbene (**14**)

Following the general procedure, **14** was obtained from 3,5-dimethoxy-4-hydroxystyrene and 3,5-dihydroxyiodobenzene; yield: 53.4%; colorless solid; mp 94–97 °C; R_F = 0.08 (silica gel, hexanes/ethyl acetate, 3:1); IR (KBr): ν = 3417*br*, 2936*w*, 1702*w*, 1608*m*, 1517*m*, 1457*w*, 1425*w*, 1344*w*, 1257*w*, 1214*w*, 1147*w*, 1111*m* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 224 (4.38), 326 (4.42) nm; ^{1}H NMR (400 MHz, CD_3CN): δ = 6.98 (*d*, 1H, ^3J (trans) = 16.2 Hz, CH= (1)), 6.91 (*d*, 1H, ^3J (trans) = 16.2 Hz, CH= (2)), 6.90 (*br s*, 2H, O*H*), 6.83 (*s*, 2H, C*H* (2) + C*H* (6)), 6.48 (*d*, 2H, ^4J = 2.1 Hz, C*H* (2′) + C*H* (6′)), 6.33 (*br s*, 1H, O*H*), 6.17 (*t*, 1H, ^4J = 2.1 Hz, C*H* (4′)), 3.85 (*s*, 6H, OCH_3) ppm; ^{13}C NMR (100 MHz, CD_3CN): δ = 159.2 (C3′ + C5′, $C_{quart.}$), 148.7 (C3 + C5, $C_{quart.}$) 141.0 (C1′, $C_{quart.}$), 136.4 (C4, $C_{quart.}$), 129.9 (*C*H=), 129.6 (C1, $C_{quart.}$), 127.4 (*C*H=), 105.9 (C2′ + C6′, *C*H), 105.0 (C2 + C6, *C*H), 102.6 (C4′, *C*H), 57.0 (OCH_3) ppm; MS (ESI, MeOH): *m*/*z* (%) = 287.5 (100% [M − H]$^-$), 333.3 (21% [M + HCO_2]$^-$), 575.0 (32% [2M − H]$^-$); analysis for $C_{16}H_{16}O_5$ (288.30): C, 66.66; H, 5.59; found: C, 66.42; H, 5.81.

4.13. (E) 4′-fluoro-4-hydroxy-3,3′,5,5′-tetramethoxystilbene (**15**)

Following the general procedure, **15** was obtained from 3,5-dimethoxy-4-hydroxystyrene and 3,5-dimethoxy-4-fluorobromobenzene; yield: 55.4%; colorless solid; mp 65–166 °C; R_F = 0.10 [silica gel, hexanes/ethyl acetate, 8:2 + AcOH (0.1%)]; IR (KBr): ν = 3505*m*, 3005*w*, 2961*w*, 2938*w*, 2841*w*, 1608*m*, 1516*s*, 1462*m*, 1429*w*, 1373*w*, 1348*m*, 1252*w*, 1219*m*, 1161*w*, 1127*s*, 1108*s*, cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 240 (4.30), 327 (4.44) nm; ^{1}H NMR (400 MHz, acetone-d_6): δ = 7.32 (*br s*, 1H, O*H*), 7.13 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (1)), 7.03 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (2)), 6.92 (*d*, 2H, $^4J_{H,F}$ = 7.3 Hz, C*H* (2′) + C*H* (6′)), 6.87 (*s*, 2H, C*H* (2) + C*H* (6)), 3.89 (*s*, 6H, OCH_3), 3.85 (*s*, 6H, OCH_3) ppm; ^{13}C NMR (100 MHz, acetone-d_6): δ = 149.2 (*d*, $^2J_{C,F}$ = 8.8 Hz, C3′ + C5′, $C_{quart.}$), 148.7 (C3 + C5, $C_{quart.}$) 142.3 (*d*, $^1J_{C,F}$ = 244.4 Hz, C4′, $C_{quart.}$), 136.9 (C4, $C_{quart.}$), 134.3 (*d*, $^4J_{C,F}$ = 5.0 Hz, C1′, $C_{quart.}$) 129.8 (*C*H=), 128.9 (C1, $C_{quart.}$), 126.3 (*C*H=), 104.8 (C2′ + C6′, *C*H), 104.4 (C2 + C6, *C*H), 56.5 (OCH_3), 56.4 (OCH_3) ppm; ^{19}F NMR (188 MHz, CD_3CN): δ = −160.6 (*t*, $^4J_{F,H}$ = 7.3 Hz, −*F*) ppm; MS (ESI, MeOH): *m*/*z* (%) = 333.2 (100% [M − H]$^-$); analysis for $C_{18}H_{19}FO_5$ (334.34): C, 64.66; H, 5.73; found: C, 64.42; H, 5.84.

4.14. (E) 4-hydroxy-2′,3,5,5′-tetramethoxystilbene (**16**)

Following the general procedure, **16** was obtained from 3,5-dimethoxy-4-hydroxystyrene and 2,5-dimethoxyiodobenzene; yield: 49.0%; off-white solid; mp 119–121 °C; R_F = 0.09 (silica gel, hexanes/ethyl acetate, 8:2); IR (KBr): ν = 3509*br*, 2997*w*, 2937*m*, 2833*m*, 2362*w*, 1780*w*, 1608*m*, 1517*s*, 1497*s*, 1463*s*, 1427*m*, 1371*m*, 1342*m*, 1312*m*, 1292*m*, 1222*s*, 1179*m*, 1163*m*, 1111*s*, 1042*s* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 214 (4.38), 342 (4.26) nm; ^{1}H NMR (400 MHz, acetone-d_6): δ = 7.29 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (1)), 7.18 (*d*, 1H, ^4J = 2.9 Hz, C*H* (6′)), 7.13 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (2)), 6.91 (*d*, 1H, ^3J = 9.9 Hz, C*H* (3′)), 6.87 (*s*, 2H, C*H* (2) + C*H* (6)), 6.78 (*dd*, ^3J = 9.9 Hz, ^4J = 2.9 Hz, C*H* (4′)), 3.87 (*s*, 6H, OCH_3), 3.82 (*s*, 3H, OCH_3), 3.77 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, acetone-d_6): δ = 154.6 (C5′, $C_{quart.}$), 151.9 (C2′, $C_{quart.}$), 148.7 (C3 + C5, $C_{quart.}$), 136.8 (C4, $C_{quart.}$), 130.4 (*C*H=), 129.5 (C1, $C_{quart.}$), 128.0 (C1′, $C_{quart.}$), 121.3 (*C*H=), 113.9 (C4′, *C*H), 113.0 (C3, *C*H), 111.9 (C6′, *C*H), 104.8 (C2 + C6, *C*H), 56.4 (OCH_3), 56.3 (OCH_3), 55.7 (OCH_3) ppm; MS (ESI, MeOH): *m*/*z* (%) = 315.2 (100% [M − H]$^-$); analysis for $C_{18}H_{20}O_5$ (316.35): C, 68.34; H, 6.37; found: C, 68.09; H, 6.54.

4.15. (E) 4′-fluoro-3′,4,5′-trimethoxystilbene (**17**)

Following the general procedure, **17** was obtained from 4-methoxystyrene and 3,5-dimethoxy-4-fluorobromobenzene; yield: 58.0%; colorless solid; mp 125–127 °C; R_F = 0.36 (silica gel, hexanes/ethyl acetate, 8:2); IR (KBr): ν = 3505*m*, 3005*w*, 2961*w*, 2938*w*, 2841*w*, 1608*m*, 1516*s*, 1462*m*, 1429*w*, 1373*w*, 1348*m*, 1252*w*, 1219*m*, 1161*w*, 1127*s*, 1108*s* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 214 (4.19), 319 (4.30) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43

(*d*, 2H, ^3J = 8.7 Hz, C*H* (2) + C*H* (6)), 6.94 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (1)), 6.88 (*d*, 2H, ^3J = 8.7 Hz, C*H* (3) + C*H* (5)), 6.85 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (2)), 6.71 (*d*, 2H, $^4J_{H,F}$ = 7.1 Hz, C*H* (2′) + C*H* (6′)), 3.91 (*s*, 6H, OCH_3), 3.81 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.4 (C4, $C_{quart.}$), 148.4 (*d*, $^2J_{C,F}$ = 9.1 Hz, C3′ + C5′, $C_{quart.}$), 142.1 (*d*, $^1J_{C,F}$ = 244.9 Hz, C4′, $C_{quart.}$), 133.1 (*d*, $^4J_{C,F}$ = 4.8 Hz, C1′, $C_{quart.}$), 129.8 (C1, $C_{quart.}$), 128.2 (*C*H=), 127.6 (C2 + C6, *C*H), 126.0 (*C*H=), 114.1 (C3 + C5, *C*H), 103.9 (C2′ + C6′, *C*H), 56.5 (O*C*H_3), 55.3 (O*C*H_3) ppm; ^{19}F NMR (188 MHz, $CDCl_3$): δ = −159.2 (*t*, $^4J_{F,H}$ = 6.7 Hz, −*F*) ppm; MS (i.e., 70 eV): *m*/*z* (%) = 288 (100), 276 (33), 257 (5), 242 (5), 230 (5), 214 (5); analysis for $C_{17}H_{17}FO_3$ (288.31): C, 70.82; H, 5.94; found: C, 70.59; H, 6.18.

4.16. (E) 2′,4,5′-trimethoxystilbene (**18**)

Following the general procedure, **18** was obtained from 4-methoxystyrene and 2,5-dimethoxyiodobenzene; yield: 56.0%; colorless solid; mp 59–61 °C (lit.: 61.9–62.7 °C [53], 67–68 °C [54]); R_F = 0.55 (silica gel, hexanes/ethyl acetate, 8:2); IR (KBr): ν = 2999*m*, 2935*m*, 2835*m*, 1603*m*, 1573*w*, 1511*s*, 1488*m*, 1458*m*, 1425*m*, 1319*w*, 1305*m*, 1281*m*, 1250*s*, 1237*m*, 1211*m*, 1175*m*, 1160*w*, 1119*m*, 1049*m*, 1022*m* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 207 (4.42), 295 (4.33), 341 (4.26) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (*d*, 2H, ^3J = 8.7 Hz, C*H* (2) + C*H* (6)), 7.30 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (1)), 7.12 (*d*, 1H, ^4J = 2.9 Hz, C*H* (6′)), 7.03 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (2)), 6.88 (*d*, 2H, ^3J = 8.7 Hz, C*H* (3) + C*H* (5)), 6.82 (*d*, 1H, ^3J = 9.0 Hz, C*H* (3′)), 6.76 (*dd*, 1H, ^3J = 9.0 Hz, ^4J = 2.9 Hz, C*H* (6′)), 3.83 (*s*, 3H, OCH_3), 3.81 (*s*, 3H, OCH_3), 3.80 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2 (C4, $C_{quart.}$), 153.8 (C5′, $C_{quart.}$), 151.3 (C2′, $C_{quart.}$), 130.6 (C1, $C_{quart.}$), 128.9 (*C*H=), 127.8 (C2 + C6, *C*H), 127.6 (C1′, $C_{quart.}$), 121.2 (*C*H=), 114.0 (C3 + C5, *C*H), 113.2 (C4′, *C*H), 112.3 (C3′, *C*H), 111.5 (C6′, *C*H), 56.3 (O*C*H_3), 55.8 (O*C*H_3), 55.3 (O*C*H_3) ppm; MS (i.e., 70 eV): *m*/*z* (%) = 270 (100), 255 (60), 227 (76), 152 (31), 115 (34); analysis for $C_{17}H_{18}O_3$ (270.32): C, 75.53; H, 6.71; found: C, 75.42; H, 6.95.

4.17. (E) 2′,5′-dihydroxy-4-methoxystilbene (**19**)

Following the general procedure, **19** was obtained from 4-methoxystyrene and 2,5-dihydroxyiodobenzene; yield: 52.8%; colorless solid; mp 141–142 °C; R_F = 0.30 (silica gel, hexanes/ethyl acetate, 3:1); IR (KBr): ν = 3227*br*, 3030*m*, 2835*w*, 1862*w*, 1605*m*, 1574*w*, 1513*s*, 1451*s*, 1360*w*, 1304*w*, 1290*w*, 1250*m*, 1189*s*, 1176*m*, 1111*w*, 1094*w*, 1032*w* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 293 (4.30), 345 (4.19) nm; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.95 (*br s*, 1H, O*H*), 8.71 (*br s*, 1H, O*H*), 7.45 (*d*, 2H, ^3J = 8.5 Hz, C*H* (2) + C*H* (6)), 7.19 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (1)), 6.99 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (2)), 6.92 (*d*, 1H, ^4J = 2.7 Hz, C*H* (6′)), 6.90 (*d*, 2H, ^3J = 8.7 Hz, C*H* (3) + C*H* (5)), 6.65 (*d*, 1H, ^3J = 8.5 Hz, C*H* (3′)), 6.50 (*dd*, 1H, ^3J = 8.5 Hz, ^4J = 2.7 Hz, C*H* (4′)), 3.75 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.8 (C4, $C_{quart.}$), 150.1 (C5′, $C_{quart.}$), 147.7 (C2′, $C_{quart.}$), 130.4 (C1, $C_{quart.}$), 127.6 (C2 + C6, *C*H), 127.2 (*C*H=), 124.6 (C1′, $C_{quart.}$), 121.6 (*C*H=), 116.6 (C3′, *C*H), 115.5 (C4′, *C*H), 114.3 (C3 + C5, *C*H), 111.7 (C6′, *C*H), 55.2 (O*C*H_3) ppm; MS (ESI, MeOH): *m*/*z* (%) = 241.3 (78% [M − H]$^-$), 287.1 (100% [M + HCO_2]$^-$), 482.9 (45% [2M − H]$^-$); analysis for $C_{15}H_{14}O_3$ (242.27): C, 74.36; H, 5.82; found: C, 74.18; H, 6.09.

4.18. (E) 2′,4,4′-trimethoxystilbene (**20**)

Following the general procedure, **20** was obtained from 4-methoxystyrene and 2,4-dimethoxyiodobenzene; yield: 57.3%; off-white solid; mp 87–90 °C (lit.: 86–89 °C [55], 94–95 °C [56]); R_F = 0.75 (silica gel, hexanes/ethyl acetate, 3:1). IR (KBr): ν = 2966*s*, 2835*s*, 1607*s*, 1575*m*, 1510*s*, 1454*s*, 1418*m*, 1320*m*, 1247*s*, 1207*s*, 1173*s*, 1158*s*, 1118*s*, 1028*s* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 210 (4.44), 294 (4.37), 329 (4.44) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (*d*, 1H, ^3J = 8.5 Hz, C*H* (6′)), 7.42 (*d*, 2H, ^3J = 8.5 Hz, C*H* (2) + C*H* (6)), 7.24 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (1)), 6.94 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (2)), 6.86 (*d*, 2H, ^3J = 8.5 Hz, C*H* (3) + C*H* (5)), 6.49 (*dd*, 1H, ^3J = 8.5 Hz, ^4J = 2.3 Hz, C*H* (5′)) 6.45 (*d*, 1H, ^3J = 2.3 Hz, C*H* (3′)), 3.85 (*s*, 3H, OCH_3), 3.81 (*s*, 3H, OCH_3), 3.80 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.2 (C4′, $C_{quart.}$), 158.8 (C4, $C_{quart.}$), 157.8 (C2′, $C_{quart.}$), 131.2 (C1, $C_{quart.}$), 127.5 (C2 + C6, *C*H), 126.9 (C6′, *C*H), 126.1 (*C*H=), 121.2 (*C*H=), 119.9 (C1′, $C_{quart.}$), 113.9 (C3 + C5, *C*H), 104.9 (C5′, *C*H), 98.5 (C3′, *C*H), 55.5 (O*C*H_3), 55.3 (O*C*H_3), 55.2 (O*C*H_3) ppm; MS (i.e., 70 eV): *m*/*z* (%) = 256 (100), 213 (44), 181 (24), 152 (16), 137 (26); analysis for $C_{17}H_{18}O_3$ (270.32): C, 75.53; H, 6.71; found: C, 75.43; H, 6.98.

4.19. (E) 3′,5′-dimethoxy-4-hydroxystilbene (**21**)

Following the general procedure, **21** was obtained from 4-hydroxystyrene and 3,5-dimethoxyiodobenzene; yield: 55.0%; colorless solid; mp 83–84 °C (lit.: 88 °C [56], 86–88 °C [57], 55–64 °C [58]); R_F = 0.16 (silica gel, hexanes/ethyl acetate, 3:1). IR (KBr): ν = 3406*br*, 2932*w*, 1598*w*, 1511*w*, 1449*w*, 1415*w*, 1233*w*, 1171*w*, 1120*w* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 209 (4.43), 326 (4.41) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (*d*, 2H, ^3J = 8.7 Hz, C*H* (2) + C*H* (6)), 6.97 (*d*, 1H, ^3J (trans) = 16.1 Hz, CH= (1)), 6.88 (*d*, 1H, ^3J (trans) = 16.1 Hz, CH= (2)), 6.80 (*d*, 2H, ^3J = 8.7 Hz, C*H* (3) + C*H* (5)), 6.67 (*d*, 2H, ^4J = 2.1 Hz, C*H* (2′) + C*H* (6′)), 6.38 (*t*, 1H, ^4J = 2.1 Hz, C*H* (4′)), 3.74 (*s*, 6H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.5 (C3′ + C5′, $C_{quart.}$), 155.2 (C4, $C_{quart.}$), 138.5 (C1′, $C_{quart.}$) 130.3 (C1, $C_{quart.}$), 127.8 (C2 + C6, *C*H), 127.7 (*C*H=), 126.9 (*C*H=), 115.6 (C3 + C5, *C*H), 104.3 (C2′ + C6′, *C*H), 99.6 (C4′, *C*H), 55.8 (O*C*H_3) ppm; MS (i.e., 70 eV): *m*/*z* (%) = 256 (100), 241 (14), 228 (9), 213 (43), 198 (15), 181 (25), 152 (22), 133 (26); analysis for $C_{16}H_{16}O_3$ (256.30): C, 74.78; H, 6.29; found: C, 74.77; H, 6.48.

4.20. (E) 3′,4,5′-trihydroxystilbene (**22**)

Following the general procedure, **22** was obtained from 4-hydroxystyrene and 3,5-dihydroxyiodobenzene; yield: 41.4%; colorless solid; mp >260 °C (lit.: 275–276 °C [59], 260 °C [60], 256–258 °C [61], 254–255 °C [62]); R_F = 0.46 (silica gel, hexanes/ethyl acetate, 1:1). IR (KBr): ν = 3287*br*, 1606*m*, 1587*m*, 1512*m*, 1462*w*, 1443*m*, 1383*m*, 1325*m*, 1300*w*, 1265*w*, 1248*m*, 1175*w*, 1148*m*, 1105*w*, 1010*w* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 217 (4.36), 305 (4.48) nm; ^{1}H NMR (400 MHz, CD_3CN): δ = 7.38 (*d*, 2H, ^3J = 8.7 Hz, C*H* (2) + C*H* (6)), 7.00 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (1)), 6.85 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (2)), 6.79 (*d*, 2H, ^3J = 8.7 Hz, C*H* (3) + C*H* (5)), 6.48 (*d*, 2H, ^4J = 2.1 Hz, C*H* (2′) + C*H* (6′)), 6.16 (*t*, 1H, ^4J = 2.1 Hz, C*H* (4′)) ppm; ^{13}C NMR (100 MHz, CD_3CN): δ = 159.1 (C3′ + C5′, $C_{quart.}$), 157.7 (C4, $C_{quart.}$), 141.0 (C1′, $C_{quart.}$) 130.0 (C1, $C_{quart.}$), 129.3 (*C*H=), 128.7 (C2 + C6, *C*H), 126.5 (*C*H=), 116.3 (C3 + C5, *C*H), 105.7 (C2′ + C6′, *C*H), 102.5 (C4′, *C*H) ppm; MS (ESI, MeOH): *m*/*z* = 227.4 (100% [M − H]$^-$), 273.0 (38% [M + HCO_2]$^-$), 454.9 (26% [2M − H]$^-$); analysis for $C_{14}H_{12}O_3$ (228.24): C, 73.67; H, 5.30; found: C, 73.46; H, 5.51.

4.21. (E) 3′,5′-dimethoxy-4′-fluoro-4-hydroxystilbene (**23**)

Following the general procedure, **23** was obtained from 4-hydroxystyrene and 3,5-dimethoxy-4-fluorobromobenzene; yield: 47.6%; off-white solid; mp 123–125 °C; R_F = 0.49 (silica gel, hexanes/ethyl acetate, 3:1); IR (KBr): ν = 3419*br*, 2940*w*, 1606*m*, 1585*w*, 1519*m*, 1455*w*, 1420*w*, 1330*w*, 1265*w*, 1249*w*, 1219*w*, 1171*w*, 1124*m* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 209 (4.49), 306

(4.53) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (*d*, 2H, ^3J = 8.5 Hz, C*H* (2) + C*H* (6)), 6.92 (*d*, 1H, ^3J (trans) = 16.2 Hz, CH═ (1)), 6.84 (*d*, 1H, ^3J (trans) = 16.2 Hz, CH═ (2)), 6.81 (*d*, 2H, ^3J = 8.5 Hz, C*H* (3) + C*H* (5)), 6.70 (*d*, 2H, $^4J_{H,F}$ = 7.1 Hz, C*H* (2′) + C*H* (6′)), 3.91 (*s*, 6H, O*CH*$_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.3 (C4, $C_{quart.}$), 148.4 (*d*, $^2J_{C,F}$ = 8.8 Hz, C3′ + C5′, $C_{quart.}$), 142.1 (*d*, $^1J_{C,F}$ = 245.8 Hz, C4′, $C_{quart.}$), 133.0 (*d*, $^4J_{C,F}$ = 5.0 Hz, C1′, $C_{quart.}$) 130.0 (C1, $C_{quart.}$), 128.1 (*C*H═), 127.8 (C2 + C6, *C*H), 126.1 (*C*H═), 115.6 (C3 + C5, *C*H), 103.9 (C2′ + C6′, *C*H), 56.5 (O*CH*$_3$) ppm; ^{19}F NMR (188 MHz, $CDCl_3$): δ = −159.1 (*t*, $^4J_{F,H}$ = 7.1 Hz, −*F*) ppm; MS (ESI, MeOH): *m*/*z* (%) = 273.6 (100% $[M-H]^-$), 319.2 (10% $[M+HCO_2]^-$), 547.0 (17% $[2M-H]^-$); analysis for $C_{16}H_{15}FO_3$ (274.28): C, 70.06; H, 5.51; found: C, 69.85; H, 5.62.

4.22. (E) 4-hydroxy-3′,4′,5′-trifluorostilbene (**24**)

Following the general procedure, **24** was obtained from 4-hydroxystyrene and 3,4,5-trifluorobromobenzene; yield: 56.9%; colorless solid; mp 149–151 °C; R_F = 0.30 (silica gel, hexanes/ethyl acetate, 9:1); IR (KBr): *ν* = 3266*br*, 2361*w*, 1889*w*, 1638*w*, 1594*s*, 1529*s*, 1508*s*, 1442*s*, 1360*m*, 1321*m*, 1269*m*, 1231*s*, 1174*m*, 1131*w*, 1106*w*, 1043*s* cm^{-1}; UV–vis (methanol): λ_{max} (log *ε*) = 230 (4.19), 321 (4.50) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 (*d*, 2H, ^3J = 8.5 Hz, C*H* (2) + C*H* (6)), 7.03 (*dt*, 1H, $^3J_{H,F}$ = 9.2 Hz, $^4J_{H,F}$ = 6.6 Hz, C*H* (2′) + C*H* (6′)), 6.92 (*d*, 1H, ^3J (trans) = 16.2 Hz, CH═ (1)), 6.81 (*d*, 2H, ^3J = 8.5 Hz, C*H* (3) + C*H* (5)), 6.75 (*d*, 1H, ^3J (trans) = 16.2 Hz, CH═ (2)) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.8 (C4, $C_{quart.}$), 151.4 (*ddd*, $^1J_{C,F}$ = 252.3 Hz, $^2J_{C,F}$ = 10.1 Hz, $^3J_{C,F}$ = 4.3 Hz, C3′ + C5′, $C_{quart.}$), 138.7 (*m*, $^1J_{C,F}$ = 250.7 Hz, C4′, $C_{quart.}$), 133.9 (*dd*, $^3J_{C,F}$ = 12.2 Hz, $^4J_{C,F}$ = 7.7 Hz, C1′, $C_{quart.}$), 130.4 (*d*, $^5J_{C,F}$ = 2.4 Hz, *C*H═), 129.2 (C1, $C_{quart.}$), 128.2 (C2 + C6, *C*H), 123.6 (*d*, $^4J_{C,F}$ = 2.8 Hz, *C*H═), 115.7 (C3 + C5, *C*H), 109.8 (*dd*, $^2J_{C,F}$ = 16.8 Hz, $^3J_{C,F}$ = 4.9 Hz, C2′ + C6′, *C*H) ppm; ^{19}F NMR (188 MHz, $CDCl_3$): δ = −135.2 (*dd*, $^3J_{F,F}$ = 19.7 Hz, $^3J_{F,H}$ = 9.2 Hz, *F* (3′) + *F* (5′)), −161.7 (*tt*, $^3J_{F,F}$ = 19.7 Hz, $^4J_{F,H}$ = 6.6 Hz, *F* (4′)) ppm; MS (ESI, MeOH): *m*/*z* (%) = 249.6 (55% $[M-H]^-$), 498.9 (100% $[2M-H]^-$); analysis for $C_{14}H_9F_3O$ (250.22): C, 67.20; H, 3.63; found: C, 66.98; H, 3.83.

4.23. (E) 2′,5′-dimethoxy-4-hydroxystilbene (**25**)

Following the general procedure, **25** was obtained from 4-hydroxystyrene and 2,5-dimethoxyiodobenzene; yield: 52.2%; off-white solid; mp 81–82 °C; R_F = 0.27 (silica gel, hexanes/ethyl acetate, 8:2 + acetic acid (0.1%)); IR (KBr): *ν* = 3341*br*, 2867*m*, 1605*m*, 1515*m*, 1497*m*, 1460*m*, 1436*m*, 1416*w*, 1359*w*, 1316*w*, 1299*w*, 1271*w*, 1215*m*, 1172*m*, 1099*w*, 1039*m*, 1009*w* cm^{-1}; UV–vis (methanol): λ_{max} (log *ε*) = 208 (4.41), 284 (4.34), 341 (4.30) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 (*d*, 2H, ^3J = 8.5 Hz, C*H* (2) + C*H* (6)), 7.28 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH═ (1)), 7.11 (*d*, 1H, ^4J = 2.9 Hz, C*H* (6′)), 7.00 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH═ (2)), 6.81 (*d*, 1H, ^3J = 9.0 Hz, C*H* (3′)), 6.79 (*d*, 2H, ^3J = 8.5 Hz, C*H* (3) + C*H* (5)), 6.76 (*dd*, 1H, ^3J = 9.0 Hz, ^4J = 2.9 Hz, C*H* (4′)), 4.92 (*br s*, 1H, O*H*), 3.82 (*s*, 3H, O*CH*$_3$), 3.80 (*s*, 3H, O*CH*$_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.1 (C4, $C_{quart.}$), 153.8 (C5′, $C_{quart.}$), 151.3 (C2′, $C_{quart.}$), 130.8 (C1, $C_{quart.}$), 128.9 (*C*H═), 128.0 (C2 + C6, *C*H), 127.6 (C1′, $C_{quart.}$), 121.2 (*C*H═), 115.5 (C3 + C5, *C*H), 113.3 (C4′, *C*H), 112.4 (C3′, *C*H), 111.5 (C6′, *C*H), 56.3 (O*CH*$_3$), 55.8 (O*CH*$_3$) ppm; MS (i.e., 70 eV): *m*/*z* (%) = 256 (100), 241 (16), 213 (56), 198 (11), 181 (16), 169 (9); analysis for $C_{16}H_{16}O_3$ (256.30): C, 74.98; H, 6.29; found: C, 74.85; H, 6.51.

4.24. (E) 2′,4,5′-trihydroxystilbene (**26**)

Following the general procedure, **26** was obtained from 4-hydroxystyrene and 2,5-dihydroxyiodobenzene; yield: 48.7%; off-white solid; mp 198–200 °C; R_F = 0.13 (silica gel, hexanes/ethyl acetate, 3:1); IR (KBr): *ν* = 3278*br*, 1605*w*, 1513*w*, 1451*w*, 1362*w*, 1253*w*, 1188*w* cm^{-1}; UV–vis (methanol): λ_{max} (log *ε*) = 209 (4.22), 296 (4.16), 345 (4.09) nm; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.53 (*br s*, 1H, O*H*), 8.93 (*br s*, 1H, O*H*), 8.71 (*br s*, 1H, O*H*), 7.33 (*d*, 2H, ^3J = 8.5 Hz, C*H* (2) + C*H* (6)), 7.12 (*d*, 1H, ^3J (trans) = 16.6 Hz, CH═ (1)), 6.93 (*d*, 1H, ^3J (trans) = 16.6 Hz, CH═ (2)), 6.89 (*d*, 1H, ^4J = 2.8 Hz, C*H* (6′)), 6.73 (*d*, 2H, ^3J = 8.5 Hz, C*H* (3) + C*H* (5)), 6.63 (*d*, 1H, ^3J = 8.5 Hz, C*H* (3′)), 6.48 (*dd*, 1H, ^3J = 8.5 Hz, ^4J = 2.8 Hz, C*H* (4′)) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 157.4 (C4, $C_{quart.}$), 150.4 (C5′, $C_{quart.}$), 147.9 (C2′, $C_{quart.}$), 129.2 (C1, $C_{quart.}$), 128.0 (C2 + C6, *C*H), 127.9 (*C*H═), 125.1 (C1′, $C_{quart.}$), 121.0 (*C*H═), 116.9 (C3′, CH), 115.9 (C3 + C5, *C*H), 115.5 (C4′, *C*H), 111.9 (C6′, *C*H) ppm; MS (ESI, MeOH): *m*/*z* (%) = 227.3 (100% $[M-H]^-$), 272.9 (17% $[M+HCO_2]^-$), 454.8 (26% $[2M-H]^-$); analysis for $C_{14}H_{12}O_3$ (228.24): C, 73.67; H, 5.30; found: C, 73.51; H, 5.32.

4.25. (E) 2′,5′-dihydrox-3-methoxystilbene (**27**)

Following the general procedure, **27** was obtained from 3-methoxystyrene and 2,5-dihydroxyiodobenzene; yield: 54.5%; slightly yellow solid; mp 139–140 °C; R_F = 0.78 (silica gel, hexanes/ethyl acetate, 1:1); IR (KBr): *ν* = 3300*br*, 2836*m*, 1862*w*, 1718*w*, 1602*m*, 1576*m*, 1515*w*, 1487*m*, 1455*s*, 1374*w*, 1328*w*, 1265*s*, 1235*s*, 1199*s*, 1152*s*, 1095*w*, 1048*m* cm^{-1}; UV–vis (methanol): λ_{max} (log *ε*) = 214 (4.74), 291 (4.60), 346 (4.45) nm; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.03 (*br s*, 1H, O*H*), 8.74 (*br s*, 1H, O*H*), 7.30 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH═ (1)), 7.22 (*t*, 1H, ^3J = 7.8 Hz, C*H* (5)), 7.07 (*d*, 1H, ^3J = 7.8 Hz, C*H* (6)), 7.03 (*s*, 1H, C*H* (2)), 7.01 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH═ (2)), 6.90 (*d*, 1H, ^4J = 2.9 Hz, C*H* (6′)), 6.77 (*dd*, 1H, ^3J = 7.8 Hz, ^4J = 2.3 Hz, C*H* (4)), 6.64 (*d*, 1H, ^3J = 8.5 Hz, C*H* (3′)), 6.51 (*dd*, 1H, ^3J = 8.5 Hz, ^4J = 2.9 Hz, C*H* (4′)), 3.74 (*s*, 3H, O*CH*$_3$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 159.7 (C3, $C_{quart.}$), 150.0 (C5′, $C_{quart.}$), 147.9 (C2′, $C_{quart.}$), 139.2 (C1, $C_{quart.}$), 129.8 (C5, *C*H), 127.5 (*C*H═), 124.2 (*C*H═), 124.1 (C1′, $C_{quart.}$), 118.7 (C6, *C*H), 116.7 (C3′, *C*H), 116.1 (C4′, CH), 113.1 (C4, *C*H), 112.0 (C6′, CH), 111.5 (C2, *C*H), 56.3 (O*CH*$_3$) ppm; MS (ESI, MeOH): *m*/*z* (%) = 241.3 (46% $[M-H]^-$), 287.0 (100% $[M+HCO_2]^-$), 482.8 (52% $[2M-H]^-$); analysis for $C_{15}H_{14}O_3$ (242.27): C, 74.36; H, 5.82; found: C, 74.11; H, 6.04.

4.26. (E) 3′,5′-dimethoxy-4′-fluoro-3-hydroxystilbene (**28**)

Following the general procedure, **28** was obtained from 3-hydroxystyrene and 3,5-dimethoxy-4-fluorobromobenzene; yield: 53.3%; off-white solid; mp 108–111 °C; R_F = 0.59 (silica gel, hexanes/ethyl acetate, 3:1); IR (KBr): *ν* = 3241*br*, 2944*w*, 1743*w*, 1601*m*, 1518*m*, 1457*m*, 1420*m*, 1336*m*, 1279*w*, 1247*m*, 1225*m*, 1184*w*, 1159*m*, 1149*m*, 1131*s* *cm*$^{-1}$; UV–vis (methanol): λ_{max} (log *ε*) = 214 (4.41), 319 (4.44) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21 (*t*, 1H, ^3J = 7.7 Hz, C*H* (5)), 7.05 (*d*, 1H, ^3J = 7.7 Hz, C*H* (6)), 6.97 (*d*, 1H, ^4J = 2.3 Hz, C*H* (2)), 6.96 (*d*, 1H, ^3J (trans) = 16.2 Hz, CH═ (1)), 6.90 (*d*, 1H, ^3J (trans) = 16.2 Hz, CH═ (2)), 6.74 (*dd*, 1H, ^3J = 7.7 Hz, ^4J = 2.3 Hz, C*H* (4)), 6.72 (*d*, 2H, $^4J_{H,F}$ = 7.1 Hz, C*H* (2′) + C*H* (6′)), 3.91 (*s*, 6H, O*CH*$_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.8 (C3, $C_{quart.}$), 148.4 (*d*, $^2J_{C,F}$ = 8.6 Hz, C3′ + C5′, $C_{quart.}$), 142.1 (*d*, $^1J_{C,F}$ = 243.1 Hz, C4′, $C_{quart.}$), 138.8 (C1, $C_{quart.}$), 132.7 (*d*, $^4J_{C,F}$ = 5.0 Hz, C1′, $C_{quart.}$), 129.9 (C5, *C*H), 128.6 (*C*H═), 128.3 (*C*H═), 119.4 (C6, *C*H), 114.8 (C4, *C*H), 112.9 (C2, *C*H), 104.4 (C2′ + C6′, *C*H), 56.7 (O*CH*$_3$) ppm; ^{19}F NMR (188 MHz, $CDCl_3$): δ = −158.3 (*t*, $^4J_{F,H}$ = 7.1 Hz, −*F*) ppm; MS (i.e., 70 eV): *m*/*z* (%) = 274 (100), 242 (10), 228 (10), 199 (15), 170 (9); analysis for $C_{16}H_{15}FO_3$ (274.28): C, 70.06; H, 5.51; found: C, 69.84; H, 5.73.

4.27. (E) 2′,3,5′-trihydroxystilbene (**29**)

Following the general procedure, **29** was obtained from 3-hydroxystyrene and 2,5-dihydroxyiodobenzene; yield: 47.9%; off-white solid; mp 208–210 °C; R_F = 0.13 (silica gel, hexanes/ethyl

acetate, 3:1); IR (KBr): ν = 3300*br*, 1613*w*, 1582*w*, 1505*w*, 1457*m*, 1377*w*, 1305*w*, 1254*w*, 1199*w*, 1156*w*, 1095*w* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 211 (4.57), 291 (4.42), 345 (4.31) nm; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.44 (*br s*, 1H, O*H*), 9.07 (*br s*, 1H, O*H*), 8.81 (*br s*, 1H, O*H*), 7.27 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (1)), 7.13 (*t*, 1H, ^3J = 7.8 Hz, C*H* (5)), 6.96 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (2)), 6.94–6.92 (*m*, 3H, C*H* (2) + C*H* (6) + C*H* (6′)), 6.66 (*d*, 1H, ^3J = 8.5 Hz, C*H* (3′)), 6.64 (*d*, 1H, ^3J = 7.8 Hz, C*H* (4)), 6.53 (*dd*, 1H, ^3J = 8.5 Hz, ^4J = 2.9 Hz, C*H* (4′)) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 157.7 (C3, $C_{quart.}$), 150.2 (C5′, $C_{quart.}$), 148.0 (C2′, $C_{quart.}$), 139.2 (C1, $C_{quart.}$), 129.9 (C5, *C*H), 127.7 (*C*H=), 124.3 (C1′, $C_{quart.}$), 123.7 (*C*H=), 117.8 (C6, *C*H), 116.8 (C3′, *C*H), 116.1 (C4′, *C*H), 114.8 (C4, *C*H), 112.7 (C6′, *C*H), 112.0 (C2, *C*H) ppm; MS (ESI, MeOH): *m*/*z* (%) = 227.4 (25% [M − H]$^-$), 273.1 (100% [M + HCO_2]$^-$), 454.9 (27% [2M − H]$^-$); analysis for $C_{14}H_{12}O_3$ (228.24): C, 73.67; H, 5.30; found: C, 73.49; H, 5.35.

4.28. (E) 2′,4′-dimethoxy-3-hydroxystilbene (**30**)

Following the general procedure, **30** was obtained from 3-hydroxystyrene and 2,4-dimethoxyiodobenzene; yield: 53.7%; off-white solid; mp 106–108 °C; R_F = 0.30 (silica gel, DCM/hexanes, 3:1); IR (KBr): ν = 3397*br*, 2945*m*, 1603*m*, 1577*m*, 1505*m*, 1468*m*, 1434*w*, 1419*w*, 1296*m*, 1277*m*, 1200*m*, 1152*m*, 1107*w*, 1023 cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 213 (4.34), 326 (4.36) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (*d*, 1H, ^3J = 8.5 Hz, C*H* (6′)), 7.35 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (1)), 7.18 (*t*, 1H, ^3J = 7.9 Hz, C*H* (5)), 7.05 (*d*, 1H, ^3J = 7.9 Hz, C*H* (6)), 6.97 (*d*, 1H, ^4J = 1.7 Hz, C*H* (2)), 6.92 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (2)), 6.68 (*dd*, 1H, ^3J = 7.9 Hz, ^4J = 1.7 Hz, C*H* (4)), 6.50 (*dd*, 1H, ^3J = 8.5 Hz, ^4J = 2.3 Hz, C*H* (5′)), 6.46 (*d*, 1H, ^4J = 2.3 Hz, C*H* (3′)), 3.85 (*s*, 3H, OCH_3), 3.82 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.7 (C4′, $C_{quart.}$), 158.1 (C2′, $C_{quart.}$), 155.7 (C3, $C_{quart.}$), 140.0 (C1, $C_{quart.}$), 129.7 (C5, *C*H), 127.3 (C6′, *C*H), 126.5 (*C*H=), 123.8 (*C*H=), 119.4 (C1′, $C_{quart.}$), 119.3 (C6, *C*H), 114.0 (C4, *C*H), 112.6 (C2, *C*H), 105.6 (C5′, *C*H), 98.5 (C3′, *C*H), 55.5 (OCH_3), 55.4 (OCH_3) ppm; MS (ESI, MeOH): *m*/*z* (%) = 255.3 (100% [M − H]$^-$), 510.8 (21% [2M − H]$^-$); analysis for $C_{16}H_{16}O_3$ (256.30): C, 74.98; H, 6.29; found: C, 74.69; H, 6.42.

4.29. (E) 2′,5′-dihydroxy-2-methoxystilbene (**31**)

Following the general procedure, **31** was obtained from 2-methoxystyrene and 2,5-dihydroxyiodobenzene; yield: 51.7%; colorless solid; mp 163–165 °C; R_F = 0.67 (silica gel, hexanes/ethyl acetate, 1:1); IR (KBr): ν = 3284*br*, 2984*w*, 1598*w*, 1511*w*, 1489*w*, 1466*m*, 1449*m*, 1362*w*, 1328*w*, 1289*w*, 1244*m*, 1195*m*, 1163*w*, 1105*w*, 1051*w*, 1023*w* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 210 (4.35), 287 (4.09), 341 (4.07) nm; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.00 (*br s*, 1H, O*H*), 8.74 (*br s*, 1H, O*H*), 7.54 (*d*, 1H, ^3J = 7.7 Hz, C*H* (6)), 7.29 (*d*, 1H, ^3J (trans) = 16.8 Hz, CH= (1)), 7.25 (*d*, 1H, ^3J (trans) = 16.8 Hz, CH= (2)), 7.19 (*t*, 1H, ^3J = 7.5 Hz, C*H* (4)), 6.96 (*d*, 1H, ^3J = 7.5 Hz, C*H* (3)), 6.91 (*t*, 1H, ^3J = 7.5 Hz, C*H* (5)), 6.89 (*d*, 1H, ^4J = 2.7 Hz, C*H* (6′)), 6.64 (*d*, 1H, ^3J = 8.7 Hz, C*H* (3′)), 6.50 (*dd*, 1H, ^3J = 8.7 Hz, ^4J = 2.7 Hz, C*H* (4′)), 3.79 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 156.7 (C2, $C_{quart.}$), 150.4 (C5′, $C_{quart.}$), 148.1 (C2′, $C_{quart.}$), 128.9 (C4, *C*H), 126.5 (C1′, $C_{quart.}$), 126.1 (C6, *C*H), 125.0 (C1, $C_{quart.}$), 124.4 (*C*H=), 122.2 (*C*H=), 121.1 (C5, *C*H), 117.1 (C3′, *C*H), 116.1 (C4′, *C*H), 112.0 (C6′, *C*H), 111.8 (C3, *C*H), 55.9 (OCH_3) ppm; MS (ESI, MeOH): *m*/*z* (%) = 241.3 (46% [M − H]$^-$), 287.1 (100% [M + HCO_2]$^-$), 482.8 (41% [2M − H]$^-$); analysis for $C_{15}H_{14}O_3$ (242.27): C, 74.36; H, 5.82; found: C, 74.21; H, 5.91.

4.30. (E) 2,2′,4′-trimethoxystilbene (**32**)

Following the general procedure, **32** was obtained from 2-methoxystyrene and 2,4-dimethoxyiodobenzene; yield: 56.4%; colorless solid; mp 91–92 °C; R_F = 0.74 (silica gel, hexanes/ethyl acetate, 3:1); IR (KBr): ν = 3052*m*, 2918*m*, 2900*m*, 2841*m*, 1643*m*, 1609*s*, 1599*s*, 1572*s*, 1503*s*, 1468*m*, 1463*s*, 1437*m*, 1423*m*, 1415*m*, 1341*s*, 1320*m*, 1289*s*, 1259*s*, 1244*s*, 1201*s*, 1185*s*, 1158*s*, 1119*s*, 1039*s* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 212 (4.21), 294 (4.12), 331 (4.30) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60 (*d*, 1H, ^3J = 7.7 Hz, C*H* (6)), 7.54 (*d*, 1H, ^3J = 8.5 Hz, C*H* (6′)), 7.37 (*d*, 1H, ^3J (trans) = 16.8 Hz, CH= (1)), 7.33 (*d*, 1H, ^3J (trans) = 16.8 Hz, CH= (2)), 7.18 (*t*, 1H, ^3J = 7.7 Hz, C*H* (4)), 6.93 (*t*, 1H, ^3J = 7.7 Hz, C*H* (5)), 6.86 (*d*, 1H, ^3J = 7.7 Hz, C*H* (3)), 6.50 (*dd*, 1H, ^3J = 8.5 Hz, ^4J = 2.5 Hz, C*H* (5′)), 6.44 (*d*, 1H, ^4J = 2.5 Hz, C*H* (3′)), 3.86 (*s*, 3H, OCH_3), 3.85 (*s*, 3H, OCH_3), 3.82 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.3 (C4′, $C_{quart.}$), 157.9 (C2′, $C_{quart.}$), 156.7 (C2, $C_{quart.}$), 127.9 (C4, *C*H), 127.4 (C1, $C_{quart.}$), 127.1 (C6′, *C*H), 126.1 (C6, *C*H), 123.4 (*C*H=), 121.5 (*C*H=), 120.7 (C5, *C*H), 120.3 (C1′, $C_{quart.}$), 110.8 (C3, *C*H), 104.9 (C5′, *C*H), 98.4 (C3′, *C*H), 55.5 (OCH_3), 55.4 (OCH_3), 55.2 (OCH_3) ppm; MS (i.e., 70 eV): *m*/*z* (%) = 270 (100), 240 (8), 225 (12), 164 (10), 151 (27); analysis for $C_{17}H_{18}O_3$ (270.32): C, 75.53; H, 6.71; found: C, 75.32; H, 6.98.

4.31. (E) 3′,5′-dimethoxy-4′-fluoro-2-hydroxystilbene (**33**)

Following the general procedure, **33** was obtained from 2-hydroxystyrene and 3,5-dimethoxy-4-fluorobromobenzene; yield: 51.1%; colorless solid; mp 63–65 °C; R_F = 0.16 (silica gel, hexanes/ethyl acetate, 8:2); IR (KBr): ν = 3418*br*, 2940*m*, 2842*w*, 1704*m*, 1605*s*, 1519*s*, 1455*s*, 1421*s*, 1349*s*, 1243*s*, 1128*s*, 1042*m* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 290 (4.12), 326 (4.18) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 (*d*, 1H, ^3J = 7.7 Hz, C*H* (6)), 7.28 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (1)), 7.11 (*t*, 1H, ^3J = 7.7 Hz, C*H* (4)), 7.01 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (2)), 6.92 (*t*, 1H, ^3J = 7.7 Hz, C*H* (5)), 6.80 (*d*, 1H, ^3J = 7.7 Hz, C*H* (3)), 6.74 (*d*, 2H, $^4J_{H,F}$ = 7.0 Hz, C*H* (2′) + C*H* (6′)) 3.88 (*s*, 6H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.3 (C2, $C_{quart.}$), 148.3 (*d*, $^2J_{C,F}$ = 8.7 Hz, C3′ + C5′, $C_{quart.}$), 142.2 (*d*, $^1J_{C,F}$ = 245.7 Hz, C4′, $C_{quart.}$), 133.3 (*d*, $^4J_{C,F}$ = 4.8 Hz, C1′, $C_{quart.}$) 129.1 (*C*H=), 128.8 (C4, *C*H), 127.0 (C6, *C*H), 124.4 (C1, $C_{quart.}$), 123.3 (*C*H=), 121.0 (C5, *C*H), 116.0 (C3, *C*H), 104.3 (C2′ + C6′, *C*H), 56.5 (OCH_3) ppm; ^{19}F NMR (188 MHz, CD_3CN): δ = −158.8 (*t*, $^4J_{F,H}$ = 7.0 Hz, *F*) ppm; MS (ESI, MeOH): *m*/*z* (%) = 273.3 (100% [M − H]$^-$); 319.0 (16.3% [M + HCO_2]$^-$); 546.8 (52% [2M − H]$^-$); analysis for $C_{16}H_{15}FO_3$ (274.28): C, 70.06; H, 5.51; found: C, 69.89; H, 5.71.

4.32. (E) 2,2′,5′-trihydroxystilbene (**34**)

Following the general procedure, **34** was obtained from 2-hydroxystyrene and 2,5-dihydroxyiodobenzene; yield: 49.8%; off-white solid; mp 218–220 °C; R_F = 0.67 (silica gel, hexanes/ethyl acetate, 1:1); IR (KBr): ν = 3287*br*, 2362*w*, 1603*w*, 1581*w*, 1508*w*, 1455*w*, 1376*w*, 1236*w*, 1197*w*, 1156*w*, 1097*w* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 284 (4.17), 341 (4.24) nm; ^{1}H NMR (400 MHz, methanol-d_4): δ = 7.52 (*d*, 1H, ^3J = 7.7 Hz, CH (6)), 7.40 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (1)), 7.35 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH= (2)), 7.03 (*t*, 1H, ^3J = 7.4 Hz, C*H* (4)), 7.01 (*d*, 1H, ^4J = 2.9 Hz, C*H* (6′)), 6.81 (*t*, 1H, ^3J = 7.4 Hz, C*H* (5)), 6.78 (*d*, 1H, ^3J = 7.4 Hz, C*H* (3)), 6.64 (*d*, 1H, ^3J = 8.5 Hz, C*H* (3′)), 6.53 (*dd*, 1H, ^3J = 8.5 Hz, ^4J = 2.9 Hz, C*H* (4′)), 4.81 (*br s*, 3H, O*H*) ppm; ^{13}C NMR (100 MHz, methanol-d_4): δ = 155.8 (C2, $C_{quart.}$), 151.2 (C5′, $C_{quart.}$), 148.9 (C2′, $C_{quart.}$), 129.0 (C4, *C*H), 127.1 (C1′, $C_{quart.}$), 127.0 (C6, *C*H), 126.4 (C1, $C_{quart.}$), 124.0 (*C*H=), 123.8 (*C*H=), 120.7 (C5, *C*H), 117.4 (C3′, *C*H), 116.5 (C3, *C*H), 116.1 (C4′, *C*H), 112.7 (C6′, *C*H) ppm; MS (ESI, MeOH): *m*/*z* (%) = 227.4 (48% [M − H]$^-$), 273.1 (58% [M + HCO_2]$^-$), 455.0 (100% [2M − H]$^-$); analysis for $C_{14}H_{12}O_3$ (228.24): C, 73.67; H, 5.30; found: C, 73.56; H, 5.44.

4.33. (E) 4′,6-difluoro-3-hydroxy-3′,4, 5′-trimethoxystilbene (**35**)

Following the general procedure, **35** was obtained from 6-fluoro-3-hydroxy-4-methoxystyrene and 3,5-dimethoxy-4-

fluorobromobenzene; yield: 56.0%; colorless solid; mp 149–151 °C; R_F = 0.39 (silica gel, hexanes/ethyl acetate, 3:1); IR (KBr): ν = 3517*br*, 3006*w*, 2944*m*, 2845*w*, 1630*m*, 1606*m*, 1518*s*, 1467*m*, 1447*m*, 1424*m*, 1375*m*, 1333*m*, 1291*m*, 1275*s*, 1252*m*, 1226*m*, 1197*s*, 1168*m*, 1152*m*, 1128*s*, 1017*m* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 210 (4.79), 300 (4.54), 331 (4.59) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.10 (*d*, 1H, $^4J_{H,F}$ = 7.3 Hz, C*H* (2)), 7.05 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH═ (1)), 6.98 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH═ (2)), 6.71 (*d*, 2H, $^4J_{H,F}$ = 7.1 Hz, C*H* (2′) + C*H* (6′)), 6.61 (*d*, 1H, $^3J_{H,F}$ = 11.4 Hz, C*H* (5)), 5.32 (*br s*, 1H, O*H*), 3.91 (*s*, 6H, OCH_3), 3.88 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.3 (*d*, $^1J_{C,F}$ = 227.3 Hz, C6, $C_{quart.}$), 148.4 (*d*, $^2J_{C,F}$ = 8.8 Hz, C3′ + C5′, $C_{quart.}$), 146.6 (*d*, $^3J_{C,F}$ = 9.1 Hz, C4, $C_{quart.}$), 142.3 (*d*, $^1J_{C,F}$ = 241.4 Hz, C4′, $C_{quart.}$), 141.9 (*d*, $^4J_{C,F}$ = 1.0 Hz, C3, $C_{quart.}$), 132.9 (*d*, $^4J_{C,F}$ = 1.8 Hz, C1′, $C_{quart.}$), 128.3 (*C*H═), 120.4 (*C*H═), 117.0 (*d*, $^2J_{C,F}$ = 12.1 Hz, C1, $C_{quart.}$), 110.9 (*d*, $^3J_{C,F}$ = 2.2 Hz, C2, *C*H), 104.1 (C2′ + C6′, *C*H), 99.4 (*d*, $^2J_{C,F}$ = 25.4 Hz, C5, *C*H), 56.6 (OCH_3), 56.2 (OCH_3) ppm; ^{19}F NMR (188 MHz, $CDCl_3$): δ = −126.1 (*dd*, $^3J_{F,H}$ = 11.4 Hz, $^4J_{F,H}$ = 7.3 Hz, *F* (6)), −158.7 (*t*, $^4J_{F,H}$ = 7.1 Hz, *F* (4′)) ppm; MS (ESI, MeOH): *m*/*z* (%) = 321.6 (71% [M − H]$^-$), 643.2 (100% [2M − H]$^-$); analysis for $C_{17}H_{16}F_2O_4$ (322.30): C, 63.35; H, 5.00; found: C, 63.54; H, 5.57.

4.34. (E) 6-fluoro-3-hydroxy-2′,4,5′-trimethoxystilbene (**36**)

Following the general procedure, **36** was obtained from 6-fluoro-3-hydroxy-4-methoxystyrene and 2,5-dimethoxyiodobenzene; yield: 56.8%; off-white solid; mp 132–134 °C; R_F = 0.19 (silica gel, hexanes/ethyl acetate, 8:2); IR (KBr): ν = 3519*br*, 2999*m*, 2942*m*, 2835*m*, 1630*m*, 1610*m*, 1582*m*, 1504*s*, 1469*s*, 1444*s*, 1429*m*, 1369*m*, 1331*m*, 1311*s*, 1285*s*, 1243*s*, 1215*s*, 1191*s*, 1170*s*, 1123*m*, 1101*m*, 1046*s*, 1018*s* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 213 (4.39), 286 (4.18), 343 (4.33) nm; ^{1}H NMR (400 MHz, acetone-d_6): δ = 7.59 (*br s*, 1H, O*H*), 7.36 (*d*, 1H, ^3J (trans) = 16.6 Hz, CH═ (1)), 7.23 (*d*, 1H, ^3J (trans) = 16.6 Hz, CH═ (2)), 7.21 (*d*, 1H, ^4J = 3.1 Hz, C*H* (6′)), 7.14 (*d*, 1H, $^4J_{H,F}$ = 7.6 Hz, C*H* (2)), 6.93 (*d*, 1H, ^3J = 9.0 Hz, C*H* (3′)), 6.82 (*dd*, 1H, ^3J = 9.0 Hz, ^4J = 3.1 Hz C*H* (4′)), 6.80 (*d*, 1H, $^3J_{H,F}$ = 11.9 Hz, C*H* (5)), 3.88 (*s*, 3H, OCH_3), 3.84 (*s*, 3H, OCH_3), 3.79 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, acetone-d_6): δ = 155.0 (*d*, $^1J_{C,F}$ = 240.6 Hz, C6, $C_{quart.}$), 154.8 (C5′, $C_{quart.}$), 152.3 (C2′, $C_{quart.}$), 148.8 (*d*, $^3J_{C,F}$ = 10.6 Hz, C4, $C_{quart.}$), 143.8 (*d*, $^4J_{C,F}$ = 2.7 Hz, C3, $C_{quart.}$), 128.0 (C1′, $C_{quart.}$), 124.2 (*d*, $^4J_{C,F}$ = 3.0 Hz, *C*H═), 121.7 (*d*, $^3J_{C,F}$ = 3.4 Hz, *C*H═), 118.0 (*d*, $^2J_{C,F}$ = 13.2 Hz, C1, $C_{quart.}$), 114.7 (C4′, *C*H), 113.4 (C3′, *C*H), 112.4 (*d*, $^3J_{C,F}$ = 4.7 Hz, C2, *C*H), 112.2 (C6′, *C*H), 100.8 (*d*, $^2J_{C,F}$ = 28.0 Hz, C5, *C*H), 56.6 (OCH_3), 56.5 (OCH_3), 55.9 (OCH_3) ppm; ^{19}F NMR (188 MHz, acetone-d_6): δ = −128.6 (*dd*, $^3J_{F,H}$ = 11.9 Hz, $^4J_{F,H}$ = 7.6 Hz, *F*) ppm; MS (ESI, MeOH): *m*/*z* (%) = 303.1 (100% [M − H]$^-$), 348.9 (8% [M + HCO_2]$^-$), 606.7 (30% [2M − H]$^-$); analysis for $C_{17}H_{17}FO_4$ (304.31): C, 67.10; H, 5.63; found: C, 66.85; H, 5.55.

4.35. (E) 6-fluoro-4-methoxy-2′,3,5′-trihydroxystilbene (**37**)

Following the general procedure, **37** was obtained from 6-fluoro-3-hydroxy-4-methoxystyrene and 2,5-dihydroxyiodobenzene; yield: 44.4%; off-white solid; mp 158–160 °C; R_F = 0.08 (silica gel, hexanes/ethyl acetate, 3:1); IR (KBr): ν = 3383*br*, 2942*w*, 1627*w*, 1508*w*, 1448*w*, 1384*w*, 1303*w*, 1195*w*, 1094*w*, 1017*w* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 291 (4.11), 349 (4.06) nm; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.16 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH═ (1)), 7.01 (*d*, 1H, ^3J (trans) = 16.4 Hz, CH═ (2)), 6.88 (*d*, 1H, ^4J = 2.3 Hz, C*H* (6′)), 6.82 (*d*, 1H, $^3J_{H,F}$ = 12.2 Hz, C*H* (5)), 6.73 (*d*, 1H, ^3J = 8.7 Hz, C*H* (3′)), 6.65 (*d*, 1H, $^4J_{H,F}$ = 8.9 Hz, C*H* (2)), 6.51 (*dd*, 1H, ^3J = 8.7 Hz, ^4J = 2.3 Hz, C*H* (4′)), 3.77 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 153.3 (*d*, $^1J_{C,F}$ = 244.3 Hz, C6, $C_{quart.}$), 150.1 (C5′, $C_{quart.}$), 148.1 (*d*, $^3J_{C,F}$ = 11.3 Hz, C4, $C_{quart.}$), 147.8 (C2′, $C_{quart.}$), 143.1 (*d*, $^4J_{C,F}$ = 2.2 Hz, C3, $C_{quart.}$), 124.3 (C1′, $C_{quart.}$), 123.7 (*d*, $^4J_{C,F}$ = 3.0 Hz, *C*H═), 119.2 (*d*, $^3J_{C,F}$ = 3.4 Hz, *C*H═), 116.8 (C4′, *C*H), 116.5 (*d*, $^2J_{C,F}$ = 13.2 Hz, C1, $C_{quart.}$), 115.8 (C3′, *C*H), 115.3 (C6′, *C*H), 111.7 (*d*, $^3J_{C,F}$ = 4.7 Hz, C2, *C*H), 100.6 (*d*, $^2J_{C,F}$ = 28.0 Hz, C5, *C*H), 56.1 (OCH_3) ppm; ^{19}F NMR (188 MHz, DMSO-d_6): δ = −128.2 (*dd*, $^3J_{F,H}$ = 12.2 Hz, $^4J_{F,H}$ = 8.9 Hz, *F*) ppm; MS (ESI, MeOH): *m*/*z* = 275.3 (45% [M − H]$^-$), 321.2 (100% [M + HCO_2]$^-$), 550.8 (16% [2M − H]$^-$); analysis for $C_{15}H_{13}FO_4$ (276.26): C, 65.21; H, 4.74; found: C, 65.03; H, 4.96.

4.36. (E) 6-fluoro-3-hydroxy-2′,4,4′-trimethoxystilbene (**38**)

Following the general procedure, **38** was obtained from 6-fluoro-3-hydroxy-4-methoxystyrene and 2, 4-dimethoxyiodobenzene; yield: 51.6%; off-white solid; mp 127–130 °C; R_F = 0.50 (silica gel, hexanes/ethyl acetate, 3:1); IR (KBr): ν = 3543*br*, 2961*w*, 1609*w*, 1513*w*, 1451*w*, 1420*w*, 1369*w*, 1327*w*, 1294*w*, 1278*w*, 1262*w*, 1197*w*, 1160*w*, 1119*w*, 1097*w*, 1041*w*, 1015*w* cm^{-1}; UV–vis (methanol): λ_{max} (log ε) = 210 (4.43), 288 (4.22), 335 (4.37) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 (*d*, 1H, ^3J = 8.5 Hz, C*H* (6′)), 7.26 (*d*, 1H, ^3J (trans) = 16.6 Hz, CH═ (2)), 7.17 (*d*, 1H, $^4J_{H,F}$ = 7.2 Hz, C*H* (2)), 7.06 (*d*, 1H, ^3J (trans) = 16.6 Hz, CH═ (1)), 6.58 (*d*, 1H, $^3J_{H,F}$ = 9.4 Hz, C*H* (5)), 6.49 (*dd*, 1H, ^3J = 8.5 Hz, ^4J = 2.5 Hz, C*H* (5′)), 6.44 (*d*, 1H, ^4J = 2.5 Hz, C*H* (3′)), 3.86 (*s*, 3H, OCH_3), 3.85 (*s*, 3H, OCH_3), 3.81 (*s*, 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.8 (C4′, $C_{quart.}$), 157.9 (C2′, $C_{quart.}$), 153.4 (*d*, $^1J_{C,F}$ = 241.3 Hz, C6, $C_{quart.}$), 146.0 (*d*, $^3J_{C,F}$ = 10.1 Hz, C4, $C_{quart.}$), 141.7 (*d*, $^4J_{C,F}$ = 2.4 Hz, C3, $C_{quart.}$), 127.1 (C6′, *C*H), 123.3 (*d*, $^4J_{C,F}$ = 3.8 Hz, *C*H═), 119.7 (C1′, $C_{quart.}$), 118.4 (*d*, $^3J_{C,F}$ = 3.8 Hz, *C*H═), 118.3 (*d*, $^2J_{C,F}$ = 12.6 Hz, C1, $C_{quart.}$), 110.7 (*d*, $^3J_{C,F}$ = 4.8 Hz, C2 *C*H), 104.9 (C5′, *C*H), 99.3 (*d*, $^2J_{C,F}$ = 28.8 Hz, C5, *C*H), 98.5 (C3′, *C*H), 56.2 (OCH_3), 55.5 (OCH_3), 55.4 (OCH_3) ppm; ^{19}F NMR (188 MHz, acetone-d_6): δ = −127.1 (*dd*, $^3J_{F,H}$ = 9.4 Hz, $^4J_{F,H}$ = 7.2 Hz, *F*) ppm; MS (ESI, MeOH): *m*/*z* (%) = 303.3 (100% [M − H]$^-$), 349.0 (11% [M + HCO_2]$^-$), 606.8 (28% [2M − H]$^-$); analysis for $C_{17}H_{17}FO_4$ (304.31): C, 67.10; H, 5.63; found: C, 66.97; H, 5.89.

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