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Substituted cinnamic anhydrides act as selective inhibitors of acetylcholinesterase

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ABSTRACT

Cinnamic anhydrides have been shown to be more than reactive reagents, but they also act as inhibitors of the enzyme acetylcholinesterease (AChE). Thus, out of a set of 33 synthesised derivatives, several of them were mixed type inhibitors for AChE (from electric eel). Thus, (*E*)-3-(2,4-dimethoxyphenyl)acrylic anhydride (**2c**) showed $K_i = 8.30 \pm 0.94\,\mu M$ and $K_i' = 9.54 \pm 0.38\,\mu M$, and for (*E*)-3-(3-chlorophenyl)acrylic anhydride (**2u**) $K_i = 8.23 \pm 0.93\,\mu M$ and $K_i' = 13.07 \pm 0.46\,\mu M$ were measured. While being not cytotoxic to many human cell lines, these compounds showed an unprecedented and noteworthy inhibitory effect for AChE but not for butyrylcholinesterase (BChE).

1. Introduction

Cinnamic acid moieties are part of a large number of natural products. Since many of them can be found in our daily nutrition [1–3] an investigation of their biological effects is of major interest. While some of these compounds have been investigated in detail [4–7], many derivatives have not been a subject of biological investigations at all. The effects of cholinesterase inhibitors in combating Alzheimer's disease (AD) remain interesting but still not completely understood. Acetyl- and butyrylcholinesterase are enzymes which influence the cognitive function and memory, thus making these enzymes of special interest in humans being affected by AD [8–10]. Approximately one percent of the world's population suffers from some kind of dementia; as a consequence, 50 million people are affected by AD [11]. Recent work from Kim et al. [12] showed derivatives of cinnamic acid to hold promising cholinesterase (ChE) inhibitory effects. Hence, we were looking for unexplored derivatives close to cinnamic acids, and interestingly cinnamic anhydrides revealed to be a class of compounds having never before tested for their ability to act as inhibitors of ChE (Fig. 1). Interestingly, quite recently another anhydride, 2,3-dimetylmaleic anhydride has been found to act as a strong inhibitor on an acetylcholinestase from insects [13].

Usually, carboxylic anhydrides are seen as reactive species to synthesize carboxylic acids derivatives that cannot be obtained directly from the carboxylic acid [14,15]. Furthermore, due to this reactivity, it is generally assumed that they are easily hydrolysed, hence resulting in a short lifetime in the presence of water. This holds true for many anhydrides, however cinnamic anhydrides are remarkable stable in aqueous solutions [16], and they should be investigated in more detail. As a consequence, anhydrides did not seem to be very appealing as potential drugs, and investigations of them are scarcely found in literature. Thus, a mixed anhydride between a triterpene and cinnamic acid [17] has been investigated as novel anti-malarial agent, and cytotoxic properties have been reported for plant extracts [18,19].

2. Results and discussion

2.1. Chemistry

Knoevenagel-Doebner-condensations [20,21] are well-known to access carboxylic acids from malonic acid and an appropriate aldehyde. To investigate the influence of the electronic profile of the aromatic system on reactivity and biologically activity, a variety of differently substituted benzaldehydes holding both electron-withdrawing and -donating substituents in various substitution patterns has been included in our investigations (Table 1).

Substituted benzaldehydes were used to prepare 13 commercially not available cinnamic acids applying Knoevenagel-Doebner reactions. These compounds are characterized by the presence of the olefinic protons in their ^{1}H NMR spectra (as exemplified for **1a**: $\delta = 7.74$ and 6.33 ppm); in the ^{13}C NMR spectra the olefinic carbons were detected at $\delta = 147.1$ and 115.0 ppm, respectively. The yields in these condensation reactions differed between moderate to very good, a fact that can be explained by the different electronic properties due to the differences

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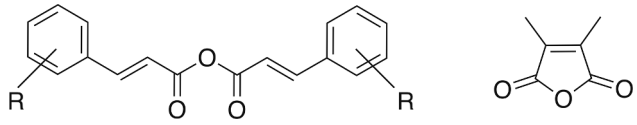


Fig. 1. Structure of cinnamic anhydrides and of 2,3-dimethylmaleic anhydride.

Table 1
Substitution pattern for cinnamic acids (**1**) and anhydrides (**2**).

	R^1	R^2	R^3	R^4
a	H	OMe	OMe	H
b	H	OMe	OMe	H
c	OMe	H	OMe	H
d	H	OMe	H	OMe
e	H	OMe	OMe	OMe
f	OH	OMe	H	H
g	H	OH	OMe	H
h	H	OMe	OH	H
i	H	OMe	OAc	H
j	H	Me	Me	H
k	NO_2	H	H	H
l	H	NO_2	H	H
m	H	H	$N(Me)_2$	H
n	H	H	H	H
o	H	OH	OH	H
p	H	OMe	OH	OMe
q	OMe	H	H	H
r	H	OMe	H	H
s	H	H	OMe	H
t	Cl	H	H	H
u	H	Cl	H	H
v	Cl/H	H/Cl	H	H
w	H	F	H	H
x	H	H	F	H

in the substitution pattern.

Symmetrical and non-symmetrical anhydrides were prepared according to Scheme 1. For the synthesis, a combination of cinnamic acids from previous reactions and commercially available compounds was used. Again, reaction yields were moderate to very good, with compounds **1f–1h** being the exceptions, reacting to polymeric structures and not forming anhydrides.

2.2. Biological evaluation

2.2.1. Inhibition of ChE

The inhibitory activity of the compounds for AChE and BChE was determined by Ellman's assays [22]. To support these experiments, some extra molecular docking calculations with the enzyme AChE (from electric eel) were performed using Autodock4 [23]. The results from the biological assays and calculations from the docking of cinnamic acid derivatives are compiled in Table 2. Interestingly, while some compounds proved to be good inhibitors for AChE, none of them was a good inhibitor for BChE.

The results from the biological assays are in excellent agreement with the results from the molecular modelling calculations. Thus, the cinnamic acid finds its way inside the enzyme pocket of AChE (Fig. 2), but shows only show weak interactions with the enzyme and cannot bind to the active site of the enzyme. In Fig. 2, the active site is located at the lower right with the corresponding amino acids His447, Glu334 and Ser203.

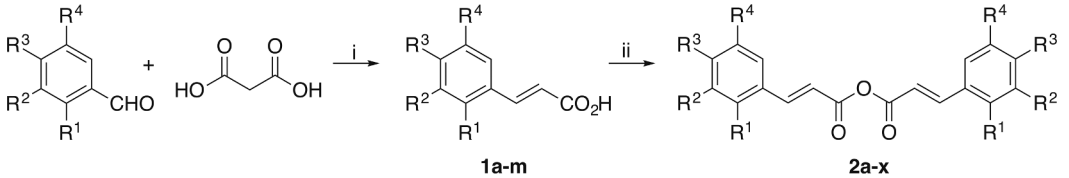
Table 2
Results from the biological screening (Ellman's assay; %-inhibition at a concentration of 10 μM) of compounds **1a**-**1m** (compounds not mentioned in the table were insoluble under the conditions of the assay) with AChE (from *electrophorus electricus*) and BChE (from *equine serum*); the inhibition [22] constants K_i and K_i' are given in μM and galantamine hydrobromide (**GH**) was used as a standard); the values are averaged from experiments performed in triplicate, and binding energies are reported in kcal/mol for AChE (PDB:1C2O).

AChE			BChE
Compounds	Inhibition [%]	Binding energy [kcal/mol]	Inhibition [%]
GH	87.70	−7.94	53.00
1a	33.70	−5.30	12.3
1b	7.22	−5.24	1.91
1c	25.91	−5.88	18.34
1d	12.65	−5.67	0.00
1e	9.75	−4.84	2.72
1g	6.89	−5.22	1.58
1h	12.32	−5.29	2.09
1i	12.09	−5.67	3.08
1j	11.85	−6.29	0.79
1k	8.52	−6.33	2.11
1l	10.60	−6.35	0.73
1m	13.61	−5.87	1.28

As depicted in Fig. 2, the anhydrides were also docked into the enzyme pocket of AChE. Although these compounds are larger, it is obvious that they fit even better than the parent acids into the pocket thus blocking the active site. The results from the biological assays showed cinnamic anhydrides **2a-2x** (Table 3) to be able of binding to the enzyme, and revealed some of them as good inhibitors. These anhydrides were only weak inhibitors for butyrylcholinesterase. Molecular modelling calculations (PDB:6EMI) revealed that these compounds have less interaction with the amino acid residues of the active site (Fig. 3).

The assays were carried out in aqueous solution, and thus it might be a valid assumption that the cinnamic anhydrides will be hydrolysed in this environment. Furthermore, one would assume that the products of hydrolysis induce the inhibitory effect. However, cinnamic acid anhydrides are rather stable under the conditions of the assays, and - as checked by TLC - even after a prolonged period of 72 h less than 10 percent of the anhydride was hydrolyzed into their corresponding acids. Therefore, the anhydride but not the cinnamic acid acts as inhibitor for AChE. The assumption that cinnamic anhydrides act as irreversible inhibitors of the enzyme could also not be confirmed since measurements of the enzyme kinetic showed these compounds as mixed type inhibitors for AChE. Thus, in this series, compounds **2c**, **2d**, **2j**, **2t**, **2u** and **2v** showed good to moderate inhibition of AChE. These biological activities are not entirely unexpected because these cinnamic anhydrides can be considered as isosteric derivatives of curcumin. Of the latter, inhibitory activity is known with respect to AChE [24–28].

Extra screening of cinnamic acids **1a**-**1m** and of anhydrides **2a**-**2x** showed them being not cytotoxic for a variety of human tumor cells lines [cut off: EC_{50} > 30 μM; cell lines: FaDu (hypopharyngeal



Scheme 1. . Synthesis of cinnamic acid derivatives and the appropriate anhydrides: (i): piperidine, pyridine, reflux 120 °C, 4 h; (ii): (1) oxalyl chloride, CH_2Cl_2, 0 °C → 25 °C, 2 h (2) pyridine, toluene, 25 °C, overnight.

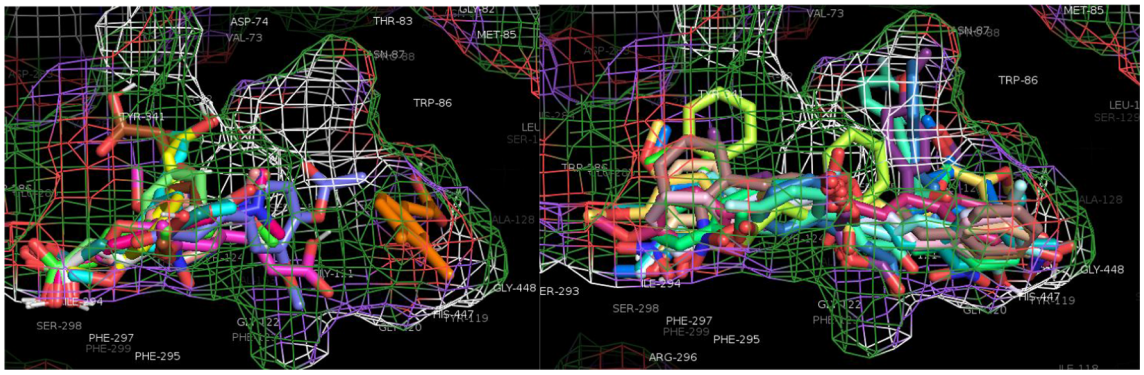


Fig. 2. Compounds **1a-1m** (left) and **2a-2x** (right) inside the AChE active site pocket.

carcinoma), A2780 (ovarian carcinoma), HT29 (colorectal carcinoma), MCF7 (breast carcinoma), SW1736 (thyroid carcinoma), A375 (malignant melanoma), A549 (epithel carcinoma)] and to non-malignant NIH 3T3 (mouse fibroblasts) cells. This finding is a prerequisite for developing anhydrides of improved properties.

3. Conclusion

As a result, cinnamic anhydrides have been shown to represent a class of interesting and promising compounds with unforeseen properties. In this study, 33 derivatives were prepared and screened for their biological activity. While these compounds exhibited no cytotoxic effect neither on malignant human tumor cells nor on non-malignant mouse fibroblasts, they proved to be moderate to good inhibitors of the enzyme acetylcholinesterase while being only negligible inhibitors for butyrylcholinesterase. As the cinnamic anhydrides are of remarkable stability in aqueous solution, derivatives of this kind might may be of interest to develop AChE inhibitors.

4. Experimental

4.1. General

The reagents were bought from commercial suppliers and used without further purification. The solvents were dried according to usual procedures. Melting points were determined on Büchi Melting Point M-565 or LEICA hot stage microscope and are uncorrected, NMR spectra were recorded on a Varian spectrometer Unity 500 (δ given in ppm, J in Hz), mass spectra were obtained on a Finnigan MAT LCQ 7000 (electrospray, voltage 4.1 kV, sheath gas nitrogen) instrument. The optical rotations were measured on a Perkin-Elmer polarimeter at 20 °C.

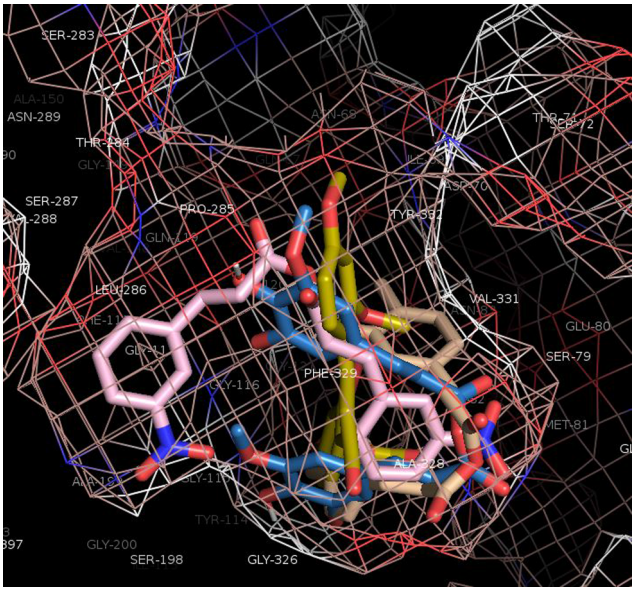


Fig. 3. Compounds **2c** (yellow), **2j** (beige), **2l** (red) and **2p** (blue) inside the BChE active site pocket.

Table 3
Results from the biological screening (Ellman's assay; %-inhibition at a concentration of 10 µM) of compounds **2a–2x** with AChE (from *electrophorus electricus*) and BChE (from *equine serum*); the inhibition constants K_i and K_i' are given in µM and galantamine hydrobromide (**GH**) was used as a standard); the values are averaged from experiments performed in triplicate, and binding energy are reported in kcal/mol for AChE (PDB:1C2O). All compounds were mixed type inhibitors.

AChE					BChE
Compounds	Inhibition [%]	K_i [µM]	K_i' [µM]	Binding energy for top 1 pose [kcal/mol]	Inhibition [%]
GH	87.70	0.54 ± 0.01	–	−7.94	53.00
2c	79.13	8.30 ± 0.94	9.54 ± 0.38	−8.46	27.50
2d	33.33	17.81 ± 0.95	53.70 ± 1.19	−8.30	0.00
2j	77.41	11.15 ± 1.36		−10.47	13.83
2k	15.36			−10.68	5.22
2m	9.02			−9.33	5.56
2n	14.14			−9.03	1.70
2p	9.14			−7.26	1.15
2q	34.85			−9.05	4.30
2r	10.54			−9.11	1.84
2t	54.55	13.42 ± 1.06	> 50	−9.94	3.60
2u	72.82	8.23 ± 0.93	13.07 ± 0.46	−9.99	13.15
2v	79.19)	12.19 ± 1.16	21.46 ± 0.13	−9.91	14.42
2w	15.70			−9.04	2.17
2x	17.15			−8.85	0.43

Macherey-Nagel ALUGRAM® Xtra SIL G/UV_{254} pre-coated silica gel 60 F254 plates were used for thin layer chromatography (detection with cerium molybdate spray reagent and UV absorption). IR spectra were recorded on a Perkin-Elmer FT-IR spectrometer Spectrum 1000 and wave numbers are expressed in cm^{-1}. The absorption spectra were measured on Perkin Elmer Lambda14 spectrometer. Microanalyses were performed with a Foss-Heraeus Vario EL (CHNS) instrument.

4.2. Molecular docking

The crystal structures of the *ee*AChE (PDB = 1C2O) *h*BChE-7 (PDB = 6EMI) were retrieved from the protein databank (rcsb.org). The enzyme was prepared according to usual procedures. Polar hydrogen atoms were added, water molecules removed, and Gasteiger charges were added. The ligand minimisation and preparation was performed with the MMFF94 force field in Datawarrior. Openbabel was used to create the pdbqt files for Autodock. Calculations were done with Autodock4 [23] Lamarckian genetic algorithm, and the analysis of the docking poses was done with MGLTools 1.5.6.; figures were created with PyMOL.

4.3. Biological screening

The Ellman's assay have been performed as previously described [29,30].

4.4. Syntheses

4.4.1. General procedure A

To a solution of the substituted benzaldehyde (1 eq.) and malonate (1.2 eq.) in pyridine (2.5 mL/mmol) at 120 °C piperidine (0.04 eq.) was added, and the reaction mixture was heated under reflux for 4 h [31]. The solvents were removed *in vacuo* as an azeotrope with toluene (3 × 70 mL). Water (100 mL) was added, and the aqueous phase was extracted with ethyl acetate (3 × 100 mL), brine (1 × 100 mL), dried ($MgSO_4$) and concentrated. Compounds **1a** and **1c–1m** were prepared following procedure A.

4.4.2. (2E)-3-(3,4-Dimethoxyphenyl)-2-propenoic acid (*1a*)

Recrystallization from ethanol gave **1a** (8.28 g, 80%) as an off-white solid; R_F = 0.05 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 178 °C (lit.: [32] 181–183 °C); IR (KBr): ν = 3440*m*, 2939*m*, 2839*m*, 1683*s*, 1625*s*, 1597*s*, 1516*s*, 1464*m*, 1426*m*, 1340*m*, 1298*m*, 1264*s*, 1210*m*, 1168*m*, 1142*s*, 1025*m* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 238 (4.05), 324 (4.20) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, *J* = 15.9 Hz, 1H, 3-H), 7.14 (dd, *J* = 8.3, 1.6 Hz, 1H, 6′-H), 7.08 (s, 1H, 5′-H), 6.88 (d, *J* = 8.3 Hz, 1H, 2′-H), 6.33 (d, *J* = 15.9 Hz, 1H, 2-H), 3.92 (s, 6H, 7′-H + 8′-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 172.4 (C-1), 151.7 (C-4′), 149.4 (C-3′), 147.1 (C-3), 127.2 (C-1′), 123.3 (C-6′), 115.0 (C-2), 111.2 (C-2′), 109.9 (C-5′), 56.1 (C-8′), 56.0 (C-7′) ppm; MS (ESI, MeOH): *m/z* (%) = 207.0 ([M − H]$^-$, 11), 415.1 ([2M − H]$^-$, 100), 436.9 ([2M − 2H + Na]$^-$, 13); analysis calcd for $C_{11}H_{12}O_4$ (208.21): C 63.45, H 5.81; found C 63.11, H 6.18.

4.4.3. 3-(3,4-Dimethoxyphenyl)propanoic acid (*1b*)

A solution of **1a** (1.0 g, 4.8 mmol) in THF (20 mL) was hydrogenated at 75 psi pressure in the presence of Pd/C (10%, 0.116 g) for 12 h. Usual work-up gave **1b** (0.83 g, 82%) as a colorless solid; R_F = 0.09 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 98 °C (lit.: [33] 98–99 °C); IR (ATR): ν = 2935*w*, 1697*s*, 1591*w*, 1516*m*, 1463*m*, 1430*m*, 1343*w*, 1306*w*, 1236*s*, 1146*s*, 1027*s*, 840*m*, 809*s*, 768*m*, 567*m* cm^{-1}; UV–vis (MeOH): λ_{max} (log ε) = 202 (4.42), 229 (3.75), 280 (3.32) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.80 (dd, *J* = 8.4, 3.2 Hz, 1H, 6′-H), 6.76 (s, 1H, 5′-H), 6.73 (d, *J* = 5.5 Hz, 1H, 2′-H), 3.87 (s, 3H, 8′-H), 3.86 (s, 3H, 7′-H), 2.91 (td, *J* = 7.8, 5.2 Hz, 2H, 3-H), 2.64 (td, *J* = 7.7, 5.1 Hz, 2H, 2-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.9 (C-1), 149.1 (C-4′), 147.8 (C-3′), 132.9 (C-1′), 120.3 (C-5′), 115.5 (C-2′), 111.8 (C-6′), 56.1 (C-8′), 56.0 (C-7′), 35.8 (C-3), 30.4 (C-2) ppm; MS (ESI, MeOH): *m/z* (%) = 209.1 ([M − H]$^-$, 100), 441 ([2M − 2H + Na]$^-$, 71); analysis calcd for $C_{11}H_{14}O_4$ (210.23): C 62.85, H 6.71; found C 62.65, H 6.92.

4.4.4. (E)-3-(2,4-Dimethoxyphenyl)acrylic acid (*1c*)

Recrystallization from ethanol gave **1c** (1.33 g, 64%) as an off-white solid; R_F = 0.25 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 190 °C (lit.: [34] 187–189 °C); IR (KBr): ν = 3448*m*, 3004*w*, 2944*w*, 2838*w*, 2586*w*, 1681*s*, 1599*s*, 1505*s*, 1459*m*, 1418*m*, 1329*s*, 1313*s*, 1298*m*, 1268*s*, 1210*s*, 1160*s*, 1117*s*, 1043*m*, 1028*m*, 987*m*, 829*m* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 254 (3.47), 316 (3.84), 354 (3.97) nm ; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 16.1 Hz, 1H, 3-H), 7.47 (d, *J* = 8.6 Hz, 1H, 3′-H), 6.52 (dd, *J* = 8.6, 2.3 Hz, 1H, 6′-H), 6.46 (d, *J* = 2.3 Hz, 1H, 5′-H), 6.45 (d, *J* = 16.0 Hz, 1H, 2-H), 3.88 (s, 3H, 7′-H), 3.85 (s, 3H, 8′-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.6 (C-1), 163.3 (C-4′), 160.3 (C-2′), 142.5 (C-3), 131.0 (C-3′), 116.5 (C-1′), 115.0 (C-2), 105.5 (C-6′), 98.6 (C-5′), 55.7 (C-7′ + C-8′) ppm; MS (ESI, MeOH): *m/z* (%) = 191.1 ([M + H-H_2O]$^+$, 100), 208.9 ([M + H]$^+$, 81), 223.0 ([M + H + MeOH-H_2O]$^+$, 25), 231.1 ([M + Na]$^+$, 8); analysis calcd for $C_{11}H_{12}O_4$ (208.21): C 63.45, H 5.81; found: C 62.35, H 6.13.

4.4.5. (E)-3-(3,5-Dimethoxyphenyl)acrylic acid (*1d*)

Compound **1d** was obtained by recrystallization from ethanol as a white solid (1.16 g, 60%); R_F = 0.08 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 173 °C (lit.: [35] 174 °C); IR (ATR): ν = 2835*w*, 1682*s*, 1632*m*, 1593*s*, 1469*m*, 1433*m*, 1356*w*, 1320*m*, 1285*s*, 1206*s*, 1163*s*, 1057*s*, 927*m*, 852*m*, 837*s*, 808*m*, 670*m*, 645*m*, 606*m*, 540*m*, 472*m* cm^{-1}; UV–vis (MeOH): λ_{max} (log ε) = 226 (4.39), 284 (4.25) nm; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.51 (d, *J* = 16.0 Hz, 1H, 3-H), 6.86 (d, *J* = 2.2 Hz, 2H, 2′-H), 6.56 (d, *J* = 16.1 Hz, 1H, 2-H), 6.53 (d, *J* = 2.2 Hz, 1H, 4′-H), 3.77 (s, 6H, 5′-H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 167.6 (C-1), 160.7 (C-3′), 143.9 (C-3), 136.2 (C-1′), 119.9 (C-2), 106.0 (C-2′), 102.4 (C-4′), 55.4 (C-5′) ppm; MS (ESI, ASAP): *m/z* (%) = 207.1 ([M − H]$^-$, 100); analysis calcd for $C_{11}H_{12}O_4$ (208.21): C 63.45, H 5.81; found C 62.29, H 6.11.

4.4.6. (E)-3-(3,4,5-Trimethoxyphenyl)acrylic acid (*1e*)

Compound **1e** was obtained by recrystallization from ethanol as an off-white solid (4.36 g, 36%); R_F = 0.04 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 125 °C (lit.: [36] 124–125 °C); IR (ATR): ν = 3004*w*, 2837*w*, 2653*w*, 1684*w*, 1625*m*, 1583*m*, 1502*m*, 1470*w*, 1454*m*, 1417*m*, 1393*m*, 1321*m*, 1283*m*, 1202*m*, 1189*m*, 1156*m*, 1117*s*, 997*s*, 982*s*, 826*m*, 739*m*, 731*m*, 620*m*, 609*m*, 527*m*, 513*m* cm^{-1}; UV–vis (MeOH): λ_{max} (log ε) = 231 (4.30), 302 (4.25) nm; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.52 (d, *J* = 15.9 Hz, 1H, 3-H), 7.02 (s, 2H, 2′-H), 6.53 (d, *J* = 15.9 Hz, 1H, 2-H), 3.81 (s, 6H, 5′-H), 3.68 (s, 3H, 6′-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 167.7 (C-1), 153.1 (C-3′), 144.1 (C-3), 139.3 (C-4′), 129.9 (C-1′), 118.5 (C-2), 105.8 (C-2′), 60.1 (C-6′), 56.0 (C-5′) ppm; MS (ESI, MeOH): *m/z* (%) = 221.1 ([M + H-H_2O]$^+$, 56), 239.0 ([M + H]$^+$, 100), 255.9 ([M + NH_4]$^+$, 10), 261.1 ([M + Na]$^+$, 37), 276.9 ([M + K]$^+$, 5), 292.7 ([M + Na + MeOH]$^+$, 10); analysis calcd for $C_{12}H_{14}O_7$ (238.24): C 60.50, H 5.92; found: C 62.39, H 6.18.

4.4.7. (E)-3-(3-Hydroxy-4-methoxyphenyl)acrylic acid (*1g*)

Compound **1g** was obtained by recrystallization from ethanol as an off-white solid (5.63 g, 58%); R_F = 0.02 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 232 °C (lit.: [37] 230–232 °C); IR (ATR): ν = 1612*m*, 1509*s*, 1442*m*, 1261*s*, 1134*s*, 1023*m*, 936*s*, 857*s*, 815*s*, 760*s*, 570*s*, 504*s* cm^{-1}; UV–vis (MeOH): λ_{max} (log ε) = 219 (4.19), 242 (4.11), 296 (4.20), 321 (4.23) nm; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.44 (d, *J* = 15.9 Hz, 1H, 3-H), 7.08 (dd, *J* = 8.2, 2.2 Hz, 1H, 6′-H), 7.06 (d, *J* = 2.1 Hz, 1H, 2′-H), 6.94 (d, *J* = 8.2 Hz, 1H, 5′-H), 6.23 (d, *J* = 15.9 Hz, 1H, 2-H), 3.80 (s, 3H, 7′-H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 167.7 (C-1), 149.8 (C-4′), 146.6 (C-3′), 144.1 (C-3), 127.1 (C-1′), 120.9 (C-6′), 116.3 (C-2), 114.1 (C-2′), 112.0 (C-5′), 55.6

(C-7′) ppm; MS (ESI, MeOH): *m/z* (%) = 193.0 ([M − H]$^-$, 100), 386.8 ([2M − H]$^-$, 16); analysis calcd for $C_{10}H_{10}O_4$ (194.19): C 61.85, H 5.19; found: C 62.03, H 5.22.

4.4.8. (E)-3-(4-Hydroxy-3-methoxyphenyl)acrylic acid (1h)

Compound **1h** was obtained by recrystallization from ethanol as a white solid (5.61 g, 57%); R_F = 0.06 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 170 °C (lit.: [37] 168–169 °C); IR (ATR): ν = 3435*w*, 1662*m*, 1590*m*, 1511*m*, 1465*m*, 1431*m*, 1323*w*, 1265*s*, 1163*s*, 1112*m*, 1033*s*, 942*s*, 851*s*, 803*s*, 751*m*, 685*m*, 598*s*, 572*s*, 519*s* cm^{-1}; UV–vis (MeOH): λ_{max} (log ε) = 218 (3.89), 321 (4.00) nm; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.48 (d, *J* = 15.9 Hz, 1H, 3-H), 7.27 (d, *J* = 1.9 Hz, 1H, 2′-H), 7.08 (dd, *J* = 8.2, 1.9 Hz, 1H, 6′-H), 6.78 (d, *J* = 8.1 Hz, 1H, 5′-H), 6.35 (d, *J* = 15.9 Hz, 1H, 2-H), 3.81 (s, 3H, 7′-H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 167.9 (C-1), 149.1 (C-4′), 147.9 (C-3′), 144.5 (C-3), 125.7 (C-1′), 122.8 (C-6′), 115.6 (C-2), 115.5 (C-5′), 111.2 (C-2′), 55.7 (C-7′) ppm; MS (ESI, ASAP): *m/z* (%) = 178.1 ([M − H-CH$_3$]$^-$, 100), 193.1 ([M − H]$^-$, 98); analysis calcd for $C_{10}H_{10}O_4$ (194.19): C 61.85, H 5.19; found C 61.75, H 6.19.

4.4.9. (E)-3-(4-Acetoxy-3-methoxyphenyl)acrylic acid (1i)

Compound **1i** was obtained by recrystallization from ethanol as a yellowish solid (2.52 g, 62%); R_F = 0.02 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 195 °C; IR (ATR): ν = 2944*w*, 1760*m*, 1682*s*, 1632*m*, 1601*m*, 1506*m*, 1469*w*, 1421*m*, 1371*w*, 1316*m*, 1260*s*, 1222*s*, 1198*s*, 1154*s*, 1120*s*, 1033*m*, 985*s*, 913*m*, 855*s*, 837*m*, 691*m*, 648*m*, 599*m*, 527*m* cm^{-1}; UV–vis (MeOH): λ_{max} (log ε) = 277 (3.83) nm; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.57 (d, *J* = 16.0 Hz, 1H, 3-H), 7.48 (d, *J* = 1.8 Hz, 1H, 2′-H), 7.26 (dd, *J* = 8.2, 1.8 Hz, 1H, 6′-H), 7.12 (d, *J* = 8.1 Hz, 1H, 5′-H), 6.58 (d, *J* = 16.0 Hz, 1H, 2-H), 3.82 (s, 3H, 7′-H), 2.26 (s, 3H, 9′-H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 168.4 (C-8′), 167.5 (C-1), 151.1 (C-3′), 143.3 (C-3), 140.8 (C-4′), 133.2 (C-1′), 123.2 (C-5′), 121.3 (C-6′), 119.6 (C-2), 111.8 (C-2′), 56.0 (C-7′), 20.4 (C-9′) ppm; MS (ESI, ASAP): *m/z* (%) = 235.1 ([M − H]$^-$, 100); analysis calcd for $C_{12}H_{12}O_5$ (236.22): C 61.02, H 5.12; found: C 6 59.77, H 5.31.

4.4.10. (E)-3-(3,4-Dimethylphenyl)acrylic acid (1j)

Compound **1j** was obtained by recrystallization from ethanol as a white solid (1.69 g, 57%); R_F = 0.19 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 174 °C; IR (ATR): ν = 2919*w*, 1672*s*, 1621*s*, 1421*m*, 1318*s*, 1285*s*, 1219*s*, 956*s*, 925*s*, 866*s*, 815*s*, 688*s*, 582*m*, 546*s* cm^{-1}; UV–vis (MeOH): λ_{max} (log ε) = 223 (4.00), 286 (4.14) nm; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.56 (d, *J* = 16.0 Hz, 1H, 3-H), 7.45 (d, *J* = 1.9 Hz, 1H, 5′-H), 7.38 (dd, *J* = 7.7, 1.9 Hz, 1H, 6′-H), 7.17 (d, *J* = 7.7 Hz, 1H, 2′-H), 6.43 (d, *J* = 16.0 Hz, 1H, 2-H), 2.23 (s, 6H, 7′-H + 8′-H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 167.7 (C-1), 144.1 (C-3), 139.0 (C-4′), 136.8 (C-3′), 131.8 (C-1′), 130.0 (C-6′), 129.1 (C-2′), 125.8 (C-5′), 117.8 (C-2), 19.3 (C-7′), 19.2 (C-8′) ppm; MS (ESI, ASAP): *m/z* (%) = 175.1 ([M − H]$^-$, 100); analysis calcd for $C_{11}H_{12}O_2$ (176.21): C 74.98, H 6.86; found: C 74.75, H 7.00.

4.4.11. (E)-3-(2-Nitrophenyl)acrylic acid (1k)

After recrystallization from ethanol compound **1k** was obtained as an off-white solid (0.89 g, 46%); R_F = 0.07 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 247 °C; IR (KBr): ν = 1694*m*, 1519*m*, 1419*m*, 1280*s*, 1202*s*, 981*m*, 865*m*, 789*s*, 754*s*, 701*s*, 594*m*, 542*m*, 486*m* cm^{-1}; UV–vis (EtOH): λ_{max} (log ε) = 286 (3.73) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (dd, *J* = 8.1, 1.2 Hz, 1H, 6′-H), 7.94 (dd, *J* = 7.8, 1.2 Hz, 1H, 3′-H), 7.86 (d, *J* = 15.9 Hz, 1H, 3-H), 7.78 (td, *J* = 7.7, 1.5 Hz, 1H, 4′-H), 7.69–7.65 (*m*, 1H, 5′-H), 6.54 (d, *J* = 15.8 Hz, 1H, 2-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 166.8 (C-1), 148.3 (C-2′), 138.7 (C-3), 133.8 (C-4′), 130.8 (C-5′), 129.3 (C-1′), 129.2 (C-3′), 124.6 (C-6′), 123.8 (C-2) ppm; MS (ESI, MeOH): *m/z* (%) = 191.9 ([M − H]$^-$, 41), 237.8 ([M + HCO$_2$]$^-$, 11), 259.9 ([M − H + NaHCO$_2$]$^-$, 6), 384.9 ([2 M − H]$^-$, 100), 406.9 ([2M − 2H + Na]$^-$, 5); analysis calcd for $C_9H_7NO_2$ (193.16): C 55.96, H 3.65, N 7.25; found: C 5571, H 3.79, N 7.07.

4.4.12. (E)-3-(3-Nitrophenyl)acrylic acid (1l)

After recrystallization from ethanol compound **1l** was obtained as an off-white solid (1.20 g, 62%); R_F = 0.02 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 204 °C; IR (KBr): ν = 2539*w*, 1683*s*, 1630*m*, 1521*s*, 1485*w*, 1434*w*, 1418*m*, 1360*s*, 1319*s*, 1306*s*, 1285*s*, 1223*m*, 1177*m*, 1108*w*, 985*m*, 922*s*, 869*m*, 825*m*, 805*s*, 747*m*, 716*s*, 667*s*, 596*m*, 567*m*, 544*m*, 486*m* cm^{-1}; UV–vis (EtOH): λ_{max} (log ε) = 295 (3.91) nm; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.60 (s, 1H, O*H*), 8.51 (t, *J* = 2.0 Hz, 1H, 4′-H), 8.23 (ddd, *J* = 8.2, 2.3, 0.9 Hz, 1H, 6′-H), 8.18 (dt, *J* = 7.7, 1.2 Hz, 1H, 5′-H), 7.72 (d, *J* = 16.2 Hz, 1H, 3-H), 7.71 (d, *J* = 7.9 Hz, 1H, 2′-H), 6.74 (d, *J* = 16.1 Hz, 1H, 2-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 167.1 (C-1), 148.3 (C-3′), 141.4 (C-3), 136.1 (C-1′), 134.0 (C-5′), 130.3 (C-2′), 124.4 (C-6′), 122.8 (C-4′), 122.3 (C-2) ppm; MS (ESI, MeOH): *m/z* (%) = 192.0 ([M − H]$^-$, 100), 237.9 ([M + HCO$_2$]$^-$, 3), 260.0 ([M − H + NaHCO$_2$]$^-$, 2), 384.8 ([2M − H]$^-$, 44), 407.0 ([2M − 2H + Na]$^-$, 14); analysis calcd for $C_9H_7NO_2$ (193.16): C 55.96, H 3.65, N 7.25; found: C 55.71, H 3.91, N 6.96.

4.4.13. (E)-3-(4-Dimethylamino)phenyl)acrylic acid (1m)

Compound **1m** was obtained by recrystallization from ethanol as an yellowish solid (3.86 g, 40%); R_F = 0.08 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 212 °C (lit.: [38] 210–212 °C); IR (ATR): ν = 2803*w*, 1665*m*, 1590*m*, 1523*m*, 1434*m*, 1366*m*, 1308*m*, 1260*m*, 1227*m*, 1163*m*, 987*m*, 940*m*, 858*m*, 812*s*, 675*m*, 513*s*, 479*m* cm^{-1}; UV–vis (MeOH): λ_{max} (log ε) = 242 (3.80), 358 (4.27) nm; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.49 (d, *J* = 2.5 Hz, 2H, 2′-H), 7.46 (d, *J* = 15.8 Hz, 1H, 3-H), 6.70 (d, *J* = 8.9 Hz, 2H, 3′-H), 6.20 (d, *J* = 15.8 Hz, 1H, 2-H), 2.96 (s, 6H, 5′-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 168.1 (C-1), 151.6 (C-4′), 144.6 (C-3), 129.7 (C-2′), 121.5 (C-1′), 112.9 (C-2), 111.8 (C-3′), 39.7 (C-5′) ppm; MS (ESI, ASAP): *m/z* (%) = 190.2 ([M − H]$^-$, 100); analysis calcd for $C_{11}H_{13}NO_2$ (191.23): C 69.09, H 6.85, N 7.32; found: C 68.88, H 7.02, N 7.15.

4.4.14. General procedure B

Under argon atmosphere, to a solution of the acid (1 eq.) in dry DCM (10 mL/mmol) at 0 °C oxalyl chloride (3 eq.) and DMF (2 drops) were added. After stirring for 1 h at 0 °C followed by 1 h at room temperature the solvent was removed *in vacuo*, and the residue was washed with dry DCM (10 mL/mmol). The residue was re-dissolved in toluene (5 mL/mmol), pyridine (2 eq.) and the corresponding acid (1 eq.) was added. The mixture was stirred over night at room temperature. Usual aqueous work-up gave a residue that was washed with ethanol.

4.4.15. (E)-3-(3,4-Dimethoxyphenyl)acrylic anhydride (2a)

Compound **2a** was obtained as a white solid (0.53 g, 55%); R_F = 0.42 (silica gel, chloroform); m.p. 177 °C; IR (ATR): ν = 2931*w*, 2835*w*, 1754*m*, 1707*s*, 1625*s*, 1598*m*, 1581*w*, 1510*s*, 1460*m*, 1438*w*, 1424*m*, 1354*w*, 1311*w*, 1266*s*, 1240*s*, 1214*s*, 1162*m*, 1144*s*, 1075*s*, 1021*s*, 1001*s*, 986*s*, 972*m*, 943*s*, 868*s*, 810*s*, 773*m*, 731*m*, 707*m*, 602*m*, 570*m*, 548*m* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 227 (3.89), 250 (3.93), 347 (4.26) nm; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 15.8 Hz, 2H, 3-H), 7.17 (dd, *J* = 8.3, 1.9 Hz, 2H, 6′-H), 7.09 (d, *J* = 1.9 Hz, 2H, 5′-H), 6.90 (d, *J* = 8.3 Hz, 2H, 2′-H), 6.40 (d, *J* = 15.8 Hz, 2H, 2-H), 3.94 (s, 6H, 7′-H), 3.93 (s, 6H, 8′-H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.1 (C-1), 152.2 (C-4′), 149.5 (C-3′), 148.7 (C-3), 127.0 (C-1′), 123.7 (C-6′), 114.6 (C-2), 111.3 (C-2′), 110.1 (C-5′), 56.2 (C-8′), 56.1 (C-7′) ppm; MS (ESI, MeOH): *m/z* (%) = 421.5 ([M + Na]$^+$, 100), 437.5 ([M + K]$^+$, 25), 453.6 ([M + Na + MeOH]$^+$); analysis calcd for $C_{22}H_{22}O_7$ (398.41): C 66.32, H 5.57; found: C 66.18, H 6.73.

4.4.16. 3-(3,4-Dimethoxyphenyl)propanoic anhydride (2b)

Compound **2b** was obtained as an off-white solid (0.09 g, 46%);

R_F = 0.04 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 178 °C; IR (ATR): ν = 2935*w*, 2838*w*, 1697*s*, 1591*w*, 1516*m*, 1463*m*, 1430*m*, 1409*w*, 1346*w*, 1306*m*, 1251*m*, 1236*s*, 1213*m*, 1146*s*, 1026*m*, 840*m*, 809*m*, 768*m* cm^{-1}; UV–vis (MeOH): λ_{max} (log ε) = 299 (3.80), 279 (3.57) nm; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.80 (dd, *J* = 8.3, 5.0 Hz, 2H, 5′-H + 5‴-H), 6.77–6.72 (*m*, 4H, 2′-H + 2‴-H + 6′-H + 6‴-H), 3.88 (s, 3H, 7′-H), 3.87 (s, 3H, 7‴-H), 3.86 (s, 3H, 8′-H), 3.85 (s, 3H, 8‴-H), 2.91 (td, *J* = 7.5, 1.2 Hz, 4H, 2-H + 2″-H), 2.73 (t, *J* = 7.6 Hz, 2H, 3-H), 2.67 (t, *J* = 7.7 Hz, 2H, 3″-H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.8 (C-1), 149.2 (C-3′), 149.1 (C-3‴), 147.9 (C-4′), 147.8 (C-4‴), 132.9 (C-1′), 132.4 (C-1‴), 120.3 (C-6′), 120.2 (C-6‴), 111.9 (C-2′ + C-2‴), 111.6 (C-5′ + C-5‴), 56.1 (C-7′ + C-7‴), 56.0 (C-8′ + C-8‴), 37.3 (C-2), 35.7 (C-2″), 30.4 (C-3), 30.0 (C-3″) ppm; MS (ESI, MeOH): *m/z* (%) = 425.1 ($[M + Na]^+$, 100), 826.9 ($[2M + Na]^+$, 8); analysis calcd for $C_{22}H_{26}O_7$ (402.44): C 65.66, H 6.51; found: C 65.41, H 6.72.

4.4.17. (E)-3-(2,4-Dimethoxyphenyl)acrylic anhydride (2c)

Compound **2c** was obtained as a white solid (0.85 g, 89%); R_F = 0.35 (silica gel, chloroform); m.p. 105–108 °C; IR (KBr): ν = 3448*w*, 2946*w*, 2843*w*, 1754*m*, 1711*m*, 1602*s*, 1566*m*, 1505*m*, 1457*m*, 1439*w*, 1418*m*, 1330*m*, 1296*s*, 1268*m*, 1215*s*, 1164*s*, 1118*m*, 1066*s*, 985*m*, 830*m* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 265 (3.81), 385 (4.35) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 16.0 Hz, 2H, 3-H), 7.48 (d, *J* = 8.6 Hz, 2H, 3′-H), 6.54 (d, *J* = 15.9 Hz, 2H, 2-H), 6.53 (dd, *J* = 8.6, 2.3 Hz, 2H, 6′-H), 6.46 (d, *J* = 2.3 Hz, 2H, 5′-H), 3.89 (s, 6H, 7′-H), 3.86 (s, 6H, 8′-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.1 (C-1), 163.7 (C-4′), 160.6 (C-2′), 144.0 (C-3), 131.5 (C-3′), 116.4 (C-1′), 114.9 (C-2), 105.7 (C-6′), 98.6 (C-5′), 55.7 (C-7′), 55.6 (C-8′) ppm; MS (ESI, MeOH): *m/z* (%) = 191.1 ($[M\text{-}C_{11}H_{11}O_4]^+$, 38), 209.0 ($[M\text{-}C_{11}H_{11}O_4 + H_2O]^+$, 3), 223.0 ($[M\text{-}C_{11}H_{11}O_4 + MeOH]^+$, 22), 421.0 ($[M + Na]^+$, 49), 818.9 ($[2\,M + Na]^+$, 100); analysis calcd for $C_{22}H_{22}O_7$ (398.41): C 66.32, H 5.57; found: C 66.11, H 5.69.

4.4.18. (E)-3-(3,5-Dimethoxyphenyl)acrylic anhydride (2d)

Compound **2d** was obtained as an off-white solid (0.31 g, 81%); R_F = 0.21 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 140 °C; IR (ATR): ν = 1778*m*, 1706*m*, 1630*m*, 1593*s*, 1471*w*, 1431*m*, 1356*w*, 1302*w*, 1284*w*, 1208*s*, 1158*s*, 1085*s*, 1065*s*, 1055*s*, 977*m*, 952*s*, 925*m*, 850*m*, 837*s*, 818*m* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 206 (4.45), 231 (4.29), 309 (4.34) nm; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 15.9 Hz, 2H, 3-H), 6.71 (d, *J* = 2.2 Hz, 4H, 2′-H), 6.55 (t, *J* = 2.2 Hz, 2H, 4′-H), 6.49 (d, *J* = 15.9 Hz, 2H, 2-H), 3.83 (s, 12H, 5′-H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.5 (C-1), 161.3 (C-3′), 148.8 (C-3), 135.7 (C-1′), 117.4 (C-2), 106.6 (C-2′), 103.7 (C-4′), 55.7 (C-5′) ppm; MS (ESI, MeOH): *m/z* (%) = 421.1 ($[M + Na]^+$, 44), 818.9 ($[2M + Na]^+$, 100); analysis calcd for $C_{22}H_{22}O_7$ (398.41): C 66.32, H 5.57; found: C 66.15, H 5.80.

4.4.19. (E)-3-(3,4,5-Trimethoxyphenyl)acrylic anhydride (2e)

Compound **2e** was obtained as a white solid (0.30 g, 77%); R_F = 0.06 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 174 °C (lit.: [39] 190–192); IR (ATR): ν = 1802*w*, 1757*w*, 1698*w*, 1623*w*, 1582*m*, 1505*m*, 1455*w*, 1422*m*, 1342*w*, 1323*w*, 1267*m*, 1251*m*, 1159*w*, 1125*s*, 1040*s*, 1008*s*, 987*m*, 959*m*, 840*m* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 236 (4.23), 335 (4.31) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 15.8 Hz, 2H, 3-H), 6.80 (s, 4H, 2′-H), 6.43 (d, *J* = 15.8 Hz, 2H, 2-H), 3.91 (s, 12H, 5′-H + 6′-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.7 (C-1), 153.7 (C-3′), 148.8 (C-3), 141.3 (C-4′), 129.3 (C-1′), 116.0 (C-2), 106.0 (C-2′), 61.2 (C-6′), 56.4 (C-5′) ppm; MS (ESI, MeOH): *m/z* (%) = 481.1 ($[M + Na]^+$, 44), 938.9 ($[2M + Na]^+$, 100); analysis calcd for $C_{24}H_{26}O_9$ (458.46): C 62.88, H 5.72; found: C 62.75, H 5.90.

4.4.20. (E)-3-(4-Acetoxy-3-methoxyphenyl)acrylic anhydride (2i)

Compound **2i** was obtained as a white solid (0.29 g, 76%); R_F = 0.06 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 122–124 °C (lit.: [40] 178–180 °C); IR (ATR): ν = 1763*s*, 1702*w*, 1627*m*, 1586*w*, 1461*w*, 1419*w*, 1371*w*, 1305*w*, 1257*m*, 1222*m*, 1169*w*, 1123*w*, 1054*s*, 1034*m*, 1001*m*, 966*m* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 206 (4.27), 297 (4.20) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 15.9 Hz, 2H, 3-H), 7.19 (dd, *J* = 8.1, 1.9 Hz, 2H, 6′-H), 7.14 (d, *J* = 1.9 Hz, 2H, 2′-H), 7.10 (d, *J* = 8.1 Hz, 2H, 5′-H), 6.47 (d, *J* = 15.9 Hz, 2H, 2-H), 3.89 (s, 6H, 7′-H), 2.33 (s, 6H, 9′-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8 (C-8′), 162.4 (C-1), 151.8 (C-3′), 148.1 (C-3), 142.5 (C-4′), 132.8 (C-1′), 123.7 (C-5′), 122.0 (C-6′), 117.0 (C-2), 111.8 (C-2′), 55.2 (C-7′), 20.8 (C-9′) ppm; MS (ESI, MeOH): *m/z* (%) = 477.1 ($[M + Na]^+$, 55), 930.9 ($[2M + Na]^+$, 100); analysis calcd for $C_{24}H_{22}O_9$ (454.43): C 63.43, H 4.88; found: C 63.21, H 5.02.

4.4.21. (E)-3-(3,4-Dimethylphenyl)acrylic anhydride (2j)

Compound **2j** was obtained as a white solid (0.23 g, 60%); R_F = 0.58 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 195 °C; IR (ATR): ν = 2919*w*, 1751*s*, 1704*s*, 1626*m*, 1605*w*, 1505*w*, 1450*w*, 1268*w*, 1234*w*, 1206*w*, 1121*s*, 1021*w*, 987*s*, 944*s*, 929*s*, 890*m*, 865*m*, 826*s*, 813*s*, 567*m* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 206 (4.44), 232 (4.36), 310 (4.64) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 15.9 Hz, 2H, 3-H), 7.35 (d, *J* = 2.0 Hz, 2H, 2′-H), 7.32 (dd, *J* = 7.8, 2.0 Hz, 2H, 6′-H), 7.18 (d, *J* = 7.8 Hz, 2H, 5′-H), 6.47 (d, *J* = 15.9 Hz, 2H, 2-H), 2.31 (s, 6H, 7′-H), 2.30 (s, 6H, 8′-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.0 (C-1), 149.0 (C-3), 140.8 (C-3′), 137.5 (C-4′), 131.7 (C-1′), 130.5 (C-5′), 129.9 (C-2′), 126.4 (C-6′), 115.7 (C-2), 20.1 (C-7′), 19.9 (C-8′) ppm; MS (ESI, MeOH): *m/z* (%) = 357.1 ($[M + Na]^+$, 74), 691.0 ($[2M + Na]^+$, 100); analysis calcd for $C_{22}H_{22}O_3$ (344.41): C 79.02, H 6.63; found: C 78.83, H 6.82.

4.4.22. (E)-3-(2-Nitrophenyl)acrylic anhydride (2k)

Compound **2k** was obtained as a yellowish solid (0.23 g, 60%); R_F = 0.31 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 184 °C; IR (ATR): ν = 1756*m*, 1706*m*, 1624*w*, 1570*w*, 1516*m*, 1341*m*, 1288*w*, 1263*w*, 1205*w*, 1148*m*, 1121*s*, 979*m*, 935*s*, 891*m*, 867*m*, 789*s*, 751*s*, 712*m*, 681*m*, 536*m*, 503*m*, 487*m* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 252 (4.29) nm; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.34 (d, *J* = 15.7 Hz, 1H, 3-H), 8.12 (dd, *J* = 8.1, 1.0 Hz, 1H, 6′-H), 7.72–7.68 (*m*, 2H, 4′-H + 3′-H), 7.62 (ddd, *J* = 8.6, 6.8, 2.1 Hz, 1H, 5′-H), 6.46 (d, *J* = 15.8 Hz, 1H, 2-H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.0 (C-1), 148.4 (C-2′), 144.3 (C-3), 133.9 (C-4′), 131.3 (C-5′), 130.1 (C-1′), 129.5 (C-3′), 125.3 (C-6′), 121.7 (C-2) ppm; MS (ESI, MeOH): *m/z* (%) = 391.0 ($[M + Na]^+$, 100), 758.8 ($[2M + Na]^+$, 79); analysis calcd for $C_{18}H_{12}N_2O_7$ (368.30): C 58.70, H 3.28, N 7.61; found: C 58.55, H 3.51, N 7.34.

4.4.23. (E)-3-(3-Nitrophenyl)acrylic anhydride (2l)

Compound **2l** was obtained as an off-white solid (0.19 g, 64%); R_F = 0.07 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 174 °C; IR (ATR): ν = 3077*w*, 1787*m*, 1714*w*, 1637*w*, 1523*s*, 1481*w*, 1443*w*, 1354*s*, 1268*w*, 1227*w*, 1204*m*, 1091*s*, 974*s*, 938*m*, 804*m*, 741*m*, 710*m*, 660*m* cm^{-1}; UV–vis (MeOH): λ_{max} (log ε) = 205 (3.98), 262 (3.95) nm; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.46 (t, *J* = 2.0 Hz, 2H, 4′-H), 8.31 (ddd, *J* = 8.2, 2.3, 1.0 Hz, 2H, 6′-H), 7.91 (d, *J* = 16.0 Hz, 2H, 3-H), 7.91–7.88 (*m*, 2H, 5′-H), 7.65 (t, *J* = 8.0 Hz, 2H, 2′-H), 6.67 (d, *J* = 16.0 Hz, 2H, 2-H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.4 (C-1), 149.0 (C-3′), 146.0 (C-3), 135.4 (C-1′), 134.2 (C-5′), 130.4 (C-2′), 125.7 (C-6′), 123.0 (C-4′), 119.8 (C-2) ppm; MS (ESI, MeOH): *m/z* (%) = 390.9 ($[M + Na]^+$, 58), 758.7 ($[2M + Na]^+$, 100); analysis calcd for $C_{18}H_{12}N_2O_7$ (368.30): C 58.70, H 3.28, N 7.61; found: C 58.61, H 3.43, N 7.47.

4.4.24. (E)-3-(4-(Dimethylamino)phenyl)acrylic anhydride (2m)

Compound **2m** was obtained as a yellowish solid (0.18 g, 48%); R_F = 0.1 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 145 °C; IR (ATR): ν = 2816*w*, 1668*m*, 1594*m*, 1523*m*, 1435*m*, 1368*m*, 1309*m*, 1261*m*, 1228*m*, 1186*s*, 988*m*, 941*m*, 814*s*, 676*m*, 514*m*, 481*m* cm^{-1}; UV–vis

(MeOH): λ_{max} (log ε) = 246 (2.49), 349 (3.02) nm; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 15.8 Hz, 2H, 3-H), 7.44 (d, *J* = 8.8 Hz, 4H, 2′-H), 6.68 (d, *J* = 8.9 Hz, 4H, 3′-H), 6.22 (d, *J* = 15.8 Hz, 2H, 2-H), 3.03 (s, 12H, 5′-H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.6 (C-1), 152.2 (C-4′), 147.6 (C-3), 130.3 (C-2′), 122.1 (C-1′), 112.0 (C-3′), 111.2 (C-2), 40.3 (C-5′) ppm; MS (ESI, MeOH): *m/z* (%) = 387.1 ([M + Na]$^+$, 15), 751.0 ([2M + Na]$^+$, 16); analysis calcd for $C_{22}H_{24}N_2O_3$ (364.44): C 72.51, H 6.64, N 7.69; found: C 72.39, H 6.87, N 7.51.

4.4.25. Cinnamic anhydride (**2n**)

Compound **2n** was obtained as a white solid (0.61 g, 65%); R_F = 0.12 (silica gel, chloroform); m.p. 136 °C (lit.: [41] 136–137 °C); IR (ATR): ν = 1764*m*, 1699*s*, 1630*m*, 1495*w*, 1450*m*, 1304*w*, 1269*w*, 1227*m*, 1200*m*, 1068*s*, 958*s*, 857*m*, 750*s*, 689*s*, 674*s*, 551*s*, 510*m*, 476*s* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 227 (4.14), 298 (4.50) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 15.9 Hz, 2H, 3-H), 7.60–7.57 (*m*, 4H, 3′-H), 7.46–7.41 (*m*, 6H, 2′-H + 4′-H), 6.54 (d, *J* = 15.9 Hz, 2H, 2-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.6 (C-1), 148.8 (C-3), 133.9 (C-1′), 131.4 (C-4′), 129.2 (C-2′), 128.7 (C-3′), 116.9 (C-2) ppm; MS (ESI, ASAP): *m/z* (%) = 301.3 ([M + Na]$^+$, 100), 333.4 ([M + Na + MeOH]$^+$, 96); analysis calcd for $C_{18}H_{14}O_3$ (278.31): C 77.68, H 5.07; found: C 77.46, H 5.18.

4.4.26. (E)-3-(3,4-Dihydroxyphenyl)acrylic anhydride (**2o**)

Compound **2o** was obtained as an off-white solid (0.51 g, 53%); R_F = 0.62 (silica gel, chloroform); m.p. 178 °C; ^{1}H NMR (400 MHz, CD_3OD): δ = 7.56 (d, *J* = 15.9 Hz, 2H, 3-H), 7.06 (d, *J* = 2.1 Hz, 2H, 5′-H), 6.96 (dd, *J* = 8.2, 2.0 Hz, 2H, 6′-H), 6.80 (d, *J* = 8.2 Hz, 2H, 2′-H), 6.24 (d, *J* = 15.9 Hz, 2H, 2-H) ppm; ^{13}C NMR (100 MHz, CD_3OD): δ = 171.0 (C-1), 149.5 (C-4′), 147.0 (C-3), 146.8 (C-3′), 127.8 (C-1′), 122.8 (C-6′), 116.5 (C-2′), 115.5 (C-2), 115.1 (C-5′) ppm; MS (ESI, MeOH): *m/z* (%) = 365.1 ([M + Na]$^+$, 21), 706.9 ([2M + Na]$^+$, 26); analysis calcd for $C_{18}H_{14}O_7$ (342.30): C 63.16, H 4.12; found: C 62.89, H 4.36.

4.4.27. (E)-3-(4-Hydroxy-3,5-dimethoxyphenyl)acrylic anhydride (**2p**)

Compound **2p** was obtained as an off-white solid (0.52 g, 52%); R_F = 0.56 (silica gel, chloroform); m.p. 187 °C; IR (ATR): ν = 2837*w*, 1659*w*, 1620*w*, 1594*w*, 1516*m*, 1460*m*, 1423*m*, 1335*m*, 1296*m*, 1268*m*, 1214*m*, 1156*m*, 1119*s*, 973*m*, 909*m*, 833*m*, 816*m*, 629*s*, 551*m* cm^{-1}; UV–vis (MeOH): λ_{max} (log ε) = 237 (4.40), 323 (4.46) nm; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 15.8 Hz, 2H, 3-H), 6.80 (s, 4H, 2′-H), 6.32 (d, *J* = 15.8 Hz, 2H, 2-H), 3.94 (s, 6H, 5′-H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.5 (C-1), 147.5 (C-3′), 147.4 (C-3), 137.8 (C-4′), 125.7 (C-1′), 114.9 (C-2), 105.6 (C-2′), 56.5 (C-5′) ppm; MS (ESI, MeOH): *m/z* (%) = 453.0 ([M + Na]$^+$, 35); analysis calcd for $C_{22}H_{22}O_9$ (430.41): C 61.39, H 5.15; found: C 61.04, H 5.31.

4.4.28. (E)-3-(2-Methoxyphenyl)acrylic anhydride (**2q**)

Compound **2q** was obtained as a white solid (0.18 g, 44%); R_F = 0.26 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 101 °C (lit.: [40] 104–106 °C); IR (ATR): ν = 2962*w*, 2838*w*, 1765*m*, 1710*m*, 1623*m*, 1599*m*, 1488*m*, 1464*m*, 1438*m*, 1324*w*, 1299*w*, 12630*m*, 1245*m*, 1198*w*, 1163*m*, 1126*s*, 1104*s*, 1046*m*, 1028*s*, 988*m*, 871*m*, 784*m*, 753*s*, 518*m* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 232 (3.87), 288 (4.05), 339 (3.97) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 16.1 Hz, 2H, 3-H), 7.55 (dd, *J* = 7.7, 1.5 Hz, 2H, 6′-H), 7.43–7.38 (*m*, 2H, 4′-H), 7.02–6.93 (*m*, 4H, 5′-H + 3′-H), 6.65 (d, *J* = 16.1 Hz, 2H, 2-H), 3.89 (s, 6H, 7′-H), 3.86 (s, 6H, 8′-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.5 (C-1), 158.9 (C-2′), 144.2 (C-3), 132.6 (C-4′), 129.8 (C-6′), 123.0 (C-1′), 121.0 (C-5′), 117.6 (C-2), 111.4 (C-3′), 55.7 (C-7′) ppm; MS (ESI, MeOH): *m/z* (%) = 361.1 ([M + Na]$^+$, 100), 698.9 ([2M + Na]$^+$, 92); analysis calcd for $C_{20}H_{18}O_5$ (338.36): C 71.00, H 5.36; found: C 70.73, H 5.47.

4.4.29. (E)-3-(3-Methoxyphenyl)acrylic anhydride (**2r**)

Compound **2r** was obtained as a white solid (0.317 g, 84%); R_F = 0.28 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 71 °C; IR (ATR): ν = 2842*w*, 1759*s*, 1694*m*, 1628*m*, 1609*w*, 1579*m*, 1491*m*, 1462*m*, 1434*m*, 1319*w*, 1272*m*, 1247*m*, 1158*m*, 1122*s*, 1046*m*, 978*s*, 935*s*, 873*m*, 849*s*, 775*s*, 720*m*, 671*m*, 577*m*, 552*m*, 510*m* cm^{-1}; UV–vis (MeOH): λ_{max} (log ε) = 216 (3.56), 285 (3.65) nm; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 15.9 Hz, 2H, 3-H), 7.34 (t, *J* = 7.9 Hz, 2H, 5′-H), 7.17 (d, *J* = 7.7 Hz, 2H, 6′-H), 7.09–7.08 (*m*, 2H, 2′-H), 7.00 (ddd, *J* = 8.3, 2.6, 0.7 Hz, 2H, 4′-H), 6.51 (d, *J* = 15.9 Hz, 2H, 2-H), 3.85 (s, 6H,7′-H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.6 (C-1), 160.2 (C-3′), 148.7 (C-3), 135.2 (C-1′), 130.2 (C-5′), 121.4 (C-6′), 117.3 (C-4′), 117.2 (C-2), 113.5 (C-2′), 55.5 (C-7′) ppm; MS (ESI, MeOH): *m/z* (%) = 361.0 ([M + Na]$^+$, 100), 698.8 ([2M + Na]$^+$, 77); analysis calcd for $C_{20}H_{18}O_5$ (338.36): C 71.00, H 5.36; found: C 70.81, H 5.51.

4.4.30. (E)-3-(4-Methoxyphenyl)acrylic anhydride (**2s**)

Compound **2s** was obtained as a white solid (0.18 g, 46%); R_F = 0.7 (silica gel, chloroform); m.p. 103 °C (lit.: [40] 104–105 °C); IR (ATR): ν = 1754*w*, 1717*m*, 1624*w*, 1597*m*, 1571*w*, 1509*m*, 1455*w*, 1439*w*, 1423*w*, 1304*w*, 1289*w*, 1255*m*, 1176*w*, 1150*w*, 1061*s*, 1022*m*, 972*s*, 923*m*, 824*s*, 804*m*, 535*m*, 518*m* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 206 (4.19), 235 (3.73), 331 (4.13) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 15.9 Hz, 2H, 3-H), 7.53 (d, *J* = 8.8 Hz, 4H, 2′-H), 6.94 (d, *J* = 8.8 Hz, 4H, 3′-H), 6.39 (d, *J* = 15.8 Hz, 2H, 2-H), 3.86 (s, 6H, 5′-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.2 (C-1), 162.3 (C-4′), 148.4 (C-3), 130.6 (C-2′), 126.7 (C-1′), 114.7 (C-3′), 114.4 (C-2), 55.6 (C-5′) ppm; MS (ESI, MeOH): *m/z* (%) = 361.1 ([M + Na]$^+$, 68), 698.9 ([2M + Na]$^+$, 100); analysis calcd for $C_{20}H_{18}O_5$ (338.36): C 71.00, H 5.36; found: C 70.72, H 5.52.

4.4.31. (E)-3-(2-Chlorophenyl)acrylic anhydride (**2t**)

Compound **2t** was obtained as white crystals (0.324 g, 92%); R_F = 0.88 (silica gel, chloroform); m.p. 156–157 °C; IR (ATR): ν = 1762*m*, 1709*m*, 1626*w*, 1588*w*, 1471*w*, 1442*w*, 1324*w*, 1259*w*, 1203*w*, 1138*s*, 1117*s*, 1051*m*, 1034*m*, 981*m*, 934*s*, 878*m*, 754*s*, 734*m*, 701*m*, 573*m* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 206 (4.02), 228 (3.38), 290 (4.09) nm; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.29 (d, *J* = 16.0 Hz, 2H, 3-H), 7.68 (dd, *J* = 7.7, 1.7 Hz, 2H, 6′-H), 7.46 (dd, *J* = 7.9, 1.2 Hz, 2H, 4′-H), 7.38 (td, *J* = 7.7, 1.7 Hz, 2H, 5′-H), 7.34–7.31 (*m*, 2H, 3′-H), 6.54 (d, *J* = 16.0 Hz, 2H, 2-H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.9 (C-1), 144.4 (C-3), 135.7 (C-2′), 132.1 (C-1′), 132.0 (C-5′), 130.5 (C-4′), 128.1 (C-6′), 127.4 (C-3′), 119.4 (C-2) ppm; MS (ESI, ASAP): *m/z* (%) = 369.3 ([M + Na]$^+$, 52), 385.3 ([M + K]$^+$, 3), 387.2 ([M + Na + H_2O]$^+$, 7), 401.3 ([M + Na + MeOH]$^+$, 100); analysis calcd for $C_{18}H_{12}Cl_2O_3$ (347.19): C 62.27, H 3.48, Cl 20.42; found: C 62.01, H 3.64.

4.4.32. (E)-3-(3-Chlorophenyl)acrylic anhydride (**2u**)

Compound **2u** was obtained as a white solid (0.20 g, 52%); R_F = 0.98 (silica gel, chloroform); m.p. 117 °C; IR (ATR): ν = 1759*m*, 1709*m*, 1630*w*, 1565*w*, 1271*w*, 1204*w*, 1130*s*, 986*m*, 939*s*, 862*m*, 785*m*, 721*m*, 687*m*, 666*s*, 564*m*, 545*m* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 228 (4.14), 291 (4.35) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 15.9 Hz, 2H, 3-H), 7.58–7.56 (*m*, 2H, 6′-H), 7.47–7.43 (*m*, 2H, 2′-H), 7.41 (t, *J* = 1.7 Hz, 2H, 5′-H), 7.40–7.35 (*m*, 2H, 4′-H), 6.52 (d, *J* = 15.9 Hz, 2H, 2-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.0 (C-1), 147.2 (C-3), 135.6 (C-1′), 135.3 (C-3′), 131.3 (C-5′), 130.5 (C-4′), 128.4 (C-6′), 126.9 (C-2′), 118.2 (C-2) ppm; MS (ESI, ASAP): *m/z* (%) = 369.3 ([M + Na]$^+$, 61), 385.3 ([M + K]$^+$, 13), 387.2 ([M + Na + H_2O]$^+$, 14), 401.3 ([M + Na + MeOH]$^+$, 100); analysis calcd for $C_{18}H_{12}Cl_2O_3$ (347.19): C 62.27, H 3.48; found: C 61.97, H 3.65.

4.4.33. (E)-3-(2-Chlorophenyl)acrylic-(E)-3-(3-Chlorophenyl)acrylic anhydride (**2v**)

Compound **2v** was obtained as an off-white solid (0.17 g, 44%);

R_F = 0.98 (silica gel, chloroform); m.p. 117 °C; IR (ATR): ν = 1758*m*, 1708*m*, 1626*w*, 1589*w*, 1565*w*, 1472*w*, 1442*w*, 1290*w*, 1203*w*, 1136*s*, 1052*m*, 1038*m*, 986*m*, 935*s*, 866*m*, 788*m*, 757*s*, 733*m*, 702*m*, 686*m*, 672*m*, 570*m* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 228 (3.99), 290 (4.22) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (dd, J = 16.0, 6.7 Hz, 1H, 3-H), 7.79 (dd, J = 15.9, 3.9 Hz, 1H, 3′-H), 7.68 (dt, J = 7.6, 2.1 Hz, 1H, 6″-H), 7.58–7.55 (*m*, 1H, 6‴-H), 7.48–7.46 (*m*, 1H, 4″-H), 7.46–7.44 (*m*, 1H, 2‴-H), 7.44–7.42 (*m*, 1H, 5‴-H), 7.41 (t, J = 1.6 Hz, 1H, 5″-H), 7.39–7.36 (m, 1H, 4‴-H), 7.35–7.32 (*m*, 1H, 3″-H), 6.53 (dd, $_J$ = 16.0, 3.5 Hz, 2H, 2-H + 2′-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.0 (C-1′), 161.9 (C-1), 147.1 (C-3′), 144.5 (C-3), 135.6 (C-1″), 135.5 (C-2″), 135.3 (C-1‴), 135.2 (C-3‴), 132.2 (C-5″), 131.3 (C-5‴), 130.6 (C-4″), 130.5 (C-4‴), 128.4 (C-6‴), 128.1 (C-6″), 127.4 (C-3″), 126.9 (C-2‴), 119.3 (C-2), 118.3 (C-2′) ppm; MS (ESI, ASAP): *m/z* (%) = 369.3 ($[M + Na]^+$, 60), 385.3 ($[M + K]^+$, 7), 387.2 ($[M + Na + H_2O]^+$, 8), 401.3 ($[M + Na + MeOH]^+$, 100); analysis calcd for $C_{18}H_{12}Cl_2O_3$ (347.19): C 62.27, H 3.48; found: C 62.11, H 3.69.

4.4.34. (E)-3-(3-Fluorophenyl)acrylic anhydride (2w)

Compound **2w** was obtained as a white solid (0.37 g, 99%); R_F = 0.48 (silica gel, *n*-hexane/ethyl acetate, 4:1); m.p. 192 °C; IR (ATR): ν = 1771*m*, 1705*m*, 1634*m*, 1585*m*, 1486*w*, 1448*w*, 1286*w*, 1270*w*, 1238*w*, 1204*m*, 1170*w*, 1149*w*, 1065*s*, 985*m*, 964*s*, 878*m*, 863*m*, 784*s*, 716*m*, 665*s*, 562*m*, 486*m* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 206 (4.19), 226 (3.71), 291 (4.22) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, J = 15.9 Hz, 2H, 3-H), 7.44–7.38 (*m*, 2H, 5′-H), 7.35 (dt, J = 7.7, 1.3 Hz, 2H, 6′-H), 7.30–7.26 (*m*, 2H, 2′-H), 7.18–7.12 (*m*, 2H, 4′-H), 6.52 (d, J = 15.9 Hz, 2H, 2-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.4 (C-3′), 162.0 (C-1), 147.4 (C-3), 136.0 (C-1′), 130.9 (C-5′), 124.8 (C-6′), 118.5 (C-4′), 118.2 (C-2), 114.9 (C-2′) ppm; MS (ESI, MeOH): *m/z* (%) = 337.1 ($[M + Na]^+$, 100), 650.8 ($[2M + Na]^+$, 48); analysis calcd for $C_{18}H_{12}F_2O_3$ (314.29): C 68.79, H 3.85; found: C 68.51, H 4.02.

4.4.35. (E)-3-(4-Fluorophenyl)acrylic anhydride (2x)

Compound **2x** was obtained as white needles (0.18 g, 49%); R_F = 0.89 (silica gel, chloroform); m.p. 128 °C (lit.: [40] 125–126 °C); IR (ATR): ν = 3078*w*, 1756*m*, 1700*m*, 1627*m*, 1595*m*, 1508*s*, 1412*w*, 1320*w*, 1301*w*, 1272*w*, 1227*s*, 1205*w*, 1163*m*, 1126*m*, 989*s*, 932*m*, 862*m*, 827*s*, 816*s*, 784*m*, 731*m*, 684*m*, 551*m*, 535*m*, 510*s*, 468*m* cm^{-1}; UV–vis ($CHCl_3$): λ_{max} (log ε) = 206 (4.32), 228 (4.31), 303 (4.63) nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, J = 15.9 Hz, 2H, 3-H), 7.61–7.55 (*m*, 4H, 2′-H), 7.16–7.09 (*m*, 4H, 3′-H), 6.45 (d, J = 15.9 Hz, 2H, 2-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.9 (C-4′), 162.5 (C-1), 147.5 (C-3), 130.7 (C-2′), 130.2 (C-1′), 116.6 (C-3′), 116.4 (C-2) ppm; MS (ESI, MeOH): *m/z* (%) = 337.1 ($[M + Na]^+$, 100), 650.8 ($[2\,M + Na]^+$, 44); analysis calcd for $C_{18}H_{12}F_2O_3$ (314.29): C 68.79, H 3.85; found: C 68.51, H 3.13.

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