A rapid and practical catalytic esterification for the preparation of caffeic acid esters

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A convenient and practical catalytic method for the preparation of caffeic acid esters is reported. This esterification was carried out with high efficiency in the presence of ytterbium triflate in nitromethane without any other auxiliary reagents. The wide scope of application and especially the higher reactivity and more convenient procedure than previous methods make it a valuable application for the synthesis of caffeic acid esters and other cinnamic acid esters.

Keywords: caffeic acid esters, cinnamic acid esters, synthesis, catalytic esterification, Lewis acid, metal triflate, ytterbium triflate

Due to their wide biological activities, such as antibacterial,[1,2] antiviral,[3,4] antitumour,[5–7] anti-inflammatory,[8,9] antioxidant,[10,11] hypoglycemic,[12,13] neuritogenic,[14] and immunomodulatory activities,[15] caffeic acid esters (CAEs), especially caffeic acid phenethyl ester (CAPE) have great application potential in the areas of food, medicine, health care and cosmetic products. These active compounds are structurally unsophisticated, but their chemical syntheses are not readily achieved by the general esterification methods in view of low reactivity, inconvenient operations and restricted scope of application (Fig. 1).

The modified acyl chloride method requires excess reactants (thionyl chloride and alcohols) and highboiling solvent *e.g.* nitrobenzene, which caused great difficulty in the purification of products (Fig. 1a, 10–70% yields in cases of aromatic alcohols).[16–18] Catalytic esterification of caffeic acid in the presence of Brønsted acids, such as H_2SO_4 and *p*-TsOH needed days of azeotropic distillation for acceptable yields (Fig. 1b).[19,20] Very poor and violently fluctuating yields (5–40% yields) were obtained when using DCC as a condensing agent (Fig. 1c).[21] Although the alkylation of caffeic acid provided CAEs with excellent yields and purities in some cases, its application is seriously limited by the reactivity and commercial availability of halides and the employment of high-boiling solvents such as DMF, DMSO and HMPT (Fig. 1d).[22]

Multi-step procedures such as the Wittig reaction[19,23] or the Knoevenagel condensation[24–26] *via* protocatechuic aldehyde have also been explored and the latter demonstrated practicality for large scale production. Nevertheless, due to the potential lower cost and simpler operation, the direct esterification of caffeic acid by alcohols is still the most worthy of investigation. We now report a simple and convenient method for direct esterification of caffeic acid by alcohols using only $Yb(OTf)_3$ as catalyst (Fig. 1e).

Results and discussion

Lewis acid catalysts including metal triflates have been well documented for the esterification of carboxylic acids.[27–29] However, to the best of our knowledge the successful catalytic esterification of caffeic acid using only Lewis acids has not yet been reported. In 2013, Mamidi and Manna[30] reported a $Zn(OTf)_2$-promoted esterification, in which an excess of Ph_3P/I_2 (2.0 equiv.) was required to activate carboxylic acids.[30] This method provided strikingly high yields (70–90%) for the synthesis of cinnamic acid ester analogues including some caffeic acid esters. Regrettably, however, both the purification of the desired esters and the disposal of excess Ph_3P and side product Ph_3PO became big problems. In view of this, we looked for a more convenient and practical catalytic method without any other additive components for preparation of CAEs.

To examine the effect of catalysts, Lewis acid catalysed condensation of caffeic acid and 2-phenylethanol was carried out under reflux in CH_3NO_2. As shown in Table 1, only trace amounts of CAPE was obtained when BF_3–Et_2O, $Ni(OAc)_2$ and $CuSO_4$ were used (entries 1–3). Low yields were found in the cases of $AlCl_3$ and $ZnCl_2$ (entries 4 and 5). Gratifyingly, however, a good yield of 54% within 15 min was obtained

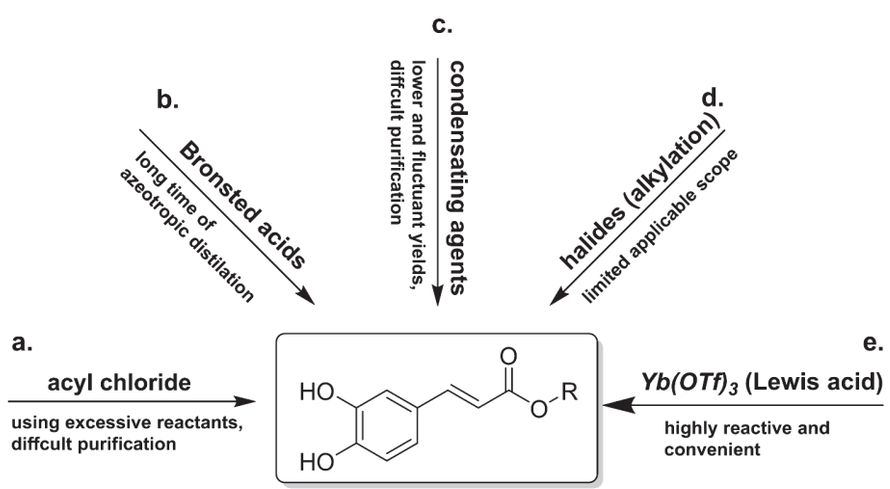

Fig. 1 Esterifications of caffeic acid.

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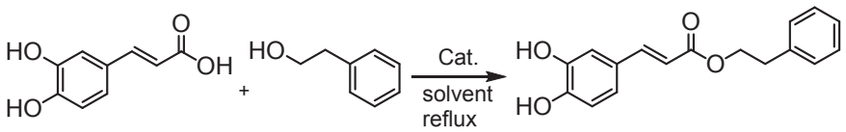
Table 1 Selection of catalysts and solvents[a]



Entry	Cat./mol%	Solvent	Time/h	Yield/%[b]
1	BF_3–Et_2O (3)	CH_3NO_2	24 h	Trace
2	$Ni(OAc)_2$ (3)	CH_3NO_2	24 h	Trace
3	$CuSO_4$ (3)	CH_3NO_2	24 h	Trace
4	$AlCl_3$ (3)	CH_3NO_2	24 h	6
5	$ZnCl_2$ (3)	CH_3NO_2	24 h	29
6	$Yb(OTf)_3$ (3)	CH_3NO_2	15 min	54
7[c]	$Yb(OTf)_3$ (3)	$C_6H_5NO_2$	15 min	51
8	$Yb(OTf)_3$ (3)	1,4-dioxane	24 h	7
9	$Yb(OTf)_3$ (3)	pyridine	6 h	–
10	$In(OTf)_3$ (3)	CH_3NO_2	200 s	45
11	$Nd(OTf)_3$ (3)	CH_3NO_2	20 min	61
12	$Dy(OTf)_3$ (3)	CH_3NO_2	25 min	58

[a]Reaction conditions: to a mixture of caffeic acid (0.4 mmol), 2-phenylethanol (0.4 mmol) in solvent (10 mL) was added catalyst. After 5 min in an ultrasonic bath, the mixture was stirred on a 120 °C oil bath under a nitrogen atmosphere.
[b]Monitored by HPLC.
[c]External oil bath temperature: 110 °C.

when $Yb(OTf)_3$ was used (entry 6). Encouraged by this result, various solvents were tested. To our surprise, only "nitro-solvents" such as CH_3NO_2 and $PhNO_2$ afforded good yields (entries 6 and 7) and most other solvents gave poor responses in the model reaction. 1,4-Dioxane showed weak reaction during 24 h (entry 8), while pyridine gave a decarboxylated product in quantitative yield (entry 9). Besides $Yb(OTf)_3$, over 20 metal triflates were subsequently tested and we fortunately found three other metal triflates with significant catalytic activity; these were indium, neodymium and dysprosium triflates (entries 10–12). Even more astonishing, indium triflate provided a yield of 45% within 200 seconds (Entry 10). The preliminary results suggested that $M_x(OTf)_y/CH_3NO_2$ might be a highly efficient catalytic system for the preparation of CAEs.

To clarify the reaction process in detail, $Yb(OTf)_3$ loading of 3 mol%, 1 mol% and 0.5 mol% were used in model reaction separately over 6 h. As shown in Fig. 2, the yield of CAPE rapidly increased and reached its peak value (54%, 65% and 61%) at 15, 35 and 120 minutes respectively and then decreased gradually with further time. When a higher catalyst loading was used, a faster decline in the yield was found. These results indicated that the $Yb(OTf)_3/CH_3NO_2$ system has significant catalytic activity to the esterification reaction and the side reactions, which involve both the starting materials and the produced esters. Therefore, the key points for better yields of CAEs are not only the appropriate amount of $Yb(OTf)_3$ but the determination of the appropriate reaction time.

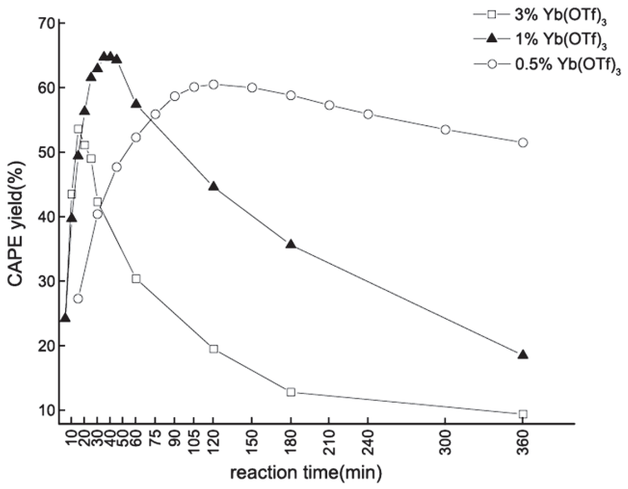


Fig. 2 The process of esterification of caffeic and phenylethanol under 3, 1 and 0.5 mol% $Yb(OTf)_3$.

The influence of water was investigated since it might inhibit the esterification or promote the side reaction (Table 2). Under 1 mol% $Yb(OTf)_3$, direct use of purchased CH_3NO_2 gave a 63% yield of CAPE (entry 1). Then the reaction was separately carried out in dry CH_3NO_2 and CH_3NO_2 containing additional water (1.0 equiv.). Very similar yields were obtained (entries 2 and 3). Further increasing the water content also provided a good result (Entry 4). The esterification reaction rate (represented by the peak time) and yield declined only when more than 3 equiv. water was added (entries 5 and 6). These results demonstrated that the $Yb(OTf)_3$-catalysed esterification reaction is tolerant to the residual water in the solvent and the water produced in the reaction. It is significantly superior to the method reported by Mamidi and Manna, which required dry CH_3CN as solvent,[30]

Table 2 The effect of water on the esterification reaction[a]

Entry	Additional water		CAPE Yield/%[b]	Time/min[c]
	Amount/mg	Equiv.		
1	0	–	63	35
2	dry	–	63	35
3	7.2	1	63	35
4	14.4	2	61	40
5	21.6	3	58	60
6	28.8	4	55	85

[a]Conditions: to a mixture of caffeic acid (0.4 mmol), 2-phenylethanol (0.44 mmol), CH_3NO_2 (10 mL) and $Yb(OTf)_3$ (1 mol%) was added the given amount of water. After 5 min in an ultrasonic bath the mixture was stirred on a 120 °C oil bath under a nitrogen atmosphere and sampled every 5 min.
[b]Peak value, monitored by HPLC.
[c]Peak time.

Table 3 Esterification reactions of caffeic acid with various alcohols[a]

Entry/Product	ROH (equiv.)	Time	Yield/%[b]
1	$C_6H_5(CH_2)_2OH$ (1)	40 min	48
2	*n*-Butanol (2)	1 h	32
3	*i*-Pentanol (2)	1 h	38
4	(±)-2-Pentanol (2)	1 h	35
5	Cyclohexanol (1.5)	2 h	34
6	*tert*-Butanol (3)	2 h	–
7	*tert*-Pentanol (3)	2 h	–
8	$2\text{-}FC_6H_4(CH_2)_2OH$ (1)	40 min	48
9	$3\text{-}FC_6H_4(CH_2)_2OH$ (1)	40 min	53
10	$4\text{-}FC_6H_4(CH_2)_2OH$ (1)	40 min	46
11	$3\text{-}ClC_6H_4(CH_2)_2OH$ (1)	40 min	47
12	$3\text{-}BrC_6H_4(CH_2)_2OH$ (1)	40 min	46
13	$2\text{-}MeC_6H_4(CH_2)_2OH$ (1)	40 min	49
14	$3\text{-}MeC_6H_4(CH_2)_2OH$ (1)	40 min	54
15	$4\text{-}MeC_6H_4(CH_2)_2OH$ (1)	40 min	47
16	$3\text{-}CF_3C_6H_4(CH_2)_2OH$ (1)	40 min	52
17	$4\text{-}CF_3C_6H_4(CH_2)_2OH$ (1)	40 min	46
18	$4\text{-}NO_2C_6H_4(CH_2)_2OH$ (1)	40 min	53
19	$4\text{-}CNC_6H_4(CH_2)_2OH$ (1)	1.5 h	61
20	$4\text{-}AcC_6H_4(CH_2)_2OH$ (1)	2 h	56
21	$3,5\text{-}Di\text{-}FC_6H_3(CH_2)_2OH$ (1)	40 min	52
22	$4\text{-}OH\text{-}3\text{-}NO_2C_6H_3(CH_2)_2OH$ (1)	2 h	58
23	$2,4,5\text{-}Tri\text{-}FC_6H_2(CH_2)_2OH$ (1)	40 min	54
24	$C_6H_5(CH_2)_3OH$ (1)	40 min	48

[a]Reaction conditions: To a mixture of caffeic acid (5.56 mmol), alcohol (6.11 mmol) in CH_3NO_2 (125 mL) was added $Yb(OTf)_3$ (1 mol%). After 5 min in an ultrasonic bath the mixture without protective gas was stirred on a 120 °C oil bath for a given time.
[b]Isolated yields after column chromatography.

let alone Brønsted acid-catalysed esterification, which required a long period of azeotropic distillation.[19,20]

To confirm further the practicability of this method, we investigated the separation process and the isolated yields of various CAEs by column chromatography (Table 3). Several fatty alcohols were first selected, among which primary and secondary alcohols gave moderate yields of 30–40% (entries 2–5), but tertiary alcohols gave no responses to the $Yb(OTf)_3$/CH_3NO_2 system (entries 6 and 7). Nevertheless, 2-phenethanol and 3-phenylpropanol afforded about a 50% yield within 2 hours (entries 1, 8–24) which is not achievable by any previous method. Furthermore, 2-phenylethanols with either electron-withdrawing or electron-donating groups gave similar results. Therefore, the current catalytic method is suitable for the synthesis of a large number of CAEs, particularly CAPEs.

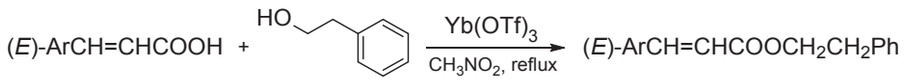
In addition to various alcohols, cinnamic acid and some substituted cinnamic acids were tested in the $Yb(OTf)_3$/CH_3NO_2 system (Table 4). To our surprise, cinnamic acid afforded an almost quantitative yield of its phenethyl ester under 5 mol% ytterbium triflate (entry 25). Other substituted cinnamic acids also gave good yields (entries 26–30). Despite a rather low reaction rate, these cinnamic acids produced less side products and gave better isolated yields than caffeic acid. Therefore the present method is also suitable for the preparation of cinnamic acid esters and esters of substituted cinnamic acids.

It is noteworthy that column chromatography is necessary in all the existing methods for preparation of CAEs due to excess substrate, side products and various added materials such as DCC and PPh_3, and high-boiling solvents which are often hard to remove. In our method, there are no other additive components except for the catalyst, stoichiometric substrate and "low-boiling" solvent, which significantly lowers the technical difficulties and cost of production. Furthermore, the catalyst (metal triflate) can be collected to a large degree by extracting the reaction mixture with water, and the solvent (CH_3NO_2) can be recycled by distillation and simple drying treatment.

Conclusion

In summary, we have found a rapid and practical esterification method for CAEs, which only uses metal triflate as catalyst in nitromethane without any other auxiliary reagents. Within an extremely short time, stoichiometric ratio caffeic acid and alcohols could readily afford various CAEs, especially CAPEs in 40–60% isolated yields without water removal. Compared to previous methods this methodology has particular advantages of a simple and highly efficient catalytic system, more convenient operations and less discharge of toxic materials. Although side products seem unavoidable, the present method exhibits a great application potential to the preparation of CAEs and other esters with the cinnamic acid structure.

Table 4 Esterification reactions of various aromatic acids with 2-phenylethanol[a]



Entry/Product	Ar	Time/h	Yield/%[b]	M.p./°C[ref]
25[c]	C_6H_5	6	95.8	54–55[31]
26[c]	$3\text{-}ClC_6H_4$	6	72.5	–
27	$4\text{-}OHC_6H_4$	1	70.6	91–92[31]
28	$4\text{-}MeOC_6H_4$	1.5	72.4	57–58[31]
29	$3\text{-}OH\text{-}4\text{-}MeOC_6H_3$	1	57.2	80–81[19]
30[d]	$3,4\text{-}Di\text{-}MeOC_6H_3$	1	60.5	101–102[31]

[a]Reaction conditions: to a mixture of cinnamic acid (1.0 g), 2-phenylethanol (1.0 equiv.), and CH_3NO_2 (125 mL) was added $Yb(OTf)_3$ (1 mol%). After 5 min of ultrasonic shaking the mixture without protective gas was stirred on a 120 °C oil bath for a given time.
[b]Isolated yields after column chromatography.
[c]1.5 equiv. 2-phenylethanol was used and 5 mol% ytterbium triflate was added in three equal doses at zero, 2 h, 4 h.
[d]Using 0.5 mol% ytterbium triflate.

Experimental

Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. Purchased metal triflates were further dehydrated at 100 °C under a high vacuum for 2 h. Silica gel column chromatography (200–300 mesh) was performed for purification of CAEs using dichloromethane and methanol (100 : 1) as the mobile phase. IR spectra were obtained on Thermo Nicolet iS10 spectrometer. NMR spectra were recorded on a Bruker 400 MHz spectrometer for ^{1}H NMR and at 100 MHz for ^{13}C NMR. High-resolution mass spectroscopy (HRMS) values were recorded on a Waters Q-Tof Premier system. The yields of CAPE in the model reaction were determined on an Agilent 1200 HPLC system (4.6 mm × 250 mm column, 5 µm, 65% MeOH in H_2O within 20 minutes at 1.0 mL min^{-1} and UV detection at 210 nm) with phenethyl acetate as the internal standard substance, which was added into reaction mixture in an equivalent amount to the caffeic acid.

Synthesis of **1**–**5**, **8**–**24***; general procedure*

To a mixture of caffeic acid fine powder (1.0 g, 5.56 mmol, 1.0 equiv.), alcohol (5.56 mmol, 1.0 equiv.) in nitromethane (125 mL) was added ytterbium triflate (34.4 mg, 0.056 mmol, 0.01 equiv.). After 5 min in an ultrasonic bath the mixture without protective gas was stirred on a 120 °C oil bath for a given time. The reaction mixture was cooled to room temperature, washed with deionised water (30 mL), 2% $NaHCO_3$ (30 mL) and brine, dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to give the crude product, which was purified on a silica gel column to give the compounds **1**–**5** and **8**–**30**.

*2-Phenethyl (*E*)-3-(3,4-dihydroxyphenyl) acrylate* (**1**): White solid; yield 758 mg, 48.0%; m.p. 128–130 °C (lit.[20] 116–123 °C); IR (KBr) ν_{max} 3480, 3328, 1683, 1601, 1362, 1301, 1279, 1182 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.46 (1H, d, J = 16 Hz, C$\underline{H}$=CHCO), 7.34–7.18 (5H, m, C_6H_5), 7.05 (1H, s, 2-ArH), 6.99 (1H, d, J = 8.0 Hz, 6-ArH), 6.77 (1H, d, J = 8.0 Hz, 5-ArH), 6.24 (1H, d, J = 16 Hz, CH=C$\underline{H}$CO), 4.32 (2H, t, J = 6.8 Hz, OCH_2), 2.94 (2H, t, J = 6.8 Hz, $OCH_2C\underline{H}_2$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.4, 148.3, 145.4, 145.1, 138.0, 128.8, 128.3, 126.3, 125.4, 121.4, 115.7, 114.7, 113.8, 64.3, 34.4 ppm; HRMS-ESI $C_{17}H_{16}O_4$ calcd [M–H]$^-$ 283.0970, found 283.0966.

*Butyl (*E*)-3-(3,4-dihydroxyphenyl)acrylate* (**2**): n-Butanol (822 mg, 11.11 mmol, 2.0 equiv.) was used. White solid; yield 420 mg, 32.0%; m.p. 109–111 °C (lit.[20] 110–111 °C); IR (KBr) ν_{max} 3489, 3343, 2953, 1685, 1638, 1604, 1301, 1279, 1193 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.47 (1H, d, J = 16 Hz, C$\underline{H}$=CHCO), 7.05 (1H, d, J = 2.0 Hz, 2-ArH), 7.00 (1H, dd, J = 8.0, 2.0 Hz, 6-ArH), 6.76 (1H, d, J = 8.0 Hz, 5-ArH), 6.25 (1H, d, J = 16 Hz, CH=C$\underline{H}$CO), 4.10 (2H, t, J = 6.8 Hz, $OC\underline{H}_2C_3H_7$), 1.60 (2H, m, $OCH_2C\underline{H}_2$Et), 1.35 (2H, m, $OCH_2CH_2C\underline{H}_2CH_3$), 0.90 (3H, t, J = 7.2 Hz, CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.5, 148.2, 145.4, 144.9, 125.4, 121.3, 115.6, 114.7, 114.0, 63.4, 30.3, 18.6, 13.5 ppm; HRMS-ESI $C_{13}H_{16}O_4$ calcd [M–H]$^-$ 235.0970, found 235.0979.

*Isopentyl (*E*)-3-(3,4-dihydroxyphenyl) acrylate* (**3**). Isopentyl alcohol (977.8 mg, 11.11 mmol, 2.0 equiv.) was used. White solid; yield 530 mg, 38.1%; m.p. 126–128 °C (lit.[17] 127–128 °C); IR (KBr) ν_{max} 3486, 3318, 2960, 1682, 1635, 1602, 1279, 1185 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.47 (1H, d, J = 16 Hz, C$\underline{H}$=CHCO), 7.05 (1H, s, 2-ArH), 7.00 (1H, d, J = 8.0 Hz, 6-ArH), 6.76 (1H, d, J = 8.0 Hz, 5-ArH), 6.25 (1H, d, J = 16 Hz, CH=C$\underline{H}$CO), 4.13 (2H, t, J = 6.8 Hz, OCH_2), 1.67 (1H, m, C$\underline{H}$Me$_2$), 1.51 (2H, td, J = 6.8, 6.8 Hz, $OCH_2C\underline{H}_2$), 0.90 (6H, t, J = 6.8 Hz, CH$\underline{Me}_2$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.5, 148.2, 145.4, 144.9, 125.4, 121.3, 115.6, 114.7, 114.0, 62.1, 37.0, 24.5, 22.3 ppm; HRMS-ESI $C_{14}H_{18}O_4$ calcd [M–H]$^-$ 249.1127, found 249.1135.

*(±)-Pentan-2-yl (*E*)-3-(3,4-dihydroxyphenyl) acrylate* (**4**): (±)-2-Pentanol (977.8 mg, 11.11 mmol, 2.0 equiv.) was used. White solid; yield 491 mg, 35.3%; m.p. 99–102 °C; IR (KBr) ν_{max} 3462, 3114, 2968, 1666, 1622, 1604, 1441, 1280, 1186 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.45 (1H, d, J = 16 Hz, C$\underline{H}$=CHCO), 7.04 (1H, s, 2-ArH), 6.99 (1H, d, J = 8.0 Hz, 6-ArH), 6.76 (1H, d, J = 8.0 Hz, 5-ArH), 6.23 (1H, d, J = 16 Hz, CH=C$\underline{H}$CO), 4.92 (1H, m, OCH), 1.53 (2H, m, CHC$\underline{H}_2$), 1.31 (2H, m, C$\underline{H}_2$CH$_3$), 1.20 (3H, d, J = 6.4 Hz, CHC$\underline{H}_3$), 0.88 (3H, t, J = 7.2 Hz, CH$_2$C$\underline{H}_3$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.2, 148.2, 145.4, 144.7, 125.4, 121.2, 115.6, 114.7, 114.4, 69.7, 37.5, 19.9, 18.1, 13.7 ppm; HRMS-ESI $C_{14}H_{18}O_4$ calcd [M–H]$^-$ 249.1127, found 249.1136.

*Cyclohexyl (*E*)-3-(3,4-dihydroxyphenyl) acrylate* (**5**): A mixture of caffeic acid fine powder (1.0 g, 5.56 mmol), cyclohexanol (833.3 mg, 8.33 mmol, 1.5 equiv.) was used. White solid; yield 500 mg, 34.3%; m.p. 152–154 °C (lit[18]: 152–154 °C); IR (KBr) ν_{max} 3446, 3273, 2940, 1686, 1634, 1601, 1274, 1182 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.45 (1H, d, J = 16 Hz, C$\underline{H}$=CHCO), 7.04 (1H, s, 2-ArH), 6.99 (1H, d, J = 8.0 Hz, 6-ArH), 6.76 (1H, d, J = 8.0 Hz, 5-ArH), 6.23 (1H, d, J = 16 Hz, CH=C$\underline{H}$CO), 4.74 (1H, m, OCH), 1.88–1.64 (4H, m, C$\underline{H}_2$CHC$\underline{H}_2$), 1.56–1.16 (6H, m, $CH_2C\underline{H}_2C\underline{H}_2C\underline{H}_2CH_2$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.9, 148.1, 145.4, 144.7, 125.5, 121.2, 115.6, 114.7, 114.4, 71.6, 31.2, 24.9, 23.3 ppm; HRMS-ESI $C_{15}H_{18}O_4$ calcd [M–H]$^-$ 261.1127, found 261.1144.

*2-(2-Fluorophenyl)ethyl (*E*)-3-(3,4-dihydroxyphenyl)acrylate* (**8**): White solid; yield 808 mg, 48.1%; m.p. 130–132 °C; IR (KBr) ν_{max} 3484, 3323, 1686, 1636, 1602, 1280, 1185 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.44 (1H, d, J = 16 Hz, C$\underline{H}$=CHCO), 7.36 (1H, m, 4′-ArH), 7.28 (1H, m, 3′-ArH), 7.19–7.12 (2H, m, 5′,6′-ArH), 7.04 (1H, d, J = 2.0 Hz, 2-ArH), 6.98 (1H, dd, J = 8.0, 2.0 Hz, 6-ArH), 6.76 (1H, d, J = 8.0 Hz, 5-ArH), 6.21 (1H, d, J = 16 Hz, CH=C$\underline{H}$CO), 4.32 (2H, t, J = 6.8 Hz, OCH_2), 2.99 (2H, t, J = 6.8 Hz, C$\underline{H}_2C_6H_4$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.3, 161.9, 159.5, 148.3, 145.4, 145.2, 131.4, 131.3, 128.6, 128.5, 125.4, 124.8, 124.6, 124.4, 124.3, 121.4, 115.6, 115.2, 115.0, 114.7, 113.7, 63.0, 27.8, 27.8 ppm; HRMS-ESI $C_{17}H_{15}FO_4$ calcd [M–H]$^-$ 301.0876, found 301.0877.

*2-(3-Fluorophenyl)ethyl (*E*)-3-(3,4-dihydroxyphenyl)acrylate* (**9**): White solid; yield 887 mg, 52.8%; m.p. 120–123 °C; IR (KBr) ν_{max} 3482, 3333, 1683, 1636, 1602, 1301, 1278, 1182 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.46 (1H, d, J = 16 Hz, C$\underline{H}$=CHCO), 7.34 (1H, m, 5′-ArH), 7.17–7.01 (5H, m, 2,6-ArH & 2′,4′,6′-ArH), 6.77 (1H, d, J = 8.0 Hz, 5-ArH), 6.23 (1H, d, J = 16 Hz, CH=C$\underline{H}$CO), 4.33 (2H, t, J = 6.8 Hz, OCH_2), 2.97 (2H, t, J = 6.8 Hz, C$\underline{H}_2C_6H_4$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.4, 163.3, 160.9, 148.3, 145.4, 145.2, 141.1, 141.0, 130.2, 130.1, 125.4, 125.0, 125.0, 121.4, 115.7, 115.4, 114.7, 113.7, 113.2, 113.0, 63.9, 34.0 ppm; HRMS-ESI $C_{17}H_{15}FO_4$ calcd [M–H]$^-$ 301.0876, found 301.0889.

*2-(4-Fluorophenyl)ethyl (*E*)-3-(3,4-dihydroxyphenyl)acrylate* (**10**): White solid; yield 776 mg, 46.2%; m.p. 145–147 °C (lit.[17] 143–144 °C); IR (KBr) ν_{max} 3475, 3360, 1684, 1633, 1597, 1534, 1511, 1362, 1276, 1181 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.45 (1H, d, J = 16 Hz, C$\underline{H}$=CHCO), 7.32 (2H, m, 2′,6′-ArH), 7.12 (2H, t, J = 8.0 Hz, 3′,5′-ArH), 7.04 (1H, d, J = 2.0 Hz, 2-ArH), 6.99 (1H, dd, J = 8.0, 2.0 Hz, 6-ArH), 6.76 (1H, d, J = 8.0 Hz, 5-ArH), 6.23 (1H, d, J = 16 Hz, CH=C$\underline{H}$CO), 4.30 (2H, t, J = 6.8 Hz, OCH_2), 2.93 (2H, t, J = 6.8 Hz, C$\underline{H}_2C_6H_4$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.4, 162.1, 159.7, 148.3, 145.4, 145.2, 134.2, 134.2, 130.7, 130.6, 125.4, 121.4, 115.6, 115.1, 114.9, 114.7, 113.7, 64.2, 33.5 ppm; HRMS-ESI $C_{17}H_{15}FO_4$ calcd [M–H]$^-$ 301.0876, found 301.0871.

*2-(3-Chlorophenyl)ethyl (*E*)-3-(3,4-dihydroxy phenyl)acrylate* (**11**): White solid; yield 837 mg, 47.3%; m.p. 130–132 °C; IR (KBr) ν_{max} 3486, 3298, 1682, 1637, 1604, 1280, 1185 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.44 (1H, d, J = 16 Hz, C$\underline{H}$=CHCO), 7.38 (1H, s, 2′-ArH), 7.36–7.23 (2H, m, 4′,5′,6′-ArH), 7.04 (1H, d, J = 2.0 Hz, 2-ArH), 6.99 (1H, dd, J = 8.0, 2.0 Hz, 6-ArH), 6.76 (1H, d, J = 8.0 Hz, 5-ArH), 6.22 (1H, d, J = 16 Hz, CH=C$\underline{H}$CO), 4.32 (2H, t, J = 6.8 Hz, OCH_2), 2.96 (2H, t, J = 6.8 Hz, C$\underline{H}_2C_6H_4$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.3, 148.3, 145.4, 145.2, 140.8, 132.9, 130.1, 128.7, 127.6, 126.3, 125.4, 121.4, 115.6, 114.7, 113.7, 63.8, 34.0 ppm; HRMS-ESI $C_{17}H_{15}ClO_4$ calcd [M–H]$^-$ 317.0581 (^{35}Cl), found 317.0596.

2-(3-Bromophenyl)ethyl (E)-3-(3,4-dihydroxyphenyl)acrylate (**12**): White solid; yield 918 mg, 45.5%; m.p. 140–142 °C; IR (KBr) ν_{max} 3472, 3315, 1686, 1624, 1604, 1442, 1278, 1180 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.52 (1H, s, 2′-ArH), 7.45 (1H, d, J = 16 Hz,

CH=CHCO), 7.42 (1H, d, *J*=7.2 Hz, 4′-ArH), 7.32–7.24 (2H, m, 5′,6′-ArH), 7.04 (1H, d, *J*=1.6 Hz, 2-ArH), 6.99 (1H, dd, *J*=8.4, 1.6 Hz, 6-ArH), 6.76 (1H, d, *J*=8.4 Hz, 5-ArH), 6.22 (1H, d, *J*=16 Hz, CH=CHCO), 4.32 (2H, t, *J*=6.8 Hz, OCH_2), 2.95 (2H, t, *J*=6.8 Hz, $CH_2C_6H_4$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.3, 148.3, 145.4, 145.2, 141.1, 131.6, 130.4, 129.2, 128.0, 125.4, 121.6, 121.4, 115.6, 114.7, 113.7, 63.9, 33.9 ppm; HRMS-ESI $C_{17}H_{15}BrO_4$ calcd $[M–H]^-$ 361.0075 (^{79}Br), found 361.0083.

*2-(2-Methylphenyl)ethyl (*E*)-3-(3,4-dihydroxyphenyl)acrylate* (**13**): White solid; yield 804 mg, 48.5%; m.p. 129–131 °C; IR (KBr) ν_{max} 3460, 3333, 1697, 1636, 1597, 1299, 1275, 1176 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.46 (1H, d, *J*=16 Hz, CH=CHCO), 7.23–7.09 (4H, m, 3′,4′,5′,6′-ArH), 7.04 (1H, d, *J*=1.6 Hz, 2-ArH), 6.99 (1H, d, *J*=8.0, 1.6 Hz, 6-ArH), 6.77 (1H, d, *J*=8.0 Hz, 5-ArH), 6.24 (1H, d, *J*=16 Hz, CH=CHCO), 4.29 (2H, t, *J*=7.2 Hz, OCH_2), 2.94 (2H, t, *J*=7.2 Hz, $CH_2C_6H_4$), 2.31 (3H, s, CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.4, 148.3, 145.4, 145.2, 136.1, 136.0, 130.0, 129.4, 126.4, 125.9, 125.4, 121.4, 115.6, 114.7, 113.8, 63.4, 31.8, 18.9 ppm; HRMS-ESI $C_{18}H_{18}O_4$ calcd $[M–H]^-$ 297.1127, found 297.1134.

*2-(3-Methylphenyl)ethyl (*E*)-3-(3,4-dihydroxyphenyl)acrylate* (**14**): White solid; yield 887 mg, 53.5%; m.p. 116–118 °C; IR (KBr) ν_{max} 3486, 3304, 1682, 1636, 1603, 1281, 1185 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 9.59 (1H, s, br, 4-OH), 9.14 (1H, s, br, 3-OH), 7.45 (1H, d, *J*=16 Hz, CH=CHCO), 7.19 (1H, t, *J*=7.2 Hz, 5′-ArH), 7.11–7.01 (4H, m, 2′,4′,6′-ArH & 2-ArH), 6.99 (1H, d, *J*=8.0, 1.6 Hz, 6-ArH), 6.76 (1H, d, *J*=8.0 Hz, 5-ArH), 6.23 (1H, d, *J*=16 Hz, CH=CHCO), 4.30 (2H, t, *J*=6.8 Hz, OCH_2), 2.90 (2H, t, *J*=6.8 Hz, $CH_2C_6H_4$), 2.28 (3H, s, CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.4, 148.4, 145.5, 145.1, 137.9, 137.3, 129.5, 128.5, 128.2, 126.9, 125.8, 125.4, 121.3, 115.7, 114.8, 113.8, 64.3, 34.4, 20.9 ppm; HRMS-ESI $C_{18}H_{18}O_4$ calcd $[M–H]^-$ 297.1127, found 297.1125.

*2-(4-Methylphenyl)ethyl (*E*)-3-(3,4-dihydroxyphenyl)acrylate* (**15**): White solid; yield 784 mg, 47.3%; m.p. 158–160 °C (lit[17]: 161–162 °C); IR (KBr) ν_{max} 3458, 3237, 1686, 1637, 1605, 1517, 1263, 1187 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.45 (1H, d, *J*=16 Hz, CH=CHCO), 7.18–7.08 (4H, m, 2′,3′,5′,6′-ArH), 7.05 (1H, d, *J*=1.6 Hz, 2-ArH), 6.99 (1H, d, *J*=8.0, 1.6 Hz, 6-ArH), 6.77 (1H, d, *J*=8.0 Hz, 5-ArH), 6.23 (1H, d, *J*=16 Hz, CH=CHCO), 4.28 (2H, t, *J*=6.8 Hz, OCH_2), 2.89 (2H, t, *J*=6.8 Hz, $CH_2C_6H_4$), 2.26 (3H, s, CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.4, 148.2, 145.4, 145.1, 135.2, 134.9, 128.9, 128.7, 125.4, 121.3, 115.6, 114.7, 113.8, 64.4, 34.0, 20.6 ppm; HRMS-ESI $C_{18}H_{18}O_4$ calcd $[M–H]^-$ 297.1127, found 297.1137.

*2-(3-Trifluoromethylphenyl)ethyl (*E*)-3-(3,4-dihydroxyphenyl) acrylate* (**16**): White solid; yield 1011 mg, 51.7%; m.p. 120–122 °C; IR (KBr) ν_{max} 3458, 3116, 1667, 1607, 1443, 1328, 1281, 1241, 1116 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.66 (1H, s, 4′-ArH), 7.63–7.51 (3H, m, 2′,5′,6′-ArH), 7.47 (1H, d, *J*=16 Hz, CH=CHCO), 7.04 (1H, d, *J*=1.6 Hz, 2-ArH), 6.97 (1H, d, *J*=8.0, 1.6 Hz, 6-ArH), 6.77 (1H, d, *J*=8.0 Hz, 5-ArH), 6.22 (1H, d, *J*=16 Hz, CH=CHCO), 4.36 (2H, t, *J*=6.8 Hz, OCH_2), 3.06 (2H, t, *J*=6.8 Hz, $CH_2C_6H_4$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.3, 148.3, 145.4, 145.2, 139.7, 133.1, 129.3, 129.2, 128.9, 125.4 (d), 125.4, 123.1 (d), 121.4, 115.6, 114.6, 113.6, 63.8, 34.0 ppm; HRMS-ESI $C_{18}H_{15}F_3O_4$ calcd $[M–H]^-$ 351.0844, found 351.0851.

*2-(4-Trifluoromethyl)phenyl)ethyl (*E*)-3-(3,4-dihydroxyphenyl) acrylate* (**17**): White solid; yield 906 mg, 46.3%; m.p. 176–178 °C; IR (KBr) ν_{max} 3480, 3318, 1685, 1635, 1602, 1336, 1279, 1179 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.66 (2H, d, *J*=8.0 Hz, 3′,5′-ArH), 7.52 (2H, d, *J*=8.0 Hz, 2′6′-ArH), 7.45 (1H, d, *J*=16 Hz, CH=CHCO), 7.04 (1H, d, *J*=2.0 Hz, 2-ArH), 6.98 (1H, d, *J*=8.0, 2.0 Hz, 6-ArH), 6.76 (1H, d, *J*=8.0 Hz, 5-ArH), 6.22 (1H, d, *J*=16 Hz, CH=CHCO), 4.36 (2H, t, *J*=6.8 Hz, OCH_2), 3.05 (2H, t, *J*=6.8 Hz, $CH_2C_6H_4$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.4, 148.3, 145.4, 145.3, 143.2, 129.7, 127.3, 126.9, 125.1 (q), 121.4, 115.6, 114.7, 113.6, 63.7, 34.2 ppm; HRMS-ESI $C_{18}H_{15}F_3O_4$ calcd $[M–H]^-$ 351.0844, found 351.0856.

*2-(4-Nitrophenethyl (*E*)-3-(3,4-dihydroxyphenyl)acrylate* (**18**): Yellow solid (970 mg, 53.0%; m.p. 174–176 °C (lit.[17] 168–169 °C); IR (KBr) ν_{max} 3474, 3420, 1691, 1633, 1597, 1508, 1355, 1340, 1299, 1277, 1169 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 9.60 (1H, br, 4-OH), 9.13 (1H, br, 3-OH), 8.17 (2H, d, *J*=12.8 Hz, 3′,5′-ArH), 7.58 (2H, d, *J*=12.8 Hz, 2′,6′-ArH), 7.44 (1H, d, *J*=16 Hz, CH=CHCO), 7.04 (1H, d, *J*=1.6 Hz, 2-ArH), 6.98 (1H, d, *J*=8.0, 1.6 Hz, 6-ArH), 6.76 (1H, d, *J*=8.0 Hz, 5-ArH), 6.21 (1H, d, *J*=16 Hz, CH=CHCO), 4.38 (2H, t, *J*=6.4 Hz, OCH_2), 3.10 (2H, t, *J*=6.4 Hz, $CH_2C_6H_4$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.3, 148.4, 146.6, 146.2, 145.5, 145.3, 130.2, 125.4, 123.3, 121.4, 115.7, 114.8, 113.6, 63.4, 34.2 ppm; HRMS-ESI $C_{17}H_{15}NO_6$ calcd $[M–H]^-$ 328.0821, found 328.0814.

*4-Cyanophenethyl (*E*)-3-(3,4-dihydroxyphenyl)acrylate* (**19**): White solid; yield 1038 mg, 60.5%; m.p. 171–173 °C; IR (KBr) ν_{max} 3465, 3339, 2222, 1696, 1634, 1597, 1533, 1357, 1300, 1275, 1178 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.77 (2H, d, *J*=8.0 Hz, 3′,5′-ArH), 7.50 (2H, d, *J*=8.0 Hz, 2′,6′-ArH), 7.43 (1H, d, *J*=16 Hz, CH=CHCO), 7.03 (1H, s, 2-ArH), 6.98 (1H, d, *J*=8.0 Hz, 6-ArH), 6.76 (1H, d, *J*=8.0 Hz, 5-ArH), 6.21 (1H, d, *J*=16 Hz, CH=CHCO), 4.35 (2H, t, *J*=6.4 Hz, OCH_2), 3.04 (2H, t, *J*=6.4 Hz, $CH_2C_6H_4$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.3, 148.3, 145.4, 145.3, 144.3, 132.1, 130.0, 125.4, 121.4, 118.9, 115.6, 114.7, 113.6, 109.2, 63.5, 34.4 ppm; HRMS-ESI $C_{18}H_{15}NO_4$ calcd $[M–H]^-$ 308.0923, found 308.0929.

*2-(4-Acetylphenyl)ethyl (*E*)-3-(3,4-dihydroxyphenyl)acrylate* (**20**): White solid; yield 1019 mg, 56.2%; m.p. 183–185 °C; IR (KBr) ν_{max} 3361, 3320, 1684, 1625, 1602, 1529, 1446, 1361, 1288, 1275, 1180 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.90 (2H, d, *J*=7.2 Hz, 3′,5′-ArH), 7.44 (1H, d, *J*=16 Hz, CH=CHCO), 7.43 (2H, d, *J*=7.2 Hz, 2′,6′-ArH), 7.04 (1H, s, 2-ArH), 6.98 (1H, d, *J*=8.0 Hz, 6-ArH), 6.76 (1H, d, *J*=8.0 Hz, 5-ArH), 6.22 (1H, d, *J*=16 Hz, CH=CHCO), 4.36 (2H, t, *J*=6.4 Hz, OCH_2), 3.03 (2H, t, *J*=6.4 Hz, $CH_2C_6H_4$), 2.55 (3H, s, $COCH_3$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 197.5, 166.4, 148.3, 145.4, 145.2, 143.9, 135.1, 129.1, 128.3, 125.4, 121.4, 115.5, 114.7, 113.7, 63.8, 26.6 ppm; HRMS-ESI $C_{19}H_{18}O_5$ calcd $[M–H]^-$ 325.1076, found 325.1072.

*2-(3,5-Difluorophenyl)ethy (*E*)-3-(3,4-dihydroxyphenyl)acrylate* (**21**): White solid; yield 918 mg, 51.6%; m.p. 148–150 °C; IR (KBr) ν_{max} 3484, 3301, 1683, 1636, 1603, 1535, 1391, 1363, 1303, 1281, 1186 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.45 (1H, d, *J*=16 Hz, CH=CHCO), 7.09–7.03 (3H, m, 2′,4′,6′-ArH), 7.03 (1H, s, 2-ArH), 6.98 (1H, d, *J*=8.4 Hz, 6-ArH), 6.77 (1H, d, *J*=8.4 Hz, 5-ArH), 6.23 (1H, d, *J*=16 Hz, CH=CHCO), 4.34 (2H, t, *J*=6.4 Hz, OCH_2), 2.98 (2H, t, *J*=6.4 Hz, $CH_2C_6H_3$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.3, 162.2 (dd), 148.3, 145.4, 145.3, 142.9 (t), 125.4, 121.4, 115.6, 114.7, 113.6, 112.0 (dd), 101.8 (t), 63.5, 34.0 ppm; HRMS-ESI $C_{17}H_{14}F_2O_4$ calcd $[M–H]^-$ 319.0782, found 319.0778.

*2-(4-Hydroxy-3-nitrophenyl)ethyl (*E*)-3-(3,4-dihydroxyphenyl) acrylate* (**22**): Yellow solid; yield 1103 mg, 57.5%; m.p. 172–174 °C; IR (KBr) ν_{max} 3478, 3310, 1686, 1634, 1604, 1536,1282, 1189 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.82 (1H, s, 2′-ArH), 7.47 (1H, d, *J*=8.4 Hz, 6′-ArH), 7.44 (1H, d, *J*=16 Hz, CH=CHCO), 7.07 (1H, d, *J*=8.4 Hz, 5′-ArH), 7.04 (1H, s, 2-ArH), 6.98 (1H, d, *J*=8.0 Hz, 6-ArH), 6.76 (1H, d, *J*=8.0 Hz, 5-ArH), 6.22 (1H, d, *J*=16 Hz, CH=CHCO), 4.29 (2H, t, *J*=6.4 Hz, OCH_2), 2.93 (2H, t, *J*=6.4 Hz, $CH_2C_6H_3$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.3, 150.6, 148.3, 145.4, 145.2, 136.3, 136.0, 129.4, 125.4, 124.9, 121.4, 119.0, 115.6, 114.7, 113.7, 63.9, 32.9 ppm; HRMS-ESI $C_{17}H_{15}NO_7$ calcd $[M–H]^-$ 344.0770, found 344.0764.

2-(2,4,5-Trifluorophenyl)ethyl (E)-3-(3,4-dihydroxyphenyl)acrylate (**23**): White solid; yield 1010 mg, 53.9%; m.p. 146–148 °C; IR (KBr) ν_{max} 3489, 3315, 1688, 1633, 1601, 1522, 1279, 1180 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 7.57–7.40 (3H, m, 3′,6′-ArH & CH=CHCO), 7.04 (1H, s, 2-ArH), 6.98 (1H, d, *J*=8.0 Hz, 6-ArH), 6.76 (1H, d, *J*=8.0 Hz, 5-ArH), 6.21 (1H, d, *J*=16 Hz, CH=CHCO), 4.31 (2H, t, *J*=6.4 Hz, OCH_2), 2.95 (2H, t, *J*=6.4 Hz, $CH_2C_6H_2$) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 166.2, 148.3, 145.4, 145.3, 125.3, 122.0 (m), 121.4, 118.9 (dd), 115.6, 114.7, 113.5, 105.6 (dd), 62.6, 37.2 ppm. HRMS-ESI $C_{17}H_{13}F_3O_4$ calcd $[M–H]^-$ 337.0688, found 337.0685.

*3-Phenylpropyl (*E*)-3-(3,4-dihydroxyphenyl)acrylate* (**24**): White solid; yield 787 mg, 47.5%; m.p. 122–124 °C (lit[20]: 123–124 °C); IR (KBr) ν_{max} 3495, 3338, 1683, 1638, 1602, 1278, 1184 cm^{-1};

^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.47 (1H, d, J=16 Hz, C<u>H</u>=CHCO), 7.32–7.13 (5H, m, $CH_2CH_2CH_2C_6\underline{H}_5$), 7.07 (1H, s, 2-ArH), 7.01 (1H, d, J=8.0 Hz, 6-ArH), 6.78 (1H, d, J=8.0 Hz, 5-ArH), 6.27 (1H, d, J=16 Hz, CH=C<u>H</u>CO), 4.10 (2H, t, J=6.8 Hz, OCH_2), 2.67 (2H, t, J=7.6 Hz, $C\underline{H}_2C_6H_5$), 1.93 (2H, m, $C\underline{H}_2CH_2C_6H_5$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.5, 148.2, 145.4, 145.0, 141.1, 128.3, 128.2, 125.8, 125.5, 121.3, 115.6, 114.7, 113.9, 63.1, 31.4, 29.8 ppm; HRMS-ESI $C_{18}H_{18}O_4$ calcd [M–H]$^-$ 297.1127, found 297.1135.

Synthesis of **25**–**30***; general procedure*

For changes in procedure see Table 4

2-Phenylethyl cinnamate (**25**): White solid; 1630 mg, 95.8%; m.p. 50–52 °C (lit.[31] 54.3–55.3 °C); IR (KBr) ν_{max} 1710, 1637, 1496, 1449, 1328, 1313, 1283, 1205, 1174 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.74–7.68 (2H, m, 2,6-ArH), 7.64 (1H, d, J=16 Hz, C<u>H</u>=CHCO), 7.42 (3H, m, 3,4,5-ArH), 7.35–7.19 (5H, m, $CH_2C_6\underline{H}_5$), 6.62 (1H, d, J=16 Hz, CH=C<u>H</u>CO), 4.36 (2H, t, J=6.8 Hz, OCH_2), 2.97 (2H, t, J=6.8 Hz, $C\underline{H}_2C_6H_5$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.5, 145.0, 138.4, 134.3, 130.9, 129.3, 129.3, 128.8, 126.8, 118.3, 65.0, 34.8 ppm; HRMS-ESI $C_{17}H_{16}O_2$ calcd [M–H]$^-$ 251.1072, found 327.1067.

*2-Phenylethyl (*E*)-3-(3-chlorophenyl)acrylate* (**26**): Colourless oil; yield 1140 mg, 72.5%; IR (KBr) ν_{max} 1713, 1639, 1314, 1201, 1173 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.85 (1H, s, 2-ArH), 7.68 (1H, d, J=7.6 Hz, 6-ArH), 7.62 (1H, d, J=16 Hz, C<u>H</u>=CHCO), 7.50–7.40 (2H, m, 4,5-ArH), 7.35–7.15 (5H, m, 2′,3′,4′,5′,6′-ArH), 6.71 (1H, d, J=16 Hz, CH=C<u>H</u>CO), 4.36 (2H, t, J=6.8 Hz, OCH_2), 2.97 (2H, t, J=6.8 Hz, $C\underline{H}_2C_6H_5$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.3, 143.4, 138.3, 136.6, 134.1, 131.0, 130.4, 129.3, 128.8, 128.3, 127.4, 126.8, 120.1, 65.1, 34.8 ppm; HRMS-ESI $C_{17}H_{15}ClO_2$ calcd [M–H]$^-$ 285.0682 (^{35}Cl), found 285.0679.

*2-Phenylethyl (*E*)-3-(4-hydroxyphenyl)acrylate* (**27**): White solid; yield 1150 mg, 70.6%; m.p. 62–64 °C (lit[31]: 90.5–91.5 °C); IR (KBr) ν_{max} 3336, 1727, 1665, 1640, 1513, 1309, 1166 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 10.01 (1H, s, 4-OH), 7.54 (3H, m, 2,6-ArH & C<u>H</u>=CHCO), 7.35–7.18 (5H, m, 2′,3′,4′,5′,6′-ArH), 6.79 (2H, d, J=7.6 Hz, 3,5-ArH), 6.36 (1H, d, J=16 Hz, CH=C<u>H</u>CO), 4.33 (2H, t, J=6.4 Hz, OCH_2), 2.95 (2H, t, J=6.4 Hz, $C\underline{H}_2C_6H_5$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.9, 160.2, 145.7, 138.5, 130.7, 129.2, 128.7, 126.7, 125.4, 116.1, 114.4, 64.7, 34.9 ppm; HRMS-ESI $C_{17}H_{16}O_3$ calcd [M–H]$^-$ 267.1021, found 267.1016.

*2-Phenylethyl (*E*)-3-(4-methoxyphenyl)acrylate* (**28**): White solid; yield 1147 mg, 72.4%; m.p. 55–56 °C (lit[31]: 56.7–57.6 °C); IR (KBr) ν_{max} 1706, 1635, 1601, 1513, 1324, 1315, 1263, 1174 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.66 (2H, d, J=8.0 Hz, 2,6-ArH), 7.58 (1H, d, J=16 Hz, C<u>H</u>=CHCO), 7.35–7.18 (5H, m, 2′,3′,4′,5′,6′-ArH), 6.97 (2H, d, J=8.0 Hz, 3,5-ArH), 6.45 (1H, d, J=16 Hz, CH=C<u>H</u>CO), 4.34 (2H, t, J=6.4 Hz, OCH_2), 2.96 (2H, t, J=6.4 Hz, $C\underline{H}_2C_6H_5$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.8, 161.5, 144.8, 138.4, 130.6, 129.2, 128.7, 127.0, 126.7, 115.6, 114.7, 64.8, 55.7, 34.8 ppm; HRMS-ESI $C_{18}H_{18}O_3$ calcd [M–H]$^-$ 281.1178, found 281.1176.

2-Phenylethyl (E)-3-(3-hydroxy-4-methoxyphenyl)acrylate (**29**): White solid; yield 878 mg, 57.2%; m.p. 79–81 °C (lit[19]: 79.5–80.5 °C); IR (KBr) ν_{max} 1703, 1632, 1614, 1511, 1265, 1160 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.57 (1H, d, J=16 Hz, C<u>H</u>=CHCO), 7.35–7.17 (5H, m, 2′,3′,4′,5′,6′-ArH), 7.13 (1H, s, 2-ArH), 7.01 (1H, d, J=8.0 Hz, 5-ArH), 6.83 (1H, d, J=8.0 Hz, 6-ArH), 6.27 (1H, d, J=16 Hz, CH=C<u>H</u>CO), 4.41 (2H, t, J=6.4 Hz, OCH_2), 3.91 (3H, s, 4-OCH_3), 3.01 (2H, t, J=6.4 Hz, $C\underline{H}_2C_6H_5$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 167.1, 148.4, 145.8, 144.6, 137.9, 128.9, 128.4, 128.0, 126.5, 121.7, 116.0, 113.0, 110.4, 77.3, 77.0, 76.70, 64.8, 55.9, 35.2 ppm; HRMS-ESI $C_{18}H_{18}O_4$ calcd [M–H]$^-$ 297.1127, found 297.1120.

2-Phenylethyl (E)-3-(3,4-dimethoxyphenyl) acrylate (**30**): White solid; yield 907 mg, 60.5%; m.p. 98–100 °C (lit[31]: 101.2–102.1 °C); IR (KBr) ν_{max} 1701, 1635, 1596, 1515, 1340, 1258, 1235, 1177, 1162, 1139 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H 7.57 (1H, d, J=16 Hz, C<u>H</u>=CHCO), 7.37–7.18 (7H, m, 2′,3′,4′,5′,6′-ArH & 2,5-ArH), 6.97 (1H, d, J=8.4 Hz, 6-ArH), 7.01 (1H, d, J=8.0 Hz, 6-ArH), 6.52 (1H, d, J=16 Hz, CH=C<u>H</u>CO), 4.35 (2H, t, J=6.4 Hz, OCH_2), 3.80 (3H, s, 3-OCH_3), 3.79 (3H, s, 4-OCH_3), 2.96 (2H, t, J=6.4 Hz, $C\underline{H}_2C_6H_5$) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ_C 166.9, 151.4, 149.4, 145.2, 138.4, 129.2, 128.8, 127.2, 126.7, 123.5, 115.8, 111.9, 110.7, 64.7, 56.0, 55.9, 34.8 ppm; HRMS-ESI $C_{19}H_{20}O_4$ calcd [M–H]$^-$ 311.1283, found 311.1300.

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