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SYNTHESIS AND cdc25B INHIBITORY ACTIVITY EVALUATION OF CHALCONES

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A library of sixty-five chalcones was prepared for screening against the protein phosphatase, cdc25B. From this library, thirteen compounds were found having good inhibitory activity. Two compounds have excellent activity and can be used for the design of more potent antiproliferative agents.

Keywords: chalcones, cdc25B, inhibition, cancer.

Mammalian cell communication and growth are regulated by protein phosphorylation, which is the product of a dynamic balance between the enzymatic activity of protein kinases and phosphatases. Cdc25 phosphatases are important members of the dual-specificity protein phosphatases (DSPases). They control cell cycle progression by activating cyclin-dependent serine/threonine protein kinases (Cdks) [1] that are responsible for the progression of eukaryotic cells through the cell cycle. The overexpression of cdc25 phosphatases is frequently associated with a wide variety of cancers. Cdc25B is one of the members of the cdc25 phosphatases and appears to be essential in the G_2/M phase transition in human cells [2]. Cdc25B is a suitable target for drug intervention, since it has been shown to be an oncogene when overexpressed, showing up in increased levels in several human breast cancers [3], and cdc25B shows more specificity than other cdc25 phosphatases. Inhibition of cdc25B could prove therapeutically useful as a treatment for cancer [4]. Recently, the structure of the catalytic domains of cdc25B has been solved by X-ray crystallography [5], and a number of small-molecule inhibitors of cdc25B have been developed, such as EK- 6136 [6], tetrahydroisoquinolines [7], pyrazole derivatives [8], vitamin K analogues [9], adociaquinone B and naphthoquinone derivatives [10, 11], etc. Efforts are currently under way to synthesize specific small-molecule cdc25B inhibitors that might have anticancer properties.

Chalcones are naturally occurring flavonoids composed of two aromatic rings connected by a three-carbon unit forming an α–β unsaturated carbonyl group. They are pharmacologically relevant because of their ability to exert antioxidant, anticarcinogenic, antibacterial, and anti-inflammatory activities, etc. [12–14]. In light of their extremely high values, chalcones have become a hot topic for research and development. Although there has been much study of the inhibitory effects of flavonoids on cdc25 phosphatases [15–17] and the inhibitory effects of chalcones on proliferation of human malignant tumor cells [18, 19], far less known are the actions of chalcones on cdc25B [20]. This is important, since the structure of chalcone is more flexible so that it can enhance the binding between compounds and enzyme or make the binding much more easier. The aim of the present study, therefore, was to probe a small compound library for potential inhibitory structures and study the structure–activity relationship so as to guide further design of chalcone analogs with more potent activity.

In this work, sixty-five compounds were synthesized and were evaluated for *in vitro* inhibitory activity against cdc25B at 20 μg/mL inhibitor concentration with 3-*O*-methylfluorescein phosphate (OMFP) as a substrate using a previously described procedure [21]. Sodium vanadate was taken as a control (IC_{50}, 9.821 ± 0.838 μmol/L). The results are summarized in Table 1.

The results demonstrated that thirteen compounds inhibited the catalytic activity of cdc25B by more than 50%. Among them, two compounds (compounds **25** and **45**) revealed a significant potency with more than 90% inhibition at the same concentration. However, the natural compounds **14** [22] and **20** [23] have almost no activity.

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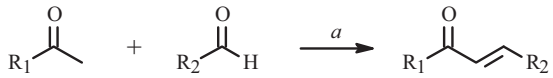

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a. 10% NaOH, C_2H_5OH, room t °C

Compound	R_1	R_2	Compound	R_1	R_2
1	2-OH-Ph	3,4-Methylenedioxy-Ph	**2**	2-OH-Ph	3-NO_2-Ph
3	2-OH-Ph	2-F-Ph	**4**	2-OH-Ph	3-F-Ph
5	2-OH-Ph	4-F-Ph	**6**	2-OH-Ph	3-Cl-Ph
7	2-OH-Ph	2,4-diCl-Ph	**8**	2-OH-Ph	3,4-diCl-Ph
9	2-OH-Ph	2,6-diCl-Ph	**10**	2-OH-Ph	2-Br-Ph
11	2-OH-Ph	4-Br-Ph	**12**	2-OH-Ph	4-CF_3-Ph
13	2-OH-Ph	4-$N(CH_3)_2$-Ph	**14**	2-OH-Ph	4-OH-3-OCH_3-Ph
15	2-OH-Ph	4-COOH-Ph	**16**	2-OH-Ph	2-Furyl
17	2-OH-Ph	5-CH_2OH-2-Furyl	**18**	2-OH-Ph	2-Thienyl
19	2-OH-Ph	2-Naphthyl	**20**	4-OCH_3-Ph	4-OCH_3-Ph
21	4-OCH_3-Ph	3,4-Methylenedioxy-Ph	**22**	4-OCH_3-Ph	3-Br-Ph
23	4-OCH_3-Ph	4-$N(CH_3)_2$-Ph	**24**	4-OCH_3-Ph	4-OH-Ph
25	4-OCH_3-Ph	2-Furyl	**26**	2-NH_2-Ph	3,4-$(OCH_3)_2$-Ph
27	2-NH_2-Ph	3-NO_2-Ph	**28**	2-NH_2-Ph	4-NO_2-Ph
29	2-NH_2-Ph	2-F-Ph	**30**	2-NH_2-Ph	3-F-Ph
31	2-NH_2-Ph	4-F-Ph	**32**	2-NH_2-Ph	2,4-diCl-Ph
33	2-NH_2-Ph	3,4-diCl-Ph	**34**	2-NH_2-Ph	2-Br-Ph
35	2-NH_2-Ph	2-Furyl	**36**	2-NH_2-Ph	2-Naphthyl
37	4-NH_2-Ph	3,4-Methylenedioxy-Ph	**38**	4-NH_2-Ph	3-Cl-Ph
39	4-NH_2-Ph	4-$N(CH_3)_2$-Ph	**40**	2-NO_2-Ph	3,4-$(OCH_3)_2$-Ph
41	2-NO_2-Ph	3,4-Methylenedioxy-Ph	**42**	2-NO_2-Ph	2-Furyl
43	4-NO_2-Ph	3,4-$(OCH_3)_2$-Ph	**44**	4-NO_2-Ph	3,4-Methylenedioxy-Ph
45	4-NO_2-Ph	3-Cl-Ph	**46**	4-NO_2-Ph	4-OH-3-OCH_3-Ph
47	2-F-Ph	4-OCH_3-Ph	**48**	2-F-Ph	3,4-Methylenedioxy-Ph
49	2-F-Ph	4-$N(CH_3)_2$-Ph	**50**	2-Cl-Ph	3,4-$(OCH_3)_2$-Ph
51	2-Cl-Ph	3,4-Methylenedioxy-Ph	**52**	2-Cl-Ph	4-OH-Ph
53	3-Cl-Ph	3,4-$(OCH_3)_2$-Ph	**54**	3-Cl-Ph	4-OCH_3-Ph
55	3-Cl-Ph	3,4-Methylenedioxy-Ph	**56**	4-Cl-Ph	3,4-$(OCH_3)_2$-Ph
57	4-Cl-Ph	3,4-Methylenedioxy-Ph	**58**	4-Cl-Ph	4-OH-3-OCH_3-Ph
59	4-Cl-Ph	2-Furyl	**60**	3-Br-Ph	3,4-$(OCH_3)_2$-Ph
61	3-Br-Ph	4-OCH_3-Ph	**62**	2-Naphthyl	4-OCH_3-Ph
63	2-Naphthyl	4-OH-Ph	**64**	2-Naphthyl	3,4-diOH- Ph
65	2-Naphthyl	3-Indolyl			

It can be concluded from the result that the introduction of groups on ring A at the 2-position or 3-position of chalcones can lower the activity regardless of electron-withdrawing or electron-donating groups, because almost all of these series have weak or no activity except for compounds **7**, **28**, **35**, and **61**, and it seems that there was no significant correlation between the inhibitory activity of cdc25B and the groups on ring B. However, the introduction of groups at the 4-position on ring A can improve the inhibitory activity to some degree, especially when the chlorine atom and 2-furyl group were introduced on ring B (compounds **25**, **45**, and **59**). It is noteworthy that the replacement of the benzene ring by the stiffer naphthalene ring as ring A is very helpful to the activity even though there are two electron-donating groups on ring B (compound **64**). This is very interesting and further study is needed.

In conclusion, sixty-five chalcones were synthesized and their preliminary cdc25B inhibitory activities *in vitro* were evaluated in this paper. Thirteen compounds (compounds **7**, **25**, **28**, **35**, **44**, **45**, **56**, **59**, and **61–65**) displayed promising inhibitory activities (inhibitory activity > 50%), and two compounds (compound **25** and **45**) showed high activities (inhibitory activity 90%) among the synthesized compounds. Study of the structure–activity relationship revealed that the introduction of groups on ring A at 4-position and the replacement of the benzene ring by the stiffer naphthalene ring can improve the activity to some degree. The present results may guide further design of chalcone analogs with high cdc25B inhibitory activity. However, further modification and biological studies, even docking studies, are necessary to better understand the binding modes between the compounds and the enzyme cdc25B. All these works are already under progress.

TABLE 1. The *in vitro* cdc25B Enzyme Inhibitory Activities of the Title Compounds

Compound	Ratio of inhibitory activity, % (20 μg/mL)	Compound	Ratio of inhibitory activity, % (20 μg/mL)	Compound	Ratio of inhibitory activity, % (20 μg/mL)
1	12.91	**23**	29.53	**45**	98.33
2	–19.27	**24**	28.06	**46**	25.02
3	–18.19	**25**	94.79	**47**	20.45
4	–9.66	**26**	–15.53	**48**	48.75
5	17.14	**27**	16.11	**49**	45.14
6	–11.10	**28**	55.98	**50**	–7.06
7	88.06	**29**	–12.41	**51**	34.98
8	14.92	**30**	20.72	**52**	44.12
9	46.09	**31**	–8.76	**53**	23.49
10	–6.58	**32**	19.61	**54**	19.13
11	38.84	**33**	40.49	**55**	–27.09
12	23.78	**34**	15.99	**56**	55.06
13	42.15	**35**	80.75	**57**	–21.46
14	5.89	**36**	18.33	**58**	33.62
15	19.74	**37**	47.17	**59**	89.17
16	23.11	**38**	29.80	**60**	29.43
17	25.56	**39**	–18.30	**61**	75.13
18	28.95	**40**	22.35	**62**	62.93
19	11.80	**41**	31.07	**63**	72.16
20	10.63	**42**	21.47	**64**	51.42
21	24.22	**43**	–1.54	**65**	80.40
22	19.20	**44**	54.45		

EXPERIMENTAL

Instruments and Equipment. The melting points were obtained using the Electrothermal digital melting point apparatus ZMD-1 and are uncorrected. ^{1}H NMR spectra were obtained on a Bruker AVANCE II-300 spectrometer, and chemical shifts are reported in parts per million relative to $CDCl_3$ (7.27 ppm for ^{1}H) and DMSO-d_6 (2.53 ppm for ^{1}H). Unless otherwise noted, the materials were obtained from commercially available sources and were used without further purification.

Synthesis of Chalcones (General Method). A solution of acetophenone (10 mmol) in ethanol (20 mL) was treated with 10% NaOH aqueous solution (40 mmol) and benzaldehyde (10 mmol) in ethanol with stirring at room temperature for 12–24 h. The reaction was monitored by TLC. When completed, the mixture was poured into an excessive amount of ice-water, then filtrated, dried, and recrystallized from ethanol to give the title compounds.

Identification of all the title compounds was performed by NMR and MS.

(*E*)-3-(Benzo[d][1,3]dioxol-5-yl)-1-(2-hydroxyphenyl)prop-2-en-1-one (1). Yellow solid. Yield 52%, mp 136–138°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.06 (2H, s, OCH_2O), 6.87 (1H, d, J = 8.1, H-5), 6.95 (1H, t, J = 8.1, H-5′), 7.03 (1H, dd, J_1 = 8.1, J_2 = 0.9, H-3′), 7.17 (1H, dd, J_1 = 8.1, J_2 = 1.5, H-6), 7.20 (1H, d, J = 1.5, H-2), 7.50 (1H, d, J = 15.3, H-α), 7.51 (1H, t, J = 8.1, H-4′), 7.87 (1H, d, J = 15.3, H-β), 7.92 (1H, dd, J_1 = 8.1, J_2 = 1.5, H-6′), 12.92 (1H, s, OH). ESI-MS *m/z* 269.56 $[M + H]^+$.

(*E*)-1-(2-Hydroxyphenyl)-3-(3-nitrophenyl)prop-2-en-1-one (2). Yellow solid. Yield 29%, mp 162–164°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.99 (1H, t, J = 8.4, H-Ar), 7.05 (1H, d, J = 8.4, H-Ar), 7.54 (1H, t, J = 7.8, H-Ar), 7.64 (1H, t, J = 7.8, H-Ar), 7.77 (1H, d, J = 15.6, H-α), 7.93 (1H, d, J = 15.6, H-β), 7.94 (2H, d, J = 7.8, H-Ar), 8.28 (1H, dd, J_1 = 7.8, J_2 = 1.8, H-Ar), 8.54 (1H, s, H-Ar), 12.60 (1H, s, OH). ESI-MS *m/z* 270.56 $[M + H]^+$.

(*E*)-3-(2-Fluorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one (3). Yellow solid. Yield 83%, mp 80–82°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.95 (1H, t, J = 7.8, H-Ar), 7.04 (1H, dd, J_1 = 8.4, J_2 = 1.2, H-Ar), 7.16 (1H, t, J = 8.4, H-Ar), 7.22 (1H, t, J = 7.8, H-Ar), 7.41 (1H, m, H-Ar), 7.51 (1H, t, J = 8.4, H-Ar), 7.66 (1H, t, J = 7.8, H-Ar), 7.79 (1H, d, J = 15.6, H-α), 7.92 (1H, dd, J_1 = 7.8, J_2 = 1.2, H-Ar), 8.00 (1H, d, J = 15.6, H-β), 12.76 (1H, s, OH). ESI-MS *m/z* 243.55 $[M + H]^+$.

(*E*)-3-(3-Fluorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one (4). Yellow solid. Yield 53%, mp 104–106°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.96 (1H, t, J = 7.8, H-Ar), 7.04 (1H, dd, J_1 = 8.4, J_2 = 1.2, H-Ar), 7.14 (1H, m, H-Ar), 7.36 (1H, d, J = 9.0, H-Ar), 7.41 (2H, m, H-Ar), 7.51 (1H, t, J = 8.4, H-Ar), 7.64 (1H, d, J = 15.6, H-α), 7.86 (1H, d, J = 15.6, H-β), 7.91 (1H, dd, J_1 = 7.8, J_2 = 1.2, H-Ar), 12.71 (1H, s, OH). ESI-MS *m/z* 243.62 $[M + H]^+$.

(*E*)-3-(4-Fluorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one (5). Yellow solid. Yield 48%, mp 114–115°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.95 (1H, t, J = 8.4, H-5′), 7.03 (1H, dd, J_1 = 8.4, J_2 = 1.2, H-3′), 7.13 (2H, d, J = 8.4, H-3, 5), 7.51 (1H, t, J = 8.4, H-4′), 7.58 (1H, d, J = 15.6, H-*α*), 7.66 (2H, d, J = 8.4, H-2, 6), 7.89 (1H, d, J = 15.6, H-*β*), 7.91 (1H, dd, J_1 = 8.4, J_2 = 1.2, H-6′), 12.77 (1H, s, OH). ESI-MS *m/z* 243.58 $[M + H]^+$.

(*E*)-3-(3-Chlorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one (6). Yellow solid. Yield 33%, mp 94–96°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.95 (1H, t, J = 7.5, H-Ar), 7.03 (1H, d, J = 8.1, H-Ar), 7.37 (2H, m, H-Ar), 7.56 (3H, m, H-Ar), 7.62 (1H, d, J = 15.3, H-*α*), 7.81 (1H, d, J = 15.3, H-*β*), 7.90 (1H, d, J = 8.1, H-Ar), 12.75 (1H, s, OH). ESI-MS *m/z* 257.82 $[M - H]^-$.

(*E*)-3-(2,4-Dichlorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one (7). Yellow solid. Yield 50%, mp 168–170°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.95 (1H, t, J = 7.8, H-Ar), 7.05 (1H, dd, J_1 = 8.4, J_2 = 0.6, H-Ar), 7.33 (1H, dd, J_1 = 8.4, J_2 = 2.4, H-Ar), 7.49 (1H, d, J = 1.8, H-Ar), 7.52 (1H, t, J = 9.0, H-Ar), 7.63 (1H, d, J = 15.0, H-*α*), 7.70 (1H, d, J = 8.4, H-Ar), 7.89 (1H, dd, J_1 = 8.4, J_2 = 1.8, H-Ar), 8.23 (1H, d, J = 15.0, H-*β*), 12.65 (1H, s, OH). ESI-MS *m/z* 291.73 $[M - H]^-$.

(*E*)-3-(3,4-Dichlorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one (8). Yellow solid. Yield 42%, mp 153–155°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.96 (1H, t, J = 7.5, H-5′), 7.04 (1H, d, J = 8.4, H-5), 7.51 (3H, m, H-Ar), 7.62 (1H, d, J = 15.6, H-*α*), 7.74 (1H, d, J = 1.2, H-2), 7.79 (1H, d, J = 15.6, H-*β*), 7.90 (1H, dd, J_1 = 8.1, J_2 = 1.2, H-6′), 12.69 (1H, s, OH). ESI-MS *m/z* 291.97 $[M - H]^-$.

(*E*)-3-(2,6-Dichlorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one (9). Yellow solid. Yield 70%, mp 98–100°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.95 (1H, t, J = 8.1, H-5′), 7.04 (1H, dd, J_1 = 8.1, J_2 = 0.9, H-3′), 7.23 (1H, t, J = 7.5, H-4), 7.40 (2H, d, J = 7.5, H-3, 5), 7.52 (1H, t, J = 8.1, H-4′), 7.83 (1H, dd, J_1 = 8.1, J_2 = 1.5, H-6′), 7.84 (1H, d, J = 15.9, H-*α*), 7.98 (1H, d, J = 15.9, H-*β*), 12.65 (1H, s, OH). ESI-MS *m/z* 291.97 $[M - H]^-$.

(*E*)-3-(2-Bromophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one (10). Yellow solid. Yield 42%, mp 92–94°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.94 (1H, t, J = 7.8, H-Ar), 7.04 (1H, dd, J_1 = 8.4, J_2 = 0.6, H-Ar), 7.28 (1H, dd, J_1 = 7.8, J_2 = 1.2, H-Ar), 7.38 (1H, t, J = 7.8, H-Ar), 7.51 (1H, t, J = 8.4, H-Ar), 7.58 (1H, d, J = 15.6, H-*α*), 7.65 (1H, dd, J_1 = 8.4, J_2 = 1.2, H-Ar), 7.75 (1H, dd, J_1 = 7.8, J_2 = 1.2, H-Ar), 7.90 (1H, dd, J_1 = 7.8, J_2 = 1.2, H-Ar), 8.26 (1H, d, J = 15.6, H-*β*), 12.71 (1H, s, OH). ESI-MS *m/z* 303.55 $[M + H]^+$.

(*E*)-3-(4-Bromophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one (11). Yellow solid. Yield 57%, mp 146–148°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.95 (1H, t, J = 7.8, H-5′), 7.04 (1H, d, J = 7.8, H-3′), 7.51 (1H, t, J = 7.8, H-4′), 7.53 (2H, d, J = 8.4, H-3, 5), 7.58 (2H, d, J = 8.4, H-2, 6), 7.65 (1H, d, J = 15.6, H-*α*), 7.85 (1H, d, J = 15.6, H-*β*), 7.91 (1H, dd, J_1 = 7.8, J_2 = 1.2, H-6′), 12.73 (1H, s, OH). ESI-MS *m/z* 303.32 $[M + H]^+$.

(*E*)-1-(2-Hydroxyphenyl)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (12). Yellow solid. Yield 80%, mp 95–97°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 7.01 (1H, t, J = 8.1, H-5′), 7.09 (1H, dd, J_1 = 8.1, J_2 = 0.9, H-3′), 7.57 (1H, t, J = 8.1, H-4′), 7.74 (2H, d, J = 8.4, H-3, 5), 7.76 (1H, d, J = 15.6, H-*α*), 7.81 (2H, d, J = 8.4, H-2, 6), 7.96 (1H, d, J = 15.6, H-*β*), 7.97 (1H, dd, J_1 = 8.1, J_2 = 1.5, H-6′), 12.73 (1H, s, OH). ESI-MS *m/z* 293.42 $[M + H]^+$.

(*E*)-3-(4-(Dimethylamino)phenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one (13). Red solid. Yield 60%, mp 172–174°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.07 (6H, s, $N(CH_3)_2$), 6.72 (2H, d, J = 9.0, H-3, 5), 6.92 (1H, t, J = 8.4, H-5′), 7.01 (1H, dd, J_1 = 8.4, J_2 = 1.2, H-3′), 7.46 (1H, t, J = 8.4, H-4′), 7.46 (1H, d, J = 15.0, H-*α*), 7.58 (2H, d, J = 9.0, H-2, 6), 7.92 (1H, d, J = 15.0, H-*β*), 7.93 (1H, dd, J_1 = 8.4, J_2 = 1.8, H-6′), 13.17 (1H, s, OH). ESI-MS *m/z* 268.66 $[M + H]^+$.

(*E*)-3-(4-Hydroxy-3-methoxyphenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one (14). Yellow solid. Yield 37%, mp 123–125°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.99 (3H, s, OCH_3), 6.01 (1H, br.s, 4-OH), 6.98 (1H, t, J = 8.4, H-5′), 7.03 (1H, d, J = 9.0, H-5), 7.15 (1H, d, J = 1.5, H-2), 7.20 (1H, d, J = 9.0, H-6), 7.28 (1H, d, J = 8.4, H-3′), 7.51 (1H, t, J = 8.4, H-4′), 7.52 (1H, d, J = 15.0, H-*α*), 7.89 (1H, d, J = 15.0, H-*β*), 7.94 (1H, d, J = 8.4, H-6′), 12.96 (1H, s, 2′-OH). ESI-MS *m/z* 271.57 $[M + H]^+$.

(*E*)-4-(3-(2-Hydroxyphenyl)-3-oxoprop-1-enyl)benzoic Acid (15). Yellow solid. Yield 41%, mp 254–255°C. ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.05 (2H, m, H-3′, 5′), 7.61 (1H, t, J = 8.1, H-4′), 7.89 (1H, d, J = 15.6, H-*α*), 8.02 (2H, d, J = 9.0, H-2, 6), 8.06 (2H, d, J = 9.0, H-3, 5), 8.16 (1H, d, J = 15.6, H-*β*), 8.28 (1H, dd, J_1 = 8.1, J_2 = 1.5, H-6′), 12.37 (1H, s, OH), 13.19 (1H, s, COOH). MS-ESI *m/z* 269.46 $[M + H]^+$.

(*E*)-3-(Furan-2-yl)-1-(2-hydroxyphenyl)prop-2-en-1-one (16). Yellow solid. Yield 57%, mp 100–102°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.55 (1H, dd, J_1 = 3.3, J_2 = 1.5, H-4), 6.78 (1H, d, J = 3.3, H-3), 6.95 (1H, t, J = 8.1, H-5′), 7.02 (1H, dd, J_1 = 8.1, J_2 = 1.2, H-3′), 7.50 (1H, t, J = 8.1, H-4′), 7.56 (1H, d, J = 15.3, H-*α*), 7.56 (1H, d, J = 1.5, H-5), 7.69 (1H, d, J = 15.3, H-*β*), 7.93 (1H, dd, J_1 = 8.1, J_2 = 1.5, H-6′), 12.92 (1H, s, OH). ESI-MS *m/z* 215.69 $[M + H]^+$.

(*E*)-3-(5-(Hydroxymethyl)furan-2-yl)-1-(2-hydroxyphenyl)prop-2-en-1-one (17). Red solid. Yield 81%, mp 92–94°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 4.72 (2H, s, CH_2), 6.46 (1H, d, J = 3.3, H-3), 6.73 (1H, d, J = 3.3, H-4), 6.95 (1H, t, J = 8.1, H-5′), 7.02 (1H, dd, J_1 = 8.1, J_2 = 1.2, H-3′), 7.49 (1H, t, J = 8.1, H-4′), 7.55 (1H, d, J = 15.0, H-*α*), 7.65 (1H, d, J = 15.0, H-*β*), 7.94 (1H, dd, J_1 = 8.1, J_2 = 1.2, H-6′), 12.92 (1H, s, OH). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 57.71 (CH_2), 110.85 (C-4), 117.57 (C-3), 118.11 (C-3′), 118.53 (C-1′), 118.84 (C-5′), 120.03 (C-*β*), 129.67 (C-*α*), 130.96 (C-6′), 136.33 (C-4′), 151.46 (C-2), 157.20 (C-5), 163.52 (C-2′). ESI-MS *m/z* 244.84 $[M + H]^+$.

(*E*)-1-(2-Hydroxyphenyl)-3-(thiophen-2-yl)prop-2-en-1-one (18). Yellow solid. Yield 29%, mp 86–88°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.99 (1H, t, J = 8.1, H-5′), 7.07 (1H, dd, J_1 = 8.4, J_2 = 0.9, H-3′), 7.16 (1H, m, H-Ar), 7.51 (3H, m, H-Ar), 7.48 (1H, d, J = 15.0, H-*α*), 7.93 (1H, dd, J_1 = 8.1, J_2 = 1.5, H-6′), 8.10 (1H, d, J = 15.0, H-*β*), 12.91 (1H, s, OH). ESI-MS *m/z* 231.44 $[M + H]^+$.

(*E*)-1-(2-Hydroxyphenyl)-3-(naphthalen-2-yl)prop-2-en-1-one (19). Yellow solid. Yield 63%, mp 152–154°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.97 (1H, t, J = 8.4, H-Ar), 7.05 (1H, dd, J_1 = 8.4, J_2 = 1.2, H-Ar), 7.54 (3H, m, H-Ar), 7.78 (1H, d, J = 15.6, H-*α*), 7.82 (1H, dd, J_1 = 8.4, J_2 = 1.8, H-Ar), 7.74 (3H, m, H-Ar), 7.99 (1H, dd, J_1 = 8.4, J_2 = 1.8, H-Ar), 8.08 (1H, s, H-Ar), 8.09 (1H, d, J = 15.6, H-*β*), 12.86 (1H, s, OH). ESI-MS *m/z* 275.65 $[M + H]^+$.

(*E*)-1,3-Bis(4-methoxyphenyl)prop-2-en-1-one (20). Yellow solid. Yield 80%, mp 101–103°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.85 (3H, s, OCH_3), 3.88 (3H, s, OCH_3), 6.93 (2H, d, J = 9.0, H-Ar), 6.97 (2H, d, J = 9.0, H-Ar), 7.42 (1H, d, J = 15.6, H-*α*), 7.59 (2H, d, J = 9.0, H-Ar), 7.77 (1H, d, J = 15.6, H-*β*), 8.03 (2H, d, J = 9.0, H-Ar). ESI-MS *m/z* 269.57 $[M + H]^+$.

(*E*)-3-(Benzo[d][1,3]dioxol-5-yl)-1-(4-methoxyphenyl)prop-2-en-1-one (21). Yellow solid. Yield 41%, mp 124–126°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.89 (3H, s, OCH_3), 6.02 (2H, s, OCH_2O), 6.84 (1H, d, J = 8.4, H-5), 6.97 (2H, d, J = 9.0, H-3′, 5′), 7.11 (1H, dd, J_1 = 8.4, J_2 = 1.8, H-6), 7.16 (1H, d, J = 1.8, H-2), 7.38 (1H, d, J = 15.6, H-*α*), 7.72 (1H, d, J = 15.6, H-*β*), 8.02 (2H, d, J = 9.0, H-2′, 6′). ESI-MS *m/z* 283.61 $[M + H]^+$.

(*E*)-3-(3-Bromophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (22). Yellow solid. Yield 28%, mp 112–115°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.90 (3H, s, OCH_3), 6.99 (2H, d, J = 9.0, H-3′, 5′), 7.29 (1H, t, J = 7.8, H-5), 7.53 (1H, d, J = 15.6, H-*α*), 7.52 (2H, d, J = 7.8, H-4, 6), 7.71 (1H, d, J = 15.6, H-*β*), 7.79 (1H, s, H-2), 8.04 (2H, d, J = 9.0, H-2′, 6′). ESI-MS *m/z* 317.51 $[M + H]^+$.

(*E*)-3-(4-(Dimethylamino)phenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (23). Red solid. Yield 63%, mp 118–120°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.04 (6H, s, $N(CH_3)_2$), 3.88 (3H, s, OCH_3), 6.69 (2H, d, J = 9.0, H-Ar), 6.97 (2H, d, J = 9.0, H-Ar), 7.35 (1H, d, J = 15.6, H-*α*), 7.54 (2H, d, J = 9.0, H-Ar), 7.78 (1H, d, J = 15.6, H-*β*), 8.03 (2H, d, J = 9.0, H-Ar). ESI-MS *m/z* 282.59 $[M + H]^+$.

(*E*)-3-(4-Hydroxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (24). Yellow solid. Yield 27%, mp 168–170°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.90 (3H, s, OCH_3), 5.30 (1H, s, OH), 6.88 (2H, d, J = 9.0, H-Ar), 6.98 (2H, d, J = 8.4, H-Ar), 7.42 (1H, d, J = 15.0, H-*α*), 7.56 (2H, d, J = 9.0, H-Ar), 7.76 (1H, d, J = 15.0, H-*β*), 8.03 (2H, d, J = 8.4, H-Ar). ESI-MS *m/z* 255.62 $[M + H]^+$.

(*E*)-3-(Furan-2-yl)-1-(4-methoxyphenyl)prop-2-en-1-one (25). Yellow solid. Yield 91%, mp 76–78°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.88 (3H, s, OCH_3), 6.50 (1H, dd, J_1 = 3.6, J_2 = 1.8, H-4), 6.69 (1H, d, J = 3.6, H-3), 6.97 (2H, d, J = 9.0, H-3′, 5′), 7.47 (1H, d, J = 15.6, H-*α*), 7.51 (1H, d, J = 1.8, H-5), 7.58 (1H, d, J = 15.6, H-*β*), 8.04 (2H, d, J = 9.0, H-2′, 6′). ESI-MS *m/z* 229.56 $[M + H]^+$.

(*E*)-1-(2-Aminophenyl)-3-(3,4-dimethoxyphenyl)prop-2-en-1-one (26). Yellow solid. Yield 88%, mp 84–86°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.92 (3H, s, OCH_3), 3.95 (3H, s, OCH_3), 6.33 (2H, br.s, NH_2), 6.70 (2H, m, H-Ar), 6.89 (1H, d, J = 8.1, H-5), 7.14 (1H, d, J = 1.8, H-2), 7.21 (1H, dd, J_1 = 8.1, J_2 = 1.8, H-6), 7.28 (1H, m, H-Ar), 7.48 (1H, d, J = 15.6, H-*α*), 7.70 (1H, d, J = 15.6, H-*β*), 7.87 (1H, dd, J_1 = 8.1, J_2 = 1.2, H-6′). ESI-MS *m/z* 282.48 $[M - H]^-$.

(*E*)-1-(2-Aminophenyl)-3-(3-nitrophenyl)prop-2-en-1-one (27). Yellow solid. Yield 56%, mp 152–153°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.40 (2H, br.s, NH_2), 6.73 (2H, m, H-Ar), 7.33 (1H, t, J = 7.2, H-Ar), 7.60 (1H, t, J = 7.8, H-Ar), 7.73 (1H, d, J = 15.0, H-*α*), 7.76 (1H, d, J = 15.0, H-*β*), 7.87 (1H, d, J = 9.0, H-Ar), 7.90 (1H, d, J = 7.8, H-Ar), 8.24 (1H, d, J = 9.0, H-Ar), 8.49 (1H, t, J = 1.8, H-Ar). ESI-MS *m/z* 269.75 $[M + H]^+$.

(*E*)-1-(2-Aminophenyl)-3-(4-nitrophenyl)prop-2-en-1-one (28). Yellow solid. Yield 30%, mp 144–147°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.42 (2H, s, NH_2), 6.71 (1H, d, J = 14.7, H-*α*), 7.76 (1H, d, J = 14.7, H-*β*), 6.72 (1H, d, J = 8.1, H-3′), 7.32 (1H, t, J = 8.1, H-5′), 7.74 (1H, m, H-4′), 7.76 (2H, d, J = 8.7, H-2, 6), 7.84 (1H, d, J = 8.1, H-6′), 8.27 (2H, d, J = 8.7, H-3, 5). ESI-MS *m/z* 269.67 $[M + H]^+$.

(*E*)-1-(2-Aminophenyl)-3-(2-fluorophenyl)prop-2-en-1-one (29). Yellow solid. Yield 50%, mp 91–93°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.39 (2H, br.s, NH_2), 6.71 (2H, m, H-Ar), 7.16 (2H, m, H-Ar), 7.34 (2H, m, H-Ar), 7.64 (1H, t, J = 7.5, H-Ar), 7.74 (1H, d, J = 15.6, H-α), 7.85 (1H, d, J = 15.6, H-β), 7.87 (1H, dd, J_1 = 7.8, J_2 = 1.5, H-Ar). ESI-MS *m/z*: 240.48 $[M - H]^-$, 242.58 $[M + H]^+$.

(*E*)-1-(2-Aminophenyl)-3-(3-fluorophenyl)prop-2-en-1-one (30). Yellow solid. Yield 54%, mp 102–104°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.36 (2H, br.s, NH_2), 6.70 (2H, m, H-Ar), 7.10 (1H, m, H-Ar), 7.34 (4H, m, H-Ar), 7.60 (1H, d, J = 15.6, H-α), 7.69 (1H, d, J = 15.6, H-β), 7.85 (1H, dd, J_1 = 8.4, J_2 = 1.2, H-6′). ESI-MS *m/z* 242.56 $[M + H]^+$.

(*E*)-1-(2-Aminophenyl)-3-(4-fluorophenyl)prop-2-en-1-one (31). Yellow solid. Yield 69%, mp 87–90°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.37 (2H, br.s, NH_2), 6.70 (2H, m, H-Ar), 7.10 (2H, d, J = 8.4, H-Ar), 7.30 (1H, t, J = 8.4, H-Ar), 7.55 (1H, d, J = 15.6, H-α), 7.61 (2H, d, J = 8.4, H-Ar), 7.71 (1H, d, J = 15.6, H-β), 7.85 (1H, dd, J_1 = 8.4, J_2 = 1.2, H-6′). ESI-MS *m/z* 242.60 $[M + H]^+$.

(*E*)-1-(2-Aminophenyl)-3-(2,4-dichlorophenyl)prop-2-en-1-one (32). Yellow solid. Yield 70%, mp 132–134°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.40 (2H, br.s, NH_2), 6.68 (1H, dd, J_1 = 7.8, J_2 = 2.1, H-5), 6.71 (1H, d, J = 7.8, H-6), 7.31 (2H, m, H-4′, 5′), 7.46 (1H, d, J = 2.1, H-3), 7.57 (1H, d, J = 15.6, H-α), 7.67 (1H, dd, J_1 = 8.4, J_2 = 1.5, H-3′), 7.82 (1H, dd, J_1 = 8.4, J_2 = 1.2, H-6′), 8.04 (1H, d, J = 15.6, H-β). ESI-MS *m/z*: 327.01 $[M + Cl]^-$, 289.90 $[M - H]^-$.

(*E*)-1-(2-Aminophenyl)-3-(3,4-dichlorophenyl)prop-2-en-1-one (33). Yellow solid. Yield 32%, mp 118–120°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.09 (2H, br.s, NH_2), 6.70 (2H, m, H-3′, 5′), 7.31 (1H, t, J = 8.4, H-4′), 7.42 (1H, dd, J_1 = 8.4, J_2 = 1.8, H-6), 7.47 (1H, d, J = 8.4, H-5), 7.56 (1H, d, J = 15.9, H-α), 7.62 (1H, d, J = 15.9, H-β), 7.69 (1H, d, J = 1.8, H-2), 7.83 (1H, dd, J_1 = 8.4, J_2 = 1.5, H-6′). ESI-MS *m/z* 289.87 $[M - H]^-$.

(*E*)-1-(2-Aminophenyl)-3-(2-bromophenyl)prop-2-en-1-one (34). Yellow solid. Yield 46%, mp 76–78°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.41 (2H, br.s, NH_2), 6.70 (2H, m, H-Ar), 7.30 (3H, m, H-Ar), 7.53 (1H, d, J = 15.6, H-α), 7.63 (1H, dd, J_1 = 8.1, J_2 = 1.2, H-Ar), 7.72 (1H, dd, J_1 = 7.8, J_2 = 1.8, H-Ar), 7.85 (1H, dd, J_1 = 7.5, J_2 = 1.5, H-Ar), 8.08 (1H, d, J = 15.6, H-β). ESI-MS *m/z* 302.55 $[M + H]^+$.

(*E*)-1-(2-Aminophenyl)-3-(furan-2-yl)prop-2-en-1-one (35). Yellow solid. Yield 45%, mp 63–66°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.38 (2H, br.s, NH_2), 6.50 (1H, m, H-Ar), 6.70 (3H, m, H-Ar), 7.29 (1H, m, H-Ar), 7.51 (1H, d, J = 15.3, H-α), 7.53 (1H, m, H-Ar), 7.57 (1H, d, J = 15.3, H-β), 7.89 (1H, dd, J_1 = 8.4, J_2 = 1.5, H-6′). ESI-MS *m/z* 212.40 $[M - H]^-$.

(*E*)-1-(2-Aminophenyl)-3-(naphthalen-2-yl)prop-2-en-1-one (36). Yellow solid. Yield 66%, mp 118–121°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.42 (2H, br.s, NH_2), 6.74 (2H, m, H-Ar), 7.33 (1H, t, J = 7.8, H-Ar), 7.53 (2H, m, H-Ar), 7.75 (1H, d, J = 15.9, H-α), 7.85 (5H, m, H-Ar), 7.92 (1H, d, J = 15.9, H-β), 8.04 (1H, s, H-Ar). ESI-MS *m/z* 274.91 $[M + H]^+$.

(*E*)-1-(4-Aminophenyl)-3-(benzo[d][1,3]dioxol-5-yl)prop-2-en-1-one (37). Yellow solid. Yield 54%, mp 198–200°C. ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 6.08 (2H, s, OCH_2O), 6.12 (2H, br.s, NH_2), 6.59 (2H, d, J = 8.4, H-3′, 5′), 6.95 (1H, d, J = 7.8, H-5), 7.24 (1H, dd, J_1 = 7.8, J_2 = 1.2, H-6), 7.53 (1H, d, J = 15.3, H-α), 7.60 (1H, d, J = 1.2, H-2), 7.73 (1H, d, J = 15.3, H-β), 7.91 (2H, d, J = 8.4, H-2′, 6′). ESI-MS *m/z* 268.46 $[M + H]^+$.

(*E*)-1-(4-Aminophenyl)-3-(3-chlorophenyl)prop-2-en-1-one (38). Yellow solid. Yield 26%, mp 166–168°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 4.25 (2H, br.s, NH_2), 6.70 (2H, d, J = 8.7, H-3′, 5′), 7.34 (2H, m, H-Ar), 7.48 (1H, m, H-Ar), 7.54 (1H, d, J = 15.6, H-α), 7.62 (1H, t, J = 1.5, H-2), 7.70 (1H, d, J = 15.6, H-β), 7.93 (2H, d, J = 8.7, H-2′, 6′). ESI-MS *m/z* 258.61 $[M + H]^+$.

(*E*)-1-(4-Aminophenyl)-3-(4-(dimethylamino) phenyl)prop-2-en-1-one (39). Red solid. Yield 31%, mp 168–170°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.05 (3H, s, CH_3), 3.08 (3H, s, CH_3), 6.69 (2H, s, NH_2), 6.70 (2H, d, J = 9.0, H-3, 5), 6.74 (2H, d, J = 9.0, H-3′, 5′), 7.40 (1H, d, J = 15.3, H-α), 7.57 (2H, d, J = 9.0, H-2, 6), 7.81 (1H, d, J = 15.3, H-β), 8.06 (2H, d, J = 9.0, H-2′, 6′). ESI-MS *m/z* 267.86 $[M + H]^+$.

(*E*)-3-(3,4-Dimethoxyphenyl)-1-(2-nitrophenyl)prop-2-en-1-one (40). Yellow solid. Yield 75%, mp 120–122°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.89 (3H, s, OCH_3), 3.90 (3H, s, OCH_3), 6.84 (1H, d, J = 8.4, H-5), 6.87 (1H, d, J = 16.2, H-α), 7.02 (1H, d, J = 1.8, H-2), 7.05 (1H, dd, J_1 = 8.4, J_2 = 1.8, H-6), 7.17 (1H, d, J = 16.2, H-β), 7.49 (1H, dd, J_1 = 7.8, J_2 = 1.2, H-6′), 7.63 (1H, t, J = 7.8, H-5′), 7.74 (1H, t, J = 7.8, H-4′), 8.15 (1H, dd, J_1 = 7.8, J_2 = 1.2, H-3′). ESI-MS *m/z* 314.53 $[M + H]^+$.

(*E*)-3-(Benzo[d][1,3]dioxol-5-yl)-1-(2-nitrophenyl)prop-2-en-1-one (41). Yellow solid. Yield 84%, mp 126–128°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.01 (2H, s, OCH_2O), 6.78 (1H, d, J = 8.1, H-5), 6.82 (1H, d, J = 15.9, H-α), 6.94 (1H, dd, J_1 = 8.1, J_2 = 1.5, H-6), 7.01 (1H, d, J = 1.5, H-2), 7.16 (1H, d, J = 15.9, H-β), 7.48 (1H, dd, J_1 = 7.8, J_2 = 1.2, H-6′), 7.64 (1H, t, J = 7.8, H-4′), 7.75 (1H, t, J = 7.8, H-5′), 8.15 (1H, dd, J_1 = 7.8, J_2 = 1.2, H-3′). ESI-MS *m/z* 298.71 $[M + H]^+$.

(*E*)-3-(Furan-2-yl)-1-(2-nitrophenyl)prop-2-en-1-one (42). Yellow solid. Yield 81%, mp 93–95°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.49 (1H, dd, J_1 = 3.3, J_2 = 1.5, H-4), 6.66 (1H, d, J = 3.3, H-3), 6.87 (1H, d, J = 15.9, H-*α*), 7.07 (1H, d, J = 15.9, H-*β*), 7.49 (1H, dd, J_1 = 7.8, J_2 = 1.2, H-6′), 7.52 (1H, d, J = 1.5, H-5), 7.64 (1H, t, J = 7.8, H-5′), 7.75 (1H, t, J = 7.8, H-4′), 8.15 (1H, dd, J_1 = 7.8, J_2 = 1.2, H-3′). ESI-MS *m/z* 242.60 $[M - H]^-$.

(*E*)-3-(3,4-Dimethoxyphenyl)-1-(4-nitrophenyl)prop-2-en-1-one (43). Yellow solid. Yield 40%, mp 162–163°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.95 (3H, s, OCH_3), 3.96 (3H, s, OCH_3), 6.92 (1H, d, J = 8.4, H-5), 7.16 (1H, d, J = 1.8, H-2), 7.26 (1H, dd, J_1 = 8.4, J_2 = 1.8, H-6), 7.33 (1H, d, J = 15.6, H-*α*), 7.79 (1H, d, J = 15.6, H-*β*), 8.13 (2H, d, J = 9.0, H-2′, 6′), 8.35 (2H, d, J = 9.0, H-3′, 5′). ESI-MS *m/z* 314.83 $[M + H]^+$.

(*E*)-3-(Benzo[d][1,3]dioxol-5-yl)-1-(4-nitrophenyl)prop-2-en-1-one (44). Yellow solid. Yield 29%, mp 202–204°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.05 (2H, s, OCH_2O), 6.87 (1H, d, J = 8.4, H-5), 7.15 (1H, d, J = 8.4, H-6), 7.18 (1H, s, H-2), 7.31 (1H, d, J = 15.0, H-*α*), 7.77 (1H, d, J = 15.0, H-*β*), 8.12 (2H, d, J = 8.4, H-2′, 6′), 8.34 (2H, d, J = 8.4, H-3′, 5′). ESI-MS *m/z* 298.82 $[M + H]^+$.

(*E*)-3-(3-Chlorophenyl)-1-(4-nitrophenyl)prop-2-en-1-one (45). Yellow solid. Yield 36%, mp 132–134°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 7.39 (1H, t, J = 7.8, H-5), 7.43 (1H, d, J = 7.8, H-4), 7.48 (1H, d, J = 16.2, H-*α*), 7.52 (1H, d, J = 7.8, H-6), 7.65 (1H, t, J = 1.8, H-2), 7.78 (1H, d, J = 16.2, H-*β*), 8.15 (2H, d, J = 9.0, H-2′, 6′), 8.36 (2H, d, J = 9.0, H-3′, 5′). ESI-MS *m/z* 288.39 $[M + H]^+$.

(*E*)-3-(4-Hydroxy-3-methoxyphenyl)-1-(4-nitrophenyl)prop-2-en-1-one (46). Yellow solid. Yield 70%, mp 178–180°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.99 (3H, s, OCH_3), 6.01 (1H, s, OH), 6.98 (1H, d, J = 8.1, H-5), 7.14 (1H, d, J = 1.8, H-2), 7.25 (1H, dd, J_1 = 8.1, J_2 = 1.8, H-6), 7.33 (1H, d, J = 15.6, H-*α*), 7.79 (1H, d, J = 15.6, H-*β*), 8.13 (2H, d, J = 8.4, H-2′, 6′), 8.36 (2H, d, J = 8.4, H-3′, 5′). ESI-MS *m/z* 298.61 $[M - H]^-$.

(*E*)-1-(2-Fluorophenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (47). Yellow solid. Yield 83%, mp 56–58°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.89 (3H, s, OCH_3), 6.96 (2H, d, J = 8.7, H-3, 5), 7.20 (1H, t, J = 9.0, H-5′), 7.30 (1H, d, J = 15.6, H-*α*), 7.31 (1H, m, H-3′), 7.54 (1H, m, H-6′), 7.62 (2H, d, J = 8.7, H-2, 6), 7.75 (1H, d, J = 15.6, H-*β*), 7.84 (1H, t, J = 7.2, H-4′). ESI-MS *m/z* 257.75 $[M + H]^+$.

(*E*)-3-(Benzo[d][1,3]dioxol-5-yl)-1-(2-fluorophenyl)prop-2-en-1-one (48). Yellow solid. Yield 99%, mp 130–132°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.03 (2H, s, OCH_2O), 6.83 (1H, d, J = 8.1, H-Ar), 7.11 (1H, d, J = 15.6, H-*α*), 7.20 (4H, m, H-Ar), 7.52 (1H, m, H-Ar), 7.67 (1H, d, J = 15.6, H-*β*), 7.80 (1H, t, J = 7.8, H-Ar). ESI-MS *m/z* 293.10 $[M + Na]^+$.

(*E*)-3-(4-(Dimethylamino)phenyl)-1-(2-fluorophenyl)prop-2-en-1-one (49). Red solid. Yield 33%, mp 74–76°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.05 (6H, s, $N(CH_3)_2$), 6.68 (2H, d, J = 9.0, H-3, 5), 7.15 (1H, d, J = 15.6, H-*α*), 7.18 (2H, m, H-Ar), 7.47 (1H, m, H-Ar), 7.52 (2H, d, J = 9.0, H-2, 6), 7.70 (1H, d, J = 15.6, H-*β*), 7.78 (1H, m, H-Ar). ESI-MS *m/z* 270.71 $[M + H]^+$.

(*E*)-1-(2-Chlorophenyl)-3-(3,4-dimethoxyphenyl)prop-2-en-1-one (50). Yellow solid. Yield 66%, mp 96–98°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.90 (6H, s, OCH_3), 6.86 (1H, d, J = 8.1, H-5), 6.98 (1H, d, J = 15.9, H-*α*), 7.08 (1H, d, J = 1.8, H-2), 7.12 (1H, dd, J_1 = 8.1, J_2 = 1.8, H-6), 7.37 (1H, d, J = 15.9, H-*β*), 7.41 (4H, m, H-Ar). ESI-MS *m/z* 303.55 $[M + H]^+$.

(*E*)-3-(Benzo[d][1,3]dioxol-5-yl)-1-(2-chlorophenyl)prop-2-en-1-one (51). Yellow solid. Yield 40%, mp 94–96°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.02 (2H, s, OCH_2O), 6.82 (1H, d, J = 7.8, H-5), 6.96 (1H, d, J = 15.6, H-*α*), 7.02 (1H, dd, J_1 = 7.8, J_2 = 1.2, H-6), 7.09 (1H, d, J = 1.2, H-2), 7.35 (1H, t, J = 7.8, H-5′), 7.37 (1H, d, J = 15.6, H-*β*), 7.40 (1H, t, J = 7.8, H-4′), 7.46 (2H, d, J = 7.8, H-3′, 6′). ESI-MS *m/z* 287.56 $[M + H]^+$.

(*E*)-1-(2-Chlorophenyl)-3-(4-hydroxyphenyl)prop-2-en-1-one (52). Yellow solid. Yield 26%, mp 138–140°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.86 (2H, d, J = 9.0, H-3, 5), 6.99 (1H, d, J = 16.2, H-*α*), 7.35 (1H, t, J = 7.8, H-5′), 7.40 (1H, d, J = 16.2, H-*β*), 7.41 (1H, t, J = 7.8, H-4′), 7.45 (2H, m, H-3′, 6′), 7.46 (2H, d, J = 9.0, H-2, 6). ESI-MS *m/z* 259.62 $[M + H]^+$.

(*E*)-1-(3-Chlorophenyl)-3-(3,4-dimethoxyphenyl)prop-2-en-1-one (53). Yellow solid. Yield 66%, mp 110–112°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.95 (3H, s, OCH_3), 3.97 (3H, s, OCH_3), 6.91 (1H, d, J = 7.8, H-5), 7.16 (1H, d, J = 2.1, H-2), 7.25 (1H, dd, J_1 = 7.8, J_2 = 2.1, H-6), 7.33 (1H, d, J = 15.6, H-*α*), 7.45 (1H, t, J = 7.8, H-5′), 7.56 (1H, d, J = 7.8, H-4′), 7.79 (1H, d, J = 15.6, H-*β*), 7.89 (1H, d, J = 7.8, H-6′), 7.98 (1H, t, J = 1.8, H-2′). ESI-MS *m/z* 303.63 $[M + H]^+$.

(*E*)-1-(3-Chlorophenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (54). Yellow solid. Yield 95%, mp 90–93°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.83 (3H, s, OCH_3), 6.92 (2H, d, J = 8.7, H-3, 5), 7.33 (1H, d, J = 15.6, H-*α*), 7.41 (1H, t, J = 7.8, H-5′), 7.51 (1H, d, J = 7.8, H-4′), 7.58 (2H, d, J = 8.7, H-2, 6), 7.78 (1H, d, J = 15.6, H-*β*), 7.86 (1H, d, J = 7.8, H-6′), 7.96 (1H, t, J = 1.5, H-2′). ESI-MS *m/z* 273.68 $[M + H]^+$.

(*E*)-3-(Benzo[d][1,3]dioxol-5-yl)-1-(3-chlorophenyl)prop-2-en-1-one (55). Yellow solid. Yield 85%, mp 124–125°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.03 (2H, s, OCH_2O), 6.84 (1H, d, J = 8.1, H-5), 7.12 (1H, dd, J_1 = 8.1, J_2 = 1.5, H-6), 7.16 (1H, d, J = 1.5, H-2), 7.29 (1H, d, J = 15.3, H-*α*), 7.43 (1H, t, J = 7.8, H-5′), 7.54 (1H, m, H-4′), 7.74 (1H, d, J = 15.3, H-*β*), 7.87 (1H, m, H-6′), 7.96 (1H, t, J = 1.8, H-2′). ESI-MS *m/z* 311.96 $[M + CN]^-$.

(*E*)-1-(4-Chlorophenyl)-3-(3,4-dimethoxyphenyl)prop-2-en-1-one (56). Yellow solid. Yield 47%, mp 102–104°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.94 (3H, s, OCH_3), 3.95 (3H, s, OCH_3), 6.90 (1H, d, J = 8.4, H-5), 7.15 (1H, d, J = 1.8, H-2), 7.23 (1H, dd, J_1 = 8.4, J_2 = 1.8, H-6), 7.33 (1H, d, J = 15.6, H-*α*), 7.47 (2H, d, J = 8.4, H-3′, 5′), 7.76 (1H, d, J = 15.6, H-*β*), 7.95 (2H, d, J = 8.4, H-2′, 6′). ESI-MS *m/z* 303.53 $[M + H]^+$.

(*E*)-3-(Benzo[d][1,3]dioxol-5-yl)-1-(4-chlorophenyl)prop-2-en-1-one (57). Yellow solid. Yield 50%, mp 120–122°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.03 (2H, s, OCH_2O), 6.84 (1H, d, J = 7.8, H-5), 7.12 (1H, dd, J_1 = 7.8, J_2 = 1.2, H-6), 7.16 (1H, d, J = 1.2, H-2), 7.31 (1H, d, J = 15.6, H-*α*), 7.46 (2H, d, J = 9.0, H-3′, 5′), 7.73 (1H, d, J = 15.6, H-*β*), 7.94 (2H, d, J = 9.0, H-2′, 6′). ESI-MS *m/z* 287.53 $[M + H]^+$.

(*E*)-1-(4-Chlorophenyl)-3-(4-hydroxy-3-methoxyphenyl)prop-2-en-1-one (58). Yellow solid. Yield 65%, mp 100–104°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.96 (3H, s, OCH_3), 6.96 (1H, d, J = 8.4, H-5), 7.12 (1H, d, J = 1.2, H-2), 7.22 (1H, dd, J_1 = 8.4, J_2 = 1.2, H-6), 7.32 (1H, d, J = 15.6, H-*α*), 7.47 (2H, d, J = 8.4, H-3′, 5′), 7.75 (1H, d, J = 15.6, H-*β*), 7.95 (2H, d, J = 8.4, H-2′, 6′). ESI-MS *m/z* 289.52 $[M + H]^+$.

(*E*)-1-(4-Chlorophenyl)-3-(furan-2-yl)prop-2-en-1-one (59). Yellow solid. Yield 64%, mp 77–78°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 6.52 (1H, dd, J_1 = 3.6, J_2 = 1.8, H-4), 6.73 (1H, d, J = 3.6, H-3), 7.40 (1H, d, J = 15.6, H-*α*), 7.46 (2H, d, J = 8.4, H-3′, 5′), 7.53 (1H, s, H-5), 7.59 (1H, d, J = 15.6, H-*β*), 7.97 (2H, d, J = 8.4, H-2′, 6′). ESI-MS *m/z* 233.52 $[M + H]^+$.

(*E*)-1-(3-Bromophenyl)-3-(3,4-dimethoxyphenyl)prop-2-en-1-one (60). Yellow solid. Yield 82%, mp 109–111°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.94 (3H, s, OCH_3), 3.96 (3H, s, OCH_3), 6.90 (1H, d, J = 8.1, H-5), 7.15 (1H, d, J = 1.5, H-2), 7.24 (1H, dd, J_1 = 8.1, J_2 = 1.5, H-6), 7.31 (1H, d, J = 15.6, H-*α*), 7.37 (1H, t, J = 7.8, H-5′), 7.69 (1H, m, H-4′), 7.77 (1H, d, J = 15.6, H-*β*), 7.92 (1H, m, H-6′), 8.12 (1H, t, J = 0.9, H-2′). ESI-MS *m/z* 347.53 $[M + H]^+$.

(*E*)-1-(3-Bromophenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (61). Yellow solid. Yield 84%, mp 78–80°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.86 (3H, s, OCH_3), 6.94 (2H, d, J = 8.7, H-3, 5), 7.34 (1H, d, J = 15.6, H-*α*), 7.37 (1H, t, J = 7.8, H-5′), 7.61 (2H, d, J = 8.7, H-2, 6), 7.69 (1H, m, H-4′), 7.80 (1H, d, J = 15.6, H-*β*), 7.92 (1H, m, H-6′), 8.13 (1H, t, J = 1.5, H-2′). ESI-MS *m/z* 513.70 $[1.5\ M + K]^+$.

(*E*)-3-(4-Methoxyphenyl)-1-(naphthalen-2-yl)prop-2-en-1-one (62). Yellow solid. Yield 75%, mp 92–94°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 3.87 (3H, s, OCH_3), 6.96 (2H, d, J = 9.0, H-3, 5), 7.56 (1H, t, J = 7.8, H-Ar), 7.58 (1H, d, J = 15.6, H-*α*), 7.60 (1H, t, J = 7.8, H-Ar), 7.65 (2H, d, J = 9.0, H-2, 6), 7.86 (1H, d, J = 15.6, H-*β*), 7.90 (1H, d, J = 8.4, H-Ar), 7.94 (1H, d, J = 8.4, H-Ar), 8.00 (1H, d, J = 8.4, H-Ar), 8.10 (1H, dd, J_1 = 8.4, J_2 = 1.2, H-Ar), 8.53 (1H, s, H-Ar). ESI-MS *m/z* 287.59 $[M - H]^-$.

(*E*)-3-(4-Hydroxyphenyl)-1-(naphthalen-2-yl)prop-2-en-1-one (63). Yellow solid. Yield 47%, mp 193–194°C. ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 6.87 (1H, m, H-Ar), 6.90 (1H, m, H-Ar), 7.64 (2H, m, H-Ar), 7.76 (1H, d, J = 15.6, H-*α*), 7.78 (1H, m, H-Ar), 7.81 (1H, m, H-Ar), 7.93 (1H, d, J = 15.6, H-*β*), 8.01 (2H, d, J = 8.1, H-3, 5), 8.13 (2H, d, J = 8.1, H-2, 6), 8.90 (1H, s, H-1′), 10.15 (1H, s, OH). ESI-MS *m/z* 273.51 $[M - H]^-$.

(*E*)-3-(3,4-Dihydroxyphenyl)-1-(naphthalen-2-yl)prop-2-en-1-one (64). Yellow solid. Yield 67%, mp 205–209°C. ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 6.84 (1H, d, J = 8.1, H-5), 7.23 (1H, dd, J_1 = 8.1, J_2 = 1.8, H-6), 7.34 (1H, d, J = 1.8, H-2), 7.62 (2H, m, H-Ar), 7.68 (1H, d, J = 15.3, H-*α*), 7.83 (1H, d, J = 15.3, H-*β*), 8.11 (4H, m, H-Ar), 8.89 (1H, s, H-1′), 9.18 (1H, s, OH), 9.79 (1H, s, OH). ESI-MS *m/z* 289.49 $[M - H]^-$.

(*E*)-3-(1*H*-Indol-3-yl)-1-(naphthalen-2-yl)prop-2-en-1-one (65). Yellow solid. Yield 21%, mp 216–218°C. ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 7.26 (2H, m, H-Ar), 7.51 (1H, m, H-Ar), 7.64 (2H, m, H-Ar), 7.84 (1H, d, J = 15.6, H-*α*), 8.03 (2H, m, H-Ar), 8.14 (1H, d, J = 15.6, H-*β*), 8.18 (4H, m, H-Ar), 8.85 (1H, s, H-1′), 11.96 (1H, s, NH). ESI-MS *m/z* 296.94 $[M - H]^-$.

Enzyme Assay. The catalytic domain corresponding to amino acid 378–566 was inserted in the pGEX-4T vector and expressed as a glutathione-*S*-transferase (GST) fusion protein in *E. coli* BL21. The GST-cdc25B fusion protein was purified on a glutathione sepharose column as previously report [24]. Briefly, enzyme assay was carried out in a final volumn of 200 μL on 96-well plates. To each well were added 20 μM FDP and 0.2 μg of cdc25B diluted in 30 mM Tris buffer (pH 8.5) containing 75 mM NaCl, 0.67 mM EDTA, and 1mM DTT with or without compounds (5% DMSO-d_6). Following incubation at room temperature for 1 h, the fluorescence released by enzyme catalysis was measured at 485 nm (excitation) and 538 nm (emission) using a fluorometer.

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