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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

# Synthesis and biologic activities of some novel heterocyclic chalcone derivatives

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**Abstract** We synthesized 36 chalcone-like (*E*)-3-(substitutedphenyl)-1-hetrylprop-2-en-1-ones by condensing 2-acetylfuran/2-acetylpyrrole with substituted benzaldehydes under basic conditions. Of the 36 molecules synthesized, 10 are new to the literature. Bio-evaluation studies of these molecules revealed that compounds **5**, **9**, **15**, **25,** and **29** were potent NorA efflux pump inhibitors against *Staphylococcus aureus* by reducing MIC of ciprofloxacin fourfold, while compounds **11**, **21**, **25**, and **26** showed promising anticancer activity in all four tested cancer cell lines (HL-60, MOLT-4, PC-3, and HeLa). Compound **25** emerged as a very good potentiator of ciprofloxacin against multidrug resistant *S. aureus* and also showed promising anticancer activity. The present communication describes syntheses, bio-evaluation, and structure-related activity of the (*E*)-3-(substitutedphenyl)-1-hetrylprop-2-en-1-ones.

**Keywords** Chalcone · (*E*)-3-(substitutedphenyl)-1-hetrylprop-2-en-1-ones · NorA efflux pump inhibitors · *Staphylococcus aureus* · Docking study

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## Introduction

Chalcones are an important class of secondary metabolites which are precursors of many naturally occurring plant pigments (Wong, 1968). These small molecules are also used as starting materials in the synthesis of UV absorption filters in polymers, photorefractive polymers, photosensitizers in color films, sweeteners in food technology, and in holographic recording technology. They have significant commercial applications in medical therapy due to the wide range of valuable biologic activities which include antimutagenic, antibacterial, antiviral, anti-inflammatory, anti-ulcerative, hepatoprotective, and anticancer activities (Forejtníkov *et al.*, 2005). Chalcones, considered as the precursors of flavonoids and isoflavones, are also known to be effective antimicrobial agents (Tsukiyama *et al.,* 2002; Friss-Möller *et al.,* 2002; Fukai *et al.,* 2002; Kromann *et al.,* 2004; Hatono *et al.,* 2000; Nielsen *et al.*, 2005; Bremner and Meyer, 1998; Belofsky *et al.,* 2004; Mustafa *et al.,* 2003; Joshi *et al.,* 2001).

Recently, bacterial resistance to antimicrobic agents has resulted in serious public health problems. Several different mechanisms have been put forward for the development of bacterial resistance. In one of these mechanisms, access of the antibiotic into the cell is prevented or reduced by decreasing the transport of the antibiotic into the cell or by

increasing the efflux of the drug from the cell to the outside medium by efflux pumps. Efflux pumps are found in both Gram-positive and -negative pathogens and some of these drug pumps confer multiple-drug resistance (MDR), and the NorA protein of *Staphylococcus aureus* is one of such pumps (Prasad *et al.,* 2007; Memurry *et al.,* 1980). NorA is a member of the major facilitator superfamily (MFS) of transport proteins, one of the most studied MDR pumps. Its substrates include antimicrobial agents such as ciprofloxacin and norfloxacin and dyes like ethidium bromide and acriflavine (Li and Nikaido, 2004). Chalcones have been found to potentiate the activity of berberine, erythromycin, and tetracycline, demonstrating a mode of action consistent with inhibition of the NorA MDR efflux pump in *S. aureus* (Poole, 2005).

Cancer is the second leading cause of human death in the developing as well as advanced countries. Among naturally occurring chalcones and their synthetic analogs (Achanta *et al.,* 2006; Romagnoli *et al.,* 2008; Echeverria *et al.,* 2009; Szliszka *et al.,* 2010; Ilango *et al.,* 2010), several compounds have been found to have cytotoxic activity (antimitotic, a cell growth inhibitor) toward cultured tumor cells. Chalcones are also known to possess antioxidant character at various extents. Activated macrophages play a key role in inflammatory responses and release a variety of mediators including nitric oxide (NO). NO is a potent vasodilator that facilitates leukocytic migration and formation of edema as well as leukocytic activity and cytokine production (Belofsky *et al*., 2004).

Keeping in view the wide range of activities of the chalcones, many research groups have synthesized these molecules (Bandgar *et al.,* 2010; Rateb and Zohdi, 2009; Bsasaif *et al.,* 2005). We designed and synthesized a number of chalcone-like molecules in which one of the phenyl rings (ring-B) has been replaced by a heterocyclic ring (pyrrole/furan ring) for bio-evaluation of their bioenhancing, anticancer, anti-inflammatory, and antioxidant activities. In this communication, we report the preparation of (*E*)-3-(substitutedphenyl)-1-hetrylprop-2-en-1-ones with chemical diversification and identification of potent lead molecules along with structure activity relationship of these analogs.

## Results and discussion

### Chemistry

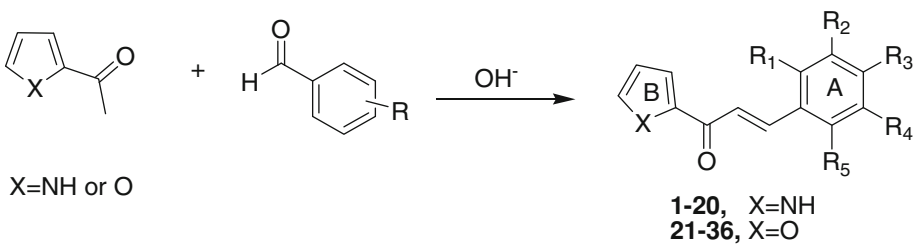
In the present investigation, 36 chalcone-like molecules viz (*E*)-3-(substitutedphenyl)-1-(1*H*-pyrrol-2-yl)prop-2-en-1-ones (**1–20**) and (*E*)-3-(substitutedphenyl)-(1-furan-2-yl) prop-2-en-1-ones (**21–36**) have been synthesized by Claisen–Schmidt's condensation of 2-acetylfuran/2-acetylpyrrol with substituted benzaldehydes under basic conditions (Scheme 1). The synthesized chemical entities (**1–36**) with diversification in chemical structures are shown in Table 1.

All the compounds were chemically characterized based on their spectral and physical data. A literature search revealed that out of 36 molecules synthesized, compounds **5, 6, 7, 9, 13, 14, 27–29,** and **36** are new to the literature.

The structure of compound **9** was further confirmed by X-ray analysis of single crystal. The crystal used for data collection was of the dimension 0.3 × 0.2 × 0.1 mm. The cell dimensions were determined by least-square fit of angular settings of 2,440 reflections in the $\theta$ range 2.59°–27.45°, Table 2. Selected bond distances and bond angles are listed in Table 3. An ORTEP view of compound **9** with atomic labeling is shown in Fig. 1 (Radwan and Abbas, 2009).

The geometry of the molecule was calculated using the WinGX and PARST software (Farrugia, 1997, 1999). Bond lengths and bond angles of the title molecule show a fair amount of agreement with some related molecules (Nardelli, 1995; Li, 2008; Tang *et al.,* 2008). The six C–C bond lengths in the phenyl ring lie in the range 1.381(4)–1.408(3) Å. The bond angles in the phenyl ring vary from 116.4(2)° to 122.7(2)° with an average of 120.0(2)°. In the title molecule, the bond lengths N1′–C5′ and N1′–C2′ are 1.345(3) and 1.378(3) Å, respectively. The C1=O1 distance [1.241(3) Å] is significantly longer than those usually observed for carbonyl bonds, probably because atom O1 is involved in intramolecular C–H···O hydrogen bond (Table 4).

The pyrrole and phenyl rings are perfectly planar (maximum deviations: 0.006(2) Å for C5′ and 0.010(2) Å for C1″). Different to most substituted chalcones, the molecule of the title compound is non-planar with a




**Scheme 1** Synthesis of (*E*)-3-(substitutedphenyl)-1-hetrylprop-2-en-1-ones by Claisen–Schmidt condensation of 2-acetyl furan/2-acetylpyrrole with substituted benzaldehydes. Substituents of aldehyde and products (**1–36**) are provided in Table 1

**Table 1** Synthesis of (*E*)-3-(substitutedphenyl)-1-hetrylprop-2-en-1-ones

| Entry | Substitutions | | | | | | Yield (%) | Reaction time (h) | m.p. (°C) |
|---|---|---|---|---|---|---|---|---|---|
| | X | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | | | |
| **1** | NH | H | H | H | H | H | 68.8 | 15 | 195.8 |
| **2** | NH | H | H | $NO_2$ | H | H | 72.72 | 15 | 205.3 |
| **3** | NH | H | $NO_2$ | H | H | H | 77.27 | 18 | 205.7 |
| **4** | NH | Cl | H | Cl | H | H | 58.33 | 15 | 172.4 |
| **5** | NH | $OCH_3$ | $OCH_3$ | H | H | H | 45.45 | 15 | 107.2 |
| **6** | NH | Cl | Cl | H | H | H | 66.66 | 15 | 193.7 |
| **7** | NH | Cl | H | H | H | Cl | 74.16 | 15 | 162.2 |
| **8** | NH | H | $OCH_3$ | H | H | H | 63.25 | 18 | 148.5 |
| **9** | NH | Br | H | H | H | H | 62.50 | 15 | 133.9 |
| **10** | NH | H | H | F | H | H | 37.57 | 15 | 139.6 |
| **11** | NH | H | H | Cl | H | H | 72.58 | 18 | 116.0 |
| **12** | NH | H | H | $N(CH_3)_2$ | H | H | 70.00 | 24 | 203.8 |
| **13** | NH | $OCH_3$ | H | H | H | $OCH_3$ | 71.0 | 15 | 128.7 |
| **14** | NH | Cl | H | H | $NO_2$ | H | 87.5 | 48 | 228.5 |
| **15** | NH | Cl | H | H | H | H | 90 | 24 | 116.0 |
| **16** | NH | H | H | Br | H | H | 87.5 | 15 | 178.5 |
| **17** | NH | $OCH_3$ | H | $OCH_3$ | H | H | 95 | 18 | 105.1 |
| **18** | NH | H | H | $OCH_3$ | H | H | 95 | 20 | 137.2 |
| **19** | NH | H | $OCH_3$ | $OCH_3$ | H | H | 95 | 20 | 166.4 |
| **20** | NH | H | [a] | [a] | H | H | 65 | 22 | 153.4 |
| **21** | O | Cl | H | H | H | Cl | 86.13 | 48 | 96.4 |
| **22** | O | Br | H | H | H | H | 70 | 16 | 60.8 |
| **23** | O | H | H | F | H | H | 90 | 15 | 114.2 |
| **24** | O | H | H | Cl | H | H | 95 | 15 | – |
| **25** | O | H | H | $N(CH_3)_2$ | H | H | 96 | 18 | 88.9 |
| **26** | O | H | $NO_2$ | H | H | H | 72.5 | 18 | 181.2 |
| **27** | O | H | H | H | H | H | 55.5 | 24 | 87.5 |
| **28** | O | Cl | H | H | $NO_2$ | H | 90 | 48 | 184.9 |
| **29** | O | $OCH_3$ | $OCH_3$ | H | H | H | 75 | 15 | 67.5 |
| **30** | O | H | [a] | [a] | H | H | 67 | 12 | 180 |
| **31** | O | H | $OCH_3$ | $OCH_3$ | H | H | 43 | 24 | 109.5 |
| **32** | O | H | H | $NO_2$ | H | H | 80 | 15 | 230.6 |
| **33** | O | H | H | Br | H | H | 89 | 15 | 131.6 |
| **34** | O | H | H | $OCH_3$ | H | H | 90 | 15 | 82.5 |
| **35** | O | H | $OCH_3$ | $OCH_3$ | $OCH_3$ | H | 67 | 10 | 149.6 |
| **36** | O | $OCH_3$ | H | H | $OCH_3$ | H | 30 | 18 | 54 |

[a] $R_2R_3$ = (–O–$CH_2$–O–)

dihedral angle of 35.16 (8)° between the pyrrole and phenyl rings (Jasinski *et al.,* 2009). The angles between the mean plane of the prop-2-en-1-one group and the mean planes of the pyrrole and phenyl rings are 15.7 (1) and 30.7(1)°, respectively. In the crystal structure, intermolecular N1′–H1′···O1 hydrogen bond links the molecules into centrosymmetric dimers (Fig. 2). Dimers are arranged in a manner to form layers (Fig. 3). Within the layers, the dimers are arranged parallel to each other.

## Biologic evaluation

### *In vitro combination study of ciprofloxacin with molecules (**1–36**)*

The MIC of the compounds (**1–36**) was determined to use these molecules at a concentration devoid of antibacterial activity, a prerequisite of any compound to be used as safe efflux pump inhibitors (EPIs). The compounds (**1–36**) were

**Table 2** Crystal data and other experimental details of compound (**9**)

| | |
|---|---|
| CCDC number | 776070 |
| Crystal description | Yellow plate |
| Crystal size | 0.3 × 0.2 × 0.1 mm |
| Empirical formula | $C_{13}H_{10}BrNO$ |
| Formula weight | 276.13 |
| Radiation, Wavelength | Mo Kα, 0.71073 Å |
| Unit cell dimensions | a = 31.524(11), b = 7.266(2), c = 10.000(3) Å, β = 93.171(9) |
| Crystal system | Monoclinic |
| Space group | *C*2/*c* |
| Unit cell volume | 2286.9(13) $Å^3$ |
| No. of molecules per unit cell (Z) | 8 |
| Temperature | 100(2) K |
| Absorption coefficient | 3.571 $mm^{-1}$ |
| F(000) | 1104 |
| $\theta$ range for entire data collection | $2.88° < \theta < 28.36°$ |
| Reflections collected/unique | 6,806/2,673 |
| Reflections observed [$I > 2\sigma(I)$] | 2,029 |
| Refinement | Full-matrix least-squares on $F^2$ |
| No. of parameters refined | 185 |
| Final R-factor | 0.0343 |
| wR($F^2$) | 0.0879 |
| Weight | $1/[\sigma^2(F_o^2) + (0.0493P)^2 + 0.0000P]$ where $P = [F_o^2 + 2F_c^2]/3$ |
| Goodness-of-fit | 1.000 |
| $(\Delta/\sigma)_{max}$ | −0.001 (for × Br1) |
| Final residual electron density | $-0.643 < \Delta\rho < 0.597 eÅ^{-3}$ |

**Table 3** Selected bond lengths (Å) and bond angles (°) for non-hydrogen atoms (e.s.d.s are given in parentheses)

| | | | |
|---|---|---|---|
| Br1–C2″ | 1.905(2) | O1–C1 | 1.241(3) |
| C1–C2 | 1.482(3) | C2–C3 | 1.340(4) |
| N1′–C5′ | 1.345(3) | N1′–C2′ | 1.378(3) |
| O1–C1–C2 | 120.8(2) | C3–C2–C1 | 119.3(2) |
| C5′–N1′–C2′ | 110.4(2) | N1′–C2′–C3′ | 106.3(2) |
| N1′–C2′–C1 | 121.7(2) | N1′–C5′–C4′ | 108.3(2) |
| C3″–C2″–Br1 | 116.5(2) | | |

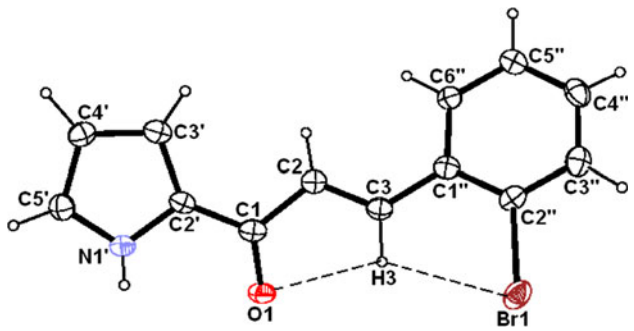



**Fig. 1** *ORTEP* view of the molecule (**9**) with displacement ellipsoids drawn at 50 % probability level. H atoms are shown as *small spheres* of arbitrary radii. The *broken lines* show the intramolecular C–H···O, C–H···Br hydrogen bonds

studied in combination with ciprofloxacin (standard drug) and bio-evaluated against NorA over expressing *S. aureus* 1199B (Bandgar *et al.,* 2010; Kaatz *et al.,*1993, 1999). Along with these synthetic molecules, two known EPIs namely reserpine and verapamil were also used for the comparative studies (Kaatz and Seo, 1995; Neyfakh *et al.,*1993). Ciprofloxacin alone showed MIC at 8 μg/mL against NorA over expressing *S. aureus* 1199B. Among the library of 36 molecules used in combination with ciprofloxacin and tested against *S. aureus* 1199B, only compounds **5**, **9**, **10**, **15**, **17**, **18**, **25**, **29**, and **33** could reduce the MIC of the drug (Table 5) and rest of the molecules failed to potentiate the antibacterial activity of the drug. However, the compounds **5**, **15**, **29**, **25**, and **33** showed the

**Table 4** Hydrogen-bonding geometry (e.s.d.s in parentheses)

Symmetry code: (i) 1/2 − x, 1/2 − y, 2 − z

| D–H···A | D–H(Å) | H···A(Å) | D···A(Å) | D–H···A(°) |
|---|---|---|---|---|
| C3–H3···Br1 | 1.00(2) | 2.76(2) | 3.187(3) | 106(1) |
| C3–H3···O1 | 1.00(2) | 2.43(2) | 2.798(3) | 101(2) |
| N1′–H1′ ···O1$^{i}$ | 0.74(3) | 2.11(3) | 2.824(3) | 162(3) |

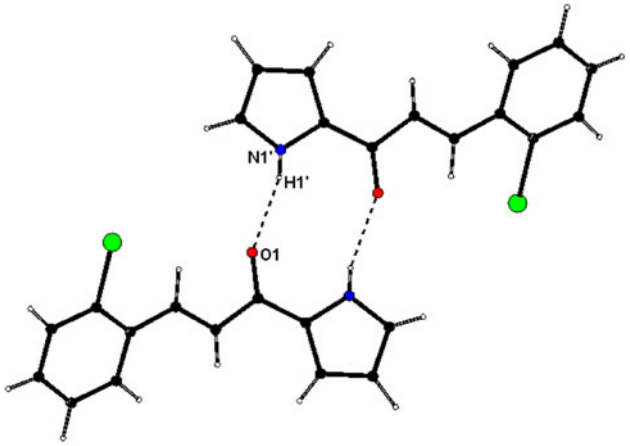



**Fig. 2** A *plot* of two molecules of the compound (**9**) showing the intermolecular N–H···O hydrogen bonds (*dashed lines*)

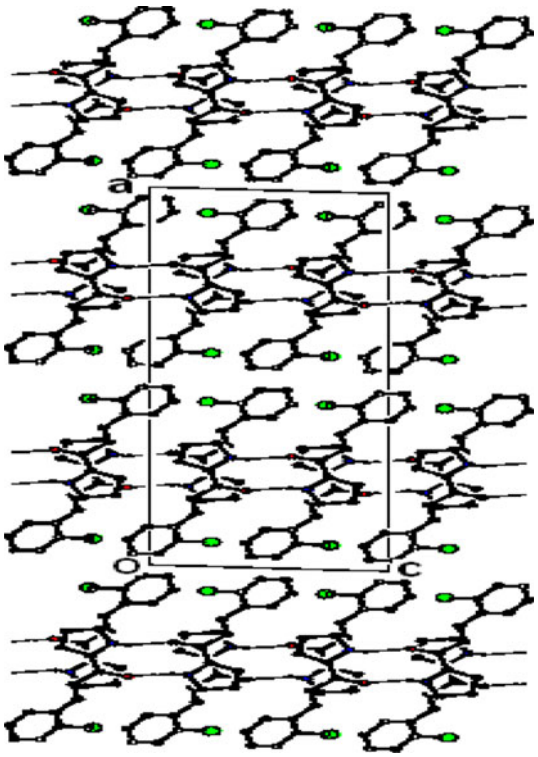



**Fig. 3** Appearance of layers of dimers of the compound (**9**) that are hydrogen bonded

fourfold reduction of MIC of ciprofloxacin and the rest of the active compounds indicated a twofold reduction in the MIC of ciprofloxacin. Compound **25** was found to be the most active compound in this study, which showed fourfold reduction in the MIC of ciprofloxacin at 12.5 μg/mL conc. against *S. aureus* 1199B.

## Anticancer activity

Among the currently identified antitumor agents, chalcones represent an important class of molecules that are abundant in edible plants. The anticancer activity of certain chalcones is believed to be a result of binding to tubulin and preventing it from polymerizing into microtubules (Lawrence *et al.,* 2006). The prepared synthetics (**1**–**36**) were also evaluated for their anticancer activity against four different cancer cell lines (HL-60, MOLT-4, PC-3, and HeLa). Out of 36, 14 molecules showed significant anticancer activity (Table 6). Compound **25** having $-N(CH_3)_2$ substitution at ring A ($R_3$) was the most active. Compounds **11**, **21**, and **24** having chloro substitution at different positions in ring A of (*E*)-3-(substitutedphenyl)-1-hetrylprop-2-en-1-ones also showed promising anticancer activity.

Compounds **2**, **3**, and **26** having nitro substitution in ring A also exhibited promising anticancer activity, while compounds **14** and **28** having both nitro and chloro substitutions in ring A of (*E*)-3-(substitutedphenyl)-1-hetrylprop-2-en-1-ones were less active. Compounds without any modification in these rings did not show any anticancer activity (**1** and **27**).

## Anti-inflammatory and antioxidant activity

Anti-inflammatory and antioxidant activities of all the synthesized molecules were determined using carrageenan-induced inflammation and DPPH methods, respectively. Out of the 36 synthetics tested, except compound **31** which showed mild anti-inflammatory activity at 100 mg/kg p.o. (23 % inhibition), others were devoid of activity (data not shown).

## Molecular docking study

A flexible docking study was performed in order to rationalize the observed cytotoxic activity of compound **25.** GOLD software was employed for this purpose and Goldscore was used to score the binding conformations. The coordinates of the colchicine-binding site of tubulin receptor

**Table 5** Ciprofloxacin activity against *S. aureus* 1199B in combination with (*E*)-3-(substitutedphenyl)-1-hetrylprop-2-en-1-ones (**1**–**36**)

| Compound | MEC[a] of compounds | MIC[b] of ciprofloxacin (μg/mL) | | |
|---|---|---|---|---|
| | | Without EPI | With EPI | Fold reduction |
| **1** | >50 | 8 | 8 | 0 |
| **2** | >50 | 8 | 8 | 0 |
| **3** | >50 | 8 | 8 | 0 |
| **4** | >50 | 8 | 8 | 0 |
| **5** | 25 | 8 | 2 | 4 |
| **6** | >50 | 8 | 8 | 0 |
| **7** | >50 | 8 | 8 | 0 |
| **8** | >50 | 8 | 8 | 0 |
| **9** | 25 | 8 | 2 | 4 |
| **10** | 25 | 8 | 4 | 2 |
| **11** | >50 | 8 | 8 | 0 |
| **12** | >50 | 8 | 8 | 0 |
| **13** | >50 | 8 | 8 | 0 |
| **14** | >50 | 8 | 8 | 0 |
| **15** | 25 | 8 | 2 | 4 |
| **16** | >50 | 8 | 8 | 0 |
| **17** | 25 | 8 | 4 | 2 |
| **18** | 25 | 8 | 4 | 2 |
| **19** | >50 | 8 | 8 | 0 |
| **20** | >50 | 8 | 8 | 0 |
| **21** | >50 | 8 | 8 | 0 |
| **22** | >50 | 8 | 8 | 0 |
| **23** | >50 | 8 | 8 | 0 |
| **24** | >50 | 8 | 8 | 0 |
| **25** | 12.5 | 8 | 2 | 4 |
| **26** | >50 | 8 | 8 | 0 |
| **27** | >50 | 8 | 8 | 0 |
| **28** | >50 | 8 | 8 | 0 |
| **29** | 25 | 8 | 2 | 4 |
| **30** | >50 | 8 | 8 | 0 |
| **31** | >50 | 8 | 8 | 0 |
| **32** | >50 | 8 | 8 | 0 |
| **33** | 25 | 8 | 4 | 2 |
| **34** | >50 | 8 | 8 | 0 |
| **35** | >50 | 8 | 8 | 0 |
| **36** | >50 | 8 | 8 | 0 |
| Reserpine | 25 | 8 | 8 | 0 |
| Verapamil | 50 | 8 | 4 | 2 |

[a] Minimum effective concentration

[b] Minimum inhibitory concentration

were obtained from a protein data bank (PDB ID: 1SA0) (Ravelli *et al.*, 2004) on which docking was performed. To validate the docking procedure for the prediction of the correct binding mode of ligands at the colchicine-binding site, colchicine was extracted from the original crystal structure (1SA0) and re-docked using GOLD. The highest scoring conformation was selected and compared with crystal structure conformation based on RMSD (0.72 Å).

The best binding conformation of the compound **25** in a colchicine-binding site was selected based on the GOLD score and visual inspection. In the binding conformation, compound **25** fits well in the binding cavity of colchicine (Fig. 4). Oxygen of the furan ring is involved in an important hydrogen bonding interaction with Met 259, which acts as an anchor to hold the compound in the cavity. Moreover, phenyl ring of compound **25** finds optimum

**Table 6** List of $IC_{50}$ values (μM) of active compounds in four human cancer cell lines

| Compounds | HL-60 | PC-3 | MOLT-4 | Hela |
|---|---|---|---|---|
| **1** | >100 | >100 | >100 | >100 |
| **2** | 14 | 13 | 15 | 26 |
| **3** | 20 | 23 | 22 | 32 |
| **4** | 22 | 22 | 13 | 26 |
| **8** | 16 | 24 | 28 | 30 |
| **9** | 42 | 44 | 38 | 44 |
| **11** | 13 | 18 | 22 | 25 |
| **14** | 38 | 55 | 42 | 68 |
| **16** | 32 | 44 | 49 | >100 |
| **21** | 12 | 14 | 25 | 26 |
| **24** | 19 | 29 | 23 | 38 |
| **25** | 12 | 13 | 12 | 20 |
| **26** | 14 | 14 | 18 | 22 |
| **27** | 100 | >100 | >100 | >100 |
| **28** | 58 | 62 | 72 | >100 |
| **33** | 48 | 58 | 62 | >100 |

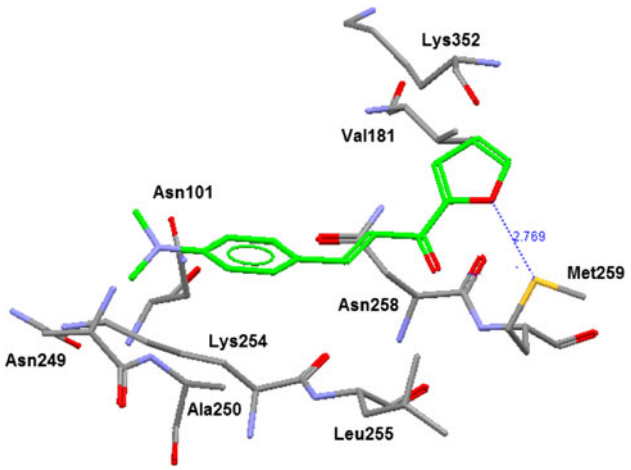



**Fig. 4** Docking conformation of compound **25** at colchicine-binding site of tubulin receptor

position over the Lys254 and Leu255, and the dimethyl amine is present in vicinity of the Asn101 and Asn249.

## Conclusion

Preparations of a series of chalcone-like derivatives, having a B ring either as pyrrole or furan, and their biologic activities are described. Compounds **11**, **21**, **25,** and **26** were found to have good anticancer activity in all four tested cancer cell lines (HL-60, MOLT-4, PC-3, and HeLa), while compounds **5**, **9**, **10**, **15**, **17**, **18**, **25**, **29,** and **33** were identified as EPIs against *S. aureus*. Compounds with methoxy substitution did not reveal any significant activity. Molecules **1**–**36** possess insignificant antioxidant and anti-inflammatory activities. The result of this study finds compound **25** as the lead molecule for the development of improved therapeutic agents designed to fight cancer as well as a NorA EPI.

## Experimental

### Materials and methods

Reagents for chemical synthesis were obtained from Sigma-Aldrich. The solvents used in reactions were distilled and dried before use. Reactions were monitored by TLC on 0.25-mm silica gel 60 $F_{254}$ plates (E. Merck) using UV light, or ceric ammonium sulfate solution for visualization of the spots. Melting points were recorded on Buchi-510 instrument and elemental analyses were performed on Elementar vario EL-III. $^{1}$H NMR and $^{13}$C NMR spectra were recorded on Bruker DPX 200/400/500 instruments using $CD_3OD/CDCl_3$/DMSO-$d_6$ as the solvent with TMS as the internal standard. Mass spectra were recorded on ESI-esquire 3000 Bruker Daltonic's instrument and IR spectra were recorded on Bruker Vector 22 instruments. X-ray intensity data were collected at 100 K on Bruker CCD area-detector diffractometer equipped with graphite monochromated Mo Kα radiation.

*General procedure for synthesis of chalcone-like (E)-3-(substitutedphenyl)-1-hetrylprop-2-en-1-ones (**1–36**)*

2-Acetylpyrrole/2-acetylfuran (4 mmol) was taken in a flask (100 mL) and dissolved in 10 mL methanol. Substituted benzaldehyde (4 mmol) was added to the solution

followed by 10 % aqueous NaOH solution (2 mL), and the reaction mixture was kept in stirred condition at 15–20 °C until completion of the reaction. Progress of the reaction was monitored by TLC (7:3, *n*-hexan:acetone). Spots on TLC were visualized by spraying with 2 % ceric ammonium sulfate spray reagent followed by heating the plate at 120 °C. After completion of the reaction, the mixture was diluted with distilled water and allowed to stand at room temperature for precipitation. Precipitated solid was filtered and recrystallized from EtOH/EtOAc. The melting point, reaction time, and yield of the products are shown in Table 1. The purity of products was monitored on TLC (30 % acetone in *n*-hexane). Spectral data and elemental analysis of synthesized molecules are given below.

*(E)-3-Phenyl-1-(1H-pyrrol-2-yl)prop-2-en-1-one* (***1***) MS: $M^+$ at *m/z* 197. Anal. Calcd for $C_{13}H_{11}NO$: C, 79.16; H, 5.62; N, 7.10 %. Found: C, 79.28; H, 5.60; N, 7.25 %. $^1$H NMR (200 MHz, $CD_3OD$): $\delta$ 6.32 (dd, 1H, $J = 2.4$ Hz and 3.8 Hz, H-4′), 7.19 (d, 1H, $J = 15.0$ Hz, H-2), 7.34 (m, 5H, H-2″, H-3″, H-4″, H-5″and H-6″), 7.45 (d, 1H, $J = 15.0$ Hz, H-3), 7.76 (bs, 2H, H-3′ and H-5′), 10.65 (s,1H, NH). $^{13}$C NMR (100 MHz, $CD_3OD$) : $\delta$ 178.81 (C-1), 140.94 (C-3), 133.12 (C-1″), 131.35 (C-2′), 130.21 (C-3″and C-5″), 130.12 (C-4″), 127.98 (C-5′), 126.08 (C-2″and C-6″), 125.90 (C-3′), 121.88 (C-2), 111.43 (C-4′).

*(E)-3-(4-Nitro-phenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one* (***2***) MS: $M^+$ at *m/z* 242. Anal. Calcd for $C_{13}H_{10}N_2O_3$: C, 64.46; H, 4.16; N, 11.56 %. Found: C, 64.57; H, 4.14; N, 11.67 %. MS. $^1$H NMR (200 MHz, DMSO-$d_6$): $\delta$ 6.34 (dd, 1H, $J = 2.4$ and 3.8 Hz, H-4′), 7.19 (d, 1H, $J = 15.2$ Hz, H-2), 7.34 (d, 1H, $J = 15.2$ Hz, H-3), 7.76 (bs, 2H, H-3′and H-5′), 7.79 (d, 2H, $J = 8.8$ Hz, H-2″ and H-6″), 8.79 (d, 2H, $J = 8.8$ Hz, H-3″and H-5″), 9.50 (s,1H, H-1′, NH). $^{13}$C NMR (100 MHz, DMSO-$d_6$): 178.10 (C-1), 162.49, (C-4″), 142.46 (C-3), 140.18 (C-2′), 133.15 (C-1″), 128.42 (C-2″ and C-6″), 128.02 (C-5′), 125.73 (C-3′), 120.6 (C-2), 120.58 (C-3″and C-5″), 111.97 (C-4′).

*(E)-3-(3-Nitrophenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one* (***3***) MS: $M^+$ at *m/z* 242. Anal. Calcd for $C_{13}H_{10}N_2O_3$: C, 64.46; H, 4.16; N, 11.56 %. Found: C, 64.38; H, 4.70; N, 11.67 %. $^1$H NMR (200 MHz, DMSO-$d_6$): $\delta$ 6.31 (bs, 1H, H-4′), 7.21(bs, 1H, H-3′),7.48 (bs, 1H, H-5′), 7.72 (dd, $J = 8.52$ Hz and 8.04 Hz, H-5″), 7.74 (dd, 1H, $J = 16.00$ Hz, H-2), 7.92 (dd, 1H, $J = 16$ Hz, H-3), 8.28 (m, 2H, H-4″ and H-6″), 8.72 (s, 1H, H-2″), 9.65 (s, 1H, H-1′, NH). $^{13}$C NMR (125 MHz, DMSO-$d_6$): 178.10 (C-1), 149.46 (C-3″), 140.29 (C-3), 135.18 (C-1″), 133.87 (C-6″), 132.15 (C-2′), 129.42 (C-5″), 128.19 (C-5′), 125.73 (C-3′), 122.19 (C-2), 122.92 (C-2″), 120.69 (C-4″), 112.91(C-4′).

*(E)-3-(2,4-Dichloro-phenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one* (***4***) MS: $M^+$ at *m/z* 266. Anal. Calcd for $C_{13}H_9Cl_2NO$: C, 58.67; H, 3.41; N, 5.26 %. Found: C, 58.76; H, 4.45; N, 5.38 %. $^1$H NMR (200 MHz, DMSO-$d_6$): $\delta$ 6.37 (bs, 1H, H-4′), 7.10 (d, 1H, $J = 15.60$ Hz, H-2), 7.30 (m, 3H, H-5″, H-6″ and H-3′), 7.47 (d, 1H, $J = 1.9$ Hz, H-3″), 7.69 (d, 1H, $J = 8.60$ Hz, H-5′), 8.13 (d, 1H, $J = 15.60$ Hz, H-3), 10.50 (s, 1H, NH). $^{13}$C NMR (100 MHz, DMSO-$d_6$): 178.10 (C-1), 140.38 (C-3), 135.81 (C-4″), 133.65 (C-2″), 133.03 (C-2′), 131.84 (C-3″), 131.23 (C-1″), 130.27 (C-6″), 128.59 (C-5′), 127.89 (C-5″), 126.21 (C-3′), 122.59 (C-2),115.89 (C-4′).

*(E)-3-(2,3-Dimethoxy-phenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one* (***5***) MS: $M^+$ at *m/z* 257. Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44 %. Found: C, 70.16; H, 4.92; N, 5.47 %. $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 3.89 (s, 6H, 2 × $OCH_3$), 6.35 (bs, 1H, H-4′), 6.96 (d, 1H, $J = 8.22$ Hz, H-4″), 7.10 (m, 2H, H-5″ and H-6″), 7.28 (m, 2H, H-3′ and H-5′), 7.42 (d, 1H, $J = 15.90$ Hz, H-2), 8.11 (d, 1H, $J = 15.90$ Hz, H-3), 10.25 (s, 1H, NH). $^{13}$C NMR (125 MHz, DMSO-$d_6$): 178.10 (C-1), 162.49 (C-3″), 159.40 (C-2″), 145.34 (C-3), 135.98 (C-2′), 129.32 (C-5′), 125.88 (C-3′), 123.24 (C-5″), 122.09 (C-2), 120.00 (C-6″), 116.77 (C-1″), 115.87 (C-4″), 109.94 (C-4′), 55.95 $(OCH_3)_2$.

*(E)-3-(2,3-Dichloro-phenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one* (***6***) MS: $M^+$ at *m/z* 266. Anal. Calcd for $C_{13}H_9Cl_2NO$: C, 58.67; H, 3.41; N, 5.26 %. Found: C, 59.72; H, 4.48; N, 5.37 %. $^1$H NMR (200 MHz, $CD_3OD$): $\delta$ 6.32 (dd, 1H, $J = 2.62$ and 3.74 Hz, H-4′), 7.16 (m, 4H, H-3′, H-4″, H-5″and H-6″), 7.23 (m, 1H, H-5′), 7.55 (d, 1H, $J = 15.90$ Hz, H-2), 8.06 (d, 1H, $J = 15.90$ Hz, H-3), 10.52 (s, 1H, NH). $^{13}$C-NMR (125 MHz, $CD_3OD$): $\delta$ 178.28 (C-1), 140.92 (C-3), 135.92 (C-1″), 135.07 (C-3″), 133.42 (C-2′), 131.92 (C-4″), 130.21 (C-5″), 129.37 (C-2″), 128.01 (C-5′), 126.52 (C-6″), 125.95 (C-3′), 122.09 (C-2), 113.05 (C-4′).

*(E)-3-(2,6-Dichloro-phenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one* (***7***) MS: $M^+$ at *m/z* 266. Anal. Calcd for $C_{13}H_9Cl_2NO$: C, 58.67; H, 3.41; N, 5.26 %. Found: C, 59.79; H, 3.18; N, 5.23 %. $^1$H-NMR (200 MHz, $CD_3OD$): $\delta$ 6.32 (dd, 1H, $J = 2.41$ Hz and 3.89 Hz, H-4′), 7.17 (m, 1H, H-3′), 7.31 (d, 1H, $J = 15.98$ Hz, H-2), 7.55 (m, 3H, H-3″, H-4″ and H-5″), 7.75 (bs, 1H, H-5′), 7.87 (d, 1H, $J = 15.98$ Hz, H-3), 10.25 (s, 1H, H-1′,NH). $^{13}$C NMR (125 MHz, $CD_3OD$): $\delta$ 179.91 (C-1), 140.59 (C-3), 136.05 (C-1″), 133.16 (C-2″ and C-6″), 132.82 (C-2′), 131.5 (C-4″), 128.52 (C-5′), 127.19 (C-3″ and C-5″), 126.05 (C-3′), 122.12 (C-2), 112.25 (C-4′).

*(E)-3-(3-Methoxyphenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (**8**)* MS: $M^+$ at *m/z* 227. Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16 %. Found: C, 74.02; H, 5.81; N, 5.27 %. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 3.84 (s, 3H, $OCH_3$), 6.33 (m, 1H, H-4′), 6.94 (dd, 1H, $J = 8.00$ Hz and 2.04 Hz, H-4″), 7.04 (m, 1H, H-3′), 7.10 (d, 1H, $J = 2.04$ Hz, H-2″), 7.26 (d, 1H, $J = 7.79$ Hz, H-6″), 7.44 (dd, 1H, $J = 8.00$ Hz and 7.79 Hz, H-5″), 7.32 (d, 1H, $J = 16.00$ Hz, H-2), 7.64 (d, 1H, $J = 1.6$ Hz, H-5′), 7.79 (d, 1H, $J = 16.00$ Hz, H-3), 10.55 (s, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): 179.06 (C-1), 159.94 (C-3″), 142.21, (C-3), 136.46 (C-1″), 133.16 (C-2′), 129.90 (C-5′), 125.97 (C-3′), 122.47 (C-5″), 120.99, (C-2) 116.99 (C-6″), 115.95 (C-4″), 113.47 (C-4′), 110.94 (C-2″) and 55.34 ($OCH_3$).

*(E)-3-(2-Bromophenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (**9**)* MS: $M^+$ at *m/z* 276. Anal. Calcd for $C_{13}H_{10}BrNO$: C, 73.99; H, 5.77; N, 6.16 %. Found: C, 74.12; H, 5.78; N, 5.17 %. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 6.35 (m, 1H, H-4′), 7.09 (m, 1H, H-4″), 7.17 (m, 1H, H-3′), 7.28 (d, 1H, $J = 16.00$ Hz, H-2), 7.35 (d, 1H, $J = 8.70$ Hz, H-6″), 7.40 (d, 1H, $J = 1.68$ Hz, H-5′), 7.62 (dd, 1H, $J = 8.70$ Hz and 1.60 Hz, H-5″), 7.74 (dd, 1H, $J = 8.70$ Hz and 1.60 Hz, H-3″), 8.18 (d, 1H, $J = 16.00$ Hz, H-3), 10.5 (bs, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): 178.59 (C-1), 140.61 (C-3), 135.21 (C-1″), 133.48 (C-4″), 132.98 (C-2′), 131.00 (C-3″), 127.82 (C-6″), 127.64 (C-5″), 126.17 (C-5′), 125.74 (C-2), 125.04 (C-3′), 117.01 (C-2″) and 111.04 (C-4′).

*(E)-3-(4-Fluorophenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (**10**)* MS: $M^+$ at *m/z* 215. Anal. Calcd for $C_{13}H_{10}FNO$: C, 72.55; H, 4.68; N, 6.51 %. Found: C, 72.65; H, 4.72; N, 6.59 %. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 6.34 (m, 1H, H-4′), 7.06 (d, 1H, $J = 2.03$ Hz, H-3′), 7.10 (m, 2H, H-3″ and H-5″), 7.16 (m, 1H, H-5′), 7.30 (d, 1H, $J = 15.66$ Hz, H-2), 7.59 (m, 2H, H-2″ and H-6″), 7.80 (d, 1H, $J = 15.66$ Hz, H-3), 10.62 (bs, 1H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): 178.81 (C-1), 165.10 (C-4″), 145.01 (C-3), 135.94 (C-2′), 133.12 (C-1″), 130.21 (C-2″), 130.21 (C-6″), 126.08 (C-5′), 121.90 (C-3′), 121.88 (C-2), 116.81 (C-3″), 116.11 (C-5″).

*(E)-3-(4-Chlorophenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (**11**)* MS: $M^+$ at *m/z* 213.5. Anal. Calcd for $C_{13}H_{10}ClNO$: C, 67.39; H, 4.35; N, 6.05 %. Found: C, 67.34; H, 4.38; N, 6.13 %. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 6.36 (m, 1H, H-4′), 7.07 (m, 1H, H-3′), 7.12 (m, 1H, H-5′), 7.31 (d, 1H, $J = 15.69$ Hz, H-2), 7.54 (d, 2H, $J = 8.0$ Hz, H-3″ and H-5″), 7.59 (d, 2H, $J = 8$ Hz, H-2″ and H-6″), 7.75 (d, 1H, $J = 15.6$ Hz, H-3), 9.73 [bs, 1H, H-1′ (NH)]. $^{13}$C NMR (100 MHz, $CDCl_3$): 178.67 (C-1), 140.79 (C-3), 136.04 (C-4″), 133.56 (C-1″), 133.08 (C-2′), 132.94 (C-5′), 129.17 (C-3″and C-5″), 129.09 (C-2″and C-6″), 125.85(C-3′), 122.57 (C-2) and 111.03 (C-4′).

*(E)-3-(4-Dimethylaminophenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (**12**)* MS: $M^+$ at *m/z* 240. Anal. Calcd for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66 %. Found: C, 75.85; H, 6.78; N, 11.68 %. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 3.05 (s, 6H, $–N(CH_3)_2$), 6.33 (m, 1H, H-4′), 6.70 (d, 2H, $J = 8.8$ Hz, H-3″ & H-5″), 7.03 (m, 1H, H-3′), 7.05 (m, 1H, H-5′), 7.17 (d, 1H, $J = 15$ Hz, H-2), 7.54 (d, 2H, $J = 8.8$ Hz, H-2″ and H-6″), 7.79 (d, 1H, $J = 15.5$, H-3), 9.55 [s, 1H, H-1′ (–NH)]. $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 179.35 (C-1), 151.85 (C-4″), 143.07 (C-3), 133.58 (C-2′), 130.15 (C-2″ and C-6″), 124.54 (C-5′), 122.89 (C-1″), 116.90 (C-3′), 115.26 (C-2), 111.89 (C-3″ and C-5″), 110.62 (C-4′), 40.14 ($–N(CH_3)_2$).

*(E)-3-(2,6-Dimethoxyphenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (**13**)* MS: $M^+$ at *m/z* 257. Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44 %. Found: C, 70.16; H, 5.92; N, 6.55 %. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 3.82 (s, 6H, $(–OCH_3)_2$), 6.35 (m, 1H, H-4′), 6.91 (d, 1H, $J = 16.48$ Hz, H-2), 6.94 (dd, 1H, $J = 3.02$ Hz and 5.9 Hz, H-3′), 7.07 (m, 2H, H-3″ and H-5″), 7.16 (t, 1H, $J = 3.2$ Hz, H-5′), 7.42 (d, 1H, $J = 16.48$ Hz, H-3), 8.08 (dd, 1H, $J = 8.00$ Hz, H-4″), 9.65 (s, 1H, NH). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 178.56 (C-1), 150.87 (C-2″and C-6″), 143.48 (C-3), 135.76 (C-4″), 133.17 (C-2′), 129.80 (C-5′), 125.96 (C-3′), 123.87(C-2), 111.98 (C-4′), 110.60 (C-1″), 109.98 (C-3″ and C-5″), 55.95 ($OCH_3$), 55.56 ($OCH_3$).

*(E)-3-(2-Chloro-5-nitrophenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (**14**)* MS: $M^+$ at *m/z* 276.5. Anal. Calcd for $C_{13}H_9ClN_2O_3$: C, 56.43; H, 3.28; N, 10.13 %. Found: C, 56.56; H, 3.32; N, 10.43 %. $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta$ 6.33 (m, 1H, H-4′), 7.25 (s, 1H, H-3′), 7.55 (s, 1H, H-5′), 7.84 (d, 1H, $J = 8.8$ Hz, H-3″), 7.90 (d, 1H, $J = 15.5$ Hz, H-2), 8.02 (d, 1H, $J = 15.5$ Hz, H-3), 8.22 (dd, 1H, $J = 2.5$ and 8.0 Hz, H-4″), 8.93 (d, 1H, $J = 2.5$ Hz, H-6″). $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta$ 176.70 (C-1), 146.85 (C-5″), 140.14 (C-3), 134.01 (C-1″), 133.41 (C-2″), 132.80 (C-2′), 131.30 (C-3″), 128.32 (C-5′), 127. 31 (C-6″), 125.19 (C-3′), 122.77 (C-2), 118.72 (C-4″), 110.39 (C-4′).

*(E)-3-(2-Chlorophenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one (**15**)* MS: $M^+$ at *m/z* 231.5. Anal. Calcd for $C_{13}H_{10}ClNO$: C, 67.39; H, 4.35; N, 6.05 %. Found: C, 67.55; H, 4.36; N, 6.08 %. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 6.35 (m, 1H, H-4′), 7.10 (m, 1H, H-4″), 7.11 (s, 1H, H-5″), 7.18 (s, 1H, H-3′), 7.30 (m, 2H, H-3″ and H-6″), 7.34 (d, 1H,

$J = 15.8$ Hz, H-2), 7.74 (m, 1H, H-5′), 8.23 (1H, d, $J = 15.$ 8 Hz, H-3), 10.59 (bs, 1H, NH). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 178.68 (C-1), 138.04 (C-3), 135.32 (C-1″), 133.36 (C-2′), 133.00 (C-2″), 130.86 (C-4″), 130.22 (C-3″), 127.70 (C-6″), 127.02 (C-5′), 126.32 (C-5″), 124.77 (C-3′), 117.15 (C-2), 111.02 (C-4′).

*(E)-3-(4-Bromophenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one* ***(16)*** MS: $M^+$ at *m/z* 276. Anal. Calcd for $C_{13}H_{10}BrNO$: C, 56.55; H, 3.65; N, 5.07 %. Found: C, 56.59; H, 3.68; N, 5.17 %. $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta$ 6.31 (m, 1H, H-4′), 7.21 (dd, 1H, $J = 1.47$ and 0.56 Hz, H-3′), 7.42 (dd, 1H, $J = 1.11$ and 2.6 Hz, H-5′), 7.64 (d, 1H, $J = 15.76$ Hz, H-2), 7.65 (d, 2H, $J = 8.36$ Hz, H-2″ and H-6″), 7.76 (d, 1H, $J = 15.7$ Hz, H-3), 7.83 (d, 2H, $J = 8.36$ Hz, H-3″ and H-5″), 10.59 (bs, 1H, NH). $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta$ 177.49 (C-1), 139.28 (C-3), 134.08 (C-1″), 132.91 (C-2′), 131.74 (C-3″and C-5″), 130.35 (C-2″and C-6″), 126.60 (C-5′), 123.75 (C-3′), 123.29 (C-4″), 117.62 (C-2), 110.22 (C-4′).

*(E)-3-(2,4-Dimethoxyphenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one* ***(17)*** MS: $M^+$ at *m/z* 257. Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44 %. Found: C, 70.12; H, 5.91; N, 5.51 %. $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta$ 3.84 (s, 6H, $(-OCH_3)_2$), 6.26 (m, 1H, H-4′), 6.63 (m, 2H, H-3″ and H-5″), 7.14 (m, 1H, H-3′), 7.27 (dd, 1H, $J = 1.05$ and 2.5 Hz, H-5′), 7.54 (d, 1H, $J = 15.77$ Hz, H-2), 7.37 (d, 1H, $J = 8.52$ Hz, H-6″), 7.92 (d, 1H, $J = 15.77$ Hz, H-3), 10.55 (s, 1H, NH) .$^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta$ 178.10 (C-1), 162.49 (C-4″), 159.46 (C-2″), 135.18 (C-3), 133.15 (C-2′), 129.42 (C-5′), 125.73 (C-3′), 120.06 (C-6″), 116.47 (C-2), 115.97 (C-4″), 109.91 (C-1″), 106.09 (C-5″), 98.16 (C-3″), 55.86 ($OCH_3$), 55.71 ($OCH_3$).

*(E)-13-(4-Methoxyphenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one* ***(18)*** MS: $M^+$ at *m/z* 228. Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.11 %. Found: C, 74.03; H, 5.80; N, 6.15 %. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 3.90 (s, 3H, $-OCH_3$), 6.35 (m, 1H, H-4′), 6.94 (d, 2H, $J = 8.76$ Hz, H-3″ and H-5″), 7.06 (m, 1H, H-3′), 7.09 (m, 1H, H-5′), 7.25 (d, 1H, $J = 15.67$, H-2), 7.60 (d, 2H, $J = 8.76$ Hz, H-2″ and H-6″), 7.81 (d,1H, $J = 15.67$, H-3), 10.59 (s, 1H, NH). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 178.28 (C-1), 163.48 (C-4″), 136.21 (C-3), 133.49 (C-2′), 131.92 (C-2′ and C-6″), 128.56 (C-1″), 127.58 (C-5′), 125.98 (C-3′), 120.06 (C-2), 118.89 (C-3″ and C-5″), 115.82 (C-4′), 55.71 ($OCH_3$).

*(E)-3-(3,4-Dimethoxyphenyl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one* ***(19)*** MS: $M^+$ at *m/z* 258. Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44 %. Found: C, 70.12; H, 5.92; N, 5.51 %. $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta$ 3.86 (s, 6H, $(OCH_3)_2$), 6.27 (d, 1H, $J = 2.45$ Hz, H-4′), 7.01 (d, 1H, $J = 8.35$ Hz, H-5″), 7.15 (s, 1H, H-2″) 7.35 (dd, 1H, $J = 1.83$ and 8.35 Hz, H-6″), 7.38 (m, 1H, H-3″), 7.48 (d, 1H, $J = 1.74$ Hz, 5′), 7.56 (d, 1H, $J = 15.84$ Hz, H-2), 7.64 (1H, d, $J = 15.84$ Hz, H-3), 10.55 (s, 1H, NH). $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta$ 177.83 (C-1), 150.68 (C-3″), 148.8 (C-4″), 140.98 (C-3), 133.07 (C-2′), 127.60 (C-1″), 125.94 (C-5′), 123.07 (C-3′), 120.60 (C-2), 116.96 (C-6″), 111.44 (C-5″), 110.50 (C-4′), 109.88 (C-2″), 55.59 ($OCH_3$), 55.45 ($OCH_3$).

*(E)-3-(Benzo[d][1,3]dioxol-6-yl)-1-(1H-pyrrol-2-yl)prop-2-en-1-one* ***(20)*** MS: $M^+$ at *m/z* 242. Anal. Calcd for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.60; N, 5.81 %. Found: C, 69.79; H, 4.67; N, 5.89 %. $^1$H NMR (500 MHz, $CDCl_3$): 6.03 (s, 2H, O–$CH_2$–O), 6.35 (m, 1H, H-4′), 6.98 (m, 1H, H-3′), 7.13 (d, 1H, $J = 8.04$ Hz, H-5′), 7.18 (d, 1H, $J = 15.62$ Hz, H-2), 7.74 (d, 1H, $J = 15.62$ Hz, H-3) 10.55 (s, 1H, NH). $^{13}$C NMR (125 MHz, $CDCl_3$) 177.89 (C-1), 152.59 (C-3″), 152.09 (C-4″), 52.05 (C-2″), 140.9 (C-3), 133.24 (C-2′), 128.28 (C-5′), 126.29 (C-3′), 123.95, (C-5″), 123.05 (C-2), 120.89 (C-6″), 118.52 (C-1″), 115.92 (C-4′), 102.61 (OCO).

*(E)-3-(2-Chlorophenyl)-1-(furan-2-yl)prop-2-en-1-one* ***(21)*** MS: $M^+$ at *m/z* 232.5. Anal. Calcd for $C_{13}H_9ClO_2$: C, 67.11; H, 3.90 %. Found: C, 67.20; H, 3.89 %. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 6.61 (dd, 1H, $J = 1.8$ & 3.5 Hz, H-4′), 7.21(m, 3H, H-4′', H-5″ and H-3′), 7.37 (m, 2H, H-3′', H-6′'), 7.58 (d, 1H, $J = 16.04$ Hz, H-2), 7.78 (bs, 1H, H-5′), 7.95 (d, 1H, $J = 16.04$ Hz, H-3). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 177.25 (C-1), 153.63 (C-2′), 149.82 (C-5′), 140.23 (C-3), 133.25 (C-2″), 133.07 (C-1″), 132.05 (C-4″), 131.83 (C-3″), 128.52 (C-6″), 127.76 (C-5″), 122.52 (C-2), 122.12 (C-3′), 112.6 (C-4′).

*(E)-3-(2-Bromophenyl)-1-(furan-2-yl)prop-2-en-1-one* ***(22)*** MS: $M^+$ at *m/z* 277. Anal. Calcd for $C_{13}H_9BrO_2$: C, 56.34; H, 3.27 %. Found: C, 56.42; H, 3.29 %. $^1$H-NMR (400 MHz, DMSO-$d_6$): $\delta$ 6.60 (m, 1H, H-4′), 7.35 (m, 1H, H-3′), 7.44 (d, 1H, $J = 16.01$ Hz, H-2), 7.55 (m, 4H, H-3″, H-4″, H-5″ and H-6″), 7.66 (m, 1H, H-5′), 7.84 (d, 1H, $J = 16.01$ Hz, H-3). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 177.73 (C-1), 153.62 (C-2′), 146.63 (C-5′), 142.53 (C-3), 135.80 (C-1″), 133.66 (C-4″), 132.21 (C-3″), 129.87 (C-6″), 129 0.04 (C-5″), 124.89 (C-2″), 121.71 (C-2),121.24 (C-3′), 112.66 (C-4′).

*(E)-3-(4-fluorophenyl)-1-(furan-2-yl)prop-2-en-1-one* ***(23)*** MS: $M^+$ at *m/z* 216. Anal. Calcd for $C_{13}H_9FO_2$: C,

72.22; H, 4.20 %. Found: C, 73.38; H, 4.19 %. $^1$H-NMR (500 MHz, $CDCl_3$): $\delta$ 6.59 (m, 1H, H-4′), 7.09 (d, 1H, $J = 8.62$ Hz, H-3″), 7.11 (d, 1H, $J = 8.62$ Hz, H-5″), 7.34 (d, 1H, $J = 3.52$ Hz, H-3′), 7.38 (d, 1H, $J = 15.76$ Hz, H-2), 7.62 (d, 1H, $J = 8.62$ Hz, H-2″), 7.63 (d, 1H, $J = 8.62$ Hz, H-6″), 7.65 (d, 1H, $J = 1.64$ Hz, H-5′), 7.83 (d, 1H, $J = 15.76$ Hz, H-3). $^{13}$C NMR (500 MHz, $CDCl_3$): $\delta$ 177.81 (C-1), 165.08 (C-4″), 153.61 (C-2′), 146.60 (C-5′), 142.63 (C-3), 130.98 (C-1″), 130.42 (C-2″ and C-6″), 120.84 (C-2), 120.83 (C-3′), 116.20 (C-3″ and C-5″), 112.62 (C-4′).

*(E)-3-(4-chlorophenyl)-1-(furan-2-yl)prop-2-en-1-one* ***(24)*** MS: $M^+$ at *m/z* 232.5. Anal. Calcd for $C_{13}H_9ClO_2$: C, 67.11; H, 3.90 %. Found: C, 67.28; H, 3.88 %. $^1$H NMR (200 MHz, $CD_3OD$): $\delta$ 6.63 (m, 1H, H-4″), 7.28 (m, 5H, H-2″, 3″, 5″, 6″ and 3″), 7.43 (d, 1H, $J = 15.78$ Hz, H-2), 7.72 (d, 1H, $J = 1.64$ Hz, H-5′), 7.79 (d, 1H, $J = 15.78$ Hz, H-3). $^{13}$C NMR (100 MHz, $CD_3OD$): $\delta$ 177.86 (C-1), 152.91 (C-2′), 148.53 (C-5′), 144.65 (C-3), 134.34 (C-4′), 134.02 (C-1′) 129.18 (C-2″ and C-6″), 130.67(C-3″ and 5″), 120.89 (C-3′), 120.08 (C-2), 111.92 (C-4′).

*(E)-3-(4-Dimethylaminophenyl)-1-(furan-2-yl)prop-2-en-1-one* ***(25)*** MS: $M^+$ at *m/z* 241. Anal. Calcd for $C_{15}H_{15}NO_2$: C, 67.11; H, 3.90 %. Found: C, 67.18; H, 3.85 %. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 3.43 [s, 6H, $N(CH_3)_2$], 6.72 (m, 1H, H-4′), 6.78 (d, 2H, $J = 8.02$ Hz, H-3″ and H-5″), 7.40 (d, 1H, $J = 15.07$ Hz, H-2), 7.63 (d, 1H, $J = 2.01$ Hz, H-3′), 7.65 (d, 1H, $J = 15.07$ Hz, H-3), 7.67 (d, 2H, $J = 8.02$ Hz, H-2″ and H-6″), 7.94 (m, 1H, H-5′). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 177.18 (C-1), 153.90 (C-2′), 152.49 (C-5′), 147.96 (C-4″), 144.36 (C-3), 131.13 (C-2″ and C-6″), 122.18 (C-1″), 118.36 (C-2), 116.41 (C-3′), 112.99 (C-4′), 112.22 (C-3″ and C-5″), 40.38 $(CH_3)_2$.

*(E)-3-(3-Nitrophenyl)-1-(furan-2-yl)-prop-2-en-1-one* ***(26)*** MS: $M^+$ at *m/z* 211. Anal. Calcd for $C_{13}H_9NO_2$: C, 64.20; H, 3.73; N, 5.76 %. Found: C, 64.28; H, 3.75; N, 5.86 %. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 6.80 (bs, 1H, H-4′), 6.98 (d, 1H, $J = 15.82$ Hz, H-2), 7.74 (m, 1H, H-3′), 7.57 (m, 1H, H-5″), 7.78 (m, 3H, H-3, H-6″, H-5′), 8.26 (m, 2H, H-4″ and H-2″). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 176.2 (C-1), 152.71 (C-2′), 148.77 (C-3′), 148.36 (C-3″), 140.32 (C-3), 136.28 (C-1″), 134.89 (C-6″), 130.31 (C-5″), 124.62 (C-2 and C-2″), 122.86 (C-3′), 120.37 (C-4″), 112.75 (C-4′).

*(E)-3-(Phenyl)-1-(furan-2-yl)prop-2-en-1-one* ***(27)*** MS : $M^+$ at *m/z* 198. Anal. Calcd for $C_{13}H_{10}O_2$: C, 78.77; H. 5.09 %. Found: C, 78.81; H. 5.11 %. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 6.62 (m, 1H, H-4′), 7.38 (dd, 1H, $J = 1.4$ Hz and 3.2 Hz, H-3′), 7.45 (d, 1H, $J = 2.0$ Hz, H-5′), 7.47 (m, 2H, H-3″, H-5″), 7.48 (d, 1H, $J = 16.02$ Hz, H-2), 7.68 (m, 3H, H-4″, H-2″ and 6″), 7.92 (d, 1H, $J = 16.02$ Hz, H-3). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 178.00 (C-1), 153.71 (C-2′), 146.54 (C-4′), 143.97 (C-3), 134.73 (C-1″), 130.61 (C-4″), 128.95 (C-3″and C-5″), 128.53 (C-2″ and C-6″), 121.18 (C-2), 117.52 (C-3′), 112.55 (C-4′).

*(E)-3-(2-Chloro-5-nitrophenyl)-1-(furan-2-yl)-prop-2-en-1-one* ***(28)*** MS: $M^+$ at *m/z* 277.5. Anal. Calcd for $C_{13}H_8ClNO_4$: C, 56.23; H, 2.90; N, 5.04 %. Found: C, 56.37; H, 2.95; N, 5.14 %. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 6.66 (m, 1H, H-4′), 7.45 (d, 1H, $J = 3.5$ Hz, H-3′), 7.58 (d, 1H, $J = 15.02$ Hz, H-2), 7.65 (d, 1H, $J = 8.32$ Hz, H-3″), 7.73 (d, 1H, $J = 1.24$ Hz, H-5′), 8.17 (m, 1H, H-4″), 8.21 (d, 1H, $J = 15.7$ Hz, H-3), 8.63 (d, $J = 2.62$ Hz, 1H, H-6″). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 176.97 (C-1), 153.22 (C-2′), 147.39 (C-5′), 146.78 (C-5″), 141.89 (C-3), 137.26 (C-2″), 134.62 (C-1″), 132.40 (C-3″), 126.13 (C-6″), 125.20 (C-4″), 122.58 (C-3′), 118.83 (C-2), 113.30 (C-4′).

*(E)-3-(2, 3-Dimethoxy-phenyl)-1-(furan-2-yl)prop-2-en-1-one* ***(29)*** MS: $M^+$ at *m/z* 258. Anal. Calcd for $C_{15}H_{14}O_4$: C, 69.76; H, 5.46 %. Found: C, 69.98; H, 6.60 %. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 3.81 (s, 6H, 2 × –$OCH_3$), 6.61 (m, 1H, H-4′), 7.00 (m, 1H, H-5″), 7.21 (d, 1H, $J = 8.00$ Hz, H-6″), 7.29 (d, 1H, $J = 3.5$ Hz, H-3′), 7.42 (d, 1H, $J = 15.67$ Hz, H-2), 7.65 (d, 1H, $J = 8.00$ Hz, H-4″), 7.73 (d, 1H, $J = 1.23$ Hz, H-5′), 8.21 (d, 1H, $J = 15.67$ Hz, H-3). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 176.19 (C-1), 153.22 (C-2′), 148.56 (C-5′), 147.39 (C-3″), 145.05 (C-2″), 141.45 (C-3), 122.85 (C-5″), 121.58 (C-2), 120.66 (C-6″), 122.02 (C-3′), 118.84 (C-1″), 113.30 (C-4″), 113.04 (C-4′), 55.96 (2″-$OCH_3$), 55.34 (3′’-$OCH_3$).

*(E)-3-(Benzo[d][1,3]dioxol-6-yl)-1-(furan-2-yl)prop-2-en-1-one* ***(30)*** MS: $M^+$ at *m/z* 242. Anal. Calcd for $C_{14}H_{10}O_4$: C, 69.42; H, 4.16 %. Found: C, 69.65; H,4.26 %. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 6.03 (s, 2H, –$OCH_2O$–), 6.70 (dd, 1H, $J = 1.62$ and 3.55 Hz, H-4′), 6.88 (d, 1H, $J = 8.05$ Hz, H-5″), 7.19 (d, 1H, $J = 1.46$ Hz, H-2″), 7.34 (bs, 1H, H-6″), 7.45 (d, 1H, $J = 15.61$ Hz, H-2), 7.56 (d, 1H, $J = 3.55$ Hz, H-3′), 7.76 (d, 1H, $J = 15.61$ Hz, H-3), 7.85 (d, 1H, $J = 1.62$ Hz, H-5′). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 177.29 (C-1), 153.29 (C-2′), 149.82 (C-5′), 149.25 (C-3″), 148.73 (C-4″), 140.52 (C-3), 123.52 (C-5″), 122.24 (C-2), 121.82 (C-3′), 120.25 (C-6″), 116.92 (C-1″), 113.26 (C-2″), 112.83 (C-4′), 102.54 (–$OCH_2O$–).

*(E)-3-(3,4-Dimethoxyphenyl)-1-(furan-2-yl)prop-2-en-1-one* ***(31)*** MS: $M^+$ at *m/z* 258. Anal. Calcd for $C_{15}H_{14}O_4$: C, 69.76; H, 5.46 %. Found: C, 69.88; H, 6.51 %. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 3.89 (s, 3H, -$OCH_3$), 3.92 (s, 3H, –$OCH_3$), 6.71 (dd, 1H, $J$ = 1.65 and 3.51 Hz, H-4′), 7.02 (d, 1H, $J$ = 8.24 Hz, H-5″), 7.46 (m, 4H, H-3′, H-2″, H-6″ and H-2), 7.81 (d, 1H, $J$ = 14.60 Hz, H-3), 7.85 (bs, 1H, H-5′). $^{13}$C NMR (125 MHz, $CDCl_3$): 178.43 (C-1), 154.196 (C-2′), 151.86 (C-5′), 149.57 (C-3′'), 148.67 (C-4″), 144.49 (C-3), 128.07 (C-1″), 123.76 (C-2), 119.34 (C-3′), 117.55 (C-6″), 112.88 (C-5″), 114.4 (C-4′), 110.42 (C-2″), 56.36 $(OCH_3)_2$.

*(E)-3-(4-Nitrophenyl)-1-(furan-2-yl)prop-2-en-1-one* ***(32)*** MS: $M^+$ at *m/z* 243 Anal. Calcd for $C_{13}H_9NO_4$: C, 64.20; H, 3.74; N, 5.76 %. Found: C, 64.31; H, 3.78; N, 5.87 %. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 6.83 (m, 1H, H-4′), 7.82 (d, 1H, $J$ = 15.18 Hz, H-2), 7.90 (d, 1H, $J$ = 3.8 Hz, H-3′), 8.11 (d, 1H, $J$ = 1.6, H-5′), 8.14 (d, 2H, $J$ = 8.8 Hz, H-2″ & H-6″), 8.20 (d, 1H, $J$ = 15.18 Hz, H-3), 8.29 (d, 2H, $J$ = 8.8 Hz, H-3″ and H-5″). $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ 176.14 (C-1), 152.7 (C-2′), 148.94 (C-5′), 148.08 (C-4″), 140.88 (C-3), 139.99 (C-1″), 129.76 (C-2″and C-6″), 125.89 (C-2), 123.93 (C-3″ and C-5″), 120.51 (C-3′), 112.87 (C-4′).

*(E)-3-(4-Bromophenyl)-1-(furan-2-yl)prop-2-en-1-one* ***(33)*** MS: $M^+$ at *m/z* 277 Anal. Calcd for $C_{13}H_9BrO_2$: C, 56.34, 3.27, H, 5.46 %. Found: C, 56.49, H, 3.29 %. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 6.60 (m, 1H, H-4′), 7.35 (dd, 1H, $J$ = 1.6 & 3.2, H-3′), 7.44 (d, 1H, $J$ = 16 Hz, H-2), 7.5 (dd, 2H, $J$ = 8.02 Hz and 1.63 Hz, H-2″ and H-6″), 7.66 (m, 1H, H-5′), 7.72 (dd, 2H, $J$ = 8.02 Hz and 1.63 Hz, H-3′' and H-5″), 7.84 (d, 1H, $J$ = 16 Hz, H-3). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 177.73 (C-1), 153.62 (C-2′), 146.63 (C-5′), 142.53 (C-3), 133.66 (C-1″), 132.21 (C-3″ and 5″), 129.87 (C-2″ and 6″), 124.89 (C-4″), 121.71 (C-2), 117.68 (C-3′), 112.66 (C-4′).

*(E)-3-(4-Methoxyphenyl)-1-(furan-2-yl)prop-2-en-1-one* ***(34)*** MS: $M^+$ at *m/z* 228. Anal. Calcd for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30 %. Found: C, 73.81; H, 5.34 %. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 3.83 (s, 3H, –$OCH_3$), 6.58 (dd, $J$ = 1.68, 2.01 Hz, 1H, H-4′), 6.92 (m, 2H, H-3″ and H-5″), 7.30 (d, 1H, $J$ = 4.4 Hz, H-3′), 7.32 (d, $J$ = 16.0 Hz, H-2), 7.60 (m, 2H, H-2″ and H-6″), 7.63 (m, 1H, H-5′), 7.84 (d, 1H, $J$ = 16 Hz, H-3). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 178.16 (C-1), 161.76 (C-4″), 153.86 (C-2′), 146.32 (C-5′), 143.82 (C-3), 130.34 (C-2″ and C-6″), 127.48 (C-1″), 118.85 (C-2), 117.35 (C-3′), 114.43 (C-3″ and C-5″), 112.4 (C-4′), 55.41 ($OCH_3$).

*(E)-3-(3,4,5-Trimethoxyphenyl)-1-(furan-2-yl)prop-2-en-1-one* ***(35)*** MS: $M^+$ at *m/z* 288. Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59 %. Found: C, 69.76; H, 5.56 %. $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 3.81 (s, 3H, –$OCH_3$), 3.91 (s, 6H, 2 × –$OCH_3$), 6.71 (dd, 1H, $J$ = 1.63 and 3.58 Hz, H-4′), 7.08 (s, 2H, H-2″ and H-6″), 7.55 (d, 1H, $J$ = 15.67 Hz, H-2), 7.63 (d, 1H, $J$ = 3.58 Hz, H-3′), 7.78 (d, 1H, $J$ = 15.67 Hz, H-3), 7.87 (bs, 1H, H-5′). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 177.82 (C-1), 162.34 (C-3″and C-5″), 153.63 (C-2′), 149.38 (C-5′), 140.59 (C-3), 140.13 (C-4″), 129.56 (C-1″), 122.56 (C-2), 121.89 (C-3′), 113.23 (C-4′), 110.6 (C-2″and C-6″), 56.52($OCH_3$), 56.23 $(OCH_3)_2$.

*(E)-3-(2,5-Dimethoxyphenyl)-1-(furan-2-yl)prop-2-en-1-one* ***(36)*** MS: $M^+$ at *m/z* 258. Anal. Calcd for $C_{15}H_{14}O_4$: C, 69.76; H, 5.46 %. Found: C, 69.88; H, 5.51 %. $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ 3.88 (s, 6H, 2 × –$OCH_3$), 6.72 (dd, 1H, $J$ = 1.58 and 3.61 Hz, H-4′), 7.13 (m, 2H, H-3″ and H-4″), 7.43 (m, 1H, H-6″), 7.56 (bs, 1H, H-3′), 7.62 (d, 1H, $J$ = 15.93 Hz, H-2), 7.88 (bs, 1H, H-5′), 8.16 (d, 1H, $J$ = 15.93 Hz, H-3). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 177.45 (C-1), 162. 43 (C-5″), 162.03 (C-2″), 153.23 (C-2′), 149.82 (C-5′), 140.25 (C-3), 121.46 (C-2), 121.35 (C-3′), 116.25 (C-1′'), 115.26 (C-3″), 115.03 (C-4″), 112.39 (C-4′), 111.37 (C-6″), 55.93 ($OCH_3$), 55.23 ($OCH_3$).

## X-ray studies

The crystal of compound **9** used for data collection was of the dimension 0.3 × 0.2 × 0.1 mm. X-ray intensity data of 6,806 reflections (of which 2,673 were unique) were collected. The cell dimensions were determined by least-square fit of angular settings of 2,440 reflections in the $\theta$ range 2.59°–27.45°. The structure was solved by direct methods using SHELXS97 (Hijova, 2006). All the hydrogen atoms were located on a difference electron density map and their positional and isotropic thermal parameters were included in the refinement. The final refinement cycles converged to an $R$ = 0.0343 and wR($F^2$) = 0.0879 for the observed data 0.59. The crystallographic data are summarized in Table 2. CCDC-776070 contains the supplementary crystallographic data for this paper.

## In vitro combination (EPI) study of ciprofloxacin in combination with compounds

The ciprofloxacin/compounds' combination studies were performed on *S. aureus* 1199B in Mueller–Hinton broth (Difco). The MIC of ciprofloxacin was determined in the presence of increasing concentrations of compounds by the broth checkerboard method in microtiter plates (Lawrence *et al*., 2006). The twofold serial dilutions of ciprofloxacin

ranging from 0.03 to 16 μg/mL were tested in combination with compounds at seven different concentrations (0.78–50 μg/mL). The final bacterial inoculum of $5 \times 10^5$ cfu/mL was added to each well. The plates were incubated for 18 h at 37 °C and the wells were assessed visually for growth. The minimum concentration of compounds that produced the maximal reduction in the MIC of ciprofloxacin was determined. The minimal effective concentration (MEC) was determined to be the minimal concentration of EPI that produced the maximal reduction in substrate MIC. No further decrease in substrate MIC was observed at EPI concentrations greater than the MEC (Sheldrick, 1997).

Anticancer activity

*Cell culture, growth conditions, and treatment*

All the cancer cell lines (HL-60, MOLT-4, PC-3, and HeLa) were obtained from the National Cancer Institute (NCI), Bethesda, USA. The cells were grown in RPMI-1640 medium supplemented with 10 % heat inactivated fetal bovine serum (FBS), penicillin (100 units/mL), streptomycin (100 μg/mL), L-glutamine (0.3 mg/mL), pyruvic acid (0.11 mg/mL), and 0.37 % $NaHCO_3$. Cells were grown in $CO_2$ incubator (Thermocon Electron Corporation, USA) at 37 °C in an atmosphere of 95 % air and 5 % $CO_2$ with 98 % humidity. Compounds (**1**–**36**) were dissolved in DMSO and delivered to cell culture in a complete medium.

*Cell proliferation assay*

HL-60 and MOLT-4 cells were plated in 96-well plates at the density of 15,000 cells per well/200 μL of the medium. Adherent cells (PC-3 and HeLa) were treated when they were 75 % confluent in 96-well plates. Cultures were treated with four different concentrations (1 μm, 10 μm, 30 μm, and 100 μm) of compounds (**1**–**36**) for 48 h to determine $IC_{50}$ values. 20μL of MTT (3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyltetrazolium bromide) of concentration (2.5 mg/mL) was added to each well and incubated at 37 °C for 3 h. The plates were centrifuged at 2,000 rpm for 15 min, and the supernatant was discarded and the MTT formazan crystals were dissolved in 150 μL of DMSO. Plates were shaken on a shaker for 3 min and then incubated at 37 °C for 5 min. The OD measured at 570 nm.

Anti-inflammatory activity

*Animal*

Wistar rats (12–16-week old, weighing between 130 and 150 mg) were housed in polycarbonate cages in the animal house. They were fed with a pellet diet and water ad libitum during the course of experimentation. The light cycle was automatically controlled for a 12-h light and dark cycle (on at 7.00 a.m. and off at 7.00 p.m.). Room temperature was regulated at 26 ± 1 °C. The animals were housed in such conditions for 3–4 days prior to the experimentation for acclimatization.

*Preparation of test material*

The test material was prepared freshly as fine homogenized suspension in 2 % gum acacia (w/v) for administration.

*Carrageenan-induced inflammation assay*

Edema was induced in groups of four rats by injecting 100 μL of 1 % (w/v) freshly prepared carrageenan solution in normal saline into the sub-planter region of the left hind paw, while the right paw received an equal volume of normal saline. Test compounds were administered orally 45 min. before carrageenan injection at 100 mg/kg. The volume of the paw was measured immediately and 4 h after carrageenan injection with a volume differential meter model 7101, Ugo Basile (Italy). Percent inhibition of the test compound was calculated.

*Statistical evaluation*

The numerical values were expressed as Mean ± SEM of the difference between the vehicle control and treatment groups, unless otherwise specified.

In vitro antioxidant activity (DPPH method)

Test solution was prepared by dissolving DPPH solution 45 μg/mL in methanol, while samples were prepared in D.W. (distilled water)/methanol/PBS. Standard ascorbic acid was prepared (Ascorbic acid 10 mg/mL or 1 mg/mL stock solution dissolved in distilled water). The free radical scavenging activity of EPA was measured in terms of the hydrogen donating or radical scavenging ability using the stable radical 1,1-diphenyl-2-picrylhydrazyl (DPPH). 0.1 mM solution of DPPH in ethanol was used. For the assay, the reaction mixture contained 10 μL of the test drug in 990 μL of DPPH solution in 48-well microtiter plates and incubated at room temperature for 30 min (Lee and Chung). Absorbance was measured at 517 nm in an ELISA reader (Thermo multiscan spectrum). The capacity to scavenge DPPH radical was calculated. DPPH was dissolved in methanol and sonicated for 5 min to obtain the stable free radical DPPH•. The test compounds were diluted in different concentrations with the DPPH• solution in a 48-well microplate. Ascorbic acid was used as control in each series.

The compounds **1–36** were tested in triplicate at different concentrations, such that a 50 % fall in absorbance of the DPPH• could be calculated. The absorbance of the reaction mixture was measured after 20-min incubation at room temperature using a microplate ELISA reader at 517 nm. The $IC_{50}$ of each sample was determined and compared with standard ascorbic acid.

Molecular modeling

The coordinates of tubulin complexed with colchicine were obtained from a protein data bank (PDB entry: 1SA0). The structure of compound **25** was drawn in MOE and subjected to energy minimization using MMFF94x force field. The ligands were docked at the colchicine-binding site of tubulin using the GOLD 4.0.1. Gold performs genetic algorithm-based ligand docking to optimize the conformation of the ligand at the receptor-binding site. It utilizes GOLD score fitness function to evaluate the various conformations of the ligand at the binding site and comprises four components: protein–ligand hydrogen bond energy, protein–ligand vander Waals (vdw) energy, ligand internal energy, and ligand torsional strain energy.

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