

Article

# Synthesis of Novel $\beta$ -Keto-Enol Derivatives Tethered Pyrazole, Pyridine and Furan as New Potential Antifungal and Anti-Breast Cancer Agents

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**Abstract:** Recently, a new generation of highly promising inhibitors bearing  $\beta$ -keto-enol functionality has emerged. Reported herein is the first synthesis and use of novel designed drugs based on the  $\beta$ -keto-enol group embedded with heterocyclic moieties such as pyrazole, pyridine, and furan, prepared in a one-step procedure by mixed Claisen condensation. All the newly synthesized compounds were characterized by FT-IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, ESI/LC-MS, elemental analysis, and evaluated for their *in vitro* antiproliferative activity against breast cancer (MDA-MB241) human cell lines and fungal strains (*Fusarium oxysporum f.sp. albedinis* FAO). Three of the synthesized compounds showed potent activity against fungal strains with IC<sub>50</sub> values in the range of 0.055–0.092  $\mu$ M. The results revealed that these compounds showed better IC<sub>50</sub> values while compared with positive controls.

**Keywords:** keto-enols; heterocycles; breast cancer; fungal strains

## 1. Introduction

Heterocyclic compounds with  $\beta$ -keto-enol moieties are well established as important, biologically effective compounds. Their versatile utility in the world of medicinal chemistry is firmly established [1,2]. Among this class of drug, we cite anti-HIV drugs S-1360 (Shionogi, Ltd., Florham Park, NJ, USA) [3] and L-708,906 (Merck Research Laboratories, Boston, MA, USA) [4] in clinical trials as well as P13 (IC<sub>50</sub> = 1.1  $\mu$ M) [5], the 5-CITEP designed by the National Cancer Institute (Bethesda, MD, USA) [3], and AIV (IC<sub>50</sub> = 0.3  $\mu$ M), an inhibitor of anti-influenza virus [6] (Figure 1), *etc.*

In this context, we note also the interest in curcumin [7] derivatives with  $\beta$ -keto-enol pharmacophore sites (Figure 1) which have spurred numerous studies in medicinal chemistry owing to their capability of eliciting antioxidant [8], anti-HIV [9], antitumor [10–12], and anti-inflammatory [13] activities.

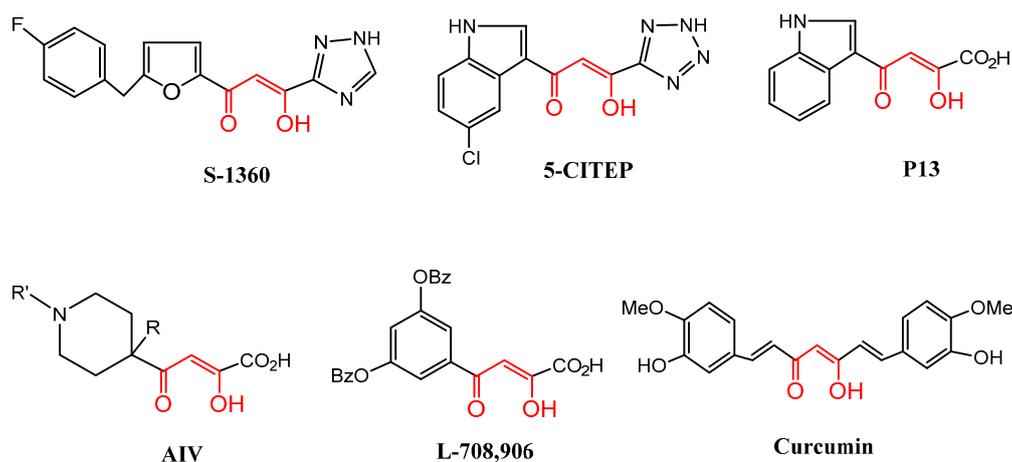


Figure 1. Representative drugs containing keto-enol functionality.

The  $\beta$ -keto-enol pharmacophore site of these hybrid drug molecules has the potential advantage of being active against all genotypes of the virus and drug-resistant variants. Multistage processes may explain the biological responses of this motif ( $\beta$ -keto-enol), such as (i) its penetration into blood vessel walls and plasma cell membranes; (ii) its interaction with the active site; (iii) its ability to chelate with metals in biological processes; and (iv) its reaction with oxygen (under aerobic conditions) or with cell macromolecules (in hypoxic conditions) resulting in oxidative stress, the modulation of gene expression, and a complex immune response to hapten-conjugate adducts.

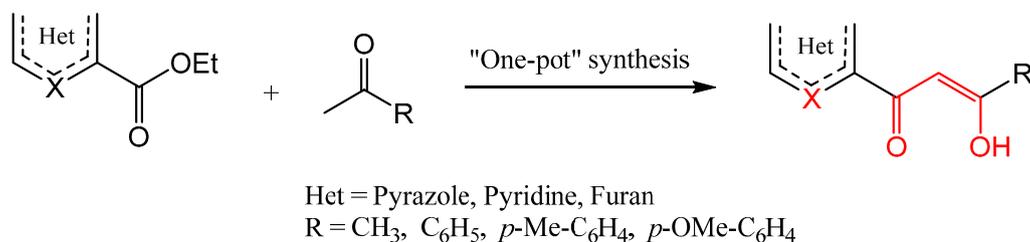
Consequently, significant effort is devoted to the search for drug-like scaffolds bearing the  $\beta$ -keto-enol pharmacophore. Recently, several molecules were designed, such as the calix[4]arene derivatives, containing the triazolyl keto-enol moiety showing potent integrase strand transfer inhibitory activity [14], keto-enol tetrazoles, and triazoles as anti-HCV agents [15], and coumarinyl chalcones, exhibiting high selectivity for the breast cancer cell lines [16].

Accordingly, described herein is the first synthesis and examination of some hybrid drug molecules bearing the  $\beta$ -keto-enol functionality as a useful motif, especially in fungal and cancer activities.

## 2. Results and Discussion

### 2.1. Chemistry

The target compounds based on  $\beta$ -keto-enol group-tethered pyrazole, pyridine, and furan were prepared by a one-pot *in situ* condensation as illustrated and outlined in Schemes 1 and 2.

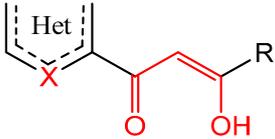


Scheme 1. Reagents and conditions: Na, Toluene, rt, two days, then acetic acid.

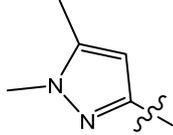
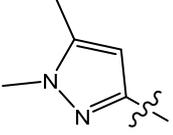
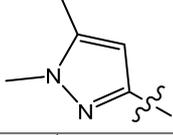
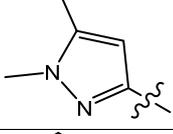
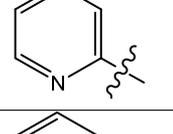
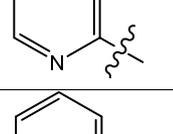
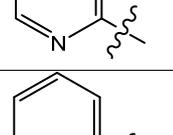
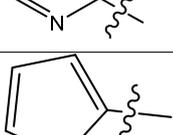
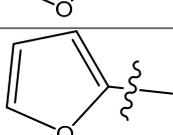
The sodium metal-mediated condensation of ketone derivatives with ethyl heterocycle-2-carboxylates exclusively afforded the target products in their enol tautomeric form. The reaction, as a mixed Claisen condensation, was carried out under mild conditions (room



**Table 1.** Breast cancer and fungal inhibitory activities of synthesized heterocycle  $\beta$ -keto-enols.



**General Structure**

No.	Products		MDA-MB241		<i>Fusarium Oxysporum f.sp Albedinis</i>	
	Heterocycles	R	IC <sub>50</sub> (μg/mL)	IC <sub>50</sub> (μM)	IC <sub>50</sub> (μg/mL)	IC <sub>50</sub> (μM)
1		CH <sub>3</sub>	46.20	256.38	0.01	0.055
2		C <sub>6</sub> H <sub>5</sub>	44.33	183.00	12.83	53.39
3		<i>p</i> -Me-C <sub>6</sub> H <sub>4</sub>	21.95	85.65	142	554.03
4		<i>p</i> -MeO-C <sub>6</sub> H <sub>4</sub>	34.93	128.30	150	550.86
5		CH <sub>3</sub>	47.00	288.04	0.013	0.079
6		C <sub>6</sub> H <sub>5</sub>	17.62	78.23	16.43	72.94
7		<i>p</i> -Me-C <sub>6</sub> H <sub>4</sub>	128.67	537.8	35.80	149.62
8		<i>p</i> -MeO-C <sub>6</sub> H <sub>4</sub>	28.97	113.50	N/A *	N/A *
9		CH <sub>3</sub>	N/A *	N/A *	0.014	0.092
10		C <sub>6</sub> H <sub>5</sub>	18.79	87.72	68.45	319.53

\* N/A means non applicable because IC<sub>50</sub> > 100 μg/mL.

However, the results of the anticancer and antifungal effects were very significant and are given in Table 1, respectively. Most of these molecules were cytotoxic against breast cancer cell lines in a dose-dependent manner. The activity followed the structure activity relationships (SARs) and showed an interesting dependence on the substitution pattern. Considering the influence of substituent R, it was found that the phenyl residue leads to a stronger growth inhibition [18]. This was especially evident for products 6 and 10. The concentration required to induce the activity (IC<sub>50</sub>) was more pronounced for compounds 3, 6 and 10 with IC<sub>50</sub> values of 21.95, 17.62, and 18.79 µg/mL, respectively. Beside this observation, we also noted the effect of the heterocycle groups for appreciable biological activity.

These structures have also led to unexpected antifungal activity. Indeed, compounds 1, 5, and 9 with methyl in the R position had the most potent activity with IC<sub>50</sub> values of 0.055, 0.079, and 0.092 µM, respectively. This result was better than all the described products. We noted that the substitution of methyl in the R position was essential for this biological activity. The aryl groups strongly decreased the activity. This suggests that the marked bioactivity of the heterocyclic compounds was sensitive to modifications and could be further exploited to determine the structure activity relationship around this novel class of fungal inhibitors. Other structural modifications to these active compounds as antifungal and anti-HIV candidates are currently in progress.

### 3. Experimental

#### 3.1. General Information

All commercial reagents were analytical grade (Aldrich, purity >99%, St. Louis, MO, USA). Melting points were measured using a BUCHI 510 m.p. apparatus (Oujda, Morocco). <sup>1</sup>H- and <sup>13</sup>C-NMR spectra were performed on a Bruker AC 300 spectrometer (CNRS, Rabat, Morocco) (300 MHz for <sup>1</sup>H and 75.47 MHz for <sup>13</sup>C spectra). JEOL JMS DX-300 mass spectrometer (Rabat, Morocco) was used for the determination of molecular weights. Infrared (IR) spectra were recorded on a Shimadzu infrared spectrophotometer (Oujda, Morocco) using the KBr disc technique. The formazan obtained at the end of the experiment in MTT assays was measured by means of a Perkin Elmer Victor X4 Microplate reader (Brussels, Belgium).

#### 3.2. General Procedure for the Synthesis of β-Keto-Enol Heterocycles

To a suspension of sodium (15.21 mmol) in 20 mL of toluene, the appropriate heterocyclic carboxylate (12.01 mmol) in 25 mL of toluene was slowly added; then acetone or aryl methyl ketones (12.01 mmol) in 10 mL of toluene was added at 0 °C. The resulting mixture was stirred at room temperature for two days. The precipitate formed was filtered, washed with toluene, dissolved in water, and neutralized with acetic acid to pH 5. After extraction with CH<sub>2</sub>Cl<sub>2</sub>, the organic layer was dried over anhydrous sodium sulfate and concentrated in *vacuo*. The obtained residue was filtered through silica using CH<sub>2</sub>Cl<sub>2</sub>/MeOH as eluant to give the desired products 1–10 as a white solid in 35%–48% yield. β-keto-enol forms were recrystallized from methanol (95%) to obtain target compounds 1–10 which were confirmed by FT-IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, elemental analysis, and mass spectroscopy.

(Z)-1-(1.5-Dimethyl-1H-pyrazol-3-yl)-3-hydroxybut-2-en-1-one (1). Yellow crystal; yield: 35%; m.p. 83–84 °C; *R<sub>f</sub>* = 0.66 (diethyl ether)/silica. IR (KBr, cm<sup>-1</sup>): ν (OH) = 3422; ν (C=O) = 1619; ν (enolic C=C) = 1509; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 2.11 (s, 3H, -CH<sub>3</sub>); 2.27 (s, 3H, Pz-CH<sub>3</sub>); 3.83 (s, 3H, N-CH<sub>3</sub>); 6.29 (s, 1H, enol, C-H). 6.54 (s, 1H, Pz-H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 11.2 (1C, Pz-CH<sub>3</sub>); 24.6 (1C, CH<sub>3</sub>); 36.7 (1C, N-CH<sub>3</sub>); 96.7 (1C, enol C-H); 106.1 (1C, Pz-CH); 140.5 (1C, Pz, C-CH<sub>3</sub>); 146.9 (1C, C=N); 180.4 (1C, C=O); 190.0 (C-OH); MS: *m/z*, 181.00 (M + H)<sup>+</sup>. Anal. Calcd. for C<sub>9</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>: C, 59.99; H, 6.71; N, 15.55. Found: C, 60.11; H, 6.83; N, 15.43.

(*Z*)-1-(1,5-Dimethyl-1H-pyrazol-3-yl)-3-hydroxy-3-phenylprop-2-en-1-one (**2**). Yellow crystal; yield: 32%; m.p. 108–110 °C;  $R_f$ : 0.88 (CH<sub>2</sub>Cl<sub>2</sub>/MeOH 9/1/silica), IR (KBr, cm<sup>-1</sup>):  $\nu$  (OH) = 3416;  $\nu$  (C=O) = 1639;  $\nu$  (enolic C=C) = 1518; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>):  $\delta$  2.29 (s, 3H, Pz-CH<sub>3</sub>); 3.83 (s, 3H, N-CH<sub>3</sub>); 6.60 (s, 1H, enol, C-H); 7.02 (s, 1H, Pz-H); 7.58 (m, 3H, Ar-H<sub>4,3,5</sub>); 7.95 (m, 2H, Ar-H<sub>2,6</sub>). <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>):  $\delta$  11.9 (1C, Pz-CH<sub>3</sub>); 37.3 (1C, CH<sub>3</sub>-N); 93.3 (1C, enol C-H); 106.1 (1C, CH-Pz); 127.3 (2C, Ar-C<sub>2,6</sub>); 128.8 (1C, Ar-C<sub>4</sub>); 129.3 (2C, Ar-C<sub>3,5</sub>); 148.8 (1C, Pz, C-CH<sub>3</sub>); 181.7 (1C, C-OH); 183.5 (1C, C=O); MS: *m/z*, 243.10 (M + H)<sup>+</sup>.

(*Z*)-1-(1,5-Dimethyl-1H-pyrazol-3-yl)-3-hydroxy-3-*p*-tolylprop-2-en-1-one (**3**). Yellow crystal; yield: 22%; m.p. 132–134 °C;  $R_f$ : 0.29 (diethyl ether)/silica. IR (KBr, cm<sup>-1</sup>):  $\nu$  (OH) = 3412;  $\nu$  (C=O) = 1642;  $\nu$  (enolic C=C) = 1536; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>):  $\delta$  2.26 (s, 3H, *p*-CH<sub>3</sub>-Ar); 2.36 (s, 3H, Pz-CH<sub>3</sub>); 3.82 (s, 3H, CH<sub>3</sub>-N); 6.67 (d, 1H, Pz-H); 6.98 (s, 1H, enol, C-H); 7.32 (m, 2H, Ar-H<sub>3,5</sub>); 7.85 (m, 2H, Ar-H<sub>2,6</sub>). <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>):  $\delta$  11.2 (1C, Pz-CH<sub>3</sub>); 21.6 (1C, *p*-CH<sub>3</sub>-Ar); 37.3 (1C, CH<sub>3</sub>-N); 92.8 (1C, enol C-H); 106.0 (1C, CH-Pz); 128.1 (2C, Ar-C<sub>2,6</sub>); 129.9 (2C, Ar-C<sub>3,5</sub>); 182.2 (1C, C-OH); 182.9 (1C, C=O); MS: *m/z*, 257.11 (M + H)<sup>+</sup>.

(*Z*)-1-(1,5-Dimethyl-1H-pyrazol-3-yl)-3-hydroxy-3-(4-methoxyphenyl)prop-2-en-1-one (**4**). Yellow crystal; yield: 31%; m.p. 122–124 °C;  $R_f$ : 0.61 (CH<sub>2</sub>Cl<sub>2</sub>/MeOH 8/2)/silica. IR (KBr, cm<sup>-1</sup>):  $\nu$  (OH) = 3432;  $\nu$  (C=O) = 1678;  $\nu$  (enolic C=C) = 1528; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>):  $\delta$  2.26 (s, 3H, O-CH<sub>3</sub>); 3.82 (s, 3H, Pz-CH<sub>3</sub>); 3.83 (s, 3H, CH<sub>3</sub>-N); 6.65 (s, 1H, Pz-H); 6.94 (s, 1H, enol, C-H); 7.04 (m, 2H, Ar-H<sub>3,5</sub>); 7.94 (m, 2H, Ar-H<sub>2,6</sub>); <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>):  $\delta$  11.1 (1C, Pz-CH<sub>3</sub>); 37.3 (1C, CH<sub>3</sub>-N); 56.0 (1C, *p*-OCH<sub>3</sub>-Ar); 92.2 (1C, enol C-H); 106.1 (1C, CH-Pz); 114.6 (2C, Ar-C<sub>3,5</sub>); 129.6 (2C, Ar-C<sub>2,6</sub>); 181.7 (1C, C-OH); 182.9 (1C, C=O); MS: *m/z*, 273.06 (M + H)<sup>+</sup>.

(*Z*)-3-Hydroxy-1-(pyridin-2-yl)but-2-en-1-one (**5**). Brown powder; yield: 48%; m.p. = 59–61 °C;  $R_f$ : 0.27 (CH<sub>2</sub>Cl<sub>2</sub>/MeOH 9/1)/silica. IR (KBr, cm<sup>-1</sup>):  $\nu$  (OH) = 3448;  $\nu$  (C=O) = 1611;  $\nu$  (enolic C=C) = 1565; <sup>1</sup>H-NMR (CDCl<sub>3</sub>):  $\delta$  2.23 (s, 3H, -CH<sub>3</sub>); 6.94 (s, 1H, enol, C-H); 7.42 (t, 1H, Py-H <sub>$\beta$</sub> ); 7.85 (t, 1H, Py-H <sub>$\gamma$</sub> ); 8.08 (d, 1H, Py-H <sub>$\delta$</sub> ); 8.66 (d, 1H, Py-H <sub>$\alpha$</sub> ); <sup>13</sup>C-NMR (CDCl<sub>3</sub>):  $\delta$  26.2 (1C, CH<sub>3</sub>-C=O); 97.8 (1C, enol, CH); 123.0 (1C, Py-C <sub>$\delta$</sub> ); 126.4 (1C, Py-C <sub>$\beta$</sub> ); 138.0 (1C, Py-C <sub>$\gamma$</sub> ); 148.5 (1C, Py-C <sub>$\alpha$</sub> ); 151.4 (1C, Py-C <sub>$\epsilon$</sub> ); 179.3 (1C, C-O), 195.6 (1C, C=OH); MS: *m/z*, 164.07 (M + H)<sup>+</sup>. Anal. Calcd. for C<sub>9</sub>H<sub>9</sub>NO<sub>2</sub>: C, 66.25, H, 5.56; N, 8.58. Found: C, 66.31; H, 5.62, N, 5.40.

(*Z*)-3-Hydroxy-3-phenyl-1-(pyridin-2-yl)prop-2-en-1-one (**6**). Red powder; yield: 32%; m.p. = 78–80 °C;  $R_f$ : 0.54 (CH<sub>2</sub>Cl<sub>2</sub>/MeOH 9/1)/silica. IR (KBr, cm<sup>-1</sup>):  $\nu$  (OH) = 3438;  $\nu$  (C=O) = 1600;  $\nu$  (enolic C=C) = 1549; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>):  $\delta$  7.51 (s, 1H, enol CH); 7.61 (m, 3H, Ar-H<sub>4,3,5</sub>); 7.66 (d, 2H, Ar-H<sub>2,6</sub>); 8.00 (t, 1H, Py-H <sub>$\beta$</sub> ); 8.04 (t, 1H, Py-H <sub>$\gamma$</sub> ); 8.11 (d, 1H, Py-H <sub>$\delta$</sub> ); 8.77 (d, 1H, Py-H <sub>$\alpha$</sub> ); <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>):  $\delta$  93.6 (1C, enol C-H); 122.5 (1C, Py-C <sub>$\delta$</sub> ); 127.7 (2C, Ar-C<sub>2,6</sub>); 128.8 (1C, Ar-C<sub>4</sub>); 129.4 (2C, Ar-C<sub>3,5</sub>); 133.7 (1C, Py-C <sub>$\beta$</sub> ); 138.3 (1C, Py-C <sub>$\gamma$</sub> ); 150.1 (1C, Py-C <sub>$\alpha$</sub> ); 184.4 (1C, C-OH); 186.1 (1C, C=O); MS: *m/z*, 226.13 (M + H)<sup>+</sup>. Anal. Calcd. for C<sub>14</sub>H<sub>11</sub>NO<sub>2</sub>: C, 74.65; H, 4.92; N, 6.22. Found: C, 74.74, H, 4.89; N, 6.25.

(*Z*)-3-Hydroxy-1-(pyridin-2-yl)-3-*p*-tolylprop-2-en-1-one (**7**). Brown powder, yield 27%, m.p.: 174–176 °C;  $R_f$ : 0.75 (CH<sub>2</sub>Cl<sub>2</sub>/MeOH 6/4)/silica. IR (KBr, cm<sup>-1</sup>):  $\nu$  (OH) = 3444;  $\nu$  (C=O) = 1602;  $\nu$  (enolic C=C) = 1542; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>):  $\delta$  2.49 (s, 3H, *p*-CH<sub>3</sub>-Ar); 6.78 (s, 1H, enol CH); 7.31 (d, 2H, Ar-H<sub>3,5</sub>); 7.46 (d, 2H, Ar-H<sub>2,6</sub>); 7.91 (dd, 2H, Py-H <sub>$\beta,\gamma$</sub> ); 8.12 (d; 1H, Py-H <sub>$\delta$</sub> ); 8.89 (d, 1H, Py-H <sub>$\alpha$</sub> ). <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>):  $\delta$  21.3 (1C, *p*-CH<sub>3</sub>-Ar); 93.8 (1C, enol CH); 121.7 (1C, Py-H <sub>$\delta$</sub> ); 126.1 (2C, Ar-C<sub>2,6</sub>); 128.1 (1C, Py-H <sub>$\beta$</sub> ); 128.9 (2C, Ar-C<sub>3,5</sub>); 136.1 (1C, Py-H <sub>$\gamma$</sub> ); 149.6 (1C, Py-H <sub>$\alpha$</sub> ); 178.1 (1C, C-OH); 186.1 (1C, C=O); MS: *m/z*, 240.13 (M + H)<sup>+</sup>. Anal. Calcd. for C<sub>15</sub>H<sub>13</sub>NO<sub>2</sub>: C, 75.30; H, 5.48, N, 5.85. Found: C, 75.49; H, 5.44; N, 5.80.

(*Z*)-3-Hydroxy-3-(4-methoxyphenyl)-1-(pyridin-2-yl)prop-2-en-1-one (**8**). Brown clear crystal, yield 33%, m.p.: 112–114 °C;  $R_f$ : 0.33 (CH<sub>2</sub>Cl<sub>2</sub>/MeOH 9/1)/silica. IR (KBr, cm<sup>-1</sup>):  $\nu$  (OH) = 3444;  $\nu$  (C=O) = 1599;  $\nu$  (enolic C=C) = 1549; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>):  $\delta$  3.83 (s, 3H, O-CH<sub>3</sub>); 7.08 (d, 2H, Ar-H<sub>3,5</sub>); 7.50 (s, 1H, enol, CH); 7.62 (t, 1H, Py-H <sub>$\delta$</sub> ); 7.97 (t, 1H, Py-H <sub>$\beta$</sub> ); 8.04 (d, 2H, Ar-H<sub>2,6</sub>); 8.08 (t, 1H, Py-H <sub>$\gamma$</sub> ); 8.76 (d, 1H, Py-H <sub>$\alpha$</sub> ). <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>):  $\delta$  56.1 (1C, OCH<sub>3</sub>); 92.8 (1C, enol, CH); 114.5 (2C, Ar-C<sub>3,5</sub>);

122.2 (1C, Py-C<sub>δ</sub>); 127.5 (2C, Ar-C<sub>2,6</sub>); 138.2 (1C, Py-C<sub>γ</sub>); 150.1 (1C, Py-C<sub>α</sub>); 182.1 (1C, C-OH); 186.6 (1C, C=O); MS: *m/z*, 256.08 (M + H)<sup>+</sup>. Anal. Calcd. for C<sub>15</sub>H<sub>13</sub>NO<sub>3</sub>: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.76; H, 5.20, N, 5.59.

(Z)-1-(Furan-2-yl)-3-hydroxybut-2-en-1-one (**9**). Red hygroscopic; yield: 39%; *R<sub>f</sub>*: 0.91 (CH<sub>2</sub>Cl<sub>2</sub>/MeOH 8/2)/silica. IR (KBr, cm<sup>-1</sup>): ν (OH) = 3434 cm<sup>-1</sup>; ν (C=O) = 1620 cm<sup>-1</sup>; ν (enolic C=C) = 1468; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): δ 2.13 (s, 3H, -CH<sub>3</sub>); 6.06 (s, 1H, enol, C-H); 6.52 (m, 1H, Fu-H<sub>β</sub>); 7.14 (d, 1H, Fu-H<sub>γ</sub>); 7.55 (m, 1H, Fu-H<sub>α</sub>); <sup>13</sup>C-NMR (CDCl<sub>3</sub>): δ 24.4 (1C, CH<sub>3</sub>-C=O); 96.0 (1C, C-H, enol); 112.4 (1C, Fu-C<sub>γ</sub>); 115.5 (1C, Fu-C<sub>β</sub>); 145.9 (1C, Fu-C<sub>α</sub>); 150.0 (1C, Fu-C<sub>δ</sub>); 176.1 (1C, C=O), 19.5 (1C, C-OH); MS: *m/z*, 153.10 (M + H)<sup>+</sup>. Anal. Calcd. for C<sub>8</sub>H<sub>8</sub>O<sub>3</sub>: C, 63.15; H, 5.30. Found: C, 63.25, H, 5.38.

(Z)-1-(Furan-2-yl)-3-hydroxy-3-phenylprop-2-en-1-one (**10**). Red powder; yield 42%; m.p. 64–66 °C; *R<sub>f</sub>*: 0.61 (CH<sub>2</sub>Cl<sub>2</sub>/silica). IR (KBr, cm<sup>-1</sup>): ν (OH) = 3431; ν (C=O) = 1621; ν (enolic C=C) = 1531; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>): δ 6.72 (d, 1H, Fu-H<sub>γ</sub>); 7.01 (s, 1H, enol, C-H); 7.52 (d, 2H, Ar-H<sub>3,5</sub>); 7.58 (t, 1H, Ar-H<sub>4</sub>); 7.64 (d, 2H, Ar-H<sub>2,6</sub>); 8.00 (t, 1H, Fu-H<sub>β</sub>); 8.04 (d, 1H, Fu-H<sub>α</sub>); <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>): δ 93.3 (1C, C-H, enol); 113.5 (1C, Fu-C<sub>γ</sub>); 120.2 (1C, Fu-C<sub>β</sub>); 127.3 (2C, Ar-C<sub>3,5</sub>); 129.2 (3C, Ar-C<sub>2,4,6</sub>); 148.7 (1C, Fu-C<sub>α</sub>); 178.5 (1C, C=O); 180.8 (1C, C-OH); MS: *m/z*, 215.12 (M + H)<sup>+</sup>.

### 3.3. Anticancer Assays

Prepared compounds were screened against breast cancer (MDA-MB241) human cell lines using normoxic conditions [20]. Tests were performed in Angiogenesis and Cancer Research Lab, Institute of Experimental and Clinical Research (UCL, Brussels, Belgium).

### 3.4. Antibacterial and Antifungal Tests

The *in vitro* antifungal activities were tested by the agar diffusion technique [21] using fungal strains (*Fusarium oxysporum f.sp. albedinis* FAO).

The results were compared with positive controls (benomyl and thiophanate-methyl). The *in vitro* antibacterial activities were tested using bacterial strains (*Echerichia coli*, *Bacillus subtilis*, and *Micrococcus luteus*).

## 4. Conclusions

In summary, we have described the first synthesis of novel β-keto-enols embedded with heterocyclic moieties and the evaluation of their *in vitro* anticancer and antifungal activities. Most of the compounds showed modest antiproliferative activity against breast cancer (MDA-MB241) human cell lines. Among the synthesized products, compounds **1**, **5**, and **9** successfully showed the most potent antifungal activity with IC<sub>50</sub> values in the range of 0.055–0.092 μM as compared with positive controls.

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**Sample Availability:** Samples of the compounds are available from the authors.



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