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Utilization of a Propenone Derivative in the Synthesis of Some New Cytotoxic Heterocyclic Compounds

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Abstract—New diaryl-substituted pyridine, pyrimidine, pyrazole, and isoxazole derivatives bearing biphenyl-4-yl and 4-(dimethylamino)phenyl substituents have been prepared by the reaction of 1-(1,1′-biphenyl-4-yl)-3-[4-(dimethylamino)phenyl]prop-2-en-1-one with different nitrogen nucleophiles such as urea, thiourea, guanidine hydrochloride, semicarbazide hydrochloride, thiosemicarbazide, and hydroxylamine hydrochloride. Nicotinonitrile derivative has been synthesized by one-pot reaction of 4-acetylbiphenyl, 4-(dimethylamino)-benzaldehyde, and malononitrile in the presence of ammonium acetate under microwave irradiation, and subsequent treatment with hydrazine hydrate gave 4,6-diaryl-1*H*-pyrazolo[3,4-*b*]pyridin-3-amine. The behavior of 4,6-diarylpyrimidin-2-amine toward carbon electrophiles has been investigated by reacting it with *p*-toluenesulfonyl chloride, acetyl chloride, ethyl acetoacetate, ethyl cyanoacetate, and nitrous acid to afford the corresponding N-substituted derivatives. 3,5-Diaryl-4,5-dihydro-1*H*-pyrazole-1-carboxamide reacted with *p*-toluenesulfonyl chloride and phenylhydrazine to produce *N*-tosyl carboxamide and carbohydrazonamide derivatives, respectively. Treatment of analogous pyrazole-1-carbothioamide with phenyl isothiocyanate, *p*-toluenesulfonyl chloride, and chloroacetyl chloride afforded *N*-(phenylcarbamothioyl), *N*-tosyl, and aminoacetamide derivatives, respectively. All the synthesized compounds were characterized by ^{1}H NMR, IR, and mass spectra and elemental analyses. Some of the newly synthesized compounds were evaluated for their *in vitro* cytotoxic activity against HePG-2 and MCF-7 cell lines. 4-(1,1′-Biphenyl-4-yl)-6-[4-(dimethylamino)phenyl]-5,6-dihydropyrimidine-2(1*H*)-thione and 4-[5-(1,1′-biphenyl-4-yl)-4,5-dihydro-1,2-oxazol-3-yl]-*N*,*N*-dimethylaniline displayed a promising growth inhibitory effect toward the two cell lines in comparison with the standard drug doxorubicin.

Keywords: pyrimidine, pyrazole, isoxazole, cyanopyridine

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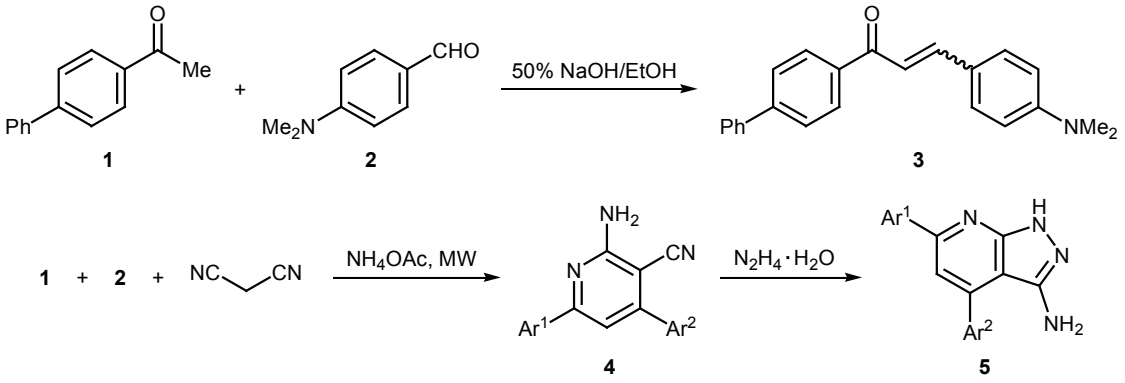
The chemistry of different chalcone compounds has been extensively studied throughout the world. Especial interest has been focused on their synthesis and pharmacological activities. Chalcone derivatives are versatile synthons, so that a variety of novel heterocycles with good pharmaceutical profiles can be designed. Chalcone compounds have a broad spectrum of biological activities, such as antibacterial [1], antioxidant [2], anti-inflammatory [3], antimalarial [4], antileishmanial [5], anticancer [6], and antitumor [7]. Different methods are available for the preparation of chalcones [8–12]. Chalcones are used to synthesize several derivatives like cyanopyridines, dihydropyrazoles, isoxazoles, and pyrimidines [6]. All these benefits encouraged us to synthesize a new chalcone compound and new heterocyclic compounds derived therefrom with potential cytotoxic activity.

Herein, we report the synthesis of a new chalcone **1** by the reaction of 4-acetylbiphenyl (**1**) with 4-(dimethylamino)benzaldehyde (**2**) in ethanol in the presence of sodium hydroxide (Scheme 1). The IR spectrum of **3** showed characteristic absorption bands at 1647 and 1603 cm^{-1} due to C=O and C=C stretching vibrations, respectively. The ^{1}H NMR spectrum of **3** showed signals at δ 3.01 and 6.75–8.20 ppm attributable to the NMe_2 group and aromatic protons, respectively. The mass spectrum of **3** showed the molecular ion peak at *m*/*z* 327 (100%, $[M]^{+\cdot}$) which coincided with the calculated molecular weight and confirmed the proposed structure.

One-pot reaction of 4-acetylbiphenyl **1**, aldehyde **2**, and malononitrile in the presence of ammonium acetate under microwave irradiation gave nicotinonitrile **4** (Scheme 1). The structure of **4** was confirmed by ana-

Scheme 1.



Ar^1 = 4-PhC_6H_4, Ar^2 = 4-$Me_2NC_6H_4$.

lytical and spectroscopic data. The IR spectrum of **4** showed bands at 3184 and 2209 cm^{-1} corresponding to ν(NH_2) and ν(C≡N), respectively. The ^1H NMR spectrum of **4** showed a two-proton D_2O exchangeable signal at δ 4.04 ppm due to the NH_2 group. The reaction of **4** with hydrazine hydrate gave pyrazolopyridine **5**. The IR spectrum of **5** showed bands at 3323 and 1610 cm^{-1} which were assigned to N–H and C=N stretchings, respectively. The NH_2 and NH protons resonated in the ^1H NMR spectrum of **5** at δ 6.40 (2H) and 10.89 ppm (1H), respectively.

Pyrimidine ring is a core of various bioactive molecules and is best known as the heterocyclic core of nucleic acid bases [13]. Compound **3** was involved in aza-Michael reactions with some nitrogen nucleophiles to give different heterocyclic compounds. The reaction of **3** with urea, thiourea, and guanidine hydrochloride afforded pyrimidinone **6**, pyrimidinethione **7**, and pyrimidin-2-amine **8**, respectively (Scheme 2). The structures of compounds **6**–**8** were confirmed by their analytical and spectroscopic data. The IR spectrum of **6** showed a carbonyl band at 1642 cm^{-1}, and its ^1H NMR spectrum contained signals at δ 2.99 and 2.87 ppm due to CH_3 and CH_2 groups in addition to aromatic proton signals. The IR spectrum of **7** showed bands at 1613 and 1184 cm^{-1} corresponding to ν(C=N) and ν(C=S), respectively. The presence of two downfield signals in the ^1H NMR spectrum of **7** at δ 8.96 and 9.76 ppm (D_2O-exchangeable) indicated that it exists in DMSO solution as a mixture of thione and thiol tautomers. The mass spectra of compounds **6**–**8** were also consistent with the postulated structures.

Chalcone **3** was also reacted with semicarbazide hydrochloride and thiosemicarbazide to obtain pyrazole-1-carboxamide **9** and pyrazole-1-carbothioamide **10**, respectively (Scheme 2). The IR spectra of compounds **9** and **10** showed bands at 3237, 3132, 3210, 3125 (N–H), 1691 (C=O), and 1362 cm^{-1} (C=S). The reaction of **3** with hydroxylamine hydrochloride gave dihydroisoxazole derivative **11**. The IR spectrum of compound **11** showed bands at 1616 and 1531 cm^{-1} corresponding to ν(C=N) and ν(C=C), respectively. The ^1H NMR spectrum of **11** displayed signals at δ 3.37, 3.78 (CH_2) and 5.59 ppm (CH). Further evidence for the proposed structure of **11** was gained from its mass spectrum which contained the molecular ion peak at *m/z* 342, as well as other important peaks.

Pyrimidin-2-amine **8** was reacted with different electrophiles to yield some new interesting heterocyclic compounds. The reactions of **8** with *p*-toluenesulfonyl chloride and acetyl chloride gave *N*-(pyrimidin-2-yl) *p*-toluenesulfonamide **12** and acetamide **13**, respectively (Scheme 3). The IR spectrum of **13** showed absorption bands at 3203 (N–H) and 1682 cm^{-1} (C=O). The ^1H NMR spectrum of **13** showed signals at δ 2.35, 3.02, and 10.34 ppm due to protons of three methyl groups and NH proton, as well as aromatic proton signals. The mass spectra of **12** and **13** displayed the molecular ion peaks with the expected *m*/*z* values, 520 and 408, respectively. The structure of **13** was also proved chemically by its reaction with 4-methoxybenzaldehyde in the presence of sodium ethoxide, which produced acrylamide derivative **14**. The spectroscopic data of **14** were in agreement with the proposed structure.

The reaction of pyrimidin-2-amine **8** with ethyl acetoacetate afforded oxobutanamide **15** which was characterized by IR bands at 3285 and 1682 cm^{-1} for the NH and C=O groups, respectively. The ^1H NMR spectrum of **15** showed three singlets at δ 2.17 (CH_3), 2.87 (CH_2), and 10.82 ppm (NH). Likewise, pyrimidin-2-amine **8** reacted with ethyl cyanoacetate to afford

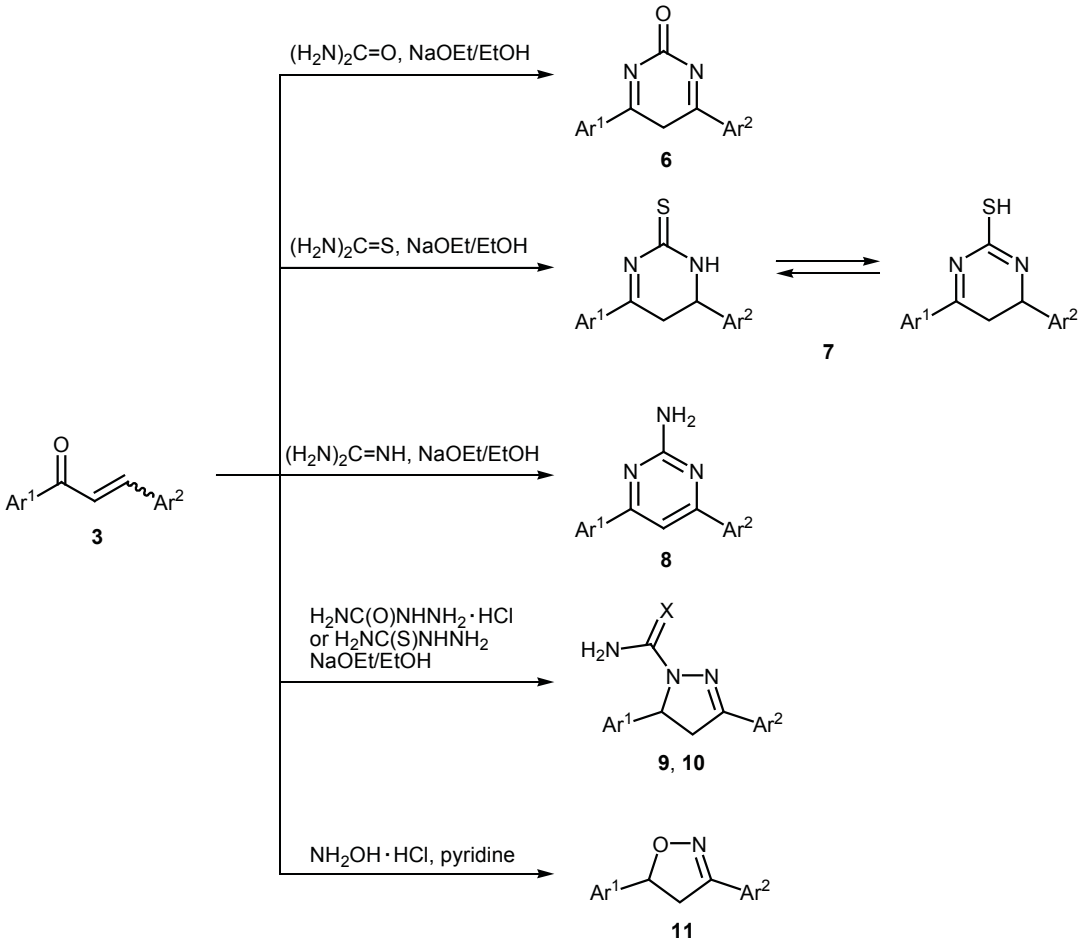
cyanoacetamide derivative **16**. The IR spectrum of **16** displayed bands at 3288 (NH), 2202 (C≡N), and 1678 cm^{-1} (C=O), and its ^1H NMR contained signals at δ 3.97, 5.89, 6.52 and 10.86 ppm attributable to the CH_2, =CH, and NH protons, respectively.

The primary amino group of **8** is capable of forming the corresponding diazonium salt upon treatment with nitrous acid at 0–5°C, and the subsequent azo coupling with ethyl cyanoacetate as a carbon nucleophile afforded triazolone derivative **17** (Scheme 3). The structure of compound **17** was confirmed by the presence of bands at 3291 and 1642 cm^{-1} for NH and C=O groups, respectively, in the IR spectrum and signals at δ 7.90 (CH=) and 7.92 ppm (NH) in the ^1H NMR spectrum.

By reacting pyrazole derivative **9** with *p*-toluenesulfonyl chloride in the presence of a few drops of triethylamine in anhydrous dioxane we obtained *N*-tosyl-1*H*-pyrazole-1-carboxamide **18** (Scheme 4). The IR spectrum of **18** contained strong absorption bands at 3185 and 1657 cm^{-1} due to NH and C=O stretching vibrations, respectively. The ^1H NMR spectrum of **18** showed singlets at δ 2.06, 3.02, and 10.08 ppm attributable to methyl groups and NH proton. Treatment of **9** with phenylhydrazine in DMF gave carbohydrazonamide derivative **19**. The IR spectrum of compound **19** displayed absorption bands at 3466 and 1663 cm^{-1}, which were assigned to NH (NH_2) and C=N stretchings, respectively. In the ^1H NMR spectrum of **19**, the CH_2 and NH protons resonated as a multiplet at δ 3.79–3.88, and the NH_2 signal appeared as a D_2O-exchangeable singlet at 6.56 ppm.

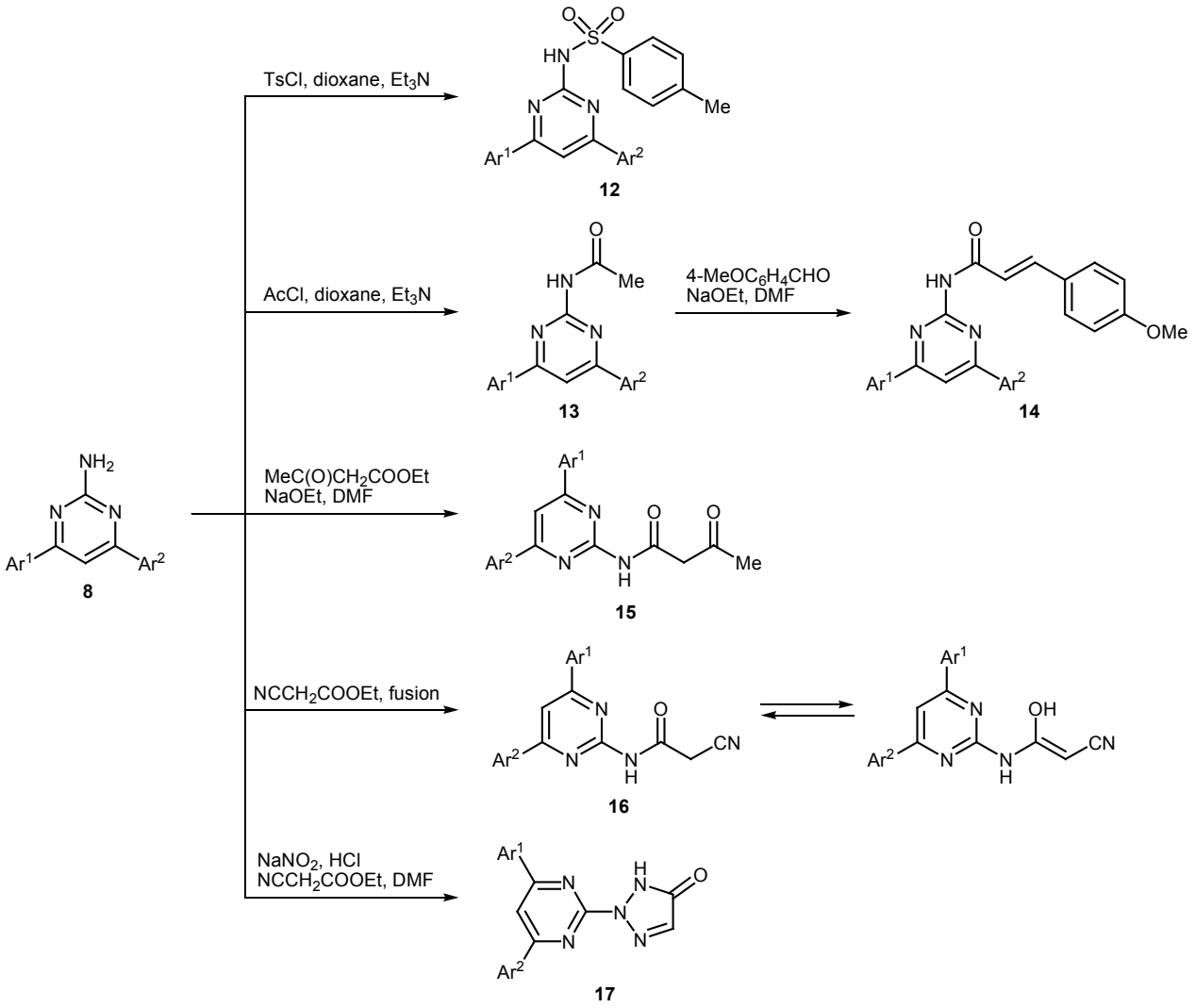
Furthermore, pyrazole-1-carbothioamide derivative **10** was treated with phenyl isothiocyanate in the presence of triethylamine as a base catalyst in boiling DMF; the product was *N*-(phenylcarbamothioyl)pyrazole-1-carbothioamide **20** which showed IR bands at 3259 and 1354 cm^{-1} for the NH and C=S groups, respectively. The ^1H NMR spectrum of **20** exhibited a singlet D_2O-exchangeable signal at δ 7.83 ppm attri-

Scheme 2.



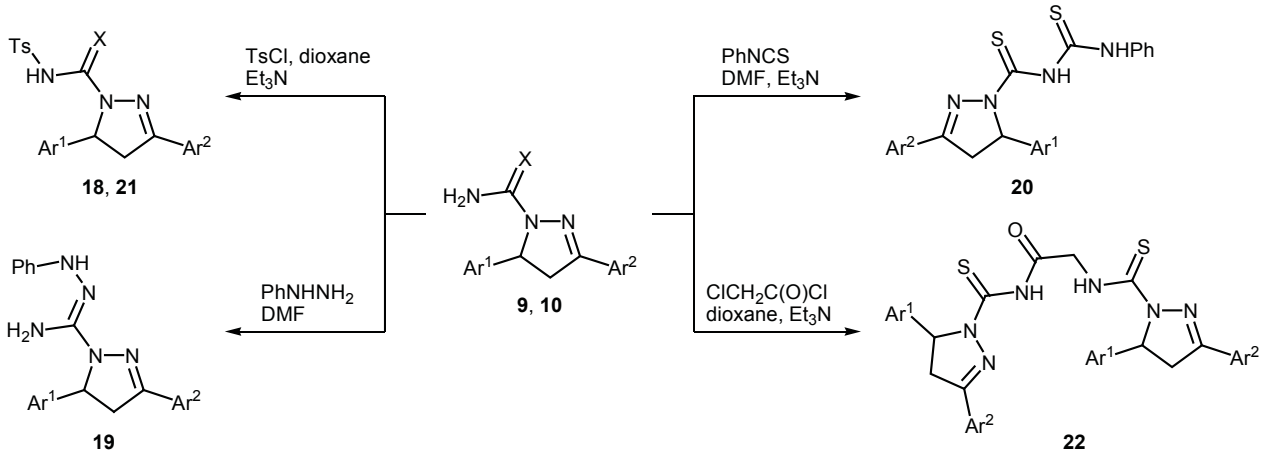
Ar^1 = 4-PhC_6H_4, Ar^2 = 4-$Me_2NC_6H_4$; **9**, X = O; **10**, X = S.

Scheme 3.



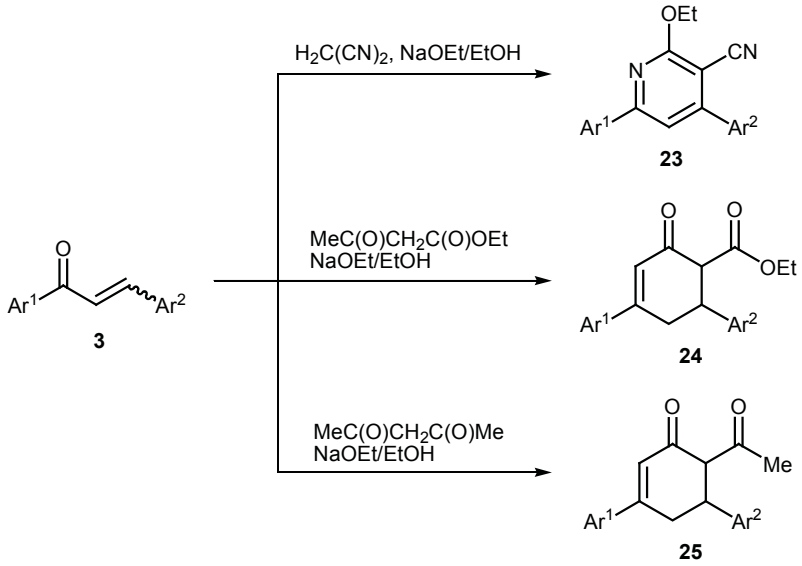
Ar^1 = 4-PhC_6H_4, Ar^2 = 4-$Me_2NC_6H_4$.

Scheme 4.



Ar^1 = 4-PhC_6H_4, Ar^2 = 4-$Me_2NC_6H_4$; **9**, **18**, X = O; **10**, **21**, X = S.

Scheme 5.



Ar^1 = 4-PhC_6H_4, Ar^2 = 4-$Me_2NC_6H_4$.

buted to two NH protons. The proposed structure of **20** was further supported by the mass spectrum where the $[M + H - PhNHCS]^+$ ion peak at *m*/*z* 400 was observed as the base peak.

The reaction of **10** with *p*-toluenesulfonyl chloride gave *N*-tosyl derivative **21.** The IR spectrum of **21** displayed NH and C=S stretching bands at 3416 and 1171 cm^{-1}, respectively. The ^1H NMR spectrum showed signals at δ 2.98, 3.02, and 10.60 ppm due to CH_3 groups and NH proton (D_2O exchangeable). Chloroacetyl chloride reacted with 2 equiv of **10** to produce acetamide derivative **22** containing two pyrazolecarbothioamide fragments (Scheme 4). The IR spectrum of **22** contained bands at 3423 (N–H), 1700 (C=O), and 1365 cm^{-1} (C=S), and its ^1H NMR spectrum displayed three methylene proton signals at δ 3.39, 3.43, and 3.89 ppm and a two-proton signal at δ 9.49 ppm due to NH protons (D_2O exchangeable).

Finally, reactions of chalcone **3** with CH acids such as malononitrile, ethyl acetoacetate, and acetylacetone in ethanolic sodium ethoxide afforded the corresponding cyclization products, 2-ethoxynicotinonitrile **23** and cyclohexenone derivatives **24** and **25** (Scheme 5). The assigned structures of **23**–**25** were confirmed by their IR and ^1H NMR spectra.

The cytotoxic activity of 16 newly synthesized compounds was evaluated using *in vitro* Ehrlich ascites assay against two human tumor cell lines, namely hepatocellular carcinoma HepG2 and breast cancer MCF-7 cell lines (Table 1). In general, the activity of the tested compounds ranged from very strong to non-cytotoxic effect. Compounds **7**, **10**, **11**, and **24** were found to be the most potent against both cancer cell lines. Compound **7** displayed a strong activity against HepG-2 (IC_{50} = 19.65±1.7 μM) and MCF-7 (IC_{50} = 12.18±1.2 μM). The activity of isoxazole derivative **11**

Table 1. Cytotoxicity (IC_{50}) of compounds **3**, **4**, **6**–**14**, **17**, and **21**–**25** against HepG2 and MCF-7 tumor cell lines

Comp. no.	IC_{50},[a] μM	
	HepG2	MCF-7
3	59.33±3.7	47.94±3.3
4	29.34±2.3	33.58±2.4
6	48.85±3.4	45.25±3.4
7	19.65±1.7	12.18±1.2
8	>100	>100
9	>100	78.37±4.4
10	31.56±2.5	18.13±1.7
11	13.71±1.2	10.02±1.0
12	89.70±4.7	81.34±4.6
13	85.50±4.5	87.41±4.9
14	>100	91.47±5.2
17	55.48±3.6	58.42±3.6
21	77.54±4.0	64.89±3.9
23	62.21±3.8	69.53±4.0
24	26.05±2.2	20.72±1.9
25	34.72±2.6	39.04±2.7
DOX[b]	4.50±0.3	4.17±0.2

[a] IC50 (μM): 1–10 (very strong); 11–20 (strong); 21–50 (moderate); 51–100 (weak); >100 (noncytotoxic).

[b] Doxorubicin.

was even higher, IC_{50} = 13.71±1.2 and 10.02±1.0 μM against HepG-2 and MCF-7, respectively. Compounds **10** and **24** showed only a moderate activity (IC_{50} = 31.56±2.5 and 26.05±2.2 μM against HepG-2 and 18.13±1.7 and 20.72±1.9 μM against MCF-7, respectively). The other compounds were either weakly active or exhibited no cytotoxic effect against the given cancer cell lines.

Analysis of the structure–activity relationship suggests that the activity of compound **7** may be due to the presence of sulfanyl (SH) and NH groups capable of adding to any unsaturated DNA moiety via thia- or aza-Michael addition or forming hydrogen bonds with nucleobases thus causing DNA damage. Likewise, the cytotoxic activity of **10** against MCF-7 cell line may be favored by the presence of NH_2 group. Dihydroisoxazole ring and cyclohexenone ring in combination with an ester group may also contribute to the activity of compounds **11** and **24**, respectively.

In summary, we have synthesized a new chalcone derivative and various new heterocyclic compounds based thereon. Some of the synthesized compounds exhibited moderate to strong cytotoxic activity against HepG2 and MCF-7 cancer cell lines.

EXPERIMENTAL

The melting points were measured on a Gallenkamp melting point apparatus and are uncorrected. The IR spectra were recorded using potassium bromide disks on a Mattson FTIR infrared spectrophotometer (USA). The ^{1}H NMR spectra were run at 400 and 300 MHz on Varian Mercury VX-400 and 300 spectrometers (Bruker, Germany) using DMSO-d_6 as solvent and tetramethylsilane as internal standard. The mass spectra (electron impact, 70 eV) were recorded on a Shimadzu GCMS-QP-1000EX mass spectrometer (Japan). The spectral measurements were carried out at the Main Defense and Cairo University Chemical Laboratories (Cairo, Egypt). The elemental analyses were carried out at the Microanalytical Center of Ain Shams University (Cairo, Egypt). The pharmaceutical activity assays were carried out at the Pharmacology Department, Faculty of Pharmacy, EL-Mansoura University (EL-Mansoura, Egypt). The progress of reactions was monitored by TLC.

1-(1,1′-Biphenyl-4-yl)-3-[4-(dimethylamino)-phenyl]prop-2-en-1-one (3). A mixture of 1.96 g (0.01 mol) of 4-acetylbiphenyl, 1.49 g (0.01 mol) of 4-(dimethylamino)benzaldehyde, and 10 g of freshly prepared 50% aqueous sodium hydroxide in 40 mL of ethanol was stirred at 0°C for 5–6 h. The mixture was left overnight in a refrigerator, and the solid product was filtered off, washed with water, dried, and recrystallized from benzene. Yield 3.1 g (95%), yellow crystals, mp 160–162°C. IR spectrum, ν, cm^{-1}: 1647 (C=O), 1603 (C=C). ^{1}H NMR spectrum, δ, ppm: 3.01 s (6H, CH_3), 6.75 d (2H, H_{arom}), 7.40–7.51 m (3H, H_{arom}), 7.63 d (1H, =CH), 7.66–7.74 m (6H, H_{arom}), 7.84 d (1H, =CH), 8.20 d (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 327 (100) $[M]^+$, 328 (23) [*M* + 1], 329 (4). Found, %: C 84.50; H 6.55; N 4.39. $C_{23}H_{21}NO$. Calculated, %: C 84.37; H 6.46; N 4.28.

2-Amino-6-(1,1′-biphenyl-4-yl)-4-[4-(dimethylamino)phenyl]pyridine-3-carbonitrile (4). A mixture of 1.96 g (0.01 mol) of 4-acetylbiphenyl, 1.49 g (0.01 mol) of 4-(dimethylamino)benzaldehyde, 0.66 g (0.01 mol) of malononitrile, and 6 g (0.08 mol) of ammonium acetate was heated for 7 min under microwave irradiation at a power of 270 W. After cooling, the solid was filtered off, washed with ethanol, dried, and recrystallized from benzene. Yield 0.62 g (16%), red crystals, mp 172–174°C. IR spectrum, ν, cm^{-1}: 3184 (NH_2), 2209 (C≡N), 1614 (C=N), 1565 (C=C). ^{1}H NMR spectrum, δ, ppm: 3.03 s (6H, CH_3), 4.04 br.s (2H, NH_2, D_2O exchangeable), 6.82 d (2H, H_{arom}), 7.44–7.50 m (5H, H_{arom}), 7.75 d (2H, H_{arom}), 7.87 m (2H, H_{arom}), 8.03 s (1H, H_{arom}), 8.22 d (2H, Harom). Mass spectrum, *m*/*z* (I_{rel}, %): 390 (38) $[M]^+$, 270 (39), 69 (100). Found, %: C 80.08; H 5.79; N 14.24. $C_{26}H_{22}N_4$. Calculated, %: C 79.97; H 5.68; N 14.35.

6-(1,1′-Biphenyl-4-yl)-4-[4-(dimethylamino)-phenyl]-1*H*-pyrazolo[3,4-*b*]pyridin-3-amine (5). A mixture of 3.9 g (0.01 mol) of compound **4** and 0.5 mL (0.01 mol) of hydrazine hydrate in 30 mL of ethanol was refluxed for 13 h. The mixture was concentrated, and the solid product was filtered off, dried, and recrystallized from ethanol. Yield 1.49 g (37%), red crystals, mp 228–230°C. IR spectrum, ν, cm^{-1}: 3323 (NH, NH_2), 1610 (C=N), 1525 (C=C). ^{1}H NMR spectrum, δ, ppm: 3.01 s (6H, CH_3), 6.40 s (2H, NH_2, D_2O exchangeable), 6.56 d (2H, H_{arom}), 6.79–6.84 m (3H, H_{arom}), 7.45 d.d (2H, H_{arom}), 7.82 d (2H, H_{arom}), 7.64–7.82 m (3H, H_{arom}), 8.36 d (2H, H_{arom}), 10.89 s (1H, NH, D_2O exchangeable). Mass spectrum, *m*/*z* (I_{rel}, %): 405 (33) $[M]^+$, 376 (55), 144 (86), 131 (100). Found, %: C 77.13; H 5.63; N 17.36. $C_{26}H_{23}N_5$. Calculated, %: C 77.01; H 5.72; N 17.27.

4-(1,1′-Biphenyl-4-yl)-6-[4-(dimethylamino)-phenyl]pyrimidin-2(5*H*)-one (6). A mixture of 3.27 g (0.01 mol) of chalcone **3** and 0.6 g (0.01 mol) of urea in a solution of sodium ethoxide prepared from

0.01 mol of sodium and 25 mL of ethanol was refluxed for 19 h. After cooling, the yellow solid was filtered off, washed with water, dried, and recrystallized from benzene. Yield 1.1 g (30%), yellow crystals, mp >300°C. IR spectrum, ν, cm^{-1}: 1642 (C=O), 1590 (C=C). ^1H NMR spectrum, δ, ppm: 2.99 s (6H, CH_3), 2.87 s (2H, CH_2), 6.57 d (1H, H_{arom}), 6.76 d (1H, H_{arom}), 7.29–7.41 m (3H, H_{arom}), 7.43–7.45 m (2H, H_{arom}), 7.63–7.79 m (2H, H_{arom}), 7.91 d (2H, H_{arom}), 8.04 d (1H, H_{arom}), 8.21 d (1H, H_{arom}), Mass spectrum, *m*/*z* (I_{rel}, %): 355 (35), 247 (19), 159 (100), 120 (43). Found, %: C 78.47; H 5.78; N 11.40. $C_{24}H_{21}N_3O$. Calculated, %: C 78.45; H 5.76; N 11.44.

4-(1,1′-Biphenyl-4-yl)-6-[4-(dimethylamino)-phenyl]-5,6-dihydropyrimidine-2(1*H*)-thione (7). A mixture of 3.27 g (0.01 mol) of chalcone **3** and 0.7 g (0.01 mol) of thiourea in a solution of sodium ethoxide prepared from 0.01 mol of sodium and 25 mL of ethanol was refluxed for 14 h. After cooling, the red solid was filtered off, washed with water, dried, and recrystallized from ethanol. Yield 0.95 g (25%), red crystals, mp 216–218°C. IR spectrum, ν, cm^{-1}: 1613 (C=N), 1561 (C=C), 1184 (C=S). ^1H NMR, δ, ppm: 2.63–2.65 m (1H, CH_2), 2.86 s (6H, CH_3), 3.00–3.03 m (1H, CH_2), 4.96 d.d (1H, CH), 6.71 d (2H, H_{arom}), 7.13 d (2H, H_{arom}), 7.34–7.47 m (5H, H_{arom}), 7.59 d (2H, H_{arom}), 7.66 d (1H, H_{arom}), 7.68 d (1H, H_{arom}), 8.96 s (1H, SH), 9.76 s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 371 (22) $[M + H - CH_2]^+$, 342 (21), 312 (100). Found: C 74.92; H 6.10; N 10.82; S 8.39. $C_{24}H_{23}N_3S$. Calculated, %: C 74.77; H 6.01; N 10.90; S, 8.32.

4-(1,1′-Biphenyl-4-yl)-6-[4-(dimethylamino)-phenyl]pyrimidin-2-amine (8). A mixture of 3.27 g (0.01 mol) of chalcone **3** and 0.96 g (0.01 mol) of guanidine hydrochloride in a solution of sodium ethoxide prepared from 0.01 mol of sodium and 25 mL of ethanol was refluxed for 25 h. After cooling, the solid product was filtered off, washed with water, dried, and recrystallized from benzene. Yield 1.31 g (36%), pale green crystals, mp 224–228°C. IR spectrum, ν, cm^{-1}: 3286, 3136 (NH_2), 1618 (C=N), 1567 (C=C). ^1H NMR spectrum, δ, ppm: 2.98 s (6H, CH_3), 6.51 d (2H, H_{arom}), 6.78 d (2H, H_{arom}), 7.34–7.50 m (3H, H_{arom}), 7.61 s (1H, H_{arom}), 7.73–7.75 m (3H, H_{arom}), 7.79 d (1H, H_{arom}), 8.08 s (2H, NH_2, D_2O exchangeable), 8.10 d (1H, H_{arom}), 8.26 d (1H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 366 (100) $[M]^+$, 367 (27) $[M + 1]^+$, 368 (10) $[M + 2]^+$. Found, %: C 78.86; H 6.00; N 15.34. $C_{24}H_{22}N_4$. Calculated, %: C 78.66; H 6.05; N 15.29.

5-(1,1′-Biphenyl-4-yl)-3-[4-(dimethylamino)-phenyl]-4,5-dihydro-1*H*-pyrazole-1-carboxamide (9). A mixture of 3.27 g (0.01 mol) of chalcone **3** and 1.12 g (0.01 mol) of semicarbazide hydrochloride in a solution of sodium ethoxide prepared from 0.01 mol of sodium and 25 mL of ethanol was refluxed for 11 h. After cooling, the solid product was filtered off, washed with water, dried, and recrystallized from ethanol. Yield 2.99 g (78%), white crystals, mp 256–258°C. IR spectrum, ν, cm^{-1}: 3210, 3125 (NH_2), 1691 (C=O), 1602 (C=N), 1573 (C=C). ^1H NMR spectrum, δ, ppm: 3.02 s (6H, CH_3), 3.82 d.d (2H, CH_2), 5.42 d.d (1H, CH), 6.53 s (2H, NH_2, D_2O exchangeable), 7.28 d (2H, H_{arom}), 7.35–7.38 m (3H, H_{arom}), 7.44–7.48 m (2H, H_{arom}), 7.69–7.73 m (2H, H_{arom}), 7.85 d (2H, H_{arom}), 7.94 d (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 384 (100) $[M]^+$, 385 (27) $[M + 1]^+$, 386 (14) $[M + 2]$. Found, %: C 75.00; H 6.36; N 14.40. $C_{24}H_{24}N_4O$. Calculated, %: C 74.97; H 6.29; N 14.57.

5-(1,1′-Biphenyl-4-yl)-3-[4-(dimethylamino)-phenyl]-4,5-dihydro-1*H*-pyrazole-1-carbothioamide (10). A mixture of 3.27 g (0.01 mol) of chalcone **3** and 0.9 g (0.01 mol) of thiosemicarbazide in a solution of sodium ethoxide prepared from 0.01 mol of sodium and 25 mL of ethanol was refluxed for 17 h. After cooling, the solid product was filtered off, washed with water, dried, and crystallized from benzene. Yield 2.04 g (51%), yellow crystals, mp 220–222°C. IR spectrum, ν, cm^{-1}: 3237, 3132 (NH_2), 1612 (C=N), 1583 (C=C), 1362 (C=S). ^1H NMR spectrum, δ, ppm: 3.10 s (6H, CH_3), 3.16 d (1H, CH_2), 3.84 d.d (1H, CH_2), 5.80 d.d (1H, CH), 6.63 d (1H, H_{arom}), 6.95 d (1H, H_{arom}), 7.34–7.37 m (4H, H_{arom}), 7.38–7.40 m (3H, H_{arom}), 7.45-7.49 m (3H, H_{arom}), 7.83 s (2H, NH_2, D_2O exchangeable), 7.94 d (1H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 400 (100) $[M]^+$, 367 (76). Found, %: C 72.14; H 6.08; N 14.00; S 8.06. $C_{24}H_{24}N_4S$. Calculated, %: C 71.97; H 6.04; N 13.99; S 8.00.

4-[5-(1,1′-Biphenyl-4-yl)-4,5-dihydro-1,2-oxazol-3-yl]-*N*,*N*-dimethylaniline (11). A mixture of 3.27 g (0.01 mol) of chalcone **3** and 0.69 g (0.01 mol) of hydroxylamine hydrochloride in 10 mL of pyridine was refluxed for 12 h. The mixture was poured into ice-cold aqueous HCl, and the solid product was filtered off, washed with water, dried, and recrystallized from ethanol. Yield 3.31 g (97%), light purple crystals, mp 188–190°C. IR spectrum, ν, cm^{-1}: 1616 (C=N), 1531 (C=C). ^1H NMR spectrum, δ, ppm: 2.87 s (6H, CH_3), 3.37 d.d (1H, CH_2), 3.78 d.d (1H, CH_2), 5.59 d.d (1H, CH), 6.71 d (2H, H_{arom}), 7.21 d (2H, H_{arom}), 7.39 d (2H, H_{arom}), 7.45–7.49 m (3H, H_{arom}), 7.70–7.79 m (4H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 342 (81) $[M]^+$, 343 (18) $[M + 1]^+$, 344 (1) $[M + 2]^+$.

Found, %: C 80.78; H 6.56; N 8.22. $C_{23}H_{22}N_2O$. Calculated, %: C 80.67; H 6.48; N 8.18.

***N*-{4-(1,1′-Biphenyl-4-yl)-6-[4-(dimethylamino)-phenyl]pyrimidin-2-yl}-4-methylbenzenesulfonamide (12).** A mixture of 3.66 g (0.01 mol) of pyrimidine **8**, 1.9 g (0.01 mol) of *p*-toluenesulfonyl chloride, and a few drops of triethylamine in 15 mL of anhydrous dioxane was refluxed for 6 h. After cooling, the solid product was filtered off, washed with dioxane, dried, and recrystallized from dioxane. Yield 2.8 g (54%), red crystals, mp 280–282°C. IR spectrum, ν, cm^{-1}: 3360 (NH), 1649 (C=N), 1595 (C=C). ^1H NMR spectrum, δ, ppm: 2.26 s (3H, CH_3), 3.05 s (6H, CH_3), 6.85 d (2H, H_{arom}), 7.09 d (2H, H_{arom}), 7.44–7.53 m (5H, H_{arom}), 7.78–7.80 m (6H, H_{arom}), 7.91 d (2H, H_{arom}), 7.85 s (1H, NH, D_2O exchangeable), 8.29 s (1H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 520 (10) $[M]^+$, 403 (25), 347 (100). Found, %: C 71.65; H 5.38; N 10.82; S 6.14. $C_{31}H_{28}N_4O_2S$. Calculated, %: C 71.51; H 5.42; N 10.76; S 6.16.

***N*-{4-(1,1′-Biphenyl-4-yl)-6-[4-(dimethylamino)-phenyl]pyrimidin-2-yl}acetamide (13).** A mixture of 3.66 g (0.01 mol) of pyrimidine **8**, 0.78 g (0.01 mol) of acetyl chloride, and a few drops of triethylamine in 15 mL of anhydrous dioxane was refluxed for 8 h. After cooling, the solid was filtered off, washed with dioxane, dried, and recrystallized from dioxane. Yield 3.87 g (95%), brown crystals, mp 240–242°C. IR spectrum, ν, cm^{-1}: 3203 (NH), 1682 (C=O), 1609 (C=N), 1575 (C=C). ^1H NMR spectrum, δ, ppm: 2.35 s (3H, $COCH_3$), 3.02 s (6H, CH_3), 6.81 d (2H, H_{arom}), 7.38–7.40 m (3H, H_{arom}), 7.76–7.78 m (4H, H_{arom}), 7.84 d (2H, H_{arom}), 8.13 s (1H, H_{arom}), 8.22 d (1H, H_{arom}), 8.38 d (1H, H_{arom}), 10.34 s (1H, NH, D_2O exchangeable). Mass spectrum, *m*/*z* (I_{rel}, %): 408 (100) $[M]^+$, 409 (31) $[M + 1]^+$, 410 (6) $[M + 2]^+$. Found, %: C 76.52; H 6.00; N 13.66. $C_{26}H_{24}N_4O$. Calculated, %: C 76.45; H 5.92; N 13.72.

***N*-{4-(1,1′-Biphenyl-4-yl)-6-[4-(dimethylamino)-phenyl]pyrimidin-2-yl}-3-(4-methoxyphenyl)prop-2-enamide (14).** A mixture of 4.08 g (0.01 mol) of compound **13**, 1.36 g (0.01 mol) of 4-methoxybenzaldehyde, 0.01 mol of sodium methoxide in 5 mL of ethanol, and 10 mL of dimethylformamide was stirred at room temperature for 10 min. The solid product was filtered off, washed with water, dried, and recrystallized from dioxane. Yield 1.87 g (36%), yellow crystals, mp 268–270°C. IR spectrum, ν, cm^{-1}: 3290 (NH), 1683 (C=O), 1609 (C=N), 1575 (C=C). ^1H NMR spectrum, δ, ppm: 3.01 s (6H, CH_3), 3.58 s (3H, OCH_3), 6.81 d (2H, H_{arom}), 7.38–7.42 m (4H, H_{arom}, =CH), 7.48–7.51 m (5H, H_{arom}, =CH), 7.77 d (2H, H_{arom}), 7.85 d (2H, H_{arom}), 8.14 s (1H, H_{arom}), 8.22 d (2H, H_{arom}), 8.40 d (2H, H_{arom}), 10.37 s (1H, NH, D_2O exchangeable). Mass spectrum, *m*/*z* (I_{rel}, %): 528 (13) $[M + 2]^+$, 394 (44), 350 (100). Found, %: C 77.46; H 5.80; N 10.72. $C_{34}H_{30}N_4O_2$. Calculated, %: C 77.54; H 5.74; N 10.64.

***N*-{4-(1,1′-Biphenyl-4-yl)-6-[4-(dimethylamino)-phenyl]pyrimidin-2-yl}-3-oxobutanamide (15).** A mixture of 3.66 g (0.01 mol) of pyrimidine **8**, 1.3 mL (0.01 mol) of ethyl acetoacetate, a solution of sodium ethoxide prepared from 0.5 g of sodium and 10 mL of ethanol, and 10 mL of of dimethylformamide was refluxed for 16 h. After cooling, the solid product was filtered off, dried, and recrystallized from ethanol. Yield 2.74 g (61%), pale yellow crystals, mp 198–200°C. IR spectrum, ν, cm^{-1}: 3285 (NH), 1682 (C=O), 1614 (C=N), 1568 (C=C). ^1H NMR , δ, ppm: 2.17 s (3H, CH_3), 2.87 s (2H, CH_2), 3.02 s (6H, CH_3), 6.51 d (2H, H_{arom}), 6.79–7.50 m (5H, H_{arom}), 7.75–7.93 m (2H, H_{arom}), 8.17–8.26 m (2H, H_{arom}), 8.28 s (1H, H_{arom}), 8.67 d (2H, H_{arom}), 10.82 s (1H, NH, D_2O exchangeable). Mass spectrum, *m*/*z* 450 (I_{rel} 4.54%) $[M]^+$. Found, %: C 74.58; H 5.71; N 12.35. $C_{28}H_{26}N_4O_2$. Calculated, %: C 74.65; H 5.82; N 12.44.

***N*-{4-(1,1′-Biphenyl-4-yl)-6-[4-(dimethylamino)-phenyl]pyrimidin-2-yl}-2-cyanoacetamide (16).** A mixture of 3.66 g (0.01 mol) of pyrimidine **8** and 10 mL of ethyl cyanoacetate was fused for 22 h at 250–260°C. The brown solid was washed with ethanol, dried, and recrystallized from ethanol. Yield 0.56 g (13%), brown crystals, mp 296–298°C. IR spectrum, ν, cm^{-1}: 3288 (NH), 2202 (C≡N), 1673 (C=O), 1615 (C=N), 1568 (C=C). ^1H NMR spectrum, δ, ppm: 3.03 s (6H, CH_3), 3.97 s (2H, CH_2), 5.89 s (1H, =CH), 6.52 s (1H, NH, D_2O exchangeable), 6.82 d.d (2H, H_{arom}), 7.39–7.61 m (3H, H_{arom}), 7.61 s (1H, H_{arom}), 7.73–7.80 m (2H, H_{arom}), 7.86 d (2H, H_{arom}), 8.22–8.28 m (2H, H_{arom}), 8.41 d (1H, H_{arom}), 8.59 d (1H, H_{arom}), 10.86 s (1H, OH, D_2O exchangeable). Mass spectrum, *m*/*z* (I_{rel}, %): 433 (6) $[M]^+$, 435 (3), 366 (81), 40.02 (100). Found, %: C 74.68; H 5.27; N 16.20. $C_{27}H_{23}N_5O$. Calculated, %: C 74.81; H 5.35; N 16.16.

2-{4-(1,1′-Biphenyl-4-yl)-6-[4-(dimethylamino)-phenyl]pyrimidin-2-yl}-3,4-dihydro-2*H*-1,2,3-triazol-4-one (17). A solution of 3.66 g (0.01 mol) of pyrimidine derivative **8** in a mixture of 10 mL of DMF and 5 mL of concentrated aqueous HCl was stirred at 0–5°C for 10 min, and a solution of 3 g of sodium nitrite in a mixture of 5 mL of water and 5 mL of DMF was added dropwise with vigorous stirring over

a period of 5 min. The obtained clear diazonium salt solution was then added dropwise with stirring to a cold (0–5°C) solution of 1.13 mL (0.01 mol) of ethyl cyanoacetate in 5 mL of DMF. The mixture was stirred for an additional 5 min at 0–5°C and diluted with 50 mL of cold water, and the solid product was filtered off, washed with water several times, dried, and recrystallized from benzene. Yield 3.99 g (92%), yellow crystals, mp 208–210°C. IR spectrum, ν, cm^{-1}: 3291 (NH), 1642 (C=O). ^1H NMR spectrum, δ, ppm: 3.07 s (6H, CH_3), 6.85 d (2H, H_{arom}), 7.08–7.12 m (3H, H_{arom}), 7.43 t (1H, H_{arom}), 7.49–7.53 m (4H, H_{arom}), 7.79 d (1H, H_{arom}), 7.90 s (1H, =CH), 7.92 s (1H, NH, D_2O exchangeable), 7.88 s (1H, H_{arom}), 8.25 d (1H, H_{arom}), 8.35 d (1H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 434 (3) $[M]^+$, 399 (14), 381 (100). Found, %: C 71.92; H 5.19; N 19.25. $C_{26}H_{22}N_6O$. Calculated, %: C 71.87; H 5.10; N 19.34.

5-(1,1′-Biphenyl-4-yl)-3-[4-(dimethylamino)-phenyl]-*N*-(4-methylbenzenesulfonyl)-4,5-dihydro-1*H*-pyrazole-1-carboxamide (18). A mixture of 3.84 g (0.01 mol) of pyrazole **9**, 1.9 g (0.01 mol) of *p*-toluenesulfonyl chloride, and a few drops of triethylamine in 15 mL of anhydrous dioxane was refluxed for 22 h. The mixture was concentrated, and the solid product was filtered off, dried, and recrystallized from ethanol. Yield 1.22 g (23%), white crystals, mp 280–282°C. IR spectrum, ν, cm^{-1}: 3360 (NH), 1657 (C=O). ^1H NMR spectrum, δ, ppm: 2.06 s (3H, CH_3), 3.02 s (6H, CH_3), 6.96–7.00 m (3H, H_{arom}), 7.38–7.46 m (5H, H_{arom}), 7.70–7.73 m (5H, H_{arom}), 7.84–7.87 m (4H, H_{arom}), 10.08 s (1H, NH, D_2O exchangeable). Mass spectrum, *m*/*z* (I_{rel}, %): 536 (5) $[M]^+$, 538 (2) $[M + 2]^+$, 366 (100), 91 (22). Found, %: C 69.24; H 5.48; N 10.48; S, 5.89. $C_{31}H_{28}N_4O_3S$. Calculated, %: C 69.38; H 5.26; N 10.44; S 5.97.

5-(1,1′-Biphenyl-4-yl)-3-[4-(dimethylamino)-phenyl]-*N*′-phenyl-4,5-dihydro-1*H*-pyrazole-1-carbohydrazonamide (19). A mixture of 3.84 g (0.01 mol) of pyrazole **9** and 1.08 mL (0.01 mol) of phenylhydrazine in 15 mL of DMF was refluxed for 17 h. The mixture was poured onto ice/aqueous HCl, and the solid product was filtered off, washed with water, dried, and recrystallized from ethanol. Yield 1.01 g (22%), brown crystals, mp 162–164°C. IR spectrum, ν, cm^{-1}: 3466, 3385 (NH, NH_2), 1663 (C=N), 1575 (C=C). ^1H NMR spectrum, δ, ppm: 3.02 s (6H, CH_3), 3.79–3.88 m (3H, CH_2, NH), 5.44 d.d (1H, CH), 6.56 s (2H, NH_2, D_2O exchangeable), 7.28 m (3H, H_{arom}), 7.37–7.41 m (3H, H_{arom}), 7.47–7.45 m (3H, H_{arom}), 7.71–7.77 m (6H, H_{arom}), 7.87–7.89 m (3H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 472 (10) $[M - 2]^+$, 355 (35), 341 (12), 167 (95), 43 (100). Found, %: C 76.02; H 6.48; N 17.65. $C_{30}H_{30}N_6$. Calculated, %: C 75.92; H 6.37; N 17.71.

5-(1,1′-Biphenyl-4-yl)-3-[4-(dimethylamino)-phenyl]-*N*-(phenylcarbamothioyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamide (20). A mixture of 4 g (0.01 mol) of pyrazole **10**, 1.35 g (0.01 mol) of phenyl isothiocyanate, and few drops of triethylamine in 15 mL of DMF was refluxed for 26 h. The mixture was concentrated, and the solid product was filtered off, dried, and recrystallized from ethanol. Yield 2.78 g (52%), brown crystals, mp 198–200°C. IR spectrum, ν, cm^{-1}: 3259 (NH), 1614 (C=N), 1575 (C=C), 1354 (C=S). ^1H NMR spectrum, δ, ppm: 2.82 s (6H, CH_3), 3.08 d.d (1H, CH_2), 3.84 d.d (1H, CH_2), 5.80 d.d (1H, CH), 6.63 d (2H, H_{arom}), 6.95 d (2H, H_{arom}), 7.36–7.39 m (2H, H_{arom}), 7.46 d and 7.48 d (2H, H_{arom}), 7.70–7.75 m (8H, H_{arom}), 7.8.3 s (2H, NH, D_2O exchangeable), 7.94 d (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 533 (1) $[M - 2]^+$, 400 (100) $[M + H - PhNHCS]^+$, 367 (38). Found, %: C 69.62; H 5.52; N 13.00; S 11.70. $C_{31}H_{29}N_5S_2$. Calculated, %: C 69.50; H 5.46; N 13.07; S 11.97.

5-(1,1′-Biphenyl-4-yl)-3-[4-(dimethylamino)-phenyl]-*N*-(4-methylbenzenesulfonyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamide (21). A mixture of 4 g (0.01 mol) of pyrazole **10**, 1.9 g (0.01 mol) of *p*-toluenesulfonyl chloride, and a few drops of triethylamine in 15 mL of anhydrous dioxane was refluxed for 24 h. The reaction mixture was concentrated, and the white solid was filtered off, dried, and recrystallized from ethanol. Yield 0.42 g (7.25%), white crystals, mp 264–266°C. IR spectrum, ν, cm^{-1}: 3416 (NH), 1171 (C=S). ^1H NMR spectrum, δ, ppm: 2.98 s (3H, CH_3), 3.02 s (6H, CH_3), 6.94 d (2H, H_{arom}), 7.01 s (1H, =CH), 7.10 d (2H, H_{arom}), 7.39 d (2H, H_{arom}), 7.46 d (2H, H_{arom}), 7.71–7.79 m (7H, H_{arom}), 7.95 d (1H, H_{arom}), 8.00 d (1H, H_{arom}), 10.60 s (1H, NH, D_2O exchangeable). Mass spectrum, *m*/*z* (I_{rel}, %): 552 (2) $[M]^+$, 408 (84), 384 (100). Found, %: C 67.42; H 5.20; N 10.18; S 11.68. $C_{31}H_{28}N_4O_2S_2$. Calculated, %: C 67.37; H 5.11; N 10.14; S 11.60.

***N*-{5-(1,1′-Biphenyl-4-yl)-3-[4-(dimethylamino)-phenyl]-4,5-dihydro-1*H*-pyrazole-1-carbonothioyl}-2-{5-(1,1′-biphenyl-4-yl)-3-[4-(dimethylamino)-phenyl]-4,5-dihydro-1*H*-pyrazole-1-carbothioamido}acetamide (22).** A mixture of 10 g (0.02 mol) of pyrazole **10**, 1.12 g (0.01 mol) of chloroacetyl chloride, and a few drops of triethylamine in 15 mL of anhydrous dioxane was refluxed for 22 h. The mixture was concentrated, and the solid product was filtered off, dried, and crystallized from dioxane. Yield 3.61 g

(43%), brown crystals, mp 130–132°C. IR spectrum, ν, cm^{-1}: 3423 (NH), 1700 (C=O), 1616 (C=N), 1577 (C=C), 1365 (C=S). ^1H NMR spectrum, δ, ppm: 2.84 s (12H, CH_3), 3.41 d.d (2H, CH_2), 3.89 s (2H, CH_2), 4.06 d.d (2H, CH), 5.66 d.d (2H, CH_2), 6.66 d (2H, H_{arom}), 7.03 d (2H, H_{arom}), 7.38–7.42 m (6H, H_{arom}), 7.47–7.52 m (8H, H_{arom}), 7.73 d (4H, H_{arom}), 7.81 d (2H, H_{arom}), 7.91 d (2H, H_{arom}), 9.49 s (2H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 840 (4) $[M]^+$, 439 (100), 428 (5), 414 (1). Found, %: C 71.08; H 5.80; N 13.28; S 7.68. $C_{50}H_{48}N_8OS_2$. Calculated, %: C 71.40; H 5.75; N 13.32; S 7.62.

6-(1,1′-Biphenyl-4-yl)-4-[4-(dimethylamino)-phenyl]-2-ethoxypyridine-3-carbonitrile (23). A mixture of 3.27 g (0.01 mol) of chalcone **3** and 0.66 g (0.01 mol) of malononitrile in a solution of sodium ethoxide prepared from 0.01 mol of sodium and 25 mL of ethanol was refluxed for 16 h. After cooling, the solid product was filtered off, washed with water, dried, and recrystallized from benzene. Yield 1.63 g (39%), phosphorescent crystals, mp 169–170°C. IR spectrum, ν, cm^{-1}: 2215 (C≡N), 1611 (C=N), 1581 (C=C). ^1H NMR spectrum, δ, ppm: 1.45 t (3H, CH_3, J = 6.9 Hz), 3.01 s (6H, CH_3), 4.62–4.64 q (2H, CH_2, J = 6.9 Hz), 6.86 d (2H, H_{arom}), 7.51 t (1H, H_{arom}), 7.68 d (2H, H_{arom}), 7.69 d (2H, H_{arom}), 7.75 d (2H, H_{arom}), 7.77 s (1H, H_{arom}), 7.83 d (2H, H_{arom}), 8.31 d (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 419 (100) $[M]^+$, 420 (27) $[M + 1]^+$, 421 (4) $[M + 2]^+$. Found, %: C 80.20; H 5.58; N 10.00. $C_{28}H_{25}N_3O$. Calculated, %: C 80.16; H 6.01; N 10.02.

Ethyl 4‴-(dimethylamino)-5″-oxo-2″,3″,4″,5″-tetrahydro[1,1′:3′,1″:3″,1‴-quaterphenyl]-4″-carboxylate (24). A mixture of 3.27 g (0.01 mol) of chalcone **3**, 1.26 mL (0.01 mol) of ethyl acetoacetate, 30 mL of ethanol, and a solution of sodium ethoxide prepared from 0.01 mol of sodium in 25 mL of ethanol was refluxed for 8 h. The mixture was poured into ice/aqueous HCl, and the solid product was filtered off, washed with water, dried, and recrystallized from ethanol. Yield 0.32 g (7.44%), brown crystals, mp 138–140°C. IR spectrum, ν, cm^{-1}: 1722 (C=O), 1664 (C=O), 1601 (C=N), 1571 (C=C). ^1H NMR spectrum, δ, ppm: 1.21 t (3H, $CH_2C\mathbf{H}_3$), 2.78–3.07 m (8H, CH_3, CH_2), 3.79–3.92 m (4H, CH, OCH_2), 6.40 s (1H, =CH), 7.00–7.25 m (2H, H_{arom}), 7.34–7.40 m (2H, H_{arom}), 7.45–7.48 m (3H, H_{arom}), 7.59–7.75 m (4H, H_{arom}), 8.00 d (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 439 (29) $[M]^+$, 441 (4) $[M + 2]^+$, 367 (100). Found, %: C 79.36; H 6.70; N 3.12. $C_{29}H_{29}NO_3$. Calculated, %: C 79.24; H 6.65; N 3.19.

6′-Acetyl-4-(dimethylamino)-1′,6′-dihydro-[1,1′:3′,1″:3′,1‴-quaterphenyl]-5′(2′*H*)-one (25). A mixture of 3.27 g (0.01 mol) of chalcone **3**, 1.02 mL (0.01 mol) of acetylacetone, 30 mL of ethanol, and a solution of sodium ethoxide prepared from 0.01 mol of sodium in 25 mL of ethanol was refluxed for 18 h. The mixture was poured into ice/aqueous HCl, and the solid product was filtered off, washed with water, dried, and recrystallized from ethanol. Yield 0.32 g (8%), brown crystals, mp 176–180°C. IR spectrum, ν, cm^{-1}: 1649 (C=O), 1602 (C=N), 1573 (C=C). ^1H NMR spectrum, δ, ppm: 2.72 m (2H, CH_2), 2.91 s (3H, CH_3), 2.99 s (6H, CH_3), 3.03 m (1H, 1′-H), 4.32 d (1H, 6′-H), 6.74 d (3H, H_{arom}, 4′-H), 7.38–7.51 m (3H, H_{arom}), 7.68–7.84 m (4H, H_{arom}), 8.03 d (2H, H_{arom}), 8.18 d (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 409 (28) $[M]^+$, 365 (100). Found, %: C 82.06; H 6.70; N 3.36. $C_{28}H_{27}NO_2$. Calculated, %: C 82.12; H 6.65; N 3.42.

Cytotoxicity assay. The cytotoxic activity of sixteen compounds was tested against two human tumor cell lines, namely hepatocellular (liver) carcinoma HepG2 and mammary gland (breast) cancer MCF-7. The cell lines were obtained from ATCC via the Holding Company for Biological Products and Vaccines (VACSERA, Cairo, Egypt). Doxorubicin was used as a standard anticancer drug for comparison. The reagents used were RPMI-1640 medium, MTT, and DMSO. The inhibitory effects of compounds on the tumor cell growth were evaluated using the MTT assay [14, 15], which is based on the conversion of the yellow tetrazolium bromide (MTT) to a purple formazan derivative by mitochondrial succinate dehydrogenase in viable cells. The cells were cultured in RPMI-1640 medium with 10% fetal bovine serum. The antibiotics added were 100 CFU/mL of penicillin and 100 μg/mL of streptomycin at 37°C in a 5% CO_2 incubator. The cells lines were seeded [16] in a 96-well plate at a density of 1.0×10^4 cells per well at 37°C for 48 h under 5% CO_2. After incubation, the cells were treated with the tested compounds at different concentrations and incubated for 24 h; 20 μL of an MTT solution at 5 mg/mL was added to each well, and the plate was incubated for 4 h. Dimethyl sulfoxide (DMSO), 100 μL, was then added to each well to dissolve the purple formazan formed, and the absorbance at λ 570 nm was measured using a BioTek ELx800 microplate reader (USA).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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