Hetaryl-1,5 Benzodiazepines—Part I: Synthesis of 3-pyrimidinyl- and Imidazolyl-1,5-benzodiazepines

Ahmed Khodairy,* Eman A. Ahmed, and Hossam Abdel Ghany

[a]Chemistry Department, Faculty of Science, Sohag University, Sohag, Egypt
*E-mail: khodairy@yahoo.com

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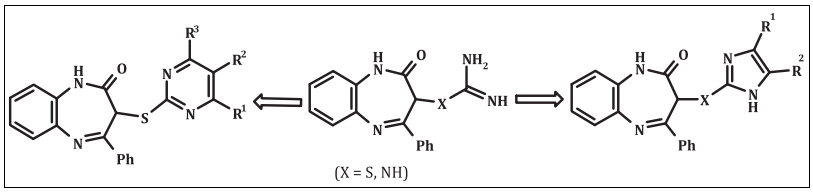

Nucleophilic substitution of 3-bromo-4-phenyl-1*H*-[1,5]benzodiazepin-2-one (**1**) with thiourea or guanidine in presence of potassium carbonate afforded 1,5-benzodiazepin-3-ylimidothiocarbamate **2** or 1,5-benzodiazepin-3-ylguanidine **3**, respectively. Pyrimidylthiobenzodiazepines **5–13** were obtained via the reaction of compound **2** with malononitrile dimer, diethyl malonate, methylenemalononitriles, or a mixture of an aldehyde and β-keto esters or acetylacetone, catalyzed using ceric ammonium nitrate. Reaction of compound **2** or **3** with α-halo esters, nitriles, and/or ketones afforded imidazoles **14–20**, respectively.

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INTRODUCTION

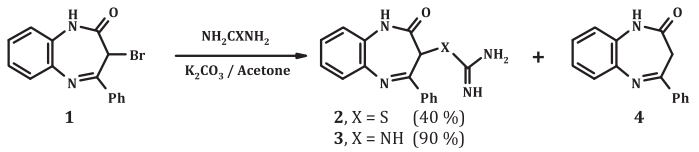
Pyrimidines are reported to possess pharmacological activities, such as antineoplastic and anticancer agents [1], analgesic, anti-pyretic [2], anti-HIV [3], and anti-tubercular [4], and are used as antibiotics [5]. On the other hand, imidazoles possess significant medicinal applications, such as antibacterial and anti-inflammatory activities [6], antifungal activity [7], antiparasitic activity [8], antiviral activity [9], and antidepressant activity [10]. In view of the previous applications, and in continuation of our interest in synthesis of some fused and spiro-1,5-benzodiazepinones [11–17], we aimed to use 2-oxo-4-phenyl-2,3-dihydro-1*H*-1,5-benzodiazepin-3-ylimidothiocarbamate (**2**) and 1-(2-oxo-4-phenyl-2,3-dihydro-1*H*-1,5-benzodiazepin-3-yl) guanidine (**3**) as building blocks for the synthesis of some new family of 3-pyrimidinyl- and imidazolyl-1,5-benzodiazepines with the hope to possess better antimicrobial activity.

RESULTS AND DISCUSSION

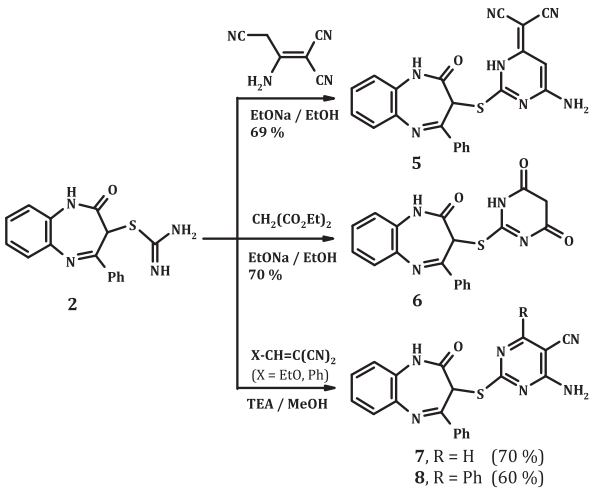
2-Oxo-4-phenyl-2,3-dihydro-1*H*-1,5-benzodiazepin-3-ylimidothiocarbamate (**2**) and 1-(2-oxo-4-phenyl-2,3-dihydro-1*H*-1,5-benzodiazepin-3-yl)guanidine (**3**) were obtained along with 4-phenyl-1*H*-1,5-benzodiazepin-2(3*H*)-one (**4**) [12] via treatment of 3-bromo-4-phenyl-1*H*-[1,5]-benzodiazepin-2(3*H*)-one (**1**) [12] with thiourea or guanidine in presence of potassium carbonate (Scheme 1). The structure of both compounds **2** and **3** was established on the basis of their spectral and analytical data. Their IR spectra displayed absorption bands corresponding to NH and NH_2 groups at $\bar{\upsilon}$ 3300, 3210, and 3197 cm^{-1}. ^{1}H-NMR spectrum of compound **2** showed three new singlet signals at δ 8.95, 4.80, and 3.60 ppm, corresponding to N–H, NH_2 (deuterium exchangeable protons), and C–H groups, respectively.

Treatment of compound **2** with 2-aminoprop-1-ene-1,1,3-tricarbo-nitrile (malononitrile dimer), in presence of sodium ethoxide, furnished malononitrile derivative **5** in 80% yield. This product was formed through nucleophilic addition of the NH_2 group (compound **2**) to the cyano group and another nucleophilic addition of the NH_2 (reagent) to the C=NH group, followed by elimination of ammonia molecule. Its IR spectrum showed appearance of cyano stretching bands at $\bar{\upsilon}$ 2201 cm^{-1} beside N–H and NH_2 groups at $\bar{\upsilon}$ 3412, 3300, and 3248 cm^{-1}. ^{1}H-NMR spectrum of the product revealed the presence of two singlet signals at δ 8.20 and 4.90, belonging to $H_{pyrimidine}$ and amino protons besides a wide range of multiplet peaks, at δ 8.00–7.10, owing to aromatic protons and NH. Compound **2** was subjected to react with diethyl malonate using sodium ethoxide as a catalyst, to afford thiobarbituric acid derivative **6**, in 70% yield (Scheme 2). Its IR spectrum represented a new stretching vibration at $\bar{\upsilon}$ 1700 and 3250 cm^{-1} owing to C=O and NH groups of pyrimidine ring. ^{1}H-NMR spectrum of compound **6** revealed the presence of new singlet signal, at δ 3.80, attributed to CH_2 group (Scheme 2). Treating compound **2** with both of benzylidenemalononitrile and ethoxymethylenemalononitrile, in presence of triethylamine, yielded 4-aminopyrimidine-5-carbonitrile derivatives **7** and **8** (Scheme 2). Their IR spectra showed new absorption band corresponding to CN groups at $\bar{\upsilon}$ 2210 and 2189 cm^{-1}, respectively, while their ^{1}H-NMR spectra showed new signals corresponding to NH_2 groups at δ 5.50 and 4.90 ppm, and CH pyrimidine at δ 6.10.

Scheme 1



Scheme 2



The reaction of compound **2** with aromatic aldehydes (namely, benzaldehyde, *p*-chlorobenzaldehyde, or *p*-anisaldehyde) along with β-keto ester or β-diketone compounds (namely, ethyl acetoacetate, ethyl benzoylacetate, and/or acetylacetone), in presence of ceric ammonium nitrate, afforded dihydropyrimidine derivatives **9–13** (Scheme 3). The reaction mechanism may proceed via a single electron transfer [18] with formation of a β-keto radical, which in turn adds to the imine intermediate and follows (Scheme 4). IR spectra of compounds **9–13** showed new absorption bands corresponding to NH groups at $\bar{\upsilon}$ 3394 and 3230 cm^{-1}, and $\bar{\upsilon}_{C=O}$ of ester group at 1716 cm^{-1} and $\bar{\upsilon}_{C=O}$ 1670 and 1660 cm^{-1}, respectively. ^{1}H-NMR spectrum of compound **8a** showed new signals corresponding to ester group at δ 1.00–1.20 as triplet and 4.00–4.20 as quartet; δ 5.90 owing to $H_{pyrimidine}$ and δ 2.39 owing to CH_3; and also, an increase in aromatic signals including NH group, appeared at δ 7.00–8.00.

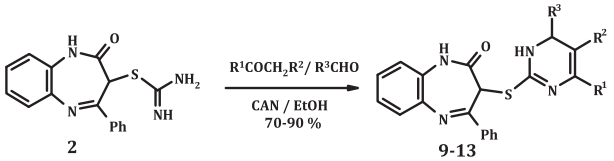
Moreover, when compounds **2** and **3** were allowed to react with active halo-compounds, namely, ethyl bromoacetate, bromomalononitrile, chloroacetonitrile, or phenacyl bromide, in presence of triethylamine in boiling ethanol, they gave 3-[(imidazol-2-yl)thio(amino)benzodiazepinones] **14–20**, in 55–90% yields (Scheme 5).

The expected imidazoles had been proved via alkylation reaction followed by a nucleophilic addition of the amino group at cyano group to form compounds **16–18** or at carbonyl group with elimination of ethanol molecule to form compound **14** or water molecule to form compounds **19** and **20**. IR spectra of the compounds **14–20** showed appearance of new absorption bands corresponding to cyano and carbonyl groups at $\bar{\upsilon}$ 2193 and 1730 cm^{-1} in imidazole moiety, respectively. The structure of these new compounds received good elucidation thorough their ^{1}H-NMR spectral data and correct elemental analyses of C, H, and N elements in which calcd./found results are within ±0.4%.

CONCLUSION

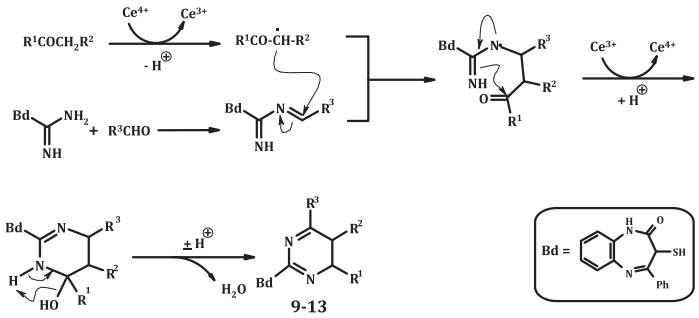
The reaction of 2-oxo-4-phenyl-2,3-dihydro-1*H*-1,5-benzodiazepin-3-yl imidothiocarbamate **2** and 1-(2-oxo-4-phenyl-2,3-dihydro-1*H*-1,5-benzodiazepin-3-yl)guanidine **3** with nitriles, a mixture of an aldehyde and β-keto esters or acetylacetone, and/or α-halo ketones or nitriles yielded new interesting pyrimidine and imidazole derivatives

Scheme 3

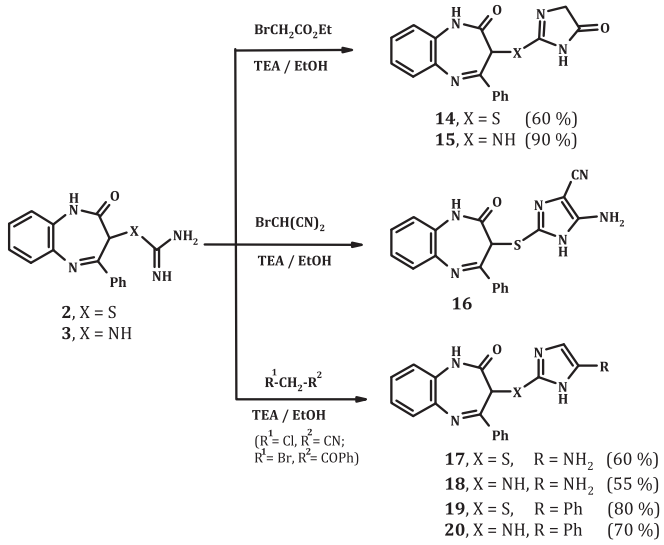


Compd.	R^1	R^2	R^3	Yield (%)
9	Me	CO_2Et	Ph	85
10	Me	CO_2Et	4-ClPh	80
11	Me	CO_2Et	4-MeOPh	70
12	Ph	CO_2Et	Ph	66
13	Ph	COMe	Ph	90

Scheme 4



Scheme 5



attached to benzodiazepine moiety. These new compounds are of promising biological applications.

EXPERIMENTAL

All melting points were determined on a MEL-TEMP II (LABORATORY DEVICES, Dubuque, NJ) and are uncorrected. IR spectra were obtained on a Nicolet 710 FT-IR spectrometer (ThermoFisher, Waltham City, MA). ^{1}H-NMR spectra, at 400 MHz, and ^{13}C-NMR spectra, at 100 MHz, were recorded on a Bruker Avance III-400MHz instrument, using DMSO-d_6 as a solvent (Bruker, Zurich, Switzerland). Elemental microanalyses were performed on a Perkin-Elmer CHN-2400 elemental analyzer (PerkinElmer, Waltham, MA). All compounds were checked their purity on thin-layer chromatography plates.

Reaction of compound 1 with thiourea and/or guanidine HCl. ***General procedure.*** A mixture of 3-bromobenzo diazepinone **1** (3.15 g, 10 mmol), thiourea (0.76 g, 10 mmol) or guanidine hydrochloride (0.95 g, 10 mmol), and potassium carbonate (3 g) in dry acetone (50 mL) was refluxed for 1 h. The reaction mixture was left to cool to room temperature and poured onto crushed ice. The separated solid was filtered, washed with cold water, and dried. This crude solid material was boiled in chloroform (54 mL) for 10 min and filtered off. The insoluble solid was washed thoroughly several times with hot chloroform (~50 mL) and crystallized from dioxane to give compounds **2** and **3**. The collected chloroform filtrate was concentrated and left to stand at room temperature overnight to give crystalline of 4-phenyl-1*H*-[1,5] benzodiazepin-2(3*H*)-one (**4**) [12].

2-Oxo-4-phenyl-2,3-dihydro-1H-1,5-benzodiazepin-3-ylimidothiocarbamate (2). Yield (40%), mp 220–222°C. IR (KBr), $\bar{\upsilon}$ (cm−1): 3331, 3250, 3190, 3157 (NH, NH_2), 1686 (C=O), 763 (C–S–C). ^{1}H-NMR (DMSO-d_6), δ: 8.80 (s, 1H, N–$H_{benzodiazepine}$), 7.81 (s, 1H, N–H disappeared on addition of D_2O), 7.69–6.58 (m, 9H, H_{arom}), 4.74 (s, 2H, NH_2 disappeared on addition of D_2O), 2.60 (s, 1H, CH). *Anal*. Calcd for $C_{16}H_{14}N_4OS$ (310.37): C, 61.92%; H, 4.55%; N, 18.05%; S, 10.33%. Found: C, 61.61%; H, 4.21%; N, 18.23%; S, 10.54%.

1-(2-Oxo-4-phenyl-2,3-dihydro-1H-1,5-benzodiazepin-3-yl) guanidine (3). Yield (90%), mp 181–183°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3430, 3350, 3200, 3183 (N–H, NH_2), 1697 (C=O). ^{1}H-NMR (DMSO-d_6), δ: 8.00 (s, 1H, N–H), 7.50–6.60 (m, 9H, H_{arom}), 5.10 (brs, 4H, $2NH_2$), 2.70 (s, 1H, C–H). *Anal*. Calcd for $C_{16}H_{15}N_5O$ (293.32): C, 65.52%; H, 5.15%; N, 23.88%. Found: C, 65.69%; H, 5.34%; N, 23.60%.

Reaction of compound 2 with malononitrile dimer and/or diethyl malonate. ***General procedure.*** A mixture of compound **2** (0.63 g, 2 mmol) and malononitrile dimer (0.26 g, 2 mmol) and/or diethyl malonate (0.32 g, 2 mmol), in ethanol (25 mL), was treated with sodium ethoxide [sodium metal (0.23 g, 10 mmol) was dissolved in absolute ethanol (5 mL)]. The reaction mixture was refluxed on water bath, for 2 h, left to cool to room temperature, and poured into ice-cold dilute hydrochloric acid solution (100 mL, 3%). The resulting solid product was filtered, washed with water, and crystallized from dioxane.

{6-Amino-2-[(2-oxo-4-phenyl-2,3-dihydro-1H-1,5-benzo diazepin-3-yl)thio]pyrimidin-4(3H)-ylidene}malononitrile (5). Yield (69%), mp 266–268°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3412, 3300, 3248, 3180 (N–H, NH_2), 2201 (C≡N), 1665 (C=O). ^{1}H-NMR (DMSO-d_6), δ: 8.70 (s, 1H, N–H), 8.20 (s, 1H, $H_{pyrimidine}$), 8.00–7.30 (m, 10H, H_{arom} + N–H), 4.90 (s, 2H, NH_2), 2.60 (s, 1H, CH). *Anal*. Calcd for $C_{22}H_{15}N_7OS$ (425.46): C, 62.10%; H, 3.55%; N, 23.04%; S, 7.54%. Found: C, 62.24%; H, 3.68%; N, 23.25%; S, 7.71%.

2-[(2-Oxo-4-phenyl-2,3-dihydro-1H-1,5-benzodiazepin-3-yl)thio]-pyrimidine-4,6-(1H,5H)-dione (6). Yield (70%), mp 172–173°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3250, 3100 (2N–H), 1700, 1683 (C=O), 1665 ($C=O_{benzodiazepine}$). ^{1}H-NMR (DMSO-d_6), δ: 8.50 (s, 1H, N–$H_{benzodiazepine}$), 7.80–7.10 (m, 10H, H_{arom} + N–H), 3.80 (s, 2H, CH_2), 2.60 (s, 1H, CH). ^{13}C-NMR δ: 182, 166, 163, 160, 143, 137, 132, 132, 131, 130, 129, 127, 126, 125, 122, 55, 41. *Anal*. Calcd for $C_{19}H_{14}N_4O_3S$ (378.40): C, 60.31%; H, 3.73%; N, 14.81%; S, 8.47%. Found: C, 60.51%; H, 3.90%; N, 14.70%; S, 8.61%.

Reaction of compound 2 with methylenemalononitriles. ***General procedure.*** A mixture of compound **2** (1.26 g, 4 mmol), benzylidenemalononitrile (0.71 g, 4 mmol), or ethoxymethylenemalononitrile (0.48 g, 4 mmol) and triethylamine (0.4 mL) in methanol (30 mL) was refluxed for 4 h. The separated product after evaporation was crystallized from dioxane.

4-Amino-2-[(2-oxo-4-phenyl-2,3-dihydro-1H-1,5-benzodiazepin-3-yl)thio]-3-phenylpyrimidine-5-carbonitrile (7). Yield (60%), mp 201–202°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3342, 3218, 3180 (N–H, NH_2), 2210 (C≡N), 1676 (C=O). ^{1}H-NMR (DMSO-d_6), δ: 8.30 (s, 1H, N–$H_{benzodiazepine}$), 8.10–7.30 (m, 14H, H_{arom}), 5.50–5.30 (br, 2H, NH_2), 2.60 (s, 1H, CH). *Anal*. Calcd for $C_{28}H_{18}N_6OS$ (462.52): C, 67.52%; H, 3.92%; N, 18.17%; S, 6.93%. Found: C, 67.70%; H, 3.75%; N, 18.30%; S, 6.60%.

4-Amino-2-[(2-oxo-4-phenyl-2,3-dihydro-1H-1,5-benzo diazepin-3-yl)thio]pyrimidine-5-carbonitrile (8). Yield (70%), mp 159–161°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3390, 3223 (NH_2), 3176 (N–H), 2189 (C≡N), 1690 (C=O). ^{1}H-NMR (DMSO-d_6), δ: 8.10 (s, 1H, N–$H_{benzodiazepine}$), 7.80–7.00 (m, 9H, H_{arom}), 6.10 (s, 1H, $H_{pyrimidine}$), 4.90 (s, 2H, NH_2), 2.60 (s, 1H, C–H). *Anal*. Calcd for $C_{20}H_{14}N_6OS$ (366.42): C, 62.16%; H, 3.65%; N, 21.75%; S, 8.30%. Found: C, 62.21%; H, 3.80%; N, 21.54%; S, 8.60%.

Ceric ammonium nitrate-catalyzed reaction of compound 2 with some aldehydes/active methylene compounds. ***General procedure.*** To a mixture of compound **2** (3.15 g, 10 mmol), 10 mmol of the appropriate aldehyde [namely, benzaldehyde (1 mL), *p*-chlorobenzaldehyde (1.42 g), or *p*-methoxybenzaldehde (1.34 mL)] and appropriate β-ketonic compound [namely, ethyl acetoacetate (1.30 mL), ethyl benzoylacetate (1.62 mL), or acetylacetone (1 mL)], in ethanol (20 mL), ceric ammonium nitrate (0.03 g) was added. Then the mixture was heated under reflux for 20 min. On completion of the reaction (thin-layer chromatography checked), the reaction mixture was diluted with cold water, and the resulting solid was filtered, dried, and crystallized from ethanol to give compounds **9–13**.

Ethyl (3-[(4-phenyl-6-methyl-1,6-dihydropyrimidin-2-yl)thio]-4-phenyl-1,3-dihydro-2H-1,5-benzodiazepin-2-one)carboxylates (9). Yield (85%), mp 232–234°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3300, 3170 (2N–H), 1730 ($C=O_{ester}$), 1688 ($C=O_{benzodiazepine}$). ^{1}H-NMR (DMSO-d_6), δ: 8.20 (s, 1H, N–$H_{benzodiazepine}$), 8.00–7.00 (m, 15H, H_{arom} + NH), 6.00 (br, 1H, $H_{pyrimidine}$), 3.95–3.80 (q, 2H, CH_2), 2.40 (s, 1H, $H_{benzodiazepine}$), 2.23 (s, 3H, CH_3), 1.32–1.00 (t, 3H, CH_3). ^{13}C-NMR (100 MHz, DMSO-d_6), δ: 170, 166, 164, 163, 160, 139, 138, 137, 136.9, 130.6, 130.7, 130.4, 130.2, 130, 129, 128, 127, 125, 121, 117, 63, 57, 51, 24, 13. *Anal*. Calcd for $C_{29}H_{26}N_4O_3S$ (510.60): C, 68.21%; H, 5.13%; N, 10.97%; S, 6.28%. Found: C, 68.04%; H, 5.28%; N, 10.75%; S, 6.43%.

Ethyl (3-[(4-p-chlorophenyl-6-methyl-1,6-dihydropy-rimidin-2-yl)thio]-4-phenyl-1,3-dihydro-2H-1,5-benzodiazepin-2-one)carboxylates (10). Yield (80%), mp 240–242°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3356, 3198 (2N–H), 1716 ($C=O_{ester}$), 1678 ($C=O_{benzodiazepine}$). ^{1}H-NMR (DMSO-d_6), δ: 8.00 (s, 1H, N–$H_{benzodiazepine}$), 7.90–7.00 (m, 14H, H_{arom} + N–H), 5.90 (s, 1H, C–H), 4.20–4.00 (q, 2H, CH_2), 2.39 (s, 3H, CH_3), 2.22 (s, 1H, $H_{benzodiazepine}$), 1.42–1.00 (t, 3H, CH3). *Anal*. Calcd for $C_{29}H_{25}ClN_4O_3S$ (545.06): C, 63.90%; H, 4.62%; N, 10.28%; S, 5.88%; Cl, 6.50%. Found: C, 63.64%; H, 4.40%; N, 10.10%; S, 5.63%; Cl, 6.70%.

Ethyl (3-[(4-methoxyphenyl-6-methyl-1,6-dihydropyrimidin-2-yl)thio]-4-phenyl-1,3-dihydro-2H-1,5-benzodiazepin-2-one) carboxylates (11). Yield (70%), mp 252–254°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3295, 3190 (2N–H), 1720 (C=O_{ester}), 1680 (C=$O_{benzodiazepine}$). ^{1}H-NMR (DMSO-d_6), δ: 8.20 (s, 1H, $NH_{benzodiazepine}$), 8.00–7.20 (m, 14H, H_{arom} + N–H), 6.10 (s, 1H, C–H), 4.40–4.02 (q, 2H, CH_2), 3.78 (s, 3H, OCH_3), 2.39 (s, 3H, CH_3), 2.22 (s, 1H, C–H), 1.33–1.00 (t, 3H, CH_3). Elemental *Anal*. Calcd for $C_{30}H_{28}N_4O_4S$ (540.63): C, 66.65%; H, 5.22%; N, 10.36%; S, 5.93%. Found: C, 66.30%; H, 5.37%; N, 10.12%; S, 5.71%.

Ethyl (3-[(4,6-diphenyl-1,6-dihydropyrimidin-2-yl)thio]-4-phenyl-1,3-dihydro-2H-1,5-benzodiazepin-2-one)carboxylate (12). Yield (66%), mp 270–272°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3230, 3190 (2N–H), 1729 (C=O), 1682 (C=O $_{benzodiazepine}$). ^{1}H-NMR (DMSO-d_6), δ: 8.30 (s, 1H, N–$H_{benzodiazepine}$), 8.10–7.20 (m, 19H, H_{arom} + NH), 5.50 (s, 1H, $CH_{pyrimidine}$), 4.20–3.90 (q, 2H, CH_2), 2.34 (s, 1H, $CH_{benzodiazepine}$), 1.40–1.10 (t, 3H, CH_3). *Anal*. Calcd for $C_{34}H_{28}N_4O_3S$ (572.67): C, 71.31%; H, 4.97%; N, 9.78%; S, 5.60%. Found: C, 71.04%; H, 4.68%; N, 9.55%; S, 5.72%

{3-[(4-Phenyl-3-acetyl-6-methyl-1,6-dihydropyrimidin-2-yl)thio]-4-phenyl-1,3-dihydro-2H-1,5-benzodiazepin-2-one} (13). Yield (90%), mp 236–237°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3294, 3190 (2N–H), 1670 (C=$O_{benzodiazepine}$). ^{1}H-NMR (DMSO-d_6), δ: 8.30 (s, 1H, N–$H_{benzodiazepine}$), 7.90–710 (m, 15H, H_{arom} + N–H), 5.95 (s, 1H, C–H), 2.60 (s, 3H, $COCH_3$), 2.40 (s, 3H, CH_3), 2.30 (s, 1H, $CH_{benzodiazepine}$). *Anal*. Calcd for $C_{28}H_{24}N_4O_2S$ (480.58): C, 69.98%; H, 5.03%; N, 11.66%; S, 6.67%. Found: C, 69.70%; H, 5.19%; N, 11.76%; S, 6.47%.

Reaction of compounds 2 and 3 with some A-halo esters, nitriles, and/or ketones. ***General procedure.*** To a mixture of 4 mmol of compound **2** (1.26 g) or **3** (1.24 g), the appropriate halocompound [chloroacetonitrile (0.45 mL), bromomalo-nonitrile (0.58 g), ethyl chloroacetate (0.49 mL), or phenacyl bromide (0.937 g)] and triethylamine (0.4 mL) in ethanol (20 mL) was refluxed for 2 h. The precipitated product after cooling was collected, dried, and recrystallized from dioxane.

3-[(5-Oxo-4,5-dihydro-1H-imidazol-2-yl)thio]-4-phenyl-1,3-dihydro-2H-1,5-benzodiazepin-2-one (14). Yield (60%), mp 186–187°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3360, 3313 (NH_2), 3171 (N–H), 1672 (C=O). ^{1}H-NMR (DMSO-d_6), δ: 8.80 (s, 1H, $NH_{benzodiazepine}$), 7.56–7.00 (m, 9H, H_{arom}), 6.00 (s, 2H, NH_2), 3.20 (s, 2H, CH_2), 2.60 (s, 1H, CH). *Anal*. Calcd for $C_{18}H_{15}N_5OS$ (349.40): C, 61.87%; H, 4.33%; N, 20.04%; S, 9.18%. Found: C, 61.44%; H, 4.64%; N, 21.24%; S, 9.34%.

3-[(5-Oxo-4,5-dihydro-1H-imidazol-2-yl)amino]-4-phenyl-1,3-dihydro-2H-1,5-benzodiazepin-2-one (15). Yield (90%), mp 159–161°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3301, 3211, 3171 (N–H), 1679 (C=O). ^{1}H-NMR (DMSO-d_6), (400 MHz, DMSO-d_6), δ: 8.80 (s, 1H, N–$H_{benzodiazepine}$), 7.56–7.00 (m, 10H, H_{arom} + N–H), 6.00 (s, 2H, NH_2), 3.05 (s, 2H, CH_2), 2.60 (s, 1H, CH). *Anal*. Calcd for $C_{18}H_{16}N_6O$ (332.35): C, 65.05%; H, 4.85%; N, 25.29%. Found: C, 65.30%; H, 4.91%; N, 25.49%.

5-Amino-2-[(2-oxo-4-phenyl-2,3-dihydro-1H-1,5-benzodiazepin-3-yl)thio]-4H-imidazole-4-carbonitrile (16). Yield (70%), mp 174–176°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3372, 3200 (NH_2), 3188 (N–H), 2193 (C≡N), 1664 (C=O). ^{1}H-NMR (DMSO-d_6), δ: 8.20 (s, 1H, $NH_{benzodiazepine}$), 7.80–7.10 (m, 10H, H_{arom} + NH), 5.00 (s, 2H, NH_2), 2.70 (s, 1H, C–H). *Anal*. Calcd for $C_{19}H_{14}N_6OS$ (374.41): C, 60.95%; H, 3.77%; N, 22.45%; S, 8.56%. Found: C, 60.60%; H, 3.58%; N, 22.70%; S, 8.80%.

3-[(5-Amino-4H-imidazol-2-yl)thio]-4-phenyl-1,3-dihydro-2H-1,5-benzodiazepin-2-one (17). Yield (60%), mp 210–212°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3452 (OH), 3200, 3150 (3N–H), 1730 (C=O), 1674 (C=O). ^{1}H-NMR (DMSO-d_6), δ: 8.10 (s, 1H, N–$H_{benzodiazepine}$), 7.60–6.90 (m, 10H, H_{arom} + N–H), 2.90 (s, 1H, CH). *Anal*. Calcd for $C_{18}H_{14}N_4O_2S$ (350.39): C, 61.70%; H, 4.03%; N, 15.99%; S, 9.15%. Found: C, 61.50%; H, 4.18%; N, 15.80%; S, 9.30%.

3-[(5-Amino-4H-imidazol-2-yl)amino]-4-phenyl-1,3-dihydro-x2H-1,5-benzodiazepin-2-one (18). Yield (55%), mp 143–145°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3270 (2NH), 3200, 3150 (NH_2), 1700 (C=O), 1684 (C=O). ^{1}H-NMR (DMSO-d_6), δ: 8.10 (s, 1H, N–$H_{benzodiazepine}$), 7.90–7.00 (m, 12H, H_{arom} + 2N–H), 6.60–6.40 (br, 1H, N–H), 2.65 (s, 1H, CH). *Anal*. Calcd for $C_{18}H_{15}N_5O_2$ (333.34): C, 64.86%; H, 4.54%; N, 21.01%. Found: C, 64.61%; H, 4.32%; N, 21.24%.

3-[(5-Phenyl-4H-imidazol-2-yl)thio]-4-phenyl-1,3-dihydro-2H-1,5-benzodiazepin-2-one (19). Yield (80%), mp 201–203°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3181 (2N–H), 1682 (C=O). ^{1}H-NMR (DMSO-d_6), δ: 8.60 (s, 1H, N–$H_{benzodiazepine}$), 7.90–7.00 (m, 16H, H_{arom} + NH), 2.65 (s, 1H, C–H). *Anal*. Calcd for $C_{24}H_{18}N_4OS$ (410.49): C, 70.22%; H, 4.42%; N, 13.65%; S, 7.81%. Found: C, 70.46%; H, 4.47%; N, 13.90%; S, 7.70%.

3-[(5-Phenyl-4H-imidazol-2-yl)amino]-4-phenyl-1,3-dihydro-2H-1,5-benzodiazepin-2-one (20). Yield (70%), mp 177–179°C. IR (KBr), $\bar{\upsilon}$ (cm^{-1}): 3211, 3181 (3N–H), 1690 (C=O). ^{1}H-NMR (DMSO-d_6), δ: 8.60 (s, 1H, N–$H_{benzodiazepine}$), 7.90–7.00 (m, 17H, H_{arom} +2N–H), 2.50 (s, 1H, C–H). *Anal*. Calcd for $C_{24}H_{19}N_5O$ (393.44): C, 73.27%; H, 4.87%; N, 17.80%. Found: C, 73.32%; H, 4.67%; N, 17.62%.

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