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Heterocyclic Synthesis Containing Bridgehead Nitrogen Atom: Synthesis of 3-[(2*H*)-2-Oxobenzo[*b*]pyran-3-yl]-*s*-triazolo[3,4-*b*]-1,3,4-thiadiazine and Thiazole Derivatives

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ABSTRACT: *The reaction of 2*H*-2-oxobenzo*[b]*-pyran-3-hydrazide (***2***) with carbon disulfide in basic DMF afforded potassium thiocarbamate* **3**, *which readily underwent heterocyclization upon its reaction with hydrazine and/or phenacyl bromide to yield 1,2,4-tiazole (***4***) and thiazole* **7** *derivatives, respectively. Condensation of* **4** *with substituted phenacyl bromide and/or chloranil gave 1,2,4-triazole[3,4-*b*]thiadiazine (***5a,b***) and 3,10-bis-[2*H*-2-oxobenzo[b]pyran-3-yl]-6,13-dichloro-bis-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazino[5′,6′-*b*:5′,6′-*e*]cyclohexa-1,4-diene (***6***), respectively. Cyclization of thiosemicarbazide* **10** *by refluxing it in sodium hydroxide and/or phosphoryl chloride afforded triazole* **13** *and thiadiazole* **15** *derivatives, respectively. Also,* **10** *reacted with phenacyl bromide in the presence of anhydrous sodium acetate to give the oxothiazolidine derivative* **17**. *The structure of the synthesized compounds were confirmed by elemental analyses, IR, ^{1}H NMR, and mass spectra.* © 2003 Wiley Periodicals, Inc. Heteroatom Chem 14:114–120, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10109

INTRODUCTION

1,2,4-Triazole derivatives have been found to be active compounds having therapeutic nature, such as antiseptic, analgesic, antiasthmatic, diuretic, antihypertensive, anticholinergic, anti-inflammatory, antitumor, and hypotensive effects [1–11]. There are known drugs containing the 1,2,4-triazole group, e.g. Triazolom and Alprazolam [12,13]. Additionally, several of the 3-substituted thio-1,2,4-triazoles have shown biological activity against tuberculosis [14,15], as anticoccidal agents in chicken [16], and in cephalosporins as antibacterial agents [17].

s-Triazolo[3,4-*b*]-1,2,4-thiadiazine derivatives constitute an important class of organic compounds with diverse biological activities such as antiparasitic, analgesic, antibacterial, and CNS depressant [18–22]. Thiazole derivatives are also associated with a broad spectrum of biological properties, including anticonvulsant [23,24], antimicrobial [25–27], antituberculous, and bacteriostatic activities [28,29]. On the other hand coumarines, an important group of organic compounds, are used as additives to food and cosmetics [30], optical brightening agent [31], and dispersed fluorescent and laser dyes [32].

Therefore, compounds containing 1,2,4-triazole, *s*-triazolo[3,4-*b*]-1,3,4-thiadiazine, thiazole, and coumarine moieties are expected to possess potential biological activities. Our previous work aimed at developing new approaches to the synthesis of polyfunctionally substituted heterocyclic compounds of expected biological activity [33–38]. Herein we report the synthesis of heterocyclic compounds containing the aforementioned rings via readily available ethyl 2*H*-2-oxobenzo[*b*]pyran-3-carboxylate.

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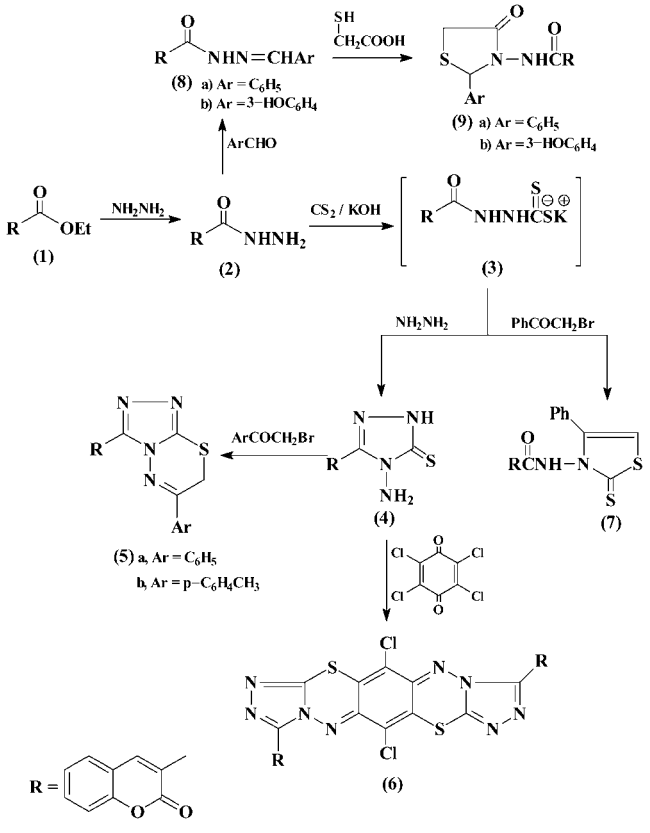
Ethyl 2*H*-2-oxobenzo[*b*]pyran-3-carboxylate (**1**) reacts with hydrazine hydrate to give 2*H*-2-oxobenzo[*b*]pyran-3-hydrazide (**2**). Hydrazide **2** reacts with carbon disulfide in *N*,*N*-dimethylformamide containing potassium hydroxide at room temperature to give the nonisolable potassium thiocarbamate salt (**3**), which was subjected to heterocyclization through its reaction with hydrazine hydrate to afford 4-amino-5-[2*H*-2-oxobenzo[*b*]pyran-3-yl]-1,2,4-triazole-3-thione (**4**). The structure of **4** was established on the basis of analytical and spectral data. Thus, the IR spectrum of reaction product **4** showed the presence of an NH_2 and an NH group at 3310 and 3180 cm^{-1}, C—H aromatic at 3050 cm^{-1}, and CO group at 1712 cm^{-1}. The ^1H NMR spectrum showed the presence of singlet signals (D_2O-exchangeable) at δ 5.21 and 13.46 ppm corresponding to NH_2 and SH protons, respectively, in addition to pyrane H-4 and phenyl protons at δ 6.69 and 7.35–8.4 ppm, respectively.

Cyclization of 4-amino-5-[2*H*-2-oxobenzo[*b*]-pyran-3-yl]-1,2,4-triazole-3-thione (**4**) with substituted phenacyl bromide has been the most useful method for the formation of *s*-triazolo[3,4-*b*]-1,3,4-thiadiazine ring system. However, this cyclization has afforded different products under various reaction conditions [39]. Thus, the treatment of **4** with 4-substituted phenacyl bromide in absolute ethanol containing potassium carbonate resulted in cyclocondensation to give the corresponding 6-substituted phenyl 3-[2*H*-2-oxobenzo[*b*]pyran-3-yl]-7*H*-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazines (**5a,b**). The structures of **5a,b** were established on the basis of elemental analyses and spectral data. IR spectra showed no absorption bands assignable to NH_2 and NH groups. The ^1H NMR spectra of **5a** exhibited a singlet signal for SCH_2 and pyran H-4 protons at δ 4.55 and 6.65 ppm, respectively, in addition to aromatic protons at δ 7.35–8.46 ppm.

Treatment of an ethanolic solution of **4** with chloranil in the presence of anhydrous sodium acetate afforded the corresponding 3,10-bis-[2*H*-2-oxobenzo-[*b*]pyran-3-yl]-6,13-dichloro-bis-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazino[5′,6′-*b*:5′,6′-*e*]cyclohexa-1,4-diene (**6**). The structure of **6** was established on the basis of elemental analyses and spectral data. The ^1H NMR spectra of **6** showed only signals for pyrane H-4 and aromatic protons.

Reaction of *N*-potassium thiocarbamate salt **3** with phenacyl bromide gave thiazole derivative **7**. The structure of **7** was established on the basis of elemental analyses and spectral data. IR spectra showed an absorption band assignable to NH group at 3450–3320 cm^{-1}, 2C=O groups at 1710, 1670 cm^{-1}, and C=S group at 1215–1190 cm^{-1}. The ^1H NMR spectra of **7** exhibited a singlet signal for thiazole H-5, pyrane H-4, and NH protons at δ 6.42, 6.72, and 9.24 ppm, respectively, in addition to aromatic protons at δ 7.23–8.31 ppm. Product **7** was found to be identical in all respects with an authentic sample prepared by an independent method [40].

Reaction of hydrazide **2** with the appropriate aromatic aldehydes afforded 3-(arylidenehydrazinocarbonyl)-2*H*-2-oxobenzo[*b*]pyrane (**8**), which on condensation with mercaptoacetic acid in dry benzene gave the corresponding3-[(2-phenyl-4-oxothiazolidinyl)aminocarbonyl]-2*H*-2-oxobenzo-[*b*]-pyrane (**9**) (Scheme 1). The IR spectrum of the compound **8a** showed NH stretching at 3340 cm^{-1} and two C=O group stretchings at 1712 and 1670 cm^{-1}, while in **9a** NH group stretching at 3211 cm^{-1} and three C=O group stretchings at 1730, 1715, and 1670 cm^{-1}. The ^1H NMR spectra of **8a** showed a singlet at δ 7.13 ppm for one proton of —N=CH, while it is shifted upfield to δ 5.84 ppm in **9a**, because the sp^2 carbon of **8a** was transformed into the sp^3 carbon of **9a**. Also, ^1H NMR of **9a** showed double doublets at δ 3.72 and 3.88 ppm for two protons of —$COCH_2S$—.

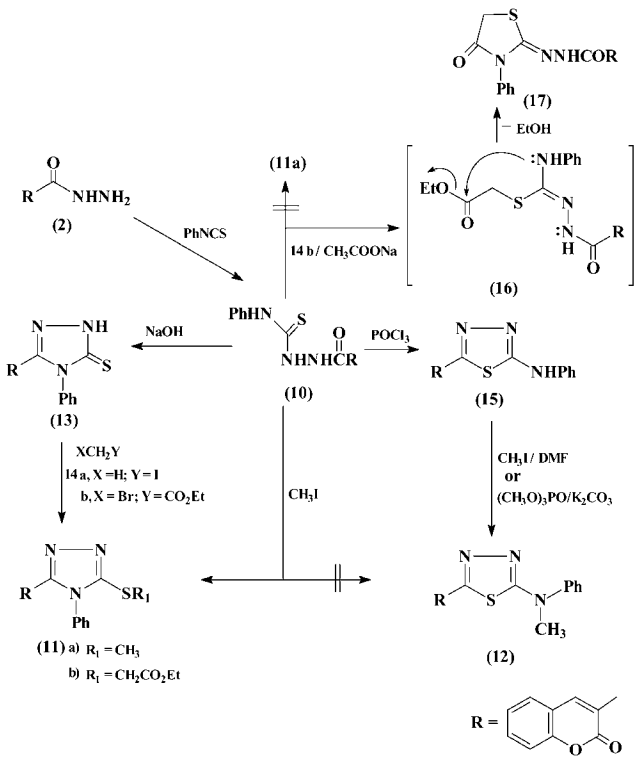


SCHEME 1

Reaction of phenyl isothiocyante with 2*H*-2-oxobenzo[*b*]pyran-3-hydrazide (**2**) in dioxane gave 1-(3-carbonyl-2*H*-2-oxobenzo[*b*]pyrane)-4-phenyl thiosemicarbazide (**10**) (Scheme 2). Structure of **10** was assigned to this product on the basis of elemental analysis and spectral data (see Experimental section).

Reaction of **10** with methyl iodide in *N*,*N*-dimethylformamide at room temperature in the presence of anhydrous potassium carbonate gave a solid product of molecular formula $C_{18}H_{13}N_3O_2S$ ($M^+ = 453$), which may be formulated as **11a** or its isomer **12**. Structure **11a** was indicated by the ^{1}H NMR spectra, which gave conclusive evidence for the triazole structure (see Experimental section). The structure of triazole **11a** was proven by the independent synthesis, which involved cyclization of **10** with sodium hydroxide to afford 4-phenyl-5-(2*H*-2-oxobenzo[*b*]pyran-3-yl)-1,2,4-triazole-3-thione (**13**). Methylation of **13** with methyl iodide yielded 3-methylthio-5-(2*H*-2-oxobenzo[*b*]pyran-3-yl)-4-phenyl-1,2,4-triazole (**11a**). In addition, the structure of **11a** was further confirmed by alternative synthesis of its isomer **12**. Heating of **10** with phosphoryl chloride gave 2-anilino-5-(2*H*-2-oxobenzo[*b*]pyran-3-yl)-1,3,4-thiadiazole (**15**). Reaction of **15** with methyl iodide in DMF and/or trimethyl phosphate in the presence of anhydrous potassium carbonate gave *N*-methyl-*N*-[5-(2*H*-2-oxobenzo-[*b*]pyran-3-yl)-1,3,4-thiadiazol-2-yl]aniline (**12**). Also, reaction of **13** with ethyl bromoacetate afforded the triazole derivative **11b**. All structures of the compounds **12, 13**, and **15** were established on the basis of elemental analysis and spectral data (see Experimental section).

Reaction of **10** with ethyl bromoacetate in absolute ethanol containing anhydrous sodium acetate did not afford the expected triazole **11b** but gave [(3-phenyl-4-oxothiazolidin-2-ylidene)hydrazonyl][2*H*-2-oxobenzo[*b*]pyran-3-yl] ketone (**17**). Formation of **17** is assumed to proceed via the intermediate **16**, which undergoes cyclization via elimination of ethanol molecule. The structure of **17** was established on the basis of elemental analyses and spectral data. Their IR spectra showed a new C=O group at 1735 cm^{-1} and the ^{1}H NMR displayed an additional singlet at δ 4.31 ppm (S–CH_2), which provided firm support for the ring closure [41].



SCHEME 2

EXPERIMENTAL

All melting points are uncorrected. IR spectra were measured as KBr pellets on a Pye Unicam SP 1000 spectrophotometer. ^{1}H NMR spectra were recorded in DMSO-d_6 at 200 MHz on a Varian Gemini NMR spectrometer, using TMS as internal reference; the chemical shifts are expressed as δ values (ppm). ^{13}C NMR spectra were measured on a Varian XL-300 (300 MHz) spectrometer. Mass spectra were obtained on a Shimadzu GCMS-QP 1000 EX mass spectrometer at 70 eV. Elemental analyses were carried out at the Microanalytical Center of Cairo University. Ethyl (2*H*)-2-oxobenzo-[*b*]pyran-3-carboxylate (**1**) was prepared according to literature procedures [42].

*(2H)-2-Oxobenzo[b]pyran-3-hydrazide (**2**)*

Hydrazine hydrate (0.25 g, 5 mmol) was added to a solution of ethyl 2*H*-2-oxobenzo[*b*]pyran-3-yl carboxylate (**1**) (0.22 g, 1 mmol) in ethanol (30 ml). The reaction mixture was heated under reflux for 2 h, concentrated in vacuum, cooled, and diluted with ice water. The precipitate obtained was filtered, washed with ice water, dried, and recrystallized from dioxane to afford **2** in 80% yield; m.p. 208°C; IR (KBr) ν 3340, 3160 (NH and NH_2), 3050 (CH aromatic), 1709, 1675 (2CO) cm^{-1}; ^{1}H NMR [DMSO-d_6]: δ = 4.72 (sbr, 2H, NH_2 D_2O-exchangeable), 6.73 (s, 1H, pyran H-4), 7.32–8.42 (m, 4H, Ar-H), 9.8 (sbr, 1H, NH D_2O-exchangeable). Calcd for $C_{10}H_8N_2O_3$: C, 58.82; H, 3.96; N, 13.72%. Found: C, 58.79; H, 3.89; N, 13.7%.

*4-Amino-5-[2H-2-oxobenzo[b]pyran-3-yl]-1,2,4-triazole-3-thione (**4**) and N-(4-Phenyl-2-thioxothiazol-3-yl)-2H-2-oxobenzo[b]pyran-3-carboxamide (**7**)*

General Procedures: To a stirred solution of a hydrazide **2** (0.2 g, 1 mmol) in DMF (20 ml), carbon disulfide (0.076 g, 1 mmol) and potassium hydroxide (0.056 g, 1 mmol) in water (5 ml) were added. The reaction mixture was heated on a boiling water bath for 2 h, then left to cool till 25°C. To this cold reaction mixture, hydrazine hydrate (0.1 g, 2 mmol) and/or phenacyl bromide (0.199 g, 1 mmol) was added. The reaction mixture was cooled, diluted with ice water (30 ml), and neutralized with hydrochloric acid. The solid product formed on standing overnight was filtered, washed thoroughly with cold water, and dried. Recrystallization from ethanol yielded the corresponding **4** and/or **7** in 70–80% yield, respectively.

4: Yield, 80%; m.p. 233°C; IR (KBr) ν 3310, 3180 (NH and NH_2), 3050 (CH aromatic), 1712 (C=O), 1560 (NC=S) cm^{-1}; ^1H NMR [DMSO-d_6]: $\delta = 5.21$ (sbr, 2H, NH_2 D_2O-exchangeable), 6.69 (s, 1H, pyran H-4), 7.35–8.40 (m, 4H, Ar-H), 13.46 (s, 1H, SH D_2O-exchangeable); *m/z* 260 (M^+). Calcd for $C_{11}H_8N_4O_2S$: C, 50.76; H, 3.01; N, 21.53; S, 12.32%. Found: C, 50.72; H, 3.1; N, 21.51; S, 12.3%.

7: Yield, 72%; m.p. 115°C; IR (KBr) ν 3450–3320 (NH), 3060 (CH aromatic), 1710, 1670 (2C=O), 1215–1190 (C=S) cm^{-1}; ^1H NMR [DMSO-d_6]: $\delta = 6.42$ (s, 1H, thiazole H-5), 6.72 (s, 1H, pyran H-4), 7.23–8.31 (m, 9H, Ar-H), 9.24 (s, 1H, NH D_2O-exchangable); ^{13}C NMR (DMSO) 126.1–154.2 (C aromatic), 146.12 (C-4 thiazole), 181.4 (C-5 thiazole), 165.2 (C=S), 182.3 (C=O pyrane), 184.5 (CONH); *m/z* 380 (M^+). Calcd for $C_{19}H_{12}N_2O_3S_2$: C, 59.98; H, 3.19; N, 7.37; S, 16.85%. Found: C, 59.94; H, 3.11; N, 7.4; S, 16.81%.

*6-Substituted Phenyl 3-[2H-2-Oxobenzo[b]-pyran-3-yl]-7H-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazines (**5a,b**)*

A mixture of **4** (0.26 g, 1 mmol), an appropriate phenacyl bromide derivative (1 mmol), and fused potassium carbonate (2 mmol) in absolute ethanol (20 ml) was refluxed for 4–6 h. After removal of the ethanol under reduced pressure, the resulting solid product was filtered and washed with water. The crude product was recrystallized from dioxane to yield the corresponding **5a,b** in 60–65% yield.

5a: Yield, 62%; m.p. 218°C; IR (KBr) ν 3059 (CH aromatic), 1706 (C=O), 1582 (C=N) cm^{-1}; ^1H NMR [DMSO-d_6]: $\delta = 4.55$ (s, 2H, CH_2), 6.65 (s, 1H, pyran H-4), 7.35–8.46 (m, 9H, Ar-H); *m/z* 360 (M^+). Calcd for $C_{19}H_{12}N_4O_2S$: C, 63.32; H, 3.36; N, 15.55; S, 8.9%. Found: C, 63.34; H, 3.22; N, 15.5; S, 8.8 %.

5b: Yield, 65%; m.p. 198°C; IR (KBr) ν 3062 (CH aromatic), 1710 (C=O), 1580 (C=N) cm^{-1}; ^1H NMR [DMSO-d_6]: $\delta = 2.43$ (s, 3H, CH_3), 4.53 (s, 2H, CH_2), 6.7 (s, 1H, pyran H-4), 7.22–8.36 (m, 8H, Ar-H); *m/z* 374 (M^+). Calcd for $C_{20}H_{14}N_4O_2S$: C, 64.15; H, 3.78; N, 14.97; S, 8.56%. Found: C, 64.2; H, 3.75; N, 14.88; S, 8.6%.

*3,10-Bis-[2H-2-oxobenzo[b]pyran-3-yl]-6,13-dichloro-bis-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazino[5′,6′-b:5′,6′-e]cyclohexa-1,4-diene (**6**)*

A mixture of **4** (0.52 g, 2 mmol), tetrachloro-1,4-benzoquinone (0.25 g, 1 mmol), and anhydrous sodium acetate (0.072 g, 1 mmol) in absolute ethanol (25 ml) was refluxed for 6–8 h (TLC control). The reaction mixture acquired a reddish color and a violet solid separated. The solid product was filtered, washed with water several times, and recrystallized from DMF to afford **6** in 55% yield; m.p. 185°C; IR (KBr) ν 3060 (CH aromatic), 1713 (C=O) cm^{-1}; ^1H NMR [DMSO-d_6]: $\delta = 6.68$ (s, 1H, pyran H-4), 7.48–8.53 (m, 8H, Ar-H); *m/z* 659 ($M^+ + 1$). Calcd for $C_{23}H_{10}N_8O_4S_2Cl_2$: C, 51.15; H, 1.54; N, 17.05; S, 9.75; Cl, 10.78%. Found: C, 51.23; H, 1.52; N, 16.99; S, 9.74; Cl, 10.77%.

*3-(Arylidenehydrazinocarbonyl)-2H-2-oxobenzo[b]pyrane (**8a,b**)*

A solution of **2** (0.21 g, 1 mmol) in ethanol (25 ml) and an appropriate aldehyde (1 mmol) was heated under reflux for 3–6 h (TLC control). The reaction mixture was cooled, the separated solid was filtered, washed with small amount of cold ethanol, and recrystallized from ethanol to yield the corresponding **8a,b** in 70–80% yield.

8a: Yield, 74%; m.p. 258°C; IR (KBr) ν 3340, 3180 (NH), 3055 (CH aromatic), 1712, 1670 (2C=O) cm^{-1}; ^1H NMR [DMSO-d_6]: $\delta = 6.71$ (s, 1H, pyran H-4), 7.13 (s, 1H, N=CH), 7.31–8.45 (m, 9H, Ar-H), 9.96 (s, 1H, NH D_2O-exchangeable); *m/z* 272 (M^+). Calcd for $C_{17}H_{12}N_2O_3$: C, 69.85; H, 4.15; N, 9.59%. Found: C, 69.86; H, 4.09; N, 9.56%.

8b: Yield, 75%; m.p. 275°C; IR (KBr) ν 3441 (OH), 3208–3180 (NH), 3060 (CH aromatic), 1708, 1675 (2C=O) cm^{-1}; ^1H NMR [DMSO-d_6]: $\delta = 6.67$ (s, 1H, pyran H-4), 7.12–8.23 (m, 10H, Ar-H and N=CH), 9.94 (s, 1H, NH D_2O-exchangeable), 11.74 (s, 1H, OH). Calcd for $C_{17}H_{12}N_2O_4$: C, 66.23; H, 3.93; N, 9.09%. Found: C, 66.21; H, 3.98; N, 9.1%.

*3-[(2-Phenyl-4-oxothiazolidinyl)-aminocarbonyl]-2H-2-oxobenzo[b]pyrane (**9a,b**)*

A mixture of **8a,b** (1 mmol) and mercaptoacetic acid (0.092 g, 1 mmol) was refluxed in dry benzene

(25 ml), using a Dean–Stark water separator. The excess benzene was evaporated in vaccuo. The resulting residue was triturated with saturated sodium bicarbonate solution until carbon dioxide evolution ceased and was allowed to stand overnight. The solid thus obtained was washed with water, dried, and recrystallized from ethanol to yield the corresponding **9a,b** in 70–75% yield.

9a: Yield, 74%; m.p. 235°C; IR (KBr) ν 3211 (NH), 3060 (CH aromatic), 1730, 1715, 1670 (3C=O) cm^{-1}; ^1H NMR [DMSO-d_6]: δ = 3.72–3.88 (dd, *J*-15.9 Hz, 2H, CH_2), 5.84 (s, 1H, NCHS), 6.82 (s, 1H, pyran H-4), 7.12–8.22 (m, 9H, Ar-H), 10.84 (s, 1H, NH D_2O-exchangeable); *m/z* 368 ($M^+ + 1$). Calcd for $C_{19}H_{14}N_2O_4S$: C, 62.28; H, 3.86; N, 7.65; S, 8.75%. Found: C, 62.25; H, 3.88; N, 7.62; S, 8.74%.

9b: Yield, 75%; m.p. 218°C; IR (KBr) ν 3398 (OH), 3225–3180 (NH), 3060 (CH aromatic), 1732, 1705, 1668 (3C=O) cm^{-1}; ^1H NMR [DMSO-d_6]: δ = 3.84–4 (dd, *J*-16 Hz, 2H, CH_2), 5.91 (s, 1H, NCHS), 6.89 (s, 1H, pyran H-4), 7.12–8.22 (m, 9H, Ar-H), 9.71 (s, 1H, OH), 10.71 (s, 1H, NH D_2O-exchangeable); ^{13}C NMR (DMSO) 126.2–156 (C aromatic), 30.12 (CH_2S), 61.4 (SCHN), 171.2 (C=O), 180.2 (C=O pyran), 181.3 (CONH). Calcd for $C_{19}H_{14}N_2O_5S$: C, 59.67; H, 3.7; N, 7.33; S, 8.38%. Found: C, 59.72; H, 3.65; N, 7.32; S, 8.31%.

*1-(3-Carbonyl-2H-2-oxobenzo[b]pyran-3-yl)-4-phenyl thiosemicarbazide (***10***)*

To a boiling solution of **2** (0.21 g, 1 mmol) in dioxane (30 ml), phenyl isothiocyanate (0.15 g, 1 mmol) was added. The reaction mixture was heated under reflux for 1 h. The reaction mixture was left to stand at room temperature overnight. The solid product which separated was filtered, washed with ether, dried, and recrystallized from dioxane to yield product **10** with 72% yield; m.p. 142°C; IR (KBr) ν 3410, 3329, 3313, 3230–3217 (NH), 3060 (CH aromatic), 1708, 1665 (2C=O), 1340 (C=S) cm^{-1}; ^1H NMR [DMSO-d_6]: δ = 6.89 (s, 1H, pyran H-4), 7.14–8.25 (m, 9H, Ar-H), 9.1, 10.35, 10.82 (3s, each 1H, 3NH D_2O-exchangeable); *m/z* 340 (M^+ + 1). Calcd for $C_{17}H_{13}N_3O_3S$: C, 60.16; H, 3.89; N, 12.39; S, 9.45%. Found: C, 60.21; H, 3.86; N, 12.4; S, 9.43%.

*3-Methylthio-5-(2H-2-oxobenzo[b]pyran-3-yl)-4-phenyl-1,2,4-triazole (***11a***)*

Methyl iodide (0.21 g, 1.5 mmol) was added to a mixture of **10** (0.34 g, 1 mmol) and anhydrous sodium carbonate (1.5 mmol) in DMF (10 ml). The reaction mixture was stirred for 3–5 h at room temperature (TLC control) and then poured into iced water. After another stirring for 1 h, the precipitated product was collected by filtration, washed with water, dried, and recrystallized from ethanol to afford **11a** with yield, 54%; m.p. 190–192°C; IR (KBr) ν 3058 (CH aromatic), 1712 (C=O) cm^{-1}; ^1H NMR [DMSO-d_6]: δ = 2.79 (s, 3H, CH_3), 6.81 (s, 1H, pyran H-4), 7.33–8.41 (m, 9H, Ar-H); *m/z* 335 (M^+). Calcd for $C_{18}H_{13}N_3O_2S$: C, 64.45; H, 3.91; N, 12.53; S, 9.56%. Found: C, 64.43; H, 3.93; N, 12.52; S, 9.62%.

*4-Phenyl-5-(2H-2-oxobenzo[b]pyran-3-yl)-1,2,4-triazole-3-thione (***13***)*

A suspension of the thiosemicarbazide **10** (0.34 g, 1 mmol) in sodium hydroxide solution (5%, 15 ml) was heated under reflux for 1 h. The reaction mixture was cooled, and then adjusted to pH 6 with 10% hydrochloric acid. The precipitate formed was filtered, washed with water several times, dried, and recrystallized from aqueous dioxane to yield **13** with 76% yield; m.p. 241–242°C; IR (KBr) ν 3190 (NH), 3050 (CH aromatic), 1708 (C=O), 1575 (C=N), 1270 (NC=S) cm^{-1}; ^1H NMR [DMSO-d_6]: δ = 6.69 (s, 1H, pyran H-4), 7.31–8.23 (m, 9H, Ar-H), 14.11 (s, 1H, SH D_2O-exchangeable). Calcd for $C_{17}H_{13}N_3O_2S$: C, 64.46; H, 3.91; N, 12.53; S, 9.56%. Found: C, 64.42; H, 3.9; N, 12.54; S, 9.52%.

*3-Methylthio-5-(2H-2-oxobenzo[b]pyran-3-yl)-4-phenyl-1,2,4-triazole (***11a***) and Ethyl [5-(2H-2-oxobenzo[b]pyran-3-yl)-4-phenyl-1,2,4-triazole-3-yl]acetate (***11b***)*

General Procedures: The Meracptotriazole **13** (0.32 g, 1 mmol) was dissolved in an ethanolic solution of sodium ethoxide prepared from sodium metal (0.023 g, 0.001 g-atom) in ethanol (50 ml) and then added methyl iodide (0.28 g, 2 mmol) and/or ethyl bromoacetate (0.17 g, 1 mmol) was added gradually to the resulting solution. The reaction mixture was heated under reflux for 2 h, concentrated, cooled, filtered, washed several times with water, and recrystallized from ethanol to afford the corresponding product **11a,b** with 63–68% yield.

11b: Yield, 64%; m.p. 235–236°C; IR (KBr) ν 3050 (CH aromatic), 2980 (CH aliphatic), 1710, 1729 (2C=O), 1600 (C=N) cm^{-1}; ^1H NMR [DMSO-d_6]: δ = 1.18 (t, 3H, *J*-7 Hz, CH_3), 4.11 (q, 2H, *J*-7 Hz, CH_2), 4.21 (s, 2H, SCH_2), 6.82 (s, 1H, pyran H-4), 7.16–8.23 (m, 9H, Ar-H). Calcd for $C_{21}H_{17}N_3O_4S$: C, 61.9; H, 4.21; N, 10.32; S, 7.87%. Found: C, 61.89; H, 4.11; N, 10.31; S, 7.85%.

*2-Anilino-5-(2H-2-oxobenzo[b]pyran-3-yl)-1,3,4-thiadiazole (**15**)*

A solution of **10** (0.34 g, 1 mmol) in phosphoryl chloride (5 ml) was refluxed for 30 min. The excess of phosphoryl chloride was removed under reduced pressure and the residue was poured into cold water. The organic layer was extracted with dichloromethane (4 × 20 ml) and the extracts were dried over sodium sulfate. The solvent was removed under reduced pressure and the resulting solid product was collected by filtration, dried, and recrystallized from methanol to yield **15** with yield, 60%; m.p. 115–117°C; IR (KBr) ν 3190 (NH), 3050 (CH aromatic), 1712 (C=O) cm^{-1}; ^1H NMR [DMSO-d_6]: $\delta = 6.78$ (s, 1H, pyran H-4), 7.21–8.27 (m, 9H, Ar-H), 10.46 (s, 1H, NH D_2O-exchangeable); *m/z* 321 (M^+). Calcd for $C_{17}H_{13}N_3O_2S$: C, 64.46; H, 3.91; N, 12.53; S, 9.56%. Found: C, 64.45; H, 3.89; N, 12.51; S, 9.57%.

*N-Methyl-N-[5-(2H-2-oxobenzo[b]pyran-3-yl)-1,3,4-thiadiazol-2-yl]aniline (**12**)*

Method A. Methyl iodide (0.17 g, 1.2 mmol) was added to solution of **15** (0.32 g, 1 mmol) containing potassium carbonate (0.14 g, 1 mmol) in DMF (10 ml). The reaction mixture was heated on a water bath with stirring for 1–2 h (TLC control). The reaction mixture was stirred for another 1 h at room temperature and then poured into ice water. The precipitated product was collected by filtration, washed with water, dried, and recrystallized from dioxane to afford **12** with yield, 73%; m.p. 256–257°C; IR (KBr) ν 3050 (CH aromatic), 2900 (CH aliphatic), 1710 (C=O) cm^{-1}; ^1H NMR [DMSO-d_6]: $\delta = 3.36$ (s, 3H, NCH_3), 6.68 (s, 1H, pyran H-4), 7.22–8.32 (m, 9H, Ar-H); *m/z* 335 (M^+). Calcd for $C_{18}H_{13}N_3O_2S$: C, 64.46; H, 3.91; N, 12.53; S, 9.56%. Found: C, 64.47; H, 3.89; N, 12.52; S, 9.57%.

Method B. A mixture of **15** (0.32 g, 1 mmol), anhydrous potassium carbonate (0.28 g, 2 mmol), and trimethyl phosphate (15 ml) was stirred for 3 h at 50°C. After pouring the reaction mixture into ice water (75 ml), the crude product was filtered and recrystallized from dioxane to yield the product identical with **12** in all respects (m.p., mixed m.p., and spectra).

*(3-Phenyl-4-oxothiazolidin-2-ylidene)hydrazonyl 2H-2-Oxobenzo[b]pyran-3-yl Ketone (**17**)*

To a suspension of the thiosemicarbazide **10** (0.34 g, 1 mmol) in absolute ethanol (25 ml) containing anhydrous sodium acetate (0.288 g, 4 mmol), ethyl bromoacetate (0.17 g, 1 mmol) was added. The reaction mixture was refluxed for 2–3 h, then cooled, diluted with water, and allowed to stand overnight. The solid product thus obtained was washed with water, dried, and recrystallized from ethanol/water to yield **17** with yield, 53%; m.p. 265–266°C; IR (KBr) ν 3450, 3201 (OH and NH), 3060 (CH aromatic), 1735, 1718, 1670 (3C=O) cm^{-1}; ^1H NMR [DMSO-d_6]: $\delta = 4.31$ (s, 2H, SCH_2), 6.82 (s, 1H, pyran H-4), 7.12–8.22 (m, 9H, Ar-H), 10.23 (s, 1H, NH D_2O-exchangeable); *m/z* 379 (M^+). Calcd for $C_{19}H_{13}N_3O_4S$: C, 60.15; H, 3.46; N, 11.08; S, 8.45%. Found: C, 60.16; H, 3.45; N, 11.05; S, 8.43%.

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