Synthesis and reactions of 3-hydrazino-2,7,8,9-tetrahydro-1*H*-benzo[6',7']cyclohepta[1',2':4,5]pyrido[2,3-*d*]pyrimidin-1-one

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Abstract

3-Hydrazino-2,7,8,9-tetrahydro-1*H*-benzo [6',7']cyclohepta[1',2':4,5] pyrido[2,3-*d*] pyrimidin-1-one (5) was prepared in good yield by reaction of 3 or 4 with hydrazine hydrate under reflux. Reaction of compound 5 with different aldehydes in acetic acid gave the corresponding hydrazono derivatives 7. Cyclization of the latter compounds with bromine in acetic acid afforded a series of novel pentacyclic compounds namely, 5,6,7,11-tetrahydro-15*H*-benzo[6",7"]cyclohepta[1",2":4',5']pyrido[2',3'-*d*][1,2,4] triazolo[4,3-*a*]pyrimidin-15-ones (11a-f). In addition, reaction of compound 5 with *β*-diketones and *α*-diketone were investigated. The structures of the so formed compounds were confirmed by elemental and spectral analyses (^{1}H NMR, ^{13}C NMR, IR and MS).

Keywords: Hydrazones, hetero-pentacyclic compounds, oxidative cyclization, pyrazoles

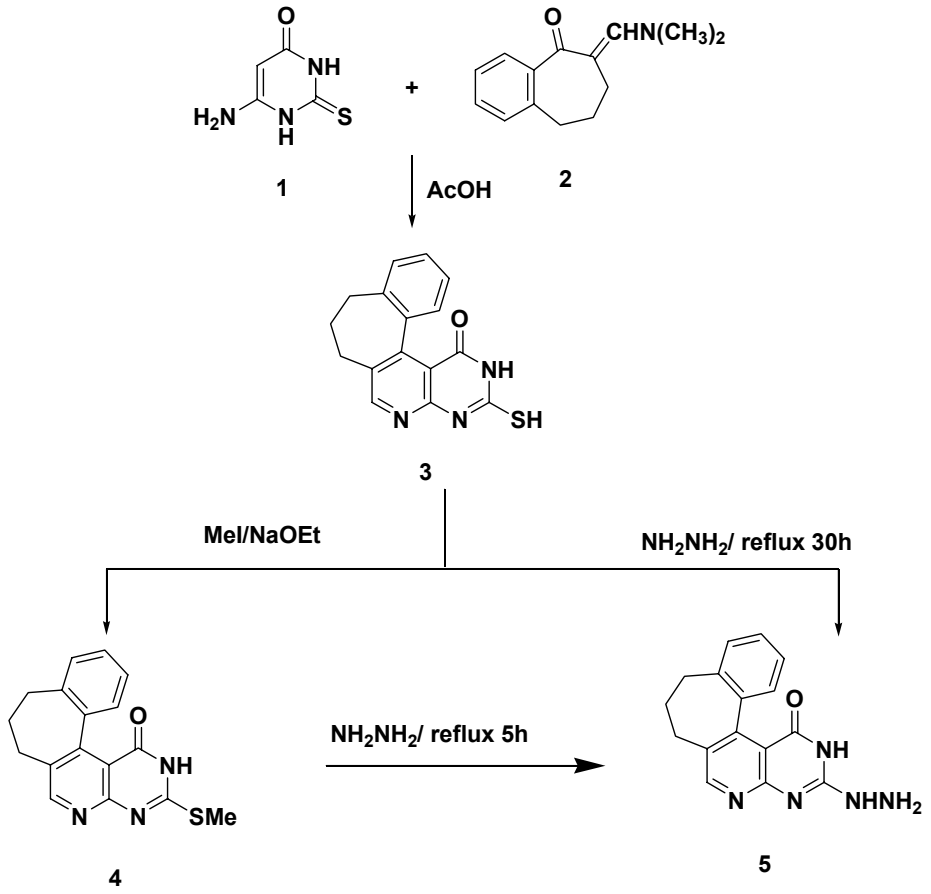
Introduction

Benzocycloheptanone and its fused ring systems play a unique role in drug discovery programs. They display a wide spectrum of biological activities such as cytotoxic, anticancer agents,[1-4] as high CB_1 receptors,[5] and have very potent antagonistic activity.[5] Substituted hydrazones are known as one of the most important classes of organic compounds, having analgesic, anticancer, antitumor, anti-inflammatory, antibacterial, and antifungal activities.[6-11] In addition, many of the poly-heterocyclic ring systems have several biological activities.[12,13] In continuation of our efforts on the synthesis of new poly-heterocyclic compounds,[14,15] and based on the above observations, we report in this context a simple method for preparation of hydrazones of a tetra-heterocyclic ring system. Cyclization of these hydrazones also afforded novel penta-heterocyclic compounds. The precursor hydrazine compound reacted with *β*-diketones to give tetra-heterocyclic compounds with a pyrazole moiety. The valuable pyrazole moiety was reported to have wide-spread biological activities.[16,17]

Results and Discussion

3-Methylthio-2,7,8,9-tetrahydro-1*H*-benzo[6',7']cyclohepta[1',2':4,5]pyrido[2,3-*d*]pyrimidin-1-one **4** was prepared by reaction of the thione **3**[14] with methyl iodide in the presence of sodium ethoxide (Scheme 1). The structure of this methylthio derivative **4** was established on the basis of spectral data and elemental analysis (see Experimental).

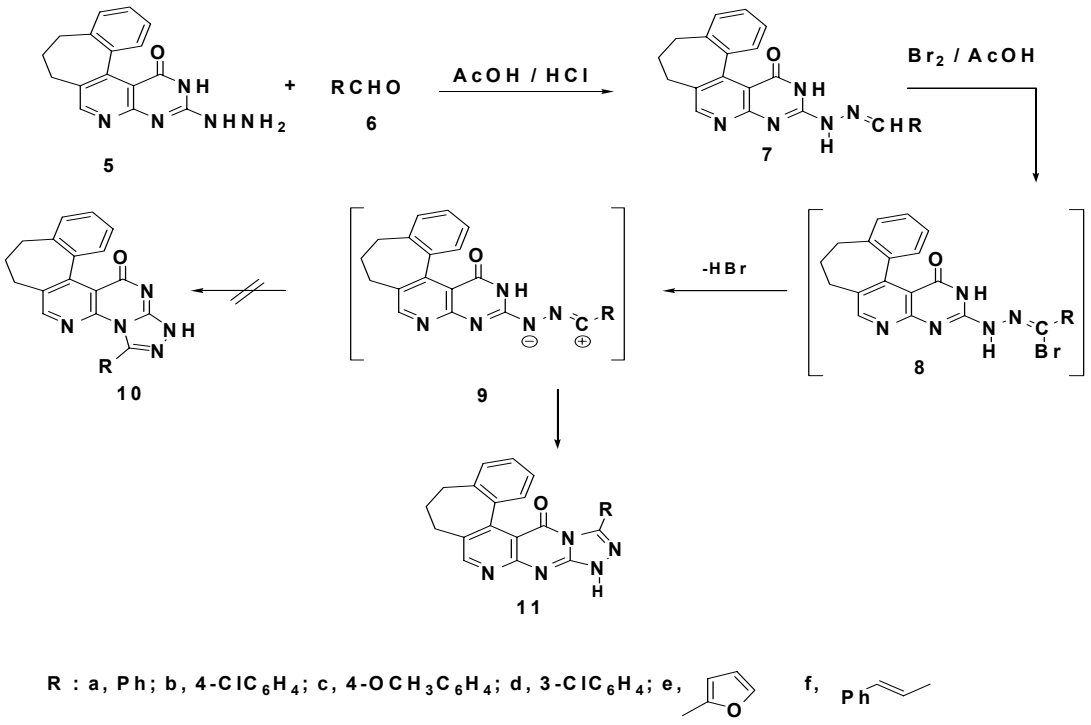
Our target 3-hydrazino-2,7,8,9-tetrahydro-1*H*-benzo[6',7']cyclohepta [1',2':4,5]pyrido [2,3-*d*]pyrimidin-1-one **5** was prepared by treating 3-methylthio-2,7,8,9-tetrahydro-1*H*-benzo[6',7']cyclohepta[1',2':4,5]pyrido[2,3-*d*]pyrimidin-1-one **4** or its thio- analogue **3**,[14] with hydrazine hydrate in absolute ethanol under reflux for 5 h or 30 h, respectively (Scheme 1). The structure of compound **5** was elucidated on the basis of spectroscopic data and microanalysis. For example, the mass spectrum of **5** showed the molecular ion peak of 100% intensity. The IR spectrum revealed absorption bands at 3367, 3338, 3185, 1683 cm^{-1} assignable to NH_2, 2-NH, and C=O, respectively. The ^1H NMR spectrum showed a characteristic singlet signal at δ 5.53, assigned to the NH_2 group.



Scheme 1

Condensation of 3-hydrazino-2,7,8,9-tetrahydro-1*H*-benzo[6',7']cyclohepta[1',2':4,5]pyrido[2,3-*d*]pyrimidin-1-one **5** with various aldehydes **6a-f** in acetic acid containing a few drops of conc. hydrochloric acid gave the corresponding hydrazone derivatives **7a-f** (Scheme 2). The mass spectra of these products **7a-f** showed the molecular ion peaks at the expected *m/z* values. Their IR spectra showed the disappearance of the NH_2 group, and revealed in each case a carbonyl band in the region 1716-1679 cm^{-1} and two bands at 3425-3239 and 3173-3100 cm^{-1} assignable to 2NH groups. Also, their ^1H NMR spectra showed the presence of the azomethine and 2NH protons at δ = 7.40-8.82 and 9.90–11.8 ppm, respectively.

Oxidative cyclization of the hydrazone derivatives **7a-f** with bromine in acetic acid at room temperature yields in each case a single group of isolable products **11** (Scheme 2), while the other isomeric structure **10** was discarded on the basis of the ^{13}C NMR spectra of the isolated products. The ^{13}C NMR of compound **11a,** taken as an example of the series prepared, revealed the signal for the carbonyl carbon resonance at δ = 163 ppm. This chemical shift value suggested that the N(4) near C=O is an sp^3 hybridized nitrogen atom (pyrrole type, as in compound **11** and **12**) and differs from the sp^2 hybridized nitrogen which appears at 170-175 ppm (compound **13**) (Chart 1).[14-20] Based on the above finding we conclude that the isolated products have structures **11** and not the isomeric structure **10**.



Scheme 2

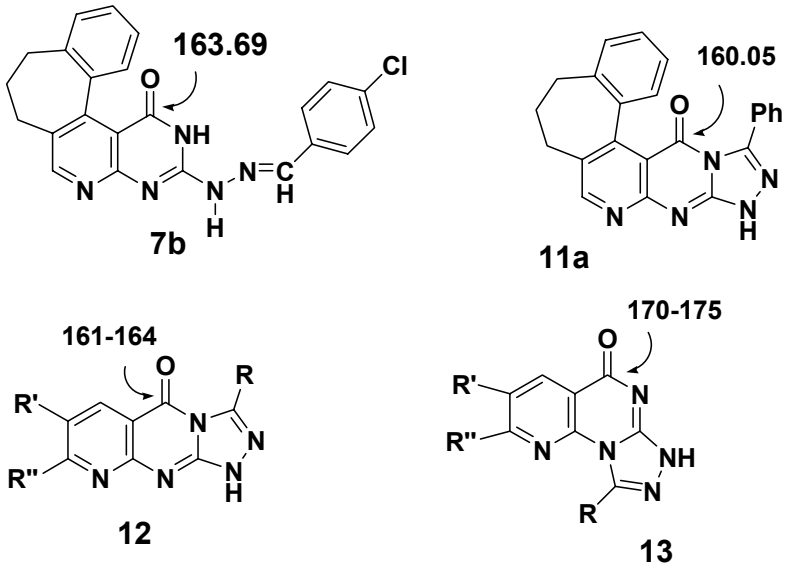
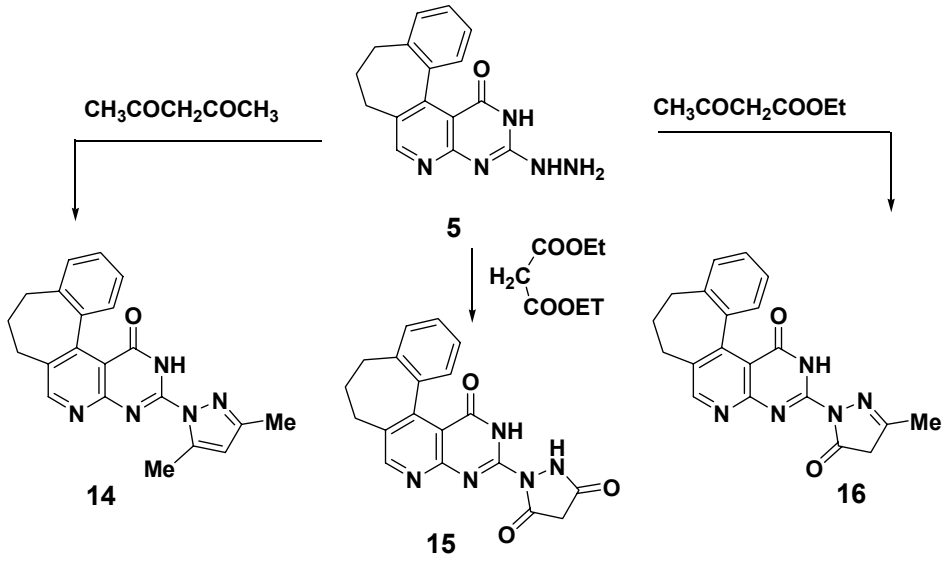


Chart 1

Our study was extended to the reaction of **5** with a variety of keto- compounds in order to synthesize new compounds have a pyrazole moiety and might be expected to be biologically active. For example, 3-hydrazino-2,7,8,9-tetrahydro-1*H*-benzo[6',7'] cyclohepta[1',2':4,5]pyrido[2,3-*d*]pyrimidin-1-one **5** reacted with acetylacetone, or diethyl malonate or ethyl acetoacetate to afford compounds **14**, **15** and **16**, respectively. The structures of **14**-**16** were confirmed on the basis of spectroscopic data and elemental analyses.

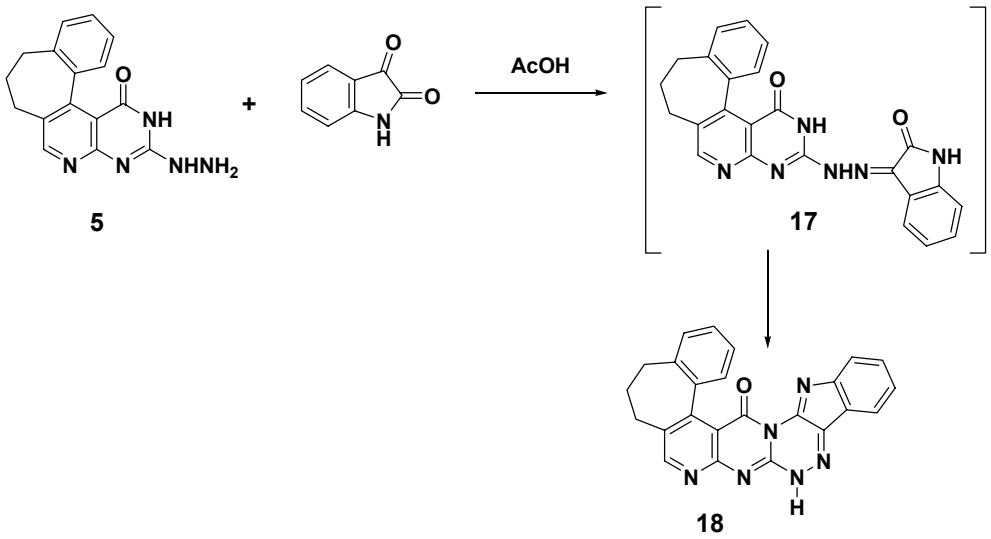


Scheme 3

We also examined the reaction of **5** with indol-2,3-dione (isatin) as an example of a *α*-diketone, which afforded the novel hepta-heterocyclic ring system **18**. The structure of the isolated product was confirmed on the basis of MS, IR, ^{1}H NMR, and elemental analysis. For example, the IR spectrum of compound **18** revealed absorption bands at 3269, 1685 cm^{-1} corresponding to NH and C=O groups, respectively, and showed the absence of the NH_2 and NH of compound **5**.

Conclusions

The synthesis of novel hydrazones of tetra-heterocyclic ring system and oxidative cyclization of these hydrazones to afford penta-heterocyclic compounds were achieved. Reaction of the precursor hydrazine derivative with *β*-diketones afforded pyrazolyl derivatives with the expected biological activities. Moreover, the reaction of hydrazine derivatives with α-diketone yielded a novel hepta-heterocyclic ring system.



Scheme 4

Experimental Section

General. Melting points were determined on a Gallenkamp apparatus and are uncorrected. IR spectra were recorded on a Pye–Unicam SP300 instrument in potassium bromide discs. ^{1}H- and ^{13}C- NMR spectra were recorded on a Varian Mercury VXR-300 spectrometer (300 MHz for ^{1}H- and 75 MHz for ^{13}C-) in DMSO-d_6, and the chemical shifts were related to that of the solvent.

Mass spectra were recorded on a GC-MS-QP 1000 EX Shimadzu Spectrometer. Elemental analyses were carried out at the Microanalytical Laboratory of Cairo University, Giza, Egypt. 3-Thioxo-2,7,8,9-tetrahydro-1H-benzo[6',7']cyclohepta[1',2':4,5]pyrido[2,3-d]pyrimidin-1-one **3** was prepared as previously described.[14]

3-Methylthio-2,7,8,9-tetrahydro-1*H*-benzo[6',7']cyclohepta[1',2':4,5]pyrido[2,3-*d*]-pyrimidin-1-one 4. To a solution of the thione **3** (1.48 g, 5 mmol) in sodium ethoxide, prepared from sodium (0.115 g, 5 mmol) in absolute ethanol (20 mL), was added methyl iodide (0.31 mL, 5 mmol). The mixture was refluxed for 10 h, and then cooled. The precipitate formed was filtered off and crystallized from ethanol to give **4**, as a pale yellow solid, (1.07 g, 69%) mp 240-242°C. ^{1}H NMR (DMSO-d_6) δ 2.15-2.61 (m, 6H, 3xCH_2), 2.68 (s, 3H, CH_3), 7.33-7.71 (m, 4H, ArH), 8.31 (s, 1H, pyridine-H), 12.78 (s, 1H, NH). ^{13}C NMR (DMSO-d_6) $\tilde{\delta}$ppm: 12.72, 28.91, 30.11, 31.88, 109.11, 120.66, 126.44, 128.44, 128.72, 129.40, 132.54, 132.77, 134.90, 135.23, 139.0, 159.65, 164.24. IR 3228, 1678 cm^{-1}. *m/z* (%) 311 (M^++2, 13), 310 (M^++1, 40), 309 (M^+, 100), 308 (33), 235 (44), 205 (17), 192 (19), 180 (16), 165 (20), 115 (23), 103 (22), 91 (16), 89 (27), 77 (42). Anal. Calcd. for $C_{17}H_{15}N_3OS$ (309.09) C, 66.00; H, 4.89; N, 13.58. Found: C, 65.89; H, 5.07; N, 13.81%.

3-Hydrazino-2,7,8,9-tetrahydro-1*H*-benzo[6',7']cyclohepta[1',2':4,5]pyrido[2,3-*d*]pyrimidin-1-one 5. To the thione **3** or its methylthio analog **4** (5 mmol) in ethanol (20 mL) was added hydrazine hydrate (10 mL, 80%). The mixture was heated at reflux until all H_2S (30 h) or MeSH (5 h) ceased to evolve, and then cooled. The solid precipitate was filtered off and crystallized from dilute dioxane to give compound **5** (1.3 g, 89%), yellow crystals, mp >300 °C. ^{1}H NMR (DMSO-d_6) δ 2.11-2.16 (m, 6H, 3xCH_2), 5.53 (s, 2H, NH_2), 7.29-7.66 (m, 6H, ArH and 2xNH), 8.13 (s, 1H, pyridine-H). ^{13}C NMR (DMSO-d_6) $\tilde{\delta}$/ppm: 28.99, 30.11, 31.80, 110.23, 122.60, 126.55, 128.76, 128.84, 130.21, 132.11, 133.32, 134.98, 135.50, 139.0, 158.32, 162.87. IR 3367, 3338, 3185, 1683 cm^{-1}. Anal. Calcd. for $C_{16}H_{15}N_5O$ (293.32) C, 65.52; H, 5.15; N, 23.88. Found: C, 65.29; H, 5.05; N, 23.67%.

Preparation of hydrazones 7a-f

A mixture of the hydrazine **5** (0.73 g, 2.5 mmol) and the appropriate aldehyde **6** (2.5 mmol) in acetic acid (20 mL) and a few drops of conc. hydrochloric acid (≈1 mL) was heated under reflux for 3 h. The mixture was then cooled and diluted with water. The so-formed solid product was then collected by filtration, dried and recrystallized from the proper solvent to afford the corresponding hydrazones **7a-f**.

3-[(Phenylmethylene)hydrazono]-2,7,8,9-tetrahydro-1*H*-benzo[6',7']cyclohepta-[1',2':4,5]-pyrido[2,3-*d*]pyrimidin-1-one 7a. Pale yellow crystals (0.71 g, 74%) mp 268-270 °C (dilute dioxane) ^{1}H NMR (DMSO-d_6) δ 1.91-2.35 (m, 6H, 3xCH_2), 7.31-7.41 and 7.95-7.97 (m, 9H, ArH), 7.68 (s, 1H, =CH), 8.19 (s, 1H, pyridine-H), 11.60 (br s, 1H, NH), 11.67 (s, 1H, NH). IR 3425, 3173, 1680 cm^{-1}. *m/z* (%) 383 (M^++2, 6), 382 (M^++1, 12), 381 (M^+, 40), 380 (28), 317 (44), 304 (92), 207 (23), 191 (26), 165 (22), 144 (21), 103 (28), 90 (85), 77 (57), 60 (100). Anal.

Calcd. for $C_{23}H_{19}N_5O$ (381.43) C, 72.42; H, 5.05; N, 18.36. Found: C, 72.31; H, 4.89; N, 18.09%.

3-[(4-Chlorophenylmethylene)hydrazono]-2,7,8,9-tetrahydro-1*H*-benzo[6',7'] cyclohepta [1',2':4,5]pyrido[2,3-*d*]pyrimidin-1-one 7b. Pale green crystals (0.79 g, 76%) mp 296-298 °C (dilute dioxane) ^{1}H NMR (DMSO-d_6) δ1.91-2.15 (m, 6H, 3xCH_2), 7.32-7.72 (m, 4H, ArH), 8.01 (s, 1H, =CH), 8.06 (d, *J* = 9.0 Hz, 2H, Ar-H), 8.16 (d, *J* = 9.0 Hz, 2H, Ar-H), 8.24 (s, 1H, pyridine-H), 11.65 (s, 1H, NH), 11.82 (s, 1H, NH). ^{13}C NMR (DMSO-d_6) δ: 28.12, 29.85, 32.25, 120.88, 126.69, 127.69, 127.88, 128.40, 128.62, 129.10, 129.33, 129.85, 129.94, 130.68, 131.89, 132.21, 132.41, 136.81, 140.29, 160.0, 163.69. IR 3369, 3165, 1679 cm^{-1}. *m/z* (%) 418 (M^++2, 5), 417 (M^++1, 18), 416 (M^+, 23), 415 (47), 414 (26), 304 (95), 207 (17), 165 (13), 153 (13), 124 (26), 111 (12), 91 (11), 90 (22), 89 (100). Anal. Calcd. for $C_{23}H_{18}ClN_5O$ (415.87) C, 66.43; H, 4.36; N, 16.84. Found: C, 66.35; H, 4.21; N, 16.65%.

3-[(4-Methoxyphenylmethylene)hydrazono]-2,7,8,9-tetrahydro-1*H*-benzo[6',7']cyclohepta [1',2':4,5]pyrido[2,3-*d*]pyrimidin-1-one 7c. Dark yellow crystals (0.80 g, 78%) mp 300-302 °C (dilute dioxane) ^{1}H NMR (DMSO-d_6) δ 1.92-2.34 (m, 6H, 3xCH_2), 3.81 (s, 3H, OCH_3), 6.96-7.35 (m, 4H, ArH), 7.40 (s, 1H, =CH), 7.79 (d, *J* = 8.0 *Hz*, 2H, Ar-H), 7.90 (d, *J* = 8.0 Hz, 2H, Ar-H), 8.60 (s, 1H, pyridine-H), 9.90 (s, 1H, NH), 11.20 (s, 1H, NH). IR 3365, 3154, 1682 cm^{-1}. *m/z* (%) 413 (M^++2, 9), 412 (M^++1, 26), 411 (M^+, 100), 304 (53), 277 (27), 208 (11), 206 (20), 192 (25), 165 (23), 121 (28), 119 (30), 115 (23), 105 (30), 91 (83), 77 (80). Anal. Calcd. for $C_{24}H_{21}N_5O_2$ (411.17) C, 70.06; H, 5.14; N, 17.02. Found: C, 70.31; H, 5.00; N, 16.92%.

3-[(3-Chlorophenylmethylene)hydrazono]-2,7,8,9-tetrahydro-1*H*-benzo[6',7'] cyclohepta[1',2':4,5]-pyrido-[2,3-*d*]-pyrimidin-1-one 7d. Yellow crystals (0.71 g, 68%) mp 258-260 °C (dioxane) ^{1}H NMR (DMSO-d_6) δ 1.91-2.20 (m, 6H, 3xCH_2), 7.40-7.82 (m, 8H, ArH), 8.30 (s, 1H, =CH), 8.43 (s, 1H, pyridine-H), 11.26 (s, 1H, NH), 11.82 (s, 1H, NH). IR 3300, 3055, 1716 cm^{-1}. *m/z* (%) 418 (M^++2, 4), 417 (M^++1, 8), 416 (M^+, 12), 415 (31), 304 (100), 207 (15), 192 (12), 165 (11), 152 (12), 140 (11), 116 (14), 111 (14), 102 (16), 89 (82), 77 (17). Anal. Calcd. for $C_{23}H_{18}ClN_5O$ (415.87) C, 66.43; H, 4.36; N, 16.84. Found: C, 66.30; H, 4.34; N, 16.55%.

3-[(2-Furfurylmethylene)hydrazono]-2,7,8,9-tetrahydro-1*H*-benzo[6',7']cyclohepta [1',2':4,5]pyrido[2,3-*d*]pyrimidin-1-one 7e. Yellow crystals (0.60g, 65%) mp 186-188°C (dioxane) ^{1}H NMR (DMSO-d_6) δ/ppm: 1.95-2.18 (m, 6H, 3xCH_2), 7.08-7.82 (m, 7H, ArH), 8.06 (s, 1H, =CH), 8.14 (s, 1H, pyridine-H), 10.86 (s, 1H, NH), 11.90 (s, 1H, NH). ^{13}C NMR (DMSO-d_6) δ 28.88, 30.44, 32.0, 110.44, 112.22, 120.77, 120.72, 120.74, 126.55, 128.88, 129.43, 130.91, 135.77, 136.64, 139.33, 142.82, 144.65, 150.11, 150.33, 156.88, 162.30. IR 3239, 3097, 1679 cm^{-1}. *m/z* (%) 372 (M^++1, 28), 371 (M^+, 100), 370 (20), 317 (16), 314 (15), 277 (15), 264 (17), 235 (11), 192 (11), 115(13), 80 (59), 77 (91). Anal. Calcd. for $C_{21}H_{17}N_5O_2$ (371.39) C, 67.91; H, 4.61; N, 18.86. Found: C, 67.75; H, 4.55; N, 18.59 %.

3-[Styrylmethylenehydrazono]-2,7,8,9-tetrahydro-1*H*-benzo[6',7']cyclohepta[1',2':4,5]-pyrido-[2,3-*d*]-pyrimidin-1-one 7f. Yellow solid (0.71 g, 70%) mp 146-148 °C (ethanol) ^{1}H NMR (DMSO-d_6) δ 1.91-2.38 (m, 6H, 3xCH_2), 5.62 (m, 1H, =CH), 7.04-8.28 (m, 11H, Ar-H

and N=CH), 8.49 (s, 1H, pyridine-H), 10.85 (s, 1H, NH), 11.82 (s, 1H, NH). IR 3240, 3100, 1682 cm^{-1}. *m/z* (%) 408 (M^++1, 12), 407 (M^+, 33), 406 (18), 405 (14), 404 (23), 317 (97), 302 (20), 293 (11), 278 (39), 277 (37), 262 (23), 207 (20), 192 (33), 152 (26), 129 (84), 115 (81), 103 (46), 91 (62), 77 (99), 55 (100). Anal. Calcd. for $C_{25}H_{21}N_5O$ (407.47) C,73.69; H, 5.19; N, 17.19. Found: C, 73.57; H, 5.02; N, 17.00 %.

5,6,7,11-Tetrahydro-15*H*-benzo[6'',7'']cyclohepta[1'',2'':4',5']pyrido[2',3'-*d*][1,2,4]-triazolo[4,3-*a*]pyrimidin-15-ones 11a-f

Bromine (0.052 g, 1 mmol) in acetic acid (5 mL) was added dropwise to a stirred solution of the appropriate hydrazone **7a-f** (1 mmol) in acetic acid (10 mL). The reaction mixture was then poured onto ice-cold water, and the solid precipitate was filtered off, washed with sodium bicarbonate solution, then with water, dried, and crystallized from the appropriate solvent to give the respective compounds **11a-f**.

13-Phenyl-5,6,7,11-tetrahydro-15*H*-benzo[6'',7'']cyclohepta[1'',2'':4',5']pyrido[2',3'-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-15-one 11a. Pale yellow crystals (0.23 g, 60%) mp 208-210 °C. ^{1}H NMR (DMSO-d_6) δ 1.90-2.39 (m, 6H, 3xCH_2), 7.27-8.24 (m, 9H, ArH), 8.48 (s, 1H, pyridine-H), 11.85 (s, 1H, NH). ^{13}C NMR (DMSO-d_6) δ 28.79, 30.31, 31.95, 126.35, 127.45, 128.29, 128.46, 128.69, 129.34, 129.41, 134.46, 134.85, 139.20, 139.41, 145.05, 145.10, 150.73, 153.0, 156.20, 157.82, 160.05. IR 3158, 1681 cm^{-1}. *m/z* (%) 379 (M^+, 23), 91 (54), 77 (100). Anal. Calcd. for $C_{23}H_{17}N_5O$ (379.41) C, 72.81; H, 4.52; N, 18.46. Found: C, 72.60; H, 4.25; N, 18.31%.

13-(4-Chlorophenyl)-5,6,7,11-tetrahydro-15*H*-benzo[6'',7'']cyclohepta[1'',2'':4',5'] pyrido-[2',3'-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-15-one 11b. Yellow solid (0.25 g, 61%) mp 230-232 °C (ethanol/dioxane) ^{1}H NMR (DMSO-d_6) δ 1.90-2.42 (m, 6H, 3xCH_2), 7.22-7.83 (m, 4H, ArH), 7.92 (d, *J* = 9.0 Hz, 2H, Ar-H), 8.02 (d, *J* = 9.0 Hz, 2H, Ar-H), 8.62 (s, 1H, pyridine-H), 10.94 (s, 1H, NH). IR 3381, 1698 cm^{-1}. *m/z* (%) 415 (M^++2, 50), 414 (M^++1, 8), 413 (M^+, 50), 297 (50), 233 (42), 180 (58), 177 (50), 138 (67), 124 (100), 115 (83), 89 (67), 77 (67). Anal. Calcd. for $C_{23}H_{16}ClN_5O$ (413.86) C, 66.75; H, 3.90; N, 16.92. Found: C, 66.51; H, 3.65; N, 16.62%.

13-(4-Methoxyphenyl)-5,6,7,11-tetrahydro-15*H*-benzo[6'',7'']cyclohepta[1'',2'':4',5'] pyrido[2',3'-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-15-one 11c. Orange solid (0.21 g, 51%) mp 130-132 °C (ethanol) ^{1}H NMR (DMSO-d_6) δ 1.90-2.39 (m, 6H, 3xCH_2), 3.90 (s, 3H, OCH_3), 6.96-8.18 (m, 8H, ArH), 8.38 (s, 1H, pyridine-H), 11.40 (s, 1H, NH). IR 3146, 1679 cm^{-1}. *m/z* (%) 409 (M^+, 62), 297 (20), 105 (52), 91 (80), 77 (100). Anal. Calcd. for $C_{24}H_{19}N_5O_2$ (409.46) C, 70.40; H, 4.68; N, 17.10. Found: C, 70.20; H, 4.36; N, 16.98%.

13-(3-Chlorophenyl)-5,6,7,11-tetrahydro-15*H*-benzo[6'',7'']cyclohepta[1'',2'':4',5'] pyrido[2',3'-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-15-one 11d. Yellow solid (0.21g, 51%) mp 250-252°C (ethanol) ^{1}H NMR ($CDCl_3$) δ 1.91-2.52 (m, 6H, 3xCH_2), 7.40 – 7.82 (m, 8H, ArH), 8.30 (s, 1H, pyridine-H), 11.21 (s, 1H, NH). IR 3256, 1686 cm^{-1}. Anal. Calcd. for $C_{23}H_{16}ClN_5O$ (413.86) C, 66.75; H, 3.90; N, 16.92. Found: C, 66.60; H, 3.59; N, 16.72%.

13-(Furan-2-yl)-5,6,7,11-tetrahydro-15*H*-benzo[6'',7'']cyclohepta[1'',2'':4',5']pyrido [2',3'-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-15-one (11e). Orange solid (0.21g, 57%) mp 270-272 °C

(dioxane/ethanol) ^{1}H NMR (DMSO-d_6) δ 1.92-2.39 (m, 6H, 3xCH_2), 7.12-8.00 (m, 7H, ArH), 8.21 (s, 1H, pyridine-H), 11.22 (s, 1H, NH). ^{13}C NMR (DMSO-d_6) δ/ppm: 28.88, 30.33, 31.94, 120.11, 121.08, 122.62, 126.76, 127.93, 128.66, 129.34, 130.21, 135.87, 136.66, 138.87, 139.92, 142.0, 143.92, 151.32, 153.41, 155.10, 162.21. IR 3320, 1685 cm^{-1}. Anal. Calcd. for $C_{21}H_{15}N_5O_2$ (369.38) C, 68.28; H, 4.09; N, 18.96. Found: C, 68.15; H, 4.25; N, 18.88%.

13-Styryl-5,6,7,11-tetrahydro-15*H*-benzo[6'',7'']cyclohepta[1'',2'':4',5']pyrido[2',3'-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-15-one 11f. Orange solid (0.21 g, 51%) mp 130-132 °C (ethanol) ^{1}H NMR (DMSO-d_6) δ: 1.90-2.36 (m, 6H, 3xCH_2), 5.50 (d, *J* = 13.0 *Hz*, 1H, =CH), 7.05-7.89 (m, 10H, ArH), 8.12 (d, *J* = 13.0 *Hz*, 1H, =CH), 8.37 (s, 1H, pyridine-H), 11.21 (s, 1H, NH). IR 3120, 1692 cm^{-1}. Anal. Calcd. for $C_{25}H_{19}N_5O$ (405.45) C, 74.06; H, 4.72; N, 17.27. Found: C, 74.20; H, 4.54; N, 17.48%.

Synthesis of compounds 14-16 A mixture of compound **5** (0.3 g, 1 mmol) and 1,3-dicarbonyl compounds (1 mmol of each) in glacial acetic acid (20 mL) was refluxed for 10 hrs. After cooling, the precipitate was collected by filtration and crystallized from the appropriate solvent to afford compounds **14-16**.

3-(3,5-Dimethylpyrazol-1-yl)-2,3,4,,7,8,9-hexahydro-1*H*-benzo[6',7']cyclohepta-[1',2':4,5]-pyrido[2,3-*d*]pyrimidin-1-one 14. Pale yellow solid (0.25g, 69%) mp 245-248°C (ethanol) ^{1}H NMR (DMSO-d_6) δ/ppm: 1.92-2.30 (m, 6H, 3xCH_2), 2.34(s, 3H, CH_3), 2.47 (s, 3H, CH_3), 6.05 (s, 1H, pyrazolyl-H), 7.31-8.37 (m, 4H, ArH), 8.48 (s, 1H, pyridine-H), 10.0 (s, 1H, NH). IR υ 3209, 1703, 1680 cm^{-1}.*m/z* (%) 357 (M^+, 80), 105 (42), 91 (65), 77 (100). Anal. Calcd. for $C_{21}H_{19}N_5O$ (357.41) C, 70.57; H, 5.36; N, 19.59. Found: C, 70.24; H, 5.11; N, 19.31%.

3-(3,5-Dioxopyrazol-1-yl)-2,3,4,,7,8,9-hexahydro-1*H*-benzo[6',7']cyclohepta[1',2':4,5] pyrido[2,3-*d*]pyrimidin-1-one 15. Pale green solid (0.26g, 72%) mp > 300 °C (ethanol) ^{1}H NMR (DMSO-d_6) δ 1.89-2.35 (m, 6H, 3xCH_2), 4.90 (s, 2H, CH_2), 7.12-7.80 (m, 4H, ArH), 8.25 (s, 1H, pyridine-H), 10.62 (s, 1H, NH), 11.21 (s, 1H, NH). ^{13}C NMR (DMSO-d_6) δ 28.91, 30.32, 32.0, 49.64, 111.32, 126.32, 128.65, 129.54, 129.84, 131.10, 135.0, 136.0, 139.10, 139.32, 150.32, 153.71, 162.0, 163.65, 166.11. IR 3234, 1703, 1690, 1679 cm^{-1}. *m/z* (%) 361 (M^+, 100), (20), 105 (25), 91 (36), 77 (100). Anal. Calcd. for $C_{19}H_{15}N_5O_3$ (361.35) C, 63.15; H, 4.18; N, 19.39. Found: C, 62.98; H, 4.30; N, 19.10%.

3-(3-Methyl-5-oxopyrazol-1-yl)-2,3,4,,7,8,9-hexahydro-1*H*-benzo[6',7']cyclohepta [1',2':4,5]pyrido [2,3-*d*]pyrimidin-1-one 16. Pale orange solid (0.25g, 72%) mp 272-274°C (ethanol) ^{1}H NMR (DMSO-d_6) δ 1.90-2.35 (m, 6H, 3xCH_2), 2.37 (s, 3H, CH_3), 4.85 (s, 2H, CH_2), 7.33–8.24 (m, 8H, ArH), 8.28 (s, 1H, pyridine-H), 11.38 (s, 1H, NH). IR 3409, 3228, 1700, 1678 cm^{-1}. *m/z* (%) 361 (M^++2, 6), 360 (M^++1, 13), 359 (M^+, 33), 347 (18), 279 (100), 264 (55), 180 (38), 166 (46), 152 (47), 129 (35), 120 (44), 96 (24), 89 (40), 77 (80). Anal. Calcd. for $C_{20}H_{17}N_5O_2$ (359.38) C, 66.84; H, 4.77; N, 19.49. Found: C, 66.62; H, 4.65; N, 19.68%.

5,6,7-Trihydro-benzo[6''',7''']cyclohepta[1''',2''':4'',5'']pyrido[2'',3'':4',5']pyrimido[2',1':3,4][1,2,4]triazino [5,6-b]indo-19(11*H*)-one 18. A mixture of compound **5** (0.3 g, 1 mmol) and indol-2,3-dione

(0.15g, 1 mmol) in acetic acid (20 mL) was refluxed for 5 h. The precipitate formed by cooling was collected by filtration, and crystallized from dioxan to give yellow solid in 88% yield. mp > 300°C; ^{1}H NMR (DMSO-d_6) δ 1.89-2.19 (m, 6H, 3xCH_2), 6.85-7.72 (m, 8H, ArH), 8.24 (s, 1H, pyridine-H), 10.58 (s, 1H, NH). ^{13}C NMR (DMSO-d_6) δ: 28.80, 30.32, 32.20, 109.87, 117.76, 120.02, 121.11, 121.52, 124.0, 126.65, 127.71, 128.88, 129.96, 130.21, 131.0, 133.20, 136.33, 138.33, 138.77, 139.52, 142.80, 153.91, 165.775, 171.90. IR 3269, 1685 cm^{-1}. *m/z* (%) 405 (M^++1, 1), 404 (M^+, 1), 368 (11), 293 (50), 256 (27), 213 (20), 185 (26), 149 (50), 129 (48), 115 (27), 92 (30), 77 (30). Anal. Calcd. for $C_{24}H_{16}N_6O$ (404.14) C, 71.28; H, 3.99; N, 20.78. Found: C, 71.06; H, 3.75; N, 20.61%.

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