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Novel Pentaheterocycles. First General Synthesis Entry to Functionalized Derivatives of Pyrido[2,3-*f*:6,5-*f*′]di[1,2,4]triazolo[4,3-*a*] pyrimidin-5(1*H*)-ones

Mosselhi A. N. Mosselhi, Magda A. Abdallah, Thoraya A. Farghaly, and **Ahmad S. Shawali***

Department of Chemistry, Faculty of Science, University of Cairo, Giza, Egypt

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Summary. Thirteen derivatives of the novel title ring system were synthesized *via* a two-step procedure that utilizes hydrazonoyl chlorides and pyridodipyrimidinones as starting materials. The mechanism and regiochemistry of the reactions studied are discussed and the compounds prepared were characterized by alternate synthesis, spectra (mass, IR, ^{1}H and ^{13}C NMR), and elemental analyses.

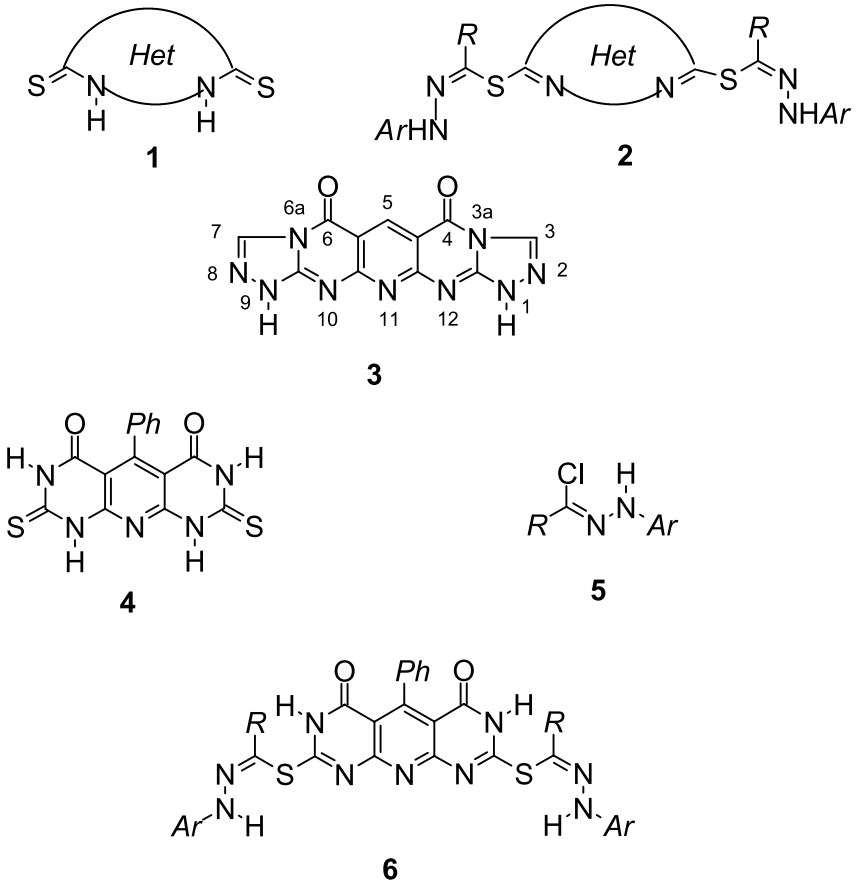
Keywords. Hydrazonoyl chlorides; Regiochemistry; Hydrazonothioates; Heterocycles.

Introduction

As a continuation of our studies of hydrazonic acid derivatives [1–4], it was decided to synthesize a series of novel bis(hydrazonothioate) esters of type **2** derived from the corresponding heterocyclic dithiones **1** (Formulae 1) and explore their utility in the synthesis of novel annelated triazoles with bridgehead nitrogen atoms. Alkyl, aryl, and heteroaryl-hydrazonate esters and their thio analogs were proved to be useful precursors for the synthesis of a variety of acyclic and heterocyclic compounds [3–7].

Recently, *Shawali et al.* reported also that such esters are useful synthons for fused heterocycles such as [1,2,4]triazolo[4,3-*b*][1,2,4]triazin-7(1*H*)-ones [8], [1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-ones [9], pyrimido[1,2-*b*][1,2,4,5]tetrazines [10], and [1,2,4]triazino[4,3-*b*][1,2,4,5]tetrazines [11]. In this paper we report the first synthesis of thirteen derivatives of the novel title ring system, namely pyrido[2,3-*f*:6,5-*f*′]di[1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one **3**. The heart of

* Corresponding author. E-mail: as_shawali@mail.com



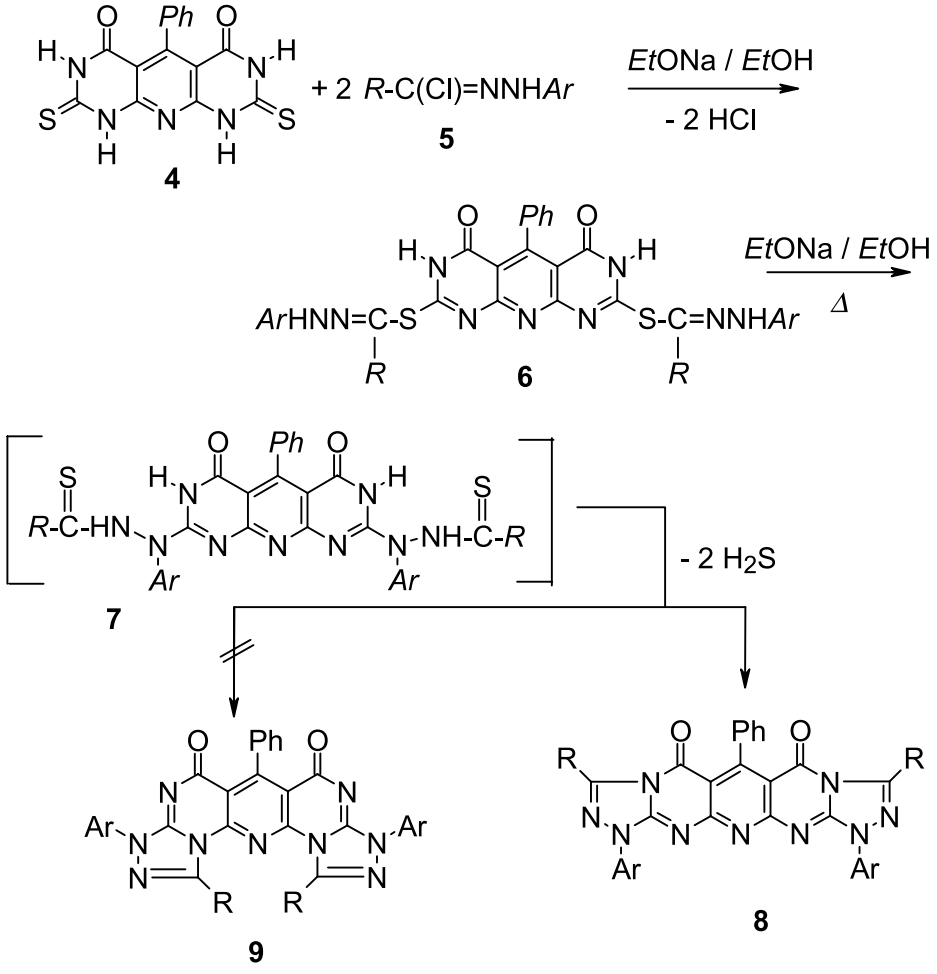
Formulae 1

our plan was the preparation of the hitherto unreported bis(hydrazonothioate) esters **6** (Formulae 1) from 5-pheny1-1,3,7,9-tetrahydro-2,8-dithioxopyrido[2,3-*d*:6,5-*d*′]-dipyrimidine-4,6(3*H*,9*H*)-dione **4** and the respective hydrazonoyl chlorides **5**.

Results and Discussion

The starting material, 5-phenyl-1,3,7,9-tetrahydro-2,8-dithioxopyrido[2,3-*d*:6,5-*d*′] dipyrimidine-4,6(1*H*,9*H*)-dione (**4**) [12] was prepared in one step by reaction of 6-amino-2-thiouracil [13] with benzaldehyde in acetic acid under reflux as previously described. Reaction of **4** with hydrazonoyl chlorides **5** in ethanol in the presence of sodium ethoxide at room temperature was found to give products that were identified as the bis(hydrazonothioate) esters **6** (Scheme 1). The structures of the latter products were established from their microanalyses and mass, IR, and ^{1}H NMR spectra which showed the expected signals. For example, like other aryl and heteroaryl hydrazonothioate esters [14], loss of elements of the corresponding thiol **4** from the molecular ions was a characteristic feature of the mass spectra of **6**.

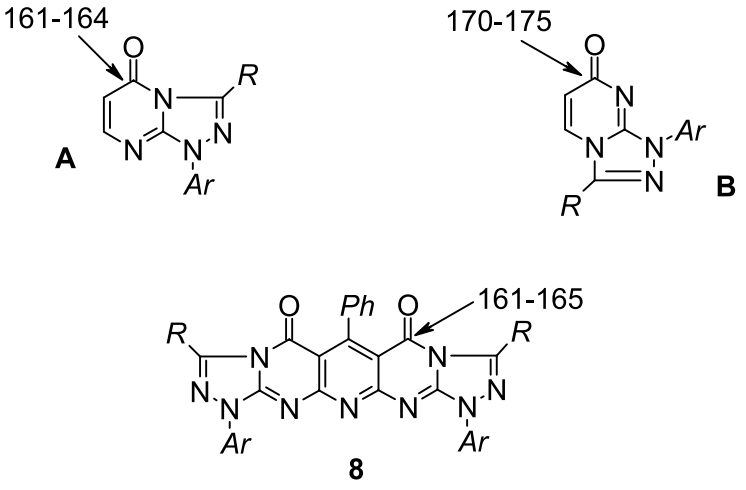
Next, we examined the *Smiles* rearrangement of the esters **6** in an attempt to get the respective bis(thiohydrazides) **7**. When each of **6** was refluxed in ethanol in the



R/*Ar*: a, *Ph*NHCO/C_6H_5; b, *Ph*NHCO/4-$CH_3C_6H_4$; c, *Ph*NHCO/4-ClC_6H_4; d, *Ph*NHCO/4-$NO_2C_6H_4$; e, CH_3CO/C_6H_5; f, CH_3CO/4-$CH_3C_6H_4$; g, CH_3CO/4-ClC_6H_4; h, CH_3CO/4-$NO_2C_6H_4$; i, *Et*OCO/C_6H_5; j, *Et*OCO/4-$CH_3C_6H_4$; k, *Et*OCO/4-ClC_6H_4; l, *Et*OCO/4-$NO_2C_6H_4$; m, C_6H_5/C_6H_5

Scheme 1

presence of sodium ethoxide, a single product was obtained in each case as evidenced by tlc analysis of the crude products. Surprisingly however, the microanalyses and mass spectral data of the isolated products showed that they were free of sulfur and such data were consistent with either one of the two isomeric structures **8** and **9** (Scheme 1). An immediate distinction between these structures was reached by comparison of the ^{13}C NMR and IR spectra of the products with those of related isomeric annelated pyrimidinones. Literature reports have shown that in the 4-pyrimidinone ring structure, the chemical shift of the carbonyl carbon is markedly affected by the nature of the adjacent nitrogen (pyrrole type in structure

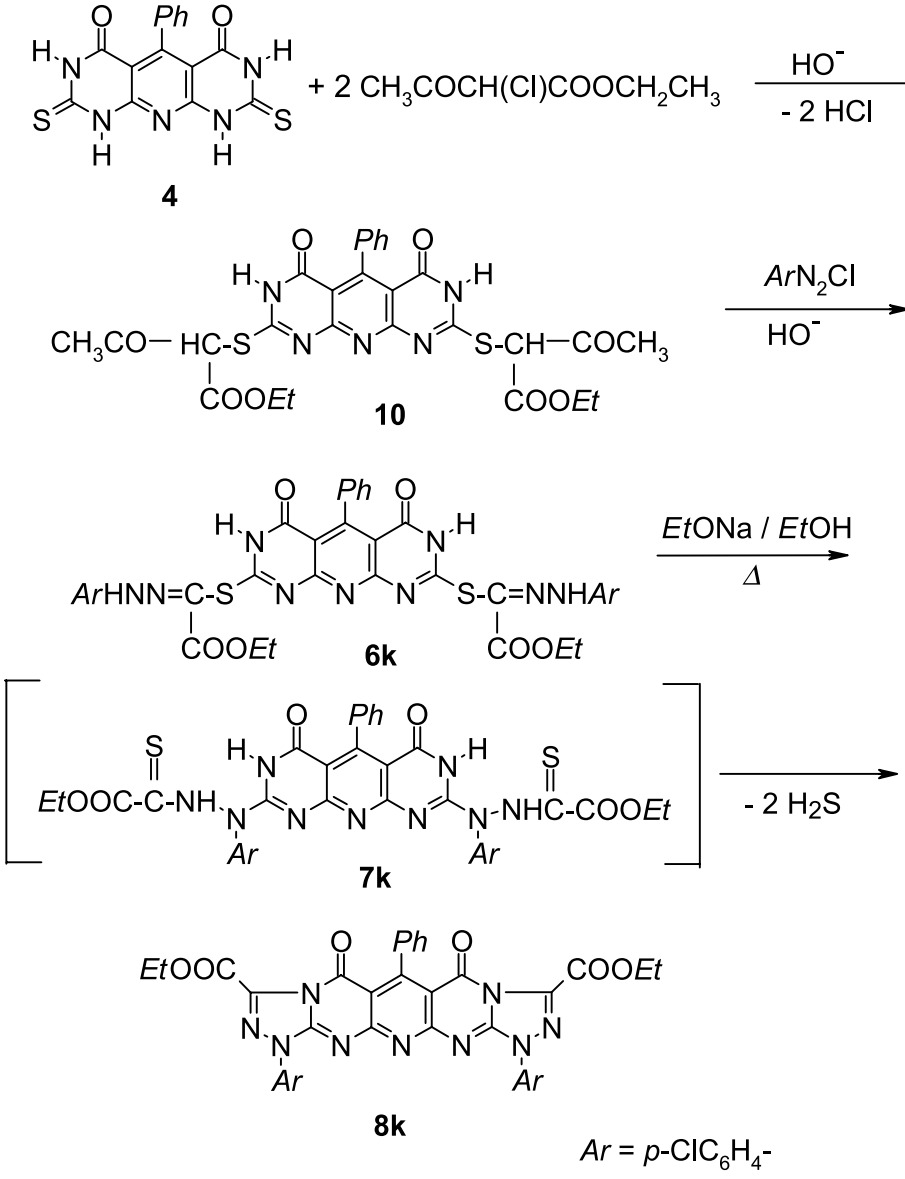


$\overline{\nu}_{C=O}$: **A**, 1680 - 1690; **B**, 1640-1660; **8**, 1670 - 1700 cm^{-1} [15-17, 22]

Formulae 2

8 and pyridine type in structure **9**). The chemical shift values of the annelated pyrimidinones **A** and **B** are shown in Formulae 2 [15–17, 22]. Since the values found for the isolated products are similar to those of **A** and not **B**, the products were assigned structure **8**. Furthermore, the assignment of structure **8** to the products isolated is also substantiated by the similarity of their carbonyl stretching frequencies ($\bar{\nu} = 1670–1700\,cm^{-1}$) with those of pyrimidinone derivatives **A**. For example, pyrimidinone derivatives **A** exhibit their CO bands in the region $\bar{\nu} = 1680–1690\,cm^{-1}$ whereas pyrimidinones **B** exhibit their CO absorption bands in the region $\bar{\nu} = 1640–1660\,cm^{-1}$ [17].

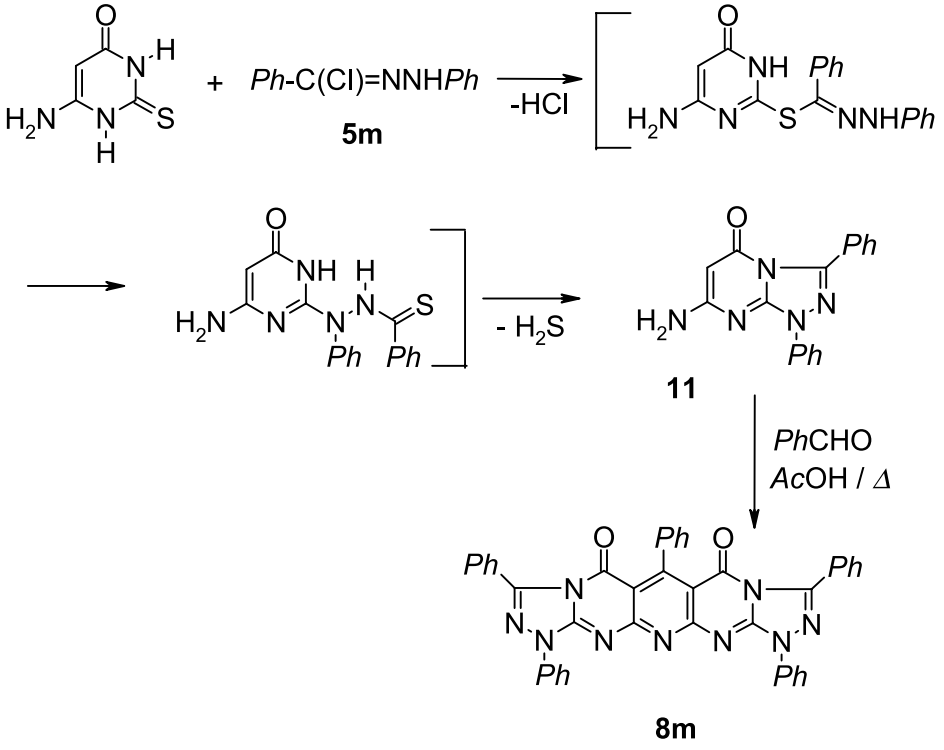
The direct formation of the products **8** from compounds **6** indicated that the intermediate thiohydrazides **7** underwent *in situ* cyclization as soon as they are formed (Scheme 1). To account for this transformation, we thought of an alternate synthesis of the products **8**. The synthesis strategy employed in this work for the preparation of the latter compounds is based on application of *Japp-Klingemann* reaction [18] and *Smiles* rearrangement [19, 20]. Thus, treatment of the dithione **4** with two molar equivalents of ethyl 2-chloro-3-oxobutanoate in ethanol in the presence of potassium hydroxide at room temperature yielded the substitution product **10** (Scheme 2). The formation of the latter derivative is analogous to *S*-alkylation reaction reported to be exhibited by 2-thiouracils [21]. The structure of the latter product was evidenced by its microanalysis and spectroscopic (mass, IR, ^{1}H NMR) data. Its ^{1}H NMR spectrum showed two characteristic singlet signals near $\delta = 2.40$ and 5.37 ppm assignable to the CH_3CO and –SCH(*R*)-protons in addition to the characteristic signals of the $–COOCH_2CH_3$ groups. Treatment of **10** with *p*-chlorobenzenediazonium chloride in ethanol in the presence of sodium acetate at low temperature (0–5°C) yielded a product identical in all respects (mp, mixed mp, IR) with that one **6k** isolated from reaction of **5k** with **4** above



Scheme 2

(Scheme 1). In our hands, attempts to get the bis(thiohydrazide) **7k** by refluxing the bis(hydrazonothioate) **6k** were found to give **8k** directly as end product.

The final structure proof was completed by alternate synthesis of **8m**, as a typical example of the series, from 7-amino-1,3-diphenyl-[1,2,4]triazolo[4,3-a]pyrimidin-5(1*H*)-one (**11**) which was reported recently from our laboratory [23]. Thus, refluxing an equimolar mixture of **11** and benzaldehyde in glacial acetic acid and work up of the reaction mixture, yielded **8m** in 70% yield and proved to be identical in all respects with that one obtained from base catalyzed cyclization of the bis(hydrazonothioate) ester **6m**.



Scheme 3

Experimental

All melting points were determined on an electrothermal *Gallenkamp* apparatus. The IR spectra were measured on a Pye-Unicam SP300 instrument in KBr discs. The ^{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 $CDCl_3$ or *DMSO*-d_6 and the chemical shifts were related to that of the solvent. The mass spectra were recorded on a GCMS-Q1000-EX spectrometer, the ionizing voltage was 70 eV. Elemental analyses were carried out by the Microanalytical Center of Cairo University, Giza, Egypt. The identification of compounds from different experiments were secured by mixed mps and superimposable IR spectra.

The reagents 4-amino-2-thiouracil [13], 5-pheny1-1,3,7,9-tetrahydro-2,8-dithioxopyrido[2,3-*d*:6,5-*d'*]dipyrimidine-4,6(1*H*,9*H*)-dione **4** [12] and the hydrazonoyl chlorides **5** [6] were prepared as previously described.

General Procedures for the Synthesis of 5-Phenylpyrido[2,3-d:6,5-d']dipyrimidine-4,6(3H,7H)-dione-2,8-diyl bis(N-arylalkanehydrazonothioates) **6**

Method A: To an ethanolic *Et*ONa solution, prepared from 0.115 g of Na (5 mmol) and 30 cm^3 of absolute *Et*OH, 0.9 g of dithione **4** (2.5 mmol) were added with stirring. To the resulting solution 5 mmol of the appropriate hydrazonoyl chloride **5** were added and the mixture was stirred at room temperature for 24 h. The precipitated solid was filtered off, washed with H_2O, dried, and finally crystallized from the appropriate solvent to give the respective bis(hydrazonothioate) ester **6**.

Reaction of **4** with **5e**, when it was carried out as above, gave the cyclized product **8e** directly. However, when the reaction mixture was stirred only for 1 h, it gave the bis(hydrazonothioate) ester **6e**.

Method B: To a solution of 0.01 mol of **10** in 40 cm^3 of *Et*OH and 10 cm^3 of *DMF* was added 3 g of *Ac*ONa · $3H_2O$ and the mixture was cooled in an ice-bath to 0–5°C while being stirred. To the resulting

cold solution a cold solution of *p*-chlorobenzenediazonium chloride, prepared as usual by diazotizing 2.55 g of *p*-chloroaniline (0.02 mol) in 12 cm^3 of 6 *M* HCl with 1.4 g of $NaNO_2$ (0.02 mol) in 10 cm^3 of H_2O, was added portionwise. After all the diazonium solution was added, the reaction mixture was stirred for further 30 min while being cooled in the ice bath. The precipitated solid was then filtered off, washed with H_2O, dried, and finally crystallized from the appropriate solvent to give the respective hydrazonothioate ester **6k**. The latter product proved to be identical in all respects (mp, mixed mp, and IR) with that obtained by Method A.

5-Phenylpyrido[2,3-d:6,5-d′]dipyrimidin-4,6(3H,7H)-dione-2,8-diyl bis(N-phenyl(phenylaminocarbonyl)methanehydrazonothioate) (**6a**, $C_{43}H_{31}N_{11}O_4S_2$)

Yield 1.61 g (78%); mp 234°C (*Et*OH dioxane); IR: $\bar{\nu} = 3394, 3178, 1682, 1663\,cm^{-1}$; ^1H NMR (*DMSO*-d_6): $\delta = 7.07–7.84$ (m, 25H), 10.12 (s, 2H), 11.68 (s, 2H), 11.97 (s, 2H) ppm.

5-Phenylpyrido[2,3-d:6,5-d′]dipyrimidin-4,6(3H,7H)-dione-2,8-diyl bis(N-(4-methylphenyl)(phenylaminocarbonyl)methanehydrazonothioate) (**6b**, $C_{45}H_{35}N_{11}O_4S_2$)

Yield 1.71 g (80%); mp 222–4°C (*Et*OH); IR: $\bar{\nu} = 3387, 3158, 1689, 1659\,cm^{-1}$; ^1H NMR (*DMSO*-d_6) $\delta = 2.40$ (s, 6H), 7.14–8.80 (m, 23H), 10.18 (s, 2H), 11.74 (s, 2H), 12.03 (s, 2H) ppm.

5-Phenylpyrido[2,3-d:6,5-d′]dipyrimidin-4,6(3H,7H)-dione-2,8-diyl bis(N-(4-chlorophenyl)(phenylaminocarbonyl)methanehydrazonothioate) (**6c**, $C_{43}H_{29}N_{11}O_4S_2Cl_2$)

Yield 1.90 g (85%); mp 236–8°C (*Et*OH dioxane); IR: $\bar{\nu} = 3395, 3194, 1688, 1658\,cm^{-1}$; ^1H NMR (*DMSO*-d_6): $\delta = 7.12–8.24$ (m, 23H), 10.25 (s, 2H), 11.66 (s, 2H), 12.1 (s, 2H) ppm.

5-Phenylpyrido[2,3-d:6,5-d′]dipyrimidin-4,6(3H,7H)-dione-2,8-diyl bis(N-(4-nitrophenyl)(phenylaminocarbonyl)methanehydrazonothioate) (**6d**, $C_{43}H_{29}N_{13}O_8S_2$)

Yield 1.88 g (82%); mp 248°C (*Et*OH dioxane); IR: $\bar{\nu} = 3333, 3186, 1680, 1653\,cm^{-1}$; ^1H NMR (*DMSO*-d_6): $\delta = 7.05–8.58$ (m, 23H), 10.35 (s, 2H), 10.72 (s, 2H), 11.5 (s, 2H) ppm.

5-Phenylpyrido[2,3-d:6,5-d′]dipyrimidin-4,6(3H,7H)-dione-2,8-diyl bis(N-phenyl-2-oxopropanehydrazonothioate) (**6e**, $C_{33}H_{25}N_9O_4S_2$)

Yield 1.14 g (68%); mp 250°C (*Et*OH); IR: $\bar{\nu} = 3333, 3186, 1720, 1666\,cm^{-1}$; ^1H NMR (*DMSO*-d_6): $\delta = 2.46$ (s, 6H), 7.01–8.13 (m, 15H), 11.90 (s, 2H), 12.08 (s, 2H) ppm.

5-Phenylpyrido[2,3-d:6,5-d′]dipyrimidin-4,6(3H,7H)-dione-2,8-diyl bis(N-(4-methylphenyl)-2-oxopropanehydrazonothioate) (**6f**, $C_{35}H_{29}N_9O_4S_2$)

Yield 1.3 g (74%); mp 210°C (dioxane); IR: $\bar{\nu} = 3325, 3186, 1720, 1666\,cm^{-1}$; ^1H NMR (*DMSO*-d_6): $\delta = 2.39$ (s, 6H), 2.5 (s, 6H), 6.8–7.94 (m, 13H), 11.85 (s, 2H), 12.19 (s, 2H) ppm.

5-Phenylpyrido[2,3-d:6,5-d′]dipyrimidin-4,6(3H,7H)-dione-2,8-diyl bis(N-(4-chlorophenyl)-2-oxopropanehydrazonothioate) (**6g**, $C_{33}H_{23}Cl_2N_9O_4S_2$)

Yield 1.48 g (80%); mp 222°C (*Et*OH dioxane); IR: $\bar{\nu} = 3410, 3194, 1712, 1660\,cm^{-1}$; ^1H NMR (*DMSO*-d_6): $\delta = 2.50$ (s, 6H), 6.8–8.18 (m, 13H), 11.86 (s, 2H), 12.08 (s, 2H) ppm.

5-Phenylpyrido[2,3-d:6,5-d′]dipyrimidin-4,6(3H,7H)-dione-2,8-diyl bis(N-(4-nitrophenyl)-2-oxopropanehydrazonothioate) (**6h**, $C_{33}H_{23}N_{11}O_8S_2$)

Yield 1.56 g (82%); mp 230°C (*Et*OH); IR: $\bar{\nu} = 3395, 3195, 1710, 1660\,cm^{-1}$; ^1H NMR (*DMSO*-d_6): $\delta = 2.50$ (s, 6H), 6.72–7.25 (m, 13H), 11.86 (s, 2H), 12.08 (s, 2H) ppm.

5-Phenylpyrido[2,3-d:6,5-d′]dipyrimidin-4,6(3H,7H)-dione-2,8-diyl bis(N-phenyl(ethoxycarbonyl)methanehydrazonothioate) (**6i**, $C_{35}H_{29}N_9O_6S_2$)

Yield 1.52 g (83%); mp 188–90°C (*Et*OH); IR: $\bar{\nu} = 3410, 3186, 1744, 1670\,cm^{-1}$; ^1H NMR (*DMSO*-d_6): $\delta = 1.31$ (t, 6H, $J = 7$ Hz), 4.40 (q, 4H, $J = 7$ Hz), 6.96–8.15 (m, 15H), 11.85 (s, 2H), 12.18 (s, 2H) ppm.

5-Phenylpyrido[2,3-d:6,5-d′]dipyrimidin-4,6(3H,7H)-dione-2,8-diyl bis(N-(4-methylphenyl)(ethoxycarbonyl)methanehydrazonothioate) (**6j**, $C_{37}H_{33}N_9O_6S_2$)

Yield 1.62 g (85%); mp 192°C (*Et*OH); IR: $\bar{\nu} = 3317, 3180, 1755, 1678\,cm^{-1}$; ^1H NMR (*DMSO*-d_6): $\delta = 1.31$ (t, 6H, $J = 7$ Hz), 2.38 (s, 6H), 4.37 (q, 4H, $J = 7$ Hz), 6.84–7.95 (m, 13H), 11.82 (s, 2H), 12.10 (s, 2H) ppm.

5-Phenylpyrido[2,3-d:6,5-d′]dipyrimidin-4,6(3H,7H)-dione-2,8-diyl bis(N-(4-chlorophenyl)(ethoxycarbonyl)methanehydrazonothioate) (**6k**, $C_{35}H_{27}Cl_2N_9O_6S_2$)

Yield 1.54 g (77%); mp 220°C (*Et*OH); IR: $\bar{\nu} = 3317, 3140, 1759, 1682\,cm^{-1}$; ^1H NMR (*DMSO*-d_6): $\delta = 1.29$ (t, 6H, $J = 7$ Hz), 4.32 (q, 4H, $J = 7$ Hz), 7.07–8.15 (m, 13H), 11.90 (s, 2H), 12.15 (s, 2H) ppm.

5-Phenylpyrido[2,3-d:6,5-d′]dipyrimidin-4,6(3H,7H)-dione-2,8-diyl bis(N-(4-nitrophenyl)(ethoxycarbonyl)methanehydrazonothioate) (**6l**, $C_{35}H_{27}N_{11}O_{10}S_2$)

Yield 1.77 g (86%); mp 205°C (*Et*OH); IR: $\bar{\nu} = 3325, 3154, 1744, 1650\,cm^{-1}$; ^1H NMR (*DMSO*-d_6): $\delta = 1.26$ (t, 6H, $J = 7$ Hz), 4.41 (q, 4H, $J = 7$ Hz), 6.78–8.49 (m, 13H), 11.8 (s, 2H), 12.1 (s, 2H) ppm.

5-Phenylpyrido[2,3-d:6,5-d′]dipyrimidin-4,6(3H,7H)-dione-2,8-diyl bis(N-phenylbenzenecarbohydrazonothioate) (**6m**, $C_{41}H_{29}N_9O_2S_2$)

Yield 1.48 g (80%); mp 240°C (*Et*OH dioxane); IR: $\bar{\nu} = 3313, 3109, 1670\,cm^{-1}$; ^1H NMR (*DMSO*-d_6): $\delta = 6.92$–8.20 (m, 25H), 11.85 (s, 2H), 12.58 (s, 2H) ppm.

General Procedures for the Synthesis of 1,3,6,9,11-Pentasubstituted Pyrido[3,2-f:6,5-f′] di([1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-ones) **8**

Method A: To a solution of *Et*ONa, prepared from 0.12 g of Na (5 mmol) and 30 cm^3 of absolute *Et*OH, 0.9 g of **4** (2.5 mmol) and 5 mmol of the appropriate hydrazonoyl chloride **5** were added. The reaction mixture was refluxed until H_2S ceased to evolve (10–20 h), and then cooled. The precipitated product was filtered off, washed with water, and crystallized from the appropriate solvent to give the respective product **8**.

Method B: To a solution of *Et*ONa, prepared from 0.23 g of Na (10 mmol) and 30 cm^3 of absolute *Et*OH, was added 5 mmol of the appropriate bis(hydrazonothioate) ester **6** and the mixture was refluxed until H_2S ceased to evolve (10–20 h), and then cooled. The precipitated product was filtered off, washed with H_2O and crystallized from the appropriate solvent to give the respective **8**. The physical constants of the products **8b**, **8f**, **8i**–**8l**, and **8m**, prepared by this method, proved to be identical in all respects with those obtained by Method A.

Method C: A mixture of 3.03 g of **11** (10 mmol) and 0.63 g of benzaldehyde (5 mmol) in 30 cm^3 of glacial *Ac*OH was refluxed for 4 h, then the reaction mixture was diluted with H_2O and allowed to cool to room temperature. The crude product was collected and crystallized from *Et*OH to give the corresponding product **8m**, which proved to be identical in all respects with that one obtained by either Method A or B.

3,9-Di(phenylaminocarbonyl)-1,6,11-triphenylpyrido[2,3-f:6,5-f′] di([1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one) (**8a**, $C_{43}H_{27}N_{11}O_4$)

Yield 5.33 g (70%); mp 298–300°C (*Et*OH dioxane); yellow-white crystals; UV (dioxane): λ_{max} ($\log \varepsilon$) = 363 (4.36) nm; IR: $\bar{\nu}$ = 3417, 1689, 1670 cm^{-1}; ^{1}H NMR (*DMSO*-d_6): δ = 7.12 (m, 25H), 11.72 (s, 2H) ppm; MS: m/z (%) = 761 (M^+, 26), 524 (28), 475 (30), 236 (53), 122 (34), 116 (64), 88 (100).

3,9-Di(4-methylphenylaminocarbonyl)-1,6,11-triphenylpyrido[2,3-f:6,5-f′] di([1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one) (**8b**, $C_{45}H_{31}N_{11}O_4$)

Yield 6.47 g (82%); mp 252°C (dioxane); yellow white crystals; UV (dioxane): λ_{max} ($\log \varepsilon$) = 336 (4.51) nm; IR: $\bar{\nu}$ = 3314, 1690, 1670 cm^{-1}; ^{1}H NMR (*DMSO*-d_6): δ = 2.51 (s, 6H), 6.84–8.30 (m, 23H), 11.72 (s, 2H) ppm; MS: m/z (%) = 788 (M^+–1, 43), 718 (67), 634 (67), 599 (62), 433 (57), 366 (62), 332 (67), 287 (71), 202 (67), 79 (100).

3,9-Di(4-chlorophenylaminocarbonyl)-1,6,11-triphenylpyrido[2,3-f:6,5-f′] di([1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one) (**8c**, $C_{43}H_{25}Cl_2N_{11}O_4$)

Yield 6.56 g (79%); mp 226°C (*Et*OH dioxane); yellow crystals; UV (dioxane): λ_{max} ($\log \varepsilon$) = 372 (4.54) nm; IR: $\bar{\nu}$ = 3386, 1700, 1658 cm^{-1}; ^{1}H NMR (*DMSO*-d_6): δ = 7.22–8.12 (m, 23H), 11.20 (s, 2H) ppm; ^{13}C NMR (*DMSO*-d_6): δ = 163.4, 157.0, 153.8, 148.2, 139.3, 138.4, 136.9, 136.7, 131.8, 130.3, 129.8, 129.5, 128.5, 128.0, 125.5, 121.7, 120.4, 98.0 ppm; MS: m/z (%) = 830 (M^+, 7), 522 (7), 453 (10), 239 (6), 122 (6), 118 (6), 88 (30), 57 (100).

3,9-Di(4-nitrophenylaminocarbonyl)-1,6,11-triphenylpyrido[2,3-f:6,5-f′] di([1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one) (**8d**, $C_{43}H_{25}N_{13}O_8$)

Yield 6.38 g (75%); mp 280°C (dioxane); yellow crystals; UV (dioxane): λ_{max} ($\log \varepsilon$) = 350 (4.57) nm; IR: $\bar{\nu}$ = 3344, 1701, 1670 cm^{-1}; ^{1}H NMR (*DMSO*-d_6): δ = 7.22–8.12 (m, 23H), 11.20 (s, 2H) ppm; MS: m/z (%) = 853 ($M^+ + 2$, 24), 849 (20), 524 (15), 451 (18), 153 (31), 121 (35), 87 (31), 56 (100).

3,9-Di(acetyl)-1,6,11-triphenylpyrido[2,3-f:6,5-f′]di([1,2,4]triazolo[4,3-a] pyrimidin-5(1H)-one) (**8e**, $C_{33}H_{21}N_9O_4$)

Yield 4.92 g (81%); mp 190°C (*Et*OH dioxane); brick red crystals; UV (dioxane): λ_{max} ($\log \varepsilon$) = 380 (4.84) nm; IR: $\bar{\nu}$ = 1717, 1677 cm^{-1}; ^{1}H NMR (*DMSO*-d_6): δ = 2.34 (s, 6H), 6.92–8.14 (m, 15H) ppm; ^{13}C NMR (*DMSO*-d_6): δ = 192.5, 163.7, 161.3, 154.1, 142.0, 138.7, 130.2, 129.9, 129.4, 129.3, 128.5, 128.3, 127.5, 126.0, 121.7, 25.1 ppm; MS: m/z (%) = 607 (M^+, 50), 408 (50), 375 (50), 199 (50), 172 (50), 141 (55), 136 (50), 69 (100).

3,9-Di(acetyl)-1,11-di(4-methylphenyl)-6-phenylpyrido[2,3-f:6,5-f′] di([1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one) (**8f**, $C_{35}H_{25}N_9O_4$)

Yield 5.40 g (85%); mp 210–12°C (*Et*OH dioxane); brown crystals; UV (dioxane): λ_{max} ($\log \varepsilon$) = 382 (3.65) nm; IR: $\bar{\nu}$ = 1715, 1670 cm^{-1}; ^{1}H NMR (*DMSO*-d_6): δ = 2.30 (s, 6H), 2.39 (s, 6H), 7.14–7.98

(m, 13H) ppm; MS: m/z (%) = 635 (M^+, 41), 528 (50), 221 (41), 157 (50), 147 (82), 104 (100), 83 (86), 56 (18).

3,9-Di(acetyl)-1,11-di(4-chlorophenyl)-6-phenylpyrido[2,3-f:6,5-f′]di([1,2,4] triazolo[4,3-a]pyrimidin-5(1H)-one) (**8g**, $C_{33}H_{19}Cl_2N_9O_4$)

Yield 5.14 g (76%); mp 248–50°C (*Et*OH dioxane); yellow solid; IR: $\bar{\nu}$ = 1712, 1670 cm^{-1}; ^{1}H NMR (*DMSO*-d_6): δ = 2.50 (s, 6H), 7.23–8.13 (m, 13H) ppm; MS: m/z (%) = 679 ($M^+ + 3$, 26), 676 (M^+, 31), 560 (31), 522 (33), 415 (36), 370 (31), 260 (64), 207 (44), 199 (62), 170 (44), 138 (44), 93 (82), 70 (100).

3,9-Di(acetyl)-1,11-di(4-nitrophenyl)-6-phenylpyrido[2,3-f:6,5-f′]di([1,2,4] triazolo[4,3-a]pyrimidin-5(1H)-one) (**8h**, $C_{33}H_{19}N_{11}O_8$)

Yield 5.51 g (79%); mp > 320°C (*Et*OH/dioxane); UV (*Et*OH/dioxane) λ_{max} (log ε) = 322 (4.40) nm; IR: $\bar{\nu}$ = 1715, 1670 cm^{-1}; ^{1}H NMR (*DMSO*-d_6): δ = 2.50 (s, 6H), 7.23–8.49 (m, 13H) ppm; MS: m/z (%) = 697 (M^+, 16), 534 (17), 507 (12), 468 (23), 377 (18), 315 (16), 267 (20), 207 (22), 199 (13), 170 (19), 115 (100), 75 (53).

3,9-Di(ethoxycarbonyl)-1,6,11-triphenylpyrido[2,3-f:6,5-f′]di([1,2,4] triazolo[4,3-a]pyrimidin-5(1H)-one) (**8i**, $C_{35}H_{25}N_9O_6$)

Yield 5.34 g (80%); mp 224°C (*Et*OH/dioxane); pale brown solid; IR: $\bar{\nu}$ = 1751, 1670 cm^{-1}; ^{1}H NMR (*DMSO*-d_6): δ = 1.29 (t, 6H, J = 7 Hz), 4.39 (q, 4H, J = 7 Hz), 6.96–8.45 (m, 15H) ppm; MS: m/z (%) = 667 (M^+, 12), 529 (18), 335 (40), 289 (20), 240 (26), 221 (18), 210 (18), 185 (18), 156 (22), 113 (16), 99 (32), 90 (32), 86 (21), 72 (20), 51 (100).

3,9-Di(ethoxycarbonyl)-1,11-di(4-methylphenyl)-6-phenylpyrido[2,3-f:6,5-f′]di([1,2,4] triazolo[4,3-a]pyrimidin-5(1H)-one) (**8j**, $C_{37}H_{29}N_9O_6$)

Yield 4.73 g (86%); mp 240°C (*Et*OH/dioxane); pale yellow crystals; UV (dioxane): λ_{max} (log ε) = 304 (4.35) nm; IR: $\bar{\nu}$ = 1743, 1674 cm^{-1}; ^{1}H NMR (*DMSO*-d_6): δ = 1.23 (t, 6H, J = 7 Hz), 2.39 (s, 6H), 4.44 (q, 4H, J = 7 Hz), 7.20–7.96 (m, 13H) ppm; ^{13}C NMR (*DMSO*-d_6): δ = 164.7, 157.8, 156,3, 146.7, 139.4, 137.9, 135.8, 134.5, 130.3, 129.7, 128.3, 127.6, 125.9, 122.0, 89.9, 63.9, 21.3, 14.5 ppm; MS: m/z (%) = 697 ($M^+ + 2$, 23), 695 (M^+, 26), 575 (31), 246 (26), 185 (23), 131 (23), 13 (23), 105 (51), 91 (100), 90 (44), 83 (44), 77 (69), 69 (74).

3,9-Di(ethoxycarbonyl)-1,11-di(4-chlorophenyl)-6-phenylpyrido[2,3-f:6,5-f′]di([1,2,4] triazolo[4,3-a]pyrimidin-5(1H)-one) (**8k**, $C_{35}H_{23}Cl_2N_9O_6$)

Yield 6.18 g (84%); mp 240°C (*Et*OH/dioxane); yellow white crystals; UV (dioxane): λ_{max} (log ε) = 305 (4.52) nm; IR: $\bar{\nu}$ = 1759, 1674 cm^{-1}; ^{1}H NMR (*DMSO*-d_6): δ = 1.31 (t, 6H, J = 7 Hz), 4.42 (q, 4H, J = 7 Hz), 7.18–8.14 (m, 13H) ppm; MS: m/z (%) = 741 ($M^+ + 5$, 22), 512 (24), 393 (24), 292 (24), 246 (26), 180 (24), 113 (28), 85 (30), 69 (52).

3,9-Di(ethoxycarbonyl)-1,11-di(4-nitrophenyl)-6-phenylpyrido[2,3-f:6,5-f′]di([1,2,4] triazolo[4,3-a]pyrimidin-5(1H)-one) (**8l**, $C_{35}H_{23}N_{11}O_{10}$)

Yield 6.43 g (85%); mp 268°C (*Et*OH/dioxane); yellow crystals; UV (dioxane): λ_{max} (log ε) = 339 (4.44) nm; IR: $\bar{\nu}$ = 1751, 1682 cm^{-1}; ^{1}H NMR (*DMSO*-d_6): δ = 1.34 (t, 6H, J = 7 Hz), 4.41 (q, 4H, J = 7 Hz), 7.16–8.51 (m, 13H) ppm; MS: m/z (%) = 759 ($M^+ + 2$, 15), 527 (30), 497 (84), 434 (62), 379 (34), 291 (22), 248 (21), 212 (60), 180 (62), 88 (100), 58 (61).

1,3,6,9,11-Pentaphenylpyrido[2,3-f:6,5-f′]di([1,2,4]triazolo[4,3-a]pyrimidin-5(1H)-one) (**8m**, $C_{41}H_{25}N_9O_2$)

Yield 5.40 g (80%); mp 210°C (*Et*OH); pale yellow crystals; UV (dioxane): λ_{max} (log ε) = 384 (3.32) nm; IR: $\bar{\nu} = 1670\,cm^{-1}$; ^1H NMR (*DMSO*-d_6): $\delta = 7.01$–8.12 (m, ArH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 163.0$, 159.0, 147.7, 144.9, 140.1, 137.5, 131.0, 130.8, 129.8, 128.2, 128.0, 127.6, 127.5, 127.4, 125.7, 121.3, 96.0, 67.0 ppm; MS: m/z (%) = 675 (M^+, 13), 650 (13), 626 (13), 393 (13), 303 (63), 236 (23), 194 (19), 160 (12), 133 (86), 103 (45), 91 (100), 76 (30), 51 (40).

2,8-Di(1-ethoxycarbonyl-2-oxopropylthio)-5-phenylpyrido[2,3-d:6,5-d′] dipyrimidine-4,6(3H,7H)-dione (**10**, $C_{27}H_{25}N_5O_8S_2$)

To a stirred solution of 0.9 g of the dithione **4** (2.5 mmol) in 40 cm^3 of *Et*OH and 10 cm^3 of *DMF* aqueous KOH solution (0.28 g, 5 mmol) in 10 cm^3 of H_2O was added. To the resulting solution was then added 0.82 g of ethyl 2-chloro-3-oxobutanoate (5 mmol). The mixture was stirred for 24 h, then diluted with H_2O. The precipitated solid was filtered off, washed with H_2O, dried, and finally crystallized from dioxane ethanol to give 1.10 g of **10** (72%); mp 210–212°C; IR: $\bar{\nu} = 3340$, 1745, 1680 cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 1.22$ (t, 6H, $J = 7$ Hz), 2.5 (s, 6H), 4.2 (q, 4H, $J = 7$ Hz), 5.37 (s, 2H), 6.73–7.24 (m, 5H), 12.03 (s, 2H) ppm.

7-Amino-1,3-diphenyl-1,2,4-triazolo[4,3-a]pyrimidin-5(1H)-one (**11**, $C_{17}H_{13}N_5O$)

To a mixture of 1.43 g of 6-amino-2-thiouracil (0.01 mol) and 2.30 g of **5m** (0.01 mol) in 30 cm^3 of dioxane 1.4 ml of Et_3N (0.01 mol) were added and the whole mixture was refluxed until H_2S ceased to evolve (10 h). Then it was cooled, and the precipitated solid was filtered off and crystallized from ethanol dioxane (1/1) to give 2.12 g of **11** (70%); mp 250°C (Ref. [23] 250°C); IR: $\bar{\nu} = 3454$, 3300, 1680 cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 4.9$ (s, 1H), 6.88 (s, 2H), 7.4–8.2 (m, 10H) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 164$, 157, 149, 144, 137, 131, 130, 128, 127, 126, 122, 121, 76 ppm.

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