

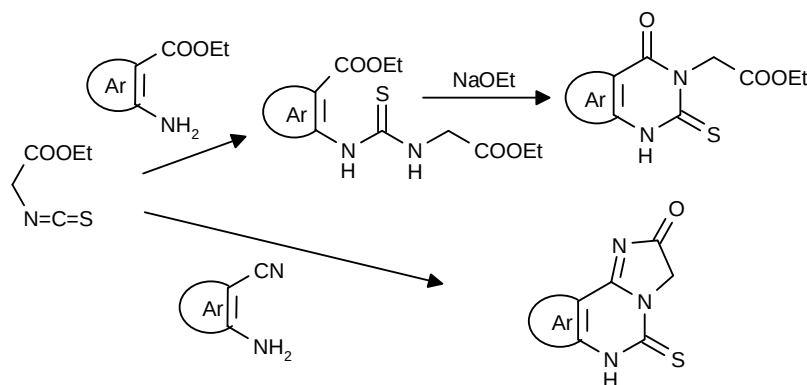
ONE POT SYNTHESIS OF FUSED PYRIMIDINES FROM 2-[N-(METHYLTHIOTHIOCARBONYL)AMINO]ACETATE

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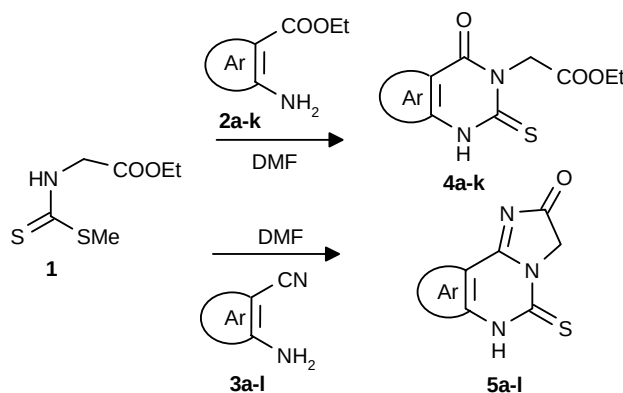
Abstract - A variety of 3-substituted fused pyrimidines (**4a-k**) are readily obtained from the 2-amino esters (**2a-k**) with 2-[N-(methylthiothiocarbonyl)-amino]acetate (**1**). Condensed imidazo[1,2-c]pyrimidine ring system was also constructed in a one-pot process by reacting heteroaromatic 2-amino nitriles (**3a-l**) with **1**, obtaining a number of novel tri- and tetracyclic compounds (**5a-l**).

Fused pyrimidines are found in a wide variety of natural products [e.g. purines, pyrrolopyrimidines, pyridopyrimidines, pteridines], pharmaceuticals, agrochemicals and veterinary products.¹⁻⁷ In recent papers,⁸⁻¹¹ we reported the reaction of heteroaromatic 2-amino esters or 2-amino nitriles with ethyl isothiocyanatoacetate giving fused pyrimidines or imidazopyrimidines, respectively (Scheme 1).



Scheme 1

As illustrated in Scheme 2, the present work is aiming at the synthesis of similar products, using ethyl 2-[N-[(methylthiothiocarbonyl)amino]acetate (**1**) in DMF.



Scheme 2

Utilization of **1** seems promising, since the corresponding isocyanatoacetate as well as 2-chloroethyl isocyanate have already been used for cyclizing anthranilonitrile (**3a**) in a 2- or 3-step procedure, respectively.^{12,13}

Here, we report a simple, one-pot reaction for the synthesis of 3-substituted pyrimidines and tri- or tetracyclic imidazopyrimidine systems by the reaction of 2-amino esters or 2-amino nitriles with ethyl 2-[N-[(methylthiothiocarbonyl)amino]acetate (**1**) in DMF.

The reaction of various 2-amino esters (**2a-k**) with **1** afforded cyclization products (**4a-k**) (Figure 1) by one-pot reactions in 40-55% yields presumably *via* an intermediate **G**.

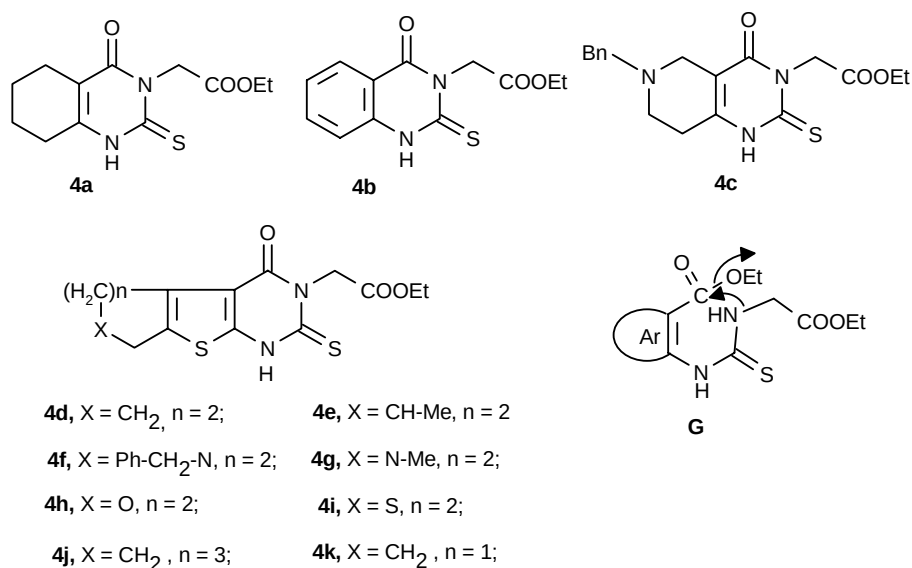


Figure 1

The conformity of the structure (**4a-k**) was proved by several evidences: comparison of chemical shifts between 2-(3,4-dihydro-2-methyl-4-oxoquinazolin-3-yl)acetic acid (from a ^{13}C NMR spectral data bank¹⁴) and methylthio derivatives^{15,16} of **4b**. Moreover, the NMR values of **4b** is also good agreements with the literature values.¹⁶

The reaction of 2-amino nitriles (**3a-l**) with **1** gave the fused pyrimidines (**5a-l**) (Figure 2) by the one-pot reactions in 36-46% yields presumably *via* a thiourea intermediate (**5I**), wherein imidazolidinyl derivative (**5L**) and diazepino derivative (**5M**) were ruled out by NMR spectroscopy. This method is useful for giving smooth access to tricyclic and tetracyclic hetero systems (**5a-l**).

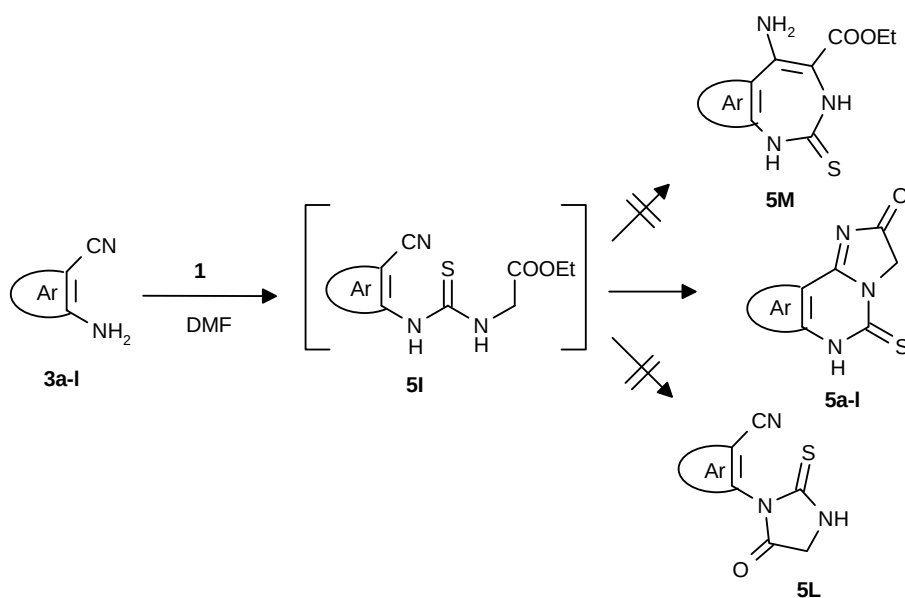


Figure 2

Thus, a series of imidazo[1,2-*c*]quinazoline (**5a**), imidazo[1,2-*c*]thiazolo[5,4-*e*]pyrimidine (**5b**), (benzo)furo[3,2-*e*]imidazo[1,2-*c*]pyrimidine (**5c,5d**), benzothieno[3,2-*e*]imidazo[1,2-*c*]pyrimidine (**5e,5f**), imidazo[1,2-*c*]pyrido[4',3':4,5]thieno[3,2-*e*]pyrimidine (**3g,3h**), imidazo[1,2-*c*](thio)pyrano[4',3':4,5]-thieno[3,2-*e*]pyrimidine (**5i,5j**), and cyclo(hepta or penta)[4,5]thieno[3,2-*e*]imidazo[1,2-*c*]pyrimidine (**5k,5l**) were easily accessible from 2-amino nitriles (**3a-l**) and ethyl 2-[N-(methylthiothiocarbonyl)amino]acetate (**1**) in DMF by a one-step reaction (Figure 3).

Annellation to such type of angular tri- and tetracyclic compounds (**5a-l**) was also established by Sauter^{15,17} and Chowdhury^{9,10,18} from 2-amino nitriles with *N*-[bis(methylthio)methylene]amino (BMMA) reagents. The structural assignment of compounds (**5a-l**) was based on the NMR spectral and elemental analytical data. Displacement reactions have been employed to create the middle ring of tricyclic or tetracyclic systems in one-step as described above. So, the concept of creating our desired tricyclic and

tetracyclic condensed systems in one-step *via* a double displacement process using **1** is demonstrated smoothly.

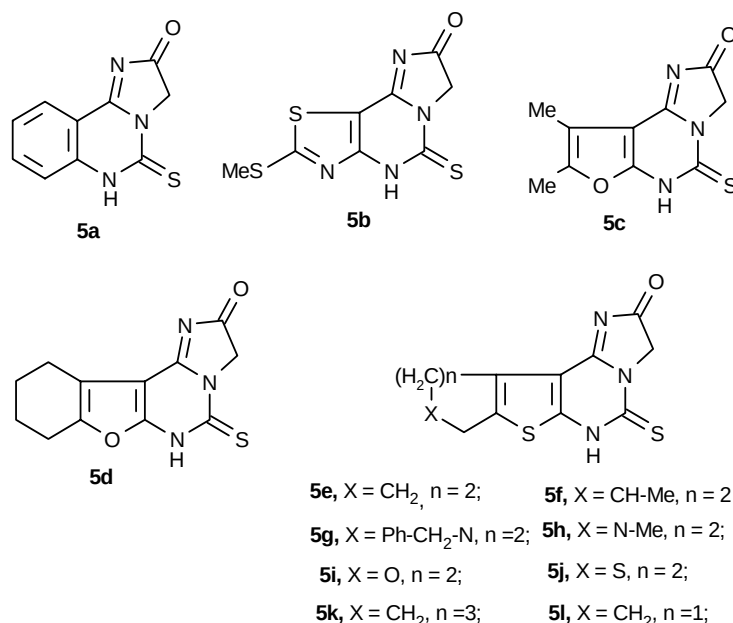


Figure 3

EXPERIMENTAL

Melting points were determined on a Yanaco hot stage apparatus and are uncorrected. ¹H and ¹³C NMR spectra were recorded on a JNM-ALPHA 500 (500 MHz) spectrometer (internal standard TMS, solvents CDCl₃ or DMSO-*d*₆ respectively, δ-values in ppm) at the National Institute for Environmental Studies, Tsukuba, Japan. Elemental analyses were performed on an EA 1108 (Fisons Instruments) Elemental Analyzer.

Ethyl 2-[*N*-(methylthiothiocarbonyl)amino]acetate (**1**) was prepared from ethyl glycinate using the method reported.^{10,15} Ethyl 2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**2d**) and -3-carbonitrile (**3e**), ethyl 2-amino-4,5,6,7-tetrahydro-6-methylbenzo[*b*]thiophene-3-carboxylate (**2e**) and -3-carbonitrile (**3f**), ethyl 2-amino-6-benzyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate (**2f**) and -3-carbonitrile (**3g**), ethyl 2-amino-4,5,6,7-tetrahydro-6-methylthieno[2,3-*c*]pyridine-3-carboxylate (**2g**) and -3-carbonitrile (**3h**), ethyl 2-amino-4,7-dihydro-5*H*-thieno[2,3-*c*]pyran-3-carboxylate (**2h**) and -3-carbonitrile (**3i**), ethyl 2-amino-4,7-dihydro-5*H*-thieno[2,3-*c*]thiopyran-3-carboxylate (**2i**) -3-carbonitrile (**3j**), ethyl 2-amino-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophene-3-carboxylate (**2j**) and -3-carbonitrile (**3k**), and ethyl 2-amino-5,6-dihydro-4*H*-cyclopenta[*b*]thiophene-3-carboxylate (**2k**) and -3-carbonitrile (**3j**) were obtained according to the literature procedures,¹⁹⁻²¹ respectively. 4-Amino-2-methylthiothiazole-5-carbonitrile (**3b**),²² 2-amino-4,5-dimethylfuran-3-carbonitrile (**3c**)²³ and 2-amino-

4,5,6,7-tetrahydrobenzofuran-3-carbonitrile (**3d**)¹⁰ were prepared according to the procedures in the literatures. Anthranilonitrile (**3a**), ethyl anthranilate (**2b**), methyl 2-amino-1-cyclohexene-1-carboxylate (**2a**) and methyl 4-amino-1-benzyl-1,2,5,6-tetrahydropyridine-3-carboxylate (**2c**) were purchased from Kanto Chemicals.

General Procedure for Cyclization Reactions: Synthesis of Compounds (4a-k and 5a-l). A solution of appropriate 2-amino ester or 2-amino nitrile (10 mmol) and 2-[N-(methylthiothiocarbonyl)-amino]acetate (**1**) (10 mmol) in 6 mL of DMF was refluxed for 8-10 h. The reaction mixture was cooled and poured onto the crushed ice. The resulting solids were collected by filtration and recrystallized from an appropriate solvent.

Ethyl 2-(1,2,3,4,5,6,7,8-octahydro-4-oxo-2-thioxoquinazolin-3-yl)acetate (4a): Prepared from **2a** as white crystals (ethanol), yield 52%, mp 187-189 °C. ¹H NMR (CDCl₃): δ 1.21 (t, *J* = 7.1 Hz, 3H, Me), 1.70 (m, 4H, 6-H and 7-H), 2.30 (t, *J* = 7.6 Hz, 4H, 5-H and 8-H), 4.18 (q, *J* = 7.1 Hz, 2H, OCH₂), 4.59 (s, 2H, CH₂), 10.35 (s, 1H, NH). ¹³C NMR (DMSO-*d*₆): δ 13.96 (q, Me), 20.98 (t, C-6), 21.04 (t, C-7), 21.45 (t, C-5), 26.07 (t, C-8), 41.25 (t, CH₂), 61.51 (t, OCH₂), 109.76 (s, C-4a), 147.52 (s, C-8a), 154.55 (s, C=O), 167.23 (s, C=O), 170.79 (s, C=S). *Anal.* Calcd for C₁₂H₁₆N₂O₃S: C, 53.72; H, 6.01; N, 10.44. Found: C, 53.81; H, 5.94; N, 10.35.

Ethyl 2-(1,2,3,4-tetrahydro-4-oxo-2-thioxoquinazolin-3-yl)acetate (4b): Prepared from **2b** as colorless crystals (ethanol), yield 47%, mp 223-225 °C. ¹H NMR (CDCl₃): δ 1.28 (t, *J* = 7.1 Hz, 3H, Me), 4.25 (q, *J* = 7.1 Hz, 2H, OCH₂), 5.15 (s, 2H, CH₂), 8.20 (m, 1H, 8-H), 7.30-7.85 (m, 3H, 5-H, 6-H and 7-H), 8.20 (m, 1H, 8-H), 10.30 (s, 1H, NH). ¹³C NMR (CDCl₃ CDCl₃): δ 14.52 (q, Me), 45.32 (t, CH₂), 61.64 (t, OCH₂), 118.68 (s, C-4a), 125.55 (d, C-6), 125.98 (d, C-7), 126.81 (d, C-5), 134.45 (d, C-8), 147.85 (s, C-8a), 156.24 (s, C=O), 167.25 (s, C=O), 173.13 (s, C=S). *Anal.* Calcd for C₁₂H₁₂N₂O₃S: C, 54.53; H, 4.57; N, 10.59. Found: C, 54.38; H, 4.61; N, 10.47.

Ethyl 2-(6-benzyl-1,2,3,4,5,6,7,8-octahydro-4-oxo-2-thioxopyrido[4,3-*d*]pyrimidin-3-yl)acetate (4c): Prepared from **2c** as brown crystals (ethanol), yield 45%, mp 188-190 °C. ¹H NMR (CDCl₃): δ 1.20 (t, *J* = 7.1 Hz, 3H, Me), 2.46 (t, *J* = 5.2 Hz, 2H, 8-H), 2.60 (t, *J* = 5.5 Hz, 2H, 7-H), 3.28 (s, 2H, 5-H), 3.60 (s, 2H, Ph-CH₂), 4.15 (q, *J* = 7.1 Hz, 2H, OCH₂), 5.11 (s, 2H, CH₂), 7.20-7.38 (m, 5H, Ar-H), 11.05 (s, 1H, NH). ¹³C NMR (CDCl₃): δ 14.05 (q, Me), 26.45 (t, C-8), 47.08 (t, C-7), 47.78 (t, C-5), 48.51 (t, CH₂), 61.65 (t, Ph-CH₂), 61.88 (t, OCH₂), 110.85 (s, C-4a), 127.24 (d, C-4'), 128.95 (d, C-3' and C-5'), 129.69

(d, C-2' and C-6'), 137.25 (s, C-1'), 146.50 (s, C-8a), 159.23 (s, C=O), 167.12 (s, C=O), 175.50 (s, C=S). *Anal.* Calcd for C₁₈H₂₁N₃O₃S: C, 60.14; H, 5.88; N, 11.69. Found: C, 59.99; H, 5.94; N, 11.75.

Ethyl 2-(1,2,3,4,5,6,7,8-octahydro-4-oxo-2-thioxo[1]benzothieno[2,3-*d*]pyrimidin-3-yl)acetate (4d): Prepared from **2d** as yellow crystals (ethanol), yield 55%, mp 220-222 °C. ¹H NMR (CDCl₃): δ 1.31 (t, *J* = 7.1 Hz, 3H, Me), 1.85 (m, 4H, 6-H and 7-H), 2.65 (m, 2H, 5-H), 2.84 (m, 2H, 8-H), 4.24 (q, *J* = 7.1 Hz, 2H, OCH₂), 5.22 (s, 2H, CH₂), 11.35 (s, 1H, NH). ¹³C NMR (CDCl₃): δ 13.75 (q, Me), 21.42 (t, C-6), 22.36 (t, C-7), 23.98 (t, C-5), 24.61 (t, C-8), 46.31 (t, CH₂), 60.72 (t, OCH₂), 115.37 (s, C-4b), 128.35 (s, C-4a), 131.12 (s, C-8a), 148.92 (s, C-9a), 156.41 (s, C=O), 167.12 (s, C=O), 173.60 (s, C=S). *Anal.* Calcd for C₁₄H₁₆N₂O₃S₂: C, 51.83; H, 4.97; N, 8.63. Found: C, 51.92; H, 4.99; N, 8.52.

Ethyl 2-(1,2,3,4,5,6,7,8-octahydro-7-methyl-4-oxo-2-thioxo[1]benzothieno[2,3-*d*]pyrimidin-3-yl)acetate (4e): Prepared from **2e** as white crystals (ethanol), yield 47%, mp 225-227 °C. ¹H NMR (CDCl₃): δ 1.05 (d, *J* = 6.4 Hz, 1H, 7-Me), 1.33 (t, *J* = 7.1 Hz, 3H, Me), 1.82-3.04 (m, 7H, 5-H, 6-H, 7-H and 8-H), 4.26 (q, *J* = 7.1 Hz, 2H, OCH₂), 5.23 (s, 2H, CH₂), 10.75 (s, 1H, NH). ¹³C NMR (CDCl₃): δ 13.65 (q, Me), 20.80 (t, 7-Me), 24.21 (t, C-6), 28.65 (d, C-7), 29.51 (t, C-5), 31.85 (t, C-8), 46.22 (t, CH₂), 60.65 (t, OCH₂), 115.16 (s, C-4b), 127.88 (s, C-4a), 130.71 (s, C-8a), 148.95 (s, C-9a), 156.09 (s, C=O), 166.92 (s, C=O), 173.55 (s, C=S). *Anal.* Calcd for C₁₅H₁₈N₂O₃S₂: C, 53.23; H, 5.36; N, 8.28. Found: C, 53.35; H, 5.28; N, 8.16.

Ethyl 2-(7-benzyl-1,2,3,4,5,6,7,8-octahydro-4-oxo-2-thioxopyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-3-yl)acetate (4f): Prepared from **2f** as red crystals (ethanol), yield 46%, mp 124-126 °C. ¹H NMR (CDCl₃): δ 1.15 (t, *J* = 7.1 Hz, 3H, Me), 2.90 (t, *J* = 5.2 Hz, 2H, 5-H), 3.33 (t, *J* = 5.5 Hz, 2H, 6-H), 3.76 (s, 2H, 8-H), 3.89 (s, 2H, CH₂-Ph), 4.20 (q, *J* = 7.1 Hz, 2H, OCH₂), 5.10 (s, 2H, CH₂), 7.29-7.54 (m, 5H, Ar-H). ¹³C NMR (DMSO-*d*₆): δ 14.01 (q, Me), 24.54 (t, C-5), 46.58 (t, C-6), 48.61 (t, C-8), 50.17 (t, CH₂), 60.24 (t, CH₂-Ph), 60.65 (t, OCH₂), 114.64 (s, C-4b), 125.27 (s, C-1'), 127.40 (d, C-4'), 128.35 (d, C-2' and C-6'), 129.15 (d, C-3' and C-5'), 129.27 (s, C-4a), 136.50 (s, C-8a), 150.67 (s, C-9a), 156.23 (s, C=O), 167.45 (s, C=O), 173.89 (s, C=S). *Anal.* Calcd for C₂₀H₂₁N₃O₃S₂: C, 57.81; H, 5.09; N, 10.11. Found: C, 57.65; H, 5.01; N, 9.85.

Ethyl 2-(1,2,3,4,5,6,7,8-octahydro-7-methyl-4-oxo-2-thioxopyrido[4',3':4,5]thieno[2,3-*d*]pyrimidin-3-yl)acetate (4g): Prepared from **2g** as brown crystals (ethanol), yield 40 %; mp 172-174 °C. ¹H NMR (DMSO-*d*₆): δ 1.22 (t, *J* = 7.1 Hz, 3H, Me), 2.60 (s, 3H, N-Me), 3.25 (m, 4H, 5-H and 6-H), 3.92 (s, 2H,

8-H), 4.10 (q, $J = 7.1$ Hz, 2H, OCH₂), 5.15 (s, 2H, CH₂). ¹³C NMR (DMSO-*d*₆): δ 14.05 (q, Me), 23.65 (t, C-6), 42.91 (q, N-Me), 48.47 (t, C-5), 50.37 (t, C-8), 51.21 (t, CH₂), 60.65 (t, OCH₂), 113.48 (s, C-4b), 120.21 (s, C-4a), 128.01 (s, C-8a), 157.41 (s, C-9a), 157.98 (s, C=O), 167.64 (s, C=O), 175.19 (s, C=S). *Anal.* Calcd for C₂₀H₂₁N₃O₃S₂: C, 57.81; H, 5.09; N, 10.11. Found: C, 57.96; H, 5.15; N, 9.86.

Ethyl 2-(1,3,4,5,6,8-hexahydro-4-oxo-2-thioxo-2H-pyrano[4',3':4,5]thieno[2,3-*d*]pyrimidin-3-yl)acetate (4h): Prepared from **2h** as yellow crystals (ethanol), yield 45%, mp 226-227 °C. ¹H NMR (DMSO-*d*₆): δ 1.29 (t, $J = 7.1$ Hz, 3H, Me), 2.81 (t, $J = 5.2$ Hz, 2H, 5-H), 3.89 (t, $J = 5.5$ Hz, 2H, 6-H), 4.25 (q, $J = 7.1$ Hz, 2H, OCH₂), 4.65 (s, 2H, CH₂), 4.68 (s, 2H, 8-H), 8.67 (s, 1H, NH). ¹³C NMR (DMSO-*d*₆): δ 14.18 (q, Me), 26.99 (t, C-5), 46.18 (t, CH₂), 60.99 (t, OCH₂), 64.67 (t, C-6), 64.94 (t, C-8), 112.45 (s, C-4b), 128.62 (s, C-4a), 136.56 (s, C-8a), 150.42 (s, C-9a), 156.45 (s, C=O), 166.84 (s, C=O), 170.77 (s, C=S). *Anal.* Calcd for C₁₃H₁₄N₂O₄S₂: C, 47.83; H, 4.32; N, 8.58. Found: C, 47.75; H, 4.40; N, 8.47.

Ethyl 2-(1,3,4,5,6,8-hexahydro-4-oxo-2-thioxo-2H-thiopyrano[4',3':4,5]thieno[2,3-*d*]pyrimidin-3-yl)acetate (4i): Prepared from **2i** as yellow needles (ethanol), yield 49%, mp 215-218 °C. ¹H NMR (CDCl₃): δ 1.26 (t, $J = 7.1$ Hz, 3H, Me), 2.84 (t, $J = 6.1$ Hz, 2H, 6-H), 2.99 (t, $J = 5.6$ Hz, 2H, 5-H), 4.25 (q, $J = 7.1$ Hz, 2H, OCH₂), 4.48 (s, 2H, CH₂), 3.70 (s, 2H, 8-H), 9.85 (s, 1H, NH). ¹³C-NMR (DMSO-*d*₆): δ 14.05 (q, Me), 25.09 (t, C-6), 25.86 (t, C-5), 26.90 (t, C-8), 46.15 (t, CH₂), 60.65 (t, OCH₂), 111.05 (s, C-4b), 125.29 (s, C-4a), 132.21 (s, C-8a), 140.14 (s, C-9a), 156.15 (s, C=O), 166.25 (s, C=O), 170.27 (s, C=S). *Anal.* Calcd for C₁₃H₁₄N₂O₃S₃: C, 45.59; H, 4.12; N, 8.18. Found: C, 45.71; H, 4.18; N, 8.25.

Ethyl 2-(1,3,4,5,6,7,8,9-octahydro-4-oxo-2-thioxo-2H-cyclohepta[4,5]thieno[2,3-*d*]pyrimidin-3-yl)acetate (4j): Prepared from **2j** as white crystals (ethanol), yield 48%, mp 202-204 °C. ¹H NMR (CDCl₃): δ 1.25 (t, $J = 7.1$ Hz, 3H, Me), 1.68 (m, 4H, 6-H and 7-H), 1.95 (m, 2H, 8-H), 2.75 (m, 2H, 5-H), 3.21 (m, 2H, 9-H), 4.20 (q, $J = 7.1$ Hz, 2H, OCH₂), 5.20 (s, 2H, CH₂), 10.25 (s, 1H, NH). ¹³C NMR (CDCl₃): δ 14.05 (q, Me), 26.75 (t, C-7), 27.08 (t, C-6), 27.45 (t, C-8), 29.35 (t, C-5), 32.14 (t, C-9), 47.15 (t, CH₂), 61.66 (t, OCH₂), 117.12 (s, C-4b), 132.97 (s, C-4a), 137.50 (s, C-9a), 146.76 (s, C-10a), 156.69 (s, C=O), 167.74 (s, C=O), 173.59 (s, C=S). *Anal.* Calcd for C₁₅H₁₈N₂O₃S₂: C, 53.23; H, 5.36; N, 8.28. Found: C, 53.11; H, 5.40; N, 8.12.

Ethyl 2-(1,3,4,5,6,7-hexahydro-4-oxo-2-thioxo-2H-cyclopenta[4,5]thieno[2,3-*d*]pyrimidin-3-yl)acetate (4k): Prepared from **2k** as yellow crystals (ethanol), yield 44%, mp 218-220 °C. ¹H NMR (CDCl₃): δ 1.25 (t, $J = 7.1$ Hz, 3H, Me), 2.43 (m, 2H, 6-H), 2.85 (m, 4H, 5-H and 7-H), 4.14 (q, $J = 7.1$ Hz, 2H,

OCH₂), 5.20 (s, 2H, CH₂), 10.21 (s, 1H, NH). ¹³C NMR (CDCl₃): δ 13.74 (q, Me), 27.60 (t, C-6), 27.95 (t, C-5), 28.34 (t, C-7), 46.31 (t, CH₂), 60.68 (t, OCH₂), 112.45 (s, C-4b), 133.61 (s, C-4a), 140.15 (s, C-7a), 153.38 (s, C-8a), 155.94 (s, C=O), 166.87 (s, C=O), 173.81 (s, C=S). *Anal.* Calcd for C₁₄H₁₆N₂O₃S₂: C, 51.83; H, 4.97; N, 8.63. Found: C, 51.85; H, 4.92; N, 8.80.

5,6-Dihydro-5-thioxoimidazo[1,2-c]quinazolin-2(3H)-one (5a): Prepared from **3a** as brown crystals (ethanol), yield 41%, mp >320 °C. ¹H NMR (DMSO-*d*₆): δ 4.59 (s, 2H, 3-H), 7.55 (m, 2H, 8-H and 9-H), 7.76 (m, 1H, 10-H), 8.05 (m, 1H, 7-H), 10.65 (s, 1H, NH). ¹³C NMR (DMSO-*d*₆): δ 53.45 (t, C-3), 110.81 (t, C-9), 116.05 (d, C-8), 125.11 (d, C-10), 127.35 (d, C-7), 136.94 (s, C-10a), 139.56 (s, C-7a), 168.02 (s, C-10b), 168.18 (s, C=S), 184.65 (s, C=O). *Anal.* Calcd for C₁₀H₇N₃OS: C, 55.29; H, 3.25; N, 19.34. Found: C, 55.19; H, 3.09; N, 19.08.

4,5-Dihydro-2-methylthio-5-thioxoimidazo[1,2-c]thiazolo[5,4-*e*]pyrimidin-8(7H)-one (5b): Prepared from **3b** as red crystals (ethanol), yield: 39%, mp >320 °C. ¹H NMR (DMSO-*d*₆): δ 4.42 (s, 2H, 7-H), 2.70 (s, 3H, Me), 10.20 (s, 1H, NH). *Anal.* Calcd. for C₈H₆N₄OS₃: C, 35.54; H, 2.24; N, 20.70. Found: C, 35.65; H, 2.45; N, 20.91.

5,6-Dihydro-8,9-dimethyl-5-thioxofuro[3,2-*e*]imidazo[1,2-*c*]pyrimidin-2(3H)-one (5c): Prepared from **3c** as red crystals (ethanol), yield 40%, mp 210-212 °C. ¹H NMR (DMSO-*d*₆): δ 2.16 (s, 3H, 9-Me), 2.28 (s, 3H, 8-Me), 4.35 (s, 2H, 3-H), 10.42 (s, 1H, NH). ¹³C NMR (DMSO-*d*₆): δ 14.15 (q, 9-Me), 14.45 (q, 8-Me), 53.32 (t, C-3), 95.48 (s, C-9), 107.55 (s, C-9a), 124.28 (s, C-8), 148.65 (s, C-9b), 166.17 (s, C=S), 170.35 (s, C-6a), 172.85 (s, C=O). *Anal.* Calcd for C₁₀H₉N₃O₂S: C, 51.05; H, 3.85; N, 17.86. Found: C, 50.91; H, 3.93; N, 17.95.

5,6,8,9,10,11-Hexahydro-5-thioxobenzofuro[3,2-*e*]imidazo[1,2-*c*]pyrimidin-2(3H)-one (5d): Prepared from **3d** as red crystals (ethanol), yield 42 %, mp 276-278 °C. ¹H NMR (DMSO-*d*₆): δ 1.65-1.90 (m, 4H, 9-H and 10-H), 2.43-2.70 (m, 4H, 8-H and 11-H), 4.60 (s, 2H, 3-H). ¹³C NMR (DMSO-*d*₆): δ 20.51 (t, C-10), 21.65 (t, C-11 and C-9), 22.18 (t, C-8), 53.49 (t, C-3), 94.26 (s, C-11a), 110.28 (s, C-11b), 149.65 (s, C-7a), 151.19 (s, C-11c), 166.48 (s, C=S), 170.01 (s, C-6a), 172.24 (s, C=O). *Anal.* Calcd for C₁₂H₁₁N₃O₂S: C, 55.16; H, 4.24; N, 16.08. Found: C, 55.30; H, 4.42; N, 16.19.

5,6,8,9,10,11-Hexahydro-5-thioxo[1]benzothieno[3,2-*e*]imidazo[1,2-*c*]pyrimidin-2(3*H*)-one (5e):

Prepared from **3e** as brown crystals (ethanol-DMF), 46%, mp >320 °C. ¹H NMR (DMSO-*d*₆): δ 1.85 (m, 4H, 9-H and 10-H), 2.55-2.80 (m, 4H, 8-H and 11-H), 4.35 (s, 2H, 3-H). ¹³C NMR (DMSO-*d*₆): δ 21.10 (t, C-10), 22.12 (t, C-9), 24.00 (t, C-11), 24.40 (t, C-8), 51.97 (t, C-3), 111.05 (s, C-11a), 129.52 (s, C-11b), 130.35 (s, C-7a), 153.85 (s, C-6a), 162.41 (s, C-11c), 166.51 (s, C=S), 182.11 (s, C=O). *Anal.* Calcd for C₁₂H₁₁N₃OS₂: C, 51.96; H, 4.00; N, 15.15. Found: C, 52.21; H, 3.95; N, 14.91.

5,6,8,9,10,11-Hexahydro-9-Methyl-5-thioxo[1]benzothieno[3,2-*e*]imidazo[1,2-*c*]pyrimidin-2(3*H*)-one (5f):

Prepared from **3f** as yellow crystals (ethanol), yield 39%, mp 299-301 °C. ¹H NMR (DMSO-*d*₆): δ 1.15 (d, *J* = 6.4 Hz, 3H, 9-Me), 1.82-2.95 (m, 7H, 8-H, 9-H, 10-H and 11-H), 4.45 (s, 2H, 3-H). *Anal.* Calcd for C₁₃H₁₃N₃OS₂: C, 55.59; H, 4.50; N, 14.42. Found: C, 55.71; H, 4.39; N, 14.56.

9-Benzyl-5,6,8,9,10,11-octahydro-2-oxo-5-thioxoimidazo[1,2-*c*]pyrido[4',3:4,5]thieno[3,2-*e*]pyrimidin-2(3*H*)-one (5g):

Prepared from **3g** as red crystals (ethanol-chloroform), yield 44%, mp 250-252 °C. ¹H NMR (CDCl₃): δ 3.30-3.38 (m, 4H, 10-H and 11-H), 4.02 (s, 2H, 8-H), 4.13 (s, 2H, CH₂-Ph), 4.25 (s, 2H, 3-H), 7.30-7.55 (m, 5H, Ar-H). ¹³C NMR (DMSO-*d*₆): δ 23.59 (t, C-11), 48.65 (t, C-10), 49.68 (t, C-8), 53.25 (t, C-3), 59.45 (t, CH₂-Ph), 109.31 (s, C-11a), 122.65 (s, C-1'), 126.92 (d, C-4'), 128.51 (d, C-2' and C-6'), 128.57 (d, C-3' and C-5') 130.12 (s, C-11b), 136.56 (s, C-8a), 133.16 (s, C-7a), 162.47 (s, C-6a), 163.38 (s, C-11c), 169.45 (s, C=S), 182.64 (s, C=O). *Anal.* Calcd for C₁₈H₁₆N₄OS₂: C, 58.67; H, 4.38; N, 15.20. Found: C, 58.45; H, 4.49; N, 15.03.

5,6,8,9,10,11-Hexahydro-9-methyl-5-thioxoimidazo[1,2-*c*]pyrido[4',3:4,5]thieno[3,2-*e*]pyrimidin-2(3*H*)-one (5h):

Prepared from **3h** as red crystals (dimethyl sulfoxide), yield 36%, mp 270-272 °C. ¹H NMR (CDCl₃): δ 2.95 (s, 3H, N-Me), 3.12 (m, 2H, 11-H), 3.54 (m, 2H, 10-H), 4.15 (s, 2H, 8-H), 4.30 (s, 2H, 3-H). *Anal.* Calcd for C₁₂H₁₂N₄OS₂: C, 49.30; H, 4.14; N, 19.16. Found: C, 49.01; H, 4.32; N, 18.99.

6,8,10,11-Tetrahydro-5-thioxo-5*H*-imidazo[1,2-*c*]pyrano[4',3':4,5]thieno[3,2-*e*]pyrimidin-2(3*H*)-one (5i):

Prepared from **3i** as red crystals (ethanol), yield 40%, mp 270 °C (decomp). ¹H NMR (DMSO-*d*₆): δ 2.82 (t, *J* = 4.8 Hz, 2H, 11-H), 3.95 (t, *J* = 5.1 Hz, 2H, 10-H), 4.40 (s, 2H, 3-H), 4.69 (s, 2H, 8-H). ¹³C NMR (DMSO-*d*₆): δ_C 25.37 (t, C-11), 52.61 (t, C-3), 63.59 (t, C-10), 64.39 (t, C-8), 111.51 (s, C-11a), 126.91 (s, C-11b), 128.24 (s, C-7a), 159.14 (s, C-6a), 161.83 (s, C-11c), 167.48 (s, C=S), 181.55 (s, C=O). *Anal.* Calcd for C₁₁H₉N₃O₂S₂: C, 47.29; H, 3.24; N, 15.04. Found: C, 47.40; H, 3.31; N, 15.19.

6,8,10,11-Tetrahydro-5-thioxo-5H-imidazo[1,2-c]thiopyrano[4',3':4,5]thieno[3,2-e]pyrimidin-2(3H)-one (5j): Prepared from **3j** as red crystals (ethanol), yield 43%, mp >320 °C. ¹H NMR (DMSO-*d*₆): δ 2.80-3.15 (m, 4H, 10-H and 11-H), 3.90 (s, 2H, 8-H), 4.35 (s, 2H, 3-H). ¹³C NMR (DMSO-*d*₆): δ 24.11 (t, C-10), 24.30 (t, C-11), 26.83 (t, C-8), 52.41 (t, C-3), 111.25 (s, C-11a), 126.88 (s, C-11b), 129.23 (s, C-7a), 161.51 (s, C-6a), 162.40 (s, C-11c), 166.86 (s, C=S), 182.49 (s, C=O). *Anal.* Calcd for C₁₁H₉N₃OS₃: C, 44.73; H, 3.07; N, 14.22. Found: C, 44.91; H, 3.18; N, 14.05.

6,8,9,10,11,12-Hexahydro-5-thioxo-5H-cyclohepta[4,5]thieno[3,2-e]imidazo[1,2-c]pyrimidin-2(3H)-one (5k): Prepared from **3e** as red crystals (ethanol-chloroform), yield 39%, mp >320 °C. ¹H NMR (DMSO-*d*₆): δ 1.50-1.90 (m, 6H, 9-H, 10-H and 11-H), 2.85 (m, 2H, 12-H), 3.32 (m, 2H, 8-H), 4.30 (s, 2H, 3-H). *Anal.* Calcd for C₁₃H₁₃N₃OS₂: C, 55.59; H, 4.50; N, 14.42. Found: C, 55.43; H, 4.36; N, 14.27.

6,8,9,10-Tetrahydro-5-thioxo-5H-cyclopenta[4,5]thieno[3,2-e]imidazo[1,2-c]pyrimidin-2(3H)-one (5l): Prepared from **3l** as red crystals (ethanol-chloroform), yield 38%, mp >320 °C. ¹H NMR (DMSO-*d*₆): δ 2.80-3.65 (m, 6H, 8-H, 9-H and 10-H), 4.55 (s, 2H, 3-H). *Anal.* Calcd for C₁₁H₉N₃OS₂: C, 50.17; H, 3.44; N, 15.96. Found: C, 50.35; H, 3.37; N, 15.85.

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