Fusions of Pyrido[4',3':4,5]thieno[2,3-*d*]pyrimidines with *N*-Heterocyclic Moieties

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Versatile 2-thioxopyrimidine-type building blocks ethyl 3-(2-ethoxy-2-oxoethyl)-4-oxo-2-thioxo-1,2,3,4,5,6,7,8-octahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidine-7-carboxylate (**4**) and ethyl 4-oxo-2-thioxo-1,2,3,4,5,6,7,8-octahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidine-7-carboxylate (**8**) were synthesized from diethyl 2-amino-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3,6-dicarboxylate (**1**). Derivatives of linear and angular heterocyclic systems having the imidazole and 1,2,4-triazole ring were obtained from the key intermediates **4** and **8**, respectively.

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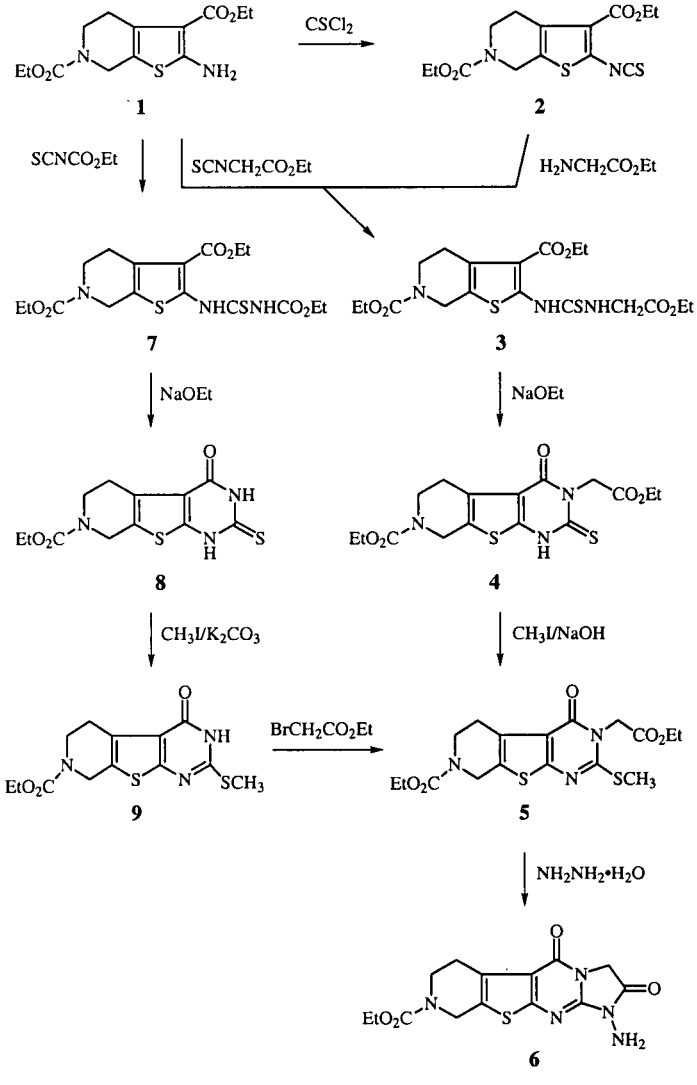
During the past few years, we have been interested in the synthesis of substituted heterocycles containing a thienopyrimidine system [1-5]. The present paper follows that line of research by reporting on a new series of linear and angular fusion reactions of pyrido[4',3':4,5]thieno[2,3-*d*]pyrimidine derivatives, in which imidazole and 1,2,4-triazole moieties were annelated, yielding novel tetracyclic ring systems. In this paper, we report the preparations and structural confirmations of the pyrido[4',3':4,5]thieno[2,3-*d*]pyrimidine derivatives **4** and **8**, of the imidazo[1,2-*a*]pyrido[4',3':4,5]-thieno[2,3-*d*]pyrimidine derivative **6** and of the pyrido[4',3':4,5]thieno[3,2-*e*][1,2,4]triazolo[4,3-*a*]-pyrimidine derivatives **11-13**.

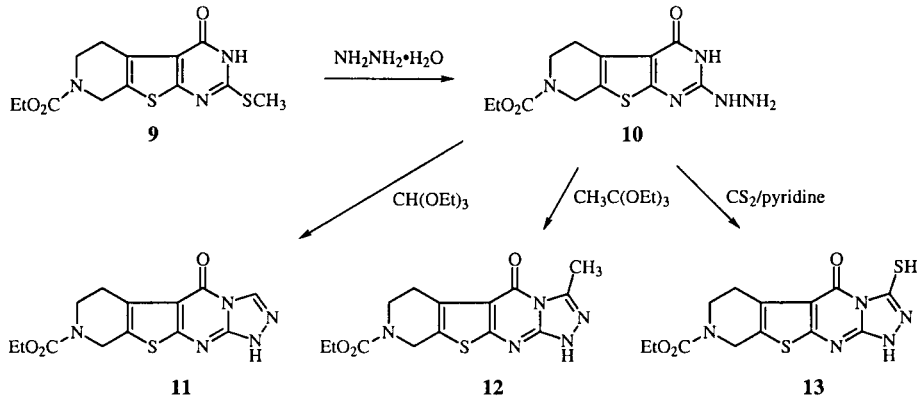
Diethyl 2-amino-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3,6-dicarboxylate (**1**) [6] was converted into ethyl 3-(2-ethoxy-2-oxoethyl)-2-(methylsulfanyl)-4-oxo-3,4,5,6,7,8-hexahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidine-7-carboxylate (**5**). As depicted in Scheme 1, the key intermediate **5** can be obtained by one of the following two sequences: 1) preparation of the thioxopyrimidone **8** by reaction of **1** with ethoxycarbonyl isothiocyanate [7] and the ensuing cyclization), followed by *S*-methylation with iodomethane to give **9**, and *N*-substitution, or, 2) preparation of intermediate **3** either from **1** and ethyl thiocyanatoacetate or, with a better yield, from isothiocyanate **2** and glycine ethyl ester hydrochloride, followed by cylization to give **4** and subsequent methylation. On reaction with hydrazine hydrate, the methylthioester **5** yielded the target *N*-aminolactam **6** (Scheme 1).

Scheme 1



Treating the *S*-methylated pyridothienopyrimidine **9** with hydrazine hydrate afforded the 2-hydrazino-substituted pyridothienopyrimidine **10**. Compound **10** was proved to be a versatile starting material for the synthesis of the new pyrido[4',3':4,5]thieno[3,2-*e*][1,2,4]triazolo[4,3-*a*]-pyrimidine derivatives **11**, **12** and **13**. Upon treatment with triethyl orthoformate, **10** yielded the triazolo compound namely ethyl 5-oxo-4,5,6,7,8,9-hexahydropyrido[4',3':4,5]-thieno[3,2-*e*][1,2,4]triazolo[4,3-*a*]pyrimidine-8-carboxylate (**11**). In the same manner, **10** treated with triethyl orthoacetate afforded the corresponding methylsubstituted triazole **12**. Another new triazolo derivative **13** was synthesized from the hydrazino compound **10** by reaction with carbon disulfide in pyridine (Scheme 2).

Scheme 2



EXPERIMENTAL

Melting points were determined on a Boetius melting point apparatus and are uncorrected. Elemental analyses were performed on a Carlo Erba CHN-S Elemental Analyzer 1108. The ^{13}C and ^{1}H nmr spectra were obtained using a Bruker AC 300 (^{1}H: 300.13 MHz, ^{13}C: 75.5 MHz). The solvents were deuterated dimethyl sulfoxide and chloroform, respectively. The δ-values are given in ppm and the internal standard was tetramethylsilane. Mass spectra were recorded on a Finnigan MAT 95-A spectrometer. The ir-spectra were recorded on a Nicolet 250 FT-IR spectrophotometer as potassium bromide pellets).

Diethyl 2-Isothiocyanato-4,5,6,7-tetrahydrothieno[2,3-*c*]-pyridine-3,6-dicarboxylate (**2**).

A suspension of **1** (0.58 g, 0.002 mole) in dichloromethane (5 ml) was added to a stirred suspension of calcium carbonate (1.8 g, 0.018 mole) in water (10 ml) and dichloromethane (20 ml) at room temperature. To the stirred mixture, thiophosgene (0.24 g, 0.002 mole) was added slowly in an ice bath. The temperature of the reaction mixture was allowed to reach room temperature. Stirring was continued for 6 hours. Inorganic salts were removed by filtration and the organic phase was washed with water and 5% aqueous sodium bicarbonate. After drying over magnesium sulfate, the dichloromethane was removed under reduced pressure and the residue was purified by column chromatography (silica gel, chloroform/acetone 20:1) as yellow crystals, mp 102-103°, 0.35 g (60%); ir: ν cm^{-1} 1707, 1770, 2150, 3070. ^{1}H nmr (deuteriochloroform): 1.30 (t, 3H, -$COOCH_2CH_3$), 1.45 (t, 3H, -$COOCH_2CH_3$), 2.90 (t, 2H, H-4), 3.60 (t, 2H, H-5), 4.20 (q, 2H, -$COOCH_2CH_3$), 4.40 (q, 2H, -$COOCH_2CH_3$), 4.60 (s, 2H, H-7); ms: m/z 340 (M^+).

Anal. Calcd. for $C_{14}H_{16}N_2O_4S_2$: C, 49.39; H, 4.73; N, 8.22; S, 18.83. Found: C, 49.30; H, 4.60, N, 8.18; S, 18.95.

Diethyl 2-({[(2-Ethoxy-2-oxoethyl)amino]carbothioyl}amino)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3,6-dicarboxylate (**3**).

Method A.

Ethoxycarbonyl methylisothiocyanate (0.80 g, 0.0055 mole) was added to a stirred solution of compound **1** (1.49 g, 0.0049 mole) in absolute ethanol (10 ml). The mixture was heated under reflux for 3 hours. On cooling, the separated solid product was collected by filtration, dried and recrystallized from ethanol as colorless crystals, mp 159-160°, 1.05 g (70%); ir: ν cm^{-1} 1550, 1669, 1669, 1740, 2980, 2990, 3120, 3255, 3430, 3440; ^{1}H nmr (deuteriochloroform): 1.20 (m, 6H, 2-$COOCH_2CH_3$), 1.30 (t, 3H, -$COOCH_2CH_3$), 2.80 (t, 2H, H-4), 3.60 (t, 2H, H-5), 4.10-4.15 (m, 4H, 2-$COOCH_2CH_3$), 4.20-4.35 (m, 4H, $COOCH_2CH_3$, H-7), 4.48 (s, 2H, CH_2COOEt), 9.97 (s, 1H, NH), 11.62 (s, 1H, NH); ^{13}C nmr (deuteriochloroform): 14.1 (q, $COOCH_2CH_3$), 14.2 (q,-$COOCH_2CH_3$), 14.4 (q, $COOCH_2CH_3$), 26.4 (t, C-4), 41.2 (t, C-5), 42.6 (t, C-7), 46.2 (t, $NHCH_2$), 60.8 (t, $COOCH_2CH_3$), 61.6 (t, $COOCH_2CH_3$), 61.8 (t, $COOCH_2CH_3$), 111.2 (s, C-3), 122.0 (s, C-7a), 129.2 (s, C-3a), 152.1 (s, CO), 155.6 (s, CO), 166.8 (s, CO), 169.3 (s, C-2), 177.7 (s, CS); ms: m/z 433 (M^+).

Anal. Calcd. for $C_{18}H_{25}N_3O_6S_2$: C, 49.86; H, 5.81; N, 9.69; S, 14.75. Found: C, 49.14; H, 5.65; N, 9.21; S, 14.57.

Method B.

To a solution of isothiocyanate **2** (0.34 g, 0.001 mole) in absolute tetrahydrofuran (10 ml), a suspension of glycine ethyl ester hydrochloride in tetrahydrofuran (10 ml) and triethylamine (3 ml) was added with stirring. The solution was stirred at room temperature for 1 hour and then the solid was filtered, washed with water, dried and recrystallized from ethanol to give colorless crystals, mp 158-160°; 0.27 g (79%). This compound was spectroscopically equivalent with the material prepared by method A, and the melting point of the two mixed materials was undepressed.

Ethyl 3-(2-Ethoxy-2-oxoethyl)-4-oxo-2-thioxo-1,2,3,4,5,6,7,8-octahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidine-7-carboxylate (**4**).

Compound **3** (0.88 g, 0.002 mole) was dissolved in a solution of sodium ethoxide (from 0.05 g, 0.0022 mole, of sodium and 10 ml of absolute ethanol) and the solution was stirred at room temperature for 10 minutes. The sodium salt of compound **3** was collected, then dissolved in water and neutralized (to *p*H = 4) with hydrochloric acid. The product which separated was collected by filtration, washed with ethanol, dried and recrystallized from ethanol to give 0.66 g (75%) of **4** as white crystals, mp 266-267° dec; ir: ν cm^{-1} 1440, 1475, 1564, 1642, 1674, 1715, 1739, 2938, 2980, 3440; ^{1}H nmr (dimethyl-d_6 sulfoxide): 1.20 (m, 6H, 2-$COOCH_2CH_3$), 2.90 (t, 2H, H-5), 3.65 (t, 2H, H-6), 4.20 (m, 4H, 2 -$COOCH_2CH_3$), 4.40 (s, 2H, H-8) 5.30 (s, 2H, CH_2COOEt), 13.80 (s, 1H, NH); ^{13}C nmr: 13.9 (q, -$COOCH_2CH_3$), 14.3 (q, $COOCH_2CH_3$), 25.1 (t, C-5), 42.5 (t, C-6), 46.9 (t, C-8), 55.8 (t, NCH_2), 59.8 (t, $COOCH_2CH_3$), 60.7 (t, $COOCH_2CH_3$), 154.6 (s, C-8a), 158.9 (s, C-9a), 165.1 (s, C-4), 168.5 (s, C-2), 175.6 (s, CO), 179.7 (s, CO); ms: m/z 397 (M^+).

Anal. Calcd. for $C_{16}H_{19}N_3O_5S_2$: C, 48.35; H, 4.81; N, 10.57; S, 16.13. Found: C, 48.20; H, 4.62; N, 10.48; S, 16.10.

Ethyl 3-(2-Ethoxy-2-oxoethyl)-2-(methylsulfanyl)-4-oxo-3,4,5,6,7,8-hexahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidine-7-carboxylate (**5**).

Method A.

A solution of **4** (0.78 g, 0.002 mole) in 1 *M* aqueous sodium hydroxide (1.5 ml) was treated with methyl iodide (0.57 g, 0.004 mole) and the mixture was stirred at 25°. The methylthio compound **5** started to crystallize almost immediately. After 1 hour, it was filtered, washed with water, dried and crystallized from ethanol as colorless crystals, mp 132-133°, 0.63 g (81%); ir: ν cm^{-1} 1568, 1680, 1700, 1736, 1746, 2360, 2860, 2980, 3260, 3400, 3450; ^1H nmr: 1.2 (t, 3H, $CO_2CH_2CH_3$), 1.25 (t, 3H, $CO_2CH_2CH_3$), 2.60 (s, 3H, SCH_3), 2.90 (t, 2H, H-5), 3.70 (t, 2H, H-6), 4.20 (q, 2H, $CO_2CH_2CH_3$), 4.35 (q, 2H, $CO_2CH_2CH_3$), 4.60 (s, 2H, H-8), 4.85 (s, 2H, CH_2CO_2Et); ^{13}C nmr: 13.7 (q, SCH_3), 14.3 (q, -$COOCH_2CH_3$), 13.7 (q, -$COOCH_2CH_3$), 24.9 (t, C-5), 40.2 (t, C-6), 42.6 (t, C-8), 44.3 (t, NCH_2), 60.9 (t, $COOCH_2CH_3$), 61.3 (-$COOCH_2CH_3$), 116.7 (s, C-4a), 127.5 (s, C-4b), 129.0 (s, C-8a), 154.5 (s, C-2), 156.0 (s, C-9a), 158.0 (s, C-4), 162.0 (s, CO), 166.6 (s, CO), ms: m/z 411 (M^+).

Anal. Calcd. for $C_{17}H_{21}N_3O_5S_2$: C, 49.61; H, 5.14; N, 10.21; S, 15.58. Found: C, 49.77; H, 5.21; N, 10.03; S, 15.67.

Method B.

To a solution of **9** (0.30 g, 0.001 mole) in dimethylformamide (10 ml), anhydrous potassium carbonate (0.17 g, 0.0012 mole) and ethyl bromoacetate (0.20 g, 0.0012 mole) were added. After stirring at 60° for 3 hours, the mixture was poured into water, acidified with 2*M* hydrochloric acid and extracted with ethyl acetate. The residue was purified using column chromatography (ethanol-toluene 1:6) and obtained as colorless crystals, mp 132-133°. The compound is identical with the compound obtained by method A.

Ethyl 1-Amino-2,5-dioxo-1,2,3,5,6,7,8,9-octahydroimidazo[1,2-*a*]-pyrido[4',3':4,5]thieno[2,3-*d*]pyrimidine-8-carboxylate (**6**).

A suspension of dry **5** (0.40 g, 0.001 mole) in 99% hydrazine hydrate (4 ml) was gently refluxed in absolute ethanol (10 ml). The solid went into solution within 10 minutes. After 30 minutes, when the solid product started separating, heating was discontinued and the reaction mixture was allowed to cool to room temperature. The solid which separated was filtered, washed with water and ethanol, dried. Recrystallization from dimethylformamide as colorless crystals, mp >330°, 0.31 g (78%); ir: ν cm^{-1} 1642, 1677, 1702, 1763, 2940, 2990, 3220, 3320, 3426; ^1H nmr (dimethyl-d_6 sulfoxide): 1.20 (t, 3H, $COOCH_2CH_3$), 2.90 (t, 2H, H-6), 3.60 (t, 2H, H-7), 4.10 (q, 2H, $COOCH_2CH_3$),4.50 (s, 2H, NH_2), 4.60 (s, 2H, H-9), 5.20 (s, 2H, H-3), ms: m/z 394 (M^+).

Anal. Calcd. $C_{14}H_{15}N_5O_4S$: C, 48.13; H, 4.32; N, 20.04; S, 9.17. Found: C, 48.30; H, 4.21; N, 20.21; S, 9.30.

Diethyl 2-({[(Ethoxycarbonyl)amino]carbothioyl}amino)-4,5,6,7-tetrahydrothieno[2,3-c]pyridine-3,6-dicarboxylate (**7**).

A solution of ethoxycarbonyl isothiocyanate, prepared by mixing ethyl chloroformate (1.08 g, 0.01 mole) in dry acetone with ammonium thiocyanate (0.76 g, 0.01 mole) and heating in a water bath for 20 minutes), was added to a stirred solution of compound **1** (2.98 g, 0.01 mole) in acetone (30 ml). The mixture was heated under reflux in a water bath for 2 hours, then evaporated *in vacuo*. The remaining product was triturated with ethanol, then collected by filtration, dried and recrystallized from ethanol as yellow crystals, mp 188-189°, 2.1 g (70%); ir: ν cm^{-1} 1689, 1738, 2980, 3012, 3190, 3380, 3400; ^1H nmr (deuteriochloroform): 1.20 (t, 3H, $COOCH_2CH_3$), 1.40 (m, 6H, 2 -$COOCH_2CH_3$) 2.90 (t, 2H, H-4), 3.60 (t, 2H, H-5), 4.20 (q, 2H, $COOCH_2CH_3$), 4.30-4.45 (m, 4H, 2 $COOCH_2CH_3$), 4.60 (s, 2H, H-7), 11.60 (s, 1H, NH), 14.10 (s, 1H, NH); ^{13}C nmr (deuteriochloroform): 14.2 (q, $COOCH_2CH_3$), 14.3 (q, $COOCH_2CH_3$), 14.7 (q, $COOCH_2CH_3$), 26.5 (t, C-4), 41.2 (t, C-5), 42.6 (s, C-7), 61.0 (t, $COOCH_2CH_3$), 61.6 (t, $COOCH_2CH_3$), 63.2 (t, $COOCH_2CH_3$), 115.5 (s, C-3), 123.8 (s, C-7a), 131.1 (s, C-3a), 148.3 (s, CO), 151.2 (s, CO), 155.5 (s, CO), 165.1 (s, C-2), 173.4 (s, CS); ms: m/z 374 (M^+).

Anal. Calcd for $C_{17}H_{23}N_3O_6S_2$: C, 47.53; H, 5.39; N, 9.78; S, 14.93. Found C, 47.52; H, 5.63; N, 9.64; S, 14.80.

Ethyl 4-Oxo-2-thioxo-1,2,3,4,5,6,7,8-octahydropyrido[4',3':4,5]-thieno[2,3-d]pyrimidine-7-carboxylate (**8**).

Compound **7** (0.43 g, 0.001 mole) was dissolved in a solution of sodium ethoxide (from 0.23 g of sodium and 15 ml of absolute ethanol) and the solution was heated under reflux for 30 minutes. The solvent was evaporated *in vacuo*, some water was added to the residue, and the *p*H of the mixture was adjusted to 4 with hydrochloric acid. The product which separated was collected and crystallized from dimethylformamide as white crystals, mp 288-289°, 0.3 g (70%); ir: ν cm^{-1} 1660, 2980, 3160, 3300, 3440; ^1H nmr (dimethyl-d_6 sulfoxide): 1.20 (t, 3H, $COOCH_2CH_3$), 2.90 (t, 2H, H-5), 3.70 (t, 2H, H-6), 4.10 (q, 2H, -$COOCH_2CH_3$), 4.60 (s, 2H, H-8), 12.40 (s, 1H, NH); 13.40 (s, 1H, NH), ^{13}C nmr (dimethyl-d_6 sulfoxide): 14.3 (q, $COOCH_2CH_3$), 24.7 (t, C-5), 40.2 (t, C-6), 42.3 (s, C-8), 60.9 (t, $COOCH_2CH_3$), 115.7 (s, C-4a), 124.5 (s, C-4b), 129.4 (s, C-8a), 150.7 (s, C-9a), 154.8 (s, C-4), 156.6 (s, CO), 172.9 (s, C-2); ms: m/z 311 (M^+).

Anal. Calcd. for $C_{12}H_{13}N_3O_3S_2$: C, 46.28; H, 4.20; N, 13.49; S, 20.59. Found: C, 46.18; H, 3.15; N, 13.32; S, 20.52.

Ethyl 2-(Methylsulfanyl)-4-oxo-3,4,5,6,7,8-hexahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidine-7-carboxylate (**9**).

To a suspension of **8** (0.3 g, 0.001 mole) in acetone (20 ml), anhydrous potassium carbonate (0.14 g) and methyl iodide (0.22 g, 0.0016 mole) were added sequentially. The reaction mixture was stirred at room temperature for 1 hour and poured into water. The solid precipitate was collected by filtration, dried and recrystallized from dimethylformamide to give white crystals, mp 133-135°, 0.24 g (80%); ir: ν cm^{-1} 1660, 1709, 2980, 3150, 3200, 3270; ^1H nmr (dimethyl-d_6 sulfoxide): 1.20 (t, 3H, -$COOCH_2CH_3$), 3.00 (t, 2H, H-5), 3.50 (s, 3H, SCH_3), 3.70 (t, 2H, H-6), 4.20 (q, 2H, -$COOCH_2CH_3$), 4.60 (t, 2H, H-8), 12.60 (s, 1H, NH); ^{13}C nmr: 14.7 (q, COO_2CH_3), 15.2 (q, SCH_3), 25.6 (t, C-5), 29.7 (t, C-6), 41.1 (t, C-8), 61.7 (t, $COOCH_2CH_3$), 117.7 (s, C-4a), 155.6 (s, C-2), 158.3 (S, C-8a), 158.4 (s, s, C-9a), 162.9 (s, C-4), 173.7 (s, CO); ms: m/z 325 (M^+).

Anal. Calcd. for $C_{13}H_{15}N_3O_3S_2$: C, 47.98; H, 4.64, N, 12.91; S, 19.70. Found: C, 47.68; H, 4.67; N, 12.76; S, 19.42.

Ethyl 2-(Methylsulfanyl)-4-oxo-3,4,5,6,7,8-hexahydropyrido[4',3':4,5]thieno[2,3-*d*]pyrimidine-7-carboxylate (**10**).

A mixture of compound **9** (0.3 g, 0.001 mole) and hydrazine hydrate (5 ml) was refluxed in 10 ml of ethanol for 1.5 hours. The hydrazino derivative **10** which precipitated during refluxing was collected and crystallized from ethanol as colorless crystals, mp

244-245°, 0.23 g (77%); ir: ν cm^{-1} 1600, 1660, 1705, 2940, 3100, 3250, 3400, 3450; ^1H nmr (dimethyl-d_6 sulfoxide): 1.20 (t, 3H, -$COOCH_2CH_3$), 2.90 (t, 2H, H-5), 3.30 (s, 2H, NH_2), 3.70 (t, 2H, H-6), 4.10 (q, 2H, $COOCH_2CH_3$), 4.50 (s, 2H, H-8), 8.30 (b, 1H, NH), 12.60 (s, 1H, NH); ^{13}C nmr: 14.9 (q, $COOCH_2CH_3$), 25.0 (t, C-5), 40.2 (t, C-6), 42.4 (t, C-8), 60.7 (t, $COOCH_2CH_3$), 112.8 (s, C-4a), 120.7 (s, C-8a), 128.5 (s, C-9a), 154.6 (s, C-2), 157.5 (s, C-4), 167.2 (CO); ms: m/z 309 (M^+).

Anal. Calcd. for $C_{12}H_{15}N_5O_3S$: C, 46.59; H, 4.88; N, 22.63; S, 10.36. Found: C, 46.19; H, 4.19; N, 22.44; S, 10.66.

5-Oxo-4,5,6,7,8,9-hexahydropyrido[4',3':4,5]thieno[3,2-*e*]-[1,2,4]triazolo[4,3-*a*]pyrimidine-8-carboxylate (**11**).

To a suspension of compound **10** (0.30 g, 0.001 mole) in triethyl orthoformate (5 ml), a few drops of glacial acetic acid was added and the mixture was refluxed for 3 hours. The precipitated product which separated from the cold solution was filtered and recrystallized from ethanol as colorless crystals, mp 250-252°, 0.23 g (77%); ^1H nmr (dimethyl-d_6 sulfoxide): 1.20 (t, 3H, -$COOCH_2CH_3$), 2.90 (t, 2H, H-6), 3.70 (t, 2H, H-7), 4.10 (q, 2H, -$COOCH_2CH_3$), 4.60 (s, 2H, H-9), 9.20 (s, 1H, CH); ms: m/z 319 (M^+).

Anal. Calcd. for $C_{13}H_{13}N_5O_3S$: C, 48.88; H, 4.11; N, 21.93, S, 10.04. Found: C, 48.70; H, 4.20, N, 21.80; S, 10.12.

Ethyl 1-Methyl-5-oxo-4,5,6,7,8,9-hexahydropyrido[4',3':4,5]-thieno[3,2-*e*][1,2,4]triazolo[4,3-*a*]pyrimidine-8-carboxylate (**12**).

Compound **10** (0.3 g, 0.001 mole) in 10 ml of triethyl orthoacetate was refluxed for 3 hours. After being cooled, the solid product was filtered and recrystallized from ethanol as yellow crystals, mp 247-248°, 0.2 g (67%); ^1H nmr (dimethyl-d_6 sulfoxide): 1.20 (t, 3H, $COOCH_2CH_3$), 2.60 (s, 3H, CH_3), 2.95 (t, 2H, H-6), 3.50 (s, 1H, NH), 3.70 (t, 2H, H-7), 4.15 (q, 2H, $COOCH_2CH_3$), 4.70 (s, 2H, H-9); ms: m/z 333 (M^+).

Anal. Calcd. for $C_{14}H_{15}N_5O_3S$: C, 50.43; H, 4.54; N, 21.01; S, 9.62. Found: C, 50.30, H, 4.62; N, 20.95; S, 9.71.

Ethyl 5-Oxo-1-sulfanyl-4,5,6,7,8,9-hexahydropyrido[4',3':4,5]-thieno[3,2-*e*][1,2,4]triazolo[4,3-*a*]pyrimidine-8-carboxylate (**13**).

A mixture of compound **10** (0.30 g, 0.001 mole) and carbon disulfide (0.20 g, 0.0026 mole) in pyridine was refluxed for 5 hours. The pyridine was removed under reduced pressure and the residue was treated with water and filtered. It was crystallized from dimethylformamide as yellow crystals, mp 235-236°, 0.19 g (63%); ^1H nmr (dimethyl-d_6 sulfoxide): 1.20 (t, 3H, $COOCH_2CH_3$), 2.90 (t, 2H, H-6), 3.70 (t, 2H, H-7), 4.10 (q, 2H, -$COOCH_2CH_3$), 4.70 (s, 2H, H-9), 14.10 (s, 1H, SH), ms: m/z 350 (M^+).

Anal. Calcd. for $C_{13}H_{13}N_5O_3S_2$: C, 44.42; H, 3.73; N, 19.93; S, 18.24. Found: C, 44.36; H, 3.60; N, 19.80; S, 18.32.

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