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Synthesis of Dihydrothiopyrano[3,4-*c*]pyridines and of Fusion Products thereof†

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Summary. Reaction of the 6-hydroxy-thiopyrano[3,4-*c*]pyridine-5-carbonitrile derivative **2** with α-halogeno-carbonyl compounds gave the O-substituted intermediates **3a–d** which on treatment with base were converted into the furo[2,3-*b*]thiopyrano[4,3-*d*]pyridines **4a–d** by fusion of a furan moiety. Cyclization of the corresponding ester **4d** led to fusion of a pyrimidine ring, thus yielding the tetracyclic product **8** as well as its N-substituted derivatives **9a–e**. Target compounds **2–9** were derived from the three novel heterocyclic parent systems **A–C**.

Keywords. Fused S,N-heterocycles; Fused S,N,O-heterocycles; Thiopyrano[3,4-*c*]pyridine; Furo[2,3-*b*]thiopyrano[4,3-*d*]pyridines; Thiopyrano[4″,3″:4′,5′]pyrido[3′,2′:4,5]furo[3,2-*d*]pyrimidine derivatives.

Synthese von Dihydrothiopyrano[3,4-*c*]pyridinen und ihrer Kondensationsprodukte

Zusammenfassung. Reaktion des 6-Hydroxy-thiopyrano[3,4-*c*]pyridin-5-carbonsäurenitril – Derivates **2** mit α-Halogencarbonylverbindungen führte über die entsprechenden O-substituierten Zwischenprodukte **3a–d** durch Furan-Anellierungen zu den Furo[2,3-*b*]thiopyrano[4,3-*d*]pyridin – Derivaten **4a–d**. Cyclisierung des entsprechenden Esters **4d** gab unter Pyrimidin-Anellierung das tetracyclische Produkt **8** sowie dessen N-Substitutionsprodukte **9a–e**. Die Zielverbindungen **2–9** leiten sich von den drei neuen heterocyclischen Grundkörpern **A–C** ab.

Introduction

Within a long-term research program aiming at the synthesis of novel fused S,N-heterocycles [1–6] the present paper is dealing with methods leading to products derived from the three new parent systems thiopyrano[3,4-*c*]pyridine (**A**), furo[2,3-*b*]thiopyrano[4,3-*d*]pyridine (**B**), and thiopyrano[4″,3″:4′,5′]pyrido[3′,2′:4,5]furo[3,2-*d*]pyrimidine (**C**) (parent system skeletons: Fig. 1).

Results and Discussion

Reaction of 4-oxo-tetrahydrothiopyran-3-carboxylic acid methyl ester (**1**, [7]) with malononitrile in methanolic benzene containing ammonium acetate and acetic acid

† Dedicated to Professor *Richard Neidlein* on the occasion of his 65th birthday

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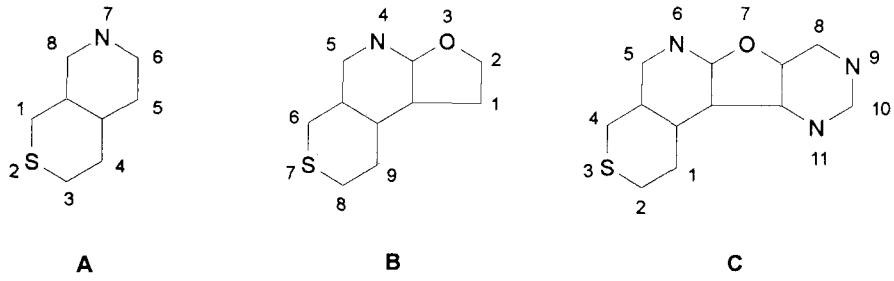
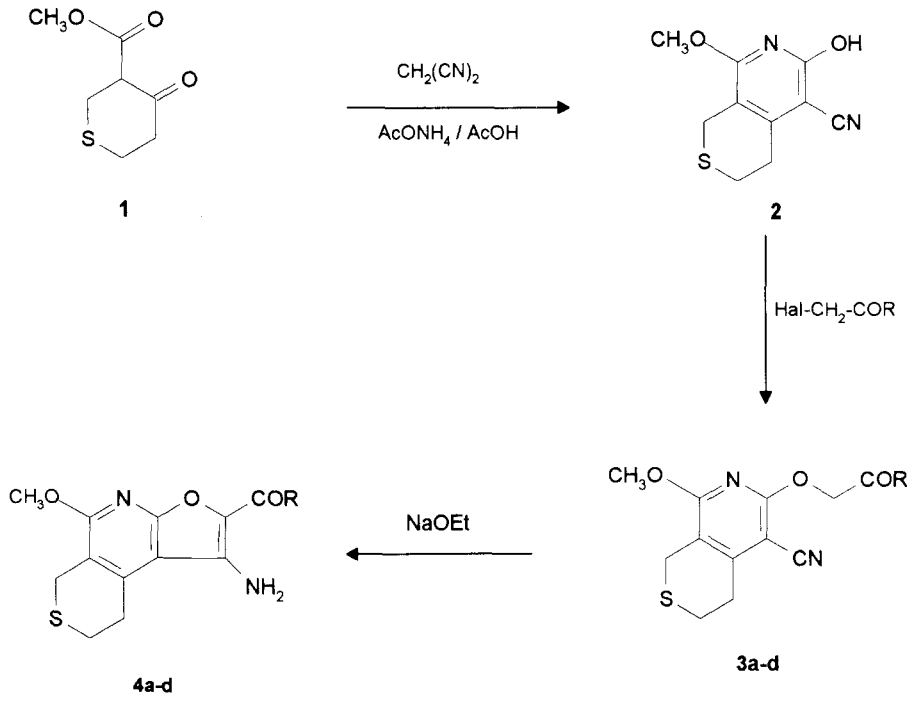


Fig. 1. Parent system skeletons of compounds **2–9**

yielded 3,4-dihydro-6-hydroxy-8-methoxy-1*H*-thiopyrano[3,4-*c*]pyridine-5-carbonitrile (**2**), obviously *via* a mechanism described by *Van der Baan* and *Bickelhaupt* [8] for structurally related cyclohexane derivatives.

Alkylations of the tautomeric hydroxy group in such lactams by chloromethyl or bromomethyl carbonyl compounds yield the corresponding α-acidic 3,4-dihydro-6-alkoxy-8-methoxy-1*H*-thiopyrano[3,4-*c*]pyridine-5-carbonitriles **3a–d** which are

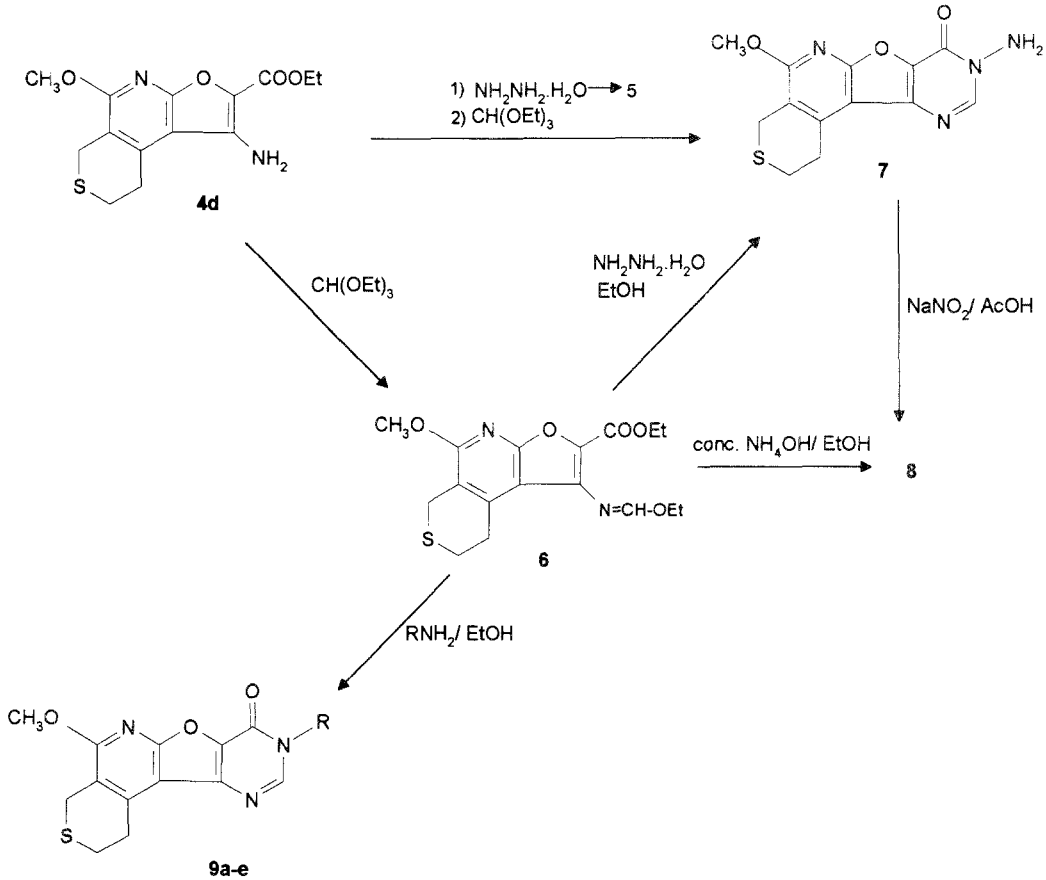


3 , 4	R
a	Me
b	Ph
c	p-Cl-Ph
d	OEt

Scheme 1

prone to undergo one more cyclization: in the presence of sodium ethoxide in ethanol, the target systems **4a–d**, *i.e.* the corresponding 1-amino-8,9-dihydro-5-methoxy-6*H*-furo[2,3-*b*]thiopyrano[4,3-*d*]pyridines were obtained in good yield (*cf.* Scheme 1).

As illustrated in Scheme 2, **4d** was also advantageously used for further cyclizations: condensation of **4d** with ethyl orthoformate gave 1-(ethoxymethylene)-amino-8,9-dihydro-5-methoxy-6*H*-furo[2,3-*b*]thiopyrano[4,3-*d*]pyridine-2-carboxylic acid ethyl ester (**6**) which proved to be a key intermediate for subsequent conversions leading to a number of related 9-substituted pyrimidines: when reacted with primary alkyl amines such as propyl amine, allylamine, 2-aminoethanol, butyl amine, and pentyl amine, the corresponding products **9a–e** were obtained. Treatment of **6** with hydrazine hydrate afforded **7** (which could alternatively be obtained from **4d** by initial conversion to the corresponding hydrazide **5**, followed



9	R
8	H
9a	propyl
9b	allyl
9c	2-hydroxyethyl
9d	butyl
9e	pentyl

Scheme 2

by cyclization with ethyl orthoformate). Deamination of **7** was effected by nitrous acid to yield 1,4-dihydro-5-methoxy-2*H*-thiopyrano[4″,3″:4′,5′]pyrido[3′,2′:4,5]furo[3,2-*d*]pyrimidin-8(9*H*)-one (**8**) which is identical to the product obtained by treatment of **6** with conc. ammonia solution in ethanol at elevated temperature in good yield.

Experimental

Melting points were determined on a Kofler melting point apparatus and are uncorrected. Elementary analyses were performed by the Microanalytical Laboratory, Institute of Physical Chemistry, University of Vienna (Mag. *J. Theiner*). ^{13}C and ^{1}H NMR spectra: Bruker AC 200(^{1}H: 200.13MHz, ^{13}C: 50.47 MHz), 5 mm dual $^{1}H/^{13}C$-VT-probe, 300 K; solvent: *DMSO*-d_6 and $CDCl_3$, respectively; δ values are given in ppm, internal standard *TMS* ($\delta = 0$ ppm); IR spectra were recorded on a Shimadzu 470 spectrophotometer (KBr pellets).

3,4-Dihydro-6-hydroxy-8-methoxy-1H-thiopyrano[3,4-c]pyridine-5-carbonitrile (**2**)

A magnetically stirred mixture of 4-oxo-tetrahydrothiopyran-3-carboxylic acid methyl ester (**1** [7], 4.35 g, 0.025 mol), malononitrile (1.8 g, 0.027 mol), glacial AcOH (1.5 ml), $AcONH_4$ (300 mg), and benzene/CH_3OH 1:1 (35 ml) was heated to reflux for 36 hours. Water was removed continuously by allowing the condensed vapors to flow back into the reaction flask through a 3 Å molecular sieve. At 4, 8, 18, and 24 hours reaction time, portions of $AcONH_4$ (100 mg each) were added. Then the mixture was evaporated *in vacuo* to dryness, the residue taken up in 1 *N* NaOH (60 ml), and the resulting solution filtered rapidly. After cooling in ice, the precipitated sodium salt of **2** was collected, washed with ice-cold 1 *N* NaOH, suspended in water (75 ml), and acidified with conc. HCl. The resulting product was collected, washed with water, dried, and recrystallized from EtOH/H_2O (1:1) to give 3.8 g (69% yield) of **2** as yellow crystals. M.p.: 178–181 °C; $C_{10}H_{10}N_2O_2S$ (222.20); calc.: C: 54.03, H: 4.53, N: 12.60; found: C: 54.03, H: 4.32, N: 12.47; ^{1}H NMR (*DMSO*-d_6): 2.80 (t, 2H, H-4), 2.90 (t, 2H, H-3), 3.50 (s, 2H, H-1), 3.90 (s, 3H, OCH_3), 12.40 (s, 1H, OH); ^{13}C NMR (*DMSO*-d_6):22.12 (t, C-4), 23.67 (t, C-3), 28.99 (s, C-1), 54.33 (OCH_3), 85.44 (C-5), 109.04 (C-8a), 115.46 (s, CN), 151.92 (C-4a), 161.50 (C-8), 163.25 (C-6); IR (KBr): 1460, 1580, 1600, 2200, 2900–3300 cm^{-1}.

General procedure for the synthesis of **3a–d**

A mixture of **2** (0.01 mol) and α-halo ketone or α-halo ester (0.01 mol) in absolute acetone (50 ml) was refluxed for 1 hour in the presence of anhydrous potassium carbonate (0.01 mol). The reaction mixture was cooled, poured onto cold water, and stirred for 1 hour at room temperature. The product was collected by filtration and recrystallized from an appropriate solvent.

3,4-Dihydro-6-(2-oxopropyl)-oxy-8-methoxy-1H-thiopyrano[3,4-c]pyridine-5-carbonitrile (**3a**)

Yellow crystals from EtOH; yield: 65%; m.p.: 118–120 °C; $C_{13}H_{14}N_2O_3S$ (278.32); calc.: C: 56.09, H: 5.06, N: 10.06; found: C: 56.23, H: 5.26, N: 10.19; ^{1}H NMR ($CDCl_3$): 2.25 (s, 3H, $COCH_3$), 2.90 (t, 2H, H-4), 3.20 (t, 2H, H-3), 3.60 (s, 2H, H-1), 3.90 (s, 3H, OCH_3), 4.90 (s, 2H, CH_2); IR (KBr): 1460, 1580, 1710, 2200, 2990 cm^{-1}.

3,4-Dihydro-6-(2-oxo-2-phenylethyl)-oxy-8-methoxy-1H-thiopyrano[3,4-c]pyridine-5-carbonitrile (**3b**)

Colorless crystals from EtOH; yield: 89%; m.p.: 148–149 °C; $C_{18}H_{16}N_2O_3S$ (340.39); calc.: C: 63.50, H: 4.73, N: 8.23; found: C: 63.69, H: 4.58, N: 8.14; ^{1}H NMR ($CDCl_3$): 2.85 (t, 2H, H-4), 3.20 (t, 2H, H-3),

3.55 (s, 2H, H-1), 3.65 (s, 3H, OCH_3), 5.60 (s, 2H, OCH_2), 7.40–7.60 (m, 3H, Ph), 7.90–8.00 (d, 2H, Ph); IR (KBr): 1460, 1580, 1700, 2200, 2990 cm^{-1}.

3,4-Dihydro-6-(2-oxo-2-(4-chlorophenyl)-ethyl)-oxy-8-methoxy-1H-thiopyrano[3,4-c]-pyridine-5-carbonitrile (**3c**)

Colorless crystals from EtOH; yield: 87.8%; m.p.: 145–146 °C; $C_{18}H_{15}ClN_2O_3S$ (374.83); calc.: C: 57.67, H: 4.03, N: 7.47; found: C: 57.87, H: 3.87, N: 7.51; ^1H NMR ($CDCl_3$): 2.85 (t, 2H, H-4), 3.10 (t, 2H, H-3), 3.60 (s, 2H, H-1), 3.65 (s, 3H, OCH_3), 5.50 (s, 2H, OCH_2), 7.45 (d, 2H, Ph), 7.90 (d, 2H, Ph); ^{13}C NMR ($CDCl_3$): 21.99 (t, C-4), 23.57 (t, C-3), 29.08 (s, C-1), 54.18 (s, OCH_3), 68.54 (s, OCH_2), 86.69 (s, C-5), 110.69 (s, C-8a), 114.55 (s, CN), 129.04 (C-phenyl), 129.85 (C-phenyl), 132.79 (C-phenyl), 138.77 (C-phenyl), 152.74 (s, C-4a), 160.78 (s, C-8), 161.18 (s, C-6), 192.92 (s, C=O); IR (KBr): 1440, 1580, 1700, 2200, 2990, 3000 cm^{-1}.

(5-Cyano-3,4-dihydro-8-methoxy-1H-thiopyrano[3,4-c]pyridin-6-yl)-oxy-acetic acid ethyl ester (**3d**)

Colorless crystals from EtOH; yield: 95.1%; m.p.: 95–96 °C; $C_{14}H_{16}N_2O_4S$ (308.35); calc.: C: 54.52, H: 5.23, N: 9.08; found: C: 54.58, H: 5.10, N: 8.94; ^1H NMR ($CDCl_3$): 1.30 (t, 3H, $COOCH_2CH_3$), 2.90 (t, 2H, H-4), 3.15 (t, 2H, H-3), 3.55 (s, 2H, H-1), 3.90 (s, 3H, OCH_3), 4.20 (q, 2H, $COOCH_2CH_3$), 4.90 (s, 2H, OCH_2); ^{13}C NMR ($CDCl_3$): 14.01 (q, OCH_2CH_3), 22.01 (t, C-4), 22.56 (t, C-3), 29.09 (s, C-1), 54.36 (s, OCH_3), 60.71 (t, OCH_2CH_3), 63.23 (s, OCH_2), 86.74 (s, C-5), 110.94 (s, C-8a), 114.36 (s, CN), 152.84 (s, C-4a), 160.88 (s, C-8), 161.07 (s, C-6), 168.13 (s, C=O); IR (KBr): 1460, 1580, 1720, 2200, 2990, 3000 cm^{-1}.

General procedure for the synthesis of **4a–d**

To a stirred suspension of compounds **3a–d** (0.01 mol) in absolute ethanol (50 ml), ethanolic sodium ethoxide (0.01 mol) was added. Stirring was continued for 15 min; then the reaction mixture was refluxed for another 10–30 min. The separated solid product was filtered off and recrystallized from an appropriate solvent.

1-(1-Amino-8,9-dihydro-5-methoxy-6H-furo[2,3-b]thiopyrano[4,3-d]pyridin-2-yl)-ethanone (**4a**)

Colorless needles from EtOH; yield 81.5%; m.p.: 236–237 °C; $C_{13}H_{14}N_2O_3S$ (278.32); calc.: C: 56.09, H: 5.06, N: 10.06; found: C: 56.34, H: 5.05, N: 10.02; ^1H NMR ($CDCl_3$): 2.40 (s, 3H, $COCH_3$), 2.90 (t, 2H, H-9), 3.40 (t, 2H, H-8), 3.70 (s, 2H, H-6), 4.00 (s, 3H, OCH_3); IR (KBr): 1480, 1510, 1580, 1620, 2990, 3300–3400 cm^{-1}.

(1-Amino-8,9-dihydro-5-methoxy-6H-furo[2,3-b]thiopyrano[4,3-d]pyridin-2-yl)-phenyl-methanone (**4b**)

Yellow crystals from EtOH; yield: 88.2%; m.p.: 194–195 °C; $C_{18}H_{16}N_2O_3S$ (340.39); calc.: C: 63.50, H: 4.73, N: 8.23; found: C: 62.83, H: 4.65, N: 8.10; ^1H NMR ($CDCl_3$): 2.90 (t, 2H, H-9), 3.40 (t, 2H, H-8), 3.70 (s, 2H, H-6), 4.00 (s, 3H, OCH_3), 6.30 (s, 2H, NH_2), 7.50 (m, 3H, Ph), 8.20 (m, 2H, Ph); IR (KBr): 1410, 1460, 1510, 1600, 2980, 2990, 3300 cm^{-1}.

(1-Amino-8,9-dihydro-5-methoxy-6H-furo[2,3-b]thiopyrano[4,3-d]pyridin-2-yl)-(4-chlorophenyl)-methanone (**4c**)

Yellow needles from EtOH; yield: 86.4%; m.p.: 220–221 °C; $C_{18}H_{15}ClN_2O_3S$ (374.83); calc.: C: 57.67, H: 4.03, N: 7.47; found: C: 57.93, H: 4.21, N: 7.86; ^1H NMR ($CDCl_3$): 2.95 (t, 2H, H-9), 3.40 (t, 2H, H-8),

3.70 (s, 2H, H-6), 6.30 (s, 2H, NH_2), 7.45 (m, 2H, Ph), 8.20 (m, 2H, Ph); ^{13}C NMR ($CDCl_3$): 22.96 (t, C-9), 23.48 (t, C-8), 27.49 (s, C-6), 54.46 (s, OCH_3), 104.30 (s, C-1), 113.18 (s, C-5a), 120.96 (s, C-9b), 128.30, 130.24, 131.31, 136.14 (aromatic carbons), 144.68 (s, C-9b), 145.07 (s, C-2), 157.38 (s, C-3a), 162.04 (s, C-5), 177.59 (s, CO); IR (KBr): 1460, 1510, 1600, 2990, 3300–3400 cm^{-1}.

1-Amino-8,9-dihydro-5-methoxy-6H-furo[2,3-b]thiopyrano[4,3-d]pyridine-2-carboxylic acid ethyl ester (**4d**)

Colorless crystals from EtOH; yield: 70%; m.p.: 156–158 °C; $C_{14}H_{16}N_2O_4S$ (308.35); calc. C: 54.52, H: 5.23, N: 9.08; found: C: 54.39, H: 5.05, N: 8.91; ^1H NMR ($CDCl_3$): 1.40 (t, 3H, $COOCH_2CH_3$), 2.90 (t, 2H, H-9), 3.35 (t, 2H, H-8), 3.70 (s, 2H, H-6), 3.95 (s, 3H, OCH_3), 4.40 (q, 2H, $COOCH_2CH_3$), 5.00 (s, 2H, NH_2); ^{13}C NMR ($CDCl_3$): 14.38 (q, $COOCH_2CH_3$), 22.93 (t, C-9), 23.53 (t, C-8), 27.15 (s, C-6), 54.15 (s, OCH_3), 59.31, (t, $COOCH_2CH_3$), 105.25 (s, C-1), 112.68 (s, C-5a), 120.96 (s, C-9b), 140.47 (s, C-9a), 144.36 (s, C-2), 156.35 (s, C-3a), 160.43 (s, C-5), 160.84 (s, COOEt); IR (KBr): 1440, 1490, 1540, 1580, 1620, 1660, 2990, 3300 cm^{-1}.

1-Amino-8,9-dihydro-5-methoxy-6H-furo[2,3-b]thiopyrano[4,3-d]pyridine-2-carboxylic acid hydrazide (**5**)

A mixture of **4d** (0.3 g, 0.001 mol) and hydrazine hydrate (2 ml, 80% solution) was refluxed in ethanol (5 ml) for 4 hours, cooled, and the colorless solid product which separated was washed with boiling ethanol to give 0.24 g (82.7% yield) of **5**. M.p.: 248–250 °C; $C_{12}H_{14}N_4O_3S$ (294.32); calc.: C: 48.96, H: 4.79, N: 19.03; found: C: 48.97, H: 4.77, N: 18.93; ^1H NMR (*DMSO*-d_6): 2.90 (t, 3H, H-9), 3.30 (t, 2H, H-8), 3.60 (s, 2H, H-6), 3.85 (s, 3H, OCH_3), 4.30 (s, 2H, NH_2), 5.70 (s, 2H, $CONH_2$), 9.20 (s, 1H, NH); ^{13}C NMR (*DMSO*-d_6): 22.96 (t, C-9), 23.69 (t, C-8), 27.02 (s, C-6), 54.12 (s, OCH_3), 106.39 (s, C-1), 112.46 (s, C-5a), 123.70 (s, C-9b), 136.26 (s, C-9a), 143.96 (s, C-2), 155.28 (s, C-3a), 159.83 (s, C-5), 161.08 (s, CO).

1-((Ethoxymethylene)-amino)-8,9-dihydro-5-methoxy-6H-furo[2,3-b]thiopyrano[4,3-d]-pyridin-2-carboxylic acid ethyl ester (**6**)

A mixture of **4d** (1 g, 0.003 mol) and ethyl orthoformate (10 g, 0.067 mol) was refluxed for 6 hours. Excess ethyl orthoformate was distilled off under vacuum and the residue was treated with ethanol. The resulting solid product was collected and recrystallized from ethanol to give 1 g (84.7%) of **6** as colorless crystals. M.p.: 130–132 °C; $C_{17}H_{20}N_2O_5S$ (364.41); calc.: C: 56.02, H: 5.53, N: 7.68; found: C: 56.16, H: 5.39, N: 7.55; ^1H NMR ($CDCl_3$): 1.30–1.50 (m, 6H, 2 $COOCH_2CH_3$), 2.90 (t, 2H, H-9), 3.40 (t, 2H, H-8), 3.70 (s, 2H, H-6), 4.00 (s, 3H, OCH_3), 4.30–4.50 (m, 4H, 2 $COOCH_2CH_3$), 7.90 (s, 1H, CH); ^{13}C NMR ($CDCl_3$): 13.92 (q, OCH_2CH_3), 22.76 (t, C-9), 23.42 (t, C-8), 27.17 (s, C-6), 54.26 (s, OCH_3), 60.12 (t, $COOCH_2CH_3$), 62.52 (s, OCH_2CH_3), 108.34 (s, C-1), 113.91 (s, C-5a), 127.58 (s, C-9b), 138.47 (s, C-9a), 144.49 (s, C-2), 155.86 (s, C-3a), 159.01 (s, N=CHOEt), 159.43 (s, C-5), 160.61 (s, COOEt); IR (KBr): 1540, 1580, 1600, 1620, 1700, 2990, 3000 cm^{-1}.

9-Amino-1,4-dihydro-5-methoxy-2H-thiopyrano[4'',3'':4',5']pyrido[3',2':4,5]furo-[3,2-d]pyrimidin-8(9H)-one (**7**)

Method A:

A mixture of **6** (0.4 g, 0.01 mol) and hydrazine hydrate (1 ml, 80% solution) was refluxed in ethanol (5 ml) for 30 min, cooled, and the resulting solid collected and recrystallized from aqueous *DMF* to give 0.3 g (90.9% yield) of **7** as colorless crystals. M.p.: 294–296 °C (dec.); $C_{13}H_{12}N_4O_3S$ (304.32); calc.: C: 51.30, H: 3.97, N: 18.41; found: C: 51.66, H: 4.13, N: 18.20; ^1H NMR (*DMSO*-d_6): 2.90 (t, 2H, H-1), 3.40

(t, 2H, H-2), 3.70 (s, 2H, H-4), 4.00 (s, 3H, OCH_3), 6.00 (s, 2H, NH_2), 8.50 (s, 1H, H-10); IR (KBr): 1540, 1580, 1600, 1700, 2990, 3300 cm^{-1}.

Method B:

A mixture of **5** (0.3 g, 0.001 mol) and ethyl orthoformate (0.2 g, 0.0017 mol) was heated at 180 °C for 1 hour. The initial melt solidified; trituration and recrystallization of the solid product from aqueous *DMF* yielded 0.22 g (70.9%) of **7**. M.p.: 294–296 °C (dec.); this compound was spectroscopically equivalent with the material prepared by method A, and a mixed melting point of the two materials was undepressed.

1,4-Dihydro-5-methoxy-2H-thiopyrano[4'',3'':4',5']pyrido[3',2':4,5]furo[3,2-d]-pyrimidin-8(9H)-one (**8**)

Method A:

A mixture of **6** (0.36 g, 0.001 mol) and conc. ammonia solution (4 ml) was heated under reflux in ethanol (5 ml) for 5 hours. The reaction mixture was allowed to cool to room temperature; the crystalline product was filtered off, washed with ethanol, dried, and recrystallized from aqueous *DMF* to give 0.19 g (67.8% yield) of **8** as white crystals. M.p.: 310 °C (dec.); $C_{13}H_{11}N_3O_3S$ (289.30); calc.: C: 53.96, H: 3.83, N: 14.52; found: C: 53.80, H: 3.68, N: 14.29; ^{1}H NMR (*DMSO*-d_6): 2.90 (t, 2H, H-1), 3.40 (t, 2H, H-2), 3.60 (s, 2H, H-4), 4.00 (s, 3H, OCH_3), 8.10 (s, 1H, NH), 12.80 (s, 1H, H-10); IR (KBr): 1460, 1580, 1600, 1640, 1680, 2990 cm^{-1}.

Method B:

A suspension of **7** (0.2 g, 0.00065 mol) in 50% aqueous acetic acid (15 ml) was warmed to 45–50 °C and then treated with sodium nitrite (0.2 g 0.002 mol) in portions. The mixture was heated (45–50 °C) until the evolution of nitrogen dioxide ceased; the resulting solution was cooled and diluted with water. The solid product was purified by dissolving in sodium hydroxide solution (10%) and reprecipitating with dilute hydrochloric acid followed by recrystallization from aqueous *DMF* to give 1.1 g (57.8% yield) of **8** as colorless crystals, m.p. 310 °C (dec.). The compound is identical to that obtained according to method A.

General procedure for the synthesis of **9a–e**

Compound **6** (0.001 mol) and the respective amine (0.0012 mol) were heated under reflux in ethanol (10 ml) for 10–50 min. The reaction mixture was allowed to cool to room temperature; the crystalline product was filtered off, washed with ethanol, dried, and recrystallized from an appropriate solvent.

9-Propyl-1,4-dihydro-5-methoxy-2H-thiopyrano[4'',3'':4',5']pyrido[3',2':4,5]furo-[3,2-d]pyrimidin-8(9H)-one (**9a**)

Colorless needles from EtOH; yield: 74.1%; m.p.: 209–210 °C; $C_{16}H_{17}N_3O_3S$ (331.38); calc.: C: 57.98, H: 5.17, N: 12.68; found: C: 57.72, H: 4.99, N: 12.73; ^{1}H NMR ($CDCl_3$): 1.00 (t, 3H, CH_3), 1.80 (m, 2H, CH_2 propyl), 2.90 (t, 2H, H-1), 3.70 (t, 2H, H-2), 3.80 (s, 2H, H-4), 4.10 (m, 5H, OCH_3, NCH_2), 8.10 (s, 1H, H-10).

9-(2-Propenyl)-1,4-dihydro-5-methoxy-2H-thiopyrano[4'',3'':4',5']pyrido[3',2':4,5]furo-[3,2-d]pyrimidin-8(9H)-one (**9b**)

Colorless needles from EtOH; yield: 70%; m.p.: 182–184 °C; $C_{16}H_{15}N_2O_3S$ (329.34); calc.: C: 58.34, H: 4.58, N: 12.75; found: C: 58.21, H: 4.32, N: 12.60; ^{1}H NMR ($CDCl_3$): 2.95 (t, 2H, H-1), 3.60 (t, 2H,

H-2), 3.70 (s, 2H, H-4), 4.10 (s, 3H, OCH_3), 4.70 (d, 2H, NCH_2), 5.20–5.30 (m, 2H, 2 =CH), 6.00 (m, 1H, =CH), 8.10 (s, 1H, H-10); IR (KBr): 1440, 1510, 1560, 1590, 1600, 1690, 2990 cm^{-1}.

9-(2-Hydroxyethyl)-1,4-dihydro-5-methoxy-2H-thiopyrano[4",3":4',5']pyrido[3',2':4,5]furo-[3,2-d]pyrimidin-8(9H)-one (**9c**)

Colorless needles from EtOH; yield: 75.8%; m.p.: 201–202 °C; $C_{15}H_{15}N_3O_4S$ (333.35); calc.: C: 54.04, H: 4.53, N: 12.60; found: C: 54.18, H: 5.64, N: 12.71; ^1H NMR ($CDCl_3$): 2.90 (t, 2H, H-1), 3.40 (t, 2H, CH_2OH), 3.70 (m, 4H, H-2, H-4), 3.90 (s, 3H, OCH_3), 4.10 (t, 2H, NCH_2), 8.40 (s, 1H, H-10); IR (KBr): 1440, 1520, 1580, 1680, 2990, 3300, 3500 cm^{-1}.

9-Butyl-1,4-dihydro-5-methoxy-2H-thiopyrano[4",3":4',5']pyrido[3',2':4,5]furo[3,2-d]-pyrimidin-8(9H)-one (**9d**)

Colorless needles from EtOH; yield: 77%; m.p.: 215 °C; $C_{17}H_{19}N_3O_3S$ (345.42); calc.: C: 59.11, H: 5.54, N: 12.16; found: C: 59.18, H: 5.64, N: 12.28; ^1H NMR ($CDCl_3$): 1.00 (t, 3H, CH_3), 1.40 (m, 2H, CH_2 butyl), 1.80 (m, 2H, CH_2 butyl), 2.95 (t, 2H, H-1), 3.70 (t, 2H, H-4), 4.10 (m, 5H, OCH_3, NCH_2), 8.10 (s, 1H, H-10).

9-Pentyl-1,4-dihydro-5-methoxy-2H-thiopyrano[4",3":4',5']pyrido[3',2':4,5]furo[3,2-d]pyrimidin-8(9H)-one (**9e**)

Colorless crystals from EtOH; yield: 80%; m.p.: 168–169 °C; $C_{18}H_{21}N_3O_3S$ (359.94); calc.: C: 60.06, H: 6.02, N: 11.67; found: C: 59.94, H: 5.89, N: 11.59; ^1H NMR ($CDCl_3$): 1.00 (t, 3H, CH_3), 1.40 (m, 4H, 2 CH_2 pentyl), 1.80 (m, 2H, CH_2 pentyl), 2.90 (t, 2H, H-1), 3.60 (t, 2H, H-2), 3.70 (s, 2H, H-4), 4.10 (m, 5H, OCH_3, NCH_2), 8.10 (s, 1H, H-10); IR (KBr): 1480, 1520, 1560, 1590, 1680, 2990 cm^{-1}.

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