SYNTHESES OF THIENO[2,3-*d*]PYRIMIDINES AND AMINO-PYRIMIDINES FROM 2-ALKOXY-5-CYANO-4-THIOXOPYRIMIDINE INTERMEDIATES

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Abstract - β-Chloro-α-cyanocinnamonitrile reacts in an one-pot reaction with potassium thiocyanate and alkanol to form 2-alkoxy-6-phenyl-5-cyano-1,4-dihydro-4-pyrimidinthions. The products were S-alkylated to yield thieno[2,3-*d*]pyrimidines on cyclization and aminopyrimidines on substitution of alkoxy and alkylthio groups.

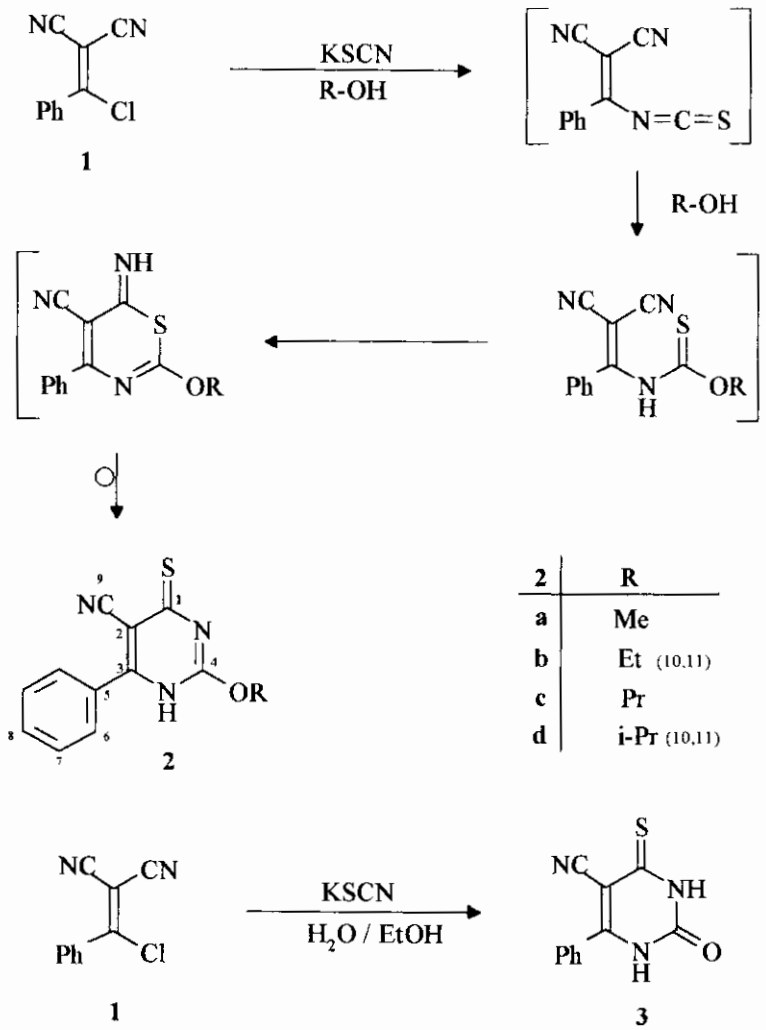
Substituted and heterocondensed pyrimidines are widespread natural products.[1] A lot of synthetic pathways are available to create substituted pyrimidines.[2]

The synthesis of 6-aminothieno[2,3-*d*]pyrimidines was earlier carried out starting with 4-chloro-pyrimidines[3] as well as using 4-mercaptopyrimidines.[4] Another synthesis route to thieno[2,3-*d*]pyrimidines was reported to apply 2,3-disubstituted derivatives of thiophene, which were condensed with various reagents to form the pyrimidine moiety.[5-11] We took advantage of a new versatile pyrimidine synthesis yielding 2-alkoxy-6-phenyl-4-thioxo-1*H*-pyrimidine-5-carbonitriles, which were S-alkylated and subjected to ring closue reaction subsequently. As building block β-chloro-α-cyanocinnamonitrile[12] was introduced in order to get easy access to the desired new substitution patterns. We have already reported on the utility of β-chloro-α-cyanocinnamonitrile in the synthesis of 2,4-diamino-3-quinolinecarbonitriles,[13] 3-amino-thiophenes,[14] and imidazo[1,2-*a*]pyridines.[15]

RESULTS AND DISCUSSION

β-Chloro-α-cyanocinnamonitrile (**1**) as starting material was obtained by chlorination of benzylidene malononitrile.[12] For the formation of the pyrimidines (**2**) the following reaction mechanism is assumed.

Substitution of chlorine by thiocyanate gives an isothiocyanato intermediate, which forms a thiocarbamate

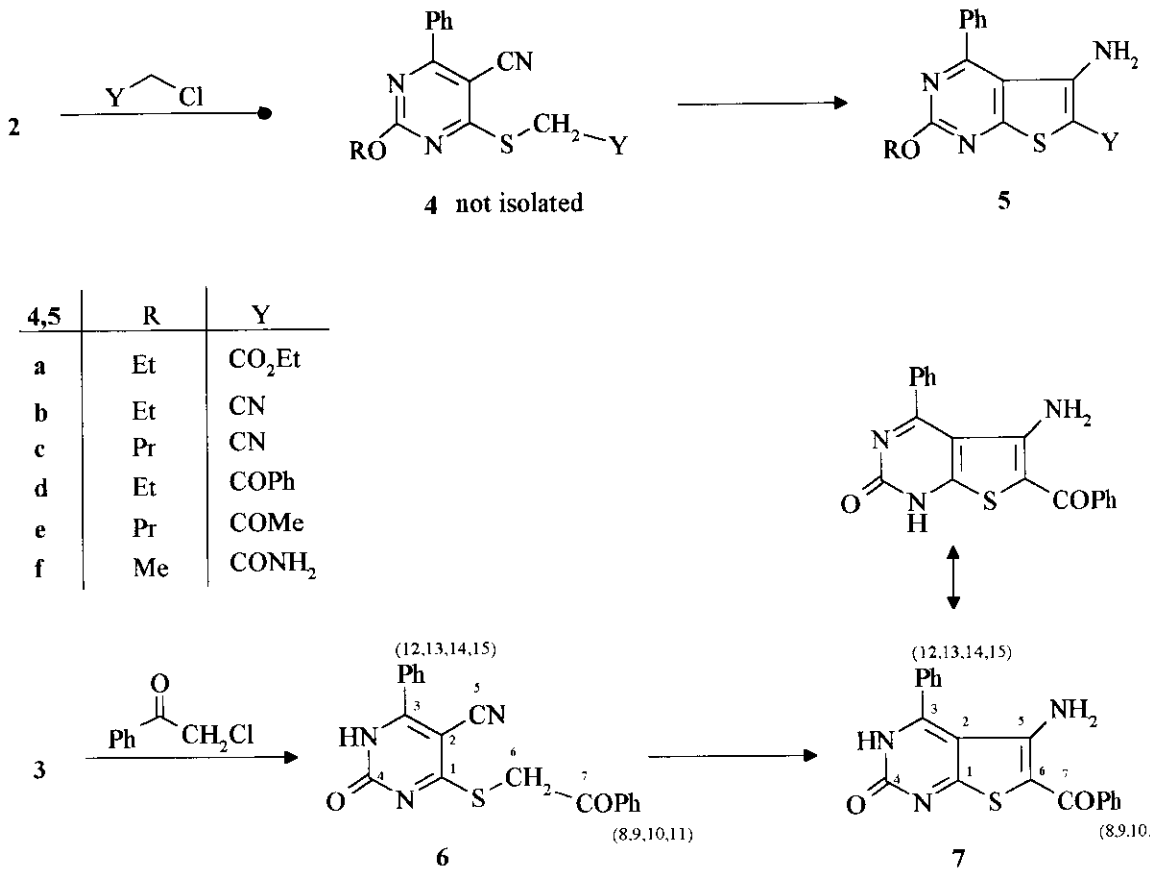


Numbering of C-atoms relates to ^{13}C NMR spectra

Scheme 1

after addition of alkanol. Dimroth rearrangement[16] of this intermediate forms finally 2-alkoxy-6-phenyl-4-thioxo-1*H*-pyrimidine-5-carbonitriles (**2**). When the reaction was carried out in the presence of water, 2-oxo-6-phenyl-4-thioxo-1*H*,3*H*-pyrimidine-5-carbonitrile was obtained dependent on composition of the solvent mixure.

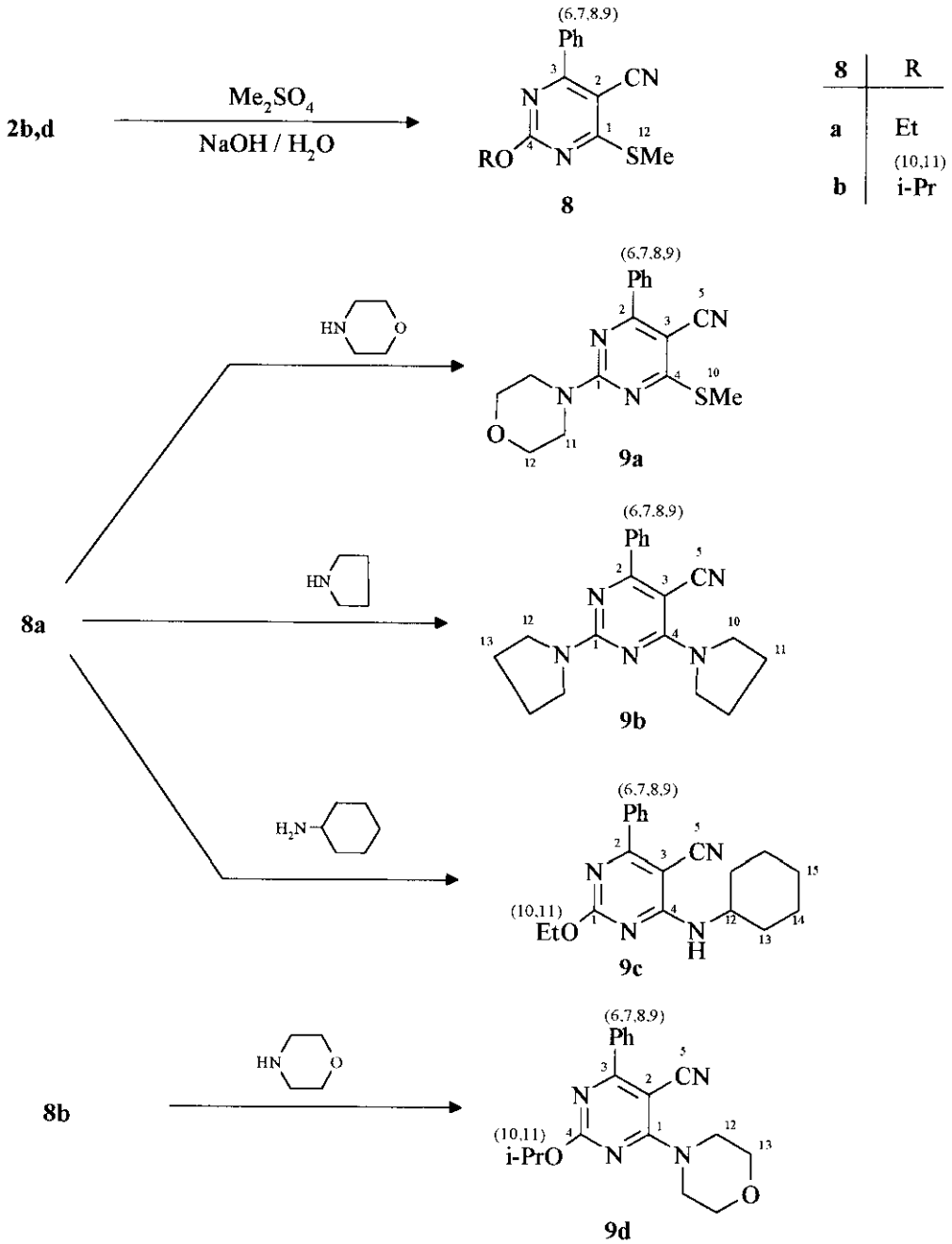
For the synthesis of 5-amino-thieno[2,3-*d*]pyrimidines, 4-thioxo-1*H*-pyrimidines (**2**) were alkylated with substituted halogenomethyl reagents such as chloroethyl acetate, chloroacetonitrile, chloroacetone, chloracetophenone, and chloroacetamide. The primary alkylation products were not isolated but subjected to ring closure reaction according to thiophene synthesis.[17,18]



Numbering of C-atoms relates to ^{13}C NMR spectra

Scheme 2

Compound	Procedure	Yield	Melting point
5a	A B	41 58	164-165 °C (n-propanol)
5b	A	44	209-211 °C (n-propanol
5c	B	65	201-203 °C (n-propanol)
5d	A B	37 51	182-183 °C (n-propanol)
5e	B	50	160-162 °C (ethanol)
5f	A	33	208-210 °C (n-propanol)



Numbering of C-atoms relates to ^{13}C NMR spectra

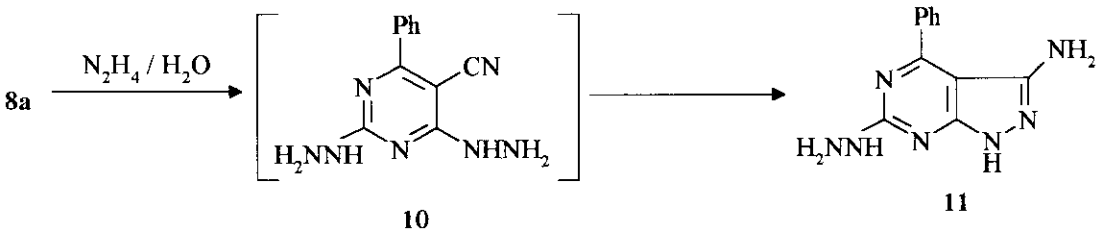
Scheme 3

The cyclization was accomplished in sodium alkoxide solution or ethanolic potassium hydroxide solution. The conversion of **4** into **5** was confirmed by recording of IR spectra showing the absence of νCN absorption. It was possible to obtain **5** directly from **1** by an one-pot reaction (procedure A),[19] otherwise the reaction was started from **2** according to procedure B. Because the yields do not differ significantly,

procedure A was advantageously applied. The alkylation of **3** with substituted halogenomethyl reagents followed by ring closure reaction was not feasible due to side reaction by *O*-alkylation in the first step. Only the reaction with chloroacetophenone gave a product (**7**) with acceptable yield and purity. The intermediate (**6**) was isolated and characterized.

For the synthesis of hitherto unknown substituted aminopyrimidine derivatives, we *S*-methylated **2** with dimethyl sulphate in aqueous sodium hydroxide solution to furnish methythiopyrimidine derivatives (**8**), which are assumed to undergo substitution reactions. Subsequently, **8a,b** were treated with amines expecting the formation of aminopyrimidine derivatives (**9**). As result alkoxy and alkylthio groups were substituted directed by steric hindrance and nucleophilicity of the respective amines. 2,4-disubstitution is attained under vigorous conditions, but we applied only reflux temperature determined by the respective reaction mixture. Surprisingly, *O*-alkyl substitution with morpholine was prevented by the isopropyl group yielding the *S*-methyl substitution product (**9d**).

A previous described synthesis of 2,4-diamino-6-phenylpyrimidines made use of the reaction between aza-analogous 1,3-dichlorotrimethinecyanine and α-iminopropylbenzene.[20]



Scheme 4

The reaction of **8a** with hydrazine hydrate was investigated. At first the formation of a bis-hydrazine substituted pyrimidine derivative is postulated, which immediately gives a ring closure product with the assigned structure. This pyrazolo[3,4-*d*]pyrimidine structure was confirmed by spectroscopic data.

ACKNOWLEDGEMENT

The authors are indebted to Mrs. Pinske for microanalyses and Dr. Gruner for NMR spectral determination.

EXPERIMENTAL

Melting points were measured on a Kofler hot-stage apparatus. ^{1}H NMR spectra and ^{13}C NMR spectra were obtained in $CDCl_3$ or DMSO-d_6 using an AC-200 MHz Bruker spectrometer. The IR spectra were recorded on a spectrophotometer Specord 75 (Fa. Carl-Zeiss Jena). Elemental analyses were determined on a EA 1108 (Fa. Carlo Erba Hofheim).

(α-Chlorobenzylidene)malononitrile (1)

This compound was prepared according to a described procedure.[12]

2-Alkoxy-6-phenyl-4-thioxo-1,4-dihydropyrimidine-5-carbonitrile (2), general procedure

A suspension of (α-chlorobenzylidene)malononitrile (18.9 g, 0.1 mol) and potassium rhodanide (1.2 g, 0.12 mol) in the respective alkanol (200 mL) was stirred and refluxed for 2 h. The reaction mixture was cooled and poured into water (600 mL) and after 1 h, the crude product was collected by filtration. Recrystallisation was carried out with the given solvent.

2-Methoxy-6-phenyl-4-thioxo-1,4-dihydropyrimidine-5-carbonitrile (2a)

Yield: 57 %, mp 187-189 °C (ethanol); Anal. Calcd for $C_{12}H_9N_3OS$: C, 59.24; H, 3.73; N, 17.27; S, 13.18. Found: C, 59.33; H, 3.74; N, 17.48; S, 12.91.

2-Ethoxy-6-phenyl-4-thioxo-1,4-dihydropyrimidine-5-carbonitrile (2b)

Yield: 54 %, mp 197-200 °C (ethanol); ^{1}H NMR (DMSO-d_6) δ 14.0-15.0 (br s, 1H, NH), 7.9-8.0 (d, J = 7 Hz, 2H, phenyl-H), 7.5-7.7 (m, 3H, phenyl-H), 4.4 (q, J = 7 Hz, 2H, OCH_2), 1.2 (t, J = 7 Hz, 3H, CH_3) ppm; Anal. Calcd for $C_{13}H_{11}N_3OS$: C, 60.68; H, 4.31; N, 16.33; S, 12.46. Found: C, 60.66; H, 4.33; N, 16.56; S, 12.60.

6-Phenyl-2-propoxy-4-thioxo-1,4-dihydropyrimidine-5-carbonitrile (2c)

Yield: 50 %, mp 213-215 °C (n-propanol); ^{13}C NMR (DMSO-d_6) δ 184.84 (s, C1), 104.27 (s, C2), 157.21 (s, C3), 166.53 (s, C4), 116.37 (s, C5), 134.94 (s, C6), 128.28 (d, C7), 128.70 (d, C8), 131.68 (d, C9), 70.91 (t, C10), 27.27 (t, C11), 9.82 (q, C12) ppm; Anal. Calcd for $C_{14}H_{13}N_3OS$: C, 61.97; H, 4.83; N, 15.49; S, 11.82. Found: C, 62.51; H, 5.06; N, 15.48; S, 11.69.

2-Isopropoxy-6-phenyl-4-thioxo-1,4-dihydropyrimidine-5-carbonitrile (2d)

Yield: 73 %, mp 200-203 °C (i-propanol); ^{1}H NMR (DMSO-d_6) δ 14.0-15.0 (br s, 1H, NH), 8.0 (d, J = 7 Hz, 2H, phenyl-H), 7.5-7.7 (m, 3H, phenyl-H), 5.5 (heptet, J = 6 Hz, 1H, CH), 1.4 (d, J = 6 Hz, 6H, $2CH_3$) ppm; ^{13}C NMR (DMSO-d_6) δ 185.00 (s, C1), 104.12 (s, C2), 156.92 (s, C3), 166.98 (s, C4), 135.21 (s, C5), 128.53 (d, C6), 128.89 (d, C7), 131.01 (d, C8), 116.73 (s, C9), 74.32 (d, C10), 21.46 (q, C11, C11′) ppm; Anal. Calcd for $C_{14}H_{13}N_3OS$: C, 61.97; H, 4.83; N, 15.49; S, 11.82. Found: C, 62.25; H, 5.04; N, 15.63; S, 11.82.

6-Phenyl-2-oxo-4-thioxo-1*H*,3*H*-pyrimidine-5-carbonitrile (3)

Potassium rhodanide (2.9 g, 30 mmol) was dissolved in a mixture of water (20 mL) and ethanol (50 mL). **1** (4.7 g, 25 mmol) was added portionwise under stirring. Subsequently, the mixture was heated at a bath temperature of 100 °C for 1 h. After cooling, the precipitate is filtered off and digested with water (75 mL) for purification. Yield: 26 %, mp 294-297 °C (H_2O); ^{1}H NMR (DMSO-d_6) δ 12.9 (s, NH), 7.6 (m, phenyl-H) ppm; ^{13}C NMR (DMSO-d_6) δ 187.71 (s, C1), 97.44 (s, C2), 187.71 (s, C3), 158.99 (s, C4), 129.70 (s,

C5), 128.44 (d, C6 and C7), 132.16 (d, C8), 115.66 (s, C9) ppm; Anal. Calcd for $C_{11}H_7N_3OS$: C, 57.63; H, 3.08; N, 18.33; S, 13.99. Found: C, 57.69; H, 3.15; N, 18.67; S, 13.67.

5-Amino-2-alkoxy-4-phenylthieno[2,3-*d*]pyrimidine (5),

General procedure A: **1** (1.88 g, 10 mmol) and potassium rhodanide (1.2 g, 12.5 mmol) were suspended in alkanol (20 mL) and then stirred at reflux temperature for 1.5 h. Subsequently, an alkoxide solution, prepared from sodium (0.46 g, 20 mmol) and alkanol (16 mL) was added, and then 20 mL of the solvent was distilled off under stirring. After cooling, the alkylating agent (10 mmol) was added, and the mixture was stirred at rt for 20 min. Afterwards, the mixture was heated on a water bath for 15 min and after cooling diluted with water (50 mL). The precipitate was filtered off after 12 h.

General procedure B: **3** (1.15 g, 5 mmol) and potassium rhodanide (1.95 g, 20 mmol) were suspended in ethanol (20 mL) and then heated to reflux for 15 min. Subsequently, an ethoxide solution, prepared from sodium (0.23 g, 10 mmol) and ethanol (8 mL) was added. After cooling, the alkylating agent (5 mmol) dissolved in ethanol (10 mL) was added, and the mixture was stirred at rt for 30 min. Afterwards, the mixture was heated on a water bath for 30 min and after cooling diluted with water (100 mL). The precipitate was filtered off after 12 h.

Ethyl 5-amino-2-ethoxy-4-phenylthieno[2,3-*d*]pyrimidine-6-carboxylate (5a)

^{1}H NMR ($CDCl_3$) δ 7.5-7.7 (m, 5H, phenyl-H), 5.9 (s, 2H, NH_2), 4.6 (q, J = 7 Hz, 2H, CH_2), 4.2 (q, J = 8 Hz, 2H, CH_2), 1.5 (t, J = 7 Hz, 3H, CH_3), 1.3 (t, J = 8 Hz, 3H, CH_3) ppm; Anal. Calcd for $C_{17}H_{17}N_3O_3S$: C, 59.45; H, 4.99; N, 12.24; S, 9.35. Found: C, 59.50; H, 5.07; N, 12.30; S, 9.31.

5-Amino-2-ethoxy-4-phenylthieno[2,3-*d*]pyrimidine-6-carbonitrile (5b)

^{1}H NMR ($CDCl_3$) δ 7.4-7.8 (m, 5H, phenyl-H), 5.9-6.2 (s, 1H, NH), 5.1-5.4 (s, 1H, NH), 4.6 (q, J = 8 Hz, 2H, CH_2), 1.5 (t, J = 8 Hz, 3H, CH_3) ppm; Anal. Calcd for $C_{15}H_{12}N_4OS$: C, 60.80; H, 4.18; N, 18.91; S, 10.80. Found: C, 60.76; H, 4.06; N, 18.44; S, 10.56.

5-Amino-4-phenyl-2-propoxythieno[2,3-*d*]pyrimidine-6-carbonitrile (5c)

Anal. Calcd for $C_{16}H_{14}N_4OS$: C, 61.93; H, 4.55; N, 18.06; S, 10.31. Found: C, 61.62; H, 4.51; N, 17.33; S, 10.23.

5-Amino-2-ethoxy-4-phenylthieno[2,3-*d*]pyrimidine-6-yl phenyl ketone (5d)

Anal. Calcd for $C_{21}H_{17}N_3O_2S$: C, 67.19; H, 4.57; N, 11.20; S, 8.53. Found: C, 67.22; H, 4.55; N, 11.23; S, 8.46.

5-Amino-4-phenyl-2-propoxythieno[2,3-*d*]pyrimidine-6-yl methyl ketone (5e)

Anal. Calcd for $C_{17}H_{17}N_3O_2S$: C, 62.37; H, 5.24; N, 12.84; S, 9.78. Found: C, 62.26; H, 5.24; N, 12.84; S, 9.86.

5-Amino-2-methoxy-4-phenylthieno[2,3-*d*]pyrimidine-6-carboxamide (5f)

Anal. Calcd for $C_{14}H_{12}N_4O_2S$: C, 56.00; H, 4.03; N, 18.66; S, 10.66. Found: C, 55.92; H, 4.08; N, 18.58; S, 10.37.

2-Oxo-4-phenylcarbonylmethylthio-6-phenyl-1*H*-pyrimidine-5-carbonitrile (6)

Phenacyl bromide (2.0 g, 10 mmol) was added to a stirred suspension of **3** (2.3 g, 10 mmol) and potassium carbonate (1.4 g, 10 mmol) in ethanol (20 mL), and the mixture was stirred at 60 °C for 1 h. After cooling, the mixture was diluted with water (120 mL) and acidified with acetic acid (5 mL). The obtained precipitate was filtered off. Yield: 2.3 g (66 %), mp 299-302 °C (n-propanol); ^{13}C NMR (DMSO-d_6) δ 175.52 (s, C1), 87.42 (s, C2), 162.85 (s, C3), 152.60 (s, C4), 114.81 (s, C5), 38.10 (t, C6), 192.30 (s, C7), 135.71, 129.42 (s, C8 and C12), 128.92, 128.80, 128.42 (d, C9, C11, C13, and C14), 133.78, 132.47 (d, C11 and C15) ppm; Anal. Calcd for $C_{19}H_{13}N_3O_2S$: C, 65.69; H, 3.77; N, 12.10; S, 9.23. Found: C, 65.97; H, 3.78; N, 11.97; S, 9.03.

5-Amino-2-oxo-4-phenyl-3*H*-thieno[2,3-*d*]pyrimidin-6-yl phenyl ketone (7)

6 (1.7 g, 5 mmol) was dissolved in a sodium ethoxide solution (prepared from sodium (0.35 g, 15 mmol) and ethanol (25 mL)) and held at a bath temperature of 110 °C for 30 min. After cooling, the mixture was diluted with water (50 mL), acidified with acetic acid (5 mL) and the precipitate filtered off. Yield: 1.3 g (75 %), mp 329-332 °C (ethanol); MS: $C_{19}H_{13}N_3O_2S$ m/z = 347; ^{13}C NMR (DMSO-d_6) δ 174.35 (s, C1), 106.16 (s, C2), 166.04 (s, C3), 152.84 (s, C4), 166.32 (s, C5), 96.05 (s, C6), 186.18 (s, C7), 142.05, 138.32 (s, C8 and C12), 128.75, 128.26, 127.90, 127.02 (d, C9, C10, C13, and C14), 130.16, 129.42 (d, C11 and C15) ppm.

2-Ethoxy-4-methylthio-6-phenylpyrimidin-5-carbonitrile (8a)

2b (5 g, 20 mmol) was suspended in 2 N sodium hydroxide solution (70 mL). Subsequently, dimethyl sulphate (2.5 g, 20 mmol) was added dropwise to this suspension. The obtained solution was stirred for 2 h and the precipitate collected by filtration afterwards. Yield: 4.1 g (76 %), mp 121-123 °C (ethanol); ^{1}H NMR (DMSO-d_6) δ 7.6 (m, 5H, phenyl-H), 4.5 (q, J = 8 Hz, 2H, CH_2), 1.4 (t, J = 8 Hz, 3H, CH_3) ppm; ^{13}C NMR (DMSO-d_6) δ 184.84 (s, C1), 104.30 (s, C2), 157.14 (s, C3), 166.69 (s, C4), 135.04 (s, C5), 128.76, 128.34 (d, C6 and C7), 132.16 (d, C8), 115.66 (s, C9), 65.76 (t, C10), 13.86 (q, C11) ppm; Anal. Calcd for $C_{14}H_{13}N_3OS$: C, 61.97; H, 4.83; N, 15.49; S, 11.82. Found: C, 61.90; H, 4.92; N, 15.42; S, 11.77.

2-Isopropoxy-4-methylthio-6-phenylpyrimidine-5-carbonitrile (8b)

2d (5.43 g, 20 mmol) was suspended in 2 N sodium hydroxide solution (70 mL). Subsequently, dimethyl sulphate (2.5 g, 20 mmol) was added dropwise to this suspension. The obtained solution was stirred for 2 h and the precipitate collected by filtration afterwards. Yield: 5.2 g (91 %), mp 131-133 °C (i-propanol); ^{1}H NMR (DMSO-d_6) δ 8.0 (d, J = 7 Hz, 2H, phenyl-H), 7.5-7.7 (m, 3H, phenyl-H), 5.4 (heptet, J = 7 Hz, 1H, CH), 2.7 (s, 3H, SCH_3), 1.4 (d, J = 7 Hz, 6H, $2CH_3$) ppm; ^{13}C NMR (DMSO-d_6) δ 177.14 (s, C1),

95.76 (s, C2), 162.94 (s, C3), 169.05 (s, C4), 115.47 (s, C5), 135.05 (s, C6), 128.71 (d, C7), 128.76 (d, C8), 131.69 (d, C9), 71.84 (d, C10), 21.56 (q, C11 and C11′), 12.77 (q, C12) ppm; Anal. Calcd for $C_{15}H_{15}N_3OS$: C, 63.13; H, 5.30; N, 14.72; S, 11.24. Found: C, 63.37; H, 5.53; N, 14.82; S, 11.23.

4-Methylthio-2-(morpholino-4-yl)-6-phenylpyrimidine-5-carbonitrile (9a)

8a (1.36 g, 5 mmol) was dissolved in morpholine (8 mL) and heated to reflux for 1.5 h. After cooling, the mixture was poured into water (50 mL), allowed to stand for 12 h and the slurry of crystallised material decanted from the aqueous mixture. After trituration with ethanol, **9a** was recrystallised from ethyl acetate. Yield: 1.0 g (64 %), mp 190-195 °C (ethyl acetate); ^{1}H NMR ($CDCl_3$) δ 7.9-8.0 (d, J = 7 Hz, 2H, phenyl-H), 7.40-7.6 (m, 3H, phenyl-H), 3.7-3.9 (t, J = 7 Hz, 4H, $N(CH_2)_2$), 3.9-4.0 (t, J = 7 Hz, 4H, $O(CH_2)_2$) ppm; ^{13}C NMR ($CDCl_3$) δ 175.26 (s, C1), 158.81 (s, C2), 90.91 (s, C3), 167.65 (s, C4), 116.74 (s, C5), 136.22 (s, C6), 128.68 (d, C7), 129.07 (d, C8), 131.05 (d, C9), 12.85 (q, C10), 44.30 (t, C11 and C11′), 66.64 (t, C12 and C12′) ppm; Anal. Calcd for $C_{16}H_{16}N_4OS$: C, 61.52; H, 5.16; N, 17.93; S, 10.26. Found: C, 61.88; H, 5.27; N, 17.94; S, 9.09.

2,4-Bis(pyrrolidino-1-yl)-6-phenylpyrimidine-5-carbonitrile (9b)

8a (1.36 g, 5 mmol) was dissolved in pyrrolidine (8 mL) and heated to reflux for 1 h. After cooling, the mixture was poured into water (50 mL), allowed to stand for 12 h, and the crystallised material collected by filtration. Yield: 0.7 g (44 %), mp 183-188 °C (ethyl acetate); ^{1}H NMR ($CDCl_3$) δ 7.8-7.9 (m, 2H, phenyl-H), 7.4-7.5 (m, 3H, phenyl-H), 3.8-3.9 (m, 4H, NCH_2), 3.6 (d, J = 7 Hz, 4H, NCH_2), 1.9-2.1 (m, 8H, CH_2CH_2) ppm; ^{13}C NMR (DMSO-d_6) δ 170.87 (s, C1), 160.43 (s, C2), 75.62 (s, C3), 158.05 (s, C4), 120.16 (s, C5), 137.84 (s, C6), 128.13 (d, C7), 128.78 (d, C8), 130.22 (d, C9), 48.53 and 46.39 (t, C10 and C12), 24.90 and 24.57 (t, C11 and C13) ppm; Anal. Calcd for $C_{19}H_{21}N_5$: C, 71.44; H, 6.63; N, 21.93. Found: C, 71.21; H, 6.78; N, 22.09.

4-Cyclohexylamino-2-ethyloxy-6-phenylpyrimidine-5-carbonitrile (9c)

8a (1.36 g, 5 mmol) was dissolved in cyclohexylamine (8 mL) and heated to reflux for 1.5 h. After cooling, the mixture was poured into water (50 mL), allowed to stand for 12 h, and the crystallised material collected by filtration. Yield: 0.7 g (43 %), mp 198-202 °C (acetonitrile); ^{1}H NMR ($CDCl_3$) δ 7.9-8.0 (d, J = 7 Hz, 2H, phenyl-H), 7.4-7.6 (m, 3H, phenyl-H), 5.5-5.6 (d, J = 10 Hz), 1H, NH), 4.0-4.2 (m, 1H, CH), 4.5 (q, J = 8 Hz, 2H, OCH_2), 1.4 (t, J = 8 Hz, 3H, CH_3), 1.1-2.1 (m, 10H, $(CH_2)_5$) ppm; ^{13}C NMR ($CDCl_3$) δ 170.09 (s, C1), 165.46 (s, C2), 81.95 (s, C3), 164.05 (s, C4), 117.05 (s, C5), 136.27 (s, C6), 128.53, 128.47 (d, C7 and C8), 131.10 (d, C9), 14.45 (q, C10), 63.81 (t, C11), 50.06 (d, C12), 32.83 (t, C13 and C13′), 24.71 (t, C14 and C14′), 25.45 (t, C15) ppm; Anal. Calcd for $C_{19}H_{22}N_4O$: C, 70.78; H, 6.88; N, 17.38. Found: C, 71.05; H, 7.02; N, 17.48.

2-Isopropoxy-4-(morpholino-4-yl)-6-phenylpyrimidine-5-carbonitrile (9d)

8c (1.43 g, 5 mmol) was dissolved and heated to reflux in a mixture of morpholine (15 mL) and i-propanol (15 mL) for 2 h on an oil-bath temperature of 170 °C. The volatile components of the mixture were distilled off *in vacuo* and the residue was recrystallized twice with i-propanol.

Yield: 1.0 g (62 %), mp 140-144 °C (i-propanol); ^{1}H NMR (DMSO-d_6) δ 7.9 (d, J = 7 Hz, 2H, phenyl-H), 7.5-7.65 (m, 3H, phenyl-H), 5.25 (heptet, J = 7 Hz, 1H, CH), 3.9 (t, J = 7 Hz, 4H, $2OCH_2$), 3.7 (t, J = 7 Hz, 4H, $2NCH_2$), 1.4 (d, J = 7 Hz, 6H, $2CH_3$) ppm; ^{13}C NMR (DMSO-d_6) δ 173.37 (s, C1), 82.11 (s, C2), 163.55 (s, C3), 164.76 (s, C4), 118.16 (s, C5), 136.45 (s, C6), 128.38 (d, C7), 129.11 (d, C8), 131.13 (d, C9), 71.84 (d, C10), 21.66 (q, C11), 47.15 (t, C12), 65.89 (t, C13) ppm; Anal. Calcd for $C_{18}H_{20}N_4O_2$: C, 66.65; H, 6.21; N, 17.27. Found: C, 66.81; H, 6.55; N, 17.30.

3-Amino-6-hydrazino-4-phenylpyrazolo[3,4-*d*]pyrimidine (11)

8a (1.36 g, 5 mmol) was heated to reflux in hydrazine hydrate solution (5 mL, 80 %) for 3 h. The precipitate was filtered off and dissolved in 10 % sodium hydroxide solution for purification. **11** was obtained as precipitate on addition of acetic acid and recrystallized from n-propanol. Yield: 0.9 g (75 %), mp 241-244 °C (n-propanol); ^{1}H NMR (DMSO-d_6) δ 11.9 (s, 1H, NH), 8.2 (s, 1H, NH), 7.7-7.9 (m, 2H, phenyl-H), 7.4-7.6 (m, 3H, phenyl-H), 4.5-4.7 (s, 2H, NH_2), 4.0-4.4 (s, 2H, NH_2) ppm; IR: 1605, 3100-3400 (br), 3460 cm^{-1}; Anal. Calcd for $C_{11}H_{11}N_7$: C, 54.70; H, 4.59; N, 40.64. Found: C, 54.84; H, 4.65; N, 40.16.

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Received, 19th January, 1998