Synthesis and Reactions of 6-Methylsulfanyl-2,4-dithioxo-1,2,3,4-tetrahydropyrimidin-5-carbonitrile

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The synthesis of 6-methylsulfanyl-2,4-dithioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile **4** is described. Compound **4** was reacted with various alkylants. The reaction with chloroacetic acid derivatives results in the formation of thieno[2,3-*d*]pyrimidines **8.** When methyl iodide was used 2,4,6-tris(methylsulfanyl)pyrimidine-5-carbonitrile **5** was obtained. The substitution of the methylsulfanyl groups in compound **5** by several *N*-nuclophiles leads to amino substituted pyrimidines.

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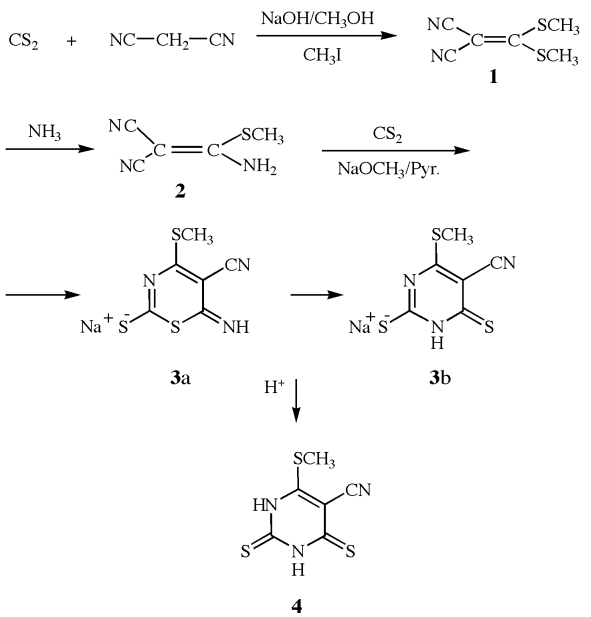
The pyrimidine ring system is found in many pharmaceuticals, herbicides and fungicides [1]. On the other hand pyrimidines, especially those with an appropriate substitution pattern, are of synthetic value for the preparation of condensed heterocycles [2]. Continuing with our work on pyrimidines we found a new and short procedure to the highly functionalised 6-methylsulfanyl-2,4-dithioxo-1,2,3,4-tetrahydropyrimidin-5-carbonitrile. On the basis of this very efficient synthetic method we investigated the reactivity of this heterocyclic compound towards electrophiles and nucleophiles in order to obtain other new heterocyclic systems.

Thus, the reaction of dicyano ketene mercaptale **1**, prepared commonly from malononitrile, carbon disulfide and an alkylating reagent with ammonia yields compound **2**

Scheme 1



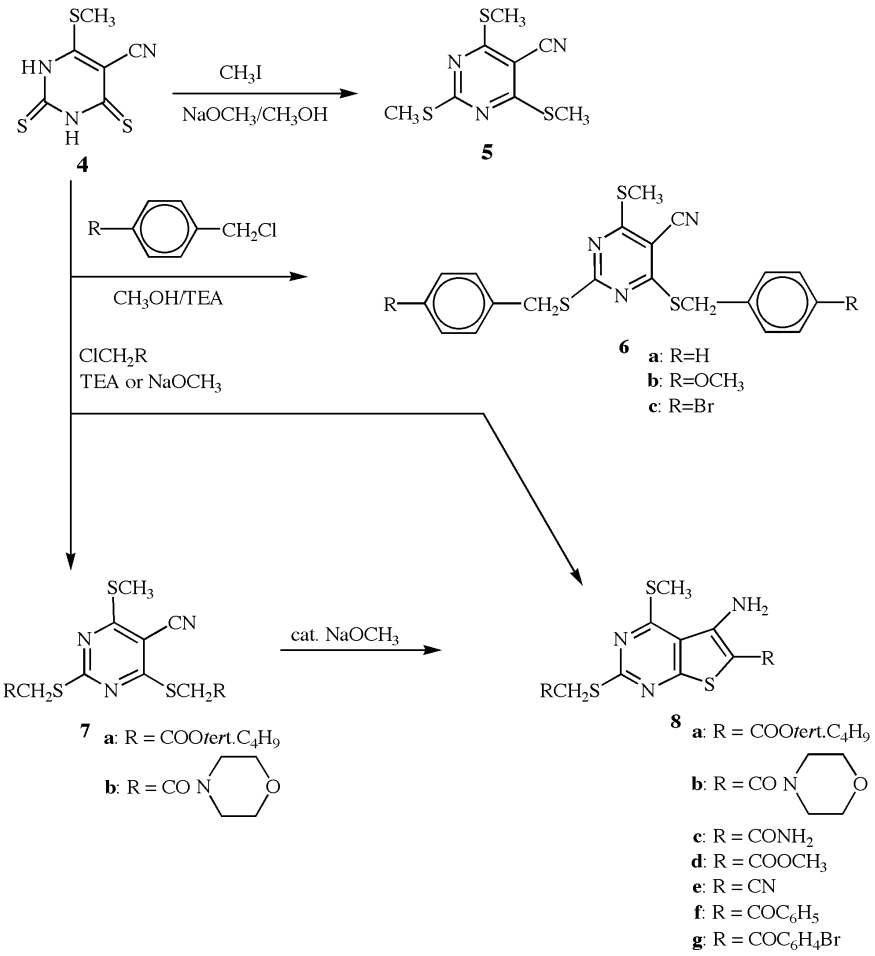
[3]. After treating this substance with carbon disulfide and sodium methoxide in pyridine the 6-methylsulfanyl-2,4-dithioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile **4** was isolated after acidic work up. The reaction of **2** with acid chlorides also yields pyrimidine a carbonitrile but with only one alkylthiosubstituent [4].

Beside the alkylated thiofunction in position 6 of the pyrimidine ring skeleton the compound **4** possesses two other SH acidic groups with potentially different reactivity. Therefore we studied the reactions of 6-methylsulfanyl-2,4-dithioxo-1,2,3,4-tetrahydropyrimidin-5-carbonitrile (**4**) with a series of alkylating reagents. Treatment of **4** with an excess of methyl iodide and two equivalents of sodium methoxide in methanol yields exclusively the 2,4,6-tris(methylsulfanyl)pyrimidin-5-carbonitrile (**5**).

However, by changing the methoxide base against triethylamine under the same conditions the reaction was not homogenous. A mixture of **5** and the bis-alkylated pyrimidines were isolated. Compared to that result the reaction of **4** with benzyl chlorides and triethylamine afforded the pyrimidines **6** without problems. Pyrimidin-5-carbonitriles with alkylthio groups in the 2,4 (and 6) position of the pyrimidine ring skeleton were prepared in an multistep procedure [5,6] starting from thiobarbituric acid according to the method of Klotzer *et al*. [7].

Alkylants containing an electron withdrawing group in α-position make the products suitable for cyclization reactions to thieno[2,3-*d*]pyrimidines. These compounds represent a class of heterocycles with interesting properties. There already exist a number of syntheses to these substances starting from pyrimidines [8a-f], but with different substituents compared with the substances described below. First we have investigated the reaction of compound **4** with some 2-chloroacetic acid derivatives and phenacyl bromides under different conditions. The reaction of **4** with 2-chloroacetic acid methyl ester and triethylamine or sodium methoxide afforded the thieno[2,3-*d*]-

Scheme 2

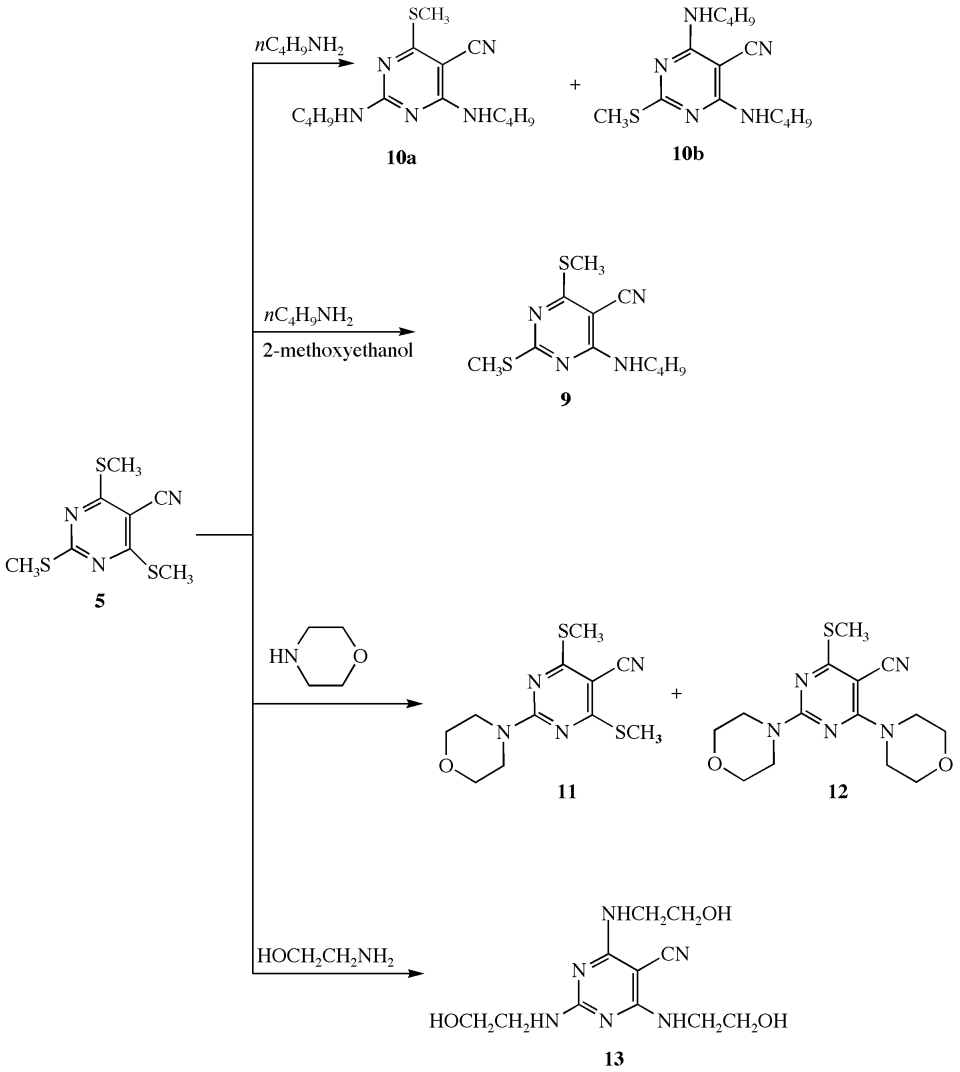


pyrimidine **8d** under mild conditions. The monocyclic product was not detected. On the other hand, the alkylation reaction with 2-chloroacetic acid *tert*-butylester using triethylamine as base yielded a mixture of monocyclic and bicyclic pyrimidine derivatives **7a** and **8a**, which are shown in nmr- and ir spectra. Addition of catalytic amounts sodium methoxide to the mixture afforded the thienopyrimidine only. However, the application of the methoxide base from the beginning of the alkylation reaction results in the formation of **8a** without the pyrimidine **7a**. In the reaction of **4** with chloroacetonitrile and sodium methoxide only decomposition products were formed. By using triethylamine the thienopyrimidine **8e** was isolated conveniently. Beside the reaction with stronger activated alkylants of the chloroacetic acid derivatives we have investigated the reaction between **4** and chloroacetic acid amides. So the 5-cyano-6-methylsulfanyl pyrimidine-2,4-bis(2-thiaacetic acid morpholide) (**7b**) was isolated with TEA as base. Application of sodium methoxide yielded again the thienopyrimidine product **8b**. The synthesis of this compound is also possible in a two-step process by transforming **7b** into **8b** using catalytic amounts sodium methoxide. The reaction of pyrimidine **4** with 2-chloroacetamide afforded with the strong methoxide base compound **8c** only. More complicated was the reaction of **4** and phenacylbromides with triethylamine yielding a mixture of mono and bis-alkylated products as well as monocylic pyrimidines and thienopyrimidines. The same situation was observed under sodium methoxide catalysis. Better results with thienopyrimidines were obtained by changing the solvent from methanol to chloroform. However the application of a two step process with triethylamine in the first step followed by the cyclization with catalytic amounts of sodium methoxide provided the best results, yielding the compounds **8f** and **8g**.

To further investigate the reactivity of the highly functionalised pyrimidine **5** was treated with representative amines under different reaction conditions (Scheme 3). Amino substituted pyrimidin-5-carbonitriles were prepared commonly starting from the corresponding chloro compounds [9] or by cyclisation reactions of 1,1 diamino-2,2-dicyanoethylene derivates [10-12].

The aim of our work was to find conditions for selective substitution of the alkylthio groups. In a first approach we

Scheme 3



have used *n*-butylamine in 2-methoxyethanol, which affords a mixture of products. The chromatographic separation of the main product yields compound **9** in 51% yield. After heating compound **5** in pure *n*-butylamine the dibutylamino product was isolated by chromatography in 53% yield. However, the nmr- spectroscopic investigation indicates a mixture of **10a** and **10b**.This is due to two different signals for the methylsulfanyl group both in ^{1}H nmr and ^{13}C nmr spectra.

The reaction with the secondary amine morpholine was carried out under the same conditions, that means in pure reagent and in solution of 2-methoxyethanol. Heating of compound **5** in morpholine for 10 hours affords a mixture of two substances, which were separated by chromatrography. Compound **11** represents a substance, in which only one methylsulfanyl group was replaced by the morpholine. The structure elucidation is based on mass spectra and elemental analysis and the interpretation of nmr spectra. Only one peak at 2.52 ppm in the ^{1}H nmr spectra, was found for the methylsulfanyl group indicating the symmetric structure of compound **11**. Similarly, in the ^{13}C nmr the resonance corresponding to the methylsulfanyl group is at 13.16 ppm. The substitution pattern in the compound **12** was evidenced by ^{13}C nmr. According to a substitution in the 4 and 6 position of the pyrimidine the molecule is symmetric, however two different values for C4 and C6 were found. This indicates that the product must be the unsymmetric one. A different result was obtained from the reaction of **5** with morpholine in 2-methyloxyethanol. After heating 20 hours in boiling solvent the starting material was detected in addition to compounds **11** and **12**, but in an reverse ratio, in contrast to the reaction with pure morpholine.

The third nucleophile used in our investigations was 2-aminoethanol. According to the strong nucleophilic power the reaction in pure reagent was always concluded within 5 hours. The resulting product was easily soluble in

water so that the isolation, especially the extraction with an organic solvent was difficult. So, after work up, the water was evaporated, the crude product isolated and purified by column chromatography. In contrast to the reaction with butylamine and morpholine the reaction of **5** in 2-aminoethanol afforded compound **13** only in which all methylsulfanyl groups are substituted by a nitrogen atom.

EXPERIMENTAL

Melting points were taken with a Boetius apparatus and are uncorrected. The ^{1}H nmr spectras have been recorded on a Bruker AC 500 using tetramethylsilane as internal reference. Chemical shifts are given in ppm and coupling constants in Hz. Mass spectrometric data were obtained on an AMD 402 (70 eV) spectrometer (Intecta GmbH, Harpstedt). Elemental analyses were performed with a CHNS-932 apparatus (LECO-Corporation, St Joseph, Michigan USA). Infrared spectra were obtained on a Spekol 1200 (Carl Zeiss), using KBr technique. UV/vis spectroscopy was performed using a Perkin Elmer Spectrum BX with acetonitrile as solvent.

The chloroacetic acid amides were prepared according to literature [13]. The phenacyl-bromides were purchased from Aldrich.

1,2,3,4-Tetrahydro-6-(methylsulfanyl)-2,4-dithioxopyrimidincarbonitrile (**4**).

Compound **2** (0.97 g, 7 mmol) was suspended with cooling in 2 ml of a 5 *M* solution of sodium methoxide in methanol and 2 ml pyridine. After adding 2 ml of carbon disulfide the mixture was allowed to stand 7 days at room temperature. After that time 20 ml of 1 *M* hydrochloric acid were added and the product was collected by suction filtration and recrystallized from DMF/water. 0.82 g (55%) yellow crystals, mp. 230° C dec.; ^{1}H nmr (DMSO-d_6): δ 2.94 (s, 3H, CH_3); ms:m/z 215 (M^+).

*Anal.*Calcd. for $C_6H_5N_3S_3$: C, 33.47; H, 2.34; N, 19.52; S, 44.67. Found: C, 33.87; H, 2.32; N, 19.21; S, 44.28.

2,4,6-Tris(methylsulfanyl)pyrimidine-5-carbonitrile (**5**).

To a suspension of compound **4** (0.32 g, 1.5 mmol) in 15 ml methanol was added a 5 *M* solution of sodium methoxide in methanol (0.9 ml, 4.5 mmol) and methyl iodide (0.4 ml, 6 mmol). After 1 hour the precipitated product was collected by suction filtration and recrystallized from 2-methoxyethanol; 0.18 g (49%), mp 150-152°; ^{1}H nmr (deuderiochloroform): δ 2.45 (s, 6H, 2xCH_3), 2.52 (s, 3H, CH_3); ms: m/z 243 (M^+).

Anal. Calcd. for $C_8H_9N_3S_3$: C, 39.48; H, 3.72; N, 17.27; S, 39.52. Found: C, 39.23; H, 3.69; N, 17.52; S, 39.81.

General Reaction of **4** with Benzyl Chlorides.

To compound **4** (0.43 g, 2 mmol) in 10 ml dry methanol were added 0.6 ml (4 mmol) TEA and 0.48 ml (4 mmol) benzyl chloride. The reaction mixture was allowed to stir for 3 days at room temperature. The white precipitate was collected by suction filtration and recrystallized from 2-methoxyethanol.

2,4-Di(benzylsulfanyl)-6-methylsulfanylpyrimidin-5-carbonitrile (**6a**).

Compound 6 was obtained in 57% yield (0.45 g); mp 96-97°; ir: 3456, 3060, 3028, 2975, 2932, 2209 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.4 (s, 3H, CH_3), 4.0 and 4.4 (2s, 4H, 2x-CH_2-), 7.2-7.4 (m, 10H, arom.); ms: m/z 395 (M^+, 81%).

Anal Calcd. for $C_{20}H_{17}N_3S_3$: C, 60.73; H, 4.33; N, 10.62; S, 24.31. Found: C, 60.75; H, 4.51; N, 10.56; S, 24.02.

2,4-Bis(*p*-methoxybenzylsulfanyl)-6-methylsulfanyl-pyrimidin-5-carbonitrile (**6b**).

Compound 6b was obtained in 57% yield (0.52 g), mp 138-139°, ms: m/z 455 (M^+,32%), ir: 3441, 2210 cm^{-1}; ^{1}H nmr (deuteriochhloroform): δ 2.6 (s, 3H, CH_3), 3.8 (s, 6H, 2x-OCH_3), 4.1 and 4.4 (2s ,4H, 2x-CH_2-), 7.2-7.3 (m, 8H, arom.).

Anal. Calcd. for $C_{22}H_{21}N_3O_2S_3$: C, 57.99; H, 4.65; N, 9.22; S, 21.11. Found: C, 57.97; H, 4.77; N, 9.18; S, 20.9.

2,4-Bis(*p*-brombenzylsulfanyl)-6-methylsulfanylpyrimidin-5-carbonitrile (**6c**).

Compound **6c** was obtained in 60% yield (0.66 g) mp 170-172°, ir: 2211 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.5 (s, 3H, CH_3), 4.0 and 4.4 (2s, 4H, 2x-CH_2-), 7.2-7.4 (m, 8H, arom.); ms: m/z 553 (M^+,48%).

*Anal.*Calcd. for $C_{20}H_{15}Br_2N_3S_3$: C, 43.41; H, 2.73; N, 7.59; S, 17.38. Found: C, 43.12; H, 2.73; N, 7.48; S, 17.72.

2,4-Bis(morpholinocarbonylmethylsulfanyl)-6-methylsulfanylpyrimidin-5-carbonitrile (**7b**).

Compound **5** (0.43 g, 2 mmol) was dissolved in 10 ml dry methanol, then 0.6 ml (4 mmol) TEA and 0.65 g (4 mmol) 2-chloroacetic acid morpholide were added. The precipitate was collected and recrystallized from 2-methoxyethanol; 0.44 g (47%), mp 172-174°, ms: m/z 469 (M^+, 31%) ir: 3436, 2962, 2923, 2859, 2211, 1620, 1500, 1480 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.55 (s, 3H, SCH_3), 3.5-3.7 (m 16H, -N(C_2H_2)$_2$O), 4.1 and 4.15 (2s, 4H, -CH_2-).

Anal. Calcd. for $C_{18}H_{23}N_5O_4S_3$: C, 46.04; H, 4.93; N, 14.91; S, 20.48. Found: C, 46.12; H, 4.91; N, 14.39; S, 20.36.

General Procedure for the Synthesis of Thienopyrimidines (**8a-d**).

To 2 mmol of the pyrimidine **4** in 10 ml dry methanol was added 4 mmol (0.8 ml) sodium methoxide (5 *M*) and 4 mmol of the 2-chloroacetic acid derivative at room temperature. After 2 days the yellow precipitate was collected by suction filtration and recrystallized from acetonitrile or 2-methoxyethanol.

5-Amino-2[(*tert*-butyloxycarbonyl)methylsulfanyl]4-methylsulfanylthieno[2.3-*d*]pyrimidin-6-carboxylic Acid *tert*-Butylester (**8a**).

Compound **8a** was obtained in 48% yield (0.42 g), mp 106-108 °C; ir: 3498, 3397, 2977, 2931, 1731, 1668, 1599 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.55, 1.44 (2s, 18H, 2x tert.C_4H_9), 2.69 (s, 3H, SCH_3), 3.86 (s, 2H, -CH_2-), 7.24 (s, 2H, NH_2); ms: m/z 443 (M^+, 4%).

Anal. Calcd. for $C_{18}H_{25}N_3O_4S_3$: C, 48.74; H, 5.68; N, 9.47; S, 21.68. Found: C, 48.97; H, 5.65; N, 9.24; S, 21.79.

5-Amino-4-methylsulfanyl-2(morpholinocarbonylmethylsulfanyl)thieno[2,3-*d*]pyrimidin-6-carboxylic Acid Morpholid (**8b**).

Compound **8b** was obtained in 56% yield (0.52 g); mp 225-227 °C; ir: 4327, 2967, 2924, 2854, 1641, 1567, 1517, 1432 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.5 (s, 3H, SCH_3), 4.4 (d, 4H, 2x –CH_2-), 7.2-7.4 (m 8H, arom.); ms: m/z 469 (M^+, 100%).

Anal. Calcd. for $C_{18}H_{23}N_5O_4S_3$: C, 46.04; H, 4.94; N, 14.91; S, 20.48. Found: C, 46.12; H, 4.91; N, 14.39; S, 20.36.

5-Amino-2-carbamoylmethylsulfanyl-4-methylsulfanylthieno[2,3-*d*]pyrimidin-6-carboxylic Acid Amide (**8c**).

Compound **8c** was obtained in 55% yield (0.36 g); mp. 257-259 °C; ir: 3349, 2970, 1684, 1645, 1589, 1527, 1434 cm^{-1}; ms: m/z 329 (M^+, 100%).

Anal. Calcd. for $C_{10}H_{11}N_5S_3O_2$: C, 36.46; H, 3.36; N, 21.26; S, 29.20. Found: C, 37.04; H, 3.45; N, 21.15; S, 28.56.

5-Amino-2-methoxycarbonylsulfanyl-4-methylsulfanylthieno-[2,3-*d*]pyrimidin-6-carboxylic Acid Methyl Ester (**8d**).

Compound **8d** was obtained in 37% yield (0.27 g); mp. 173-175 °C; ir: 3454, 3343, 2950, 2921, 1737, 1673, 1602, 1510, 1472 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.7 (s, 3H, SCH_3), 3.74 (s, 3H, $COOCH_3$), 3.84 (s, 3H, $COOCH_3$), 3.98 (s, 2H, -CH_2-), 7.24 (s, 2H, NH_2); ms: m/z 359 (M^+, 100%).

Anal. Calcd. for $C_{12}H_{13}N_3O_4S_3$: C, 40.10; H, 3.65; N, 11.69; S, 26.76. Found: C, 40.11; H, 3.69; N, 11.62; S, 26.69.

5-Amino-2-cyanomethylsulfanyl-4-methylsulfanylthieno[2,3-*d*]-pyrimidin-6-carbonitrile (**8e**).

To a suspension of 0.43 g (2 mmol) of compound **4** 0.6 ml (4 mmol) TEA and 0.25 ml (4 mmol) chloracetonitrile were added at room temperature. After 5 hours the yellow precipitate was collected and recrystallized from 2-methoxyethanol or acetonitrile to yield 0.32 g (54%), mp. 246-247 °C; ms: m/z 293 (M^+, 100%); ir: 3444, 3343, 3230, 3007, 2983, 2910, 2198 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.75 (s, 3H, SCH_3), 4.33 (s, 2H, -CH_2-), 6.67 (s, 2H, NH_2).

Anal. Calcd. for $C_{10}H_7N_5S_3$: C, 40.94; H, 2.41; N, 23.87; S, 32.79. Found: C, 40.78; H, 2.43; N, 23.88; S, 32.71.

Procedure for the Conversion of **7b** into **8b**.

Compound **7b** (1.5 g, 3.2 mmol) were suspended in 30 ml ethanol. After addition of five drops of a 5 *M* solution of sodium methoxide in methanol the mixture was stirred 20 minutes at room temperature. The reaction was allowed to stand over night at that temperature and the product was collected by suction filtration, washed three times with 20 ml water and 3 ml methanol an dried *in vacuo*. After recrystallization from 2-methoxyethanol, 1.43 g (95%) of **8b** was isolated.

General Procedure for the Synthesis of 5-Amino-2-(2-aryl-2-oxoethylsulfanyl)-4-methylsulfanylthieno[2,3-*d*]pyrimidin-6-yl)-phenyl-ketones (**8f**, **8g**).

Compound **4** (0.43g, 2 mmol) were suspended in 10 ml dry methanol, then 0.6 ml TEA (4 mmol) and 4 mmol of the phenacyl bromide were added. After 15 minutes the product, which consists of two substances, was isolated by filtration. A 100 mg sample of this mixture was suspended in 5 ml methyl glycol, then 5 drops of a 5 *M* solution of sodium methoxide was added and the mixture was stirred for 1 hour at room temperature. The pure thienopyrimidines **8f** and **8g** were isolated and recrystallized from 2-methoxyethanol.

{5-Amino-4-methylsulfanyl-2-(2-phenyl-2-oxoethylsulfanyl)-thieno[2,3-*d*]pyrimidin-6-yl}phenyl ketone (**8f**).

Compound **8f** was obtained in 33% yield (0.3 g); mp 174-175 °C; ms: m/z 451 (M^+, 64%); ir: 3450, 3059, 2908, 1682, 1593, 1515, 1447 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.63 (s, 3H, SCH_3), 4.68 (s, 2H, -CH_2-), 7.24 (s, 2H, NH_2), 7.41-8.04 (m, 10H, arom.).

Anal. Calcd. for $C_{22}H_{17}N_3O_2S_3$: C,58.51; H, 3.79; N, 9.30; S, 21.30. Found: C, 58.65; H, 3.84; N, 9.15; S, 21.09.

{5-Amino-2[2-(*p*-bromophenyl)-2-oxoethylsulfanyl]-4-methylsulfanylthieno[2,3-*d*]pyrimidin-6-yl}-6-bromophenyl ketone (**8g**).

Compound **8g** was obtained in 48% yield (0.58 g); mp. 240-241 °C; ms: m/z 609 (M^+, 60%); ir: 3448, 2924, 1684 cm^{-1}.

Anal. Calcd. for $C_{22}H_{15}Br_2N_3O_2S_3$: C, 43.36; H, 2.48; N, 6.89; S, 15.78. Found: C, 43.14; H, 2.55; N, 6.37; S, 15.13.

4-Butylamino-2,6-bis(methylsulfanyl)pyrimidin-5-carbonitrile (**9**).

Compound **5** (0.24 g, 1 mmol) was dissolved in methyl glycol. Then 0.3 ml (3 mmol) *n*-butyl amine was added and the mixture was heated under reflux for 15 hours. The solution was diluted with 20 ml water, acidified with 3 *N* HCl and the mixture extracted 3 times with chloroform. After drying over calcium chloride the solvent was evaporated and the residue purified by column chromatography to give 0.14 g (51%), mp 90-93 °C; ms: m/z 268 (M^+, 69%); ir: 3381, 2957, 2927, 2854, 2203 cm^{-1}; ^1H nmr (deuteriochloroform): δ= 1.04 (t, 3H, -CH_3), 1.58 (m, 4H, -CH_2-CH_2-), 2.45 (s, 3H, SCH_3), 2.56 (s, 3H, SCH_3), 3.58 (m, 2H, -CH_2-NH-).

Anal. Calcd. for $C_{11}H_{16}N_4S_2$: C, 49.23; H, 6.01; N, 20.87; S, 23.89. Found: C, 49.13; H, 6.24; N, 19.10; S, 22.45.

2,4-Bis(butylamino)-6-methylsulfanylpyrimidin-5-carbonitril (**10a**) and 4,6-Bis(butylamino)-2-methylsulfanylpyrimidin-5-carbonitrile (**10b**).

Compound **5** (0.72 g, 3 mmol) was heated in 7.5 ml of *n*-butylamine for 10 hours. The reaction mixture was diluted with 100 ml water and acidified with 3 *N* HCl. The solution was extracted 3 times with chloroform and the combined extract dried and evaporated. The crude product was purified by chromatography to give 0.46 g (53%) (mixture of the isomers **10a** and **10b**); mp. 73-76 °C, ms: m/z 293 (M^+, 100%); ir: 3340, 2850-300, 2200 cm^{-1}; ^1H nmr (deuteriochloroform): δ 0.96 (t, 3H, -CH_3), 1.23 (t, 3H, -CH_3), 1.39 (m, 4H, -CH_2-CH_2-), 1.56 (m, 8H, -CH_2-CH_2-), 2.47 (s, 3H, SCH_3), 2.53 (s, 3H, SCH_3), 3.33 (m, 2H, -CH_2-NH-), 3.58 (m, 4H, -CH_2-NH-), 10.59 (m, 2H, -NH-), 10.89 (m, 2H, -NH-).

Anal. Calcd. for $C_{14}H_{23}N_5S$: C, 57.31; H, 7.90; N, 23.86; S, 10.92. Found: C, 57.38; H, 7.92; N, 22.24; S, 9.99.

Synthesis of 4,6-Bis(methylsulfanyl)-2-morpholino-pyrimidin-5-carbonitrile (**11**) and 6-Methylsulfanyl-2,4-dimorpholino-pyrimidin-5-carbonitrile (**12**).

Compound **5** (0.72 g, 3 mmol) of and 7.5 ml morpholine were heated 10 hours under reflux. The reaction mixture was diluted with 100 ml water and acidified with 3 *N* HCl then extracted three times with chloroform. The chloroform extracts were dried over calcium chloride and the solvent was removed *in vacuo*. The compounds **11** and **12** were separated by column chromatography (silica gel 60 Merck, 0.063-0.2 mm) with chloroform and methanol using gradient technique (starting from $CHCl_3$/MeOH=95:5, final polarity $CHCl_3$/MeOH=8:2).

Compound **11**.

Compound **11** was obtained in 11% yield (0.09 g); mp 224-225 °C; ms: m/z 282 (M^+, 100%); ir: 2977, 2927, 2865, 2195 cm^{-1}; ^1H

nmr (deuteriochloroform): δ= 2.52 (s, 6H, SCH_3), 3.78 (m, 4H, $-CH_2N$), 3.92 (m, 4H, $-CH_2O$); ^{13}C nmr (deuteriochloroform): δ 13.16, 44.91, 67.22, 113.25, 115.47, 158.14, 173.34.

Anal. Calcd. for $C_{11}H_{14}N_4OS_2$: C, 46.78; H, 5.00; N, 19.84; S, 22.71. Found: C, 46.81; H, 4.98; N, 19.74; S, 21.30.

Compound **12**.

Compound **12** was obtained in 32% yield (0.3 g); mp 176-178 °C, ms: m/z 321 (M^+, 100%); ir: 3455, 2991, 2967, 2920, 2865, 2195 cm^{-1}; ^1H nmr (deuteriochloroform): d 2.46 (s, 3H, SCH_3), 3.61 and 3.65 (m, 8H, $-CH_2N$), 3.72 and 3.75 (m, 8H, $-CH_2O$); ^{13}C nmr (DMSO-d_6): d 13.19, 44.69, 47.33, 66.69, 66.77, 76.31, 118.62, 158.70, 162.82, 175.94.

Anal. Calcd. for $C_{14}H_{19}N_5O_2S$: C, 52.31; H, 5.96; N, 21.79; S, 9.97. Found: C, 52.24; H, 5.95; N, 22.15; S, 9.87.

2,4,6-Tris(2-hydroxyethylamino)pyrimidin-5-carbonitril (**13**).

Compound **5** (0.72 g, 3 mmol) and 7.5 ml 2-aminoethanol were refluxed for 5 hours. The reaction mixture was diluted with 100 ml water and the solution extracted with 30 ml chloroform. The water phase was then evaporated. The residue was purified by column chromatography (silica gel 60, Merck, 0.063-0.2 mm) with chloroform and methanol using gradient technique to give 0.29g (34%); mp 113-117 °C; ms.: m/z 282 (M^+, 38%); ir: 3369, 2936, 2875, 2194 cm^{-1}.

Anal. Calcd. For $C_{11}H_{18}N_6O_3$: C, 46.80; H, 6.43; N, 29.77. Found: C, 46.98; H, 6.68; N, 28.99.

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