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The reaction of thiobenzamide with 3-alkoxy-3-aryl(or alkyl)-2-cyanopropenenitriles **1** and sodium 2-propoxide in 2-propanol afforded after acidic treatment 6-aryl(or alkyl)-5-cyano-2-phenyl-4-thioxo-3,4-dihydropyrimidines **3** through formation of the 3-aryl(or alkyl)-2-cyano-3-thiobenzamidopropenenitrile **2** that has been isolated in one case (**2a**, R<sup>1</sup> = Ph).

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General preparative methods for the synthesis of 4-thioxo-3,4-dihydropyrimidines have been reported [2-7]. Yamamoto and Muraoka [8] have recently described the synthesis of 2-aryl-4-thioxo-3,4-dihydropyrimidines from 1,3-thiazine-2,6-dithiones. In a previous paper [9] we achieved the formation of 5-cyano-2-methyl-4-thioxo-3,4-dihydropyrimidines from thioacetamide and 3-alkoxy-2-cyanopropenenitriles. Now we wish to report the synthesis of 6-aryl(or alkyl)-5-cyano-2-phenyl-4-thioxo-3,4-dihydropyrimidines (**3**) from thiobenzamide and 3-alkoxy-3-aryl(or alkyl)-2-cyanopropenenitriles (**1**). The reactions were performed by stirring at room temperature equimolar amounts of the propenenitriles **1** and thiobenzamide in 2-propanol with one molar equivalent of sodium 2-propoxide and further treatment with dilute hydrochloric acid. As side products we obtained the disulfides **4** resulting from the oxidation of pyrimidines **3**.

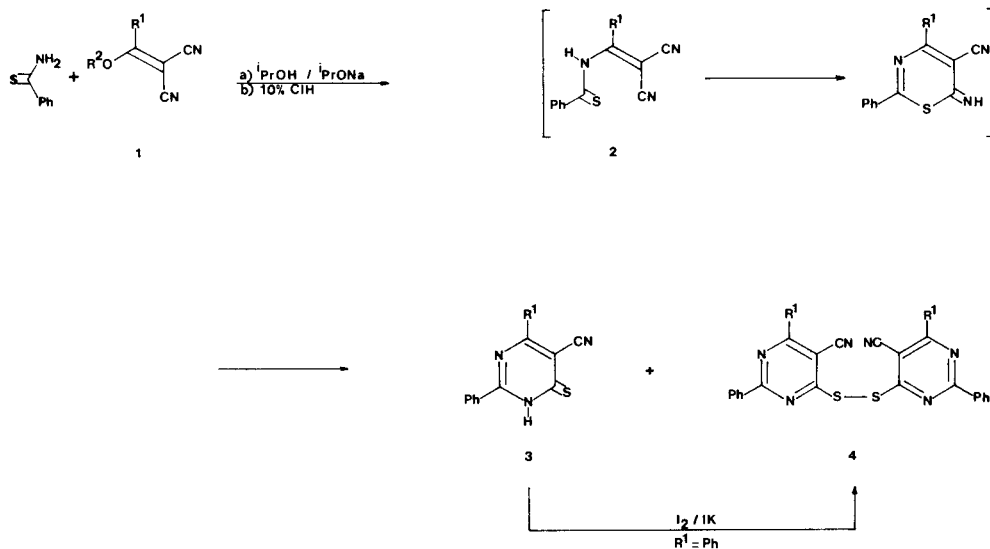
The reaction proceeds through formation of the 2-cyano-3-thiobenzamidopropenenitrile **2** that cyclizes to 6-imino-1,3-thiazine which rearranges [10] to the corresponding 4-thioxo-3,4-dihydropyrimidine **3**.

The structure of the 4-thioxopyrimidines **3** was confirmed by their transformation in 4-oxopyrimidines **6**, that were obtained from ethyl (*E*)-2-cyano-3-phenylpropenoate (**7**) and benzamidine.

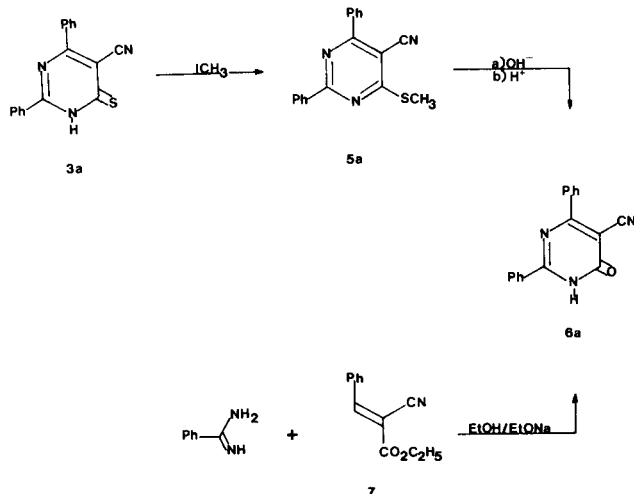
#### EXPERIMENTAL

Melting points were determined on a Büchi SMP-20 or a Bühler metal block (> 290°) and are uncorrected. The ir spectra were obtained as potassium bromide pellets using a Perkin Elmer 700. The pmr spectra were recorded on a Varian FT-80 A with TMS as internal Standard. Mass spectra were obtained on a Varian MAT 711 mass spectrometer at 70 eV. For the column chromatography silicagel 60 Merck was used.

Scheme 1



Scheme 2



The 3-alkoxy-3-aryl(or alkyl)-2-cyanopropenenitriles were prepared by the reported procedures [11-14].

6-Aryl(or alkyl)-5-cyano-2-phenyl-4-thioxo-3,4-dihydropyrimidines (3). General Procedure.

To a solution of sodium (69 mg) in dry 2-propanol (50 ml), thiobenzam-

ide (3 mmoles) and 3-aryl-2-cyano-3-methoxypropenenitrile **1** (2-cyano-3-ethoxy-2-butenitrile in the case **1e**) (3 mmoles) were added. The mixture was stirred at room temperature until tlc indicated complete consumption of the starting material and then was acidified with 10% hydrochloric acid. After a few hours solvent was removed *in vacuo* and the oil obtained treated with water, afforded a precipitate that was purified on a silicagel column and further recrystallization.

bis-(5-Cyano-2,6-diphenyl-4-pyrimidinyl) Disulfide (**4a**).

To a stirred mixture of 289 mg (1 mmole) of **3a** in 40 ml of ethanol, iodine and potassium iodide were added. The mixture was then stirred at room temperature for a few minutes. After the solvent was removed *in vacuo* and the residue was treated with water, collected, washed with water and recrystallized from dimethylsulfoxide, yield 80%, mp 285-286°; ir (potassium bromide): 2200, 1510, 1470, 1420, 1370  $\text{cm}^{-1}$ ; ms: (relative intensity) 576 ( $\text{M}^+$ , 92), 575 (100), 289 (94), 186 (85), 153 (94).

Anal. Calcd. for  $\text{C}_{34}\text{H}_{20}\text{N}_6\text{S}_2$ : C, 70.81; H, 3.50; N, 14.57; S, 11.12. Found: C, 71.08; H, 3.68; N, 14.41; S, 10.98.

2-Cyano-3-phenyl-3-thiobenzamidopropenenitrile (**2a**).

Thiobenzamide (274 mg, 2 mmoles) and 2-cyano-3-methoxy-3-phenylpropenenitrile (**1a**, 368 mg, 2 mmoles) were added to a solution of sodium (46 mg) in dry 2-propanol (40 ml). After 10 hours with stirring at room temperature the solvent was removed and the residue obtained, dissolved in water and acidified with 2% hydrochloric acid. The precipitate was collected and recrystallized from hexane-toluene, yield 69% mp 241-242°; ir (potassium bromide): 3200, 2190, 1570, 1550, 1515, 1480, 1460, 1425  $\text{cm}^{-1}$ ; pmr (acetone):  $\delta$  8.19-7.79 (m, aromatic, 4H), 7.69-7.29 (m, aromatic, 6H); ms: (relative intensity) 289 ( $\text{M}^+$ , 54), 262 (100), 186 (28), 159 (50), 153 (25).

Table

6-Aryl(or alkyl)-5-cyano-2-phenyl-4-thioxo-3,4-dihydropyrimidines **3**.

Compound No.	R <sup>1</sup>	Yield (%)	Mp (°C)	Recrystallization Solvent	Analysis % Found/(Calcd.)				IR ( $\nu$ $\text{cm}^{-1}$ )	NMR [a] ( $\delta$ values)
					C	H	N	S		
<b>3a</b>	$\text{C}_6\text{H}_5$	70	272-273 (253) [6]	ethanol/acetonitrile	70.32 (70.57)	3.97 (3.83)	14.66 (14.52)	11.05 (11.08)	3150 (NH), 2210 (CN), 1190 (C=S)	8.33-7.80 (m, aromatic, 4H), 7.71-7.27 (m, aromatic, 6H)
<b>3b</b>	$4\text{-H}_3\text{C-C}_6\text{H}_4$	82	266-267 (266.5-266.5) [8]	ethanol/acetonitrile	71.04 (71.25)	4.10 (4.32)	14.26 (13.85)	10.60 (10.57)	3150 (NH), 2220 (CN), 1190 (C=S)	8.34-8.03 (m, aromatic, 2H), 7.71-7.46 (m, aromatic, 3H), 7.91, 7.36 ( $\text{A}_2\text{B}_2$ , J = 8 Hz, aromatic, 4H), 2.40 (s, 3H, $\text{CH}_3$ )
<b>3c</b>	$2\text{-H}_3\text{C-C}_6\text{H}_4$	26	237-238	ethanol/acetonitrile	71.50 (71.25)	4.01 (4.32)	14.11 (13.85)	10.38 (10.57)	3200 (NH), 2200 (CN), 1180 (C=S)	8.34-7.90 (m, aromatic, 2H), 7.78-7.15 (m, aromatic, 7H), 2.34 (s, 3H, $\text{CH}_3$ )
<b>3d</b>	$3\text{-Cl-C}_6\text{H}_4$	61	228-229	ethanol/acetonitrile	63.22 (63.05)	3.58 (3.11)	12.80 (12.98)	9.89 (9.90)	3160 (NH), 2215 (CN), 1180 (C=S)	8.30-8.02 (m, aromatic, 2H), 8.02-7.80 (m, aromatic, 2H), 7.80-7.30 (m, aromatic, 5H)
<b>3e</b>	$\text{CH}_3$	10	233-234 (230) [5]	ethanol	63.04 (63.40)	4.04 (3.99)	18.86 (18.49)	14.06 (14.11)	3200 (NH), 2215 (CN), 1185 (C=S)	8.24-7.84 (m, aromatic, 2H), 7.84-7.34 (m, aromatic, 3H), 2.50 (s, 3H, $\text{CH}_3$ )

[a] All pmr spectra were determined in hexadeuteriodimethylsulfoxide as the solvent.

*Anal.* Calcd. for  $C_{17}H_{11}N_3S$ : C, 70.57; H, 3.83; N, 14.52; S, 11.08. Found: C, 70.58; H, 4.02; N, 14.23; S, 11.37.

Cyclization of **2a**: 5-Cyano-2,6-diphenyl-4-thioxo-3,4-dihydropyrimidine (**3a**).

A solution of **2a** (289 mg, 1 mmole) in dry 2-propanol (20 ml) was acidified with 2 ml of 10% hydrochloric acid. After 6 hours with stirring at room temperature the solvent was removed and the residue treated with water afforded a solid that was recrystallized from ethanol-acetonitrile, yield 75%.

5-Cyano-4-methylthio-2,6-diphenylpyrimidine (**5a**).

To an ethanolic solution of sodium ethoxide (prepared from sodium metal) (23 mg) and 90 ml of dry ethanol were added 289 mg (1 mmole) of **3a** and 254 mg (2 mmoles) of methyl iodide. The mixture was stirred at room temperature for 2 hours and cooled. Then the precipitate was collected and recrystallized from ethanol, yield 75%, mp 168-169° (lit [15] mp 169-171°); ir (potassium bromide): 2200, 1510, 1485, 1440, 1375, 1300  $cm^{-1}$ ; pmr (hexadeuteriodimethylsulfoxide):  $\delta$  8.69-8.39 (m, aromatic, 2H), 8.28-7.94 (m, aromatic, 2H), 7.81-7.43 (m, aromatic, 6H), 2.78 (s,  $CH_3$ , 3H); ms: (relative intensity) 241 ( $M^+$ , 100), 153 (5), 127 (13), 77 (6).

*Anal.* Calcd. for  $C_{18}H_{13}N_3S$ : C, 71.26; H, 4.32; N, 13.85; S, 10.57. Found: C, 71.10; H, 4.40; N, 13.70; S, 10.81.

Hydrolysis of **5a**: 5-Cyano-4-oxo-2,6-diphenyl-3,4-dihydropyrimidine (**6a**).

A solution of **5a** (303 mg, 1 mmole) in ethanol (15 ml) was basified with 30 ml of 20% aqueous sodium hydroxide and stirred at room temperature for 48 hours. Upon acidification with dilute hydrochloric acid a precipitate separated which was collected and recrystallized from acetone, yield 30%, mp 350-354° (lit [16] mp 350-356°); ir (potassium bromide): 3210, 2220, 1660, 1545, 1540, 1505, 1315  $cm^{-1}$ ; pmr (hexadeuteriodimethylsulfoxide):  $\delta$  14.22-13.16 (br s, NH, 1H), 8.46-7.80 (m, aromatic, 4H), 7.75-7.00 (m, aromatic, 6H).

*Anal.* Calcd. for  $C_{17}H_{11}N_3O$ : C, 74.71; H, 4.06; N, 15.38. Found: C, 74.42; H, 4.19; N, 15.11.

5-Cyano-4-oxo-2,6-diphenyl-3,4-dihydropyrimidine (**6a**).

Benzamidinium hydrochloride (783 mg, 5 mmoles) and ethyl (*E*)-2-cyano-3-phenylpropenoate (**7**, 1 g, 5 mmoles) were added to a solution of sodium (173 mg) in dry ethanol (40 ml). The mixture was stirred at room temperature for 1 hour and afterwards the precipitate of sodium chloride filtered. The filtrate was concentrated to one third of the initial volume, affording a precipitate that was dissolved by adding water. Upon acidification with dilute hydrochloric acid a precipitate separated that was collected and recrystallized from acetone, yield 57%.

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