An Efficient Synthesis of 4-Alkoxy-5,6-dihydro-furo(and -thieno)[2,3-*d*]pyrimidines Using Zinc Chloride/Triethylamine Reagent System

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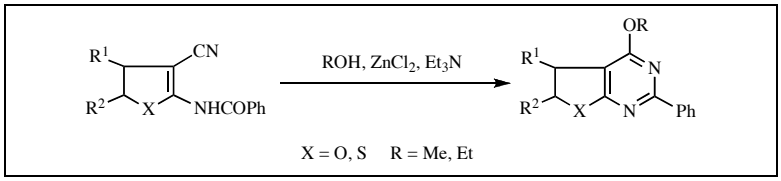

The one-pot synthesis of 4-alkoxy-5,6-dihydro-furo(and -thieno)[2,3-*d*]pyrimidines is described. The reactions of 2-benzamido-4,5-dihydro-3-furan(and -3-thiophene)carbonitriles **1a-d** and **2a-c** with ethanol and/or methanol in the presence of zinc chloride and triethylamine gave the corresponding 4-alkoxy-5,6-dihydro-furo(and -thieno)[2,3-*d*]pyrimidines **3a-d**, **4a-d**, **5a-c** and **6a-c**.

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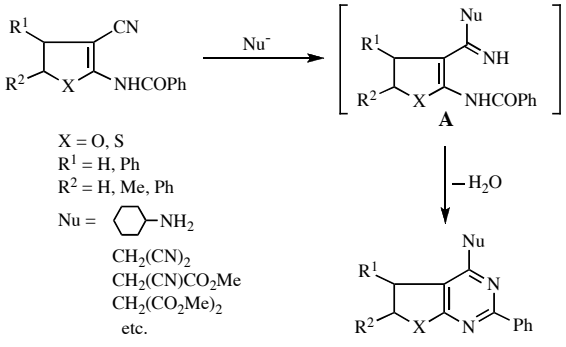
INTRODUCTION

The fused pyrimidine ring system is a ubiquitous heterocycle in nature. Owing to the great structural diversity of biologically active fused pyrimidines such as quinazoline derivatives, it is not surprising that the fused pyrimidine ring system has become an important structural component in many pharmaceutical agents. In this context, the synthesis [1-16] of fused pyrimidine derivatives continues to attract attention due to their biological activities [17-25] and provides an interesting challenge. For the reasons given above, we have been interested in the development of the methods for the construction of fused pyrimidines. In our previous papers [26-28] we have shown that the reactions of heterocyclic β-enaminonitriles with various nucleophiles give the 5,6-dihydro-furo(and -thieno)[2,3-*d*]pyrimidines (Scheme 1). This reaction probably occurs *via* the initial attack of nucleophile to the carbon atom of the cyano group to form the intermediate imino derivatives **A**, which undergo intramolecular cyclo-condensation to produce the fused pyrimidines. In keeping with our interest in the synthetic chemistry of fused pyrimidine derivatives, we now wish to describe an efficient method for preparing 4-alkoxy-5,6-dihydro-furo(and -thieno)[2,3-*d*]pyrimidines by means of a zinc chloride/triethylamine reagent system.

Scheme 1

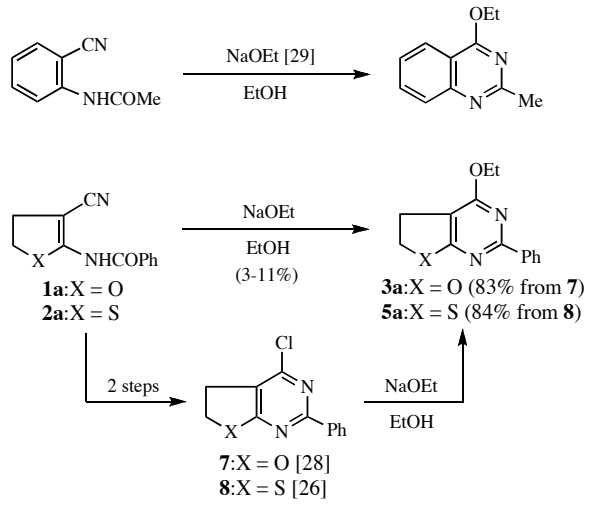


RESULTS AND DISCUSSION

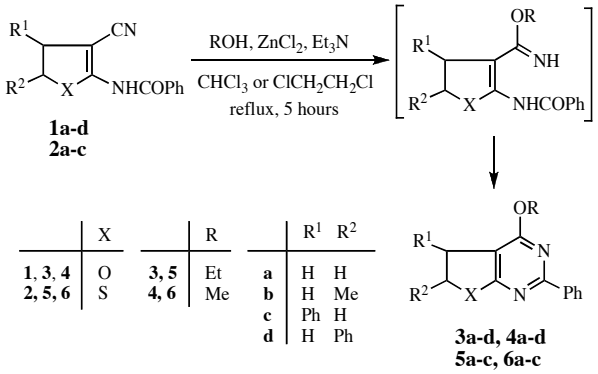
An available synthetic route to 4-ethoxy-2-methyl-quinazoline was developed by Breukink and coworkers and proceeds from 2-acetamidobenzonitrile [29]. To our surprise, however, the reactions of 2-benzamido-4,5-dihydro-3-furancarbonitrile **1a** [30] and its thia analogue **2a** [31] with sodium ethoxide according to the method of Breukink *et al.* [29] produced the desired furo[2,3-*d*]-pyrimidine **3a** and thieno[2,3-*d*]pyrimidine **5a** in very low yields. This result indicates that this type of the direct preparation of fused pyrimidines **3a** and **5a** starting from **1a** and **2a** in a one-pot process is not easy. Thus, we synthesized **3a** and **5a** by the reaction of 4-chloro-5,6-dihydro-2-phenylfuro[2,3-*d*]pyrimidine **7** [28] and its thia analogue **8** [26] with sodium ethoxide in good yields (Scheme 2). However, this method has obviously proved to have a disadvantage such as a long reaction time. Hence, in order to overcome this limitation, we tried one-pot synthesis of **3a** from **1a** and ethanol.

We have previously shown that the reactions of 2-amino-4,5-dihydro-3-furan(and -3-thiophene)carbo-nitriles with active methylene compounds, *e.g.* ethyl acetoacetate, dimethyl malonate and diethyl malonate, by using a combination of tin(IV) chloride and triethylamine afford the fused pyrimidines bearing an

Scheme 2



Scheme 3



active methine group at the 4-position [28]. Therefore we anticipated that, by analogy to our earlier work, the reaction of **1a** with ethanol in the presence of Lewis acid and triethylamine would provide **3a**. Thus, we tested the reactions in the presence of several Lewis acids. Best result was obtained when **1a** was treated with ethanol in the presence of zinc chloride and triethylamine, and the expected fused pyrimidine **3a** was isolated in 59% yield (Scheme 3 and entry 1 in Table 1). The use of other Lewis acids such as titanium(IV) chloride and tin(IV) chloride was not successful. Although the reason is not clear at present, this is probably because the reaction of titanium(IV) chloride or tin(IV) chloride with ethanol would occur. It makes us believe that the nucleophilic addition of ethanol to cyano group and cyclocondensation of the intermediate imino derivative can only be promoted by using a couple zinc chloride and triethylamine reagents. Based on these results, we started the reactions of **1a-d** and **2a-c** with ethanol and/or methanol in the presence of zinc chloride and triethylamine.

Table 1

One-Pot Synthesis of 4-Alkoxy-5,6-dihydro-furo(and -thieno)[2,3-*d*]pyrimidines **3-6**

Entry	Substrate	Product	Yieid (%)
1	**1a**	**3a**	59
2	**1b**	**3b**	44
3	**1c**	**3c**	58
4	**1d**	**3d**	55
5	**2a**	**5a**	89
6	**2b**	**5b**	90
7	**2c**	**5c**	73
8	**1a**	**4a**	57
9	**1b**	**4b**	58
10	**1c**	**4c**	47
11	**1d**	**4d**	47
12	**2a**	**6a**	86
13	**2b**	**6b**	88
14	**2c**	**6c**	86

When a mixture of **1a-d** and **2a-c** with ethanol or methanol in the presence of zinc chloride and triethylamine in chloroform or 1,2-dichloroethane was refluxed for 5 hours, the expected 4-alkoxy-5,6-dihydro-2-phenyl-furo(and -thieno)[2,3-*d*]pyrimidines **3a-d**, **4a-d**, **5a-c** and **6a-c** were obtained in moderate to good yields. The results are listed in Table 1. The ir spectra of **3-6** lacked characteristic bands of both, benzoylamino and cyano group. The ^{1}H nmr spectra of **3** and **5** exhibit a two-proton quartet near δ 4.5 attributable to the methylene protons of an ethoxy group and a three-proton triplet near δ 1.3 due to the methyl protons of an ethoxy group. The ^{1}H nmr spectra of **4** and **6** show a three-proton singlet near δ 4.0 assignable to the methyl protons of a methoxy group. Elemental analyses and spectral data of **3-6** are consistent with the proposed structures (see experimental section). In addition, compounds **3a** and **5a** were shown to be identical with samples prepared from 4-chloro-5,6-dihydro-2-phenyl-furo(and -thieno)[2,3-*d*]pyrimidines (**7** and **8**) with sodium ethoxide on the basis of a mixed melting point determination and a comparison of the ir spectra.

In conclusion, we have developed a convenient straight-forward method for the construction of 4-alkoxy-5,6-dihydrofuro[2,3-*d*]pyrimidines and their thieno analogues, proceeding by zinc chloride/triethylamine promoted nucleophilic addition of alcohol to the cyano group and cyclocondensation of the non-isolable imino intermediate. This methodology offers significant advantages with regard to the simplicity of operation. Functionalized fused pyrimidines are important synthons in organic synthesis and for the preparation of biologically active compounds with interest in medicinal chemistry.

EXPERIMENTAL

All melting points are uncorrected. The ^{1}H and ^{13}C nmr spectra were recorded on a JEOL JNM-A 500 spectrometer at

500 and 125 MHz, respectively. The ^{1}H and ^{13}C chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane as internal standard. The positive FAB mass spectra were obtained on a JEOL JMS-HX 110 spectrometer. The elemental analyses were performed on a HERAUS CHNO-RAPID analyzer. The starting materials, 2-benzamido-4,5-dihydro-3-furan(and -3-thiophene)carbonitriles **1a-d** and **2a-c** were easily prepared by previously reported our method [30,31].

General Procedure for the Preparation of 4-Alkoxy-furo(and -thieno)[2,3-*d*]pyrimidines 3a-d, 4a-d, 5a-c and 6a-c. To a stirred solution of **1a-d** [30] (10 mmoles) or **2a-c** [31] (10 mmoles), ethanol (0.92 g, 20 mmoles) or methanol (0.64 g, 20 mmoles) and triethylamine (2.02 g, 20 mmoles) in chloroform (20 mL, in the case of the preparation of **3a-d** and **4a-d**) or in 1,2-dichloroethane (20 mL, in the case of the preparation of **5a-c** and **6a-c**) was added zinc chloride (4.08 g, 30 mmoles). After the mixture was refluxed for 5 hours, a 5% hydrochloric acid solution (20 mL) was added to the reaction mixture with stirring and ice-cooling. The resulting mixture was extracted with chloroform (60 mL). The extract was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with chloroform as the eluent to afford **3a-d, 4a-d, 5a-c** and **6a-c**.

4-Ethoxy-5,6-dihydro-2-phenylfuro[2,3-*d*]pyrimidine (3a). This compound was obtained as colorless needles (1.42 g, 59%), mp 103-105 °C (diethyl ether-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 1.44 (t, J = 7.0 Hz, 3H, OCH$_2$*Me*), 3.17 (t, J = 8.9 Hz, 2H, 5-H), 4.60 (q, J = 7.0 Hz, 2H, OC*H*$_2$M*e*), 4.68 (t, J = 8.9 Hz, 2H, 6-H), 7.42-7.44 (m, 3H, Ph-H), 8.40-8.42 ppm (m, 2H, Ph-H); ^{13}C nmr (deuteriochloroform): δ 14.7 (OCH$_2$*Me*), 24.7 (C-5), 62.3 (O*C*H$_2$Me), 70.1 (C-6), 97.0 (C-4a), 128.2, 130.4, 137.5 (Ph-C), 163.9 (C-2), 166.0 (C-4), 177.0 ppm (C-7a); ms: m/z 243 [M+H]$^+$. *Anal.* Calcd. for $C_{14}H_{14}N_2O_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.58; H, 5.94; N, 11.62.

4-Ethoxy-5,6-dihydro-6-methyl-2-phenylfuro[2,3-*d*]pyrimidine (3b). This compound was obtained as colorless columns (1.13 g, 44%), mp 82-83 °C (diethyl ether-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 1.44 (t, J = 7.0 Hz, 3H, OCH$_2$*Me*), 1.52 (d, J = 6.1 Hz, 3H, 6-Me), 2.74 (dd, J = 6.7, 15.6 Hz, 1H, 5-H), 3.29 (dd, J = 9.2, 15.6 Hz, 1H, 5-H), 4.59 (q, J = 7.0 Hz, 2H, OC*H*$_2$M*e*), 5.03-5.07 (m, 1H, 6-H), 7.41-7.44 (m, 3H, Ph-H), 8.40-8.43 ppm (m, 2H, Ph-H); ^{13}C nmr (deuteriochloroform): δ 14.7 (OCH$_2$*Me*), 22.1 (6-Me), 32.1 (C-5), 62.3 (O*C*H$_2$Me), 79.2 (C-6), 97.1 (C-4a), 128.2, 130.4, 137.5 (Ph-C), 163.9 (C-2), 165.9 (C-4), 176.0 ppm (C-7a); ms: m/z 257 [M+H]$^+$. *Anal.* Calcd. for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.36; H, 6.48; N, 10.96.

4-Ethoxy-5,6-dihydro-2,5-diphenylfuro[2,3-*d*]pyrimidine (3c). This compound was obtained as colorless prisms (1.84 g, 58%), mp 117-118 °C (acetone-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 1.25 (t, J = 7.0 Hz, 3H, OCH$_2$*Me*), 4.48 (q, J = 7.0 Hz, 2H, OC*H*$_2$M*e*), 4.59 (dd, J = 5.5, 8.9 Hz, 1H, 6-H), 4.67 (dd, J = 5.5, 9.8 Hz, 1H, 5-H), 4.99 (dd, J = 8.9, 9.8 Hz, 1H, 6-H), 7.20-7.33 (m, 5H, Ph-H), 7.43-7.46 (m, 3H, Ph-H), 8.42-8.44 ppm (m, 2H, Ph-H); ^{13}C nmr (deuteriochloroform): δ 14.4 (OCH$_2$*Me*), 43.8 (C-5), 62.3 (O*C*H$_2$Me), 78.1 (C-6), 100.6 (C-4a), 127.2, 128.3, 128.4, 128.7, 130.6, 137.4, 141.4 (Ph-C), 164.7 (C-2), 166.2 (C-4), 176.5 ppm (C-7a); ms: m/z 319 [M+H]$^+$. *Anal.* Calcd. for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.57; H, 5.72; N, 8.87.

4-Ethoxy-5,6-dihydro-2,6-diphenylfuro[2,3-*d*]pyrimidine (3d). This compound was obtained as colorless scales (1.74 g, 55%), mp 144-145 °C (acetone-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 1.44 (t, J = 7.0 Hz, 3H, OCH$_2$*Me*), 3.15 (dd, J = 7.3, 15.6 Hz, 1H, 5-H), 3.62 (dd, J = 9.8, 15.6 Hz, 1H, 5-H), 4.60 (q, J = 7.0 Hz, 2H, OC*H*$_2$M*e*), 5.90 (dd, J = 7.3, 9.8 Hz, 1H, 6-H), 7.31-7.46 (m, 8H, Ph-H), 8.43-8.45 ppm (m, 2H, Ph-H); ^{13}C nmr (deuteriochloroform): δ 14.7 (OCH$_2$*Me*), 33.4 (C-5), 62.4 (O*C*H$_2$Me), 83.0 (C-6), 96.8 (C-4a), 125.6, 128.3, 128.7, 130.5, 137.5, 140.9 (Ph-C), 164.2 (C-2), 165.9 (C-4), 176.2 ppm (C-7a); ms: m/z 319 [M+H]$^+$. *Anal.* Calcd. for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.59; H, 5.83; N, 9.02.

5,6-Dihydro-4-methoxy-2-phenylfuro[2,3-*d*]pyrimidine (4a). This compound was obtained as colorless needles (1.31 g, 57%), mp 107-108 °C (diethyl ether-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 3.16 (t, J = 8.9 Hz, 2H, 5-H), 4.10 (s, 3H, OMe), 4.68 (t, J = 8.9 Hz, 2H, 6-H), 7.43-7.44 (m, 3H, Ph-H), 8.42-8.44 ppm (m, 2H, Ph-H); ^{13}C nmr (deuteriochloroform): δ 24.6 (C-5), 53.7 (OMe), 70.1 (C-6), 97.0 (C-4a), 128.2, 128.3, 137.4 (Ph-C), 164.1 (C-2), 166.2 (C-4), 177.0 ppm (C-7a); ms: m/z 229 [M+H]$^+$. *Anal.* Calcd. for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.51; H, 5.24; N, 11.97.

5,6-Dihydro-4-methoxy-6-methyl-2-phenylfuro[2,3-*d*]pyrimidine (4b). This compound was obtained as colorless needles (1.40 g, 58%), mp 55-56 °C (diethyl ether-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 1.52 (d, J = 6.1 Hz, 3H, 6-Me), 2.74 (dd, J = 6.7, 15.6 Hz, 1H, 5-H), 3.29 (dd, J = 9.2, 15.6 Hz, 1H, 5-H), 4.10 (s, 3H, OMe), 5.03-5.08 (m, 1H, 6-H), 7.42-7.44 (m, 3H, Ph-H), 8.42-8.44 ppm (m, 2H, Ph-H); ^{13}C nmr (deuteriochloroform): δ 22.0 (6-Me), 37.0 (C-5), 53.6 (OMe), 79.2 (C-6), 97.1 (C-4a), 128.2, 130.5, 137.4 (Ph-C), 164.1 (C-2), 166.2 (C-4), 176.0 ppm (C-7a); ms: m/z 243 [M+H]$^+$. *Anal.* Calcd. for $C_{14}H_{14}N_2O_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.51; H, 5.85; N, 11.48.

5,6-Dihydro-4-methoxy-2,5-diphenylfuro[2,3-*d*]pyrimidine (4c). This compound was obtained as colorless needles (1.44 g, 47%), mp 129-131 °C (acetone-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 3.98 (s, 3H, OMe), 4.55 (dd, J = 5.5, 9.2 Hz, 1H, 6-H), 4.67 (dd, J = 5.5, 9.8 Hz, 1H, 5-H), 4.98 (dd, J = 9.2, 9.8 Hz, 1H, 6-H), 7.18-7.20 (m, 2H, Ph-H), 7.26-7.27 (m, 1H, Ph-H), 7.31-7.33 (m, 2H, Ph-H), 7.44-7.46 (m, 3H, Ph-H), 8.45-8.47 ppm (m, 2H, Ph-H); ^{13}C nmr (deuteriochloroform): δ 43.9 (C-5), 53.7 (OMe), 78.2 (C-6), 100.5 (C-4a), 127.2, 127.3, 128.3, 128.4, 128.8, 130.7, 137.2, 141.4 (Ph-C), 164.8 (C-2), 166.5 (C-4), 176.2 ppm (C-7a); ms: m/z 305 [M+H]$^+$. *Anal.* Calcd. for $C_{19}H_{16}N_2O_2$: C, 74.98; H, 5.30; N, 9.20. Found: C, 74.89; H, 5.39; N, 9.17.

5,6-Dihydro-4-methoxy-2,6-diphenylfuro[2,3-*d*]pyrimidine (4d). This compound was obtained as colorless scales (1.43 g, 47%), mp 123-125 °C (acetone-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 3.15 (dd, J = 7.3, 15.8 Hz, 1H, 5-H), 3.62 (dd, J = 9.8, 15.8 Hz, 1H, 5-H), 4.11 (s, 3H, OMe), 5.90 (dd, J = 7.3, 9.8 Hz, 1H, 6-H), 7.33-7.46 (m, 8H, Ph-H), 8.45-8.47 ppm (m, 2H, Ph-H); ^{13}C nmr (deuteriochloroform): δ 33.3 (C-5), 53.7 (OMe), 83.1 (C-6), 96.8 (C-4a), 125.6, 128.3, 128.4, 128.8, 130.5, 130.6, 137.4, 140.8 (Ph-C), 164.4 (C-2), 166.1 (C-4), 176.2 ppm (C-7a); ms: m/z 305 [M+H]$^+$. *Anal.* Calcd. for $C_{19}H_{16}N_2O_2$: C, 74.98; H, 5.30; N, 9.20. Found: C, 74.99; H, 5.36; N, 9.22.

4-Ethoxy-5,6-dihydro-2-phenylthieno[2,3-*d*]pyrimidine (5a). This compound was obtained as colorless columns (2.30 g, 89%), mp 130-132 °C (acetone-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 1.43 (t, J = 7.0 Hz, 3H, OCH$_2$*Me*), 3.23-

3.27 (m, 2H, 5-H), 3.39-3.43 (m, 2H, 6-H), 4.56 (q, J = 7.0 Hz, 2H, OCH_2M*e*), 7.41-7.44 (m, 3H, Ph-H), 8.37-8.40 ppm (m, 2H, Ph-H); ^{13}C nmr (deuteriochloroform): δ 14.6 (OCH$_2$*Me*), 29.2 (C-5), 30.3 (C-6), 62.1 (O*C*H$_2$Me), 113.0 (C-4a), 128.2, 130.4, 137.5 (Ph-C), 163.8 (C-2), 164.2 (C-4), 176.4 ppm (C-7a); ms: m/z 259 [M+H]$^+$. *Anal*. Calcd. for $C_{14}H_{14}N_2OS$: C, 65.09; H, 5.46; N, 10.84. Found: C, 65.05; H, 5.44; N, 10.93.

4-Ethoxy-5,6-dihydro-6-methyl-2-phenylthieno[2,3-*d*]pyrimidine (5b). This compound was obtained as colorless prisms (2.45 g, 90%), mp 105-106 ˚C (acetone-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 1.43 (t, J = 7.0 Hz, 3H, OCH$_2$*Me*), 1.51 (d, J = 6.7 Hz, 3H, 6-Me), 2.90 (dd, J = 6.0, 16.0 Hz, 1H, 5-H), 3.37 (dd, J = 8.4, 16.0 Hz, 1H, 5-H), 4.00-4.05 (m, 1H, 6-H), 4.56 (q, J = 7.0 Hz, 2H, OCH_2M*e*), 7.41-7.44 (m, 3H, Ph-H), 8.37-8.40 ppm (m, 2H, Ph-H); ^{13}C nmr (deuteriochloroform): δ 14.6 (OCH$_2$*Me*), 22.9 (6-Me), 37.5 (C-5), 42.9 (C-6), 62.1 (O*C*H$_2$Me), 112.6 (C-4a), 128.2, 130.4, 137.5 (Ph-C), 163.8 (C-2), 164.2 (C-4), 175.7 ppm (C-7a); ms: m/z 273 [M+H]$^+$. *Anal*. Calcd. for $C_{15}H_{16}N_2OS$: C, 66.15; H, 5.92; N, 10.29. Found: C, 66.36; H, 5.95; N, 10.46.

4-Ethoxy-5,6-dihydro-2,5-diphenylthieno[2,3-*d*]pyrimidine (5c). This compound was obtained as colorless prisms (2.45 g, 73%), mp 129-130 ˚C (acetone-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 1.19 (t, J = 7.0 Hz, 3H, OCH$_2$*Me*), 3.35 (dd, J = 4.3, 11.3 Hz, 1H, 6-H), 3.92 (dd, J = 9.5, 11.3 Hz, 1H, 6-H), 4.42 (q, J = 7.0 Hz, 2H, OCH_2M*e*), 4.73 (dd, J = 4.3, 9.5 Hz, 1H, 5-H), 7.23-7.31 (m, 5H, Ph-H), 7.42-7.45 (m, 3H, Ph-H), 8.39-8.41 ppm (m, 2H, Ph-H); ^{13}C nmr (deuteriochloroform): δ 14.3 (OCH$_2$*Me*), 38.6 (C-6), 47.6 (C-5), 62.0 (O*C*H$_2$Me), 115.9 (C-4a), 127.1, 127.2, 128.3, 128.5, 130.6, 137.3, 142.4 (Ph-C), 164.4 (C-2 and 4), 176.2 ppm (C-7a); ms: m/z 335 [M+H]$^+$. *Anal*. Calcd. for $C_{20}H_{18}N_2OS$: C, 71.83; H, 5.43; N, 8.38. Found: C, 71.96; H, 5.34; N, 8.54.

5,6-Dihydro-4-methoxy-2-phenylthieno[2,3-*d*]pyrimidine (6a). This compound was obtained as colorless prisms (2.10 g, 86%), mp 110-112 ˚C (acetone-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 3.23-3.27 (m, 2H, 5-H), 3.40-3.43 (m, 2H, 6-H), 4.07 (s, 3H, OMe), 7.42-7.44 (m, 3H, Ph-H), 8.39-8.41 ppm (m, 2H, Ph-H); ^{13}C nmr (deuteriochloroform): δ 29.1 (C-5), 30.3 (C-6), 53.4 (OMe), 113.0 (C-4a), 128.2, 130.5, 137.3 (Ph-C), 163.9 (C-2), 164.4 (C-4), 176.5 ppm (C-7a); ms: m/z 245 [M+H]$^+$. *Anal*. Calcd. for $C_{13}H_{12}N_2OS$: C, 63.91; H, 4.95; N, 11.47. Found: C, 63.98; H, 5.04; N, 11.43.

5,6-Dihydro-4-methoxy-6-methyl-2-phenythieno[2,3-*d*]pyrimidine (6b). This compound was obtained as colorless prisms (2.26 g, 88%), mp 87-88 ˚C (diethyl ether-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 1.50 (d, J = 6.7 Hz, 3H, 6-Me), 2.90 (dd, J = 5.8, 16.0 Hz, 1H, 5-H), 3.37 (dd, J = 8.3, 16.0 Hz, 1H, 5-H), 4.00-4.06 (m, 1H, 6-H), 4.07 (s, 3H, OMe), 7.42-7.45 (m, 3H, Ph-H), 8.39-8.41 ppm (m, 2H, Ph-H); ^{13}C nmr (deuteriochloroform): δ 22.9 (6-Me), 37.4 (C-5), 42.9 (C-6), 53.4 (OMe), 112.5 (C-4a), 128.2, 130.4, 137.4 (Ph-C), 163.9 (C-2), 164.5 (C-4), 175.7 ppm (C-7a); ms: m/z 259 [M+H]$^+$. *Anal*. Calcd. for $C_{14}H_{14}N_2OS$: C, 65.09; H, 5.46; N, 10.84. Found: C, 65.20; H, 5.21; N, 10.74.

5,6-Dihydro-4-methoxy-2,5-diphenylthieno[2,3-*d*]pyrimidine (6c). This compound was obtained as colorless needles (2.76 g, 86%), mp 146-147 ˚C (acetone-petroleum ether); ^{1}H nmr (deuteriochloroform): δ 3.34 (dd, J = 3.5, 11.1 Hz, 1H, 6-H), 3.93 (dd, J = 9.6, 11.1 Hz, 1H, 6-H), 3.93 (s, 3H, OMe), 4.74 (dd, J = 3.5, 9.6 Hz, 1H, 5-H), 7.24-7.30 (m, 5H, Ph-H), 7.43-7.45 (m, 3H, Ph-H), 8.42-8.44 ppm (m, 2H, Ph-H); ^{13}C nmr (deuteriochloroform): δ 38.9 (C-6), 47.4 (C-5), 53.4 (OMe), 115.8 (C-4a), 126.9, 127.3, 128.3, 128.7, 130.7, 137.2, 142.2 (Ph-C), 164.6 (C-2), 164.8 (C-4), 176.5 ppm (C-7a); ms: m/z 321 [M+H]$^+$. *Anal*. Calcd. for $C_{19}H_{16}N_2OS$: C, 71.22; H, 5.03; N, 8.74. Found: C, 71.19; H, 5.05; N, 8.66.

The Preparation of 4-Ethoxy-furo(and -thieno)[2,3-*d*]-pyrimidines 3a and 5a from 7 and 8. To a solution of sodium (0.17 g, 7.4 mmoles) in anhydrous ethanol (10 mL) was added **7** [28] (1.16 g, 5 mmoles) or **8** [26] (1.24 g, 5 mmoles) with stirring. After the mixture was refluxed for 1 hour, a 5% hydrochloric acid solution (30 mL) was added to the reaction mixture with stirring and ice-cooling. The precipitate was isolated by filtration, washed with water, dried and recrystallized from diethyl ether-petroleum ether (in the case of **3a**) or from acetone-petroleum ether (in the case of **5a**) to yield **3a** (1.00 g, 83%) and **5a** (1.09 g, 84%). These products **3a** and **5a** were shown to be identical with samples prepared from **1a** and/or **2a** and ethanol in the presence of zinc chloride and triethylamine on the basis of a mixed melting point determination and a comparison of the ir spectra.

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