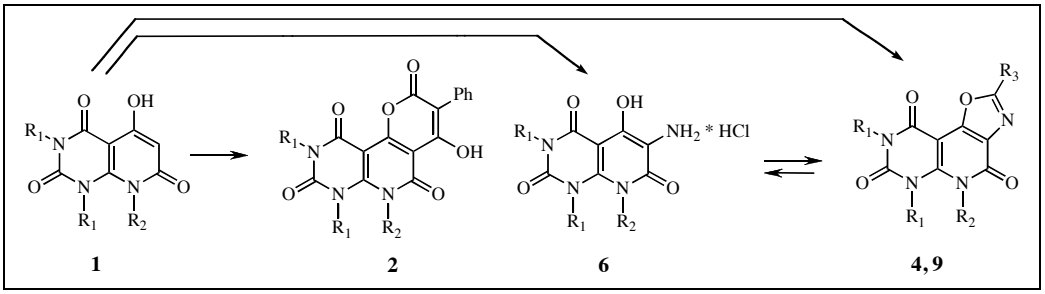
Ring Closure Reactions of Pyrido[2,3-*d*]pyrimidines to Pyrano[2',3':4,5]- and Oxazolo[5',4':4,5]pyrido[2,3-*d*]pyrimidines

Dang Van Tinh[a] and Wolfgang Stadlbauer* [b]

[a]University of Medicine and Pharmacy at Hochiminh City
41 Dinh Tien Hoang Str., Dist. 1, Ho Chi Minh City (Viet Nam)
[b] Institute of Chemistry, Organic Synthesis Group, Karl-Franzens University of Graz,
Heinrichstrasse 28, A-8010 Graz (Austria)
wolfgang.stadlbauer@uni-graz.at

Received January 11, 2008



The cyclocondensation of 5-hydroxy-pyrido[2,3-*d*]pyrimidines **1** with malonates gives pyrano[2',3':4,5]-pyrido[2,3-*d*]pyrimidines **2**. Nitration of **1** and reduction with zinc in the presence of carboxylic acids/anhydrides gave 2-alkyloxazolo[5',4':4,5]pyrido[2,3-*d*]pyrimidines **4**, which were ring-opened to 6-aminopyrido[2,3-*d*]pyrimidines **5, 6** and **7**. Cyclization of 6-aminopyrido[2,3-*d*]pyrimidines **6** with benzoylchlorides **8** gave 2-aryloxazolo[5',4':4,5]pyrido[2,3-*d*]pyrimidines **9**. Reaction conditions for the cyclization have been studied by differential scanning calorimetry (DSC).

J. Heterocyclic Chem., **45**, 1359 (2008).

INTRODUCTION

Pyrido[2,3-*d*]pyrimidine derivatives form a class of fused heterocyclic compounds which reveal interesting pharmacological and biological properties. Thus, they have been used as effective antitumor agents, as antibacterial, anticonvulsant or enzyme inhibitors or as a new class of antileishmanial agents [1]. Oxazolo-, isoxazolo-, oxadiazolo- and indoloheterocycles in the quinoline and pyrimidine series were investigated thoroughly in the last decades and many representatives were found which show antihypertensive and dopaminergic properties [2], antiulcer [3], anticancer [4], antiallergic and antidepressive [5] or herbicidal activity [6]. These findings prompted us to study the combination of these biologically interesting nuclei by synthesis of pyrido[2,3-*d*]pyrimidinetriones anellated to the f-side by pyrano- and oxazolo rings. The ring closure reactions intended for this project involve cyclocondensation reactions of ortho-substituted hydroxy-pyrido[2,3-*d*]pyrimidinetriones with C1- or C3-fragments leading to pyrano- and oxazolo-derivatives.

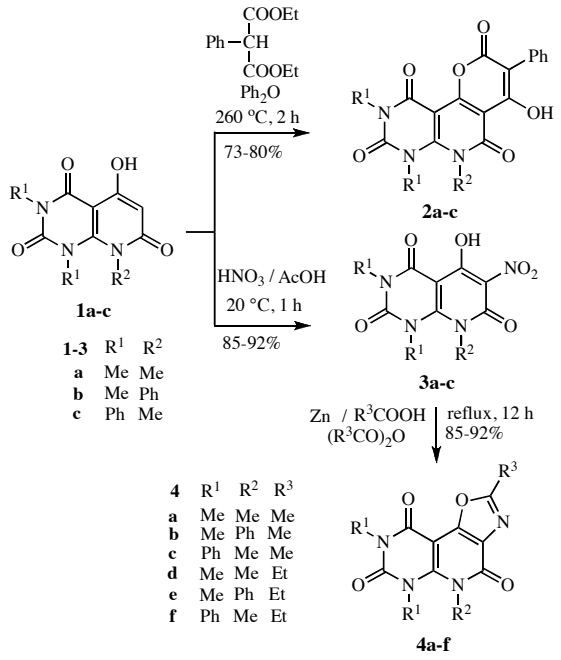
RESULTS AND DISCUSSION

The syntheses started from 6-unsubstituted 5-hydroxy-pyrido[2,3-*d*]pyrimidines **1a-c** [7]. The thermal cyclocondensation of **1a-c** as 1,3-dinucleophiles with diethyl phenylmalonate as an electrophilic C3-fragment gave in good yields in a ring closure reaction to six-membered heterocycles pyrano[2',3':4,5]pyrido[2,3-*d*]pyrimidines **2a-c**. The cyclization was carried out in diphenylether solution and can be observed to proceed in two steps: in the first step by liberation of one equivalent of ethanol trans-esterification of the malonate with the hydroxy-heterocycle **1** takes place. In the next step, at high temperatures an internal cleavage of ethanol takes place to form a ketene-ester moiety from the malonate part, which reacts thermally without catalyst with the heteroaromatic position 6 of the pyrido[2,3-*d*]pyrimidine, similar as observed earlier with other heterocyclic systems [10]. This mechanism is supported by findings, that **1a-c** with alkylmalonates or unsubstituted malonate gave either no ring closure products or only decomposition products depending on the substituents and reaction conditions, which can be explained in terms of the formation of the ketene intermediate, which is facilitated by the phenyl substituent of phenylmalonate forming **2a-c**, but hindered by alkyl substituents in alkylmalonates, and giving multiple condensation reactions with unsubstituted malonates.

A further ring closure sequence was intended starting from *ortho*-aminosubstituted hydroxyheterocycles as 1,4-dinucleophiles, which can be cyclized with electrophilic C1-fragments to five membered heterocycles. The pathway to *ortho*-amino derivatives was planned to lead *via* an *ortho*-nitro group. Nitration of similar pyrido[2,3-

d]pyrimidines at elevated temperatures was reported earlier [8a,b]. The nitration of **1a-c** with fuming nitric acid and sodium nitrite as catalyst in acetic acid gave already at room temperature 6-nitropyrido[2,3-*d*]pyrimidinetriones **3**. These mild conditions can be explained by initial nitrosation of **1** with sodium nitrite and subsequent oxidation to the desired nitro group [8c]. The conversion of the nitro group of 6-nitropyrido[2,3-*d*]pyrimidines **3a-c** to a 6-amino group was planned by reduction with zinc dust in the presence of acetic anhydride. In this way stable 6-acetylamino-5-hydroxy-pyrido[2,3-*d*]pyrimidine-2,4,7-triones **5** should be obtained which avoids the isolation of the sensitive free amino derivatives such as **6** or **7**.

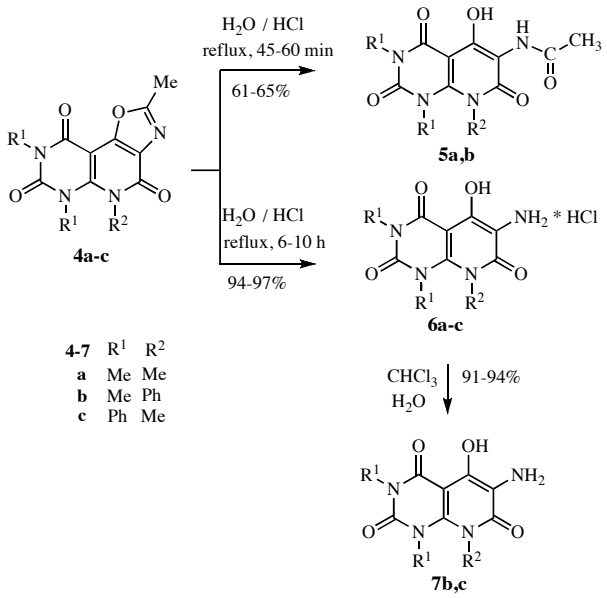
Scheme 1



However, acetylamino derivatives **5** could not be obtained in a pure form from 6-nitropyrido[2,3-*d*]-pyrimidines **3**, because the acetyl group acts already as a reactive C1-fragment and a consecutive ring closure to oxazolo[5',4':4,5]pyrido[2,3-*d*]pyrimidinetriones **4** occurred before the reduction to **5** was completed. Therefore we synthesized 2-alkyloxazolo[5',4':4,5]pyrido[2,3-*d*]pyrimidines **4a-f** both as stable intermediates for the generation of further amino derivatives and as cyclization examples of alkyl-substituted oxazoles. This synthesis pathway led directly from 6-nitro compounds **3** with zinc dust in mixtures of acetic or propionic acid and their anhydrides by heating under reflux to oxazoles **4**. Attempts to apply another method for the reduction of the nitro group of **3a-c** to amines using sodium dithionite as reduction agent, which we have used successfully earlier in the 4-hydroxy-3-nitro-quinolone series [9], failed.

The transformation of oxazolo[5',4':4,5]pyrido[2,3-*d*]-pyrimidinetriones **4a-c** to amino derivatives could be achieved by kinetically controlled acid catalyzed ring opening. The reaction with 0.5 *M* hydrochloric acid in ethanolic solution gave after 45-60 minutes the 6-acetylamino-5-hydroxy-pyrido[2,3-*d*]pyrimidinetriones **5** together with small amounts of amino hydrochlorides **6**. Extraction of the mixture with chloroform gave in good yields acetylamino compounds **5a,b**. When the reaction time was extended to 6-10 hours, the hydrochlorides of the 6-amino-5-hydroxy-pyrido[2,3-*d*]pyrimidinetriones **6a-c** were isolated, which were rather stable and allowed us to record all physical and spectroscopical data. To obtain the free amino bases from hydrochlorides **6**, the salts **6a-c** were dissolved in water and extracted with chloroform. This allowed the isolation of the free amino bases **7b,c**, whereas the isolation of the free amino base **7a** failed. Attempts to liberate the free amino bases **7** from hydrochlorides **6** by addition of sodium hydroxide as a base failed due to decomposition.

Scheme 2



For further ring closure reactions, amine hydrochlorides **6a-c** have been found as the most suitable reagents, both stable enough and reactive towards benzoic acid derivatives as arylsubstituted C-1 fragments. The ring closure reaction of amine hydrochlorides **6a-c** with the appropriately substituted benzoyl chlorides **8a-h** were intended to be carried out in polyphosphoric acid. Suitable reaction conditions were determined by means of differential scanning calorimetry (DSC), a method used successfully earlier for the investigation of reaction conditions [11]. The DSC diagram of a 1:1 mixture of the amino hydrochloride **6a** and benzoyl chloride **8a** in

polyphosphoric acid (Figure 1) shows an onset at 123 °C and a peak maximum at 153 °C.

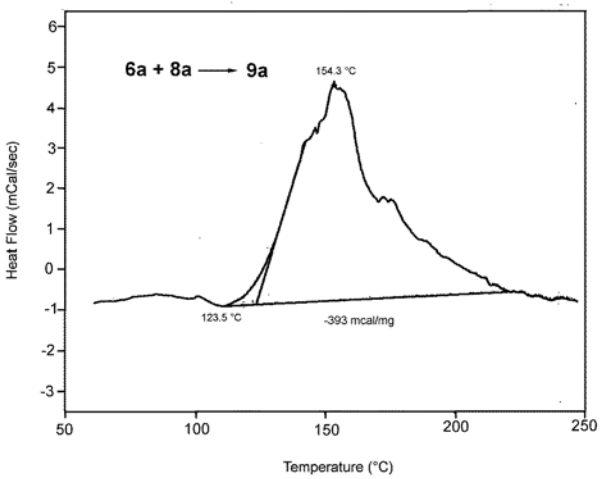
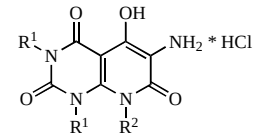


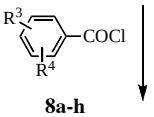
Figure 1. Differential scanning diagram of the reaction of salt 6a with benzoylchloride 8a and polyphosphoric acid.

Similar findings were obtained with a mixture of the salts **6b,c** and benzoyl chloride **8a** (onset: 120-125 °C, peak maximum 155-160 °C). Reaction mixtures of amine hydrochlorides **6a-c** and acetyl chloride, which were investigated for comparison, showed remarkable lower onset points of about 60-80° C (peak maximum at 95-115 °C), followed by a second exothermic signal (peak maximum: 150-160 °C), which explains the quick cyclization reaction during the reduction of nitro compounds **3** to oxazoles **4**. In a preparative scale, the reaction of amine hydrochlorides **6a-c** and benzoyl chlorides **8a-h** in polyphosphoric acid gave in good yields at 150 °C as cyclization products the 2-aryloxazolo-[5',4':4,5]pyrido[2,3-*d*]pyrimidines **9a-o**.

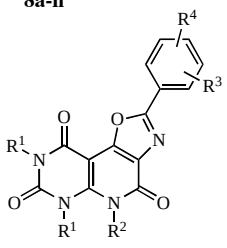
Scheme 3



6a-c



8a-h



9a-o

8	R^3	R^4
a	H	H
b	4-Me	H
c	4-OMe	H
d	4-Cl	H
e	4-NO_2	H
f	2-Cl	4-Cl
g	3-Cl	4-Cl
h	2-OMe	6-OMe

9	R^1	R^2	R^3	R^4
a	Me	Me	H	H
b	Me	Me	4-Me	H
c	Me	Me	4-OMe	H
d	Me	Me	4-Cl	H
e	Me	Me	4-NO_2	H
f	Me	Ph	H	H
g	Me	Ph	4-Me	H
h	Me	Ph	4-Cl	H
i	Me	Ph	4-NO_2	H
j	Ph	Me	4-Cl	H
k	Me	Me	2-Cl	4-Cl
l	Me	Me	3-Cl	4-Cl
m	Me	Me	2-OMe	6-OMe
n	Me	Ph	2-Cl	4-Cl
o	Me	Ph	3-Cl	4-Cl

In conclusion, the synthesis of several new fused pyrido[2,3-*d*]pyrimidines is described, having as anellated ring either a six-membered pyrano ring, or a five-membered oxazole ring. The cyclization reaction takes place by cyclocondensation of bifunctional pyrido[2,3-*d*]-pyrimidines with carboxylic acid derivatives applied either as C1 or C3 fragments. Reaction conditions were studied in advance by differential scanning calorimetry (DSC).

EXPERIMENTAL

Melting points were obtained on a Gallenkamp Melting Point Aparatus, Mod. MFB 595 in open capillary tubes. ^{1}H and ^{13}C nmr spectra were recorded on a Bruker AMX 360 instrument (360 or 90 MHz) or on a Bruker Avance DRX 500 instrument (500 or 125 MHz). Chemical shifts are reported in ppm from internal tetramethylsilan standard and are given in δ-units. The solvent was $CDCl_3$ unless otherwise stated. Infrared spectra were taken on a Mattson Galaxy Series FTIR 7020 instrument with potassium bromide discs. Elemental analyses were performed on a Fisons EA 1108 C,H,N-automatic analyzer and are within ± 0.4 of the theoretical percentages. Calorimetric data were obtained on a Rheometric Scientific DSC-Plus instrument with the software Orchestrator V6.5.8. between 25 - 700 °C, a heating rate of 2-10 °C/min, and 1.5-3 mg compound in sealed aluminium crucibles (11 bar).

5-Hydroxy-1,3,8-trimethyl-pyrido[2,3-*d*]pyrimidine-2,4,7-trione (**1a**), 5-hydroxy-1,3-dimethyl-8-phenyl-pyrido[2,3-*d*]pyrimidine-2,4,7-trione (**1b**) and 5-hydroxy-8-methyl-1,3-diphenylpyrido[2,3-*d*]pyrimidine-2,4,7-trione (**1c**) were obtained according to ref. [7].

4-Hydroxy-6,7,9-trimethyl-3-phenyl-2*H*-pyrano[2',3':4,5]pyrido[2,3-*d*]pyrimidine-2,5,8,10(6*H*,7*H*,9*H*)-tetrone (2a). A mixture of 5-hydroxypyrido[2,3-*d*]pyrimidinetrione **1a** (2.37 g, 10 mmol) and diethyl phenylmalonate (4.72 g, 20 mmol) in diphenylether (15 mL) was heated for 2 hours to 250-260 °C using a short air condenser to remove the liberated ethanol. After cooling, the reaction mixture was digested with cyclohexane (50 mL), the obtained precipitate was collected by filtration, washed with cold cyclohexane and dried. Then the precipitate was boiled with ethanol for 10 minutes, cooled, collected by suction filtration, washed with ethanol and recrystallized from dimethylformamide. The yield was 2.8 g (73%), yellow prisms, mp 310-312 °C (dimethylformamide); ir: 1720 s, 1680 s, 1655 s cm^{-1}; ^{1}H nmr: δ 3.46 (s, 3 H, NMe), 3.70 (s, 6 H, NMe), 7.25-7.45 (m, 5 H, PhH), 12.40 (s, 1 H, OH). *Anal*. Calcd. for $C_{19}H_{15}N_3O_6$ (381.35): C, 59.84; H, 3.96; N, 11.02. Found: C, 59.45; H, 3.93; N, 11.05.

4-Hydroxy-7,9-dimethyl-3,6-diphenyl-2*H*-pyrano[2',3':4,5]pyrido[2,3-*d*]pyrimidine-2,5,8,10(6*H*,7*H*,9*H*)-tetrone (2b). This compound was obtained from 5-hydroxypyrido[2,3-*d*]-pyrimidinetrione **1b** (2.99 g, 10 mmol) according to the procedure described for **2a**; the yield was 3.54 g (80%), yellow prisms, mp 320 °C (dimethylformamide); ir: 1750 s, 1720 s, 1685 s, 1665 s cm^{-1}; ^{1}H nmr (CF_3COOD): δ 2.78 (s, 3 H, NMe), 3.30 (s, 3 H, NMe), 7.19-7.22 (m, 7 H, ArH), 7.42-7.44 (m, 3 H, ArH). *Anal*. Calcd. for $C_{24}H_{17}N_3O_6$ (443.42): C, 65.01; H, 3.86; N, 9.48. Found: C, 64.67; H, 3.85; N, 9.70.

4-Hydroxy-6-methyl-3,7,9-triphenyl-2*H*-pyrano[2',3':4,5]-pyrido[2,3-*d*]pyrimidine-2,5,8,10 (6*H*,7*H*,9*H*)-tetrone (2c). This compound was obtained from 5-hydroxypyrido[2,3-*d*]-pyrimidinetrione **1c** (3.61 g, 10 mmol) according to the procedure described for **2a**; the yield was 3.8 g (75%), yellow prisms, mp 301-303 °C (toluene); ir: 1720 s, 1690 s, 1660 s cm^{-1}; ^1H nmr ($CDCl_3$): δ 3.00 (s, 3 H, NMe), 7.30-7.60 (m, 15 H, ArH), 12.45 (s, 1 H, OH). *Anal*. Calcd. for $C_{29}H_{19}N_3O_6$ (505.49): C, 68.91; H, 3.79; N, 8.31. Found: C, 68.72; H, 3.66; N, 8.26.

5-Hydroxy-1,3,8-trimethyl-6-nitropyrido[2,3-*d*]pyrimidine-2,4,7(1*H*,3*H*,8*H*)-trione (3a). A suspension of 5-hydroxypyrido[2,3-*d*]pyrimidinetrione **1a** (18.00 g, 76 mmol) in glacial acetic acid (140 mL) was treated with fuming nitric acid (14.0 mL, 213 mmol) and then with sodium nitrite (0.40 g, 5.8 mmol) to start the slightly exothermic reaction. The starting material dissolved, followed immediately by precipitation of the product. The mixture was stirred for 60 minutes at 20 °C and diluted with ice water (1 L). The product was collected by suction filtration, washed with water (200 mL) and dried. The yield was 19.00 g (89%), yellow prisms, mp 223-225 °C (dimethylformamide/ethanol); ir: 1720 s, 1670 s cm^{-1}; ^1H nmr δ 3.39 (s, 3 H, NMe), 3.53 (s, 3 H, NMe), 3.55 (s, 3 H, NMe). *Anal*. Calcd. for $C_{10}H_{10}N_4O_6$ (282.21): C, 42.56; H, 3.57; N, 19.85. Found: C, 42.38; H, 3.60; N, 19.76.

5-Hydroxy-1,3-dimethyl-6-nitro-8-phenylpyrido[2,3-*d*]pyrimidine-2,4,7(1*H*,3*H*,8*H*)-trione (3b). This compound was obtained from 5-hydroxypyrido[2,3-*d*]pyrimidinetrione **1b** (22.70 g, 76 mmol) according to the procedure described for **3a**; the yield was 22.00 g (84%), yellow prisms, mp 246-249 °C (dimethylformamide/ethanol); ir: 1725 s, 1700 s, 1660 s cm^{-1}; ^1H nmr δ2.66 (s, 3 H, NMe), 3.30 (s, 3 H, NMe), 7.57-7.60 (m, 5 H, PhH). *Anal*. Calcd. for $C_{15}H_{12}N_4O_6$ (344.29): C, 52.33; H, 3.51; N, 16.27. Found: C, 52.28; H, 3.50; N, 16.15.

5-Hydroxy-8-methyl-6-nitro-1,3-diphenylpyrido[2,3-*d*]pyrimidine-2,4,7(1*H*,3*H*,8*H*)-trione (3c). This compound was obtained from 5-hydroxypyrido[2,3-*d*]pyrimidinetrione **1c** (26.80 g, 76 mmol) according to the procedure described for **3a**; the yield was 28.00 g (91 %), yellow prisms, mp 283-285 °C (dimethylformamide/ethanol); ir: 1740 s, 1670 s cm^{-1}; ^1H nmr δ 2.76 (s, 3 H, NMe), 7.40-7.59 (m, 10 H, ArH). *Anal*. Calcd. for $C_{20}H_{14}N_4O_6$ (406.36): C, 59.12; H, 3.47; N, 13.79. Found: C, 59.40; H, 3.47; N, 13.88.

2,5,6,8-Tetramethyl[1,3]oxazolo[5',4':4,5]pyrido[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (4a). A mixture of 5-hydroxy-6-nitropyrido[2,3-*d*]pyrimidinetrione **3a** (2.82 g, 10 mmol) and zinc dust (46 mmol, 3.0 g) in glacial acetic acid (70 mL) and acetic anhydride (48 mL) was heated under reflux for 12 hours. The hot reaction mixture was filtered still hot, then the filtrate was taken to dryness *in vacuo* and the residue triturated with ethanol (50 mL). The solid product was collected by filtration, washed with ethanol and dried. The yield was 2.30 g (83%), colorless prisms, mp 282 °C (dimethylformamide); ir: 1720 s, 1690 s, 1665 s cm^{-1}; ^1H nmr: δ 2.68 (s, 3 H, NMe), 3.43 (s, 3 H, NMe), 3.63 (s, 3 H, NMe), 3.70 (s, 3 H, NMe). *Anal*. Calcd. for $C_{12}H_{12}N_4O_4$ (276.25): C, 52.17; H, 4.38; N, 20.28. Found: C, 52.02; H, 4.35; N, 20.30.

2,6,8-Trimethyl-5-phenyl[1,3]oxazolo[5',4':4,5]pyrido[2,3-*d*]-pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (4b). This compound was obtained from 5-hydroxy-6-nitropyrido[2,3-*d*]pyrimidine-trione **3b** (3.44 g, 10 mmol) according to the procedure described for **4a**; the yield was 2.90 g (86%), colorless prisms, mp 318 °C (dimethylformamide); ir: 1730 m, 1700 s, 1665 s, 1620 m cm^{-1}; ^1H nmr δ 2.70 (s, 3 H, NMe), 2.83 (s, 3 H, NMe), 3.44 (s, 3 H, NMe), 7.30-7.35 (m, 2 H, PhH), 7.55-7.57 (m, 3 H, PhH). *Anal*. Calcd. for $C_{17}H_{14}N_4O_4$ (338.33): C, 60.35; H, 4.17; N, 16.56. Found: C, 60.59; H, 4.03; N, 16.69.

2,5-Dimethyl-6,8-diphenyl[1,3]oxazolo[5',4':4,5]pyrido-[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (4c). This compound was obtained from 5-hydroxy-6-nitropyrido[2,3-*d*]-pyrimidinetrione **3c** (4.06 g, 10 mmol) according to the procedure described for **4a**; the yield was 3.40 g (85%) colorless prisms, mp 352 °C (dimethylformamide); ir: 1730 m, 1690 s, 1620 m cm^{-1}; ^1H nmr δ 2.68 (s, 3 H, NMe), 3.05 (s, 3 H, NMe), 7.25-7.50 (m, 10 H, ArH). *Anal*. Calcd. for $C_{22}H_{16}N_4O_4$ (400.40): C, 66.00; H, 4.03; N, 13.99. Found: C, 65.89; H, 3.93; N, 13.97.

2-Ethyl-5,6,8-trimethyl[1,3]oxazolo[5',4':4,5]pyrido[2,3-*d*]-pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (4d). This compound was obtained from 5-hydroxy-6-nitropyrido[2,3-*d*]pyrimidine-trione **3a** (2.82 g, 10 mmol) according to the procedure described for **4a**; the yield was 2.20 g (76%), colorless prisms, mp 369 °C (dimethylformamide/ethanol); ir: 1720 m, 1690 s, 1660 s, 1620 m cm^{-1}; ^1H nmr: δ 1.40 (t, 3 H, J = 7 Hz, ethyl-CH_3), 2.93 (q, 2 H, J = 7 Hz, ethyl-CH_2), 3.41 (s, 3 H, NMe), 3.61 (s, 3 H, NMe), 3.68 (s, 3 H, NMe). *Anal*. Calcd. for $C_{13}H_{14}N_4O_4$ (290.28): C, 53.79; H, 4.86; N, 19.30. Found: C, 53.81; H, 4.86; N, 19.16.

2-Ethyl-6,8-dimethyl-5-phenyl[1,3]oxazolo[5',4':4,5]pyrido-[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (4e). This compound was obtained from 5-hydroxy-6-nitropyrido[2,3-*d*]-pyrimidine-trione **3b** (3.44 g, 10 mmol) according to the procedure described for **4a**; the yield was 2.64 g (75%), colorless prisms, mp 280-282 °C (dimethylformamide); ir: 1720 w, 1690 s, 1655 s, 1620 s cm^{-1}; ^1H nmr δ 1.42 (t, 3 H, J = 7 Hz, ethyl-CH_3), 2.81 (s, 3 H, NMe), 2.95 (q, 2 H, J = 7 Hz, ethyl-CH_2), 3.45 (s, 3 H, NMe), 7.30-7.34 (m, 2 H, ArH), 7.50-7.52 (m, 3 H, ArH). *Anal*. Calcd. for $C_{18}H_{16}N_4O_4$ (352.35): C, 61.36; H, 4.58; N, 15.90. Found: C, 61.16; H, 4.51; N, 15.97.

2-Ethyl-5-methyl-6,8-diphenyl[1,3]oxazolo[5',4':4,5]pyrido[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (4f). This compound was obtained from 5-hydroxy-6-nitropyrido[2,3-*d*]-pyrimidinetrione **3c** (4.06 g, 10 mmol) according to the procedure described for **4a**; the yield was 3.10 g (75%), colorless prisms, mp 307-309 °C (dimethylformamide); ir: 1730 m, 1690 s, 1625 m cm^{-1}; ^1H nmr δ 1.40 (t, 3 H, J = 7 Hz, ethyl-CH_3), 2.94 (q, 2 H, J = 7 Hz, ethyl-CH_2), 3.07 (s, 3 H, NMe), 7.28-7.48 (m, 10 H, ArH). *Anal*. Calcd. for $C_{23}H_{18}N_4O_4$ (414.42): C, 66.66; H, 4.38; N, 13.52. Found: C, 66.65; H, 4.27; N, 13.50.

***N*-(5-Hydroxy-1,3,8-trimethyl-2,4,7-trioxo-1,2,3,4,7,8-hexahydropyrido[2,3-*d*]pyrimidin-6-yl)acetamide (5a).** A mixture of oxazolo[5',4':4,5]pyrido[2,3-*d*]pyrimidinetrione **4a** (2.76 g, 10 mmol) in 0.2 *M* hydrochloric acid (100 mL) and ethanol (80 mL) was heated under reflux for about 45 minutes (until a solution was obtained). The reaction mixture was filtered and the filtrate taken to dryness under reduced pressure. The residue was diluted with water (50 mL) and the aqueous solution extracted with chloroform (3 x 50 mL). From the aqueous layer 6-aminopyrido[2,3-*d*]pyrimidinetrione hydrochloride **6a** could be isolated (work up described at **6a**, method A). The organic layer was dried over sodium sulfate and the solvent removed *in vacuo*. The crystalline residue was dried by the addition and destillative removal of abs. ethanol (2 x 50 mL). The yield was 1.80 g (61%) colorless prisms, mp 222-223 °C (ethanol); ir: 3200 w, 1710 m, 1650 s cm^{-1}; ^1H nmr: δ 2.20 (s, 3 H, acetyl-CH_3), 3.40 (s, 3 H, NMe), 3.56 (s, 6 H, 2 NMe), 6.87 (s, 1 H,

NH), 12.40 (s, OH). *Anal*. Calcd. for $C_{12}H_{14}N_4O_5$ (294.27): C, 48.98; H, 4.80; N, 19.04. Found: C, 49.36; H, 4.56; N, 18.78.

N-(5-Hydroxy-1,3-dimethyl-2,4,7-trioxo-8-phenyl-1,2,3,4,7,8-hexahydropyrido[2,3-*d*]pyrimidin-6-yl)acetamide (5b). This compound was obtained from oxazolo[5',4':4,5]-pyrido[2,3-*d*]pyrimidinetrione **4b** (3.38 g, 10 mmol) according to the method described for **5a**; the yield was 2.32 g (65%), colorless prisms, mp 233-235 °C (ethanol); ir: 3280 m, 2950 w, 1720 m, 1690 s, 1640 s cm^{-1}; ^{1}H nmr: δ 2.04 (s, 3 H, acetyl-CH_3), 2.38 (s, 3 H, NMe), 2.70 (s, 3 H, NMe), 6.48 (s, 1 H, NH), 6.63-6.65 (m, 2 H, PhH), 6.73-6.74 (m, 3 H, PhH), 12.35 (s, OH). *Anal*. Calcd. for $C_{17}H_{16}N_4O_5$ (356.34): C, 57.30; H, 4.53; N, 15.72. Found: C, 57.56; H, 4.51; N, 15.44.

6-Amino-5-hydroxy-1,3,8-trimethylpyrido[2,3-*d*]pyrimidine-2,4,7(1*H*,3*H*,8*H*)-trione hydrochloride (6a). Method A. From the aqueous layer during the work-up of **5a** 6-amino-pyrido[2,3-*d*]pyrimidinetrione hydrochloride **6a** was isolated: The aqueous layer was taken to dryness at reduced pressure, and the residue dried by the addition and destillative removal of abs. ethanol (2 x 50 mL). The yield was 1.00 g (33%), colorless prisms.

Method B. A mixture of oxazolo[5',4':4,5]pyrido[2,3-*d*]-pyrimidinetrione **4a** (2.76 g, 10 mmol) in 0.5 *M* hydrochloric acid (100 mL) and ethanol (80 mL) was heated under reflux for 8 hours. The reaction mixture was taken to dryness under reduced pressure. The crystalline residue was dried by the addition and removal of two portions of abs. ethanol (50 mL). The yield was 2.70 g (94%), colorless prisms, mp 212 °C (ethanol); ir: 1720 w, 1650 w cm^{-1}; ^{1}H nmr (D_2O): δ 3.30 (s, 3 H, NMe), 3.55 (s, 3 H, NMe), 3.58 (s, 3 H, NMe). *Anal*. Calcd. for $C_{10}H_{13}ClN_4O_4$ (288.69): C, 41.61; H, 4.54; N, 19.41. Found: C, 41.98; H, 4.18; N, 19.76.

6-Amino-5-hydroxy-1,3-dimethyl-8-phenyl-pyrido[2,3-*d*]-pyrimidine-2,4,7(1*H*,3*H*,8*H*)-trione hydrochloride (6b). This compound was obtained from oxazolo[5',4':4,5]pyrido[2,3-*d*]-pyrimidinetrione **4b** (3.38 g, 10 mmol) according to the procedure described for **6a** (method B); the yield was 3.40 g (95%), colorless prisms, mp 150 °C (ethanol); ir: 1720 w, 1670 m cm^{-1}; ^{1}H nmr (D_2O): δ 2.78 (s, 3 H, NMe), 3.35 (s, 3 H, NMe), 7.33-7.40 (m, 2 H, ArH), 7.57-7.60 (m, 3 H, ArH). *Anal*. Calcd. for $C_{15}H_{15}ClN_4O_4$ (350.76): C, 51.36; H, 4.31; N, 15.97. Found: C, 51.72; H, 3.97; N, 15.58.

6-Amino-5-hydroxy-8-methyl-1,3-diphenylpyrido[2,3-*d*]-pyrimidine-2,4,7(1*H*,3*H*,8*H*)-trione hydrochloride (6c). This compound was obtained from oxazolo[5',4':4,5]pyrido[2,3-*d*]-pyrimidinetrione **4c** (4.00 g, 10 mmol) according to the procedure described for **6a** (method B); the yield was 4.00 g (97%), colorless prisms, mp 170 °C (ethanol); ir: 1730 m, 1660 s cm^{-1}; ^{1}H nmr (D_2O): δ 2.80 (s, 3 H, NMe), 7.25-7.45 (m, 10 H, ArH). *Anal*. Calcd. for $C_{20}H_{17}ClN_4O_4$ (412.84): C, 58.19; H, 4.15; N, 13.57. Found: C, 57.79; H, 3.87; N, 13.88.

6-Amino-5-hydroxy-1,3-dimethyl-8-phenylpyrido[2,3-*d*]-pyrimidine-2,4,7(1*H*,3*H*,8*H*)-trione (7b). A solution of 6-amino-5-hydroxypyrido[2,3-*d*]pyrimidinetrione hydrochloride **6b** (3.50 g, 10 mmol) and water (30 mL) was extracted with chloroform (3 x 50 mL), dried over sodium sulfate and the solution was taken to dryness. In this way the free base **7b** was obtained. The residue was treated with ethanol, and the precipitate was collected by filtration and dried at room temperature *in vacuo*. The yield was 2.86 g (91%), yellow prisms, mp 250-252 °C (ethanol); ir: 3450 w, 3360 w, 1720 s, 1700 s, 1660 s, 1610 m cm^{-1}; ^{1}H nmr: δ 2.81 (s, 3 H, NMe), 3.45 (s, 3 H, NMe), 7.29-7.32 (m, 2 H, ArH), 7.49-7.56 (m, 3 H, ArH), 11.69 (s, 1 H, OH). *Anal*. Calcd. for $C_{15}H_{14}N_4O_4$ (314.30): C, 57.32; H, 4.49; N, 17.83. Found: C, 56.94; H, 4.31; N, 17.45.

6-Amino-5-hydroxy-8-methyl-1,3-diphenyl-pyrido[2,3-*d*]-pyrimidine-2,4,7(1*H*,3*H*,8*H*)-trione (7c). This compound was obtained from 6-amino-5-hydroxy-pyrido[2,3-*d*]pyrimidine-trione hydrochloride **6c** (4.13 g, 10 mmol) according to the method described for **7b**; the yield was 3.54 g (94%), yellow prisms, mp 258-260 °C (ethanol); ir: 3440 m, 3350 m, 1710 s, 1685 s, 1650 s, 1610 m cm^{-1}; ^{1}H nmr: δ 2.98 (s, 3 H, NMe), 3.75 (s, 2 H, NH_2), 7.28-7.47 (m, 10 H, ArH), 11.13 (s, 1 H, OH). *Anal*. Calcd. for $C_{20}H_{16}N_4O_4$ (376.37): C, 63.83; H, 4.28; N, 14.89. Found: C, 63.71; H, 4.24; N, 14.78.

General Procedure for the Preparation of Oxazolo-[5',4':4,5]pyrido[2,3-*d*]pyrimidinetriones 9a-o. A mixture of the corresponding 6-amino-5-hydroxypyrido[2,3-*d*]pyrimidine-trione hydrochloride **6a-c** (10 mmol) with the appropriate substituted benzoyl chloride **8a-h** (20 mmol) in polyphosphoric acid (20.00 g) was heated to 150 °C for 4 hours. The warm reaction mixture was poured into ice/water (400 mL), brought to pH 6-7 with aqueous concentrated sodium hydroxide. The formed precipitate was collected by suction filtered, washed with water and dried. The obtained colorless crystals were recrystallized from dimethylformamide.

5,6,8-Trimethyl-2-phenyl[1,3]oxazolo[5',4':4,5]pyrido[2,3-*d*]-pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (9a). The yield was 2.64 g (78%), mp 318 °C; ir: 1720 m, 1695 s, 1670 s, 1620 s cm^{-1}; ^{1}H nmr (CF_3COOD): δ 3.63 (s, 3 H, NMe), 3.85 (s, 3 H, NMe), 3.94 (s, 3 H, NMe), 7.65-7.83 (m, 3 H, PhH), 8.29-8.33 (m, 2 H, PhH). *Anal*. Calcd. for $C_{17}H_{14}N_4O_4$ (338.33): C, 60.35; H, 4.17; N, 16.56. Found: C, 60.33; H, 4.04; N, 16.70.

5,6,8-Trimethyl-2-(4-methylphenyl)[1,3]oxazolo[5',4':4,5]-pyrido[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (9b). The yield was 2.72 g (76%), mp 319 °C; ir: 1720 w, 1690 s, 1665 s, 1620 s cm^{-1}; ^{1}H nmr (CF_3COOD): δ 2.50 (s, 3 H, 4'-Me), 3.58 (s, 3 H, NMe), 3.81 (s, 3 H, NMe), 3.92 (s, 3 H, NMe), 7.48 and 8.20 (2 d, J = 7 Hz, AA'BB' pattern, 4 H, PhH). *Anal*. Calcd. for $C_{18}H_{16}N_4O_4$ (352.35): C, 61.36; H, 4.58; N, 15.90. Found: C, 61.19; H, 4.48; N, 15.94.

2-(4-Methoxyphenyl)-5,6,8-trimethyl[1,3]oxazolo-[5',4':4,5]pyrido[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (9c). The yield was 2.39 g (65%), mp 317 °C; ir: 1720 w, 1690 s, 1660 s, 1610 s cm^{-1}; ^{1}H nmr (CF_3COOD): δ 3.60 (s, 3 H, NMe), 3.80 (s, 3 H, NMe), 3.95 (s, 3 H, NMe), 4.02 (s, 3 H, 4'-OMe), 7.20 and 8.32 (2 d, J = 7 Hz, AA'BB' pattern, 4 H, PhH). *Anal*. Calcd. for $C_{18}H_{16}N_4O_5$ (368.35): C, 58.69; H, 4.38; N, 15.21. Found: C, 58.41; H, 4.19; N, 15.00.

2-(4-Chlorophenyl)-5,6,8-trimethyl[1,3]oxazolo[5',4':4,5]-pyrido[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (9d). The yield was 2.76 g (74%), mp 336 °C; ir: 1720 m, 1690 s, 1665 s, 1620 s cm^{-1}; ^{1}H nmr (CF_3COOD): δ 3.58 (s, 3 H, NMe), 3.80 (s, 3 H, NMe), 3.92 (s, 3 H, NMe), 7.60 and 8.18 (2 d, J = 7 Hz, AA'BB' pattern, 4 H, PhH). *Anal*. Calcd. for $C_{17}H_{13}ClN_4O_4$ (372.77): C, 54.78; H, 3.52; N, 15.03. Found: C, 54.51; H, 3.25; N, 14.90.

5,6,8-Trimethyl-2-(4-nitrophenyl)[1,3]oxazolo[5',4':4,5]-pyrido[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (9e). The yield was 2.72 g (71%), mp 350 °C; ir: 1720 m, 1690 s, 1660 s, 1620 s cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 2.69 (s, 3 H, NMe), 3.17 (s, 3 H, NMe), 3.61 (s, 3 H, NMe), 8.33 and 8.42 (2 d, J = 7 Hz, AA'BB' pattern, 4 H, PhH). *Anal*. Calcd. for $C_{17}H_{13}N_5O_6$ (383.32): C, 53.27; H, 3.42; N, 18.27. Found: C, 53.52; H, 3.18; N, 18.36.

6,8-Dimethyl-2,5-diphenyl[1,3]oxazolo[5',4':4,5]pyrido-[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (9f). The yield was

2.92 g (73%), mp 312 °C; ir: 1730 m, 1700 s, 1665 s, 1620 s cm^{-1}; ^{1}H nmr (CF_3COOH): δ 3.12 (s, 3 H, NMe), 3.71 (s, 3 H, NMe), 7.51-7.56 (m, 2 H, ArH), 7.71-7.88 (m, 6 H, ArH), 8.38-8.42 (m, 2 H, ArH). *Anal*. Calcd. for $C_{22}H_{16}N_4O_4$ (400.40): C, 66.00; H, 4.03; N, 13.99. Found: C, 66.28; H, 3.82; N, 13.81.

6,8-Dimethyl-2-(4-methylphenyl)-5-phenyl[1,3]oxazolo-[5',4':4,5]pyrido[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (9g). The yield was 3.15 g (76%), mp 304 °C; ir: 1690 s, 1665 s, 1610 s cm^{-1}; ^{1}H nmr (CF_3COOD): δ 2.43 (s, 3 H, 4-Me), 2.85 (s, 3 H, NMe), 3.38 (s, 3 H, NMe), 7.30-7.35 (m, 2 H, ArH), 7.35 and 8.12 (2 d, J = 7 Hz, AA'BB' pattern, 4 H, ArH), 7.56-7.58 (m, 3 H, ArH). *Anal*. Calcd. for $C_{23}H_{18}N_4O_4$ (414.42): C, 66.66; H, 4.38; N, 13.52. Found: C, 66.62; H, 4.22; N, 13.56.

2-(4-Chlorophenyl)-6,8-dimethyl-5-phenyl[1,3]oxazolo-[5',4':4,5]pyrido[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (9h). The yield was 3.26 g (75%), mp 323 °C; ir: 1720 w, 1700 s, 1670 s, 1610 s cm^{-1}; ^{1}H nmr (CF_3COOD): δ 3.02 (s, 3 H, NMe), 3.63 (s, 3 H, NMe), 7.45 and 8.20 (2 d, J = 7 Hz, AA'BB' pattern, 4 H, PhH), 7.58-7.65 (m, 5 H, PhH). *Anal*. Calcd. for $C_{22}H_{15}ClN_4O_4$ (434.84): C, 60.77; H, 3.48; N, 12.88. Found: C, 60.99; H, 3.30; N, 13.00.

6,8-Dimethyl-2-(4-nitrophenyl)-5-phenyl[1,3]oxazolo-[5',4':4,5]pyrido[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (9i). The yield was 3.12 g (70%), mp 334 °C; ir: 1720 w, 1695 s, 1670 s, 1615 s cm^{-1}; ^{1}H nmr (DMSO): δ 2.66 (s, 3 H, NMe), 3.16 (s, 3 H, NMe), 7.57 (m, 5 H, PhH), 8.36 and 8.48 (2 d, J = 7 Hz, AA'BB' pattern, 4 H, PhH). *Anal*. Calcd. for $C_{22}H_{15}N_5O_6$ (445.39): C, 59.33; H, 3.39; N, 15.72. Found: C, 59.66; H, 3.13; N, 15.47.

2-(4-Chlorophenyl)-5-methyl-6,8-diphenyl[1,3]oxazolo-[5',4':4,5]pyrido[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (9j). The yield was 3.38 g (68%), mp 322 °C; ir: 1730 m, 1700 s, 1680 s, 1615 m cm^{-1}; ^{1}H nmr (CF_3COOD): δ 3.25 (s, 3 H, NMe), 7.35 and 8.18 (2 d, J = 7 Hz, AA'BB' pattern, 4 H, PhH), 7.55-7.60 (m, 10 H, ArH). *Anal*. Calcd. for $C_{27}H_{17}ClN_4O_4$ (496.91): C, 65.26; H, 3.45; N, 11.27. Found: C, 65.22; H, 3.30; N, 11.41.

2-(2,4-Dichlorophenyl)-5,6,8-trimethyl[1,3]oxazolo-[5',4':4,5]pyrido[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (9k). The yield was 2.85 g (70%), mp 348 °C; ir: 1720 m, 1685 s, 1660 s, 1620 s cm^{-1}; ^{1}H nmr (CF_3COOD): δ 3.58 (s, 3 H, NMe), 3.75 (s, 3 H, NMe), 3.85 (s, 3 H, NMe), 7.45 (d, J = 7 Hz, 1 H, ArH), 7.63 (s, 1 H, ArH), 7.98 (d, J = 7 Hz, 1 H, ArH). *Anal*. Calcd. for $C_{17}H_{12}Cl_2N_4O_4$ (407.22): C, 50.14; H, 2.97; N, 13.76. Found: C, 49.91; H, 2.70; N, 13.67.

2-(3,4-Dichlorophenyl)-5,6,8-trimethyl[1,3]oxazolo-[5',4':4,5]pyrido[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (9l). The yield was 2.93 g (72%), mp 305 °C; ir: 1720 s, 1695 s, 1670 s, 1620 s cm^{-1}; ^{1}H nmr (CF_3COOD): δ 3.35 (s, 3 H, NMe, 3.57 (s, 3 H, NMe), 3.66 (s, 3 H, NMe), 7.38 (d, J = 7 Hz, 1 H, ArH), 7.77 (d, J = 7 Hz, 1 H, ArH), 8.02 (s, 1 H, ArH). *Anal*. Calcd. for $C_{17}H_{12}Cl_2N_4O_4$ (407.22): C, 50.14; H, 2.97; N, 13.76. Found: C, 50.10; H, 2.76; N, 13.78.

2-(2,6-Dimethoxyphenyl)-5,6,8-trimethyl[1,3]oxazolo-[5',4':4,5]pyrido[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (9m). The yield was 2.76 g (68%), mp 302 °C; ir: 1715 m, 1690 s, 1665 s, 1620 s cm^{-1}; ^{1}H nmr (CF_3COOD): δ 3.32 (s, 3 H, NMe), 3.52 (s, 3 H, NMe), 3.65 (s, 3 H, NMe), 3.75 (s, 3 H, OMe), 3.99 (s, 3 H, OMe), 6.53 (s, 1 H, ArH), 6.65 (d, J = 7 Hz, 1 H, ArH), 8.09 (d, J = 7 Hz, 1 H, ArH). *Anal*. Calcd. for $C_{19}H_{18}N_4O_6$ (398.38): C, 57.29; H, 4.55; N, 14.06. Found: C, 57.62; H, 4.57; N, 14.0.

2-(2,4-Dichlorophenyl)-6,8-dimethyl-5-phenyl[1,3]oxazolo-[5',4':4,5]pyrido[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (9n). The yield was 2.88 g (71%), mp 313 °C; ir: 1695 s, 1665 s, 1610 s. cm^{-1}; ^{1}H nmr (CF_3COOD): δ 3.00 (s, 3 H, NMe), 3.65 (s, 3 H, NMe), 7.40 (d, J = 7 Hz, 1 H, ArH), 7.45-7.64 (m, 5 H, ArH), 7.65 (s, 1 H, ArH), 8.05 (d, J = 7 Hz, 1 H, ArH). *Anal*. Calcd. for $C_{22}H_{14}Cl_2N_4O_4$ (469.29): C, 56.31; H, 3.01; N, 11.94. Found: C, 56.26; H, 2.80; N, 11.89.

2-(3,4-Dichlorophenyl)-6,8-dimethyl-5-phenyl[1,3]oxazolo-[5',4':4,5]pyrido[2,3-*d*]pyrimidine-4,7,9(5*H*,6*H*,8*H*)-trione (9o). The yield was 2.92 g (72%), mp 334 °C; ir: 1730 w, 1710 s, 1670 s cm^{-1}; ^{1}H nmr (CF_3COOD): δ 2.76 (s, 3 H, NMe), 3.35 (s, 3 H, NMe), 7.13-7.15 (m, 2 H, ArH), 7.35-7.42 (m, 4 H, ArH), 7.76-7.82 (m, 1 H, ArH), 8.03-8.06 (m, 1 H, ArH). *Anal*. Calcd. for $C_{22}H_{14}Cl_2N_4O_4$ (469.29): C, 56.31; H, 3.01; N, 11.94. Found: C, 56.66; H, 2.88; N, 11.91.

Acknowledgement: This work was supported by an ASEA-Uninet scholarship (D.V.T).

REFERENCES

[1a] Grivsky, E. M.; Lee, S.; Sigel, C. W.; Duch, D. S.; Nichols, C. A. *J. Med. Chem.* **1980**, *23*, 327; [b] Bulicz, J.; Bertarelli, D. C. G.; Baumert, D.; Fülle, F.; Müller, C. E.; Heber, D. *Bioorg. Med. Chem.* **2006**, *14*, 2837; [c] Heber, D.; Heers, C.; Ravens, U. *Pharmazie* **1993**, *48*, 537; [d] Girreser, U.; Heber, D.; Schütt, M. *Proceedings of ECSOC-5, The Fifth International Electronic Conference on Synthetic Organic Chemistry, 2001*, poster A0008; Kappe, C. O.; Merino, P.; Marzinzik, A.; Wennemers, H.; Wirth, T.; Van den Eynde, J.-J.; Lin, S.-K. (Eds). CD-ROM edition, ISBN 3-906980-06-5, MPDI, Basel (Switzerland), 2001; [e] Agarwal, A.; Ramesh; A.; Goyal, N.; Chauhan, P. M. S.; Gupta, S. *Bioorg. Med. Chem.* **2005**, *13*, 6678; [f] Sladowska, H.; Sabiniarz, A.; Filipek, B.; Kardasz, M.; Maciag, D. *Farmaco* **2003**, *58*, 25.

[2a] Schaus, J. M.; Titus, R. D. (Eli Lilly & Co.), *U. S. Patent* **1987**, 4,659,832; *Chem. Abstr.* **1987**, *107*, 23329; [b] Caprathe, B. W.; Jaen, J. C., Wise, L. D. (Warner Lambert Co.), *European Patent Appl.* **1988**, 260,642; *Chem. Abstr.* **1988**, *109*, 92992v.

[3] Decktor, D. L.; Fitzpatrick, L. R.; Campbell, H. F. (Rorer Pharmaceutical Corporation), *U. S. Patent* **1989**, 4,831,040; *Chem. Abstr.* **1990**, *112*, 16278p.

[4] Inamoto, Y.; Kawai, S.; Sanada, K.; Endo, T. (Fuji Chemical Industry Co. Ltd., Japan), *Japan Kokai Tokkyo Koho* **1991**, 03 109388; *Chem. Abstr.* **1991**, *115*, 279995.

[5a] Musser, J. H.; Brown, R. E. (USV Pharmaceutical Corporation), *U. S. Patent* **1986**, 4,563,463; *Chem. Abstr.* **1987**, *106*, 50187u; [b] Renaud, A.; Schoofs, A. R.; Guiraudie, J. M.; Brochet D. (Delalande S. A.), *European Patent Appl.* **1989**, 322263; *Chem. Abstr.* **1990**, *112*, 216909g.

[6a] Brill, G.; Hagen, H.; Westphalen, K. O.; Würzer, B. (BASF AG), *European Patent Appl.* **1990**, 401582; *Chem. Abstr.* **1991**, *114*, 122372r; [b] Brill, G.; Hagen, H.; Westphalen, K. O.; Würzer, B. (BASF AG), *German Offen.* **1990**, 3,917,883; *Chem. Abstr.* **1991**, *114*, 185503e.

[7] Khattab, A. F. A.; Dang, V. T.; Stadlbauer, W. *J. Prakt. Chem-Chem. Ztg.* **1996**, *338*, 151.

[8a] Burova, O. A.; Bystryakova, I. D.; Smirnova, N. M.; Safonova, T. S. *Khim. Geterotsikl. Soedin.* **1990**, 662; [b] Burova, O. A.; Bystryakova, I. D.; Smirnova, N. M.; Safonova, T. S. *Khim. Geterotsikl. Soedin.* 1991, 497; [c] Seidenfaden, W.; Pawellek, D. in *Houben-Weyl, Methoden der Organischen Chemie*, 4th ed, Müller, E. (Ed), Vol 10/1, Georg Thieme Verlag, Stuttgart, 1971, p 849.

[9] Steinschifter, W.; Fiala, W.; Stadlbauer, W. *J. Heterocyclic Chem.* **1994**, *31*, 1647.

[10] Stadlbauer, W.; Badawey, E.-S.; Hojas, G.; Roschger, P.; Kappe, T. *Molecules* **2001**, *6*, 338.

[11a] Dang, V. T.; Stadlbauer, W. *Molecules* **1996**, *1*, 201; [b] Kappe, T.; Stadlbauer, W. *Molecules* **1996**, *1*, 255.