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Synthesis of 6-substituted 7-aryl-5,6-dihydropyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-diones using the Vilsmeier reaction☆

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Abstract—The reaction of 6-amino-1,3-dimethyluracil with equimolar amounts of arylalkanone Mannich bases under optimized reaction conditions leads to 7-aryl-5,6-dihydropyrido[2,3-*d*]pyrimidines in a yield of 50–80%. Functionalization of these dihydropyridopyrimidine(1*H*,3*H*)-2,4-diones with the Vilsmeier reagent affords, depending on the reaction conditions, either 6-dimethylaminomethylidene substituted 5*H*-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-diones or the corresponding pyridopyrimidine(1*H*,3*H*)-2,4-diones bearing a carboxaldehyde function in position 6 of the heterocycle. Some further transformations of the aldehyde function demonstrate the synthetic potential of the synthesized structures, introducing pharmacologically relevant basic substituents into the side chain of these pyrido[2,3-*d*]pyrimidine derivatives.

1. Introduction

Among the methods for the synthesis of 1,3-dimethylpyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-diones,[2–8] the condensation of 6-amino-1,3-dimethyluracil with suitable electrophiles is a straightforward and often used approach. The substitution pattern of the annelated pyridine ring formed is determined in these reactions by the structure of the biselectrophile. When an arylalkanone Mannich base is employed, formation of mixtures of dihydropyridopyrimidine(1*H*,3*H*)-2,4-dione **5** and pyridopyrimidine(1*H*,3*H*)-2,4-dione **6** has been reported.[3] However, the formation of the regioisomeric 5-aryl substituted pyridopyrimidines is not observed. The reaction mechanism is outlined in Scheme 1, in cyclocondensations performed with 6-aminouracil analogs and Mannich bases the postulated intermediates **3** und **4** could be isolated.[8]

We considered position 6 of the pyridopyrimidine **5** an interesting target for further modifications and employed the Vilsmeier reaction, as the structures obtainable are of interest regarding their pharmacological properties. The biological activity of this class of compounds, that is, their antitumor, antifolate and antibacterial properties are referenced elsewhere.[8] There are also only a few 6- or 7-substituted 5,6,7,8-tetrahydropyrido[2,3-*d*]pyrimidines used as drugs described in the literature,[9,10] for example, the antineoplastic lometrexol sodium.[10]

2. Results and discussion

6-Amino-1,3-dimethyluracil (**1**) was reacted with an equimolar amount of the Mannich bases **2a–c** according to the reported procedure.[3] We performed this reaction under an atmosphere of nitrogen in order to prevent oxidation to **6**, thus it was not necessary to purify the reaction mixture by column chromatography. The pyridopyrimidines **6** can be obtained directly, when the cyclocondensation is performed in acetic acid as the solvent.[3] The 5,6-dihydropyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-diones **5** were then converted to the red colored dimethylaminomethylidene derivatives **7** by treatment with the Vilsmeier mixture of phosphorous oxychloride and *N*,*N*-dimethylformamide at room temperature and subsequent hydrolysis (Scheme 1). Crystals of **7** decolorized with formation of the carbaldehyde **8**, which was also the main product, when the Vilsmeier reaction was performed at 80 °C followed by hydrolysis. The position 6 of the carbaldehyde group is evidenced by a H,H long-range coupling observed in the two dimensional spectrum with the proton in position 5 and

☆ See Ref. 1.

Keywords: Cyclization; Cyclocondensation; 6-Amino-1,3-dimethyluracil; Mannich bases; Vilsmeier reaction; Pyrido[2,3-*d*]pyrimidines.
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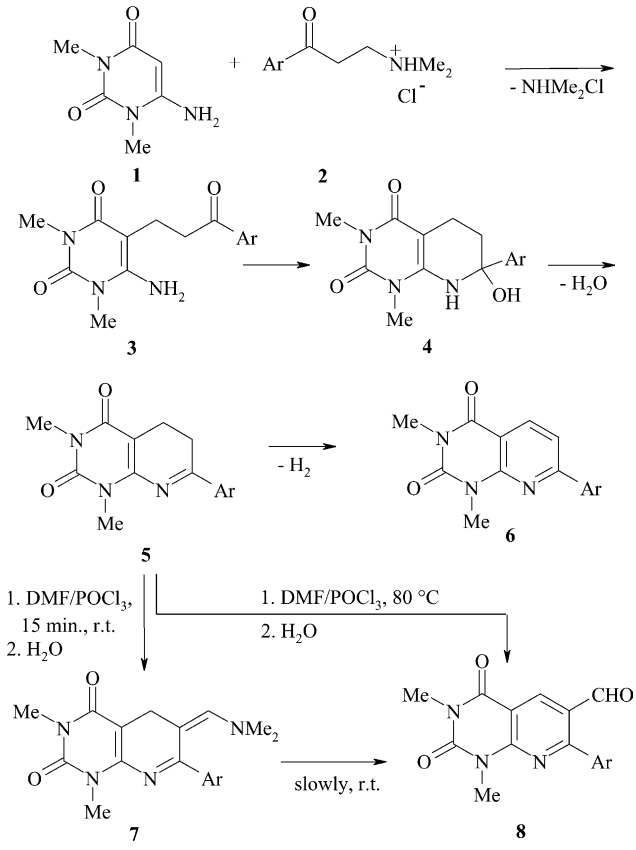
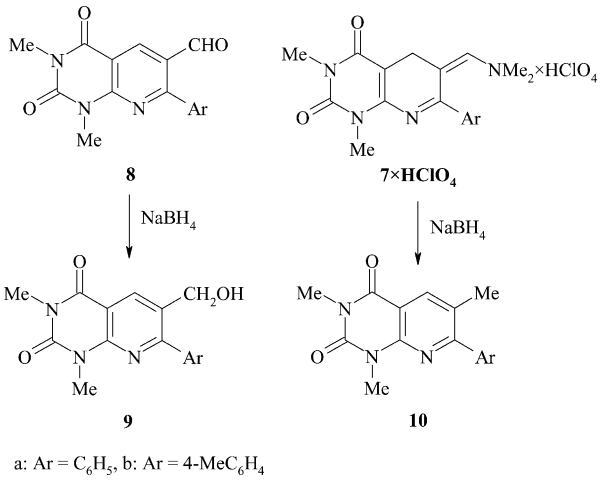


Scheme 1.

also a weak cross peak in the NOESY spectrum which showed additionally a strong cross peak with the protons in *ortho* position of the phenyl group. Two dimensional C,H-correlations aided also in the assignment of the ^{13}C NMR data of all the structures prepared.

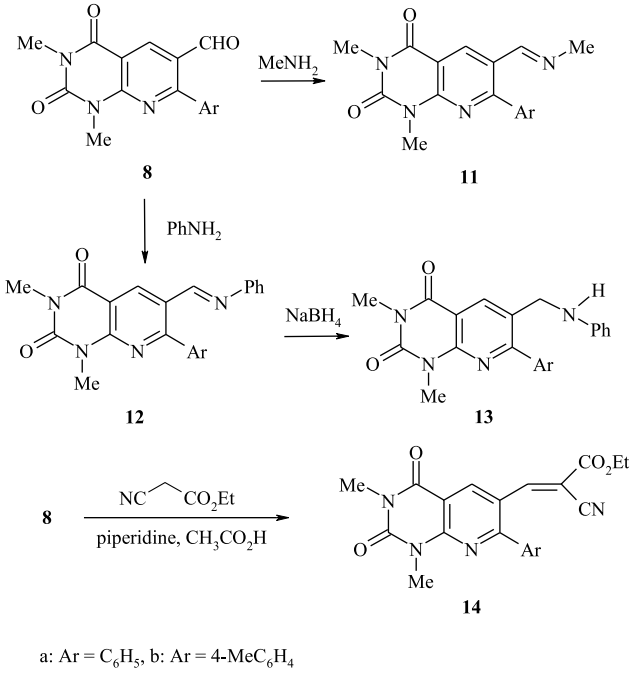
Thus, oxidation of the dihydropyridine moiety is occurring together with hydrolysis. The red dimethylaminomethylidene derivatives **7**, which are very sensitive towards air and water, can be precipitated as yellow hydroperchlorates, however, the salts do show only a slightly higher stability towards hydrolysis and, for example, completely decompose during the recording of the ^{13}C NMR spectra under routine conditions. The UV/vis spectra of the hydroperchlorates **7**×$HClO_4$ show an absorption band at about 465–470 nm with only a small bathochromic shift compared with the bases **7** of about 5 nm. Upon reduction of the carbaldehydes **8** with sodium borohydride, the expected hydroxymethylderivatives **9** are obtained. However, when performing the reduction of the hydroperchlorates **7** under the same reaction conditions, a complex mixture was obtained, the major product being the pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-diones **10**. The dimethylaminomethyl derivative is not formed, instead cleavage of the amino group and reduction to the methyl residue is observed, the pyridine moiety being unaffected (Scheme 2).

Another approach to pharmacological relevant structures is the introduction of a basic center into the side chain of the heterocycle, presenting the characteristic string of aromatic



Scheme 2.

moiety connected via an aliphatic side chain to a basic function.[11] In order to modify the carbaldehydes **8**, reactions with a primary amine afforded the imines **11** and **12**, the reduction of which allowed access to the anilinomethyl derivative **13**, again without reduction of the pyridine nucleus (Scheme 3).



Scheme 3.

Finally, under the reaction of the carbaldehydes **8** with numerous C–H acidic compounds we describe here only the one with ethyl cyano acetate under Knoevenagel conditions, affording the expected acrylate derivatives in about 60–70% yield.

3. Conclusions

The synthetic approach to 6-substituted pyrido[2,3-*d*]-pyrimidine(1*H*,3*H*)-2,4-diones presented here using the

Vilsmeier reaction of 5,6-dihydropyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-diones, allows access to a great number of structures and introduction of functionalities via the intermediate carboxaldehydes.

4. Experimental

4.1. General

Electron impact (EI) mass spectra were obtained with an ionization energy of 70 eV using a HP 5989A mass spectrometer and a direct inlet probe with a tungsten wire; *m*/*z* values are reported followed by the relative intensity in parentheses. APCI mass spectra were obtained on a Bruker Esquire LC. Nuclear Magnetic Resonance (^{1}H and ^{13}C) spectra were recorded on a Bruker instrument ARX300. In all cases DMSO-d_6 was used as the solvent. Chemical shifts are reported in parts per million (δ) downfield from an internal TMS reference. Coupling constants (*J*) are reported in Hertz (Hz), and spin multiplicities are indicated by the following symbols s (singlet), d (doublet), t (triplet), q (quartet), quint. (quintet), m (multiplet), br (broad signal). Multiplets were analyzed according to first order coupling. Elemental analyses were either performed by the Mikroanalytisches Labor Beetz or at the Institute of Inorganic Chemistry of the University of Kiel. High resolution mass spectra were performed by the Institute or Organic Chemistry at the University of Kiel. UV/vis spectra were recorded with a HP 8542A spectrophotometer in MeOH as the solvent. The wavelengths of the three or four strongest absorption bands together with the logarithm of the extinction coefficient ε in l/(mol×cm) are given. IR spectra were recorded as KBr pellets on a Perkin–Elmer 1600 PC FT-IR machine. Melting points were recorded with a Thiele (Büchi SMP-20) melting point apparatus and are not corrected. For preparative column chromatography silica gel 60 (Merck) was used.

4.2. 5,6-Dihydropyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-diones 5a–c and pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-diones 6a–c

A solution of 620 mg (4 mmol) of 4-amino-1,3-dimethyluracil (**1**) (Merck, Darmstadt, Germany) and 4 mmol of the corresponding arylalkanone Mannich bases **2a–c** was heated to reflux in 20 mL of deoxygenated water for 90 min under an atmosphere of nitrogen. After cooling to rt the yellow crystals were filtered and recrystallized from ethanol. In order to obtain pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-diones **6a–c**, the reaction was performed on the same scale as described above for **5**, acetic acid was employed as the solvent and air was not excluded. After cooling to rt the slightly yellow crystals were filtered and recrystallized from ethanol.

4.2.1. 1,3-Dimethyl-7-phenyl-5,6-dihydropyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione (5a). 540 mg (2.0 mmol, 50%), mp 180 °C, mp[3] 180 °C. UV/vis λ: 218 (4.1), 276 (4.2), 368 (3.8). IR ν: 1688, 1644/1640. MS *m*/*z*: 269 (M^+, 84), 268 (100), 192 (38), 154 (19), 81 (40). ^{1}H NMR data in accordance with Ref. 5. ^{13}C NMR δ: 16.3 (C-5), 24.2 (C-6), 28.2 (1-CH_3), 29.9 (3-CH_3), 94.2 (C-4a), 128.0 (C-3′), 128.8 (C-2′), 132.7 (C-4′), 136.8 (C-1′), 149.4 (C-8a), 152.1 (C-2), 163.0 (C-4), 174.6 (C-7).

4.2.2. 1,3-Dimethyl-7-(4-tolyl)-5,6-dihydropyrido[2,3-*d*]-pyrimidine(1*H*,3*H*)-2,4-dione (5b). 690 mg (2.4 mmol, 61%), mp 181 °C. UV/vis λ: 218 (4.2), 276 (4.2), 362 (3.9). IR ν: 1692, 1660/1650. MS *m*/*z*: 283 (M^+, 71), 282 (100), 281 (21), 192 (26), 81 (40). ^{1}H NMR δ: 2.44 (s, 3H, 4′-CH_3), 2.68/2.89 (2×t, J=9.0 Hz, 2×2H, 5-H, 6-H), 3.42/3.56 (2×s, 2×3H, 1-CH_3, 3-CH_3), 7.30/7.98 (2×d, J=8.3 Hz, 2×2H, 2′-H, 3′-H). ^{13}C NMR δ: 16.4 (C-5), 21.7 (4′-CH_3), 24.1 (C-6), 28.2 (1-CH_3), 30.0 (3-CH_3), 94.4 (C-4a), 128.2 (C-2′), 129.6 (C-3′), 134.2 (C-1′), 43.7 (C-4′), 149.7 (C-8a), 152.2 (C-2), 163.1 (C-4), 174.5 (C-7). HRMS Calcd for $C_{15}H_{12}N_3O_2$: 283.1321, found: 283.1319.

4.2.3. 7-(4-Bromophenyl)-1,3-dimethyl-5,6-dihydropyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione (5c). 1.09 g (3.1 mmol, 78%), mp 178–180 °C. UV/vis λ: 218 220 (4.2), 284 (4.3), 370 (3.9). IR ν: 1692, 1638 (br). MS *m*/*z*: 349 (M^+, ^{81}Br, 76), 348 (100), 347 (M^+, ^{79}Br, 88), 346 (85), 345 (23), 192 (59), 81 (64). ^{1}H NMR δ: 2.69/2.88 (2×t, J=9 Hz, 2×2H, 5-H, 6-H), 3.41/3.64 (2×s, 2×3H, 1-CH_3, 3-CH_3), 7.64/7.95 (2×d, J=8.7 Hz, 2×2H, 2′-H, 3′-H). ^{13}C NMR δ: 16.3 (C-5), 24.0 (C-6), 28.3 (1-CH_3), 30.0 (3-CH_3), 94.5 (C-4a), 127.8 (C-1′), 129.4 (C-2′), 132.1 (C-3′), 135.6 (C-4′), 149.3 (C-8a), 152.0 (C-2), 163.0 (C-4), 173.5 (C-7).

4.2.4. 1,3-Dimethyl-7-phenylpyrido[2,3-*d*]pyrimidine-(1*H*,3*H*)-2,4-dione (6a). 570 mg (2.2 mmol, 54%), mp 184 °C, mp[3] 156–157 °C. UV/vis λ: 220 (4.5), 252 (4.1), 272 (4.0), 332 (4.2). IR ν: 1706, 1658, 1602. MS *m*/*z*: 267 (M^+, 100), 239 (47), 238 (42), 155 (44), 154 (19). ^{1}H NMR data in accordance with Ref. 3. ^{13}C NMR δ: 28.4 (1-CH_3), 29.4 (3-CH_3), 109.0 (C-4a), 115.0 (C-6), 127.5 (C-3′), 128.9 (C-2′), 130.7 (C-4′), 137.4 (C-1′), 138.3 (C-5), 150.7 (C-8a), 151.6 (C-2), 161.1 (C-7), 161.3 (C-4).

4.2.5. 1,3-Dimethyl-7-(4-tolyl)-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione (6b). 550 mg (2.0 mmol, 49%), mp 183 °C, mp[3] 173–174 °C. UV/vis λ: 220 (4.6), 254 (4.1), 336 (4.1), 336 (4.4). IR ν: 1704, 1660, 1596. MS *m*/*z*: 281 (M^+, 100), 253 (46), 252 (43), 169 (34). ^{1}H NMR δ: 2.44 (s, 3H, 4′-CH_3), 3.50/3.82 (2×s, 2×3H, 1-CH_3, 3-CH_3), 7.31/8.02 (2×d, J=8.0 Hz, 2×2H, 2′-H, 3′-H), 7.62/8.46 (2×d, J=8.2 Hz, 2×1H, 6-H, 5-H). ^{13}C NMR δ: 21.4 (4′-CH_3), 28.4 (1-CH_3), 29.3 (3-CH_3), 108.7 (C-4a), 114.7 (C-6), 127.4 (C-2′), 129.6 (C-3′), 134.6 (C-1′), 138.1 (C-5), 141.4 (C-4′), 150.6 (C-8a), 151.6 (C-2), 161.1 (C-7), 161.3 (C-4).

4.2.6. 7-(4-Bromophenyl)-1,3-dimethylpyrido[2,3-*d*]-pyrimidine(1*H*,3*H*)-2,4-dione (6c). 910 mg (2.6 mmol, 66%), mp 216 °C. UV/vis λ: 222 (4.5), 256 (4.2), 276 (4.2), 336 (4.3). IR ν: 1704, 1656, 1598. MS *m*/*z*: 347 (M^+, ^{81}Br, 100), 319 (36), 318 (35), 317 (36), 316 (29), 235 (35), 233 (36). ^{1}H NMR δ: 3.51/3.81 (2×s, 2×3H, 1-CH_3, 3-CH_3), 7.60/8.47 (2×d, J=8.1 Hz, 2×1H, 6-H, 5-H), 7.63/7.97 (2×d, J=8 Hz, 2×2H, 2′-H, 3′-H). ^{13}C NMR δ: 28.5 (1-CH_3), 29.4 (3-CH_3), 109.3 (C-4a), 114.8 (C-6), 125.4 (C-1′), 129.0 (C-3′), 132.2 (C-2′), 136.3 (C-4′), 138.6 (C-5), 150.8 (C-8a), 151.6 (C-2), 160.0 (C-7), 161.2 (C-4).

HRMS Calcd for $C_{15}H_{12}N_3O_2^{79}Br$ 345.0113, found: 345.0113.

4.3. 6-(Dimethylaminomethylidene)-5*H*-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-diones 7a–c, hydroperchlorates 7a–c×HClO$_4$, and 1,3-dimethyl-2,4-dioxo-(1*H*,3*H*)-pyrido[2,3-*d*]pyrimidine-6-carbaldehydes 8a–c

To a suspension of 1.0 mmol of **5** in 2 mL of DMF was added dropwise 200 µl (0.33 g, 2.1 mmol) of $POCl_3$ while cooling with an ice/water bath. The reaction mixture was stirred for 15 min at rt, followed by the addition of 10 mL of cold water. Solid sodium bicarbonate was added to the yellow solution until alkaline. The red solution was extracted with three 10 mL portions of dichloromethane, the combined organic layers were washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated. The remainder was treated with diethyl ether and the solids of **7a–c** obtained were filtered and dried in vacuo. The corresponding hydroperchlorates were obtained by dissolving 1 mmol of **7** in 25 mL of methanol and 0.2 mL of $HClO_4$ (70%) was added while cooling with an ice/water bath. After about 15 min a precipitate was formed, which was filtered off and dried in vacuo. In all cases the yield was quantitative. The carbaldehydes **8a–c** were obtained when performing the reaction on the same scale as described above for **7a–c**, after stirring the reaction mixture for 30 min at rt, then the reaction mixture was heated to 80 °C for 3 h. After cooling 15 g of ice was added and the mixture was stirred vigorously. The yellow precipitate was filtered, dried, and recrystallized.

4.3.1. 1,3-Dimethyl-6-(dimethylaminomethylidene)-7-phenyl-5*H*-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione (7a). 165 mg (0.51 mmol, 51%), mp 141 °C, decomposition upon recrystallization. UV/vis λ: 260 (3.9), 324 (3.8), 464 (3.6). IR ν: 2910 (w), 1662, 1636 (w). MS *m/z*: 324 (M^+, 21), 323 (17), 309 (53), 280 (38), 166 (35), 58 (100). ^{1}H NMR δ: 3.16 (s, 6H, $N(CH_3)_2$), 3.38/3.56 (2×s, 2×3H, 1-CH_3, 3-CH_3), 3.87 (br s, 2H, 5-H), 6.69 (t, J=1 Hz, 1H, 6=CH), 7.30–7.60 (m, 5H, phenyl-H). ^{13}C NMR δ: 22.9 (C-5), 27.9 (1-CH_3), 29.4 (3-CH_3), 43.9 (N-CH_3), 89.9 (C-6), 100.2 (C-4a), 128.1 (C-3′), 130.1 (C-2′), 130.3 (C-4′), 140.3 (C-1′), 151.5 (C-2), 152.5 (C-8a), 155 (6=CH), 162.9 (C-4), 176.9 (C-7).

4.3.2. 1,3-Dimethyl-6-(dimethylaminomethylidene)-7-(4-tolyl)-5*H*-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione (7b). 210 mg (0.61 mmol, 61%), mp 166 °C, decomposition upon recrystallization. UV/vis λ: 276 (4.1), 326 (4.1), 466 (3.9). IR ν: 1684, 1644 (s), 1610. MS *m/z*: 338 (M^+, 54), 337 (51), 323 (94), 294 (82), 180 (48), 58 (100). ^{1}H NMR δ: 2.38 (s, 3H, 4′-CH_3), 3.16 (s, 6H, $N(CH_3)_2$), 3.38/3.57 (2×s, 2×3H, 1-CH_3, 3-CH_3), 3.83 (br s, 2H, 5-H), 6.72 (t, J=1 Hz, 1H, 6=CH), 7.21/7.46 (2×d, J=8.1 Hz, 2×2H, 2′-H, 3′-H). ^{13}C NMR δ: 21.4 (4′-CH_3), 22.9 (C-5), 27.9 (1-CH_3), 29.4 (3-CH_3), 43.8 (N-CH_3), 89.9 (C-6), 100.1 (C-4a), 128.9 (C-2′), 130.2 (C-3′), 137.4 (C-1′), 140.8 (C-4′), 151.6 (C-2), 152.5 (C-8a), 155.2 (6=CH), 163.0 (C-4), 176.9 (C-7).

4.3.3. 7-(4-Bromophenyl)-1,3-dimethyl-6-(dimethylaminomethylidene)-5*H*-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione (7c). 250 mg (0.63 mmol, 63%), mp 143 °C, decomposition upon recrystallization. UV/vis λ: 218 (4.4), 276 (4.3), 368 (4.1), 466 (3.8). IR ν: 1686, 1640 (s). MS *m/z*: 402 (M^+, ^{79}Br, 8), 387 (21), 279 (55), 58 (100). ^{1}H NMR δ: 3.17 (s, 6H, $N(CH_3)_2$), 3.37/3.54 (2×s, 2×3H, 1-CH_3, 3-CH_3), 3.86 (br s, 2H, 5-H), 6.64 (br s, 1H, 6=CH), 7.42/7.54 (2×d, J=8.4 Hz, 2×2H, 2′-H, 3′-H). ^{13}C NMR δ: 22.9 (C-5), 27.9 (1-CH_3), 29.4 (3-CH_3), 43.9 (N-CH_3), 90.0 (C-6), 100.1 (C-4a), 124.8 (C-1′), 131.6 (C-3′), 131.9 (C-2′), 139.2 (C-4′), 151.3 (C-2), 152.4 (C-8a), 155.0 (6=CH), 162.9 (C-4), 175.6 (C-7).

4.3.4. 1,3-Dimethyl-6-(dimethylaminomethylidene)-7-phenyl-5*H*-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione hydroperchlorate (7a×HClO$_4$). Mp 206–208 °C, decomposition upon recrystallization. UV/vis λ: 204 (4.4), 268 (4.2), 316 (4.1), 456 (3.9). IR ν: 3200 (br), 1690, 1664, 1090 (s). MS *m/z*: 325 [M+H$^+$] in MeOH/10 mM NH_4OAc by APCI. ^{1}H NMR δ: 3.20/3.47 (2×s, 2×3H, 1-CH_3, 3-CH_3), 3.50 (br s, 6H, $N(CH_3)_2$), 3.73 (br s, 2H, 5-H), 7.55–7.75 (m, 6H, phenyl-H, 6=CH), 10.31 (br s, 1H, NH). ^{13}C NMR δ: 22.2 (C-5), 27.8 (1-CH_3), 30.3 (3-CH_3), 43–49 (very br, N-CH_3), 86.9 (C-6), 102.6 (C-4a), 128.9 (C-3′), 131.3 (C-2′), 132.4 (C-1′), 132.8 (C-4′), 143.0 (C-8a), 150.5 (C-2), 160.7 (C-4), 160.8 (C-7), 166.4 (6=CH).

4.3.5. 1,3-Dimethyl-6-(dimethylaminomethylidene)-7-(4-tolyl)-5*H*-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione hydroperchlorate (7b×HClO$_4$). Mp 192–194 °C, decomposition upon recrystallization. UV/vis λ: 278 (4.2), 322 (4.1), 462 (4.0). IR ν: 3200–2800 (w), 1694, 1664, 1092 (br, s). MS *m/z*: 339 [M+H$^+$] in MeOH/10 mM NH_4OAc by APCI. ^{1}H NMR δ: 2.43 (s, 3H, 4′-CH_3), 3.19/3.47 (2×s, 2×3H, 1-CH_3, 3-CH_3), 3.49 (br s, 6H, $N(CH_3)_2$), 3.70 (br s, 2H, 5-H), 7.52 (m, 5H, phenyl-H, 6=CH), 10.26 (br s, 1H, NH). ^{13}C NMR δ: 21.1 (4′-CH_3), 22.2 (C-5), 27.8 (1-CH_3), 30.2 (3-CH_3), 43-47 (very br, N-CH_3), 87.0 (C-6), 102.1 (C-4a), 129.4 (C-2′), 129.7 (C-1′), 131.3 (C-3′), 143.3 (C-8a), 143.9 (C-4′), 150.6 (C-2), 160.7 (C-4), 161.0 (C-7), 166.2 (6=CH).

4.3.6. 7-(4-Bromophenyl)-1,3-dimethyl-6-(dimethylaminomethylidene)-5*H*-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione hydroperchlorate (7c×HClO$_4$). Mp 195–197 °C, decomposition upon recrystallization. UV/vis λ: 220 (4.3), 274 (4.3), 326 (4.1), 470 (4.0). IR ν: 3400–2900 (w), 1694, 1666, 1090 (br, s). MS *m/z*: 404/406 [M+H$^+$] in MeOH/10 mM NH_4OAc by APCI. ^{1}H NMR δ: 3.19/3.45 (2×s, 2×3H, 1-CH_3, 3-CH_3), 3.50 (br s, 6H, $N(CH_3)_2$), 3.72 (br s, 2H, 5-H), 7.60-7.80 (m, 5H, phenyl-H, 6=CH), 10.25 (br s, 1H, NH). ^{13}C NMR δ: 22.2 (C-5), 27.8 (1-CH_3), 30.2 (3-CH_3), 43-50 (very br, N-CH_3), 86.8 (C-6), 103.0 (C-4a), 126.6 (C-1′), 131.6 (C-4′), 131.8 (C-3′), 132.1 (C-2′), 143.9 (C-8a), 150.5 (C-2), 159.7 (C-7), 160.7 (C-4), 166.2 (6=CH).

4.3.7. 1,3-Dimethyl-2,4-dioxo-7-phenyl-(1*H*,3*H*)-pyrido[2,3-*d*]pyrimidine-6-carbaldehyde (8a). 210 mg (0.71 mmol, 71%), mp 189 °C (ethyl acetate). UV/vis λ: 222 (4.4), 256 (4.0), 276 (4.1), 336 (4.2). IR ν: 1718, 1680, 1658. MS *m/z*: 295 (M^+, 95), 294 (100), 267 (17), 239 (27), 238 (24). ^{1}H NMR δ: 3.52/3.81 (2×s, 2×3H, 1-CH_3,

3-CH_3), 7.50–7.80 (m, 5H, phenyl-H), 9.06 (s, 1H, 5-H), 10.05 (s, 1H, CHO). ^{13}C NMR δ: 28.6 (1-CH_3), 30.0 (3-CH_3), 109.6 (C-4a), 125.5 (C-6), 128.8 (C-3′), 130.5 (C-2′), 130.8 (C-4′), 136.1 (C-1′), 139.3 (C-5), 151.3 (C-2), 152.3 (C-8a), 160.5 (C-4), 166.2 (C-7), 189.2 (6-CHO). Anal. Calcd: C: 65.08, H: 4.44, N: 14.23, found: C: 65.40, H: 4.48, N: 14.12.

4.3.8. 1,3-Dimethyl-2,4-dioxo-7-(4-tolyl)-(1*H*,3*H*)-pyrido[2,3-*d*]pyrimidine-6-carbaldehyde (8b). 220 mg (0.70 mmol, 70%), mp 194 °C (ethyl acetate). UV/vis λ: 220 (4.4), 274 (4.3), 326 (4.2). IR ν: 1718, 1686, 1662. MS *m/z*: 309 (M^+, 100), 308 (82), 294 (61), 253 (33), 252 (31), 169 (34). ^{1}H NMR δ: 2.49 (s, 3H, 4′-CH_3), 3.51/3.80 (2×s, 2×3H, 1-CH_3, 3-CH_3), 7.38/7.57 (2×d, J=7.9 Hz, 2×2H, 2′-H, 3′-H), 9.05 (s, 1H, 5-H), 10.06 (s, 1H, CHO). ^{13}C NMR δ: 21.5 (4′-CH_3), 28.6 (1-CH_3), 29.9 (3-CH_3), 109.4 (C-4a), 125.4 (C-6), 129.6 (C-2′), 130.6 (C-3′), 133.3 (C-1′), 139.3 (C-5), 141.3 (C-4′), 151.4 (C-2), 152.2 (C-8a), 160.6 (C-4), 166.2 (C-7), 189.4 (6-CHO). Anal. Calcd: C: 66.01, H: 4.89, N: 13.58, found: C: 65.82, H: 5.14, N: 13.41.

4.3.9. 7-(4-Bromophenyl)-1,3-dimethyl-2,4-dioxo-(1*H*,3*H*)-pyrido[2,3-*d*]pyrimidine-6-carbaldehyde (8c). 250 mg (0.67 mmol, 67%), mp 203 °C (toluene). UV/vis λ: 220 (4.4), 258 (4.3), 324 (4.1). IR ν: 1720, 1684, 1660. MS *m/z*: 375 (M^+, ^{81}Br, 96), 374 (71), 373 (M^+, ^{79}Br, 100), 372 (53), 294 (47), 293 (35). ^{1}H NMR δ: 3.52/3.79 (2×s, 2×3H, 1-CH_3, 3-CH_3), 7.54/7.72 (2×d, J=8.6 Hz, 2×2H, 2′-H, 3′-H), 9.05 (s, 1H, 5-H), 10.04 (s, 1H, CHO). ^{13}C NMR δ: 28.7 (1-CH_3), 30.0 (3-CH_3), 109.9 (C-4a), 125.4 (C-6), 125.7 (C-1′), 131.9 (C-3′), 132.1 (C-2′), 135.0 (C-4′), 139.6 (C-5), 151.3 (C-2), 152.4 (C-8a), 160.4 (C-4), 164.9 (C-7), 188.7 (6-CHO). Anal. Calcd: C: 51.36, H: 3.23, N: 11.23, found: C: 51.07, H: 3.13, N: 11.56.

4.4. 6-Hydroxymethyl-1,3-dimethylpyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-diones 9a–b and 1,3,6-trimethylpyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-diones 10a–b

0.5 mmol of **8** and 100 mg (2.65 mmol) of sodium borohydride were suspended in 10 mL of ethanol and stirred for 45 min at rt. The mixture was concentrated in vacuo and vigorously stirred with 20 mL of cold water. Then the mixture was acidified by addition of diluted HCl, the precipitate was filtered, washed with water, and recrystallized from ethanol. The trimethyl derivatives **10a–b** were obtained by heating 1 mmol of **7**×$HClO_4$ and 100 mg (2.65 mmol) of sodium borohydride in 25 mL of ethanol to 50 °C for 90 min. After cooling the reaction mixture was concentrated in vacuum and 20 mL of cold water was added to the remainder. The mixture was stirred vigorously and the precipitate was filtered off, dried in vacuum and subjected to column chromatography on silica gel (cyclohexane/ethyl acetate 6/4) to afford the colorless derivatives **10**.

4.4.1. 6-Hydroxymethyl-1,3-dimethyl-7-phenylpyrido-[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione (9a). 120 mg (0.41 mmol, 81%), mp 193 °C. UV/vis λ: 220 (4.5), 250 (4.3), 326 (4.1). IR ν: 3438 (br), 1714, 1670, 1608. MS *m/z*: 297 (M^+, 100), 296 (77), 268 (19), 239 (16), 220 (15). ^{1}H NMR δ: 2.57 (br s, 1H, OH), 3.47/3.72 (2×s, 2×3H, 1-CH_3, 3-CH_3), 4.76 (s, 2H, 6-CH_2), 7.50/7.69 (2×m, 5H, phenyl-H), 8.66 (s, 1H, 5-H). ^{13}C NMR δ: 28.5 (1-CH_3), 29.5 (3-CH_3), 61.7 (6-CH_2), 109.1 (C-4a), 128.4 (C-3′), 129.3 (C-2′), 129.6 (two overlapping signals, C-6, C-4′), 138.3 (C-1′), 138.8 (C-5), 149.5 (C-8a), 151.6 (C-2), 161.4 (C-4), 162.5 (C-7). HRMS Calcd for $C_{16}H_{15}N_3O_3$ 297.1133, found: 297.1114.

4.4.2. 6-Hydroxymethyl-1,3-dimethyl-7-(4-tolyl)-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione (9b). 140 mg (0.45 mmol, 90%), mp 198 °C. UV/vis λ: 220 (4.6), 254 (4.2), 328 (4.2). IR ν: 3400 (br), 1700, 1640, 1605. MS *m/z*: 311 (M^+, 100), 310 (76), 296 (17), 282 (16). ^{1}H NMR δ: 2.44 (s, 3H, 4′-CH_3), 2.61 (br s, 1H, OH), 3.46/3.71 (2×s, 2×3H, 1-CH_3, 3-CH_3), 4.76 (s, 2H, 6-CH_2), 7.31/7.59 (2×d, J=8.0 Hz, 2×2H, 2′-H, 3′-H), 8.47 (s, 1H, 5-H). ^{13}C NMR δ: 21.4 (4′-CH_3), 28.5 (1-CH_3), 29.5 (3-CH_3), 61.8 (6-CH_2), 108.8 (C-4a), 129.2 (two overlapping signals C-2′, C-3′), 129.5 (C-6), 135.5 (C-1′), 138.7 (C-5), 139.9 (C-4′), 149.5 (C-8a), 151.7 (C-2), 161.4 (C-4), 162.5 (C-7). Anal. Calcd: C: 65.58, H: 5.50, N: 13.50, found: C: 65.46, H: 5.42, N: 13.55.

4.4.3. 1,3,6-Trimethyl-7-phenylpyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione (10a). 56 mg (0.20 mmol, 20%), mp 165 °C, mp[3] 162–163 °C. UV/vis λ: 218 (4.5), 248 (4.2), 330 (4.1). IR ν: 1706, 1670, 1606. MS *m/z*: 281 (M^+, 98), 280 (100), 253 (23), 252 (32), 169 (37). ^{1}H NMR δ: 2.45 (s, 3H, 6-CH_3), 3.50/3.73 (2×s, 2×3H, 1-CH_3, 3-CH_3), 7.49/7.62 (2×m, 3H/2H, phenyl-H), 8.33 (s, 1H, 5-H). ^{13}C NMR δ: 19.2 (6-CH_3), 27.3 (1-CH_3), 28.9 (3-CH_3), 108.5 (C-4a), 125.8 (C-6), 127.8 (C-3′), 128.6 (two overlapping signals C-2′,C-4′), 138.8 (C-1′), 139.1 (C-5), 148.2 (C-8a), 151.2 (C-2), 161.0 (C-4), 162.3 (C-7). HRMS Calcd for $C_{16}H_{15}N_3O_2$ 281.1164, found: 281.1164.

4.4.4. 1,3,6-Trimethyl-7-(4-tolyl)-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione (10b). 44 mg (0.15 mmol, 15%), mp 166 °C. UV/vis λ: 220 (4.6), 252 (4.1), 332 (4.1). IR ν: 1702, 1654 (s), 1604. MS *m/z*: 295 (M^+, 92), 294 (100), 267 (16), 266 (22), 183 (18). ^{1}H NMR δ: 2.44 (s, 6H, 6-CH_3, 4′-CH_3), 3.49/3.71 (2×s, 2×3H, 1-CH_3, 3-CH_3), 4.76 (s, 2H, 6-CH_2), 7.30/7.59 (2×d, J=8.0 Hz, 2×2H, 2′-H, 3′-H), 8.29 (s, 1H, 5-H). ^{13}C NMR δ: 19.6 (6-CH_3), 21.3 (4′-CH_3), 28.3 (1-CH_3), 29.3 (3-CH_3), 108.6 (C-4a), 126.2 (C-6), 128.9 (C-2′), 129.0 (C-3′), 136.4 (C-1′), 139.1 (C-4′), 139.4 (C-5), 148.6 (C-8a), 151.6 (C-2), 161.4 (C-4), 162.7 (C-7). HRMS Calcd for $C_{17}H_{17}N_3O_2$ 295.1321, found: 295.1320.

4.5. Substituted 6-iminomethylpyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-diones 11a–b, 12a–b, and substituted 6-aminomethylpyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-diones 13a–b

2 mmol of **8** and 4 mmol of aniline or the corresponding amount of a solution of methyl amine in ethanol were suspended in 20 mL of ethanol and heated to reflux for 30 min. The solids **11a–b**, **12a–b** formed upon cooling of the mixture were filtered off, dried in vacuo, and used as such for further reactions. **13a–b** was obtained by reaction of 0.5 mmol of **12** and 100 mg (2.65 mmol) of sodium borohydride in 25 mL of ethanol, the mixture was stirred overnight at rt. The solvent was evaporated in vacuum,

25 mL of cold water was added and the mixture was stirred vigorously. The precipitate which formed was filtered off, dried, and subjected to column chromatography on silica gel (ethyl acetate/cyclohexane, 3:7).

4.5.1. 1,3-Dimethyl-6-(*N*-methyliminomethyl)-7-phenyl-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione (11a). 350 mg (1.1 mmol, 57%), mp 208 °C (ethanol). UV/vis λ: 206 (4.4), 228 (4.6), 332 (4.3). IR ν: 1712, 1676, 1600.MS *m/z*: 308 (M^+, 20), 307 (100), 250 (11), 193 (8). ^{1}H NMR δ: 3.50 (br s, 6H, 1-CH_3, N-CH_3), 3.76 (s, 3H, 3-CH_3), 7.52/7.62 (2× m, 5H, phenyl-H), 8.31 (q, J=1.6 Hz, 1H, 6-CH), 9.08 (s, 1H, 5-H). ^{13}C NMR δ: 28.5 (1-CH_3), 29.6 (C-3-CH_3), 48.4 (N-CH_3), 109.7 (C-4a), 125.7 (C-6), 128.5 (C-3′), 129.8 (C-4′), 130.2 (C-2′), 137.5 (C-1′), 138.0 (C-5), 150.6 (C-8a), 151.5 (C-2), 158.7 (C-6-CH), 160.9 (C-4), 162.7 (C-7). Anal. Calcd: C: 66.22, H: 5.23, N: 18.17, found: C: 65.97, H: 5.11, N: 18.05.

4.5.2. 1,3-Dimethyl-6-(*N*-methyliminomethyl)-7-(4-tolyl)-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione (11b). 390 mg (1.2 mmol, 60%), mp 190 °C (ethanol). UV/vis λ: 228 (4.5), 268 (4.4), 334 (4.1). IR ν: 1710, 1684, 1600. MS *m/z*: 322 (M^+, 22), 321 (100), 264 (7), 132 (7). ^{1}H NMR δ: 2.46 (s, 3H, 4′-CH_3), 3.49 (s, 3H, N-CH_3) 3.51/3.76 (2×s, 2×3H, 1-CH_3, 3-CH_3), 7.33/7.52 (2×d, J=8.0 Hz, 2×2H, phenyl-H), 8.32 (q, J=1.6 Hz, 1H, 6-CH), 9.06 (s, 1H, 5-H). ^{13}C NMR δ: 21.4 (4′-CH_3), 28.5 (1-CH_3), 29.6 (3-CH_3), 48.3 (N-CH_3), 109.4 (C-4a), 125.6 (C-6), 129.2 (C-2′), 130.0 (C-3′), 134.7 (C-1′), 137.9 (C-5), 140.1 (C-4′), 150.5 (C-8a), 151.5 (C-2), 158.9 (6-CH), 160.9 (C-4), 162.8 (C-7). Anal. Calcd: C: 67.07, H: 5.63, N: 17.38, found: C: 66.93, H: 5.39, N: 17.13.

4.5.3. 1,3-Dimethyl-7-phenyl-6-(*N*-phenyliminomethyl)-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione (12a). 460 mg (1.26 mmol, 63%), mp 210 °C (ethanol). UV/vis λ: 232 (4.3), 254 (4.2), 300 (4.1), 334 (4.2). IR ν: 1718, 1670 (s), 1605. MS *m/z*: 370 (M^+, 30), 369 (100), 312 (4), 278 (8), 255 (5). ^{1}H NMR δ: 3.51/3.79 (2×s, 2×3H, 1-CH_3, 3-CH_3), 7.10–7.70 (m, 10H, phenyl-H, aniline-H), 8.52 (s, 1H, 5-H), 9.33 (s, 1H, 6-CH). ^{13}C NMR δ: 28.6 (1-CH_3), 29.7 (3-CH_3), 109.8 (C-4a), 121.1 (aniline-C2), 125.7 (C-6), 128.6 (aniline-C3), 129.2 (C-3′), 130.1 (C-4′), 130.2 (C-2′), 137.4 (C-1′), 138.4 (C-5), 138.4 (aniline-C4), 151.0 (C-8a), 151.2 (aniline-C 1), 151.5 (C-2), 156.0 (6-CH), 160.9 (C-4), 163.7 (C-7). HRMS Calcd for $C_{23}H_{17}N_4O_2$ $(M\text{-}H)^+$ 369.1352, found: 369.1351.

4.5.4. 1,3-Dimethyl-6-(*N*-phenyliminomethyl)-7-(4-tolyl)-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione (12b). 445 mg (1.16 mmol, 58%), mp 209 °C (ethanol). UV/vis λ: 232 (4.6), 270 (4.6), 336 (4.5). IR ν: 1712, 1664, 1600. MS *m/z*: 384 (M^+, 30), 383 (100), 326 (3), 292 (7). ^{1}H NMR δ: 2.45 (s, 3H, 4′-CH_3), 3.51/3.78 (2×s, 2×3H, 1-CH_3, 3-CH_3), 7.18-7.57 (m, 9H, phenyl-H, aniline-H), 8.53 (s, 1H, 5-H), 9.30 (s, 1H, 6-CH). ^{13}C NMR δ: 21.4 (4′-CH_3), 28.5 (1-CH_3), 29.6 (3-CH_3), 109.5 (C-4a), 121.0, (aniline-C2), 125.5 (C-6), 129.1 (aniline-C3), 129.3 (C-2′), 130.1 (C-3′), 134.5 (C-1′), 138.3 (C-5), 138.4 (aniline-C4), 140.4 (C-4′), 150.9 (C-8a), 151.2 (aniline-C1), 151.7 (C-2), 156.2 (6-CH), 161.0 (C-4), 163.7 (C-7). Anal. Calcd: C: 71.86, H: 5.24, N: 14.57, found: C: 71.78, H: 5.24, N: 14.58.

4.5.5. 1,3-Dimethyl-7-phenyl-6-(*N*-phenylaminomethyl)-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione (13a). 37 mg (0.10 mmol, 20%), mp 131 °C (ethyl acetate). UV/vis λ: 218 (4.6), 248 (4.4), 328 (4.0). IR ν: 3350 (m), 1708, 1652, 1640 (s). MS *m/z*: 372 (M^+, 19), 281 (25), 280 (100), 223 (51). ^{1}H NMR δ: 2.44 (s, 1H, NH), 3.48/3.73 (2×s, 2×3H, 1-CH_3, 3-CH_3), 4.39 (s, 2H, 6-CH_2), 6.48 (d, J=7.7 Hz, 2H, aniline-2H), 6.71 (t, J=7.3 Hz, 1H, aniline-4H), 7.12 (br t, J=7.8 Hz, 2H, aniline-3H), 7.50/7.63 (2×m, 5H, phenyl-H), 8.60 (s, 1H, 5-H). ^{13}C NMR δ: 28.5 (1-CH_3), 29.5 (3-CH_3), 45.3 (6-CH_2), 109.3 (C-4a), 113.2 (aniline-C2), 118.3 (aniline-C4), 128.2 (C-6), 128.5 (C-3′), 129.0 (C-2′), 129.3 (aniline-C3), 129.5 (C-4′), 138.6 (C-5), 139.6 (C-1′), 146.9 (aniline-C1), 149.4 (C-8a), 151.6 (C-2), 161.3 (C-7), 162.8 (C-4). HRMS Calcd for $C_{22}H_{20}N_4O_2$ 372.1586, found: 372.1584.

4.5.6. 1,3-Dimethyl-6-(*N*-phenylaminomethyl)-7-(4-tolyl)-pyrido[2,3-*d*]pyrimidine(1*H*,3*H*)-2,4-dione (13b). 60 mg (0.16 mmol, 32%), mp 195 °C (ethanol). UV/vis λ: 220 (4.6), 250 (4.4), 328 (4.1). IR ν: 3408, 1702, 1666, 1602. MS *m/z*: 384 (M^+, 22), 295 (20), 294 (100), 237 (36). ^{1}H NMR δ: 2.46 (s, 3H, 4′-CH_3), 3.47/3.72 (2×s, 2×3H, 1-CH_3, 3-CH_3), 4.07 (br s, 1H, NH), 4.38 (br s, 2H, 6-CH_2), 6.48 (d, J=7.9 Hz, 2H, aniline-2H), 6.68 (t, J=7.3 Hz, 1H, aniline-4H), 7.12 (t, J=7.8 Hz, 2H, aniline-3H), 7.31/7.59 (2×d, 2×2H, 4H, phenyl-H), 8.56 (s, 1H, 5-H). ^{13}C NMR δ: 21.8 (4′-CH_3), 28.4 (1-CH_3), 29.4 (3-CH_3), 45.2 (6-CH_2), 109.0 (C-4a), 113.0 (aniline-C2), 118.1 (aniline-C4), 128.0 (C-6), 129.0 (C-2′), 129.2 (C-3′), 129.2 (aniline-C3), 135.7 (C-1′), 138.6 (C-4′), 139.8 (C-5), 147.1 (aniline-C1), 149.4 (C-8a), 151.6 (C-2), 161.3 (C-7), 162.9 (C-4), Anal. Calcd: C: 71.48, H: 5.74, N: 14.50, found: C: 71.41, H: 5.81, N: 14.43.

4.6. Ethyl 2-cyano-3-(pyrido[2,3-*d*]pyrimidin-6-yl)acrylates 14a–b

2 mmol of **8** was dissolved together with 2.5 mmol of ethyl cyano acetate in 20 mL of toluene, three drops of piperidine and eight drops of acetic acid were added and the reaction mixture was heated to reflux until no more water condensed. After cooling the mixture was washed with brine, dried, and concentrated in vacuo. The precipitate was treated with diethyl ether, filtered, and recrystallized from ethyl acetate to afford yellow crystals of **14**.

4.6.1. Ethyl 2-cyano-3-(1,3-dimethyl-2,4-dioxo-7-phenyl-(1*H*,3*H*)-pyrido[2,3-*d*]pyrimidine-6-yl)acrylate (14a). 490 mg (1.26 mmol, 63%), mp 171 °C (ethyl acetate). UV/vis λ: 262 (4.3), 338 (4.3). IR ν: 2210, 1720, 1680, 1600. MS *m/z*: 390 (M^+, 21), 361 (8), 318 (26), 317 (100). ^{1}H NMR δ: 1.28 (t, J=7.1 Hz, 3H, OCH_2CH_3), 3.51/3.79 (2×s, 2×3H, 1-CH_3, 3-CH_3), 4.37 (q, J=7.1 Hz, 2H, OCH_2CH_3), 7.56 (m, 5H, phenyl-H), 8.27 (d, J=0.6 Hz, 1H, 5-H), 9.28 (d, J=0.6 Hz, 1H, 6-CH). ^{13}C NMR δ: 14.1 (CH_3), 28.6 (1-CH_3), 29.8 (3-CH_3), 62.9 (CH_2), 105.8 (C≡N), 109.3 (C-4a), 114.6 (C=C), 121.0 (C-6), 128.8 (C-3′), 130.4 (C-2′), 130.9 (C-4′), 137.1 (C-1′), 139.0 (C-5), 151.3 (C-2), 151.6 (C-8a), 151.8 (C=CH), 160.2 (C-7), 161.7 (C-4), 164.5 (C=O). Anal. Calcd: C: 64.61, H: 4.65, N: 14.35, found: C: 64.76, H: 4.65, N: 14.04.

4.6.2. Ethyl 2-cyano-3-(1,3-dimethyl-2,4-dioxo7-(4-tolyl)-(1*H*,3*H*)-pyrido[2,3-*d*]pyrimidine-6-yl)acrylate (14b). 525 mg (1.30 mmol, 65%), mp 188 °C (ethyl acetate). UV/vis λ: 284 (4.3), 342 (4.4). IR ν: 2239, 1718, 1714, 1670, 1590. MS *m/z*: 404 (M^+, 6), 332 (14), 331 (53), 45 (100). ^{1}H NMR δ: 1.39 (t, $J=7.1$ Hz, 3H, OCH_2CH_3), 2.46 (s, 3H, 4′-CH_3), 3.52/3.79 (2×s, 2×3H, 1-CH_3, 3-CH_3), 4.37 (q, $J=7.1$ Hz, 2H, OCH_2CH_3), 7.34/7.49 (2× d, $J=8.0$ Hz, 2×2H, phenyl-H), 8.28 (s, 1H, 5-H), 9.26 (s, 1H, 6-CH). ^{13}C NMR δ: 14.1 (CH_3), 21.4 (4′-CH_3), 28.6 (1-CH_3), 29.7 (3-CH_3), 62.9 (CH_2), 105.4 (C≡N), 109.0 (C-4a), 114.6 (C=C), 120.9 (C-6), 129.5 (C-2′), 130.4 (C-3′), 134.3 (C-1′), 139.0 (C-5), 141.5 (C-4′), 151.3 (C-2), 151.6 (C-8a), 152.0 (C=CH), 160.2 (C-7), 161.8 (C-4), 164.5 (C=O). HRMS Calcd for $C_{22}H_{20}N_4O_4$, 404.1485, found: 404.1483.

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