

# Convenient Selective Synthesis of Substituted Pyrido[2,3-*d*]pyrimidones and Annulated Derivatives

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The reaction of 6-aminouracil (**1**) with the appropriate  $\alpha,\beta$ -unsaturated ketones, gave the corresponding pyrido[2,3-*d*]pyrimidin-2,4-diones **3**, **6**, **8** and **10**, respectively. Treatment of **1** with salicylaldehyde, 6-carboethoxy-3,5-diphenyl-2-cyclohexenone (**13**) or 2,6-bis(phenylmethylidene)cyclohexanone (**15**) afforded the corresponding pyrimido[4,5-*d*]quinoline-2,4-diones **12**, **14** and **16**, respectively. Furthermore, a pyrido[2,3-*d*]pyrimidine incorporating 3,2'-bis(quinoline) derivative **18** was synthesized. Annulation of pyrido[2,3-*d*]pyrimidine with pyrazole or imidazole moieties was achieved *via* reaction of **1** with benzylidene derivatives of pyrazolone, imidazolone or 3-carboethoxycoumarin (**23**) to give **21**, **22** and **24**, respectively.

**Key words:** Uracil, Annulation, Biselectrophilic Reagent, Cyclocondensation

## Introduction

The one-step assemblage of monocyclic as well as polycyclic heterocycles represents a practical approach in modern organic synthesis. These reactions are of particular interest in combinatorial chemistry [1] because they allow the production of vast arrays of molecules in an efficient mode. Recently, Quiroga [2] has reported the selective preparation of a number of condensed heterocycles as potential biologically active compounds. Amongst these, pyrido[2,3-*d*]pyrimidine derivatives known as deazalumazines [3, 4] present interesting biological properties. These compounds have been used as dihydrofolate reductase inhibitors and antitumor agents [5–9]; some of them have shown a broad spectrum of antimicrobial activity [10–13], diuretic properties [14] and activity against platelet aggregation [15].

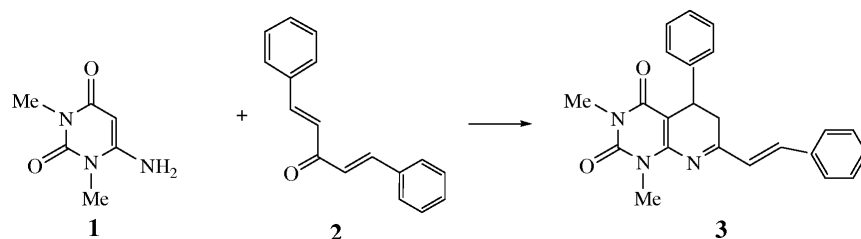
The therapeutic importance of this molecular framework motivated us to develop selective procedures of synthesis in which constituents could be arranged in a pharmacophoric pattern to display a high degree of pharmacological activities.

## Results and Discussion

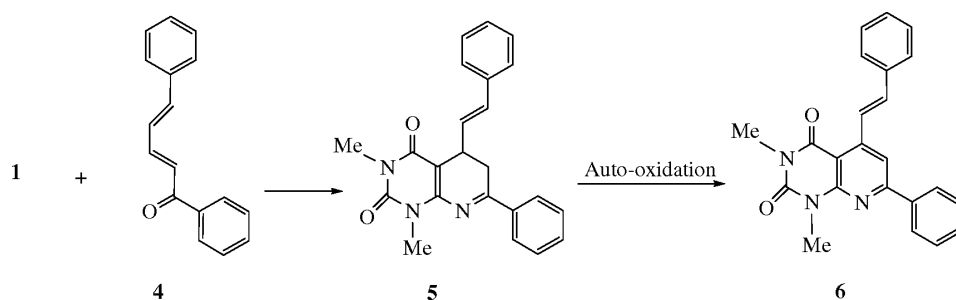
From early studies [16–18], an empirical rule has emerged which specifies that in annulation reactions involving substituted 6-aminopyrimidines, which have multiple competing sites for possible ring-annulation

and biselectrophiles, the 5-position of the pyrimidine is the most nucleophilic and attacks the most electrophilic carbon atom of the biselectrophile, followed by ring closure between the 6-amino group and the second electrophilic center. This experimental observation was supported by computational studies, which revealed a direct correlation between charge densities at the C-5 carbon atom of the 6-aminopyrimidine and their enamine-like nucleophilicity toward enones [19, 20]. However, unexpected reactions have also been observed in some cases, depending on the substitution in the pyrimidine, the biselectrophile, and the solvent used [21].

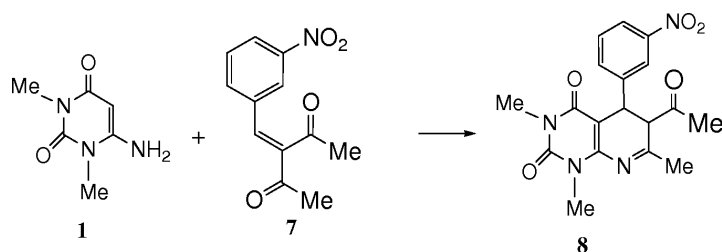
A wide variety of polycyclic molecules have been shown to interfere with the replication of DNA through intercalation between adjacent partially unwound base pairs as first described by Lerman [22]. Actinomycin [23], ethidium bromide [24], acridines [25] and proflavine [26] are known to bind to DNA by this intercalative process. This type of binding to DNA was also observed for other planar heterocyclic ring systems such as ellipticine, a pyridocarbazole derivative with a high degree of activity against leukemia [27–29]. Therefore, this study provides a convenient method for the selective synthesis of 7-styrylpyrido[2,3-*d*]pyrimidine **3** by reactions of 6-aminouracil **1** with 1,5-diphenyl-1,4-pentadien-3-one (**2**) in acetic acid in good yield *via* cyclocondensation reaction (Scheme 1). We have found that this reaction



Scheme 1.



Scheme 2.



Scheme 3.

was regioselective and no other compound was formed (TLC control). It is analogous to reactions of other aminopyrimidines and biselectrophiles [16, 30].

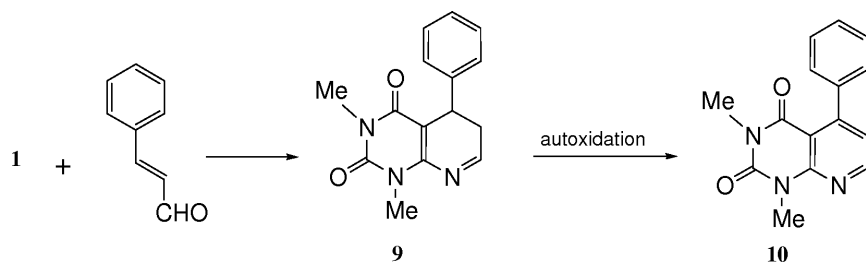
The constitution of **3** is supported by elemental analysis, IR,  $^1\text{H}$  NMR and MS spectra. The  $^1\text{H}$  NMR spectrum of **3** displayed signals corresponding to a methylene group (a doublet at  $\delta = 2.13$ ), and a methine proton (triplet at  $\delta = 4.01$ ). Its MS fragmentation pattern showed good agreement with the proposed structure.

The pyrimidine-2,4-dione ring is frequently encountered in drugs used for the treatment of hypothyroidy, hypertension, cancer and HIV infections [31]. Also, highly conjugated pyrimidine-2,4-dione derivatives have antiparasitic activities [32]. According to the interest toward pyrido[2,3-*d*]pyrimidines, considerable attention has been focused on the synthesis of highly conjugated pyrido[2,3-*d*]pyrimidines for biological evaluation.

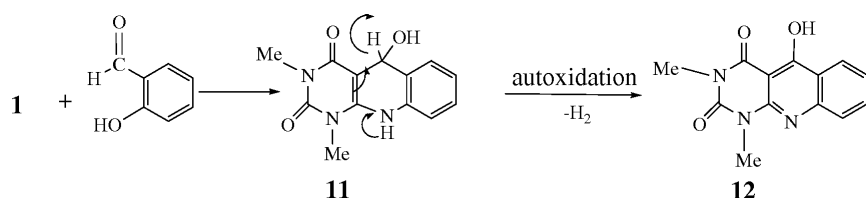
Accordingly, it seemed interesting to explore the Michael addition of 6-amino-1,3-dimethyl-2,4-pyrimidinedione (**1**) to the highly conjugated  $\alpha,\beta$ -unsaturated ketone **4** to afford **6**. The dihydropyridine

adduct from a Hantzsch synthesis in this case afforded the fully oxidized (aromatic) pyridine derivative presumably due to the highly conjugated system formed (Scheme 2). The constitution of **6** was affirmed through its  $^1\text{H}$  NMR and MS spectra. The mass spectrum gave a molecular ion peak at  $m/z = 369$  ( $\text{M}^+$ , 66 %), 368 ( $\text{M}^+ - 1$ , 35 %) and a base peak at  $m/z = 292$ .

In view of the interesting biological implication of nitrogen-containing heterocycles we aimed to synthesize novel bicyclic compounds which include an acetyl group at the pyridine ring. The synthesis of 6-acetyl-substituted pyrido[2,3-*d*]pyrimidine-2,4(1*H*, 3*H*)-dione **8** was achieved by condensation of the 6-aminouracil derivative **1** with *m*-nitrobenzylidene-acetylacetone (**7**) (Scheme 3). Its  $^1\text{H}$  NMR spectrum shows a singlet at  $\delta = 2.14$  for the methyl group, a singlet at  $\delta = 3.09$  for three protons ( $\text{COCH}_3$ ), a singlet at  $\delta = 5.1$  for  $\text{HC-Ar}$ , a multiplet at  $\delta = 7.5 - 8.06$  for four aromatic protons and a singlet at  $\delta = 8.83$  for  $\text{HC-CO}$ . Additionally, the mass spectrometric fragmentation pattern of **8** coincides with the proposed structure.



Scheme 4.



Scheme 5.

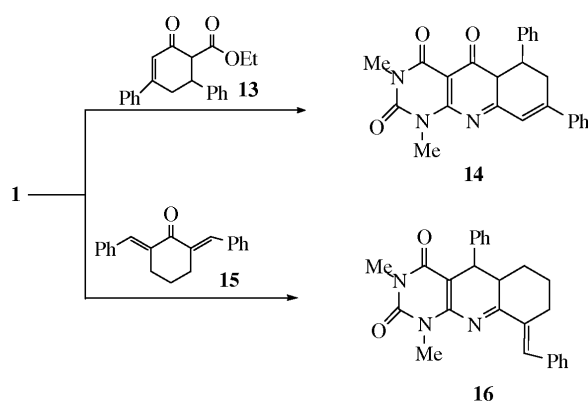
Furthermore, the condensation of **1** with cinnamaldehyde in glacial acetic acid furnished compound **10** in low yield (Scheme 4). Compatible analytical and spectroscopic evidence was gained for the structure of compound **10**. The mass spectra gave a molecular ion peak at  $m/z = 267$  ( $M^+$ ) and a base peak at  $m/z = 266$  ( $M^+ - 1$ ).

In a similar manner, 2-hydroxy-benzaldehyde was used to assure this finding. Thus, 5-hydroxy-1,3-dimethylpyrimido[4,5-*b*]quinoline-2,4-(1*H*,3*H*)-dione (**12**) was synthesized by reaction of **1** with salicylaldehyde in acidic medium (Scheme 5). Its structure was confirmed by IR, <sup>1</sup>H NMR and MS spectra.

It has been reported in the literature [33] that compound **1** reacted with an excess of ethyl acetoacetate to give 5-oxopyrido[2,3-*d*]pyrimidine in 2% yield in a basic medium or by thermal condensation [34].

In the present investigation it was also found that condensation of **1** with 6-carboethoxy-3,5-diphenyl-2-cyclohexenone (**13**) [35–37] as a  $\beta$ -ketoester (not as an  $\alpha,\beta$ -unsaturated ketone, because its  $\beta$ -position is blocked) furnished pyrimido[4,5-*b*]quinoline-2,4,5-(1*H*,3*H*,5*aH*)trione **14** (Scheme 6). Its structure was confirmed by elemental analysis and MS spectrum (see Experimental Section).

In addition, the reaction of **1** and dibenzylidenecyclohexanone (**15**) [38] in acidic medium afforded pyrimido[4,5-*b*]quinoline-2,4-(1*H*,3*H*)-dione **16** as a sole product in high yield (Scheme 6). In contrast, Diaz [39] separated three adducts (one of them as a monoadduct and two isomeric bisadducts) from the reaction of compound **1** with dibenzylidencyclohex-

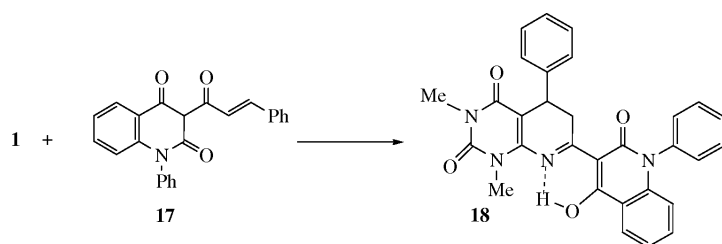


Scheme 6.

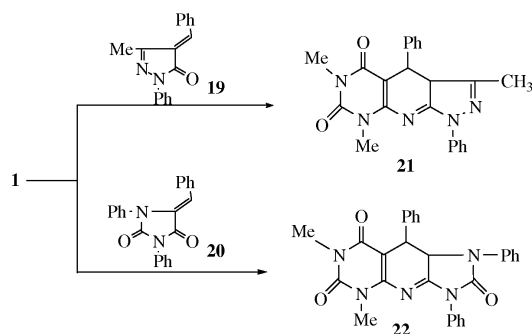
anone in the presence of Triton B as a base in moderate yields. The conformation of such skeletons was reported earlier [39].

The structural formula of **16** was deduced from spectral data. The <sup>1</sup>H NMR spectrum showed signals at  $\delta = 1.66$ , 2.09 and 2.57–2.75 (three  $CH_2$  groups), 3.14 and 3.54 (two N- $CH_3$  groups), 4.53 and 6.49 (two  $CH$  protons) and also 7.20–7.35 (2 Ph and Ph- $CH=$ ) protons. In addition, the mass spectrum of compound **16** indicated a molecular ion peak at  $m/z = 411$  ( $M^+$ , 6%) corresponding to the molecular formula  $C_{26}H_{25}N_3O_2$ .

In addition, the interesting pharmacological activity of quinoline in different areas of chemotherapy [40] prompted us to prepare the 7-(quinolin-3-yl)-pyrido[2,3-*d*]pyrimidine-2,4-(1*H*,3*H*)-dione derivative **18** through the cyclocondensation of **1** with 3-cinnamoyl-1-phenyl-2,4-(1*H*,3*H*)-quinolinedione (**17**)



Scheme 7.



Scheme 8.

[41] (Scheme 7). Its structure was confirmed by the  $^1\text{H}$  NMR spectrum which showed a singlet at  $\delta = 2.08$  ( $\text{CH}_2$ ), two singlet signals at  $\delta = 3.36$  and  $3.9$  ( $2 \text{ NCH}_3$ ), a singlet at  $3.78$  ( $\text{PhCH}$ ), multiplet at  $\delta = 7.18$ – $7.63$  for 14 aromatic protons, and finally a singlet at  $\delta = 17.76$  ppm for enolic  $\text{OH}$ . In addition, the mass spectrum of compound **18** indicated a molecular ion peak at  $m/z = 504$  ( $\text{M}^+$ , 8 %) and a base peak at  $427$  ( $\text{M}^+ - \text{Ph}$ ).

No attention has been paid to the similar reaction with the benzylidenepyrazolone derivative **19** or the benzylidenehydantoin derivative **20** which can be used as key intermediates for the construction of a pyridopyrimidine moiety fused with pyrazole or with imidazole rings, respectively. The reaction of **1** with **19** [42] or **20** [43] in the presence of glacial acetic acid gave **21** and **22**, respectively (Scheme 8). Formulation of structures **21** and **22** is based on elemental analysis, IR and mass spectra fragmentation.

## Experimental Section

All melting points (uncorrected) were determined on a Gallenkamp electric melting point apparatus. Elemental microanalyses were carried out at the Microanalytical Unit, Faculty of Science, Cairo University. Infrared spectra measured using KBr discs on a Mattson 5000 FTIR spectrometer.  $^1\text{H}$  NMR data were obtained in  $\text{CDCl}_3$  or DMSO solution on a Varian XL 200 MHz instrument using TMS as inter-

nal standard. Chemical shifts are reported in ppm ( $\delta$ ) downfield from internal TMS. Mass spectra recorded on a GC-MS (Shimadzu QP-1000 EX). Reactions were monitored by thin layer chromatography (TLC) using silica gel (EM science) coated plates.

### Pyrido[2,3-*d*]pyrimidines **3**, **6** and **10**; general procedure

A mixture of 6-amino-1,3-dimethyl-uracil (1 g, 6.5 mmol) and the appropriate  $\alpha,\beta$ -unsaturated compounds, namely, 1,5-diphenyl-1,4-pentadien-3-one (**2**), 1,5-diphenyl-1,3-pentadien-5-one (**4**) or cinnamaldehyde (6.5 mmol), in glacial acetic acid (20 mL) was refluxed for 1 h on a steam bath, kept overnight at r. t., diluted with water, then basified by ammonia. The precipitate formed was collected by filtration, then purified by crystallization from an appropriate solvent to give compounds **3**, **6** and **10**, respectively.

#### 5,6-Dihydro-1,3-dimethyl-5-phenyl-7-styrylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**3**)

M. p.  $129$ – $130$  °C (acetic acid). –  $R_f = 0.58$  (pet. ether  $40$ – $60$  °C / ethyl acetate, (1 : 1)). – Yield: 94 % (yellow crystals). – IR (KBr):  $\nu = 3060$ ,  $2975$  (CH),  $1637$  (CO),  $1620$   $\text{cm}^{-1}$  (C=N). –  $^1\text{H}$  NMR (200 MHz,  $[\text{D}_6]$ -DMSO):  $\delta = 2.13$  (d,  $J = 6.4$  Hz, 2H),  $2.80$  (s, 3H),  $3.09$  (s, 3H),  $4.01$  (t,  $J = 6.4$  Hz, 1H),  $6.26$  (d,  $J = 16.5$  Hz, 1H),  $6.93$ – $7.28$  (m, 11H). – MS (EI, 70 eV):  $m/z$  (%) =  $371$  (94) [ $\text{M}^+$ ],  $370$  (51) [ $\text{M}^+ - 1$ ],  $369$  (4) [ $\text{M}^+ - 2$ ],  $294$  (100),  $244$  (48),  $217$  (2),  $205$  (6),  $191$  (2),  $155$  (43),  $153$  (9). –  $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}_2$  (371.42): calcd. C 74.37, H 5.69; found C 74.46, H 5.80.

#### 1,3-Dimethyl-7-phenyl-5-styrylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**6**)

M. p.  $185$  °C (ethanol). –  $R_f = 0.65$  (pet. ether  $40$ – $60$  °C / ethyl acetate (4 : 1)). – Yield: 92 % (yellow crystals). – IR (KBr):  $\nu = 2946$  (CH),  $1708$ ,  $1660$  (CO),  $1625$  (C=N),  $1589$   $\text{cm}^{-1}$  (C=C). –  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta = 3.26$  (s, 3H),  $3.62$  (s, 3H),  $7.41$ – $7.70$  (m, 9H),  $8.07$  (s, 1H),  $8.27$ – $8.30$  (m, 21H),  $8.51$ – $8.59$  (m, 1H). – MS (EI, 70 eV):  $m/z$  (%) =  $369$  (66) [ $\text{M}^+$ ],  $368$  (35) [ $\text{M}^+ - 1$ ],  $292$  (100),  $242$  (3),  $215$  (7),  $192$  (4),  $186$  (2),  $155$  (5),  $153$  (7). –  $\text{C}_{23}\text{H}_{19}\text{N}_3\text{O}_2$  (369.42): calcd. C 74.78, H 5.18; found C 74.75, H 5.17.

**1,3-Dimethyl-5-phenylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (10)**

M. p. 170 °C (methanol). –  $R_f$  = 0.7 (pet. ether 40–60 °C / ethyl acetate (1 : 2)). – Yield: 37 % (yellow crystals). – IR (KBr):  $\nu$  = 1709, 1680 (CO), 1584  $\text{cm}^{-1}$  (C=C). – MS (EI, 70 eV):  $m/z$  (%) = 267 (54) [ $\text{M}^+$ ], 266 (100), 238 (2), 200 (2), 181 (3), 155 (30), 127 (16), 81 (8). –  $\text{C}_{15}\text{H}_{13}\text{N}_3\text{O}_2$  (267.27): calcd. C 67.40, H 4.90; found C 67.49, H 5.04.

**6-Acetyl-5,6-dihydro-1,3,7-trimethyl-5-(3-nitrophenyl)pyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (8)**

A mixture of 6-amino-1,3-dimethyl-uracil (**1**) (1 g, 6.5 mmol) and *m*-nitrobenzylidene-acetylacetone **7** (6.5 mmol) in ethanol (30 mL) containing 3 drops of acetic acid was heated at reflux for 2 h. The reaction mixture was kept at r. t., diluted with  $\text{H}_2\text{O}$  whereby the precipitate formed was filtered off and crystallized from ethanol to furnish compound **8**. – M. p. 236 °C (ethanol). –  $R_f$  = 0.63 (pet. ether 40–60 °C / ethyl acetate (1 : 1)). – Yield: 48 % (yellow crystals). – IR (KBr):  $\nu$  = 3138 (CH), 1693, 1668 (CO), 1592  $\text{cm}^{-1}$  (C=C). –  $^1\text{H}$  NMR (200 MHz,  $[\text{D}_6]$ -DMSO):  $\delta$  = 2.14 (s, 3H), 3.09 (s, 3H), 3.32 (s, 3H), 3.43 (s, 3H), 5.1 (s, 1H), 7.5–8.06 (m, 4H), 8.83 (s, 1H). – MS (EI, 70 eV):  $m/z$  (%) = 370 (10) [ $\text{M}^+$ ], 368 (6) [ $\text{M}^+ - 2$ ], 359 (3), 353 (21), 327 (47), 313 (7) 248 (100), 205 (28), 191 (15), 123 (5). –  $\text{C}_{18}\text{H}_{18}\text{N}_4\text{O}_5$  (370.35) calcd. C 58.37, H 4.89; found C 58.46, H 4.98.

**Pyrimido[4,5-*b*]quinolines 12 and 16; general procedure**

A mixture of 6-amino-1,3-dimethyl-uracil (**1**) (1 g, 6.5 mmol) and salicylaldehyde or 2,6-dibenzylidenecyclohexanone **15** (6.5 mmol) in glacial acetic acid (20 mL) was heated for 1 h on a steam bath, kept overnight at r. t., diluted with water, then basified with ammonia. The precipitate formed was collected by filtration, and then purified by crystallization from an appropriate solvent to give compound **12** and **16**, respectively.

**5-Hydroxy-1,3-dimethyl pyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-dione (12)**

M. p. 240 °C (acetone). –  $R_f$  = 0.65 (pet. ether (40–60 °C) / ethyl acetate (1 : 2)) – Yield: 38 % (yellow crystals). – IR (KBr):  $\nu$  = 3570, 3519 (OH), 2956 (CH), 1708, 1659  $\text{cm}^{-1}$  (CO). –  $^1\text{H}$  NMR (200 MHz,  $[\text{D}_6]$ -DMSO):  $\delta$  = 3.32 (m, 3H), 3.56 (m, 3H), 5.05 (br, 1H), 7.27 (m, 4H). – MS (EI, 70 eV):  $m/z$  (%) = 257 (10) [ $\text{M}^+$ ], 230 (14), 120 (22), 123 (17), 215 (11), 54 (100). –  $\text{C}_{13}\text{H}_{11}\text{N}_3\text{O}_3$  (257.24): calcd. C 60.69, H 4.31; found C 60.61, H 4.39.

**9-Benzylidene-5,5a,6,7,8,9-hexahydro-1,3-dimethyl-5-phenylpyrimido[4,5-*b*]quinoline-2,4(1*H*,3*H*)-dione (16)**

M. p. 258 °C (acetic acid). –  $R_f$  = 0.57 (pet. ether (40–60 °C) / ethyl acetate (1 : 1)). – Yield: 93 % (yellow crystals). – IR (KBr):  $\nu$  = 3134 (CH), 1695, 1665 (CO), 1604  $\text{cm}^{-1}$  (C=C). –  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.66 (t,  $J$  = 8.0 Hz, 2H), 2.09 (t,  $J$  = 8.0 Hz, 2H), 2.57–2.75 (m, 2H), 3.14 (s, 3H), 3.54 (s, 3H), 4.53 (s, 1H), 6.49 (s, 1H), 7.20–7.35 (m, 11H). – MS (EI, 70 eV):  $m/z$  (%) = 411 (6) [ $\text{M}^+$ ], 410 (4) [ $\text{M}^+ - 1$ ], 409 (5), 334 (100), 320 (5), 256 (1), 91 (11), 77 (3). –  $\text{C}_{26}\text{H}_{25}\text{N}_3\text{O}_2$  (411.50): calcd C 75.89, H 6.12; found C 75.78, H 6.21.

**6,7-Dihydro-1,3-dimethyl-6,8-diphenylpyrimido[4,5-*b*]quinoline-2,4,5(1*H*,3*H*,5*aH*)-trione (14)**

A mixture of 6-amino-1,3-dimethyl-uracil (**1**) (0.34 g, 2.16 mmol), 6-carboethoxy-3,5-diphenyl-2-cyclohexenone **13** (2.16 mmol) in diphenyl ether (10 mL) was refluxed until disappearance of the starting materials as evidenced by TLC. After the reaction was over, removal of the solvent under vacuum followed by crystallization of the residue from ethanol afforded **14**. – M. p. 306 °C (ethanol). –  $R_f$  = 0.66 (pet. ether (40–60 °C) / ethyl acetate (3 : 2)). – Yield: 51 % (brown crystals). – IR (KBr):  $\nu$  = 3134, 2875 (CH), 1708, 1658, 1641, 1612  $\text{cm}^{-1}$  (CO). – MS (EI, 70 eV):  $m/z$  (%) = 411 (77) [ $\text{M}^+$ ], 410 (23) [ $\text{M}^+ - 1$ ], 409 (3) [ $\text{M}^+ - 2$ ], 334 (100), 333 (7), 256 (8), 227 (7), 226 (6), 178 (4). –  $\text{C}_{25}\text{H}_{21}\text{N}_3\text{O}_3$  (411.44): calcd. C 72.98, H 5.15; found C 72.29, H 5.05.

**5,6-Dihydro-7-(1,2-dihydro-4-hydroxy-2-oxo-1-phenylquinolin-3-yl)-1,3-dimethyl-5-phenylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (18)**

A mixture of 6-amino-1,3-dimethyl-uracil (**1**) (1 g, 6.5 mmol), 3-cinnamoyl-1-phenyl-2,4(1*H*,3*H*)-quinoline-dione (2.4 g, 6.5 mmol) in glacial acetic acid (20 mL) was heated for 1 h on a steam bath, kept overnight at r. t., diluted with water, and then basified with ammonia. The precipitate formed was collected by filtration, and then purified by crystallization from acetic acid to give **18**. – M. p. 160 °C (acetic acid). –  $R_f$  = 0.63 (pet. ether (40–60 °C) / ethyl acetate (1 : 2)). – Yield: 97 % (yellow crystals). – IR (KBr):  $\nu$  = 3454 (OH intermolecular), 3057, 2952 (CH), 1712, 1671, 1645  $\text{cm}^{-1}$  (CO). –  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 2.08 (s, 2H), 3.36 (s, 3H), 3.78 (s, 1H), 3.9 (s, 3H), 7.18–7.63 (m, 14H), 9.05 (s, 1H), 17.76 (s, 1H). – MS (EI, 70 eV):  $m/z$  (%) = 504 (8) [ $\text{M}^+$ ], 502 (67), [ $\text{M}^+ - 2$ ], 427 (100), 367 (10), 308 (30), 237 (30), 196 (65). –  $\text{C}_{30}\text{H}_{24}\text{N}_4\text{O}_4$  (504.52): calcd. C 71.41, H 4.79; found C 71.49, H 4.89.

*Pyrido[2,3-*d*]pyrimidines 21 and 22, general procedure*

A mixture of 6-amino-1,3-dimethyl-uracil (1 g, 6.5 mmol), and the benzylidenepyrazolone derivative **19** [43] or the benzylidenehydantoin derivative **20** [44] (6.5 mmol) in glacial acetic acid (20 mL) was heated for 1 h on a steam bath, kept overnight at room temperature, diluted with water, then basified with ammonia. The precipitate formed collected by filtration, and then purified by crystallization from the appropriate solvent to give **21** and **22**.

*5,5a-Dihydro-5,8-diphenyl-1,3,6-trimethylpyrazolo[4',3':5,6]-pyrido[2,3-*d*]pyrimidine-2,4 (1*H*,3*H*)-dione (21)*

M.p. 140 (acetic acid). –  $R_f$  = 0.58 (pet. ether (40–60 °C) / ethyl acetate (1 : 1)). – Yield: 51 % (yellow crys-

tals). – IR (KBr):  $\nu$  = 3068 (CH), 1695, 1669 (CO), 1617 (C=N), 1582  $\text{cm}^{-1}$  (C=C). – MS (EI, 70 eV):  $m/z$  (%) = 399 (5) [ $\text{M}^+$ ], 368 (5) [ $\text{M}^+ - \text{CH}$ ], 334 (5), 284 (4) 262 (36), 89 (100). –  $\text{C}_{23}\text{H}_{21}\text{N}_5\text{O}_2$  (399.44): calcd. C 69.16, H 5.30; found C 69.35, H 5.39.

*5,5a-Dihydro-5,6,8-triphenyl-1,3-dimethyl-imidazolo[4',5':5,6]pyrido[2,3-*d*]pyrimidine-2,4,7(1*H*,3*H*,6*H*)-trione (22)*

M.p. 112 °C (ethanol). –  $R_f$  = 0.62 (pet. ether (40–60 °C) / ethyl acetate (3 : 2)). – Yield: 86 % (green crystals). – IR (KBr):  $\nu$  = 2953 (CH), 1777, 1710, 1641 (CO), 1610 (C=N), 1597  $\text{cm}^{-1}$  (C=C). – MS (EI, 70 eV):  $m/z$  (%) = 477 (3) [ $\text{M}^+$ ], 465 (2), 439 (3), 412 (2), 353 (1), 307 (2), 267 (5), 190 (6), 112 (15), 210 (2), 104 (100). –  $\text{C}_{28}\text{H}_{23}\text{N}_5\text{O}_3$  (477.5): calcd. C 70.43, H 4.85; found C 70.32, H 4.93.

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