1,2-Fused Pyrimidines. V. Synthesis of 1-Alkyl or Phenyl-2*H*-dipyrido-[1,2-*a*:2′,3′-*d*]pyrimidine-2,5(1*H*)-diones

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The reaction of 2-[(*N*-acyl, *N*-alkyl or phenyl)amino]-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones **8a-g** with the *N*,*N*-dimethylformamide/phosphorus oxychloride Vilsmeier reagent **1** (95°, 90 minutes) afforded 1-alkyl or phenyl-2*H*-dipyrido[1,2-*a*:2′,3′-*d*]pyrimidine-2,5(1*H*)-diones, 3-alkyl substituted or not, **10a-g**.

The starting compounds **8** were prepared by treating 2-amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones *N*-alkyl substituted **7a,b** or *N*-phenyl substituted **4** with excess anhydrides (130°, 7 hours); when the 2-(alkylamino) derivatives **7** were used in the reaction, compounds **8** were obtained along with very small amounts of 3-acyl-2-(alkylamino)-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones **9**.

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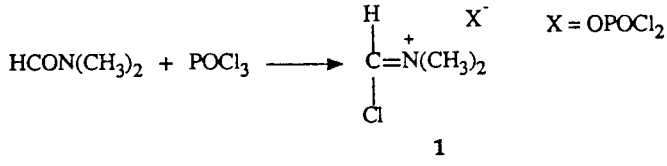
We previously described [1-3] the cyclization of the *N*-phenyl substituted heterocyclic β-enaminocarbonylic compounds when treated with the *N*,*N*-dimethylformamide/phosphorus oxychloride electrophilic reagent **1**, with the formation of a 2,3-fused quinoline nucleus. For instance, the reaction of **1** with compounds **2** or **4** afforded 14*H*-naphtho[1′,2′:5,6]pyrano[2,3-*b*]quinolin-14-one **3** [2] or 12*H*-pyrido[1′,2′:1,2]pyrimido[4,5-*b*]quinolin-12-one **5** [3], respectively.

Continuing our interest both in cyclizations involving the Vilsmeier reagent **1** and in the chemistry of pyrido[1,2-*a*]pyrimidines, we have now chosen the *N*-acyl derivatives **8** as suitable starting compounds for the easy preparation of novel 2*H*-dipyrido[1,2-*a*:2′,3′-*d*]pyrimidine derivatives (**10**), by reaction with reagent **1**. Only few examples of dipyrido[1,2-*a*:2′,3′-*d*]pyrimidine derivatives have been until now reported in the literature [4-9].

Thus, the reaction of 2-chloro-4*H*-pyrido[1,2-*a*]pyrimi-



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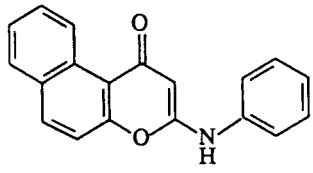

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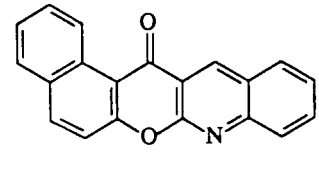

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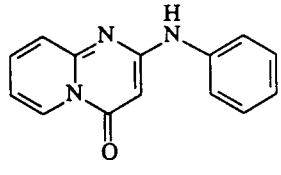

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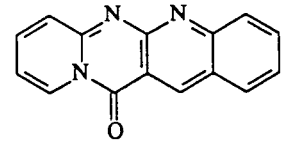

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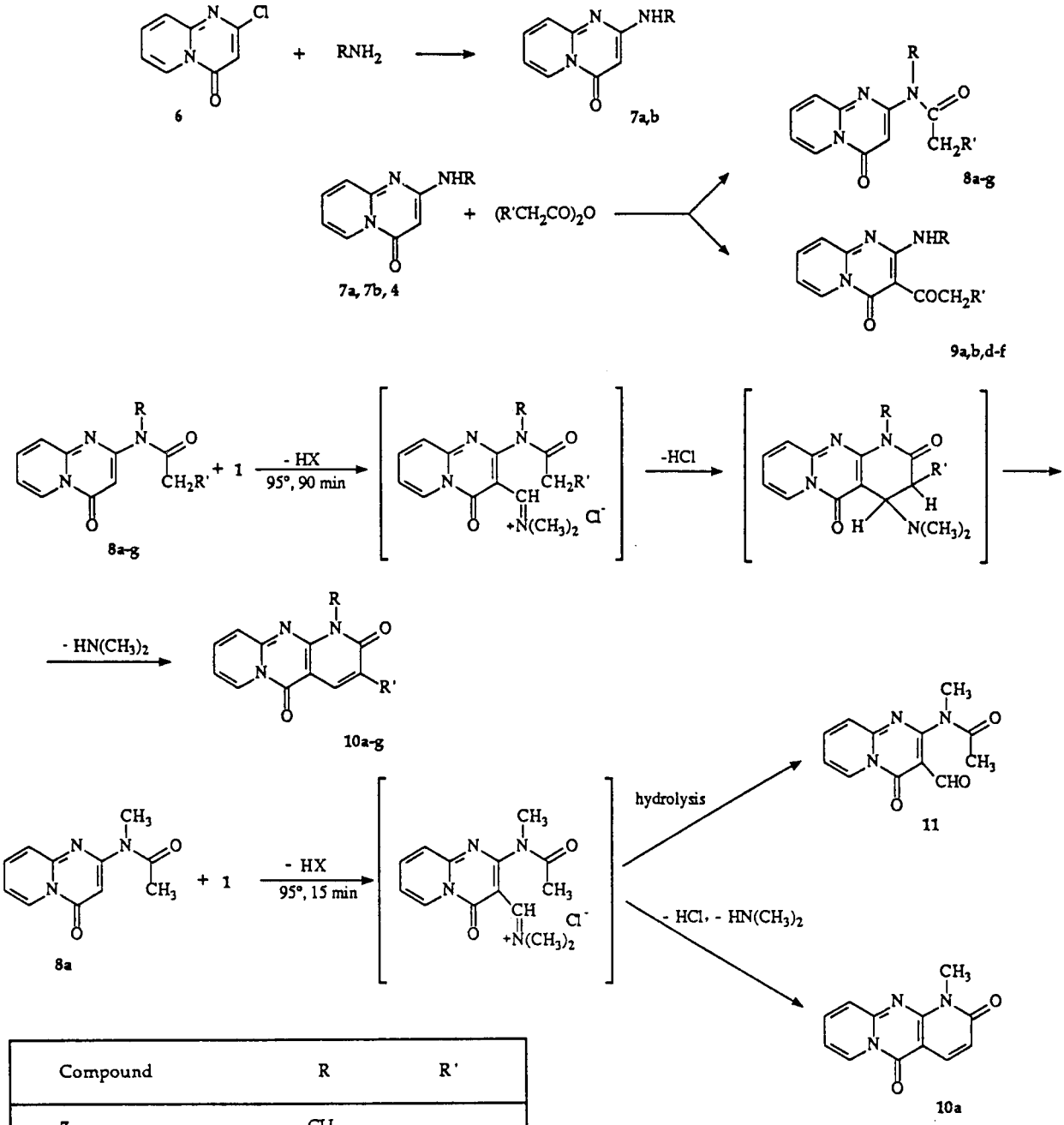
Scheme 1



Compound	R	R'
7a	CH_3	–
7b	C_2H_5	–
8a, 9a, 10a	CH_3	H
8b, 9b, 10b	C_2H_5	H
8c, 10c	C_6H_5	H
8d, 9d, 10d	CH_3	CH_3
8e, 9e, 10e	C_2H_5	CH_3
8f, 9f, 10f	CH_3	C_2H_5
8g, 10g	C_6H_5	C_2H_5

din-4-one **6** [10] with methylamine or ethylamine (ethanol at reflux, 24 hours) afforded high yields of 2-(alkylamino) derivatives **7a** or **7b**. Compounds **7a,b** and **4** [3] were then treated with a large excess of the suitable anhydride (130°, 7 hours) to give good yields of the desired *N*-acyl derivatives **8**, usually (R = alkyl) along with very small amounts of 3-acyl derivatives **9**. Finally, the reaction of compounds **8a-g** with reagent **1** (95°, 90 minutes, *N,N*-dimethylformamide as solvent) afforded the expected substituted 2*H*-dipyrido[1,2-*a*:2′,3′-*d*]pyrimidine-2,5(1*H*)-diones **10a-g** in good yields. Significantly, when compound **8a** (chosen as an example) was treated with reagent **1** under the same conditions, but heating for 15 minutes only, a mixture of formyl derivative **11** and tricyclic compound **10a** was obtained (Scheme 1).

Considering this latter result and the presence in compounds **8** of two nucleophilic sites in proper positions (*i.e.* the C-3 atom and the α-methylene group of *N*-acyl substituent) the formation of tricyclic derivatives **10** may be explained through the reaction pattern depicted in Scheme 1 [3].

It is interesting to observe that when compounds **8c,g** (*N*-acyl derivatives of **4**) were treated with reagent **1** (95°, 90 minutes) only tricyclic derivatives **10c,g** were obtained (Scheme 1), no trace of tetracyclic derivatives analogous to **5** having been isolated from the reaction mixture. This result was most likely due to the deactivating effect of *N*-acyl substituent on the *N*-phenyl position 2. Actually, from the reaction of **12** [*i.e.* the *N*-(ethoxycarbonyl) derivative of **4**] with reagent **1**, under the same conditions, only 3-formyl derivative **14** was obtained, no proper nucleophilic site being available in this case for the cyclization of intermediate **13** and for the formation of the quinoline nucleus (Scheme 2).

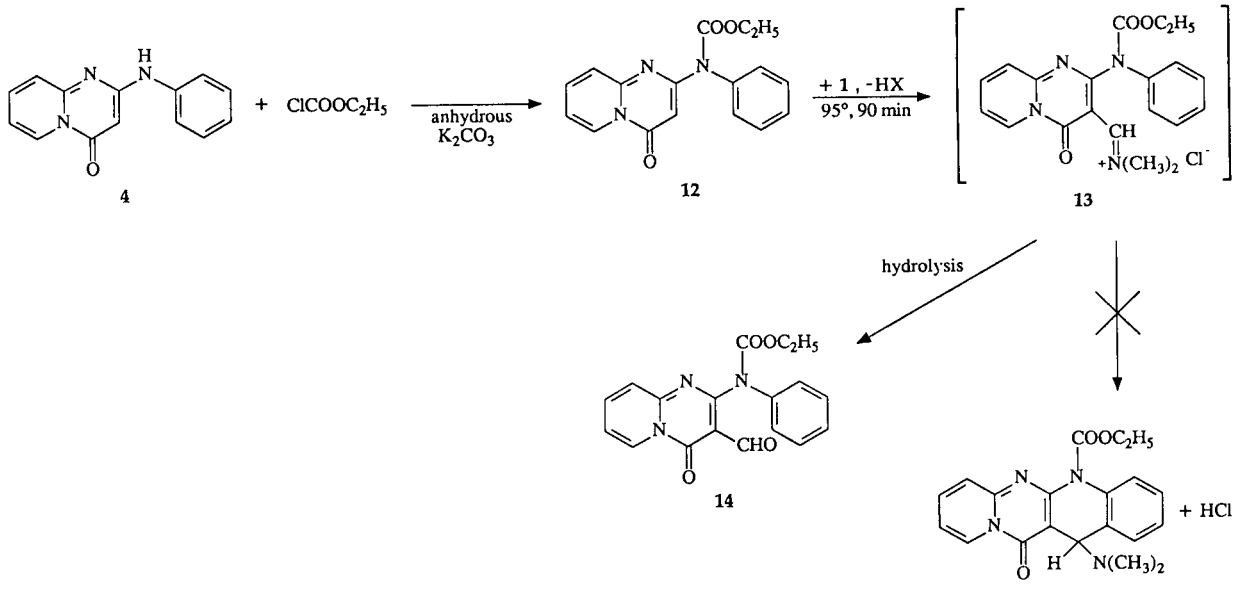
Results of elemental analyses, and ir and ^{1}H-nmr spectral data (see Experimental) were consistent with the structures attributed to the compounds described in this paper [3,11].

Referring to compounds **9a,b,d-f**, an intramolecular hydrogen bond seems to be responsible of ir low stretching frequencies (not affected by change of concentration) of NH and acyl CO groups, as well as of the low-field position of the ^{1}H-nmr NH signal. Similar spectral characteristics were shown by 2-(phenylamino)-4-oxo-4*H*-pyrido[1,2-*a*]-pyrimidine-3-carbaldehyde, an analogous compound that we previously described [3]. We can further observe that the ^{1}H-nmr NH signal (deuteriochloroform) of compounds **9a,b,d-f** did not disappear by treatment with deuterium oxide, but it was absent when the ^{1}H-nmr spectra were run using deuteriotrifluoroacetic acid as solvent.

EXPERIMENTAL

Melting points were determined with a Fisher-Johns (Electrothermal when above 300°) apparatus and are uncorrected. Infrared spectra were obtained with a Perkin-Elmer 398 spectrophotometer. The ^{1}H-nmr spectra were recorded on a Hitachi Perkin-Elmer R-600 spectrometer (60 MHz), using tetramethylsilane as an internal reference (δ = 0). Elemental analyses were performed by Laboratorio di Microanalisi, Istituto di Scienze Farmaceutiche dell'Università di Genova.

Scheme 2



2-(Methylamino)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**7a**) and 2-(Ethylamino)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**7b**).

A mixture of 15.0 mmoles (2.71 g) of 2-chloro-4*H*-pyrido[1,2-*a*]-pyrimidin-4-one **6** [10], 75.0 mmoles of methylamine hydrochloride (5.06 g) or ethylamine hydrochloride (6.12 g), 75.0 mmoles (7.59 g) of triethylamine, and 100 ml of ethanol was refluxed for 24 hours, while stirring. The solution obtained was evaporated *in vacuo* to dryness and 100 ml of water was added to the solid residue. The resulting aqueous solution was made alkaline by the addition of sodium carbonate, then exhaustively extracted with chloroform. The combined extracts were dried (anhydrous sodium sulfate), then evaporated under reduced pressure to afford a white solid which was taken up in a little ethyl ether and collected by filtration. There was obtained the nearly pure compound **7a** (2.49 g, 95%) or **7b** (2.57 g, 91%).

Compound **7a**.

After crystallization from ethyl acetate, white needles melting at 156-157° were obtained; ir (chloroform): 3450 (NH), 1672 (CO), 1644, 1578, 1550 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.94 (d, J = 5 Hz, 3H, CH_3; s after treatment with deuterium oxide), 5.49 (s, 1H, H-3), 5.93 (broad signal, 1H, NH; disappeared with deuterium oxide), 6.88 (mc, 1H, H-7), 7.25 (mc, 1H, H-9), 7.64 (mc, 1H, H-8), 8.95 (mc, 1H, H-6).

Anal. Calcd. for $C_9H_9N_3O$: C, 61.70; H, 5.18; N, 23.99. Found: C, 61.60; H, 5.10; N, 23.81.

Compound **7b**.

After crystallization from cyclohexane, white crystals melting at 107-108° were obtained; ir (chloroform): 3435 (NH), 1674 (CO), 1642, 1575, 1548 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.27 (t, 3H, CH_3), 3.32 (mc, 2H, CH_2; q after treatment with deuterium oxide), 5.15 (broad signal, 1H, NH; disappeared with deuterium oxide), 5.46 (s, 1H, H-3), 6.84 (mc, 1H, H-7), 7.20 (mc, 1H, H-9), 7.57 (mc, 1H, H-8), 8.90 (mc, 1H, H-6).

Anal. Calcd. for $C_{10}H_{11}N_3O$: C, 63.48; H, 5.86; N, 22.21. Found: C, 63.73; H, 5.81; N, 22.43.

2-[(*N*-Acyl,*N*-alkyl or phenyl)amino]-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones **8a-g** and 3-Acyl-2-(alkylamino)-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones **9a,b,d-f**.

A 1.50 g quantity of **7a**, **7b**, or **4** [3] was suspended in 15 ml of the proper anhydride and the mixture was heated at 130° for 7 hours, while stirring. The resulting solution was poured onto crushed ice and water and the mixture allowed to stir at room temperature until the excess anhydride was destroyed. After addition of excess sodium bicarbonate, a sticky solid separated out and the mixture was then exhaustively extracted with chloroform. The combined extracts (dried over anhydrous sodium sulfate), after removal of the solvent, gave a nearly solid or oily residue from which compounds **8a-g** and **9a,b,d-f** were recovered according to the below described procedures.

2-[(*N*-Acetyl,*N*-methyl)amino]-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**8a**) and 3-Acetyl-2-(methylamino)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**9a**).

By treating with a little ethyl ether the nearly solid residue obtained from the reaction of **7a** with acetic anhydride, pure **8a** (1.68 g) separated out, white needles melting at 164-165° after crystallization from ethyl acetate; ir (chloroform): 1689 (CO), 1662 (CO), 1633 (shoulder), 1562, 1522 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.38 (s, 3H, $COCH_3$), 3.44 (s, 3H, N-CH_3), 6.44 (s, 1H, H-3), 7.25 (mc, 1H, H-7), 7.63 (mc, 1H, H-9), 7.90 (mc, 1H, H-8), 9.07 (mc, 1H, H-6).

Anal. Calcd. for $C_{11}H_{11}N_3O_2$: C, 60.82; H, 5.10; N, 19.34. Found: C, 60.72; H, 4.99; N, 19.33.

The filtrate was then evaporated to dryness and the residue was dissolved in a little chloroform and subjected to column chromatography (silica gel). By eluting with ethyl acetate, compound **9a** (0.02 g, 1.1%) was recovered, white crystals, mp 188-189°, after crystallization from isopropyl ether; ir (chloroform): 3225 (broad, NH), 1680 (4-CO), 1638, 1607 (broad, acyl CO), 1553, 1525 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.74 (s, 3H, $COCH_3$), 3.11 (d, J = 5 Hz, 3H, N-CH_3) (in deuteriotrifluoroacetic acid the N-CH_3 signal is a singlet at δ = 3.36), 6.87 (mc, 1H, H-7), 7.25 (mc, 1H, H-9), 7.68 (mc, 1H, H-8), 8.90 (mc, 1H, H-6), 10.46 (broad signal, 1H, NH) (for this compound and **9b,d-f**, in deuteriotrifluoroacetic acid the NH signal is absent).

Anal. Calcd. for $C_{11}H_{11}N_3O_2$: C, 60.82; H, 5.10; N, 19.34. Found: C, 60.71; H, 5.05; N, 19.23.

By further elution of the column with a mixture chloroform-ethyl acetate-methanol (9:9:1), an additional crop (0.06 g) of **8a** was obtained (total yield 94%).

In the same manner as for compounds **8a** and **9a**, there were obtained the following compounds **8d-f** and **9d-f**:

2-[(*N*-Methyl,*N*-propionyl)amino]-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**8d**) and 2-(Methylamino)-3-propionyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**9d**).

The nearly solid residue resulting from the reaction of **7a** with propionic anhydride afforded 1.79 g (90%) of **8d** (two amounts of 1.69 g and 0.1 g, respectively), whitish solid that melted at 138-139° after crystallization from ethyl acetate, and 0.03 g (1.5%) of **9d**, white crystals, mp 151-152°, after crystallization from isopropyl ether.

Compound **8d**.

This compound had ir (chloroform): 1687 (CO), 1662 (CO), 1636 (shoulder), 1560, 1521 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.18 (t, 3H, CH_2CH_3), 2.65 (q, 2H, CH_2), 3.42 (s, 3H, N-CH_3), 6.43 (s, 1H, H-3), 7.20 (mc, 1H, H-7), 7.59 (mc, 1H, H-9), 7.86 (mc, 1H, H-8), 9.07 (mc, 1H, H-6).

Anal. Calcd. for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.23; H, 5.64; N, 17.98.

Compound **9d**.

This compound had ir (chloroform): 3227 (broad, NH), 1682 (4-CO), 1639, 1607 (acyl CO), 1592 (shoulder), 1554, 1524 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.15 (t, 3H, CH_2CH_3), 3.09 (d, J = 5 Hz, 3H, N-CH_3) (in deuteriotrifluoroacetic acid the N-CH_3 signal is a singlet at δ = 3.39), 3.18 (q, 2H, CH_2), 6.85 (mc, 1H, H-7), 7.21 (mc, 1H, H-9), 7.63 (mc, 1H, H-8), 8.87 (mc, 1H, H-6), 10.53 (broad signal, 1H, NH).

Anal. Calcd. for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.04; H, 5.68; N, 17.83.

2-[(*N*-Ethyl,*N*-propionyl)amino]-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**8e**) and 2-(Ethylamino)-3-propionyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**9e**).

The treatment of the thick oil obtained from the reaction of **7b** with propionic anhydride yielded 1.50 g (77%) of **8e** (1.12 g +

0.38 g), white needles melting at 91-92° after crystallization from isopropyl ether, and 0.14 g (7.2%) of **9e**, whitish needles, mp 152-153°, after crystallization from the same solvent.

Compound **8e**.

This compound had ir (chloroform): 1687 (CO), 1660 (CO), 1635 (shoulder), 1562, 1521 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.16 (t, 3H, $COCH_2CH_3$), 1.21 (t, 3H, $N-CH_2CH_3$), 2.56 (q, 2H, $COCH_2$), 3.95 (q, 2H, $N-CH_2$), 6.37 (s, 1H, H-3), 7.21 (mc, 1H, H-7), 7.60 (mc, 1H, H-9), 7.84 (mc, 1H, H-8), 9.08 (mc, 1H, H-6).

Anal. Calcd. for $C_{13}H_{15}N_3O_2$: C, 63.66; H, 6.16; N, 17.13. Found: C, 63.69; H, 6.15; N, 16.97.

Compound **9e**.

This compound had ir (chloroform): 3220 (broad, NH), 1679 (4-CO), 1638, 1604 (acyl CO), 1583, 1552, 1524 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.16 (t, 3H, $COCH_2CH_3$), 1.27 (t, 3H, $N-CH_2CH_3$), 3.17 (q, 2H, $COCH_2$), 3.62 (mc, 2H, $N-CH_2$) (in deuteriotrifluoroacetic acid the $N-CH_2$ signal is a quartet at δ = 3.73), 6.84 (mc, 1H, H-7), 7.19 (mc, 1H, H-9), 7.63 (mc, 1H, H-8), 8.86 (mc, 1H, H-6), 10.56 (broad signal, 1H, NH).

Anal. Calcd. for $C_{13}H_{15}N_3O_2$: C, 63.66; H, 6.16; N, 17.13. Found: C, 63.56; H, 6.11; N, 17.05.

2-[(*N*-Butyryl,*N*-methyl)amino]-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**8f**) and 3-Butyryl-2-(methylamino)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**9f**).

The final oily residue obtained from the reaction of **7a** with butyric anhydride afforded 1.79 g (85%) of **8f** (1.63 g + 0.16 g), white crystals, mp 114-115°, after crystallization from ethyl acetate, and 0.03 g (1.4%) of **9f**, white solid melting at 133-134°, after crystallization from isopropyl ether.

Compound **8f**.

This compound had ir (chloroform): 1687 (CO), 1660 (CO), 1636 (shoulder), 1562, 1521 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.93 (t, 3H, $CH_2CH_2CH_3$), 1.74 (mc, 2H, $CH_2CH_2CH_3$), 2.60 (t, 2H, $CH_2CH_2CH_3$), 3.41 (s, 3H, $N-CH_3$), 6.41 (s, 1H, H-3), 7.21 (mc, 1H, H-7), 7.60 (mc, 1H, H-9), 7.88 (mc, 1H, H-8), 9.07 (mc, 1H, H-6).

Anal. Calcd. for $C_{13}H_{15}N_3O_2$: C, 63.66; H, 6.16; N, 17.13. Found: C, 63.73; H, 6.15; N, 16.93.

Compound **9f**.

This compound had ir (chloroform): 3225 (broad, NH), 1680 (4-CO), 1639, 1603 (broad, acyl CO), 1553, 1525 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.01 (t, 3H, $CH_2CH_2CH_3$), 1.64 (mc, 2H, $CH_2CH_2CH_3$), 3.11 (d, J = 5 Hz, 3H, $N-CH_3$) (in deuteriotrifluoroacetic acid the $N-CH_3$ signal is a singlet at δ = 3.36), 3.16 (t, 2H, $CH_2CH_2CH_3$), 6.86 (mc, 1H, H-7), 7.24 (mc, 1H, H-9), 7.66 (mc, 1H, H-8), 8.90 (mc, 1H, H-6), 10.55 (broad signal, 1H, NH).

Anal. Calcd. for $C_{13}H_{15}N_3O_2$: C, 63.66; H, 6.16; N, 17.13. Found: C, 63.38; H, 6.03; N, 16.98.

2-[(*N*-Acetyl,*N*-ethyl)amino]-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**8b**) and 3-Acetyl-2-(ethylamino)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**9b**).

The thick oil obtained from the reaction of **7b** with acetic anhydride was dissolved in a little chloroform and chromatographed on a silica gel column. The first fractions eluted with ethyl acetate yielded 0.04 g (2.2%) of **9b**, white solid that melted at 154-155° after crystallization from isopropyl ether; ir (chloroform): 3215 (broad, NH), 1679 (4-CO), 1637, 1604 (acyl CO), 1586, 1551, 1522 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.25 (t, 3H, CH_2CH_3), 2.71 (s, 3H, $COCH_3$), 3.62 (mc, 2H, CH_2) (in deuteriotrifluoroacetic acid the CH_2 signal is a quartet at δ = 3.73), 6.85 (mc, 1H, H-7), 7.21 (mc, 1H, H-9), 7.65 (mc, 1H, H-8), 8.87 (mc, 1H, H-6), 10.45 (broad signal, 1H, NH).

Anal. Calcd. for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.14; H, 5.64; N, 17.93.

By further elution of the column, at first with ethyl acetate and then with a mixture chloroform-ethyl acetate-methanol (9:9:1), compound **8b** (1.40 g, 76%) was recovered, white solid melting at 83-84° after crystallization from isopropyl ether; ir (chloroform): 1687 (CO), 1660 (CO), 1635 (shoulder), 1563, 1522 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.24 (t, 3H, CH_2CH_3), 2.29 (s, 3H, $COCH_3$), 4.01 (q, 2H, CH_2), 6.41 (s, 1H, H-3), 7.27 (mc, 1H, H-7), 7.64 (mc, 1H, H-9), 7.90 (mc, 1H, H-8), 9.09 (mc, 1H, H-6).

Anal. Calcd. for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.33; H, 5.66; N, 18.00.

2-[(*N*-Acetyl,*N*-phenyl)amino]-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**8c**).

By treating with a little ethyl ether the nearly solid residue obtained from the reaction of **4** [3] with acetic anhydride and filtering, nearly pure **8c** (1.71 g, 97%) was recovered, white crystalline solid melting at 167-168°, after crystallization from ethyl acetate with charcoal; ir (chloroform): 1689 (CO), 1670 (CO), 1638, 1596, 1564, 1522 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.26 (s, 3H, CH_3), 6.52 (s, 1H, H-3), 6.96-7.90 (m, 8H, H-7,8,9 + phenyl H's), 9.02 (mc, 1H, H-6).

Anal. Calcd. for $C_{16}H_{13}N_3O_2$: C, 68.81; H, 4.69; N, 15.04. Found: C, 68.57; H, 4.73; N, 15.17.

2-[(*N*-Butyryl,*N*-phenyl)amino]-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**8g**).

By proceeding in the same manner as for **8c**, from the reaction of **4** with butyric anhydride, **8g** (1.87 g, 96%) was obtained, white crystals mp 146-147°, after crystallization from isopropyl ether; ir (chloroform): 1689 (CO), 1670 (CO), 1637, 1596, 1563, 1523 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.93 (t, 3H, $CH_2CH_2CH_3$), 1.73 (mc, 2H, $CH_2CH_2CH_3$), 2.48 (t, 2H, $CH_2CH_2CH_3$), 6.55 (s, 1H, H-3), 6.93-7.94 (m, 8H, H-7,8,9 + phenyl H's), 9.05 (mc, 1H, H-6).

Anal. Calcd. for $C_{18}H_{17}N_3O_2$: C, 70.34; H, 5.58; N, 13.67. Found: C, 70.59; H, 5.59; N, 13.56.

Preparation of Substituted 2*H*-Dipyrido[1,2-*a*:2',3'-*d*]pyrimidine-2,5(1*H*)-diones **10a-g**.

General Procedure.

Phosphorus oxychloride (0.92 g, 6.0 mmoles) was added dropwise with stirring to 2 ml of *N*,*N*-dimethylformamide which was contained in a flask cooled with an ice bath and protected from atmospheric moisture with a calcium chloride tube. The resulting solution was stirred at room temperature for 30 minutes, then a suspension of proper compound **8** (4.0 mmoles) in 8 ml of *N*,*N*-dimethylformamide was added and the stirred mixture was heated at 95° for 90 minutes. After cooling, the mixture was poured onto crushed ice and the resulting suspension was treated with excess saturated aqueous solution of sodium acetate and stirred for 1 hour at room temperature. The yellowish solid that separated out was collected by filtration, washed with water and dried: there was so obtained the nearly pure compound **10** which was then crystallized from the suitable solvent.

By the above procedure the following compounds **10a-g** were prepared:

1-Methyl-2*H*-dipyrido[1,2-*a*:2',3'-*d*]pyrimidine-2,5(1*H*)-dione (**10a**).

Starting from **8a** (0.87 g), compound **10a** (0.80 g, 88%) was obtained, pale yellow needles melting at 285-286° after crystallization from dichloromethane; ir (potassium bromide): 1698 (CO), 1678 (CO), 1633, 1604 (weak), 1561, 1531, 1502 cm^{-1}; ^{1}H-nmr (deuteriotrifluoroacetic acid): δ 4.12 (s, 3H, CH_3), 7.10 (d, J = 9 Hz, 1H, H-3), 7.92 (mc, 1H, H-8), 8.17-8.84 (m, 3H, H-4,9,10), 9.50 (mc, 1H, H-7).

Anal. Calcd. for $C_{12}H_9N_3O_2$: C, 63.43; H, 3.99; N, 18.49. Found: C, 63.39; H, 3.91; N, 18.36.

1-Ethyl-2*H*-dipyrido[1,2-*a*:2',3'-*d*]pyrimidine-2,5(1*H*)-dione (**10b**).

Starting from **8b** (0.93 g) compound **10b** (0.70 g, 73%) was obtained, orange yellow needles, mp 203-204°, after crystallization from ethyl acetate; ir (potassium bromide): 1708 (CO), 1650 (broad, CO), 1601 (weak), 1553, 1526 (weak), 1500 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.33 (t, 3H, CH_3), 4.52 (q, 2H, CH_2), 6.53 (d, J = 9 Hz, 1H, H-3), 7.14 (mc, 1H, H-8), 7.46-8.03 (m, 2H, H-9,10), 8.13 (d, J = 9 Hz, 1H, H-4), 8.99 (mc, 1H, H-7).

Anal. Calcd. for $C_{13}H_{11}N_3O_2$: C, 64.72; H, 4.60; N, 17.42. Found: C, 64.45; H, 4.47; N, 17.26.

1-Phenyl-2*H*-dipyrido[1,2-*a*:2',3'-*d*]pyrimidine-2,5(1*H*)-dione (**10c**).

From **8c** (1.12 g) compound **10c** (0.95 g, 82%) was obtained, yellow crystalline solid that melted at 305-306° after crystallization from dichloromethane; ir (potassium bromide): 1702 (CO), 1660 (CO), 1632, 1606 (weak), 1557, 1519, 1494 cm^{-1}; ^{1}H-nmr (deuteriotrifluoroacetic acid): δ 7.04 (d, J = 9 Hz, 1H, H-3), 7.32-8.82 (m, 9H, H-4,8,9,10 + phenyl H's), 9.52 (mc, 1H, H-7).

Anal. Calcd. for $C_{17}H_{11}N_3O_2$: C, 70.58; H, 3.83; N, 14.52. Found: C, 70.61; H, 3.81; N, 14.71.

1,3-Dimethyl-2*H*-dipyrido[1,2-*a*:2',3'-*d*]pyrimidine-2,5(1*H*)-dione (**10d**).

The reaction of **8d** (0.93 g) afforded **10d** (0.69 g, 72%), yellow crystals mp 249-250° after crystallization from dichloromethane; ir (potassium bromide): 1696 (CO), 1642 (CO), 1563, 1531, 1501 cm^{-1}; ^{1}H-nmr (deuteriotrifluoroacetic acid): δ 2.37 (s, 3H, 3-CH_3), 4.05 (s, 3H, 1-CH_3), 7.94 (mc, 1H, H-8), 8.20-8.87 (m, 3H, H-4,9,10), 9.50 (mc, 1H, H-7).

Anal. Calcd. for $C_{13}H_{11}N_3O_2$: C, 64.72; H, 4.60; N, 17.42. Found: C, 64.87; H, 4.57; N, 17.27.

1-Ethyl-3-methyl-2*H*-dipyrido[1,2-*a*:2',3'-*d*]pyrimidine-2,5(1*H*)-dione (**10e**).

Compound **10e** was obtained (0.76 g, 74%) from **8e** (0.98 g), yellow needles melting at 207-208° after crystallization from ethyl acetate; ir (potassium bromide): 1693 (CO), 1640 (CO), 1557, 1530, 1500 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.32 (t, 3H, CH_2CH_3), 2.21 (s, 3H, 3-CH_3), 4.52 (q, 2H, CH_2), 7.11 (mc, 1H, H-8), 7.43-7.94 (m, 2H, H-9,10), 7.96 (s, 1H, H-4), 8.96 (mc, 1H, H-7).

Anal. Calcd. for $C_{14}H_{13}N_3O_2$: C, 65.87; H, 5.13; N, 16.46. Found: C, 65.94; H, 5.10; N, 16.22.

3-Ethyl-1-methyl-2*H*-dipyrido[1,2-*a*:2',3'-*d*]pyrimidine-2,5(1*H*)-dione (**10f**).

The reaction of 0.98 g of **8f** afforded 0.85 g (83%) of **10f**, yellow crystals, mp 192-193°, after crystallization from ethyl acetate; ir (potassium bromide): 1698 (CO), 1642 (CO), 1563, 1535, 1503 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.23 (t, 3H, CH_2CH_3), 2.61 (q, 2H, CH_2), 3.75 (s, 3H, 1-CH_3), 7.11 (mc, 1H, H-8), 7.41-7.91 (m, 2H, H-9,10), 7.92 (s, 1H, H-4), 8.97 (mc, 1H, H-7).

Anal. Calcd. for $C_{14}H_{13}N_3O_2$: C, 65.87; H, 5.13; N, 16.46. Found: C, 66.01; H, 5.13; N, 16.29.

3-Ethyl-1-phenyl-2*H*-dipyrido[1,2-*a*:2',3'-*d*]pyrimidine-2,5(1*H*)-dione (**10g**).

Starting from **8g** (1.23 g) compound **10g** (1.07 g, 84%) was obtained, yellow crystalline solid that melted at 235-236° after crystallization from acetone; ir (potassium bromide): 1690 (CO), 1659 (CO), 1634, 1595 (weak), 1558, 1522, 1495 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.27 (t, 3H, CH_3), 2.66 (q, 2H, CH_2), 6.89-7.85 (m, 8H, H-8,9,10 + phenyl H's), 8.11 (s, 1H, H-4), 9.01 (mc, 1H, H-7).

Anal. Calcd. for $C_{19}H_{15}N_3O_2$: C, 71.91; H, 4.76; N, 13.24. Found: C, 71.81; H, 4.73; N, 13.11.

The Reaction of **8a** with the Reagent **1** to Give **10a** and 2-[(*N*-Acetyl,*N*-methyl)amino]-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carbaldehyde (**11**).

Compound **8a** (0.87 g, 4.0 mmoles) was treated with the *N*,*N*-dimethylformamide/phosphorus oxychloride reagent **1** under the same conditions as those described in the general procedure for the preparation of compounds **10a-g**, but the reaction was carried out for 15 minutes only. After cooling, the final mixture was poured onto crushed ice and water and the resulting suspension was treated with excess saturated aqueous solution of sodium acetate and stirred for 1 hour at room temperature.

By filtering, washing with water, and drying the yellowish solid that separated out, nearly pure compound **10a** (0.48 g, 53%) was recovered.

The aqueous filtrate was then exhaustively extracted with chloroform and the combined extracts were dried (anhydrous sodium sulfate) and evaporated *in vacuo* to dryness. The dark oil obtained was dissolved in a little chloroform and chromatographed on a silica gel column. The column was first eluted with a mixture chloroform-ethyl acetate (1:1) until some impurities were removed, then with acetone to recover compound **11**. The acetone eluate was evaporated to dryness and a little ethyl ether was added to the oily residue: after standing, the crystalline compound **11** (0.30 g, 31%) separated out, pale yellow needles melting at 158-159°, after recrystallization from ethyl acetate; ir (potassium bromide): 1700 (CO), 1676 (CO), 1662 (CO), 1628, 1552, 1508 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.13 (s, 3H, $COCH_3$), 3.35 (s, 3H, N-CH_3), 7.45 (mc, 1H, H-7), 7.74 (mc, 1H, H-9), 8.13 (mc, 1H, H-8), 9.22 (mc, 1H, H-6), 10.32 (s, 1H, CHO).

Anal. Calcd. for $C_{12}H_{11}N_3O_3$: C, 58.77; H, 4.52; N, 17.13. Found: C, 59.04; H, 4.54; N, 17.00.

2-[[*N*-(Ethoxycarbonyl),*N*-phenyl]amino]-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**12**).

A mixture of 1.0 g of **4** [3], 15 ml of dry toluene, 15 ml of ethyl chloroformate, and 0.50 g of anhydrous potassium carbonate was heated at 130° for 18 hours, while stirring.

The mixture was then evaporated *in vacuo* to dryness and the residue partitioned between chloroform and water. The aqueous phase was extracted several times with chloroform. The combined organic phases were dried (anhydrous sodium sulfate) and the solvent removed to afford a thick oil from which, after addi-

tion of a little ethyl ether and standing, 1.18 g (91%) of pure compound **12** separated out, pale yellow solid melting at 120-121° after crystallization from cyclohexane; ir (potassium bromide): 1727 (urethane CO), 1676 (4-CO), 1640, 1600, 1563, 1536, 1524 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.22 (t, 3H, CH_3), 4.25 (q, 2H, CH_2), 6.72 (s, 1H, H-3), 6.86-7.78 (m, 8H, H-7,8,9 + phenyl H's), 8.93 (mc, 1H, H-6).

Anal. Calcd. for $C_{17}H_{15}N_3O_3$: C, 66.01; H, 4.89; N, 13.58. Found: C, 66.08; H, 4.93; N, 13.65.

2-[[*N*-(Ethoxycarbonyl),*N*-phenyl]amino]-4-oxo-4*H*-pyrido[1,2-*a*]-pyrimidine-3-carbaldehyde (**14**).

Following the procedure above described for the preparation of compounds **10a-g**, a suspension of 1.24 g (4.0 mmoles) of compound **12** in 8 ml of *N*,*N*-dimethylformamide was added to a mixture of 0.92 g (6.0 mmoles) of phosphorus oxychloride and 2 ml of *N*,*N*-dimethylformamide, heating then for 90 minutes at 95°, while stirring. After cooling and pouring the final mixture onto crushed ice, the resulting solution was treated with excess saturated aqueous solution of sodium acetate and stirred for 1 hour at room temperature. The whitish solid that separated was collected by filtration, washed with water and dried: there was so obtained the nearly pure compound **14** (1.25 g, 93%) which was then crystallized from ethanol to give ivory white crystals melting at 198-199°; ir (potassium bromide): 1714 (urethane CO), 1692 (CO), 1680 (CO), 1630, 1598, 1586 (weak), 1560, 1515 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 1.13 (t, 3H, CH_3), 4.10 (q, 2H, CH_2), 7.09-7.74 (m, 7H, H-7,9 + phenyl H's), 8.16 (mc, 1H, H-8), 9.10 (mc, 1H, H-6), 10.38 (s, 1H, CHO).

Anal. Calcd. for $C_{18}H_{15}N_3O_4$: C, 64.09; H, 4.48; N, 12.46. Found: C, 64.31; H, 4.47; N, 12.23.

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