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TRANSFORMATIONS OF DIETHYL 2-[(DIMETHYLAMINO)METHYLENE]-3-OXOPENTANEDIOATE. A SIMPLE SYNTHESIS OF SUBSTITUTED 2-AMINO-5-OXO-5,6-DIHYDROPYRIDO[4,3-*d*]PYRIMIDINE-8-CARBOXYLATES

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Dedicated to Professor Emeritus Keiichiro Fukumoto on the occasion of his 75th birthday

Abstract – Diethyl 2-[(dimethylamino)methylene]-3-oxopentanedioate (**2**), prepared from acetone-1,3-dicarboxylates (**1**) and *N,N*-dimethylformamide dimethyl acetal (DMFDMA) was, without isolation, transformed by treatment with guanidine hydrochloride into ethyl 2-amino-4-(2-ethoxycarbonylmethyl)-pyrimidine-5-carboxylate (**3**). Compound **3** was transformed with DMFDMA first into intermediate **4** and with an excess of DMFDMA into ethyl 4-[1-(dimethylamino)-3-ethoxy-3-oxoprop-1-en-2-yl]-2-[(dimethylamino)methylene amino]pyrimidine-5-carboxylate (**5**). By treatment of compound **5** with ammonia, primary amines, hydrazine or hydroxylamine intermediates **6a-j** were formed, which cyclized into 6-substituted 2-amino-5-oxo-5,6-dihydro-pyrido[4,3-*d*]pyridine-8- carboxylates (**7a-j**).

INTRODUCTION

There are many methods described in the literature for the synthesis of pyridopyrimidines [1-3] Recently, they have been prepared from 4-amino-6-chloro-5-phenyl-2-methylthiopyrimidine[4] and from 4-amino-1-benzyl-1,2,5,6-tetrahydropyridine-3-carboxylate.[5] They are well-known pharmacophores,[6,7] PDE-inhibitors,[8] inhibitors of tyrosine kinase activity in the epidermal growth factor receptor.[9,10]

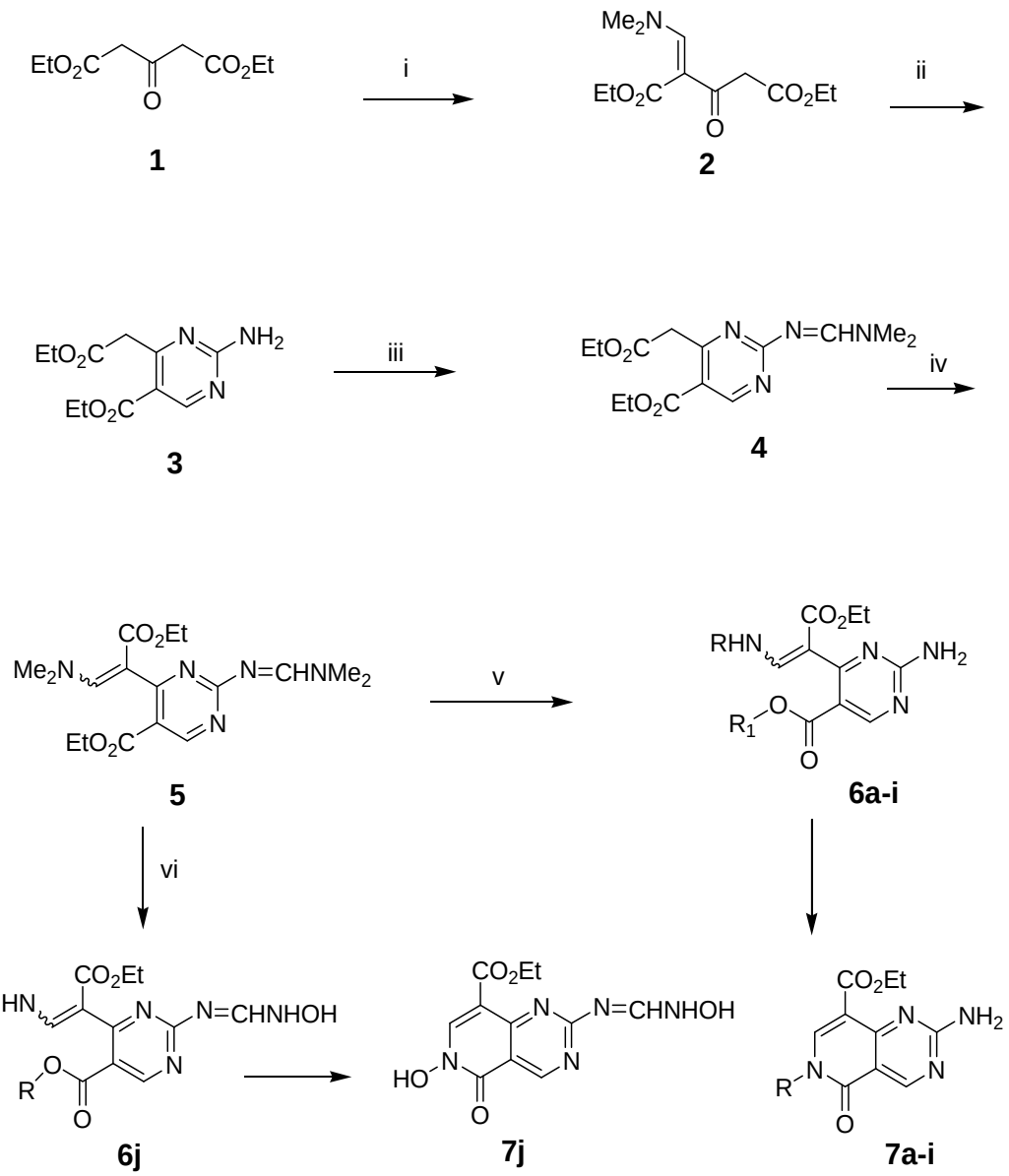
In connection with our interest in enaminones and related compounds, as building blocks for the preparation of various heterocyclic systems,[11] including also some natural products,[12,13] dialkyl acetone-1,3-dicarboxylates have been recently employed for the synthesis of heteroaryl substituted pyrimidines,[14] dialkyl 1-substituted 4-oxo-1,4-dihydropyridine-3,5-dicarboxylates,[15] pyrazolo[4,3-*d*]-pyridine-7-carboxylates,[16] pyrazolyl substituted pyridopyrimidines, pyranopyranediones, chromene-diones,[17] and pyrazolo[4,3-*d*][1,2]diazepines.[18,19] We recently reported an efficient method for the preparation and functionalisation of highly substituted 1-aminopyrroline, 1-aminopyrrole and oxazoline-pyrroline fused systems from 1,2-diaza-1,3-butadienes and 3-dimethylaminopropenoates,[20] and the regio- and stereoselective one-pot synthesis of oxazoline-fused pyridazine via a "Michael addition-pyridazine-cyclisation-oxazoline cyclisation" cascade reaction.[21] Many fused pyrimidines are formed by cyclisation of 3-heteroarylaminopropenoates, derived from 2-substituted 3-(dimethyl-amino)propenoates and heterocylic α-amino compounds.[11,22]

RESULTS AND DISCUSSION

Diethyl acetone-1,3-dicarboxylate (**1**) gave with *N,N*-dimethylformamide dimethyl acetal (DMFDMA) diethyl 2-[(2-dimethylamino)methylene]-3-oxopentanedioate (**2**), which was without isolation transformed with guanidine hydrochloride into ethyl 2-amino-4-(2-ethoxycarbonylmethyl)pyrimidine-5-carboxylate (**3**). When compound **3** was treated with one equivalent of DMFDMA in EtOH, amino group at 2 position was transformed into dimethylaminomethylene amino group to form intermediate **4**. By further treatment with DMFDMA in *n*-propyl acetate as solvent under reflux also active methylene group at 6-position was transformed into dimethylaminomethylene group to give ethyl 4-[1-(dimethyl-amino)-3-ethoxy-3-oxoprop-1-en-2-yl]-2-[(dimethylamino)methyleneamino]pyrimidine-5-carboxylate (**5**). In the reaction of compound **5** with ammonia, primary amines, or hydrazine first the dimethylaminomethylene group at 2-position was transformed into free amino group, followed by substitution of the dimethylamino group on the side chain to give intermediates **6a-j,** which were without isolation cyclised into ethyl 6-substittued 2-amino-5-oxo-5,6-dihydropyrido[4,3-*d*]pyrimidine-8-carboxylates (**7a-i**). Compound **5** was with hydroxylamine hydrochloride transformed into the corresponding 6-hydroxy derivative (**7j**) (Scheme 1, Table 1).

STRUCTURE DETERMINATION

The structures of new compounds were determined by spectroscopic methods (IR, ^{1}H and ^{13}C NMR spectroscopy, MS) and by elemental analyses for C, H, and N. ^{1}H NMR spectrum of compound **3** exhibits



Scheme 1. (i) DMFDMA, EtOH, rt, 45 min; (ii) guanidine hydrochloride, EtOH, reflux, 1h; (iii) DMFDMA (1 equiv.), EtOH, reflux, 1h; (iv) DMFDMA (1.5 equiv.) EtOH, reflux, 6h; (v) RNH_2 (3 equiv.), *n*-PrOAc, aq. HCl, (catalytic amount), reflux, 5h; (vi) NH_2OH x HCl (3 equiv.), EtOH, reflux, 5h.

Table 1. 6-Substituted 2-amino-5-oxo-5,6-dihydropyrido[4,3-*d*]pyrimidine-8-carboxylates (7a-j)

Comp		Yield (%)	Mp (^{o}C) solvent
7	R		
a	H	96.5	289 – 291 (DMF)
b	Me	93.1	298 – 300 (DMF)
c	CH_2CH_2OH	39.5	240 – 245 (EtOH)

d	iPr	83.6	170 –174 (EtOH)
e	cyclopropyl	74.7	239 – 240 (DMF)
f	benzyl	87.9	204 – 209 (DMF)
g	4-methoxybenzyl	67.7	238 – 245 (EtOH)
h	ethoxycarbonylmethyl	96.2	240 – 246 (DMF)
i	NH_2	93.9	278 – 290 (DMF)
j	OH	92.6	245 – 250 (DMF)

two triplets at δ = 1.17 and 1.26 ppm and two quartets at δ = 4.07 and 4.20 ppm for two ester groups, a singlet at δ = 3.91 ppm for CH_2 group, a singlet at δ = 7.52 ppm for NH_2 and a singlet at δ = 8.71 ppm for H_4. Compound **4** shows two triplets at δ = 1.25 and 1.38 ppm and two quartets at δ = 4.15 and 4.35 ppm for two ester groups, a singlet at δ = 4.15 ppm for CH_2 group and a singlet at δ = 8.81 ppm for H_4 two sinlets at δ = 3.22 and 3.25 ppm for NMe_2 group and a singlet at δ = 9.01 ppm for the amidine proton. Compound **5** shows again two triplets at δ = 1.13 and 1.32 ppm and two quartets at δ = 4.05 and 4.27 ppm for two ester groups, a singlet at δ = 8.73 ppm for H_4, a broad singlet at δ = 2.83 ppm for the NMe_2 group and a singlet at δ = 7.62 ppm of the dimethylaminomethylene group, two singlets at δ = 3.16 and 3.29 ppm for NMe_2 and a singlet at δ = 8.87 ppm for the amidine part of the molecule. ^{1}H NMR spectra of compounds **7** exhibit two characteristic singlets for protons H_4 and H_7. While the signal for H_4 appears for all bicyclic compounds at δ_{H4} = 9.00 ppm, the signal for the H_7 appears in the range of δ_{H7} = 8.00-8.50 ppm, dependent on the group R attached at 6-position, and the signals characteristic for R group.

EXPERIMENTAL

Melting points were determined on a Kofler micro hot stage. The ^{1}H NMR spectra were obtained on a Bruker Avance DPX 300 at 300 MHz for ^{1}H and 75.5 MHz for ^{13}C nucleus, using DMSO–d_6 and $CDCl_3$, with TMS as the internal standard, as solvents (δ in ppm, *J* in Hz). All NMR experiments were carried out at 302 K. Mass spectra were recorded on an AutoSpecQ spectrometer and Q-TOF Premier spectrometer, IR spectra on a Perkin-Elmer Spectrum BX FTIR spectrophotometer (ν in cm^{-1}). Microanalyses were performed on a Perkin-Elmer Series II CHN Analyser 2400. Column chromatography (CC) was performed on silica gel (Fluka, silica gel 60, 0.04–0.06 mm)

Ethyl 2-amino-4-(2-ethoxy-2-oxoethyl)pyrimidine-5-carboxylate (3)

To a solution of diethyl 1,3-acetonedicarboxylate (0.95 , 5 mmol), in EtOH (10 mL), DMFDMA (0.72 mL, 5 mmol) was added and the mixture was stirred at rt for 45 min. Guanidine hydrochloride (478 mg, 5

mmol) was then added and the mixture was stirred under reflux for 1 h. The volatile components were evaporated and the crude product was recrystallized from EtOH to give **1**. Yield 23% (290 mg), mp 125-127 °C. ^{1}H NMR (DMSO-d_6) δ: 1.17 (t, 3H: $OCH_2C\underline{H}_3$, J = 7.2 Hz), 1.26 (t, 3H: $OCH_2C\underline{H}_3$, J = 7.2 Hz), 3.91 (s, 2H: $C\underline{H}_2COOEt$), 4.07 (q, 2H: $OC\underline{H}_2CH_3$, *J* = 7.2 Hz), 4.20 (q, 2H: $OC\underline{H}_2CH_3$, *J* = 7.2 Hz), 7.52 (s, 2H: $N\underline{H}_2$), 8.71 (s, 1H: H_4); ^{13}C NMR (DMSO-d_6) δ: 14.00, 43.03, 60.18, 60.29, 111.61 (C_5), 161.12, 163.89, 164.48, 165.61, 169.19; IR (KBr) ν (cm^{-1}): 3327, 3157, 1732, 1715, 1667, 1266; MS (M+) m/z: 253. *Anal*. Calcd for $C_9H_{11}N_3O_4$ (253.2): C 52.17, H 5.97, N 16.59. Found: C 51.95, H 6.24, N 16.37.

Ethyl 2-[(dimethylamino)methyleneamino]-4-(2-ethoxy-2-oxoethyl)pyrimidine-5-carboxylate (4)

2-Amino-5-ethoxycarbonyl-4-ethoxycarbonylmethylpirimidine (**2**; 253 mg, 1 mmol) was suspended in EtOH (3 mL), DMFDMA (0.14 mL, 1 mmol) was added and the mixture was stirred under reflux for 1 h. Then additional 0.07 mL DMFDMA (0.07 mL, 5 mmol) was added and the reaction mixture was heated under reflux for 1 h. The mixture was cooled and concentrated under reduced pressure to give an oily residue, to which Et_2O (3 mL) was added and the precipitate was collected by filtration to give **4** Yield 83 % (255 mg), mp 99-101 °C (from *t*-BuOMe). ^{1}H NMR ($CDCl_3$) δ: 1.25 (t, 3H: $OCH_2C\underline{H}_3$, *J* = 7.2 Hz), 1.38 (t, 3H: $OCH_2C\underline{H}_3$, *J* = 7.2 Hz), 3.22 (s, 3H: $N(C\underline{H}_3)_2$), 3.25 (s, 3H: $N(C\underline{H}_3)_2$), 4.15 (s, 2H: $C\underline{H}_2COOEt$), 4.15 (q, 2H: $OC\underline{H}_2CH_3$, *J* = 7.2 Hz), 4.35 (q, 2H: $OC\underline{H}_2CH_3$, *J* = 7.2 Hz), 8.81 (s, 1H: H_4), 9.01 (s, 1H: =C$\underline{H}$); ^{13}C NMR ($CDCl_3$) δ: 14.11, 35.35, 41.36, 43.84, 60.85, 60.96, 116.84, 159.46, 161.07, 164.96, 165.85, 167.61, 169.66; IR (KBr) ν (cm^{-1}): 2980, 1709, 1634, 1515; MS (M+) m/z: 308. *Anal.* Calcd for $C_{14}H_{20}N_4O_4$ (308.3): C 54.54, H 6.54, N 18.17. Found: C 54.91, H 6.76, N 18.30.

Ethyl 4-[1-(dimethylamino)-3-ethoxy-3-oxoprop-1-en-2-yl]-2-[(dimethylamino)methyleneamino]pyrimidine-5-carboxylate (5)

To a solution of compound **2** (3.10 g, 10 mmol) in *n*-propyl acetate (25 mL) DMFDMA (2.1 mL, 15 mmol) was added. The mixture was stirred under reflux for 6 hours. Then the mixture was cooled and concentrated under reduced pressure to give an oily residue to which Et_2O (5 mL) was added and the precipitate was collected by filtration to give **5**. Yield 55 % (1.78 g), mp 142-144 °C (from *tert*-butyl methyl ether). ^{1}H NMR ($CDCl_3$) δ: 1.13 (t, 3H: $OCH_2C\underline{H}_3$, *J* = 7.2 Hz), 1.32 (t, 3H: $OCH_2C\underline{H}_3$, *J* = 7.2 Hz), 2.83 (br s, 6H: C=CHN($C\underline{H}_3$)$_2$), 3.16 (s, 3H: N=CHN($C\underline{H}_3$)$_2$), 3.19 (s, 3H: N=CHN($C\underline{H}_3$)$_2$), 4.05 (q, 2H: $OC\underline{H}_2CH_3$, *J* = 7.2 Hz), 4.27 (q, 2H: $OC\underline{H}_2CH_3$, *J* = 7.2 Hz), 7.62 (s, 1H: C=C$\underline{H}$N(CH_3)$_2$), 8.73 (s, 1H: H_4), 8.87 (s, 1H: N=C$\underline{H}$N(CH_3)$_2$); ^{13}C NMR ($CDCl_3$) δ: 14.17, 14.30, 35.22, 41.15, 43.93, 59.52, 60.63, 98.35, 119.35, 151.34, 158.77, 159.54, 165.76, 165.93, 166.63, 168.20; IR (KBr) ν (cm^{-1}): 3420, 2984, 1690, 1600, 1563, 1426; MS (M+) m/z: 363. *Anal.* Calcd for $C_{17}H_{25}N_5O_4$ (363.4): C 56.19, H 6.93,

N 19.27. Found: C 56.34, H 7.16, N 19.25.

6-Substituted ethyl 2-amino-5-oxo-5,6-dihydropyrido[4,3-*d*]pyrimidine-8-carboxylate (7a-j). General procedure.

363 mg (1 mmol) of compound **3** was dissolved in 5 mL of EtOH and 3 mmol of the corresponding amine and one drop of concentrated HCl was added. The mixture was stirred under reflux for 5 h. Then the mixture was cooled on the ice bad and the product was filtered. The crude product was recrystallised from corresponding solvent.

Ethyl 2-amino-5-oxo-5,6-dihydropyrido[4,3-*d*]pyrimidine-8-carboxylate (7a)

This compound was prepared from **3** (363 mg, 1 mmol), EtOH (5 mL), and 25 % NH_4OH (0.20 mL, 3 mmol). Yield 97 % (225 mg), mp 289-291 ^oC (from DMF). ^1H NMR (DMSO-d_6) δ: 1.30 (t, 3H: $OCH_2C\underline{H}_3$, J = 6.9 Hz), 4.22 (q, 2H: $OC\underline{H}_2CH_3$, J = 6.9 Hz), 7.44(br s, 2H: $N\underline{H}_2$), 8.01 (s, 1H: H_7), 8.97 (s, 1H: H_4), 11.69 (br s, 1H: N$\underline{H}$); ^{13}C NMR (DMSO-d_6) δ: 14.17, 60.08, 106.83, 109.59, 143.17, 158.67, 160.33, 161.22, 163.22, 164.19; IR (KBr) ν (cm^{-1}): 3429, 3140, 1717, 1674, 1614, 1443; MS (M+) m/z: 234. *Anal.* Calcd. for $C_{10}H_{10}N_4O_3$ (234.2): C 51.28, H 4.30, N 23.92. Found: C 51.42, H 4.02, N 23.60; HRMS: Calcd. for $C_{10}H_{10}N_4O_3$: 234,075290, found: 234,076020.

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Ethyl 2-amino-6-methyl-5-oxo-5,6-dihydropyrido[4,3-*d*]pyrimidine-8-carboxylate (7b)

This compound was prepared from **3** (363 mg, 1 mmol), EtOH (5mL), and methylamine (aqueous sol. 11.8 M, 0.25 mL, 3 mmol) Yield 93 % (230 mg), mp 298-300 ^oC (from DMF). ^1H NMR (DMSO-d_6) δ: 1.31 (t, 3H: $OCH_2C\underline{H}_3$, J = 7.2 Hz), 3.48 (s, 3H: $C\underline{H}_3$), 4.24 (q, 2H: $OC\underline{H}_2CH_3$, J = 7.2 Hz) , 7.43 (br.s, 2H: $N\underline{H}_2$), 8.40 (br s, 1H: H_7), 9.00 (s, 1H: H_4); ^{13}C NMR (DMSO-d_6) δ: 14.22, 36.17, 60.15, 106.71, 108.96, 147.41, 157.82, 160.55, 160.84, 163.23, 163.99; IR (KBr) ν (cm^{-1}): 3375, 3184, 1729, 1641, 1574; MS (M+) m/z: 248. *Anal*. Calcd for $C_{11}H_{12}N_4O_3$ (248.2): C 53.22, H 4.87, N 22.57. Found: C 53.17, H 4.92, N 22.63.

Ethyl 2-amino-6-(2-hydroxyethyl)-5-oxo-5,6-dihydropyrido[4,3-*d*]pyrimidine-8-carboxylate (7c)

This compound was prepared from **3** (363 mg, 1 mmol), EtOH (5mL), and ethanolamine (0.18 mL, 3 mmol). Yield 40 % (112 mg), mp 240-245 ^oC (from EtOH). ^1H NMR (DMSO-d_6) δ: 1.31 (t, 3H: $OCH_2C\underline{H}_3$, J = 6.9 Hz), 3.65 (m, 2H: $NC\underline{H}_2$), 4.01 (m, 2H: $C\underline{H}_2OH$), 4.25 (q, 2H: $OC\underline{H}_2CH_3$, J = 6.9 Hz) 4.93 (t, 1H: $CH_2O\underline{H}$, J = 5.7 Hz), 7.44 (br s, 2H: $N\underline{H}_2$), 8.30 (s, 1H: H_7), 9.01 (s, 1H: H_4); ^{13}C NMR (DMSO-d_6) δ: 14.24, 50.96, 58.56, 60.16, 106.27, 109.07, 147.72, 157.87, 160.52, 160.66, 163.35, 164.03; IR (KBr) ν (cm^{-1}): 3385, 3177, 1716, 1680, 1650, 1611, 1468; MS (M+) m/z: 278. *Anal*. Calcd

for $C_{12}H_{14}N_4O_4$ (278.3): C 51.80, H 5.07, N 20.13. Found: C 52.09, H 5.33, N 20.07.

Ethyl 2-amino-6-isopropyl-5-oxo-5,6-dihydropyrido[4,3-*d*]pyrimidine-8-carboxylate (7d)

This compound was prepared from **3** (363 mg, 1 mmol), EtOH (5 mL), and isopropylamine (0.26 mL, 3 mmol). Yield 84 % (232 mg), mp 170-174 °C (from EtOH). ^{1}H NMR (DMSO-d_6) δ: 1.34 (m, 9H: $OCH_2C\underline{H}_3$, $CH(C\underline{H}_3)_2$), 4.26 (q, 2H: $OC\underline{H}_2CH_3$, J = 7.2 Hz), 5.01 (m, 1H: C<u>H</u>, J = 6.6 Hz), 7.44 (br s, 2H: $N\underline{H}_2$), 8.25 (s, 1H: H_7), 9.02 (s, 1H: H_4); ^{13}C NMR (DMSO-d_6) δ: 14.19, 21.03, 46.83, 60.36, 107.90, 109.05, 141.86, 157.15, 160.14, 160.88, 163.60, 164.07; IR (KBr) ν (cm^{-1}): 3430, 3175, 1735, 1630, 1574, 1188. *Anal*. Calcd for $C_{13}H_{16}N_4O_3$ (276.3): C 56.51, H 5.84, N 20.28. Found: C 56.60, H 5.94, N 20.06.

Ethyl 2-amino-6-cyclopropyl-5-oxo-5,6-dihydropyrido[4,3-*d*]pyrimidine-8-carboxylate (7e)

This compound was prepared from **3** (363 mg, 1 mmol), EtOH (5mL), and cyclopropylamine (0.21 mL, 3 mmol). Yield 75 % (206 mg), mp 239-240 °C (from DMF). ^{1}H NMR (DMSO-d_6) δ: 0.85-0.92 (m, 2H: C<u>H</u>$_2$ (cyclopropyl)), 0.96 - 1.06 (m, 2H: C<u>H</u>$_2$ (cyclopropyl)), 1.31 (t, 3H: $OCH_2C\underline{H}_3$, J = 7.2 Hz), 3.22.-.3.31 (m, 1H: C<u>H</u> (cyclopropyl)), 4.24 (q, 2H: $OC\underline{H}_2CH_3$, J = 7.2 Hz), 7.44 (br s, 2H: $N\underline{H}_2$), 8.11 (s, 1H: H_7), 8.99 (s, 1H: H_4); ^{13}C NMR (DMSO-d_6) δ: 6.35, 14.21, 31.86, 60.29, 106.96, 109.08, 145.90, 157.51, 160.60, 161.51, 163.27, 164.09; IR (KBr) ν (cm^{-1}): 3414, 3163, 1723, 1670, 1634, 1574. *Anal*. Calcd for $C_{13}H_{14}N_4O_3$ (274.3): C 56.93, H 5.14, N 20.43. Found: C 57.01, H 5.25, N 20.34.

Ethyl 2-amino-6-benzyl-5-oxo-5,6-dihydropyrido[4,3-*d*]pyrimidine-8-carboxylate (7f)

This compound was prepared from **3** (363 mg, 1 mmol), EtOH (5 mL), and benzylamine (0.33 mL, 3 mmol). Yield 88 % (285 mg), mp 204-209 °C (from DMF). ^{1}H NMR (DMSO-d_6) δ: 1.30 (t, 3H: $OCH_2C\underline{H}_3$, J = 7.2 Hz), 4.24 (q, 2H: $OC\underline{H}_2CH_3$, J = 7.2 Hz), 5.19 (s, 2H: $C\underline{H}_2Ph$), 7.26 - 7.40 (m, 5H: Ph), 7.50 (br s, 2H: $N\underline{H}_2$), 8.50 (s, 1H: H_7), 9.02 (s, 1H: H_4); ^{13}C NMR (DMSO-d_6) δ: 14.19, 50.81, 60.34, 107.75, 109.13, 127.55, 127.63, 128.66, 136.90, 146.30, 157.80, 160.44, 160.82, 163.28, 164.11; IR (KBr) ν (cm^{-1}): 3475, 3175, 1640, 1579, 1456. *Anal*. Calcd for $C_{17}H_{16}N_4O_3$ (324.3): C 62.95, H 4.97, N 17.27. Found: C 63.23, H 4.87, N 17.28.

Ethyl 2-amino-6-(4-methoxybenzyl)-5-oxo-5,6-dihydropyrido[4,3-*d*]pyrimidine-8-carboxylate (7g)

This compound was prepared from **3** (363 mg, 1 mmol), EtOH (5 mL), and 4-methoxybenzylamine (0.39 mL, 3 mmol). Yield 68 % (240 mg), mp 238-245 °C (from EtOH). ^{1}H NMR (DMSO-d_6) δ: 1.30 (t, 3H: $OCH_2C\underline{H}_3$, J = 7.2 Hz), 3.73 (s, 3H: $OC\underline{H}_3$), 4.24 (q, 2H: $OC\underline{H}_2CH_3$, J = 7.2 Hz), 5.10 (s, 2H: $C\underline{H}_2Ph$), 6.91 (d, 2H: Ar, J = 9.0 Hz), 7.30 (d, 2H: Ar, J = 9.0 Hz), 7.48 (br s, 2H: $N\underline{H}_2$), 8.47 (s, 1H: H_7), 9.01 (s, 1H: H_4); ^{13}C NMR (DMSO-d_6) δ: 14.18, 50.19, 55.09, 60.31, 107.65, 109.12, 144.05, 128.81, 129.34,

146.06, 157.71, 158.84, 160.41, 160.78, 163.32, 164.07; IR (KBr) ν (cm^{-1}): 3398, 3190, 1727, 1677, 1632, 1568. *Anal*. Calcd for $C_{18}H_{18}N_4O_4$ (354.4): C 61.01, H 5.12, N 15.81. Found: C 60.69, H 5.21, N 15.82.

Ethyl 2-amino-6-(2-ethoxycarbonylmethyl)-5-oxo-5,6-dihydropyrido[4,3-*d*]pyrimidine-8-carboxylate (7h)

This compound was prepared from **3** (363 mg, 1 mmol), EtOH (5mL), and glycine ethyl ester hydrochloride (419 mg, 3 mmol). Yield 96 % (307 mg), mp 240-246 °C (from DMF). ^{1}H NMR (DMSO-d_6) δ: 1.22 (t, 3H: $CH_2COOCH_2C\underline{H}_3$, J = 7.2 Hz), 1.31 (t, 3H: $OCH_2C\underline{H}_3$, J = 7.2 Hz), 4.16 (q, 2H: $CH_2COOC\underline{H}_2CH_3$, J = 7.2 Hz), 4.23 (q, 2H: $OC\underline{H}_2CH_3$, J = 7.2 Hz), 4.79 (s, 2H: $C\underline{H}_2COOCH_2CH_3$), 7.55 (br s, 2H: $N\underline{H}_2$), 8.45 (s, 1H: H_7), 8.99 (s, 1H: H_4); ^{13}C NMR (DMSO-d_6) δ: 14.02, 14.21, 49.51, 60.33, 61.22, 107.46, 108.69, 146.96, 158.08, 160.33, 160.67, 163.13, 164.20, 168.03; IR (KBr) ν (cm^{-1}): 3501, 3170, 1750, 1687, 1663, 1631, 1576. *Anal*. Calcd for $C_{14}H_{16}N_4O_5$ (320.3): C 52.50, H 5.03, N 17.49. Found: C 52.78, H 5.08, N 17.29.

Ethyl 2,6-diamino-5-oxo-5,6-dihydropyrido[4,3-*d*]pyrimidine-8-carboxylate (7i)

This compound was prepared from **3** (363 mg, 1 mmol), EtOH (5mL), and hydrazine (0.094 mL, 3 mmol) Yield 94 % (234 mg), mp 278-290 °C (from DMF). ^{1}H NMR (DMSO-d_6) δ: 1.30 (t, 3H: $OCH_2C\underline{H}_3$, J = 7.2 Hz), 4.23 (q, 2H: $OC\underline{H}_2CH_3$, J = 7.2 Hz), 5.99 (s, 2H: $NN\underline{H}_2$), 7.46 (rs, 2H: $N\underline{H}_2$), 8.31 (s, 1H: H_7), 9.04 (s, 1H: H_4); ^{13}C NMR (DMSO-d_6) δ: 14.17, 60.18, 105.48, 108.69, 146.48, 157.17, 159.93, 160.58, 162.72, 163.93; IR (KBr) ν (cm^{-1}): 3373, 3178, 1728, 1650, 1619, 1573, 1205; MS (M+) m/z: 249. *Anal*. Calcd for $C_{10}H_{11}N_5O_3$ (249.2): C 48.19, H 4.45, N 28.10. Found: C 47.96, H 4.72, N 28.05.

Ethyl 6-hydroxy-2-[(hydroxyamino)methyleneamino]-5-oxo-5,6-dihydropyrido[4,3-*d*]pyrimidine-8-carboxylate (7j)

This compound was prepared from **3** (363 mg, 1 mmol), EtOH (5mL), and hydroxylamine (50 % aqueous sol. 0.20 mL, 3 mmol). Yield 93 % (272 mg), mp 245-250 °C (from DMF). ^{1}H NMR (DMSO-d_6) δ: 11.33 (t, 3H: $OCH_2C\underline{H}_3$, J = 7.2 Hz), 4.29 (q, 2H: $OC\underline{H}_2CH_3$, J = 7.2 Hz), 7.94 (d, 1H: $NHC\underline{H}$=NOH, J = 9.6 Hz), 8.63 (s, 1H: H_7), 9.26 (s, 1H: H_4), 9.69 (br d, 1H: $N\underline{H}$CH=NOH), 10.61 (br s, 2H: OH, NHCH=NO$\underline{H}$); IR (KBr) ν (cm^{-1}): 3342, 1725, 1677, 1588, 1541; MS (M+) m/z: 293. *Anal*. Calcd for $C_{11}H_{11}N_5O_5$ (293.3): C 45,06, H 3,78, N 23,88. Found: C 44,88, H 4,01, N 23,62.

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