Catalytic Hydrogenation of 3-Benzyloxycarbonylaminoazino[1,2-*x*]-azin-4-ones. A Facile Access to 3-Amino-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyridin-4-ones and 3-Amino-6,7,8,9-tetrahydro-4*H*-azino[1,2-*x*]pyrimidin-4-ones

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By catalytic hydrogenation of 3-(benzyloxycarbonyl)amino-4*H*-pyrido[1,2-*a*]pyridin-4-ones **28** and **29**, and azino[1,2-*x*]pyrimidin-4-ones **32-35**, **41**, and **42**, partial saturation of the heterocyclic systems and removal of the benzyloxycarbonyl moiety was observed to give 3-amino-6,7,8,9-tetrahydro-4*H*-pyrido[1,2 *a*]pyridin-4-ones **30** and **31**, and 3-amino-6,7,8,9-tetrahydro-4*H*-azino[1,2-*x*]pyrimidin-4-ones **36-39**, **43**, and **44** in high yields. The methods represent a simple two step synthesis, starting from heterocyclic α-amino compounds and methyl (*Z*)-2-(benzyloxycarbonyl)amino-3-dimethylaminopropenoate followed by catalytic hydrogenation.

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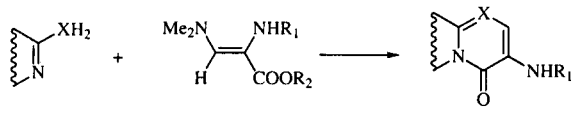
The pyridine moiety of 4*H*-pyrido[1,2-*a*]pyrimidin-4-one could be generally saturated by catalytic hydrogenation over Pd/C or Raney nickel at atmospheric pressure as well as under pressure at room temperature in acetic acid, in an alcohol, or mixture of alcohols to give 6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones [1]. If the pyridine ring bears a nitro group, only the reduction of nitro group occurs, without saturation of the pyridine ring of 4*H*-pyrido[1,2-*a*]pyrimidin-4-one [2].

Recently, a series of alkyl 2-acylamino-3-dimethylaminopropenoates and alkyl 2-(2,2-disubstituted ethenyl)amino-3-dimethylaminopropenoates [3-14] have been prepared and employed as three carbon synthons for preparation of substituted fused 3-amino pyranones, pyridinones and pyrimidinones from the corresponding heterocyclic compounds with an active methylene or amino group in α- position in respect to the ring nitrogen atom according to the following scheme: (Scheme 1).

Scheme 1



1a: X = C-COOEt
b: X = C-CN
c: X = N

2a: R_1 = -COPh, R_2 = Me
b: R_1 = -COMe, R_2 = Me
c: R_1 = -COMe, R_2 = Et
d: R_1 = -$COOCH_2Ph$, R_2 = Me
e: R_1 = -CH=C$(COMe)_2$, R_2 = Me
f: R_1 = -CH=C(COMe)$COOCH_2Ph$, R_2 = Me
g: R_1 = -CH=C(COMe)COOEt, R_2 = Et

3

3-Amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones have been recently studied as flourescent probes for hypoxic cells in solid tumors [15]. They have been prepared by condensation of substituted 2-aminopyridines with ethyl 3-ethoxy-2-nitropropenoate followed by cyclization in polyphosphoric acid, to give substituted 3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones. Reduction of the nitro group has been achieved using either titanium (III) chloride or Pd/C in the presence of hydrogen [16]. They have been also prepared by hydrolysis of the benzoylamino group of 3-benzoylamino-4*H*-pyrido[1,2-*a*]-pyrimidin-4-ones in concentrated hydrochloric acid in yields below 30% [17].

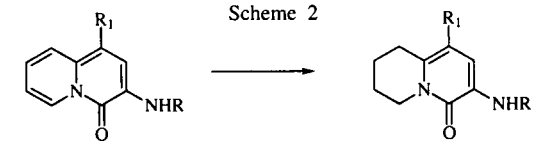
Methyl (*Z*)-2-(benzyloxycarbonyl)amino-3-dimethylaminopropenoate (**2d**) has been used as a reagent for preparation of 3-(benzyloxycarbonyl)amino substituted 4*H*-pyrido[1,2-*a*]pyrimidin-4-ones, 4*H*-pyrimido-[1,2-*b*]pyridazin-4-ones, 5*H*-[1,2,4]triazolo[2,3-*a*]pyrimidin-5-ones, 5*H*-thiazolo[3,2-*c*]pyrimidin-5-ones, and 4*H*-pyrazino[1,2-*a*]pyrimidin-4-ones (**3**), from which benzyloxycarbonyl group has been removed selectively by catalytic transfer hydrogenation with Pd/C in the presence of cyclohexene to give the corresponding 3-amino derivatives in high yields [12, 14].

In connection with our interest in heterocyclic diazo compounds, we decided to apply the above methodology for the preparation of 3-amino-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyridin-4-ones and 3-amino-6,7,8,9-tetrahydro-4*H*-azino[1,2-*x*]pyrimidin-4-ones.

In this paper we report on catalytic hydrogenation of substituted 3-aminopyrido[1,2-*a*]pyridin-4-ones and 3-aminoazino[1,2-*x*]pyrimidin-4-ones in the presence of Pd/C to give corresponding 6,7,8,9-tetrahydropyrido[1,2-*a*]pyridin-4-ones and 6,7,8,9-tetrahydroazino[1,2-*x*]pyrimidin-4-ones. In the case of benzyloxycarbonylamino compounds the benzyloxycarbonyl group was removed at the same time to give free amino compounds.

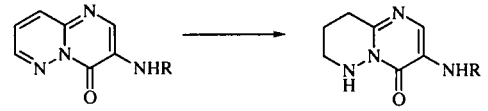
The following 3-benzoylamino and 3-acetylamino compounds have been selected: 3-benzoylamino-1-ethoxycarbonyl-4*H*-pyrido[1,2-*a*]pyridin-4-one (**4**) [18], 3-benzoylamino-1-cyano-4*H*-pyrido[1,2-*a*]pyridin-4-one (**5**) [18], 3-acetylamino-1-ethoxycarbonyl-4*H*-pyrido[1,2-*a*]pyridin-4-one (**6**), 3-acetylamino-1-cyano-4*H*-pyrido[1,2-*a*]pyridin-4-one (**7**), 3-benzoylamino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**12**) [19], 3-benzoylamino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**13**) [19], 3-benzoylamino-9-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**14**), 3-acetylamino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**15**) [20], 3-acetylamino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**16**) [20], 3-benzoylamino-4*H*-pyrimido[1,2-*b*]pyridazin-4-one (**22**), 3-acetylamino-4*H*-pyrimido[1,2-*b*]pyridazin-4-one (**23**), and 3-benzoylamino-4*H*-pyrazino[1,2-*a*]pyrimidin-4-one (**26**) [19], to give the corresponding 3-benzoylamino tetrahydro compounds **8**, **9**, **17-19**, **24**, and **27**, and 3-acetylamino tetrahydro compounds **10**, **11**, **20**, **21**, and **25** (Scheme 2).

Scheme 2

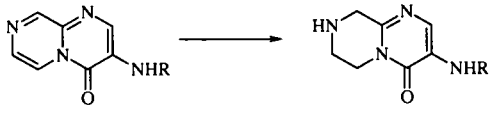


4	R = COPh, R_1 = COOEt	**8**
5	R = COPh, R_1 = CN	**9**
6	R = COMe, R_1 = COOEt	**10**
7	R = COMe, R_1 = CN	**11**

12	R = COPh, R_1 = R_2 = H	**17**
13	R = COPh, R_1 = CH_3, R_2 = H	**18**
14	R = COPh, R_1 = H, R_2 = CH_3	**19**
15	R = COMe, R_1 = R_2 = H	**20**
16	R = COMe, R_1 = CH_3, R_2 = H	**21**



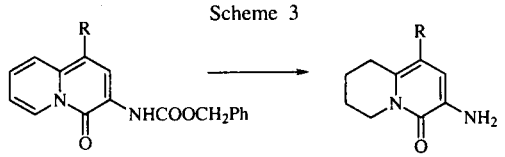
22	R = COPh	**24**
23	R = COMe	**25**



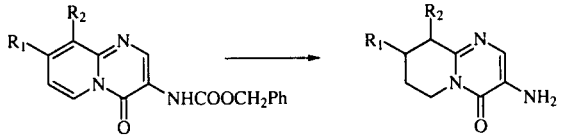
26	R = COPh	**27**

On the other hand, 3-(benzyloxycarbonyl)amino compounds, such as 3-(benzyloxycarbonyl)amino-1-ethoxycarbonyl-4*H*-pyrido[1,2-*a*]pyridin-4-one (**28**) [12], 3-(benzyloxycarbonyl)amino-1-cyano-4*H*-pyrido[1,2-*a*]-pyridin-4-one (**29**) [12], 3-(benzyloxycarbonyl)amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**32**) [14], 3-(benzyloxycarbonyl)amino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**33**) [14], 3-(benzyloxycarbonyl)amino-9-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**34**) [14], 3-(benzyloxycarbonyl)amino-9-hydroxy-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**35**) [14], 3-(benzyloxycarbonyl)amino-4*H*-pyrimido[1,2-*b*]pyridazin-4-one (**41**) [14], and 3-(benzyloxycarbonyl)amino-4*H*-pyrazino[1,2-*a*]pyrimidin-4-one (**42**) [14], gave under the same conditions the corresponding 3-amino tetrahydro derivatives **30**, **31**, **36-39**, **43**, and **44**. (Scheme 3). However, when 10% Pt/C was used instead of Pd/C, only saturation of the pyridine ring took place. For example, 3-(benzyloxycarbonyl)amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**32**) gave 3-(benzyloxycarbonyl)amino-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**40**) (Scheme 3).

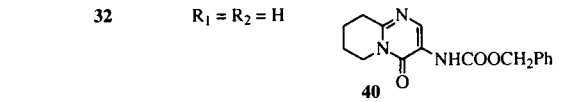
Scheme 3



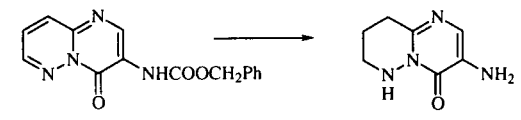
28	R = COOEt	**30**
29	R = CN	**31**



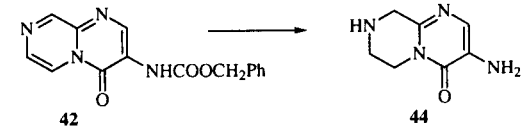
32	R_1 = R_2 = H	**36**
33	R_1 = CH_3, R_2 = H	**37**
34	R_1 = H, R_2 = CH_3	**38**
35	R_1 = H, R_2 = OH	**39**



32	R_1 = R_2 = H	**40**



41		**43**

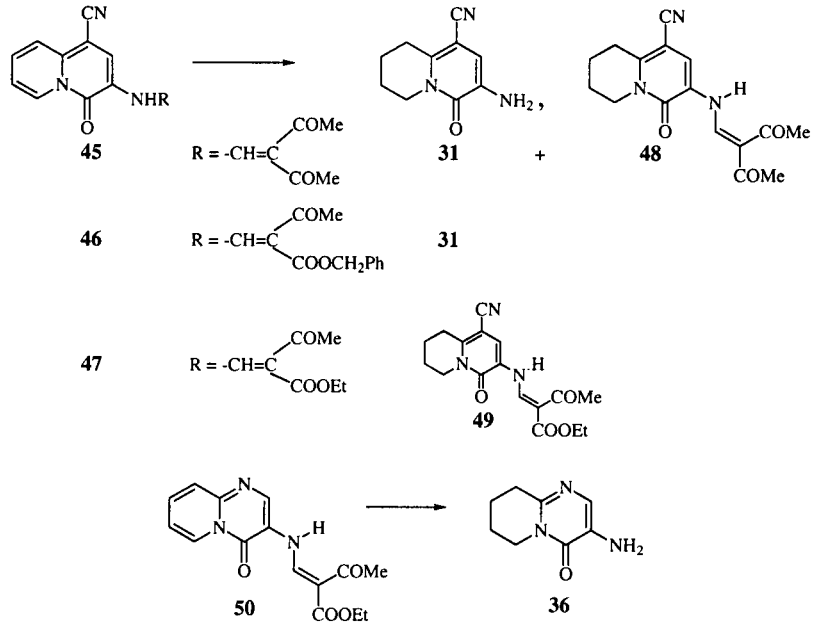


42		**44**

Similarly, 3-(2-acetyl-2-benzyloxycarbonyl-1-ethenyl)-amino-1-cyano-4*H*-pyrido[1,2-*a*]pyridin-4-one (**46**) [6] gave under analogous conditions the corresponding

3-amino derivative **31**, [2,2-bis(acetyl)ethenyl]amino-derivative **45** [21] gave a mixture of 3-amino-6,7,8,9-tetrahydro derivative **31** and 3-[2,2bis(acetyl)ethenyl]-amino-1-cyano-6,7,8,9-tetrahydro derivative **48**, while in the case of 3-(2-acetyl-2-ethoxycarbonyl-1-ethenyl)amino-1-cyano- derivative **47** [12] only the 6,7,8,9-tetrahydro derivative **49** was isolated. 3-(2-Acetyl-2-ethoxycarbonyl-1-ethenyl)amino-4*H*-pyrido-[1,2-*a*]pyrimidin-4-one (**50**) [11] gave at 50° the corresponding 3-amino-6,7,8,9-tetrahydro derivative **36** (Scheme 4).

Scheme 4



The structures of new compounds were determined on the basis of elemental analysis for C, H, and N, and ^{1}H nmr spectra including COSY-45 technique.

The catalytic hydrogenation of fused 3-benzyloxycarbonylamino derivatives in the presence of Pd/C represents a simple two step synthesis of 3-amino-6,7,8,9-tetrahydro-4*H*-azino[1,2-*x*]pyrimidin-4-ones starting from heteroaromatic amino compounds.

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ^{1}H nmr spectra were obtained on a Bruker Avance DPX 300 MHz spectrometer, ir spectra on a Perkin-Elmer 1310 instrument and micro analyses for C, H and N on a Perkin-Elmer Analyzer 2400.

The following compounds were prepared according to the procedures described in the literature: 4-dimethylaminomethylene-2-methyl-5(4*H*)-oxazolone [20], methyl (*Z*)-2-benzoylamino-3-dimethylaminopropenoate (**2a**) [19, 23], methyl 2-acetylamino-3-dimethylaminopropenoate (**2b**) [20], methyl 2-(benzyloxycarbonyl)amino-3-dimethylaminopropenoate (**2d**) [12], methyl 2-[2,2-bis(acetyl)ethenyl]amino-3-dimethylaminopropenoate (**2e**) [21], methyl 2-(2-acetyl-2-benzyloxycarbonylethenyl)amino-3-dimethylaminopropenoate (**2f**) [6], ethyl 2-(2-acetyl-2-ethoxycarbonyl-1-ethenyl)amino-3-dimethylaminopropenoate (**2g**) [11], 3-benzoylamino-1-ethoxycarbonyl-4*H*-pyrido[1,2-*a*]pyridin-4-one (**4**) [18], 3-benzoylamino-1-cyano-4*H*-pyrido[1,2-*a*]pyridin-4-one (**5**) [18], 3-benzoylamino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**12**) [19], 3-benzoylamino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**13**) [19], 3-acetylamino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**15**) [20], 3-benzoylamino-4*H*-pyrazino[1,2-*a*]pyrimidin-4-one (**26**) [19], 3-(benzyloxycarbonyl)amino-1-ethoxycarbonyl-4*H*-pyrido[1,2-*a*]pyridin-4-one (**28**) [12], 3-(benzyloxycarbonyl)amino-1-cyano-4*H*-pyrido[1,2-*a*]pyridin-4-one (**29**) [12], 3-(benzyloxycarbonyl)amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**32**) [14], 3-(benzyloxycarbonyl)amino-8-methyl-4*H*-pyrido-[1,2-*a*]pyrimidin-4-one (**33**) [14], 3-(benzyloxycarbonyl)amino-9-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**34**) [14], 3-(benzyloxycarbonyl)amino-9-hydroxy-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**35**) [14], 3-(benzyloxycarbonyl)amino-4*H*-pyrimido[1,2-*b*]pyridazin-4-one (**41**) [14], 3-(benzyloxycarbonyl)amino-4*H*-pyrazino[1,2-*a*]-pyrimidin-4-one (**42**) [14], 3-[2,2-bis(acetyl)-1-ethenyl]amino-1-cyano-4*H*-pyrido[1,2-*a*]pyridin-4-one (**45**) [21], 3-(2-acetyl-2-benzyloxycarbonyl-1-ethenyl)amino-1-cyano-4*H*-pyrido[1,2-*a*]-pyridin-4-one (**46**) [6], 3-[2-acetyl-2-ethoxycarbonyl-1-ethenyl]amino-1-cyano-4*H*-pyrido[1,2-*a*]pyridin-4-one (**47**) [11], 3-(2-acetyl-2-ethoxycarbonyl-1-ethenyl)amino-4*H*-pyrido[1,2-*a*]-pyrimidin-4-one (**50**) [11].

Ethyl 2-Acetylamino-3-dimethylaminopropenoate (2c)

This compound was prepared according to a slightly modified procedure described in the literature for preparation of methyl 2-acetylamino-3-dimethylaminopropenoate [20].

A mixture of 4-dimethylaminomethylene-2-methyl-5(4*H*)-oxazolone (0.154 g, 1.0 mmole) in 3 ml of ethanol and sodium hydroxide (0.020 g, 0.5 mmole) was heated under reflux for 15 minutes. The solvent was evaporated *in vacuo*, water (7ml) was added and extracted with chloroform (5 x 5 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated *in vacuo*. The oily residue crystallized from diethyl ether to give **3** in 70% yield, mp 105°, ^{1}H nmr (deuteriochloroform): δ 1.24, 1.25 (2t, 3H, $COOCH_2CH_3$), 1.92, 2.09 (2s, 3H, $COCH_3$), 3.01, 3.08 (2s, 6H, $N(CH_3)_2$),4.12 (q, 2H, $COOCH_2CH_3$), 6.16, 6.38 (2br s, 1H, N*H*), 7.33, 7.37 (2s, 1H, C*H*), J_{CH-CH} = 7.1 Hz.

Anal. Calcd. for $C_9H_{16}N_2O_3$: C, 53.99; H, 8.05; N, 13.99. Found: C, 53.94; H, 8.18; N, 13.92.

The Synthesis of 3-Acylamino-4*H*-azino[1,2-*x*]azin-4-ones.

The following compounds were prepared according to procedures described in the literature for the synthesis of other 3-acylamino-4*H*-azino[1,2-*x*]azin-4-ones [18, 19, 20].

General Procedure:

To a solution of 2-pyridylacetic acid derivative (**1a**, **1b**) or heterocyclic amine (**1c**) (5.0 mmoles) in acetic acid (20 ml) alkyl 2-acylamino-3-dimethylaminopropenoate (5.0 mmoles) was added and the mixture was heated under reflux for several hours. The reaction was followed by tlc (DC-Alufolien Kieselgel 60 F 254, 0.2 mm, E. Merck, and chloroform/methanol, 25:1 as a solvent). After reaction was completed, acetic acid was evaporated *in vacuo* and the solid residue was recrystallized from an appropriate solvent.

3-Acetylamino-1-ethoxycarbonyl-4*H*-pyrido[1,2-*a*]pyridin-4-one (**6**).

This compound was prepared from ethyl 2-pyridinylacetate (0.825 g) and ethyl 2-acetylamino-3-dimethylaminopropenoate (**2c**) (1.000 g), three hours of reflux, in 42% yield, mp 193-196° (washed with ethanol); ^{1}H nmr (deuteriochloroform): δ 1.43 (t, 3H, $COOCH_2CH_3$), 2.27 (s, 3H, $NHCOCH_3$), 4.40 (q, 2H, $COOCH_2CH_3$), 7.14 (ddd, 1H, H_7), 7.50 (ddd, 1H, H_8), 8.24 (br s, 1H, N*H*), 9.15 (dd, 1H, H_6), 9.24 (dd, 1H, H_9), 9.56 (s, 1H, H_2), $J_{H6,H7}$ = 7.2 Hz, $J_{H7,H8}$ = 6.4 Hz, $J_{H8,H9}$ = 9.4 Hz, $J_{H7,H9}$ = 1.1 Hz, $J_{H6,H8}$ = 1.5 Hz, J_{CH-CH} = 7.2 Hz.

Anal. Calcd. for $C_{14}H_{14}N_2O_4$: C, 61.31; H, 5.14; N, 10.21. Found: C, 61.21; H, 5.26; N, 10.32.

3-Acetylamino-1-cyano-4*H*-pyrido[1,2-*a*]pyridin-4-one (**7**).

This compound was prepared from 2-pyridinylacetonitrile (0.590 g) and ethyl 2-acetylamino-3-dimethylaminopropenoate (**2c**) (1.000 g), one hour and forty five minutes of reflux, in 74% yield, mp 243-245° (washed with ethanol); ^{1}H nmr (deuteriochloroform): δ 2.27 (s, 3H, $NHCOCH_3$), 7.18 (ddd, 1H, H_7), 7.55 (ddd, 1H, H_8), 7.97 (dd, 1H, H_9), 8.27 (br s, 1H, N*H*), 9.08 (dd, 1H, H_6), 9.11 (s, 1H, H_2), $J_{H6,H7}$ = 7.1 Hz, $J_{H8,H9}$ = 9.1 Hz, $J_{H7,H8}$ = 6.4 Hz, $J_{H7,H9}$ = 1.1 Hz.

Anal. Calcd. for $C_{12}H_9N_3O_2$: C, 63.43; H, 3.99; N, 18.49. Found: C, 63.40; H, 4.05; N, 18.49.

3-Benzoylamino-9-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**14**).

This compound was prepared from 2-amino-3-methylpyridine (0.540 g) and methyl (*Z*)-2-benzoylamino-3-dimethylaminopropenoate (**2a**) (1.240 g), 4 hours of reflux, in 50% yield, mp 167-168° (washed with ethanol); (lit. [24] mp 171.5-173°); ^{1}H nmr (deuteriochloroform): δ 2.64 (s, 3H, Het-CH_3), 7.08 (dd, 1H, H_7), 7.45-7.60 (m, 4H, Ph, H_8), 7.95-8.00 (m, 2H, Ph), 8.79 (br s, 1H, N*H*), 8.88 (dd, 1H, H_6), 9.75 (s, 1H, H_2), $J_{H6,H7}$ = 7.2 Hz, $J_{H7,H8}$ = 6.8 Hz, $J_{H6,H8}$ = 1.5 Hz.

Anal. Calcd. for $C_{16}H_{13}N_3O_2$: C, 68.81; H, 4.69; N, 15.04. Found: C, 68.96; H, 4.77; N, 15.11.

3-Acetylamino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**16**).

This compound was prepared from 2-amino-4-methylpyridine (0.540 g) and ethyl 2-acetylamino-3-dimethylaminopropenoate (**2c**) (1.000 g), two and one half hours of reflux, in 85% yield, mp 292-293° (washed with ethanol); ^{1}H nmr (deuteriochloroform): δ 2.25 (s, 3H, Het-CH_3), 2.47 (s, 3H, $NHCOCH_3$), 6.96 (dd, 1H, H_7), 7.44 (d, 1H, H_9), 7.93 (br s, 1H, N*H*), 8.84 (d, 1H, H_6), 9.48 (s, 1H, H_2), $J_{H6,H7}$ = 7.5 Hz, $J_{H7,H9}$ = 1.9 Hz.

Anal. Calcd. for $C_{11}H_{11}N_3O_2$: C, 60.82; H, 5.10; N, 19.34. Found: C, 60.65; H, 5.13; N, 19.32.

3-Benzoylamino-4*H*-pyrimido[1,2-*b*]pyridazin-4-one (**22**).

This compound was prepared from 3-aminopyridazine (0.475 g) and methyl (*Z*)-2-benzoylamino-3-dimethylaminopropenoate (**2a**) (1.240 g), four and one half hours of reflux, in 86% yield, mp 243-244° (from toluene), ^{1}H nmr (deuteriochloroform): δ 7.35 (dd, 1H, H_8), 7.50-7.64 (m, 3H, Ph), 7.93 (dd, 1H, H_9), 7.96-8.01 (m, 2H, Ph), 8.66 (dd, 1H, H_7), 9.00 (br s, 1H, N*H*), 9.72 (s, 1H, H_2), $J_{H7,H8}$ = 3.8 Hz, $J_{H7,H9}$ = 1.5 Hz, $J_{H8,H9}$ = 9.0 Hz.

Anal. Calcd. for $C_{14}H_{10}N_4O_2$: C, 63.15; H, 3.79; N, 21.04. Found: C, 63.05; H, 3.72; N, 21.29.

3-Acetylamino-4*H*-pyrimido[1,2-*b*]pyridazin-4-one (**23**).

This compound was prepared from 3-aminopyridazine (0.475 g) and ethyl 2-acetylamino-3-dimethylaminopropenoate (**2c**) (1.000 g), three and one half hours of reflux, in 71% yield, mp 312-314° (washed with ethanol); ^{1}H nmr (deuteriochloroform): δ 2.30 (s, 3H, $NHCOCH_3$), 7.33 (dd, 1H, H_8), 7.90 (dd, 1H, H_9), 8.23 (br s, 1H, N*H*), 8.64 (dd, 1H, H_7), 9.53 (s, 1H, H_2), $J_{H7,H8}$ = 4.1 Hz, $J_{H7,H9}$ = 1.9 Hz, $J_{H8,H9}$ = 9.0 Hz.

Anal. Calcd. for $C_9H_8N_4O_2$: C, 52.94; H, 3.95; N, 27.44. Found: C, 52.70; H, 3.98; N, 27.25.

Catalytic Hydrogenation of 3-Amino Substituted 4*H*-Azino-[1,2-*x*]azin-4-ones

General procedure:

A solution of 3-amino substituted-4*H*-azino[1,2-*x*]azin-4-ones in ethanol or in a mixture of ethanol and acetic acid was mixed with commercial 10% Pd/C catalyst (ratio catalyst: substrate = 1 : 5 by weight). The mixture was hydrogenated at normal pressure for several hours. The reaction was followed by tlc (DC-Alufolien Kieselgel 60 F 254, 0.2 mm, E. Merck, and chloroform/methanol, 5:1 or ethyl acetate/n-heptane, 2:1 as a solvent). The catalyst was removed by filtration of warm mixture. The filtrate was evaporated *in vacuo* and the solid residue was recrystallized from an appropriate solvent. The following compounds were prepared in this manner:

3-Benzoylamino-1-ethoxycarbonyl-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyridin-4-one (**8**).

This compound was prepared from 3-benzoylamino-1-ethoxycarbonyl-4*H*-pyrido[1,2-*a*]pyridin-4-one (**4**) (0.366 g, 1 mmole), five and one half hours of hydrogenation at 50°, in quantitative

yield, mp 179-182° (from a mixture of ethyl acetate and *n*-heptane); ^{1}H nmr (deuteriochloroform): δ 1.40 (t, 3H, CH_2CH_3), 1.84 (tt, 2H, H_8, H_8'), 1.98 (tt, 2H, H_7, H_7'), 3.39 (t, 2H, H_9, H_9'), 4.15 (t, 2H, H_6, H_6'), 4.33 (q, 2H, CH_2CH_3), 7.46-7.59 (m, 3H, Ph), 7.91-7.97 (m, 2H, Ph), 9.05 (br s, 1H, N*H*), 9.08 (s, 1H, H_2), $J_{H6,H7}$ = 6.0 Hz, $J_{H8,H9}$ = 6.4 Hz, J_{CH-CH} = 7.2 Hz.

Anal. Calcd. for $C_{19}H_{20}N_2O_4$: C, 67.05; H, 5.92; N, 8.23. Found: C, 66.96; H, 6.09; N, 8.16.

3-Benzoylamino-1-cyano-6,7,8,9-tetrahydro-4*H*-pyrido-[1,2-*a*]pyridin-4-one (**9**).

This compound was prepared from 3-benzoylamino-1-cyano-4*H*-pyrido[1,2-*a*]pyridin-4-one (**5**) (0.289g, 1 mmole), six hours of hydrogenation at 40°, in 85% yield, mp 171-174° (from a mixture of ethyl acetate and *n*-heptane); ^{1}H nmr (deuteriochloroform): δ 1.87-1.97 (m, 2H, H_8, H_8'), 1.98-2.08 (m, 2H, H_7, H_7'), 3.10 (t, 2H, H_9, H_9'), 4.09 (t, 2H, H_6, H_6'), 7.47-7.62 (m, 3H, Ph), 7.88-7.95 (m, 2H, Ph), 8.66 (s, 1H, H_2), 9.03 (br s, 1H, N*H*), $J_{H6,H7}$ = 6.0 Hz, $J_{H8,H9}$ = 6.8 Hz.

Anal. Calcd. for $C_{17}H_{15}N_3O_2$: C, 69.61; H, 5.15; N, 14.33. Found: C, 69.30; H, 5.31; N, 14.23.

3-Acetylamino-1-ethoxycarbonyl-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyridin-4-one (**10**).

This compound was prepared from 3-acetylamino-1-ethoxycarbonyl-4*H*-pyrido[1,2-*a*]pyridin-4-one (**6**) (0.200 g, 0.7 mmole), three hours of hydrogenation at 40°, in 86% yield, mp 151-154°; ^{1}H nmr (deuteriochloroform): δ 1.37 (t, 3H, CH_2CH_3), 1.82 (tt, 2H, H_8, H_8'), 1.94 (tt, 2H, H_7, H_7'), 2.20 (s 3H, NHCOCH_3), 3.35 (t, 2H, H_9, H_9'), 4.11 (t, 2H, H_6, H_6), 4.30 (q, 2H, CH_2CH_3), 8.19 (br s, 1H, N*H*), 8.89 (s, 1H, H_2), $J_{H6,H7}$ = 6.4 Hz, $J_{H8,H9}$ = 6.8 Hz, J_{CH-CH} = 7.2 Hz.

Anal. Calcd. for $C_{14}H_{18}N_2O_4$: C, 60.42; H, 6.52; N, 10.07. Found: C, 60.43; H, 6.69; N, 10.18.

3-Acetylamino-1-cyano-6,7,8,9-tetrahydro-4*H*-pyrido-[1,2-*a*]pyridin-4-one (**11**).

This compound was prepared from 3-acetylamino-1-cyano-4*H*-pyrido[1,2-*a*]pyridin-4-one (**7**) (0.200g, 0.9 mmole), three and one half hours of hydrogenation at 40°, in 94% yield, mp 179-180° (from ethanol); ^{1}H nmr (deuteriochloroform): δ 1.84-1.94 (m, 2H, H_8, H_8'), 1.96-2.06 (m, 2H, H_7, H_7'), 2.20 (s, 3H, NHCOCH_3), 3.06 (t, 2H, H_9, H_9'), 4.05 (t, 2H, H_6, H_6'), 8.20 (br s, 1H, N*H*), 8.46 (s, 1H, H_2), $J_{H6,H7}$ = 6.0 Hz, $J_{H8,H9}$ = 6.8 Hz .

Anal. Calcd. for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.49; H, 5.74; N, 18.26.

3-Benzoylamino-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**17**).

This compound was prepared from 3-benzoylamino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**12**) (0.265 g, 1 mmole), five hours and fifteen minutes of hydrogenation at 40°, in quantitative yield, mp 118-121° (from a mixture of ethyl acetate and n-heptane); ^{1}H nmr (deuteriochloroform): δ 1.88-2.10 (m, 4H, H_8, H_8', H_7, H_7'), 2.97 (t, 2H, H_9, H_9'), 4.05 (t, 2H, H_6, H_6'), 7.46-7.60 (m, 3H, Ph), 7.88-7.95 (m, 2H, Ph), 8.74 (br s, 1H, N*H*), 9.11 (s, 1H, H_2), $J_{H6,H7}$ = 6.0 Hz, $J_{H8,H9}$ = 6.4 Hz.

Anal. Calcd. for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60. Found: C, 66.59; H, 5.79; N, 15.42.

3-Benzoylamino-8-methyl-6,7,8,9-tetrahydro-4*H*-pyrido-[1,2-*a*]pyrimidin-4-one (**18**).

This compound was prepared from 3-benzoylamino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**13**) (0.279 g, 1 mmole), six hours of hydrogenation at 50°, in quantitative yield, mp 132-136° (from a mixture of ethyl acetate and *n*-heptane); ^{1}H nmr (deuteriochloroform): δ 1.14 (d, 3H, Het-CH_3), 1.52-1.67 (m, 1H, H_7), 2.00-2.20 (m, 2H, H_7', H_8), 2.55 (dd, 1H, H_9), 3.07 (ddd, 1H, H_9'), 3.78 (ddd, 1H, H_6), 4.35 (ddd, 1H, H_6'), 7.46-7.60 (m, 3H, Ph), 7.89-7.94 (m, 2H, Ph), 8.74 (br s, 1H, N*H*), 9.11 (s, 1H, H_2), $J_{CH3,H8}$ = 6.4 Hz, $J_{H9,H9'}$ = 17.7 Hz, $J_{H8,H9}$ = 10.2 Hz, $J_{H8,H9'}$ = 4.9 Hz, $J_{H7,H9'}$ = 1.9 Hz, $J_{H6,H6'}$ = 15.3 Hz, $J_{H6,H7'}$ = 10.9 Hz, $J_{H6,H7}$ = 5.3 Hz, $J_{H6',H7}$ = 5.7 Hz, $J_{H6',H7'}$ = 3.8 Hz.

Anal. Calcd. for $C_{16}H_{17}N_3O_2$: C, 67.83; H, 6.05; N, 14.83. Found: C, 67.79; H, 6.21; N, 15.03.

3-Benzoylamino-9-methyl-6,7,8,9-tetrahydro-4*H*-pyrido-[1,2-*a*]pyrimidin-4-one (**19**).

This compound was prepared from 3-benzoylamino-9-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**14**) (0.250 g, 0.9 mmole), four hours of hydrogenation at 40°, in quantitative yield, mp 133° (from a mixture of ethanol and water); ^{1}H nmr (deuteriochloroform): δ 1.45 (d, 3H, Het-CH_3), 1.59-1.68 (m, 1H, H_8), 1.91-2.17 (m, 3H, H_7, H_7', H_8'), 2.93-3.03 (m, 1H, H_9), 3.92-4.02 (m, 1H, H_6), 4.12-4.21 (ddd, 1H, H_6'), 7.46-7.59 (m, 3H, Ph), 7.89-7.95 (m, 2H, Ph), 8.74 (br s, 1H, N*H*), 9.15 (s, 1H, H_2), $J_{CH3,H9}$ = 6.8 Hz, $J_{H6,H6'}$ = 14.3 Hz, $J_{H6',H7}$ = 7.2 Hz, $J_{H6',H7'}$ = 5.7 Hz.

Anal. Calcd. for $C_{16}H_{17}N_3O_2$: C, 67.83; H, 6.05; N, 14.83. Found: C, 67.62; H, 6.13; N, 14.80.

3-Acetylamino-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**20**).

This compound was prepared from 3-acetylamino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**15**) (0.200 g, 1.0 mmole), two and one half hours of hydrogenation at 40°, in quantitative yield, mp 130-133° (from ethanol); ^{1}H nmr (deuteriochloroform): δ 1.85-2.05 (m, 4H, H_8, H_8', H_7, H_7'), 2.02 (s, 3H, NHCOCH_3), 2.93 (t, 2H, H_9, H_9'), 4.01 (t, 2H, H_6, H_6'), 7.94 (br s, 1H, N*H*), 8.91 (s, 1H, H_2), $J_{H6,H7}$ = 6.2 Hz, $J_{H8,H9}$ = 6.6 Hz.

Anal. Calcd. for $C_{10}H_{13}N_3O_2$: C, 57.96; H, 6.32; N, 20.28. Found: C, 57.70; H, 6.21; N, 20.34.

3-Acetylamino-8-methyl-6,7,8,9-tetrahydro-4*H*-pyrido-[1,2-*a*]pyrimidin-4-one (**21**).

This compound was prepared from 3-acetylamino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**16**) (0.200 g, 0.7 mmole), two hours of hydrogenation at 40°, in 85% yield, mp 186-188°; ^{1}H nmr (deuteriochloroform): δ 1.12 (d, 3H, Het-CH_3), 1.54-1.64 (m, 1H, H_7), 1.96-2.16 (m, 2H, H_7', H_8), 2.19 (s, 3H, NHCOCH_3), 2.51 (dd, 1H, H_9), 3.03 (ddd, 1H, H_9'), 3.72 (ddd, 1H, H_6), 4.30 (ddd, 1H, H_6'), 7.92 (br s, 1H, N*H*), 8.91 (s, 1H, H_2), $J_{CH3,H8}$ = 6.4 Hz, $J_{H6,H6'}$ = 15.2 Hz, $J_{H6,H7}$ = 4.9 Hz, $J_{H6,H7'}$ = 10.6 Hz, $J_{H6',H7'}$ = 3.4 Hz, $J_{H6',H7}$ = 5.7 Hz, $J_{H9,H9'}$ = 17.7 Hz, $J_{H8,H9}$ = 10.6 Hz, $J_{H9',H8}$ = 5.3 Hz, $J_{H9',H7}$ = 2.3 Hz.

Anal. Calcd. for $C_{11}H_{15}N_3O_2$: C, 59.71; H, 6.83; N, 18.99. Found: C, 59.36; H, 6.95; N, 19.13.

3-Benzoylamino-6,7,8,9-tetrahydro-4*H*-pyrimido[1,2-*b*]-pyridazin-4-one (**24**).

This compound was prepared from 3-benzoylamino-4*H*-pyrimido[1,2-*b*]pyridazin-4-one (**22**) (0.266 g, 1 mmole), twenty

four hours of hydrogenation at room temperature. The solvent was evaporated *in vacuo* and the solid residue was purified by radial chromatography by chromatotrone (Silica gel 60 PF_{254} containing gypsum, Merck, and ethyl acetate/*n*-heptane; 2:1 as eluent) to give **24** in 37% yield, mp 156-158° (from a mixture of ethyl acetate and *n*-heptane); ^{1}H nmr (deuteriochloroform): δ 2.01 (tt, 2H, H_8, H_8'), 2.92 (t, 2H, H_9, H_9'), 3.16 (td, 2H, H_7, H_7'), 7.50-7.64 (m, 4H, Ph, H_6), 7.92-7.98 (m, 2H, Ph), 8.42 (s, 1H, H_2), 9.45 (br s, 1H, N*H*), $J_{H7,H8}$ = 6.4 Hz, $J_{H8,H9}$ = 7.2 Hz, $J_{H6,H7}$ = 2.6 Hz.

Anal. Calcd. for $C_{14}H_{14}N_4O_2$: C, 62.21; H, 5.22; N, 20.73. Found: C, 62.17; H, 5.34; N, 20.81.

3-Acetylamino-6,7,8,9-tetrahydro-4*H*-pyrimido[1,2-*b*]-pyridazin-4-one (**25**).

This compound was prepared from 3-acetylamino-6,7,8,9-tetrahydro-4*H*-pyrimido[1,2-*b*]pyridazin-4-one (**23**) (0.200 g, 1.0 mmole), eighteen hours of hydrogenation at 35°. The solvent was evaporated *in vacuo* and the solid residue was purified by radial chromatography by chromatotrone (Silica gel 60 PF_{254} containing gypsum, Merck, and chloroform/methanol; 25:1 as eluent) to give **25** in 50% yield, mp 134-136°; ^{1}H nmr (deuteriochloroform): δ 2.16 (tt, 2H, H_8, H_8'), 2.21 (s, 3H, NHCOCH_3), 2.98 (t, 2H, H_9, H_9'), 3.28 (td, 2H, H_7, H_7'), 7.04 (br s, 1H, H_6), 7.79 (br s, 1H, N*H*), 8.93 (s, 1H, H_2), $J_{H6,H7}$ =2.2 Hz, $J_{H7,H8}$ = 6.8 Hz, $J_{H8,H}$ = 7.2 Hz.

Anal. Calcd. for $C_9H_{12}N_4O_2$: C, 51.92; H, 5.81; N, 26.91. Found: C, 51.65; H, 5.86; N, 26.51.

3-Benzoylamino-6,7,8,9-tetrahydro-4*H*-pyrazino[1,2-*a*]-pyrimidin-4-one (**27**).

This compound was prepared from 3-benzoylamino-4*H*-pyrazino[1,2-*a*]pyrimidin-4-one (**26**) (0.200 g, 0.8 mmole), seven and one half hours of hydrogenation at 25-30°. The solvent was evaporated *in vacuo* and the solid residue was purified by radial chromatography by chromatotrone (Silica gel 60 PF_{254} containing gypsum, Merck, and chloroform/methanol; 50 :1 as eluent) to give **27** in 45% yield, mp 151-154°; ^{1}H nmr (deuteriochloroform): δ 3.31 (t 2H, H_7, H_7'), 4.01 (t, 2H, H_6, H_6'), 4.09 (s, 2H, H_9, H_9'), 7.46-7.60 (m, 3H, Ph), 7.89-7.94 (m, 2H, Ph), 8.73 (br s, 1H, N*H*), 9.12 (s, 1H, H_2), $J_{H6,H7}$ = 5.6 Hz.

Anal. Calcd. for $C_{14}H_{14}N_4O_2$: C, 62.21; H, 5.22; N, 20.73. Found: C, 62.30; H, 5.49; N, 20.87.

3-Amino-1-ethoxycarbonyl-6,7,8,9-tetrahydro-4*H*-pyrido-[1,2-*a*]pyridin-4-one (**30**).

This compound was prepared from 3-(bezyloxycarbonyl)-amino-1-ethoxycarbonyl-4*H*-pyrido[1,2-*a*]pyridin-4-one (**28**) (0.183 g, 0.5 mmole), four hours of hydrogenation at 50°, in 89% yield, mp 112-115° (from a mixture of ethyl acetate and *n*-heptane); ^{1}H nmr (deuteriochloroform): δ 1.35 (t, 3H, CH_2CH_3), 1.78 (tt, 2H, H_8, H_8'), 1.92 (tt, 2H, H_7, H_7'), 3.28 (t, 2H, H_9, H_9'), 4.05 (br s, 2H, NH_2), 4.11 (t, 2H, H_6, H_6'), 4.27 (q, 2H, CH_2CH_3), 7.14 (s, 1H, H_2), $J_{H6,H7}$ = 6.2 Hz, $J_{H7,H8}$ = 6.4 Hz, $J_{H8,H9}$ = 6.8 Hz, J_{CH-CH} = 7.1 Hz.

Anal. Calcd. for $C_{12}H_{16}N_2O_3$: C, 61.00; H, 6.83; N, 11.86. Found: C, 60.98; H, 7.05; N, 11.80.

3-Amino-1-cyano-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyridin-4-one (**31**).

Method A:

This compound was prepared from 3-(benzyloxycarbonyl)-amino-1-cyano-4*H*-pyrido[1,2-*a*]pyridin-4-one (**29**) (0.170g, 0.5 mmole), four hours of hydrogenation at 50°, in quantitative yield, mp 162-165° (from a mixture of ethyl acetate and *n*-heptane); ^{1}H nmr (deuteriochloroform): δ 1.85 (tt, 2H, H_8, H_8'), 1.97 (tt, 2H, H_7, H_7'), 2.99 (t, 2H, H_9, H_9'), 4.04 (t, 2H, H_6, H_6'), 4.22 (br s, 2H, NH_2), 7.26 (s, 1H, H_2), $J_{H6,H7}$ = 6.3 Hz, $J_{H7,H8}$ = 6.4 Hz, $J_{H8,H9}$ = 6.6 Hz.

Anal. Calcd. for $C_{10}H_{11}N_3O$: C, 63.48; H, 5.86; N, 22.21. Found: C, 63.57; H, 6.06; N, 22.06.

Method B:

The compound was also prepared from 3-(2-acetyl-2-benzyloxycarbonyl-1-ethenyl)amino-1-cyano-4*H*-pyrido-[1,2-*a*]pyridin-4-one (**46**) (0.250 g, 0.7 mmole), seventeen hours of hydrogenation at 35°, in 90% yield (from ethanol), mp 155-158°.

3-Amino-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**36**).

Method A:

This compound was prepared from 3-(benzyloxycarbonyl)-amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**32**) (0.149 g, 0.5 mmole), three hours of hydrogenation at 50°, in 86% yield, mp 108-110° (from a mixture of ethyl acetate and n-heptane); ^{1}H nmr (deuteriochloroform): δ 1.82-2.01 (m, 4H, H_8, H_8', H_7, H_7'), 2.84 (t, 2H, H_9, H_9'), 3.83 (br s, 2H, NH_2), 4.01 (t, 2H, H_6, H_6'), 7.35 (s, 1H, H_2), $J_{H6,H7}$ = 6.6 Hz, $J_{H8,H9}$ = 6.4 Hz.

Anal. Calcd. for $C_8H_{11}N_3O$: C, 58.17; H, 6.71; N, 25.44. Found: C, 58.25; H, 6.83; N, 25.36.

Method B:

The compound was also prepared from 3-(2-acetyl-2-ethoxycarbonyl-1-ethenyl)amino-4*H*-pyrido[1,2-*a*]pyrimidine-4-one (**50**) (0.152 g, 0.5 mmole), five hours of hydrogenation at 50°, in 95% yield, mp 105-108°.

3-Amino-8-methyl-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**37**).

This compound was prepared from 3-(benzyloxycarbonyl)-amino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**33**) (0.171 g, 0.6 mmole), three hours of hydrogenation at 50°, in 95% yield, mp 152-154°; ^{1}H nmr (deuteriochloroform): δ 1.10 (d, 3H, Het-CH_3), 1.47-1.60 (m, 1H, H_7), 1.97-2.12 (m, 2H, H_7', H_8), 2.44 (dd, 1H, H_9), 2.93 (ddd, 1H, H_9'), 3.73 (ddd, 1H, H_6), 3.82 (br s, 2H, NH_2), 4.31 (ddd, 1H, H_6'), 7.35 (s, 1H, H_2), $J_{CH3,H8}$ = 6.4 Hz, $J_{H6,H6'}$ = 14.7 Hz, $J_{H6,H7}$ = 5.3 Hz, $J_{H6,H7'}$ = 10.6 Hz, $J_{H6',H7}$ = 5.7 Hz, $J_{H6',H7'}$ = 3.8 Hz, $J_{H9,H9'}$ = 17.3 Hz, $J_{H9,H8}$ = 10.6 Hz, $J_{H8,H9'}$ = 4.9 Hz, $J_{H7,H9'}$ = 1.9 Hz.

Anal. Calcd. for $C_9H_{13}N_3O$: C, 60.32; H, 7.31; N, 23.45. Found: C, 60.14; H, 7.63; N, 23.26.

3-Amino-9-methyl-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**38**).

This compound was prepared from 3-(benzyloxycarbonyl)-amino-9-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**34**) (0.175 g, 0.6 mmole), four hours of hydrogenation at 50°. The solvent was evaporated *in vacuo* and the oily residue was purified by column

chromatography (Silica gel 60, chloroform/methanol; 50 :1 as eluent) to give **38** in 89% yield, mp 75-78°; ^{1}H nmr (deuteriochloroform): δ 1.37 (d, 3H, CH_3), 1.48-1.60 (m, 1H, H_8), 1.85-2.10 (m, 3H, H_7, H_7', H_8'), 2.87 (m, 1H, H_9), 3.82 (br s, 2H, NH_2), 3.92 (m, 1H, H_6), 4.15 (ddd, 1H, H_6'), 7.40 (s, 1H, H_2), $J_{CH3,H9}$ = 6.8 Hz, $J_{H6,H6'}$ =14.3 Hz, $J_{H6,H7'}$ =7.2 Hz, $J_{H6,H7}$ = 5.7 Hz.

Anal. Calcd. for $C_9H_{13}N_3O$: C, 60.32; H, 7.31; N, 23.45. Found: C, 60.17; H, 7.44; N, 23.36.

3-Amino-9-hydroxy-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**39**).

This compound was prepared from 3-(benzyloxycarbonyl)-amino-9-hydroxy-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**35**) (0.103 g, 0.3 mmole), three and one half hours of hydrogenation at 50°, in 97% yield, mp 203-206° (from a mixture of ethanol and toluene); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 1.78-1.93 (m, 3H, H_8, H_8', H_7), 1.96-2.08 (m, 1H, H_7'), 3.72-3.81 (m, 1H, H_6), 3.92-4.00 (m, 1H, H_6'), 4.41-4.46 (m, 1H, H_9), 4.95 (br s, 2H, NH_2), 5.43 (d, 1H, Het-O*H*), 7.25 (s, 1H, H_2), $J_{OH,H9}$ = 3.8 Hz.

Anal. Calcd. for $C_8H_{11}N_3O_2$: C, 53.03; H, 6.12; N, 23.19. Found: C, 53.29; H, 6.38; N, 23.03.

3-Amino-6,7,8,9-tetrahydro-4*H*-pyrimido[1,2-*b*]pyridazin-4-one (**43**).

This compound was prepared from 3-(benzyloxycarbonyl)-amino-4*H*-pyrimido[1,2-*b*]pyridazin-4-one (**41**) (0.200g, 0.7 mmole), eight hours of hydrogenation at 30°. The solvent was evaporated *in vacuo* and the solid residue was purified by radial chromatography by chromatotrone (Silica gel 60 PF_{254} containing gypsum, Merck, and chloroform/methanol; 10 :1 as eluent) to give **43** in 49% yield, mp 185-186° (recrystallized from ethyl acetate); ^{1}H nmr (deuteriochloroform): δ 2.13 (tt, 2H, H_8, H_8'), 2.90 (t, 2H, H_9, H_9'), 3.24 (td, 2H, H_7, H_7'), 3.80 (br s, 2H, NH_2), 7.10 (br s, 1H, H_6), 7.36 (s, 1H, H_2), $J_{H6,H7}$ = 2.3 Hz, $J_{H7,H8}$ = 7.1 Hz, $J_{H8,H9}$ = 7.2 Hz.

Anal. Calcd. for $C_7H_{10}N_4O$: C, 50.59; H, 6.07; N, 33.71. Found: C, 50.67; H, 6.24; N, 33.71.

3-Amino-6,7,8,9-tetrahydro-4*H*-pyrazino[1,2-*a*]pyrimidin-4-one (**44**).

This compound was prepared from 3-(benzyloxycarbonyl)-amino-4*H*-pyrazino[1,2-*a*]pyrimidin-4-one (**42**) (0.153 g, 0.5 mmole), five hours of hydrogenation at 30°. The solvent was evaporated *in vacuo* and the solid residue was purified by radial chromatography by chromatotrone (Silica gel 60 PF_{254} containing gypsum, Merck, and chloroform/methanol; 10 :1 as eluent) to give **44** in 69% yield, mp 215-218° (recrystallized from a mixture of ethyl acetate and ethanol); ^{1}H nmr (deuteriochloroform): δ 3.26 (t, 2H, H_7, H_7'), 3.49 (br s, 2H, NH_2), 3.96 (t, 2H, H_6, H_6'), 3.97 (s, 2H, H_9, H_9'), 7.35 (s, 1H, H_2), $J_{H6,H7}$ = 5.7 Hz.

Anal. Calcd. for $C_7H_{10}N_4O$: C, 50.59; H, 6.07; N, 33.71. Found: C, 50.55; H, 6.10; N, 33.68.

3-[2,2-Bis(acetyl)ethenyl]amino-1-cyano-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyridin-4-one (**48**) and 3-Amino-1-cyano-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyridin-4-one (**31**).

These compounds (**48** and **31**) were prepared from 3-[2,2-bis-(acetyl)ethenyl]amino-1-cyano-4*H*-pyrido[1,2-*a*]pyridin-4-one (**45**) (0.250g, 0.8 mmole), twelve hours of hydrogenation at 30°. The catalyst was removed by filtration of the warm mixture and the solvent was evaporated *in vacuo*. The solid residue was dissolved in 15 ml of chloroform and extracted with 10% HCl (3 x 10 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated *in vacuo*. The solid residue was recrystallized from ethanol to give **48** in 66% yield, mp 169-171°; ^{1}H nmr (deuteriochloroform): δ 1.92 (tt, 2H, H_8, H_8'), 2.03 (tt, 2H, H_7, H_7'), 2.40, 2.54 (2s, 6H, 2 x COCH_3), 3.09 (t, 2H, H_9, H_9'), 4.09 (t, 2H, H_6, H_6'), 7.17 (s, 1H, H_2), 8.30 (d, 1H, C*H*NH), 12.62 (d, 1H, CHN*H*), $J_{H6,H7}$ = 6.0 Hz, $J_{H8,H9}$ = 6.8 Hz, J_{CHNH} = 12.8 Hz.

Anal. Calcd. for $C_{16}H_{17}N_3O_3$: C, 64.20; H, 5.72; N, 14.04. Found: C, 64.04; H, 5.81; N, 13.91.

The water layer was neutralized with sodium hydrogen carbonate and extracted with chloroform (3 x 5 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated *in vacuo*. The solid residue was recrystallized from ethanol to give **31** in 32% yield, mp 158-161°.

3-(2-Acetyl-2-ethoxycarbonyl-1-ethenyl)amino-1-cyano-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyridin-4-one (**49**).

This compound was prepared from 3-(2-acetyl-2-ethoxycarbonyl-1-ethenyl)amino-1-cyano-4*H*-pyrido[1,2-*a*]pyridin-4-one (**47**) (0.162g, 0.5 mmole), five hours of hydrogenation at 30°, in 47% yield, mp 170-173°; ^{1}H nmr (deuteriochloroform): δ 1.37, 1.42 (2t, 3H, 2 x CH_2CH_3, (*E*)-form, (*Z*)-form), 1.85-2.06 (m, 4H, H_7, H_7', H_8, H_8'), 2.55, 2.51 (2s, 3H, COCH_3, (*E*)-form, (*Z*)-form), 3.08 (t, 2H, H_9, H_9'), 4.09 (t, 2H, H_6, H_6'), 4.28, 4.36 (2q, 2H, CH_2CH_3, (*E*)-form, (*Z*)-form), 7.19, 7.21 (s, 1H, H_2, (*E*)-form, (*Z*)-form), 8.33, 8.39 (d, 1H, C*H*NH, (*E*)-form, (*Z*)-form), 12.60 (d, 1H, CHN*H*), $J_{H6,H7}$ = 6.4 Hz, $J_{H8,H9}$ = 6.6 Hz, J_{CHCH} = 7.1 Hz, J_{CHNH} = 13.2 Hz, ratio *E*:*Z* = 96 : 4.

Anal. Calcd. for $C_{17}H_{19}N_3O_4$: C, 62.00; H, 5.81; N, 12.76. Found: C, 62.11; H, 5.85; N, 12.76.

Catalytic Hydrogenation of 3-(Benzyloxycarbonyl)amino-4*H*-pyrido[1,2-*a*]pyrimidine-4-one (32) with Pt/C Catalyst.

3-(Benzyloxycarbonyl)amino-6,7,8,9-tetrahydro-4*H*-pyrido-[1,2-*a*]pyrimidin-4-one (**40**).

A solution of 3-(benzyloxycarbonyl)amino-4*H*-pyrido[1,2-*a*]-pyrimidin-4-one (**32**) (0.168 g, 0.6 mmole) in ethanol was mixed with commercial 10% Pt/C catalyst (ratio catalyst : substrate = 1:5 by weight). The mixture was hydrogenated at normal pressure at 40° for seven hours. The reaction was followed by tlc (DC-Alufolien Kieselgel 60 F 254, 0.2 mm, E. Merck, and chloroform/methanol, 25:1 as a solvent). The catalyst was removed by filtration of warm mixture. The filtrate was evaporated *in vacuo* and the solid residue was purified by radial chromatography by chromatotrone, (eluent chloroform : methanol = 100:1), to give **40** in 84% yield, mp 100-103°; ^{1}H nmr (deuteriochloroform): δ 1.85-2.02 (m, 4H, H_8, H_8', H_7, H_7'), 2.91 (t, 2H, H_9, H_9'), 4.00 (t, 2H, H_6, H_6'), 7.31-7.43 (m, 6H, Ph, N*H*), 8.60 (s, 1H, H_2), $J_{H6,H7}$ = 6.4 Hz, $J_{H8,H9}$ = 6.8 Hz.

Anal. Calcd. for $C_{16}H_{17}N_3O_3$: C, 64.20; H, 5.72; N, 14.04. Found: C, 64.19; H, 5.90; N, 14.02.

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