

**THE SYNTHESIS OF ETHYL 2-(2-CYANO-2-ETHOXYCARBONYL-ETHENYL)AMINO-3-DIMETHYLAMINOPROPENOATE.
THE SYNTHESIS OF SUBSTITUTED AMINOAZOLO-, AMINOAZINO-
PYRIMIDINONES AND 2H-1-BENZOPYRAN-2-ONES**

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Dedicated to Dr. Bernhard Witkop on the occasion of his 80th birthday

Abstract - Ethyl 2-(2-cyano-2-ethoxycarbonylethenyl)amino-3-dimethylamino-propenoate (**3**) was prepared in two steps from ethyl 2-cyano-3-ethoxypropenoate, and used as a reagent for the preparation of *N*-protected 3-amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones (**9a-c**), 5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**10**), 4*H*-pyrido[1,2-*a*]pyridin-4-one (**11**), 2*H*-1-benzopyranones (**12a,b**), and their tetrahydro derivatives (**13a,b**). Free amino 4*H*-pyrido[1,2-*a*]pyrimidin-4-ones (**14a-c**), 5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**15**) and 4*H*-pyrido[1,2-*a*]pyridin-4-one (**16**), were prepared from **9-13** by removal of the 2-cyano-2-ethoxycarbonylethenyl as *N*-protecting group by heating with hydrazine hydrate.

Recently, the synthesis of various derivatives of pyran-2-ones and fused pyran-2-ones has attracted an interest, since many of them have been found as nonpeptide HIV protease inhibitors.^{1,2} Substituted 3-amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones have been recently studied as candidate fluorescent probes for hypoxic cells in solid tumors.³ 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, Pd/C in the presence of hydrogen or cyclohexene by transfer hydrogenation in 53-82% yield.⁴

They have also been 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%.⁵

Recently, we have prepared a series of substituted alkyl 2-(2,2-disubstituted ethenyl)amino-3-dimethylaminopropenoates,⁶⁻¹⁵ masked α -formyl- α -amino acid derivatives, as versatile reagents in the synthesis of many heterocyclic systems such as indolizines, quinolizines, pyranones, benzo- and naphthopyranones, pyranopyrimidines, azolo- and azinopyrimidines, with a monosubstituted amino group at position 3 in the newly formed ring.¹⁶

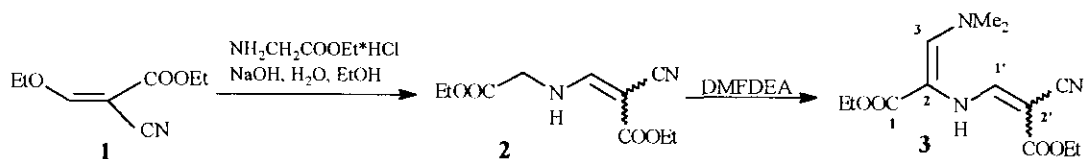
On the other hand, we have also observed that 2,2-disubstituted ethenyl groups, such as 2-benzoyl-2-(ethoxycarbonyl)ethenyl and 2-benzoyl-2-(methoxycarbonyl)ethenyl groups can be applied as *N*-protecting groups in the synthesis of didehydropeptides containing *N*-terminal 3-heteroaryl-amino-2,3-didehydroalanine moiety, since they can be easily removed with hydrazine or hydroxylamine under mild conditions.¹⁷

Similarly, 3-amino substituted fused pyrimidinones have been prepared in high yields.^{8-10,12}

In this paper we present, as an extension of our research in this area, the synthesis of ethyl 2-(2-cyano-2-ethoxycarbonylethenyl)amino-3-dimethylaminopropenoate (**3**) and its application for the synthesis of fused pyrimidines and pyranones with an amino group attached at position 3 in the newly formed system.

Ethyl 2-(2-cyano-2-ethoxycarbonylethenyl)amino-3-dimethylaminopropenoate (**3**) was prepared in the following way: ethyl 2-cyano-3-ethoxypropenoate (**1**) was converted with ethyl glycinate hydrochloride in ethanol at room temperature to give ethyl *N*-(2-cyano-2-ethoxycarbonylethenyl)glycinate (**2**) in 80% yield. This was treated with *N,N*-dimethylformamide diethyl acetal (DMFDEA) in acetonitrile to give **3** in 47% yield. (Scheme 1).

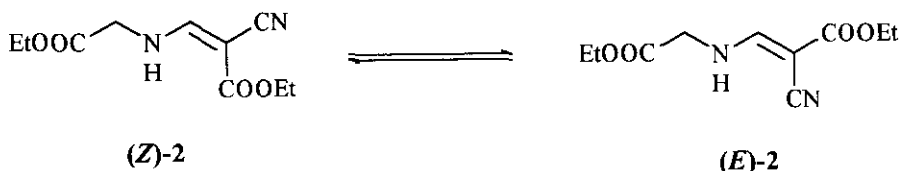
Scheme 1



The structure of **2** and **3** was determined by ^1H NMR spectroscopy. The chemical shift differences of the two sets of signals showed that compound (**2**) exists in solution in an equilibrium of (*Z*)-**2** and (*E*)-**2** isomers in ratio 1:1. (Scheme 2).

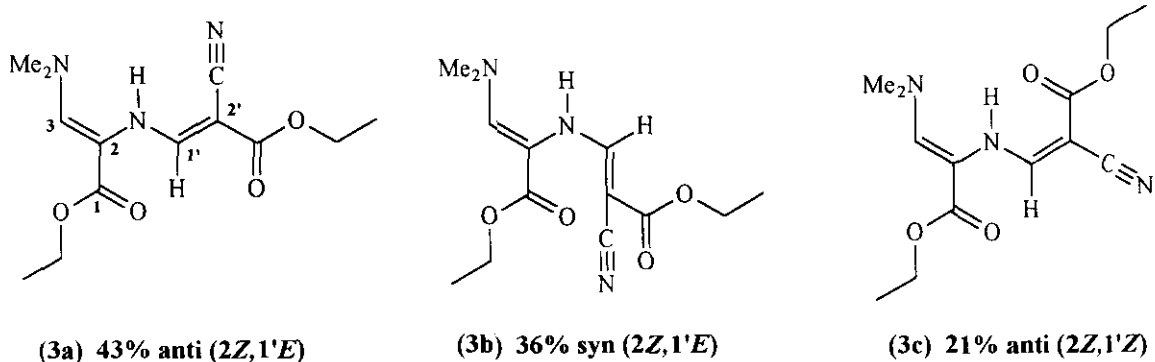
The most characteristic difference was observed for NHCH structural element, at $\delta = 6.60$ ppm (NHCH) and $\delta = 7.84$ ppm (NHCH) with the coupling constant $J_{\text{CHNH}} = 15.0$ Hz for (*E*)-isomer and $\delta = 9.10$ ppm (NHCH) and $\delta = 7.28$ ppm (NHCH) with the coupling constant $J_{\text{CHNH}} = 13.7$ Hz for (*Z*)-isomer.

Scheme 2



Compound (3) showed in the ^1H NMR three sets of signals. The most characteristic are three singlets for H_3 at $\delta = 7.25$, 7.27 and 7.28 ppm, and three pairs of doublets for CHNH structural element at $\delta = 7.56$, 7.60 and 7.79 ppm for CH part and at $\delta = 9.57$, 9.30 and 9.22 ppm for the NH part, with the coupling constants $J_{\text{CHNH}} = 14.05$, 14.05 and 7.52 Hz, respectively. These data indicate that there are three isomers in equilibrium, two isomers having *anti* orientation of CHNH protons, while the orientation in the third isomer is *syn*. It has been shown that ^{13}C - ^1H long range coupling constants may be used in the configuration assignment of some trisubstituted alkenes. It has been successfully applied as a criterion for the *E,Z*-differentiation of ethyl 2-acyloxy-2-alkenoates¹⁸ and NOESY, ROESY and HMBC techniques have been successfully employed for orientation of groups in 2,3-diaminopropenoates even if only one isomer is available.¹⁹

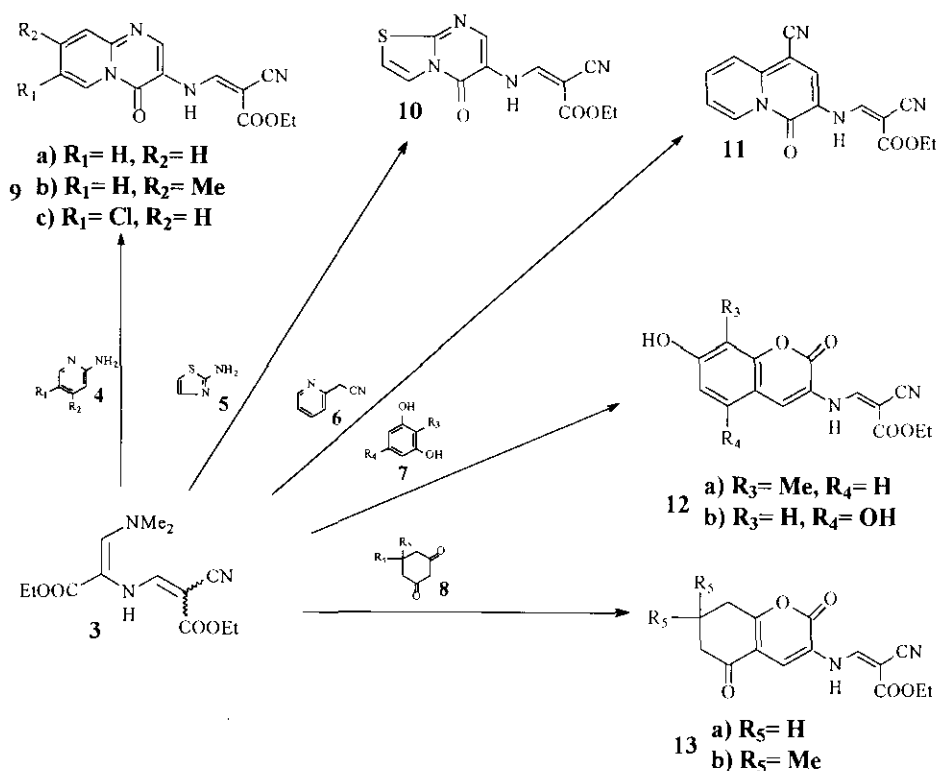
Scheme 3



Since the assignment of isomers was not possible on the basis of ^1H NMR characteristics, the structures of isomers and the ratio among them was finally established by NOESY and chemical exchange techniques to be 43% *anti*(2*Z*,1'*E*) (**3a**), 36% *syn*(2*Z*,1'*E*) (**3b**), and 21% *anti*(2*Z*,1'*Z*) (**3c**). (Scheme 3).

The dimethylamino group in compound (**3**) can be formally substituted with *N*- and *C*-nucleophiles. The following *N*-nucleophiles were selected: 2-aminopyridine (**4a**), 2-amino-4-methylpyridine (**4b**), 2-amino-5-chloropyridine (**4c**), and 2-aminothiazole (**5**). They were treated with an equimolar amount of **3** in acetic acid under reflux. After 2.5 - 3 hours, derivatives of 4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**9**) and 5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**10**) were isolated. (Scheme 4).

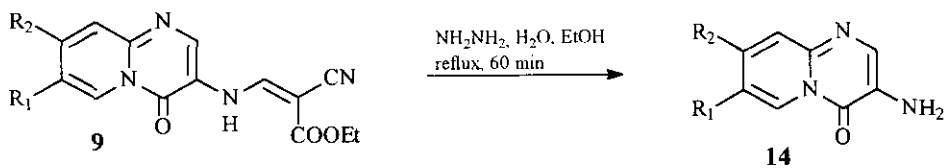
Scheme 4



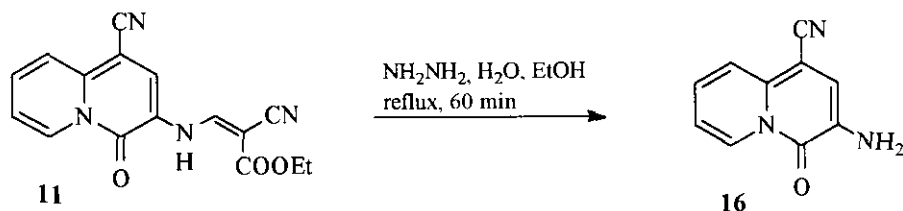
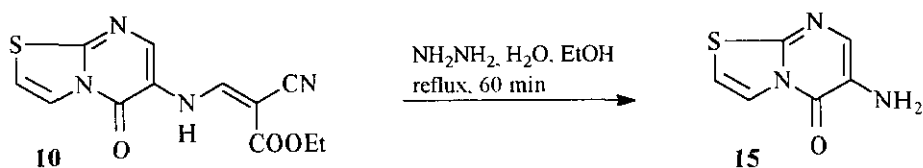
Two types of *C*-nucleophiles were used: 2-pyridylacetonitrile (**6**) was transformed with compound (**3**) in acetic acid into 4*H*-pyrido[1,2-*a*]pyrimidin-4-one derivative (**11**), while 2-methylbenzene-1,3-diol (**7a**), and benzene-1,3,5-triol (**7b**), and cyclic 1,3-diketones, such as cyclohexane-1,3-dione (**8a**) and dimedone (**8b**) gave 2*H*-1-benzopyran-2-one derivatives (**12**) and 5,6,7,8-tetrahydro-2*H*-1-benzopyran-2-one derivatives (**13**), respectively. (Scheme 4).

Removal of the 2-cyano-2-ethoxycarbonyl ethenyl group at the N³ atom of compounds (9 - 11) was achieved by treatment with hydrazine hydrate in ethanol at reflux temperature to give the free amino compounds (14 - 16) in 45 - 98% yield, respectively. (Scheme 5).

Scheme 5



9,14	R ₁	R ₂	Yield (%)
a	H	H	45
b	H	Me	98
c	Cl	H	61



EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ¹H NMR spectra were obtained on a Bruker Avance DPX 300 spectrometer with TMS as the internal standard, IR spectra on a Perkin-Elmer 1310 or 727 B spectrophotometer and elemental analyses for C, H and N on a Perkin-Elmer CHN Analyser 240 C.

Ethyl *N*-(2-Cyano-2-ethoxycarbonylethenyl)glycinate (2). To a solution of ethyl glycinate hydrochloride (150 mmol, 20.94 g) in water (100 mL), sodium hydroxide (150 mmol, 6.00 g) was added. After sodium hydroxide was completely dissolved, ethyl 2-cyano-3-ethoxypropenoate (**1**, 150 mmol, 25.38 g) in ethanol (100 mL) was added to the stirred solution. Mixture was stirred for 1 h and then left overnight at -10° to -20°C . Precipitate was collected by filtration and recrystallized from ethanol to give **2** in 80% yield (27.15 g), (50% (*Z*)-configuration, 50% (*E*)-configuration), mp $116\text{--}118^{\circ}\text{C}$; IR 2210 cm^{-1} (CN); $^1\text{H NMR}$ (CDCl_3): δ 1.30 and 1.31 (t, $\text{COOCH}_2\text{CH}_3$), 4.07 (d, CH_2NH), 4.22 and 4.26 (q, $\text{COOCH}_2\text{CH}_3$), 6.60 (m, *E*-NH), 7.28 (d, *Z*-CHNH), 7.84 (d, *E*-CHNH), 9.10 (m, *Z*-NH); $J_{\text{CHNH}(E)} = 15.0\text{ Hz}$, $J_{\text{CHNH}(Z)} = 13.7\text{ Hz}$, $J_{\text{CH}_2\text{CH}_3} = 7.0\text{ Hz}$, $J_{\text{CH}_2\text{NH}} = 6.3\text{ Hz}$. $^1\text{H NMR}$ ($\text{DMSO-}d_6$) δ 1.22 (t, $2\times\text{COOCH}_2\text{CH}_3$), 4.08-4.19 (m, $2\times\text{COOCH}_2\text{CH}_3$, CH_2NH), 7.74 (d, *Z*-CHNH), 8.02 (d, *E*-CHNH), 8.64 (m, *E*-NH), 9.12 (m, *Z*-NH). *Anal.* Calcd for $\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}_4$: C, 53.09; H, 6.24; N, 12.38. Found: C, 52.81; H, 6.15; N, 12.35.

Ethyl 2-(2-Cyano-2-ethoxycarbonylethenyl)amino-3-dimethylaminopropenopate (3). Ethyl *N*-(2-cyano-2-ethoxycarbonylethenyl)glycinate (**2**, 100 mmol, 22.62 g) and dimethylformamide diethyl acetal (DMFDEA, 240 mmol, 41 mL) in acetonitrile (50 mL) were heated at reflux for 4 h. Volatile components were evaporated *in vacuo* and ethanol (20 mL) was added for crystallization. Precipitate was collected by filtration and recrystallized from ethanol to give **3** in 47% yield (13.22 g), (3 isomers), mp $99\text{--}101^{\circ}\text{C}$; IR 2200 cm^{-1} (CN); $^1\text{H NMR}$ ($\text{DMSO-}d_6$): δ 1.17 and 1.20 (t, $\text{COOCH}_2\text{CH}_3$), 2.99 (s, Me_2N), 4.02-4.20 (2xq, $2\times\text{COOCH}_2\text{CH}_3$), 7.25 and 7.27 and 7.28 (s, H_3), CHNH pairs for three isomers: 7.56 and 9.57 (21%, $J=14.05\text{ Hz}$), 7.60 and 9.30 (43%, $J=14.05\text{ Hz}$), 7.79 and 9.22 (36%, $J=7.52\text{ Hz}$); $J_{\text{CH}_2\text{CH}_3}=7.0\text{ Hz}$. *Anal.* Calcd for $\text{C}_{13}\text{H}_{19}\text{N}_3\text{O}_4$: C, 55.51; H, 6.81; N, 14.94. Found: C, 55.65; H, 7.12; N, 14.64.

General Procedure for Reactions of Compound (3) with Heteroaryl Amines and *C*-Nucleophiles. To a solution of heteroaryl amine (1 mmol) or *C*-nucleophile (1 mmol) in acetic acid (4 mL), equimolar amount of compound (**3**) (281 mg, 1 mmol) was added, and the mixture was heated under reflux for several hours. Reaction was followed by TLC (DC-Alufolien Kieselgel 60 F 254, 0.2 mm, E. Merck, and chloroform/methanol 10:1 as a solvent). After the reaction was completed, acetic acid was evaporated and the solid residue recrystallized from an appropriate solvent. The following compounds were prepared in this manner:

3-(2-Cyano-2-ethoxycarbonylethenyl)amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (9a). This compound was prepared from 2-aminopyridine (**4a**), 3 h of reflux, in 33% yield (67% (*Z*)-configuration), mp $233\text{--}235^{\circ}\text{C}$ (from toluene); $^1\text{H NMR}$ ($\text{DMSO-}d_6$): δ 1.29 (t, $\text{COOCH}_2\text{CH}_3$), 4.26 (q, $\text{COOCH}_2\text{CH}_3$), 7.41 (dd,

H₇), 7.75 (dd, H₉), 7.89 (dd, H₈), 8.71 (d, CHNH), 8.84 (s, H₂), 8.94 (dd, H₆); J_{H₆H₇} = 6.8 Hz, J_{H₈H₉} = 8.9 Hz, J_{CH₂CH₃} = 7.1 Hz, J_{CHNH} = 13.5 Hz. *Anal.* Calcd for C₁₄H₁₂N₄O₃: C, 59.15; H, 4.26; N, 19.71. Found: C, 59.12; H, 4.11; N, 19.79.

8-Methyl-3-(2-cyano-2-ethoxycarbonylethenyl)amino-4H-pyrido[1,2-a]pyrimidin-4-one (9b). This compound was prepared from 2-amino-4-methylpyridine (4b), 3 h of reflux, in 31% yield (67% (Z)-configuration), mp 263-264°C (from toluene); ¹H NMR (DMSO-d₆): δ 1.28 (t, COOCH₂CH₃), 2.47 (s, 8-Me), 4.25 (q, COOCH₂CH₃), 7.28 (dd, H₇), 7.57 (d, H₉), 8.67 (d, CHNH), 8.78 (s, H₂), 8.93 (d, H₆), 10.86 (d, NH); J_{H₆H₇} = 7.3 Hz, J_{H₇H₉} = 1.8 Hz, J_{CH₂CH₃} = 7.3 Hz, J_{CHNH} = 13.1 Hz. *Anal.* Calcd for C₁₅H₁₄N₄O₃: C, 60.40; H, 4.73; N, 18.78. Found: C, 60.51; H, 4.55; N, 18.98.

7-Chloro-3-(2-cyano-2-ethoxycarbonylethenyl)amino-4H-pyrido[1,2-a]pyrimidin-4-one (9c). This compound was prepared from 2-amino-5-chloropyridine (4c), 3 h of reflux, in 55% yield (67% (Z)-configuration), mp 225-238°C (from toluene); ¹H NMR (DMSO-d₆): δ 1.29 (t, COOCH₂CH₃), 4.22 (q, COOCH₂CH₃), 7.76 (d, H₉), 7.92 (dd, H₈), 8.72 (d, CHNH), 8.84 (s, H₂), 9.01 (d, H₆), 10.86 (d, NH); J_{H₆H₈} = 2.2 Hz, J_{H₈H₉} = 9.5 Hz, J_{CH₂CH₃} = 7.1 Hz, J_{CHNH} = 14.0 Hz. *Anal.* Calcd for C₁₄H₁₁N₄O₃Cl: C, 52.76; H, 3.48; N, 17.58. Found: C, 52.52; H, 3.44; N, 17.29.

6-(2-Cyano-2-ethoxycarbonylethenyl)amino-5H-thiazolo[3,2-a]pyrimidin-5-one (10). This compound was prepared from 2-aminothiazole (5), 3 h of reflux, in 25% yield (67% (Z)-configuration), mp 242-243°C (from toluene); ¹H NMR (DMSO-d₆): δ 1.27 (t, COOCH₂CH₃), 4.24 (q, COOCH₂CH₃), 7.65 (d, H₂), 8.12 (d, H₃), 8.52 (s, H₇), 8.59 (d, CHNH), 10.69 (d, NH); J_{H₂H₃} = 4.9 Hz, J_{CH₂CH₃} = 7.1 Hz, J_{CHNH} = 13.9 Hz. *Anal.* Calcd. for C₁₂H₁₀N₄O₃S: C, 49.65; H, 3.47; N, 19.30. Found: C, 49.77; H, 3.37; N, 19.00.

1-Cyano-3-(2-cyano-2-ethoxycarbonylethenyl)amino-4H-pyrido[1,2-a]pyridin-4-one (11). This compound was prepared from 2-pyridylacetonitrile (6), 2.5 h of reflux, in 30% yield (85% (Z)-configuration, mp over 270°C (from mixture of DMF and ethanol); ¹H NMR (DMSO-d₆): δ 1.29 (t, COOCH₂CH₃), 4.26 (q, COOCH₂CH₃), 7.47 (dd, H₇), 7.86 (dd, H₈), 7.93 (d, H₉), 8.56 (s, H₂), 8.68 (d, CHNH), 9.06 (d, H₆), 11.00 (d, NH); J_{H₆H₇} = 7.2 Hz, J_{H₈H₉} = 8.5 Hz, J_{H₈H₇} = 6.7 Hz, J_{CH₂CH₃} = 7.1 Hz, J_{CHNH} = 13.9 Hz. *Anal.* Calcd for C₁₆H₁₂N₄O₃: C, 62.33; H, 3.92; N, 18.17. Found: C, 61.93; H, 3.62; N, 18.29.

7-Hydroxy-8-methyl-3-(2-cyano-2-ethoxycarbonylethenyl)amino-2H-1-benzopyran-2-one (12a). This compound was prepared from 2,6-dihydroxytoluene (7a), 3.5 h of reflux in 3% yield (82% (Z)-

configuration), mp over 270°C (from ethanol); $^1\text{H NMR}$ (DMSO- d_6): δ 1.28 (t, $\text{COOCH}_2\text{CH}_3$), 2.23 (s, 8-Me), 4.25 (q, $\text{COOCH}_2\text{CH}_3$), 6.92 (d, H_5), 7.29 (d, H_6), 8.13 (s, H_4), 8.56 (d, CHNH), 10.44 (bs, 7-OH), 10.73 (d, NH); $J_{\text{H}_5\text{H}_6} = 8.3$ Hz, $J_{\text{CH}_2\text{CH}_3} = 7.2$ Hz, $J_{\text{CHNH}} = 13.9$ Hz. *Anal.* Calcd for $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}_5 \cdot \frac{1}{2}\text{H}_2\text{O}$: C, 59.44; H, 4.68; N, 8.66. Found: C, 59.62; H, 4.45; N, 8.80.

5,7-Dihydroxy-3-(2-cyano-2-ethoxycarbonylethenyl)amino-2H-1-benzopyran-2-one (12b). This compound was prepared from 1,3,5-trihydroxybenzene (**7b**), 1 h of reflux in 44% yield (100% (*Z*)-configuration), mp over 270°C decomp (from mixture of DMF and ethanol); $^1\text{H NMR}$ (DMSO- d_6): δ 1.27 (t, $\text{COOCH}_2\text{CH}_3$), 4.21 (q, $\text{COOCH}_2\text{CH}_3$), 6.25 and 6.32 (2xd, H_6 , H_8), 8.15 (s, H_4), 8.67 (d, CHNH), 10.36 (bs, 5-OH, 7-OH), 10.73 (d, NH); $J_{\text{H}_8\text{H}_6} = 1.6$ Hz, $J_{\text{CH}_2\text{CH}_3} = 7.1$ Hz, $J_{\text{CHNH}} = 13.8$ Hz. *Anal.* Calcd for $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_6$: C, 56.97; H, 3.82; N, 8.86. Found: C, 56.71; H, 3.53; N, 9.01.

5-Oxo-3-(2-cyano-2-ethoxycarbonylethenyl)amino-5,6,7,8-tetrahydro-2H-1-benzopyran-2-one (13a). This compound was prepared from 1,3-cyclohexandione (**8a**), 2.5 h of reflux, in 46% yield (78% (*Z*)-configuration), mp 227-231°C (from toluene); $^1\text{H NMR}$ (DMSO- d_6): δ 1.27 (t, $\text{COOCH}_2\text{CH}_3$), 2.06 (t, CH_2), 2.52 (m, CH_2), 2.88 (t, CH_2), 4.24 (t, $\text{COOCH}_2\text{CH}_3$), 7.97 (s, H_4), 8.75 (d, CHNH), 10.68 (d, NH); $J_{\text{CH}_2\text{CH}_2} = 6.1$ Hz, $J_{\text{CH}_2\text{CH}_3} = 7.1$ Hz, $J_{\text{CHNH}} = 13.6$ Hz. *Anal.* Calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_5$: C, 59.60; H, 4.67; N, 9.27. Found: C, 59.59; H, 4.51; N, 9.24.

7,7-Dimethyl-5-oxo-3-(2-cyano-2-ethoxycarbonylethenyl)amino-5,6,7,8-tetrahydro-2H-1-benzopyran-2-one (13b). This compound was prepared from 5,5-dimethyl-1,3-cyclohexandione (**8b**), 2.5 h of reflux, in 96% yield (78% (*Z*)-configuration), mp 234-235°C (from mixture of DMF and ethanol); $^1\text{H NMR}$ (DMSO- d_6): δ 1.07 (s, 2x7-Me), 1.27 (t, $\text{COOCH}_2\text{CH}_3$), 2.44 (s, CH_2), 2.81 (s, CH_2), 4.24 (q, $\text{COOCH}_2\text{CH}_3$), 7.96 (s, H_4), 8.76 (d, CHNH), 10.68 (d, NH); $J_{\text{CH}_2\text{CH}_3} = 7.1$ Hz, $J_{\text{CHNH}} = 13.6$ Hz. *Anal.* Calcd. for $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_5$: C, 61.81; H, 5.49; N, 8.48. Found: C, 61.59; H, 5.44; N, 8.48.

General Procedure for Removal of the 2-Cyano-2-ethoxycarbonyl Group. To a starting compound (1 mmol), 0.5M solution of hydrazine hydrate in ethanol (4 mL), was added. The mixture was heated under reflux for 1 h. After that, mixture was cooled until precipitate was formed, which was further collected by filtration. Compounds were recovered in analytical pure form without further purification. The following compounds were prepared in this manner:

3-Amino-4H-pyrido[1,2-a]pyrimidin-4-one (14a). This compound was prepared from **9a** (0.284 g, 1 mmol), in 45% yield; mp 176-178°C (from ethanol), (lit.,⁵: 180-182°C); ¹H NMR (DMSO-d₆): δ 5.18 (s, NH₂), 7.10 (ddd, H₇), 7.40-7.52 (m, H₈, H₉), 7.91 (s, H₂), 8.73 (ddd, H₆), J_{H₆H₇} = 7.3 Hz, J_{H₈H₉} = 9.0 Hz, J_{H₇H₈} = 5.6 Hz, J_{H₆H₈} = 1.1 Hz, J_{H₇H₉} = 2.2 Hz, J_{H₆H₉} = 0.6 Hz.

3-Amino-8-methyl-4H-pyrido[1,2-a]pyrimidin-4-one (14b). This compound was prepared from **9b** (0.298 g, 1 mmol), in 98% yield; mp 225-226°C (from ethanol), (lit.,²⁰: 215-225°C); ¹H NMR (DMSO-d₆): δ 2.34 (s, 8-Me), 5.01 (s, NH₂), 6.97 (dd, H₇), 7.26 (d, H₉), 7.86 (s, H₂), 8.66 (d, H₆), J_{H₆H₇} = 7.2 Hz, J_{H₇H₉} = 1.9 Hz.

3-Amino-7-chloro-4H-pyrido[1,2-a]pyrimidin-4-one (14c). This compound was prepared from **9c** (0.318 g, 1 mmol), in 61% yield; mp 192-193°C (from methanol), (lit.,⁴: 189-190°C); ¹H NMR (DMSO-d₆): δ 5.42 (s, NH₂), 7.43 (dd, H₈), 7.49 (dd, H₉), 7.89 (s, H₂), 8.72 (dd, H₆), J_{H₈H₉} = 9.6 Hz, J_{H₈H₆} = 2.2 Hz, J_{H₆H₉} = 0.5 Hz.

6-Amino-5H-thiazolo[3,2-a]pyrimidin-5-one (15). This compound was prepared from **10** (0.290 g, 1 mmol), in 72% yield; mp 169-172°C (from ethanol); ¹H NMR (DMSO-d₆): δ 4.88 (s, NH₂), 7.42 (d, H₂), 7.52 (s, H₇), 7.90 (d, H₃); J_{H₂H₃} = 4.9 Hz. *Anal.* Calcd for C₆H₅N₃OS: C, 43.11; H, 3.01; N, 25.13. Found: C, 42.77; H, 3.13; N, 25.50.

3-Amino-1-cyano-4H-pyrido[1,2-a]pyridin-4-one (16). This compound was prepared from **11** (0.308 g, 1 mmol), in 85% yield; mp 202-204°C (from ethanol), (lit.,¹¹: 190-192°C); ¹H NMR (DMSO-d₆): δ 5.63 (s, NH₂), 7.15 (dd, H₇), 7.22 (s, H₂), 7.38 (ddd, H₈), 7.64 (dd, H₉), 8.82 (dd, H₆); J_{H₆H₇} = 7.5 Hz, J_{H₇H₉} = 1.1 Hz, J_{H₆H₈} = 1.1 Hz, J_{H₈H₉} = 9.0 Hz.

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