HETEROCYCLES, Vol. 55, No. 4, 2001, pp. 705 - 727, Received, 22nd December, 2000

REACTIONS OF ALKYL (*Z*)-2-[(*E*)-2-CYANO-2-(2-PYRIDINYL)ETHENYL]AMINO-3-DIMETHYLAMINOPROPENOATES WITH *C*- AND *N*-NUCLEOPHILES. THE SYNTHESIS OF FUSED 2*H*,5*H*-PYRAN-2,5-DIONES, 4*H*-PYRIMIDIN-4-ONES, AND 1-HETEROARYL-1*H*-IMIDAZOLE-4-CARBOXYLATES

Lucija Jukić, Jurij Svete*, and Branko Stanovnik*

Faculty of Chemistry and Chemical Technology, University of Ljubljana, Aškerčeva 5, P.O. Box 537, 1000 Ljubljana, Slovenia
e-mail: Branko.Stanovnik@uni-lj.si

Abstract - Alkyl (*Z*)-2-[(*E*)-2-cyano-2-(2-pyridinyl)ethenyl]amino-3-dimethylaminopropenoates (**2**) and (**3**) were transformed with *C*-and *N*-nucleophiles into alkyl 2-[2-cyano-2-(2-pyridinyl)ethenyl]amino-3-heteroarylpropenoates (**10-13**), 2*H*,5*H*-benzo-[*b*]pyran-2,5-diones (**14**) and (**15**), 2*H*,5*H*-pyrano[4,3-*b*]pyran-2,5-dione (**16**), 2*H*,5*H*-pyrano[3,2-*c*]benzo[*b*]pyran-2,5-dione (**17**), alkyl 2-[2-cyano-2-(2-pyridinyl)ethenyl]amino-3-arylamino- (**28-40**), and 3-heteroarylaminopropenoates (**41-43**), pyrido[1,2-*a*]pyrimidin-4-ones (**50-53**), thiazolo[3,2-*a*]pyrimidin-4-one (**54**), benzothiazolo[3,2-*a*]pyrimidin-4-one (**55**), and 1-heteroaryl-1*H*-imidazole-4-carboxylate (**56**). Compounds (**28-43**) exist in (2*E*, 2'*E*) form or as a mixture of (2*E*, 2'*E*) as a major and (2*Z*,2'*E*) form as a minor isomer.

α-Amino acids and their derivatives play an important role in organic synthesis,[1-6] especially as building blocks for the preparation of many heterocyclic systems. Recently, several comprehensive reviews have been published describing the preparation of the following heterocyclic systems: pyranones and fused pyranones,[7] fused pyridinones,[8] fused pyrimidinones,[9] pyrroles,[10] pyrazoles,[11] imidazoles,[12] and 1,2,4-oxadiazoles.[13]

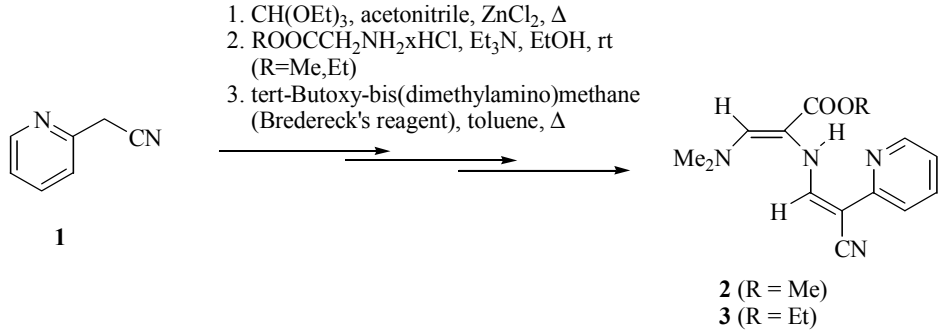
Quinolizines, pyridopyrimidines, benzopyrans, pyranopyrans and related fused systems are the basic structures of many alkaloids and their synthetic derivatives exhibiting various biological activity.[14-18]

Since there has been no general method known for the preparation of those heterocyclic systems, in which an amino acid is incorporated or partially incorporated into the heterocyclic ring, we have prepared a series of 2-substituted 3-dimethylaminopropenoates, 2-[(2,2-disubstituted ethenyl)amino]-3-dimethyl-aminopropenoates and related compounds, stable masked 2-formylglycine derivatives, as versatile reagents for the preparation of various heterocyclic systems,[19] among others alkyl 3,4-disubstituted and alkyl 1-acyl-3,4-disubstituted pyrrole-2-carboxylates,[20,21] and dialkyl 3-aminopyrrole-2,4-dicarboxylates,[22] which have been further transformed into 5*H*-pyrrolo[3,2-*d*]pyrimidine derivatives,[23] and other systems,[24-30] including some natural products, such as aplysinopsins.[31]

This methodology has opened also an easy access to substituted 4*H*-quinolizin-4-ones, pyridopyrimidines and other heterocyclic systems with an amino group in 3 position of the newly formed heterocyclic system.[28,32,33] The substituents attached at 2,2-disubstituted ethenyl group of the substituted amino group are ester groups or a combinations of an ester and an acyl, two acyl, an ester and an amino, an ester and a cyano, two cyano, or an ester and a phenyl group.[19]

Recently, alkyl (*Z*)-2-[(*E*)-2-cyano-2-(2-pyridinyl)ethenyl]amino-3-dimethylaminopropenoates (**2**) and (**3**) have been prepared from 2-pyridinylacetonitrile (**1**) in three steps (Scheme 1) and converted by heating in acetic acid into substituted 3-aminopyrrole-2-carboxylates and by treatment with aliphatic amines into 5*H*-pyrrolo[3,2-*d*]pyrimidin-4-ones.[34]

Scheme 1

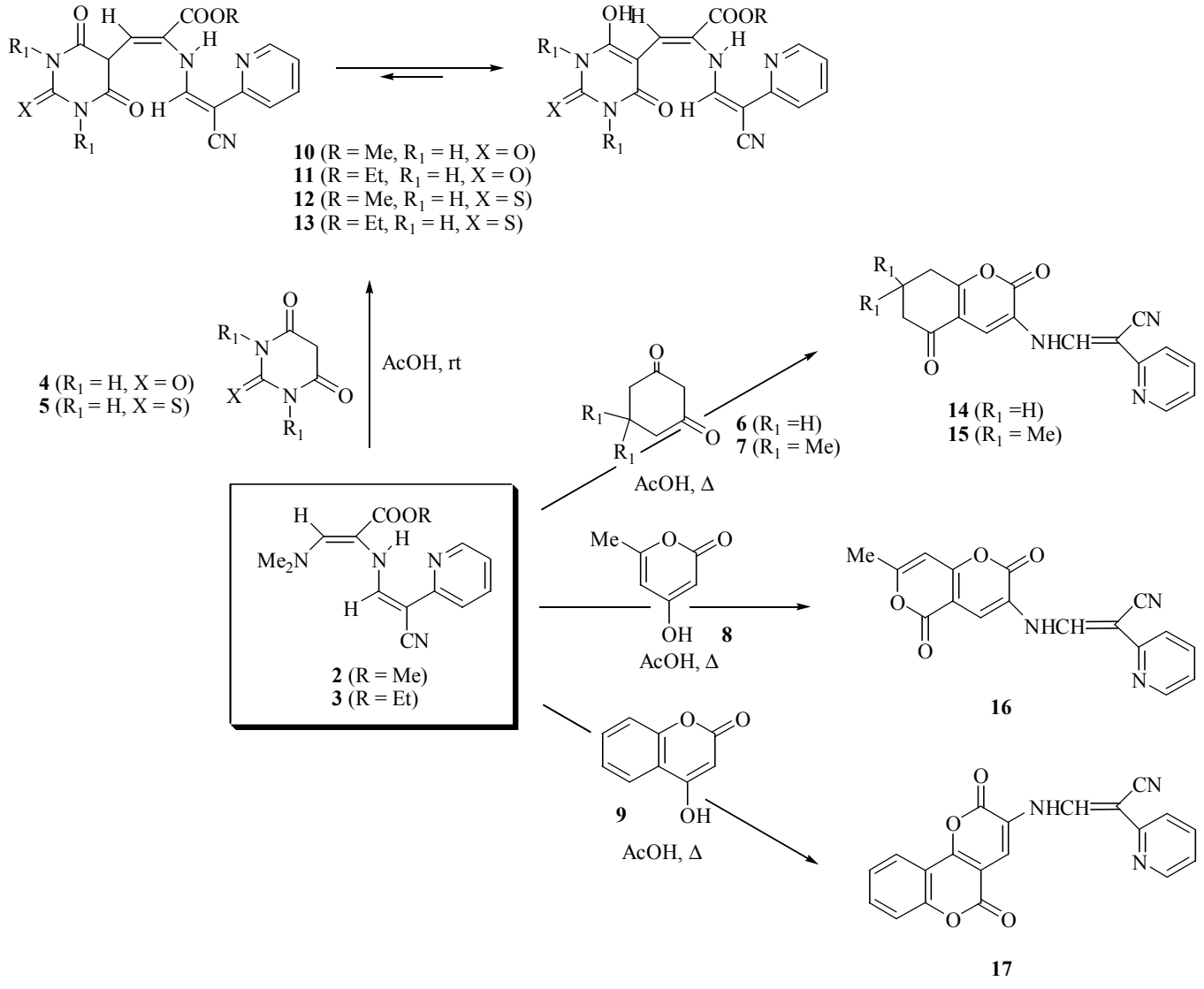


In this paper we report the transformations of compounds (**2**) and (**3**), with *C*- and *N*-nucleophiles into β-heteroaryl-, β-arylamino- and β-heteroarylamino-α,β-didehydro-α-amino acid derivatives, and various heterocyclic systems in which heteroaryl and cyano substituted ethenylamino groups are introduced into the newly formed ring.

Compounds (**2**) and (**3**) were treated with barbituric (**4**) and thiobarbituric acid (**5**) in acetic acid at room temperature for 1.5 to 2 h to form the corresponding 2-[2-cyano-2-(2-pyridinyl)ethenyl]aminopyrimidinyl-

propenoates (**10-13**) in 54-91% yield. By treatment with cyclohexane-1,3-diones (**6**) and (**7**) in acetic acid under reflux for several hours 5,6,7,8-tetrahydro-2*H*,5*H*-benzo[*b*]pyran-2,5-diones (**14**) and (**15**) were obtained in 27-48% yield. 4-Hydroxy-6-methyl-2*H*-pyran-2-one (**8**) and 4-hydroxy-2*H*-ben-zo[*b*]pyran-2-one (**9**) afforded 2*H*,5*H*-pyrano[4,3-*b*]pyran-2,5-dione (**16**) and 2*H*,5*H*-pyrano[3,2-*c*]ben-zo[*b*]pyran-2,5-dione (**17**) derivatives in 47-58% yield. (Scheme 2).

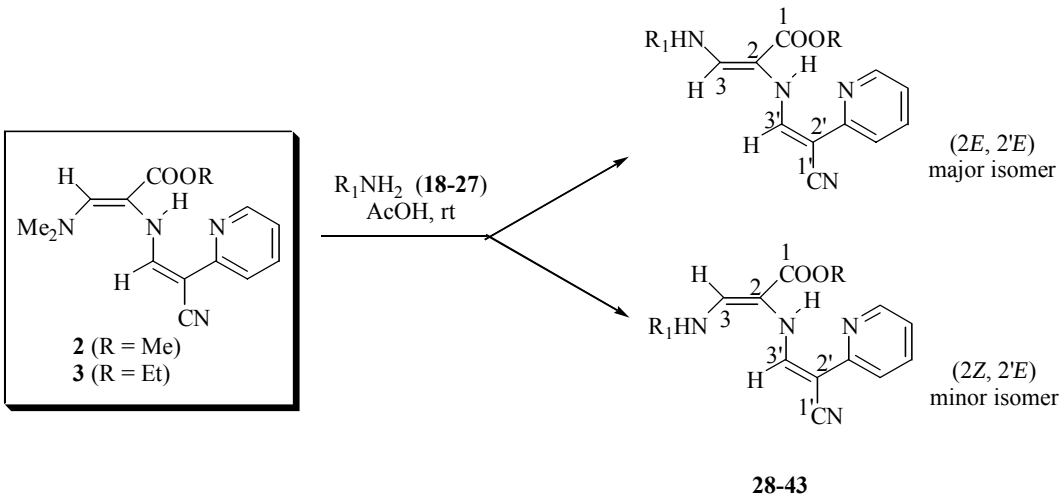
Scheme 2



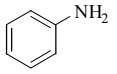
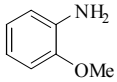
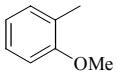
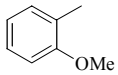
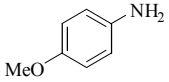
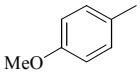
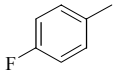
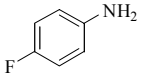
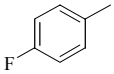
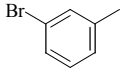
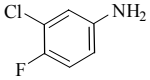
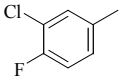
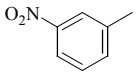
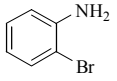
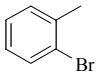
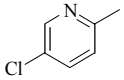
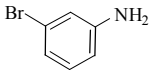
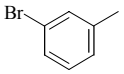
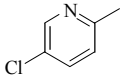
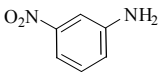
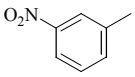
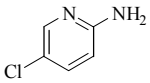
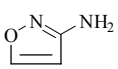
Since we have not isolated the noncyclized intermediates resulting from substitution of the dimethylamino group with aliphatic amines,[34] we extended our studies to the reaction of compounds (**2**) and (**3**) with aromatic and heteroaromatic amines in order to prepare intermediates from which other heterocycles can be prepared. In this respect, compounds (**2**) and (**3**) were treated with anilines (**18-25**), 2-amino-5-chloropyridine (**26**)**,** and 3-aminoisoxazole (**27**) in acetic acid for several hours at room

temperature to give alkyl 2-[2-cyano-2-(2-pyridinyl)ethenyl]amino-3-arylamino (or heteroarylamino)propenoates (**28-43**) in 70-99% yield with few exceptions. (Scheme 3).

Scheme 3

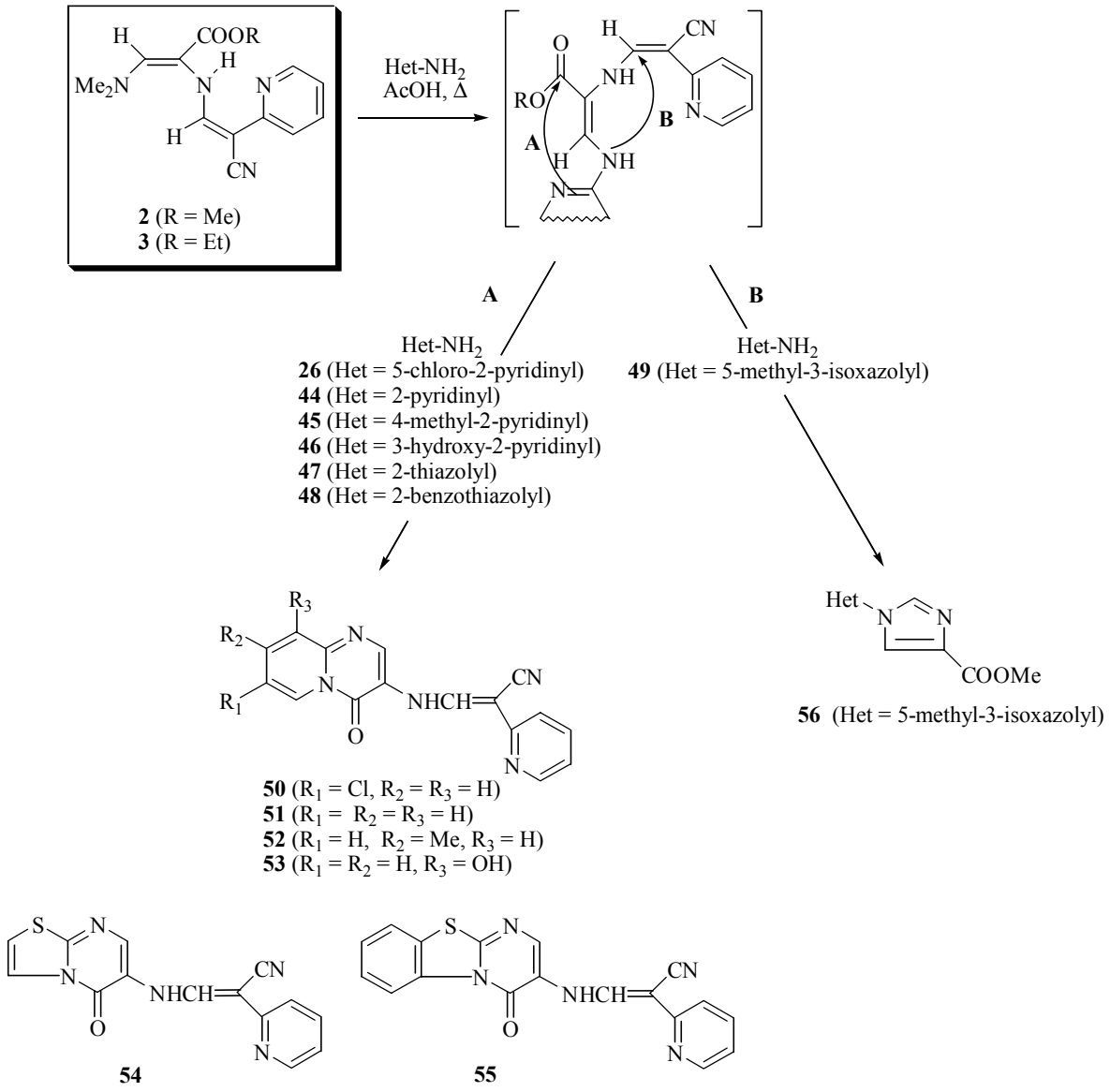


28-43

amines (R_1NH_2)		**products**					
			R	**R_1-**		**R**	**R_1-**
18		**28**	Me		**36**	Et	
19		**29**	Me		**37**	Et	
20		**30**	Me		**38**	Et	
21		**31**	Me		**39**	Et	
22		**32**	Me		**40**	Et	
23		**33**	Me		**41**	Me	
24		**34**	Me		**42**	Et	
25		**35**	Me		**43**	Me	
26							
27							

Further transformations with *N*-nucleophiles can proceed in two different manners: with sterically unhindered heteroarylamines the reaction proceeds according to path A to form fused pyrimidin-4-ones, while with sterically hindered heteroarylamines the reaction proceeds according to path B to form 1-heteroaryl-1*H*-imidazole-4-carboxylates, similary as observed earlier.[35] Thus, compounds (**2**) and (**3**) react with pyridines (**26**, **44-46**), 2-aminothiazole (**47**), and 2-aminobenzothiazole (**48**) to give 4*H*-pyrido[1,2-*a*]pyrimidin-4-ones (**50-53**), 5*H*-thiazolo[3,2-*a*]pyrimidin-4-one (**54**), and 4*H*-benzothiazolo[3,2-*a*]pyrimidin-4-one (**55**) derivatives, respectively, in low yields (11-42%), while 3-amino-5-methylisoxazole (**49**) gives 1-(5-methyl-3-isoxazolyl)-1*H*-imidazole-4-carboxylate (**56**) in 20% yield. (Scheme 4).

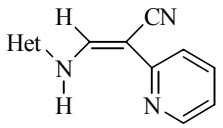
Scheme 4



STRUCTURE DETERMINATION

The structures of new compounds were determined on the basis of their MS spectra, elemental analyses for *C*, *H*, and *N* and ^{1}H NMR spectra. In ^{1}H NMR spectra of compounds (**14-17**) and (**50-55**) the chemical shifts for protons attached to the heteroaromatic systems are in agreement with the data reported earlier for other derivatives of these systems.[19a] The protons attached to the substituted amino group show the following characteristics. The C*H*NH appear as dublets in the range of δ = 7.68-7.93 ppm and CHN*H* as dublets or broad singlet (compound (**16**)) in the range of δ = 12.74-13.20 ppm with the coupling constants $J_{CH\text{-}NH}$ = 11.1-13.0 Hz. From the chemical shifts one can conclude that the orientation around the C=C bond is *trans* and from the magnitude of coupling constants that the orientation around the CHNH bond is *trans* (*antiperiplanar*).[36] (Figure 1).

Figure 1



14-17, 50-55

The compounds (**28-43**) show in ^{1}H NMR spectra in deuteriochloroform one or two sets of signals indicating that they exist in (2*E*, 2'*E*) and (2*Z*, 2'*E*) forms with (2*E*, 2'*E*) being the only one or the predominating form. The ratios between isomers were determined on the basis of peaks for methyl and ethyl groups in esters. The orientations around the both double bonds were deducted from analogous chemical shifts for C*H*NH and CHN*H*, and $J_{CH\text{-}NH}$ coupling constants in ^{1}H NMR spectra.[36] In all cases the orientation in major isomer is (*E*) for C(2)=C(3) and (*E*) for C(2')=C(3'), while in the minor isomer the orientation is (*Z*) around the C(2)=C(3) and (*E*) around the C(2')=C(3') double bonds. (Table 1).

Table 1. Characteristic peaks in ^{1}H NMR ($CDCl_3$) (δ in ppm, J in Hz) for compounds (**28-43**).

	δ_{R1NHCH}	δ_{R1NHCH}	δ_{CHNH}	δ_{CHNH}	J_{R1NHCH}	J_{CHNH}
28 (2*E*, 2'*E*)	7.91	6.65	7.04	11.24	13.2	10.4
29 (2*E*, 2'*E*)	7.43	9.90	7.27	11.54	13.0	11.6
37 (2*E*, 2'*E*)	7.41	9.80	7.30	11.72	13.0	12.4

38						
(2*E*, 2'*E*)	7.29	9.58	7.28	11.67	12.5	12.7
41						
(2*E*, 2'*E*)	8.32	7.15	7.33	11.36	12.5	10.3
42						
(2*E*, 2'*E*)	8.29	7.37	7.35	11.33	12.7	-
30						
(2*E*, 2'*E*)	7.82	6.59	7.24	11.16	13.2	11.7
(2*Z*, 2'*E*)	7.32	9.55	7.30	11.45	13.2	11.7
31						
(2*E*, 2'*E*)	7.80	6.78	7.24	11.20	13.1	12.4
(2*Z*, 2'*E*)	7.32	9.60	7.28	11.50	13.1	12.4
32						
(2*E*, 2'*E*)	7.75	6.58	7.24	11.25	13.2	10.7
(2*Z*, 2'*E*)	7.75	9.60	7.29	11.55	13.2	10.7
33						
(2*E*, 2'*E*)	7.81	7.16	7.29	11.67	12.7	12.4
(2*Z*, 2'*E*)	7.50	10.05	7.38	11.67	12.7	12.4
34						
(2*E*, 2'*E*)	7.82	6.66	7.25	11.28	12.7	11.7
(2*Z*, 2'*E*)	7.33	9.62	7.30	11.57	12.7	11.7
35						
(2*E*, 2'*E*)	7.87	7.31	7.07	9.85	12.1	12.5
(2*Z*, 2'*E*)	7.86	7.31	7.41	11.67	12.1	12.5
36						
(2*E*, 2'*E*)	7.39	9.61	7.29	11.69	12.3	12.1
(2*Z*, 2'*E*)	7.39	9.61	7.29	11.69	12.3	12.1
39						
(2*E*, 2'*E*)	7.78	6.73	7.29	11.29	12.8	12.3
(2*Z*, 2'*E*)	7.32	9.61	7.31	11.75	12.8	12.3
40						
(2*E*, 2'*E*)	7.86	7.00	7.32	11.37	12.8	12.4
(2*Z*, 2'*E*)	7.84	9.84	7.38	11.85	12.8	12.4
43						
(2*E*, 2'*E*)	7.82	6.95	7.28	11.35	12.4	11.5
(2*Z*, 2'*E*)	7.49	9.47	7.30	11.71	12.4	11.5

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ^{1}H NMR spectra were obtained on a Bruker Avance DPX 300 (300 MHz) spectrometer in such solvent as DMSO-d_6 and $CDCl_3$ with TMS as the internal standard, MS spectra on an AutoSpecQ spectrometer, IR spectra on a Perkin-Elmer 1310 infrared spectrophotometer and elemental analyses for *C*, *H* and *N* on a Perkin-Elmer CHN Analyser 2400. Methyl and ethyl (*Z*)-2-[(*E*)-2-cyano-2-(2-pyridinyl)ethenyl]amino-3-dimethylaminopropenoates **2** and **3** were prepared according to the procedure described in the literature.[34]

General Procedure for the Preparation of β-Heteroaryl-α,β-didehydro-α-amino Acid Derivatives (10-13):

To compound (**2**) (136 mg, 0.5 mmol) or (**3**) (143 mg, 0.5 mmol) the corresponding aromatic amines (**5**) and (**6**) (0.5 mmol) and acetic acid (2 mL) were added and the mixture was stirred at rt for 1.5 to 2 h. The precipitate was collected by filtration and washed with ethanol.

Methyl 2-[2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(4-hydroxy-2,6-dioxo-5-pyrimidinyl)propenoate (10). This compound was prepared from compound (**2**) (136 mg, 0.5 mmol) and barbituric acid (**5**) (64 mg, 0.5 mmol), 2 h, 91% yield (162 mg), mp >350°C (from ether), MS 355 (M^+), HRMS: Calcd: 355.091669, Found: 355.092530, IR 2200 cm^{-1} (CN), 3400 cm^{-1} (OH), ^{1}H NMR (DMSO-d_6) δ: 3.74 (3H, s, COOMe), 7.22 (1H, dd, J_{H4-H5} = 7.7 Hz, J_{H5-H6} = 6.0 Hz, H_5), 7.54 (1H, s, CH), 7.74 (1H, ddd, J_{H3-H4} = 8.1 Hz, J_{H4-H5} = 7.7 Hz, J_{H4-H6} = 1.8 Hz, H_4), 7.99 (1H, d, J_{H3-H4} = 8.1 Hz, H_3), 8.32 (1H, dd, J_{H4-H6} = 1.8 Hz, J_{H5-H6} = 6.0 Hz, H_6), 8.60 (1H, d, J_{CH-NH} = 12.8 Hz, C*H*NH), 10.09 (2H, s, 2x NH), 13.31 (1H, br s, CHN*H*). *Anal.* Calcd for $C_{16}H_{13}N_5O_5$ + ½ H_2O: C, 52.75; H, 3.87; N, 19.22. Found: C, 52.52; H, 4.15; N, 19.25.

Ethyl 2-[2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(4-hydroxy-2,6-dioxo-5-pyrimidinyl)propenoate (11). This compound was prepared from compound (**3**) (143 mg, 0.5 mmol) and barbituric acid (**5**) (64 mg, 0.5 mmol), 1.5 h, 67% yield (124 mg), mp 149-153°C (from ether), MS 369 (M^+), HRMS: Calcd: 369.107319, Found: 369.10798, IR 2190 cm^{-1} (CN), 3420 cm^{-1} (OH), ^{1}H NMR (DMSO-d_6) δ: 1.27 (3H, t, $J_{CH2-CH3}$ = 7.2 Hz, $COOCH_2CH_3$), 4.21 (2H, q, $J_{CH2-CH3}$ = 7.2 Hz, $COOCH_2CH_3$), 7.26 (1H, dd, J_{H4-H5} = 7.0 Hz, J_{H5-H6} = 5.3 Hz, H_5), 7.55 (1H, s, CH), 7.58 (1H, d, J_{H3-H4} = 8.7 Hz, H_3), 8.04 (1H, dd, J_{H3-H4} = 8.7 Hz, J_{H4-H5} = 7.0 Hz, H_4), 8.31 (1H, d, J_{H5-H6} = 5.3 Hz, H_6), 8.61 (1H, d, J_{CH-NH} = 12.8 Hz, C*H*NH), 10.10

(2H, s, 2x NH), 13.43 (1H, br s, CHN*H*). *Anal.* Calcd for $C_{17}H_{15}N_5O_5$ + 1 H_2O: C, 52.71; H, 4.42; N, 18.08. Found: C, 53.02; H, 4.75; N, 17.98.

Methyl 2-[2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(4-hydroxy-2-thio-6-oxo-5-pyrimidinyl)propenoate (12). This compound was prepared from compound (**2**) (136 mg, 0.5 mmol) and 2-thiobarbituric acid (**6**) (72 mg, 0.5 mmol), 2 h, 83% yield (154 mg), mp >350°C (from ether), MS 371 (M^+), HRMS: Calcd: 371.068826, Found: 371.06956, IR 2200 cm^{-1} (CN), 3460 cm^{-1} (OH), ^{1}H NMR (DMSO-d_6) δ: 3.76 (3H, s, COOMe), 7.29 (1H, dd, J_{H4-H5} = 7.3 Hz, J_{H5-H6} = 5.7 Hz, H_5), 7.45 (1H, s, CH), 7.60 (1H, d, J_{H3-H4} = 8.7 Hz, H_3), 8.05 (1H, dd, J_{H3-H4} = 8.7 Hz, J_{H4-H5} = 7.3 Hz, H_4), 8.35 (1H, d, J_{H5-H6} = 5.7 Hz, H_6), 8.58 (1H, d, J_{CH-NH} = 13.2 Hz**,** C*H*NH), 11.37 (2H, s, 2x NH), 12.90 (1H, br s, CHN*H*). *Anal.* Calcd for $C_{16}H_{13}N_5O_4S$ + ½ H_2O: C, 50.52; H, 3.71; N, 18.41. Found: C, 50.74; H, 3.70; N, 18.59.

Ethyl 2-[2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(4-hydroxy-2-thio-6-oxo-5-pyrimidinyl)propenoate (13). This compound was prepared from compound (**3**) (143 mg, 0.5 mmol) and 2-thiobarbituric acid (**6**) (72 mg, 0.5 mmol), 1.5 h, 54% yield (104 mg), mp 246-250°C (from ethanol (decomp)), MS 385 (M^+), HRMS: Calcd: 385.084476, Found: 385.08524, IR 2200 cm^{-1} (CN), 3440 cm^{-1} (OH), ^{1}H NMR (DMSO-d_6) δ: 1.27 (3H, t, $J_{CH2-CH3}$ = 7.1 Hz, $COOCH_2CH_3$), 4.24 (2H, q, $J_{CH2-CH3}$ = 7.1 Hz, $COOCH_2CH_3$), 7.35 (1H, ddd, J_{H3-H5} = 0.8 Hz, J_{H4-H5} = 7.1 Hz, J_{H5-H6} = 6.1 Hz, H_5), 7.49 (1H, s, CH), 7.69 (1H, dd, J_{H3-H4} = 8.7 Hz, J_{H3-H5} = 0.8 Hz, H_3), 8.14 (1H, ddd, J_{H3-H4} = 8.7 Hz, J_{H4-H5} = 7.1 Hz, J_{H4-H6} = 1.5 Hz, H_4), 8.35 (1H, dd, J_{H4-H6} = 1.5 Hz, J_{H5-H6} = 6.1 Hz, H_6), 8.61 (1H, d, J_{CH-NH} = 13.2 Hz, C*H*NH), 11.41 (2H, s, 2x NH), 13.17 (1H, d, J_{CH-NH} = 13.2 Hz, CHN*H*). *Anal.* Calcd for $C_{17}H_{15}N_5O_4S$: C, 52.98; H, 3.92; N, 18.17. Found: C, 52.77; H, 3.74; N, 17.95.

General Procedure for the Preparation of Pyranones (14-17):

To compound (**2**) (136 mg, 0.5 mmol) or (**3**) (143 mg, 0.5 mmol) the corresponding *C*-nucleophilic compounds (**6-9**) (0.5 mmol) and acetic acid (2 mL) were added and the mixture was heated under reflux for 0.5 to 6 h. The volatile compounds were evaporated *in vacuo*, ethanol (3 mL) was added and the precipitate was collected by filtration.

3-[2-Cyano-2-(2-pyridinyl)ethenyl]amino-5,6,7,8-tetrahydro-2*H*,5*H*-benzo[*b*]pyran-2,5-dione (14). This compound was prepared from compound (**2**) (136 mg, 0.5 mmol) and 1,3-cyclohexanedione (**6**) (56 mg, 0.5 mmol), 2 h, 41% yield (63 mg), and from compound (**3**) (143 mg, 0.5 mmol) and 1,3-cyclohexane-

dione (**6**) (56 mg, 0.5 mmol), 2.5 h, 27% yield (41 mg), mp 249-252°C (from a mixture of ethanol and toluene), IR 2220 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: 2.15-2.24 (2H, m, CH_2), 2.58-2.62 (2H, m, CH_2), 2.90 (2H, t, $J_{CH2-CH2}$ = 6.4 Hz, CH_2), 7.17 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.35 (1H, s, H_4), 7.58 (1H, ddd, $J_{H3'-H4'}$ = 8.1 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 0.9 Hz, H_3'), 7.69 (1H, d, J_{CH-NH} = 11.9 Hz, C*H*NH), 7.76 (1H, ddd, $J_{H3'-H4'}$ = 8.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.8 Hz, H_4'), 8.63 (1H, ddd, $J_{H3'-H6'}$ = 0.9 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 12.83 (1H, d, J_{CH-NH} = 11.9 Hz, CHN*H*). *Anal.* Calcd for $C_{17}H_{13}N_3O_3$: C, 66.44; H, 4.26; N, 13.67. Found: C, 66.75; H, 4.26; N, 13.49.

3-[2-Cyano-2-(2-pyridinyl)ethenyl]amino-7,7-dimethyl-5,6,7,8-tetrahydro-2*H*,5*H*-benzo[*b*]pyran-2,5-dione (15). This compound was prepared from compound (**2**) (136 mg, 0.5 mmol) and 5,5-dimethyl-1,3-cyclohexanedione (**7**) (70 mg, 0.5 mmol), 2 h, 48% yield (80 mg), and from compound (**3**) (143 mg, 0.5 mmol) and 5,5-dimethyl-1,3-cyclohexanedione (**7**) (70 mg, 0.5 mmol), 2.5 h, 36% yield (60 mg), mp 250-253°C (from ethanol), IR 2210 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: 1.17 (6H, s, 2x 7-Me), 2.46 (2H, s, CH_2), 2.75 (2H, s, CH_2), 7.17 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H5'-H6'}$ = 4.9 Hz, H_5'), 7.34 (1H, s, H_4), 7.58 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.69 (1H, d, J_{CH-NH} = 11.9 Hz, C*H*NH), 7.76 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H4'-H6'}$ = 1.8 Hz, H_4'), 8.63 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 4.9 Hz, H_6'), 12.84 (1H, d, J_{CH-NH} = 11.9 Hz, CHN*H*). *Anal.* Calcd for $C_{19}H_{17}N_3O_3$: C, 68.05; H, 5.11; N, 12.53. Found: C, 68.13; H, 5.31; N, 12.44.

3-[2-Cyano-2-(2-pyridinyl)ethenyl]amino-7-methyl-2*H*,5*H*-pyrano[4,3-*b*]pyran-2,5-dione (16). This compound was prepared from compound (**2**) (136 mg, 0.5 mmol) and 4-hydroxy-6-methyl-2*H*-pyran-2-one (**8**) (63 mg, 0.5 mmol), 6 h, 2.5 h, 49% yield (79 mg), and from compound (**3**) (143 mg, 0.5 mmol) and 4-hydroxy-6-methyl-2*H*-pyran-2-one (**8**) (63 mg, 0.5 mmol), 2.5 h, 51% yield (82 mg), mp 305-308°C (from a mixture of ethanol and toluene), IR 2230 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: 2.37 (3H, d, $J_{7-Me-H8}$ = 0.9 Hz, 7-Me), 6.23 (1H, d, $J_{7-Me-H8}$ = 0.9 Hz, H_8), 7.19 (1H, ddd, $J_{H3'-H5'}$ = 1.0 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.35 (1H, s, H_4), 7.61 (1H, ddd, $J_{H3'-H4'}$ = 8.1 Hz, $J_{H3'-H5'}$ = 1.0 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.68 (1H, d, J_{CH-NH} = 12.0 Hz, C*H*NH), 7.78 (1H, ddd, $J_{H3'-H4'}$ = 8.1 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 8.64 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 13.08 (1H, br s, CHN*H*). *Anal.* Calcd for $C_{17}H_{11}N_3O_4$: C, 63.55; H, 3.45; N, 13.08. Found: C, 63.80; H, 3.37; N, 13.35.

3-[2-Cyano-2-(2-pyridinyl)ethenyl]amino-2*H*,5*H*-pyrano[3,2-*c*]benzo[*b*]pyran-2,5-dione (17). This compound was prepared from compound (**2**) (136 mg, 0.5 mmol) and 4-hydroxy-2*H*-benzo[*b*]pyran-2-one (**9**) (81 mg, 0.5 mmol), 1.5 h, 47% yield (84 mg), and from compound (**3**) (143 mg, 0.5 mmol) and 4-

hydroxy-2*H*-benzo[*b*]pyran-2-one (**9**) (81 mg, 0.5 mmol), 30 min, 58% yield (104 mg), mp 329-327°C (from ethanol), IR 2260 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: 7.22 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.6 Hz, $J_{H5'-H6'}$ = 5.1 Hz, H_5'), 7.42 (1H, dd, J_{H7-H8} = 8.4 Hz, J_{H7-H9} = 1.2 Hz, H_7), 7.43 (1H, ddd, J_{H7-H9} = 1.2 Hz, J_{H8-H9} = 7.2 Hz, J_{H9-H10} = 8.4 Hz, H_9), 7.48 (1H, s, H_4), 7.63 (1H, ddd, $J_{H3'-H4'}$ = 8.3 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.65 (1H, ddd, J_{H7-H8} = 8.4 Hz, J_{H8-H9} = 7.2 Hz, J_{H8-H10} = 1.4 Hz, H_8), 7.74 (1H, d, J_{CH-NH} = 11.1 Hz, C*H*NH), 7.81 (1H, ddd, $J_{H3'-H4'}$ = 8.3 Hz, $J_{H4'-H5'}$ = 7.6 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 8.05 (1H, dd, J_{H8-H10} = 1.4 Hz, J_{H9-H10} = 8.4 Hz, H_{10}), 8.68 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.1 Hz, H_6'), 13.20 (1H, d, J_{CH-NH} = 11.1 Hz, CHN*H*). *Anal.* Calcd for $C_{20}H_{11}N_3O_4$: C, 67.23; H, 3.10; N, 11.76. Found: C, 67.59; H, 2.92; N, 11.98.

General Procedure for the Preparation of β-Arylamino-α,β-didehydro-α-amino Acid Derivatives (28-40):

To compound (**2**) (136 mg, 0.5 mmol) or (**3**) (143 mg, 0.5 mmol) the corresponding aromatic amines (**18-25**) (0.5 mmol) and acetic acid (2 mL) were added and the mixture was stirred at rt for several hours. The volatile compounds were evaporated *in vacuo*, ethanol (3 mL) was added and the precipitate was collected by filtration.

Methyl (*E*)-2-[(*E*)-2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-phenylaminopropenoate (28). This compound was prepared from compound (**2**) (136 mg, 0.5 mmol) and aniline (**18**) (47 mg, 0.5 mmol), 5.5 h, 80% yield (128 mg), mp 182-186°C (from ethanol), IR 2210 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: 3.80 (3H, s, COOMe), 6.65 (1H, d, $J_{R1NH-CH}$ = 13.2 Hz, R_1N*H*CH), 7.00-7.03 (2H, m, 2H(Ph)), 7.04 (1H, d, J_{CH-NH} = 10.4 Hz, C*H*NH), 7.07 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.31-7.36 (3H, m, 3H(Ph)), 7.52 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.72 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.8 Hz, H_4'), 7.91 (1H, d, $J_{R1NH-CH}$ = 13.2 Hz, R_1NHC*H*), 8.46 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 11.24 (1H, d, J_{CH-NH} = 10.4 Hz, CHN*H*). *Anal.* Calcd for $C_{18}H_{16}N_4O_2$: C, 67.49; H, 5.03; N, 17.49. Found: C, 67.48; H, 4.96; N, 17.51.

Methyl (*E*)-2-[(*E*)-2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(2-methoxyphenyl)aminopropenoate (29). This compound was prepared from compound (**2**) (136 mg, 0.5 mmol) and 2-methoxyaniline (**19**) (62 mg, 0.5 mmol), 5 h, 77% yield (135 mg), mp 189-193°C (from ethanol), IR 2200 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: 3.87 (3H, s, COOMe), 3.95 (3H, s, OMe), 6.90-7.09 (4H, m, 4H(Ph)), 7.03 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.27 (1H, d, J_{CH-NH} = 11.6 Hz, C*H*NH), 7.43 (1H, d, $J_{R1NH-CH}$ =

13.0 Hz, R_1NHCH), 7.47 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.68 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.8 Hz, H_4'), 8.44 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 9.90 (1H, d, $J_{R1NH-CH}$ = 13.0 Hz, R_1NHCH), 11.54 (1H, d, J_{CH-NH} = 11.6 Hz, CHNH). *Anal.* Calcd for $C_{19}H_{18}N_4O_3$: C, 65.13; H, 5.18; N, 15.99. Found: C, 65.38; H, 5.02; N, 16.12.

Methyl (*E*)-2-[(*E*)-2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(4-methoxyphenyl)aminopropenoate and (*Z*)-2-[(*E*)- Isomer (30). These compounds were prepared from compound (**2**) (136 mg, 0.5 mmol) and 4-methoxyaniline (**20**) (62 mg, 0.5 mmol) in 3:1 ratio, 24 h, 75% yield (131 mg), mp 143-155°C (from ethanol), IR 2210 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: (2*E*, 2'*E*): 3.77, 3.79 (6H, 2x s, COOMe, OMe), 6.59 (1H, d, $J_{R1NH-CH}$ = 13.2 Hz, R_1NHCH), 6.86-6.98 (4H, m, 4H(Ph)), 7.05 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.24 (1H, d, J_{CH-NH} = 11.7 Hz, CHNH), 7.50 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.70 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.8 Hz, H_4'), 7.82 (1H, d, $J_{R1NH-CH}$ = 13.2 Hz, R_1NHCH), 8.45 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 11.16 (1H, d, J_{CH-NH} = 11.7 Hz, CHNH). Addition of D_2O causes the loss of d at δ = 6.59 ppm and d at δ = 11.16 ppm; d at δ = 7.24 ppm turns to s and d at δ = 7.82 turns to s. (2*Z*, 2'*E*): 3.80, 3.84 (6H, 2x s, COOMe, OMe), 7.02 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.30 (1H, d, J_{CH-NH} = 11.7 Hz, CHNH), 7.32 (1H, d, $J_{R1NH-CH}$ = 13.2 Hz, R_1NHCH), 7.46 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.67 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.8 Hz, H_4'), 8.43 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 9.55 (1H, d, $J_{R1NH-CH}$ = 13.2 Hz, R_1NHCH), 11.45 (1H, d, J_{CH-NH} = 11.7 Hz, CHNH). Addition of D_2O causes the loss of d at δ = 9.55 ppm and d at δ = 11.45 ppm; d at δ = 7.30 ppm turns to s and d at δ = 7.32 turns to s. *Anal.* Calcd for $C_{19}H_{18}N_4O_3$: C, 65.13; H, 5.18; N, 15.99. Found: C, 65.43; H, 4.92; N, 16.23.

Methyl (*E*)-2-[(*E*)-2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(4-fluorophenyl)aminopropenoate and (*Z*)-2-[(*E*)- Isomer (31). These compounds were prepared from compound (**2**) (136 mg, 0.5 mmol) and 4-fluoroaniline (**21**) (56 mg, 0.5 mmol) in 3:1 ratio, 3 h, 85% yield (144 mg), mp 201-205°C (from ethanol), IR 2180 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: (2*E*, 2'*E*): 3.78 (3H, s, COOMe), 6.78 (1H, d, $J_{R1NH-CH}$ = 13.1 Hz, R_1NHCH), 6.94-7.07 (5H, m, H_5', 4H(Ph)), 7.24 (1H, d, J_{CH-NH} = 12.4 Hz, CHNH), 7.45 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.0 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.67 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H4'-H6'}$ = 1.8 Hz, H_4'), 7.80 (1H, d, $J_{R1NH-CH}$ = 13.1 Hz, R_1NHCH), 8.45 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 11.20 (1H, d, J_{CH-NH} = 12.4 Hz, CHNH). (2*Z*, 2'*E*): 3.85 (3H, s, COOMe), 7.28 (1H, d, J_{CH-NH} = 12.4 Hz, CHNH), 7.32 (1H, d, $J_{R1NH-CH}$ = 13.1 Hz, R_1NHCH), 8.43 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 9.60 (1H, d, $J_{R1NH-CH}$ = 13.1 Hz, R_1NHCH), 11.50 (1H, d,

J_{CH-NH} = 12.4 Hz, CHN*H*). *Anal.* Calcd for $C_{18}H_{15}N_4O_2F$: C, 63.90; H, 4.47; N, 16.56. Found: C, 63.96; H, 4.43; N, 16.70.

Methyl (*E*)-2-[(*E*)-2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(3-chloro-4-fluorophenyl)aminopropenoate and (*Z*)-2-[(*E*)- Isomer (32). These compounds were prepared from compound (**2**) (136 mg, 0.5 mmol) and 3-chloro-4-fluoroaniline (**22**) (73 mg, 0.5 mmol) in 7:1 ratio, 1.5 h, 90% yield (168 mg), mp 213-215°C (from ethanol), IR 2180 cm^{-1} (CN), ^{1}H NMR ($CDCl_3$) δ: (2*E*, 2'*E*): 3.80 (3 H, s, COOMe), 6.58 (1H, d, $J_{R1NH-CH}$ = 13.2 Hz, R_1N*H*CH), 6.84-6.89 (1H, m, 1H(Ph)), 7.07 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.1 Hz, H_5'), 7.06-7.14 (2H, m, 2H(Ph)), 7.24 (1H, d, J_{CH-NH} = 10.7 Hz, C*H*NH), 7.52 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.72 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 7.75 (1H, d, $J_{R1NH-CH}$ = 13.2 Hz, R_1NHC*H*), 8.45 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.1 Hz, H_6'), 11.25 (1H, d, J_{CH-NH} = 10.7 Hz, CHN*H*). (2*Z*, 2'*E*): 3.86 (3H, s, COOMe), 7.29 (1H, d, J_{CH-NH} = 10.7 Hz, C*H*NH), 7.48 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.69 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 8.43 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.1 Hz, H_6'), 9.60 (1H, d, $J_{R1NH-CH}$ = 13.2 Hz, R_1N*H*CH), 11.55 (1H, d, J_{CH-NH} = 10.7 Hz, CHN*H*). *Anal.* Calcd for $C_{18}H_{14}N_4O_2ClF$: C, 57.99; H, 3.79; N, 15.03. Found: C, 57.81; H, 3.53; N, 15.00.

Methyl (*E*)-2-[(*E*)-2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(2-bromophenyl)aminopropenoate and (*Z*)-2-[(*E*)- Isomer (33). These compounds were prepared from compound (**2**) (136 mg, 0.5 mmol) and 2-bromoaniline (**23**) (86 mg, 0.5 mmol) in 3:2 ratio, 2.5 h, 61% yield (122 mg), mp 218-221°C (from ethanol), IR 2190 cm^{-1} (CN), ^{1}H NMR ($CDCl_3$) δ: (2*E*, 2'*E*): 3.83 (3H, s, COOMe), 6.87-6.94 (1H, m, 1H(Ph)), 7.07 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.1 Hz, H_5'), 7.10-7.20 (1H, m, 1H(Ph)), 7.16 (1H, d, $J_{R1NH-CH}$ = 12.7 Hz, R_1N*H*CH), 7.29 (1H, d, J_{CH-NH} = 12.4 Hz, C*H*NH), 7.30-7.36 (1H, m, 1H(Ph)), 7.54 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.52-7.59 (1H, m, 1H(Ph)), 7.73 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 7.81 (1H, d, $J_{R1NH-CH}$ = 12.7 Hz, R_1NHC*H*), 8.47 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.1 Hz, H_6'), 11.67 (1H, d, J_{CH-NH} = 12.4 Hz, CHN*H*). (2*Z*, 2'*E*): 3.91 (3H, s, COOMe), 7.04 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.1 Hz, H_5'), 7.38 (1H, d, J_{CH-NH} = 12.4 Hz, C*H*NH), 7.48 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.50 (1H, d, $J_{R1NH-CH}$ = 12.7 Hz, R_1NHC*H*), 7.69 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 8.45 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.1 Hz, H_6'), 10.05 (1H, d, $J_{R1NH-CH}$ = 12.7 Hz, R_1N*H*CH). *Anal.* Calcd for $C_{18}H_{15}N_4O_2Br$: C, 54.15; H, 3.79; N, 14.03. Found: C, 54.30; H, 3.70; N, 14.12.

Methyl (*E*)-2-[(*E*)-2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(3-bromophenyl)aminopropenoate and (*Z*)-2-[(*E*)- Isomer (34). These compounds were prepared from compound (**2**) (136 mg, 0.5 mmol) and 3-bromoaniline (**24**) (86 mg, 0.5 mmol) in 3:1 ratio, 4 h, 80% yield (160 mg), mp 203-210°C (from ethanol), IR 2190 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: (2*E*, 2'*E*): 3.81 (3H, s, COOMe), 6.66 (1H, d, $J_{R1NH-CH}$ = 12.7 Hz, R_1NHCH), 6.90-6.95 (1H, m, 1H(Ph)), 7.07 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.16-7.20 (3H, m, 3H(Ph)), 7.25 (1H, d, J_{CH-NH} = 11.7 Hz, C*H*NH), 7.51 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.71 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 7.82 (1H, d, $J_{R1NH-CH}$ = 12.7 Hz, R_1NHCH), 8.46 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 11.28 (1H, d, J_{CH-NH} = 11.7 Hz, CHN*H*). (2*Z*, 2'*E*): 3.86 (3H, s, COOMe), 7.04, (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.30 (1H, d, J_{CH-NH} = 11.7 Hz, C*H*NH), 7.33 (1H, d, $J_{R1NH-CH}$ = 12.7 Hz, R_1NHCH), 7.48 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.69 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 8.44 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 9.62 (1H, d, $J_{R1NH-CH}$ = 12.7 Hz, R_1NHCH), 11.57 (1H, d, J_{CH-NH} = 11.7 Hz, CHN*H*). *Anal.* Calcd for $C_{18}H_{15}N_4O_2Br$: C, 54.15; H, 3.79; N, 14.03. Found: C, 54.38; H, 3.56; N, 14.22.

Methyl (*E*)-2-[(*E*)-2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(3-nitrophenyl)aminopropenoate and (*Z*)-2-[(*E*)- Isomer (35). These compounds were prepared from compound (**2**) (136 mg, 0.5 mmol) and 3-nitroaniline (**25**) (69 mg, 0.5 mmol) in 5:1 ratio, 4 h, 99% yield (181 mg), mp 200-208°C (from ethanol), IR 2180 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: (2*E*, 2'*E*): 3.83 (3H, s, COOMe), 7.07 (1H, d, $J_{R1NH-CH}$ = 12.1 Hz, R_1NHCH), 7.08 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.31 (1H, br s, C*H*NH), 7.31-7.35 (1H, m, 1H(Ph)), 7.47 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.47-7.53 (1H, m, 1H(Ph)), 7.69 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 7.84-7.90 (2H, m, 2H(Ph)), 7.87 (1H, d, $J_{R1NH-CH}$ = 12.1 Hz, R_1NHCH), 8.46 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 9.85 (1H, d, J_{CH-NH} = 12.5 Hz, CHN*H*). (2*Z*, 2'*E*): 3.89 (3H, s, COOMe), 7.41 (1H, d, $J_{R1NH-CH}$ = 12.1 Hz, R_1NHCH), 7.86 (1H, d, $J_{R1NH-CH}$ = 12.1 Hz, R_1NHCH), 8.45 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 11.67 (1H, d, J_{CH-NH} = 12.5 Hz, CHN*H*). *Anal.* Calcd for $C_{18}H_{15}N_5O_4$: C, 59.18; H, 4.14; N, 19.17. Found: C, 59.03; H, 4.16; N, 19.26.

Ethyl (*E*)-2-[(*E*)-2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-phenylaminopropenoate and (*Z*)-2-[(*E*)- Isomer (36). These compounds were prepared from compound (**3**) (143 mg, 0.5 mmol) and aniline (**18**) (47 mg, 0.5 mmol) in 8:1 ratio, 24 h, 61% yield (102 mg), mp 181-183°C (from ethanol), IR 2190 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: (2*E*, 2'*E*): 1.38 (3H, t, $J_{CH2-CH3}$ = 7.1 Hz, $COOCH_2CH_3$), 4.32 (2H, q, $J_{CH2-CH3}$ =

7.1 Hz, COOC*H*$_2$CH$_3$), 6.98-7.09 (3H, m, 3H(Ph)), 7.03 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.29 (1H, d, J_{CH-NH} = 12.1 Hz, C*H*NH), 7.31-7.36 (2H, m, 2H(Ph)), 7.39 (1H, d, $J_{R1NH-CH}$ = 12.3 Hz, R_1NHC*H*), 7.48 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.68 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 8.42 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 9.61 (1H, d, $J_{R1NH-CH}$ = 12.3 Hz, R_1N*H*CH), 11.69 (1H, d, J_{CH-NH} = 12.1 Hz, CHN*H*). (2*Z*, 2'*E*): 1.32 (3H, t, $J_{CH2-CH3}$ = 7.1 Hz, COOCH$_2$C*H*$_3$), 4.27 (2H, q, $J_{CH2-CH3}$ = 7.1 Hz, COOC*H*$_2$CH$_3$), 7.07 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.53 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.72 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 8.46 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'). *Anal.* Calcd for $C_{19}H_{18}N_4O_2$: C, 68.25; H, 5.43; N, 16.76. Found: C, 68.40; H, 5.37; N, 16.97.

Ethyl (*E*)-2-[(*E*)-2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(2-methoxyphenyl)aminopropenoate (37). This compound was prepared from compound (**3**) (143 mg, 0.5 mmol) and 2-methoxyaniline (**19**) (62 mg, 0.5 mmol), 24 h, 79% yield (144 mg), mp 177-189°C (from ethanol), IR 2190 cm^{-1} (CN), ^{1}H NMR ($CDCl_3$) δ: 1.39 (3H, t, $J_{CH2-CH3}$ = 7.1 Hz, COOCH$_2$C*H*$_3$), 3.94 (3H, s, OMe), 4.34, (2H, q, $J_{CH2-CH3}$ = 7.1 Hz, COOC*H*$_2$CH$_3$), 6.89-7.09 (4H, m, 4H(Ph)), 7.02 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.30 (1H, d, J_{CH-NH} = 12.4 Hz, C*H*NH), 7.41 (1H, d, $J_{R1NH-CH}$ = 13.0 Hz, R_1NHC*H*), 7.47 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.67 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.8 Hz, H_4'), 8.43 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 9.80 (1H, d, $J_{R1NH-CH}$ = 13.0 Hz, R_1N*H*CH), 11.72 (1H, d, J_{CH-NH} = 12.4 Hz, CHN*H*). *Anal.* Calcd for $C_{20}H_{20}N_4O_3$: C, 65.92; H, 5.53; N, 15.37. Found: C, 66.02; H, 5.51; N, 15.12.

Ethyl (*E*)-2-[(*E*)-2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(4-fluorophenyl)aminopropenoate (38). This compound was prepared from compound (**3**) (143 mg, 0.5 mmol) and 4-fluoroaniline (**21**) (56 mg, 0.5 mmol), 24 h, 70% yield (123 mg), mp 202-205°C (from ethanol), IR 2190 cm^{-1} (CN), ^{1}H NMR ($CDCl_3$) δ: 1.38 (3H, t, $J_{CH2-CH3}$ = 7.1 Hz, COOCH$_2$C*H*$_3$), 4.31 (2H, q, $J_{CH2-CH3}$ = 7.1 Hz, COOC*H*$_2$CH$_3$), 6.93-6.99 (2H, m, 2H(Ph)), 7.01-7.07 (2H, m, 2H(Ph)), 7.03 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.28 (1H, d, J_{CH-NH} = 12.7 Hz, C*H*NH), 7.29 (1H, d, $J_{R1NH-CH}$ = 12.5 Hz, R_1N*H*CH), 7.47 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.68 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.8 Hz, H_4'), 8.42 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 9.58 (1H, d, $J_{R1NH-CH}$ = 12.5 Hz, R_1N*H*CH), 11.67 (1H, d, J_{CH-NH} = 12.7 Hz, CHN*H*). *Anal.* Calcd for $C_{19}H_{17}N_4O_2F$: C, 64.76; H, 4.86; N, 15.90. Found: C, 64.91; H, 4.83; N, 15.61.

Ethyl (*E*)-2-[(*E*)-2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(3-bromophenyl)aminopropenoate and (*Z*)-2-[(*E*)- Isomer (39). These compounds were prepared from compound (**3**) (143 mg, 0.5 mmol) and 3-bromoaniline (**24**) (86 mg, 0.5 mmol) in 2:1 ratio, 24 h, 35% yield (72 mg), mp 143-163°C (from ethanol), IR 2180 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: (2*E*, 2'*E*): 1.33 (3H, t, $J_{CH2-CH3}$ = 7.1 Hz, $COOCH_2CH_3$), 4.27 (2H, q, $J_{CH2-CH3}$ = 7.1 Hz, $COOCH_2CH_3$), 6.73 (1H, d, $J_{R1NH-CH}$ = 12.8 Hz, R_1NHCH), 6.89-6.95 (1H, m, 1H(Ph)), 7.07 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.15-7.19 (3H, m, 3H(Ph)), 7.29 (1H, d, J_{CH-NH} = 12.3 Hz, C*H*NH), 7.49 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.70 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.8 Hz, H_4'), 7.78 (1H, d, $J_{R1NH-CH}$ = 12.8 Hz, R_1NHCH), 8.45 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 11.29 (1H, d, J_{CH-NH} = 12.3 Hz, CHN*H*). (2*Z*, 2'*E*): 1.38 (3H, t, $J_{CH2-CH3}$ = 7.1 Hz, $COOCH_2CH_3$), 4.32 (2H, q, $J_{CH2-CH3}$ = 7.1 Hz, $COOCH_2CH_3$), 7.03 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.31 (1H, d, J_{CH-NH} = 12.3 Hz, C*H*NH), 7.32 (1H, d, $J_{R1NH-CH}$ = 12.8 Hz, R_1NHCH), 7.47 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.68 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.8 Hz, H_4'), 8.42 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 9.61 (1H, d, $J_{R1NH-CH}$ = 12.8 Hz, R_1NHCH), 11.75 (1H, d, J_{CH-NH} = 12.3 Hz, CHN*H*). *Anal.* Calcd for $C_{19}H_{17}N_4O_2Br$: C, 55.22; H, 4.15; N, 13.56. Found: C, 55.60; H, 4.21; N, 13.59.

Ethyl (*E*)-2-[(*E*)-2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(3-nitrophenyl)aminopropenoate and (*Z*)-2-[(*E*)- Isomer (40). These compounds were prepared from compound (**3**) (143 mg, 0.5 mmol) and 3-nitroaniline (**25**) (69 mg, 0.5 mmol) in 1:1 ratio, 24 h, 45% yield (85 mg), mp 192-195°C (from ethanol), IR 2190 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: (2*E*, 2'*E*): 1.34 (3H, t, $J_{CH2-CH3}$ = 7.1 Hz, $COOCH_2CH_3$), 4.30 (2H, q, $J_{CH2-CH3}$ = 7.1 Hz, $COOCH_2CH_3$), 7.00 (1H, d, $J_{R1NH-CH}$ = 12.8 Hz, R_1NHCH), 7.08 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.27-7.35 (1H, m, 1H(Ph)), 7.32 (1H, d, J_{CH-NH} = 12.4 Hz, C*H*NH), 7.46-7.53 (1H, m, 1H(Ph)), 7.49 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.70 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 7.83-7.90 (2H, m, 2H(Ph)), 7.86 (1H, d, $J_{R1NH-CH}$ = 12.8 Hz, R_1NHCH), 8.46 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 11.37 (1H, d, J_{CH-NH} = 12.4 Hz, CHN*H*),. (2*Z*, 2'*E*): 1.40 (3H, t, $J_{CH2-CH3}$ = 7.1 Hz, $COOCH_2CH_3$), 4.35 (2H, q, $J_{CH2-CH3}$ = 7.1 Hz, $COOCH_2CH_3$), 7.06 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.38 (1H, d, J_{CH-NH} = 12.4 Hz, C*H*NH), 7.69 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 7.84 (1H, d, $J_{R1NH-CH}$ = 12.8 Hz, R_1NHCH), 8.43 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 9.84 (1H, d, $J_{R1NH-CH}$ = 12.8 Hz, R_1NHCH), 11.85 (1H, d, J_{CH-NH} = 12.4 Hz, CHN*H*). *Anal.* Calcd for $C_{19}H_{17}N_5O_4$: C, 60.15; H, 4.52; N, 18.46. Found: C, 59.83; H, 4.59; N, 18.07.

General Procedure for the Preparation of β-Heteroarylamino-α,β-didehydro-α-amino Acid Derivatives (41-43):

To compound (**2**) (136 mg, 0.5 mmol) or (**3**) (143 mg, 0.5 mmol) the corresponding heteroarylamines (**26**, **27**) (0.5 mmol) and acetic acid (2 mL) were added and the mixture was stirred at rt for several days. The volatile compounds were evaporated *in vacuo*, ethanol (3 mL) was added and the precipitate was collected by filtration.

Methyl (*E*)-2-[(*E*)-2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(5-chloro-2-pyridinyl)aminopropenoate (41). This compound was prepared from compound (**2**) (136 mg, 0.5 mmol) and 2-amino-5-chloropyridine (**26**) (64 mg, 0.5 mmol), 24 h, 83% yield (148 mg), mp 225-227°C (from ethanol), IR 2180 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: 3.80 (3H, s, COOMe), 6.78 (1H, dd, J_{H3-H4} = 8.7 Hz, J_{H3-H6} = 0.7 Hz, H_3(Ar)), 7.07 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.15 (1H, d, $J_{R1NH-CH}$ = 12.5 Hz, R_1NHCH), 7.33 (1H, d, J_{CH-NH} = 10.3 Hz, C*H*NH), 7.50 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.59 (1H, dd, J_{H3-H4} = 8.7 Hz, J_{H4-H6} = 2.5 Hz, H_4(Ar)), 7.71 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 8.23 (1H, dd, J_{H3-H6} = 0.7 Hz, J_{H4-H6} = 2.5 Hz, H_6(Ar)), 8.32 (1H, d, $J_{R1NH-CH}$ = 12.5 Hz, R_1NHCH), 8.46 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 11.36 (1H, br s, CHN*H*). Addition of D_2O causes the loss of d at δ = 7.15 ppm and br s at δ = 11.36 ppm; d at δ = 7.33 ppm turns to s and d at δ = 8.32 turns to s. *Anal.* Calcd for $C_{17}H_{14}N_5O_2Cl$: C, 57.39; H, 3.97; N, 19.68. Found: C, 57.06; H, 3.95; N, 19.82.

Ethyl (*E*)-2-[(*E*)-2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(5-chloro-2-pyridinyl)aminopropenoate (42). This compound was prepared from compound (**3**) (143 mg, 0.5 mmol) and 2-amino-5-chloropyridine (**26**) (64 mg, 0.5 mmol), 24 h, 29% yield (54 mg), mp 180-184°C (from ethanol), IR 2190 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: 1.33 (3H, t, $J_{CH2-CH3}$ = 7.1 Hz, $COOCH_2CH_3$), 4.28 (2H, q, $J_{CH2-CH3}$ = 7.1 Hz, $COOCH_2CH_3$), 6.80 (1H, dd, J_{H3-H4} = 8.7 Hz, J_{H3-H6} = 0.7 Hz, H_3(Ar)), 7.05 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.35 (1H, br s, C*H*NH), 7.37 (1H, br s, R_1NHCH), 7.44 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.58 (1H, dd, J_{H3-H4} = 8.7 Hz, J_{H4-H6} = 2.5 Hz, H_4(Ar)), 7.67 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.8 Hz, H_4'), 8.23 (1H, dd, J_{H3-H6} = 0.7 Hz, J_{H4-H6} = 2.5 Hz, H_6(Ar)), 8.29 (1H, d, $J_{R1NH-CH}$ = 12.7 Hz, R_1NHCH), 8.45 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 11.33 (1H, br s, CHN*H*),. Addition of D_2O causes the loss of br s at δ = 7.37 ppm and br s at δ = 11.33 ppm; br s at δ = 7.35 ppm turns to s and d at δ = 8.29 turns to s. *Anal.* Calcd for $C_{18}H_{16}N_5O_2Cl$: C, 58.46; H, 4.36; N, 18.94. Found: C, 58.18; H, 4.04; N, 19.03.

Methyl (*E*)-2-[(*E*)-2-Cyano-2-(2-pyridinyl)ethenyl]amino-3-(3-isoxazolyl)aminopropenoate and (*Z*)-2-[(*E*)- Isomer (43).These compounds were prepared from compound (**2**) (136 mg, 0.5 mmol) and 3-aminoisoxazol (**27**) (48 mg, 0.5 mmol) in 3:2 ratio, 7 days, 80% yield (125 mg), mp 181-184°C (from ethanol), IR 2190 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: (2*E*, 2'*E*): 3.81 (3H, s, COOMe), 6.12 (1H, d, J_{H4-H5} = 1.8 Hz, H_4(Ar)), 6.95 (1H, d, $J_{R1NH-CH}$ = 12.4 Hz, R_1N*H*CH), 7.08 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.28 (1H, d, J_{CH-NH} = 11.5 Hz, C*H*NH), 7.51 (1H, ddd, $J_{H3'-H4'}$ = 8.1 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.72 (1H, ddd, $J_{H3'-H4'}$ = 8.1 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H4'-H6'}$ = 1.8 Hz, H_4'), 7.82 (1H, d, $J_{R1NH-CH}$ = 12.4 Hz, R_1NHC*H*), 8.27 (1H, d, J_{H4-H5} = 1.8 Hz, H_5(Ar)), 8.43 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 11.35 (1H, d, J_{CH-NH} = 11.5 Hz, CHN*H*). Addition of D_2O causes the loss of d at δ = 6.95 ppm and d at δ = 11.35 ppm; d at δ = 7.28 ppm turns to s and d at δ = 7.82 turns to s. (2*Z*, 2'*E*): 3.89 (3H, s, COOMe), 6.21 (1H, d, J_{H4-H5} = 1.8 Hz, H_4(Ar)), 7.05 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.30 (1H, d, J_{CH-NH} = 11.5 Hz, C*H*NH), 7.48 (1H, ddd, $J_{H3'-H4'}$ = 8.1 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.49 (1H, d, $J_{R1NH-CH}$ = 12.4 Hz, R_1NHC*H*), 7.69 (1H, ddd, $J_{H3'-H4'}$ = 8.1 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H4'-H6'}$ = 1.8 Hz, H_4'), 8.25 (1H, d, J_{H4-H5} = 1.8 Hz, H_5(Ar)), 8.45 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 9.47 (1H, d, $J_{R1NH-CH}$ = 12.4 Hz, R_1N*H*CH), 11.71 (1H, d, J_{CH-NH} = 11.5 Hz, CHN*H*). Addition of D_2O causes the loss of d at δ = 9.47 ppm and d at δ = 11.71 ppm; d at δ = 7.30 ppm turns to s. *Anal.* Calcd for $C_{15}H_{13}N_5O_3$: C, 57.88; H, 4.21; N, 22.50. Found: C, 57.63; H, 4.27; N, 22.26.

General Procedure for the Preparation of Pyrido[1,2-*a*]pyrimidin-4-ones (50-53), Thiazolo[3,2-*a*]pyrimidin-4-one (54) and Benzothiazolo[3,2-*a*]pyrimidin-4-one (55):

To compound (**2**) (136 mg, 0.5 mmol) or (**3**) (143 mg, 0.5 mmol) the corresponding heteroarylamine (**26**, **44-48**) (0.5 mmol) and acetic acid (2 mL) were added and the reaction mixture was heated under reflux for 1 to 1.5 h. The volatile compounds were evaporated *in vacuo*, ethanol (3 mL) was added, the precipitate was collected by filtration and washed with ethanol.

3-[2-Cyano-2-(2-pyridinyl)ethenyl]amino-7-chloro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (50). This compound was prepared from compound (**2**) (136 mg, 0.5 mmol) and 2-amino-5-chloropyridine (**26**) (64 mg, 0.5 mmol), 1 h, 42% yield (68 mg), and from compound (**3**) (143 mg, 0.5 mmol) and 2-amino-5-chloropyridine (**26**) (64 mg, 0.5 mmol), 1.5 h, 13% yield (21 mg), mp 286-288°C (from ethanol), IR 2180 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: 7.16 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.52 (1H, dd, J_{H6-H8} = 2.3 Hz, J_{H8-H9} = 9.5 Hz, H_8), 7.58 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$

= 1.0 Hz, H_3'), 7.61 (1H, dd, J_{H6-H9} = 0.8 Hz, J_{H8-H9} = 9.5 Hz, H_9), 7.76 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 7.91 (1H, d, J_{CH-NH} = 12.0 Hz, C*H*NH), 8.33 (1H, s, H_2), 8.66 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 9.02 (1H, dd, J_{H6-H8} = 2.3 Hz, J_{H6-H9} = 0.8 Hz, H_6), 12.96 (1H, d, J_{CH-NH} = 12.0 Hz, CHN*H*). *Anal.* Calcd for $C_{16}H_{10}N_5OCl$: C, 59.36; H, 3.11; N, 21.63. Found: C, 59.43; H, 2.99; N, 21.74.

3-[2-Cyano-2-(2-pyridinyl)ethenyl]amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (51). This compound was prepared from compound (**2**) (136 mg, 0.5 mmol) and 2-aminopyridine (**44**) (47 mg, 0.5 mmol), 1.5 h, 18% yield (26 mg), and from compound (**3**) (143 mg, 0.5 mmol) and 2-aminopyridine (**44**) (47 mg, 0.5 mmol), 1.5 h, 16% yield (23 mg), mp 275-276°C (from ethanol), IR 2220 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: 7.14 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.16 (1H, ddd, J_{H6-H7} = 7.3 Hz, J_{H7-H8} = 6.3 Hz, J_{H7-H9} = 1.7 Hz, H_7), 7.57 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.61 (1H, ddd, J_{H6-H8} = 1.5 Hz, J_{H7-H8} = 6.3 Hz, J_{H7-H9} = 1.7 Hz, J_{H8-H9} = 9.0 Hz, H_8), 7.67 (1H, ddd, J_{H6-H9} = 0.9 Hz, J_{H7-H9} = 1.7 Hz, J_{H8-H9} = 9.0 Hz, H_9), 7.75 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 7.93 (1H, d, J_{CH-NH} = 13.0 Hz, C*H*NH), 8.37 (1H, s, H_2), 8.66 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 9.01 (1H, ddd, J_{H6-H7} = 7.3 Hz, J_{H6-H8} = 1.5 Hz, J_{H6-H9} = 0.9 Hz, H_6), 12.88 (1H, d, J_{CH-NH} = 13.0 Hz, CHN*H*). *Anal.* Calcd for $C_{16}H_{11}N_5O$: C, 66.43; H, 3.83; N, 24.21. Found: C, 66.23; H, 3.68; N, 24.22.

3-[2-Cyano-2-(2-pyridinyl)ethenyl]amino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (52). This compound was prepared from compound (**2**) (136 mg, 0.5 mmol) and 2-amino-4-methylpyridine (**45**) (54 mg, 0.5 mmol), 1.5 h, 19% yield (29 mg),and from compound (**3**) (143 mg, 0.5 mmol) and 2-amino-4-methylpyridine (**45**) (54 mg, 0.5 mmol), 1.5 h, 11% yield (17 mg), mp 283-285°C (from ethanol), IR 2210 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: 2.49 (3H, d, $J_{8-Me-H9}$ = 1.2 Hz, 8-Me), 7.00 (1H, dd, J_{H6-H7} = 7.4 Hz, J_{H7-H9} = 2.0 Hz, H_7), 7.12 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.44 (1H, ddq, J_{H6-H9} = 0.9 Hz, J_{H7-H9} = 2.0 Hz, $J_{8-Me-H9}$ = 1.2 Hz, H_9), 7.56 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.74 (1H, ddd, $J_{H3'-H4'}$ = 8.2 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H4'-H6'}$ = 1.8 Hz, H_4'), 7.91 (1H, d, J_{CH-NH} = 12.3 Hz, C*H*NH), 8.32 (1H, s, H_2), 8.64 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 8.92 (1H, dd, J_{H6-H7} = 7.4 Hz, J_{H6-H9} = 0.9 Hz, H_6), 12.81 (1H, d, J_{CH-NH} = 12.3 Hz, CHN*H*). *Anal.* Calcd for $C_{17}H_{13}N_5O$: C, 67.32; H, 4.32; N, 23.09. Found: C, 67.33; H, 4.31; N, 23.27.

3-[2-Cyano-2-(2-pyridinyl)ethenyl]amino-9-hydroxy-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (53). This compound was prepared from compound (**2**) (136 mg, 0.5 mmol) and 2-amino-3-hydroxypyridine (**46**)

(55 mg, 0.5 mmol), 1.5 h, 15% yield (23 mg), and from compound (**3**) (143 mg, 0.5 mmol) and 2-amino-3-hydroxypyridine (**46**) (55 mg, 0.5 mmol), 1.5 h, 11% yield (17 mg), mp 279-283°C (from ethanol (decomp)), IR 2180 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: 7.06 (1H, dd, J_{H6-H8} = 2.0 Hz, J_{H7-H8} = 7.5 Hz, H_8), 7.10 (1H, dd, J_{H6-H7} = 6.5 Hz, J_{H7-H8} = 7.5 Hz, H_7), 7.15 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.58 (1H, ddd, $J_{H3'-H4'}$ = 8.1 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.76 (1H, ddd, $J_{H3'-H4'}$ = 8.1 Hz, $J_{H4'-H5'}$ = 7.4 Hz, $J_{H4'-H6'}$ = 1.8 Hz, H_4'), 7.89 (1H, d, J_{CH-NH} = 12.3 Hz, C*H*NH), 8.28 (1H, s, H_2), 8.53 (1H, dd, J_{H6-H7} = 6.5 Hz, J_{H6-H8} = 2.0 Hz, H_6), 8.66 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 12.90 (1H, d, J_{CH-NH} = 12.3 Hz, CHN*H*). *Anal.* Calcd for $C_{16}H_{11}N_5O_2$: C, 62.95; H, 3.63; N, 22.94. Found: C, 62.74; H, 3.44; N, 23.00.

6-[2-Cyano-2-(2-pyridinyl)ethenyl]amino-5*H*-thiazolo[3,2-*a*]pyrimidin-4-one (54). This compound was prepared from compound (**2**) (136 mg, 0.5 mmol) and 2-aminothiazole (**47**) (50 mg, 0.5 mmol), 1 h, 18% yield (27 mg), mp 297-299°C (from ethanol), IR 2180 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: 7.09 (1H, d, J_{H2-H3} = 4.9 Hz, H_2), 7.13 (1H, ddd, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.56 (1H, ddd, $J_{H3'-H4'}$ = 8.3 Hz, $J_{H3'-H5'}$ = 1.1 Hz, $J_{H3'-H6'}$ = 1.0 Hz, H_3'), 7.74 (1H, ddd, $J_{H3'-H4'}$ = 8.3 Hz, $J_{H4'-H5'}$ = 7.5 Hz, $J_{H4'-H6'}$ = 1.9 Hz, H_4'), 7.82 (1H, d, J_{CH-NH} = 12.8 Hz, C*H*NH), 8.01 (1H, d, J_{H2-H3} = 4.9 Hz, H_3), 8.02 (1H, s, H_7), 8.62 (1H, ddd, $J_{H3'-H6'}$ = 1.0 Hz, $J_{H4'-H6'}$ = 1.9 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 12.74 (1H, d, J_{CH-NH} = 12.8 Hz, CHN*H*). *Anal.* Calcd for $C_{14}H_9N_5OS$: C, 56.94; H, 3.07; N, 23.71. Found: C, 56.65; H, 3.16; N, 23.44.

3-[2-Cyano-2-(2-pyridinyl)ethenyl]amino-4*H*-benzothiazolo[3,2-*a*]pyrimidin-4-one (55). This compound was prepared from compound (**2**) (136 mg, 0.5 mmol) and 2-aminobenzothiazole (**48**) (75 mg, 0.5 mmol), 1 h, 13% yield (22 mg), mp 288-290°C (from ethanol), IR 2200 cm^{-1} (CN), ^1H NMR ($CDCl_3$) δ: 7.16 (1H, ddd, $J_{H3'-H5'}$ = 1.0 Hz, $J_{H4'-H5'}$ = 8.2 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_5'), 7.53-7.59 (3H, m, H_3', 2H(Ph)), 7.69-7.79 (2H, m, H_4', 1H(Ph)), 7.77 (1H, d, J_{CH-NH} = 11.6 Hz, C*H*NH), 7.93 (1H, s, H_2), 8.69 (1H, ddd, $J_{H3'-H6'}$ = 0.8 Hz, $J_{H4'-H6'}$ = 1.8 Hz, $J_{H5'-H6'}$ = 5.0 Hz, H_6'), 9.12-9.15 (1H, m, 1H(Ph)), 12.79 (1H, d, J_{CH-NH} = 11.6 Hz, CHN*H*). *Anal.* Calcd for $C_{18}H_{11}N_5OS$: C, 62.60; H, 3.21; N, 20.28. Found: C, 62.43; H, 3.31; N, 20.04.

Methyl 1-(5-Methyl-3-isoxazolyl)-1*H*-imidazole-4-carboxylate (56). To compound (**2**) (136 mg, 0.5 mmol) 3-amino-5-methylisoxazole (**49**) (50 mg, 0.5 mmol) and acetic acid (2 mL) were added and the reaxtion mixture was heated under reflux for 5 h. The volatile compounds were evaporated *in vacuo* and ethanol (3 mL) was added to precipitate **56** in 20% yield (21 mg), mp 197-198°C (from ethanol), ^1H NMR

($CDCl_3$) δ: 2.53 (3H, d, $J_{H4'\text{-}5\text{-}Me}$ = 0.9 Hz, 5'-Me), 3.94 (3H, s, COOMe), 6.23 (1H, q, $J_{H4'\text{-}5\text{-}Me}$ = 0.9 Hz, H_4'), 8.02 (1H, d, $J_{H2\text{-}H5}$ = 1.4 Hz, H_5), 8.05 (1H, d, $J_{H2\text{-}H5}$ = 1.4 Hz, H_2). *Anal.* Calcd for $C_9H_9N_3O_3$: C, 52.17; H, 4.38; N, 20.28. Found: C, 63.69; H, 6.02; N, 14.00.

ACKNOWLEDGMENT

The financial support by the Ministry of Science and Technology of Slovenia is gratefully acknowledged.

REFERENCES

1. R.M. Williams, *"Synthesis of Optically Active α-Amino Acids"*, Pergamon Press, Oxford 1989.
2. R.O. Duthaler, *Tetrahedron*, 1994, **50**, 1539.
3. P. Kolar, A. Petrič, and M. Tišler, *J. Heterocycl. Chem.*, 1997, **34**, 1067.
4. I. Wagner and H. Musso, *Angew. Chem.*, 1983, **95**, 827; *Angew. Chem., Inter. Ed. Engl.*, 1983, **22**, 816.
5. U. Schmidt, A. Lieberknecht, and J. Wild, *Synthesis*, 1988, 159.
6. M. Tišler and P. Kolar, *Adv. Heterocyclic Chem.*, 1995, **64**, 1.
7. J.D. Hepworth, C.D. Gabbutt, and B.M. Heron, *"Pyrans and Their Benzo Derivatives: Synthesis"* in "*Comprehensive Heterocyclic Chemistry II*", ed. by A.R. Katritzky, C.W. Rees, and E.F.V. Scriven, Vol. 5, Elsevier Science Ltd., Oxford 1996, pp. 351-468.
8. G. Jones, *"Pyridines and Their Benzo Derivatives: Synthesis"* in "*Comprehensive Heterocyclic Chemistry II*", ed. by A.R. Katritzky, C.W. Rees, and E.F.V. Scriven, Vol. 5, Elsevier Science Ltd., Oxford 1996, pp. 167-243.
9. K. Undheim and T. Benneche, *"Pyrimidines and Their Benzo Derivatives "* in "*Comprehensive Heterocyclic Chemistry II*", ed. by A.R. Katritzky, C.W. Rees, and E.F.V. Scriven, Vol. 6, Elsevier Science Ltd., Oxford 1996, pp. 93-231.
10. R.J. Sundberg, *"Pyrroles and Their Benzo Derivatives: Synthesis"* in "*Comprehensive Heterocyclic Chemistry II*", ed. by A.R. Katritzky, C.W. Rees, and E.F.V. Scriven, Vol. 2, Elsevier Science Ltd., Oxford 1996, pp. 119-206.
11. J. Elguero, *"Pyrazoles"* in "*Comprehensive Heterocyclic Chemistry II*", ed. by A.R. Katritzky, C.W. Rees, and E.F.V. Scriven, Vol. 3, Elsevier Science Ltd., Oxford 1996, pp. 1-75.

12. M.R. Grimmett, *"Imidazoles"* in "*Comprehensive Heterocyclic Chemistry II*", ed. by A.R. Katritzky, C.W. Rees, and E.F.V. Scriven, Vol. 3, Elsevier Science Ltd., Oxford 1996, pp. 77-220.
13. J.C. Jochims, *"1,2,4-Oxadiazoles"* in "*Comprehensive Heterocyclic Chemistry II*", ed. by A.R. Katritzky, C.W. Rees, and E.F.V. Scriven, Vol. 4, Elsevier Science Ltd., Oxford 1996, pp. 179-228.
14. W. Flitsch, "*Bicyclic 5-6 Systems with One Ring Junction Nitrogen Atom: No Extra Heteroatom*" in "*Comprehensive Heterocyclic Chemistry II*", ed. by A.R. Katritzky, C.W. Rees, and E.F.V. Scriven, Vol. 8, G. Jones, ed., Elsevier Science Ltd., Oxford 1996, pp. 237-248.
15. C. Avendano and J.C. Menéndez, "*Bicyclic 6-6 Systems with One Ring Junction Nitrogen Atom: No Extra Heteroatom*" in "*Comprehensive Heterocyclic Chemistry II*", ed. by A.R. Katritzky, C.W. Rees, and E.F.V. Scriven, Vol. 8, G. Jones, ed., Elsevier Science Ltd., Oxford 1996, pp. 507-562.
16. I. Hermecz, L. Vasvári-Debreczy, and P. Mátyus "*Bicyclic 6-6 Systems with One Ring Junction Nitrogen Atom: One Extra Heteroatom 1:0*" in "*Comprehensive Heterocyclic Chemistry II*", ed. by A.R. Katritzky, C.W. Rees, and E.F.V. Scriven, Vol. 8, G. Jones, ed., Elsevier Science Ltd., Oxford 1996, pp. 563-595.
17. S.P. Stanforth, "*Bicyclic 6-6 Systems: Two Heteroatoms 1:1*" in "*Comprehensive Heterocyclic Chemistry II*", ed. by A.R. Katritzky, C.W. Rees, and E.F.V. Scriven, Vol. 7, C.A. Ramsden, ed., Elsevier Science Ltd., Oxford 1996, pp. 527-559.
18. G.R. Geen, J.M. Evans, and A.K. Vong, "*Pyrans and their Benzo Derivatives: Applications*" in "*Comprehensive Heterocyclic Chemistry II*", ed. by A.R. Katritzky, C.W. Rees, and E.F.V. Scriven, Vol. 5, A. McKillop, ed., Elsevier Science Ltd., Oxford 1996, pp. 469-500.
19. For recent reviews see: a) B. Stanovnik and J. Svete, *Synlett*, 2000, 1077. b) B. Stanovnik, *J. Heterocycl. Chem.*, 1999, **36**, 1581.
20. M. Malešič, A. Krbavčič, A. Golobič, L. Golič, and B. Stanovnik, *J. Heterocycl. Chem.*, 1997, **34**, 1757.
21. L. Selič and B. Stanovnik, *Synthesis*, 1999, 479.
22. L. Selič and B. Stanovnik, *Helv. Chim. Acta*, 1998, **81**, 1634.
23. L. Selič and B. Stanovnik, *Heterocycles*, 1999, **51**, 1087.
24. L. Pizzioli, B. Ornik, J. Svete, and B. Stanovnik, *Helv. Chim. Acta*, 1998, **81**, 231.
25. M. Škof, J. Svete, M. Kmetič, S. Golič Grdadolnik, and B. Stanovnik, *Eur. J. Org. Chem.*, 1999, 1581.
26. L. Selič, S. Golič Grdadolnik, and B. Stanovnik, *Helv. Chim. Acta*, 1997, **80**, 2418.
27. M. Škof, J. Svete, and B. Stanovnik, *Heterocycles*, 1999, **51**, 1051.
28. S. Rečnik, R. Toplak, J. Svete, L. Pizzioli, and B. Stanovnik, *J. Heterocycl. Chem.*, 2000, **37**, 783.
29. L. Selič, S. Golič Grdadolnik, and B. Stanovnik, *Heterocycles*, 1998, **49**, 133.

30. M. Škof, J. Svete, B. Stanovnik, L. Golič, S. Golič Grdadolnik, and L. Selič, *Helv. Chim. Acta*, 1998, **81**, 2332.
31. L. Selič, R. Jakše, K. Lampič, L. Golič, S. Golič Grdadolnik, and B. Stanovnik, *Helv. Chim. Acta*, 2000, **83**, 2802.
32. R. Toplak, J. Svete, B. Stanovnik, and S. Golič Grdadolnik, *J. Heterocycl. Chem.*, 1999, **36**, 225.
33. R. Toplak, J. Svete, S. Golič Grdadolnik, and B. Stanovnik, *Collect. Czech. Chem. Commun.*, 1999, **64**, 177.
34. L. Jukić, J. Svete, A. Golobič, L. Golič, and B. Stanovnik, *Heterocycles*, 2000, **53**, 805.
35. L. Selič and B. Stanovnik, *J. Heterocycl. Chem.*, 1998, **35**, 1527.
36. L. Selič, B. Stanovnik, and S. Golič Grdadolnik, *Acta Chim. Slov.*, 2000, **47**, 413.