Alkyl (*E,Z*)-2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-dimethylaminopropenoates in the Synthesis of Fused Pyrimidinones. A Facile Route to 3-Aminoazino-4*H*-pyrimidin-4-ones

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Alkyl (*E,Z*)-2-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-dimethylaminopropenoates **1a,b** react with heteroarylamines **2** to give alkyl 2-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-heteroarylaminopropenoates **3-13**. These were cyclized into fused 3-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-4*H*-azolo- (or azino)-pyrimidin-4-ones **14-18**. 2-Benzoyl-2-ethoxycarbonyl-1-ethenyl group can be easily removed from 3-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**14**) to give 3-amino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**19**). The structure of **1a** was confirmed by X-ray analysis.

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Recently, substituted 2-amino-3-dimethylaminopropenoates have been used for the synthesis of heterocyclic systems [1-4]. As an extension of these studies, alkyl 2-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-dimethylaminopropenoates **1a,b** (Figure 1) have been prepared and applied to the synthesis of fused substituted 3-aminopyranones [5].

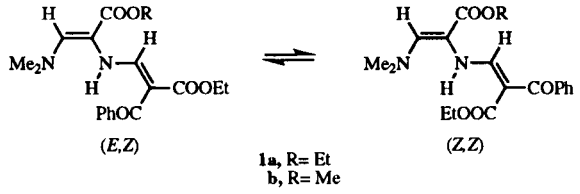


Figure 1

The orientation around the double bonds of compounds **1** in solution was shown by the NOE technique and by long range ^{13}C-^{1}H coupling constants to be solvent dependent, in dimethyl sulfoxide solution there is a mixture of (*E,Z*) and (*Z,Z*) isomers in the ratio 5:3, while in chloroform the (*E,Z*) isomer is present in over 95% [6]. We present now the results of X-ray analysis for ethyl 2-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-dimethylaminopropenoate (**1a**), which shows, that the compound exists in the solid state in the (*E,Z*) form. (Figures 2,3 and Tables 1,2).

In this paper we report on the reactions of alkyl 2-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-dimethylaminopropenoates **1a, b** with heterocyclic amines **2**, in which the amino group is attached at α-position with respect to the ring nitrogen atom. A series of heterocyclic amines were selected: 2-aminopyridine (**2a**), 2-amino-4-methylpyridine (**2b**), 2-amino-5-chloropyridine (**2c**), 2-amino-3-hydroxypyridine (**2d**), 3-amino-6-chloropyridazine (**2e**), 2-amino-4,6-dimethylpyrimidine (**2f**), 2-aminopyrazine (**2g**), 3-aminoisoxazole (**2h**), 2-amino-5-methylisoxazole (**2i**), 3-amino-5-cyanopyrazole (**2j**).

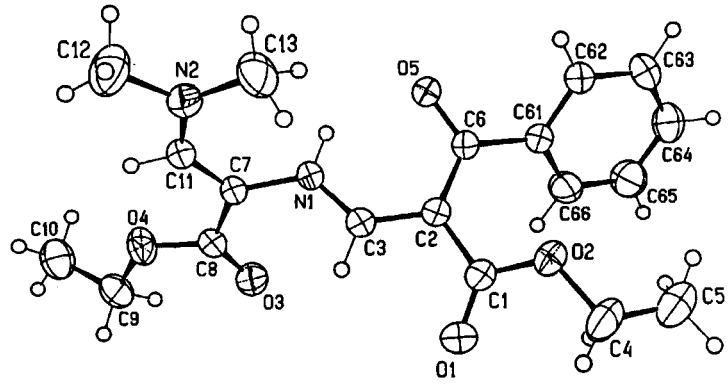


Figure 2. Ortep view of the molecule of **1a** with labeling of nonhydrogen atoms. (Ellipsoids at 40% probability level.)

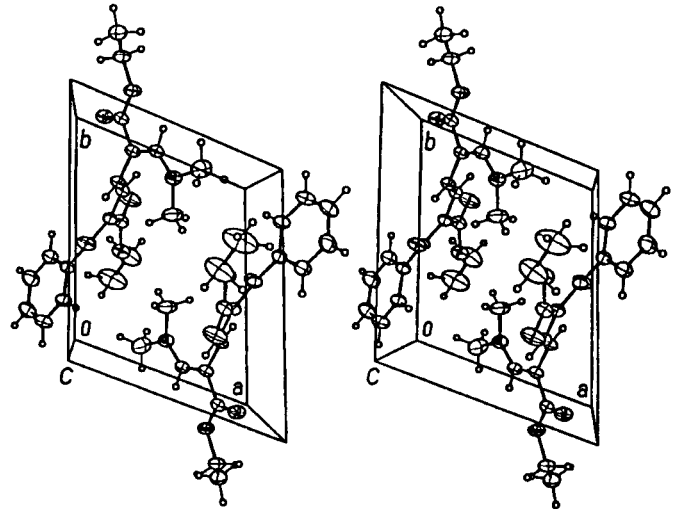


Figure 3. Ortep stereoview of the molecular packing in the unit cell of **1a**.

In this reaction, the substitution of the dimethylamino group with a heterocyclic amine took place in acetic acid

Table 1

Fractional Coordinates and Equivalent Temperature Factors (Å²). U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor

	x/a	y/b	z/c	U_{eq}
O(1)	0.6949(3)	0.2842(2)	0.8111(1)	0.081(1)
O(2)	0.7442(3)	0.5306(2)	0.8334(1)	0.0654(8)
O(3)	0.8397(3)	0.0028(2)	0.5655(1)	0.0604(7)
O(4)	0.6983(2)	-0.1293(2)	0.4006(1)	0.0602(7)
O(5)	0.9338(3)	0.5604(2)	0.5824(1)	0.0585(7)
N(1)	0.7677(2)	0.2571(2)	0.5214(1)	0.0441(6)
N(2)	0.4962(3)	0.1672(2)	0.3097(1)	0.0534(7)
C(1)	0.7468(3)	0.4003(2)	0.7828(2)	0.0510(8)
C(2)	0.8080(3)	0.4129(2)	0.6893(1)	0.0429(7)
C(3)	0.7428(3)	0.2767(2)	0.6142(1)	0.0432(7)
C(4)	0.6985(7)	0.5338(5)	0.9303(3)	0.115(2)
C(5)	0.789(1)	0.6678(6)	1.0018(4)	0.146(3)
C(6)	0.9210(3)	0.5525(2)	0.6705(1)	0.0422(7)
C(7)	0.6955(3)	0.1130(2)	0.4481(1)	0.0425(7)
C(8)	0.7538(3)	-0.0058(2)	0.4794(2)	0.0458(7)
C(9)	0.7527(4)	-0.2540(3)	0.4172(2)	0.061(1)
C(10)	0.7767(5)	-0.3233(4)	0.3184(3)	0.073(1)
C(11)	0.5793(3)	0.0850(2)	0.3533(1)	0.0437(7)
C(12)	0.3679(6)	0.0992(5)	0.2077(3)	0.086(2)
C(13)	0.4972(6)	0.3109(3)	0.3619(3)	0.081(1)
C(61)	1.0358(3)	0.6889(2)	0.7571(1)	0.0442(7)
C(62)	1.0538(3)	0.8321(2)	0.7429(2)	0.0513(8)
C(63)	1.1631(4)	0.9591(3)	0.8212(2)	0.067(1)
C(64)	1.2567(4)	0.9448(3)	0.9129(2)	0.075(1)
C(65)	1.2435(4)	0.8037(3)	0.9271(2)	0.074(1)
C(66)	1.1329(4)	0.6756(3)	0.8495(2)	0.0584(9)

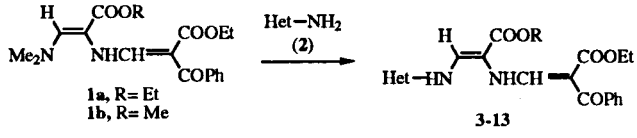
Table 2

Bond Distances (Å) and Bond Angles (°) with e.s.d.'s in parentheses

O(1)-C(1)	1.209(3)	C(2)-C(3)	1.393(3)
O(2)-C(1)	1.340(3)	C(2)-C(6)	1.449(3)
O(2)-C(4)	1.439(5)	C(4)-C(5)	1.355(6)
O(3)-C(8)	1.209(3)	C(6)-C(61)	1.496(2)
O(4)-C(8)	1.347(2)	C(7)-C(8)	1.460(3)
O(4)-C(9)	1.441(4)	C(7)-C(11)	1.361(3)
O(5)-C(6)	1.236(3)	C(9)-C(10)	1.483(5)
N(1)-C(3)	1.314(3)	C(61)-C(62)	1.384(3)
N(1)-C(7)	1.431(2)	C(61)-C(66)	1.389(3)
N(2)-C(11)	1.329(3)	C(62)-C(63)	1.380(3)
N(2)-C(12)	1.454(4)	C(63)-C(64)	1.374(4)
N(2)-C(13)	1.446(4)	C(64)-C(65)	1.372(5)
C(1)-C(2)	1.466(3)	C(65)-C(66)	1.383(3)
C(1)-O(2)-C(4)	117.8(3)	N(1)-C(7)-C(8)	116.6(2)
C(8)-O(4)-C(9)	118.7(2)	N(1)-C(7)-C(11)	123.0(2)
C(3)-N(1)-C(7)	123.7(2)	C(8)-C(7)-C(11)	120.4(2)
C(11)-N(2)-C(12)	118.7(3)	O(3)-C(8)-O(4)	123.2(2)
C(11)-N(2)-C(13)	125.2(2)	O(3)-C(8)-C(7)	125.0(2)
C(12)-N(2)-C(13)	115.2(3)	O(4)-C(8)-C(7)	111.8(2)
O(1)-C(1)-O(2)	121.7(2)	O(4)-C(9)-C(10)	107.3(3)
O(1)-C(1)-C(2)	125.0(2)	N(2)-C(11)-C(7)	132.3(2)
O(2)-C(1)-C(2)	113.3(2)	C(6)-C(61)-C(62)	119.3(2)
C(1)-C(2)-C(3)	114.2(2)	C(6)-C(61)-C(66)	121.4(2)
C(1)-C(2)-C(6)	125.2(2)	C(62)-C(61)-C(66)	119.2(2)
C(3)-C(2)-C(6)	120.6(2)	C(61)-C(62)-C(63)	119.9(2)
N(1)-C(3)-C(2)	126.9(2)	C(62)-C(63)-C(64)	120.6(3)
O(2)-C(4)-C(5)	114.3(4)	C(63)-C(64)-C(65)	120.2(2)
O(5)-C(6)-C(2)	120.9(1)	C(64)-C(65)-C(66)	119.8(3)
O(5)-C(6)-C(61)	117.3(2)	C(61)-C(66)-C(65)	120.4(3)

at room temperature to produce alkyl 2-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-heteroarylaminopropenoates **3-13**, which were isolated in pure form. (Scheme 1). In the ^{1}H nmr spectra of compounds **3-13** two sets of peaks for one CHNH structural element appear, with similar chemical shifts as those in the starting compounds **1**, while the signals for the Het-NHCH structural element appear usually as only one set of signals. This means that these compounds exist in solution in equilibrium of two isomers (*E,Z*) and (*Z,Z*), dependent on the solvent, similarly as the starting compounds **1**.

Scheme 1

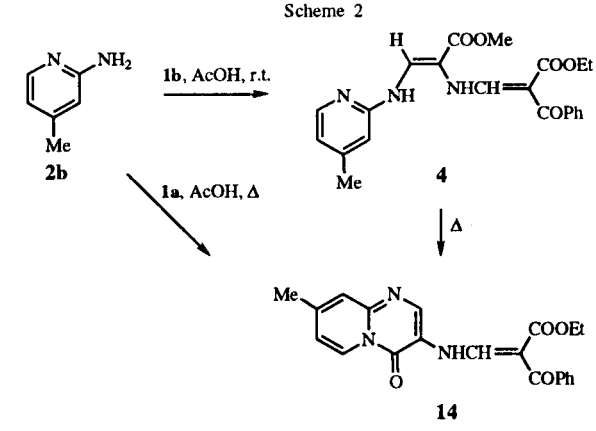


2	Het
a	pyridinyl-2
b	4-methylpyridinyl-2
c	5-chloropyridinyl-2
d	3-hydroxypyridinyl-2
e	6-chloropyridazinyl-3
f	4,6-dimethylpyrimidinyl-2
g	pyrazinyl
h	isoxazolyl-3
i	5-methylisoxazolyl-3
j	5-cyanopyrazolyl-3

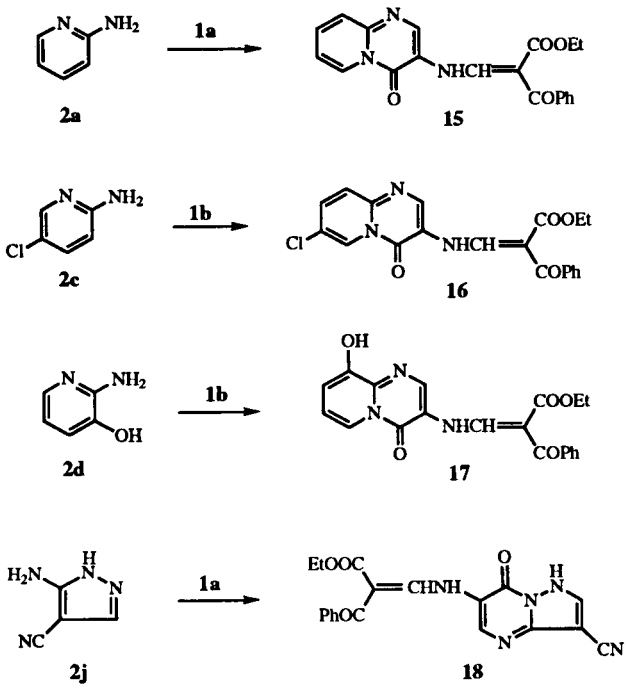
	R	Het
3	Et	pyridinyl-2
4	Me	4-methylpyridinyl-2
5	Et	5-chloropyridinyl-2
6	Me	5-chloropyridinyl-2
7	Et	6-chloropyridazinyl-3
8	Me	6-chloropyridazinyl-3
9	Et	4,6-dimethylpyrimidinyl-2
10	Et	pyrazinyl
11	Me	pyrazinyl
12	Et	isoxazolyl-3
13	Et	5-methylisoxazolyl-3

Further cyclization of the ester group to the ring nitrogen atom at the α-position gives fused azolo- and azinopyrimidinones. For example, when methyl 2-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-(4-methylpyridinyl-2)aminopropenoate (**4**) was heated in acetic acid under reflux for 45 minutes 3-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**14**) was obtained in 91% yield. Compound **14** was prepared also directly from **1a** and **2b**, without isolation of the intermediate, by heating in acetic acid for 1 hour, in 67% yield. (Scheme 2). The

Scheme 2



Scheme 3



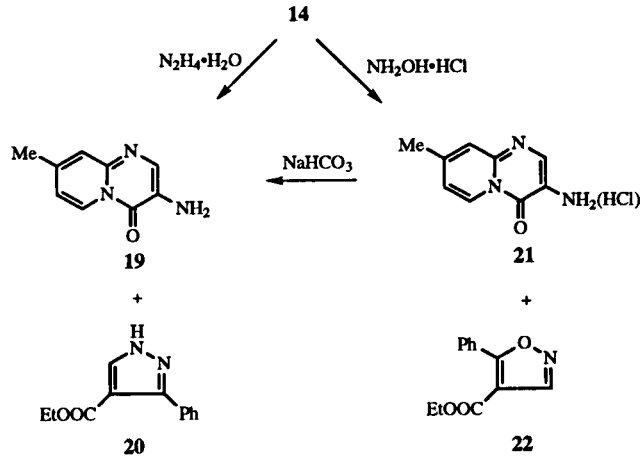
following compounds were obtained in this manner: 3-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-4*H*-pyrido-[1,2-*a*]pyrimidin-4-one (**15**) and its 7-chloro- **16** and 9-hydroxy- **17** analogues, and 6-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-cyano-7*H*-pyrazolo[1,5-*a*]-pyrimidin-7-one (**18**) in 44-67% yields (Scheme 3).

It has been reported, that dimethylaminomethylene derivatives (enaminones) react with hydrazine to give the corresponding pyrazoles [7-9] and with hydroxylamine to give the corresponding isoxazoles [10]. Recently, 2-benzoyl-2-ethoxycarbonyl-1-vinyl and 2-benzoylamino-2-methoxycarbonyl-1-vinyl groups have been used as *N*-protecting group in peptide synthesis, which can be removed easily by hydrazine or hydroxylamine [11].

We applied this reaction for the preparation of fused pyrimidin-4-ones with a free amino group at position 3. When 3-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**14**) was treated with hydrazine hydrate (99%) under reflux for 20 minutes, 3-amino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**19**) was obtained in 91% yield, as well as 4-ethoxycarbonyl-3-phenylpyrazole (**20**). Treatment of compound **14** with hydroxylamine hydrochloride gave 3-amino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one hydrochloride (**21**), from which the free amino compound was obtained by neutralizing the aqueous solution with sodium hydrogen carbonate, along with 4-ethoxycarbonyl-5-phenylisoxazole (**22**) (Scheme 4).

This removal of the *N*-protecting group represents a simple route to fused azolo- and azinopyrimidinones with a free amino group attached at position 3 of the

Scheme 4



pyrimidinone ring in comparison to other methods which require nitration followed by reduction [12]. Further research in this respect is in progress.

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ^1H nmr spectra were obtained on a Bruker Avance 300 DPX spectrometer with TMS as an internal standard, ir spectra on a Perkin-Elmer 1310 instrument, mass spectra on an Autospeck Q spectrometer and microanalyses for C, H and N on a Perkin-Elmer Analyser 2400.

The following compounds were prepared according to the procedures described in the literature: ethyl (*E,Z*)-2-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-dimethylaminopropenoate (**1a**) [5] and methyl (*E,Z*)-2-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-dimethylaminopropenoate (**1b**) [5].

Synthesis of Alkyl 2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)-amino-3-heteroarylaminopropenoates **3-13**.

Ethyl 2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-(pyridinyl-2)aminopropenoate (**3**).

A mixture of **1a** (1 mmole, 0.360 g) and 2-aminopyridine (**2a**, 1 mmole, 0.094 g) in acetic acid (5 ml) was stirred at room temperature for 7 hours. After the volatile components were evaporated *in vacuo*, 2-propanol (2 ml) was added. The precipitate, formed after cooling, was collected by filtration and recrystallized from 2-propanol to give **3** in 48% yield, mp 169-171°; ^1H nmr (DMSO-d_6): δ 0.91 and 0.93, 1.24 and 1.26 (2 x 2t, 2 x 3H, 2 x CH_2CH_3), 3.92 and 4.02, 4.18 and 4.21 (2 x 2q, 2 x 2H, 2 x CH_2CH_3), 6.99-7.74 (m, 8H, COPh, $H_{3'}$, $H_{4'}$, $H_{5'}$), 7.56 and 7.94 (2d, 1H, *CH*NH), 8.28 (dd, 1H, $H_{6'}$), 8.53 and 8.57 (2d, 1H, *CH*NHHet), 9.93 and 10.02 (2d, 1H, CHN*H*Het), 9.53 and 10.76 (2d, 1H, CHN*H*), J_{CH2CH3} = 7.0 Hz, J_{CHNH} = 13.8 Hz, $J_{CHNHHet}$ = 12.3 Hz.

Anal. Calcd. for $C_{22}H_{23}N_3O_5$: C, 64.53; H, 5.66; N, 10.26. Found: C, 64.09; H, 5.38; N, 10.22.

Methyl 2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-(4-methylpyridinyl-2)aminopropenoate (**4**).

A mixture of **1b** (1 mmole, 0.346 g) and 2-amino-4-methylpyridine (**2b**, 1 mmole, 0.108 g) in acetic acid (5 ml) was stirred at room temperature for 7 hours. After the volatile components were

evaporated *in vacuo*, ethanol (2 ml) was added. The precipitate, formed after cooling, was collected by filtration and recrystallized from ethanol to give **4** in 45% yield, mp 185-186°; ms: 409 (M^+); ^{1}H nmr (DMSO-d_6): δ 0.98 and 1.01 (2t, 3H, CH_2CH_3), 2.30 (s, 3H, 4'-Me), 3.81 (s, 3H, $COOCH_3$), 4.03 and 4.07 (2q, 2H, CH_2CH_3), 6.85 (dd, 1H, $H_{5'}$), 6.93 (d, 1H, $H_{3'}$), 6.99-7.74 (m, 5H, COPh,), 7.56 and 7.94 (2d, 1H, CHNH), 8.28 (dd, 1H, $H_{6'}$), 8.53 and 8.57 (2d, 1H, CHNHHet), 9.93 and 10.02 (2d, 1H, CHNHHet), 9.53 and 10.76 (2d, 1H, CHNH), $J_{CH_2CH_3}$ = 7.0 Hz, J_{CHNH} = 13.8 Hz, $J_{CHNHHet}$ = 12.4 Hz, $J_{H5'H6'}$ = 10.3 Hz, $J_{H3'H5'}$ = 5.1 Hz.

Anal. Calcd. for $C_{22}H_{23}N_3O_5$: C, 64.53; H, 5.66; N, 10.26. Found: C, 65.03; H, 5.68; N, 10.31.

Ethyl 2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-(5-chloropyridinyl-2)aminopropenoate (**5**).

A mixture of **1a** (1 mmole, 0.360 g) and 2-amino-5-chloropyridine (**2c**, 1 mmole, 0.128 g) in acetic acid (3 ml) was heated in an oil bath at 100 for 1.5 hour. After the volatile components were evaporated *in vacuo*, and a mixture of ethanol (2 ml) and water (1 ml) was added. The precipitate, formed after cooling, was collected by filtration and recrystallized from a mixture of ethanol and water to give **5** in 43% yield, mp 176-179°; ^{1}H nmr (DMSO-d_6): δ 0.91 and 0.930, 1.24 and 1.25 (2 x 2t, 2 x 3H, 2 x CH_2CH_3), 3.91 and 4.02, 4.18 and 4.23 (2 x 2q, 2 x 2H, 2 x CH_2CH_3), 7.13 (d, 1H, $H_{4'}$), 7.38-7.83 (m, 7H, COPh, $H_{3'}$, CHNH), 7.97 and 8.44 (2d, 1H, CHNH), 8.32 (s, 1H, $H_{6'}$), 9.54 in 10.76 (2d, 1H, CHNH), 10.11 (br s, 1H, CHNHHet), $J_{CH_2CH_3}$ = 7.1 Hz, J_{CHNH} = 13.9 Hz, $J_{H3'H4'}$ = 8.8 Hz.

Anal. Calcd. for $C_{22}H_{22}N_3O_5Cl$: C, 59.53; H, 5.00; N, 9.47. Found: C, 59.03; H, 4.92; N, 9.41.

Methyl 2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-(5-chloropyridinyl-2)aminopropenoate (**6**).

A mixture of **1b** (1 mmole, 0.346 g) and 2-amino-5-chloropyridine (**2c**, 1 mmole, 0.128 g) in acetic acid (3 ml) was stirred at room temperature for 12 hours. The precipitate formed during this time was collected by filtration and recrystallized from a mixture of 2-propanol and water to give **6** in 61% yield, mp 194-196°; ^{1}H nmr (DMSO-d_6): δ 0.91 and 0.93 (2t, 3H, CH_2CH_3), 3.73 (s, 3H, COOMe), 3.91 and 4.00 (2q, 2H, CH_2CH_3), 7.13 (d, 1H, $H_{4'}$), 7.38-7.83 (m, 7H, COPh, $H_{3'}$, CHNH), 7.93 and 8.46 (2d, 1H, CHNH), 8.32 (s, 1H, $H_{6'}$), 9.54 and 10.75 (2d, 1H, CHNH), 10.14 (br s, 1H, CHNHHet), $J_{CH_2CH_3}$ = 7.1 Hz, J_{CHNH} = 13.8 Hz, $J_{H3'H4'}$ = 8.8 Hz.

Anal. Calcd. for $C_{21}H_{20}N_3O_5Cl$: C, 58.68; H, 4.69; N, 9.77. Found: C, 58.57; H, 4.65; N, 9.67.

Ethyl 2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-(6-chloropyridazinyl-3)aminopropenoate (**7**).

A mixture of **1a** (1 mmole, 0.360 g) and 3-amino-6-chloropyridazine (**2e**, 1 mmole, 0.130 g) in acetic acid (3 ml) was heated in an oil bath at 100 for 2 hours. After the volatile components were evaporated *in vacuo*, the mixture of ethanol (2 ml) and water (1 ml) was added. The precipitate, formed after cooling, was collected by filtration and recrystallized from a mixture of ethanol and water to give **7** in 38% yield, mp 200-202°; ms: 444 (M^+); ^{1}H nmr (DMSO-d_6): δ 0.91 and 0.93, 1.26 and 1.28 (2 x 2t, 2 x 3H, 2 x CH_2CH_3), 3.91 and 4.02 (2 x 2q, 2 x 2H, 2 x CH_2CH_3), 7.38-7.50 (m, 5H, COPh), 7.57 (d, 1H, $H_{5'}$), 7.61 and 7.97 (2d, 1H, CHNH), 7.76 (d, 1H, $H_{4'}$), 8.49 (d, 1H, CHNHHet), 9.54 and 10.75 (2d, 1H, CHNH), 10.21 (br s, 1H, CHNHHet), $J_{CH_2CH_3}$ = 7.1 Hz, J_{CHNH} = 14.0 Hz, $J_{H4'H5'}$ = 9.2 Hz.

Anal. Calcd. for $C_{21}H_{21}N_4O_5Cl$: C, 56.70; H, 4.76; N, 12.59. Found: C, 55.81; H, 4.69; N, 12.18.

Methyl 2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-(6-chloropyridazinyl-3)aminopropenoate (**8**).

A mixture of **1b** (1 mmole, 0.346 g) and 3-amino-6-chloropyridazine (**8e**, 1 mmole, 0.130 g) in acetic acid (3 ml) was stirred at room temperature for 15 minutes. The precipitate formed during this time was collected by filtration and recrystallized from a mixture of ethanol and water to give **8** in 41% yield, mp 187-189°; ^{1}H nmr (DMSO-d_6): δ 0.91 and 0.93 (2t, 3H, CH_2CH_3), 3.76 (s, 3H, COOMe), 3.92 and 4.02 (2q, 2H, CH_2CH_3), 7.38-7.50 (m, 5H, COPh), 7.57 (d, 1H, $H_{5'}$), 7.61 and 7.97 (2d, 1H, CHNH), 7.76 (d, 1H, $H_{4'}$), 8.49 (d, 1H, CHNHHet), 9.54 and 10.75 (2d, 1H, CHNH), 10.23 (br s, 1H, CHNHHet), $J_{CH_2CH_3}$ = 7.1 Hz, J_{CHNH} = 14.0 Hz, $J_{CHNHHet}$ = 17.0 Hz, $J_{H4'H5'}$ = 9.2 Hz.

Anal. Calcd. for $C_{20}H_{19}N_4O_5Cl$: C, 55.75; H, 4.44; N, 13.00. Found: C, 55.61; H, 4.33; N, 12.99.

Ethyl 2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-(4,6-dimethylpyrimidinyl-2)aminopropenoate (**9**).

A mixture of **1a** (1 mmole, 0.360 g) and 2-amino-4,6-dimethylpyrimidine (**2f**, 1 mmole, 0.123 g) in acetic acid (3 ml) was heated in an oil bath at 100 for 2.5 hours. After the volatile components were evaporated *in vacuo*, a mixture of ethanol (2 ml) and water (1 ml) was added. The precipitate, formed after cooling, was collected by filtration and recrystallized from ethanol to give **9** in 45% yield, mp 174-176°; ^{1}H nmr (DMSO-d_6): δ 0.90 (t, 3H, CH_2CH_3), 1.24 and 1.26 (2t, 3H, CH_2CH_3), 2.36 (s, 6H, 4'-Me, 6'-Me), 3.90 and 3.99 (2q, 2H, CH_2CH_3), 4.22 (q, 2H, CH_2CH_3), 6.86 (s, 1H, $H_{5'}$), 7.38-7.93 (m, 6H, Ph, CHNH), 8.39 (br s, 1H, CHNHHet), 9.52 and 10.61 (2d, 1H, CHNH), 10.11 (br s, 1H, NHHet), $J_{CH_2CH_3}$ = 7.1 Hz, J_{CHNH} = 13.7 Hz.

Anal. Calcd. for $C_{23}H_{26}N_4O_5$: C, 63.00; H, 5.98; N, 12.78. Found: C, 62.80; H, 6.06; N, 12.84.

Ethyl 2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-(pyrazinyl-2)aminopropenoate (**10**).

A mixture of **1a** (1 mmole, 0.360 g) and 2-aminopyrazine (**2g**, 1 mmole, 0.085 g) in acetic acid (3 ml) was heated in an oil bath at 100 for 2 hours. After the volatile components were evaporated *in vacuo*, a mixture of 2-propanol (2 ml) and water (1 ml) was added. The precipitate, formed after cooling, was collected by filtration and recrystallized from a mixture of 2-propanol and water to give **10** in 52% yield, mp 168-170°; ^{1}H nmr (DMSO-d_6): δ 0.91 and 0.93, 1.24 and 1.25 (2 x 2t, 2 x 3H, 2 x CH_2CH_3), 3.91 and 4.02, 4.18 and 4.23 (2 x 2q, 2 x 2H, 2 x CH_2CH_3), 7.41-8.48 (m, 10H, COPh, $H_{3'}$, $H_{5'}$, $H_{6'}$, 2 x CHNH), 9.54 and 10.76 (2d, 1H, CHNH), 10.31 (br s, 1H, CHNHHet), $J_{CH_2CH_3}$ = 7.1 Hz, J_{CHNH} = 13.9 Hz.

Anal. Calcd. for $C_{21}H_{22}N_4O_5$: C, 61.46; H, 5.40; N, 13.65. Found: C, 61.71; H, 5.47; N, 13.81.

Methyl 2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-(pyrazinyl-2)aminopropenoate (**11**).

A mixture of **1b** (1 mmole, 0.346 g) and 2-aminopyrazine (**2g**, 1 mmole, 0.085 g) in acetic acid (3 ml) was heated in an oil bath at 100 for 2 hours. After the volatile components were evaporated *in vacuo*, a mixture of 2-propanol (2 ml) and water (1 ml) was added. The precipitate, formed after cooling, was collected by filtration and recrystallized from a mixture of 2-propanol and water to give **11** in 55% yield, mp 171-173°; ^{1}H nmr (DMSO-d_6): δ 1.24 and

1.25 (2t, 3H, CH_2CH_3), 3.83 (s, 3H, COOMe), 4.18 and 4.23 (2 x 2q, 2 x 2H, 2 x CH_2CH_3), 7.14-8.48 (m, 9H, COPh, $H_{3'}$, $H_{5'}$, $H_{6'}$, CHNH), 8.47 and 8.52 (2d, 1H, CHNH), 9.13 and 9.17 (2d, 1H, CHNHHet), 9.79 and 11.70 (2d, 1H, CHNH), $J_{CH_2CH_3}$ = 7.1 Hz, J_{CHNH} = 13.9 Hz, $J_{CHNHHet}$ = 12.4 Hz.

Anal. Calcd. for $C_{20}H_{20}N_4O_5$: C, 60.60; H, 5.09; N, 14.13. Found: C, 60.53; H, 5.21; N, 14.16.

Ethyl 2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-(isoxazolyl-3)aminopropenoate (**12**).

A mixture of **1a** (1 mmole, 0.360 g) and 3-aminoisoxazole (**2h**; 1 mmole, 0.084 g) in acetic acid (4 ml) was heated in an oil bath at 120 for 1 hour. After the volatile components were evaporated *in vacuo*, a mixture of ethanol (2 ml) and water (1 ml) was added. The precipitate, formed after cooling, was collected by filtration and recrystallized from a mixture of ethanol and water to give **12** in 54% yield, mp 144-145°; ms: 399 (M^+); ^1H nmr (DMSO-d_6): δ 0.91 and 0.92, 1.23 and 1.25 (2 x 2t, 2 x 3H, 2 x CH_2CH_3), 3.93 and 4.00, 4.16 and 4.18 (2 x 2q, 2 x 2H, 2 x CH_2CH_3), 6.42 (d, 1H, $H_{4'}$), 7.41-7.94 (m, 7H, COPh, 2 x CHNH), 8.73 (d, 1H, $H_{5'}$), 10.01 (br s, 1H, CHNHHet), 9.47 and 10.67 (2d, 1H, CHNH), $J_{CH_2CH_3}$ = 7.1 Hz, J_{CHNH} = 14.0 Hz, $J_{H4'H5'}$ = 1.6 Hz.

Anal. Calcd. for $C_{20}H_{21}N_3O_6$: C, 60.15; H, 5.30; N, 10.52. Found: C, 59.56; H, 5.34; N, 10.42.

Ethyl 2-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-(5-methylisoxazolyl-3)aminopropenoate (**13**).

A mixture of **1a** (1 mmole, 0.360 g) and 3-amino-5-methylisoxazole (**2i**, 1 mmole, 0.098 g) in acetic acid (4 ml) was heated in an oil bath at 120 for 1 hour. After the volatile components were evaporated *in vacuo*, a mixture of ethanol (2 ml) and water (1 ml) was added. The precipitate, formed after cooling, was collected by filtration and recrystallized from a mixture of ethanol and water to give **13** in 51% yield, mp 155-157°; ^1H nmr (DMSO-d_6): δ 0.91 and 0.92, 1.23 and 1.25 (2 x 2t, 2 x 3H, 2 x CH_2CH_3), 2.35 (s, 3H, 5'-CH_3), 3.93 and 4.00, 4.16 and 4.18 (2 x 2q, 2 x 2H, 2 x CH_2CH_3), 6.11 (s, 1H, 5'-CH_3), 7.41-7.93 (m, 7H, COPh, 2 x CHNH), 9.92 (br s, 1H, CHNHHet), 9.48 and 10.67 (2d, 1H, CHNH), $J_{CH_2CH_3}$ = 7.1 Hz, J_{CHNH} = 14.0 Hz.

Anal. Calcd. for $C_{21}H_{23}N_3O_6$: C, 61.01; H, 5.61; N, 10.16. Found: C, 60.76; H, 5.79; N, 10.12.

The Synthesis of (2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-substituted Fused Pyrimidinones **14-18**.

General Procedure (Method A).

A mixture of reagent **1** (1 mmole) and heterocyclic amine **2** (1 mmole) in acetic acid (5 ml) was heated in an oil bath at 110° for several hours. The reaction was followed by tlc (DC-Alufolien Kieselgel 60 F 254, 0.2 mm, E. Merck, and ether as a solvent). After the reaction was completed, the volatile components were evaporated *in vacuo*. To the oily residue a mixture of ethanol and water was added. The precipitate, formed after cooling, was collected by filtration and recrystallized from an appropriate solvent to give productes **14-18**.

The following compounds were prepared in this manner:

3-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**14**).

This compound was prepared from **1a** (0.360 g) and 2-amino-4-methylpyridine (**2b**, 0.108 g), by heating for 1 hour, to give **14** in 67% yield, mp 178-180° (from ethanol); ^1H nmr (DMSO-d_6): δ 0.89 and 0.94 (2t, 3H, CH_2CH_3), 2.50 (s, 3H, 8-CH_3), 3.96 and 4.02 (2q, 2H, CH_2CH_3), 7.25-7.63 (m, 7H, COPh, H_7, H_9), 8.47-8.91 (m, 3H, CHNH, H_2, H_6), 10.79 and 11.99 (2d, 1H, CHNH), $J_{CH_2CH_3}$ = 7.1 Hz, J_{CHNH} = 14.0 Hz.

Anal. Calcd. for $C_{21}H_{19}N_3O_4$: C, 66.88; H, 5.07; N, 11.13. Found: C, 66.82; H, 5.01; N, 11.14.

Method B.

A solution of methyl 2-(2-benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-(4-methylpyridinyl-2)aminopropenoate (**4**, 0.5 mmole, 0.205 g) in acetic acid (3 ml) was heated in an oil bath at 110° for 45 minutes. The volatile components were evaporated *in vacuo*. To the oily residue ethanol (2 ml) was added. The precipitate, formed after cooling, was collected by filtration and recrystallized from ethanol to give a product identical to compound **14** in 91% yield.

3-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-4*H*-pyrido-[1,2-*a*]pyrimidin-4-one (**15**).

This compound was prepared from **1a** (0.360 g) and 2-aminopyridine (**2a**, 0.094 g), by heating for 1 hour, to give **15** in 59% yield, mp 143-144° (from 2-propanol); ^1H nmr (DMSO-d_6): δ 0.89 and 0.94 (2t, 3H, CH_2CH_3), 3.97 and 4.01 (2q, 2H, CH_2CH_3), 7.40-7.89 (m, 8H, COPh, H_7, H_8, H_9), 8.46-9.01 (m, 3H, CHNH, H_2, H_6), 10.83 and 11.99 (2d, 1H, CHNH), $J_{CH_2CH_3}$ = 7.1 Hz, J_{CHNH} = 14.0 Hz.

Anal. Calcd. for $C_{20}H_{17}N_3O_4$: C, 66.11; H, 4.72; N, 11.56. Found: C, 66.20; H, 4.55; N, 11.64.

3-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-7-chloro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**16**).

This compound was prepared from **1b** (0.346 g) and 2-amino-5-chloropyridine (**2c**, 0.128 g), by heating for 5 hours, to give **16** in 50% yield, mp 150-151° (from a mixture of 2-propanol and water); ^1H nmr (DMSO-d_6): δ 0.88 and 0.93 (2t, 3H, CH_2CH_3), 3.95 and 4.01 (2q, 2H, CH_2CH_3), 7.39-7.91 (m, 7H, COPh, H_8, H_9), 8.43-8.97 (m, 3H, CHNH, H_2, H_6), 10.78 and 11.90 (2d, 1H, CHNH), $J_{CH_2CH_3}$ = 7.1 Hz, J_{CHNH} = 14.0 Hz.

Anal. Calcd. for $C_{20}H_{16}N_3O_4Cl$: C, 60.38; H, 4.05; N, 10.56. Found: C, 59.99; H, 3.63; N, 10.80.

3-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-9-hydroxy-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**17**).

This compound was prepared from **1b** (0.346 g) and 2-amino-3-hydroxypyridine (**2d**, 0.111 g), by heating for 2 hours, to give **17** in 64% yield, mp 168-170° (from a mixture of ethanol and water); ms: 379 (M^+); ^1H nmr (DMSO-d_6): δ 0.89 and 0.93 (2t, 3H, CH_2CH_3), 3.96 and 4.02 (2q, 2H, CH_2CH_3), 7.16-7.64 (m, 7H, COPh, H_7, H_8), 8.51-8.82 (m, 3H, CHNH, H_2, H_6), 10.78 and 11.90 (2d, 1H, CHNH), OH exchanged, $J_{CH_2CH_3}$ = 7.1 Hz, J_{CHNH} = 14.0 Hz.

Anal. Calcd. for $C_{20}H_{17}N_3O_5$: C, 63.32; H, 4.52; N, 11.08. Found: C, 62.97; H, 4.33; N, 10.51.

6-(2-Benzoyl-2-ethoxycarbonyl-1-ethenyl)amino-3-cyano-7*H*-pyrazolo[1,5-*a*]pyrimidin-7-one (**18**).

This compound was prepared from **1b** (0.346 g) and 3-amino-5-cyanopyrazole (**2j**, 0.108 g), by heating for 2.5 hours, to give **18** in 56% yield, mp 215-217° (from a mixture of methanol and water); ^1H nmr (DMSO-d_6): δ 0.88 and 0.93 (2t, 3H, CH_2CH_3), 3.95 and 4.01 (2q, 2H, CH_2CH_3), 7.41-7.62 (m, 6H, COPh, H_5), 8.44 (s, 1H,

H_2), 8.17 and 8.54 (2d, 1H, C*H*NH), 10.56 and 11.78 (2d, 1H, CHN*H*), NH exchanged, $J_{CH_2CH_3}$ = 7.0 Hz, J_{CHNH} = 13.7 Hz.

Anal. Calcd. for $C_{19}H_{15}N_5O_4$: C, 60.48; H, 4.01; N, 18.56. Found: C, 60.42; H, 3.96; N, 18.76.

Removal of the *N*-protecting Group.

3-Amino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**19**).

Method A.

To a suspension of the fused pyrimidine **14** (0.377 g, 1 mmole) in ethanol (4 ml) hydrazine hydrate (99%, 0.4 ml) was added. The mixture was heated under reflux temperature for 20 minutes. The volatile components were evaporated *in vacuo*. To the oily residue methanol (3 ml) was added. The precipitate was collected by filtration and recrystallized from an appropriate solvent to give compound **19** in 91% yield, mp 217-218° (from methanol), (lit [13] 215-225°); ^{1}H nmr (DMSO-d_6): δ 2.34 (s, 3H, CH_3-Het), 5.01 (s, 2H, NH_2), 6.97 (dd, 1H,H_7), 7.26 (d, 1H, H_9), 7.86 (s, 1H, H_2), 8.66 (d, 1H, H_6), $J_{H6,H7}$ = 7.4 Hz, $J_{H6,H9}$ = 1.7 Hz.

Anal. Calcd. for $C_9H_9N_3O$: C, 61.70; H, 5.18; N, 23.99. Found: C, 61.68; H, 5.15; N, 24.36.

4-Ethoxycarbonyl-3-phenylpyrazole (**20**).

The filtrate after reaction with hydrazine was evaporated *in vacuo*. The oily residue crystallizes after a long period at room temperature to give pyrazole **20**, mp 71-73°; ms: 216 (M^+); ^{1}H nmr (deuteriochloroform): δ 1.28 (t, 3H, CH_2CH_3), 4.25 (q, 2H, CH_2CH_3), 7.42-7.47 (m, 3H, Ph), 7.66-7.70 (m, 2H, Ph), 8.02 (s, 1H, H_5), $J_{CH_2CH_3}$ = 7.1 Hz.

Method B.

3-Amino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one hydrochloride (**21**, 0.5 mmole, 0.106 g) was dissolved in water (5 ml) and a saturated solution of sodium bicarbonate was dropwise added to *p*H = 7-8. The precipitate was collected by filtration and recrystallized from a mixture of methanol and water to give a product identical to compound **19** in 89% yield.

3-Amino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one Hydrochloride (**21**).

A mixture of **14** (0.5 mmole, 0.188 g) and hydroxylamine hydrochloride (0.5 mmole, 0.034 g) in ethanol (3 ml) was heated under reflux for 9 hours. The precipitate formed during this time was collected by filtration and recrystallized from a mixture of ethanol and water to give **21** in 84% yield, mp 222-224°; ^{1}H nmr (DMSO-d_6): δ 2.50 (s, 3H, CH_3-Het), 7.350 (dd, 1H, H_7), 7.59 (d, 1H, H_9), 7.89 (s, 1H, H_2), 8.85 (d, 1H, H_6), NH_3^+ exchanged, $J_{H6,H7}$ = 7.4 Hz, $J_{H6,H9}$ = 1.7 Hz.

Anal. Calcd. for $C_9H_{10}N_3OCl$: C, 51.07; H, 4.76; N, 19.85. Found: C, 51.16; H, 4.77; N, 20.15.

4-Ethoxycarbonyl-5-phenylisoxazole (**22**).

The filtrate after a reaction with hydoxylamine was evaporated *in vacuo* to give the oily product **22** [14]; ms: 217 (M^+); ^{1}H nmr (deuteriochloroform): δ 1.35 (t, 3H, CH_2CH_3), 4.33 (q, 2H, CH_2CH_3), 7.45-7.53 (m, 3H, Ph), 8.09-8.12 (m, 2H, Ph), 8.63 (s, 1H, H_3), $J_{CH_2CH_3}$ = 7.1 Hz.

Anal. Calcd. for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.18; H, 5.10; N, 6.90.

X-ray Structure Determination.

A yellow crystal with dimensions 0.48 0.33 0.24 mm was used for data collection on an Enraf Nonius CAD-4 diffractometer with graphite monochromatized MoKα radiation. Accurate unit-cell parameters were obtained from a least-squares refinement of the angular settings of 73 reflections in the range $8.1° < \theta < 15.0°$. Crystals are triclinic with cell dimensions a = 8.109(1), b = 9.607(2), c = 13.607(2) Å, α = 99.06(2), β = 101.77(1), γ = 109.16(1)° and space group P$\bar{1}$ (no. 2). Other crystal data are $C_{19}H_{24}N_2O_5$, M_r = 360.4, V = 950.9(3) Å^3, Z = 2, D_x = 1.259 Mg/m^3, μ = 0.0855 mm^{-1}, F(000) = 384, T = 293(2) K. Intensity data were collected in the ω-2θ scan mode with a scan width (0.80 + 0.3 tgθ)°, aperture (2.4+0.9 tgθ) mm and maximum scan time 60 seconds. Background was measured at 1/4 of the scan at each limit. Entire sphere to θ_{max} 28° of data was measured with an index range $-10 \le h \le 10$, $-12 \le k$ 12 and $-17 \le l \le 17$. The intensity check reflections (1,5,2; 1,1,5; 1,4,1) were monitored periodically every 20000 seconds of the scanning time. A change of -1.44% of intensities of check reflections was observed and correction applied. Orientation control using reflections (2,-5,4; 4,-2,-6; 2,1,-6) was every 600 reflections. Due to the low value of the linear absorption coefficient (0.0855 mm^{-1}) absorption was ignored. 9247 reflections were collected, averaging gave 4580 independent reflections with R_{int} = 0.050; 3199 of them were observed ($I > 2.5\ \sigma(I)$).

The structure was solved by direct methods using the SIR92 [15] program. The positions of hydrogen atoms were partially obtained from an intermediate difference Fourier map and partially calculated on the basis of standard geometry. Full-matrix least-squares refinement minimizing $\Sigma w(|F_O|-|F_C|)^2$ with an empirical weighting scheme was employed. Most of the hydrogen atom positions with their isotropic temperature factors were refined. Also the correction for secondary extinction [16] was applied with g = 0.98(14)•10^4. In the final cycle were 3902 contributing reflections (including were those unobserved reflections for which F_c was greater than F_o) and 324 parameters. The final R and R_w values were 0.058 and 0.073 respectively. Average and maximum shift to e.s.d. ratio were 0.0045 and 0.0634. The residual density in the final difference map was max. 0.293 and min. -0.362 e/Å^3.

The Xtal3.4 [17] system of crystallographic programs was used for the correlation and reduction of data, structure refinement and interpretation. ORTEPII [18] was used to produce molecular graphics. All calculations were performed on 486 PC computer.

Final atomic coordinates and equivalent isotropic thermal parameters with their e.s.d.'s are reported in Table 1. Bond lengths and bond angles for nonhydrogen atoms are listed in Table 2. An ORTEP drawing [18] of the asymmetric unit showing the atom-labeling scheme is presented in Figure 2 and molecular packing in Figure 3.

Bond C(7)=C(11) [1.361(3) Å] is longer than the unpolarised double bond in ethylene [1.314(6) Å] [19]. This is the result of the conjugation of this double bond with the nitrogen atom lone pair and carbonyl group of the ethoxycarbonyl moiety. This is reflected also in the bond lengths of C(7)-C(8) [1.460(3) Å] and C(11)-N(2) [1.329(3) Å] which are shorter than corresponding unconjugated single bonds (C(sp2)-C(sp2) 1.484(17) Å [20] and C(sp2)-N(sp2) 1.470(5) Å [21]). Bond C(2)=C(3) [1.393 Å] is even longer than C(7)=C(11). There are two reasons for greater π electron delocalization in this part of molecules. On C(7) there was bonded only one typical electron accepting group (ethoxycarbonyl), while on C(2) are bonded two groups with such character. The above mentioned increased delocalization is also consistent with RAHB theory [22] which tells that π conjugated system undergoes greater

delocalization when it forms either intramolecular or infinite chain intermolecular hydrogen bonding. In our case π conjugated system includes N(1)-H..O(5) intramolecular hydrogen bond with N(1)..O(5) contact distance 2.683(2) Å, O(5)..H distance 2.02(3) Å and N(1)-H..O(5) angle 130(3)°. Delocalization of π electrons results also in the shortening of bonds C(3)-N(1) [1.314(3) Å], C(2)-C(6) [1.449(3) Å] and C(1)-C(2) [1.466(3) Å] comparing to formal single bonds. C(2)-C(6) bond is shorter (and thus have more double bond character) than C(1)-C(2) bond and C(6)=O(5) is longer (and thus have more single bond character) than C(1)=O(1) bond. This is in accordance with above mentioned RAHB theory since benzoyl carbonyl group which takes part in the intramolecular hydrogen bonding participates more in the π electron delocalization than does C(1)=O(1) carbonyl group. Intermolecular contacts which result in the molecular packing are dominated by van der Waals interactions.

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REFERENCES AND NOTES

[1] B. Stanovnik, *Molecules*, **1**, 123 (1996); and references cited therein.

[2] G. Soršak, A. Sinur, L. Golič, and B. Stanovnik, *J. Heterocyclic Chem.*, **32**, 921 (1995).

[3] L. Selič and B. Stanovnik, *J. Heterocyclic Chem.*, in print.

[4] R. Toplak, L. Selič, G. Sorčak, and B. Stanovnik, *Heterocycles*, **45**, 555 (1997).

[5] S. Strah, S. Golič Grdadolnik, and B. Stanovnik, *J. Heterocyclic Chem.*, **34**, 263 (1997).

[6] S. Golič Grdadolnik and B. Stanovnik, *Magn. Reson. Chem.*, **35**, 482 (1997).

[7] G. Menozzi, L. Mosti, and P. Schenone, *J. Heterocyclic Chem.*, **24**, 1669 (1987).

[8] J. R. Beck and M. P. Lynch, *J. Heterocyclic Chem.*, **24**, 693 (1987).

[9] P. Schenone, L. Mosti , and G. Menozzi, *J. Heterocyclic Chem.*, **19**, 1355 (1982).

[10] G. Menozzi, P. Schenone, and L. Mosti, *J. Heterocyclic Chem.*, **20**, 645 (1983).

[11] J. Svete, M. Aljaž-Rožič, and B. Stanovnik, *J. Heterocyclic Chem.*, **34**, 177 (1997).

[12] G. Horváth, I. Hermecz, Á. Horvath, M. Pongor-Csákvári, L. Pusztay, Á. I. Kiss, L. Czakó, and O. H. Abdirizak, *J. Heterocyclic Chem.*, **22**, 481 (1985).

[13] J. Smodiš, B. Stanovnik, and M. Tišler, *J. Heterocyclic Chem.*, **31**, 125 (1994).

[14] R. Huisgen and M. Christl, *Chem. Ber.*, **106**, 3291 (1973).

[15] A. Altomare, M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, A. Guagliardi, and G. Polidori, *J. Appl. Cryst.*, **27**, 435 (1994).

[16] A. C. Larson, *Crystallographic Computing*, F. R. Ahmed, S. R. Hall and C. P. Huber, eds, Munksgaard, Copenhagen, 1970, p 291.

[17] S. R. Hall, G. S. D. King, and J. M. Stewart, The Xtal3.4 User's Manual, University of Western Australia, Lamb, Perth, 1995.

[18] C. K. Johnson, ORTEPII. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA, 1976.

[19] G. J. H. van Nes and A. Vos, *Acta Cryst.* **B33**, 1653 (1977).

[20] F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, and R. Taylor, *J. Chem. Soc., Perkin Trans.* **2**, S1-S19 (1987).

[21] A. Camerman, L. H. Jensen, and A. T. Balaban, *Acta Cryst.*, **B25**, 2623 (1969).

[22] C. Giacovazzo, H. L. Monaco, D. Viterbo, F. Scordari, G. Gili, G. Zanotti, and M. Catti, Fundamentals of Crystallography, Oxford University Press: Oxford, 1992, p 521.