Amino Acids in the Synthesis of Heterocyclic Systems. Synthesis of γ-(5-(1,2,4-Triazinylidene))-α,β-dehydro-α-amino Acid Derivatives and 6*H*-Pyrido[1,2-*d*][1,2,4]triazin-6-ones

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Dedicated to Professor Dr. Fritz Sauter, Technical University of Vienna, on the occasion of his 65th birthday.

5-(1,2,4-Triazinyl) substituted enamines **3** react with 5(4*H*)-oxazolones **4** in acetic anhydride to give acetylated products **5**, while in toluene-acetic acid mixture nonacetylated products **9** are formed. Both types of products were isolated as (*E*,*Z*) mixtures. Compounds **5** and **9** rearrange into 6*H*-pyrido[1,2-*d*]-[1,2,4]triazin-6-ones **12** by heating in formic acid or in xylene, respectively. Compounds **5** are transformed in the presence of nucleophiles, such as sodium alkoxides or sodium amides *via* anionic form **10** into corresponding esters **13** and amides **14** of γ-(5-(1,2,4-triazinylidene)) substituted derivatives of α-amino-2-butenoic acid, which exist in 2-(*Z*),4-(*Z*) form.

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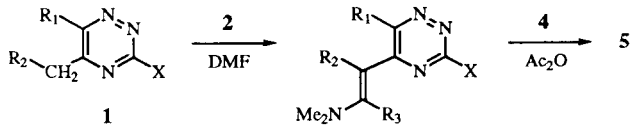
The methods for the preparation of heteroaryl substituted α-amino acids are very limited. γ-Pyridinyl substituted α-amino acids have been prepared by addition of acetamidomalonates to vinylpyridine [1-3]. *N*-Acylamino acid analogues of 2(1*H*)-quinolinone have been synthesized and tested for antiulcer activity against acetic acid induced gastric ulcer in rats [4] and 2-amino-4-(3-pyridinyl)butyric acid derivatives have been synthesized and tested as weak inhibitors of human leucocytic elastase [5]. Some nonproteinogenic amino acids exhibit ACE inhibition and antihypertensive activity [6]. Many of them have been isolated from natural sources, mostly as components of microbial metabolites [7].

Recently, two novel methods for the preparation of unsaturated α-amino acids have been developed in our laboratory. According to the first method, *N*,*N*-dimethyl-*N*-heteroarylformamidines, prepared from heterocyclic amines and *N*,*N*-dimethylformamide dimethyl acetal (DMFDMA), have been treated with 5-oxo-2-phenyl-1,3-oxazole in the presence of acetic anhydride to give heteroarylaminomethyleneoxazolones as intermediates. They have been converted with nucleophiles to give various derivatives of β-heteroarylamino-α,β-dehydro-α-amino acid derivatives [8,9]. According to the second method, methyl 2-benzoylamino-3-dimethylaminopropenoate has been employed as a versatile reagent, in which dimethylamino group can be substituted either with *N*- or *C*-nucleophiles to give β-aryl (or heteroaryl) amino- and β-aryl (or heteroaryl)-α,β-dehydro-α-amino acid derivatives, respectively [10-13]. Many of these compounds easily cyclize under reaction conditions to give α-pyranones, benzopyranones, pyranoazoles and pyranoazines, azolo- and azinopyridines, and azolo- and azinopyrimidines [14]. Heterocyclic compounds with an active methyl group attached at α-position in respect to the ring nitrogen atom give the corresponding enamines, which cyclize into fused pyridinones [15].

In this communication, we describe the reactions of enamines **3**, prepared from 1,2,4-triazine derivatives **1**, with an active methyl or methylene group at 5 position, and amide acetals **2**, with various 2-substituted 5(4*H*)-oxazolones **4**, formed *in situ* from the corresponding *N*-acylated derivatives of glycine and acetic anhydride. In these reactions, a red precipitate **5** is formed (Scheme 1). From 5-((*E*)-2-(dimethylamino)ethenyl)-3-ethylmercapto-6-methyl-1,2,4-triazine (**3a**) and 2-phenyl-5(4*H*)-oxazolone the compound **5a** was obtained, for which the molecular formula $C_{19}H_{18}N_4O_3S$ was established on the basis of microanalyses for C, H, and N, supported by mass spectrum (M^+ 382). The ^1H nmr spectrum shows that this material is a mixture of two isomeric compounds, each of them containing one acetyl group. The coupling constant for olefinic protons (J = 12.0 Hz) excluded the *cis* orientation around the double bond. On this basis, three different structures **6**, **7**, and **8** are possible (Scheme 2). The attempts to separate both isomers by tlc on silica gel were unsuccessful. However, by hydrolysis only one isomer was hydrolyzed. The nonhydrolyzed isomer was used for the NOESY experiments in order to elucidate its structure by observing both protons in the chain between the oxazolone and 1,2,4-triazine part of the molecule. The structures **6** and **7** are excluded, since they exist only in one isomeric form, and the observed chemical shifts for protons of the acetyl group, δ = 2.43 ppm, equal for both isomers, exclude the mixture of them. Therefore, three possible isomeric pairs of the general structure **8** were further discussed.

Scheme 1

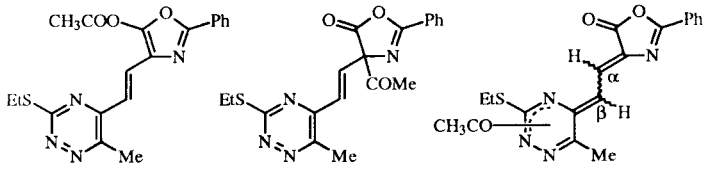


1,3	R_1	R_2	R_3	X
a	Me	H	H	SEt
b	Me	H	H	SMe
c	Me	H	H	OMe
d	Me	H	Me	SEt
e	$CH_2CH_2CH_2$		H	SEt

2a (R_3 = H)
2b (R_3 = Me)

4
(for R, Y see Table 1)

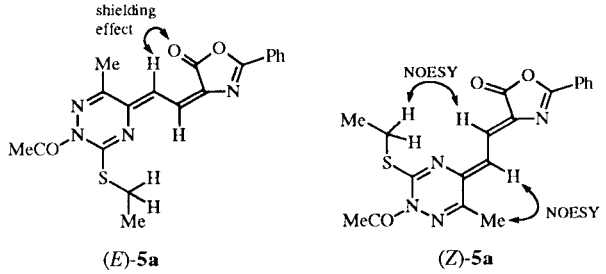
Scheme 2



6 **7** **8**

The acetyl group must be attached to one of the nitrogens of the 1,2,4-triazine part of the molecule. The acetyl group is attached to nitrogen at 2 position, since the nitrogen at 4 position is less favorable and could be excluded on the basis of the weak NOESY correlation between α-H and SCH_2CH_3 group. The orientation around the 5-*exo* double bond of the triazine ring is supposed to be (*Z*) due to the steric reasons supported by the NOESY correlation between β-H and 6-Me group. On this basis, we can conclude that the product **5a** is 4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone and consists of two compounds (*E*)-**5a** and (*Z*)-**5a** that are geometric isomers with respect to the 4-*exo* double bond of the oxazole ring (Scheme 3). The differentiation between them was made on the basis of the chemical shifts for β-H protons. To the isomer with the β-H at higher field (δ = 6.60 ppm) was assigned the structure (*E*)-**5a** and to the isomer with the β-H at lower field (δ = 7.08 ppm) the structure (*Z*)-**5a**, due to shielding effect of the carbonyl group.

Scheme 3



(*E*)-**5a** (*Z*)-**5a**

When the reaction of 5-(1,2,4-triazinyl) substituted enamines **3** and 2-phenyl-5(4*H*)-oxazolone was carried out in an inert solvent in the presence of small amounts of acetic acid, the nonacetylated 4-((*Z*)-2-(2,5-dihydro-5-(1,2,4-triazinylidene))ethylidene-2-phenyl-5(4*H*)-oxazolone isomeric pairs **9** were isolated (Scheme 4). These compounds are identical with the compounds obtained by deacetylation of the acetylated analogues **5** in sodium hydroxide solution followed by acidification. The alkaline solution is of purple color, indicating a high delocalization of the intermediate anion **10**. Methylation of such anion, obtained from **5a**, with methyl iodide gave 4-((*Z*)-2-(2,5-dihydro-2,6-dimethyl-3-ethylmercapto-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**11**).

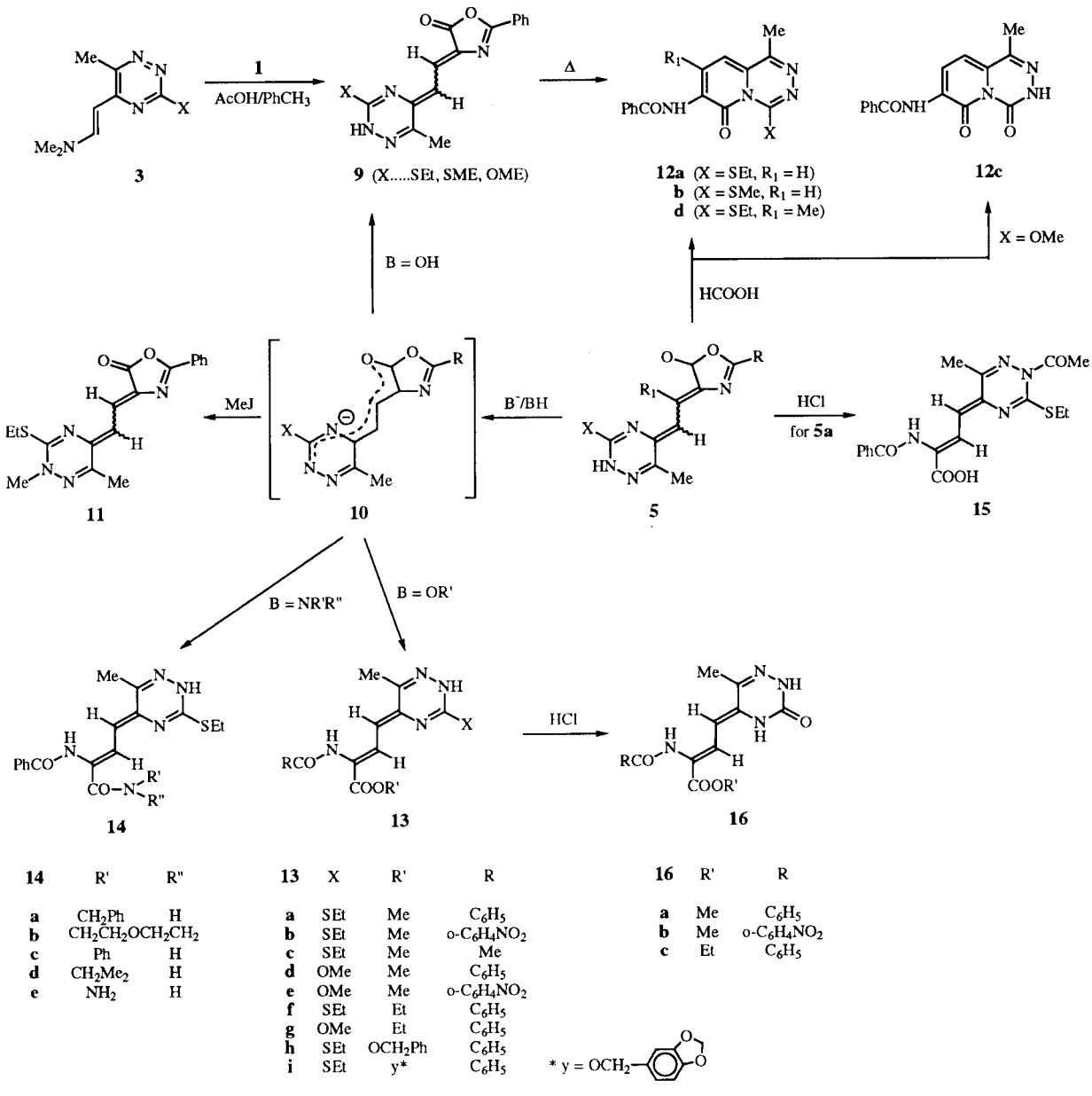
4-((*Z*)-2-(2,5-Dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone mixture **9a**, when heated in xylene, was cyclized into 7-benzoylamino-4-ethylmercapto-1-methyl-6*H*-pyrido[1,2-*d*][1,2,4]triazin-6-one (**12a**). The derivatives of the same bicyclic systems were obtained also from acetylated analogues **5** by heating in formic acid in order to remove the acetyl group before cyclization. Methoxy group at 3 position in 4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-methoxy-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5h**) was hydrolyzed during this procedure to give 7-benzoylamino-3,4-dihydro-1-methyl-6*H*-pyrido[1,2-*d*][1,2,4]triazine-4,6-dione (**12c**).

The treatment of various acetylated 4-((*Z*)-2-(2,5-dihydro-5-(1,2,4-triazinylidene))ethylidene)-5(4*H*)-oxazolone mixtures **5** with an alkoxide in the corresponding alcohol produced 4-(2-(2,5-dihydro-5-(1,2,4-triazinylidene))-2-acylamino-2-butenoic esters **13** with simultaneous removing of the acetyl group. Analogously, the corresponding butenamides **14** were prepared by treatment of the isomeric mixture **5** with amines in the presence of sodium hydride. Esters **13** and amides **14** exist only in one isomeric form.

The NOESY experiments for methyl 2-benzoylamino-4-(2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-2-butenoate (**13a**) show the same orientation of the 1,2,4-triazine ring as for the compounds **5**, while the correlation between 2-NH and 4-H confirms the (*Z*) orientation around 2,3-double bond.

The (*E*) isomer of 4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5a**) was almost completely hydrolyzed into (*Z*)-4-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-2-benzoylamino-(*Z*)-2-butenoic acid (**15**) by refluxing in hydrochloric acid while the (*Z*) isomer was recovered. Trials to obtain acids from esters **13** or amides **14** by refluxing in aqueous or ethanolic hydrochloric acid led in some cases only to the hydrolysis at the 3 position of the

Scheme 4



14	R'	R"
a	CH_2Ph	H
b	$CH_2CH_2OCH_2CH_2$	
c	Ph	H
d	CH_2Me_2	H
e	NH_2	H

13	X	R'	R
a	SEt	Me	C_6H_5
b	SEt	Me	o-$C_6H_4NO_2$
c	SEt	Me	Me
d	OMe	Me	C_6H_5
e	OMe	Me	o-$C_6H_4NO_2$
f	SEt	Et	C_6H_5
g	OMe	Et	C_6H_5
h	SEt	OCH_2Ph	C_6H_5
i	SEt	y*	C_6H_5

16	R'	R
a	Me	C_6H_5
b	Me	o-$C_6H_4NO_2$
c	Et	C_6H_5

* y = OCH_2

triazine part of the molecule isolating various 2-acylamino-(*Z*)-4-(6-methyl-3-oxo-2,3,4,5-tetrahydro-5-(1,2,4-triazinylidene))-(*Z*)-2-butenoic esters (**16**).

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ^1H nmr spectra were obtained on a Varian EM-360 or a Varian VXR-300 instrument with TMS as internal standard and elemental analyses for C, H, and N on a Perkin-Elmer Analyzer 2400.

The following compounds were prepared according to the procedures described in literature: 2-phenyl-5(4*H*)-oxazolone [16], *N*-dithiocarbobenzoxyglycine [17], various *N*-acylglycines [18]. All chromatographic purifications were carried out on silica gel E. Merck 0.063-0.200 mm.

[1,2,4]Triazines **1**.

These compounds were synthesized according to the procedure in literature [19], which was applied on the following new compounds:

5,6-Dimethyl-3-ethylmercapto-1,2,4-triazine (**1a**).

Diacetyl (1.03 g, 12 mmoles), dissolved in the water solution of sodium hydrogencarbonate (9 g/500 ml), was cooled to 0° and added into a solution of *S*-ethylcarbazonium bromide (20 g, 10 mmoles) in water (300 ml) at 0°. The mixture was stirred one hour at 0° and was left for further five hours in the refrigerator (about 5°). The product was extracted with chloroform (30 ml,

Table 1

5	R_1	R_2	R_3	X	Y	R	Procedure	Reaction Time	(*E*)-**5**:(*Z*)-**5**	Color	Mp (°C)	Yield %
a	Me	H	H	SEt	O	C_6H_5	A	10 min	1:1	orange red	187-190 [a]	77
b	Me	H	H	SEt	O	*p*-ClC_6H_4	A	1 h	5:4	red	199-203 [b]	29
c	Me	H	H	SEt	O	*p*-MeC_6H_4	A	30 min	1:1	red	187-190 [b]	57
d	Me	H	H	SEt	O	*p*-$NO_2C_6H_4$	A	5 min	1:1	deep red	238-240 [c]	51
e	Me	H	H	SEt	O	*o*-$NO_2C_6H_4$	A	2 h	3:2	orange red	184-187 [b]	12
f	Me	H	H	SEt	O	Me	B	30 min	3:1	brownish yellow	191-192 [b]	74
g	Me	H	H	SMe	O	C_6H_5	A	10 min	3:1	red	252-256 [a]	81
h	Me	H	H	OMe	O	C_6H_5	A	10 min	varies	red	189-192 [c]	82
i	Me	H	H	OMe	O	o-$NO_2C_6H_4$	A	2 h	(*E*)>>(*Z*)	orange red	196-198 [c]	10
j	Me	H	Me	SEt	O	C_6H_5	A	20 min	2:1	red	216-218 [a]	16 [d]
k	$CH_2CH_2CH_2$		H	SEt	O	C_6H_5	A	10 min	3:2	red	231-235 [a]	29 [d]
l	Me	H	H	SEt	S	$SCH_2C_6H_5$	B	2 h	only one [e]	red	181-183 [a]	91

[a] From toluene. [b] From acetonitrile. [c] From acetic anhydride. [d] Calculated on **1**. [e] The nmr data for **5l** were closer to nmr data for (*E*)-**5** than for (*Z*)-**5**.

ten times), the combined extract was dried over magnesium sulfate and evaporated to the oily residue, which was fractionally distilled under reduced pressure, bp 134-136° (5.5 mbar), yield 90%; ^{1}H nmr (deuteriochloroform): δ 1.44 (t, 3H, CH_2*Me*), 2.51 (s, 3H, 6-Me), 2.64 (s, 3H, 5-Me), 3.27 (q, 2H, CH_2Me), $J_{CH_2CH_3}$ = 8.0 Hz.

3-Ethylmercapto-5,6,7,8-tetrahydrobenzo[1,2,4]triazine (**1d**).

This compound was prepared according to the procedure for 5,6-dimethyl-3-ethylmercapto-1,2,4-triazine (**1a**), from 1,2-cyclohexandione in 90% yield, mp 31-32° (from hexane); ^{1}H nmr (deuteriochloroform): δ 1.43 (t, 3H, CH_2*Me*), 1.92 (deg tt, 4H, 6,7-CH_2), 2.7-3.2 (m, 4H, 5,8-CH_2), 3.25 (q, 2H, CH_2Me), $J_{CH_2CH_3}$ = 8.0 Hz.

Anal. Calcd. for $C_9H_{13}N_3S$: C, 55.35; H, 6.71; N, 21.52. Found: C, 55.62; H, 6.86; N, 21.81.

5-((*E*)-2-(*N*,*N*-Dimethylamino)ethenyl)-1,2,4-triazines **3a-d**. General Procedure.

A mixture of triazine **1** (10 mmoles), *N*,*N*-dimethylformamide (90 ml) and DMFDMA (**2a**) (2.4 g, 20 mmoles) was heated under reflux for ten minutes. Volatile compounds were evaporated *in vacuo*, the residue was crystallized from cyclohexane.

5-((*E*)-2-(*N*,*N*-Dimethylamino)ethenyl)-3-ethylmercapto-6-methyl-1,2,4-triazine (**3a**).

This compound was prepared from 5,6-dimethyl-3-ethylmercapto-1,2,4-triazine (**1a**) in 71% yield, mp 98-100°; ^{1}H nmr (deuteriochloroform): δ 1.43 (t, 3H, CH_2*Me*), 2.44 (s, 3H, 6-Me), 3.09 (s, 6H, NMe_2), 3.25 (q, 2H, CH_2Me), 4.89 (d, C*H*=CHN), 8.14 (d, CH=C*H*N), $J_{CH_2CH_3}$ = 8.0 Hz, $J_{CH=CH}$ = 12.0 Hz.

Anal. Calcd. for $C_{10}H_{16}N_4S$: C, 53.54; H, 7.19; N, 24.98. Found: C, 53.68; H, 7.15; N, 24.98.

5-((*E*)-2-(*N*,*N*-Dimethylamino)ethenyl)-6-methyl-3-methylmercapto-1,2,4-triazine (**3b**).

This compound was prepared from 2,6-dimethyl-3-methylmercapto-1,2,4-triazine (**1b**) [19] in 75% yield, mp 126-128°; ^{1}H nmr (deuteriochloroform): δ 2.44 (s, 3H, 6-Me), 2.61 (s, 3H, SMe), 3.08 (s, 6H, NMe_2), 4.82 (d, C*H*=CHN), 8.08 (d, CH=C*H*N), $J_{CH=CH}$ = 12.5 Hz.

Anal. Calcd. for $C_9H_{14}N_4S$: C, 51.40; H, 6.71; N, 26.64. Found: C, 51.50; H, 6.94; N, 26.64.

5-((*E*)-2-(*N*,*N*-Dimethylamino)ethenyl)-3-methoxy-6-methyl-1,2,4-triazine (**3c**).

This compound was prepared from 2,6-dimethyl-3-methoxy-1,2,4-triazine (**1c**) [19] in 66% yield, mp 101-102°; ^{1}H nmr (deuteriochloroform): δ 2.35 (s, 3H, 6-Me), 3.07 (s, 6H, NMe_2), 3.91 (s, 3H, OMe), 4.97 (d, C*H*=CHN), 8.09 (d, CH=C*H*N), $J_{CH=CH}$ = 12.5 Hz.

Anal. Calcd. for $C_9H_{14}N_4O$: C, 55.65; H, 7.27; N, 28.84. Found: C, 55.15; H, 7.27; N, 28.44.

5-((*E*)-2-(*N*,*N*-Dimethylamino)ethenyl)-3-ethylmercapto-5,6,7,8-tetrahydrobenzo[1,2,4]triazine (**3d**).

This compound was prepared from 3-ethylmercapto-5,6,7,8-tetrahydrobenzo[1,2,4]triazine (**1d**) and was used further without purification, yield not determined, mp 110-114°; ^{1}H nmr (deuteriochloroform): δ 1.42 (t, 3H, CH_2*Me*), 1.84 (deg tt, 2H, 7-CH_2), 2.73 (t, 2H, 6-CH_2), 2.89 (t, 2H, 8-CH_2), 3.16 (q, 2H, CH_2Me), 3.18 (s, 6H, NMe_2), 7.88 (s, α-CH), $J_{CH_2CH_3}$ = 6.0 Hz, $J_{6\text{-}CH_2,7\text{-}CH_2}$ = 7.0 Hz, $J_{7\text{-}CH_2 8\text{-}CH_2}$ = 7.0 Hz.

5-(2-(*N*,*N*-Dimethylamino)prop-1-en-1-yl)-3-ethylmercapto-6-methyl-1,2,4-triazine (**3e**).

A mixture of 5,6-dimethyl-3-ethylmercapto-1,2,4-triazine (**1a**) (1.7 g, 10 mmoles), *N*,*N*-dimethylformamide (90 ml) and *N*,*N*-dimethylacetamide dimethyl acetal (**2b**) (2.7 g, 20 mmoles) was heated under reflux for ten minutes. Volatile compounds were removed *in vacuo*, the residue was used further without crystallization, mp 59-65° (crude residue); ^{1}H nmr (deuteriochloroform): δ 1.39 (t, 3H, CH_2*Me*), 2.43 (s, 3H, 6-Me), 2.67 (s, 3H, β-Me), 3.12 (s, 6H, NMe_2), 3.18 (q, CH_2Me), 4.88 (s, α-CH), $J_{CH_2CH_3}$ = 7.5 Hz.

4-(2-(2-Acetyl-2,5-dihydro-5-(1,2,4-triazinylidene))-substituted-5(4*H*)-oxazolones and 5(4*H*)-Thiazolones **5**.

Procedure A.

N-Acylglycine (11 mmoles) and acetic anhydride (16 ml) were heated at 80-90° for thirty minutes, the mixture was then filtered and cooled to 50-60°. Enamine **3** was added and the mixture was then stirred at the same temperature. After cooling to 0° the precipitated crystals were collected by filtration and washed with ether. The purification by column chromatography (silica gel, chloroform) was necessary only for elemental analysis.

Procedure B.

Enamine **3**, *N*-acylglycine and acetic anhydride were mixed together, stirred at 50-60° and isolated as described in the method A.

The experimental data are summarized in Table 1. The following compounds were prepared according to these procedures:

(*E*)-4 and (*Z*)-4-((*Z*)-2-(2-Acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5a**).

This mixture was prepared from 5-((*E*)-2-(*N*,*N*-dimethylamino)ethenyl)-3-ethylmercapto-6-methyl-1,2,4-triazine (**3a**) and hippuric acid; ^{1}H nmr (deuteriochloroform): (*E*)-**5a**: δ 1.40 (t, 3H, CH_2*Me*), 2.27 (s, 3H, 6-Me), 2.43 (s, 3H, COMe), 3.09 (q, 2H, C*H*$_2$Me), 6.6 (d, β-CH), 7.4-7.6 (m, 3H, 3,4,5-H_{Ph}), 7.83 (d, α-CH), 8.0-8.1 (m, 2H, 2,6-H_{Ph}), $J_{CH_2CH_3}$ = 7.5 Hz, $J_{\alpha\text{-H},\beta\text{-H}}$ = 12.0 Hz; (*Z*)-**5a**: δ 1.39 (t, 3H, CH_2*Me*), 2.25 (s, 3H, 6-Me), 2.43 (s, 3H, COMe), 3.09 (q, 2H, C*H*$_2$Me), 7.08 (d, β-CH), 7.97 (d, α-CH), $J_{CH_2CH_3}$ = 7.5 Hz, $J_{\alpha\text{-H},\beta\text{-H}}$ = 12.0 Hz, multiplets for H_{Ph}, are overlapped [20].

Anal. Calcd. for $C_{19}H_{18}N_4O_3S$: C, 59.67; H, 4.74; N, 14.65. Found: C, 59.63; H, 4.74; N, 14.37.

(*E*)-4 and (*Z*)-4-((*Z*)-2-(2-Acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-(4-chlorophenyl)-5(4*H*)-oxazolone (**5b**).

This mixture was prepared from 5-((*E*)-2-(*N*,*N*-dimethylamino)ethenyl)-3-ethylmercapto-6-methyl-1,2,4-triazine (**3a**) and *N*-(4-chlorobenzoyl)glycine; ^{1}H nmr (deuteriochloroform): (*E*)-**5b**: δ 1.37 (t, 3H, CH_2*Me*), 2.45 (s, 3H, COMe), 2.77 (s, 3H, 6-Me), 3.12 (q, 2H, C*H*$_2$Me), 6.59 (d, β-CH), 7.48 (d, 2H, 3,5-H_{Ar}), 7.89 (d, α-CH), 7.85-8.2 (m, 2H, 2,6-H_{Ar}), $J_{CH_2CH_3}$ = 7.0 Hz, $J_{\alpha\text{-H},\beta\text{-H}}$ = 12.0 Hz, $J_{2\text{-H(Ar)},3\text{-H(Ar)}}$ = 9.0 Hz; (*Z*)-**5b**: δ 2.24 (s, 6-Me), 7.07 (d, β-CH), other signals are identical or overlapped.

Anal. Calcd. for $C_{19}H_{17}ClN_4O_3S$: C, 54.74; H, 4.11; N, 13.44. Found: C, 54.46; H, 4.13; N, 13.46.

(*E*)-4 and (*Z*)-4-((*Z*)-2-(2-Acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-(4-methylphenyl)-5(4*H*)-oxazolone (**5c**).

This mixture was prepared from 5-((*E*)-2-(*N*,*N*-dimethylamino)ethenyl)-3-ethylmercapto-6-methyl-1,2,4-triazine (**3a**) and *N*-(4-methylbenzoyl)glycine; ^{1}H nmr (deuteriochloroform): (*E*)-**5c**: δ 1.41 (t, 3H, CH_2*Me*), 2.26 (s, 3H, 6-Me), 2.46 (s, 6H, COMe, C_6H_4*Me*), 3.05 (q, 2H, C*H*$_2$Me), 6.57 (d, β-CH), 7.30 (d, 2H, 3,5-H_{Ar}), 7.80 (d, α-CH), 7.80-8.15 (m, 2H, 2,6-H_{Ar}), $J_{CH_2CH_3}$ = 7.0 Hz, $J_{\alpha\text{-H},\beta\text{-H}}$ = 12.5 Hz, $J_{2\text{-H(Ar)},3\text{-H(Ar)}}$ = 9.0 Hz; (*Z*)-**5c**: δ 2.23 (s, 6-Me), 7.04 (d, β-CH), other signals are identical or overlapped.

Anal. Calcd. for $C_{20}H_{20}N_4O_3S$: C, 60.59; H, 5.08; N, 14.13. Found: C, 60.65; H, 5.44; N, 13.75.

(*E*)-4 and (*Z*)-4-((*Z*)-2-(2-Acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-(4-nitrophenyl)-5(4*H*)-oxazolone (**5d**).

This mixture was prepared from 5-((*E*)-2-(*N*,*N*-dimethylamino)ethenyl)-3-ethylmercapto-6-methyl-1,2,4-triazine (**3a**) and *N*-(4-nitrophenyl)glycine; ^{1}H nmr (deuteriochloroform): (*E*)-**5d**: δ 1.39 (t, 3H, CH_2*Me*), 2.32 (s, 3H, 6-Me), 2.48 (s, 3H, COMe), 3.09 (q, 2H, C*H*$_2$Me), 6.55 (s, β-CH), 7.92 (d, α-CH), 8.27 (m, 4H, Ar), $J_{CH_2CH_3}$ = 8.0 Hz, $J_{\alpha\text{-H},\beta\text{-H}}$ = 12.5 Hz; (*Z*)-**5d**: δ 2.28 (s, 3H, 6-Me), 6.99 (d, β-H), 8.04 (d, α-H), other signals are identical or overlapped.

Anal. Calcd. for $C_{19}H_{17}N_5O_5S$: C, 53.39; H, 4.01; N, 16.38. Found: C, 53.11; H, 4.10; N, 16.32.

(*E*)-4 and (*Z*)-4-((*Z*)-2-(2-Acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-(2-nitrophenyl)-5(4*H*)-oxazolone (**5e**).

This mixture was prepared from 5-((*E*)-2-(*N*,*N*-dimethylamino)ethenyl)-3-ethylmercapto-6-methyl-1,2,4-triazine (**3a**) and *N*-(2-nitrophenyl)glycine; ^{1}H nmr (deuteriochloroform): (*E*)-**5e**: δ 1.33 (t, 3H, CH_2*Me*), 2.26 (s, 3H, 6-Me), 2.43 (s, 3H, COMe), 3.04 (q, 2H, C*H*$_2$Me), 6.43 (d, β-CH), 7.6-8.2 (m, 5H, β-CH, Ar), $J_{CH_2CH_3}$ = 7.0 Hz, $J_{\alpha\text{-H},\beta\text{-H}}$ = 12.5 Hz; (*Z*)-**5e**: δ 6.87 (d, β-H), other signals are identical or overlapped.

Anal. Calcd. for $C_{19}H_{17}N_5O_5S$: C, 53.39; H, 4.01; N, 16.38. Found: C, 53.13; H, 3.99; N, 16.37.

(*E*)-4 and (*Z*)-4-((*Z*)-2-(2-Acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-methyl-5(4*H*)-oxazolone (**5f**).

This mixture was prepared from 5-((*E*)-2-(*N*,*N*-dimethylamino)ethenyl)-3-ethylmercapto-6-methyl-1,2,4-triazine (**3a**) and *N*-acetylglycine; ^{1}H nmr (deuteriochloroform): (*E*)-**5f**: δ 1.37 (t, 3H, CH_2*Me*), 2.26 (s, 3H, 6'-Me), 2.37 (s, 3H, 2-Me), 2.47 (s, 3H, COMe), 3.08 (q, 2H, C*H*$_2$Me), 6.43 (d, β-CH), 7.79 (d, α-CH), $J_{CH_2CH_3}$ = 7.5 Hz, $J_{\alpha\text{-H},\beta\text{-H}}$ = 12.0 Hz; (*Z*)-**5f**: δ 7.17 (d, β-CH), 7.93 (d, α-CH), other signals are identical.

Anal. Calcd. for $C_{14}H_{16}N_4O_3S$: C, 52.49; H, 5.03; N, 17.49. Found: C, 52.16; H, 5.18; N, 17.42.

(*E*)-4 and (*Z*)-4-((*Z*)-2-(2-Acetyl-2,5-dihydro-6-methyl-3-methylmercapto-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5g**).

This mixture was prepared from 5-((*E*)-2-(*N*,*N*-dimethylamino)ethenyl)-6-methyl-3-methylmercapto-1,2,4-triazine (**3b**) and hippuric acid; ^{1}H nmr (deuteriochloroform): (*E*)-**5g**: δ 2.39 (s, 3H, 6-Me), 2.52 (s, 6H, COMe, SMe), 6.80 (d, β-CH), 7.6-8.5 (m, 6H, α-CH, Ph), $J_{\alpha\text{-H},\beta\text{-H}}$ = 13.0 Hz; (*Z*)-**5g**: δ 2.32 (s, 3H, 6-Me), 7.30 (d, β-CH), 8.14 (d, α-CH), other signals were identical or overlapped.

Anal. Calcd. for $C_{18}H_{16}N_4O_3S$: C, 58.68; H, 4.38; N, 15.21. Found: C, 58.94; H, 4.48; N, 15.23.

(*E*)-4 and (*Z*)-4-((*Z*)-2-(2-Acetyl-2,5-dihydro-3-methoxy-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5h**).

This mixture was prepared from 5-((*E*)-2-(*N*,*N*-dimethylamino)ethenyl)-3-methoxy-6-methyl-1,2,4-triazine (**3c**) and hippuric acid; ^{1}H nmr (deuteriochloroform): (*E*)-**5h**: δ 2.32 (s, 3H, 6-Me), 2.52 (s, 3H, COMe), 4.13 (s, 3H, OMe), 6.62 (d, β-CH), 7.6-8.3 (m, 6H, α-CH, Ph), $J_{\alpha\text{-H},\beta\text{-H}}$ = 12.0 Hz; (*Z*)-**5h**: δ 2.29 (s, 3H, 6-Me), 7.07 (d, β-H), other signals are identical or overlapped.

Anal. Calcd. for $C_{18}H_{16}N_4O_4$: C, 61.38; H, 4.58; N, 15.90. Found: C, 61.04; H, 4.68; N, 15.70.

(*E*)-4 and (*Z*)-4-((*Z*)-2-(2-Acetyl-2,5-dihydro-3-methoxy-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-(2-nitrophenyl)-5(4*H*)-oxazolone (**5i**).

This mixture was prepared from 5-((*E*)-2-(*N*,*N*-dimethylamino)ethenyl)-3-methoxy-6-methyl-1,2,4-triazine (**3c**) and

N-(2-nitrobenzyl)glycine; ^{1}H nmr (deuteriochloroform): (*E*)-**5i**: δ 2.24 (s, 3H, 6-Me), 2.43 (s, 3H, COMe), 4.01 (s, 3H, OMe), 6.47 (d, β-CH), 7.74 (d, α-CH), 7.2-7.5 and 7.7-8.0 (m, 4H, Ar), $J_{\alpha\text{-H, }\beta\text{-H}}$ = 12.0 Hz; (*Z*)-**5i**: δ 6.94 (d, β-H), 7.94 (d, α-H), other signals are identical or overlapped.

Anal. Calcd. for $C_{18}H_{15}N_5O_6$: C, 54.41; H, 3.81; N, 17.63. Found: C, 54.84; H, 4.01; N, 17.88.

(*E*)-4 and (*Z*)-4-((*Z*)-1-(2-Acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-2-propylidene)-2-phenyl-5(4*H*)-oxazolone (**5j**).

This mixture was prepared from crude 5-(2-(*N*,*N*-dimethylamino)prop-1-en-1-yl)-3-ethylmercapto-6-methyl-1,2,4-triazine (**3e**) (obtained from 10 mmoles of 5,6-dimethyl-3-ethylmercapto-1,2,4-triazine (**1a**)) and hippuric acid; ^{1}H nmr (deuteriochloroform): (*E*)-**5j**: δ 1.33 (t, 3H, CH_2*Me*), 2.32 (s, 3H, 6-Me), 2.44 (s, 3H, COMe), 2.86 (s, β-CMe), 3.00 (q, 2H, C*H*$_2$Me), 6.96 (s, α-CH), 7.43-7.57 and 8.03-8.09 (m, 5H, Ph), $J_{CH_2CH_3}$ = 7.3 Hz; (*Z*)-**5j**: δ 1.35 (t, 3H, CH_2*Me*), 2.28 (s, 3H, 6-Me), 2.43 (s, 3H, COMe), 2.79 (s, 3H, β-CMe), 3.01 (q, 2H, C*H*$_2$Me), 7.42 (s, α-CH), other signals are identical or overlapped.

Anal. Calcd. for $C_{20}H_{20}N_4O_3S$: C, 60.59; H, 5.08; N, 14.13. Found: C, 60.91; H, 5.25; N, 13.82.

(*E*)-4 and (*Z*)-4-(2-Acetyl-3-ethylmercapto-2,6,7,8-tetrahydro-5-benzo[1,2,4]triazinyl)methylene)-2-phenyl-5(4*H*)-oxazolone (**5k**).

This mixture was prepared from 5-((*E*)-2-(*N*,*N*-dimethylamino)ethenyl)-3-ethylmercapto-5,6,7,8-tetrahydrobenzo[1,2,4]-triazine (**3d**) (obtained from 10 mmoles from 3-ethylmercapto-5,6,7,8-tetrahydrobenzo[1,2,4]-triazine (**1d**)) and hippuric acid; ^{1}H nmr (deuteriochloroform): (*E*)-**5k**: δ 1.38 (t, 3H, CH_2*Me*), 1.96 (deg tt, 2H, 7-CH_2), 2.43 (s, 3H, COMe), 2.3-2.8 (m, 4H, 6-CH_2, 8-CH_2), 3.07 (q, 2H, C*H*$_2$Me), 7.20 (s, CH), 7.3-8.2 (m, 5H, Ph), $J_{CH_2CH_3}$ = 7.0 Hz; (*Z*)-**5k**: δ 2.36 (s, 3H, COMe), 7.31 (s, CH), other signals are identical or overlapped.

Anal. Calcd. for $C_{21}H_{20}N_4O_3S$: C, 61.75; H, 4.94; N, 13.72. Found: C, 61.56; H, 5.19; N, 13.72.

(*E*)-4 or (*Z*)-4-((*Z*)-2-(2-Acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-benzylmercapto-5(4*H*)-thiazolone (**5l**).

This compound was prepared from 5-((*E*)-2-(*N*,*N*-dimethylamino)ethenyl)-3-ethylmercapto-6-methyl-1,2,4-triazine (**3a**) and *N*-dithiocarbobenzoxyglycine; ^{1}H nmr (deuteriochloroform): δ 1.38 (t, 3H, CH_2*Me*), 2.23 (s, 3H, 6'-Me), 2.45 (s, 3H, COMe), 3.06 (q, 2H, C*H*$_2$Me), 4.55 (s, 2H, C*H*$_2$Ph), 6.58 (d, β-CH), 7.2-7.6 (m, 5H, Ph), 7.65 (d, α-CH), $J_{CH_2CH_3}$ = 7.0 Hz, $J_{\alpha\text{-H, }\beta\text{-H}}$ = 12.5 Hz.

Anal. Calcd. for $C_{20}H_{20}N_4O_2S_3$: C, 54.03; H, 4.53; N, 12.60. Found: C, 53.85; H, 4.67; N, 12.49.

4-(2-(2,5-Dihydro-5-(1,2,4-triazinylidene))ethylidene)-5(4*H*)-oxazolones (**9**).

Procedure A.

Enamine **3** (1.5 mmoles), 2-phenyl-5(4*H*)-oxazolone (320 mg, 2 mmoles), acetic acid (0.5 ml) and toluene (6 ml) were heated together under reflux for 20 minutes. Volatile components were then evaporated and the residue was purified by column chromatography (silica gel, chloroform).

Procedure B.

Isomeric mixture **5** (6 mmoles) was stirred for 1 hour at room temperature in the mixture of 2*M* sodium hydroxide solution (40 ml) and dioxane (15 ml). The mixture was then acidified by acetic acid and the precipitated product was collected by filtration.

(*E*)-4 and (*Z*)-4-((*Z*)-2-(2,5-Dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**9a**).

This mixture was prepared from 5-((*E*)-2-(*N*,*N*-dimethylamino)ethenyl)-3-ethylmercapto-6-methyl-1,2,4-triazine (**3a**) according to the procedure A in 52% yield or from 4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5a**) according to the procedure B in 91% yield, mp 259-262° (from toluene); ^{1}H nmr (deuteriochloroform): (*E*)-**9a**: δ 1.37 (t, 3H, CH_2*Me*), 2.15 (s, 3H, 6-Me), 3.15 (q, 2H, C*H*$_2$Me), 6.30 (d, β-CH), 7.2-7.6 and 7.8-8.2 (m, 5H, Ph), 7.95 (d, α-CH), $J_{\alpha\text{-H, }\beta\text{-H}}$ = 12.0 Hz; (*Z*)-**9a**: δ 6.81 (d, β-CH), other signals are identical or overlapped. Ratio (*E*)-**9a**/(*Z*)-**9a** was 2:1.

Anal. Calcd. for $C_{17}H_{16}N_4O_2S$: C, 59.98; H, 4.74; N, 16.46. Found: C, 60.03; H, 4.90; N, 16.20.

(*E*)-4 and (*Z*)-4-((*Z*)-2-(2,5-Dihydro-3-methoxy-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**9b**).

This mixture was prepared from 5-((*E*)-2-(*N*,*N*-dimethylamino)ethenyl)-3-methoxy-6-methyl-1,2,4-triazine (**3c**) according to the procedure A in 31% yield or from 4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-methoxy-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5h**) according to the procedure B in 62% yield, mp 184-185° (from toluene); ^{1}H nmr (deuteriochloroform): (*E*)-**9b**: δ 2.14 (s, 3H, 6-Me), 3.88 (s, 3H, OMe), 6.03 (d, β-CH), 7.3-8.0 (m, 6H, Ph, α-CH), $J_{\alpha\text{-H, }\beta\text{-H}}$ = 12.5 Hz; δ 2.07 (s, 3H, 6-Me), 6.44 (d, β-CH), other signals are identical or overlapped. Ratio (*E*)-**9b**/(*Z*)-**9b** was 7:1.

Anal. Calcd. for $C_{16}H_{14}N_4O_3$: C, 61.93; H, 4.55; N, 18.05. Found: C, 61.64; H, 4.68; N, 17.97.

(*E*)-4 and (*Z*)-4-((*Z*)-2-(2,5-Dihydro-2,6-dimethyl-3-ethylmercapto-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**11**).

To the mixture of 40% solution of sodium hydroxide (1 ml) and acetone (5 ml) first 4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5a**) (380 mg, 1 mmole) and then methyl iodide (1 ml) were added. After 20 minutes of stirring at room temperature ether (5 ml) was added. The obtained red crystals were collected by filtration and purified by column chromatography (silica gel, chloroform) to give **11** in 41% yield, mp 231-237° (from toluene); ^{1}H nmr (deuteriochloroform): (*E*)-**11**: δ 1.43 (t, 3H, CH_2*Me*), 2.19 (s, 3H, 6-Me), 3.22 (q, 2H, C*H*$_2$Me), 3.53 (s, 3H, 2-Me), 6.30 (d, β-CH), 7.96 (d, α-CH), 7.3-7.6 and 7.9-8.03 (m, 5H, Ph), $J_{\alpha\text{-H, }\beta\text{-H}}$ = 13.0 Hz; (*Z*)-**11**: δ 2.16 (s, 3H, 6-Me), 6.80 (d, β-H), other data were identical or nonidentified. Ratio (*E*)-**11**/(*Z*)-**11** was 2:1.

Anal. Calcd. for $C_{18}H_{18}N_4O_2S$: C, 61.00; H, 5.12; N, 15.81. Found: C, 60.78; H, 5.33; N, 15.74.

7-Benzoylamino-6*H*-pyrido[1,2-*d*][1,2,4]triazin-6-ones **12**.

Procedure A.

7-Benzoylamino-4-ethylmercapto-1-methyl-6*H*-pyrido[1,2-*d*][1,2,4]triazin-6-one (**12a**).

4-((Z)-2-(2,5-Dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**9a**) (1.36 g, 4 mmoles) was heated in xylene (20 ml) for twelve hours and after cooling the mixture to 0° the precipitate was collected by filtration in 50% yield, mp 271-272° (from toluene), ^{1}H nmr (deuteriochloroform): δ 1.40 (t, 3H, CH_2*Me*), 2.58 (s, 3H, 1-Me), 3.19 (q, 2H, C*H*$_2$Me), 6.84 (d, 9-H), 7.4-8.1 (m, 5H, Ph), 8.94 (d, 8-H), 9.3 (s, broad, NH), $J_{CH_2CH_3}$ = 7.5 Hz, $J_{8\text{-H, }9\text{-H}}$ = 8.5 Hz.

Anal. Calcd. for $C_{17}H_{16}N_4O_2S$: C, 59.98; H, 4.74; N, 16.46. Found: C, 59.60; H, 4.82; N, 16.01.

Procedure B.

The isomeric mixture **5** (2 mmoles) was heated under reflux in 99% formic acid (8 ml). Volatile compounds were removed *in vacuo*, the residue was treated with water, filtered and dried over silica gel.

According to this procedure **12a** was prepared from 4-((Z)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5a**), reaction time 20 minutes, yield 36%. Analogously the following other compounds were prepared:

7-Benzoylamino-1-methyl-4-methylmercapto-6*H*-pyrido[1,2-*d*]-[1,2,4]triazin-6-one (**12b**).

This compound was prepared from 4-((Z)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-ethylidene)-2-(4-chlorophenyl)-5(4*H*)-oxazolone (**5b**), reaction time 50 minutes, yield 83%, mp 278-280° (from dioxane); ^{1}H nmr (DMSO-d$_6$, 150°): δ 2.52 (s, 3H, SMe), 2.71 (s, 3H, 1-Me), 7.01 (d, 9-H), 7.4-8.1 (m, 5H, Ph), 8.64 (d, 8-H), 9.3 (s, NH), $J_{8\text{-H, }9\text{-H}}$ = 8.5 Hz.

Anal. Calcd. for $C_{16}H_{14}N_4O_2S$: C, 58.88; H, 4.32; N, 17;17. Found: C, 58.61; H, 4.49; N, 17.17.

7-Benzoylamino-3,4-dihydro-1-methyl-6*H*-pyrido[1,2-*d*]-[1,2,4]triazine-4,6-dione (**12c**).

This compound was prepared from 4-((Z)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-ethylidene)-2-(4-methylphenyl)-5(4*H*)-oxazolone (**5c**), reaction time 15 minutes, yield 75%, mp 306-311° (from dioxane); ^{1}H nmr (DMSO-d$_6$, 70°): δ 2.24 (s, 3H, Me), 6.75 (d, 9-H), 7.5-8.0 (m, 5H, Ph), 8.42 (d, 8-H), 9.55 (s, NHCO), 11.9 (s, broad, 3-H).

Anal. Calcd. for $C_{15}H_{12}N_4O_3$: C, 60.81; H, 4.08; N, 18.91. Found: C, 60.80; H, 4.12; N, 18.80.

7-Benzoylamino-1,8-dimethyl-4-ethylmercapto-6*H*-pyrido-[1,2-*d*][1,2,4]triazin-6-one (**12d**).

This compound was prepared from 4-((Z)-1-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-2-propylidene)-2-phenyl-5(4*H*)-oxazolone (**5j**), reaction time 10 minutes, yield 92%, mp 217-218° (from acetonitrile), ^{1}H nmr (deuteriochloroform): δ 1.29 (t, 3H, CH_2*Me*), 2.29 (s, 3H, 8-Me), 2.53 (s, 3H, 1-Me), 3.03 (q, 2H, C*H*$_2$Me), 6.95 (s, 9-H), 7.4-7.7 and 7.9-8.1 (m, 5H, Ph), 9.94 (s, NH), $J_{CH_2CH_3}$ = 7.5 Hz.

Anal. Calcd. for $C_{18}H_{18}N_4O_2S$: C, 61.00; H, 5.12; N, 15.81. Found: C, 61.26; H, 5.37; N, 15.91.

Esters **13** and Amides **14** of 2-Benzoylamino-4-(2,5-dihydro-5-(1,2,4-triazinylidene))-2-butenoic Acid.

Procedure A.

The isomeric mixture **5** (15 mmoles) was stirred at room temperature in the solution of alkoxide previously prepared from sodium (750 mg, 33 mmoles) and alcohol (50 ml). Alcohol was removed *in vacuo* to obtain viscous mass to which water (20 ml) and ether (50 ml) were added. The two-phase mixture was acidified with acetic acid, the precipitated crystals were collected by filtration and washed by ether.

The following compounds were prepared according to this procedure:

Methyl 2-Benzoylamino-(Z)-4-(2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-(Z)-2-butenoate (**13a**).

This compound was prepared from 4-((Z)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5a**) and methanol, reaction time 90 minutes, yield 95%, mp 176-178° (from toluene); ^{1}H nmr (DMSO-d$_6$): δ 1.38 (t, 3H, CH_2*Me*), 1.96 (s, 3H, 6'-Me), 3.12 (q, 2H, C*H*$_2$Me), 3.67 (s, 3H, OMe), 5.55 (d, β-H), 7.4-7.7 and 7.9-8.1 (m, 5H, Ph), 7.83 (d, α-H), 9.71 (s, NHCO), 12.18 (s, 2-H), $J_{CH_2CH_3}$ = 7.9 Hz, $J_{\alpha\text{-H, }\beta\text{-H}}$ = 11.7 Hz.

Anal. Calcd. for $C_{18}H_{20}N_4O_3S$: C, 58.05; H, 5.41; N, 15.04. Found: C, 57.90; H, 5.40; N, 14.91.

Methyl (Z)-4-(2,5-Dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-2-(2-nitrobenzoylamino)-(Z)-2-butenoate (**13b**).

This compound was prepared from 4-((Z)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-ethylidene)-2-(2-nitrophenyl)-5(4*H*)-oxazolone (**5e**) and methanol, reaction time 90 minutes, yield 50%, mp 227-233° (from acetonitrile); ^{1}H nmr (DMSO-d$_6$): δ 1.33 (t, 3H, CH_2*Me*), 2.01 (s, 3H, 6'-Me), 3.09 (q, 2H, C*H*$_2$Me), 3.68 (s, 3H, COOMe), 5.59 (d, 4-H), 7.4-8.2 (m, 5H, Ar, 3-H), 9.82 (NHCO), $J_{CH_2CH_3}$ = 7.5 Hz, $J_{3\text{-H, }4\text{-H}}$ = 12.0 Hz.

Anal. Calcd. for $C_{18}H_{19}N_5O_5S$: C, 51.79; H, 4.59; N, 16.78. Found: C, 51.58; H, 4.68; N, 16.86.

Methyl 2-Acetylamino-(Z)-4-(2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-(Z)-2-butenoate (**13c**).

This compound was prepared from 4-((Z)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-ethylidene)-2-methyl-5(4*H*)-oxazolone (**5f**) and methanol, reaction time 90 minutes, yield 32%, mp 191-195° (from acetonitrile); ^{1}H nmr (DMSO-d$_6$): δ 1.34 (t, 3H, CH_2*Me*), 1.99 (s, 6H, 6'-Me, COMe), 3.21 (q, 2H, C*H*$_2$Me), 3.64 (s, 3H, COOMe), 5.48 (d, 4-H), 7.74 (d, 3-H), 9.23 (s, NHCO), 11.7-12.6 (s, broad, 2'-H), $J_{CH_2CH_3}$ = 7.5 Hz, $J_{3\text{-H, }4\text{-H}}$ = 12.0 Hz.

Anal. Calcd. for $C_{13}H_{18}N_4O_3S$: C, 50.31; H, 5.85; N, 18.05. Found: C, 50.44; H, 5.84; N, 18.03.

Methyl 2-Benzoylamino-(Z)-4-(2,5-dihydro-3-methoxy-6-methyl-5-(1,2,4-triazinylidene))-(Z)-2-butenoate (**13d**).

This compound was prepared from 4-((Z)-2-(2-acetyl-2,5-dihydro-3-methoxy-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5h**) and methanol, reaction time one hour, yield 74%, mp 211-213° (from acetonitrile); ^{1}H nmr (DMSO-d$_6$): δ 1.96 (s, 3H, 6'-Me), 3.68 (s, 3H, COOMe), 3.92 (s, 3H, 3'-OMe), 5.67 (d, 4-H), 7.4-8.2 (m, 5H, Ph), 7.92 (d, 3-H), 9.80 (s, NHCO), 12.0 (s, broad, 2'-H), $J_{3\text{-H, }4\text{-H}}$ = 12.0 Hz.

Anal. Calcd. for $C_{17}H_{18}N_4O_4$: C, 59.64; H, 5.30; N, 16.37. Found: C, 59.86; H, 5.45; N, 16.50.

Methyl (Z)-4-(2,5-Dihydro-3-methoxy-6-methyl-5-(1,2,4-triazinylidene))-2-(2-nitrobenzoyl)-(Z)-2-butenoate (**13e**).

This compound was prepared from 4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-methoxy-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-(2-nitrophenyl)-5(4*H*)-oxazolone (**5i**) and methanol, reaction time two hours, yield 70%, mp 231-234° (from acetonitrile); ^{1}H nmr (DMSO-d_6): δ 2.06 (s, 3H, 6'-Me), 3.73 (s, 3H, COOMe), 3.91 (s, 3H, 3'-OMe), 5.69 (d, 4-H), 7.5-8.3 (m, 5H, Ar, 3-H), 9.94 (s, NHCO), 12.1 (s, broad, 2'-H), $J_{3\text{-H, }4\text{-H}}$ = 12.0 Hz.

Anal. Calcd. for $C_{17}H_{17}N_5O_6$: C, 52.71; H, 4.42; N, 18.08. Found: C, 52.99; H, 4.50; N, 17.97.

Ethyl 2-Benzoylamino-(*Z*)-4-(2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-(*Z*)-2-butenoate (**13f**).

This compound was prepared from 4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5a**) and ethanol reaction time 90 minutes, yield 70%, mp 191-198° (from toluene); ^{1}H nmr (deuteriochloroform): δ 1.23 (t, 3H, SCH_2*Me*), 1.38 (t, 3H, OCH_2*Me*), 1.97 (s, 3H, 6'-Me), 3.15 (q, 2H, SCH_2Me), 4.16 (q, 2H, OCH_2Me), 5.57 (d, 4-H), 7.4-8.1 (m, 6H, Ph, 3-H), 9.69 (s, NHCO), 12.3 (s, broad, 2'-H), $J_{SCH_2CH_3}$ = 7.5 Hz, $J_{OCH_2CH_3}$ = 7.0 Hz, $J_{3\text{-H, }4\text{-H}}$ = 12.0 Hz.

Anal. Calcd. for $C_{19}H_{22}N_4O_3S$: C, 59.05; H, 5.74; N, 14.50. Found: C, 59.12; H, 5.90; N, 14.24.

Ethyl 2-Benzoylamino-(*Z*)-4-(2,5-dihydro-3-methoxy-6-methyl-5-(1,2,4-triazinylidene))-(*Z*)-2-butenoate (**13g**).

This compound was prepared from 4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-methoxy-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5h**) and ethanol, reaction time one hour, yield 74%, mp 179-182° (from toluene); ^{1}H nmr (deuteriochloroform): δ 1.33 (t, 3H, CH_2*Me*), 1.97 (s, 3H, 6'-Me), 3.95 (s, 3H, OMe), 4.27 (q, 2H, CH_2Me), 5.44 (d, 4-H), 7.3-8.1 (m, 5H, Ph), 8.14 (d, 3H), 9.75 (s, NHCO), $J_{CH_2CH_3}$ = 7.5 Hz, $J_{3\text{-H, }4\text{-H}}$ = 12.0 Hz.

Anal. Calcd. for $C_{18}H_{20}N_4O_4$: C, 60.67; H, 5.66; N, 15.72. Found: C, 60.40; H, 5.93; N, 15.61.

Procedure B.

An alcohol or an amine (5 ml) was heated up to 60° and sodium hydride was added. The mixture was stirred at 60° for one hour, isomeric mixture **5** was added with continuation of stirring at the same conditions. The mixture was cooled, first ether (25 ml) and then slowly water (10 ml) were added and the mixture was acidified with acetic acid. The precipitated crystals were filtrated and washed by ether.

The following compounds were prepared according to this procedure:

Benzyl 2-Benzoylamino-(*Z*)-4-(2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-(*Z*)-2-butenoate (**13h**).

This compound was prepared from 4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5a**) and benzylic alcohol, reaction time three hours, yield 62%, mp 198-202° (from toluene); ^{1}H nmr (deuteriochloroform): δ 1.20 (t, 3H, CH_2*Me*), 1.94 (s, 6'-Me), 3.00 (q, 2H, CH_2Me), 5.26 (s, CH_2Ph), 5.52 (d, 4-H), 7.1-8.1 (m, 5H, *Ph*CO), 7.42 (s, CH_2Ph), 8.32 (d, 3-H), 9.85 (s, broad, NHCO), $J_{CH_2CH_3}$ = 7.0 Hz, $J_{3\text{-H, }4\text{-H}}$ = 12.0 Hz.

Anal. Calcd. for $C_{24}H_{24}N_4O_3S$: C, 64.27; H, 5.39; N, 12.49. Found: C, 63.99; H, 5.45; N, 12.56.

3,4-(Methylenedioxy)benzyl 2-Benzoylamino-(*Z*)-4-(2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-(*Z*)-2-butenoate (**13i**).

This compound was prepared from 4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5a**) and 3,4-methylenedioxybenzylic alcohol, reaction time three hours, yield 20%, mp 201-205° (from acetonitrile); ^{1}H nmr (deuteriochloroform): δ 1.26 (t, 3H, CH_2*Me*), 1.94 (s, 3H, 6'-Me), 3.09 (q, 2H, CH_2Me), 5.07 (s, CH_2Ph), 5.57 (d, 4-H), 6.05 (s, 2H, OCH_2O), 6.9-7.0 (m, 3H, C_6H_3), 7.4-7.7 and 7.8-8.2 (m, 6H, Ph, 3-H), 9.69 (s, NHCO), $J_{CH_2CH_3}$ = 7.5 Hz, $J_{3\text{-H, }4\text{-H}}$ = 12.0 Hz.

Anal. Calcd. for $C_{25}H_{24}N_4O_5S$: C, 60.96; H, 4.91; N, 11.37. Found: C, 60.61; H, 5.04; N, 11.54.

2-Benzoylamino-*N*-benzyl-(*Z*)-4-(2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-(*Z*)-2-butenamide (**14a**).

This compound was prepared from 4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5a**) and benzylamine, reaction time three hours, yield 58%, mp 214-216° (from acetonitrile); ^{1}H nmr (DMSO-d_6): δ 1.32 (t, 3H, CH_2*Me*), 2.54 (s, 3H, 6'-Me), 3.13 (q, 2H, CH_2Me), 4.39 (d, 2H, CH_2Ph), 5.52 (d, 4-H), 7.36 (s, CH_2*Ph*), 7.4-8.2 (m, 6H, COPh, 3-H), 8.43 (t, N*H*CH_2), 9.74 (s, N*H*COPh), 12.13 (s, 2'-H), $J_{CH_2CH_3}$ = 7.5 Hz, J_{CH_2NH} = 6.0 Hz, $J_{3\text{-H, }4\text{-H}}$ = 12.0 Hz.

Anal. Calcd. for $C_{24}H_{25}N_5O_2S$: C, 64.41; H, 5.63; N, 15.65. Found: C, 64.48; H, 5.88; N, 15.55.

N-(2-Benzoylamino-(*Z*)-4-(2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-(*Z*)-2-butenoyl)morpholine (**14b**).

This compound was prepared from 4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5a**) and morpholine, reaction time one hour, yield 92%, mp 166-169° (from acetonitrile); ^{1}H nmr (DMSO-d_6): δ 1.31 (t, 3H, CH_2*Me*), 1.93 (s, 3H, 6'-Me), 3.04 (q, 2H, CH_2Me), 3.56 (s, 8H, NCH_2CH_2O), 5.68 (d, 4-H), 6.73 (d, 3-H), 7.4-8.1 (m, 5H, Ph), 10.05 (s, NHCO), 11.4-11.9 (s, broad, 2'-H), $J_{CH_2CH_3}$ = 7.5 Hz, $J_{3\text{-H, }4\text{-H}}$ = 11.5 Hz.

Anal. Calcd. for $C_{21}H_{25}N_5O_3S$: C, 59.00; H, 5.89; N, 16.38. Found: C, 58.62; H, 6.04; N, 15.98.

2-Benzoyl-(*Z*)-4-(2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-*N*-phenyl-(*Z*)-2-butenamide (**14c**).

This compound was prepared from 4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5a**) and aniline, reaction time one hour, yield 43%, mp 176-178° (from acetonitrile); ^{1}H nmr (DMSO-d_6): δ 1.31 (t, 3H, CH_2*Me*), 1.92 (s, 3H, 6'-Me), 3.13 (q, 2H, CH_2Me), 5.56 (d, 4-H), 7.0-8.3 (m, 11H, 3-H, COPh, NH*Ph*), 9.76 (s, N*H*COPh), $J_{CH_2CH_3}$ = 7.0 Hz, $J_{3\text{-H, }4\text{-H}}$ = 11.5 Hz.

Anal. Calcd. for $C_{23}H_{23}N_5O_2S$: C, 63.72; H, 5.35; N, 16.15. Found: C, 63.94; H, 5.31; N, 16.03.

2-Benzoylamino-(*Z*)-4-(2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-*N*-(2-propyl)-(*Z*)-2-butenamide (**14d**).

Isopropylamine (20 ml) and sodium hydride (750 mg, 33 mmoles) were heated under reflux for one hour, then 4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5a**) (5.7 g, 15 mmoles) was added. The reaction mixture was heated under reflux for further three hours, isopropylamine was then evapo-

rated *in vacuo*, ether (10 ml) and then slowly water (10 ml) was added to the residue. The mixture was acidified with acetic acid and the precipitate was collected by filtration and washed by ether, yield 49%, mp 200-203° (from acetonitrile); ^{1}H nmr (DMSO-d_6): δ 1.06 (d, 6H, CH*Me*$_2$), 1.31 (t, 3H, CH_2*Me*), 1.83 (s, 3H, 6'-Me), 3.09 (q, 2H), 3.9 (m, C*H*Me$_2$), 5.38 (d, 4-H), 7.2-8.1 (m, 7H, Ph, 3-H, N*H*CH), 9.46 (s, N*H*COPh), 11.82 (s, 2'-H), J_{CHMe_2} = 6.5 Hz, $J_{CH_2CH_3}$ = 7.0 Hz, $J_{3\text{-H, }4\text{-H}}$ = 11.5 Hz.

Anal. Calcd. for $C_{20}H_{25}N_5O_2S$: C, 60.13; H, 6.31; N, 17.53. Found: C, 59.93; H, 6.42; N, 17.61.

2-Benzoylamino-(*Z*)-4-(2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-(*Z*)-2-butenoylhydrazine (**14e**).

4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5a**) (1.14 g, 3 mmoles), 80% hydrazine hydrate (1 ml) and ethanol (10 ml) were stirred at room temperature for one hour. The precipitate was collected by filtration and washed by ethanol, yield 73%, mp 179-184° (from *N*,*N*-dimethylformamide/water); ^{1}H nmr (DMSO-d_6): δ 1.36 (t, 3H, CH_2*Me*), 1.89 (s, 3H, 6'-Me), 3.15 (q, 2H, C*H*$_2$Me), 4.3 (s, broad, 2H, NH_2), 5.47 (d, 4-H), 7.4-8.2 (m, 6H, Ph, 3-H), 9.23 (s, N*H*NH$_2$), 9.64 (s, NHCO), 12.0 (s, broad, 2'-H), $J_{CH_2CH_3}$ = 7.0 Hz, $J_{3\text{-H, }4\text{-H}}$ = 11.5 Hz.

Anal. Calcd. for $C_{17}H_{20}N_6O_2S$: C, 54.82; H, 5.41; N, 22.56. Found: C, 55.13; H, 5.45; N, 22.20.

(*Z*)-4-(2-Acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-2-benzoylamino-(*Z*)-2-butenoic Acid (**15**).

4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (**5a**) (1.15 g, 3 mmoles) was heated under reflux in the mixture of concentrated hydrochloric acid (6 ml) and water (25 ml) for 12 hours. The precipitate was, after cooling to 0°, collected by filtration and washed by boiling five minutes in toluene (25 ml) to give, after repeated filtration, **15** in 18% yield, mp 232-235° (from *N*,*N*-dimethylformamide/water); ^{1}H nmr (DMSO-d_6): δ 1.33 (t, 3H, CH_2*Me*), 2.10 (s, 3H, 6'-Me), 2.36 (s, 3H, COMe), 2.94 (q, 2H, C*H*$_2$Me), 6.00 (d, 4-H), 7.4-8.1 (m, 6H, Ph, 3-H), 9.81 (s, NHCO), $J_{CH_2CH_3}$ = 7.0 Hz, $J_{3\text{-H, }4\text{-H}}$ = 11.5 Hz.

Anal. Calcd. for $C_{19}H_{20}N_4O_4S\cdot 1/2H_2O$: C, 55.73; H, 5.17; N, 13.68. Found: C, 56.14; H, 5.07; N, 13.80.

The toluene extract was evaporated *in vacuo*, the residue was purified in column chromatography (silica gel, chloroform) to give pure (*Z*)-4-((*Z*)-2-(2-acetyl-2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))ethylidene)-2-phenyl-5(4*H*)-oxazolone (*Z*-**5a**), yield 34%.

2-Benzoylamino-4-(3-oxo-2,3,4,5-tetrahydro-5-(1,2,4-triazinylidene))-2-butenoates **16**.

Procedure A.

Ester **13** (2 mmoles) was heated under reflux in 10% solution of hydrochloric acid (6 ml) for 15 minutes. The precipitate was, after cooling to 0°, collected by filtration and washed with water.

The following compounds were prepared according to this procedure:

Methyl 2-Benzoylamino-(*Z*)-4-(6-methyl-3-oxo-2,3,4,5-tetrahydro-5-(1,2,4-triazinylidene))-(*Z*)-2-butenoate Monohydrate (**16a**).

This compound was prepared from methyl 2-benzoylamino-(*Z*)-4-(2,5-dihydro-3-methoxy-6-methyl-5-(1,2,4-triazinylidene))-(*Z*)-2-butenoate (**13d**) in 85% yield, mp 302-306° dec (from *N*,*N*-dimethylformamide/water); ^{1}H nmr (DMSO-d_6): δ 1.97 (s, 3H, 6'-Me), 3.71 (s, 3H, COOMe), 5.42 (d, 4-H), 7.4-8.2 (m, 6H, Ph, 3-H), 9.87 (s, NHCO), 10.7 and 11.1 (s, s, 2'-H, 4'-H), $J_{3\text{-H, }4\text{-H}}$ = 12.5 Hz.

Anal. Calcd. for $C_{16}H_{16}N_4O_4\cdot H_2O$: C, 55.49; H, 5.24; N, 16.18. Found: C, 56.14; H, 5.21; N, 16.24.

Methyl (*Z*)-4-(6-Methyl-3-oxo-2,3,4,5-tetrahydro-5-(1,2,4-triazinylidene))-2-(2-nitrobenzoyl)-(*Z*)-2-butenoate (**16b**).

This compound was prepared from methyl (*Z*)-4-(2,5-dihydro-3-methoxy-6-methyl-5-(1,2,4-triazinylidene))-2-(2-nitrobenzoyl)-(*Z*)-2-butenoate (**13e**) in 88% yield, mp 284-286° dec (from *N*,*N*-dimethylformamide/water); ^{1}H nmr (DMSO-d_6): δ 2.07 (s, 3H, 6'-Me), 3.80 (s, 3H, COOMe), 5.57 (d, 4-H), 7.5-8.3 (m, 5H, Ar, 3-H), 10.08 (s, NHCO), 10.8 and 11.15 (s, s, 2'-H, 4'-H), $J_{3\text{-H, }4\text{-H}}$ = 13.0 Hz.

Anal. Calcd. for $C_{16}H_{15}N_5O_6$: C, 51.48; H, 4.05; N, 18.76. Found: C, 51.24; H, 4.22; N, 18.67.

Ethyl 2-Benzoylamino-(*Z*)-4-(6-methyl-3-oxo-2,3,4,5-tetrahydro-5-(1,2,4-triazinylidene))-(*Z*)-2-butenoate (**16c**).

This compound was obtained from ethyl 2-benzoylamino-(*Z*)-4-(2,5-dihydro-3-methoxy-6-methyl-5-(1,2,4-triazinylidene))-(*Z*)-2-butenoate (**13g**) in 91% yield, mp 298-301° (from acetonitrile); ^{1}H nmr (DMSO-d_6): δ 1.24 (t, 3H, CH_2*Me*), 1.98 (s, 3H, 6'-Me), 4.20 (q, 2H, C*H*$_2$Me), 5.44 (d, 4-H), 7.5-8.2 (m, 6H, Ph, 3-H), 9.93 (s, NHCO), 10.74 and 11.14 (s, s, 2'-H, 4'-H), $J_{CH_2CH_3}$ = 8.0 Hz, $J_{3\text{-H, }4\text{-H}}$ = 13.0 Hz.

Anal. Calcd. for $C_{17}H_{18}N_4O_4$: C, 59.64; H, 5.30; N, 16.37. Found: C, 60.02; H, 5.32; N, 16.76.

Procedure B.

Methyl 2-benzoylamino-(*Z*)-4-(2,5-dihydro-3-ethylmercapto-6-methyl-5-(1,2,4-triazinylidene))-(*Z*)-2-butenoate (**13a**) (370 mg, 1 mmole) was heated under reflux in the mixture of methanol (5 ml) and concentrated hydrochloric acid (3 ml) for two hours. Methyl 2-benzoylamino-(*Z*)-4-(6-methyl-3-oxo-2,3,4,5-tetrahydro-5-(1,2,4-triazinylidene))-(*Z*)-2-butenoate monohydrate (**16a**) was, after cooling to 0°, collected by filtration and washed with water, yield 38%.

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