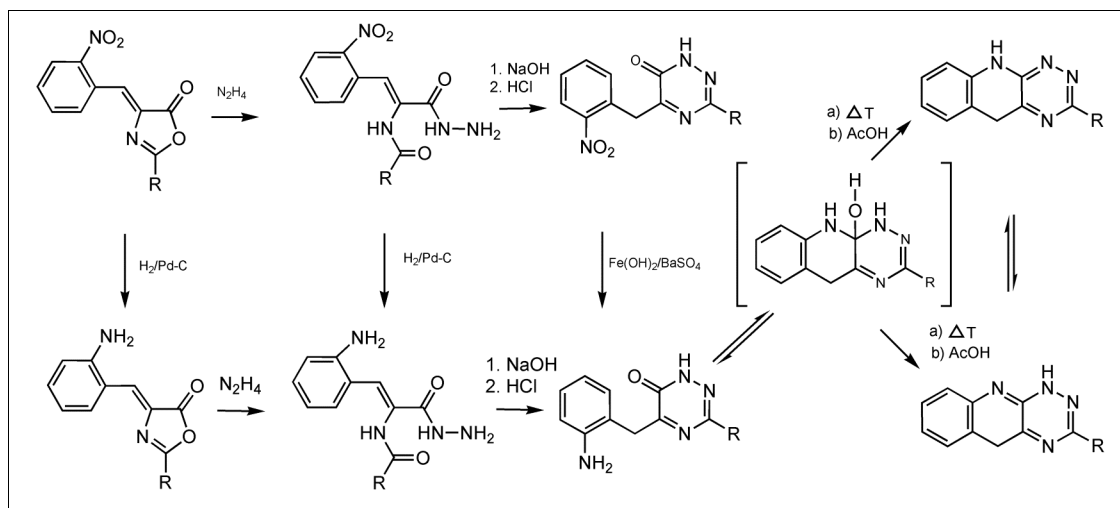


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A series of 2-substituted-4-(2-nitrobenzylidene)-4,5-dihydrooxazol-5-ones (**2a-2i**) was prepared by the Erlenmeyer's synthesis of 2-nitrobenzaldehyde with acylglycines (**1a-1i**) and the series of corresponding aminoderivatives (**3b-3d** and **3g-3i**) was synthesised by catalytic hydrogenation of (**2b-2d** and **3g-3i**). Hydrazinolysis of azlactones (**2**) and (**3**) gave hydrazides (**4**) and (**5**). The hydrazides (**5**) were also obtained by catalytic hydrogenation of corresponding nitroderivatives (**4**). The cyclization reaction of hydrazides (**4**) or (**5**) proceeded to 3,5-disubstituted-1,6-dihydro-[1,2,4]triazine-6-ones (**6**) or (**7**). Aminoderivatives (**7**) were also obtained by reduction of nitro group of compounds (**6**). The aminoderivatives (**7**) were then cyclized to 3-substituted-1,5-dihydro-[1,2,4]triazino[6,5-*b*]quinolines (**9**), resp. its tautomers (**10**).

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## Introduction.

A large number of [1,2,4]triazines substituted with 2-aminophenyl [2-11] or 2-aminobenzyl [12-13] group have been found as advantageous synthons for preparation of various condensed heterocyclic systems which bear [1,2,4]triazine ring. Contrary to 6-azauracile derivatives substituted with mentioned groups analogous derivatives of 1,6-dihydro[1,2,4]triazin-6-one substituted with 2-aminobenzylgroup (**7**) have not been synthesized up to this time and their cyclocondensation reactions could not be studied. They were described only as probable and unisolable intermediates in the synthesis of some [1,2,4]triazino[6,5-*b*]quinolines which was the matter of one of our previous communications [14].

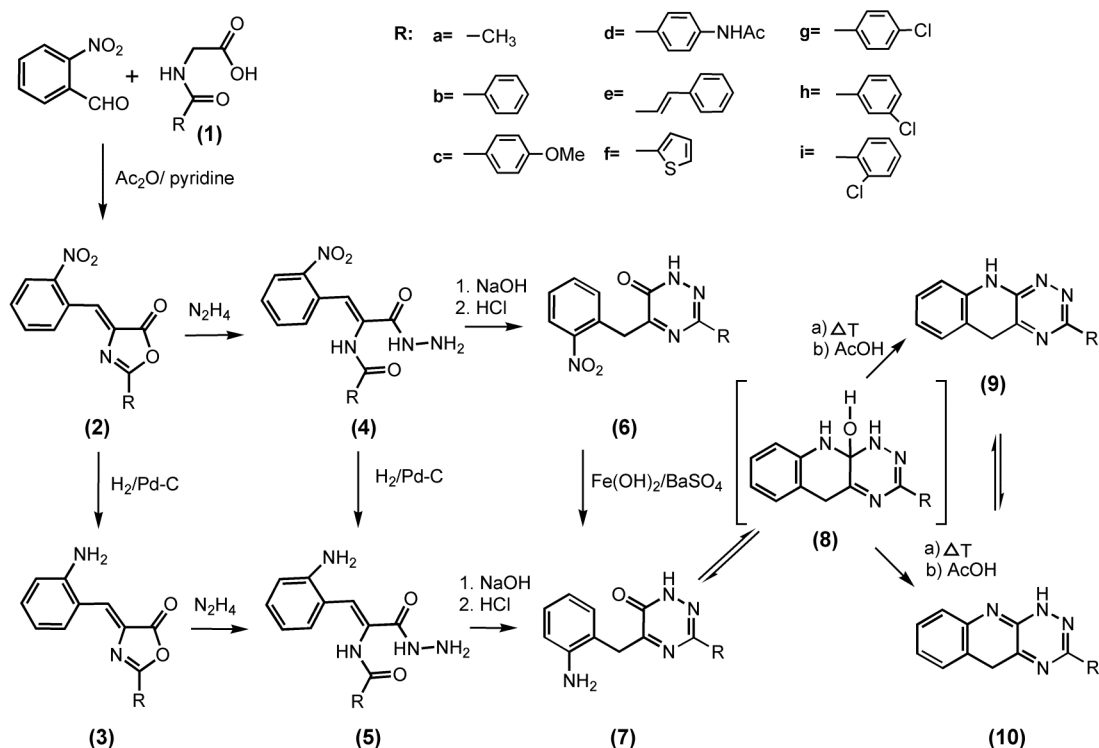
## Results and Discussion.

Now we focused on possibility of isolation of aminoderivatives (**7**) and study of their cyclocondensation

reactions. As starting compounds we used 2-substituted-4-(2-nitrobenzylidene)-4,5-dihydrooxazol-5-ones (**2**) which were prepared by Erlenmeyer's synthesis. The corresponding 2-substituted-4-(2-aminobenzylidene)-4,5-dihydrooxazol-5-ones (**3b-3d** and **3g-3i**) were obtained by catalytic hydrogenation of nitroderivatives (**2b-2d** and **3g-3i**) under atmospheric pressure. The hydrogenation of exocyclic double bond of azlactones (**2**) is much slower than hydrogenation of the nitrogroup and the crude product is therefore contaminated with only small amount of 3-acylamino-1,2,3,4-tetrahydroquinoline-2-ones. We were able to isolate azlactones (**3b-3d** and **3g-3i**) in very good yield and purity after one crystallization.

We were also interested in assignment of geometry on exocyclic double bond of prepared azalactones (**2**) and (**3**). We supposed that only *Z*- isomers were formed because we did not observe any formation of 3-acylamino-1,2-dihydroquinoline-2-ones (**13**) during

Scheme 1



catalytic hydrogenation of azlactones (**2**). In accordance to ref. [14] the azlactone (**3**) with *E*- configuration would probably cyclise easily to mentioned quinolines (**13**). The assignment of geometric isomery was performed by determination of vicinal coupling constant between <sup>13</sup>C carbon in position 5- of oxazolone ring and olefinic

proton of exocyclic double bond and vicinal coupling constant between <sup>15</sup>N in position 3- of oxazolone ring and the same olefinic proton. We used the GE-HSQC method [15] and the values are given in Table 1. The found values of <sup>13</sup>C-<sup>1</sup>H coupling constants are in agreement with value found for comparable *Z*- 2-phenyl-4-benzylidene-4,5-dihydrooxazol-5-one [16].

The reaction of azalactones (**2**) or (**3**) with hydrazine hydrate under mild conditions gave hydrazides of 2-acylamino-3-(2-nitrophenyl)acrylic acids (**4**) or hydrazides of 2-acylamino-3-(2-aminophenyl)acrylic acids (**5**), respectively. The hydrazides (**5**) were also synthesized by catalytic hydrogenation of the nitroderivatives (**4**).

Cyclization of these hydrazides in alkaline medium proceeded smoothly to the 3-substituted-5-(2-substituted-benzyl)-1,6-dihydro-[1,2,4]-triazine-6-ones (**6**) or (**7**). However, this cyclisation reaction failed in the cases of **4i**

Scheme 2

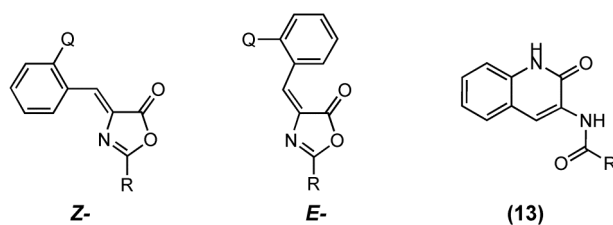
Geometric isomery of azlactones (**2**) and (**3**)

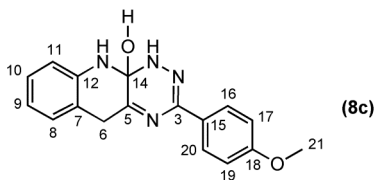
Table 1

Compound	Q	R	δ(ppm) H	δ(ppm) C <sub>5</sub>	J ( <sup>1</sup> H- <sup>13</sup> C) (Hz)	J ( <sup>1</sup> H- <sup>15</sup> N) (Hz)
<b>2b</b>	NO <sub>2</sub>	Ph	7.57	166.7	5.4	-
<b>2c</b>	NO <sub>2</sub>	4-MeOPh	7.46	154.1	5.4	4.8
<b>2i</b>	NO <sub>2</sub>	2-ClPh	7.61	167.6	5.5	-
<b>2f</b>	NO <sub>2</sub>	2-C <sub>4</sub> H <sub>3</sub> S	7.57	166.7	5.4	-
<b>3c</b>	NH <sub>2</sub>	4-MeOPh	7.45	167.8	5.4	4.8

and **5i**. Prolongation of reaction time in these cases resulted in the hydrolysis of the hydrazido group. The 3-substituted-5-(2-aminobenzyl)-1,6-dihydro-[1,2,4]triazine-6-ones (**7**) were also prepared by the reduction of the corresponding nitro derivatives with ferrous hydroxide precipitated on baryum sulfate.

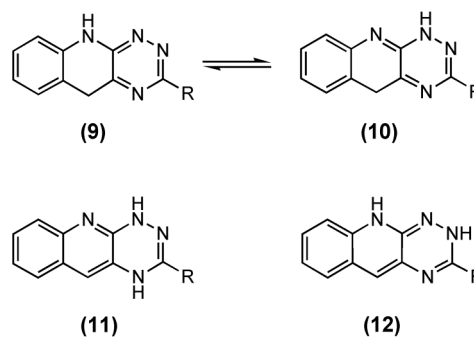
The structure of prepared 3-substituted-5-(2-aminobenzyl)-1,6-dihydro[1,2,4]triazine-6-ones seems to be different in solid state and in solution. In the solid state, characteristic frequencies of carbonyl group as well as of aminogroup were observed in IR spectra. Surprisingly, we did not observe the signal of methylene group in the  $^1\text{H}$  NMR spectra as singlet but as two doublets ( $J=16.5\text{-}17.0$ ) and, instead of a broad signal of aminogroup, we observed three singlets of relatively acidic protons. We proposed structure (**8**) for explanation of these facts which is also the probable intermediate of further cyclisation reaction to the [1,2,4]triazino[6,5-*b*]quinolines (**9**) or (**10**). In this rigid structure without possibility of free rotation, the methylene group is *prochiral* and chemical shifts of both methylene protons should be different. Two acidic NH protons and OH proton are also present in this structure. For further study we have chosen compound **7c**. We proved the proposed structure (**8c**) with the help of  $^{13}\text{C}$  APT,  $^1\text{H}$ - $^1\text{H}$  COSY,  $^1\text{H}$ - $^{13}\text{C}$  HMQC and  $^1\text{H}$ - $^{13}\text{C}$  HMQC spectra. Thus we were able to assign the protons to corresponding carbons and determine the position of quaternary carbons. The results of are summarized in Table 2. The numbering of carbons is shown in Scheme 3.

Scheme 3



The most important part of this work was the study of cyclocondensation reaction of 3-substituted-5-(2-aminobenzyl)-1,6-dihydro[1,2,4]triazine-6-ones (**7**) to the 3-substituted-[1,2,4]triazino[6,5-*b*]quinolines (**9**). The cyclocondensation reaction proceeded smoothly in boiling acetic acid for 10 hours, as well as thermal cyclisation performed in boiling anisole. Finally, [1,2,4]triazino[6,5-*b*]quinolines (**9**) were also synthesized by the action of phosphorous oxychloride. No dependence of yields or reaction times on substituents on position 3- was observed.

Scheme 4



Beside tautomeric forms (**9**) and (**10**) it is also possible to suppose 1,4-dihydro form (**11**) or 2,10-dihydrotautomeric form (**12**). In the NMR spectra of prepared triazino[6,5-*b*]quinolines we observed only the signal of methylene group protons which evidences of only presence of 5,10-dihydro (**9**), resp. 1,5-dihydro (**10**) forms. Similar structure has been assigned for 2,3,4,10-tetrahydro[1,2,4]triazino[5,6-*b*]quinolin-3-one [13].

## EXPERIMENTAL

Melting points were determined on a Boetius stage and are not corrected. Infrared spectra were measured in KBr disks and scanned on an ATI Unicam Genesis FTIR instrument and values are described in  $\text{cm}^{-1}$ . NMR spectra were measured in solutions in  $\text{dms}\text{-}d_6$  on a Bruker AMX-300 spectrometer (300 MHz); the chemical shifts reported are in ppm, coupling constants in Hz).

Table 2

Carbon position	$^{13}\text{C}$ $\delta$ (ppm)	$^1\text{H}$ $\delta$ (ppm)	Carbon position	$^{13}\text{C}$ $\delta$ (ppm)	$^1\text{H}$ $\delta$ (ppm)
3	144.2	-	12 or 7	126.2	-
5	162.9	-	14	73.8	-
6	39.1	3.13, 3.85	15	125.4	-
7 or 12	149.0	-	16, 20	128.2	7.73
8	124.0	7.04	17, 19	114.0	6.94
9	127.5	6.94	18	160.9	-
10	117.8	6.59	21	55.7	3.79
11	107.6	6.38			

Elemental analyses were performed by using an EA 1108 Elemental Analyzer (Fison Instrument). Mass spectrometric experiments were performed using an LCQ ion trap mass spectrometer (Finnigan MAT, San Jose, CA, USA).

#### *N*-Acylglycines (**1a-1i**).

The *N*-acylglycines (**1a-1e** and **1g-1i**) were prepared according to literature: acetylglycine **1a** [19], benzoylglycine **1b** [20], 4-methoxybenzoylglycine **1c** and 3-chlorobenzoylglycine **1h** [21], 4-acetylamino benzoylglycine **1d** [22], *trans*-cinnamoylglycine **1e** [23], 4-chlorobenzoylglycine **1g** and 2-chlorobenzoylglycine **1i** [24].

The *N*-(2-thienyl)karbonylglycine **1f** has not been described up to this time and was prepared according to the following procedure:

The stirred mixture of 2-thiophenecarboxylic acid (15.00 g, 117.05 mmol), thionylchloride (21.0 g, 176 mmol) and anhydrous pyridine (100  $\mu$ l) was heated at 110 °C for 2 hours. After cooling to room temperature, the excess of thionylchloride was removed *in vacuo*. The oily residue was slowly added to a stirred ice cooled solution of glycine (8.75 g, 116.50 mmol) in 6 *M* sodium hydroxide (40 ml) for a period 10 minutes and it was then stirred at room temperature for a further 30 minutes. The solution was acidified with conc. hydrochloric acid to pH=1-2. The solid was collected by filtration and washed a few times with ice-cold water. The crude product was crystallized from a mixture water-ethanol (1:1). Yield: 74%, mp: 168-170 °C.

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*Anal.* Calcd. For C<sub>7</sub>H<sub>7</sub>NO<sub>3</sub>S 45.40 C, 3.81 H, 7.56 N, 17.31 S. Found 45.25 C, 3.72 H, 7.39 N, 17.01 S.

#### 2-Substituted 4-(2-nitrobenzylidene)-4,5-dihydrooxazol-5-ones (**2**).

##### General Procedure.

A stirred mixture of 2-nitrobenzaldehyde (1.00 g, 6.62 mmol), corresponding *N*-acylglycine (6.62 mmol), dry pyridine (0.5 ml) and acetic anhydride (1.4 ml) was heated using a boiling water bath for 30 minutes. After cooling to room temperature the mixture was allowed to stand at 0 °C overnight. The precipitate was collected by filtration, washed with diethylether (10 ml) and ethanol (20 ml) and crystallized from an appropriate solvent.

2-Methyl-4-(2-nitrobenzylidene)-4,5-dihydrooxazol-5-one (**2a**), see [17].

4-(2-Nitrobenzylidene)-2-phenyl-4,5-dihydrooxazol-5-one (**2b**), see [18].

2-(4-Methoxyphenyl)-4-(2-nitrobenzylidene)-4,5-dihydrooxazol-5-one (**2c**).

Yield 93%, m.p. 183-185 °C (toluene), ir 3107, 3068, 1800, 1659, 1603, 1514, 1475, 1439, 1337, 1262, 1222, 1171, 1140,

1011, 1034, 978, 865, 740, 783, <sup>1</sup>H nmr (DMSO): 3.92(s, 3H, -OCH<sub>3</sub>), 7.18(d, 2H, ArH, J=8.7 Hz), 7.46(s, 1H, C=H), 7.72(t, 1H, ArH, J=8.4 Hz), 7.90(t, 1H, ArH, J=8.4 Hz), 8.05-8.14(m, 3H, ArH), 8.62(d, 1H, J=9.0 Hz), <sup>13</sup>C nmr (DMSO): 45.40; 104.62; 106.31; 111.86; 114.51; 120.21; 120.64; 122.47; 123.07; 125.90; 138.63; 153.74; 154.16.

*Anal.* Calcd. for C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>O<sub>5</sub>: 62.96 C, 3.73 H, 8.64 N. Found: 61.68 C, 3.56 H, 8.99 N.

2-(4-Acetylamino phenyl)-4-(2-nitrobenzylidene)-4,5-dihydrooxazol-5-one (**2d**).

Yield 95%, mp 218-220 °C (toluene), ir 3331, 3082, 1784, 1764, 1702, 1649, 1597, 1524, 1411, 1345, 1316, 1258, 1229, 1175, 992, 888, 849, <sup>1</sup>H nmr (DMSO): 1.91(s, 3H, CH<sub>3</sub>), 7.47(s, 1H, =CH), 7.72(t, 1H, ArH, J=9.0Hz), 7.82-7.92(m, 4H, ArH), 8.04(d, 2H, ArH, J=9.0Hz), 8.13(d, 1H, ArH, J=7.2Hz), 8.62(d, 1H, ArH, J=7.8Hz), 10.43(s, 1H, NH), <sup>13</sup>C nmr (DMSO): 21.49, 119.35, 122.98, 125.36, 127.82, 130.14, 131.54, 133.93, 136.74, 145.13, 149.49, 164.90, 166.94, 169.61, 172.44.

*Anal.* Calcd. for C<sub>18</sub>H<sub>13</sub>N<sub>3</sub>O<sub>5</sub>: 61.54 C, 3.73 H, 11.96 N. Found: 61.45 C, 3.59 H, 11.84 N.

4-(2-Nitrobenzylidene)-2-styryl-4,5-dihydrooxazol-5-one (**2e**).

Yield 88%, mp 152-155 °C (toluene-ethanol (1:1)), ir 3181, 1680, 1444, 1209, 1140, 845, 804, 725, <sup>1</sup>H nmr (DMSO): 7.6(d, 1H, ArH, J=7.2 Hz), 7.46-7.48(m, 3H, ArH), 7.50(s, 1H, =CH), 7.73(t, 1H, ArH, J=8.7 Hz), 7.84-7.92(m, 4H, ArH), 8.15(d, 1H, =CH(styryl), J=7.8), 8.51(d, 1H, =CH(styryl), J=7.8) <sup>13</sup>C nmr (DMSO): 113.67, 123.90, 125.43, 127.89, 129.28, 129.54, 131.66, 133.28, 133.01, 134.79, 136.80, 145.54, 149.33, 165.43, 166.61, 172.43.

*Anal.* Calcd. For C<sub>18</sub>H<sub>12</sub>N<sub>2</sub>O<sub>4</sub>: 67.50 C, 3.78 H, 8.75 N. Found: 67.71 C, 3.65 H, 8.60 N.

4-(2-Nitrobenzylidene)-2-(2-thienyl)-4,5-dihydrooxazol-5-one (**2f**).

Yield 91%, mp 148-150 °C (toluene), ir 3004, 1717, 1593, 1552, 1438, 1343, 1281, 1094, 781, 847, 1015, <sup>1</sup>H nmr (DMSO): 7.36(t, 1H, ArH, J=4.5Hz), 7.49(s, 1H, =CH), 7.72(t, 1H, ArH, J=7.8Hz), 7.91(t, 1H, ArH, J=7.5Hz), 7.05(d, 1H, ArH, J=3.9Hz), 8.12-8.17(m, 2H, ArH), 8.49(d, 1H, ArH, J=7.8Hz), <sup>13</sup>C nmr (DMSO): 112.57, 114.56, 116.92, 119.06, 120.74, 122.29, 123.11, 123.86, 125.44, 125.59, 138.52, 150.16, 155.56.

*Anal.* Calcd. for C<sub>14</sub>H<sub>10</sub>N<sub>2</sub>O<sub>4</sub>S: 56.00 C, 2.69 H, 9.33 N, 10.68 S. Found: 55.78 C, 2.54 H, 9.44 N, 10.46 S.

2-(4-Chlorophenyl)-4-(2-nitrobenzylidene)-4,5-dihydrooxazol-5-one (**2g**).

Yield 79%, mp 227-229 °C (toluene), ir: 3075, 1792, 1656, 1593, 1526, 1485, 1405, 1349, 1294, 1227, 1175, 1091, 982, 871, 841, 785, <sup>1</sup>H nmr (DMSO): 7.57(d, 2H, ArH, J=8.4), 7.61(s, 1H, C=H), 7.71-7.82(m, 2H, ArH), 7.94(d, 2H, ArH, J=8.4), 8.10(d, 1H, ArH, J=8.7), *Anal.* Calcd. For C<sub>16</sub>H<sub>9</sub>N<sub>2</sub>O<sub>4</sub>Cl: 58.46 C, 2.76 H, 8.52 N. Found: 58.24 C, 2.74 H, 8.44 N.

2-(3-Chlorophenyl)-4-(2-nitrobenzylidene)-4,5-dihydrooxazol-5-one (**2h**).

Yield 79%, mp 227-229 °C (toluene), ir: 3073, 1803, 1651, 1583, 1518, 1432, 1342, 1303, 1224, 1171, 876, 998, 739, <sup>1</sup>H nmr (DMSO): 7.57(d, 2H, ArH, J=8.4), 7.61(s, 1H, C=H), 7.71-7.82(m, 2H, ArH), 7.94(d, 2H, ArH, J=8.4), 8.10(d, 1H, ArH, J=8.7).

*Anal.* Calcd. For  $C_{16}H_9N_2O_4Cl$ : 58.46 C, 2.76 H, 8.52 N, Found: 58.24 C, 2.74 H, 8.44 N.

2-(2-Chlorophenyl)-4-(2-nitrobenzylidene)-4,5-dihydrooxazol-5-one (**2i**).

Yield 86%, mp 164-166°C (toluene), ir: 3108, 3073, 1799, 1654, 1578, 1519, 1474, 1431, 1337, 1262, 1221, 1173, 980, 874, 728.

*Anal.* Calcd. For  $C_{16}H_9N_2O_4Cl$ : 58.46 C, 2.76 H, 8.52 N, Found: 58.18 C, 3.02 H, 8.57 N

2-Substituted-4-(2-aminobenzylidene)-4,5-dihydrooxazol-5-ones (**3**).

General Procedure.

2-Substituted-4-(2-nitrobenzylidene)-4,5-dihydrooxazol-5-one (**2**) (10.20 mmol) was suspended in amount *x* of solvent **A** and palladium on charcoal (10%) was added (150 mg). The hydrogenation was performed under atmospheric pressure in a Parr hydrogenation apparatus. After consumption of hydrogen (685 ml, 30.60 mmol) the reaction mixture was filtered and the solvent evaporated *in vacuo*. The crude product was recrystallized from toluene.

4-(2-Aminobenzylidene)-2-phenyl-4,5-dihydrooxazol-5-one (**3b**).

Yield: 97% mp 170-172°C (toluene), **A**=ethylacetate, *x*=60ml, ir:3399, 3375, 3063, 1757, 1649, 1598, 1556, 1531, 1489, 1449, 1404, 1325, 1295, 1263, 1181, 1109, 1068, 1001, 891, 874, 762, 746, 696. <sup>1</sup>H nmr (DMSO): 6.23 (s(br), 2H, NH<sub>2</sub>), 6.65 (t, 1H, ArH, J= 7.8), 6.75 (d, 1H, ArH, J=7.9), 7.16 (t, 1H, Ar, J=7.7), 7.47 (s, 1H, =CH), 7.75-7.51 (m, 3H, ArH), 8.08 (d, 2H, ArH, J= 7.7), 8.18 (d, 1H, ArH, J=8.1).

*Anal.* Calcd. for  $C_{16}H_{12}N_2O_2$  72.72 C, 4.58 H, 10.60 N, Found 72.63 C, 4.31 H, 10.79 N.

4-(2-Aminobenzylidene)-2-(4-methoxyphenyl)-4,5-dihydrooxazol-5-one (**3c**).

Yield: 98% mp 201-203°C (toluene), **A**=ethylacetate, *x*=300ml, ir: 3345, 3171, 1771, 1637, 1603, 1551, 1507, 1449, 1310, 1264, 1233, 1175, 1100, 1020, 988, 898, 837, 737 <sup>1</sup>H nmr: 6.32(s(br), 2H, NH<sub>2</sub>), 6.64(t, 1H, ArH, J=7.8), 6.74(d, 1H, ArH, J=8.1), 7.13-7.18(m, 3H, ArH), 7.45(s, 1H, =CH), 8.01(d, 2H, ArH, J=9.0), 8.44(d, 1H, ArH, J=8.1), <sup>13</sup>C nmr: 56.09, 115.33, 116.79, 117.09, 127.24, 128.65, 130.07, 133.28, 151.11, 161.07, 163.66, 167.78.

*Anal.* Calcd. for  $C_{17}H_{14}N_2O_3$ : 69.38 C, 4.79 H, 9.52 N, Found: 69.32 C, 5.09 H, 9.78 N.

2-(4-Acetylaminophenyl)-4-(2-aminobenzylidene)-4,5-dihydrooxazol-5-one (**3d**).

Yield: 98%, mp 138-140°C (toluene), **A**=acetic acid, *x*=175ml, ir: 1669, 1636, 1597, 1526, 1507, 1407, 1373, 1321, 1264, 1184, 3253, 852, 1016, 755.

*Anal.* Calcd. for  $C_{18}H_{15}N_3O_3$ : 67.28 C, 4.71 H, 13.08 N, Found 67.12 C, 4.39 H, 13.27 N.

4-(2-Aminobenzylidene)-2-(4-chlorophenyl)-4,5-dihydrooxazol-5-one (**3g**).

Yield: 98%, mp: 208-210°C (toluene), **A**=ethylacetate, *x*=200ml, ir: 3412, 3335, 3092, 3062, 1771, 1647, 1595, 1553, 1486, 1458, 1414, 1321, 1269, 1169, 1095, 988, 878, 839, 761, 727, <sup>1</sup>H nmr

(DMSO): 6.39(s(br), 1H, NH<sub>2</sub>), 7.56(s, 1H, C=H), 7.62-7.73(m, 4H, ArH), 7.98(d, 2H, ArH, J=8.4), 8.07(d, 2H, ArH, J=8.4).

*Anal.* Calcd. for  $C_{16}H_{11}N_2O_2Cl$ : 64.33 C, 3.71 H, 9.38 N, Found: 63.96 C, 3.41 H, 9.46 N.

4-(2-Aminobenzylidene)-2-(3-chlorophenyl)-4,5-dihydro-oxazol-5-one (**3h**).

Yield: 98%, mp: 144-146°C (toluene), **A**=ethylacetate, *x*=100ml, ir: 3410, 3396, 3075, 1759, 1643, 1580, 1458, 1430, 1298, 1261, 1179, 1015, 899, 763.

*Anal.* Calcd. for  $C_{16}H_{11}N_2O_2Cl$ : 64.33 C, 3.71 H, 9.38 N, Found 64.12 C, 3.99 H, 9.35 N.

4-(2-Aminobenzylidene)-2-(2-Chlorophenylphenyl)-4,5-dihydrooxazol-5-one (**3i**).

Yield: 96%, mp: 107-109°C (toluene), **A**=ethanol, *x*=150ml, ir: 3422, 3166, 1771, 1642, 1540, 1478, 1316, 1163, 1265, 1050, 986, 885, 864, 760, 730.

*Anal.* Calcd. for  $C_{16}H_{11}N_2O_2Cl$  : 64.33 C, 3.71 H, 9.38 N, Found: 64.62 C, 3.83 H, 9.61 N.

*N*-[1-Hydrazinocarbonyl-2-(2-nitrophenyl)vinyl]acetyl amides (**4**).

General Procedure.

Well powdered 2-substituted-4-(2-nitrobenzylidene)-4,5-dihydrooxazol-5-one (**2**) (8.70 mmol) was suspended in ethanol (5.0 ml) and 99% hydrazin hydrate (10.44 mmol) was slowly added over a 2 minutes period and the reaction mixture was stirred for 15 minutes. It was then allowed to stand for 30 minutes at 0°C. The precipitate was collected, washed with water (10 ml), then ethanol (15 ml). It was recrystallized from ethanol.

*N*-[1-Hydrazinocarbonyl-2-(2-nitrophenyl)vinyl]acetyl amide (**4a**).

Yield: 75%, mp 162-165°C (ethanol), ir: 3315, 3245, 3060, 2984, 1674, 1523, 1373, 1308.

*Anal.* Calcd. For  $C_{13}H_{16}N_4O_3$ : 50.00 C, 4.58 H, 21.20 N, Found: 50.25 C, 4.55 H, 21.07 N.

*N*-[1-Hydrazinocarbonyl-2-(2-nitrophenyl)vinyl]benzamide (**4b**), see [25].

*N*-[1-Hydrazinocarbonyl-2-(2-nitrophenyl)vinyl]-4-methoxybenzamide (**4c**).

Yield: 97%, mp: 168-170°C (ethanol), ir: 3324, 3243, 2971, 2845, 1640, 1607, 1572, 1518, 1495, 1476, 1344, 1264, 1186, 1026, 845, 973, 774, 735.

*Anal.* Calcd. for  $C_{17}H_{16}N_4O_3$ : 57.30 C, 4.53 H, 15.72 N, Found: 57.20 C, 4.77 H, 15.90 N.

*N*-[1-Hydrazinocarbonyl-2-(2-nitrophenyl)vinyl]-4-acetylaminobenzamide (**4d**).

Yield: 95%, mp: 154-156°C (ethanol), ir: 3315, 3206, 2901, 1692, 1631, 1593, 1520, 1341, 1316, 1258, 1184, 857.

*Anal.* Calcd. for  $C_{18}H_{17}N_5O_3$ : 56.40 C, 4.47 H, 18.27 N, Found: 56.65 C, 4.22 H, 18.09 N.

*N*-[1-Hydrazinocarbonyl-2-(2-nitrophenyl)vinyl]-3-phenylacrylamide (**4e**).

Yield: 83%, mp: 208-209°C (ethanol), ir: 3298, 3266, 3213, 3024, 2982, 1658, 1620, 1514, 1338, 1186, 1071, 987, 863, 735.

*Anal.* Calcd. for  $C_{18}H_{16}N_4O_4$ : 61.36 C, 4.58 H, 15.90 N, Found: 61.65 C, 4.82 H, 15.83 N.

*N*-[1-Hydrazinocarbonyl-2-(2-nitrophenyl)vinyl]-2-Thienylkarbonylaminoamide (**4f**).

Yield: 91%, mp: 188-190°C (ethanol), ir: 3250, 3080, 1643, 1519, 1495, 1346, 1291, 1128, 973, 853, 736.

*Anal.* Calcd. for C<sub>14</sub>H<sub>12</sub>N<sub>4</sub>O<sub>4</sub>S: 50.60 C, 3.64 H, 16.86 N, 9.65 S, Found: 50.55 C, 3.83 H, 17.02 N, 9.73 S.

*N*-[1-Hydrazinocarbonyl-2-(2-nitrophenyl)vinyl]-4-chlorobenzamide (**4g**).

Yield: 65%, mp: 105-110°C (ethanol), ir: 3330, 2928, 1718, 1626, 1573, 1536, 1462, 1310, 1243, 1198, 1088, 890, 697, 1682, <sup>1</sup>H nmr (DMSO): 4.46(s(br), 2H, NH<sub>2</sub>), 7.44(d, 2H, ArH, J=7.20), 7.50-7.55(m, 3H, ArH, C=H), 7.64(t, 3H, ArH, J=8.40), 7.80(d, 2H, ArH, J=8.40), 8.11(d, 2H, ArH, J=8.40), 9.63(s, 1H, NH), 9.77(s, 1H, NH), <sup>13</sup>C nmr (DMSO): 125.03, 125.60, 128.65, 129.69, 130.20, 130.69, 130.95, 131.52, 132.87, 134.12, 136.90, 147.81, 163.87.

*Anal.* Calcd. for C<sub>16</sub>H<sub>13</sub>N<sub>4</sub>O<sub>4</sub>Cl: 53.27 C, 3.63 H, 15.53 N, Found: 53.69 C, 3.66 H, 15.75 N.

*N*-[1-Hydrazinocarbonyl-2-(2-nitrophenyl)vinyl]-3-chlorobenzamide (**4h**).

Yield: 94%, mp: 162-164°C (ethanol), ir: 3300, 3229, 3067, 1649, 1612, 1518, 1469, 1341, 1290, 1100, 963, 731, 767. <sup>1</sup>H nmr (DMSO): 4.50(s(br), 2H, NH<sub>2</sub>), 7.33(s, 1H, C=H), 7.56-7.81(m, 6H, ArH), 8.01(d, 1H, ArH, J=9.00), 8.14(d, 1H, ArH, J=8.10), 9.40(s, 1H, NH), 10.16(s, 1H, NH) <sup>13</sup>C nmr (DMSO): 124.49, 125.00, 129.97, 130.56, 130.91, 131.46, 131.74, 133.78, 134.26, 147.64, 163.99, 164.97.

*Anal.* Calcd. for C<sub>16</sub>H<sub>13</sub>N<sub>4</sub>O<sub>4</sub>Cl: 53.27 C, 3.63 H, 15.53 N, Found 52.98 C, 3.73 H, 15.82 N.

*N*-[1-Hydrazinocarbonyl-2-(2-nitrophenyl)vinyl]-2-chlorobenzamide (**4i**).

Yield: 89%, mp: 174-176°C (ethanol), ir: 3340, 3245, 1660, 1625, 1516, 1468, 1341, 1297, 1208, 1053, 972, 860, 795.

*Anal.* Calcd. for C<sub>16</sub>H<sub>13</sub>N<sub>4</sub>O<sub>4</sub>Cl: 53.27 C, 3.63 H, 15.53 N, Found 53.53 C, 3.30 H, 15.25 N.

*N*-[2-(2-Aminophenyl)-1-hydrazinocarbonylvinyl]acylamides (**5**).

General Procedures.

Method A.

Well powdered 2-substituted-4-(2-aminobenzylidene)-4,5-dihydrooxazol-5-one (**3**) (8.70 mmol) was suspended in ethanol (5.0 ml) and 99% hydrazin hydrate (10.44 mmol) was slowly added over a 2 minutes period with stirring. The reaction mixture was refluxed for 1 minute and cooled to room temperature. It was then allowed to stand for 30 minutes at 0 °C. The precipitate was collected, washed with ethanol (10 ml), then crystallized from ethanol.

Method B.

The hydrazide of 2-acylamino-3-(2-nitrophenyl)acrylic acid (**4**) (3.00 mmol) was suspended in *y* (ml) of absolute ethanol and palladium on charcoal (10%) was added (50 mg). The hydrogenation was performed under atmospheric pressure in a Parr hydrogenation apparatus. After consumption of hydrogen the catalyst was filtered off and the filtrate evaporated *in vacuo*. The crude product was crystallized from ethanol.

*N*-[2-(2-Aminophenyl)-1-hydrazinocarbonylvinyl]acetylamide (**5a**).

Yield: 96% (method B), mp: 168-169°C (ethanol), *y*=50ml, ir: 3375, 3300, 3210, 3034, 1649, 1513, 1458, 1338, 1268, 758, <sup>1</sup>H nmr (DMSO): 1.89(s, 3H, CH<sub>3</sub>), 4.28(s(br), 2H, NH<sub>2</sub>), 5.16(s(br), 2H, NH<sub>2</sub>), 6.52(t, 1H, ArH, J=7,5), 6.67(d, 1H, ArH, J=8,1), 6.84(s, 1H, C=H), 6.99(t, 1H, ArH, J=8,1), 7.23(d, 1H, ArH, J=7,5), 9.16(s, 1H, NH), 9.29(s, 1H, NH), <sup>13</sup>C nmr (DMSO): 23.19, 115.74, 116.28, 118.56, 123.77, 129.13, 129.31, 129.53, 147.43, 165.54, 169.76.

*Anal.* Calcd. for C<sub>11</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>: 56.40 C, 6.02 H, 23.92 N, Found: 56.21 C, 4.53 H, 23.29 N.

*N*-[2-(2-Aminophenyl)-1-hydrazinocarbonylvinyl]benzamide (**5b**).

Yield: 89% (method A); 95% (method B), mp: 183-185°C (ethanol), *y*=250ml, ir: 3275, 3237, 3199, 3027, 1641, 1601, 1577, 1505, 1486, 1335, 1302, 1263, 1189, 909, 752, 714, <sup>1</sup>H nmr (DMSO): 4.38(s(br), 2H, NH<sub>2</sub>), 5.25(s, 2H, NH<sub>2</sub>), 6.49(t, 1H, ArH, J=7,2), 6.69(d, 1H, ArH, J=8,1), 7.01(s, 1H, C=H), 7.30(d, 1H, ArH, J=7,2), 7.44-7.56(m, 4H, ArH), 7.92(d, 2H, ArH, J=7,2), 9.45(s, 1H, NH), 9.73(s, 1H, NH).

*Anal.* Calcd. for C<sub>16</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub>: 64.85 C, 5.44 H, 18.91 N, Found: 64.59 C, 5.12 H, 18.67 N.

*N*-[2-(2-Aminophenyl)-1-hydrazinocarbonylvinyl]-4-methoxybenzamide (**5c**).

Yield: 92% (method A), 92% (method B), mp: 197-200°C (ethanol), *y*=300ml, ir: 3345, 3325, 3200, 3060, 2834, 1629, 1604, 1493, 1373, 1333, 1313, 1258, 1178, 1033, 969, 943, 843, 753.

*Anal.* Calcd. for C<sub>17</sub>H<sub>18</sub>N<sub>4</sub>O<sub>3</sub>: 62.57 C, 5.56 H, 17.17 N, Found: 62.41 C, 5.43 H, 16.92 N.

*N*-[2-(2-Aminophenyl)-1-hydrazinocarbonylvinyl]-4-chlorobenzamide (**5g**).

Yield: 93% (method A), 96% (method B), mp: 198-200°C (ethanol), *y*=400ml, ir: 3341, 3285, 3200, 2957, 2866, 1636, 1615, 1508, 1476, 1334, 1274, 1182, 1093, 1012, 972, 901, 753, <sup>1</sup>H nmr (DMSO): 4.37(s(br), 2H, NH<sub>2</sub>), 5.25(s(br), 2H, NH<sub>2</sub>), 6.45(t, 1H, ArH, J=7,80), 6.68(d, 1H, ArH, J=8,10), 6.97(t, 1H, ArH, J=6,90), 7.04(s, 1H, C=H), 7.24-7.32(m, 1H, ArH), 7.55(d, 2H, ArH, J=8,40), 7.93(d, 2H, ArH, J=8,40), 9.46(s, 1H, NH), 9.80(s, 1H, NH).

*Anal.* Calcd. for C<sub>16</sub>H<sub>15</sub>N<sub>4</sub>O<sub>2</sub>Cl: 58.10 C, 4.57 H, 16.94 N, Found: 58.29 C, 4.88 H, 16.53 N.

*N*-[2-(2-Aminophenyl)-1-hydrazinocarbonylvinyl]-3-chlorobenzamide (**5h**).

Yield: 78% (method A), 95% (method B), mp: 198-200°C (ethanol), *y*=250ml, ir: 3345, 3325, 3225, 3063, 1659, 1639, 1604, 1513, 1489, 1313, 1286, 1156, 1033, 987, 768.

*Anal.* Calcd. for C<sub>16</sub>H<sub>15</sub>N<sub>4</sub>O<sub>2</sub>Cl: 58.10 C, 4.57 H, 16.94 N, Found: 58.36 C, 4.74 H, 16.85 N.

*N*-[2-(2-aminophenyl)-1-hydrazinocarbonylvinyl]-2-chlorobenzamide (**5i**).

Yield: 92% (method A), 95% (method B), mp: 183-185°C (ethanol), *y*=400ml, ir: 3369, 3260, 3013, 1644, 1501, 1464, 1337, 1263, 747.

*Anal.* Calcd. for  $C_{16}H_{15}N_4O_2Cl$ : 58.10 C, 4.57 H, 16.94 N. Found: 57.93 C, 4.32 H, 16.75 N.

3-Substituted-1,6-dihydro-5-(2-nitrobenzyl)-1H-[1,2,4]triazine-6-ones (**6**).

General Procedures.

Method A.

The hydrazide of 2-acylamino-3-(2-nitrophenyl)acrylic acid (**4**) (1.00 mmol) was refluxed for 2 minutes in aqueous 1 *M* sodium hydroxide solution (2.50 ml). The mixture was filtered while hot with charcoal and after cooling to room temperature the filtrate was neutralized with acetic acid. The precipitate was collected by filtration, then washed with water (20 ml). The crude product was purified by flash column chromatography using chloroform-methanol (10:1) (v/v) as the eluent.

Method B.

The hydrazide of 2-acylamino-3-(2-nitrophenyl)acrylic acid (**4**) (1.00 mmol) was stirred for 18 hours at room temperature in 1 *M* aqueous sodium hydroxide solution (2.50 ml). The reaction mixture was acidified with acetic acid and the precipitate was filtered and washed with water (20 ml).

3-Methyl-5-(2-nitrobenzyl)-1H-[1,2,4]triazine-6-one (**6a**).

Yield: 33% (method A), 58% (method B), mp: 162-165°C, ir: 3200, 3065, 2964, 1679, 1528, 1448, 1348, 1298, 1258, 1203, 863, 758.

*Anal.* Calcd. for  $C_{11}H_{10}N_4O_3$ : 53.66 C, 4.09 H, 22.75 N. Found: 53.38 C, 4.43 H, 22.82 N.

3-Phenyl-5-(2-nitrobenzyl)-1H-[1,2,4]triazine-6-one (**6b**).

Yield: 56% (method A), 85% (method B), mp: 202-204°C, lit.: 205-208°C, ir: 3200, 3135, 1674, 1594, 1574, 1528, 1488, 1448, 1343, 1268, 1133, 1083, 933, 863, 793, 743, 698,  $^1H$  nmr (DMSO): 4.76(s, 2H,  $CH_2$ ), 7.35-7.39(m, 3H, ArH), 7.46(d, 1H, ArH,  $J=7.5$ ), 7.55(t, 1H, ArH,  $J=8.1$ ), 7.66(t, 1H, ArH,  $J=7.2$ ), 7.86(d, 2H, ArH,  $J=7.2$ ), 8.18(d, 1H, ArH,  $J=8.1$ ),  $^{13}C$  nmr (DMSO): 37.26, 125.20, 126.75, 128.56, 130.27, 130.50, 133.30, 133.50, 148.71, 149.60, 154.29, 168.16, 179.26.

*Anal.* Calcd. for  $C_{16}H_{12}N_4O_3$ : 62.34 C, 3.92 H, 18.17 N. Found: 62.02 C, 3.79 H, 17.94 N.

3-(4-Methoxyphenyl)-5-(2-nitrobenzyl)-1H-[1,2,4]triazine-6-one (**6c**).

Yield: 86% (method B), mp: 110-115°C, ir: 3201, 3004, 2841, 1659, 1606, 1571, 1522, 1462, 1346, 1254, 1176, 1132, 1027, 841, 789.

*Anal.* Calcd. for  $C_{18}H_{15}N_5O_4$ : 60.35 C, 4.17 H, 16.56 N. Found: 60.52 C, 4.19 H, 16.87 N.

3-(4-Acetylaminophenyl)-5-(2-nitrobenzyl)-1H-[1,2,4]triazine-6-one (**6d**).

Yield: 91% (method B), mp: 169-171°C, ir: 3268, 3186, 3036, 2856, 1665, 1647, 1584, 1510, 1456, 1412, 1228, 1145, 964, 678.

*Anal.* Calcd. for  $C_{18}H_{15}N_5O_4$ : 59.18 C, 4.14 H, 19.17 N. Found: 59.35 C, 4.22 H, 19.08 N.

3-(Styryl)-5-(2-nitrobenzyl)-1H-[1,2,4]triazine-6-one (**6e**).

Yield: 83% (method B), mp: 136-138°C, ir: 3200, 3065, 3029, 2944, 1669, 1584, 1523, 1448, 1343, 1203, 978, 858, 746, 695.

*Anal.* Calcd. for  $C_{18}H_{14}N_4O_3$ : 64.67 C, 4.22 H, 16.76 N. Found: 64.34 C, 4.56 H, 16.73 N.

3-(4-Thienyl)-5-(2-nitrobenzyl)-1H-[1,2,4]triazin-6-one (**6f**).

Yield: 66% (method B), mp: 118-120°C, ir: 3263, 3019, 1662, 1578, 1520, 1342, 1290, 1132, 853, 788, 726.

*Anal.* Calcd. for  $C_{14}H_{10}N_4O_3S \cdot H_2O$ : 50.60 C, 3.64 H, 16.86 N, 9.65 S. Found: 50.31 C, 3.45 H, 16.39 N, 9.89 S.

3-(4-Chlorophenyl)-5-(2-nitrobenzyl)-1H-[1,2,4]triazin-6-one (**6g**).

Yield: 94% (method B), mp: 168-170°C, ir: 3242, 3088, 1667, 1595, 1520, 1485, 1406, 1341, 1299, 1090, 1013, 961, 845, 788.  $^1H$  nmr (DMSO): 4.25(s, 2H,  $CH_2$ ), 6.45(t, 1H, ArH,  $J=7.8$ ), 6.72(d, 1H, ArH,  $J=8.1$ ), 7.12(t, 1H, ArH,  $J=6.9$ ), 7.45-7.68(m, 1H, ArH), 8.05(d, 2H, ArH,  $J=8.40$ ), 8.41(d, 2H, ArH,  $J=8.40$ ), 10.12(s, 1H, NH).

*Anal.* Calcd. for  $C_{16}H_{11}N_4O_3Cl$ : 56.07 C, 3.23 H, 16.35 N. Found: 55.89 C, 3.48 H, 16.04 N.

3-(3-Chlorophenyl)-5-(2-nitrobenzyl)-1H-[1,2,4]triazin-6-one (**6h**).

Yield: 87% (method B), mp: 148-150°C, ir: 3196, 3068, 1669, 1632, 1601, 1519, 1488, 1379, 1299, 1249, 1076, 901, 749.

*Anal.* Calcd. for  $C_{16}H_{11}N_4O_3Cl$ : 56.07 C, 3.23 H, 16.35 N. Found: 56.19 C, 3.52 H, 16.74 N.

3-Substituted-5-(2-aminobenzyl)-1H-[1,2,4]triazin-6-ones (7).

General Procedures.

Method A.

A solution of ferrous sulfate heptahydrate (2.78 g) in water (15 ml) was added with stirring to a hot solution of baryum hydroxide octahydrate (3.16 g) in water (30 ml). The precipitate was collected by suction filtration and washed with hot water (15 ml), then ethanol (15 ml).

The precipitate of ferrous hydroxide on baryum sulfate was suspended in solution of 3-substituted-1,6-dihydro-1,2,4-triazin-6-one (1.00 mmol) in ethanol (40 ml). The reaction mixture was heated on boiling water bath with intensive stirring for 60 minutes. It was then filtered hot and the precipitate was washed twice with ethanol (25 ml). After cooling to room temperature, it was allowed to stand for a further 60 minutes and filtered again. The filtrate was concentrated *in vacuo* to volume cca 20 ml and allowed to stand at room temperature for 48 hours. The crystalline compound was collected by filtration and washed with a little of ethanol. The crude product was crystallized from an appropriate solvent.

Method B.

The hydrazide of 2-acylamino-3-(2-aminophenyl)acrylic acid (**5**) (1.00 mmol) was refluxed for 5 minutes in a 1 *M* sodium hydroxide water solution. The mixture was filtered hot with charcoal and after cooling to room temperature the solution was neutralized with acetic acid. The precipitate was collected by filtration, then washed with water (20 ml). The crude product was crystallized from an appropriate solvent.

3-Methyl-5-(2-aminobenzyl)-1H-[1,2,4]triazin-6-one (**7a**).

Yield: 33% (method A), 58% (method B), mp: 162-165°C, ir: 3290, 3045, 2869, 1659, 1639, 1528, 1483, 1468, 1423, 1253, 1203, 1158, 1123, 1103, 1053, 948, 798, 773, 748.

*Anal.* Calcd. for  $C_{11}H_{10}N_4O_3$ : 53.66 C, 4.09 H, 22.75 N. Found: 53.38 C, 4.43 H, 22.82 N.

3-Phenyl-(2-aminobenzyl)-1*H*-[1,2,4]triazin-6-one (**7b**).

Yield: 57% (method A), 86% (method B), mp: 162-165°C (ethanol), ir: 3325, 3310, 3279, 1640, 1613, 1521, 1485, 1421, 1403, 1322, 1129, 1090, 1033, 917, 755, 689,  $^1H$  nmr (DMSO): 3.15(d, 1H,  $CH_2$ ,  $J=16.5$ ), 3.88(d, 1H,  $CH_2$ ,  $J=16.5$ ), 6.38(d, 1H, ArH,  $J=7.8$ ), 6.59(t, 1H, ArH,  $J=7.2$ ), 6.94(t, 1H, ArH,  $J=7.8$ ), 7.05(d, 1H, ArH,  $J=7.2$ ), 7.41-7.47(m, 4H, ArH, NH), 7.78(d, 2H, ArH,  $J=8.1$ ), 8.28(s, 1H, NH), 10.81(s, 1H, NH),  $^{13}C$  NMR (DMSO): 73.87, 107.65, 117.79, 124.06, 126.15, 126.69, 127.51, 128.64, 130.12, 133.03, 144.33, 148.94, 162.89. ms ( $M^++1$ ) 279.

*Anal.* Calcd. for  $C_{16}H_{14}N_4O$ : 69.05 C, 5.07 H, 20.13 N. Found: 69.06 C, 5.21 H, 19.98 N.

3-(4-Methoxyphenyl)-5-(2-aminobenzyl)-1*H*-[1,2,4]triazin-6-one (**7c**).

Yield: 73% (method A), 95% (method B), mp: 223-225°C (ethanol-toluene (1:1)), ir: 3201, 3004, 2841, 1659, 1606, 1571, 1522, 1462, 1346, 1254, 1176, 1132, 1027, 841, 789,  $^1H$  nmr (DMSO): 3.14(d, 1H,  $CH_2$ ,  $J=16.5$ ), 3.79(s, 3H,  $OCH_3$ ), 3.87(d, 1H,  $CH_2$ ,  $J=16.5$ ), 6.38(d, 1H, ArH,  $J=7.8$ ), 6.59(t, 1H, ArH,  $J=7.2$ ), 6.91-6.99(m, 4H, ArH, NH), 7.04(d, 1H, ArH,  $J=7.8$ ), 7.72(d, 2H, ArH,  $J=9.0$ ), 8.17(s, 1H, NH), 10.72(s, 1H, NH),  $^{13}C$  nmr: 39.1, 55.7, 73.8, 107.6, 114.0, 17.8, 124.0, 125.4, 126.2, 127.5, 128.2, 144.2, 149.0, 160.9, 162.9. ms ( $M^++1$ ) 309.

*Anal.* Calcd. for  $C_{17}H_{16}N_4O_2$ : 66.22 C, 5.23 H, 18.17 N. Found: 66.48 C, 5.34 H, 18.15 N.

3-(4-Acetylamino-phenyl)-5-(2-aminobenzyl)-1*H*-[1,2,4]triazin-6-one (**7d**).

Yield: 51% (method B), mp: 138-140°C, ir: 3285, 3110, 3050, 1684, 1644, 1609, 1528, 1508, 1418, 1377, 1323, 1255, 1188, 1036, 848, 748.

*Anal.* Calcd. for  $C_{18}H_{17}N_5O_2$ : 64.47 C, 5.11 H, 20.88 N. Found: 64.31 C, 5.19 H, 20.33 N.

3-(4-Styryl)-5-(2-aminobenzyl)-1*H*-[1,2,4]triazin-6-one (**7e**).

Yield: 43% (method A), mp: 144-146°C, ir: 3244, 3210, 3154, 3059, 3029, 1666, 1580, 1524, 1449, 1346, 1303, 1183, 1130, 973, 860, 787, 748, 693.

*Anal.* Calcd. for  $C_{18}H_{16}N_4O$ : 71.04 C, 5.30 H, 18.41 N. Found: 70.82 C, 5.02 H, 18.06 N.

3-(2-Thienyl)-5-(2-aminobenzyl)-1*H*-[1,2,4]triazin-6-one (**7f**).

Yield: 51% (method A), mp: 149-152°C (ethanol), ir: 3263, 3019, 1662, 1578, 1520, 1342, 1290, 1132, 853, 788, 726.

*Anal.* Calcd. for  $C_{14}H_{12}N_4OS$ : 59.14 C, 4.25 H, 19.70 N, 11.28 S. Found: 59.21 C, 4.45 H, 19.39 N, 11.59 S.

3-(4-Chlorophenyl)-5-(2-aminobenzyl)-1*H*-[1,2,4]triazin-6-one (**7g**).

Yield: 45% (method A), 94% (method B), mp: 168-170°C, ir: 3242, 3088, 1667, 1595, 1520, 1485, 1406, 1341, 1299, 1090, 1013, 961, 845, 788,  $^1H$  nmr (DMSO): 3.16(d, 1H,  $CH_2$ ,  $J=16.8$ ), 3.89(d, 1H,  $CH_2$ ,  $J=16.8$ ), 6.38(d, 1H, ArH,  $J=8.1$ ), 6.60(t, 1H, ArH,  $J=7.2$ ), 6.94(t, 1H, ArH,  $J=8.1$ ), 7.00(s, 1H, NH), 7.05(d, 1H, ArH,  $J=7.2$ ), 7.50(d, 2H, ArH,  $J=8.7$ ), 7.80(d, 2H, ArH,  $J=8.7$ ), 8.35(s, 1H, NH), 10.87(s, 1H, NH). ms ( $M^++1$ ) 313, 314.

*Anal.* Calcd. for  $C_{16}H_{13}N_4O_3Cl$ : 61.45 C, 4.19 H, 17.91 N. Found: 61.58 C, 4.63 H, 17.84 N.

3-(3-Chlorophenyl)-5-(2-aminobenzyl)-1*H*-[1,2,4]triazin-6-one (**7h**).

Yield: 92%, (method B), mp: 143-145°C, ir: 3196, 3068, 1669, 1632, 1601, 1519, 1488, 1379, 1299, 1249, 1076, 901, 749.

*Anal.* Calcd. for  $C_{16}H_{13}N_4OCl$ : 61.45 C, 4.19 H, 17.91 N. Found: 61.28 C, 4.36 H, 17.62 N.

3-Substituted-5,10-dihydro[1,2,4]triazino[6,5-*b*]quinolines (**9**) and 3-Substituted-1,5-dihydro[1,2,4]triazino[6,5-*b*]quinolines (**10**).

General Procedures.

Method A.

3-Substituted-5-(2-aminobenzyl)-1*H*-[1,2,4]triazin-6-one (**7**) (1.00 mmol) was refluxed for 10 hours in acetic acid (5.0 ml). After cooling to room temperature, the solvent was evaporated *in vacuo*. The crude product was crystallized from an appropriate solvent.

Method B.

3-Substituted-5-(2-aminobenzyl)-1*H*-[1,2,4]triazin-6-one (**7**) (1.00 mmol) and *p*-toluenesulphonic acid (100 mg) was refluxed for 5 hours in anisole (5.0 ml). The solvent was evaporated *in vacuo*. The residue was then dissolved in ethanol and evaporated again *in vacuo*. The residue was suspended in water (10.0 ml), the precipitate was collected by filtration and washed with water.

Method C.

3-Substituted-5-(2-aminobenzyl)-1*H*-[1,2,4]triazin-6-one (**7**) (1.00 mmol) was heated at 110 °C for 1 hour in phosphorous oxychloride (3.0 ml). The mixture was evaporated *in vacuo*. The residue was dissolved in dioxane (5.0 ml) and poured over crushed ice (30 g). The precipitate was collected by filtration and washed with water. The crude product was crystallized from an appropriate solvent.

3-Methyl-5,10-dihydro[1,2,4]triazino[6,5-*b*]quinoline (**9a**).

Yield: 73% (method A), 76% (method C), mp: 222-225°C (toluene) [14], ir: 3053, 1618, 1553, 1521, 1386, 1209, 1027.

*Anal.* Calcd. for  $C_{11}H_{10}N_4$ : 66.65 C, 5.08 H, 28.26 N. Found: 66.37 C, 5.38 H, 27.98 N.

3-Phenyl-5,10-dihydro-[1,2,4]triazino[6,5-*b*]quinoline (**9b**).

Yield: 88% (method A), 92% (method B), 90% (method C), mp: 251-253°C (ethanol-toluene (1:1)) [14], ir: 3070, 1634, 1553, 1488, 1393, 1323, 1233, 1048, 1023.  $^1H$  nmr(DMSO): 3.75(s, 2H,  $CH_2$ ), 6.37(d, 1H, ArH,  $J=7.2$ ), 6.51(t, 1H, ArH,  $J=7.2$ ), 6.70(t, 2H, ArH,  $J=7.5$ ), 6.83-7.22(m, 3H, ArH), 7.70(d, 2H, ArH,  $J=7.5$ ), 9.53(s, 1H, NH),  $^{13}C$  nmr (DMSO): 24.10, 83.16, 96.37, 108.40, 108.84, 112.75, 114.17, 115.60, 127.52, 127.90, 132.17, 145.68, 150.63, 174.27. ms ( $M^++1$ ) 261.

*Anal.* Calcd. for  $C_{16}H_{12}N_4$ : 73.83 C, 4.65 H, 21.52 N. Found: 73.56 C, 4.88 H, 21.32 N.

3-(4-Methoxyphenyl)-5,10-dihydro-[1,2,4]triazino[6,5-*b*]quinoline (**9c**).

Yield: 90% (method A), 92% (method C), mp: 198-200 (ethanol), ir: 3185, 3055, 2899, 1609, 1548, 1503, 1458, 1393,



1303, 1258, 1178, 1093, 1028, 968, 838, 753, <sup>1</sup>H nmr: 4.22(s, 2H, CH<sub>2</sub>), 3.84(s, 3H, OCH<sub>3</sub>), 7.04-7.22(m, 3H, ArH), 7.47(d, 1H, ArH, J=8.1), 7.61(d, 1H, ArH, J=7.5), 7.72(t, 1H, ArH, J=8.1), 8.08(d, 2H, ArH, J=9.0), 11.77(s, 1H, NH). ms (M<sup>+</sup>+1) 291.

Anal. Calcd. for C<sub>17</sub>H<sub>14</sub>N<sub>4</sub>O: 70.33 C, 4.86 H, 19.30 N. Found: 70.25 C, 4.69 H, 18.96 N.

3-(4-Acetylamino-phenyl)-5,10-dihydro-[1,2,4]triazino[6,5-*b*]quinoline (**9d**).

Yield: 92% (method C), mp: 256-258°C (ethylacetate), ir: 3225, 3060, 1659, 1604, 1543, 1491, 1385, 1299, 1264, 1163, 1073, 965.

Anal. Calcd. for C<sub>16</sub>H<sub>11</sub>N<sub>4</sub>Cl: 68.13 C, 4.76 H, 22.07 N. Found: 68.49 C, 4.52 H, 21.83 N.

3-Styryl-5,10-dihydro-[1,2,4]triazino[6,5-*b*]quinoline (**9e**).

Yield: 85% (method C), mp: 225-227°C (ethanol-toluene (1:1)), ir: 3225, 3060, 1620, 1594, 1553, 1498, 1453, 1393, 1338, 1258, 1218, 1168, 1073, 973, 758, 693.

Anal. Calcd. for C<sub>18</sub>H<sub>14</sub>N<sub>4</sub>: 75.51 C, 4.93 H, 19.57 N. Found: 75.38 C, 5.12 H, 19.37 N.

3-(2-Thienyl)-5,10-dihydro-[1,2,4]triazino[6,5-*b*]quinoline (**9f**).

Yield: 85% (method C), mp: 261-263°C, ir: 3311, 3058, 1619, 1594, 1533, 1480, 1463, 1383, 1338, 1201, 1152, 973.

Anal. Calcd. for C<sub>14</sub>H<sub>10</sub>N<sub>4</sub>S: 63.14 C, 3.78 H, 21.04 N. Found: 63.27 C, 3.46 H, 20.82 N.

3-(4-Chlorophenyl)-5,10-dihydro-[1,2,4]triazino[6,5-*b*]quinoline (**9g**).

Yield: 85% (method C), mp: 227-229°C (ethanol-toluene (1:1)), ir: 3220, 3050, 1604, 1553, 1488, 1348, 1293, 1263, 1178, 1093, 1013, 833, 753, <sup>1</sup>H nmr (DMSO): 4.23(s, 2H, CH<sub>2</sub>) 7.09(t, 1H, ArH, J=7.5), 7.26(t, 1H, ArH, J=7.8), 7.49(d, 1H, ArH, J=7.8), 7.70(d, 1H, ArH, J=7.5), 7.79(d, 2H, ArH, J=8.7), 7.94(d, 2H, ArH, J=8.7), 10.22(s, 1H, NH).

Anal. Calcd. for C<sub>16</sub>H<sub>11</sub>N<sub>4</sub>Cl: 65.20 C, 3.76 H, 19.01 N. Found: 64.93 C, 3.48 H, 18.97 N.

3-(3-Chlorophenyl)-5,10-dihydro[1,2,4]triazino[6,5-*b*]quinoline (**9h**).

Yield: 93% (method C), mp: 210-212°C (ethanol), ir: 3200, 3075, 1599, 1558, 1533, 1488, 1448, 1408, 1363, 1343, 1293, 1265, 1230, 1088, 1018, 833, 753.

Anal. Calcd. for C<sub>16</sub>H<sub>11</sub>N<sub>4</sub>Cl: 65.20 C, 3.76 H, 19.01 N. Found: 65.44 C, 4.01 H, 18.76 N.

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