The cleavage of heterocyclic compounds.  
Synthesis of 1-phenyl-5-naphthyl-6-azacytosines

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Abstract
A series of 6-azacytosines were prepared by nucleophilic cleavage of the furan ring of phenyl derivatives of naphto[1´,2´:4,5]furo[2,3-e][1,2,4]triazines. Some were then used for the preparation of 1,2,4-triazolo[4,3-d][1,2,4]triazines and tetrazolo[1,5-d][1,2,4]triazines.

Keywords: 1,2,4-Triazine, condensed 1,2,4-triazine, 1-aryl-6-azacytosine

Introduction
Multinuclear heterocycles form a very large group of biologically active compounds, in which biological activity is often linked to mutual conformations of the cycles. Heterocyclic aryl-derivatives are mostly represented by variously substituted phenyl derivatives. Interesting heterocyclic aryl derivatives also include naphthyl derivatives, such as antiplateled active naphtyloxadiazoles or naphtylmaleinimids that act as inhibitors of protein kinases. Some naphtylisoquinolines are important from the perspective of atropoisomery.

From the perspective of biological activity, some naphthyl derivatives of 6-azauracil may be interesting; however, these form just a very small group. In this report, we focused on the straightforward fission of furo[2,3-e][1,2,4]triazines.

Results and Discussion
As starting material we prepared 2-phenyl-2,3-dihyronaphto[1´,2´:4,5]furo[2,3-e][1,2,4] triazine-3-on 1, using the straightforward synthesis described before. Using this compound, all cleavage reactions with oxygen, sulfur or nitrogen nucleophiles are very easy and lead to good yields of the end products.
While the hydrolytic cleavage leads – as previously described\textsuperscript{6} – to the relevant substituted 6-azauracil, the ethanolysis with non-aqueous ethanol provided 5-ethoxy-6-(2-hydroxy-1-naphtyl)-2-phenyl-1,2,4-triazin-3(2H)-one (2). The ammonolysis was also easily completed, using an aqueous ammonia solution, giving rise to 1-fenyl-5-(2-hydroxy-1-naphtyl)-6-azacytosin (3a). A number of other 6-azacytosine 3b-3d derivatives were obtained from the reaction of 1 with primary amines. The mono substitution with diamines were also successful. Thus, 6-azacytosine 3e was obtained from a reaction with ethylenediamine, derivative 3f from hexan-1,6-diamine and 3g from reaction with lysine. Reactions with hexan-1,6-diamine were both amino-groups reacted, gave rise to binuclear 6-azacytosine 3j. We observed that the cleavage of the furan cycle took place with secondary amines, such as piperidine or diethylamine, giving rise to the corresponding derivatives 3h and 3i.

\begin{equation}
\begin{array}{c}
2 \\
\text{EtOH} \\
H_2S \\
\text{HNR}_1R_2 \\
R\text{-NH-NH}_2
\end{array}
\end{equation}

\begin{equation}
\begin{array}{c}
1 \\
3a R_1 = R_2 = H \\
3b R_1 = H; R_2 = CH_3 \\
3c R_1 = H; R_2 = \text{phenyl} \\
3d R_1 = H; R_2 = \text{cyclohexyl} \\
3e R_1 = H; R_2 = \text{CH}_2\text{CH}_2\text{NH}_2 \\
3f R_1 = H; R_2 = \text{CH}_2\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2 \\
3g R_1 = H; R_2 = (\text{CH}_2)_3\text{CH(\text{NH}_2)_2}\text{COOH} \\
3h R_1 = R_2 = \text{CH}_2\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2 \\
3i R_1 = R_2 = \text{CH}_2\text{CH}_3 \\
4a R = H \\
4b R = \text{phenyl} \\
4c R = \text{CONH}_2
\end{array}
\end{equation}

Scheme 1
The hydrazinolysis using hydrazine, phenylhydrazine and semicarbazide, leading to the corresponding 2-phenyl-5-hydrazino-6-(2-hydroxy-1-naphthyl)-1,2,4-triazin-3(2\(H\))-ones 4a-4c could also be performed without problems.

Hydrazine derivative 4a served as starting compound for the preparation of derivatives of 1,2,4-triazolo[4,3-\(d\)]-[1,2,4]triazine 5a-5c and tetrazolo[1,5-\(d\)]-[1,2,4]triazine 6. Heating of compound 4a in formic acid gave compound 5a without formylation of the phenolic OH group. In contrast, acetic anhydride acetylated the hydroxy group leading to the derivative 5b as expected. The closure of the fused triazole ring was also successful using carbon disulfide affording compound 5c. 8-(2-Hydroxy-1-naphtyl)-6-phenyltetrazolo[1,5-\(d\)]-[1,2,4]triazin-5(6\(H\))-one (6) was obtained smoothly by the nitrosation of the hydrazino derivative 4a.

Scheme 3
Finally, a very interesting aspect was the cleavage of the furan cycle by hydrogen sulfide, providing 1-phenyl-4-thio-5-(2-hydroxy-1-naphthyl)-6-azauracil 7.

The prepared compounds were tested for biological activity. Human adenocarcinoma cell line MCF7 and K-562 was used for cytotoxicity determination by the calcein AM assay. The tested new compounds showed poor cytostatic activity (IC₅₀ = 70–200 µmol/l), with the exception of the moderately active cytosines 3j (K-562: IC₅₀ = 12.4 µmol/l; MCF7: IC₅₀ = 8.0 µmol/l), 4a (K-562: IC₅₀ = 21.6 µmol/l; MCF7: IC₅₀ = 13.8 µmol/l) and 4b (K-562: IC₅₀ = 3.1 µmol/l; MCF7: IC₅₀ = 7.5 µmol/l).

**Experimental Section**

**General Procedures.** Melting points were determined on a Boetius stage and are uncorrected. The IR spectra were recorded in KBr wafers on an ATI Unicam Genesis FTIR instrument. The NMR spectra were registered on a Bruker Avance 300 MHz DRX spectrometer; chemical shifts are reported in ppm, the coupling constants J in Hz. Elemental analyses were performed with an EA 1108 Elemental Analyser (Fison Instruments). Mass spectrometric experiments were performed using an LCQ ion trap mass spectrometer (Finnigan MAT, San Jose, CA, USA).

**5-Ethoxy-6-(2-hydroxy-1-naphthyl)-2-phenyl-1,2,4-triazin-3(2H)-one (2).** Compound 1 (63.7 mg, 0.203 mmol) was dissolved in anhydrous ethanol (15 ml) in a sealed vial. After 90 min of stirring at room temperature, the product was obtained in quantitative yield (TLC). The solution was evaporated and the resulting oily product mixed with hexane (5 ml). Solids were filtered off, washed with hexane and crystallized from a small amount of ethanol by standing at – 20 °C. Yield 52.7 mg (72.3 %), mp 151-153 °C (dec.); MS (ESI, m/z (rel. %)) 360.3 (100) [M+H]^+; IR [cm⁻¹]: 3424, 3190, 2966, 1654, 1595, 1436, 1261, 1147, 755; ¹H-NMR (DMSO-d₆): δ 1.53 (t, 3H, CH₃, J = 7.4 Hz); 4.60 (q, 2H, CH₂, J = 7.4 Hz); 6.98-7.06 (m, 2H, arom.); 7.33-7.42 (m, 4H, arom.); 7.52 (t, 2H, arom.); 7.64 (d, 2H, arom.); 7.96 (d, 1H, arom.); 9.74 (bs, 1H, OH). Anal. calcd for C21H17N3O3 (359.4): C, 70.18; H, 4.77; N, 11.69. Found C, 70.32; H, 4.60; N, 11.47.

**6-(2-Hydroxy-1-naphthyl)-5-imino-2-phenyl-4,5-dihydro-1,2,4-triazin-3(2H)-one (3a).** A mixture of compound 1 (67.5 mg, 0.215 mmol) and 26% aqueous ammonia was stirred until a solution was obtained (6 h). The yellow solution was evaporated in vacuo to dryness and the solid was dried at 130°C for 1 h. A sample for analysis was prepared by the crystallization from ethanol and dried at 130°C. Yield 70.5 mg (99.0 %), mp 263-265°C; MS (ESI, m/z (rel. %)) 331.1 (90) [M+H]^+; IR [cm⁻¹]: 3453, 3187, 1653, 1508, 1488, 1347, 1277, 749; ¹H-NMR (DMSO-d₆): δ 6.60 (bs, 1H, NH); 6.72-7.01 (m, 2H, arom.); 7.43-7.49 (m, 4H, arom.); 7.62-7.69 (m, 2H, arom.); 7.76-7.87 (m, 3H, arom.); 8.23 (bs, 1H, NH) 9.93 (bs, 1H, OH). Anal. calcd for C₁₉H₁₄N₄O₂ (330.3): C, 69.08; H, 4.27; N, 16.96. Found C, 69.16; H, 4.36; N, 16.60.

**6-(2-Hydroxy-1-naphthyl)-5-methylamino-2-phenyl-1,2,4-triazin-3(2H)-one (3b).** A mixture of 1 (21.5 mg, 0.069 mmol) and 35% aqueous methylvamine (3 ml) was stirred for 60 min at
room temperature. The obtained solution was evaporated in vacuo to dryness to yield 22.4 mg (94.8 %). A sample for analysis was prepared by crystallization from ethanol and drying at 130°C for 1 h. Mp 273-275°C; MS (ESI, m/z (rel. %)) 345.2 (100) [M+H]+; IR [cm⁻¹]: 3352, 3065, 2941, 1652, 1578, 1437, 1358, 1250, 745; ¹H-NMR (DMSO-d₆): δ 2.77 (s, 3H, CH₃); 7.27 (d, 1H, arom., J = 8.7 Hz); 7.30-7.46 (m, 5H, arom.); 7.51-7.56 (m, 3H, arom.); 7.87 (d, 1H, arom. J = 7.8 Hz); 7.92 (d, 1H, arom. J = 9.0 Hz); 10.09 (bs, 1H, OH), NH proton is missing in spectrum. ¹³C-NMR (DMSO-d₆): δ 27.6, 109.6, 119.5, 122.1, 122.6, 125.0, 126.6, 126.8, 127.3, 128.0, 128.2, 131.0, 133.9, 134.9, 141.9, 152.8, 156.6, 157.1. Anal. calcd for C₂₀H₁₆N₄O₂ (344.4): C, 69.76; H, 4.68; N, 16.27. Found C, 69.85; H, 4.91; N, 15.97.

5-Anilino-6-(2-hydroxy-1-naphthyl)-2-phenyl-1,2,4-triazin-3(2H)-one (3c).
Compound 1 (34.1 mg, 0.109 mmol) was dissolved in aniline (0.7 ml) with stirring at room temperature. After 60 min, water (10 ml) was added to the solution and compound 3c was slowly precipitated under stirring with dilute acetic acid. After 2 h stirring, the precipitate was collected on a filter, washed with water and dried. A sample for analysis was prepared by crystallization from ethanol. Yield: 37.5 mg (84.7%), mp 235-238°C; MS (ESI, m/z (rel. %)) 407.2 (100) [M+H]+; IR [cm⁻¹]: 3361, 3190, 3052, 1642, 1512, 1451, 1254, 743; ¹H-NMR (DMSO-d₆): δ 7.17 (t, 1H, arom., J = 7.2 Hz); 7.28-7.66 (m, 12H, arom.); 7.71 (d, 1H, arom. J = 8.1 Hz); 7.90 (d, 1H, arom., J = 7.5 Hz); 7.94 (d, 1H, arom., J = 9.0 Hz); 8.95 (s, 1H, NH); 10.23 (s, 1H, OH). Anal. calcd for C₂₅H₁₈N₄O₂ (406.5): C, 73.88; H, 4.46; N, 13.78. Found C, 73.75; H, 4.10; N, 13.55.

5-(Cyclohexylamino)-6-(2-hydroxy-1-naphthyl)-2-phenyl-1,2,4-triazin-3(2H)-one (3d).
Compound 1 (65.1 mg, 0.208 mmol) was dissolved in cyclohexylamine (0.8 ml) at room temperature. After 120 min with occasional stirring, the solid began to precipitate from the solution. The mixture was diluted with water (10 ml) and neutralized with dilute acetic acid to pH ~ 8. The precipitate was collected by suction, washed with water and dried. A sample for analysis was prepared by crystallization from methanol. Yield 77.4 mg (90.3%), mp 267-269°C; MS (ESI, m/z (rel. %)) 413.2 (100) [M+H]+; IR [cm⁻¹]: 3373, 3094, 2933, 2855, 1643, 1585, 1538, 1513, 1335, 1152, 745; ¹H-NMR (DMSO-d₆): δ 0.93-1.78 (m, 10H, CH₂); 4.03 (bs, 1H, CH); 6.96 (bs, 1H, NH); 7.24-7.55 (m, 9H, arom.); 7.88 (d, 1H, arom., J = 8.1 Hz); 7.94 (d, 1H, arom., J = 8.7 Hz); 10.10 (bs, 1H, OH). Anal. calcd for C₂₅H₂₄N₄O₂ (412.5): C, 72.80; H, 5.86; N, 13.58. Found C, 72.95; H, 5.46; N, 13.26.

5-[2-Aminoethylamino]-6-(2-hydroxy-1-naphthyl)-2-phenyl-1,2,4-triazin-3(2H)-one (3e).
Compound 1 (75.6 mg, 0.241 mmol) was dissolved in ethylene diamine (0.5 ml). After 60 min of stirring the mixture was diluted with water (13 ml) and neutralized with dilute acetic acid to pH ~ 8. The precipitate was collected by suction, washed with water and dried. A sample for analysis was prepared by crystallization from ethanol. Yield 55.5 mg (61.7%), mp 233-235°C; MS (ESI, m/z (rel. %)) 374.1 (100) [M+H]+; IR [cm⁻¹]: 3451, 3310, 3031, 2880, 1661, 1589, 1548, 1348, 703; ¹H-NMR (DMSO-d₆): δ 2.68 (t, 2H, CH₂; J = 7.0 Hz); 3.33 (bs, 2H, CH₂); 3.6-4.2 (bs, NH); 7.23-7.33 (m, 3H, arom.); 7.40-7.57 (m, 6H, arom.); 7.85 (d, 1H, arom., J = 7.8 Hz); 7.91 (d, 1H, arom., J = 9.0 Hz); OH protons are missing in spectrum. ¹³C-NMR (DMSO-d₆): δ 40.5, 42.5, 109.7, 119.3, 122.3, 122.8, 125.0, 126.7, 126.8, 127.5, 128.0, 128.2, 131.1, 133.8, 134.6, 141.8,
5-[(6-Aminohexyl)amino]-6-(2-hydroxy-1-naphthyl)-2-phenyl-1,2,4-triazin-3(2H)-one (3f). Compound 1 (95.3 mg, 0.304 mmol) was dissolved in a solution of hexan-1,6-diamine (174.3 mg, 1.50 mmol) in chloroform (10 ml). After 18 h stirring, the precipitated solid was filtered off, washed with chloroform (2 x 2 ml) and dried. This product was suspended in water (5 ml) and the pH of the mixture was adjusted by dilute acetic acid to pH ~ 8 (to remove traces of hexan-1,6-diamine) and after 30 min stirring it was again filtered off and dried. A sample for analysis was prepared by crystallization from ethanol. Yield 96.0 mg (73.5%), mp 193-195°C; MS (ESI, m/z (rel. %)) 430.2 (100) [M+H]+; IR [cm⁻¹]: 3342, 3069, 2945, 1648, 1588, 1533, 1365, 818; ¹H-NMR (DMSO-d₆): δ 1.23 (bs, 4H, CH₂); 1.47 (bs, 4H, CH₂); 4.36-4.80 (bs, 6H, 2x CH₂, NH₂); 7.26-7.75 (m, 9H, arom.); 7.82-7.90 (m, 2H, arom.), OH protons are missing in spectrum. Anal. calcd for C₂₅H₂₇N₅O₂ (429.5): C, 69.91; H, 6.34; N, 16.30. Found C, 69.52; H, 6.18; N, 16.18.

N⁶-[6-(2-Hydroxy-1-naphthyl)-3-oxo-2-phenyl-2,3-dihydro-1,2,4-triazin-5-yl]lysine (3g). Compound 1 (52.3 mg, 0.167 mmol) was suspended in a solution of DL-lysine prepared from DL-lysine hydrochloride (60.9 mg, 0.334 mmol), an equivalent amount of sodium hydroxide (13.3 mg, 0.334 mmol), water (10 ml) and ethanol (10 ml). The mixture was refluxed for 6 h, the obtained solution was neutralized with dilute acetic acid to pH ~ 8. After 1 h stirring, the precipitate was collected on a filter, washed with water and dried. Yield 53.9 mg (70.3%), mp 287-288°C; MS (ESI, m/z (rel. %)) 460.3 (68) [M+H]+; IR [cm⁻¹]: 3361, 3054, 2921, 1649, 1586, 1543, 1323, 1208, 743; ¹H-NMR (DMSO-d₆): δ 1.44-1.96 (m, 6H, CH₂), 3.0-4.0 (bs COOH, CH, CH₂ and NH protons together with residue of water); 7.24-7.64 (m, 9H, arom.); 7.87 (d, 1H, arom., J = 8.4 Hz); 7.93 (d, 1H, arom., J = 8.7 Hz); Anal. calcd for C₂₅H₂₅N₅O₄ (459.5): C, 65.35; H, 5.48; N, 15.24. Found C, 65.17; H, 5.21; N, 14.96.

6-(2-Hydroxy-1-naphthyl)-2-phenyl-5-piperidino-1,2,4-triazin-3(2H)-one (3h). This compound was prepared in a similar way as compound 3c using compound 1 (55.9 mg, 0.178 mmol) and piperidine (0.7 ml). Yield 65.1 mg (91.5%), mp 274-276°C; MS (ESI, m/z (rel. %)) 399.3 (78) [M+H]+; IR [cm⁻¹]: 3293, 3066, 2937, 1633, 1566, 1443, 1228, 1134, 769; ¹H-NMR (DMSO-d₆): δ 1.29 (bs, 4H, CH₂); 1.42-1.53 (m, 2H, CH₂); 3.60 (bs, 4H, CH₂); 7.25-7.50 (m, 6H, arom.); 7.54-7.57 (m, 2H, arom.); 7.68 (d, 1H, arom., J = 8.1 Hz); 7.85-7.92 (m, 2H, arom.), OH protons are missing in spectrum. ¹³C-NMR (DMSO-d₆): δ 23.5, 25.2, 46.6, 115.0, 118.3, 123.1, 123.4, 124.6, 126.8, 127.2, 127.8, 128.1, 128.2, 130.6, 132.2, 132.4, 141.4, 151.8, 153.1, 156.7 Anal. calcd for C₂₄H₂₂N₄O₂ (398.5): C, 72.34; H, 5.57; N, 14.06. Found C, 71.89; H, 6.06; N, 13.79.

5-(Diethylamino)-6-(2-hydroxy-1-naphthyl)-2-phenyl-1,2,4-triazin-3(2H)-one (3i). This compound was prepared in a similar way as compound 3c using compound 1 (51.3 mg, 0.163 mmol) and diethylamine (0.6 ml). Yield 57.7 mg (91.2%), mp 155-157°C; MS (ESI, m/z (rel. %)) 387.3 (100) [M+H]+; IR [cm⁻¹]: 3297, 3209, 2909, 1632, 1562, 1434, 1351, 1048, 648; ¹H-NMR (DMSO-d₆): δ 1.03 (bs, 6H, CH₃); 3.44 (bs, 4H, CH₂); 7.26 (d, 1H, arom., J = 9.0 Hz); 7.28-7.40 (m, 4H, arom.); 7.47 (t, 1H, arom., J = 6.9 Hz); 7.52-7.60 (m, 2H, arom.); 7.62 (d, 1H,
arom., $J = 8.1$ Hz); 7.87 (d, 1H, arom., $J = 8.1$ Hz); 7.92 (d, 1H, arom., $J = 9.0$ Hz); 10.21 (bs, 1H, OH). Anal. calcd for C$_{23}$H$_{22}$N$_{4}$O$_{2}$ (386.5): C, 71.47; H, 5.74; N, 14.49. Found C, 71.58; H, 5.67; N, 14.23.

5,5’-[((Hexan-1,6-diyl)diamino]bis[6-(2-hydroxy-1-naphthyl)-2-phenyl-1,2,4-triazin-3(2H)-one] (3j). Compound 1 (106.6 mg, 0.334 mmol) was dissolved in a solution of hexan-1,6-diamine (19.4 mg, 0.167 mmol) in anhydrous chloroform (5 ml). After 24 h of stirring in a sealed glass vial, the precipitate was filtered off and washed with chloroform (2 x 0.5 ml). Sample for analysis was prepared by crystallization from ethanol (1 ml per 1 mg). Yield 114.5 mg (92.3 %), mp 257-259°C; MS (ESI, m/z (rel. %)) 743.6 (100) [M+H]$^+$; IR [cm$^{-1}$]: 3357, 3071, 2943, 1644, 1590, 1554, 1513, 1349, 815; $^1$H-NMR (DMSO-$d_6$): $\delta$ 1.22 (bs, 4H, CH$_2$); 1.46 (bs, 4H, CH$_2$); 3.26 (t, 2H, CH$_2$, $J = 6.9$ Hz ); 3.40-4.0 (bs, 4H, CH$_2$, 2x NH); 7.26-7.38 (m, 6H, arom.); 7.39-7.47 (m, 6H, arom.); 7.50-7.57 (m, 6H, arom.); 7.84-7.90 (m, 3H, arom.); 7.93 (d, 1H, arom., $J = 8.1$ Hz); OH protons are missing in spectrum. Anal. calcd for C$_{44}$H$_{38}$N$_{8}$O$_{4}$ (742.8): C, 71.14; H, 5.16 N, 15.08. Found C, 70.85; H, 5.26; N, 15.27.

5-Hydrazino-6-(2-hydroxy-1-naphthyl)-2-phenyl-1,2,4-triazin-3(2H)-one (4a). Compound 1 (190.0 mg, 0.606 mmol) was dissolved in 80% hydrazine hydrate (3.5 ml). After 90 min of stirring at 50°C, the solution was diluted with water (10 ml) and neutralized with dilute acetic acid. The precipitated solid was collected on a filter and washed with water. A sample for analysis was prepared by crystallization from anhydrous ethanol (2 ml per 1 mg). Yield 192.3 mg (91.8%), mp 266-269°C; MS (ESI, m/z (rel. %)) 346.2 (100) [M+H]$^+$; IR [cm$^{-1}$]: 3249, 1659, 1575, 1457, 1268, 927, 705; $^1$H-NMR (DMSO-$d_6$): $\delta$ 3.2-4.0 (bs, NH protons together with residue of water); 5.90-6.30 (bs, 1H, NH); 7.17 (d, 1H, arom., $J = 9.0$ Hz); 7.23-7.30 (m, 2H, arom.); 7.37-7.43 (m, 3H, arom.); 7.50-7.54 (m, 2H, arom.); 7.63 (d, 1H, arom., $J = 8.4$ Hz); 7.76 (m, 2H, arom.); 9.70 (bs, 1H, OH). $^{13}$C-NMR (DMSO-$d_6$): $\delta$ 113.4, 118.3, 122.5, 123.7, 124.8, 126.1, 126.4, 127.4, 127.7, 128.2, 129.7, 130.8, 133.5, 140.9, 143.5, 147.8, 153.0. Anal. calcd for C$_{19}$H$_{15}$N$_{5}$O$_{2}$ (345.4): C, 66.08; H, 4.38; N, 20.28. Found C, 66.17; H, 4.25; N, 19.94.

6-(2-Hydroxy-1-naphthyl)-2-phenyl-5-(phenylhydrazino)-1,2,4-triazin-3(2H)-one (4b). Compound 1 (79.5 mg, 0.254 mmol) was suspended in phenylhydrazine (0.8 ml) at room temperature. After 4 h of stirring, water (5 ml) was added to the bright yellow suspension, which was then neutralized with dilute acetic acid, then filtered off, washed with water and crystallized for analysis from ethanol (1 ml per 1 mg). Yield 94.0 mg (89.9%), mp 172-175°C; MS (ESI, m/z (rel. %)) 422.4 (68) [M+H]$^+$; IR [cm$^{-1}$]: 3329, 3273, 3055, 1691, 1600, 1498, 1353, 1249, 1125, 748; $^1$H-NMR (DMSO-$d_6$): $\delta$ 6.55-7.05 (m, 4H, arom.); 7.10-7.59 (m, 9H, arom.); 7.76 (m, 2H, arom.); 9.70 (bs, 1H, OH). Anal. calcd for C$_{25}$H$_{19}$N$_{5}$O$_{2}$ (421.6): C, 71.25; H, 4.54; N, 16.62. Found C, 71.50; H, 4.32; N, 16.30.

2-[6-(2-Hydroxy-1-naphthyl)-3-oxo-2-phenyl-2,3-dihydro-1,2,4-triazin-5-yl]hydrazinecarboxamide (4c). A mixture of 1 (110.3 mg, 0.352 mmol), semicarbazide hydrochloride (669.2 mg, 6.00 mmol) and solution of sodium hydroxide (240.2 mg, 6.00 mmol) in water (5 ml) and ethanol (10 ml) was refluxed for 4 h. After cooling, water was added to the mixture (25 ml) and after 2 h of stirring a pale yellow solid was filtered off and washed with
water. A sample for analysis was prepared by crystallization from ethanol. Yield 133.4 mg (97.6 %), mp 197-200 °C; MS (ESI, m/z (rel. %)) 389.1 (100) [M+H]+; IR [cm⁻¹]: 3476, 3275, 3054, 2942, 1716, 1572, 1328, 1123, 750; ¹H-NMR (DMSO-d₆): δ 5.85 (bs, 2H, NH); 7.27-7.56 (m, 7H, arom.); 7.74-7.88 (m, 3H, arom.); 9.22 (s, 1H, NH); 9.80 (bs, 1H, NH); 10.77 (bs, 1H, OH). Anal. calcd for C₂₀H₁₆N₆O₃ (388.4): C, 61.85; H, 4.15; N, 21.64. Found C, 61.53; H, 3.92; N, 21.35.

8-(2-Hydroxy-1-naphthyl)-6-phenyl-1,2,4-triazolo[4,3-d][1,2,4]triazin-5(6H)-one (5a). A solution of compound 4a (75.2 mg, 0.218 mmol) in formic acid (3 ml) was refluxed for 90 min. Upon cooling, the solution was diluted with water (10 ml) and the precipitate was collected on a filter and washed with water. A sample for analysis was prepared by crystallization from methanol (1 ml per 2 mg). Yield 67.5 mg (87.1%), mp 238-240°C; MS (ESI, m/z (rel. %)) 356.1 (100) [M+H]+; IR [cm⁻¹]: 3108, 3079, 1735, 1465, 1369, 1286, 1170, 752; ¹H-NMR (DMSO-d₆): δ 7.29-7.48 (m, 4H, arom.); 7.53-7.59 (m, 2H, arom.); 7.68-7.71 (m, 2H, arom.); 7.83 (d, 1H, arom., J = 8.4 Hz); 7.90 (d, 1H, arom., J = 7.5 Hz); 8.00 (d, 1H, arom., J = 9.0 Hz); 9.75 (s, 1H, arom.). ¹³C-NMR (DMSO-d₆): δ 110.5, 118.4, 123.0, 123.9, 126.0, 126.8, 127.5, 127.8, 128.2, 131.5, 133.2, 136.6, 138.6, 139.9, 142.3, 145.2, 154.1. Anal. calcd for C₂₀H₁₃N₅O₂ (355.4): C, 67.60; H, 3.69; N, 19.71. Found C, 67.27; H, 3.51; N, 19.47.

2-(3-Methyl-5-oxo-6-phenyl-5,6-dihydro-1,2,4-triazolo[4,3-d][1,2,4]triazin-8-yl)naphthyl acetate (5b). A mixture of 4a (91.5 mg, 0.265 mmol) and acetic anhydride (1.0 ml) in anhydrous pyridine (3 ml) was heated on a boiling water bath for 2 h. Upon cooling to 2 °C, the solution was diluted with water to 50 ml. The precipitate was filtered off, washed with water and (for analysis) crystallized from an ethanol-water mixture. Yield 88.5 mg (81 %), mp 198-200°C; MS (ESI, m/z (rel. %)) 412.1 (100) [M+H]+; IR [cm⁻¹]: 3056, 1760, 1739, 1485, 1323, 1199, 758; ¹H-NMR (DMSO-d₆): δ 2.13 (s, 3H, COCH₃); 2.93 (s, 3H, CH₃); 7.47 (d, 1H, arom., J = 9.0 Hz); 7.90 (d, 1H, arom., J = 7.5 Hz); 8.02-8.09 (m, 2H, arom.); 8.21 (d, 1H, arom., J = 7.4 Hz). ¹³C-NMR (DMSO-d₆): δ 12.5, 20.5, 119.4, 122.2, 125.5, 126.0, 126.1, 127.1, 128.0, 128.2, 128.8, 131.0, 131.2, 132.1, 134.9, 139.9, 143.6, 145.5, 147.2, 149.6, 168.7. Anal. calcd for C₂₃H₁₇N₅O₃ (411.4): C, 67.15; H, 4.16; N, 17.02. Found C, 66.98; H, 4.01; N, 17.27.

8-(2-Hydroxy-1-naphthyl)-6-phenyl-3-thioxo-2,3-dihydro-1,2,4-triazolo[4,3-d][1,2,4]triazin-5(6H)-one (5c). A mixture of 4a (67.4 mg, 0.195 mmol) and carbon disulfide (0.3 ml) in pyridine (4 ml) was stirred in a sealed glass vial at room temperature. After 20 h, the vial was heated on a water bath (70 °C) for 10 min and evaporated to dryness in vacuo. The residue was mixed with water (3 ml), collected on a filter, washed with water and crystallized from ethanol (1 ml per 1 mg). Yield 67.1 mg (88.7 %), mp 264-266 °C; MS (ESI, m/z (rel. %)) 388.1 (65) [M+H]+, negative mode: 386.4 (100) [M-H]; IR [cm⁻¹]: 3495, 3127, 3059, 2920, 1716, 1459, 1251, 1148, 653; ¹H-NMR (DMSO-d₆): δ 7.17 (d, 1H, arom, J = 8.7 Hz); 7.26-7.62 (m, 5H, arom.); 7.76-7.99 (m, 3H, arom.); 8.57-8.59 (m, 2H, arom.); 9.92 (bs, 1H, NH-arom). Anal. calcd for C₂₀H₁₃N₅O₂S (387.4): C, 62.01; H, 3.38; N, 18.08; S, 8.42. Found C, 62.07; H, 3.51; N, 17.57; S, 8.42.

8-(2-Hydroxy-1-naphthyl)-6-phenyltetrazolo[1,5-d][1,2,4]triazin-5(6H)-one (6). Compound 4a (50.2 mg, 0.145 mmol) was dissolved in solution of 35% hydrochloric acid (0.2 ml) and water
(15 ml) at 60-70 °C and then cooled to 0-5 °C. To this mixture, a solution of sodium nitrite (10.0 mg, 0.145 mmol) in water (3 ml) was added. After 4 h stirring at 0-5 °C, the precipitate was filtered off and washed with water. Sample for analysis was prepared by crystallization from methanol (1 ml per 1 mg). Yield 43.3 mg (83.9 %), mp 282-284 °C; MS (ESI, m/z (rel. %)) 357.1 (90) [M+H]+; IR [cm⁻¹]: 3435, 3187, 3080, 1683, 1594, 1328, 1163, 763; ¹H-NMR (DMSO-d₆): δ 7.17 (d, 1H, arom., J = 8.7 Hz); 7.23-7.30 (m, 2H, arom.); 7.37-7.43 (m, 3H, arom.); 7.52-7.55 (m, 2H, arom.); 7.62-7.82 (m, 3H, arom.); 9.70 (bs, 1H, OH). Anal. calcd for C₂₀H₁₂N₆O₂ (356.3): C, 64.04; H, 3.39; N, 23.58. Found C, 63.87; H, 3.32; N, 23.69.

6-(2-Hydroxy-1-naphthyl)-2-phenyl-5-thioxo-4,5-dihydro-1,2,4-triazin-3(2H)-one (7).

Compound 1 (95.3 mg, 0.304 mmol) was suspended in a solution of NaOH (ca. 400 mg of NaOH in 5 ml of water) saturated with H₂S at room temperature. The mixture was stirred for 3 h at room temperature to obtain a solution. After 20 h, the solution was diluted with water (10 ml) and carefully neutralized with dilute acetic acid to pH 7-8. The precipitate was collected on filter and washed with water. A sample for analysis was obtained by crystallization from ethanol. Yield 50.4 mg (47.8 %), mp 241-245 °C; MS (ESI, m/z (rel. %)) 348.1 (35) [M+H]+, negative mode: 346.4 (100) [M-H]-; IR [cm⁻¹]: 3222, 3074, 1722, 1694, 1597, 1462, 1309, 1122, 749. ¹H-NMR (DMSO-d₆): δ 7.16 (d, 1H, arom., J = 8.7 Hz); 7.29-7.62 (m, 7H, arom.); 7.70-7.86 (m, 3H, arom.); 9.71 (s, 1H, OH); 13.85 (bs, 1H, NH-arom). Anal. calcd for C₁₉H₁₃N₃O₂S (347.4): C, 65.69; H, 3.77; N, 12.10; S, 9.23. Found C, 65.54; H, 3.52; N, 11.82 S, 8.96.

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