

# Synthesis of 4,4-dialkyl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazol-2-amines

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Synthesis of a series of 4,4-dialkyl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazol-2-amines by the cyclocondensation reaction of the corresponding 2-guanidinobenzimidazoles with various ketones is described.

**Key words:** [1,3,5]triazino[1,2-*a*]benzimidazoles, 2-guanidinobenzimidazoles, cyclocondensation, ketones

## INTRODUCTION

*s*-Triazino[1,2-*a*]benzimidazole derivatives exhibit antibacterial [1] and dihydrofolate reductase (DHFR) inhibitory activities [2–5]. It is well known that compounds capable of inhibiting the enzyme dihydrofolate reductase (DHFR) can be used in the treatment of some tumours [6, 7]. In this context and continuing our studies on the synthesis of fused heterocyclic compounds with antitumor properties [8, 9], it was of interest to synthesize some novel derivatives of 4,4-dialkyl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazol-2-amines for biological evaluation.

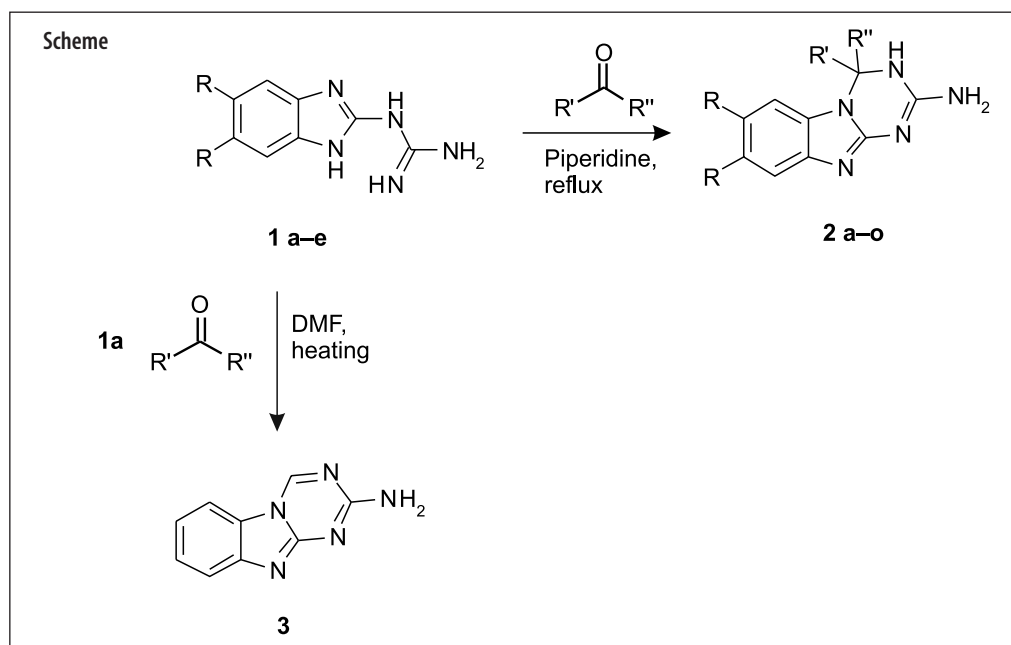
## RESULTS AND DISCUSSION

The target 4,4-dialkyl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazol-2-amines were prepared by cyclocondensation reaction of various 2-guanidinobenzimidazoles (1 *a*–*e*) with alifatic ketones by the method reported earlier [10] (Scheme). The equimolar amount of base piperidine was added to the solution of the starting materials in an appropriate ketone, and the resulted reaction mixtures were refluxed for the indicated period of time (Table). It is noteworthy that the cyclization of starting 2-guanidinobenzimidazoles bearing alkoxy

substituents in the benzene ring proceeded more smoothly. Overall, the yields of the products were good, ranging from 40 to 95%. Moreover, we tried to study the analogous synthetic method of the target compounds in solvent dimethylformamide either via convectional or microwave heating conditions. In both cases we isolated [1,3,5]triazino[1,2-*a*]benzimidazol-2-amine (3) as a sole reaction product. We presume that dimethylformamide acts not only as a solvent, but also reacts with the starting 2-guanidinobenzimidazole (1*a*) as a formyl synthon donor (Scheme).

The spectral characteristics and analytical data were in accordance with the structure of the synthesized 4,4-dialkyl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazol-2-amines 2 *a*–*o*. It should be noted that in <sup>1</sup>H NMR spectra of 4,4-diethyl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazol-2-amines 2 *l*–*o*, there are two different multiplets of methylene groups at 1.71–1.85 and 2.34–2.45 ppm, respectively. After the selective irradiation of the neighbouring methyl groups, the multiplets of methylene groups became doublets with coupling constants from 15 to 16.2 Hz. Therefore, in compounds 2 *l*–*o* we observed the geminal coupling between diastereotopic protons (Figure). It is worth noting that no diastereotopicity was observed in <sup>1</sup>H NMR spectra of 4-ethyl-4-methyl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazol-2-amines 2 *f*–*j* and 7,8-diethoxy-*spiro*[1,4']-cyclopentano-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazol-2-amine 2*k*.

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Table. Data of the synthesis of 4,4-dialkyl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazol-2-amines 2 a-o

Entry	Starting comp.	R	Product	R'	R''	Yield, %; (reaction time, h)
1	1a	-H	2a	-Me	-Me	95 (7)
2	1b	-(CH <sub>2</sub> ) <sub>3</sub> -	2b	-Me	-Me	40 (8)
3	1c	-OEt	2c	-Me	-Me	75 (16)
4	1d	-OMe	2d	-Me	-Me	61 (14)
5	1e	-OCH <sub>2</sub> O-	2e	-Me	-Me	92 (12)
6	1a	-H	2f	-Me	-Et	94 (7)
7	1b	-(CH <sub>2</sub> ) <sub>3</sub> -	2g	-Me	-Et	96 (7)
8	1c	-OEt	2h	-Me	-Et	62 (7)
9	1d	-OMe	2i	-Me	-Et	58 (5)
10	1e	-OCH <sub>2</sub> O-	2j	-Me	-Et	76 (12)
11	1c	-OEt	2k		-(CH <sub>2</sub> ) <sub>4</sub> -	44 (3)
12	1c	-OEt	2l	-Et	-Et	84 (18)
13	1a	-H	2m	-Et	-Et	48 (6.5)
14	1b	-(CH <sub>2</sub> ) <sub>3</sub> -	2n	-Et	-Et	42 (6.5)
15	1e	-OCH <sub>2</sub> O-	2o	-Et	-Et	50 (12)

The newly synthesized compounds were tested for antiproliferative activity *in vitro*. All compounds were inactive against the human solid tumour cancer cell lines tested (HeLa (cervix), Ishikawa (endometrial), SW1573 (non-small cell lung), T-47D (breast), and WiDr (colon)).

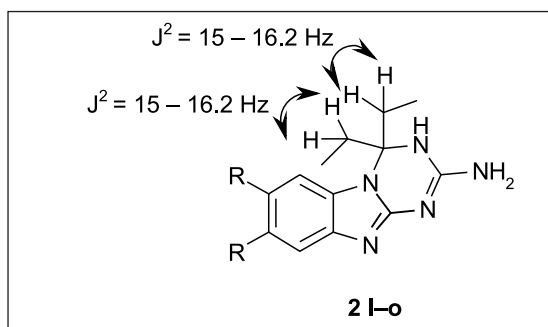
## EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were run in Nujol mulls or in KBr discs on a Perkin-Elmer FT Spectrum BX II spectrophotometer. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded with a Varian Unity INOVA spectrometer (300 MHz) using tetramethylsilane as the internal standard. Results of elemental analyses (C, N, H) were found to be in good agreement ( $\pm 0.4\%$ ) with

the calculated values. All reactions and the purity of the synthesized compounds were monitored by TLC using Silica gel 60 F<sub>254</sub> aluminium plates (Merck). Visualization was accomplished with UV light.

The starting 2-guanidinobenzimidazoles (1 a-e) were synthesized from the corresponding benzene-1,2-diamines and cyanoguanidine by the known procedure [11].

**4,4-Dialkyl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazol-2-amines (2 a-o).** To a solution of the corresponding 2-guanidinobenzimidazoles 1 a-e (0.1 mmol) in an appropriate ketone (5 ml), piperidine (0.1 mmol) was added. The reaction mixture was heated under stirring at reflux for 3–14 h. After cooling to room temperature, the precipitate was filtered off and recrystallized.



Figure

**2a:** Yield: 95%, m. p. 291–293 °C (from acetone)

$^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ ,  $\delta$ , ppm): 1.83 (6H, s., 2CH<sub>3</sub>), 6.95 (2H, br. s., NH<sub>2</sub>), 6.98–7.07 (2H, m., C(7)H and C(8)H), 7.29 (1H, d.,  $J = 7.8$  Hz, C(6)H or C(9)H), 7.34 (1H, d.,  $J = 7.5$  Hz, C(6)H or C(9)H), 8.18 (1H, br. s., NH).

$^{13}\text{C}$  NMR (75 MHz, DMSO- $d_6$ ,  $\delta$ , ppm): 34.1, 74.9, 115.2, 121.3, 124.6, 126.2, 136.1, 148.8, 159.1, 160.8.

Data for compound **2a** are in agreement with those published elsewhere [10].

**2b:** Yield: 40%, m. p. 305–306 °C (from DMSO).

$^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ ,  $\delta$ , ppm): 1.82 (6H, s., 2CH<sub>3</sub>), 2.04–2.06 (2H, m., CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.89–2.91 (4H, m., CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 6.23 (2H, br. s., NH<sub>2</sub>), 7.13 (1H, s., C(6)H or C(9)H), 7.26 (1H, s., C(6)H or C(9)H), 7.90 (1H, br. s., NH).

$^{13}\text{C}$  NMR (75 MHz, DMSO- $d_6$ ,  $\delta$ , ppm): 26.7, 29.3, 31.4, 33.0, 33.2, 70.0, 106.2, 112.8, 130.2, 135.4, 136.7, 143.1, 153.9, 155.8.

IR (v, cm<sup>-1</sup>): 3 330, 3 295, 3 096 (NH, NH<sub>2</sub>).

Elemental analysis data: found, %: C 65.91; H 6.75; N 27.36; formula C<sub>14</sub>H<sub>17</sub>N<sub>5</sub>; calculated, %: C 65.86; H 6.71; N 27.43.

**2c:** Yield: 75%, m. p. >275 °C (from ethyl acetate).

$^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ ,  $\delta$ , ppm): 1.32 (6H, t.,  $J = 6.6$  Hz, 2OCH<sub>2</sub>CH<sub>3</sub>), 1.77 (6H, s., 2CH<sub>3</sub>), 3.98–4.04 (4H, m., 2OCH<sub>2</sub>CH<sub>3</sub>), 6.55 (2H, br. s., NH<sub>2</sub>), 6.90 (1H, s., C(6)H or C(9)H), 6.97 (1H, s., C(6)H or C(9)H), 7.84 (1H, br. s., NH).

$^{13}\text{C}$  NMR (75 MHz, DMSO- $d_6$ ,  $\delta$ , ppm): 15.7, 31.4, 65.4, 66.3, 70.0, 99.3, 103.8, 124.9, 138.4, 143.8, 145.5, 153.8, 155.5.

IR (v, cm<sup>-1</sup>): 3 331, 3 279, 3 095 (NH, NH<sub>2</sub>).

Elemental analysis data: found, %: C 59.28; H 7.21; N 22.98; formula C<sub>15</sub>H<sub>21</sub>N<sub>5</sub>O<sub>2</sub>; calculated, %: C 59.39; H 6.98; N 23.09.

**2d:** Yield: 61%, m. p. 261 °C (decomp.) (from ethyl acetate and ethanol mixture).

$^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ ,  $\delta$ , ppm): 1.89 (6H, s., 2CH<sub>3</sub>), 3.80 (3H, s., OCH<sub>3</sub>), 3.85 (3H, s., OCH<sub>3</sub>), 6.96 (1H, s., C(6)H or C(9)H), 7.17 (1H, s., C(6)H or C(9)H), 7.37 (2H, br. s., NH<sub>2</sub>), 9.01 (1H, br. s., NH).

$^{13}\text{C}$  NMR (75 MHz, DMSO- $d_6$ ,  $\delta$ , ppm): 29.1, 56.8, 57.5, 71.1, 97.6, 98.2, 121.7, 127.1, 146.2, 147.2, 150.9, 156.4.

IR (v, cm<sup>-1</sup>): 3 395, 3 154, 3 057 (NH, NH<sub>2</sub>).

Elemental analysis data: found, %: C 56.78; H 6.25; N 25.37; formula C<sub>13</sub>H<sub>17</sub>N<sub>5</sub>O<sub>2</sub>; calculated, %: C 56.71; H 6.22; N 25.44.

**2e:** Yield: 92%, m. p. 224 °C (decomp.) (from ethanol).

$^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ ,  $\delta$ , ppm): 1.77 (6H, s., 2CH<sub>3</sub>), 5.92 (2H, s., OCH<sub>2</sub>O), 6.61 (2H, br. s., NH<sub>2</sub>), 6.85 (1H, s., C(6)H or C(9)H), 7.13 (1H, s., C(6)H or C(9)H), 7.92 (1H, br. s., NH).

$^{13}\text{C}$  NMR (75 MHz, DMSO- $d_6$ ,  $\delta$ , ppm): 29.2, 70.2, 93.1, 97.7, 100.8, 124.8, 138.0, 142.0, 143.0, 153.4, 155.3.

IR (v, cm<sup>-1</sup>): 3 319, 3 232, 3 105 (NH, NH<sub>2</sub>).

Elemental analysis data: found, %: C 55.69; H 5.29; N 26.85; formula C<sub>12</sub>H<sub>13</sub>N<sub>5</sub>O<sub>2</sub>; calculated, %: C 55.59; H 5.05; N 27.01.

**2f:** Yield: 94%, m. p. 241 °C (decomp.) (from ethyl acetate and ethanol mixture).

$^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ ,  $\delta$ , ppm): 0.72 (3H, t.,  $J = 7.2$  Hz CH<sub>2</sub>CH<sub>3</sub>), 1.83 (3H, s., CH<sub>3</sub>), 2.36–2.43 (2H, m., CH<sub>2</sub>CH<sub>3</sub>), 6.78 (2H, br. s., NH<sub>2</sub>), 6.97–7.09 (2H, m., C(7)H, C(8)H), 7.29 (1H, d.,  $J = 7.5$  Hz, C(6)H or C(9)H), 7.40 (1H, d.,  $J = 7.5$  Hz C(6)H or C(9)H), 8.06 (1H, br. s., NH).

$^{13}\text{C}$  NMR (75 MHz, DMSO- $d_6$ ,  $\delta$ , ppm): 8.0, 28.8, 33.9, 39.3, 73.0, 110.4, 116.5, 119.8, 121.5, 131.1, 143.9, 154.9, 156.5.

IR (v, cm<sup>-1</sup>): 3 327, 3 253, 3 117 (NH, NH<sub>2</sub>).

Elemental analysis data: found, %: C 62.98; H 6.74; N 30.68; formula C<sub>12</sub>H<sub>15</sub>N<sub>5</sub>; calculated, %: C 62.86; H 6.59; N 30.54.

**2g:** Yield: 96%, m. p. 218 °C (decomp.) (from ethyl acetate and 2-propanol mixture).

$^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ ,  $\delta$ , ppm): 0.72 (3H, br. s., CH<sub>2</sub>CH<sub>3</sub>), 1.83 (3H, s., CH<sub>3</sub>), 2.03 (2H, br. s., CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.46 (2H, br. s., CH<sub>2</sub>CH<sub>3</sub>), 2.90 (4H, br. s., CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 6.84 (2H, br. s., NH<sub>2</sub>), 7.11 (1H, s., C(6)H or C(9)H), 7.20 (1H, s., C(6)H or C(9)H), 7.98 (1H, br. s., NH).

$^{13}\text{C}$  NMR (75 MHz, DMSO- $d_6$ ,  $\delta$ , ppm): 8.1, 26.6, 28.9, 33.0, 33.2, 33.9, 72.9, 106.9, 112.0, 130.9, 135.4, 136.8, 143.0, 154.5, 156.1.

IR (v, cm<sup>-1</sup>): 3 330, 3 253, 3 104 (NH, NH<sub>2</sub>).

Elemental analysis data: found, %: C 66.85; H 7.24; N 26.06; formula C<sub>15</sub>H<sub>19</sub>N<sub>5</sub>; calculated, %: C 66.89; H 7.11; N 26.00.

**2h:** Yield: 62%, m. p. 248–250 °C (from 2-butanone).

$^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ ,  $\delta$ , ppm): 0.72 (3H, t.,  $J = 6.9$  Hz CH<sub>2</sub>CH<sub>3</sub>), 1.30–1.35 (6H, m., 2OCH<sub>2</sub>CH<sub>3</sub>), 1.80 (3H, s., CH<sub>3</sub>), 2.33–2.40 (2H, m., CH<sub>2</sub>CH<sub>3</sub>), 3.98–4.06 (4H, m., 2OCH<sub>2</sub>CH<sub>3</sub>), 6.58 (2H, br. s., NH<sub>2</sub>), 6.90 (1H, s., C(6)H or C(9)H), 6.92 (1H, s., C(6)H or C(9)H), 7.72 (1H, br. s., NH).

$^{13}\text{C}$  NMR (75 MHz, DMSO- $d_6$ ,  $\delta$ , ppm): 8.0, 15.7, 28.8, 34.0, 65.3, 66.3, 72.8, 99.1, 103.7, 124.7, 138.2, 143.7, 145.5, 154.3, 155.9.

IR ( $\nu$ ,  $\text{cm}^{-1}$ ): 3 356, 3 266, 3 105 (NH, NH<sub>2</sub>).

Elemental analysis data: found, %: C 60.78; H 7.11; N 22.06; formula C<sub>16</sub>H<sub>23</sub>N<sub>5</sub>O<sub>2</sub>; calculated, %: C 60.55; H 7.30; N 22.07.

**2i**: Yield: 58%, m. p. >275 °C (from 2-propanol).

<sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>,  $\delta$ , ppm): 0.76 (3H, t, *J* = 6.9 Hz CH<sub>2</sub>CH<sub>3</sub>), 1.91 (3H, s, CH<sub>3</sub>), 2.42–2.47 (2H, m, CH<sub>2</sub>CH<sub>3</sub>), 3.80 (3H, s, OCH<sub>3</sub>), 3.84 (3H, s, OCH<sub>3</sub>), 6.99 (1H, s, C(6)H or C(9)H), 7.13 (1H, s, C(6)H or C(9)H), 7.45 (2H, br. s., NH<sub>2</sub>), 9.19 (1H, br. s., NH).

<sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>,  $\delta$ , ppm): 7.8, 28.3, 33.7, 56.8, 57.5, 74.3, 97.1, 97.7, 120.7, 123.6, 146.9, 147.7, 150.8, 157.3.

IR ( $\nu$ ,  $\text{cm}^{-1}$ ): 3 369, 3 331, 3 167 (NH, NH<sub>2</sub>).

Elemental analysis data: found, %: C 58.31; H 6.68; N 24.15; formula C<sub>14</sub>H<sub>19</sub>N<sub>5</sub>O<sub>2</sub>; calculated, %: C 58.12; H 6.62; N 24.21.

**2j**: Yield: 76%, m. p. >275 °C (from 2-propanol).

<sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>,  $\delta$ , ppm): 0.71 (3H, br. s., CH<sub>2</sub>CH<sub>3</sub>), 1.82 (3H, s, CH<sub>3</sub>), 2.34–2.41 (2H, m, CH<sub>2</sub>CH<sub>3</sub>), 3.90 (1H, br. s., NH + H<sub>2</sub>O), 5.97 (2H, s, OCH<sub>2</sub>O), 6.96 (1H, s, C(6)H or C(9)H), 7.15 (2H, br. s., NH<sub>2</sub>), 7.20 (1H, s, C(6)H or C(9)H).

<sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>,  $\delta$ , ppm): 7.9, 28.4, 33.6, 73.6, 93.6, 96.6, 101.4, 123.4, 132.7, 143.1, 143.8, 152.7, 156.3.

IR ( $\nu$ ,  $\text{cm}^{-1}$ ): 3 330, 3 266, 3 125 (NH, NH<sub>2</sub>).

Elemental analysis data: found, %: C 57.19; H 5.49; N 25.48; formula C<sub>13</sub>H<sub>15</sub>N<sub>5</sub>O<sub>2</sub>; calculated, %: C 57.13; H 5.53; N 25.63.

**2k**: Yield: 44%, m. p. = 204–205 °C (from 2-propanol).

<sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>,  $\delta$ , ppm): 1.30–1.35 (6H, m., 2OCH<sub>2</sub>CH<sub>3</sub>), 1.86 (8H, br. s., CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 3.99–4.02 (4H, m., 2OCH<sub>2</sub>CH<sub>3</sub>), 6.32 (2H, br. s., NH<sub>2</sub>), 6.76 (1H, s, C(6)H or C(9)H), 6.92 (1H, s, C(6)H or C(9)H), 7.92 (1H, br. s., NH).

<sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>,  $\delta$ , ppm): 15.7, 24.0, 38.9, 65.2, 66.1, 79.4, 98.6, 103.3, 124.1, 136.8, 143.9, 145.6, 154.0, 155.2.

IR ( $\nu$ ,  $\text{cm}^{-1}$ ): 3 340, 3 269, 3 134 (NH, NH<sub>2</sub>).

Elemental analysis data: found, %: C 62.07; H 7.09; N 21.48; formula C<sub>17</sub>H<sub>23</sub>N<sub>5</sub>O<sub>2</sub>; calculated, %: C 61.99; H 7.04; N 21.26.

**2l**: Yield: 84%, m. p. = 252–254 °C (from ethanol).

<sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>,  $\delta$ , ppm): 0.70 (6H, t, *J* = 6.9 Hz, 2CH<sub>2</sub>CH<sub>3</sub>), 1.31–1.33 (6H, m., 2OCH<sub>2</sub>CH<sub>3</sub>), 1.74–1.78 (2H, m., 2CH<sub>2</sub>CH<sub>3</sub>), 2.36–2.43 (2H, m., 2CH<sub>2</sub>CH<sub>3</sub>), 3.98–4.01 (4H, m., 2OCH<sub>2</sub>CH<sub>3</sub>), 6.42 (2H, br. s., NH<sub>2</sub>), 6.86 (1H, s, C(6)H or C(9)H), 6.89 (1H, s, C(6)H or C(9)H), 7.46 (1H, br. s., NH).

<sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>,  $\delta$ , ppm): 7.7, 15.7, 15.7, 33.2, 65.3, 66.3, 75.9, 98.8, 103.6, 124.5, 137.9, 143.7, 145.5, 155.0, 156.4.

IR ( $\nu$ ,  $\text{cm}^{-1}$ ): 3 375, 3 275, 3 096 (NH, NH<sub>2</sub>).

Elemental analysis data: found, %: C 61.31; H 7.89; N 21.09; formula C<sub>17</sub>H<sub>23</sub>N<sub>5</sub>O<sub>2</sub>; calculated, %: C 61.61; H 7.60; N 21.13.

**2m**: Yield: 48%, m. p. = 192–194 °C (from ethyl acetate and 2-propanol mixture).

<sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>,  $\delta$ , ppm): 0.70 (6H, br. s., 2CH<sub>2</sub>CH<sub>3</sub>), 1.80–1.85 (2H, m., 2CH<sub>2</sub>CH<sub>3</sub>), 2.45 (2H, br. s., 2CH<sub>2</sub>CH<sub>3</sub>), 6.92–7.04 (4H, m., NH<sub>2</sub>, C(7)H, C(8)H), 7.26–7.32 (2H, m., C(6)H, C(9)H), 8.70 (1H, br. s., NH).

<sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>,  $\delta$ , ppm): 7.8, 33.3, 76.2, 110.2, 116.4, 120.0, 121.7, 130.8, 143.3, 155.6, 157.2.

IR ( $\nu$ ,  $\text{cm}^{-1}$ ): 3 334, 3 214, 3 094 (NH, NH<sub>2</sub>).

Elemental analysis data: found, %: C 64.12; H 7.15; N 28.91; formula C<sub>13</sub>H<sub>17</sub>N<sub>5</sub>; calculated, %: C 64.17; H 7.04; N 28.78.

**2n**: Yield: 42%, m. p. > 240 °C (decomp.) (from ethyl acetate and 2-propanol mixture).

<sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>,  $\delta$ , ppm): 0.69 (6H, br. s., 2CH<sub>2</sub>CH<sub>3</sub>), 1.73–1.77 (2H, m., 2CH<sub>2</sub>CH<sub>3</sub>), 2.02 (2H, br. s., CH<sub>2</sub>CH<sub>2</sub>), 2.42–2.45 (2H, m., 2CH<sub>2</sub>CH<sub>3</sub>), 2.46 (2H, br. s., CH<sub>2</sub>CH<sub>2</sub>), 2.86–2.88 (4H, m., CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 6.38 (2H, br. s., NH<sub>2</sub>), 7.08 (1H, s, C(6)H or C(9)H), 7.14 (1H, s, C(6)H or C(9)H), 7.43 (1H, br. s., NH).

<sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>,  $\delta$ , ppm): 7.8, 26.6, 33.0, 33.2, 75.9, 105.7, 112.2, 129.9, 135.4, 136.8, 142.9, 156.6, 157.0.

IR ( $\nu$ ,  $\text{cm}^{-1}$ ): 3 318, 3 214, 3 104 (NH, NH<sub>2</sub>).

Elemental analysis data: found, %: C 66.97; H 7.95; N 24.69; formula C<sub>16</sub>H<sub>21</sub>N<sub>5</sub>; calculated, %: C 67.82; H 7.47; N 24.71.

**2o**: Yield: 76%, m. p. >275 °C (from 2-propanol).

<sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>,  $\delta$ , ppm): 0.66–0.71 (6H, m., 2CH<sub>2</sub>CH<sub>3</sub>), 1.68–1.75 (2H, m., 2CH<sub>2</sub>CH<sub>3</sub>), 2.38–2.45 (2H, m., 2CH<sub>2</sub>CH<sub>3</sub>), 5.91 (2H, s, OCH<sub>2</sub>O), 6.48 (2H, br. s., NH<sub>2</sub>), 6.82 (1H, s, C(6)H or C(9)H), 7.04 (1H, s, C(6)H or C(9)H), 7.45 (1H, br. s., NH).

<sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>,  $\delta$ , ppm): 7.7, 33.2, 76.1, 92.7, 97.8, 100.8, 124.5, 138.0, 141.9, 143.0, 154.8, 156.3.

IR ( $\nu$ ,  $\text{cm}^{-1}$ ): 3 321, 3 215, 3 105 (NH, NH<sub>2</sub>).

Elemental analysis data: found, %: C 58.69; H 6.03; N 24.45; formula C<sub>14</sub>H<sub>17</sub>N<sub>5</sub>O<sub>2</sub>; calculated, %: C 58.52; H 5.96; N 24.38.

### [1,3,5]Triazino[1,2-*a*]benzimidazol-2-amine (3)

*Method A.* A solution of the 2-guanidinobenzimidazole **1a** (0.2 g, 1.1 mmol) in dimethylformamide (5 ml) was heated at 120 °C for 5 h. After cooling to room temperature the precipitate was filtered off and recrystallized.

*Method B.* A solution of the 2-guanidinobenzimidazole **1a** (0.2 g, 1.1 mmol) in dimethylformamide (3 ml) was placed in a closed vessel (15 ml) and irradiated in a domestic microwave oven (model DAEWOO KOR6305A) at 610 W for

30 min. After cooling to room temperature, the precipitate was filtered off and recrystallized.

Yield: 36% (method A), 69% (method B).

Data for compound 3 are in agreement with those published previously [12].

## CONCLUSIONS

A series of some novel 4,4-dialkyl-3,4-dihydro[1,3,5]triazino[1,2-*a*]benzimidazol-2-amines was prepared. It was shown that the synthesized compounds were not able to inhibit the growth of human solid tumour cancer cell lines as had been expected.

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## 4,4-DIALKIL-3H-1,3,5-TRIAZINO[1,2-*a*]- BENZIMIDAZOL-2-AMINŲ SINTEZĖ

### Santrauka

Reaguojant 2-guanidinobenzimidazolams su įvairiais ketonais susintetinti keli nauji 4,4-dialkil-3H-1,3,5-triazino[1,2-*a*]benzimidazol-2-aminai.