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5,6-DIHYDRO-[1,2,4]TRIAZOLO[1,5-*c*]QUINAZOLINES. MESSAGE 2. [5+1]-CYCLOCONDENSATION OF [2-(3-ARYL-1*H*-1,2,4-TRIAZOL-5-YL)PHENYL]AMINES WITH ALIPHATIC AND AROMATIC KETONES

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Key words: 5-[2-(3-aryl-1H-1,2,4-triazol-5-yl)phenyl]amines; ketones; [5+1]-cyclocondensation; spectral characteristics

The reactions of [5+1]-cyclocondensation of [2-(3-aryl-1H-1,2,4-triazol-5-yl)phenyl]amines with aliphatic and aromatic ketones result in the corresponding 5-R-5-R1-2-aryl-5,6-dihydro-[1,2,4]triazolo[1,5-c]quinazolines with good yields. Modification of the synthetic protocol by variation of the solvent and duration of the reaction does not lead to the changes in target products yields. Conducting of the interaction between [2-(3-aryl-1H-1,2,4-triazol-5-yl)phenyl]amines and ketones in acetic acid leads to formation of the mixture the corresponding 2-aryl-5-R-5-R1-5,6-dihydro[1,2,4]triazolo[1,5-c]quinazolines and 5-methyl-2-aryl-[1,2,4]triazolo[1,5-c]quinazolin. The compounds mentioned above have been prepared using alternative synthetic approaches, namely via refluxing of [2-(3-aryl-1H-1,2,4-triazol-5-yl)phenyl]amines in acetic acid. The formation of 5-methyl-2-aryl-[1,2,4]triazolo[1,5-c]quinazolines occurs as a competitive acylation followed by the condensation process. It can be explained by the low reactivity and spatial structure of the corresponding ketones. The purity and the structure of the compounds synthesized have been proven by the complex of physicochemical methods, including IR-, LC-MS, ^{1}H-, ^{13}C-NMR-spectrometry and elemental analysis. It has been found that the characteristic signal of sp^{3}-carbon atom of position 5 for the compounds synthesized is observed at the 75.57-61.64 ppm.

5,6-ДИГІДРО-[1,2,4]ТРИАЗОЛО[1,5-c]ХІНАЗОЛІНИ. ПОВІДОМЛЕННЯ 2. РЕАКЦІЇ [5+1]-ЦИКЛОКОНДЕНСАЦІЇ [2-(3-АРИЛ-1Н-1,2,4-ТРИАЗОЛ-5-ІЛ)ФЕНІЛ]АМІНІВ З КЕТОНАМИ АЛІФАТИЧНОГО ТА АРОМАТИЧНОГО РЯДУ

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***Ключові слова**: [2-(3-арил-1Н-1,2,4-триазол-5-іл)феніл]аміни; кетони; [5+1]-циклоконденсація; спектральні характеристики*

Реакції [5+1]-циклоконденсації [2-(3-арил-1Н-1,2,4-триазол-5-іл)феніл]амінів з кетонами аліфатичного та ароматичного ряду перебігають з утворенням 5-R-5-R$_1$-2-арил-5,6-дигідро-[1,2,4]триазоло[1,5-c]хіназолінів з задовільними виходами. Модифікація синтетичного протоколу шляхом варіювання розчинника та тривалості реакції не приводить до збільшення виходів цільових продуктів. Реалізація реакції [2-(3-арил-1Н-1,2,4-триазол-5-іл)феніл]амінів з кетонами у льодяній оцтовій кислоті привела до утворення суміші відповідних 2-арил-5-R-5-R$_1$-5,6-дигідро[1,2,4]триазоло[1,5-c]хіназолінів та 5-метил-2-арил-[1,2,4]триазоло[1,5-c]хіназолінів. Останні синтезовані зустрічним синтезом, а саме кип'ятінням [2-(3-арил-1Н-1,2,4-триазол-5-іл)феніл]амінів у льодяній оцтовій кислоті. Формування 5-метил-2-арил-[1,2,4]триазоло[1,5-c]хіназолінів відбувається як конкуруюче ацилювання з наступною гетероциклізацією і є можливим у зв'язку з низькою реакційною здатністю кетонів та просторовою будовою їх молекули. Індивідуальність та будова синтезованих сполук підтверджені хроматомас-, ІЧ-, ^{1}Н-, ^{13}С-ЯМР-спектрами та елементним аналізом. Встановлено, що характеристичний сигнал sp^{3}-гібридизованого атома Карбону положення 5 реєструється при 75,57-61,64 м.ч.

5,6-ДИГИДРО-[1,2,4]ТРИАЗОЛО[1,5-c]ХИНАЗОЛИНЫ. СООБЩЕНИЕ 2. РЕАКЦИИ [5+1]-ЦИКЛОКОНДЕНСАЦИИ [2-(3-АРИЛ-1Н-1,2,4-ТРИАЗОЛ-5-ИЛ)ФЕНИЛ]АМИНОВ С КЕТОНАМИ АЛИФАТИЧЕСКОГО И АРОМАТИЧЕСКОГО РЯДА

С.В.Холодняк, К.П.Шабельник, А.Ю.Воскобойник, А.Н.Антипенко, Г.Г.Берест, С.И.Коваленко

***Ключевые слова:** [2-(3-арил-1Н-1,2,4-триазол-5-ил)фенил]амины; кетоны; [5+1]-циклоконденсация; спектральные характеристики*

Реакции [5+1]-циклоконденсации [2-(3-арил-1Н-1,2,4-триазол-5-ил)фенил]аминов с кетонами алифатического и ароматического ряда протекают с образованием 5-R-5-R$_1$-2-арил-5,6-дигидро-[1,2,4]триазоло[1,5-c]хиназолинов с хорошими выходами. Модификация синтетического протокола путем варьирования растворителя и длительности реакции не приводит к увеличению выходов целевых продуктов. Реализация реакции [2-(3-арил-1Н-1,2,4-триазол-5-ил)фенил]аминов с кетонами в ледяной уксусной кислоте приводит к образованию смеси соответствующих 2-арил-5-R-5-R$_1$-5,6-дигидро[1,2,4]триазоло[1,5-c]хиназолинов и 5-метил-2-арил-[1,2,4]триазоло[1,5-c]хиназолинов. Последние синтезированы встречным синтезом, а именно кипячением [2-(3-арил-1Н-1,2,4-триазол-5-ил)фенил]аминов в ледяной уксусной кислоте. Формирование 5-метил-2-арил-[1,2,4]триазоло[1,5-c]хиназолинов происходит как конкурентное ацилирование с последующей гетероциклизацией и возможно ввиду низкой реакционной способности кетонов и их пространственного строения. Индивидуальность и строение синтезированных веществ подтверждено хроматомасс-, ИК-, ^{1}Н-, ^{13}С-ЯМР-спектрами и элементным анализом. Установлено, что характеристический сигнал sp^{3}-гибридизованного атома углерода положения 5 регистрируется при 75,57-61,64 м.ч.

In our previous paper [1] the features of the interaction between [2-(3-aryl-1*H*-1,2,4-triazol-5-yl)phenyl] amines (**1**) and aldehydes were reported. There the possibility of spontaneous 5,6-dihydro-[1,2,4]triazolo [1,5-*c*]quinazoline oxidation to the corresponding aromatic analogues was described. Probably some differences in [5+1]-cyclocondensation between amines **1.1-1.5** and ketones would be expected. Moreover, the reactivity of ketones as electrophiles is much more lower compared to aldehydes, and steric complications when forming the 5,6-dihydro-[1,2,4]triazolo [1,5-*c*]quinazoline cycle is possible [2].

The aim of the present work was to study the features of the interaction of [2-(3-aryl-1*H*-1,2,4-triazol-5-ylphenyl]amines with aliphatic and aromatic ketones, and the effects of the solvent and conditions of the reaction course on the structure of the products, as well as to confirm the structure of the compounds synthesized by the complex of physicochemical methods.

Results and Discussion

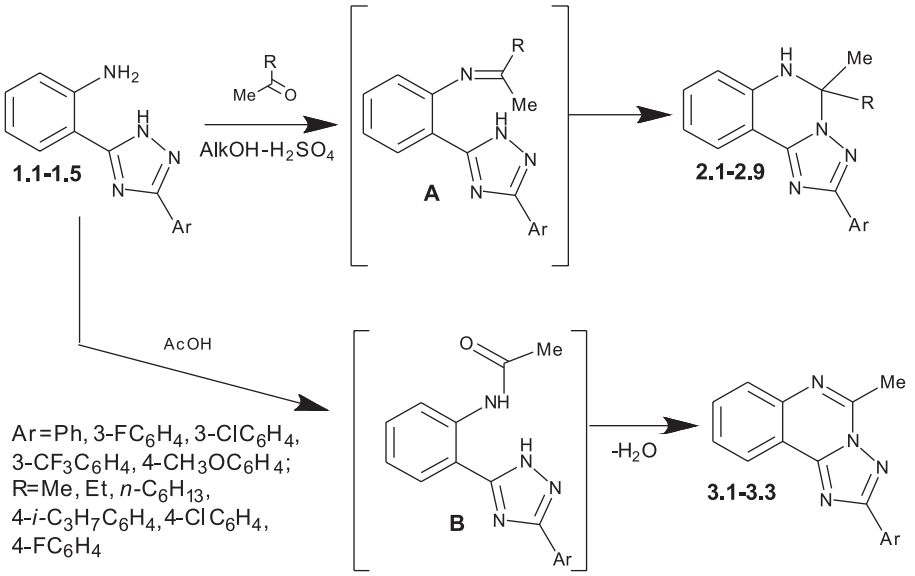
It was determined that the interaction of equimolar quantities of anilines **1.1-1.5** with ketones in propan-2-ol in the presence of an acidic catalyst resulted in formation of the corresponding 2-aryl-5-R-5-R_1-5,6-dihydro[1,2,4]triazolo[1,5-*c*]quinazolines (**2.1-2.9**) with good yields (Scheme, Table). Modification of the synthetic protocol by means of variation of the solvent (lowest alcohols, dioxane) and duration of the process (up to 6 h) did not led to the increase of yields and oxidation of **2.1-2.9**. As in case of [5+1]-cyclocondensation between anilines **1.1-1.5** and aldehydes, this reaction is a binucleophilic addition, wherein Schiff base plays the role of an intermediate, and is not stereoselective [2].

At the same time, according to LC-MS data, the interaction between anilines **1.1-1.5** with ketones in acetic acid led to the unexpected result, namely to formation of the mixture consisting of the corresponding 2-aryl-5-R-5-R_1-5,6-dihydro[1,2,4]triazolo[1,5-*c*] quinazolines (**2**, 5-19%) and 5-methyl-2-aryl-[1,2,4] triazolo[1,5-*c*]quinazolines (**3**, 61-79%). Compounds **2** and **3** were isolated *via* recrystallization using propan-2-ol as a solvent.

The formation of compounds **3.1-3.3** could occur as a competitive acylation of anilines **1** followed by cyclization of intermediate **B**. Probably, acylation was possible as the result of the low reactivity of ketones as electrophiles and the spatial structure of their molecules. Really, refluxing of anilines **1.2, 1.4, 1.5** in glacial acetic acid for 6 h resulted in compounds **3.1-3.3** with the yields of 31-57% (Scheme).

The purity and structure of the compounds synthesized were proven by the complex of physicochemical methods, including LC-MS, ^{1}H-, ^{13}C-NMR- and elemental analysis. In the LC-MS spectra of compounds **2.1-2.9** and **3.1-3.3** the low intensive signals of molecular ions [M+1] were registered. They corresponded to the calculated target compounds, and undoubtedly confirmed the condensation process. Moreover, LC-MS spectra of compounds **2.3**, **2.7** and **2.8** were characterized by the ion [M+3] indicated the presence of ^{37}Cl isotope.

IR-spectra of compounds **2.1-2.9** were different from patterns of the initial amines **1.1-1.5** [5, 6] and had stretching vibrations of the n_{NHR_2}-group as one band at 3265-3062 cm^{-1}, deformation vibrations of the d_{NH}-group at – 1625-1611 cm^{-1} and vibrations of the g_{NHR_2}-group at 1606-1587 cm^{-1}, respectively. Moreover, compounds **2.1-2.9** were characterized by intensive bands of stretching vibrations of n_{asCH_3}, n_{sCH_3}-group, n_{asCH_2}-, n_{sCH_2}-bonds at 3023-2950 and 2885-2860 cm^{-1} and deformation vibrations at 1470-1435 and 1385-1370 cm^{-1}. It is important to note that intensive stretching vibrations at 1340-1100 cm^{-1} and 700-600 cm^{-1} indicated the presence of halogens (Chlorine, Fluorine) in the compounds studied [3]. But the bands of the secon-



Scheme. The interaction of [2-(3-aryl-1*H*-1,2,4-triazol)phenyl]amines with ketones.

Table

The physicochemical properties

Compounds, No.	Ar	R	M.p.	Yields		Formula
				A	B	
2.1	Ph	Me	246-248	70.7	–	$C_{17}H_{16}N_4$
2.2	Ph	Et	137-139	89.7	–	$C_{18}H_{18}N_4$
2.3	3-ClC_6H_4	Et	164-166	70.3	–	$C_{18}H_{17}ClN_4$
2.4	Ph	*н*-C_6H_{13}	135-136	89.0	–	$C_{22}H_{26}N_4$
2.5	Ph	Ph	234-235	63.0	–	$C_{22}H_{18}N_4$
2.6	3-FC_6H_4	4-*i*-PrC_6H_4	157-158	78.0	–	$C_{25}H_{23}FN_4$
2.7	Ph	4-ClC_6H_4	182-183	88.2	–	$C_{22}H_{17}ClN_4$
2.8	4-$MeOC_6H_4$	4-ClC_6H_4	204-205	76.3	–	$C_{23}H_{19}ClN_4O$
2.9	3-$CF_3C_6H_4$	4-FC_6H_4	190-191	54.0	–	$C_{23}H_{16}F_4N_4$
3.1	3-$CF_3C_6H_4$		140-142	41.2	31.4	$C_{17}H_{11}F_3N_4$
3.2	3-FC_6H_4	–	165-167	56.9	42.6	$C_{16}H_{11}FN_4$
3.3	4-$MeOC_6H_4$	–	149-151	31.2	46.8	$C_{17}H_{14}N_4O$

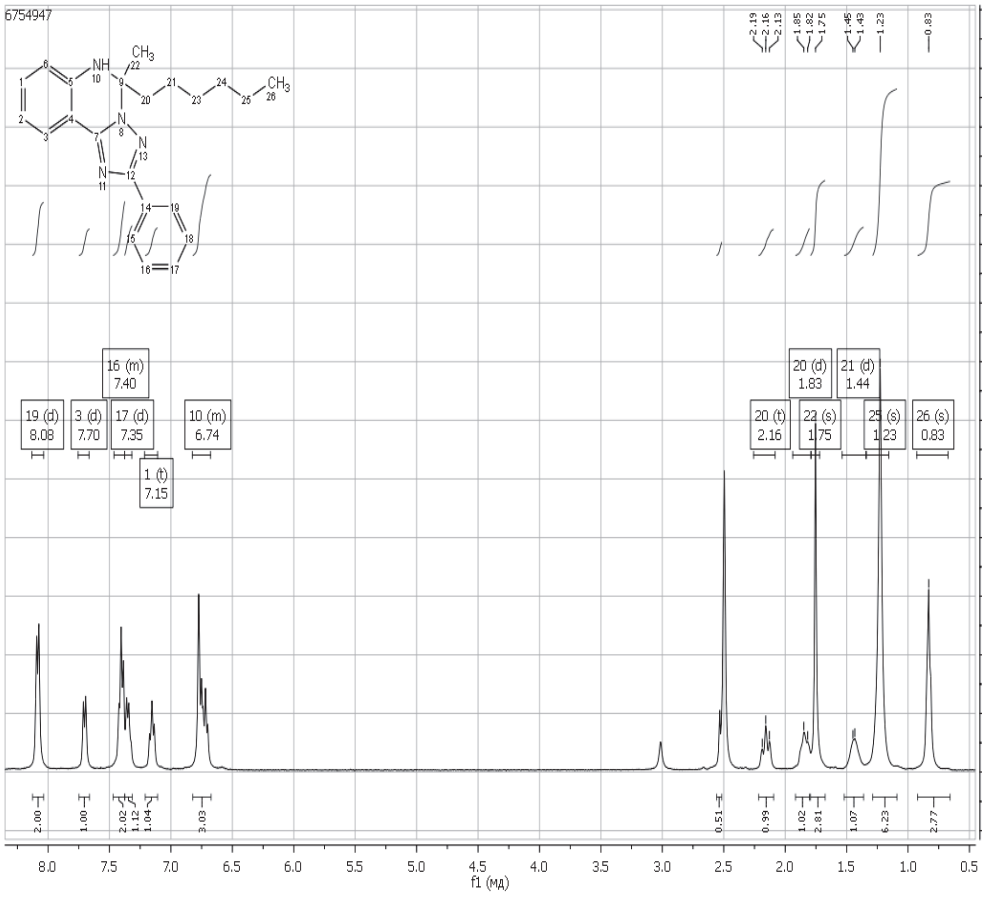


Fig. 1. The fragment of ^{1}H NMR-spectra (400 MHz) of compound **2.4** in DMSO-d_6.

dary NHR_2-group for compounds **3.1-3.2** were absent. The given compounds were characterized by intensive bands of CH_3-group deformation vibrations at 3009-2860 cm^{-1} and 1480-1412 cm^{-1}, respectively.

The formation of **2.1-2.9** was also proven by the presence of NH-group proton signals registered as singlets at 7.33-6.83 ppm for compounds with the aliphatic moiety in position 5 of the triazoloquinazoline cycle (**2.1-2.4**) and at 7.93-7.75 ppm for compounds with aromatic fragments (**2.5-2.9**, Fig. 1). Signals of the methyl group in position 5 of compounds **2.1-2.9** were observed as singlets at 2.26-1.75 ppm. Aliphatic moieties in position 5 of compounds **2.2-2.4** were characterized by diastereotopic splitting of methylene group signals,

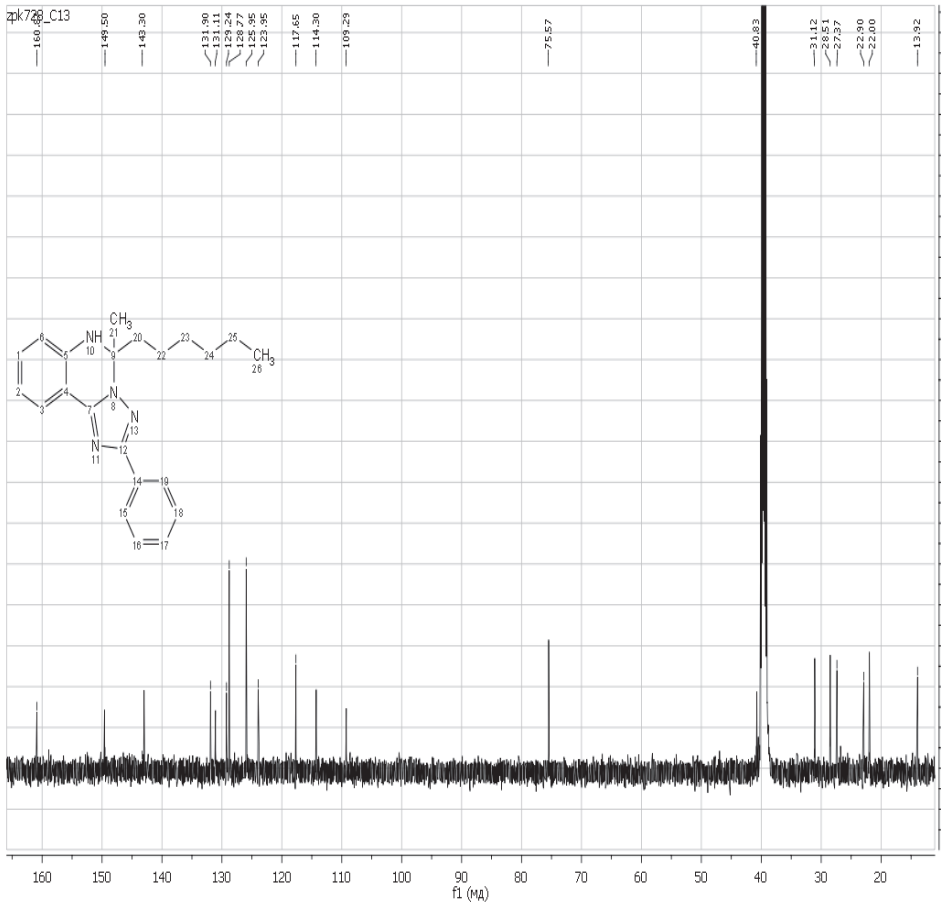


Fig. 2. The fragment of ^{13}C-NMR spectrum (100 MHz) of compound **13.4** in DMSO-d_6.

they were observed at 2.32-2.16 and 1.99-1.83 ppm. All other protons had shifts and multiplicities corresponding to the structure of proper moieties (Fig. 1) [4].

Protons of the hydrogenated triazoloquinazoline cycle of compounds **2.1-2.9** were observed as doublets for H-10 (7.86-7.70 ppm), triplets for H-8 (7.24-7.15 ppm), doublets for H-7 (6.97-6.78 ppm) and triplets for H-9 (6.82-6.67 ppm). In some cases protons H-7 and H-9 were overlapped and were registered as an individual two-proton multiple (**2.1**) or a multiplet with other aromatic protons (**2.2**, **2.4**, **2.8**). Protons of phenyl substituents in positions 2 and 5 of **2.1**, **2.2**, **2.5**, **2.7** were observed as two-proton doublets (H-2 and H-6), doublets (H-4) and multiplets (H-3 and H-5). Introduction of substituents to the phenyl moiety led to changes in the spectral pattern; as a rule, the signals had "classic" chemical shifts and multiplicity [4].

At the same time, ^{1}H NMR-spectra of compounds **3.1-3.4** had significant differences. The signals of heterocyclic H-10, H-9, H-8 and H-7 were shifted in low field. This statement may be illustrated by location of H-10 doublet at 8.53-8.48 ppm. Protons of the methyl group in position 5 of compounds **3.1-3.4** were significantly deshielded and registered at 3.07-2.51 ppm. The facts mentioned undoubtedly proved the formation of the aromatic triazoloquinazoline cycle.

According to the ^{13}C NMR spectra C-2 (160.87 and 167.30 ppm), C-10b' (149.50 and 149.93 ppm), C-6a' (143.30 and 143.01 ppm) were the most deshielded in compounds **2.4**, **2.7**, and the signals of the *sp*^{3}-hybridized Carbon atom in position 5 were observed at 75.57 ppm and 61.64 ppm, respectively (Fig. 2). These signals proved the formation of 5,6-dihydro-[1,2,4]triazolo[1,5-*c*]quinazoline. At the same time, the signals of Carbon atoms in the ^{13}C NMR-spectrum of compound **3.3** were more deshielded, and the signal of C-2 was registered at 163.24 ppm, C-10b' at 151.36 ppm, C-6a' at 148.13 ppm. The signal of C-5 was registered at 161.63, and it proved its sp^2-hybridezed nature.

Experimental Part

Melting points were determined in open capillary tubes and were uncorrected. The elemental analyses (C, H, N, S) were performed using an ELEMENTAR vario EL Cube analyzer (USA). Analyses were indicated by the symbols of the elements or functions within ±0.3% of the theoretical values. ^{1}H NMR-spectra (400 M*Hz*) and ^{13}C NMR-spectra (100 M*Hz*) were recorded on a Varian-Mercury 400 (Varian Inc., Palo Alto, CA, USA) spectrometer with TMS as an internal standard in DMSO-d_6 solution. LC-MS were recorded using the chromatography/mass spectrometric system con-sisting of an "Agilent 1100 Series" high performance liquid

chromatograph (Agilent, Palo Alto, CA, USA) equipped with a diode-matrix and an "Agilent LC/MSD SL" mass-selective detector (atmospheric pressure chemical ionization – APCI).

Synthetic procedures were conducted according to common approaches for the synthesis of promising biologically active agents. All reagents were commercially available ("Sigma-Aldrich", Missouri, USA and "Enamine", Kyiv, Ukraine) and were used without additional purification. 2-(3-Aryl-1*H*-1,2,4-triazole-5-yl) phenyl]amines (**1.1-1.9)** were obtained according to the synthetic protocols described [5, 6].

The general method for the synthesis of 5-R-5-R^1-2-aryl-5,6-dihydro[1,2,4]triazolo[1,5-c]quinazolines (2.1-2.9). To the solution of 10 mmol of the corresponding {2-[3-aryl-1*H*-1,2,4-triazolo-5-yl]phenyl}amine (**1.1-1.5**) in 10 ml of propan-2-ol add 10 mmol of aromatic or aliphatic ketones. If propan-2-ol-2 is used as a solvent, add also 2 drops of sulphuric or hydrochloric acid. Reflux the mixture obtained for 2-6 h. Then cool the mixture and pour into the saturated solution of sodium acetate. Filter the precipitate formed and dry. In case of insufficient purity recrystallize the compounds obtained from methanol.

5,5-Dimethyl-2-phenyl-5,6-dihydro-[1,2,4] triazolo[1,5-c]quinazoline (2.1). IR, ν, cm^{-1}: 3265, 2960, 2907, 2895, 2864, 2843, 2795, 2600, 2540, 1729, 1621, 1574, 1563, 1556, 1543, 1510, 1503, 1494, 1475, 1462, 1440, 1414, 1389, 1366, 1345, 1318, 1289, 1270, 1201, 1134, 1106, 1072, 1040, 1018, 987, 958, 930, 857, 806, 789, 776, 755, 739, 723, 713, 697, 688, 668, 643, 632, 616; ^{1}H NMR (400 MHz, DMSO_d$_6$+ccl$_4$) δ 8.21 (d, *J* = 6.7 Hz, 2H, H-2,6 Ph), 7.86 (d, *J* = 7.4 Hz, 1H, H-10), 7.57-7.33 (m, 4H, H-3,4,5 Ph, NH), 7.21 (t, *J* = 7.4 Hz, 1H, H-8), 6.80 (m, 2H, H-7, 9), 1.77 (s, 6H, (-CH$_3$)$_2$); LC-MS, *m/z* = 277 [M+1]; Anal. calcd. for $C_{17}H_{16}N_4$: C, 73.89; H, 5.84; N, 20.27; Found: C, 73.83; H, 5.80; N, 20.23.

5-Ethyl-5-methyl-2-phenyl-5,6-dihydro-[1,2,4]triazolo[1,5-c]quinazoline (2.2). IR, ν, cm^{-1}: 3229, 3203, 3110, 3037, 2967, 2924, 1621, 1591, 1518, 1483, 1470, 1454, 1442, 1410, 1372, 1348, 1331, 1308, 1273, 1248, 1196, 1157, 1143, 1128, 1110, 1073, 1049, 1027, 1012, 994, 981, 936, 918, 846, 784, 767, 747, 721, 687, 668, 642, 617, 607; ^{1}H NMR (400 MHz, DMSO_d$_6$+ccl$_4$) δ 8.10 (d, *J* = 7.1 Hz, 2H, H-2,6 Ph), 7.72 (d, *J* = 7.3 Hz, 1H, H-10), 7.48-7.38 (m, 2H, H-3,5 Ph), 7.36 (d, *J* = 7.0 Hz, 1H, H-4 Ph), 7.16 (t, *J* = 7.3 Hz, 1H, H-8), 6.83-6.75 (m, 2H, NH, H-7), 6.72 (t, *J* = 7.3 Hz, 1H, H-9), 2.32-2.16 (m, 1H, -C<u>H</u>$_2$CH$_3$), 1.99-1.83 (m, 1H, -C<u>H</u>$_2$CH$_3$), 1.77 (s, 3H, -CH$_3$), 0.92 (t, *J* = 7.1 Hz, 3H, -CH$_2$C<u>H</u>$_3$); LC-MS, *m/z* = 291 [M+1]; Anal. calcd. for $C_{18}H_{18}N_4$: C, 74.46; H, 6.25; N, 19.30; Found: C, 74.43; H, 6.22; N, 19.29.

5-Ethyl-5-methyl-2-(3-chlorophenyl)-5,6-dihydro-[1,2,4]triazolo[1,5-c]quinazoline (2.3). IR, ν, cm^{-1}: 3062, 2917, 2849, 1625, 1605, 1558, 1509, 1474, 1442, 1429, 1403, 1382, 1363, 1332, 1308, 1286, 1253, 1155, 1135, 1108, 1086, 1071, 986, 975, 912, 900, 888, 861, 782, 763, 737, 702, 677, 660, 633; ^{1}H NMR (400 MHz, DMSO_d$_6$+ccl$_4$) δ 8.06 (s, 1H, H-2 3-ClPh), 8.01 (d, *J* = 7.5 Hz, 1H, H-6, 3-ClPh), 7.70 (d, *J* = 7.5 Hz, 1H, H-10), 7.41 (t, *J* = 7.7 Hz, 1H, H-5 3-ClPh), 7.35 (d, *J* = 7.8 Hz, 1H, H-4, 3-ClPh), 7.16 (t, *J* = 7.4 Hz, 1H, H-8), 6.84 (s, 1H, NH), 6.78 (d, *J* = 8.0 Hz, 1H, H-7), 6.72 (t, *J* = 7.4 Hz, 1H, H-9), 2.27 (m, 1H, -C<u>H</u>$_2$CH$_3$), 1.85 (m, 4H, -C<u>H</u>$_2$CH$_3$, -C<u>H</u>$_3$), 0.90 (t, *J* = 7.2 Hz, 3H, -C<u>H</u>$_3$); LC-MS, *m/z* = 325 [M+1], 327 [M+3]; Anal. calcd. for $C_{18}H_{17}ClN_4$: C, 66.56; H, 5.28; N, 17.25; Found: C, 66.53; H, 5.26; N, 17.24.

5-(n-Hexyl)-5-methyl-2-phenyl-5,6-dihydro-[1,2,4]triazolo[1,5-c]quinazoline (2.4). IR, ν, cm^{-1}: 3234, 3211, 3109, 3041, 2953, 2922, 2853, 1623, 1592, 1524, 1484, 1470, 1444, 1412, 1374, 1347, 1334, 1279, 1267, 1204, 1176, 1156, 1135, 1121, 1108, 1071, 1027, 1011, 981, 938, 921, 852, 787, 764, 745, 724, 692, 669, 641, 608; ^{1}H NMR (400 MHz, DMSO_d$_6$+ccl$_4$) δ 8.08 (d, *J* = 6.8 Hz, 2H, H-2,6 Ph), 7.70 (d, *J* = 7.4 Hz, 1H, H-10), 7.46-7.38 (m, 2H, H-3,5 Ph), 7.35 (t, *J* = 7.1 Hz, 1H, H-4 Ph), 7.15 (t, *J* = 7.6 Hz, 1H, H-8), 6.83-6.68 (m, 3H, NH, H-7, H-9), 2.16 (t, *J* = 11.7 Hz, 1H, -C<u>H</u>$_2$(CH$_2$)$_4$CH$_3$), 1.83 (t, *J* = 11.5 Hz, 1H, -C<u>H</u>$_2$(CH$_2$)$_4$CH$_3$), 1.75 (s, 3H, -CH$_3$), 1.44 (m, 2H, -CH$_2$C<u>H</u>$_2$(CH$_2$)$_3$CH$_3$), 1.23 (m, 7H, -CH$_2$C<u>H</u>$_2$(C<u>H</u>$_2$)$_3$CH$_3$), 0.83 (s, 3H, -(CH$_2$)$_5$C<u>H</u>$_3$); ^{13}C NMR (126 MHz, DMSO) δ 160.87, 149.50, 143.30, 131.90, 131.11, 129.24, 128.77, 125.95, 123.95, 117.65, 114.30, 109.29, 75.57, 40.83, 31.12, 28.51, 27.37, 22.90, 22.00, 13.92; LC-MS, *m/z* = 347 [M+1]; Anal. calcd. for $C_{22}H_{26}N_4$: C, 76.27; H, 7.56; N, 16.17; Found: C, 76.25; H, 7.56; N, 16.14.

2,5-Diphenyl-5-methyl-5,6-dihydro-[1,2,4] triazolo[1,5-c]quinazoline (2.5). ^{1}H NMR (400 MHz, DMSO_d$_6$) δ 8.42 (m, 2H, H-2, 6 Ph), 8.19 (d, *J* = 7.1 Hz, 1H, H-2,6 Ph), 7.93 (s, 1H, NH), 7.75 (d, *J* = 7.3 Hz, 1H, H-10), 7.44 (m, 3H, H-3,4,5 Ph), 7.24 (t, *J* = 7.5 Hz, 1H, H-8), 7.16 (m, 3H, H-3, 4,5 Ph), 6.97 (d, *J* = 8.0 Hz, 1H, H-7), 6.82 (t, *J* = 7.3 Hz, 1H, H-9), 2.26 (s, 3H, -CH$_3$); LC-MS, *m/z* = 340 [M+2]; Anal. calcd. for $C_{22}H_{18}N_4$: C, 78.08; H, 5.36; N, 16.56; Found: C, 78.06; H, 5.35; N, 16.57.

5-Methyl-5-(4-i-propylphenyl)-2-(3-fluorophenyl)-5,6-dihydro-[1,2,4]triazolo[1,5-c]quinazoline (2.6). ^{1}H NMR (400 MHz, DMSO_d$_6$) δ 7.99 (d, *J* = 7.7 Hz, 1H, H-2, PhF-3), 7.86 (d, *J* = 9.0 Hz, 1H, H-6 PhF-3), 7.75 (s, 1H, NH), 7.71 (d, *J* = 7.4 Hz, 1H, H-10), 7.47 (dd, *J* = 13.9, 7.8 Hz, 1H, H-5 PhF-3), 7.21 (t, *J* = 7.6 Hz, 1H, H-8), 7.18-7.10 (m, 3H, H-4 PhF-3, H-2,6 PhCH(CH$_3$)$_2$-4), 7.10-7.03 (m, 2H, H-3,5 PhCH(CH$_3$)$_2$-4), 6.95 (d, *J* = 8.0 Hz, 1H, H-7), 6.78 (t, *J* = 7.3 Hz, 1H, H-9), 2.81 (dt, *J* = 13.7, 6.8 Hz, 1H, -C<u>H</u>(CH$_3$)$_2$), 2.23 (s, 3H, CH$_3$), 1.16 (d, *J* = 6.8 Hz, 6H, C<u>H</u>(CH$_3$)$_2$); LC-MS, *m/z* = 399 [M+1]; Anal. calcd. for $C_{25}H_{23}FN_4$: C, 75.35; H, 5.82; N, 14.06; Found: C, 75.32; H, 5.83; N, 14.05.

5-Methyl-5-(4-chlorophenyl)-2-phenyl-5,6-dihydro-[1,2,4]triazolo[1,5-c]quinazolin (2.7). IR, ν, cm^{-1}: 3195, 3072, 3023, 2998, 2957, 1728, 1620, 1591,

1541, 1517, 1482, 1469, 1440, 1403, 1377, 1344, 1322, 1264, 1219, 1207, 1165, 1152, 1107, 1094, 1071, 1029, 1010, 983, 933, 920, 875, 853, 822, 811, 786, 738, 723, 690, 670, 642, 615; ^{1}H NMR (400 MHz, DMSO_d_6+ccl_4) δ 8.15 (d, *J* = 7.2 Hz, 2H, H-2,6 Ph), 7.80 (s, 1H, NH), 7.71 (d, *J* = 7.3 Hz, 1H, H-10), 7.50-7.35 (m, 3H, H-3,4,5 Ph), 7.26-7.18 (m, 5H, H-8, H-2,3,5,6 4-ClPh), 6.93 (d, *J* = 8.0 Hz, 1H, H-7), 6.79 (t, *J* = 7.2 Hz, 1H, H-9), 2.22 (s, 3H, -CH_3); ^{13}C NMR (126 MHz, DMSO) δ 167.30, 149.93, 143.01, 137.88, 134.60, 125.47, 124.90, 116.14, 108.24, 61.64, 14.07; LC-MS, *m/z* = 373 [M+1], 375 [M+3]; Anal. calcd. for $C_{22}H_{17}ClN_4$: C, 70.87; H, 4.60; N, 15.03; Found: C, 70.82; H, 4.58; N, 15.01.

5-Methyl-2-(4-methoxyphenyl)-5-(4-chlorophenyl)-5,6-dihydro-[1,2,4]-triazolo[1,5-c] quinazolin (2.8). ^{1}H NMR (400 MHz, DMSO_d_6) δ 8.07 (d, *J* = 8.5 Hz, 2H, H-2, 6 $PhOCH_3$-4), 7.77 (s, 1H, NH), 7.71 (d, *J* = 7.5 Hz, 1H, H-10), 7.26-7.18 (m, 5H, H-8, H-2,3,5,6 PhCl-4), 6.95 (m, 3H, H-7, H-3, 5 $PhOCH_3$-4), 6.79 (t, *J* = 7.4 Hz, 1H, H-9), 3.86 (s, 3H, -OCH_3), 2.22 (s, 3H, -CH_3); LC-MS, *m/z* = 403 [M+1], 405 [M+3]; Anal. calcd. for $C_{23}H_{19}ClN_4O$: C, 68.57; H, 4.75; N, 13.91; Found: C, 68.52; H, 4.71; N, 13.89.

5-Methyl-2-[(3-trifluoromethyl)phenyl]-5-(4-fluorophenyl)-5,6-dihydro-[1,2,4]triazolo [1,5-c]quinazoline (2.9). ^{1}H NMR (400 MHz, DMSO_d_6) δ 8.40 (m, 2H, H-2,6 $PhCF_3$-3), 7.84 (s, 1H, NH), 7.75 (d, *J* = 7.6 Hz, 1H, H-10), 7.72-7.63 (m, 2H, H-4, 5 $PhCF_3$-3), 7.25 (m, 2H, H-2,6 PhF-4), 7.11 (t, *J* = 7.6 Hz, 1H, H-8), 6.96 (t, *J* = 6.9 Hz, 1H, H-3,5 PhF-4), 6.82 (d, *J* = 7.7 Hz, 1H, H-7), 6.67 (t, 1H, H-9), 2.25 (s, 3H, -CH_3); LC-MS, *m/z* = 425 [M+1]; Anal. calcd. for $C_{23}H_{16}F_4N_4$: C, 65.09; H, 3.80; N, 13.20; Found: C, 65.05; H, 3.78; N, 13.18.

The general method for the synthesis of 5-R-5-R^1-2-aryl-5,6-dihydro[1,2,4]triazolo[1,5-c]quinazolines (3.1-3.9). To the solution of 10 mmol of the corresponding {2-[3-aryl-1*H*-1,2,4-triazolo-5-yl]phenyl}amine (**1.3-1.5**) add 10 ml of acetic acid. Reflux the solution obtained for 6-8 h. Then cool it and pour into the saturated solution of sodium acetate. Filter the precipitate formed and dry. In case of insufficient purity recrystallize the compounds obtained from propan-2-ol.

5-Methyl-2-(3-(trifluoromethyl)phenyl)-[1,2,4]triazolo[1,5-c]quinazolin (3.1). IR, ν, cm^{-1}: 1629, 1561, 1531, 1514, 1468, 1415, 1388, 1353, 1324, 1306, 1268, 1162, 1118, 1091, 1068, 1007, 989, 978, 934, 913, 898, 880, 861, 817, 777, 746, 731, 698, 685, 666, 651, 638; ^{1}H NMR (400 MHz, DMSO_d_6+ccl_4) δ 8.59 (m, 2H, H-2,6 $PhCF_3$-3), 8.53 (d, *J* = 7.6 Hz, 1H, H-10), 7.98 (d, *J* = 7.8 Hz, 1H, H-7), 7.88 (t, 1H, H-9), 7.85-7.72 (m, 3H, H-8, H-4,5 $PhCF_3$-3), 3.07 (s, 3H, -CH_3); LC-MS, *m/z* = 329 [M+1]; Anal. calcd. for $C_{17}H_{11}F_3N_4$: C, 62.20; H, 3.38; N, 17.07; Found: C, 62.18; H, 3.34; N, 17.03.

5-Methyl-2-(3-fluorophenyl)-[1,2,4]triazolo [1,5-c]quinazoline (3.2). IR, ν, cm^{-1}: 3062, 3009, 2917, 2848, 1675, 1631, 1591, 1560, 1530, 1512, 1480, 1452, 1412, 1386, 1357, 1327, 1306, 1275, 1262, 1221, 1210, 1163, 1113, 1093, 1068, 1027, 982, 958, 877, 858, 833, 794, 777, 743, 720, 677, 660, 637, 617; ^{1}H NMR (400 MHz, DMSO_d_6+ccl_4) δ 8.51 (d, *J* = 7.7 Hz, 1H, H-10), 8.16 (d, *J* = 7.5 Hz, 1H, H-7), 8.03 (d, *J* = 8.4 Hz, 1H, H-2 PhF-3), 7.97 (d, *J* = 8.4 Hz, 1H, H-6 PhF-3), 7.88 (t, *J* = 7.5 Hz, 1H, H-9), 7.75 (t, *J* = 7.5 Hz, 1H, H-8), 7.57 (dd, *J* = 14.0, 7.2 Hz, 1H, H-4 PhF-3), 7.26 (t, *J* = 7.7 Hz, 1H, H-5 PhF-3), 3.00 (s, 3H, -CH_3); LC-MS, *m/z* = 279 [M+1]; Anal. calcd. for $C_{16}H_{11}FN_4$: C, 69.06; H, 3.98; N, 20.13; Found: C, 69.03; H, 3.94; N, 20.13.

5-Methyl-2-(4-methoxyphenyl)-[1,2,4]triazolo [1,5-c]quinazololine (3.3). IR, ν, cm^{-1}: 2989, 2955, 2935, 2835, 2376, 2354, 2344, 2280, 2057, 2000, 1908, 1737, 1665, 1630, 1607, 1585, 1555, 1529, 1476, 1452, 1442, 1420, 1389, 1351, 1316, 1301, 1252, 1170, 1106, 1028, 985, 971, 955, 861, 844, 836, 811, 799, 779, 750, 728, 711, 667, 657, 649, 633, 611; ^{1}H NMR (400 MHz, DMSO_d_6+ccl_4) δ 8.48 (d, *J* = 7.7 Hz, 1H, H-10), 8.24 (d, *J* = 7.0 Hz, 2H, H-2,6 4-CH_3OPh), 7.93 (d, *J* = 7.9 Hz, 1H, H-7), 7.83 (t, *J* = 7.4 Hz, 1H, H-8), 7.71 (t, *J* = 7.3 Hz, 1H, H-9), 7.03 (d, *J* = 7.0 Hz, 2H, H-3,5 4-CH_3OPh), 3.89 (s, 3H, -OCH_3), 2.51 (s, 3H, -CH_3); ^{13}C NMR (101 MHz, DMSO) δ 163.24, 161.63, 151.36, 148.13, 142.72, 132.61, 129.35, 128.44, 128.13, 123.95, 122.69, 117.07, 114.88, 55.73, 20.23; LC-MS, *m/z*=291 [M+1]; Anal. calcd. for $C_{17}H_{14}N_4O$: C, 70.33; H, 4.86; N, 19.30; Found: C, 70.29; H, 3.84; N, 19.28.

Conclusions

The reaction of [2-(3-aryl-1*H*-1,2,4-triazole-5-yl) phenyl]amines with aliphatic and aromatic ketones is a suitable method for the synthesis of 5-methyl-5-alkyl-(aryl-)-2-aryl-5,6-dihydro[1,2,4]triazolo[1,5-*c*]quinazolines. The use of acetic acid as a solventis limited taking into account the possibility of a competitive acylation followed by cyclization and formation of the corresponding 5-methyl-2-aryl-[1,2,4]triazolo[1,5-*c*]quinazolines.

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