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5,6-DIHYDRO-[1,2,4]TRIAZOLO[1,5-c]QUINAZOLINES. MESSAGE 3. SYNTHESIS OF 2-ARYL-5-TRICHLOROMETHYL- 5,6-DIHYDRO[1,2,4]TRIAZOLO[1,5-c]QUINAZOLINES AND THEIR REACTIVITY TOWARDS N-NUCLEOPHILES

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Key words: 2-aryl-5-trichloromethyl-5,6-dihydro[1,2,4]triazolo[1,5-c]quinazolines; [5+1]-cyclocondensation; N-nucleophiles; elimination

Features of 5-trichloromethyl-2-aryl-5,6-dihydro-[1,2,4]triazolo[1,5-c]quinazolines formation as result of [5+1]-cyclocondensation of the corresponding [2-(3-aryl-1H-1,2,4-triazole-5-yl)phenyl]amines with chloral hydrate are described in the article. It has been shown that this transformation is regioselective, occurs by refluxing of the initial compounds in acetic acid with formation of 2-aryl-5-trichloromethyl-5,6-dihydro-[1,2,4]triazolo[1,5-c]quinazolines. The possible mechanism of 5,6-dihydro-[1,2,4]triazolo[1,5-c]quinazolines has been proposed and substantiated. It has been shown that the reaction proceeds as step-by-step transformation that includes A_NE and A_N processes. The 2-phenyl-5-trichloromethyl-5,6-dihydro-[1,2,4]triazolo[1,5-c]quinazoline obtained was studied in reactions with N-nucleophiles. It has been found that regardless of the nature of nucleophile the reaction mentioned above leads to formation of 2-phenyl-5-(dichloromethyl)-[1,2,4]triazolo[1,5-c]quinazoline. The mechanism of the transformation mentioned above is given; it is β-elimination on the E_{1cb}-mechanism followed by isomerisation. The structure of the compounds synthesized has been confirmed by the complex of physicochemical methods, including ¹H-, ¹³C-NMR-spectrometry, chromatomass-spectrometry, mass-spectrometry and X-ray structural study. A detailed analysis of ¹H and ¹³C-NMR spectral data of the compounds synthesized has been conducted. It has been found that the signals of the carbon atom in position 5 at 79.25-77.95 ppm were characteristic for 2-aryl-5-trichloromethyl-5,6-dihydro-[1,2,4]triazolo[1,5-c]quinazolines, whereas aromatization of the molecule leads to significant deshielding of this carbon atom (163.41 ppm). The prospects of further chemical modification of 2-aryl-5-(dichloromethyl)-[1,2,4]triazolo[1,5-c]quinazolines has been discussed.

5,6-ДИГІДРО-[1,2,4]ТРИАЗОЛО[1,5-с]ХІНАЗОЛІНИ. ПОВІДОМЛЕННЯ 3. СИНТЕЗ 5-ТРИХЛОРОМЕТИЛ-2-АРИЛ-5,6-ДИГІДРО-[1,2,4]ТРИАЗОЛО[1,5-с]ХІНАЗОЛІНІВ І ЇХ РЕАКЦІЙНА ЗДАТНІСТЬ ПО ВІДНОШЕННЮ ДО N-НУКЛЕОФІЛІВ

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Ключові слова: 2-арил-5-трихлорометил-5,6-дигідро-[1,2,4]триазоло[1,5-с]хіназоліни; [5+1]-циклоконденсація; N-нуклеофіли; елімінація

У представленій роботі описано формування 5-трихлорометил-2-арил-5,6-дигідро-[1,2,4]триазоло[1,5-с]хіназолінів як результат [5+1]циклоконденсації відповідних [2-(3-арил-1H-1,2,4-триазол-5-іл)феніл]амінів з хлоралгідратом. Показано, що зазначене перетворення є регіоселективним та легко відбувається при кип'ятінні вихідних сполук у оцтовій кислоті або пропанолі-2 впродовж 6 годин з утворенням 2-арил-5-трихлорометил-5,6-дигідро-[1,2,4]триазоло[1,5-с]хіназолінів. Запропоновано та обґрунтовано ймовірний механізм формування 5,6-дигідро-[1,2,4]триазоло[1,5-с]хіназолінів, який являє собою тандемне перетворення, що включає A_NE та A_N процеси. Одержаний 2-феніл-5-трихлорометил-5,6-дигідро-[1,2,4]триазоло[1,5-с]хіназолін був досліджений у реакціях з N-нуклеофілами. Показано, що зазначена реакція незалежно від природи нуклеофілу веде до утворення 2-феніл-5-(дихлорометил)-[1,2,4]триазоло[1,5-с]хіназоліну. Представлено механізм зазначеного вище перетворення, який являє собою послідовність β-елімінування за E_{1cb} механізмом та ізомеризації. Структура синтезованих сполук доведена за допомогою комплексу фізико-хімічних методів аналізу, зокрема ¹H-, ¹³C-ЯМР спектроскопії, хромато-мас-спектрометрії, мас-спектрометрії та рентгеноструктурного дослідження. Проведено детальний аналіз даних ¹H- та ¹³C-ЯМР спектроскопії синтезованих сполук. Показано, що для 2-арил-5-трихлорометил-5,6-дигідро-[1,2,4]триазоло[1,5-с]хіназолінів характерними є сигнали атома карбону положення 5 при 79.25-77.95 м.ч., тоді як ароматизація системи веде до його дезекранування (163.41 м.ч.). Показана перспективність подальшої хімічної модифікації 2-арил-5-(дихлорометил)-[1,2,4]триазоло[1,5-с]хіназолінів.

5,6-ДИГІДРО-[1,2,4]ТРИАЗОЛО[1,5-с]ХІНАЗОЛИНЫ. СООБЩЕНИЕ 3. СИНТЕЗ 5-ТРИХЛОРОМЕТИЛ-2-АРИЛ-5,6-ДИГІДРО-[1,2,4]ТРИАЗОЛО[1,5-с]ХІНАЗОЛИНОВ И ИХ РЕАКЦИОННАЯ СПОСОБНОСТЬ ПО ОТНОШЕНИЮ К N-НУКЛЕОФИЛАМ

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Ключевые слова: 2-арил-5-трихлорометил-5,6-дигідро-[1,2,4]триазоло[1,5-с]хіназоліни; [5+1]-циклоконденсації; N-нуклеофіли; елімінація

В представленной работе описано формирование 5-трихлорометил-2-арил-5,6-дигідро-[1,2,4]триазоло[1,5-с]хіназолинов в результате [5+1]циклоконденсации соответствующих [2-(3-арил-1H-1,2,4-триазол-

5-ил)фенил]аминов с хлоралгидратом. Показано, что данное превращение является региоселективным и легко происходит при кипячении исходных соединений в уксусной кислоте или пропанол-2 с образованием 2-арил-5-трихлорметил-5,6-дигидро-[1,2,4]триазоло[1,5-с]хиназолинов. Предложен и обоснован возможный механизм формирования 5,6-дигидро-[1,2,4]триазоло[1,5-с]хиназолинов, который представляет собой тандемное превращение, которое включает A_NE и A_N процессы. Полученный 2-фенил-5-трихлорметил-5,6-дигидро-[1,2,4]триазоло[1,5-с]хиназолин был исследован в реакциях с *N*-нуклеофилами. Показано, что упомянутая выше реакция вне зависимости от природы нуклеофила приводит к образованию 2-фенил-5-(дихлорметил)-[1,2,4]триазоло[1,5-с]хиназолина. Представлен механизм упомянутого превращения, который представляет собой последовательность β -элиминирования по E_{1cb} -механизму изомеризации. Структура синтезированных соединений подтверждена с помощью комплекса физико-химических методов анализа, в частности 1H -, ^{13}C -ЯМР спектроскопии, хромато-масс-спектрометрии, масс-спектрометрии и рентгеноструктурного исследования. Проведен детальный анализ данных 1H - и ^{13}C -ЯМР спектров синтезированных соединений. Показано, что для 2-арил-5-трихлорметил-5,6-дигидро-[1,2,4]триазоло[1,5-с]хиназолинов характеристическими являются сигналы атома углерода положения 5 при 79.25-77.95 м.д., в то время как ароматизация ведет к его дезэкранированию (163.41 м.д.). Показана перспективность дальнейшей химической модификации 2-арил-5-(дихлорметил)-[1,2,4]триазоло[1,5-с]хиназолинов.

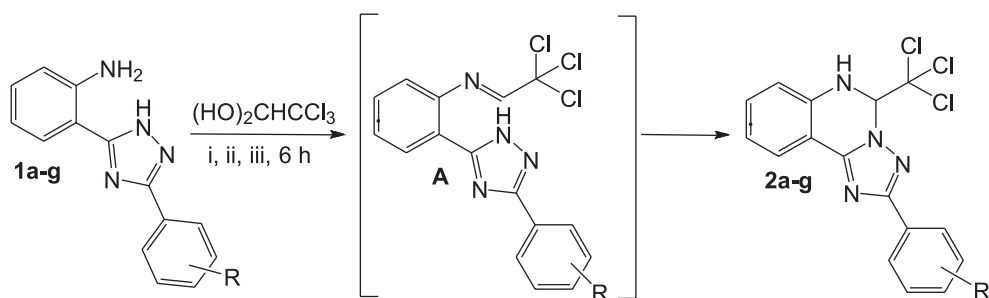
Characteristics of chemical transformations of compounds with the trichloromethyl moiety in heterocyclic fragments were widely discussed in recent publication. The authors described the features of their interaction with *N*-, *O*-nucleophiles by S_{NAr} - or $tele-S_N$ -mechanisms and formation of the corresponding *N*-, *O*-substituted heterocyclic fragments [1-3]. In order to expand the synthetic potential of the reaction mentioned above it would be interesting to study the interaction of non-aromatic heterocyclic compounds with trichloromethyl substituent at sp^3 hybridized carbon atom.

The aim of the work is to study the features of the reaction between [2-(3-aryl-1*H*-1,2,4-triazol-5-yl)phenyl]amines with chloralhydrate and transformations of the non-aromatic heterocyclic compounds obtained with the trichlormethyl moiety at sp^3 -hybridized carbon atom under the action of *N*-nucleophiles.

The reactions were carried out by refluxing equimolar amounts of diamines **1a-g** and chloral hydrate in acetic acid or methanol with an acidic catalyst (Scheme 1). It is worth noting that **1a-g** normally exist in two tautomeric forms, which may invoke parallel formation of isomeric [1,2,4]triazolo[1,5-*c*]- and -[4,3-*c*]quinazolines. Nevertheless, our experiments have demonstrated that the reaction proceeds regioselectivity through an azomethine intermediate **A** with the subsequent intramolecular nucleophilic cyclization into tricycles **2a-g** (Scheme 1). We attribute such selectivity to a +*M*-effect (α -effect) of the neighbouring nitrogen atom.

Purity of the compounds synthesized was confirmed by LC-MS (APCI) analysis; the structure was determined using 1H and ^{13}C NMR, IR spectroscopic and MS (EI) spectrometric methods. In 1H NMR-spectra, 6-NH and H5 protons were observed as broad singlets or doublets at 8.41-8.26 ppm ($J = 3.3$ -4.0 Hz) and 6.96-6.69 ppm ($J = 3.7$ -4.1 Hz), respectively. Other protons of the heterocyclic fragment were registered as sequentially located doublets of H10 (7.96-7.78 ppm) and H7 (7.06-7.04 ppm), as well as triplets of H8 (7.33-7.27 ppm) and H-9 (6.88-6.86 ppm). The ^{13}C NMR-spectral data for compounds **2a**, **2e** and **2g** additionally substantiated our structural conclusions. The low field signals of Csp^2 atoms were observed at 163.6-157.7 ppm (C2), 150.8-150.7 ppm (C6a) and 145.2-141.1 ppm (C10b). Characteristic Csp^3 signals were located at 117.6-102.6 ppm (CCl_3) and 79.25-77.95 ppm (C5).

The crystals of compound **2a** were also studied by X-ray diffraction (Fig. 1). The compound crystallized in a non-centrosymmetric space group, which indicated the presence of only one enantiomer in the crystal phase. Configuration of the chiral C8 atom was unambiguously determined using the Flack parameter (-0.04(8)). The dihydropyrimidine ring was in an intermediate conformation between a twist-boat and sofa (puckering parameters [4] were: $S = 0.41$, $\theta = 53.1^\circ$, $\psi = 28.3^\circ$). Deviations of N3 and C8 from the mean plane of other atoms were 0.20 Å and 0.49 Å, respectively. The N2 atom had a pyramidal configuration with a small degree of pyramidity (the sum of centred



i = *i*-Pr, H_2SO_4 , ii = *i*-Pr, HCl, iii = CH_3COOH ; R = H, *o*-OCH₃, *m*-CH₃, *m*-CF₃, *m*-F, *m*-OCH₃, *p*-OCH₃

Scheme 1. The synthesis of 5-trichloromethyl-2-aryl-5,6-dihydro[1,2,4]triazolo[1,5-*c*]quinazolines.

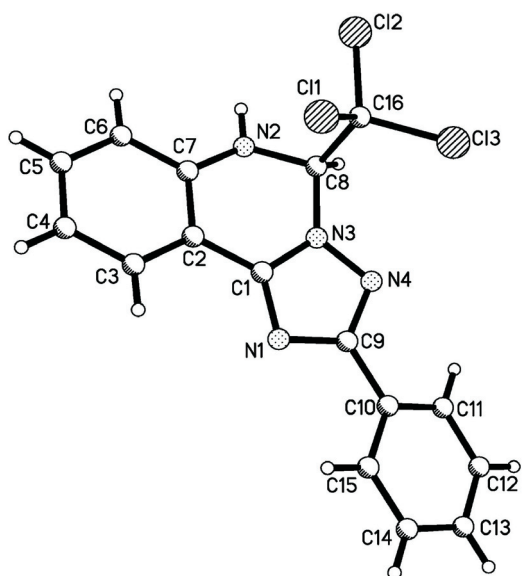


Fig. 1. The molecular structure of compound **2a** according to the data of the X-ray diffraction study.

bond angles was 357°). The trichloromethyl substituent was located in the axial position and turned in such a way that the C16-Cl2 bond was antiperiplanar to the N3-C8 bond (the C1-N3-C8-C16 and N3-C8-C16-Cl2 torsion angles were $100.6(3)^\circ$ and $179.6(2)^\circ$, respectively). We also observed shortened intramolecular Cl3...N4 and H(N2)...Cl2 bonds (3.18 \AA and 2.77 \AA vs. the sums of van der Waals radii as 3.40 \AA and 3.06 \AA [5], respectively). Despite the presence of H11...N4 and H15...N1 attractive interactions (the H...N distance for both was 2.62 \AA) the phenyl substituent was slightly out of the triazole ring plane (the N4-C9-C10-C11 torsion angle was $-15.6(5)^\circ$). In the crystal phase the intermolecular hydrogen bonds between the molecules of **2a** were observed: N-H(N2)...C3' (p) ($1-x, -0.5+y, 0.5-z$) H...C 2.78 \AA N-H...C 135° and (C6)H...N-1' ($1-x, -0.5+y, 0.5-z$) H...N 2.64 \AA C-H...N 143° .

The experiments have shown that the reaction of **2a** with different *N*-nucleophiles ((2,2-dimethoxyethyl) amine, benzylamine, morpholine, piperidine and triethylamine) results in the same product, namely dichloromethylated aromatic heterocycle **3a** (Scheme 2). Most likely the reaction proceeds *via* the step-by-step mechanism with E_{1cb} b-elimination followed by iso-

merization of the resulting enamine (intermediate **B**). It starts with elimination of the acidic hydrogen in position 5 in the presence of a base giving a carbanion (intermediate **A**). Next the negative charge is displaced towards the electron withdrawing trichloromethyl group causing elimination of a chloride anion. At the final stage isomerization into a heterocyclic aromatic system takes place (Scheme 2).

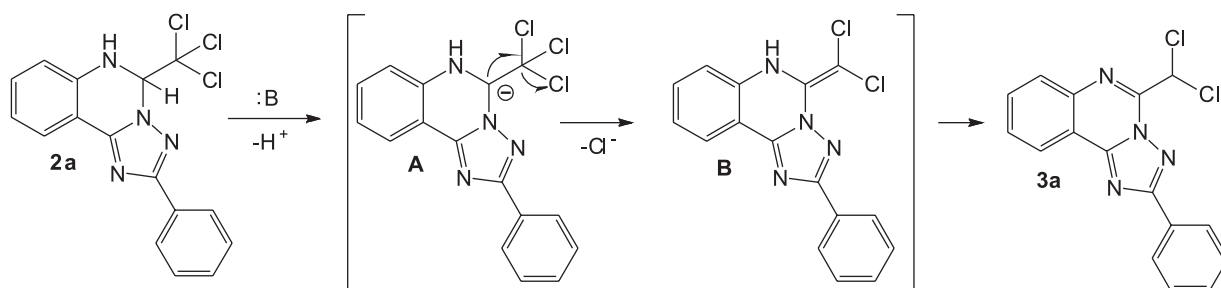
The structure of **3a** was confirmed using NMR-spectroscopy. In ^1H NMR-spectrum the NH-proton signal in position 5 vanished; instead a new one appeared at 7.80 ppm indicating the presence of the CHCl_2 group. Most importantly, we observed a significant paramagnetic shift of protons in the annelated benzene fragment (H-7 (8.60 ppm), H-10 (8.17 ppm), H-9 (7.98 ppm) and H-8 (7.89 ppm)), which demonstrated formation of the aromatic triazinoquinazoline system (Fig. 2).

Additionally, characteristic Csp^2 signals in the ^{13}C NMR-spectrum: 163.41 ppm (C-5), 152.01 ppm (C-2), 143.43 ppm (C-6a), 141.55 ppm (C-7) were observed. The resonance of Csp^3 in CHCl_2 was noted at 65.24 ppm (Fig. 3).

Experimental Part

Melting points were determined in open capillary tubes in a Thiele apparatus and were given uncorrected. The elemental analysis (C, H, N, S) was performed using an ELEMENTAR vario EL cube analyzer (Elementar Analysensysteme GmbH, Hanau, Germany). IR-spectra ($4000\text{-}600 \text{ cm}^{-1}$) were recorded on a Bruker ALPHA FT-IR spectrometer (Bruker Bioscience, Germany) using an ATR eco ZnSe module. ^1H NMR-spectra (400 MHz) were recorded on a Varian-Mercury 400 spectrometer (Varian, Palo Alto, CA) in DMSO-d_6 with SiMe_4 as an internal standard. LC-MS were recorded using the chromatography/mass spectrometric system consisting of an "Agilent 1100 Series" (Agilent, Palo Alto, CA) HPLC chromatograph equipped with an "Agilent LC/MSD SL" diode-matrix and mass-selective detector (atmospheric pressure chemical ionization – APCI). Electron impact mass spectra (EI-MS) were measured on a Varian 1200 L instrument (Varian, USA) at 70 eV .

Compounds **1a-g** were obtained according to the protocols described [6, 7]. All other reactants and sol-



Scheme 2. The reactivity of 5-trichloromethyl-2-aryl-5,6-dihydro[1,2,4]triazolo[1,5-c]quinazolines towards *N*-nucleophiles.

ν , cm^{-1} : 3411, 3067, 3023, 2936, 1622, 1594, 1552, 1532, 1501, 1474, 1455, 1413, 1338, 1313, 1277, 1257, 1237, 1178, 1157, 1120, 1109, 1086, 1036, 1019, 962, 945, 919, 866, 827, 815, 749, 740, 707, 690, 647, 636, 611; $^1\text{H NMR}$, δ , ppm (J , Hz): 8.39 (d, $J = 4.0$ Hz, 1H, NH), 7.96 (d, $J = 8.0$ Hz, 2H, H-2,6 Ar), 7.78 (d, $J = 7.7$ Hz, 1H, H-10), 7.38-7.27 (m, 3H, H-4,5 Ar, H-8), 7.06 (d, $J = 8.2$ Hz, 1H, 7), 6.93 (d, $J = 4.0$ Hz, 1H, H-5), 6.87 (t, $J = 7.5$ Hz, 1H, H-9), 2.34 (s, 3H, CH_3); Found: %: C, 53.75; H, 3.40; N, 14.75; Calculated for $\text{C}_{17}\text{H}_{13}\text{Cl}_3\text{N}_4\text{O}$: %: C, 53.78; H, 3.45; N, 14.76.

5-(Trichloromethyl)-2-(3-(trifluoromethyl)phenyl)-5,6-dihydro-[1,2,4]triazolo[1,5-c]quinazoline (2c). Yield – 99.9%; white crystals. M. p. – 96-98°C; IR, ν , cm^{-1} : 3442, 2932, 1624, 1597, 1553, 1536, 1515, 1502, 1479, 1452, 1434, 1414, 1348, 1315, 1282, 1258, 1240, 1188, 1166, 1155, 1124, 1114, 1089, 1066, 1021, 983, 960, 940, 917, 904, 829, 807, 757, 742, 723, 691, 668, 654, 638, 606; $^1\text{H NMR}$, δ , ppm (J , Hz): 8.44-8.35 (m, 2H, H-2,6 Ar), 8.32 (bs, 1H, NH), 7.86 (d, $J = 7.4$, 1H, H-10), 7.76-7.65 (m, 2H, H-4,5 Ar), 7.30 (t, $J = 7.6$, 1H, H-8), 7.06 (d, $J = 8.0$, 1H, H-7), 6.87 (t, $J = 7.1$, 1H, H-9), 6.72 (d, $J = 3.7$ Hz, 1H, H-5); LC-MS, $m/z = 435$ [M+2], 437 [M+4], 439 [M+6]; Found: %: C, 47.05; H, 2.28; N, 12.95; $\text{C}_{17}\text{H}_{10}\text{Cl}_3\text{F}_3\text{N}_4$; Calculated, %: C, 47.09; H, 2.32; N, 12.92.

5-(Trichloromethyl)-2-(3-fluorophenyl)-5,6-dihydro-[1,2,4]triazolo[1,5-c]quinazoline (2d). Yield – 99.9%; white crystals. M. p. – 144-146°C; IR, ν , cm^{-1} : 3416, 1621, 1587, 1548, 1518, 1498, 1446, 1337, 1321, 1283, 1258, 1239, 1216, 1187, 1160, 1112, 1101, 1089, 1070, 1049, 1020, 987, 969, 947, 919, 885, 875, 838, 816, 796, 750, 741, 713, 697, 680, 642, 609; $^1\text{H NMR}$, δ , ppm (J , Hz): 8.30 (bs, 1H, NH), 7.96 (d, $J = 7.4$ Hz, 1H, H-10), 7.83 (d, $J = 8.0$ Hz, 2H, H-2,6 Ar), 7.48 (dd, $J = 13.6, 6.4$ Hz, 1H, H-5 Ar), 7.29 (t, $J = 7.6$ Hz, 1H, H-8), 7.16 (t, $J = 7.2$ Hz, 1H, H-4 Ar), 7.05 (d, $J = 8.0$ Hz, 1H, H-7), 6.87 (t, $J = 7.1$ Hz, 1H, H-9), 6.70 (d, 1H, H-5); LC-MS, $m/z = 385$ [M+3], 387 [M+5], 389 [M+7]; Found: %: C, 50.05; H, 2.60; N, 14.58; Calculated for $\text{C}_{16}\text{H}_{10}\text{Cl}_3\text{FN}_4$: %: C, 50.09; H, 2.63; N, 14.60.

2-(2-Methoxyphenyl)-5-(trichloromethyl)-5,6-dehydro-[1,2,4]triazolo[1,5-c]quinazoline (2e). Yield – 56.9%; white crystals. M. p. – 201-202°C; IR, ν , cm^{-1} : 3196, 3015, 2965, 2934, 2836, 1618, 1603, 1586, 1547, 1513, 1475, 1462, 1436, 1342, 1310, 1268, 1244, 1174, 1164, 1153, 1134, 1117, 1099, 1052, 1041, 1023, 979, 965, 946, 855, 832, 813, 760, 746, 721, 694, 651, 615; $^1\text{H NMR}$, δ , ppm (J , Hz): 8.37 (d, $J = 4.0$ Hz, 1H, NH), 7.82-7.69 (m, 2H, H-10, H-3 Ar), 7.43 (t, 1H, H-4 Ar), 7.31 (t, 1H, 7.6 Hz, 1H, H-8), 7.14 (d, $J = 8.4$ Hz, 1H, H-3 Ar), 7.09-7.00 (m, 2H, H-5 Ar, H-7), 6.93 (dd, $J = 4.1, 1.6$ Hz, 1H, H-5), 6.86 (t, $J = 7.5$ Hz, 1H, H-9), 3.79 (c, 3H, CH_3O); $^{13}\text{C NMR}$, δ , ppm: 157.76 (C-2), 151.85 (C-2 ϕ), 150.63 (C-6a), 145.17 (C-10b), 139.87, 135.09, 132.18, 131.20, 130.93, 125.01, 120.74, 120.46, 114.00, 113.96, 112.04, 112.00 (CCl_3), 78.84 (C-5),

56.47 (CH_3O); Found: %: C, 51.63; H, 3.30; N, 14.15; C; Calculated for $^{17}\text{H}_{13}\text{Cl}_3\text{N}_4\text{O}$, %: C, 51.60; H, 3.31; N, 14.16.

2-(3-Methoxyphenyl)-5-trichloromethyl)-5,6-dihydro-[1,2,4]triazolo[1,5-c]quinazolin (2f). Yield – 72.6%; white crystals. M. p. – 72-74°C; IR, ν , cm^{-1} : 3256, 3236, 3213, 3111, 3040, 2962, 2933, 2829, 1624, 1606, 1590, 1517, 1482, 1463, 1438, 1427, 1409, 1349, 1317, 1284, 1273, 1236, 1193, 1154, 1112, 1078, 1026, 990, 953, 862, 848, 829, 808, 792, 771, 757, 741, 710, 688, 639, 613; $^1\text{H NMR}$, δ , ppm (J , Hz): 8.41 (d, $J = 3.6$ Hz, 1H, NH), 7.80 (d, $J = 7.6$ Hz, 1H, H-10), 7.67 (d, $J = 7.5$ Hz, 1H, H-6 Ar), 7.59 (s, 1H, H-2 Ar), 7.41 (t, $J = 7.9$ Hz, 1H, H-5 Ar), 7.33 (t, $J = 7.7$ Hz, 1H, H-8), 7.10-7.00 (m, 2H, H-4 Ar, H-7), 6.96 (d, $J = 4.0$ Hz, 1H, H-5), 6.88 (t, $J = 7.5$ Hz, 1H, H-9), 3.81 (s, 3H, CH_3O); Found: %: C, 51.62; H, 3.34; N, 14.17; Calculated for $\text{C}_{17}\text{H}_{13}\text{Cl}_3\text{N}_4\text{O}$, %: C, 51.60; H, 3.31; N, 14.16.

2-(4-Methoxyphenyl)-5-(trichloromethyl)-5,6-dihydro[1,2,4]triazolo[1,5-c]quinazolin (2g). Yield – 70.9%; white crystals. M. p. – 168-170°C; IR, ν , cm^{-1} : 3402, 3060, 3001, 2958, 2934, 2885, 2834, 1611, 1594, 1553, 1503, 1474, 1456, 1423, 1339, 1305, 1289, 1279, 1252, 1181, 1170, 1156, 1123, 1109, 1084, 1034, 1018, 956, 945, 842, 813, 751, 707, 689, 648, 630, 613, 604; $^1\text{H NMR}$, δ , ppm (J , Hz): 8.38 (d, $J = 4.0$ Hz, 1H, NH), 8.01 (d, $J = 8.8$ Hz, 2H, H-2,6 Ar), 7.78 (d, $J = 7.7$ Hz, 1H, H-10), 7.31 (t, $J = 7.8$ Hz, 1H, H-8), 7.08-7.02 (m, 3H, H-3,5 Ar, H-7), 6.91 (d, $J = 4.0$ Hz, 1H, H-5), 6.87 (t, $J = 7.5$ Hz, 1H, H-9), 3.79 (s, 3H, CH_3O); $^{13}\text{C NMR}$, δ , ppm: 161.32 (C-2), 160.42 (C-4 ϕ), 150.75 (C-6a), 141.11 (C-10b), 132.34, 127.67, 123.84, 123.02, 118.92, 114.58, 114.22, 109.92, 102.61 (CCl_3), 77.95 (C-5), 55.41 (CH_3O); Found: %: C, 51.60; H, 3.29; N, 14.13; Calculated for $\text{C}_{17}\text{H}_{13}\text{Cl}_3\text{N}_4\text{O}$, %: C, 51.60; H, 3.31; N, 14.16.

The reaction of 2-phenyl-5-(trichloromethyl)-5,6-dihydro[1,2,4]triazolo[1,5-c]quinazoline (2a) with N-nucleophiles. To a solution of 3.65 g (10 mmol) of 2-phenyl-5-(trichloromethyl)-5,6-dihydro[1,2,4]triazolo-[1,5-c]quinazoline (2a) in 10 ml of isopropanol add 11 mmol of the corresponding nucleophile ((2,2-dimethoxymethyl)amine, benzylamine, morpholine, piperidine, triethylamine). Then reflux the mixture for 1-1.5 h. While cooling to room temperature filter the precipitate and dry in the air.

2-Phenyl-5-(dichloromethyl)-[1,2,4]triazolo[1,5-c]quinazoline (3a). Yield – 39-75%; white crystals. M. p. – 240-242°C; IR, ν , cm^{-1} : 3072, 3010, 2958, 2920, 2852, 1624, 1608, 1556, 1521, 1476, 1443, 1397, 1348, 1319, 1298, 1279, 1265, 1215, 1176, 1134, 1113, 1072, 1024, 964, 928, 894, 874, 806, 791, 780, 745, 722, 690, 669, 660, 629; $^1\text{H NMR}$, δ , ppm (J , Hz): 8.60 (d, $J = 7.6$, 1H, H-7), 8.35 (d, $J = 7.0$, 2H, H-2,6 Ph), 8.17 (d, $J = 8.0$, 1H, H-10), 7.98 (t, $J = 7.6$, 1H, H-9), 7.89 (t, $J = 7.3$, 1H, H-8), 7.80 (s, 1H, $-\text{CHCl}_2$), 7.54 (m, 3H, H-3,4,5 Ph); $^{13}\text{C NMR}$, δ , ppm: 163.41 (C-5), 152.01 (C-2), 143.43 (C-6a), 141.55 (C-7), 133.05, 131.15,

130.26, 129.44, 129.24, 128.97, 127.43, 123.76, 117.56 (C-10a), 65.24 (CHCl₂); LC-MS, *m/z* = 329 [M+1], 330 [M+2], 331 [M+3]; Found, %: C, 58.38; H, 3.09; N, 17.05; Calculated for C₁₆H₁₀Cl₂N₄, %: C, 58.38; H, 3.06; N, 17.02.

X-ray study

The colourless crystals of **2a** (C₁₆H₁₁N₄Cl₃) were rhombic. At 293 K, *a* = 6.1949(4), *b* = 10.9669(5), *c* = 23.453(2) Å, *V* = 1593.4(2) Å³, *M_r* = 365.64, *Z* = 4, space group P2₁2₁2₁, *d_{calc}* = 1.524 g/cm³, μ(MoK_α) = 0.578 mm⁻¹, F(000) = 744. Intensities of 8685 reflections (4625 independent, *R_{int}* = 0.072) were measured on a "Xcalibur-3" diffractometer (graphite-monochromated MoK_α radiation, a CCD detector, ω-scanning, 2θ_{max} = 60°). The structure was solved using a SHELXTL package [8]. Positions of the hydrogen atoms were located on electron density difference maps and refined by "riding" the model with *U_{iso}* = 1.2*U_{eq}* of the carrier atom. A hydrogen atom of the amino group was refined using isotropic approximation. Full-matrix least-squares refinement against *F*² in anisotropic approximation for non-hydrogen atoms using 4582

reflections was converged to *wR₂* = 0.124 (*R₁* = 0.060 for 2645 reflections with *F* > 4σ(*F*), *S* = 0.940). The final atomic coordinates and crystallographic data for molecule **2a** were deposited to the Cambridge Crystallographic Data Centre, 12 Union Road, CB2 1EZ, UK (fax: +44-1223-336033; E-mail: deposit@ccdc.cam.ac.uk). They are available on request quoting the deposition number CCDC 1408958).

Conclusions

It has been shown that [5+1] cyclocondensation of [2-(3-aryl-1*H*-1,2,4-triazole-5-yl)phenyl]amines with chloral hydrate leads to 5-trichloromethyl-2-aryl-5,6-dihydro-[1,2,4]triazolo[1,5-*c*]quinazolines, and it has allowed to expand their combinatorial library. When treating with *N*-nucleophiles the products eliminate hydrogen chloride to yield 2-phenyl-5-(dichloromethyl)-[1,2,4]triazolo[1,5-*c*]quinazolines. This happens irrespective of the nature of *N*-nucleophile used. The mechanism of this reaction has been discussed.

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