Synthesis and Reactivity of [1,2,4]Triazolo-annelated Quinazolines

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Abstract: This paper reports the synthesis of phenyl-substituted 2-alkoxy(methylsulfanyl)-1,2,4-triazolo[1,5-a]quinazolines starting from N-cyanoimidocarbonates and substituted hydrazinobenzoic acids as building blocks. Thionation or chlorination of the inherent lactam moiety in the target compounds followed by treatment with multifunctional nucleophiles provided access to a variety of derivatives.

Keywords: triazolo[1,5-a]quinazolines; thionation; alkylation; chlorination; tetracyclic systems

1. Introduction

Triazolo-annelated quinazolines are known to constitute a pharmacologically interesting class of compounds. For instance, the novel compound Ia is effective adenosine antagonist whereas the related compound Ib was found to be benzodiazepine receptor antagonist [1-3]. The recently reported 1,2,4-triazoloquinazolines of type II were also found to exhibit promising antihistaminic activity against histamine induced bronchospasms and showed negligible sedation, compared to chlorpheniramine maleate, and could therefore serve as lead molecules for further modification to obtain a clinically useful class of non-sedative antihistamines [4,5]. Furthermore, some triazoloquinazolines IIIa which originated from N-cyanoimidocarbonates as synthons, have been described as potent protein kinase inhibitors [6].

In our previous paper on the 1,2,4-triazolo[1,5-a]quinazolines series IIIb, the corresponding alkylated derivatives have been proven as excellent agents for controlling the plant growth diseases.
caused by fungal pathogens, and some chlorinated compounds have shown an interesting affinity towards adenosine receptors [7].

In continuation of our ongoing studies of the chemistry of 1,2,4-triazolo[1,5-\(a\)]quinazolines, we report herein the synthesis of several phenyl-substituted 2-alkoxy(methylsulfanyl)-1,2,4-triazolo[1,5-\(a\)]quinazolines and their derivatives.

\[
\begin{align*}
\text{Ia} & \quad \text{X} = \text{NH}_2, \text{R} : \text{furan} \\
\text{Ib} & \quad \text{X} = \text{OH}, \text{R} : \text{P-fluorophenyl} \\
\text{II} & \quad \text{R} : \text{alkyl, aryl, aralkyl} \\
\text{X} & \quad \text{R} : \text{alkyl, aryl, aralkyl} \\
\text{IIIa} & \quad \text{X} = \text{NH} \\
\text{IIIb} & \quad \text{X} = \text{O}, \text{R} : \text{H, alkyl, aryl, aralkyl} \\
\text{R} & \quad \text{R} : \text{alkyl, aryl, aralkyl}
\end{align*}
\]

2. Results and Discussion

The cornerstone of the strategy for the synthesis of our target products was the preparation of compounds 5a-h (Scheme 1, Table 1). The first step, the preparation of several dialkyl \(N\)-cyanoimido-carbonates 1 from equimolar amounts of cyanogen bromide and the corresponding alcohol was reported previously [8]. In addition, it has been found that, the reaction of cyanamide with carbon disulfide in the presence of KOH followed by the alkylation with methyl iodide gives dimethyl \(N\)-cyanoimidodithiocarbonate [9].

\textbf{Scheme 1. Synthesis of [1,2,4]triazolo[1,5-\(a\)]quinazolin-5-ones 5a-h.}

\[
\begin{align*}
\text{RX} & \quad + \quad \text{OH} \cdot \text{HCl} \quad \text{i) Et}_3\text{N, EtOH; 11) conc. HCl, 80 °C}
\end{align*}
\]

Reagents and conditions: i) \text{Et}_3\text{N, EtOH; 11) conc. HCl, 80 °C}
Table 1. Prepared compounds 5-9.

| Compounds | R       | R¹     | R²     | X     |
|-----------|---------|--------|--------|-------|
| 5a        | CH₃     | COOH   | -      | O     |
| 5b        | CH₂CH₂- | COOH   | -      | O     |
| 5c        | CH₂CH₂CH₂CH₂CH₂- | CH₃ | -      | O     |
| 5d        | CH₂=CHCH₂- | CH₃ | -      | O     |
| 5e        | C₆H₅CH₂- | di-OCH₃ | -     | O     |
| 5f        | C₆H₅CH₂CH₂- | di-OCH₃ | -     | O     |
| 5g        | CH₃     | CH₃    | -      | S     |
| 5h        | CH₃     | di-OCH₃ | -      | S     |
| 6a        | CH₃     | CH₃    | C₆H₅CH₂CH₂- | S   |
| 6b        | C₆H₅CH₂- | di-OCH₃ | CH₂=CHCH₂- | O   |
| 6c        | CH₃     | COOH   | CH₂CH₂- | O   |
| 6d        | CH₂=CHCH₂- | CH₃ | C₆H₅CH₂- | O   |
| 7a        | CH₃     | CH₃    | -      | S     |
| 7b        | CH₂=CHCH₂- | CH₃ | -      | O     |
| 7c        | C₆H₅CH₂- | di-OCH₃ | -     | O     |
| 7d        | C₆H₅CH₂CH₂- | di-OCH₃ | -     | O     |
| 8a        | CH₃     | CH₃    | -      | S     |
| 8b        | CH₂=CHCH₂- | CH₃ | -      | O     |
| 8c        | C₆H₅CH₂- | di-OCH₃ | -     | O     |
| 8d        | C₆H₅CH₂CH₂- | di-OCH₃ | -     | O     |
| 9a        | CH₂CH₂- | COOH   | -      | O     |
| 9b        | CH₂CH₂CH₂CH₂CH₂- | CH₃ | -      | O     |
| 9c        | C₆H₅CH₂- | di-OCH₃ | -     | O     |
| 9d        | CH₂=CHCH₂- | CH₃ | -      | O     |
| 9e        | C₆H₅CH₂CH₂- | di-OCH₃ | -     | O     |
| 9f        | CH₃     | CH₃    | -      | S     |

Diazotization of the corresponding anthranilic acids [10] followed by the reduction with sulphur dioxide afforded the substituted 2-hydrazinobenzoic acids 2. Based on the high reactivity of N-cyanoimidocarbonates towards hydrazines to produce 1,2,4-triazole derivatives [11-13], reaction of 1 with 2 in ethanol in the presence of triethylamine under ice cooling analogously provided the intermediate 1,2,4-triazole derivatives 4, which upon treatment with hydrochloric acid produced the target [1,2,4]triazolo[1,5-a]quinazolin-5-ones 5a-h in 50-68% yield [14]. The structures of the novel compounds 5a-h have been established on the basis of their IR, ¹H-NMR and ¹³C-NMR spectra and microanalysis.

The IR spectra of compounds 5a-h are characterized by a strong (C=O)-stretching band at 1,685-1,712 cm⁻¹.

Alkylation of the lactam functionality may occur at the N- or (and) O-atom, giving rise to the formation of N-alkyllactams or (and) cyclic imido esters [15-17]. Regioselective N-alkylation has been well documented in the literature [18,19]. Accordingly, when the [1,2,4]triazolo[1,5-a]quinazolin-5-ones 5 were allowed to react with alkyl halides in a molar ratio of 1:1.5 in absolute dimethyl
formamide at room temperature in the presence of potassium carbonate, the corresponding 4-alkyl[1,2,4]triazolo[1,5-a]quinazolin-5-ones 6a-d resulted in 62-85% yield (Scheme 2, Table 1) [18].

Scheme 2. Synthesis of compounds 6-9.

\[
\begin{align*}
&\text{Reagents and conditions: i) } K_2CO_3, \text{ alkyl halides, DMF; ii) } \text{LiAlH}_4, \text{ THF; iii) } \text{P}_2\text{S}_5, \text{ pyridine; iv) } \text{POCl}_3, \text{ benzene or C}_2\text{O}_2\text{Cl}_2, \text{ trichloroethane.}
\end{align*}
\]

The products 6a-d were obtained as colored solid compounds and their IR spectra display a strong (C=O) absorption band at 1,670-1,682 cm\(^{-1}\). Treatment of compounds 5 with lithium aluminum hydride in absolute tetrahydrofuran at room temperature furnished the expected 4,5-dihydro[1,2,4]triazolo[1,5-a]quinazolines 7a-d in 55-70% yield [20]. The compounds 7a-d were obtained as colorless solids after column chromatography and their structures were verified by elemental analyses and spectral (NMR, MS and IR) data. The IR revealed the disappearance of the (C=O) absorption band at 1,685-1,712 cm\(^{-1}\) (previously found in compounds 5) and confirmed the formation of the products 7. When equimolar amounts of [1,2,4]triazolo[1,5-a]quinazolin-5-ones 5 and phosphorus pentasulfide were allowed to react in absolute pyridine under reflux for 2 h, the desired 2-alkoxy(methylsulfanyl)-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-thiones 8a-d could be isolated as yellow solids in excellent yields of 89-95% [21]. The IR spectra of compounds 8a-d displayed a weak (C=S) absorption band at around 1,249-1,268 cm\(^{-1}\) and the \(^{13}\)C-NMR spectra were characterized by a (C=S) resonance at 184.91-186.62 ppm.

Conversion of [1,2,4]triazoloquinazolin-5-ones 5 into 5-chloro-[1,2,4]triazolo[1,5-a]quinazolines 9a-f has been successfully achieved by chlorination with either oxalyl chloride in boiling 1,1,2-trichloroethane for 19 h [14] or with phosphorus oxychloride in boiling benzene for 2 h, followed
by trituration with a saturated aqueous solution of potassium carbonate [22]. Although both methods
gave acceptable yields, the reaction of 5 with phosphorus oxychloride is more advantageous with
regard to short reaction time and higher yields. The formation of 9 was accompanied by the gradual
disappearance of the characteristic (C=O) band of 5 at 1,685-1,712 cm⁻¹.

Scheme 3. Synthesis of compounds 10-18.

Reagents and conditions: i) hydrazine hydrate, EtOH; ii) aldehyde or ketone, EtOH; iii)
carbonyldiimidazole, toluene or carbon disulfide, pyridine; iv) hydrazides, toluene; v) carba-zides,
benzene; vi) POCl₃; vii) NaN₃, toluene; viii) methyl-3-aminothiophene-2-carboxylate, dioxane.

As outlined in Scheme 3, hydrazinolysis of 9 in refluxing ethanol led to the corresponding
[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazines 10a-d in good yields of 60-78% [23], which upon
treatment with an equimolar amount of aldehyde or ketone furnished the respective hydrazones 11a-d
in 68-83% yield (Table 2) [24]. The ¹H-NMR spectra of compounds 10 showed signals of NH₂, NH at
δ 4.65-5.40 and 9.37-9.90 ppm respectively, whereas the structure of the hydrazones 11 was confirmed
by disappearance of the signal of NH₂ group in the ¹H-NMR spectra. Reaction of 10 with
1,1'-carbonyldiimidazole in a molar ratio of 1:1.2 in boiling absolute toluene for 3 h provided the
hitherto unknown bis[1,2,4]triazolo[1,5-a:4,3-c]quinazolin-3-ones 12a,b in 49 and 57% yield [25].
Similarly, the corresponding thioxo derivatives 13a,b could be obtained in 56 and 61 % yield from the reaction of 10 with carbon disulfide in a molar ratio of 1:10 in refluxing pyridine for 2 h [26]. The IR spectra of 12 display strong (C=O) absorption bands at 1,702 and 1,711 cm⁻¹, and the ¹³C-NMR spectra of 13 are characterized by a (C=S) resonance at 185.05 and 185.73 ppm. Replacement of the chlorine in compounds 9 by different hydrazides occurred smoothly in refluxing toluene to produce the [1,2,4]triazoloquinazolin-5-yl-carbohydrazides 14a,b in 65 and 76% yield [27]. The IR spectra of 14 are characterized by a strong (C=O) absorption band at 1,660, 1,673 and a weak (NH) absorption band at 3,184, 3,207 cm⁻¹, respectively. Like the reaction with hydrazides, the corresponding reaction of compounds 9 with carbazides according to literature [27] produced the respective [1,2,4]triazoloquinazolin-5-yl-hydrazine-carboxylic acid esters of type 15a,b in 75 and 80% yield as colorless solids. The IR spectra of 15 display a strong (C=O) absorption band at 1,708, 1,718 and a weak (NH) absorption band at 3,198, 3,261 cm⁻¹.

After having successfully elaborated the synthesis of the carbohydrazides 14, we became interested in seeing whether these compounds could be cyclo-condensed to the novel bis[1,2,4]triazoloquinazolines of type 16. In fact when amidrazones 14 were treated with phosphorus oxychloride at refluxing temperature for 2 h, followed by subsequent neutralization with saturated potassium carbonate solution or aqueous ammonia, the desired compounds 16a,b were obtained in 70 and 75% yield [28]. The completion of the internal cyclization was monitored by IR spectroscopy: disappearance of the (C=O) and (NH) absorption bands at 1,660, 1,673 and 3,184, 3,207 cm⁻¹ signaled complete conversion of 14 to the tetracyclic compounds 16. When 5-chloro[1,2,4]triazoloquinazolines 9 were reacted with sodium azide in a molar ratio of 1:1.2 in absolute dimethyl formamide for 24 h at 90°C, the corresponding 2-alkoxy(methylsulfanyl)-tetrazolo[4,3-c][1,2,4]triazolo[1,5-a]quinazolines 17a-c were formed as colorless solids in 51-60% yield (Scheme 3, Table 2) [29].

The aforementioned facile nucleophilic displacement of the chlorine atom in 9 prompted us to investigate the reaction of 9 with methyl 3-aminothiophene-2-carboxylate, which theoretically should provide access to the novel pentacyclic compounds of type 18. Thus, when compounds 9 were reacted with methyl 3-aminothiophene-2-carboxylate in absolute dioxane in a molar ratio of 1:1.6, followed by addition of sodium hydride, the target compounds 18a,b could be isolated from the reaction mixture in 69 and 81% yield [27]. The IR spectra of compounds 18 are characterized by (C=O) stretching bands at 1,670 and 1,677 cm⁻¹.
Table 2. Prepared compounds 10-18.

| Compounds | R   | R^1 | R^2 | R^3 | X/Z |
|-----------|-----|-----|-----|-----|-----|
| 10a       | CH₃ | CH₃ | -   | -   | S   |
| 10b       | CH₃ CH₂⁻ | COOH | -   | -   | O   |
| 10c       | CH₂=CHCH₃⁻ | CH₃ | -   | -   | O   |
| 10d       | C₆H₅CH₂⁻ | di-OCH₃ | -   | -   | O   |
| 11a       | CH₃ | CH₃ | CH₃ | CH₃ | S   |
| 11b       | CH₃ | CH₃ | C₆H₅ | H   | S   |
| 11c       | C₆H₅CH₂⁻ | di-OCH₃ | CH₃ | CH₃ | O   |
| 11d       | C₆H₅CH₂CH₃⁻ | di-OCH₃ | C₆H₅ | CH₃ | O   |
| 12a       | CH₂=CHCH₃⁻ | CH₃ | -   | -   | O/O |
| 12b       | C₆H₅CH₂⁻ | di-OCH₃ | -   | -   | O/O |
| 13a       | C₆H₅CH₂⁻ | di-OCH₃ | -   | -   | O/S |
| 13b       | CH₃ | CH₃ | -   | -   | S/S |
| 14a       | CH₃ | CH₃ | C₆H₅ | -   | S   |
| 14b       | CH₃ | CH₃ | C₃H₇N | -   | S   |
| 15a       | CH₂=CHCH₃⁻ | CH₃ | CH₂CH₃⁻ | -   | O   |
| 15b       | CH₃ | CH₃ | C₆H₅CH₂⁻ | -   | S   |
| 16a       | CH₃ | CH₃ | C₆H₅ | -   | S   |
| 16b       | CH₃ | CH₃ | C₆H₅ | -   | S   |
| 17a       | CH₃ | CH₃ | -   | -   | S   |
| 17b       | C₆H₅CH₂⁻ | di-OCH₃ | -   | -   | O   |
| 17c       | C₆H₅CH₂CH₃⁻ | di-OCH₃ | -   | -   | O   |
| 18a       | CH₃CH₂CH₂CH₂CH₂⁻ | CH₃ | -   | -   | O   |
| 18b       | C₆H₅CH₂CH₂CH₂⁻ | di-OCH₃ | -   | -   | O   |

Table 3. Melting points, crystallization solvents, yields, molecular formulae and molecular weights of compounds 5-18.

| Comp. No. | Mp (°C) | Cryst. Solv. | Yield (%) | Molecular Formula. (Mol. Wt) |
|-----------|---------|--------------|-----------|------------------------------|
| 5a        | 228-230 | THF          | 58        | C₁₁H₈N₄O₄ (260.21)          |
| 5b        | 239-241 | THF          | 64        | C₁₂H₁₀N₄O₄ (274.24)         |
| 5c        | 254-257 | THF          | 50        | C₁₃H₁₂N₄O₂ (286.34)         |
| 5d        | 232-234 | THF          | 55        | C₁₃H₁₂N₄O₂ (256.27)         |
| 5e        | 243-245 | THF          | 65        | C₁₃H₁₄N₄O₄ (352.35)         |
| 5f        | 265-267 | THF          | 60        | C₁₉H₁₈N₄O₄ (366.38)         |
| 5g        | 227-229 | THF          | 68        | C₁₁H₁₀N₄OS (246.29)         |
| 5h        | 216-218 | THF          | 62        | C₁₂H₁₃N₄O₃S (292.32)        |
| 6a        | 180-182 | THF          | 85        | C₁₉H₁₈N₄OS (350.35)         |
| 6b        | 172-174 | THF          | 81        | C₂₁H₂₀N₄O₄ (392.42)         |
| 6c        | 165-167 | THF          | 62        | C₁₉H₁₂N₄O₄ (288.26)         |
| 6d        | 202-204 | THF          | 82        | C₂₁H₁₈N₄O₂ (346.39)         |
| 7a        | 133-135 | EtOAc-hexane | 60        | C₁₁H₁₂N₄S (232.31)          |
| 7b        | 145-147 | EtOAc-hexane | 55        | C₁₃H₁₄N₄O (242.28)          |
| 7c        | 158-160 | EtOAc-hexane | 70        | C₁₃H₁₈N₄O₃ (338.37)         |
| 7d        | 179-181 | EtOAc-hexane | 64        | C₁₉H₂₀N₄O₃ (352.40)         |
Table 3. Cont.

|   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|
| 8a | 220-222 | DMF | 90 | C_{12}H_{12}N_{6}O_{2}S_{2} (308.38) |
| 8b | 212-214 | DMF | 95 | C_{13}H_{12}N_{6}O_{2} (272.33) |
| 8c | 253-255 | DMF | 92 | C_{16}H_{12}N_{6}O_{2}S (368.42) |
| 8d | 241-243 | DMF | 89 | C_{19}H_{16}N_{6}O_{2}S (382.44) |
| 9a | 128-130 | THF-hexane | 90 | C_{12}H_{12}N_{6}O_{3} (292.68) |
| 9b | 144-46 | THF-hexane | 88 | C_{15}H_{15}O_{2} (304.78) |
| 9c | 163-165 | THF-hexane | 91 | C_{18}H_{15}O_{2} (370.80) |
| 9d | 132-135 | THF-hexane | 87 | C_{13}H_{13}O_{2} (274.71) |
| 9e | 157-159 | THF-hexane | 93 | C_{19}H_{15}O_{2} (384.83) |
| 9f | 176-178 | THF-hexane | 86 | C_{14}H_{12}O_{2} (264.74) |
| 10a | 230-232 | EtOH | 60 | C_{16}H_{12}O_{2} (260.32) |
| 10b | 215-217 | EtOH | 69 | C_{13}H_{12}O_{2} (288.27) |
| 10c | 223-225 | EtOH | 71 | C_{16}H_{14}O_{2} (296.29) |
| 10d | 243-245 | EtOH | 78 | C_{19}H_{16}O_{2} (366.38) |
| 11a | 189-191 | EtOH | 70 | C_{18}H_{16}O_{2} (300.39) |
| 11b | 208-210 | EtOH | 83 | C_{18}H_{16}O_{2} (348.43) |
| 11c | 198-200 | EtOH | 73 | C_{20}H_{22}O_{2} (406.45) |
| 11d | 213-215 | EtOH | 68 | C_{20}H_{22}O_{2} (482.55) |
| 12a | 219-221 | EtOH | 49 | C_{16}H_{12}O_{2} (296.29) |
| 12b | 230-232 | EtOH | 57 | C_{19}H_{16}O_{2} (392.38) |
| 13a | 248-250 | MeOH | 61 | C_{19}H_{16}O_{2} (408.44) |
| 13b | 225-227 | MeOH | 56 | C_{19}H_{16}O_{2} (320.38) |
| 14a | 178-179 | MeOH | 65 | C_{18}H_{16}O_{2} (364.43) |
| 14b | 149-151 | MeOH | 76 | C_{18}H_{16}O_{2} (365.42) |
| 15a | 127-129 | MeOH | 75 | C_{18}H_{18}O_{2} (342.36) |
| 15b | 191-193 | MeOH | 80 | C_{19}H_{18}O_{2} (394.46) |
| 16a | 186-188 | MeOH | 75 | C_{19}H_{18}O_{2} (346.42) |
| 16b | 200-202 | MeOH | 70 | C_{17}H_{17}O_{2} (347.40) |
| 17a | 170-172 | MeOH | 60 | C_{19}H_{18}O_{2} (271.31) |
| 17b | 224-226 | MeOH | 54 | C_{19}H_{18}O_{2} (377.37) |
| 17c | 206-208 | MeOH | 51 | C_{19}H_{18}O_{2} (391.39) |
| 18a | 242-244 | MeOH | 81 | C_{20}H_{19}O_{2} (393.47) |
| 18b | 231-233 | MeOH | 69 | C_{24}H_{19}O_{2} (473.51) |

3. Experimental

3.1. General

Melting points (°C) were determined on open glass capillaries using a Mettler FP 62 apparatus and are uncorrected. Elemental analyses (C, H, N, S) were in full agreement with the proposed structures within ± 0.4% of the theoretical values, and were carried out with a Heraeus CHN-O-Rapid Instrument. The IR (KBr) spectra were recorded on a Shimadzu FT-IR 8300. ¹H-NMR (400 MHz) and ¹³C-NMR (100 MHz) spectra were recorded on a Bruker AMX 400 spectrometer and chemical shifts are giving in a (ppm) downfield from tetramethylsilane (TMS) as an internal standard, DMSO is used as solvent. Mass spectra were recorded on a Finnigan MAT 311A and on a VG 70-250S (VG
Analytical) instrument. Follow up of the reactions and checking the purity of compounds was made by TLC on DC-Mikrokarten polygram SIL G/UV254, from the Macherey-Nagel Firm, Duren. Thickness: 0.25 m. Column chromatography was conducted on silica gel (ICN Silica 100-200, active 60 Å)

3.2. Chemistry

3.2.1. Synthesis of compounds 5a-h

10 mmol of substituted hydrazinobenzoic acid 2 was added portionwise to a stirred solution of 1 (10 mmol) in EtOH (20 mL) at 0°C. Afterwards triethylamine (30 mmol) was added dropwise over a period of 30 min. After the addition was complete, the reaction mixture was left to stir overnight at room temperature. Acidification of the mixture was performed by conc. HCl under ice cooling followed by refluxing for 1-3 h. After cooling, the mixture was poured into ice/water, the resulting solid was filtered, washed with water and dried. Recrystallization from THF gave analytically pure colored compounds 5a-h.

8-Carboxylic acid-2-methoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one (5a). IR (cm⁻¹): ν 1,685, 1,712 (C=O). ¹H-NMR (DMSO-d₆): δ 3.19 (s, 1H, OH), 3.99 (s, 3H, OCH₃), 7.48-8.05 (m, 3H, Ar-H), 13.15 (s, 1H, NH). ¹³C-NMR: 57.16, 114.31, 116.53, 125.58, 128.08, 135.12, 136.18, 147.87, 159.70, 161.83, 168.02. MS, m/z (%): 260 (M⁺, 100).

8-Carboxylic acid-2-ethoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one (5b). IR (cm⁻¹): ν 1,689, 1,703 (C=O). ¹H-NMR (DMSO-d₆): δ 1.38 (t, J = 7.02 Hz, 3H, OCH₂CH₃), 3.34 (s, 1H, OH), 4.35 (q, J = 14.10 Hz, 2H, OC₂H₂CH₃), 7.67-8.12 (m, 3H, Ar-H), 13.01 (s, 1H, NH). ¹³C-NMR: 14.86, 65.64, 114.29, 116.79, 125.43, 128.25, 135.62, 136.12, 147.24, 156.14, 159.86, 167.52. MS, m/z (%): 274 (M⁺, 95).

8-Methyl-2-pentyloxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one (5c). IR (cm⁻¹): ν 1,690 (C=O). ¹H-NMR (DMSO-d₆): δ 0.98 (t, J = 7.32 Hz, 3H, OCH₂CH₂CH₂CH₂CH₃), 1.37-1.44 (m, 4H, OCH₂CH₂CH₂CH₂CH₃), 1.63-1.79 (m, 2H, OCH₂CH₂CH₂CH₂CH₃), 2.78 (s, 3H, CH₃), 4.42 (t, J = 7.41 Hz, 2H, OC₂H₂CH₂CH₂CH₃), 7.45-8.51 (m, 3H, Ar-H), 12.83 (s, 1H, NH). ¹³C-NMR: 13.39, 14.47, 22.24, 27.73, 28.07, 69.74, 114.65, 116.80, 125.45, 128.68, 135.72, 136.11, 147.74, 159.91, 167.70. MS, m/z (%): 286 (M⁺, 85).

2-Allyloxy-8-methyl-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one (5d). IR (cm⁻¹): ν 1,697 (C=O). ¹H-NMR (DMSO-d₆): δ 3.39 (s, 3H, CH₃), 4.86 (d, J = 5.68 Hz, 2H, CH₂=CHCH₂), 5.42-5.61 (m, 2H, CH₂=CHCH₂), 6.05-6.15 (m, 1H, CH₂=CHCH₂), 7.68-8.25 (m, 3H, Ar-H), 13.41 (s, 1H, NH). ¹³C-NMR: 23.89, 69.60, 113.82, 116.44, 118.25, 125.16, 128.13, 134.11, 135.30, 135.62, 147.30, 159.45, 166.92. MS, m/z (%): 256 (M⁺, 100).

2-Benzyl oxy-7,8-dimethoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one (5e) IR (cm⁻¹): ν 1,710 (C=O). ¹H-NMR (DMSO-d₆): δ 3.48 (s, 3H, OCH₃), 3.98 (s, 3H, OCH₃), 5.39 (s, 2H, OCH₂Ph), 7.37-8.16 (m, 7H, Ar-H), 13.44 (s, 1H, NH). ¹³C-NMR: 54.23, 58.09, 71.18, 114.34, 116.81, 125.53, 127.74, 128.03, 128.85, 135.75, 136.11, 136.77, 147.11, 160.40, 167.58. MS, m/z (%): 352 (M⁺, 92).
7,8-Dimethoxy-2-phenethyloxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one (5f). IR (cm\(^{-1}\)): \(\nu\) 1,689 (C=O). \(^1\)H-NMR (DMSO-d\(_6\)): \(\delta\) 3.09 (t, \(J = 7.44\) Hz, 2H, OCH\(_2\)CH\(_2\)Ph), 3.80 (s, 3H, OCH\(_3\)), 4.01 (s, 3H, OCH\(_3\)), 4.50 (t, \(J = 7.41\) Hz, 2H, OCH\(_2\)CH\(_2\)Ph), 7.20-8.19 (m, 7H, Ar-H), 13.75 (s, 1H, NH). \(^13\)C-NMR: 34.91, 51.73, 56.71, 70.23, 116.81, 114.32, 126.80, 125.51, 128.29, 128.74, 129.37, 136.14, 138.33, 147.72, 159.91, 167.57. MS, \(m/z\) (%): 366 (M\(^+\), 53).

8-Methyl-2-methylsulfanyl-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one (5g). IR (cm\(^{-1}\)): \(\nu\) 1,687 (C=O). \(^1\)H-NMR (DMSO-d\(_6\)): \(\delta\) 2.94 (s, 3H, CH\(_3\)), 3.27 (s, 3H, SCH\(_3\)) 7.64-8.25 (m, 3H, Ar-H), 13.68 (s, 1H, NH). \(^13\)C-NMR: 13.92, 24.60, 114.65, 116.23, 125.50, 128.58, 135.72, 136.12, 149.11, 159.90, 162.30. MS, \(m/z\) (%): 246 (M\(^+\), 87).

7,8-Dimethoxy-2-methylsulfanyl-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-one (5h). IR (cm\(^{-1}\)): \(\nu\) 1,698 (C=O). \(^1\)H-NMR (DMSO-d\(_6\)): \(\delta\) 2.87 (s, 3H, SCH\(_3\)), 3.07 (s, 3H, OCH\(_3\)), 3.84 (s, 3H, OCH\(_3\)), 7.59-8.36 (m, 2H, Ar-H), 13.90 (s, 1H, NH). \(^13\)C-NMR: 13.78, 56.45, 58.01, 114.05, 115.91, 126.34, 129.08, 135.09, 136.52, 149.11, 159.72, 165.30. MS, \(m/z\) (%): 292 (M\(^+\), 100).

3.2.2. Synthesis of compounds 6a-d

To a solution of 5 (1 mmol) in DMF (5 mL) was added potassium carbonate (1.2 mmol) portion wise over a period of 10 min at room temperature. After stirring for 20 min, the appropriate alkyl halide (1.5 mmol) was added dropwise and the reaction mixture was stirred for 18 h at room temperature. The mixture was poured into ice/water, the precipitate was filtered off, washed with water and dried. Analytically pure products 6a-d were obtained after recrystallization from THF.

8-Methyl-2-methylsulfanyl-4-phenethyl[1,2,4]triazolo[1,5-a]quinazolin-5-one (6a). IR (cm\(^{-1}\)): \(\nu\) 1,671 (C=O). \(^1\)H-NMR (DMSO-d\(_6\)): \(\delta\) 2.98 (s, 3H, SCH\(_3\)), 3.37 (t, \(J = 7.54\) Hz, 2H, NC\(_\text{H}_2\)CH\(_2\)Ph), 4.02 (s, 3H, CH\(_3\)), 4.31 (t, \(J = 7.51\) Hz, 2H, NCH\(_2\)CH\(_2\)Ph), 7.22-8.20 (m, 8H, Ar-H). \(^13\)C-NMR: 13.98, 24.74, 34.48, 64.26, 114.68, 116.13, 125.82, 126.88, 128.87, 135.42, 135.84, 138.39, 147.59, 158.76, 167.91. MS, \(m/z\) (%): 350 (M\(^+\), 90).

2-Benzylloxy-7,8-dimethoxy-4-allyl[1,2,4]triazolo[1,5-a]quinazolin-5-one (6b). IR (cm\(^{-1}\)): \(\nu\) 1,678 (C=O). \(^1\)H-NMR (DMSO-d\(_6\)): \(\delta\) 3.11 (s, 3H, OCH\(_3\)), 3.90 (s, 3H, OCH\(_3\)), 4.45 (d, \(J = 5.62\) Hz, 2H, CH\(_2\)=CHCH\(_2\)), 5.17-5.29 (m, 2H, CH\(_2\)=CHCH\(_2\)), 5.31 (s, 2H, CH\(_2\)), 6.25-6.33 (m, 1H, CH\(_2\)=CHCH\(_2\)), 7.50-8.30 (m, 7H, Ar-H). \(^13\)C-NMR: 24.11, 49.89, 57.34, 69.60, 113.82, 116.44, 118.25, 124.03, 124.98, 125.16, 128.13, 131.54, 134.91, 135.30, 135.62, 147.30, 159.05, 165.82. MS, \(m/z\) (%): 392 (M\(^+\), 79).

8-Carboxylic acid-4-ethyl-2-methoxy[1,2,4]triazolo[1,5-a]quinazolin-5-one (6c). IR (cm\(^{-1}\)): \(\nu\) 1,675, 1,682 (C=O). \(^1\)H-NMR (DMSO-d\(_6\)): \(\delta\) 1.37 (t, \(J = 7.02\) Hz, 3H, NCH\(_2\)CH\(_3\)), 3.52 (s, 1H, OH), 4.09 (q, \(J = 14.22\) Hz, 2H, NCH\(_2\)CH\(_3\)), 4.32 (s, 3H, OCH\(_3\)), 7.58-8.09 (m, 3H, Ar-H). \(^13\)C-NMR: 14.23, 52.34, 57.18, 114.13, 116.27, 125.71, 128.79, 135.20, 135.42, 148.49, 158.64, 162.34, 167.99. MS, \(m/z\) (%): 288 (M\(^+\), 67).
2-Allyloxy-4-benzyl-8-methyl[1,2,4]triazolo[1,5-a]quinazolin-5-one (6d). IR (cm$^{-1}$): ν 1,670 (C=O).

$^1$H-NMR (DMSO-$d_6$): δ 3.57 (s, 3H, CH$_3$), 4.83 (d, $J = 4.60$ Hz, 2H, CH$_2$=CHCH$_2$), 5.20 (s, 2H, CH$_2$), 5.30-5.42 (m, 2H, CH$_2$=CHCH$_2$), 6.04-6.14 (m, 1H, CH$_2$=CHCH$_2$), 7.46-8.15 (m, 8H, Ar-H). $^{13}$C-NMR: 24.29, 44.53, 63.14, 114.47, 116.10, 117.18, 125.83, 128.82, 130.23, 131.45, 134.45, 134.90, 135.32, 135.86, 148.79, 157.81, 168.43. MS, $m/z$ (%): 346 (M$^+$, 80).

3.2.3. Synthesis of compounds 7a-d

A solution of 5 (1 mmol) in dry THF (5 mL) was added dropwise to a stirred suspension of LiAlH$_4$ (3 mmol) in dry THF (10 mL). After stirring at room temperature for 3 h, water (0.4 mL) was added carefully and the mixture was stirred for an additional 30 min. The reaction mixture was filtered and the solvent removed under reduced pressure, the residue was dissolved in THF and passed through a short column chromatography, the solvent was removed under reduced pressure, and the obtained solid was recrystallized from EtOAc/n-hexane.

4,5-Dihydro-8-methyl-2-methylsulanyl[1,2,4]triazolo[1,5-a]quinazoline (7a). IR (cm$^{-1}$): ν 3,167, (NH). $^1$H-NMR (DMSO-$d_6$): δ 2.83 (s, 3H, CH$_3$), 3.50 (s, 3H, SCH$_3$), 4.20 (s, 2H, CH$_2$-quinazoline), 7.28-7.82 (m, 3H, Ar-H), 7.95 (s, 1H, NH). $^{13}$C-NMR: 13.23, 25.23, 43.22, 112.72, 119.64, 124.50, 126.23, 130.75, 134.16, 155.18, 165.29. MS, $m/z$ (%): 232 (M$^+$, 100).

2-Allyloxy-4,5-dihydro-8-methyl[1,2,4]triazolo[1,5-a]quinazoline (7b). IR (cm$^{-1}$): ν 3,153, (NH). $^1$H-NMR (DMSO-$d_6$): δ 2.76 (s, 3H, CH$_3$), 4.76 (d, $J = 6.74$ Hz, 2H, CH$_2$=CHCH$_2$), 4.92 (s, 2H, CH$_2$-quinazoline), 5.22-5.33 (m, 2H, CH$_2$=CHCH$_2$), 6.09-6.16 (m, 1H, CH$_2$=CHCH$_2$), 7.48-8.10 (m, 3H, Ar-H), 8.25 (s, 1H, NH). $^{13}$C-NMR: 23.45, 69.63, 113.87, 116.45, 118.20, 125.33, 128.12, 134.57, 135.25, 135.51, 159.47, 167.70. MS, $m/z$ (%): 242 (M$^+$, 89).

2-Benzylloxy-4,5-dihydro-7,8-dimethoxy[1,2,4]triazolo[1,5-a]quinazoline (7c). IR (cm$^{-1}$): ν 3,189, (NH). $^1$H-NMR (DMSO-$d_6$): δ 2.93 (s, 3H, OCH$_3$), 3.30 (s, 3H, OCH$_3$), 4.50 (s, 2H, CH$_2$-quinazoline), 5.26 (s, 2H, OCH$_2$Ph), 7.01-7.56 (m, 7H, Ar-H), 7.91 (s, 1H, NH). $^{13}$C-NMR: 52.07, 55.39, 69.94, 112.27, 119.23, 124.10, 126.30, 127.12, 127.75, 128.23, 128.85, 133.27, 136.44, 154.55, 166.87. MS, $m/z$ (%): 338 (M$^+$, 93).

4,5-Dihydro-7,8-dimethoxy-2-phenethyloxy[1,2,4]triazolo[1,5-a]quinazoline (7d). IR (cm$^{-1}$): ν 3,180, (NH). $^1$H-NMR (DMSO-$d_6$): δ 2.89 (s, 3H, OCH$_3$), 3.22 (s, 3H, OCH$_3$), 3.44 (t, $J = 7.45$ Hz, 2H, OCH$_2$CH$_2$Ph), 4.39 (t, $J = 7.41$ Hz, 2H, OCH$_2$CH$_2$Ph), 4.48 (s, 2H, CH$_2$-quinazoline), 7.10-7.52 (m, 7H, Ar-H), 7.77 (s, 1H, NH). $^{13}$C-NMR: 34.90, 45.07, 49.38, 68.95, 113.33, 119.27, 124.23, 126.80, 128.51, 129.37, 131.09, 135.74, 136.11, 138.33, 154.90, 166.85. MS, $m/z$ (%): 352 (M$^+$, 90).

3.2.4. Synthesis of compounds 8a-d

Compound 5 (1 mmol) was refluxed with phosphorus pentasulfide (1 mmol) in absolute pyridine (5 mL) for 2 h. Afterwards the reaction mixture was cooled and poured into ice/water, the yellow precipitate was separated by filtration and washed thoroughly with water. Recrystallization from aqueous DMF furnished analytically pure 8a-d.
7,8-Dimethoxy-2-methylsulfanyl-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-thione (8a). IR (cm⁻¹): ν 1,268 (C=S). ¹H-NMR (DMSO-d₆): δ 3.32 (s, 3H, SCH₃), 3.70 (s, 3H, OCH₃), 4.02 (s, 3H, OCH₃), 7.52-7.96 (m, 2H, Ar-H), 14.72 (s, 1H, NH). ¹³C-NMR: 13.72, 54.43, 56.84, 114.21, 122.43, 125.83, 132.41, 135.88, 149.59, 162.78, 185.71. MS, m/z (%): 308 (M⁺, 100).

2-Allyloxy-8-methyl-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-thione (8b). IR (cm⁻¹): ν 1,258 (C=S).

1H-NMR (DMSO-d₆): δ 2.86 (s, 3H, CH₃), 4.85 (d, J = 6.36 Hz, 2H, CH₂=CHCH₂), 5.31-5.46 (m, 2H, C₆H₂=CHCH₂), 6.08-6.15 (m, 1H, CH₂=CHCH₂), 7.48-8.12 (m, 3H, Ar-H), 14.48 (s, 1H, NH). ¹³C-NMR: 25.09, 69.92, 114.27, 118.39, 122.53, 125.92, 128.21, 131.83, 132.42, 135.92, 145.75, 167.31, 184.91. MS, m/z (%): 272 (M⁺, 94).

2-Benzylloxy-7,8-dimethoxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-thione (8c). IR (cm⁻¹): ν 1,255 (C=S).

1H-NMR (DMSO-d₆): δ 3.20 (s, 3H, OCH₃), 3.78 (s, 3H, OCH₃), 5.42 (s, 2H, OCH₂CH₂Ph), 7.37-8.62 (m, 7H, Ar-H), 14.74 (s, 1H, NH). ¹³C-NMR: 45.21, 48.34, 70.60, 114.24, 122.40, 125.37, 128.06, 128.30, 131.72, 132.33, 135.38, 145.90, 167.34, 185.11. MS, m/z (%): 368 (M⁺, 65).

7,8-Dimethoxy-2-phenethyloxy-4H-[1,2,4]triazolo[1,5-a]quinazolin-5-thione (8d). IR (cm⁻¹): ν 1,249 (C=S).

1H-NMR (DMSO-d₆): δ 2.95 (s, 3H, OCH₃), 3.11 (t, J = 6.35 Hz, 2H, OCH₂CH₂CH₂CH₃), 3.58 (s, 3H, OCH₃), 4.55 (t, J = 6.63 Hz, 2H, OCH₂CH₂CH₂CH₃), 7.24-8.61 (m, 7H, Ar-H), 14.70 (s, 1H, NH). ¹³C-NMR: 34.45, 47.21, 53.34, 69.72, 114.23, 122.42, 125.00, 125.82, 126.30, 128.85, 131.76, 135.83, 137.80, 145.63, 165.20, 186.62. MS, m/z (%): 382 (M⁺, 78).

3.2.5. Synthesis of compounds 9a-f

Method-A: Compound 5 (2 mmol) was refluxed with oxalyl chloride (6 mmol) in 1,1,2-trichloroethane (12 mL) for 19 h at 105°C. The solution was cooled and MeOH (0.2 mL) was added drop-wise, the obtained solid was filtered, washed with hexane, dried and recrystallized from THF-hexane.

Method-B: Compound 5 (1 mmol) was refluxed with Phosphorus oxychloride (1 mL) in benzene (7 mL) for 2 h. The solvent was evaporated and the residue was treated with saturated aqueous solution of potassium carbonate. The solid was filtered, washed thoroughly with water, dried and recrystallized from THF-hexane.

8-Carboxylic acid-5-chloro-2-ethoxy[1,2,4]triazolo[1,5-a]quinazoline (9a). IR (cm⁻¹): ν 1,683 (C=O). ¹H-NMR (DMSO-d₆): δ 1.30 (t, J = 7.07 Hz, 3H, OCH₂CH₃), 3.03 (s, 1H, OH), 4.34 (q, J = 14.10 Hz, 2H, OCH₂CH₂CH₃), 7.49-8.15 (m, 3H, Ar-H). ¹³C-NMR: 14.56, 64.57, 114.38, 116.05, 125.39, 128.22, 135.58, 136.43, 142.70, 154.32, 159.38. MS, m/z (%): 292 (M⁺, 88).

5-Chloro-8-methyl-2-pentyloxy[1,2,4]triazolo[1,5-a]quinazoline (9b). ¹H-NMR (DMSO-d₆): δ 0.81 (t, J = 7.45 Hz, 3H, OCH₂CH₂CH₂CH₂CH₃), 1.46-1.63 (m, 4H, OCH₂CH₂CH₂CH₂CH₂CH₃), 1.83-1.89 (m, 2H, OCH₂CH₂CH₂CH₂CH₂CH₃), 3.11 (s, 3H, CH₃), 4.43 (t, J = 7.60 Hz, 2H, OCH₂CH₂CH₂CH₂CH₂CH₃), 7.45-8.16 (m, 3H, Ar-H). ¹³C-NMR: 13.75, 21.70, 27.35, 28.16, 45.82, 69.52, 114.70, 116.81, 126.54, 127.95, 136.57, 146.63, 155.33, 160.07. MS, m/z (%): 304 (M⁺, 91).
2-Benzyl-5-chloro-7,8-dimethoxy[1,2,4]triazolo[1,5-a]quinazoline (9c). $^1$H-NMR (DMSO-d$_6$): $\delta$ 3.23 (s, 3H, OCH$_3$), 3.64 (s, 3H, OCH$_3$), 5.79 (s, 2H, OCH$_2$Ph), 7.37-8.45 (m, 7H, Ar-H). $^{13}$C-NMR: 50.01, 53.74, 71.34, 115.20, 117.42, 125.50, 126.71, 127.14, 128.25, 128.70, 132.41, 135.90, 136.11, 136.77, 155.93, 162.65. MS, m/z (%): 370 (M$^+$, 69).

2-Allyloxy-5-chloro-8-methyl[1,2,4]triazolo[1,5-a]quinazoline (9d). $^1$H-NMR (DMSO-d$_6$): $\delta$ 3.01 (s, 3H, CH$_3$), 4.21 (d, $J$ = 5.50 Hz, 2H, CH$_2$=CHC$_2$H$_2$), 5.33-5.52 (m, 2H, C$_2$H$_2$=CHCH$_2$), 6.10-6.16 (m, 1H, CH$_2$=CHCH$_2$), 7.73-8.34 (m, 3H, Ar-H). $^{13}$C-NMR: 25.89, 69.60, 113.82, 116.44, 118.25, 125.16, 128.13, 134.11, 135.30, 135.62, 145.87, 158.33, 163.12. MS, m/z (%): 274 (M$^+$, 100).

5-Chloro-7,8-dimethoxy-2-phenethyloxy[1,2,4]triazolo[1,5-a]quinazoline (9e): $^1$H-NMR (DMSO-d$_6$): $\delta$ 3.09 (s, 3H, OCH$_3$), 3.21 (t, $J$ = 7.50 Hz, 2H, OC$_2$H$_2$CH$_2$), 3.52 (s, 3H, OCH$_3$), 4.65 (t, $J$ = 7.51 Hz, 2H, OCH$_2$C$_2$H$_2$Ph), 7.22-8.37 (m, 7H, Ar-H). $^{13}$C-NMR: 35.09, 49.60, 54.11, 69.61, 114.59, 124.40, 126.72, 129.30, 134.29, 134.94, 138.49, 153.37, 156.84, 161.31. MS, m/z (%): 384 (M$^+$, 100).

5-Chloro-8-methyl-2-methylsulfanyl[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazine (10a). IR (cm$^{-1}$): $\nu$ 3,189, 3,231 (NH-NH$_2$). $^1$H-NMR (DMSO-d$_6$): $\delta$ 2.80 (s, 3H, CH$_3$), 3.78 (s, 3H, S.CH$_3$), 4.84 (s, 2H, NH$_2$), 7.97-8.30 (m, 3H, Ar-H), 9.37 (s, 1H, NH). $^{13}$C-NMR: 13.87, 26.48, 114.48, 124.06, 124.77, 125.40, 127.35, 134.24, 134.88, 153.31, 169.73. MS, m/z (%): 260 (M$^+$, 100).

8-Carboxylic acid-2-ethoxy[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazine (10b). IR (cm$^{-1}$): $\nu$ 3,182, 3,201 (NH-NH$_2$), 1,686 (C=O). $^1$H-NMR (DMSO-d$_6$): $\delta$ 1.32 (t, $J$ = 7.07 Hz, 3H, OCH$_2$CH$_3$), 3.34 (s, 1H, OH), 4.37 (q, $J$ = 14.15 Hz, 2H, OCH$_2$CH$_3$), 4.65 (s, 2H, NH$_2$), 7.89-8.05 (m, 3H, Ar-H), 9.42 (s, 1H, NH). $^{13}$C-NMR: 14.73, 65.61, 114.12, 116.45, 125.62, 128.43, 135.13, 136.29, 145.38, 157.82, 167.92. MS, m/z (%): 288 (M$^+$, 78).

2-Allyloxy-8-methyl[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazine (10c). IR (cm$^{-1}$): $\nu$ 3,210, 3,267 (NH-NH$_2$). $^1$H-NMR (DMSO-d$_6$): $\delta$ 3.21 (s, 3H, CH$_3$), 4.81 (s, 2H, NH$_2$), 4.85 (d, $J$ = 5.30 Hz, 2H, CH$_2$=CHCH$_2$), 5.29-5.43 (m, 2H, CH$_2$=CHCH$_2$), 6.06-6.12 (m, 1H, CH$_2$=CHCH$_2$) 7.87-8.31 (m, 3H, Ar-H), 9.90 (s, 1H, NH). $^{13}$C-NMR: 25.34, 69.53, 70.55, 113.12, 114.59, 118.32, 124.41, 133.52, 134.26, 134.95, 150.72, 161.12, 168.50. MS, m/z (%): 270 (M$^+$, 94).
2-Benzyl-7,8-dimethoxy[1,2,4]triazolo[1,5-a]quinazolin-5-yl-hydrazine (10d). IR (cm⁻¹): ν 3,205, 3,286 (NH-NH). ¹H-NMR (DMSO-d₆): δ 3.08 (s, 3H, OCH₃), 3.43 (s, 3H, OCH₃), 4.82 (s, 2H, OCH₂Ph), 5.40 (s, 2H, NH₂), 7.93-8.32 (m, 7H, Ar-H), 9.84 (s, 1H, NH). ¹³C-NMR: 34.21, 47.87, 69.63, 113.85, 116.43, 118.20, 125.12, 128.15, 132.62, 135.15, 135.66, 147.34, 159.45, 166.93. MS, m/z (%): 366 (M⁺, 72).

3.2.7. Synthesis of compounds 11a-d

A mixture of 10 (1 mmol) and aldehyde or ketone (1 mmol) was refluxed in EtOH (10 mL) for 3 h. The solvent was removed under reduced pressure, and the resulting solids were recrystallized from EtOH.

N-Isopropylidene-N’-(8-methyl-2-methylsulfanyl[1,2,4]triazolo[1,5-a]quinazolin-5-yl)hydrazine (11a). ¹H-NMR (DMSO-d₆): δ 2.21 (s, 3H, CH₃-isopropyl), 2.63 (s, 3H, CH₃-isopropyl), 2.85 (s, 3H, CH₃), 3.45 (s, 3H, SCH₃), 7.37-7.94 (m, 3H, Ar-H), 10.45 (s, 1H, NH). ¹³C-NMR: 13.80, 18.67, 25.27, 45.34, 115.08, 124.90, 125.75, 126.06, 134.24, 134.96, 162.37, 164.54. MS, m/z (%): 300 (M⁺, 79).

N-Benzylidene-N’-(8-methyl-2-methylsulfanyl[1,2,4]triazolo[1,5-a]-quinazolin-5-yl)hydrazine (11b). ¹H-NMR (DMSO-d₆): δ 2.92 (s, 3H, CH₃), 3.34 (s, 3H, SCH₃), 4.33 (s, 1H, CH-benzylidene), 7.45-8.05 (m, 8H, Ar-H), 11.83 (s, 1H, NH). ¹³C-NMR: 13.78, 25.17, 69.79, 110.23, 114.12, 115.37, 124.65, 127.54, 129.20, 131.76, 133.54, 141.32, 154.20, 168.97. MS, m/z (%): 348 (M⁺, 90).

N-(2-Benzyloxy-7,8-dimethoxy[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-N’-isopropylidene-hydrazine (11c). ¹H-NMR (DMSO-d₆): δ 2.12 (s, 3H, CH₃-isopropyl), 2.30 (s, 3H, CH₃-isopropyl), 2.87 (s, 3H, OCH₃), 3.33 (s, 3H, OCH₃), 5.54 (s, 2H, OCH₂Ph), 6.34 (s, 1H, NH). ¹³C-NMR: 12.71, 13.43, 52.65, 58.43, 70.88, 103.16, 109.37, 114.05, 121.53, 124.69, 128.18, 128.76, 136.08, 136.74, 143.30, 150.85, 152.63, 169.21. MS, m/z (%): 406 (M⁺, 80).

N-(2-Phenethyloxy)-7,8-dimethoxy[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-N’-(1-phenyl-ethylidene)-hydrazine (11d). ¹H-NMR (DMSO-d₆): δ 3.01 (s, 3H, OCH₃), 3.17 (t, J = 7.74 Hz, 2H, OCH₂CH₂Ph), 3.34 (s, 3H, CH₃-ethylidene), 3.83 (s, 3H, OCH₃), 4.77 (t, J = 7.71 Hz, 2H, OCH₂CH₂Ph), 7.25-8.55 (m, 12H, Ar-H), 9.91 (s, 1H, NH). ¹³C-NMR: 12.71, 35.10, 51.11, 56.43, 69.79, 110.73, 114.62, 116.73, 124.65, 125.33, 126.23, 128.11, 129.20, 131.11, 131.58, 132.27, 135.78, 139.52, 141.32, 145.34, 152.20, 161.57. MS, m/z (%): 482 (M⁺, 64).

3.2.8. Synthesis of compounds 12a,b

A mixture of 10 (0.5 mmol) and 1,1'-carbonyldiimidazole (0.6 mmol) was refluxed in absolute toluene (7 mL) for 3 h. The solvent was removed under reduced pressure and the residue was treated with CHCl₃. The resulting solid was separated by filtration and recrystallized from EtOH.

2-Allyloxy-8-methyl-bis[1,2,4]triazolo[1,5-a:4',3'-c]quinazolin-3-one (12a). IR (cm⁻¹): ν 1,702 (C=O). ¹H-NMR (DMSO-d₆): δ 3.01 (s, 3H, CH₃), 4.60 (d, J = 5.54 Hz, 2H, CH₂=CHCH₂), 5.20-5.39 (m, 2H, CH₂=CHCH₂), 6.10-6.18 (m, 1H, CH₂=CHCH₂), 7.31-7.92 (m, 3H, Ar-H), 12.24 (s, 1H, NH). ¹³C-
NMR: 24.74, 65.09, 114.92, 125.12, 127.64, 129.03, 131.23, 135.66, 136.76, 148.73, 157.43, 168.37. MS, m/z (%): 296 (M⁺, 75).

2-Benzylxy-7,8-dimethoxy-bis[1,2,4]triazolo[1,5-a:4',3'-c]quinazolin-3-one (12b). IR (cm⁻¹): ν 1,711 (C=O). ¹H-NMR (DMSO-d₆): δ 3.75 (s, 3H, OCH₃), 4.03 (s, 3H, OCH₃), 5.41 (s, 2H, OCH₂Ph), 7.38-8.22 (m, 7H, Ar-H), 12.87 (s, 1H, NH). ¹³C-NMR: 54.76, 56.65, 70.53, 70.53, 110.38, 114.59, 120.67, 124.87, 128.48, 133.33, 134.30, 134.86, 147.67, 153.38, 156.80, 168.62. MS, m/z (%): 392 (M⁺, 82).

3.2.9. Synthesis of compounds 13a,b

A mixture of 10 (0.5 mmol) and CS₂ (2.5 mmol) in pyridine (5 mL) was refluxed for 2 h. After cooling, the mixture was poured into ice/water, the yellow precipitate was filtered off, washed with water and recrystallized from MeOH.

2-Benzylxy-7,8-dimethoxy-bis[1,2,4]triazolo[1,5-a:4',3'-c]quinazolin-3-thione (13a). ¹H-NMR (DMSO-d₆): δ 3.88 (s, 3H, OCH₃), 4.43 (s, 3H, OCH₃), 5.11 (s, 2H, OCH₂Ph), 7.43-8.18 (m, 7H, Ar-H), 14.60 (s, 1H, NH). ¹³C-NMR: 49.06, 55.78, 71.52, 112.05, 115.19, 124.16, 125.63, 126.87, 128.34, 128.83, 133.33, 134.42, 136.15, 142.06, 157.12, 163.17, 185.73. MS, m/z (%): 408 (M⁺, 90).

8-Methyl-2-methylsulfanyl-bis[1,2,4]triazolo[1,5-a:4',3'-c]quinazolin-3-thione (13b). ¹H-NMR (DMSO-d₆): δ 2.82 (s, 3H, CH₃), 3.90 (s, 3H, SCH₃) 7.74-8.15 (m, 3H, Ar-H), 14.68 (s, 1H, NH). ¹³C-NMR: 13.72, 24.60, 114.75, 115.23, 126.57, 129.53, 135.0, 136.32, 148.91, 159.94, 162.30, 185.05. MS, m/z (%): 302 (M⁺, 83).

3.2.10. Synthesis of compounds 14a,b

A mixture of 9 (1 mmol) and the corresponding carbohydrazide (2.2 mmol) was refluxed in toluene (10 mL) for 2.5 h. After cooling, the solid was collected by filtration. Analytically pure products 14a,b were obtained by recrystallization from MeOH.

8-Methyl-N-(2-methylsulfanyl[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-benzohydrazide (14a). IR (cm⁻¹): ν 1,660 (C=O), 3,184 (NH). ¹H-NMR (DMSO-d₆): δ 2.98 (s, 3H, CH₃), 4.01 (s, 3H, SCh₃), 7.53-8.51 (m, 8H, Ar-H), 10.39 (s, 1H, NH), 10.97 (s, 1H, NH). ¹³C-NMR: 13.78, 25.67, 109.83, 114.88, 124.93, 125.29, 127.41, 127.99, 128.87, 129.07, 132.21, 132.81, 133.04, 135.09, 157.07, 168.00. MS, m/z (%): 364 (M⁺, 92).

8-Methyl-N-(2-methylsulfanyl[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-isonicotinichydrazide (14b). IR (cm⁻¹): ν 1,673 (C=O), 3,207 (NH). ¹H-NMR (DMSO-d₆): δ 3.08 (s, 3H, CH₃), 3.94 (s, 3H, SCh₃), 7.65-8.50 (m, 7H, Ar-H), 10.66 (s, 1H, NH), 11.14 (s, 1H, NH). ¹³C-NMR: 13.56, 24.69, 109.70, 114.94, 121.73, 124.88, 125.36, 128.45, 132.20, 135.21, 139.74, 150.94, 155.50, 164.82. MS, m/z (%): 365 (M⁺, 76).
3.2.11. Synthesis of compounds 15a,b

A mixture of 9 (1 mmol) and benzyl carbazate or ethyl carbazate (2.2 mmol) was refluxed in benzene (10 mL) for 2.5 h. The solvent was removed under reduced pressure, the resulting solid was filtered off and recrystallized from MeOH.

Ethyl-N-(2-allyloxy-8-methyl[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-hydrazine-carboxylate (15a). IR (cm⁻¹): ν 1708 (C=O), 3198 (NH). ¹H-NMR (DMSO-d₆): δ 1.13 (t, J = 7.61 Hz, 3H, OCH₂CH₃), 2.87 (s, 3H, CH₃), 4.08 (q, J = 10.12 Hz, 2H, OC₂H₂CH₃), 4.60 (d, J = 5.54 Hz, 2H, CH₂=CHCH₂), 5.07-5.19 (m, 2H, CH₂=CHCH₂), 6.06-6.13 (m, 1H, CH₂=CHCH₂) 7.54-7.93 (m, 3H, Ar-H), 9.50 (s, 1H, NH), 10.34 (s, 1H, NH). ¹³C-NMR: 14.92, 23.89, 57.33, 63.75, 109.26, 114.60, 124.79, 126.21, 127.07, 134.70, 156.69, 169.23. MS, m/z (%): 342 (M⁺, 80).

Benzyl-N-(8-methyl-2-methylsulfanyl[1,2,4]triazolo[1,5-a]quinazolin-5-yl)-hydrazine-carboxylate (15b). IR (cm⁻¹): ν 1718 (C=O), 3261 (NH). ¹H-NMR (DMSO-d₆): δ 3.74 (s, 3H, CH₃), 4.11 (s, 3H, SCH₃), 5.35 (s, 2H, OC₂H₂Ph), 7.25-8.43 (m, 8H, Ar-H), 9.88 (s, 1H, NH), 10.44 (s, 1H, NH). ¹³C-NMR: 13.54, 25.03, 66.48, 109.62, 114.85, 124.75, 125.25, 126.54, 128.81, 135.11, 135.33, 136.98, 152.74, 157.10, 168.42. MS, m/z (%): 394 (M⁺, 100).

3.2.12. Synthesis of compounds 16a,b

A mixture of 14 (0.5 mmol) and POCl₃ (5 mL) was refluxed at 100°C for 2 h. After cooling, the excess of POCl₃ was removed under reduced pressure and the residue was treated with saturated aqueous solution of K₂CO₃ under ice cooling. The resulting solids were collected by filtration and recrystallized from MeOH to afford 16a,b as colored pure products.

8-Methyl-2-methylsulfanyl-bis[1,2,4]triazolo[1,5-a:4',3'-c]quinazoline (16a). ¹H-NMR (DMSO-d₆): δ 3.33 (s, 3H, CH₃), 3.91 (s, 3H, SCH₃), 7.74-8.48 (m, 8H, Ar-H). ¹³C-NMR: 13.65, 24.06, 111.94, 115.17, 124.56, 126.12, 127.09, 128.35, 129.80, 130.59, 131.09, 141.82, 143.67, 149.47, 167.34. MS, m/z (%): 346 (M⁺, 82).

8-Methyl-2-methylsulfanyl-3-pyridyl-bis[1,2,4]triazolo[1,5-a:4',3'-c]quinazoline (16b). ¹H-NMR (DMSO-d₆): δ 3.66 (s, 3H, CH₃), 4.19 (s, 3H, SCH₃), 7.53-8.41 (m, 7H, Ar-H). ¹³C-NMR: 13.42, 25.03, 111.24, 115.23, 124.39, 125.75, 128.21, 129.33, 131.16, 133.35, 142.52, 145.67, 150.03, 161.24. MS, m/z (%): 347 (M⁺, 95).

3.2.13. Synthesis of compounds 17a-c

A mixture of 9 (1 mmol) and NaN₃ (1.2 mmol) in absolute DMF (5 mL) was heated at 90 °C for 24 h. After cooling, the reaction mixture was poured into water and saturated with brine solution. The resulting solid was filtered off, dried and recrystallized from MeOH.

8-Methyl-2-methylsulfanyl-tetrazolo[4,3-c][1,2,4]triazolo[1,5-a]quinazoline (17a). ¹H-NMR (DMSO-d₆): δ 3.32 (s, 3H, CH₃), 3.99 (s, 3H, SCH₃), 7.48-7.95 (m, 3H, Ar-H). ¹³C-NMR: 13.89, 24.67, 114.67, 116.23, 125.81, 128.27, 134.74, 136.49, 145.01, 157.32, 167.54. MS, m/z (%): 271 (M⁺, 77).
2-Benzylx-7,8-dimethoxy-tetrazolo[4,3-c][1,2,4]triazolo[1,5-a]quinazoline (17b). $^1$H-NMR (DMSO-d$_6$): $\delta$ 3.48 (s, 3H, OCH$_3$), 4.50 (s, 3H, OCH$_3$), 5.75 (s, 2H, OCH$_2$Ph), 7.44-8.28 (m, 7H, Ar-H). $^{13}$C-NMR: 45.98, 51.72, 71.57, 109.58, 115.08, 125.5, 127.72, 128.23, 130.36, 134.21, 134.53, 135.47, 148.17, 160.43, 167.16. MS, m/z (%): 377 (M$^+$, 90).

7,8-Dimethoxy-2-phenethyloxy-tetrazolo[4,3-c][1,2,4]triazolo[1,5-a]quinazoline (17c). $^1$H-NMR (DMSO-d$_6$): $\delta$ 3.42 (t, $J = 7.50$ Hz, 2H, OCH$_2$CH$_2$Ph), 3.62 (s, 3H, OCH$_3$), 4.53 (s, 3H, OCH$_3$), 4.79 (t, $J = 7.51$ Hz, 2H, OCH$_2$CH$_2$Ph), 7.23-8.67 (m, 7H, Ar-H). $^{13}$C-NMR: 41.43, 44.76, 64.83, 71.21, 115.57, 124.39, 126.10, 126.87, 127.56, 128.80, 129.35, 130.23, 134.99, 138.27, 142.32, 156.34, 167.54. MS, m/z (%): 391 (M$^+$, 100).

3.2.14. Synthesis of compounds 18a,b

A mixture of 9 (1 mmol) and 3-aminothiophene-2-methylcarboxylic acid ester (2.2 mmol) in absolute dioxane (10 mL) was refluxed in the presence of NaH (0.4 mmol) for 21 h. The solvent was removed under reduced pressure and the residue was treated with water and MeOH. The resulting solid was filtered off and dried.

8-Methyl-2-pentyloxy-(3H-thieno[3,2-d]pyrimidin-4-one[4,3-c][1,2,4]triazolo[1,5-a]quinazoline (18a). IR (cm$^{-1}$): $\nu$ 1,677 (C=O). $^1$H-NMR (DMSO-d$_6$): $\delta$ 0.73 (t, $J = 7.54$ Hz, 3H, OCH$_2$CH$_2$CH$_2$CH$_2$CH$_3$), 1.14-1.20 (m, 4H, OCH$_2$CH$_2$CH$_2$CH$_2$CH$_3$), 1.48-1.67 (m, 2H, OCH$_2$CH$_2$CH$_2$CH$_2$CH$_3$), 2.87 (s, 3H, CH$_3$), 4.08 (t, $J = 7.60$ Hz, 2H, OCH$_2$CH$_2$CH$_2$CH$_2$CH$_3$), 6.78-8.35 (m, 5H, Ar-H). $^{13}$C-NMR: 14.63, 22.18, 24.65, 27.69, 28.63, 69.35, 114.82, 123.71, 124.25, 124.80, 134.33, 134.89, 147.72, 153.60, 167.84. MS, m/z (%): 393 (M$^+$, 61).

7,8-Dimethoxy-2-phenethyloxy-(3H-thieno[3,2-d]pyrimidin-4-one[4,3-c][1,2,4]triazolo[1,5-a]-quinazoline (18b). IR (cm$^{-1}$): $\nu$ 1,670 (C=O). $^1$H-NMR (DMSO-d$_6$): $\delta$ 3.67 (s, 3H, OCH$_3$), 3.90 (t, $J = 7.61$ Hz, 2H, OCH$_2$CH$_2$Ph), 4.31 (s, 3H, OCH$_3$), 4.60 (t, $J = 7.63$ Hz, 2H, OCH$_2$CH$_2$Ph), 6.38-8.15 (m, 9H, Ar-H). $^{13}$C-NMR: 36.40, 40.61, 54.70, 63.57, 109.08, 116.08, 124.25, 127.02, 128.13, 128.75, 131.36, 131.93, 133.23, 133.91, 134.53, 135.47, 148.17, 160.43, 167.16. MS, m/z (%): 473 (M$^+$, 70).

4. Conclusions

In summary, the obtained [1,2,4]triazolo[1,5-a]quinazolin-5-ones 5a-h have been used successfully as valuable intermediates in the syntheses of various multifunctional heterocyclic systems. The biological properties of the prepared compounds are still under investigation and will be reported elsewhere.

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*Sample Availability*: Samples of the compounds **5-18** are available from the author.

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