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NOVEL SYNTHESIS OF 2-ALKOXY(ARALKOXY)-5-CHLORO[1,2,4]TRIAZOLO[1,5-*a*]QUINAZOLINES AND THEIR DERIVATIVES

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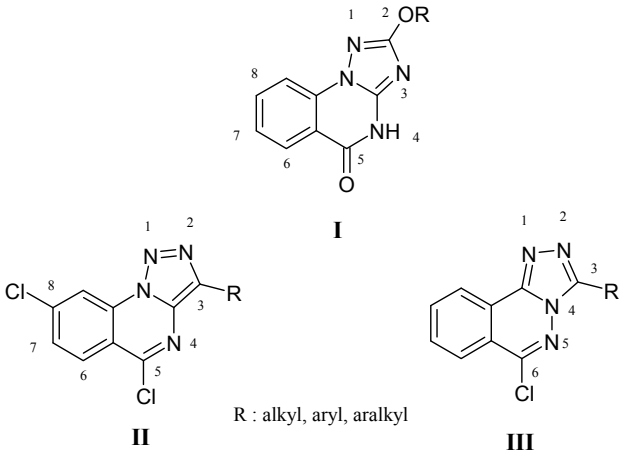
Abstract – 2-Alkoxy(aralkoxy)-5-chloro[1,2,4]triazolo[1,5-*a*]quinazolines have been synthesized. The corresponding 2-alkoxy(aralkoxy)[1,2,4]triazolo[1,5-*a*]quinazolin-5-ones were chlorinated with either oxalyl chloride or phosphorus oxychloride. The chlorine atom at 5-position of the targeted [1,2,4]triazolo[1,5-*a*]quinazolines was replaced with multifunctional *N*-nucleophiles. This provided the preparation of the heterocyclic system bearing a variety of substituents at 5-position.

INTRODUCTION

We have already reported that, the alkylated derivatives of novel 2-alkoxy(aralkoxy)[1,2,4]triazolo[1,5-*a*]quinazolin-5-ones (**I**) have been proven as excellent agents for controlling the plant growth diseases caused by fungal pathogen.[1] It has been demonstrated that subject of electron withdrawing atoms or groups in ring positions 5, 6 and 8 of the [1,2,3]triazolo[1,5-*a*]quinazolines (**II**) or [1,2,4]triazolo[3,4-*a*]phthalazines (**III**) enhances strongly the binding affinity towards benzodiazepine and adenosine A_1, A_{2A} receptors.[2,3]

This work has done in continuation of our program with the aim of obtaining an interesting series of chlorinated [1,2,4]triazolo[1,5-*a*]quinazoline compounds which was not only expected to be a valuable compound by further nucleophilic displacement reactions but also may contribute as a pharmacophore to the bioactivity of **I.**



I **II** **III**

RESULTS AND DISCUSSION

The synthetic strategy is outlined in Scheme 1. First, the 5-chloro[1,2,4]triazolo[1,5-*a*]quinazolines **2** required as our key starting materials were synthesized by chlorination of the corresponding **I** (previously prepared by condensation reaction of *N*-cyanoimidocarbonates with hydrazinobenzoic acid)[4] with either oxalyl chloride in boiling 1,1,2-trichloroethane for 19 h or with phosphorus oxychloride in boiling benzene for 2 h, followed by trituration with a saturated aqueous solution of potassium carbonate.[5] Although both methods gave acceptable yields, the reaction of **I** with phosphorus oxychloride is more advantageous with regard to short reaction time and higher yields (Table 1).

The formation of **2** was accompanied by the gradual disappearance of the characteristic (C=O) band of **I** at 1685-1705 cm^{-1}. The structure of the novel 5-chloro[1,2,4]triazolo[1,5-*a*]quinazolines **2** was confirmed by IR, ^{1}H NMR, ^{13}C NMR spectra and microanalyses.

Hydrazinolysis of **2** in refluxing ethanol were formed the corresponding [1,2,4]triazolo[1,5-*a*]quinazolin-5-yl-hydrazines **3a-f** in good yields of 60-78%,[6] which upon treatment with equimolar amout of aldehyde or ketone furnished the targeted hydrazones **4a-d** in 70-83%.[7]

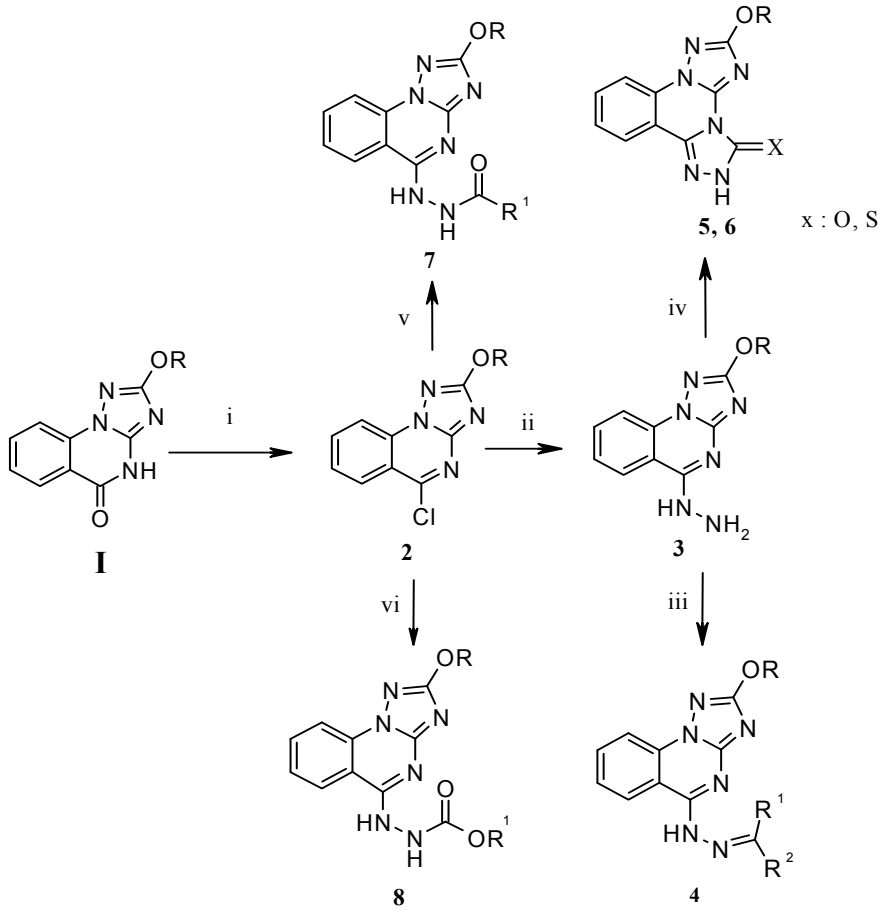
Reaction of **3b,e** with 1,1′-carbonyldiimidazole in a molar ratio of 1:1.2 in boiling absolute toluene for 3 h provided the until hitherto unknown bis[1,2,4]triazolo[1,5-*a*:4′,3′-*c*]quinazolin-3-ones **5a,b** in 45-50% yield.[8] Similarly, the corresponding thioxo derivatives **6a,b** could be obtained in 56-61% yield [9] from the reaction of **3e,f** with carbon disulfide in a molar ratio of 1:10 in boiling pyridine for 2 h. The IR spectra of **5a,b** display strong (C=O) absorption bands at 1705 and 1709 cm^{-1}, and the ^{13}C NMR spectra of **6a,b** are characterized by a (C=S) resonance at 185.00 and 185.7 ppm.

Replacement of the chlorine in compounds **2** by different hydrazides occurred smoothly in refluxing toluene to produce the [1,2,4]triazoloquinazolin-5-yl-carbohydrazides **7a-e** in 65-76% yield,[10] which as

themselves deserve interest as suitable intermediates and furthermore should open access to a number of triazolo-annelated compounds such as bis[1,2,4]triazoloquinazolines.

Analogously to the reaction with hydrazides, the corresponding reaction of compounds **2** with carbazates according to literature[10] produced the respective [1,2,4]triazoloquinazolin-5-yl-hydrazine carboxylic acid esters of type **8a-d** in 73-80 % yield as colorless solids.

The IR spectra of **7a-f** are characterized by a strong (C=O) absorption band at 1660-1670 and a weak (NH) band at 3189-3210 cm^{-1} respectively, while compounds **8a-d** display a strong (C=O) absorption band at 1706-1718 and a weak (NH) absorption band at 3198-3261 cm^{-1}.



R, R^1, R^2, : alkyl, aryl, aralkyl

i : $POCl_3$, benzene or oxalyl chloride, 1,1,2 trichloroethane ii: hydrazine hydrate, EtOH iii: aldehyde or ketone, EtOH iv : carbonyl diimidazole, toluene or CS_2 , pyridine v : hydrazides, toluene vi: carbazates, benzene.

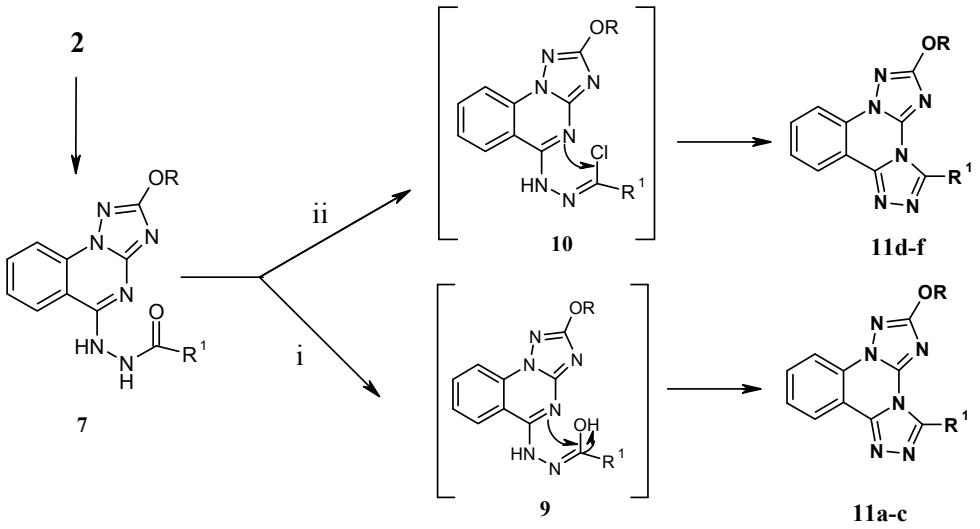
Scheme 1. Reaction of chlorinated triazoloquinazolines 2 with multifunctional N-nucleophiles

Table 1. Synthesis of 5-chloro[1,2,4]triazolo[1,5-*a*]quinazolines and derivatives

Compound	R	R^1	R^2	Yield (%)
2a	Me	-	-	80
2b	Et	-	-	89
2c	CH_2=$CHCH_2$-	-	-	87
2d	$CH_3CH_2CH_2CH_2CH_2$-	-	-	81
2e	$C_6H_5CH_2$-	-	-	90
2f	$C_6H_5CH_2CH_2$-	-	-	91
3a	Me	-	-	60
3b	Et	-	-	69
3c	CH_2=$CHCH_2$-	-	-	71
3d	$CH_3CH_2CH_2CH_2CH_2$-	-	-	62
3e	$C_6H_5CH_2$-	-	-	78
3f	$C_6H_5CH_2CH_2$-	-	-	72
4a	Me	Me	Me	70
4b	$C_6H_5CH_2$-	Me	Me	73
4c	$C_6H_5CH_2CH_2$-	H	C_6H_5	79
4d	$C_6H_5CH_2CH_2$-	Me	C_6H_5	68
5a	Et	-	-	45
5b	$C_6H_5CH_2$-	-	-	50
6a	$C_6H_5CH_2$-	-	-	61
6b	$C_6H_5CH_2CH_2$-	-	-	56
7a	Me	Me	-	67
7b	Me	C_6H_5	-	71
7c	Me	3-pyridyl	-	65
7d	Et	C_6H_5	-	68
7e	Et	3-pyridyl	-	70
7f	$C_6H_5CH_2$-	Me	-	76
8a	Me	Et	-	73
8b	Me	$C_6H_5CH_2$-	-	75
8c	Et	Et	-	74
8d	Et	$C_6H_5CH_2$-	-	80

After having successfully elaborated the synthesis of the carbohydrazides **7a-f,** our interest arose wether these compounds could be cyclo-condensed to the novel bis[1,2,4]triazoloquinazolines of type **11**. Actually, when **2a,b,f** were treated with acylhydrazines in a molar ratio of 1:2 in absolute toluene, the primarily formed acylamidrazones **9** (Scheme 2) underwent smoothly a base-catalyzed cyclization to provide the corresponding bis[1,2,4]triazolo[1,5-*a*:4′,3′-*c*]quinazolines **11**.[10] This approach proved to be

successful for the preparation of **11a-c** (Table 2) but failed in the case of **11d-f**. Therefore, the amidrazones **7b,c,d** were treated with phosphorus oxychloride at refluxing temperature for 2 h to furnish the respective intermediates **10**, which upon subsequent neutralization with saturated aqueous potassium carbonate solution or aqueous ammonia delivered the targeted **11d-f**.[11] The completion of the internal cyclization was monitored by IR spectroscopy: disappearence of the (C=O) and (NH) absorption bands at 1650-1670, 3173-3194 cm^{-1} signaled complete conversion of **9** or **10** to the tetracyclic compounds **11**. In addition, the structure of compound **11b** has been unambiguously proven by X-ray crystallography (Figure 1).



R, R^1 : alkyl, aryl, aralkyl

i: toluene, NaH ii: $POCl_3$

Scheme 2. Synthesis of tetracyclic systems of type 11

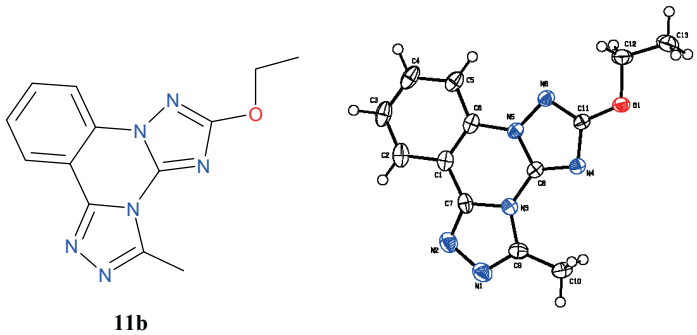


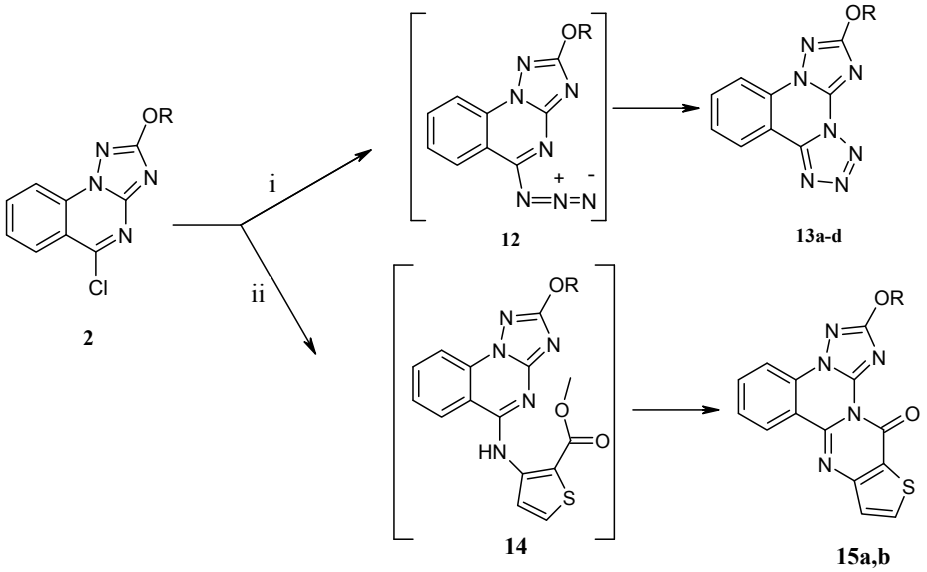
Figure 1

Table 2. Synthesis of tetracyclic and pentacyclic systems

Compound	R	R^1	Yield (%)
11a	Et	H	50
11b	Et	Me	55
11c	$C_6H_5CH_2CH_2$-	H	51
11d	Et	C_6H_5	68
11e	Me	C_6H_5	75
11f	Me	3-pyridyl	77
13a	Me	-	54
13b	Et	-	53
13c	$C_6H_5CH_2$-	-	51
13d	$C_6H_5CH_2CH_2$-	-	60
15a	$CH_3CH_2CH_2CH_2CH_2$-	-	81
15b	$C_6H_5CH_2$-	-	69

Treatment of 5-chloro[1,2,4]triazoloquinazolines **2a,b,e,f** with sodium azide in a molar ratio of 1:1.2 in absolute dimethyl formamide for 24 h at 90 ^oC, furnished the aimed tetrazolo[4,3-*c*][1,2,4]triazolo[1,5-*a*]quinazolines **13a-d** via the (not isolated) intermediates **12** as colorless solids in 51-60% yield[12] (Scheme 3). Furthermore, treatment of **3** with nitrous acid at -5 ^oC for 30-40 min afforded also the tetrazole products **13** in 53-58% yield.[10] The beforementioned facile nucleophilic displacement of the chlorine atom in **2** prompted us to investigate the reaction of **2** with methyl 3-aminothiophene-2-carboxylate, which theoretically should provide access to the novel pentacyclic compounds of type **15**. In fact, when **2d,e** 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 targeted **15a,b** could be isolated from the reaction mixture in 69 and 81% yield (Scheme 3).[10] The IR spectra of compounds **15a,b** are characterized by a (C=O) stretching at 1670 and 1667 cm^{-1} respectively.

In conclusion, replacement of the chlorine atom in the targeted compounds by different nucleophiles has been achieved successfully and provided access to a series of tetracyclic, pentacyclic systems and a variety of open chained derivatives.



i : NaN_3, toluene, ii : methyl-3-aminothiophene-2-carboxylate, dioxane

Scheme 3. Synthesis of novel tetracyclic and pentacyclic systems of types 13 and 15

EXPERIMENTAL

Melting points were determined on open glass capillaries using a Mettler FP 62 apparatus and are uncorrected. Elemental analyses were carried out with a Heraeus CHN-O-Rapid Instrument. The IR (KBr) spectra were recorded on a Shimadzu FT-IR 8300. ^{1}H-NMR (400.1 MHz) and ^{13}C-NMR 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 using 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/$UV_{254,}$ from the Macherey-Nagel Firm, Duren Thickness: 0.25 m. Column chromatography was conducted on silica gel (ICN Silica 100-200, active 60 Å).

General procedure for the synthesis of 2-Alkoxy(aralkoxy)-5-chloro[1,2,4]triazolo[1,5-*a*]quinazolines (2a-f).

Method A: Compound **I** (2 mmol) was heated with oxalyl chloride (6 mmol) in 1,1,2-trichloroethane (12 mL) for 19 h at 105 ^{o}C. The solution was cooled and MeOH (0.2 mL) was added dropwise. The obtained solid was filtered, washed with hexane, dried and recrystallized from THF-hexane.

Method B: Compound **I** (1 mmol) was heated with $POCl_3$ (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.

5-Chloro-2-methoxy[1,2,4]triazolo[1,5-*a*]quinazoline (2a): This compound obtained as white solid with 0.187 g (80%). mp 146-148 °C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 3.99 (s, 3H), 7.48-8.15 (m, 4H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 57.16, 114.20, 116.83, 125.51, 128.57, 135.74, 136.19, 141.11, 159.90, 168.26; MS m/z: $(234)^+$; Anal. Calcd for $C_{10}H_7ClN_4O$ (234.65): C 51.19, H 3.01, N 23.88. Found: C 51.12, H 3.18, N 23.98.

5-Chloro-2-ethoxy[1,2,4]triazolo[1,5-*a*]quinazoline (2b): This compound obtained as white solid with 89% (0.220 g). mp 131-134 °C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.37 (t, 3H, J = 7.07 Hz), 4.34 (q, 2H, J = 14.13 Hz), 7.49-8.15 (m, 4H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 14.83, 65.67, 114.17, 116.75, 125.52, 128.80, 135.18, 136.13, 142.20, 159.92, 167.38; MS m/z: $(248)^+$; Anal. Calcd for $C_{11}H_9ClN_4O$ (248.67): C 53.13, H 3.65, N 22.53. Found: C 53.33, H 3.98, N 22.33.

2-Allyloxy-5-chloro[1,2,4]triazolo[1,5-*a*]quinazoline (2c): This compound obtained as yellow solid with 0.226 g (87%). mp 113-115 °C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 4.86 (d, 2H, J = 6.53 Hz), 5.42-5.65 (m, 2H), 6.15-6.20 (m, 1H), 7.48-8.04 (m, 4H); ^{13}C-NMR (DMSO-d_6): δ 70.32, 115.17, 117.44, 118.80, 127.13, 128.17, 134.10, 135.30, 135.62, 137.19, 159.11, 167.90; MS m/z: $(260)^+$; Anal. Calcd for $C_{12}H_9ClN_4O$ (260.68): C 55.29, H 3.48, N 21.49. Found: C 54.94, H 3.67, N 21.09.

5-Chloro-2-pentyloxy[1,2,4]triazolo[1,5-*a*]quinazoline (2d): This compound obtained as pale brown solid with 0.234 g (81%). mp 108-110 °C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 0.96 (t, 3H, J = 7.45 Hz), 1.37-1.47 (m, 4H), 1.83-1.89 (m, 2H), 4.43 (t, 2H, J = 7.60 Hz), 7.45-8.16 (m, 4H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 13.75, 21.70, 27.35, 28.16, 69.52, 114.70, 116.81, 126.54, 127.95, 135.57, 136.63, 155.33, 166.57; MS m/z: $(290)^+$; Anal. Calcd for $C_{14}H_{15}ClN_4O$ (290.75): C 57.83, H 5.20, N 19.27. Found: C 57.93, H 5.29, N 18.98**.**

2-Benzyloxy-5-chloro[1,2,4]triazolo[1,5-*a*]quinazoline (2e): This compound obtained as white solid with 0.279 g (90%). mp 128-130 °C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.79 (s, 2H), 7.37-8.45 (m, 9H), ^{13}C-NMR (100 MHz, DMSO-d_6): δ 71.34, 115.20, 117.42, 125.50, 126.71, 127.14, 128.07, 128.70, 132.41, 135.90, 136.11, 136.77, 155.93, 165.25; MS m/z: $(310)^+$; Anal. Calcd for $C_{16}H_{11}ClN_4O$ (310.75): C 61.84, H 3.57, N 18.03. Found: C 61.80, H 3.82, N 17.88.

5-Chloro-2-phenethyloxy[1,2,4]triazolo[1,5-*a*]quinazoline (2f): This compound obtained as white solid with 0.294 g (91%). mp 137-140 °C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 3.15 (t, 2H, J = 7.50 Hz), 4.65 (t, 2H, J = 7.51 Hz), 7.22-8.37 (m, 9H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 35.09, 69.61, 114.59, 124.40, 124.83, 126.72, 128.74, 129.30, 134.29, 134.94, 138.49, 153.37, 156.84, 168.61; MS m/z: $(324)^+$; Anal.

Calcd for $C_{17}H_{13}ClN_4O$ (324.77): C 62.87, H 4.03, N 17.25. Found: C 62.57, H 4.22, N 17.15.

General procedure for the synthesis of 2-Alkoxy(aralkoxy)[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl-hydrazines (3a-f): Compound **2** (1 mmol) was heated under reflux with hydrazine hydrate (5 mmol) in EtOH (8 mL) for 3 h. After cooling, the precipitate was filtered off and washed with water. Recrystallization from EtOH afforded **3a-f** as colored pure solids.

2-Methoxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl-hydrazine (3a): This compound obtained as white solid with 0.138 g (60%). mp 233-235 ^oC; IR (KBr) ν max cm^{-1}: 3205, 3250; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 3.98 (s, 3H), 4.94 (s, 2H), 7.47-8.30 (m, 4H), 9.37 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 56.48, 114.48, 124.40, 124.77, 125.40, 127.35, 134.24, 134.98, 153.51, 169.23; MS m/z: $(230)^+$; Anal. Calcd for $C_{10}H_{10}N_6O$ (230.23): C 52.17, H 4.38, N 36.50. Found: C 52.46, H 4.25, N 36.15.

2-Ethoxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl-hydrazine (3b): This compound obtained as white solid with 0.168 g (69%). mp 215-218 ^oC; IR (KBr) ν max cm^{-1}: 3189, 3231; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.30 (t, 3H, J = 7.07 Hz), 4,37 (q, 2H, J = 14.13 Hz), 4.65 (s, 2H), 7.49-8.15 (m, 4H), 9.42 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 14.73, 65.61, 114.12, 116.45, 125.62, 128.43, 135.13, 136.29, 142.38, 159.82, 167.92; MS m/z: $(244)^+$; Anal. Calcd for $C_{11}H_{12}N_6O$ (244.26): C 54.09, H 4.95, N 34.41. Found: C 54.37, H 5.12, N 34.27.

2-Allyloxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl-hydrazine (3c): This compound obtained as yellow solid with 0.181 g (71%). mp 220-223 ^oC; IR (KBr) ν max cm^{-1}: 3210, 3267; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 4.81 (s, 2H), 4.85 (d, 2H, J = 5.30 Hz), 5.29-5.43 (m, 2H), 6.06-6.12 (m, 1H) 7.47-8.30 (m, 4H), 9.90 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 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: $(256)^+$; Anal. Calcd for $C_{12}H_{12}N_6O$ (256.27): C 56.24, H 4.72, N 32.79. Found: C 56.50, H 4.54, N 32.93.

2-Pentyloxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl-hydrazine (3d): This compound obtained as white solid with 0.177 g (62%). mp 197-200 ^oC; IR (KBr) ν max cm^{-1}: 3183, 3256; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 0.94 (t, 3H, J = 7.40 Hz), 1.34-1.44 (m, 4H), 1.71-1.77 (m, 2H), 4.35 (t, 2H, J = 7.60 Hz), 4.93 (s, 2H), 7.55-8.17 (m, 4H), 9.98 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 14.23, 22.18, 27.89, 28.63, 69.05, 114.2, 124.41, 124.55, 124.70, 134.20, 134.99, 147.72, 153.90, 167.74; MS m/z: $(286)^+$; Anal. Calcd for $C_{14}H_{18}N_6O$ (286.34): C 58.73, H 6.34, N 29.35. Found: C 59.21, H 6.02, N 29.28.

2-Benzyloxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl-hydrazine (3e): This compound obtained as white solid with 0.238 g (78%). mp 213-215 ^oC; IR (KBr) ν max cm^{-1}: 3209, 3286; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 4.82 (s, 2H), 5.40 (s, 2H), 7.33-8.32 (m, 9H), 9.91 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-

d$_6$): δ 69.63, 113.85, 116.43, 118.20, 125.12, 128.15, 132.62, 135.30, 135.66, 147.34, 159.45, 166.93; MS m/z: $(306)^+$; Anal. Calcd for $C_{16}H_{14}N_6O$ (306.33): C 62.74, H 4.61, N 27.43. Found: C 62.54, H 4.43, N 27.24.

2-Phenethyloxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl-hydrazine (3f): This compound obtained as yellow solid with 0.230 g (72%). mp 187-190 °C; IR (KBr) ν max cm^{-1}: 3217, 3280; ^{1}H-NMR (400 MHz, DMSO-*d*$_6$): δ 3.40 (t, 2H, *J* = 7.70 Hz), 4.62 (t, 2H, *J* = 7.45 Hz), 4.95 (s, 2H), 7.20-8.24 (m, 9H), 9.94 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-*d*$_6$): δ 34.66, 69.13, 109.89, 114.12, 125.51, 126.8, 128.59, 128.74, 133.76, 134.75, 136.15, 138.30, 152.94, 156.35, 168.18; MS m/z: $(320)^+$; Anal. Calcd for $C_{17}H_{16}N_6O$ (320.36): C 63.74, H 5.03, N 26.23. Found: C 63.47, H 4.94, N 26.43.

General procedure for the synthesis of *N*-Alkylidene-*N*′-(2-alkoxy(aralkoxy)[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)hydrazine (4a-e):

A mixture of **3a,e,f (**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*′-(2-methoxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)hydrazine (4a):** This compound obtained as yellow solid with 0.189 g (70 %). mp 186-189 °C; ^{1}H-NMR (400 MHz, DMSO-*d*$_6$): δ 2.21 (s, 3H), 2.63 (s, 3H), 2.85 (s, 3H), 7.37-8.54 (m, 4H), 10.45 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-*d*$_6$): δ 13.80, 18.67, 25.27, 115.08, 124.90, 125.75, 126.06, 134.24, 134.96, 163.37, 164.54; MS m/z: $(270)^+$; Anal. Calcd for $C_{13}H_{14}N_6O$ (270.30): C 57.77, H 5.22, N 31.09. Found: C 57.52, H 4.94, N 31.42.

***N*′-(2-Benzyloxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)-*N*-isopropylidene-hydrazine (4b):** This compound obtained as yellow solid with 0.252 g (73%). mp 195-198 °C; ^{1}H-NMR (400 MHz, DMSO-*d*$_6$): δ 2.12 (s, 3H), 2.30 (s, 3H), 5.54 (s, 2H), 6.34 (s, 1H), 7.37-8.63 (m, 9H); ^{13}C-NMR (100 MHz, DMSO-*d*$_6$): δ 12.71, 13.43, 70.88, 103.16, 109.37, 114.05, 121.53, 124.69, 128.18, 128.46, 136.08, 136.74, 143.30, 150.85, 152.63, 169.21; MS m/z: $(346)^+$; Anal. Calcd for $C_{19}H_{18}N_6O$ (346.39): C 65.88, H 5.24, N 24.26. Found: C 65.73, H 4.98, N 24.31.

***N*-Benzylidene-*N*′-(2-phenethyloxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)hydrazine (4c):** This compound obtained as yellow solid with 0.322 g (79%). mp 215-218 °C; ^{1}H-NMR (400 MHz, DMSO-*d*$_6$): δ 3.12 (t, 2H, *J* = 7.34 Hz), 3.33 (s, 1H), 4.57 (t, 2H, *J* = 7.23 Hz), 7.25-8.55 (m, 14H), 11.83 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-*d*$_6$): δ 35.11, 69.79, 110.23, 114.12, 115.37, 124.65, 126.43, 127.54, 128.61, 129.20, 130.11, 131.58, 132.27, 135.78, 139.52, 141.32, 154.20, 168.97; MS m/z: $(408)^+$; Anal. Calcd for $C_{24}H_{20}N_6O$ (408.47): C 70.57, H 4.94, N 20.57. Found: C 70.29, H 5.14, N 20.41.

***N*′-(2-Phenethyloxy)[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)-*N*-(1-phenylethylidene)hydrazine (4d):**

This compound obtained as yellow solid with 0.286 g (68%). mp 198-203 ^{o}C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.87 (s, 3H), 3.43 (t, 2H, J = 7.74 Hz), 4.77 (t, 2H, J = 7.83 Hz), 7.25-8.55 (m, 14H), 9.91 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 14.65, 35.10, 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: $(422)^{+}$; Anal. Calcd for $C_{25}H_{22}N_6O$ (422.49): C 71.07, H 5.25, N 19.89. Found: C 70.81, H 5.01, N 20.28.

General procedure for the synthesis of 2-Alkoxy(aralkoxy)-bis[1,2,4]triazolo[1,5-*a*:4′,3′-*c*]quinazolin-3-ones (5a,b): A mixture of **3b,e** (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 $CHCl_3$. The resulting solid was separated by filtration and recrystallized from EtOH.

2-Ethoxy-bis[1,2,4]triazolo[1,5-*a*:4′,3′-*c*]quinazolin-3-one (5a): This compound obtained as white solid with 0.61 g (45%). mp 208-211 ^{o}C; IR (KBr) ν max cm^{-1}: 1709 ; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.47 (t, 3H, J = 7.24 Hz), 4.14 (q, 2H, J = 13.77 Hz), 7.31-7.92 (m, 4H), 12.24 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 13.73, 66.15, 114.63, 116.43, 125.12, 127.64, 135.66, 136.76, 147.73, 157.43, 168.37; MS m/z: $(270)^{+}$; Anal. Calcd for $C_{12}H_{10}N_6O_2$ (270.25): C 53.33, H 3.73, N 31.10. Found: C 53.68, H 4.02, N 30.89.

2-Benzyloxy-bis[1,2,4]triazolo[1,5-*a*:4′,3′-*c*]quinazolin-3-one (5b): This compound obtained as yellow solid with 0.83 g (50%). mp 203-206 ^{o}C; IR (KBr) ν max cm^{-1}: 1705; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.41 (s, 2H), 7.28-8.22 (m, 9H), 12.87 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 70.53, 110.38, 114.59, 120.67, 124.87, 128.48, 133.33, 134.30, 134.89, 136.89, 147.67, 153.38, 156.80, 168.62; MS m/z: $(332)^{+}$; Anal. Calcd for $C_{17}H_{12}N_6O_2$ (332.32): C 61.44, H 3.64, N 25.29. Found: C 61.58, H 3.40, N 25.42.

General procedure for the synthesis of 2-Aralkoxy-bis[1,2,4]triazolo[1,5-*a*:4′,3′-*c*]quinazolin-3-thiones (6a,b): A mixture of **3e,f** (0.5 mmol) and CS_2 (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-Benzyloxy-bis[1,2,4]triazolo[1,5-*a*:4′,3′-*c*]quinazolin-3-thione (6a): This compound obtained as yellow solid with 0.106 g (61%). mp 228-230 ^{o}C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.48 (s, 2H), 7.38-822 (m, 9H), 14.60 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 71.52, 112.05, 115.19, 124.16, 125.63, 126.87, 128.74, 128.83, 133.33, 134.42, 136.15, 142.06, 157.12, 163.17, 185.67; MS m/z: $(348)^{+}$; Anal. Calcd for $C_{17}H_{12}N_6OS$ (348.39): C 58.61, H 3.47, N 24.12, S 9.20. Found: C 58.37, H 3.42, N 24.43, S

8.93.

2-Phenethyloxy-bis[1,2,4]triazolo[1,5-*a*:4′,3′-*c*]quinazolin-3-thione (6b): This compound obtained as yellow solid with 0.102 g (56%). mp 192-195 °C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 3.25 (t, 2H, J = 7.82 Hz), 4.76 (t, 2H, J = 7.65 Hz), 7.10-8.45 (m, 9H), 14.54 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 34.45, 69.99, 114.23, 122.43, 125.83, 126.32, 128.28, 128.85, 131.75, 132.38, 135.86, 137.80, 145.64, 167.35, 184.98; MS m/z: $(362)^+$; Anal. Calcd for $C_{18}H_{14}N_6OS$ (362.42): C 59.66, H 3.89, N 23.19, S 8.85. Found: C 60.04, H 3.95, N 23.02, S 8.53.

General procedure for the synthesis of *N*-(2-Alkoxy(aralkoxy)[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)-carbohydrazides (7a-f): A mixture of **2a,b,e (**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 **7a-f** were obtained by recrystallization from MeOH.

***N*-(2-Methoxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)acetohydrazide (7a):** This compound obtained as white solid with 0.182 g (67%). mp 208-210 °C; IR (KBr) ν max cm^{-1}: 1669, 3206; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.02 (s, 3H), 4.00 (s, 3H), 7.58-8.42 (m, 4H), 10.17 (s, 1H), 10.31 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 12.07, 61.22, 109.71, 114.80, 124.06, 125.14, 134.98, 135.34, 152.81, 156.69, 166.23, 169.46; MS m/z: $(272)^+$; Anal. Calcd for $C_{12}H_{12}N_6O_2$ (272.27): C 52.94, H 4.44, N 30.87. Found: C 52.71, H 4.31, N 30.69.

***N*-(2-Methoxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)benzohydrazide (7b):** This compound obtained as white solid with 0.237 g (71%). mp 178-180 °C; IR (KBr) ν max cm^{-1}: 1665, 3193; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 3.98 (s, 3H), 7.53-8.51 (m, 9H), 10.52 (s, 1H), 10.81 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 56.67, 109.83, 114.88, 124.93, 125.29, 127.81, 127.99, 128.87, 129.07, 132.21, 132.81, 133.04, 135.09, 157.07, 169.44; MS m/z: $(334)^+$; Anal. Calcd for $C_{17}H_{14}N_6O_2$ (334.34): C 61.07, H 4.22, N 25.14. Found: C 61.35, H 4.34, N 24.90.

***N*-(2-Methoxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)isonicotinichydrazide (7c):** This compound obtained as white solid with 0.217 g (65%). mp 147-150 °C; IR (KBr) ν max cm^{-1}: 1668, 3210; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 3.98 (s, 3H), 7.65-8.50 (m, 8H), 10.66 (s, 1H), 11.14 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 65.69, 109.73, 114.94, 121.73, 124.88, 125.36, 128.45, 133.20, 135.21, 139.74, 150.94, 152.66, 155.50, 164.82; MS m/z: $(335)^+$; Anal. Calcd for $C_{16}H_{13}N_7O_2$ (335.33): C 57.31, H 3.91, N 29.24. Found: C 57.57, H 3.73, N 28.93.

***N*-(2-Ethoxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)benzohydrazide (7d):** This compound obtained as white solid with 0.236 g (68%). mp 160-164 °C; IR (KBr) ν max cm^{-1}: 1660, 3189; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.36 (t, 3H, J = 7.20 Hz), 4.35 (q, 2H, J = 13.99 Hz), 7.53-8.51 (m, 9H), 10.57 (s, 1H),

10.81 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 14.94, 65.16, 109.83, 114.88, 124.94, 125.26, 127.96, 128.96, 132.42, 132.81, 135.09, 135.36, 152.60, 157.04, 166.39, 168.73; MS m/z: $(348)^+$; Anal. Calcd for $C_{18}H_{16}N_6O_2$ (348.37): C 62.06, H 4.63, N 24.12. Found: C 62.30, H 4.52, N 23.95.

***N*-(2-Ethoxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)isonicotinichydrazide (7e):** This compound obtained as white solid with 0.244 g (70%). mp 170-173 °C; IR (KBr) ν max cm^{-1}: 1664, 3206; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.35 (t, 3H, J = 7.50 Hz), 4.38 (q, 2H, J = 14.04 Hz), 7.51-8.48 (m, 8H), 10.42 (s, 1H), 10.91 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 14.46, 64.80, 109.30, 114.45, 122.18, 122.70, 124.92, 134.79, 147.91, 148.92, 156.25, 163.54, 168.03; MS m/z: $(349)^+$; Anal. Calcd for $C_{17}H_{15}N_7O_2$ (349.35): C 58.45, H 4.33, N 28.07. Found: C 58.61, H 4.22, N 28.35.

***N*-(2-Benzyloxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)acetohydrazide (7f):** This compound obtained as yellow solid with 0.264 g (76%). mp 189-192 °C; IR (KBr) ν max cm^{-1}: 1670, 3197; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.27 (s, 3H), 5.66 (s, 2H), 7.59-8.76 (m, 9H), 10.48 (s, 1H), 10.59 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 12.09, 71.67, 114.88, 115.24, 124.78, 125.21, 127.67, 128.46, 128.80, 131.16, 135.60, 136.06, 137.08, 156.68, 168.72, 169.22; MS m/z: $(348)^+$; Anal. Calcd for $C_{18}H_{16}N_6O_2$ (348.37): C 62.06, H 4.63, N 24.12. Found: C 62.44, H 4.51, N 24.21.

General procedure for the synthesis of Alkyl(aralkyl)-*N*-(2-alkoxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)hydrazine carboxylate (8a-d): A mixture of **2a,b (**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-methoxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)hydrazine carboxylate (8a): This compound obtained as white solid with 0.220 g (73%). mp 127-130 °C; IR (KBr) ν max cm^{-1}: 1707, 3198; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.23 (t, 3H, J = 7.91 Hz), 4.00 (q, 2H, J = 10.12 Hz), 4.10 (s, 3H), 7.59-8.27 (m, 4H), 9.50 (s, 1H), 10.34 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 14.92, 57.33, 61.15, 109.71, 114.83, 124.75, 125.21, 127.07, 134.70, 135.06, 137.15, 156.69, 169.23; MS m/z: $(302)^+$; Anal. Calcd for $C_{13}H_{14}N_6O_3$ (302.29): C 51.65, H 4.67, N 27.80. Found: C 51.93, H 4.55, N 27.64.

Benzyl-*N*-(2-methoxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)hydrazine carboxylate (8b): This compound obtained as white solid with 0.273 g (75%). mp 197-200 °C; IR (KBr) ν max cm^{-1}: 1718, 3215; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 4.01 (s, 3H), 5.15 (s, 2H), 7.20-8.41 (m, 9H), 9.68 (s, 1H), 10.40 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 56.69, 66.98, 109.67, 114.85, 124.75, 125.25, 126.25, 128.54, 128.81, 135.11, 135.33, 136.98, 152.74, 157.10, 168.42; MS m/z: $(364)^+$; Anal. Calcd for $C_{18}H_{16}N_6O_3$ (364.37): C 59.34, H 4.43, N 23.06. Found: C 59.16, H 4.33, N 22.85.

Ethyl-*N*-(2-ethoxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)hydrazine carboxylate (8c): This compound obtained as white solid with 0.233 g (74%). mp 165-167 °C; IR (KBr) ν max cm^{-1}: 1710, 3261; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.30 (t, 3H, J = 7.75 Hz), 1.73 (t, 3H, J = 7.89 Hz), 4.20 (q, 2H, J = 14.04 Hz), 4.65 (q, 2H, J = 14.06 Hz), 7.50-8.40 (m, 4H), 9.89 (s, 1H), 10.54 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 14.70, 14.96, 61.15, 65.12, 114.84, 124.71, 125.18, 127.24, 128.11, 129.34, 131.87, 135.05, 151.12, 167.32; MS m/z: $(316)^+$; Anal. Calcd for $C_{14}H_{16}N_6O_3$ (316.32): C 53.16, H 5.10, N 26.57. Found: C 53.56, H 4.96, N 26.41.

Benzyl-*N*-(2-ethoxy[1,2,4]triazolo[1,5-*a*]quinazolin-5-yl)hydrazine-carboxylate (8d): This compound obtained as white solid with 0.302 g (80%). mp 119-122 °C; IR (KBr) ν max cm^{-1}: 1706, 3215; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.39 (t, 3H, J = 7.30 Hz), 4.40 (q, 2H, J = 14.20 Hz), 5.20 (s, 2H), 7.19-8.39 (m, 9H), 9.69 (s, 1H), 10.37 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 14.97, 65.16, 66.45, 109.66, 114.85, 124.71, 125.19, 128.08, 128.79, 135.07, 135.33, 136.99, 152.62, 156.90; MS m/z: $(378)^+$; Anal. Calcd for $C_{19}H_{18}N_6O_3$ (378.39): C 60.31, H 4.79, N 22.21. Found: C 60.04, H 4.90, N 22.21.

General procedure for the synthesis of 2-Alkoxy(aralkoxy)-3-alkyl-bis[1,2,4]triazolo[1,5-*a*:4′,3′-*c*]quinazolines (11a-c): A mixture of **2b,f** (1 mmol) and formohydrazide or acetohydrazide (2.2 mmol) was refluxed in absolute toluene (15 mL) in the presence of sodium hydride (0.8 mmol) for 14-20 h. The solvent was removed under reduced pressure, and the residue was crystallized from MeOH.

2-Ethoxy-bis[1,2,4]triazolo[1,5-*a*:4′,3′-*c*]quinazoline (11a): This compound obtained as yellow solid with 0.127 g (50%). mp 192-195 °C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.48 (t, 3H, J = 7.75 Hz), 4.48 (q, 2H, J = 14.12 Hz), 7.65-8.30 (m, 4H), 9.90 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 14.84, 66.37, 111.71, 115.18, 123.57, 124.77, 126.99, 134.34, 137.50, 142.17, 152.17, 164.25; MS m/z: $(254)^+$; Anal. Calcd for $C_{12}H_{10}N_6O$ (254.25): C 56.69, H 3.96, N 33.05. Found: C 57.11, H 4.17, N 33.30.

2-Ethoxy-3-methyl-bis[1,2,4]triazolo[1,5-*a*:4′,3′-*c*]quinazoline (11b): This compound obtained as yellow solid with 0.147 g (55%). mp 203-205 °C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.43 (t, 3H, J = 7.49 Hz), 2.89 (s, 3H), 4.46 (q, 2H, J = 14.97 Hz), 7.62-8.42 (m, 4H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 12.10, 14.70, 66.29, 111.99, 115.16, 124.38, 126.94, 131.07, 132.61, 146.83, 151.12, 162.17; MS m/z: $(268)^+$; Anal. Calcd for $C_{13}H_{12}N_6O$ (268.28): C 58.20, H 4.51, N 31.33. Found: C 58.87, H 4.40, N 31.49.

2-Phenethyloxy-bis[1,2,4]triazolo[1,5-*a*:4′,3′-*c*]quinazoline (11c): This compound obtained as yellow solid with 0.168 g (51%). mp 226-228 °C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 3.15 (t, 2H, J = 7.23 Hz), 4.64 (t, 2H, J = 7.13 Hz), 7.25-8.50 (m, 9H), 9.68 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 35.05, 69.43, 112.73, 119.68, 124.58, 126.79, 128.71, 129.27, 134.10, 138.51, 154.98, 167.32; MS m/z: $(330)^+$;

Anal. Calcd for $C_{18}H_{14}N_6O$ (330.35): C 65.45, H 4.27, N 25.44. Found: C 65.96, H 3.98, N 25.25.

General procedure for the synthesis of 2-Alkoxy(aralkoxy)-3-aryl-bis[1,2,4]triazolo[1,5-*a*:4′,3′-*c*]quinazolines (11d-f): A mixture of **7b,c,d** (0.5 mmol) and $POCl_3$ (5 mL) was refluxed at 100 °C for 2 h. After cooling, the excess of $POCl_3$ was removed under reduced pressure and the residue was treated with saturated aqueous solution of K_2CO_3 under ice cooling. The resulting solids were collected by filtration and recrystallized from MeOH to afford **9d-f** as colored pure products.

2-Ethoxy-3-phenyl-bis[1,2,4]triazolo[1,5-*a*:4′,3′-*c*]quinazoline (11d): This compound obtained as yellow solid with 0.224 g (68%). mp 222-225 °C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.68 (t, 3H, J = 7.85 Hz), 4.58 (q, 2H, J =13.98 Hz), 7.65-8.81 (m, 9H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 14.73, 66.21, 111.71, 114.88, 115.18, 124.89, 125.24, 126.99, 127.04, 130.59, 132.22, 134.34, 137.50, 142.17, 152.17, 164.25; MS m/z: $(330)^+$; Anal. Calcd for $C_{18}H_{14}N_6O$ (330.35): C 65.45, H 4.27, N 25.44. Found: C 65.98, H 3.98, N 25.37.

2-Methoxy-3-phenyl-bis[1,2,4]triazolo[1,5-*a*:4′,3′-*c*]quinazoline (11e): This compound obtained as white solid with 0.237 g (75%). mp 196-198 °C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 4.02 (s, 3H), 7.62-8.76 (m, 9H), ^{13}C-NMR (100 MHz, DMSO-d_6): δ 57.46, 111.94, 115.17, 124.56, 126.12, 127.09, 128.35, 129.80, 130.59, 130.89, 131.09, 141.82, 147.67, 149.47, 167.34; MS m/z: $(316)^+$; Anal. Calcd for $C_{17}H_{12}N_6O$ (316.32): C 64.55, H 3.82, N 26.57. Found: C 65.08, H 3.67, N 26.41.

2-Methoxy-3-pyridyl-bis[1,2,4]triazolo[1,5-*a*:4′,3′-*c*]quinazoline (11f): This compound obtained as white solid with 0.244 g (77%). mp 207-210 °C; ^{1}H-NMR (400 MHZ, DMSO-d_6): δ 4.12 (s, 3H), 7.75-8.89 (m, 8H), ^{13}C-NMR (100 MHz, DMSO-d_6): δ 57.39, 111.24, 115.23, 124.39, 124.75, 127.29, 129.80, 130.59, 133.35, 142.52, 145.67, 150.03, 161.24; MS m/z: $(317)^+$; Anal. Calcd for $C_{16}H_{11}N_7O$ (317.31): C 60.56, H 3.49, N 30.90. Found: C 61.10, H 3.52, N 31.27.

General procedure for the synthesis of 2-Alkoxy(aralkoxy)-tetrazolo[4,3-*c*][1,2,4]triazolo[1,5-*a*]quinazolines (13a-d):

Method A: A mixture of **2a,b,e,f** (1 mmol) and NaN_3 (1.2 mmol) in absolute DMF (5 mL) was heated at 90 °C in a nitrogen atmosphere 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.

Method B: To a stirred solution of sodium nitrite (1.2 mmol) in water (5 mL) was added dropwise at -5 °C a mixture of **3a,b,e,f** (0.8 mmol) in 10% hydrochloric acid (1.6 mL). After stirring for 30 min, the precipitate was collected by filtration, washed thoroughly with water, dried and recrystallized from MeOH.

2-Methoxy-tetrazolo[4,3-*c*][1,2,4]triazolo[1,5-*a*]quinazoline (13a): This compound obtained as white

solid with 0.130 g (54%). mp 174-178 ^{o}C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 3.99 (s, 3H), 7.18-7.95 (m, 4H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 56.36, 114.67, 116.23, 125.81, 128.27, 134.74, 136.49, 145.01, 157.32, 167.54; MS m/z: $(241)^{+}$; Anal. Calcd for $C_{10}H_7N_7O$ (241.21): C 49.79, H 2.93, N 40.65. Found: C 50.12, H 3.18, N 40.42.

2-Ethoxy-tetrazolo[4,3-*c*][1,2,4]triazolo[1,5-*a*]quinazoline (13b): This compound obtained as white solid with 0.135 g (53%). mp 157-160 ^{o}C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.38 (t, 3H, J = 7.54 Hz), 4.46 (q, 2H, J = 13.98 Hz), 7.51-8.53 (m, 4H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 14.81, 66.81, 109.97, 115.52, 126.11, 127.51, 132.65, 134.99, 148.61, 167.43; MS m/z: $(255)^{+}$; Anal. Calcd for $C_{11}H_9N_7O$ (255.24): C 51.76, H 3.55, N 38.41. Found: C 52.10, H 3.51 , N 38.56.

2-Benzyloxy-tetrazolo[4,3-*c*][1,2,4]triazolo[1,5-*a*]quinazoline (13c): This compound obtained as white solid; 0.161 g (51%), mp 178-180 ^{o}C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.75 (s, 2H), 7.37-8.35 (m, 9H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 71.57, 109.58, 115.08, 125.5, 127.72, 128.23, 128.75, 130.36, 134.21, 134.53, 135.47, 148.17, 160.43, 167.16; MS m/z: $(317)^{+}$; Anal. Calcd for $C_{16}H_{11}N_7O$ (317.31): C 60.56, H 3.49, N 30.90. Found: C 60.96, H 3.64 , N 30.98.

2-Phenethyloxy-tetrazolo[4,3-*c*][1,2,4]triazolo[1,5-*a*]quinazoline (13d): This compound obtained as white solid with 0.198 g (60%). mp 169-173 ^{o}C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 3.22 (t, 2H, J = 7.50 Hz), 4.79 (t, 2H, J = 7.51 Hz), 7.23-8.67 (m, 9H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 34.83, 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: $(331)^{+}$; Anal. Calcd for $C_{17}H_{13}N_7O$ (331.34): C 61.63, H 3.95, N 29.59. Found: C 61.88, H 3.73, N 29.68.

General procedure for the synthesis 2-Alkoxy(aralkoxy)-(3*H*-thieno[3,2-*d*]pyrimidin-4-one[4,3-*c*][1,2,4]triazolo[1,5-*a*]quinazolines (15a,b): A mixture of **2d,e (**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.

2-Pentyloxy-(3*H*-thieno[3,2-*d*]pyrimidin-4-one[4,3-*c*][1,2,4]triazolo[1,5-*a*]quinazoline (15a): This compound obtained as yellow solid with 0.307 g (81%). mp 236-240 ^{o}C; IR (KBr) ν max cm^{-1}: 1670; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 0.68 (t, 3H, J = 7.40 Hz), 1.14-1.18 (m, 4H), 1.50-1.65 (m, 2H), 4.02 (t, 2H, J = 7.60 Hz), 6.18-8.05 (m, 6H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 14.63, 22.18, 27.69, 28.63, 69.35, 114.82, 124.71, 124.25, 124.80, 134.50, 134.19, 147.72, 153.60, 167.84; MS m/z: $(379)^{+}$; HRMS $[M-H]^{-}$ Calcd for $C_{19}H_{17}N_5O_2S$ (379.44), found: 379.40.

2-Benzyloxy-(3*H*-thieno[3,2-*d*]pyrimidin-4-one[4,3-*c*][1,2,4]triazolo[1,5-*a*]quinazoline (15b): This compound obtained as yellow solid with 0.274 g (69%). mp 203-207 ^{o}C; IR (KBr) ν max cm^{-1}: 1667; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.32 (s, 2H), 6.48-8.05 (m, 11H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 73.57, 109.08, 116.08, 124.25, 127.02, 128.13, 128.75, 131.36, 131.93, 133.23, 134.21, 134.53, 135.47, 148.17, 160.43, 167.16; MS m/z: $(399)^{+}$; HRMS $[M-H]^{-}$ Calcd for $C_{21}H_{13}N_5O_2S$ (399.43), found: 399.47.

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