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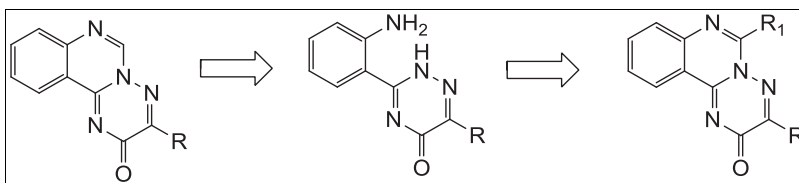
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The series of 6-substituted 3-R¹-2H-[1,2,4]triazino[2,3-*c*]quinazolin-2-one was prepared via condensation of 3-(2-aminophenyl)-6-R¹-1,2,4-triazin-5-ones with acylating reagents. Particularities of ¹H NMR spectra have been also discussed based on the comparison of experimental and theoretical results for 3-methyl-6-phenyl-2H-[1,2,4]triazino[2,3-*c*]quinazolin-2-one and its 4,3-isomer.

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INTRODUCTION

Triazino[*c*]quinazolines are heterocyclic compounds, which have been proved to be very useful in the synthetic chemistry, especially in various one-step heterocyclization reactions. The most common among the extensively discussed literature methods, which lead to the formation of such type of heterocyclic systems, is [4 + 2]-cyclocondensation [1–3]. Especial attention should be given to the series of publications [4,5] describing the formation of 3-R¹-2H-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones via condensation of 4-hydrazinoquinazoline with α -ketocarboxylic acid esters. Authors have found that the formation of the aforementioned substances proceeds through [4,3-*c*] systems intermediate resulted from specific Dimroth's type rearrangement. However, they obtained only 3-substituted 2H-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones, despite the possibility of compound formation with substitutions in other positions that greatly expand their potential particularly as biologically active agents. Nevertheless, we synthesized an unexpected series of the 6-substituted compounds. The main purpose of the presented investigation is the elaboration of preparative methods for 6-substituted 3-R¹-2H-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones.

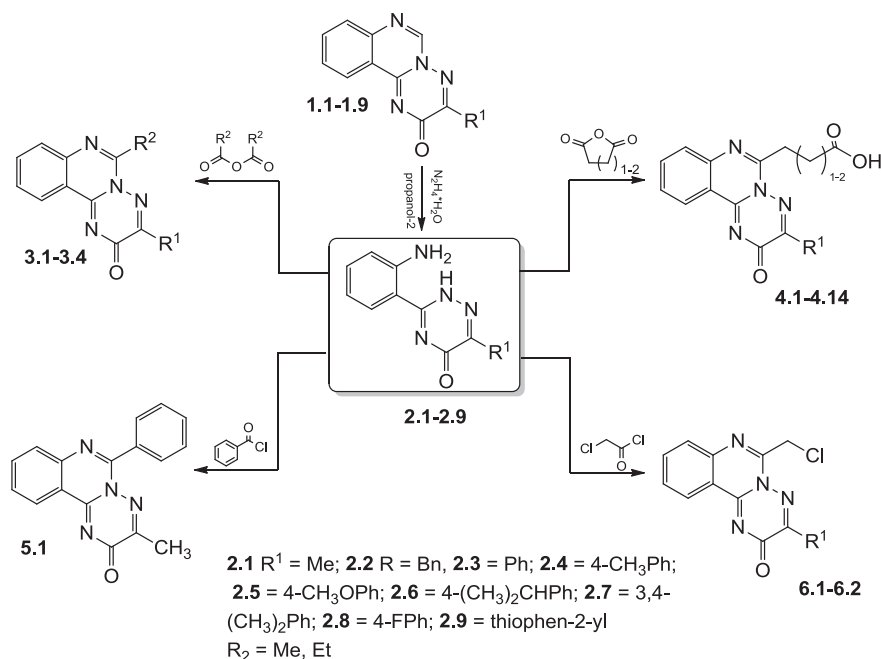
RESULT AND DISCUSSION

According to [4], we attempted to obtain 6-substituted 3-R¹-2H-[1,2,4]triazino[2,3-*c*]quinazolin-2-one via condensation of

2-substituted-4-hydrazinoquinazolines with α -ketocarboxylic acid esters. Unfortunately, LC–MS data showed that refluxing of the mentioned compounds in acetic acid did not lead to the formation of the expected products. Inability of target compound formation can be explained by the fact that the substituent in position 2 complicates the ANRORC-rearrangement.

In continuation of our ongoing interest for the synthesis of 6-substituted 3-R¹-2H-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones, we proposed the alternative approach through [5 + 1]-condensation. It is known that 3-R¹-2H-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones under hydrazine hydrate action undergo the nucleophilic cleavage, accompanied by the formation of 3-(2-aminophenyl)-6-R¹-1,2,4-triazin-5-ones [6]. The products of the reaction were formed with high yield and determined as NCCCN-binucleophiles. Thus, they can be used like a starting compound for the synthesis of 6-substituted 3-R¹-2H-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones. During the studying of the [5 + 1]-cyclocondensation, the acetic, propionic, succinic, and glutaric anhydrides and benzoyl and chloracetic chlorides were utilized as 1,1-bielectrophiles.

The obtained results indicated that refluxing of initial 3-(2-aminophenyl)-6-R¹-1,2,4-triazin-5-ones in acetic and propionic anhydrides over 3 h has led to the corresponding 6-methyl(ethyl)-3-R¹-2H-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones **3.1–3.4** (Scheme 1). Interactions of **2.1–2.9** with cyclic anhydrides of dicarboxylic acids were performed

Scheme 1. Interaction of 3-(2-aminophenyl)-6-R¹-1,2,4-triazin-5-ones with acylating agents.

in acetic acid. Refluxing of the afore mentioned compounds over 4 h led to the formation of (3-R¹-2-oxo-2H-[1,2,4]triazino[2,3-*c*]quinazolin-6-yl)carboxylic acids **4.1–4.14** in high yields. Under similar conditions, the interaction of 3-(2-aminophenyl)-6-methyl-1,2,4-triazin-5-one with benzoylchloride resulted in the 6-phenyl-3-methyl-2H-[1,2,4]triazino[2,3-*c*]quinazolin-2-one **5.1** formation. The presence of two high reactive electrophilic centers in the molecule of chloroacetylchloride causes the necessity of mild conditions during the reaction. Interaction of chloroacetylchloride with 3-(2-aminophenyl)-6-R¹-1,2,4-triazin-5-ones at 60°C in acetic acid yields to 6-(chloromethyl)-3-R¹-2H-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones **6.1** and **6.2**.

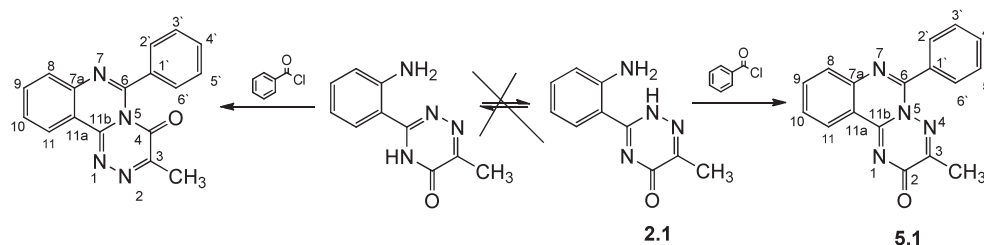
The structures of the synthesized compounds were proved by a complex of spectral methods: ¹H NMR, ¹³C NMR, EIMS, LC–MS, and X-ray analysis. The intensive signals of molecular ions (MH⁺) are presented in the LC–MS spectra of compounds **3.1–3.4**, **4.1–4.14**, **5.1**, **6.1**, and **6.2**. The LC–MS spectra of compounds **3.2**, **3.4**, **4.7**, and **4.14** also contain signals [M+3] caused by isotopic composition of the sulfur.

Mass spectra data for compounds **3.1**, **4.1–4.14** and **5.1** show molecular ion instability. The main route for the decomposition of triazine cycle is its degradation on C(10b)–N(1) and N(3)–N(4) bonds. In the case of compounds **4.1–4.7**, breakdown of ions F⁺, detected after the expansion of triazine ring, included formation of [F–H₂O]⁺ (*m/z* 225), [F–CO₂]⁺ (*m/z* 199), [F–COOH]⁺ (*m/z* 198), and [F–H₂O–CO]⁺ (*m/z* 197) ions, where [F–COOH]⁺ has the maximum intensity. The same dissociative

ionization mechanism could also be applied to compounds **4.8–4.14**. [F–CO₂]⁺ (*m/z* 213), [F–COOH]⁺ (*m/z* 212), and [F–CH₂COOH]⁺ (*m/z* 198) ions formation resulted from F⁺ ions with *m/z* 257. Elimination of CO and C₂H₅ from [F–CO₂]⁺ and [F–COOH]⁺ gives an ion with maximal intensity (*m/z* 185).

¹H NMR spectra of compounds **3.1–3.4**, **4.1–4.14**, **5.1**, **6.1**, and **6.2** were characterized by the presence of four signals belonging to the aromatic protons of triazinoquinazoline system with the corresponding splitting [4]. The spectra of compounds **3.1–3.4** contain the signals of an aliphatic substitute that is observed in high field as a three-proton singlet (**3.1** and **3.2**) or a combination of a three-proton triplet and a two-proton quartet (**3.3** and **3.4**). The ¹H NMR spectroscopic data of compounds **4.1–4.14** are also consistent with the assigned structure. Triplet signals due to ethylene fragment in compounds **4.1–4.7** are located at 3.63–3.55 and 3.03–2.98 ppm, and propylene fragment signals (**4.8–4.14**) are observed at around 3.04, 2.47–2.30, and 2.11–1.71 ppm, respectively. ¹H NMR spectra of compounds **6.1** and **6.2** prove the structure by the presence of a two-proton singlet at 5.16–5.18 ppm, caused by the chloromethylene group. The signals related to the substitutes in position 3 are also presented in all ¹H NMR spectra.

For better understanding of the particularities of ¹H NMR spectra of 2,3- and 4,3-isomers of quinazolin-2-ones, we have performed quantum-chemical calculations of ¹H chemical shifts of isomeric 3-methyl-6-phenyl-2H-[1,2,4]triazino[4,3-*c*]quinazolin-2-one (**5.1**) and 3-methyl-6-phenyl-2H-[1,2,4]triazino[4,3-*c*]quinazolin-2-one that may be formed as a result of possible tautomeric processes (Scheme 2).

Scheme 2. Theoretical formation of isomeric 3-methyl-6-phenyl-2*H*-[1,2,4]triazino[4,3-*c*]quinazolin-2-one as a result of tautomeric processes.

For the calculations, we have used a DFT approach with B3LYP [7,8], PBE1PBE [9,10], and M06L [11] functionals in combination with Continuous Set of Gauge Transformations (CSGT) [12] and Gauge-Independent Atomic Orbital (GIAO) [13] techniques for geometry optimization at the same levels of theory. Magnetically consistent 6–31G^{##} (I) basis set, proposed in [14] and tested for the calculations of chemical shifts in [15–17], has been used herein. Taking into account the effect of the solvent (DMSO), the calculations were performed via the Polarizable continuum model (PCM) method [18–20]. All calculations were performed using Gaussian 09 program [21]. Chemical shifts were obtained by subtracting the calculated magnetic shielding for the corresponding nuclei of interest from the shielding of the reference compound (TMS). As could be seen from Table 1, the B3LYP and PBE1PBE functionals, in contrast to M06L, give good agreement with the experiment and could be used for signal assignments and identification of the structure of such heterocyclic compounds. Calculations clearly demonstrate that the difference of chemical shifts of ortho- and meta-protons of the 6-phenyl fragment could be used for the unambiguous assignment of isomers. Thus, in the case of 4,3-isomer, chemical shifts of those protons are almost equal, while in the case of 2,3-isomer, the $\Delta\delta_{o-m}$ value in experimental spectrum reaches 0.24 ppm, which is very close to calculations with the B3LYP and PBE1PBE functionals. Analysis of chemical shifts of protons at positions 8, 11 and 9, 10 reveals in conclusion that protons H_{11} and H_9 are more deshielded if compared with H_8 and H_{10} , respectively.

Formation of the aforementioned tricyclic system was also confirmed by the carboxylic carbon signal at 174.77–173.67 ppm and the C6 atom signal at 153.95–151.34 ppm detected in the ^{13}C NMR spectra of compounds **4.1**, **4.3**, **4.8**, and **4.10**.

The complex of spectral data did not give us an ability to determine the type of heterocyclic system that was formed. Final conclusion about the structure of the synthesized compounds was made on the basis of the results (Fig. 1) of the XRD study of the compound (**4.8**).

Quinazoline fragment is planar within 0.021 Å. Triazinone ring adopts a very flattened boat conformation. The deviations of the N(2) and C(8) atoms from the mean plane of the remaining atoms of ring are 0.03 and 0.04 Å, respectively. There is a well-defined alternation of the bonds within the

pyrimidine ring. The N(1)–C(11) and N(2)–C(7) bonds [1.278(1) and 1.377(1) Å, respectively] are shorter than the C(1)–N(1) and N(2)–C(11) bonds [1.390(1) and 1.409(1) Å, respectively]. The same effect was observed in the previously studied structure [4]. The substituent at the C(11) atom has all-trans conformation [the corresponding torsion angles are as follows: C(11)–C(12)–C(13)–C(14) –175.98(9)°, C(12)–C(13)–C(14)–C(15) 174.4(1)°, and C(13)–C(14)–C(15)–O(3) 166.72(9)°]. Such conformation of substituent is stabilized by attractive intramolecular contacts: H(13B)...N(1) 2.62 Å, H(12A)...N(3) 2.55 Å, and H(12B)...N(3) 2.65 Å (the sum of van der Waals radii is 2.67 Å [22]). Angular structure of the tricyclic system causes formation of the H(5)...N(4) 2.53 Å (2.67 Å) attractive interaction that cannot be considered as an intramolecular hydrogen bond because of the small value of the C–H...N angle (100°).

CONCLUSIONS

The title synthetic protocol allowed the preparation of hard accessible 6-substituted 3-*R*-2*H*-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones starting from proper 3-(2-aminophenyl)-6-*R*-1,2,4-triazin-5-ones. The proposed method characterized by good yields and purity of target products. Comparison of experimental and theoretical results for 3-methyl-6-phenyl-2*H*-[1,2,4]triazino[2,3-*c*]quinazolin-2-one and its 4,3-isomer and X-ray study confirm the formation of 2,3-isomer series.

EXPERIMENTAL

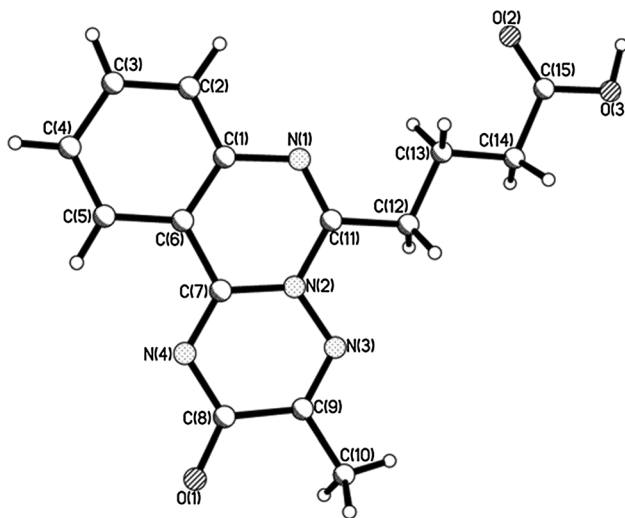
Melting points were determined using Stuart Scientific SMP30 apparatus (Stone, Staffordshire, UK). The elemental analyses (C, H, N, and S) were performed using the Elementar vario EL cube analyzer (Hanau, Germany). Analyses were indicated by the symbols of the elements or functions within $\pm 0.3\%$ of the theoretical values. IR spectra (4000–600 cm^{-1}) were recorded on a Bruker ALPHA FTIR spectrometer (Coventry, UK) using a module for measuring ATR. ^1H (400 MHz) and ^{13}C NMR spectra (100 MHz) were recorded on a Varian-Mercury 400 (Varian Inc., Palo Alto, CA) spectrometer with TMS as internal standard in DMSO- d_6 solution. LC–MS data were recorded using a chromatography/mass spectrometric system that consists of an HPLC “Agilent 1100 Series” (Palo Alto, CA) equipped with a diode-matrix and a mass-selective detector “Agilent LC/MSD SL” (atmospheric pressure chemical ionization). EIMS data were recorded on a Varian

Table 1

Experimental ^1H chemical shifts (ppm) for 3-methyl-6-phenyl-2H-[1,2,4]triazino[2,3-c]quinazolin-2-one (**5.1**), calculated values for (**5.1**) and its 4,3-isomer, and parameters of the linear regression equation $\delta_{\text{expt}} = A \times \delta_{\text{calc}} + B$.

Atoms	Experiment	B3LYP/6-31G ^{##} (I)				PBE1PBE/6-31G ^{##} (I)				M06L/6-31G ^{##} (I)			
		2,3-Isomer		4,3-Isomer		2,3-Isomer		4,3-Isomer		2,3-Isomer		4,3-Isomer	
		CSGT	GIAO	CSGT	GIAO	CSGT	GIAO	CSGT	GIAO	CSGT	GIAO	CSGT	GIAO
2', 6'	7.80	7.97	8.10	7.72	7.82	8.08	8.23	7.82	7.94	8.08	8.51	7.73	8.06
3', 5'	7.56	7.74	7.85	7.67	7.78	7.82	7.94	7.75	7.86	7.69	7.71	7.61	7.73
4	7.56	7.77	7.92	7.70	7.85	7.86	8.01	7.79	7.93	7.71	7.97	7.65	7.90
8	7.93	8.08	8.21	8.05	8.16	8.16	8.30	8.14	8.26	7.96	8.44	7.98	8.32
9	8.02	8.18	8.31	8.08	8.22	8.25	8.40	8.17	8.32	8.06	8.59	8.03	8.10
10	7.78	7.88	8.03	7.86	8.02	7.96	8.11	7.94	8.11	7.80	8.17	7.80	7.97
11	8.57	8.89	9.06	9.06	9.27	8.99	9.18	9.17	9.39	8.77	9.31	8.98	9.50
1-CH ₃	2.22	2.28	2.28	2.52	2.49	2.28	2.28	2.53	2.50	2.34	2.44	2.59	2.74
$\Delta\delta_{\text{o-m}}$	0.24	0.23	0.25	0.05	0.04	0.26	0.29	0.07	0.08	0.39	0.8	0.12	0.33
R ¹		0.991	0.990	0.970	0.963	0.989	0.988	0.971	0.968	0.965	0.963	0.977	0.952
A		0.87	0.84	0.69	0.64	0.86	0.82	0.68	0.63	0.90	0.65	0.71	0.56
B		0.85	0.97	2.37	2.64	0.87	1.06	2.39	2.65	0.67	2.46	2.19	3.30

Protons of methyl group have not been included to the correlation for better estimation of the region of aromatic protons.

Figure 1. Structure of **2h** according to XRD data.

1200 L instrument at 70 eV. The purity of all obtained compounds was checked by ^1H NMR and LC-MS.

Substances **1.1–1.9** and **2.1–2.9** were synthesized according to the reported procedures [4,6]. Other starting materials and solvents were obtained from commercially available sources and used without additional purification.

General method for the preparation of 6-alkyl-3-R¹-2H-[1,2,4]triazino[2,3-c]quinazolin-2-ones (3.1–3.4). The 5 mmol of corresponded 3-(2-aminophenyl)-6-R-1,2,4-triazin-5(2H)-one (**2.1** and **2.9**) was suspended in 15 mL of acetic or propionic anhydride and refluxed during 3 h. The mixture was cooled, and the formed precipitate was filtered off, washed with propanol 2, and dried.

3,6-Dimethyl-2H-[1,2,4]triazino[2,3-c]quinazolin-2-one (3.1). Yield: 72.5%; mp 222–224°C; ^1H NMR 2.36 (s, 3H, 3-CH₃),

2.77 (s, 3H, 6-CH₃), 7.70 (t, 1H, $J=8.1$ Hz, H-10), 7.80 (d, 1H, $J=8.1$ Hz, H-8), 7.96 (t, 1H, $J=8.0$ Hz, H-9), 8.48 (d, 1H, $J=8.0$ Hz, H-11); EIMS m/z (I rel, %) 227 (2.2), 226 (8.4), 186 (12.7), 185 (100.0), 145 (5.5), 144 (5.5), 102 (25.3), 90 (5.2), 76 (12.4), 75 (14.5); LC-MS $m/z=227$ [M+1]; Anal. Calcd for C₁₂H₁₀N₄O: C, 63.71; H, 4.46; N, 24.76; Found: C, 63.74; H, 4.52; N, 24.77.

6-Methyl-3-(thiophen-2-yl)-2H-[1,2,4]triazino[2,3-c]quinazolin-2-one (3.2). Yield: 76.1%; mp 264–266°C; ^1H NMR 2.89 (s, 3H, 6-CH₃), 7.31 (t, 1H, $J=3.7$ Hz, H-4 thioph), 7.74 (t, 1H, $J=7.8$ Hz, H-10), 7.86 (d, 1H, $J=7$ Hz, H-8), 7.98 (m, 2H, H-9, H-5 thioph), 8.41 (d, 1H, $J=3.7$ Hz, H-3 thioph), 8.54 (d, 1H, $J=8.2$ Hz, H-11); LC-MS $m/z=295$ [M+1]; Anal. Calcd for C₁₅H₁₀N₄OS: C, 61.21; H, 3.42; N, 19.04; Found: C, 61.23; H, 3.43; N, 19.08.

6-Ethyl-3-methyl-2H-[1,2,4]triazino[2,3-c]quinazolin-2-one (3.3). Yield: 75.0%; mp 170–172°C; ^1H NMR 1.36 (t, 3H, $J=7.4$ Hz, $6\text{-CH}_2\text{CH}_3$), 2.36 (s, 3H, 3-CH_3), 3.16 (q, 2H, $J=7.4$ Hz, CH_2CH_3), 7.70 (t, 1H, $J=8.2$ Hz, H-10), 7.82 (d, 1H, $J=8.2$ Hz, H-8), 7.96 (t, 1H, $J=8.0$ Hz, H-9), 8.47 (d, 1H, $J=8.0$ Hz, H-11); LC–MS $m/z=241$ [$M+1$]; *Anal.* Calcd for $\text{C}_{13}\text{H}_{12}\text{N}_4\text{O}$: C, 64.99; H, 5.03; N, 23.32; Found: C, 65.00; H, 5.05; N, 23.32.

6-Ethyl-3-(thiophen-2-yl)-2H-[1,2,4]triazino[2,3-c]quinazolin-2-one (3.4). Yield: 86.3%; mp 190–192°C; ^1H NMR 1.36 (t, 3H, $J=7.2$ Hz, $6\text{-CH}_2\text{CH}_3$), 3.16 (q, 2H, $J=7.2$ Hz, $6\text{-CH}_2\text{CH}_3$), 7.30 (1H, $J=3.9$ Hz, H-4 thioph.), 7.73 (t, 1H, H-10, $J=8.1$ Hz), 7.88 (d, 1H, $J=8.1$ Hz, H-8), 7.96 (m, 2H, H-9, H-5), 8.40 (d, 1H, $J=3.9$ Hz, H-3 thioph.), 8.53 (d, 1H, $J=8.2$ Hz, H-11); LC–MS $m/z=309$ [$M+1$]; *Anal.* Calcd for $\text{C}_{16}\text{H}_{12}\text{N}_4\text{OS}$: C, 62.32; H, 3.92; N, 18.17; Found: C, 62.35; H, 3.96; N, 18.18.

General procedure for the preparation of (3-R¹-2-oxo-2H-[1,2,4]triazino[2,3-c]quinazolin-6-yl)carboxylic acids (4.1–4.14). To a 5 mmol of corresponding 6-R-3-(2-aminophenyl)-[1,2,4]triazin-5-ones (**2.1–2.5**, **2.7**, and **2.9**) in 10 mL of acetic acid, 5.25 mmol of succinic or glutaric anhydride was added. The resulting mixture was refluxed for 4 h. The solvent was removed in vacuum. After the addition of methanol, the solid was filtered off and washed with ethyl ether. If necessary, additional purification could be performed by crystallization from acetic acid.

(3-Methyl-2-oxo-2H-[1,2,4]triazino[2,3-c]quinazolin-6-yl)propanoic acid (4.1). Yield: 95.7%; mp 234–236°C; ^1H NMR 2.37 (s, 3H, CH_3), 2.83 (t, 2H, $J=6.8$ Hz, $\text{CH}_2\text{CH}_2\text{COOH}$), 3.38 (t, 2H, $J=6.8$ Hz, $\text{CH}_2\text{CH}_2\text{COOH}$), 7.69 (t, 1H, $J=8.1$ Hz, H-10), 7.76 (d, 1H, $J=8.1$ Hz, H-8), 7.95 (t, 1H, $J=8.1$ Hz, H-9), 8.46 (d, 1H, $J=8.1$ Hz, H-11), 12.28 (s, 1H, COOH); ^{13}C NMR: $\delta=18.34$ (CH_3), 28.26 ($\text{CH}_2\text{CH}_2\text{COOH}$), 30.27 ($\text{CH}_2\text{CH}_2\text{COOH}$), 119.93 (11a-C), 125.79 (8-C), 127.71 (11-C), 128.73 (10-C), 135.69 (9-C), 142.22 (3-C), 143.79 (11b-C), 152.28 (6-C), 153.34 (7a-C), 154.97 (2-C), 173.67 (COOH); IR (cm^{-1}): 3106, 3003, 2922, 2859, 2779, 2677, 2601; 1702; 1660; 1625; 1592; 1568; 1510; 1464; 1421; 1408; 1359; 1335; 1286; 1273; 1259; 1222, 1204, 1181, 1155, 1129, 1104, 1081, 1036, 1018, 1005, 984, 967, 944, 873, 846, 777, 705, 689, 677, 668, 622; EIMS m/z (I rel, %) = 284 (M^+ , 1.3), 244 (5.2), 243 (20.7), 225 (2.7), 199 (19.0), 198 (100.0), 171 (10.6), 170 (5.1), 155 (18.3), 143 (11.4), 129 (7.2), 118 (6.4), 102 (12.1), 90 (8.7), 76 (6.6), 75 (9.6); LC–MS $m/z=286$ ($[M+2]^+$), 285 (MH^+); *Anal.* Calcd for $\text{C}_{14}\text{H}_{12}\text{N}_4\text{O}_3$: C, 59.15; H, 4.25; N, 19.71; Found: C, 59.16; H, 4.26; N, 19.71.

(3-Benzyl-2-oxo-2H-[1,2,4]triazino[2,3-c]quinazolin-6-yl)propanoic acid (4.2). Yield: 66.3%; mp 194–196°C; ^1H NMR 2.76 (t, 2H, $J=7.0$ Hz, $\text{CH}_2\text{CH}_2\text{COOH}$), 3.31 (t, 2H, $J=7.0$ Hz, $\text{CH}_2\text{CH}_2\text{COOH}$), 4.10 (s, 2H, CH_2), 7.23 (t, 1H, $J=7.6$ Hz, H-4'), 7.31 (t, 2H, $J=7.6$ Hz, H-3', 5'), 7.38 (d, 2H, $J=7.5$ Hz, H-2', 6'), 7.69 (t, 1H, $J=8.1$ Hz, H-10), 7.77 (d, 1H, $J=8.1$ Hz, H-8), 7.95 (t, 1H, $J=8.1$ Hz, H-9), 8.48 (d, 1H, $J=8.1$ Hz, H-11), 12.25 (s, 1H, COOH); IR (cm^{-1}): 2910, 2710, 2619, 2550, 1713, 1634, 1606, 1592, 1568, 1494, 1475, 1454, 1441, 1425, 1349, 1334, 1295, 1268, 1247, 1227, 1178, 1158, 1102, 1076, 1029, 1003, 975, 917, 890, 873, 893, 829, 773, 748, 735, 697, 670, 657, 627, 605; EIMS m/z (I rel, %) = 361 ($[M+1]^+$, 5.3), 360 (M^+ , 22.0), 243 (4.7), 225 (2.8), 199 (23.0), 198 (100.0), 197 (11.5), 171 (20.5), 170 (6.6), 156 (7.6), 155 (51.6), 145 (6.3), 143 (19.3), 129 (17.0), 118 (12.9), 117 (19.7), 116 (24.2), 103 (6.0), 102 (25.9), 91 (18.5), 90 (25.1), 89 (17.7), 77

(10.8), 76 (6.1), 75 (6.1), 65 (7.5), 63 (6.5), 56 (6.3), 55 (14.4), 51 (8.9), 43 (5.8); LC–MS $m/z=362$ ($[M+2]^+$), 361 (MH^+); *Anal.* Calcd for $\text{C}_{20}\text{H}_{16}\text{N}_4\text{O}_3$: C, 66.66; H, 4.48; N, 15.55; Found: C, 66.64; H, 4.47; N, 15.54.

(3-Phenyl-2-oxo-2H-[1,2,4]triazino[2,3-c]quinazolin-6-yl)propanoic acid (4.3). Yield: 89.2%; mp 280–282°C; ^1H NMR 2.88 (t, 2H, $J=6.8$ Hz, $\text{CH}_2\text{CH}_2\text{COOH}$), 3.51 (t, 2H, $J=6.8$ Hz, $\text{CH}_2\text{CH}_2\text{COOH}$), 7.60–7.53 (m, 3H, H-3', 4', 5'), 7.73 (t, 1H, $J=8.1$ Hz, H-10), 7.81 (d, 1H, $J=8.1$ Hz, H-8), 7.98 (t, 1H, $J=8.1$ Hz, H-9), 8.25 (d, 2H, $J=7.7$ Hz, H-2', 6'), 8.53 (d, 1H, $J=8.1$ Hz, H-11), 12.30 (s, 1H, COOH); ^{13}C NMR: $\delta=28.21$ ($\text{CH}_2\text{CH}_2\text{COOH}$), 30.25 ($\text{CH}_2\text{CH}_2\text{COOH}$), 119.64 (11a-C), 125.89 (8-C), 127.77 (11-C), 128.77 (10-C), 128.88 (4'-C), 129.76 (3'-C, 5'-C), 131.72 (2'-C, 6'-C), 132.56 (1'-C), 135.79 (9-C), 143.68 (3-C), 149.78 (11b-C), 151.34 (6-C), 153.56 (7a-C), 159.80 (2-C), 173.92 (COOH); IR (cm^{-1}): 3011, 2916, 2848, 1733, 1663, 1639, 1630, 1615, 1602, 1573, 1544, 1498, 1474, 1448, 1420, 1343, 1331, 1317, 1293, 1247, 1179, 1163, 1100, 1015, 982, 945, 920, 874, 816, 802, 780, 755, 707, 690, 644, 631; EIMS m/z (I rel, %) = 347 ($[M+1]^+$, 1.3), 243 (30.0), 225 (6.2), 199 (44.0), 198 (100.0), 197 (19.3), 171 (24.9), 170 (7.0), 156 (5.3), 155 (43.1), 149 (6.4), 143 (12.9), 129 (11.2), 118 (8.8), 103 (22.1), 102 (16.5), 90 (5.5), 76 (11.6), 75 (5.5), 41 (6.6); LC–MS $m/z=348$ ($[MH+2]^+$), 347 (MH^+); *Anal.* Calcd for $\text{C}_{19}\text{H}_{14}\text{N}_4\text{O}_3$: C, 65.89; H, 4.07; N, 16.18; Found: C, 65.91; H, 4.09; N, 16.20.

(3-(4'-Methylphenyl)-2-oxo-2H-[1,2,4]triazino[2,3-c]quinazolin-6-yl)propanoic acid (4.4). Yield: 89.5%; mp 262–264°C; ^1H NMR 2.38 (s, 3H, CH_3), 2.87 (t, 2H, $J=6.8$ Hz, $\text{CH}_2\text{CH}_2\text{COOH}$), 3.50 (t, 2H, $J=6.8$ Hz, $\text{CH}_2\text{CH}_2\text{COOH}$), 7.35 (d, 3H, $J=7.7$ Hz, H-3', 5'), 7.73 (t, 1H, $J=8.1$ Hz, H-10), 7.81 (d, 1H, $J=8.1$ Hz, H-8), 7.97 (t, 1H, $J=8.1$ Hz, H-9), 8.19 (d, 2H, $J=7.7$ Hz, H-2', 6'), 8.53 (d, 1H, $J=8.1$ Hz, H-11), 12.24 (s, 1H, COOH); IR (cm^{-1}): 2973, 2917, 2848, 2668, 1745, 1626, 1603, 1570, 1546, 1494, 1469, 1389, 1362, 1341, 1308, 1284, 1264, 1239, 1214, 1180, 1162, 1142, 1110, 1015, 969, 944, 869, 835, 788, 777, 713, 699, 690, 678, 637, 623; EIMS m/z (I rel, %) = 361 ($[M+1]^+$, 2.4), 243 (31.6), 225 (5.3), 199 (42.9), 198 (100.0), 197 (14.9), 171 (25.4), 170 (7.3), 156 (6.0), 155 (48.5), 143 (16.5), 129 (14.2), 118 (13.4), 117 (18.6), 116 (20.5), 103 (5.6), 102 (21.0), 91 (5.0), 90 (16.1), 89 (11.8), 77 (6.4), 76 (5.0); LC–MS $m/z=362$ ($[MH+2]^+$), 361 (MH^+); *Anal.* Calcd for $\text{C}_{20}\text{H}_{16}\text{N}_4\text{O}_3$: C, 66.66; H, 4.48; N, 15.55; Found: C, 66.61; H, 4.45; N, 15.52.

(3-(3',4'-Dimethylphenyl)-2-oxo-2H-[1,2,4]triazino[2,3-c]quinazolin-6-yl)propanoic acid (4.5). Yield: 97.3%; mp 240–244°C; ^1H NMR: 2.28 (s, 3H, 4'- CH_3), 2.24 (s, 3H, 3'- CH_3), 2.87 (t, 2H, $J=6.8$ Hz, $\text{CH}_2\text{CH}_2\text{COOH}$), 3.49 (t, 2H, $J=6.8$ Hz, $\text{CH}_2\text{CH}_2\text{COOH}$), 7.27 (d, 1H, $J=8.3$ Hz, H-5'), 7.73 (t, 1H, $J=8.1$ Hz, H-10), 7.81 (d, 1H, $J=8.1$ Hz, H-8), 7.97 (t, 1H, $J=8.1$ Hz, H-9), 8.01 (d, 1H, $J=8.3$ Hz, H-6'), 8.03 (s, 1H, H-2'), 8.51 (d, 1H, $J=8.1$ Hz, H-11), 12.34 (s, 1H, COOH); IR (cm^{-1}): 3020, 2916, 2848, 2752, 2651, 2565, 1700, 1662, 1630, 1604, 1573, 1574, 1506, 1494, 1468, 1439, 1415, 1396, 1369, 1355, 1335, 1245, 1214, 1178, 1160, 1125, 1106, 1058, 1021, 995, 948, 911, 896, 857, 841, 829, 783, 745, 708, 686, 667, 625; EIMS m/z (I rel, %) = 375 ($[M+1]^+$, 1.4), 243 (27.8), 225 (5.2), 199 (40.5), 198 (100.0), 197 (15.1), 171 (22.7), 170 (5.8), 155 (40.5), 143 (12.6), 131 (9.5), 130 (7.9), 129 (10.8), 118 (8.1), 117 (6.8), 116 (25.0), 103 (6.7), 102 (13.3), 89 (5.2); LC–MS $m/z=376$ ($[MH+2]^+$), 375 (MH^+); *Anal.* Calcd for $\text{C}_{21}\text{H}_{18}\text{N}_4\text{O}_3$: C, 67.37; H, 4.85; N, 14.66; Found: C, 67.33; H, 4.80; N, 14.63.

(3-(4'-Methoxyphenyl)-2-oxo-2H-[1,2,4]triazino[2,3-c]quinazolin-6-yl)propanoic acid (4.6). Yield: 91.1%; mp 256–260; ^1H NMR: δ =2.87 (t, 2H, J =6.8 Hz, $\text{CH}_2\text{CH}_2\text{COOH}$), 3.51 (t, 2H, J =6.8 Hz, $\text{CH}_2\text{CH}_2\text{COOH}$), 3.83 (s, 3H, OCH_3), 7.09 (d, 2H, J =8.9 Hz, H-3', 5'), 7.72 (t, 1H, J =8.1 Hz, H-10), 7.81 (d, 1H, J =8.1 Hz, H-8), 7.97 (t, 1H, J =8.1 Hz, H-9), 8.33 (d, 2H, J =9.0 Hz, H-2', 6'), 8.52 (d, 1H, J =8.1 Hz, H-11), 12.22 (s, 1H, COOH); IR (cm^{-1}): 2914, 2839, 1725, 1655, 1627, 1599, 1570, 1537, 1489, 1470, 1438, 1410, 1347, 1312, 1256, 1168, 1143, 1113, 1041, 1019, 975, 943, 904, 884, 842, 815, 788, 776, 723, 705, 690, 678, 636, 621; EIMS m/z (I rel, %)=376 (M^+ , 2.2), 243 (13.8), 225 (3.8), 198 (100.0), 197 (10.1), 185 (24.1), 171 (17.5), 170 (6.8), 156 (5.6), 155 (42.0), 149 (10.4), 145 (7.4), 144 (7.2), 143 (34.3), 134 (9.3), 133 (90.3), 131 (5.4), 130 (6.9), 129 (20.6), 118 (18.6), 117 (16.5), 116 (21.1), 115 (6.8), 111 (5.8), 104 (7.9), 103 (41.9), 102 (47.8), 91 (11.7), 90 (47.5), 89 (11.3), 87 (5.9), 83 (16.9), 81 (7.8), 77 (10.5), 76 (21.4), 75 (18.0), 74 (5.6), 73 (12.4), 71 (15.2), 70 (5.9), 69 (15.1), 67 (7.1), 65 (9.6), 64 (12.7), 63 (11.5), 60 (17.7), 57 (24.7), 56 (11.1), 55 (35.8), 54 (6.5), 51 (12.2), 50 (9.4), 45 (17.9), 43 (34.1), 42 (8.2), 41 (21.7); LC-MS m/z =378 ($[\text{MH}+2]^+$), 377 (MH^+); Anal. Calcd for $\text{C}_{20}\text{H}_{16}\text{N}_4\text{O}_4$: C, 63.83; H, 4.28; N, 14.89; Found: C, 63.81; H, 4.26; N, 14.86.

(3-(Tienyl-2)-2-oxo-2H-[1,2,4]triazino[2,3-c]quinazolin-6-yl)propanoic acid (4.7). Yield: 69.6%; mp 284–286°C; ^1H NMR: δ =2.89 (t, 2H, J =7.0 Hz, $\text{CH}_2\text{CH}_2\text{COOH}$), 3.52 (t, 2H, J =6.9 Hz, $\text{CH}_2\text{CH}_2\text{COOH}$), 7.30 (t, 1H, J =3.9 Hz, H-4'), 7.74 (t, 1H, J =8.1 Hz, H-10), 7.84 (d, 1H, J =8.2 Hz, H-8), 7.97 (m, 2H, H-9, 5'), 8.39 (d, 1H, J =3.9 Hz, H-3'), 8.53 (d, 1H, J =8.2 Hz, H-11), 12.26 (s, 1H, COOH); IR (cm^{-1}): 2915, 1731, 1633, 1617, 1600, 1570, 1531, 1519, 1485, 1464, 1407, 1344, 1296, 1249, 1224, 1178, 1165, 1110, 1095, 1045, 993, 968, 928, 887, 852, 795, 772, 750, 736, 725, 691, 668, 626; EIMS m/z (I rel, %)=352 (M^+ , 2.3), 244 (5.1), 243 (34.2), 225 (5.2), 199 (41.9), 198 (100.0), 197 (18.0), 171 (23.4), 170 (6.9), 156 (5.2), 155 (44.2), 145 (5.4), 143 (14.2), 129 (13.1), 118 (10.0), 117 (5.5), 103 (5.7), 102 (18.8), 97 (6.5), 90 (6.4), 85 (6.6), 83 (7.9), 76 (5.4), 71 (7.7), 69 (7.7), 57 (13.3), 56 (5.7), 55 (12.3), 45 (7.8), 43 (10.0), 41 (6.5); LC-MS m/z =355 ($[\text{MH}+3]^+$), 353 (MH^+); Anal. Calcd for $\text{C}_{17}\text{H}_{12}\text{N}_4\text{O}_4\text{S}$: C, 57.95; H, 3.43; N, 15.90; S, 9.10; Found: C, 57.93; H, 3.42; N, 15.87; S, 9.08.

(3-Methyl-2-oxo-2H-[1,2,4]triazino[2,3-c]quinazolin-6-yl)butanoic acids (4.8). Yield: 85.8%; mp 210–212°C; ^1H NMR 2.05 (q, 2H, J =7.0 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 2.35 (s, 3H, CH_3), 2.42 (t, 2H, J =6.9 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 3.16 (t, 2H, J =7.0 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 7.68 (t, 1H, J =8.1 Hz, H-10), 7.78 (d, 1H, J =8.1 Hz, H-8), 7.93 (t, 1H, J =8.1 Hz, H-9), 8.44 (d, 1H, J =8.1 Hz, H-11), 12.08 (s, 1H, COOH); ^{13}C NMR 18.35 (CH_3), 21.61 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 32.33 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 33.29 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 119.96 (C-11a), 125.70 (C-8), 127.69 (C-11), 128.60 (C-10), 135.58 (C-9), 143.92 (C-3), 152.30 (C-11b), 153.95 (C-6), 154.79 (C-7a), 160.74 (C-2), 174.66 (COOH); IR (cm^{-1}): 3052, 2985, 2916, 2846, 2602, 1698, 1657, 1631, 1608, 1593, 1572, 1505, 1467, 1435, 1409, 1379, 1362, 1339, 1291, 1277, 1247, 1226, 1206, 1132, 1106, 1088, 1059, 1021, 1003, 969, 931, 889, 797, 784, 740, 725, 691, 657, 624; EIMS m/z (I rel, %)=299 ($[\text{M}+1]^+$, 13.4), 298 (M^+ , 7.6), 258 (5.3), 257 (33.0), 213 (7.3), 212 (52.5), 199 (22.2), 198 (96.1), 186 (27.0), 185 (100.0), 171 (5.9), 170 (6.3), 169 (15.4), 156 (5.5), 155 (32.3), 145 (16.6), 144 (5.3), 143 (38.7), 142 (20.8), 129 (21.0), 118 (6.4), 117 (13.4), 116 (12.9), 115 (10.3), 105 (5.1), 103 (7.9), 102 (41.6), 90 (13.3),

89 (7.2), 85 (9.2), 83 (13.0), 77 (5.0), 76 (9.8), 75 (10.2), 60 (5.3), 56 (13.7), 55 (6.5), 45 (19.3), 43 (6.6), 42 (9.0), 41 (11.8); LC-MS m/z =300 ($[\text{MH}+2]^+$), 299 (MH^+); Anal. Calcd for $\text{C}_{15}\text{H}_{14}\text{N}_4\text{O}_3$: C, 60.40; H, 4.73; N, 18.78; Found: C, 60.43; H, 4.75; N, 18.79.

(3-Benzyl-2-oxo-2H-[1,2,4]triazino[2,3-c]quinazolin-6-yl)butanoic acids (4.9). Yield: 72.9%; mp 152–154°C; ^1H NMR (q, 2H, J =7.0 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 2.30 (t, 2H, J =7.0 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 3.04 (t, 2H, J =7.0 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 4.09 (s, CH_2), 7.24 (t, 1H, J =7.2 Hz, H-4'), 7.31 (t, 2H, J =7.5 Hz, H-3', 5'), 7.37 (d, 2H, J =7.5 Hz, H-2', 6'), 7.68 (t, 1H, J =8.1 Hz, H-10), 7.78 (d, 1H, J =8.1 Hz, H-8), 7.92 (t, 1H, J =7.7 Hz, H-9), 8.46 (d, 1H, J =8.1 Hz, H-11), 12.07 (s, 1H, COOH); IR (cm^{-1}): 3061, 3026, 2971, 2907, 2671, 2575, 1700, 1663, 1627, 1607, 1590, 1508, 1467, 1414, 1377, 1351, 1332, 1317, 1288, 1249, 1224, 1184, 1164, 1150, 1124, 1098, 1071, 1025, 976, 922, 779, 754, 721, 700, 639, 614; EIMS m/z (I rel, %)=375 ($[\text{M}+1]^+$, 6.9), 374 (M^+ , 26.1), 213 (4.0), 212 (28.0), 199 (11.6), 198 (83.3), 186 (12.8), 185 (100.0), 171 (4.0), 170 (4.2), 169 (11.7), 155 (23.6), 145 (12.7), 143 (18.9), 142 (10.9), 129 (11.4), 118 (5.4), 117 (15.9), 116 (18.1), 115 (5.2), 102 (17.4), 91 (13.6), 90 (15.3), 89 (11.4), 77 (6.1), 65 (5.0), 56 (9.2), 55 (8.7), 51 (5.0), 45 (5.0), 41 (9.8); LC-MS m/z =376 ($[\text{MH}+2]^+$), 375 (MH^+); Anal. Calcd for $\text{C}_{21}\text{H}_{18}\text{N}_4\text{O}_3$: C, 67.37; H, 4.85; N, 14.96; Found: C, 67.39; H, 4.87; N, 14.97.

(3-Phenyl-2-oxo-2H-[1,2,4]triazino[2,3-c]quinazolin-6-yl)butanoic acids (4.10). Yield: 74.4%; mp 220–222°C; ^1H NMR: δ =2.11 (q, 2H, J =7.0 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 2.46 (t, 2H, J =7.0 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 3.30 (t, 2H, J =7.1 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 7.60–7.53 (m, 3H, H-3', 4', 5'), 7.74 (t, 1H, J =8.1 Hz, H-10), 7.86 (d, 1H, J =8.1 Hz, H-8), 7.98 (t, 1H, J =8.1 Hz, H-9), 8.27 (d, 2H, J =7.2 Hz, H-2', 6'), 8.54 (d, 1H, J =8.1 Hz, H-11), 12.10 (s, 1H, COOH); ^{13}C NMR 21.67 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 32.47 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 33.30 ($\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 119.83 (11a-C), 125.89 (8-C), 127.86 (11-C), 128.82 (10-C), 128.87 (3'-C, 5'-C), 129.78 (2'-C, 6'-C), 131.72 (4'-C), 132.47 (1'-C), 135.62 (9-C), 143.95 (3-C), 149.47 (11b-C), 151.54 (6-C), 154.31 (7a-C), 159.96 (2-C), 174.77 (COOH); IR (cm^{-1}): 3039, 2943, 2884, 2728, 2653, 2578, 1721, 1616, 1602, 1572, 1545, 1498, 1483, 1470, 1441, 1409, 1346, 1312, 1282, 1251, 1180, 1151, 1139, 1107, 1076, 1046, 1017, 999, 977, 946, 895, 844, 815, 778, 757, 693, 672, 649, 627, 615; EIMS m/z (I rel, %)=257 (11.8), 212 (19.8), 199 (10.1), 198 (75.8), 186 (13.0), 185 (100.0), 171 (3.1), 170 (3.9), 169 (8.8), 155 (21.8), 145 (11.2), 143 (19.0), 142 (11.2), 129 (12.9), 117 (8.1), 116 (7.1), 115 (5.7), 103 (18.8), 102 (19.8), 90 (6.2), 89 (6.6), 77 (7.9), 76 (13.2), 75 (5.5), 57 (5.6), 56 (10.3), 55 (8.0), 51 (5.3), 45 (6.8), 43 (5.0), 41 (11.9); LC-MS m/z =362 ($[\text{MH}+2]^+$), 361 (MH^+); Anal. Calcd for $\text{C}_{20}\text{H}_{16}\text{N}_4\text{O}_3$: C, 66.66; H, 4.48; N, 15.55; Found: C, 66.63; H, 4.46; N, 15.53.

(3-(4'-Methylphenyl)-2-oxo-2H-[1,2,4]triazino[2,3-c]quinazolin-6-yl)butanoic acids (4.11). Yield: 83.5%; mp 226–228°C; ^1H NMR 2.11 (q, 2H, J =7.1 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 2.36 (s, 3H, CH_3), 2.45 (t, 2H, J =7.0 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 3.28 (t, 2H, J =7.1 Hz, $\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}$), 7.33 (d, 2H, J =8.0 Hz, H-3', 5'), 7.72 (t, 1H, J =8.1 Hz, H-10), 7.84 (d, 1H, J =8.1 Hz, H-8), 7.96 (t, 1H, J =8.1 Hz, H-9), 8.19 (d, 2H, J =8.0 Hz, H-2', 6'), 8.51 (d, 1H, J =8.1 Hz, H-11), 12.10 (s, 1H, COOH); IR (cm^{-1}): 3067, 3039, 2977, 2914, 2731, 2659, 2582, 1719, 1639, 1619, 1604, 1573, 1545, 1492, 1470, 1426, 1409, 1348, 1328, 1311, 1252, 1182, 1165, 1140, 1058, 1039, 1021, 947, 899, 838, 783, 772, 713, 692, 677, 660; 624; EIMS m/z (I rel,

(%)=257 (11.8), 212 (19.4), 199 (11.2), 198 (82.0), 186 (12.9), 185 (100.0), 171 (3.6), 170 (3.4), 169 (9.1), 155 (19.6), 149 (5.0), 145 (10.4), 143 (18.7), 142 (8.8), 129 (10.3), 118 (6.1), 117 (16.2), 116 (16.6), 103 (5.1), 102 (17.5), 90 (11.8), 89 (8.7), 77 (5.9), 56 (7.6), 55 (6.5), 41 (9.1); LC-MS m/z =376 ($[MH+2]^+$), 375 (MH^+); *Anal.* Calcd for $C_{21}H_{18}N_4O_3$: C, 67.37; H, 4.85; N, 14.96; Found: C, 67.38; H, 4.90; N, 14.97.

(3-(3',4'-Dimethylphenyl)-2-oxo-2H-[1,2,4]triazino[2,3-c]quinazolin-6-yl)butanoic acids (4.12). Yield: 91.2%; mp 232–234°C; 1H NMR 2.10 (q, 2H, $J=7.0$ Hz, $CH_2CH_2CH_2COOH$), 2.17 (s, 3H, 3'-CH₃), 2.24 (s, 3H, 4'-CH₃), 2.46 (t, 2H, $J=6.9$ Hz, $CH_2CH_2CH_2COOH$), 3.24 (t, 2H, $J=7.0$ Hz, $CH_2CH_2CH_2COOH$), 7.20 (d, 1H, $J=7.9$ Hz, H-5'), 7.70 (t, 1H, $J=8.1$ Hz, H-10), 7.82 (d, 1H, $J=8.1$ Hz, H-8), 8.01–7.93 (m, 3H, H-2', 6', 9), 8.47 (d, 1H, $J=8.1$ Hz, H-11), 12.12 (s, 1H, COOH); IR (cm^{-1}): 3152, 3062, 2947, 2911, 1724, 1649, 1624, 1606, 1573, 1544, 1505, 1490, 1469, 1445, 1400, 1372, 1342, 1326, 1288, 1233, 1221, 1201, 1160, 1127, 1107, 1023, 996, 959, 899, 877, 861, 839, 772, 711, 688, 626; EIMS m/z (I rel, %)=257 (11.0), 212 (19.4), 199 (10.1), 198 (70.7), 186 (12.1), 185 (100.0), 169 (10.6), 159 (5.3), 155 (20.7), 149 (7.1), 145 (14.7), 143 (22.4), 142 (12.1), 131 (18.1), 130 (15.3), 129 (16.2), 118 (6.1), 117 (15.6), 116 (52.9), 115 (10.5), 104 (5.2), 103 (17.6), 102 (29.8), 97 (7.2), 91 (10.2), 90 (11.3), 89 (14.0), 85 (9.5), 83 (9.8), 79 (6.1), 77 (16.0), 76 (8.4), 75 (7.4), 73 (6.6), 71 (6.3), 70 (7.5), 69 (13.1), 65 (6.2), 60 (7.8), 57 (11.3), 56 (18.9), 55 (23.5), 51 (9.2), 50 (7.4), 45 (12.2), 43 (9.5), 41 (23.7); LC-MS m/z =390 ($[MH+2]^+$), 389 (MH^+); *Anal.* Calcd for $C_{22}H_{20}N_4O_3$: C, 68.03; H, 5.19; N, 14.42; Found: C, 68.03; H, 5.20; N, 14.45.

(3-(4'-Methoxyphenyl)-2-oxo-2H-[1,2,4]triazino[2,3-c]quinazolin-6-yl)butanoic acids (4.13). Yield: 71.4%; mp 218–222°C; 1H NMR 2.11 (q, 2H, $J_2=14.4$ Hz, $J_3=7.2$ Hz, $CH_2CH_2CH_2COOH$), 2.46 (t, 2H, $J=7.0$ Hz, $CH_2CH_2CH_2COOH$), 3.29 (t, 2H, $J=7.2$ Hz, $CH_2CH_2CH_2COOH$), 3.83 (s, 3H, OCH₃), 7.07 (d, 2H, $J=8.9$ Hz, H-3', 5'), 7.71 (t, 1H, $J=7.7$ Hz, H-10), 7.84 (d, 1H, $J=8.1$ Hz, H-8), 7.96 (t, 1H, $J=7.7$ Hz, H-9), 8.33 (d, 2H, $J=8.9$ Hz, H-2', 6'), 8.50 (d, 1H, $J=8.1$ Hz, H-11), 11.97 (s, 1H, COOH); IR (cm^{-1}): 3171, 1741, 1642, 1624, 1603, 1571, 1537, 1514, 1488, 1471, 1455, 1417, 1400, 1372, 1347, 1332, 1305, 1290, 1268, 1218, 1175, 1111, 1098, 1061, 1026, 948, 906, 847, 814, 772, 750, 726, 689, 633, 622; EIMS m/z (I rel, %)=391 ($[M+1]^+$, 2.4), 390 (M^+ , 2.4), 257 (9.0), 212 (16.7), 199 (8.6), 198 (63.1), 186 (14.9), 185 (100.0), 169 (6.7), 159 (5.8), 155 (13.0), 145 (8.1), 143 (32.2), 142 (6.5), 134 (6.8), 133 (64.7), 129 (7.8), 119 (4.5), 118 (8.1), 117 (5.2), 116 (5.3), 103 (18.5), 102 (21.2), 90 (19.6), 76 (8.2), 45 (10.5), 43 (5.7); LC-MS m/z =392 ($[MH+2]^+$), 391 (MH^+); *Anal.* Calcd for $C_{21}H_{18}N_4O_4$: C, 64.61; H, 4.65; N, 14.35; Found: C, 64.63; H, 4.69; N, 14.37.

(3-(Thienyl-2)-2-oxo-2H-[1,2,4]triazino[2,3-c]quinazolin-6-yl)butanoic acids (4.14). Yield: 92.6%; mp 236–240°C; 1H NMR 1.71 (quintet, 2H, $J=7.1$ Hz, $CH_2CH_2CH_2COOH$), 2.47 (t, 2H, $J=7.0$ Hz, $CH_2CH_2CH_2COOH$), 3.29 (t, 2H, $J=7.1$ Hz, $CH_2CH_2CH_2COOH$), 7.59–7.71 (m, 2H, H-10, 4'), 7.86 (d, 1H, $J=8.1$ Hz, H-8), 8.00–7.96 (m, 2H, H-9, 5'), 8.41 (d, 1H, $J=3.3$ Hz, H-3'), 8.54 (d, 1H, $J=8.1$ Hz, H-11), 12.11 (s, 1H, COOH); IR (cm^{-1}): 3081, 2976, 2904, 1731, 1643, 1622, 1605, 1572, 1541, 1524, 1479, 1411, 1387, 1369, 1411, 1380, 1353, 1326, 1293, 1254, 1183, 1148, 1111, 1058, 994, 907, 876, 850, 772, 732, 714, 690, 665, 682; EIMS m/z (I rel, %)=367 ($[M+1]^+$, 1.1),

366 (M^+ , 1.1), 257 (10.4), 212 (17.9), 199 (9.8), 198 (67.9), 186 (12.8), 185 (100.0), 169 (8.6), 155 (17.6), 145 (9.9), 143 (19.7), 142 (9.1), 129 (9.4), 117 (6.1), 109 (8.4), 102 (16.5), 69 (5.3), 56 (5.5), 41 (6.5); LC-MS m/z =369 ($[MH+2]^+$), 367 (MH^+); *Anal.* Calcd for $C_{18}H_{14}N_4O_3S$: C, 59.01; H, 3.85; N, 15.29; S, 8.75; Found: C, 59.03; H, 3.89; N, 15.27; S, 8.75.

Method for preparation of 3-methyl-6-phenyl-2H-[1,2,4]triazino[2,3-c]quinazolin-2-one (5.1). To a 5 mmol of 6-methyl-3-(2-aminophenyl)-[1,2,4]-triazin-5-one (**2.1**) in 10 mL of acetic acid, 5.25 mmol of benzoyl chloride was added. The resulting mixture was refluxed for 4 h. The solvent was removed in vacuum. After the addition of methanol, the solid was filtered off and washed with ethyl ether. If necessary, additional purification could be achieved by crystallization from acetic acid.

3-Methyl-6-phenyl-2H-[1,2,4]triazino[2,3-c]quinazolin-2-one (5.1). Yield: 83.2%; mp 250–252°C; 1H NMR (400 MHz) 2.22 (s, 3H, 3-CH₃), 7.56 (m, 3H, H-3, H-4, H-5 Ph), 7.78 (t, 1H, $J=8.2$ Hz, H-10), 7.80 (d, 2H, $J=8.2$ Hz, H-2, H-6 Ph), 7.93 (d, 1H, $J=8.2$ Hz, H-8), 8.02 (t, 1H, $J=8.2$ Hz, H-9), 8.57 (d, 1H, $J=8.2$ Hz, H-11); EIMS m/z (I rel, %)=288 (5.2), 248 (14.0), 247 (100.0), 206 (12.0), 205 (78.5), 103 (13.2), 102 (28.0), 90 (9.1), 77 (39.0), 76 (23.4); LC-MS m/z =289 $[M+1]$; *Anal.* Calcd for $C_{17}H_{12}N_4O$: C, 70.82; H, 4.20; N, 19.43; Found: C, 70.85; H, 4.22, N, 19.45.

General method for the preparation of 6-(chloromethyl)-3-R¹-2H-[1,2,4]triazino[2,3-c]quinazolin-2-ones (6.1 and 6.2). The 5 mmol of corresponded 3-(2-aminophenyl)-6-R-1,2,4-triazin-5(2H)-one (**2.6** and **2.8**) was suspended in 15 mL of acetic acid then 8.5 mmol of chloroacetylchloride was added and hold at 60°C during 30 min. The mixture was cooled, and the formed precipitate was filtered off, dried, and crystallized from acetone.

6-(Chloromethyl)-3-(4-isopropylphenyl)-2H-[1,2,4]triazino[2,3-c]quinazolin-2-one (6.1). Yield: 83.2%; mp 250–252°C; 1H NMR 1.33 (d, 6H, $J=6.8$ Hz, $CH(CH_3)_2$), 3.04–2.97 (m, 1H, $CH(CH_3)_2$), 5.16 (s, 2H, CH_2Cl), 7.39 (d, 2H, $J=8.2$ Hz, 2H, H-3', H-5'), 7.81 (t, 1H, $J=7.5$ Hz, H-10), 7.92 (d, 1H, $J=7.0$ Hz, H-8), 8.02 (t, 1H, $J=7.2$ Hz, H-9), 8.30 (d, 2H, $J=8.2$ Hz, H-2', H-6'), 8.66 (d, 1H, $J=7.7$ Hz, H-11); LC-MS m/z =365 $[M+1]$; *Anal.* Calcd for $C_{20}H_{17}ClN_4O$: C, 65.84; H, 4.70; N, 15.36; Found: C, 65.87; H, 4.71, N, 15.38.

6-(Chloromethyl)-3-(4-fluorophenyl)-2H-[1,2,4]triazino[2,3-c]quinazolin-2-one (6.2). Yield: 83.2%; mp 250–252°C; 1H NMR (400 MHz) 5.18 (s, 2H, CH_2Cl), 7.29 (t, 1H, $J=8.7$ Hz, H-3', H-5'), 7.81 (t, 1H, $J=7.4$ Hz, H-10), 7.93 (d, 1H, $J=8.0$ Hz, H-8), 8.03 (t, 1H, $J=7.1$ Hz, H-9), 8.48 (dd, 2H, $J=8.7$, 5.6 Hz, H-2', H-6'), 8.66 (d, 1H, $J=7.7$ Hz, H-11); EIMS m/z (I rel, %)=221 (30.1), 220 (11.00), 219 (100.0), 185 (6.9), 184 (11.4), 177 (5.1), 143 (5.3), 142 (9.9), 122 (5.4), 121 (62.0), 116 (10.8), 115 (5.1), 107 (13.8), 102 (30.1), 95 (9.0), 94 (29.1), 90 (9.7), 89 (9.2), 88 (5.2), 81 (6.2), 76 (17.6), 75 (18.2), 64 (5.5), 63 (7.7), 57 (10.3), 56 (40.7), 51 (12.7), 50 (8.3), 49 (14.7); LC-MS m/z =341 $[M+1]$; *Anal.* Calcd for $C_{17}H_{10}ClFN_4O$: C, 59.92; H, 2.96; N, 16.44; Found: C, 59.98; H, 3.01, N, 16.48.

X-ray diffraction study of 4.8. Crystals are triclinic, $C_{13}H_{14}N_4O_3$, at 20°C. $a=9.2355(4)$, $b=9.4258(4)$, $c=9.7498(5)$ Å, $\alpha=67.780(4)^\circ$, $\beta=75.948(4)^\circ$, $\gamma=66.363(4)^\circ$, $V=715.62(6)$ Å³, $M_r=298.30$, $Z=2$, space group $P\bar{1}$, $d_{sub}=1.384$ g/sm³, $(MoK)=0.100$ mm⁻¹, and $F(000)=312$. Data collection was performed on an “Xcalibur-3” diffractometer (MoK radiation,

CCD detector, graphite monochromator, ω -scanning, $2_{\max} = 60$). A total of 8445 reflections was collected (4375 independent, $R_{\text{int}} = 0.021$).

Structure was solved by direct methods and refined against F^2 by full-matrix least squares procedure using SHELXTL program package [23]. All nonhydrogen atoms were refined in anisotropic approximation. Hydrogen atom positions were initially located from difference electron density maps and refined isotropically. Final refinement was converged at $wR_2 = 0.104$ for all 4050 reflections ($R_1 = 0.039$ for 2660 reflections with $F > 4(F)$, $S = 0.89$).

Atom coordinates and crystallographic parameters have been deposited to the Cambridge Crystallographic Data Centre (CCDC 771094). These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

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