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Synthesis of spiro-fused (C5)-pyrazolino-(C6)-triazinones, a new heterocyclic system

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ABSTRACT

Reaction of 4-hydrazinoquinazoline with 2,4-diketoesters gives the corresponding 3-acylmethyl-2*H*-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones in a one-step procedure via cyclocondensation–Dimroth-like rearrangement. Spectroscopic studies as well as X-ray analysis reveal that the obtained triazinoquinazolines exist in their ketoimine tautomeric form. Treatment of these compounds with hydrazine hydrate affords 3′-(2-aminophenyl)-3-(het)aryl-spiro[pyrazoline-5,6′(1′*H*)-1,2,4-triazin]-5′(4′*H*)-ones or 5-(het)arylpyrazole-3-carboxylic acid hydrazides depending on the reaction conditions. The structure of the spiro-heterocycles was elucidated by means of single-crystal X-ray analysis and confirmed by spectroscopic investigations.

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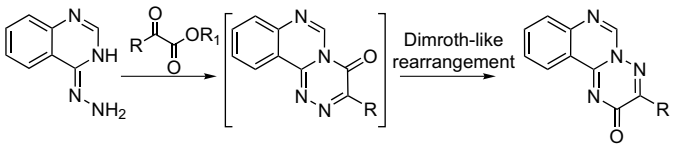
1. Introduction

Triazino-annulated quinazolines are important in both heterocyclic and medicinal chemistry.[1,2] Several cases of biological activities have been claimed for [1,2,4]triazino[2,3-*c*]quinazolines[3,4] but insignificant amount of research activity has so far been directed toward this class of compounds.[5–16] Recently, we have presented a novel one-step synthesis of 2*H*-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones starting from 4-hydrazinoquinazoline and α-ketocarboxylic acids or their esters (Scheme 1).[17] However, this approach was only applied to derivatives substituted with alkyl and (hetero)aryl groups. Consequently, our interest was kindled by the desire to extend the scope of the method for preparation of the corresponding 3-acylmethyl derivatives in order to examine their susceptibility for attack of strong nitrogen nucleophiles, namely hydrazine hydrate.



Scheme 1.

Our strategy was based on employing 2,4-diketoesters, which are easily accessible key building blocks for heterocyclic systems construction[18–20] and are known as a novel class of inhibitors of HIV-1 integrase.[21,22] These compounds, when treated with hydrazines, react at the β-dicarbonyl fragment whereas aromatic 1,2-binucleophiles react at the α-ketoester group, although formation of pyridazine derivatives could not be excluded a priori.[18,19] The use of α-hydrazinoazines in this reaction was substantially restricted.[23–25]

2. Results and discussion

Condensation of 4-hydrazinoquinazoline (**1**) with different (hetero)aryl substituted 2,4-diketoesters in glacial acetic acid afforded the corresponding 3-acylmethyl derivatives **4** in good to moderate yields (Scheme 2). Apparently, the key steps of this synthesis were the formation of Schiff bases **2**, and their cyclization to the supposed intermediate triazinoquinazolines **3** followed by its Dimroth-like rearrangement to [2,3-*c*] isomers **4**; this was inferred from related processes.[17] Such an approach to **4** was found to be advantageous for achieving the introduction of the acylmethyl moiety into the triazinoquinazoline core.

The obtained triazinoquinazolines **4** are novel compounds and were characterized by means of elemental analyses and spectroscopic data as well. This allows to exclude possible formation of pyrazole derivatives, which are considered as an alternative structures to the target **4**. Thus, in the ^{1}H and ^{13}C NMR spectra, the

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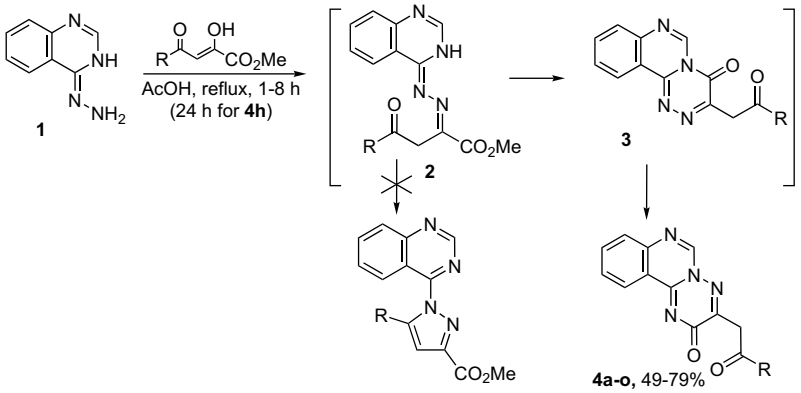


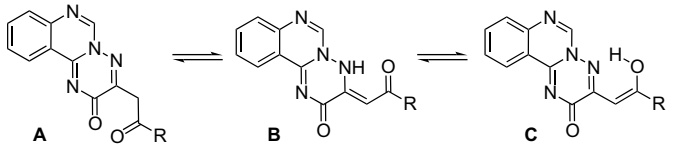
	a	b	c	d	e	f	g	h
R	Ph	4-MeC_6H_4	4-$MeOC_6H_4$	3-$NO_2C_6H_4$	4-$NO_2C_6H_4$	2-FC_6H_4	4-FC_6H_4	2,5-$F_2C_6H_3$

	i	j	k	l	m	n	o
R	2-ClC_6H_4	4-ClC_6H_4	3-BrC_6H_4	4-BrC_6H_4	thiophen-2-yl	furan-2-yl	benzo[*b*]furan-2-yl

Scheme 2.

resonances of the triazinoquinazoline protons and carbons are diagnostic since they appear in the areas typical for this heterocycle[17] and for CH_2CO-group. Of particular use is the singlet of H-6 and doublet of H-11, which occur in the narrow range of 8.94–9.01 and 8.55–8.59 ppm, respectively. The same deshielding was observed also in a series of substituted 1,2,4-triazolo[1,5-*c*]quinazolines.[26,27] Furthermore, signals occurring at lowest field values in the ^{13}C NMR spectra belong to the two C=O groups of the acylmethyl moiety and C-2 at 183.0–195.4 and 160.5–164.1 ppm, respectively. The measurement of the ^1H NMR spectrum of **4e** was unsuccessful due to low solubility in DMSO-d_6.

In a similar way to the parent acylmethyl derivatives,[28] compounds **4** can also exist in ketoimine (**A**), enaminone (**B**) and enol (**C**) tautomeric forms (Scheme 3). According to the ^1H and ^{13}C NMR spectra, ketoimine form **A** is the only present tautomer of 3-acylmethyl triazinoquinazolines **4b**–**d**,**g**,**h**,**k**–**n**. Other derivatives **4a**,**f**,**i**,**j**,**o** also favor form **A** in DMSO-d_6 solution, however minor amounts of other tautomers were observed in the ^1H NMR spectra. The latter shows a low-field shift of H-6 (9.23–9.32 ppm) relative to the H-6 of form **A**. This fact along with the distinctive position of the methine proton (5.97–6.53 ppm) discloses slight changes in the structure of the heterocycle thus indicating the presence of enol **C** as a minor tautomeric form. According to the integral intensities in the ^1H NMR spectra, the equilibrium solutions of **4a**,**f**,**i**,**j**,**o** in DMSO-d_6 were found to contain 2.5–15% of enol tautomer **C**.



Scheme 3.

The LC–MS positive-ion atmospheric pressure chemical ionization (APCI) show the appropriately protonated molecular ions $[MH]^+$, which confirm the expected molecular weights of **4**. The MS (EI) pattern is typical for this class of heterocyclic system[17] and is connected mainly with two processes. The first one is related to the cleavage of the CH_2–CO bond, leaving a characteristic $ArC{\equiv}O^+$ fragment (**4c**,**e**,**g**,**j**,**l**). The second route is concerned with C(2)–C(3) and N(4)–N(5) bond breaking of the triazinoquinazoline, which gives fragment ions with *m*/*z* 171 (base peak for **4e**,**g**,**j**,**l**) or *m*/*z* 170 (**4m**). The mass spectrum of 4-chlorophenyl substituted derivative **4j** is also characterized by clusters of rearrangement peaks $[4\text{-}ClC_6H_4C{\equiv}O{+}M]^+$ and $[4\text{-}ClC_6H_4C{\equiv}O{+}M]^+$.

Ultimately, the structure of **4c** was determined by an X-ray diffraction study as 3-[2-(4-methoxyphenyl)-2-oxoethyl]-2*H*-[1,2,4]triazino[2,3-*c*]quinazolin-2-one (Fig. 1). According to the crystal data (the numbering is given according to the structural analysis), **4c** includes two planar fragments, which are turned relatively to each other due to the rotation around the C(10)–C(11) bond (the C(9)–C(10)–C(11)–C(12) torsion angle is −74.9(4)°). The non-planarity of molecule probably results from the repulsion between two carbonyl groups. The length of the O(2)–C(12) bond (1.217(4) Å) reflects double character of this bond. This fact in combination with the clearly single character of the C(10)–C(11) and C(11)–C(12) bonds (1.495(4) Å and 1.512(5) Å, respectively) indicates the existence of molecule **4c** in its ketoimine tautomeric form **A**. A shortened intramolecular contact H(6)…N(4) 2.57 Å(the van der Waals radii sum[29] is 2.67 Å) is observed. This is in complete agreement with the above deshielding of this proton observed in ^1H NMR spectra.

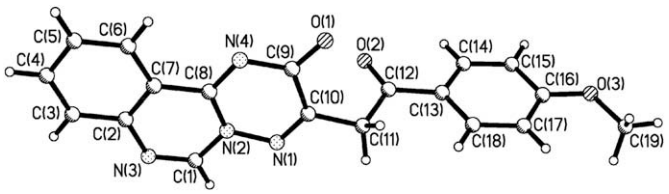
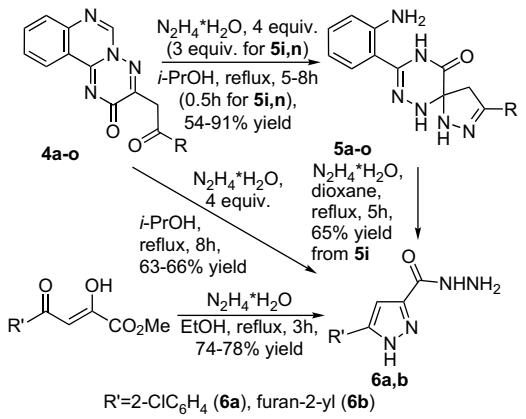


Figure 1. The molecular structure of compound **4c** according to X-ray diffraction data with the atom numbering used in structural analysis.

In continuation of our investigations regarding the chemistry and synthetic potential of fused quinazolines,[16,17,26,27] the obtained triazinoquinazolines were subjected to the reaction with excess of hydrazine hydrate (Scheme 4). Employing 3-acylmethyl derivatives **4** furnished the corresponding spiro-substituted heterocycles **5** in good yields, providing derivatives of the novel heterocyclic system spiro[pyrazoline-5,6′(1′*H*)-1,2,4-triazin]-5′(4′*H*)-one. However, it was found that prolonged heating of 2-chloro (**4i**) and furan-2-yl (**4n**) substituted triazinoquinazolines with a fourfold excess of hydrazine hydrate in *i*-propanol did not lead to anticipated spiro-

derivatives. Instead, the unexpected 5-(het)aryl-1*H*-pyrazole-3-carboxylic acid hydrazides (**6a**,**b**) were isolated. Their structure was deduced via spectroscopic studies and independent synthesis, which was performed starting from the appropriate benzoylpyruvates using a known procedure.[30] To elaborate feasible method for the synthesis of spiro-derivatives **5i**,**n** different conditions were examined. As a result, it was found that proper stoichiometry (3 rather than 4 equiv of hydrazine hydrate) and reaction time (heating for 30 min only) is crucial to keep the reaction on the desired pathway. Further hydrazinolysis of **5i** led to the 5-(2-chlorophenyl)-1*H*-pyrazole-3-carboxylic acid hydrazide (**6a**), which proves that hydrazides **6** arised from triazinoquinazolines **4** through successive degradation of the triazine ring in spiro-heterocycles **5**.



Scheme 4.

Comparing the ^{1}H NMR spectroscopic data of compounds **5** with those of **4** reveals the disappearance of the signal of H-6. Instead, the two-proton singlet of the NH_2-group occurs at ca. 6.30 ppm together with some upfield shift of the 2-aminophenyl protons, which clearly indicates pyrimidine ring degradation. The diastereotopic hydrogens of the CH_2-group of the pyrazoline ring appear as two distinct doublets with $^2J_{HH}$=17.6 Hz in the range 2.89–3.07 and 3.77–4.04 ppm. Thus, spiranes **5** were formed as the only tautomers. Besides, in the ^{13}C NMR spectra more significant differences are obvious; thus, in compounds **5**, the signal of the spiro C-atom occurred at 77.3–78.2 ppm serving as reliable evidence of spiro-heterocycle formation. The imine carbon C(3) of the pyrazoline ring is subjected to the influence of substituents in the het(aryl) ring and its signal is predictably shifted in the ^{13}C NMR spectra (142.3–150.4 ppm). Atom C(10) of the amide group is observed almost in the same region (163.5–164.1 ppm) as the one in the starting triazinoquinazolines.

Whereas quasimolecular ions $[MH]^+$ were observed in the LC–MS of **5**, the MS(EI) showed the appropriate fragmentation pattern, thus additionally confirming their structure. A characteristic abundant peaks $[M-H_2O]^{+\bullet}$ were formed due to cascade intramolecular rearrangement–dehydration processes. In some cases (**5e**,**m**), $[M-H_2O]^{+\bullet}$ becomes the base peak in the MS(EI).

The structure of compound **5g** was established by an X-ray diffraction study (Fig. 3). According to the crystallographic data (the numbering is given according to the structural analysis), the five-membered ring in compound **5g** adopts an envelope conformation. Deviation of the C(9) atom from the mean plane of the remaining atoms of the ring is 0.36 Å. The six-membered ring adopts a twist-boat conformation (the puckering parameters[31] are S=0.66, θ=53°, Ψ=29°). The C(8) and C(9) atoms deviate from the mean plane of the remaining atoms of the ring by 0.35 Å and 0.80 Å, respectively. The N(2) atom has an almost planar configuration (the sum of the bond angles centered at this atom is 358°). The C(7)–N(2) bond (1.404(2) Å) is longer than its average value[32] for acyclic compounds (1.347 Å), but barely differs from the known bond lengths of the structures **7** and **8**, containing a similar six-membered heterocycle (Fig. 2).[33,34] The amide fragment is somewhat nonplanar (the O(1)–C(8)–N(2)–H(2 N) torsion angle is 14°) owing to some pyramidality of the nitrogen atom. This perturbation, probably, results in elongation of the N(2)–C(8) bond to 1.356(2) Å and shortening of the C(8)–O(1) bond to 1.220(2) Å in comparison with their average values in acyclic amides and δ-lactams (1.334 Å and 1.235 Å, respectively), which was also observed in structure **7**. These observations suggest the presence of certain distortion of π-conjugation in the amide group and its presence mainly within the N(2)–C(7)–N(3) fragment.

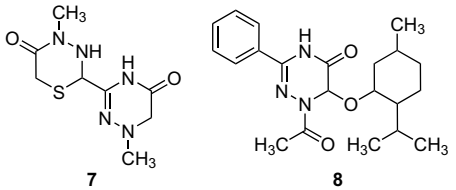


Figure 2. Selected 3-(het)aryl-1,6-dihydro-4*H*-[1,2,4]triazin-5-ones.

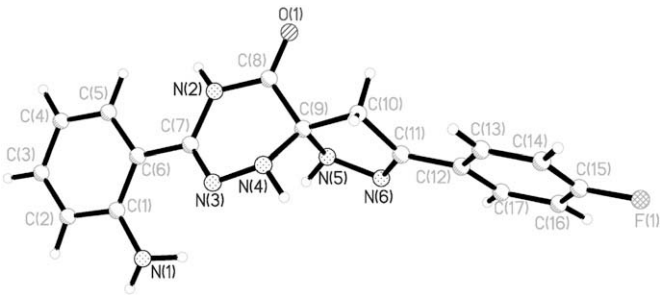
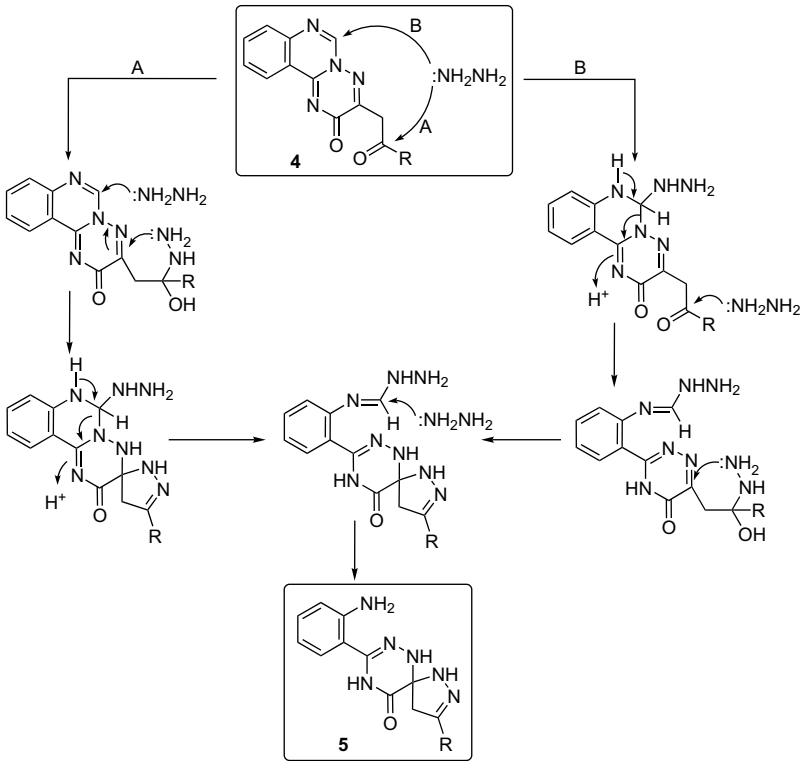


Figure 3. The molecular structure of compound **5g** according to X-ray diffraction data with the atom numbering used in structural analysis.

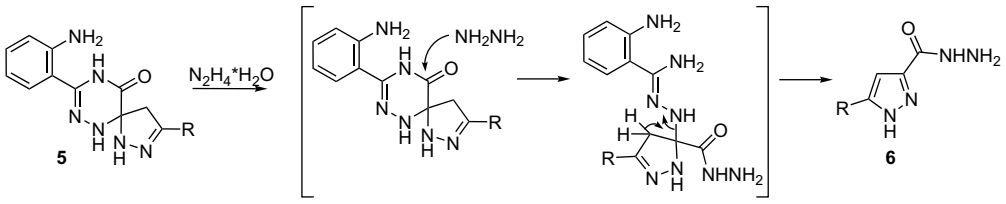
The N(4) and N(5) atoms have a pyramidal configuration (the sum of bond angles centered at these atoms are 336° and 331°, respectively). The N(4)–N(3) 1.393(2) Å and N(5)–N(6) 1.412(2) Å bond lengths are considerably longer their average value 1.366 Å indicating significant weakening of n-π conjugation with π-systems of neighboring double bonds.

In Scheme 5, a possible reaction mechanism accounting for the formation of spiro[pyrazoline-5,6′(1′*H*)-1,2,4-triazin]-5′(4′*H*)-ones (**5**) is hypothesized. Triazinoquinazolines **4** contain several electrophilic centers, which can serve as possible sites for hydrazine attack. The most significant ones are the carbons of the exocyclic C=O group and C-6 of the ring. An attempt to establish a place of initial nucleophilic attack through isolation of possible intermediates failed since an interaction with 1 equiv of hydrazine hydrate led to mixtures of starting material with the spiro-compound. Thus, we stipulated that at the first stage simultaneous addition of hydrazine at the indicated carbons occurs. Following the successive interaction with another molecule of hydrazine, the pyrimidine ring opens and the subsequent intermediate is produced. This, in turn, is attacked by hydrazine and spiro derivative (**5**) is formed.

A supposed mechanism of the side process, which results in formation of pyrazole-3-carboxylic acid hydrazides (**6**), is outlined in Scheme 6. Some distortion of π-conjugation in NHC(O) group of **5** emerged from X-ray data and makes this site rather susceptible for the nucleophilic attack. Therefore, we expect that the reaction of hydrazine at the lactam carbon gives rise to eliminative triazine ring fission in which hydrazide (**6**) is produced.



Scheme 5.



Scheme 6.

3. Conclusions

We have presented the straightforward synthesis of variously substituted derivatives of new spiro-heterocyclic system (**5**) starting from easily available 4-hydrazinoquinazoline (**1**). At the first stage 3-[2-(het)aryl-2-oxoethyl]-2*H*-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones (**4**) were obtained by the regioselective reaction of the starting hydrazine **1** with various 2,4-diketoesters. This approach represents a cascade cyclocondensation–Dimroth-like rearrangement, and was found to be advantageous for achieving the introduction of the acylmethyl moiety into the triazinoquinazoline core. Next, the obtained triazinoquinazolines **4** were subjected to the hydrazinolysis reaction, which leads to the novel spiro-ring system through a tandem process. Applications of these new spiro[pyrazoline-5,6′(1′*H*)-1,2,4-triazine] derivatives (**5**) in the synthesis of nitrogen containing heterocycles will be reported in due course.

4. Experimental section

4.1. General

Melting points were determined in open capillary tubes. IR spectra (4000–600 cm^{-1}) were recorded on a Bruker ALPHA FTIR spectrometer using a module for measuring attenuated total reflection (ATR) or Bruker Tensor 27 spectrometer (KBr) and expressed in cm^{-1}. ^1H and ^{13}C NMR spectra (500 MHz for ^1H and 125 MHz for ^{13}C) were recorded on a Bruker Avance DRX-500 spectrometer with $SiMe_4$ as internal standard in DMSO-d_6 solution. LC–MS were recorded using chromatography/mass spectrometric system, which consists of high-performed liquid chromatograph 'Agi1ent 1100 Series' equipped with diode-matrix and mass-selective detector 'Agi1ent LC/MSD SL' (atmospheric pressure chemical ionization—APCI). Electron impact mass spectra (EI-MS) were recorded on a Varian 1200 L instrument at 70 eV. The purity of all obtained compounds was checked by ^1H NMR and LC–MS.

4-Hydrazinoquinazoline (**1**) was synthesized according to the reported procedure.[35] Other starting materials and solvents were obtained from commercially available sources and used without additional purification.

4.2. Typical procedure for the synthesis of 3-[2-(het)aryl-2-oxoethyl]-2*H*-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones (4)

An appropriate 2,4-diketoester (11 mmol) was added to a solution of 4-hydrazinoquinazoline (**1**) (1.6 g, 10 mmol) in glacial acetic acid (30 mL) and resulting mixture was refluxed for 1–8 h or 24 h (**4h**). Then, it was concentrated to a volume of ca. 10 mL under reduced pressure. The residue so obtained was treated with EtOH (50 mL) and the mixture was kept several hours for

crystallization. The precipitate was filtered and washed thoroughly with EtOH.

4.2.1. 3-(2-Phenyl-2-oxoethyl)-2H-[1,2,4]triazino[2,3-c]quinazolin-2-one (**4a**)

Pale yellow solid (2.35 g, 74%), mp 286–288 °C. IR (ATR, cm^{-1}): 3063, 1623, 1511, 1471, 1440, 1417, 1318, 1269, 1255, 1203, 1123, 902, 775, 723, 689, 637, 621. ^1H NMR: δ=4.58 (s, 2H, CH_2)/6.51* (s, CH), 7.54*/7.59 (t, 2H, J=7.8, H-3′,5′), 7.72 (t, 1H, J=7.8, H-4′), 7.82 (t, 1H, J=7.8, H-10), 7.94 (d, 1H, J=8.0, H-8), 8.04 (t, 1H, J=7.8, H-9), 8.09 (d, 2H, J=8.0, H-2′,6′), 8.31*/8.58 (d, 1H, J=8.0, H-11), 8.99/9.31* (s, 1H, H-6) (tautomeric ratio, %: CH_2/CH*=97.5:2.5). ^{13}C NMR δ=41.7, 120.1, 125.9, 128.3, 128.9 (2C), 129.3 (2C), 129.6, 134.3, 136.0, 136.5, 144.3, 144.4, 152.3, 155.4, 160.6, 195.4. LC–MS, m/z=317 (MH^+). Anal. Calcd for $C_{18}H_{12}N_4O_2$: C, 68.35; H, 3.82; N, 17.71. Found: C, 68.41; H, 3.75; N, 17.79.

4.2.2. 3-[2-(4-Methylphenyl)-2-oxoethyl]-2H-[1,2,4]triazino-[2,3-c]quinazolin-2-one (**4b**)

Yellow solid (1.70 g, 51%), mp 236–238 °C. IR (ATR, cm^{-1}): 3065, 3038, 2988, 2923, 1681, 1663, 1628, 1595, 1510, 1464, 1407, 1319, 1305, 1276, 1260, 1200, 1183, 1121, 1101, 979, 912, 823, 797, 787, 688, 624. ^1H NMR: δ=2.41 (s, 3H, CH_3), 4.54 (s, 2H, CH_2), 7.39, 7.98 (d, 2H, J=8.0, H_{Phenyl}), 7.82 (t, 1H, J=7.8, H-10), 7.94 (d, 1H, J=8.0, H-8), 8.05 (t, 1H, J=7.8, H-9), 8.57 (d, 1H, J=8.0, H-11), 8.99 (s, 1H, H-6). ^{13}C NMR δ=21.7, 41.6, 120.2, 125.9, 128.3, 129.0 (2C), 129.6, 129.9 (2C), 134.1, 136.0, 144.3, 144.4, 144.8, 152.3, 155.5, 160.6, 194.9. LC–MS, m/z=331 (MH^+). Anal. Calcd for $C_{19}H_{14}N_4O_2$: C, 69.08; H, 4.27; N, 16.96. Found: C, 69.19; H, 4.21; N, 16.84.

4.2.3. 3-[2-(4-Methoxyphenyl)-2-oxoethyl]-2H-[1,2,4]triazino-[2,3-c]quinazolin-2-one (**4c**)

Yellow solid (2.48 g, 71%), mp 276–278 °C. IR (ATR, cm^{-1}): 3071, 2977, 2901, 1662, 1620, 1592, 1572, 1517, 1470, 1457, 1439, 1417, 1397, 1385, 1324, 1314, 1272, 1249, 1202, 1182, 1170, 1126, 1110, 1023, 1007, 977, 910, 838, 802, 775, 751, 699, 687, 668, 622. ^1H NMR: δ=3.88 (s, 3H, OCH_3), 4.52 (s, 2H, CH_2), 7.10 (d, 2H, J=8.1, H-3′,5′), 7.82 (t, 1H, J=7.8, H-10), 7.94 (d, 1H, J=8.0, H-8), 8.05 (m, 3H, H-9,2′,6′), 8.58 (d, 1H, J=8.0, H-11), 8.98 (s, 1H, H-6). ^{13}C NMR δ=41.4, 56.1, 114.5 (2C), 120.2, 125.9, 128.3, 129.5, 129.6, 131.3 (2C), 136.1, 144.3, 144.4, 152.3, 155.6, 160.6, 164.1, 193.7. EI-MS, m/z (I_{rel}, %)=346 ($M^{+\bullet}$, 13.8), 175 (5.2), 172 (6.1), 171 (40.4), 136 (10.9), 135 (100.0), 129 (17.8), 102 (5.2), 92 (5.2). LC–MS, m/z=348, 347 (MH^+). Anal. Calcd for $C_{19}H_{14}N_4O_3$: C, 65.89; H, 4.07; N, 16.18. Found: C, 65.95; H, 3.92; N, 16.31.

4.2.4. 3-[2-(3-Nitrophenyl)-2-oxoethyl]-2H-[1,2,4]triazino-[2,3-c]quinazolin-2-one (**4d**)

Dark red solid (2.25 g, 62%), mp 264–266 °C (DMF–H_2O). IR (ATR, cm^{-1}): 3034, 2987, 2902, 1652, 1605, 1563, 1522, 1501, 1479, 1463, 1395, 1347, 1323, 1285, 1256, 1217, 1200, 1158, 1129, 1107, 1066, 1033, 1011, 962, 911, 887, 831, 809, 786, 742, 697, 687, 651. ^1H NMR: δ=4.68 (s, 2H, CH_2), 7.82 (t, 1H, J=7.8, H-10), 7.90 (t, 2H, J=7.8, H-5′), 7.94 (d, 1H, J=8.0, H-8), 8.05 (t, 1H, J=7.8, H-9), 8.51 (d, 2H, J=7.8, H-4′,6′), 8.59 (d, 1H, J=7.9, H-11), 8.76 (s, 1H, H-2′), 8.94 (s, 1H, H-6). LC–MS, m/z=363, 362 (MH^+). Anal. Calcd for $C_{18}H_{11}N_5O_4$: C, 59.84; H, 3.07; N, 19.38. Found: C, 59.94; H, 2.95; N, 19.24.

4.2.5. 3-[2-(4-Nitrophenyl)-2-oxoethyl]-2H-[1,2,4]triazino-[2,3-c]quinazolin-2-one (**4e**)

Black solid (2.30 g, 64%), mp >300 °C. IR (ATR, cm^{-1}): 3064, 1665, 1615, 1604, 1594, 1564, 1516, 1500, 1465, 1425, 1389, 1338, 1318, 1294, 1256, 1216, 1194, 1184, 1159, 1129, 1108, 1068, 1030, 1015, 979, 937, 914, 900, 856, 832, 809, 784, 754, 729, 710, 690, 670, 622. EI-MS: m/z (I, %)=361 ($M^{+\bullet}$, 13.8), 172 (14.9), 171 (100.0), 150 (10.9), 129 (23.9), 104 (8.8), 102 (10.5). Anal. Calcd for $C_{18}H_{11}N_5O_4$: C, 59.84; H, 3.07; N, 19.38. Found: C, 59.92; H, 2.96; N, 19.24.

4.2.6. 3-[2-(2-Fluorophenyl)-2-oxoethyl]-2H-[1,2,4]triazino-[2,3-c]quinazolin-2-one (**4f**)

Yellow solid (2.40 g, 72%), mp 240–242 °C. IR (ATR, cm^{-1}): 3035, 2975, 2936, 1680, 1660, 1626, 1593, 1506, 1478, 1467, 1452, 1384, 1318, 1275, 1262, 1225, 1209, 1194, 1177, 1150, 1125, 1099, 1031, 975, 910, 858, 825, 812, 780, 767, 753, 691, 680, 623. ^1H NMR: δ=4.47 (s, 2H, CH_2)/6.46* (s, CH), 7.39 (m, 2H, H-3′,5′), 7.73 (m, 1H, H-4′), 7.81 (t, 1H, J=7.8, H-10), 7.93 (m, 2H, H-8,6′), 8.04 (t, 1H, J=7.8, H-9), 8.57 (d, 1H, J=7.8, H-11), 8.98/9.32* (s, 1H, H-6) (tautomeric ratio, %: CH_2/CH*=95:5). ^{13}C NMR δ=45.3 (^4J=6.6 Hz), 117.5 (^2J=22.6 Hz), 120.1, 125.2 (^2J=11.1 Hz), 125.4, 125.9, 128.3, 129.7, 131.0, 136.1, 136.2 (^3J=9.3 Hz), 144.3, 144.4, 152.4, 154.8, 160.5, 161.5 (^1J=254.8 Hz), 192.9. LC–MS, m/z=335 (MH^+). Anal. Calcd for $C_{18}H_{11}FN_4O_2$: C, 64.67; H, 3.32; N, 16.76. Found: C, 64.55; H, 3.28; N, 16.84.

4.2.7. 3-[2-(4-Fluorophenyl)-2-oxoethyl]-2H-[1,2,4]triazino-[2,3-c]quinazolin-2-one (**4g**)

Yellow solid (1.90 g, 57%), mp 224–226 °C (dioxane–H_2O). IR (ATR, cm^{-1}): 3061, 3036, 1682, 1652, 1627, 1595, 1508, 1469, 1410, 1390, 1369, 1343, 1327, 1279, 1263, 1225, 1204, 1163, 1130, 1102, 1035, 1013, 991, 980, 912, 862, 839, 817, 776, 776, 688, 625. ^1H NMR: δ=4.58 (s, 2H, CH_2), 7.42 (t, 2H, J=8.7, H-2′,6′), 7.82 (t, 1H, J=7.8, H-10), 7.94 (d, 1H, J=8.0, H-8), 8.05 (t, 1H, J=7.8, H-9), 8.18 (dd, 2H, ^3J=8.7, $^3J_{H-F}$=3.1, H-3′,5′), 8.57 (d, 1H, J=8.0, H-11), 8.94 (s, 1H, H-6). ^{13}C NMR δ=41.7, 116.4 (2C, $^2J_{CF}$=22.1 Hz), 120.2, 125.9, 128.3, 129.7, 132.0 (2C, $^3J_{CF}$=9.7 Hz), 133.3, 136.1, 144.3, 144.4, 152.4, 155.3, 160.1 ($^1J_{CF}$=254.8 Hz), 160.6, 194.1. EI-MS, m/z (I_{rel}, %)=335 (4.1), 334 ($M^{+\bullet}$, 21.8), 238 (6.2), 197 (3.7), 172 (16.6), 171 (100.0), 170 (6.4), 163 (3.4), 155 (3.2), 144 (4.5), 135 (5.6), 129 (35.7), 123 (9.7), 103 (5.5), 102 (5.6), 95 (13.3), 75 (18.4), 70 (6.1), 63 (3.8), 53 (3.1), 50 (3.1). LC–MS, m/z=335 (MH^+). Anal. Calcd for $C_{18}H_{11}FN_4O_2$: C, 64.67; H, 3.32; N, 16.76. Found: C, 64.52; H, 3.26; N, 16.85.

4.2.8. 3-[2-(2,5-Difluorophenyl)-2-oxoethyl]-2H-[1,2,4]-triazino[2,3-c]quinazolin-2-one (**4h**)

Pink solid (2.80 g, 79%), mp 260–262 °C. IR (ATR, cm^{-1}): 3035, 2988, 2929, 1687, 1660, 1629, 1602, 1512, 1486, 1468, 1420, 1385, 1327, 1276, 1261, 1218, 1193, 1177, 1146, 1125, 1105, 1033, 1025, 971, 957, 911, 894, 778, 760, 687, 625, 605. ^1H NMR: δ=4.49 (s, 2H, CH_2), 7.49, 7.62, 7.73 (m, 1H, H-3′,4′,6′), 7.82 (t, 1H, J=7.8, H-10), 7.94 (d, 1H, J=8.0, H-8), 8.05 (t, 1H, J=7.8, H-9), 8.58 (d, 1H, J=8.0, H-11), 8.98 (s, 1H, H-6). LC–MS, m/z=353 (MH^+). Anal. Calcd for $C_{18}H_{10}F_2N_4O_2$: C, 61.37; H, 2.86; N, 15.90. Found: C, 61.30; H, 2.92; N, 15.77.

4.2.9. 3-[2-(2-Chlorophenyl)-2-oxoethyl]-2H-[1,2,4]triazino-[2,3-c]quinazolin-2-one (**4i**)

Pink solid (2.23 g, 64%), mp 237–239 °C. IR (ATR, cm^{-1}): 3034, 2976, 2925, 1688, 1661, 1625, 1597, 1585, 1508, 1466, 1427, 1383, 1322, 1302, 1275, 1261, 1186, 1175, 1125, 1066, 1042, 1031, 976, 910, 783, 767, 757, 723, 689, 669, 623. ^1H NMR: δ=4.50 (s, 2H, CH_2)/5.97* (s, CH), 7.47*/7.54 (m, 1H, H-3′), 7.61 (m, 2H, H-4′,5′), 7.82 (t, 1H, J=7.8, H-10), 7.95 (m, 2H, H-8,6′), 8.05 (t, 1H, J=7.8, H-9), 8.57 (d, 1H, J=8.0, H-11), 9.01/9.23* (s, 1H, H-6) (tautomeric ratio, %: CH_2/CH*=90:10). ^{13}C NMR δ=45.1, 120.1, 126.0, 128.0, 128.3, 129.7, 130.7, 130.8, 131.2, 133.5, 136.1, 137.7, 144.3, 144.4, 152.4, 154.6, 160.5, 196.6. LC–MS, m/z=354, 353, 351 (MH^+). Anal. Calcd for $C_{18}H_{11}ClN_4O_2$: C, 61.64; H, 3.16; N, 15.97. Found: C, 61.55; H, 3.11; N, 15.88.

4.2.10. 3-[2-(4-Chlorophenyl)-2-oxoethyl]-2H-[1,2,4]triazino-[2,3-c]quinazolin-2-one (**4j**)

Yellow solid (2.65 g, 75%), mp 256–258 °C. IR (ATR, cm^{-1}): 3095–2842, 1689, 1660, 1618, 1604, 1587, 1512, 1468, 1398, 1386, 1368, 1324, 1271, 1254, 1203, 1178, 1125, 1089, 1026, 1005, 977, 956, 909, 836, 820, 769, 728, 686, 659, 622. ^1H NMR: δ=4.58 (s, 2H, CH_2)/

6.50* (s, CH), 7.82 (td, 1H, ^3J=8.0, ^4J=1.5, H-10), 7.93 (d, 2H, J=8.0, H-8), 8.05 (td, 1H, ^3J=8.0, ^4J=1.5, H-9), 8.10, 7.57*/7.66 (d, 2H, J=8.0, H_{Phenyl}), 8.57 (dd, 1H, ^3J=7.9, ^4J=1.5, H-11), 8.99/9.30* (s, 1H, H-6) (tautomeric ratio, %: CH_2/CH*=95:5). ^{13}C NMR δ=41.7, 120.1, 125.9, 128.3, 129.5 (2C), 129.6, 130.8 (2C), 135.2, 136.0, 139.2, 144.3, 144.4, 152.3, 155.2, 160.6, 194.5. EI-MS, m/z (I_{rel}, %)=493 (2.8), 492 (3.6), 491 (13.2), 490 (5.6), 489 ([4-$ClC_6H_4C{\equiv}O$+M]$^+$, 21.3), 464 (2.2), 463 (7.1), 461 ([4-ClC_6H_4+M]$^+$, 10.5), 452 (3.9), 426 (3.1), 425 (4.4), 354 (10.5), 353 (44.7), 352 ([M+2]$^{+\bullet}$, 54.5), 351 (75.9), 350 (M$^{+\bullet}$, 78.8), 333 (4.8), 327 (3.0), 326 (3.1), 325 (4.4), 324 (4.6), 322 (5.0), 239 (8.1), 213 (3.5), 212 (3.0), 211 (3.4), 197 (3.8), 181 (6.6), 179 (14.8), 172 (27.7), 171 (100.0), 143 (3.0), 141 (9.0), 139 (27.7), 129 (23.0), 111 (8.8), 102 (3.5), 76 (3.9), 75 (5.7). LC–MS, m/z=353 ([MH+2]$^+$), 351 (MH$^+$). Anal. Calcd for $C_{18}H_{11}ClN_4O_2$: C, 61.64; H, 3.16; N, 15.97. Found: C, 61.56; H, 3.07; N, 15.90.

4.2.11. 3-[2-(3-Bromophenyl)-2-oxoethyl]-2H-[1,2,4]triazino-[2,3-c]quinazolin-2-one (**4k**)

Pink solid (2.83 g, 72%), mp >300 °C. IR (ATR, cm^{-1}): 3047, 2988, 2925, 1693, 1663, 1625, 1594, 1562, 1506, 1467, 1407, 1392, 1323, 1277, 1261, 1209, 1177, 1156, 1127, 1101, 1091, 1067, 1033, 1012, 979, 964, 911, 872, 853, 819, 791, 781, 724, 697, 688, 677, 664, 642, 624. ^{1}H NMR: δ=4.60 (s, 2H, CH_2), 7.56 (t, 1H, J=8.0, H-5′), 7.82 (t, 1H, J=8.0, H-10), 7.92 (d, 2H, J=7.8, H-6′), 7.94 (d, 1H, J=8.0, H-8), 8.04 (t, 1H, J=8.0, H-9), 8.09 (d, 1H, J=8.1, H-4′), 8.23 (s, 1H, H-2′), 8.58 (d, 1H, J=8.0, H-11), 8.98 (s, 1H, H-6). LC–MS, m/z=397 ([MH+2]$^+$), 396, 395 (MH$^+$). Anal. Calcd for $C_{18}H_{11}BrN_4O_2$: C, 54.70; H, 2.81; N, 14.18. Found: C, 54.81; H, 2.93; N, 14.10.

4.2.12. 3-[2-(4-Bromophenyl)-2-oxoethyl]-2H-[1,2,4]triazino-[2,3-c]quinazolin-2-one (**4l**)

Pink solid (2.75 g, 70%), mp >300 °C (DMF–H_2O). IR (ATR, cm^{-1}): 3034, 2987, 2927, 2902, 1683, 1654, 1627, 1596, 1584, 1508, 1468, 1391, 1370, 1342, 1327, 1280, 1261, 1204, 1179, 1158, 1128, 1103, 1070, 1034, 1018, 1007, 989, 912, 857, 831, 820, 806, 791, 776, 753, 719, 707, 688, 660, 625. ^{1}H NMR: δ=4.57 (s, 2H, CH_2), 7.83 (t, 1H, J=7.8, H-10), 7.95 (d, 1H, J=8.0, H-8), 7.81, 8.02 (d, 2H, J=8.2, H-2′,3′,5′,6′), 8.05 (t, 1H, J=7.8, H-9), 8.58 (d, 1H, J=8.0, H-11), 8.99 (s, 1H, H-6). EI-MS, m/z (I_{rel}, %)=396 ([M+2]$^{+\bullet}$, 8.2), 394 (M$^{+\bullet}$, 8.7), 324 (5.8), 185 (29.6), 183 (38.4), 172 (16.5), 171 (100.0), 157 (10.3), 155 (10.3), 129 (29.0), 102 (8.9). LC–MS, m/z=397 ([MH+2]$^+$), 396, 395 (MH$^+$). Anal. Calcd for $C_{18}H_{11}BrN_4O_2$: C, 54.70; H, 2.81; N, 14.18. Found: C, 54.83; H, 2.90; N, 14.07.

4.2.13. 3-[2-Thiophen-2-yl-2-oxoethyl]-2H-[1,2,4]triazino-[2,3-c]quinazolin-2-one (**4m**)

Yellow solid (2.35 g, 73%), mp 256–258 °C. IR (ATR, cm^{-1}): 3087, 2973, 2936, 2904, 1655, 1620, 1606, 1586, 1506, 1466, 1405, 1385, 1361, 1325, 1240, 1201, 1174, 1123, 1099, 1082, 1047, 1026, 1004, 976, 946, 907, 860, 774, 741, 699, 687, 669, 661, 644, 623. ^{1}H NMR: δ=4.52 (s, 2H, CH_2), 7.31 (t, 1H, J=4.0, H-4′), 7.79 (t, 1H, J=7.8, H-10), 7.91 (d, 1H, J=7.9, H-8), 8.03 (t, 1H, J=8.0, H-9), 8.09 (d, 1H, J=4.9, H-3′), 8.18 (d, 1H, J=3.2, H-5′), 8.55 (d, 1H, J=8.0, H-11), 8.97 (s, 1H, H-6). ^{13}C NMR δ=42.0, 120.1, 125.9, 128.3, 129.4, 129.6, 135.2, 136.1, 136.2, 143.4, 144.3, 144.4, 152.3, 154.7, 160.6, 188.0. EI-MS, m/z (I_{rel}, %)=325 (5.2), 324 ([M+2]$^{+\bullet}$, 13.4), 322 (M$^{+\bullet}$, 34.5), 321 (100.0), 170 (13.1), 168 (6.3). LC–MS, m/z=323 (MH$^+$). Anal. Calcd for $C_{16}H_{10}N_4O_2S$: C, 59.62; H, 3.13; N, 17.38. Found: C, 59.70; H, 3.21; N, 17.29.

4.2.14. 3-(2-Furan-2-yl-2-oxoethyl)-2H-[1,2,4]triazino-[2,3-c]quinazolin-2-one (**4n**)

Yellow solid (2.40 g, 78%), mp 266–268 °C. IR (ATR, cm^{-1}): 3132, 3108, 3040, 2921, 2852, 1679, 1658, 1622, 1589, 1507, 1460, 1387, 1328, 1266, 1212, 1151, 1126, 1079, 1037, 1010, 986, 909, 881, 797, 771, 688, 650, 620. ^{1}H NMR: δ=4.37 (s, 2H, CH_2), 6.79 (m, 1H, H-4′), 7.66 (d, 1H, J=3.4, H-3′), 7.81 (t, 1H, J=7.8, H-10), 7.94 (d, 1H, J=7.9, H-8), 8.05 (m, 2H, H-9,5′), 8.57 (d, 1H, J=7.9, H-11), 8.99 (s, 1H, H-6). ^{13}C NMR δ=41.3, 113.3, 120.1, 120.2, 125.9, 128.3, 129.6, 136.1, 144.3, 144.4, 148.8, 151.8, 152.4, 154.6, 160.5, 183.0. LC–MS, m/z=307 (MH$^+$). Anal. Calcd for $C_{16}H_{10}N_4O_3$: C, 62.75; H, 3.29; N, 18.29. Found: C, 62.88; H, 3.41; N, 18.25.

4.2.15. 3-(2-Benzo[b]furan-2-yl-2-oxoethyl)-2H-[1,2,4]triazino-[2,3-c]quinazolin-2-one (**4o**)

Yellow solid (1.75 g, 49%), mp 283–285 °C (DMF–H_2O). IR (ATR, cm^{-1}): 3057, 3036, 2929, 1686, 1662, 1629, 1596, 1561, 1509, 1468, 1332, 1324, 1277, 1262, 1155, 1133, 912, 881, 823, 782, 751, 744, 689, 640. ^{1}H NMR: δ=4.53 (s, 2H, CH_2)/6.53* (s, CH), 7.33*/7.41, 7.48*/7.59 (t, 1H, J=8.0, H-5′,6′), 7.82 (t, 1H, J=7.8, H-10), 7.71*/7.75, 7.84*/7.89 (d, 1H, J=8.0, H-4′,7′), 7.94 (d, 1H, J=7.9, H-8), 7.97*/8.05 (t, 1H, J=7.8, H-9), 8.12 (s, 1H, H-3′), 8.58 (d, 1H, J=7.9, H-11), 9.00/9.25* (s, 1H, H-6) (tautomeric ratio, %: CH_2/CH*=85:15). LC–MS, m/z=358, 357 (MH$^+$). Anal. Calcd for $C_{20}H_{12}N_4O_3$: C, 67.41; H, 3.39; N, 15.72. Found: C, 67.49; H, 3.48; N, 15.62.

4.3. Typical procedure for the synthesis of 3′-(2-aminophenyl)-3-(het)aryl-spiro[pyrazoline-5,6′(1′*H*)-1,2,4-triazin]-5′(4′*H*)-ones (5)

To an appropriate triazinoquinazoline **4** (10 mmol) in *i*-PrOH (15 mL) was added N_2H_4•H_2O (2.0 mL, 40 mmol) and resulting mixture was refluxed for 6–8 h. On cooling, the precipitate was filtered and washed with *i*-PrOH.

Compounds **4i**,**n** under these reaction conditions afforded **6a** (1.57 g, 66%, *i*-propanol–H_2O) and **6b** (1.22 g, 63%) correspondingly.

4.3.1. 3′-(2-Aminophenyl)-3-phenyl-spiro[pyrazoline-5,6′(1′H)-1,2,4-triazin]-5′(4′H)-one (**5a**)

White solid (2.80 g, 87%), mp 236–238 °C (dioxane–H_2O). IR (ATR, cm^{-1}): 3374, 3260, 3221, 1690, 1616, 1568, 1526, 1494, 1445, 1350, 1300, 1262, 1130, 1063, 1008, 998, 971, 863, 745, 685, 660, 640, 611. ^{1}H NMR: δ=2.95, 3.84 (d, 1H, J=17.6, CH_2), 6.32 (br s, 2H, NH_2), 6.55 (t, 1H, J=7.6, H-5′), 6.71 (d, 1H, J=7.8, H-3′), 7.05 (t, 1H, J=7.8, H-4′), 7.35 (d, 1H, J=7.6, H-6′), 7.40 (t, 3H, J=7.6, H-3,4,5), 7.65 (d, 2H, J=7.4, H-2,6), 8.22, 8.14 (s, 1H, NH), 10.84 (s, 1H, NH–CO). ^{13}C NMR δ=39.0, 77.7, 113.2, 115.3, 116.0, 125.6, 125.9, 127.9, 128.8, 129.0, 129.4, 129.9, 133.3, 140.3, 147.6, 148.1, 164.0. LC–MS, m/z=322, 321 (MH$^+$). Anal. Calcd for $C_{17}H_{16}N_6O$: C, 63.74; H, 5.03; N, 26.23. Found: C, 63.88; H, 5.12; N, 26.11.

4.3.2. 3′-(2-Aminophenyl)-3-(4-methylphenyl)-spiro[pyrazoline-5,6′(1′H)-1,2,4-triazin]-5′(4′H)-one (**5b**)

White solid (2.30 g, 69%), mp 206–208 °C (dioxane–H_2O). IR (ATR, cm^{-1}): 3382, 3215, 1689, 1613, 1595, 1503, 1436, 1363, 1348, 1313, 1233, 1216, 1131, 1076, 1039, 1009, 972, 932, 884, 864, 813, 788, 753, 741, 690, 666, 647, 614. ^{1}H NMR: δ=2.92, 3.80 (d, 1H, J=17.6, CH_2), 6.32 (br s, 2H, NH_2), 6.54 (t, 1H, J=7.6, H-5′), 6.70 (d, 1H, J=8.1, H-3′), 7.04 (t, 1H, J=7.8, H-4′), 7.20 (d, 2H, J=8.1, H-3,5), 7.41 (d, 1H, J=7.8, H-6′), 7.54 (d, 2H, J=8.1, H-2,6), 8.13, 8.10 (s, 1H, NH), 10.82 (s, 1H, NH–CO). ^{13}C NMR δ=21.4, 39.1, 77.6, 113.1, 115.2, 116.0, 125.8 (2C), 127.8, 129.6 (2C), 129.8, 130.6, 138.2, 140.2, 147.6, 148.2, 164.0. LC–MS, m/z=335 (MH$^+$). Anal. Calcd for $C_{18}H_{18}N_6O$: C, 64.66; H, 5.43; N, 25.13. Found: C, 64.77; H, 5.51; N, 25.05.

4.3.3. 3′-(2-Aminophenyl)-3-(4-methoxyphenyl)-spiro[pyrazoline-5,6′(1′H)-1,2,4-triazin]-5′(4′H)-one (**5c**)

White solid (3.20 g, 91%), mp 214–216 °C (dioxane–H_2O). IR (KBr, cm^{-1}): 3470, 3299, 3252, 1703, 1620, 1606, 1589, 1516, 1499, 1451, 1417, 1402, 1351, 1260, 1179, 1130, 1047, 1029, 979, 903, 867, 835, 781, 758, 734, 661, 604. ^{1}H NMR: δ=2.91, 3.80 (d, 1H, J=17.6, CH_2), 6.32 (br s, 2H, NH_2), 6.54 (t, 1H, J=7.6, H-5′), 6.70 (d, 1H, J=8.1,

H-3′), 6.95 (d, 2H, *J*=8.5, H-3,5), 7.04 (t, 1H, *J*=7.8, H-4′), 7.41 (d, 1H, *J*=7.8, H-6′), 7.59 (d, 2H, *J*=8.5, H-2,6), 7.97, 8.11 (s, 1H, NH), 10.81 (s, 1H, NH–CO). ^{13}C NMR δ=39.3, 55.7, 77.6, 113.2, 114.5 (2C), 115.3, 116.0, 126.0, 127.4 (2C), 127.8, 129.8, 140.2, 147.6, 148.3, 160.0, 164.1. LC–MS, *m*/*z*=351 (MH^+). EI-MS, *m*/*z* (I_{rel}, %)=351 (13.7), 350 ($M^{+\bullet}$, 100.0), 344 (9.8), 334 (16.4), 333 (26.8), 332 ($[M-H_2O]^{+\bullet}$, 71.1), 331 (27.6), 321 (10.7), 319 (34.8), 200 (22.9), 198 (24.9), 197 (5.9), 159 (16.3). Anal. Calcd for $C_{18}H_{18}N_6O_2$: C, 61.70; H, 5.18; N, 23.99. Found: C, 61.79; H, 5.25; N, 23.85.

4.3.4. 3′-(2-Aminophenyl)-3-(3-nitrophenyl)-spiro[pyrazoline-5,6′(1′H)-1,2,4-triazin]-5′(4′H)-one (**5d**)

Yellow solid (2.90 g, 79%), mp 216–218 °C (dioxane–H_2O). IR (ATR, cm^{-1}): 3466, 3363, 3267, 3206, 1698, 1613, 1592, 1529, 1502, 1450, 1349, 1292, 1021, 970, 915, 884, 856, 833, 791, 760, 751, 736, 694, 670. ^{1}H NMR: δ=3.02, 3.90 (d, 1H, *J*=17.6, CH_2), 6.30 (br s, 2H, NH_2), 6.55 (t, 1H, *J*=7.6, H-5′), 6.71 (d, 1H, *J*=8.1, H-3′), 7.05 (t, 1H, *J*=7.8, H-4′), 7.42 (d, 1H, *J*=7.8, H-6′), 7.69 (t, 1H, *J*=7.8, H-5), 8.03 (d, 1H, *J*=7.8, H-6), 8.15 (d, 1H, *J*=8.1, H-4), 8.18 (s, 1H, NH), 8.39 (s, 1H, H-2), 8.64 (s, 1H, NH), 10.88 (br s, 1H, NH–CO). ^{13}C NMR δ=38.6, 78.2, 113.1, 115.3, 116.0, 119.6, 122.9, 127.9, 129.9, 130.7, 131.9, 135.1, 140.4, 145.8, 147.6, 148.6, 163.6. LC–MS, *m*/*z*=365 (M^+), 364. Anal. Calcd for $C_{17}H_{15}N_7O_3$: C, 55.89; H, 4.14; N, 26.84. Found: C, 55.98; H, 4.20; N, 26.75.

4.3.5. 3′-(2-Aminophenyl)-3-(4-nitrophenyl)-spiro[pyrazoline-5,6′(1′H)-1,2,4-triazin]-5′(4′H)-one (**5e**)

Orange solid (2.60 g, 71%), mp 228–230 °C (dioxane–H_2O). IR (KBr, cm^{-1}): 3464, 3352, 3288, 1711, 1615, 1565, 1507, 1452, 1407, 1370, 1338, 1293, 1167, 1109, 1042, 1009, 974, 908, 851, 832, 767, 750. ^{1}H NMR: δ=2.99, 3.88 (d, 1H, *J*=17.6, CH_2), 6.31 (br s, 2H, NH_2), 6.54 (t, 1H, *J*=7.6, H-5′), 6.70 (d, 1H, *J*=8.1, H-3′), 7.05 (t, 1H, *J*=7.8, H-4′), 7.41 (d, 1H, *J*=7.8, H-6′), 7.86 (d, 2H, *J*=8.8, H-3,5), 8.23 (m, 3H, NH, H-2,6), 8.98 (s, 1H, NH), 10.92 (s, 1H, NH–CO). ^{13}C NMR δ=38.3, 78.2, 113.0, 115.3, 116.1, 124.4 (2C), 126.3 (2C), 127.9, 129.9, 139.8, 140.4, 145.3, 146.8, 147.6, 163.4. LC–MS, *m*/*z*=364 ($[M-H]^+$). EI-MS, *m*/*z* (I_{rel}, %)=366 (21.0), 365 ($M^{+\bullet}$, 67.1), 349 (20.0), 348 (62.0), 347 ($[M-H_2O]^{+\bullet}$, 100.0), 337 (27.1), 334 (15.4), 306 (14.2), 301 (13.7), 247 (16.0), 217 (14.0), 216 (73.3), 205 (10.0), 176 (11.9), 171 (12.9), 170 (12.2), 162 (18.5), 161 (27.1), 135 (14.6), 133 (17.3), 129 (10.5), 120 (10.3), 119 (66.7), 118 (84.0), 105 (11.0), 104 (15.6), 103 (11.6), 102 (13.2), 92 (19.9), 91 (24.0), 90 (10.9). Anal. Calcd for $C_{17}H_{15}N_7O_3$: C, 55.89; H, 4.14; N, 26.84. Found: C, 55.96; H, 4.21; N, 26.71.

4.3.6. 3′-(2-Aminophenyl)-3-(2-fluorophenyl)-spiro[pyrazoline-5,6′(1′H)-1,2,4-triazin]-5′(4′H)-one (**5f**)

White solid (2.84 g, 84%), mp 190–192 °C (dioxane–H_2O). IR (ATR, cm^{-1}): 3373, 3273, 3228, 1691, 1613, 1591, 1488, 1448, 1429, 1340, 1294, 1218, 1130, 1098, 1008, 971, 864, 814, 743, 688, 651. ^{1}H NMR: δ=2.99, 3.90 (d, 1H, *J*=17.6, CH_2), 6.31 (br s, 2H, NH_2), 6.54 (t, 1H, *J*=7.6, H-5′), 6.70 (d, 1H, *J*=8.1, H-3′), 7.05 (t, 1H, *J*=7.8, H-4′), 7.25 (m, 2H, H-3,5), 7.37 (t, 1H, *J*=7.1, H-4), 7.41 (d, 1H, *J*=7.8, H-6′), 7.78 (t, 1H, *J*=7.8, H-6), 8.16, 8.41 (s, 1H, NH), 10.85 (s, 1H, NH–CO). ^{13}C NMR δ=40.9, 77.5, 113.1, 115.3, 116.0, 116.8 ($^2J_{CF}$=22.1 Hz), 121.1 ($^2J_{CF}$=11.5 Hz), 125.1 ($^4J_{CF}$=2.7 Hz), 127.9, 128.5 ($^3J_{CF}$=4.0 Hz), 129.9, 130.5 ($^3J_{CF}$=8.4 Hz), 140.3, 143.5 ($^3J_{CF}$=3.5 Hz), 147.6, 159.8 ($^1J_{CF}$=250.0 Hz), 163.8. LC–MS, *m*/*z*=339 (MH^+). Anal. Calcd for $C_{17}H_{15}FN_6O$: C, 60.35; H, 4.47; N, 24.84. Found: C, 60.47; H, 4.54; N, 24.78.

4.3.7. 3′-(2-Aminophenyl)-3-(4-fluorophenyl)-spiro[pyrazoline-5,6′(1′H)-1,2,4-triazin]-5′(4′H)-one (**5g**)

Off-white solid (2.90 g, 86%), mp 214–216 °C (dioxane–H_2O). IR (KBr, cm^{-1}): 3380, 3265, 3225, 1692, 1621, 1604, 1512, 1450, 1413, 1356, 1303, 1234, 933, 834, 760, 695, 668, 651, 615. ^{1}H NMR: δ=2.95, 3.82 (d, 1H, *J*=17.6, CH_2), 6.24 (br s, 2H, NH_2), 6.54 (t, 1H, *J*=7.6, H-5′), 6.70 (d, 1H, *J*=8.1, H-3′), 7.05 (t, 1H, *J*=7.8, H-4′), 7.21 (m, 2H, H-3,5), 7.41 (d, 1H, *J*=7.8, H-6′), 7.68 (m, 2H, H-2,6), 8.06, 8.11 (s, 1H, NH), 10.74 (s, 1H, NH–CO). ^{13}C NMR δ=39.1, 77.8, 113.1, 115.3, 116.0 (2C, $^2J_{CF}$=21.7 Hz), 116.0, 127.8, 127.9 (2C, $^3J_{CF}$=8.4 Hz), 129.9, 130.0, 140.3, 147.3, 147.6, 162.5 ($^1J_{CF}$=245.5 Hz), 163.9. LC–MS, *m*/*z*=338 (M^+), 337. EI-MS, *m*/*z* (I_{rel}, %)=339 (10.1), 338 ($M^{+\bullet}$, 100.0), 321 (12.4), 320 ($[M-H_2O]^{+\bullet}$, 42.4), 188 (25.1), 172 (15.9), 71 (9.9). Anal. Calcd for $C_{17}H_{15}FN_6O$: C, 60.35; H, 4.47; N, 24.84. Found: C, 60.49; H, 4.58; N, 24.72.

4.3.8. 3′-(2-Aminophenyl)-3-(2,5-difluorophenyl)-spiro-[pyrazoline-5,6′(1′H)-1,2,4-triazin]-5′(4′H)-one (**5h**)

Beige solid (1.92 g, 54%), mp 212–214 °C (dioxane–H_2O). IR (ATR, cm^{-1}): 3471, 3369, 3253, 1694, 1611, 1591, 1566, 1492, 1444, 1363, 1336, 1290, 1245, 1171, 1045, 1024, 968, 908, 891, 812, 788, 748, 698, 664. ^{1}H NMR: δ=2.99, 3.89 (d, 1H, *J*=17.6, CH_2), 6.28 (br s, 2H, NH_2), 6.54 (t, 1H, *J*=7.6, H-5′), 6.70 (d, 1H, *J*=8.1, H-3′), 7.05 (t, 1H, *J*=7.8, H-4′), 7.21 (m, 1H, H-3), 7.31 (m, 1H, H-5), 7.40 (d, 1H, *J*=7.8, H-6′), 7.51 (m, 1H, H-6), 8.15, 8.60 (s, 1H, NH), 10.85 (s, 1H, NH–CO). ^{13}C NMR δ=39.5, 77.7, 113.0, 113.8 ($^2J_{CF}$=26.1 Hz, $^3J_{CF}$=4.4 Hz), 115.2, 116.0, 116.8 ($^2J_{CF}$=24.3 Hz, $^3J_{CF}$=9.3 Hz), 118.6 ($^2J_{CF}$=24.8 Hz, $^3J_{CF}$=9.3 Hz), 122.7, 127.9, 129.9, 140.3, 142.3, 147.6, 155.9 ($^1J_{CF}$=245.9 Hz), 158.6 ($^1J_{CF}$=239.7 Hz), 163.6. LC–MS, *m*/*z*=357 (MH^+). Anal. Calcd for $C_{17}H_{14}F_2N_6O$: C, 57.30; H, 3.96; N, 23.58. Found: C, 57.41; H, 4.08; N, 23.48.

4.3.9. 3′-(2-Aminophenyl)-3-(2-chlorophenyl)-spiro[pyrazoline-5,6′(1′H)-1,2,4-triazin]-5′(4′H)-one (**5i**)

To a suspension of **4i** (3.51 g, 10 mmol) in *i*-PrOH (15 mL) was added $N_2H_4{\bullet}H_2O$ (1.5 mL, 30 mmol) and resulting mixture was refluxed for 0.5 h. On cooling, the precipitate was filtered, washed with *i*-PrOH and air-dried to give yellow solid (2.74 g, 77%), mp 186–188 °C (dioxane–H_2O). IR (ATR, cm^{-1}): 3451, 3338, 3080, 2923, 1693, 1629, 1607, 1571, 1501, 1456, 1429, 1401, 1365, 1345, 1320, 1291, 1269, 1155, 1073, 1032, 1005, 967, 902, 871, 826, 750, 673, 650, 637. ^{1}H NMR: δ=3.07, 4.04 (d, 1H, *J*=17.6, CH_2), 6.32 (br s, 2H, NH_2), 6.54 (t, 1H, *J*=7.6, H-5′), 6.71 (d, 1H, *J*=7.8, H-3′), 7.05 (t, 1H, *J*=7.8, H-4′), 7.35 (m, 2H, H-4,5), 7.41 (d, 1H, *J*=7.8, H-6′), 7.48 (dd, 1H, ^3J=7.2, ^4J=2.0, H-3), 7.74 (dd, ^3J=7.2, ^4J=2.0, H-6), 8.19, 8.46 (s, 1H, NH), 10.87 (s, 1H, NH–CO). ^{13}C NMR δ=41.5, 77.9, 113.1, 115.3, 116.0, 127.6, 127.9, 129.9, 130.0, 130.4, 131.1, 131.2, 132.0, 140.3, 146.2, 147.6, 163.7. LC–MS, *m*/*z*=357, 355 (MH^+). Anal. Calcd for $C_{17}H_{15}ClN_6O$: C, 57.55; H, 4.26; N, 23.69. Found: C, 57.69; H, 4.31; N, 23.55.

4.3.10. 3′-(2-Aminophenyl)-3-(4-chlorophenyl)-spiro[pyrazoline-5,6′(1′H)-1,2,4-triazin]-5′(4′H)-one (**5j**)

White solid (3.04 g, 86%), mp 206–208 °C (dioxane–H_2O). IR (KBr, cm^{-1}): 3386, 3303, 3256, 3214, 1690, 1620, 1595, 1494, 1450, 1402, 1352, 1312, 1093, 1038, 1010, 933, 865, 758, 693, 670, 647, 615, 538. ^{1}H NMR: δ=2.93, 3.82 (d, 1H, *J*=17.6, CH_2), 6.32 (br s, 2H, NH_2), 6.54 (t, 1H, *J*=7.8, H-5′), 6.70 (d, 1H, *J*=8.1, H-3′), 7.05 (t, 1H, *J*=7.8, H-4′), 7.41 (d, 1H, *J*=8.1, H-6′), 7.45 (d, 2H, *J*=8.5, H-3,5), 7.66 (d, 2H, *J*=8.5, H-2,6), 8.16, 8.36 (s, 1H, NH), 10.86 (s, 1H, NH–CO). ^{13}C NMR δ=38.8, 77.8, 113.1, 115.2, 116.0, 127.5 (2C), 127.8, 129.1 (2C), 129.9, 132.2, 133.1, 140.3, 146.9, 147.6, 163.8. EI-MS, *m*/*z* (I_{rel}, %)=358 (7.6), 357 (34.3), 356 ($[M+2]^{+\bullet}$, 44.3), 354 ($M^{+\bullet}$, 100.0), 340 (9.1), 339 (23.2), 337 (52.2), 336 ($[M-H_2O]^{+\bullet}$, 78.6), 327 (4.2), 326 (4.9), 325 (12.9), 324 (5.2), 323 (9.2), 310 (4.1), 309 (5.0), 296 (3.1), 294 (5.8), 206 (6.0), 205 (14.7), 204 (29.9), 203 (22.4), 192 (4.7), 191 (4.8), 162 (3.5). LC–MS, *m*/*z*=355 (MH^+), 353. Anal. Calcd for $C_{17}H_{15}ClN_6O$: C, 57.55; H, 4.26; N, 23.69. Found: C, 57.67; H, 4.32; N, 23.56.

4.3.11. 3′-(2-Aminophenyl)-3-(3-bromophenyl)-spiro[pyrazoline-5,6′(1′H)-1,2,4-triazin]-5′(4′H)-one (**5k**)

Pale yellow solid (3.40 g, 85%), mp 216–218 °C (dioxane–H_2O). IR (ATR, cm^{-1}): 3375, 3265, 3221, 1688, 1616, 1554, 1521, 1503, 1469, 1448, 1422, 1359, 1299, 1259, 1160, 1129, 1069, 1040, 1010, 972, 885, 863, 756, 728, 693, 665, 640, 615. ^{1}H NMR: δ=2.94, 3.82 (d, 1H,

J=17.6, CH_2), 6.30 (br s, 2H, NH_2), 6.54 (t, 1H, J=7.6, H-5′), 6.70 (d, 1H, J=8.1, H-3′), 7.05 (t, 1H, J=7.8, H-4′), 7.35 (t, 1H. J=7.8, H-5), 7.41 (d, 1H, J=7.8, H-6′), 7.51 (d, 1H, J=7.8, H-4), 7.63 (d, 1H, J=7.8, H-6), 7.79 (s, 1H, H-2), 8.14, 8.44 (s, 1H, NH), 10.85 (s, 1H, NH–CO). ^{13}C NMR δ=38.7, 77.9, 113.1, 115.2, 116.0, 122.5, 124.8, 127.9, 128.1; 129.9, 131.2 (2C), 135.7, 140.3, 146.4, 147.6, 163.7. LC–MS, m/z=399 ([M−H]$^+$), 397. Anal. Calcd for $C_{17}H_{15}BrN_6O$: C, 51.14; H, 3.79; N, 21.05. Found: C, 51.26; H, 3.90; N, 20.92.

4.3.12. 3′-(2-Aminophenyl)-3-(4-bromophenyl)-spiro[pyrazoline-5,6′(1′H)-1,2,4-triazin]-5′(4′H)-one (**5l**)

Yellow solid (2.90 g, 73%), mp 220–222 °C (dioxane–H_2O). IR (KBr, cm^{-1}): 3419, 3315, 1700, 1608, 1587, 1491, 1451, 1416, 1399, 1342, 1312, 1295, 1162, 1132, 1071, 1007, 903, 875, 821, 754, 715, 670, 610. ^{1}H NMR: δ=2.93, 3.82 (d, 1H, J=17.6, CH_2), 6.31 (br s, 2H, NH_2), 6.54 (t, 1H, J=7.6, H-5′), 6.70 (d, 1H, J=8.1, H-3′), 7.04 (t, 1H, J=7.8, H-4′), 7.40 (d, 1H, J=7.8, H-6′), 7.58 (s, 4H, H-2,3,5,6), 8.15, 8.36 (s, 1H, NH), 10.85 (s, 1H, NH–CO). ^{13}C NMR δ=38.8, 77.8, 113.1, 115.2, 116.0, 121.7, 127.7 (2C), 127.8, 129.9, 132.0 (2C), 132.6, 140.3, 146.9, 147.6, 163.8. LC–MS, m/z=399 ([M−H]$^+$), 397. EI-MS, m/z (I_{rel}, %)=400 ([M+2]$^{+\bullet}$, 6.1), 398 (M$^{+\bullet}$, 5.7), 383 (5.8), 382 (8.9), 381 (5.0), 380 ([M−H_2O]$^{+\bullet}$, 6.4), 283 (8.4), 282 (55.9), 281 (7.0), 280 (46.6), 252 (11.5), 251 (99.5), 250 (9.7), 249 (100.0), 197 (3.8), 196 (13.7), 195 (5.1), 194 (16.2), 184 (9.1), 183 (3.1), 182 (6.1), 171 (5.1), 170 (8.5), 169 (4.4), 157 (7.1), 155 (8.7), 143 (3.1), 129 (3.1), 119 (11.5), 118 (10.9), 115 (9.8), 114 (11.1), 113 (9.6), 103 (4.5), 102 (6.3), 91 (3.4). Anal. Calcd for $C_{17}H_{15}BrN_6O$: C, 51.14; H, 3.79; N, 21.05. Found: C, 51.25; H, 3.88; N, 20.94.

4.3.13. 3′-(2-Aminophenyl)-3-(thiophen-2-yl)-spiro[pyrazoline-5,6′(1′H)-1,2,4-triazin]-5′(4′H)-one (**5m**)

Brown solid (2.24 g, 69%), mp 256–258 °C (dioxane–H_2O). IR (KBr, cm^{-1}): 3475, 3300, 2914, 1703, 1622, 1607, 1586, 1496, 1451, 1392, 1371, 1335, 1308, 1276, 1125, 1017, 986, 902, 859, 840, 776, 747, 704, 661. ^{1}H NMR: δ=2.95, 3.83 (d, 1H, J=17.6, CH_2), 6.31 (br s, 2H, NH_2), 6.53 (t, 1H, J=7.6, H-5′), 6.69 (d, 1H, J=8.1, H-3′), 7.04 (t, 1H, J=7.8, H-4′), 7.08 (dd, 1H, J_{H4-H5}=5.1, J_{H4-H3}=3.6, H-4), 7.24 (d, 1H, J_{H3-H4}=3.6, H-3), 7.40 (d, 1H, J=7.8, H-6′), 7.50 (d, 1H, J_{H5-H4}=5.1, H-5), 8.13, 8.16 (s, 1H, NH), 10.84 (s, 1H, NH–CO). ^{13}C NMR δ=39.5, 77.8, 113.1, 115.3, 116.0, 126.9, 127.0, 127.8, 128.0, 129.9, 136.9, 140.3, 144.5, 147.6, 163.8. EI-MS, m/z (I_{rel}, %)=328 (6.6), 327 (15.5), 326 (M$^{+\bullet}$, 88.5), 311 (5.3), 310 (19.0), 309 (69.3), 308 ([M−H_2O]$^{+\bullet}$, 100.0), 295 (17.5), 293 (5.2), 279 (7.1), 208 (11.4), 177 (55.6), 165 (12.0), 162 (7.2), 136 (9.0), 134 (8.9), 133 (6.1), 125 (5.9), 121 (6.6), 119 (36.0), 118 (33.2), 110 (12.7), 109 (11.3), 108 (6.3), 104 (6.3), 92 (9.6), 91 (12.8). LC–MS, m/z=327 (MH$^+$). Anal. Calcd for $C_{15}H_{14}N_6OS$: C, 55.20; H, 4.32; N, 25.75. Found: C, 55.32; H, 4.44; N, 25.70.

4.3.14. 3′-(2-Aminophenyl)-3-(furan-2-yl)-spiro[pyrazoline-5,6′(1′H)-1,2,4-triazin]-5′(4′H)-one (**5n**)

Compound **5n** was prepared from **4n** (3.06 g, 10 mmol) and N_2H_4•H_2O (1.5 mL, 30 mmol) in a similar manner as **5i**.

Dark-brown solid (2.02 g, 65%), mp 193–195 °C. IR (ATR, cm^{-1}): 3474, 3299, 1697, 1621, 1585, 1496, 1449, 1394, 1368, 1327, 1276, 1256, 1228, 1181, 1155, 1125, 1005, 974, 898, 884, 841, 745, 708, 650. ^{1}H NMR: δ=2.89, 3.77 (d, 1H, J=17.6, CH_2), 6.32 (br s, 2H, NH_2), 6.56 (t, 1H, J=7.6, H-5′), 6.59 (dd, 1H, J_{H4-H5}=3.4, J_{H4-H3}=1.8, H-4), 6.72 (m, 2H, H-3′,3), 7.06 (t, 1H, J=7.6, H-4′), 7.42 (d, 1H, J=7.8, H-6′), 7.75 (d, 1H, J=1.7, H-5), 8.16, 8.23 (s, 1H, NH), 10.86 (s, 1H, NH–CO). ^{13}C NMR δ=39.0, 77.3, 109.7, 112.2, 113.1, 115.2, 116.0, 127.9, 129.9, 140.3, 140.4, 143.9, 147.6, 148.5, 163.7. LC–MS, m/z=311 (MH$^+$). Anal. Calcd for $C_{15}H_{14}N_6O_2$: C, 58.06; H, 4.55; N, 27.08. Found: C, 58.20; H, 4.59; N, 26.94.

4.3.15. 3′-(2-Aminophenyl)-3-(benzo[b]furan-2-yl)-spiro-[pyrazoline-5,6′(1′H)-1,2,4-triazin]-5′(4′H)-one (**5o**)

Off-white solid (3.10 g, 86%), mp 240–242 °C (dioxane–H_2O). IR (ATR, cm^{-1}): 3420, 3289, 3243, 1698, 1613, 1589, 1499, 1449, 1363, 1326, 1277, 1255, 1234, 1119, 1019, 969, 928, 872, 846, 821, 799, 752, 698, 636, 612. ^{1}H NMR: δ=2.97, 3.86 (d, 1H, J=17.6, CH_2), 6.30 (br s, 2H, NH_2), 6.54 (t, 1H, J=7.6, H-5′), 6.70 (d, 1H, J=8.1, H-3′), 7.05 (t, 1H, J=7.8, H-4′), 7.12 (s, 1H, H-3), 7.26 (t, 1H, J=7.8, H-5), 7.32 (t, 1H, J=7.8, H-6), 7.41 (d, 1H, J=7.8, H-6′), 7.58 (d, 1H, J=8.1, H-7), 7.64 (d, 1H, J=7.8, H-4), 8.23, 8.68 (s, 1H, NH), 10.90 (br s, 1H, NH–CO). ^{13}C NMR δ=38.7, 77.7, 105.7, 111.5, 113.1, 115.3, 116.0, 121.8, 123.8, 125.5, 127.9, 128.7, 129.9, 139.4, 140.4, 147.6, 150.4, 154.8, 163.5. LC–MS, m/z=361 (MH$^+$). Anal. Calcd for $C_{19}H_{16}N_6O_2$: C, 63.33; H, 4.48; N, 23.32. Found: C, 63.45; H, 4.59; N, 23.21.

4.4. Reaction of 5i with hydrazine hydrate

To a **5i** (10 mmol) in dioxane (10 mL) was added N_2H_4•H_2O (2.0 mL, 40 mmol) and resulting mixture was refluxed for 8 h. After cooling, the mixture was poured into water. Obtained precipitate was filtered.

Otherwise the compounds **6a**,**b** was also prepared using the reported method.[30]

4.4.1. 5-(2-Chlorophenyl)-1H-pyrazole-3-carboxylic acid hydrazide (**6a**)

White solid (1.76 g, 74%), mp 194–196 °C (lit.[30] mp 195–196 °C). IR (ATR, cm^{-1}): 3321, 3219, 2974, 1658, 1600, 1538, 1475, 1452, 1394, 1286, 1252, 1199, 1074, 1045, 962, 927, 880, 831, 787, 747, 716, 675, 625. ^{1}H NMR: δ=4.80 (s, 2H, NH_2), 6.8–8.0 (m, 5H, H_{Ar}), 9.61 (s, 1H, NH), 13.66 (s, 1H, NH). LC–MS, m/z=239 (MH$^+$), 237. Anal. Calcd for $C_{10}H_9ClN_4O$: C, 50.75; H, 3.83; N, 23.67. Found: C, 50.62; H, 3.70; N, 23.81.

4.4.2. 5-(Furan-2-yl)-1H-pyrazole-3-carboxylic acid hydrazide (**6b**)

Off-white solid (1.50 g, 78%), mp 185–187 °C (*i*-propanol–H_2O). IR (ATR, cm^{-1}): 3278, 3180, 1650, 1583, 1555, 1531, 1515, 1407, 1391, 1369, 1320, 1257, 1124, 1078, 1012, 954, 895, 828, 791, 724. ^{1}H NMR: δ=4.47 (s, 2H, NH_2+H_2O), 6.58 (s, 1H, $H_{pyrazol}$), 6.76 (m, 1H, H-4$_{furan}$), 6.95 (m, 1H, H-3$_{furan}$), 7.73 (m, 1H, H-5$_{furan}$), 9.64 (s, 1H, NH), 9.94 (s, 1H, NH). LC–MS, m/z=191 ([M−H]$^+$). Anal. Calcd for $C_8H_8N_4O_2$: C, 50.00; H, 4.20; N, 29.15. Found: C, 50.12; H, 4.09; N, 29.26.

4.5. X-ray diffraction

The crystals of $C_{19}H_{14}N_4O_3$ (**4c**) are monoclinic. At 100 K a=13.781(5), b=8.091(5), c=14.656(5) Å, β=107.57(1)°, V=1558(1) Å^3, M_r=346.34, Z=4, space group $P2_1/n$, d_{calcd}=1.477 g/cm^3, μ(MoK$_\alpha$)=0.104 mm^{-1}, F(000)=720. Intensity of 6443 reflections (2731 independent, R_{int}=0.056) were measured on an automatic 'Xcalibur-3' diffractometer (graphite monochromated MoK$_\alpha$ radiation, CCD detector, ω scanning, 2Θ_{max}=50°).

The crystals of $C_{17}H_{15}FN_6O$ (**5g**) are monoclinic. At 293 K a=16.488(7), b=10.570(4), c=9.513(3) Å, β=106.24(7)°, V=1591.8(8) (2) Å^3, M_r=338.35, Z=4, space group $P2_1/c$, d_{calcd}=1.412 g/cm^3, μ(MoK$_\alpha$)=0.102 mm^{-1}, F(000)=704. Intensity of 106,047 reflections (5990 independent, R_{int}=0.0265) were measured on an automatic 'Xcalibur-3' diffractometer (graphite monochromated MoK$_\alpha$ radiation, CCD detector, ω scanning, 2Θ_{max}=55°).

The structures were solved by direct method using SHELXTL package.[36] Positions of the hydrogen atoms were located from electron density difference maps and refined usding 'riding' model with Uiso=nUeq of the carrier atom (n=1.5 for methyl group and n=1.2 for other hydrogen atoms) for structure **4c** and using isotropic approximation for structure **5g**.

Full-matrix least-squares refinement of the structures against F^2 in anisotropic approximation for non-hydrogen atoms using 2680 (**4c**), 3596 (**5g**) reflections was converged to: wR_2=0.149 (R_1=0.070 for 1687 reflections with F>4σ(F), S=1.112) for structure **4c** and

wR_2=0.096 (R_1=0.039 for 2289 reflections with $F>4\sigma(F)$, S=0.998) for structure **5g**. The final atomic coordinates, and crystallographic data for molecules **4c** and **5g** have been deposited to the Cambridge Crystallographic Data Centre, 12 Union Road, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk) and are available on request quoting the deposition numbers CCDC 722354 for **4c** and CCDC 722356 for **5g**.

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