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## A NEW ONE-STEP SYNTHESIS OF 1,2,4-TRIAZINO[2,3-*c*]-QUINAZOLINES

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**Abstract** – A new and efficient one-step protocol for the synthesis of 3-substituted 2*H*-1,2,4-triazino[2,3-*c*]quinazolin-2-ones (**5**) was developed starting from 4-hydrazinoquinazoline (**1**) and  $\alpha$ -ketocarboxylic acids and their esters. Corresponding hydrazones (**2a,c** and **3a,c,e**) were isolated as intermediate products. Further cyclocondensation followed by acid-catalyzed Dimroth rearrangement resulted in the title derivatives **5**.

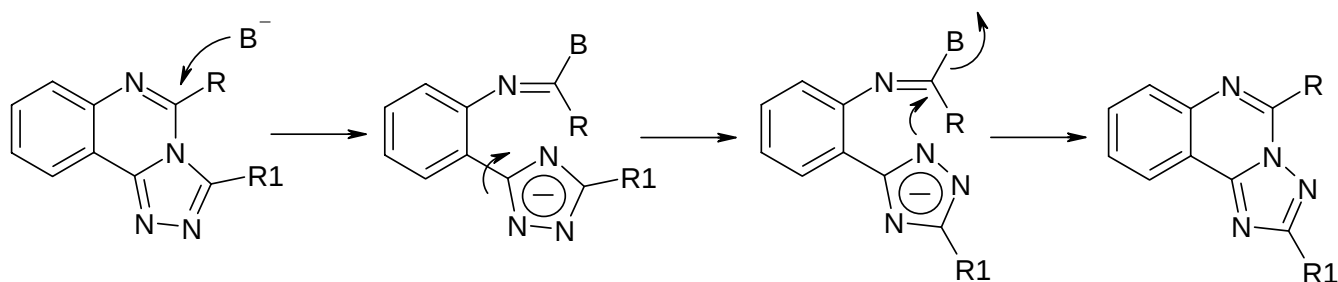
## INTRODUCTION

Development of efficient syntheses of 1,2,4-triazino[2,3-*c*]quinazolines is of considerable current interest. These compounds contain the pharmacologically relevant heterocyclic skeleton and exhibit a significant activity spectrum. Thus, 3,4-dihydro-2*H*-1,2,4-triazino[2,3-*c*]quinazolin-2-ones and the isomeric 2*H*-1,2,4-triazino[2,3-*c*]quinazolin-3(4*H*)-ones have been shown to possess antibacterial activity against *S. aureus*, *S. marcescens*, *B. subtilis*, and *E. Coli*.<sup>1</sup> Modification of the 3-hydrazino group in substituted 4*H*-1,2,4-triazino[2,3-*c*]quinazolines allowed to reveal lead compounds with high anti-inflammatory activity.<sup>2</sup>

1,2,4-Triazino[2,3-*c*]quinazolines have been synthesized by the formation of either pyrimidine<sup>3</sup> or triazine<sup>1,2,4-6</sup> ring. However, the bottleneck of the first approach is the availability of the key 3-(*o*-aminophenyl)-1,2,4-triazines, which are usually prepared in multi-step sequence. Therefore, it is of significant importance to elaborate a method for the annulation of the 1,2,4-triazine ring to quinazolines

starting from the readily available materials and reagents. Thus, one of the general synthetic methods for the preparation of 2*H*-1,2,4-triazino[2,3-*c*]quinazolin-3(4*H*)-ones is the reaction of 2-chloro-*N*-(4-oxo-4*H*-quinazolin-3-yl)acetamides with ammonium acetate in the presence of acetic acid.<sup>1,2,4,5</sup> Another route consists of interaction of 3-amino-3*H*-quinazolin-4-ones with chloroacetamide in DMF<sup>1,5</sup> or by melting<sup>6</sup> that yields 3,4-dihydro-2*H*-1,2,4-triazino[2,3-*c*]quinazolin-2-ones. However, these methods do not allow to prepare 3-substituted 2-oxo-2*H*-1,2,4-triazino[2,3-*c*]quinazolines, which significantly complicates investigation of their chemical properties and biological activity.

Another well-known method of direct 1,2,4-triazinone ring annulation to heteroarenes is based on cyclocondensation of heterylhydrazines with an  $\alpha$ -ketocarboxylic acids or their esters.<sup>7</sup> Moreover, Shaban and co-workers described the synthesis of 3-substituted 4-oxo-1,2,4-triazino[4,3-*c*]quinazolines via acid-catalyzed heterocyclization of the corresponding hydrazones obtained by condensation of 4-hydrazinoquinazoline with pyruvic acid, ethyl pyruvate and methyl phenylglyoxylate.<sup>8</sup> Since an extremely facile Dimroth rearrangement of triazolo[*c*]quinazolines was observed (Scheme 1)<sup>9</sup>, it was of particular interest to investigate the possibility of similar isomerization in the triazino[*c*]quinazoline series.

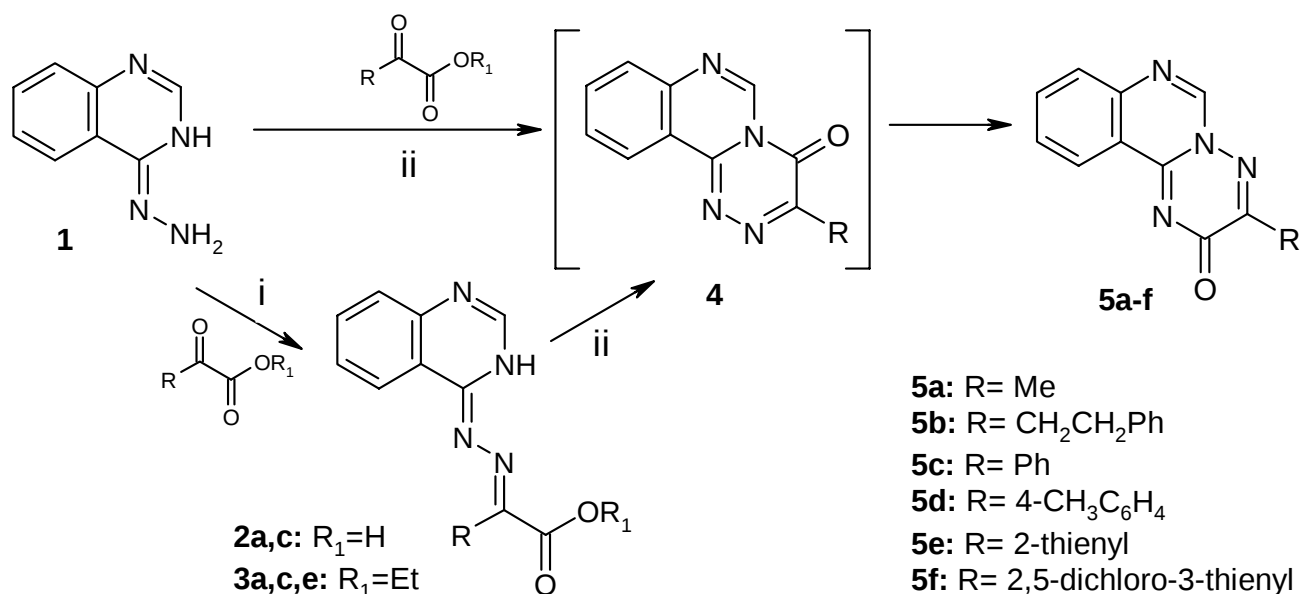


**Scheme 1.** Isomerization of the 1,2,4-triazolo[4,3-*c*]quinazolines into 1,2,4-triazolo[1,5-*c*]quinazolines

## RESULTS AND DISCUSSION

When 4-hydrazinoquinazoline (**1**) was allowed to react with  $\alpha$ -ketocarboxylic acids and their esters in isopropanol, the corresponding hydrazones (**2a,c** and **3a,c,e**) were isolated in good yields. The structure of obtained compounds was confirmed by their spectral data.<sup>8</sup> Further cyclocondensation of **2a,c** and **3a,c,e** in acetic acid afforded the 3-substituted 2-oxo-2*H*-1,2,4-triazino[2,3-*c*]quinazolines (**5a,c,e**) apparently through a facile Dimroth-like rearrangement of intermediate [4,3-*c*] isomers (**4**) (Scheme 2).

Further efforts were directed towards elaboration of the one-step synthesis of the 1,2,4-triazinoquinazolines **5** without isolation of intermediate hydrazones **2,3**. Thus, treatment of 4-hydrazinoquinazoline (**1**) with  $\alpha$ -ketocarboxylic acid esters in acetic acid was found to result in derivatives **5a-f** as sole products. The reaction occurs *via* initial cyclocondensation with formation of intermediates **4** followed by their quick Dimroth-like rearrangement yielding compounds **5**. This transformation can be considered as a first example of the Dimroth-like rearrangement in a series of triazino-annulated heteroarenes.

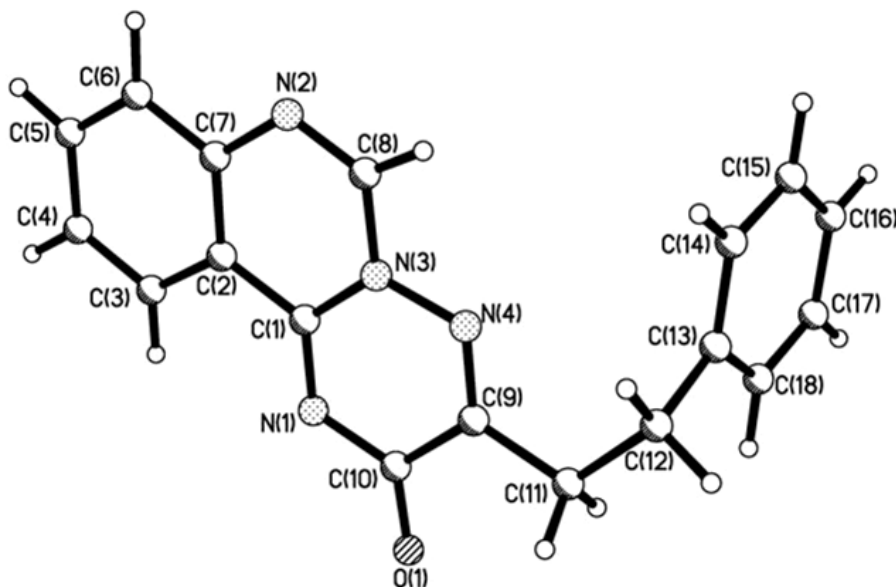


**Scheme 2.** Reagents and conditions: i, *i*-PrOH, reflux, 1 h; ii, AcOH, reflux, 3-4 h.

The structural assignment of synthesized compounds **5a-f** was initially deduced from their spectral data. Thus, in LC/MS, the base peaks of appropriately protonated molecular ions  $[MH]^+$  were observed. The mass spectrum (EI) of 3-phenyl-2*H*-1,2,4-triazino[2,3-*c*]quinazolin-2-one (**5c**) gives molecular ion peak with low abundance. The base peak in the mass spectrum related to the fragment ion ( $m/z$  171), which formed due to C(2)–C(3) and N(4)–N(5) bond breaking. The  $^1H$  NMR spectra of **5a-f** recorded in DMSO- $d_6$  showed signals from the 1,2,4-triazinoquinazoline moiety and substituents. An unusually downfield singlet of H-6 at 9.09–8.81 ppm was observed. Such strong deshielding would be due to the ring nitrogen and C=O group. However, there was nothing downfield from 8.62 ppm in the spectra of compound **5c** reported.<sup>8</sup> The signals of the other 1,2,4-triazinoquinazoline skeleton protons observed as ABCD spin system. The  $^{13}C$  NMR spectra were also in good agreement with the assigned structures of **5a,c,e**.

The structure of prepared compound **5b** was unambiguously proved by X-ray crystallographic study (Figure 1). According to the crystallographic data, the tricyclic fragment as well as the O(1), C(11), C(12) atoms are coplanar within 0.02 Å. It results in the shortened intramolecular contacts H(12b)...N(4) 2.58 Å (the sum of the van der Waals radii<sup>10</sup> is 2.67 Å) and H(3)...N(1) 2.60 Å. The presence of the contact H(3)...N(1) is confirmed by spectral data. Thus, the doublet of 11-H was observed in  $^1H$  NMR spectra of **5b** at 8.56 ppm and was shifted noticeably downfield from the rest of benzene moiety protons. Apparently, this is due to deshielding of the proton by the neighboring triazine ring and indicates their close mutual arrangement. The same effect was present throughout the series of compounds **5a-f**. Bond lengths in the triazinone cycle are close to those previously investigated.<sup>11</sup> The phenyl ring adopts *sc*-conformation with respect to the C(9)–C(11) bond [the C(9)–C(11)–C(12)–C(13) torsion angle is  $-75.2(1)^\circ$ ] and it is turned relatively the C(11)–C(12) bond [the C(11)–C(12)–C(13)–C(14) torsion angle is  $129.5(1)^\circ$ ]. Such

orientation of the aromatic ring results in repulsion between the H(11a) atom and atoms of the phenyl ring [shortened intramolecular contacts H(11a)...C(18) 2.77 Å (2.87 Å), H(11a)...H(18) 2.30 Å (2.34 Å)]. In the crystal molecules **5b** form stacks along the crystallographic direction [1 0 0], bounded by the very weak intermolecular hydrogen bond C(3)–H(3)...N(2)' (x, 1+y, z) H...N 2.55 Å, C–H...N 146°. Also, it was found shortened intermolecular contact H(18)...C(13)' (-1-x, 0.5+y, 0.5-z) 2.79 Å (2.87 Å). At this point, we were able to re-evaluate earlier work of Shaban.<sup>8</sup>



**Figure 1.** X-Ray molecular structure of compound **5b** with the atom numbering used in crystallographic analysis

In conclusion, the present investigation has resulted in a new one-step synthesis of the 3-substituted 2*H*-1,2,4-triazino[2,3-*c*]quinazolin-2-ones **5**. The availability and simplicity of the starting materials and experimental procedures make this approach useful and convenient. Moreover, to the best of our knowledge, it is the first case of Dimroth rearrangement in the fused 1,2,4-triazines.

## EXPERIMENTAL

4-Hydrazinoquinazoline (**1**) was prepared as reported.<sup>12</sup> The other starting materials were commercially available and used without additional purification. All mps were determined in open capillary tubes in a Thiele's apparatus and are uncorrected. <sup>1</sup>H NMR spectra were recorded on a Mercury 400 (400 MHz) spectrometer in DMSO-*d*<sub>6</sub> solution. Chemical shifts (δ) are given in ppm downfield from internal SiMe<sub>4</sub>. *J* values are in Hz. <sup>13</sup>C NMR spectra were recorded on a Bruker Avance 500 (125 MHz for <sup>13</sup>C) spectrometer in DMSO-*d*<sub>6</sub> solution. LC/MS were determined on an Agilent 1100 instrument. Mass spectrum of

3-phenyl-2*H*-1,2,4-triazino[2,3-*c*]quinazolin-2-one (**5c**) was determined on a Varian 1200L instrument (EI, 70 eV). The purity of all compounds prepared was checked by <sup>1</sup>H NMR and LC/MS. For all compounds, satisfactory elemental analyses were obtained.

**[(3*H*-Quinazolin-4-ylidene)hydrazono]acetic acids (2a,c). General Procedure:** An appropriate  $\alpha$ -ketocarboxylic acid (11 mmol) was added to a suspension of **1** (1.6 g, 10 mmol) in *i*-PrOH (20 mL) and the resulting mixture was refluxed for 1 h. Upon cooling, a crystalline precipitate formed was filtered off and washed with *i*-PrOH. Further purification by dissolving in aqueous NaHCO<sub>3</sub> followed by re-precipitation by HCl yielded derivatives **2a,c**.

**2-[(3*H*-Quinazolin-4-ylidene)hydrazono]propionic acid (2a):** (1.9 g, 82.6%). mp 206-208°C. <sup>1</sup>H NMR:  $\delta$  = 2.26 (s, 3H, CH<sub>3</sub>), 7.53 (t, 1H, *J* = 7.8, 6-H), 7.61 (d, 1H, *J* = 8.0, 8-H), 7.78 (t, 1H, *J* = 8.0, 7-H), 8.13 (s, 1H, 2-H), 8.37 (d, 1H, *J* = 7.8, 5-H), 12.00 (s, 1H, NH), 12.28 (s, 1H, COOH). LC/MS: *m/z* = 231 (MH<sup>+</sup>). Anal. Calcd for C<sub>11</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>: C 57.39, H 4.38, N 24.34. Found: 57.31, H, 4.39, N 24.30.

**Phenyl[(3*H*-quinazolin-4-ylidene)hydrazono]acetic acid (2c):** (2.9 g, 99.2%). mp 208-210°C. <sup>1</sup>H NMR:  $\delta$  = 7.42 (m, 4H, 6-H, 3',4',5'-H<sub>Ph</sub>), 7.50 (d, 1H, *J* = 8.0, 8-H), 7.63 (t, 1H, *J* = 8.0, 7-H), 7.87 (s, 1H, 2-H), 7.93 (m, 2H, 2',6'-H), 8.21 (d, 1H, *J* = 7.8, 5-H). LC/MS: *m/z* = 294, 293 (MH<sup>+</sup>). Anal. Calcd for C<sub>16</sub>H<sub>12</sub>N<sub>4</sub>O<sub>2</sub>: C 65.75, H 4.14, N 19.17. Found: C 65.79, H 4.11, N 19.21.

**General Procedure for the Synthesis of Compounds (3a,c,e):** An appropriate  $\alpha$ -ketocarboxylic acid ethyl ester (11 mmol) was added to a suspension of **1** (1.6 g, 10 mmol) in *i*-PrOH (20 mL) and the resulting mixture was refluxed for 1 hour. After cooling, the reaction mixture was diluted with H<sub>2</sub>O (150 mL). The product was filtered off, washed with diethyl ether and recrystallized from *i*-PrOH-H<sub>2</sub>O (1:1) to give compounds **3a,c,e**.

**2-[(3*H*-Quinazolin-4-ylidene)hydrazono]propionic acid ethyl ester (3a):** (1.27 g, 49.0%); mp 141-143°C. <sup>1</sup>H NMR:  $\delta$  = 1.44 (t, 3H, *J* = 7.1, CH<sub>2</sub>CH<sub>3</sub>), 2.42 (s, 3H, CH<sub>3</sub>), 4.44 (q, 2H, *J* = 7.1, OCH<sub>2</sub>), 7.53 (t, 1H, *J* = 7.8, 6-H), 7.61 (d, 1H, *J* = 8.0, 8-H), 7.78 (t, 1H, *J* = 8.0, 7-H), 8.13 (s, 1H, 2-H), 8.37 (d, 1H, *J* = 7.8, 5-H), 11.41 (s, 1H, NH). LC/MS: *m/z* = 259 (MH<sup>+</sup>). Anal. Calcd for C<sub>13</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub>: C 60.46, H 5.46, N 21.69. Found: C 60.40, H 5.48, N 21.73.

**Phenyl[(3*H*-quinazolin-4-ylidene)hydrazono]acetic acid ethyl ester (3c):** (2.52 g, 78.7%); mp 174-176°C. <sup>1</sup>H NMR:  $\delta$  = 1.37 (t, 3H, *J* = 7.1, CH<sub>3</sub>), 4.47 (q, 2H, *J* = 7.1, CH<sub>2</sub>), 7.44 (m, 5H, 6,8-H, 3,4,5-H<sub>Ph</sub>), 7.88 (m, 2H, 2,6-H<sub>Ph</sub>), 7.71 (t, 1H, *J* = 8.0, 7-H), 7.94 (s, 1H, 2-H), 8.12 (d, 1H, *J* = 7.8, 5-H), 11.86 (s, 1H, NH). LC/MS: *m/z* = 322, 321 (MH<sup>+</sup>). Anal. Calcd for C<sub>18</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub>: C 67.49, H 5.03, N 17.49. Found: C 67.52, H 4.99, N 17.45.

**[(3*H*-Quinazolin-4-ylidene)hydrazono](2-thienyl)acetic acid ethyl ester (3e):** (2.46 g, 75.5%); mp 76-78°C. <sup>1</sup>H NMR:  $\delta$  = 1.37 (t, 3H, *J* = 7.0, CH<sub>3</sub>), 4.40 (q, 2H, *J* = 7.0, CH<sub>2</sub>), 7.19 (t, 1H, *J* = 4.4, 4-H<sub>Thioph</sub>), 7.60 (m, 3H, 6,8-H, 3-H<sub>Thioph</sub>), 7.77 (t, 1H, *J* = 8.0, 7-H), 7.93 (m, 2H, 2-H, 5-H<sub>Thioph</sub>), 8.50 (d, 1H, *J* = 7.8,

5-H), 11.88 (s, 1H, NH). LC/MS:  $m/z$  = 327 ( $MH^+$ ). Anal. Calcd for  $C_{16}H_{14}N_4O_2S$ : C 58.88, H 4.32, N 17.17. Found: C 58.92, H 4.36, N 17.21.

### **2H-1,2,4-Triazino[2,3-*c*]quinazolin-2-ones (5a–f). General Procedure:**

**Method A.** An appropriate ethyl ester (**3a,c,e**, 10 mmol) was dissolved in acetic acid (20 mL) and refluxed for 3–4 h. On cooling, EtOH (20 mL) was added and the mixture was allowed to stand several hours for crystallization. The precipitate was filtered and washed thoroughly with EtOH and then with Et<sub>2</sub>O. The substances obtained were analytically pure. If necessary, additional purification could be achieved by recrystallization from dioxane–H<sub>2</sub>O.

**Method B.** 2H-1,2,4-Triazino[2,3-*c*]quinazolin-2-ones (**5a,c**) were prepared according to the method A starting from the appropriate acids (**2a,c**).

**Method C.** An appropriate  $\alpha$ -ketocarboxylic acid ethyl ester (11 mmol) was added to a solution of **1** (1.6 g, 10 mmol) in acetic acid (10 mL) and resulting mixture was refluxed for 3–4 h. Further work-up as in method A afforded derivatives **5a–f**.

**3-Methyl-2H-1,2,4-triazino[2,3-*c*]quinazolin-2-one (5a):** (Method A: 1.53 g, 72.0%; Method B: 0.96 g, 45.2%; Method C: 1.26 g, 59.4%); mp 240–242°C. <sup>1</sup>H NMR:  $\delta$  = 2.50 (s, 3H, CH<sub>3</sub>), 7.79 (t, 1H,  $J$  = 7.8, 10-H), 7.90 (d, 1H,  $J$  = 7.8, 8-H), 8.02 (t, 1H,  $J$  = 7.8, 9-H), 8.53 (d, 1H,  $J$  = 7.8, 11-H), 8.94 (s, 1H, 6-H). <sup>13</sup>C NMR:  $\delta$  = 18.1 (q, CH<sub>3</sub>, <sup>1</sup> $J_{CH}$  = 130.1), 120.2 (m, 11a-C, <sup>2</sup> $J_{CH}$  = 6.9), 125.8 (dd, 8-C, <sup>1</sup> $J_{CH}$  = 166.3, <sup>2</sup> $J_{CH}$  = 8.0), 128.2 (dd, 10-C, <sup>1</sup> $J_{CH}$  = 165.6, <sup>2</sup> $J_{CH}$  = 7.6), 129.5 (dd, 11-C, <sup>1</sup> $J_{CH}$  = 164.0, <sup>2</sup> $J_{CH}$  = 8.0), 135.8 (dd, 9-C, <sup>1</sup> $J_{CH}$  = 163.6, <sup>2</sup> $J_{CH}$  = 8.8), 144.3 (m, 7a-C), 144.5 (d, 6-C, <sup>1</sup> $J_{CH}$  = 219.5), 152.1 (m, 11b-C), 156.5 (q, 3-C, <sup>2</sup> $J_{CH}$  = 7.2), 161.3 (q, 4-C, <sup>3</sup> $J_{CH}$  = 2.5). LC/MS:  $m/z$  = 213 ( $MH^+$ ). Anal. Calcd for  $C_{11}H_8N_4O$ : C 62.26, H 3.80, N 26.40. Found: C 62.21, H 3.76, N 26.46.

**3-(2-Phenylethyl)-2H-1,2,4-triazino[2,3-*c*]quinazolin-2-one (5b):** (Method C: 2.5 g, 82.7%); mp 210–212°C. <sup>1</sup>H NMR:  $\delta$  = 3.04 (s, 4H, CH<sub>2</sub>CH<sub>2</sub>), 7.20 (m, 1H, H<sub>Ph</sub>), 7.31 (m, 4H, H<sub>Ph</sub>), 7.80 (t, 1H,  $J$  = 8.0, 10-H), 7.92 (d, 1H,  $J$  = 7.8, 8-H), 8.03 (t, 1H,  $J$  = 7.8, 9-H), 8.56 (d, 1H,  $J$  = 8.0, 11-H), 8.98 (s, 1H, 6-H). LC/MS:  $m/z$  = 303 ( $MH^+$ ). Anal. Calcd for  $C_{18}H_{14}N_4O$ : C 71.51, H 4.67, N 18.53. Found: C 71.48, H 4.69, N 18.48.

**3-Phenyl-2H-1,2,4-triazino[2,3-*c*]quinazolin-2-one (5c):** (Method A: 2.40 g, 87.6%; Method B: 1.46 g, 53.3%; Method C: 2.0 g, 72.9%); mp 246–248°C. <sup>1</sup>H NMR:  $\delta$  = 7.58 (m, 3H, 3,4,5-H<sub>Ph</sub>), 7.83 (dt, 1H, <sup>3</sup> $J$  = 8.0, <sup>4</sup> $J$  = 0.8, 10-H), 7.95 (d, 1H,  $J$  = 8.0, 8-H), 8.05 (dt, 1H, <sup>3</sup> $J$  = 8.0, <sup>4</sup> $J$  = 1.3, 9-H), 8.21 (d, 2H, <sup>3</sup> $J$  = 8.0, <sup>4</sup> $J$  = 1.2, 2,6-H<sub>Ph</sub>), 8.59 (dd, 1H, <sup>3</sup> $J$  = 8.0, <sup>4</sup> $J$  = 0.8, 11-H), 9.09 (s, 1H, 6-H). <sup>13</sup>C NMR:  $\delta$  = 119.8 (11a-C), 125.9 (8-C), 128.2 (10-C), 128.7 (3,5-C<sub>Ph</sub>), 129.7 (11-C), 129.8 (2,6-C<sub>Ph</sub>), 131.7 (4-C<sub>Ph</sub>), 132.2 (1-C<sub>Ph</sub>), 135.9 (9-C), 144.2 (7a-C), 144.7 (6-C), 151.3 (11b-C), 151.7 (3-C), 160.4 (4-C). LC/MS:  $m/z$  = 276, 275 ( $MH^+$ ). MS (EI):  $m/z$  (%) = 275 (4.7), 274 ( $M^+$ , 2.1), 248 (4.3), 205 (3.3), 172 (9.8), 171 (100.0), 143 (3.7), 129 (14.2), 103 (11.1), 102 (6.2), 77 (3.3), 76 (19.5), 75 (6.3), 74 (2.7), 64 (5.5), 63 (20.3), 62 (11.2), 61 (3.0),

52 (4.9), 51 (5.5), 50 (6.9). Anal. Calcd for  $C_{16}H_{10}N_4O$ : C 70.07, H 3.67, N 20.43. Found: C 70.03, H 3.64, N 20.40.

**3-(4-Methylphenyl)-2H-1,2,4-triazino[2,3-c]quinazolin-2-one (5d):** (Method C: 1.90 g, 65.9%); mp 292-294°C.  $^1H$  NMR:  $\delta$  = 2.46 (s, 3H,  $CH_3$ ), 7.28 (d, 2H,  $J$  = 8.2,  $H_{Ph}$ ), 7.77 (t, 1H,  $J$  = 7.8, 10-H), 7.89 (d, 1H,  $J$  = 8.0, 8-H), 7.97 (t, 1H,  $J$  = 8.0, 9-H), 8.22 (d, 2H,  $J$  = 8.2,  $H_{Ph}$ ), 8.67 (d, 1H,  $J$  = 7.8, 11-H), 8.81 (s, 1H, 6-H). LC/MS:  $m/z$  = 289 ( $MH^+$ ). Anal. Calcd for  $C_{17}H_{12}N_4O$ : C 70.82, H 4.20, N 19.43. Found: C 70.78, H 4.16, N 19.46.

**3-(2-Thienyl)-2H-1,2,4-triazino[2,3-c]quinazolin-2-on (5e):** (Method A: 2.17 g, 77.6%); mp 280-282°C.  $^1H$  NMR:  $\delta$  = 7.31 (t, 1H,  $J$  = 4.3, 4- $H_{Thioph}$ ), 7.82 (t, 1H,  $J$  = 7.8, 10-H), 7.94 (d, 1H,  $J$  = 8.0, 8-H), 7.98 (d, 1H,  $J$  = 5.0, 3- $H_{Thioph}$ ), 8.04 (t, 1H,  $J$  = 8.0, 9-H), 8.40 (d, 1H,  $J$  = 3.2, 5- $H_{Thioph}$ ), 8.58 (d, 1H,  $J$  = 7.8, 11-H), 9.04 (s, 1H, 6-H).  $^{13}C$  NMR:  $\delta$  = 120.0 (11a-C), 125.9 (8-C), 128.3 (10-C), 128.6 (5- $C_{Thioph}$ ), 129.7 (11-C), 133.0 (4- $C_{Thioph}$ ), 133.6 (3- $C_{Thioph}$ ), 134.4 (2- $C_{Thioph}$ ), 135.8 (9-C), 144.1 (7a-C), 144.4 (6-C), 146.7 (11b-C), 151.1 (3-C), 159.4 (4-C). LC/MS:  $m/z$  = 282, 281 ( $MH^+$ ). Anal. Calcd for  $C_{14}H_8N_4OS$ : C 59.99, H 2.88, N 19.99. Found: C 59.95, H 2.86, N 20.04.

**3-(2,5-Dichloro-3-thienyl)-2H-1,2,4-triazino[2,3-c]quinazolin-2-one (5f):** (Method C: 2.30 g, 65.9%); mp 269-271°C.  $^1H$  NMR:  $\delta$  = 7.57 (s, 1H, 4- $H_{Thioph}$ ), 7.84 (t, 1H,  $J$  = 7.8, 10-H), 7.95 (d, 1H,  $J$  = 8.0, 8-H), 8.06 (t, 1H,  $J$  = 8.0, 9-H), 8.59 (d, 1H,  $J$  = 7.8, 11-H), 9.02 (s, 1H, 6-H). LC/MS:  $m/z$  = 352, 351, 349 ( $M^+$ ). Anal. Calcd for  $C_{14}H_6Cl_2N_4OS$ : C 48.15, H 1.73, N 16.04. Found: C 48.11, H 1.69, N 16.08.

**X-Ray Crystal Structure Determination of 5b:** The crystals of  $C_{18}H_{14}N_4O$  are monoclinic. At 100 K  $a$  = 11.508(2),  $b$  = 6.792(1),  $c$  = 18.161(2) Å,  $\beta$  = 92.85(1)°,  $V$  = 1417.7(4) Å<sup>3</sup>,  $M_r$  = 302.33,  $Z$  = 4, space group  $P2_1/c$ ,  $d_{calc}$  = 1.417 g/cm<sup>3</sup>,  $\mu(MoK_\alpha)$  = 0.092 mm<sup>-1</sup>,  $F(000)$  = 632. Intensity of 11560 reflections (4107 independent,  $R_{int}$  = 0.022) were measured on an automatic "Xcalibur" diffractometer (graphite monochromated  $MoK_\alpha$  radiation, CCD detector,  $\omega$  scanning,  $2\Theta_{max}$  = 60°). The structure was solved by direct method using SHELXTL program package.<sup>13</sup> Positions of hydrogen atoms were located from electron density difference maps and refined isotropically. Full-matrix least-squares refinement against  $F^2$  in anisotropic approximation using 4053 reflections was converged to  $R_1$  = 0.044 (for 3543 reflections with  $F > 4\sigma(F)$ ),  $wR_2$  = 0.117,  $S$  = 1.095. Atomic coordinates and crystallographic parameters have been deposited to the Cambridge Crystallographic Data Centre (CCDC 616485). These data can be obtained from the Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).

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