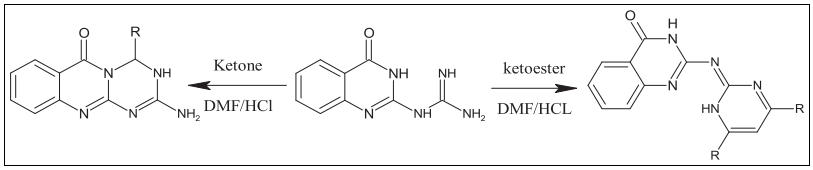
Rapidly and Highly Yielded Synthesis of Pyrimidine, Dihydropyrimidinone, and Triazino[2,1-*b*]quinazolin-6-ones Derivatives

Shaaban K. Mohamed,[a] Ahmed M. Soliman,[b] Mahmoud A. A. El Remaily,[b]* and H. Abdel-Ghany[b]

[a]School of Biology, Chemistry and Material Science, Manchester Metropolitan University, Manchester, United Kingdom
[b]Department of Chemistry, Sohag University, Egypt
*E-mail: msremaily@yahoo.com

Received April 18, 2011
DOI 10.1002/jhet.1092
Published online 9 September 2013 in Wiley Online Library (wileyonlinelibrary.com).



The reaction of 4-oxo-3,4-dihydroquinazolinyl-2-guanidine **1** with several active methylene compounds has revealed formation of the corresponding hydropyrimidine and dihydropyrimidnone (DHPMs) derivatives *via* cycloaddition reaction mechanism. Satisfactory results were obtained with good yields, short time, and simplicity in the experimental procedure. Reaction with ketones in DMF proceeded *via* (5+1) heterocyclization and resulted in the formation of 2-amino-4-(het)aryl-4,6-dihydro-1(3)(11)H-[1,3,5] triazino[2,1-b]quinazolin-6-ones **8-13**, respectively. All compounds have been characterized based on IR, ^{1}H-NMR, and mass spectrum.

J. Heterocyclic Chem., **50**, 1425 (2013).

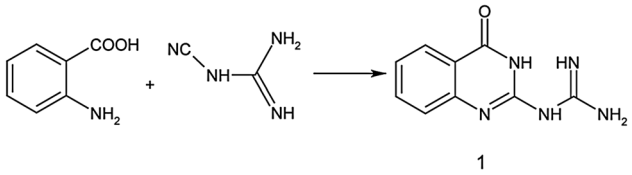
INTRODUCTION

Due to their broad range of pharmacological properties such as calcium channels blockers, antioxidant, anticancer, and anti-inflammatory activity, 3,4-dihydropyrimidinone nucleus have increasingly attracted the attention of synthetic chemists [1–5]. In addition, antimicrobial activity of 3,4-dihydropyrimidone derivatives has been extensively studied and well established in the literature [6–12]. However, there are relatively very few reports on the anti-inflammatory activity of the 3,4-dihydropyrimidinone derivatives [5], [13]. And most importantly, the potential of 3,4-dihydropyrimidinone nucleus as to their anti-inflammatory activity against the pro-inflammatory cytokines (TNF-α and IL-6) hitherto remained untested. Non-steroidal anti-inflammatory drugs (NSADs) are therapeutically important in the treatment of rheumatic arthritis and in various types of inflammatory conditions, but their therapeutic utility has been limited due to their frequently observed gastrointestinal side effects. Thus, there is an urgent need for new targets that are required for the design and development of novel anti-inflammatory agents as an alternative to NSAIDs [14]. Tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6), the two important multifunctional pro-inflammatory cytokines, are involved in the pathogenesis of autoimmune, inflammatory, cardiovascular, neurodegenerative, and cancer diseases through a series of cytokine signaling pathways [15], [16]. IL-6 contributes to the initiation and extension of the inflammatory process and considered as a central mediator in a range of inflammatory diseases but has not received the desired attention in drug discovery [14]. TNF-α and IL-6 are thus pharmaceutically important molecular targets for the treatment of the abovementioned diseases. Biologically important heterocyclic derivatives of aryl ureas have been reported in the literature. For example, *N*-2,4-pyrimidine-*N*-*N*-phenyl/alkyl ureas were reported to be inhibitor of tumor necrosis factor alpha (TNF-α) [17], [18], SA13353, substituted urea derivatives, is reported as a potent inhibitor of TNF-α production [19].

Naturally occurring and synthetic quinazolinone derivatives, including fused systems, are known to possess a wide range of biological activities [20–22]. Three isomeric structures are possible for quinazoline fused with 1,3,5-triazine nucleus, *viz.*, 1,3,5-triazino[1,2-*a*] quinazoline, 1,3,5-triazino[1,2-*c*]quinazoline, and 1,3,5-triazino[2,1-*b*]quinazoline heterocyclic systems. The known methods of the synthesis of these compounds are limited. The system with [1,2-*a*] ring junction has been prepared *via* (2+2+2) cycloaddition of two isocyanate molecules to the side "a" of quinazolines [23], [24] or by (3+3) heterocyclization of 2-aminoquinazolines with chlorocarbonyl isocyanate [25]. The annulation of 1,3,5-triazine ring onto the side "c" of the quinazolines with the formation of 1,3,5-triazino[1,2-*c*]quinazolines was also reported [26–29].

Among the methods of 1,3,5-triazino[2,1-*b*]-quinazolines synthesis [26], [30–32], only one annulations of 1,3,5-triazine

Scheme 1



1

ring onto an existing quinazoline skeleton has been reported [26] using thermal ring closure of 2-benzamido-3-cyano-3,4-dihydroquinazolin-4-one. It has been reported that 1,3,5-triazino[2,1-*b*]-quinazoline compounds have been synthesized by reaction of 4-oxo-3,4-dihydroquinazolinyl-2-guanidines with different aldehydes [33–37].

RESULTS AND DISCUSSION

V. Dolzhenko *et al*. [35] reported that heating of DCD with anthranilic acid in aqueous sulfuric acid medium for 20 min, and then treating with sodium hydroxide gave compound **1**. As a mater of modification for this method, we have obtained product **1** (Scheme 1) by direct reflux of DCD with anthranilic acid in sulfuric acid medium. The product has been formed in high temperature with a very good yield. Excess of acid has been washed out by water. IR and melting point of the product (317°C, [38,39], 316–317°C) did not change and were in accordance with the literature.

Compound **1** reacted with acetylacetone in DMF and the addition of a few drops of hydrochloric acid as a catalyst rapidly and highly yielded pyrimidine derivative **2**. IR spectra of compound **2** showed the disappearance of absorption bands corresponding to NH, NH_2 groups. Their ^{1}H-NMR spectra showed new signals corresponding to CH group at 6.05 ppm, $2CH_3$ at 2.5 ppm and NH in aromatic region, respectively. Mass spectra of compound **2** gave the molecular ion peak at *m*/*z* 267.

It has been reported that the reaction of biguanides with ethyl cyanoacetate gave triazineacetonitrile [37]. On the reaction **1** with ethyl cyanoacetate gave 2,3-dihydropyrimidin-4(1H)-one **3** (Scheme 2). Their reaction mechanism was proceeding *via* a condensation reaction between the amino group and ester group with the elimination of ethanol molecule and then the addition of the amino group to cyano group. IR spectra of compound **3** showed new absorption bands corresponding to NH_2 group at 3383, 3290 cm^{-1}. MS of compound **3** showed molecular ion peak at *m*/*z* 270.

The same mechanism when the reaction compound **1** with malononitrile gave compound **4** showed new absorption bands corresponding to NH_2 groups at 3321, 3213 cm^{-1}. 6-Methyl-, 6-phenyl, and 6-hydroxy-2,3-dihydropyrimidin-4(1H)-ones **5–7** were synthesized *via* the reaction of compound **1** with ethyl acetoacetate, ethyl benzoylacetate, or diethyl malonate in the presence of the benign catalyst hydrochloric acid (Scheme 2). ^{1}H-NMR spectra showed new signals corresponding to CH groups at δ 5.17, 6.37, and 5.01 ppm. Mass spectra of compounds **5-7** showed molecular ion peaks at *m*/*z* 269, 331, and 271, respectively (Scheme 2).

The reaction of 4-oxo-3,4-dihydroquinazolinyl-2-guanidine **1** with ketones in DMF proceeded *via* (5+1) heterocyclization and resulted in the formation of hitherto unknown 2-amino-4-(het)aryl-4,6-dihydro-1(3)(11)H-[1,3,5]triazino[2,1-*b*]quinazolin-6-ones **8-13**, respectively.

The structures of the products were established using data of IR, 1H-NMR, 13C-NMR, and 2D NOESY spectroscopy by V. Dolzhenko *et al*. [34].

The reaction of compound **1** with cyclopentanone, cyclohexanon, thiazolidione, pyrazolone, barbaturic acid, and camphor in DMF in the presence of a few drops of hydrochloric acid as a benign catalyst rapidly and highly yielded 2-amino-4-(het)aryl-4,6-dihydro-1(3)(11)H-[1,3,5] triazino[2,1-*b*]quinazolin-6-ones **8-13**, respectively (Scheme 3). Mass spectra of compounds **8-13** showed molecular ion peaks at *m*/*z* 269, 283, 302, 359, 313, and 337, respectively (Scheme 3).

EXPERIMENTAL

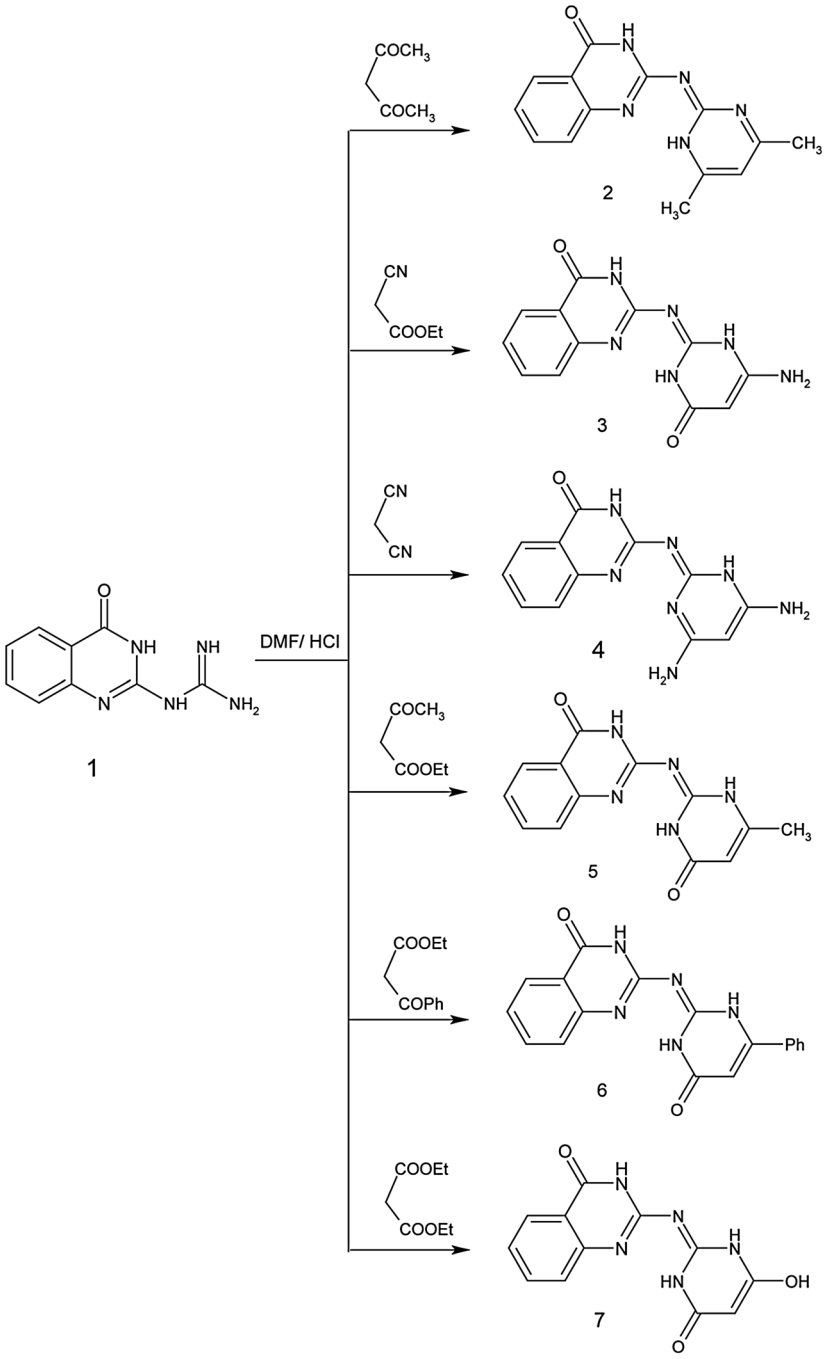
All melting points are uncorrected and were recorded on Melt-Temp II melting point apparatus. IR spectra were measured as KBr pellets on a Shimadzu DR-8001 spectrometer. ^{1}H-NMR spectra were recorded on a Varian Gemini at 280 MHz using TMS as an internal reference and DMSO-d_6 as a solvent. Mass spectra were performed on a Shimadzu GCMS-QP 1000 mass spectrometer at 70 ev. The elemental analyses were carried out on a Perkin-Elmer 240C Microanalyzer. All compounds were checked for their purity on TLC plates.

Synthesis of 1-(4-oxo-3,4-dihydroquinazolin-2-yl)guanidine 1. Anthranilic acid (50 mmol) was dissolved on 50 mL of 10% sulfuric acid and dicyandiamide (75 mmol) was added. The reaction mixture was refluxed for 20 min and the product precipitate on the hot solid was collected by filtration and washed with water.

Yield 84%; mp 340°C; IR (potassium bromide): NH 3402, NH 3340, CH 3048, C O 1702, 1669, 1624, 1585, 1502, 1456,1315, 767 cm^{-1}; ^{1}H-NMR (300 MHz) dimethyl sulfoxide-d_6/TMS, δ (ppm): 7.18 (t, *J* = 7.3 Hz, 1H, H-6), 7.37 (d, *J* = 7.9 Hz, 1H, H-8), 7.60 (t, *J* = 7.5 Hz, 1H, H-7), 7.83 (br s, 4H,NH-C(NH) NH2), 7.95 (d, *J* = 7.9 Hz, 1H, H-5), 11.37 (br s,1H, N(3)H); ^{13}C-NMR (75 MHz) dimethyl sulfoxide-d_6/TMS, δ(ppm): 118.1 (C-4a), 122.3 (C-6), 124.2 (br s, C-8), 125.7 (C-5), 133.5 (C-7), 149.2 (br s, C-8a), 156.1 (C-2), 159.4 (NHC(NH)NH2), 165.4 (C O).

General procedure for preparation of compounds 2-7. A mixture of compound **1** (50 mmol) and (50 mmol) of acetylacetone, ethylcyanoacetate, malononitrile, ethyl acetoacetate,

Scheme 2

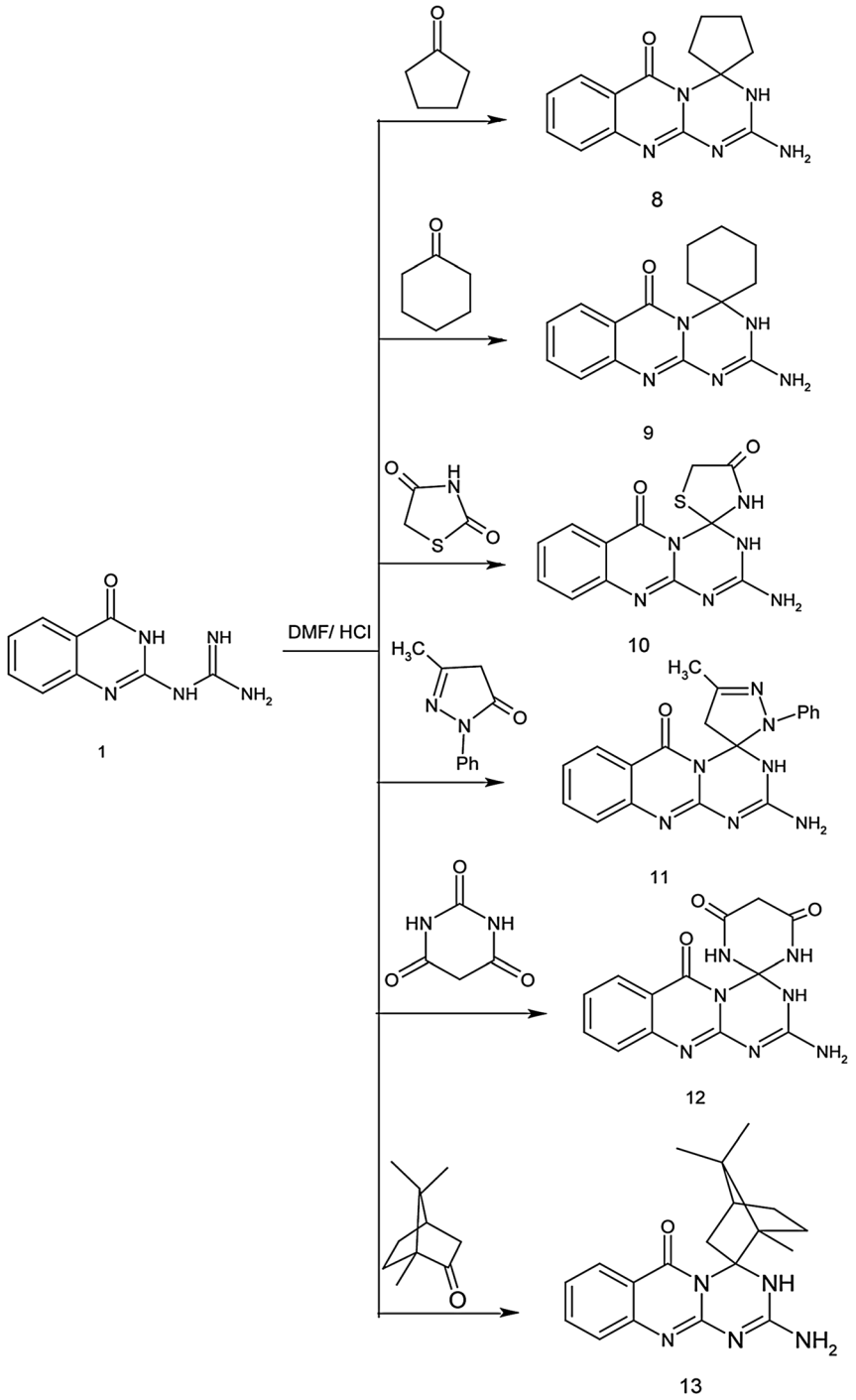


ethyl benzoylacetate, or diethyl malonate in DMF and the presence of a few drops of hydrochloric acid as a catalyst was refluxed at 200°C, solid products were observed after 30 min. The reaction was proceeded with reflux for further 1 h. After cooling down, the solid crystalline products were filtered, washed, and recrystallized from ethanol.

2-{[(2E)-4,6-Dimethylpyrimidin-2(1H)-ylidene]amino} quinazolin-4(3H)-one 2. Yield 77%, mp >350°C; IR: cm^{-1} 3283, 3133 (2NH), 1683 (CO); ^{1}H-NMR: δ 13.14 (s, 1H, NH), 7.82–7.31 (br, 4H, arom), 6.88 (s,1H, NH), 6.05 (s, 1H, CH), 2.5 (s, 6H, $2CH_3$); MS *m/z* (%): M^+ 267 (22.47), 203 (36.94), 144 (81.61), 119 (100); Anal. Calc. For $C_{14}H_{13}N_5O$ (267.28):C(62.91%) H(4.90%) N(26.20%). Found: C(62.33%) H(4.10%) N(25.98%).

2-{[(2Z)-6-Amino-4-oxo-3,4-dihydropyrimidin-2(1H)-ylidene]amino}quinazolin-4(3H)-one 3. Yield 81%, mp

Scheme 3



>360°C; IR: cm^{-1} 3383, 3290, 3185 (2NH, NH_2), 1687 (CO), 1670 (CO); ^{1}H-NMR: δ 12.75 (s,1H, NH), 9.15 (s,1H, NH), 8.33 (s,2H, NH_2), 7.82–7.61 (br, 4H, arom), 6.28 (s, 1H, CH), 5.99 (s, 1H, NH); MS *m*/*z* (%): M^+ 270 (18.49), 228 (36.14), 186 (51.61), 77 (100); Anal. Calc. For $C_{12}H_{10}N_6O_2$ (270.25): C(53.33%) H (3.73%) N(31.10%). Found: C(54.01%) H(3.29%) N(31.01%).

2-{[(2Z)-4,6-Diaminopyrimidin-2(1H)-ylidene]amino} quinazolin-4(3H)-one 4. Yield 73%, mp 320°C ; IR: cm^{-1} 3403, 3310, 3185, 3107 (2NH, $2NH_2$); ^{1}H-NMR: δ 12.77 (s, 1H, NH), 7.82–7.54 (br, 4H, arom), 6.26 (s, 1H, CH), 6.01 (s, 1H, NH), 5.42 (s,4H, $2NH_2$); MS *m*/*z* (%): M^+ 269 (23.49), 226 (56.94), 185 (71.41), 77 (100); Anal. Calc.

For $C_{12}H_{11}N_7O$ (269.26):C(53.53%) H(4.12%) N(36.41%). Found: C(53.39%) H(3.99%) N(36.02%).

2-{[(2Z)-6-Methyl-4-oxo-3,4-dihydropyrimidin-2(1H)-ylidene]amino}quinazolin-4(3H)-one 5. Yield 83%, mp 350°C; IR: cm^{-1} 3257, 3187 (2NH), 1686 (CO), 1673 (CO); ^{1}H-NMR: δ 13.41 (s, 1H, NH), 12.61 (s, 1H, NH), 7.85–7.66 (br, 4H, arom), 5.99 (s, 1H, NH), 5.17 (s, 1H, CH), 2.41 (s, 3H, CH_3); MS *m/z* (%): M^+ 269 (37.42), 228 (3.94), 203 (97.61), 186 (85.31), 161 (67.10), 119 (100), 77 (13.01); Anal. Calc. For $C_{13}H_{11}N_5O_2$ (269.26):C(57.99%) H(4.12%) N(26.01%). Found: C(57.39%) H(4.02%) N(25.66%).

2-{[(2Z)-4-Oxo-6-phenyl-3,4-dihydropyrimidin-2(1H)-ylidene]amino}quinazolin-4(3H)-one 6. Yield 78%, mp 360°C; IR: cm^{-1} 3214, 3185 (3NH), 1680 (CO), 1658 (CO); ^{1}H-NMR: δ 13.40 (s, 1H, NH), 12.63 (s, 1H, NH), 7.89–7.63 (br, 9H, 2 arom), 6.37 (s, 1H, CH), 5.99 (s, 1H, NH); MS *m/z* (%): M^+ 331 (21.57), 301 (36.94), 228 (81.61), 77 (100); Anal. Calc. For $C_{18}H_{13}N_5O_2$ (331.33):C(65.25%) H(3.93%) N (21.14%). Found: C(65.29%) H(3.42%) N(21.43%).

2-{[(2Z)-6-Hydroxy-4-oxo-3,4-dihydropyrimidin-2(1H)-ylidene]amino}quinazolin-4(3H)-one 7. Yield 86%, mp >350°C; IR: cm^{-1} 3438 (OH), 3245, 3218 (3NH), 1689 (CO), 1668 (CO); ^{1}H-NMR: δ 14.01 (s, 1H, NH), 12.54 (s, 1H, NH), 11.49 (s, 1H, OH), 7.85–7.60 (br, 4H, arom), 5.99 (s, 1H, NH), 5.01 (s, 1H, CH); MS *m/z* (%): M^+ 271 (27.47), 132 (36.94), 107 (81.61), 67 (100); Anal. Calc. For $C_{12}H_9N_5O_2$ (271.23):C(53.14%) H(3.34%) N(25.82%). Found: C(53.33%) H(3.01%) N(25.03%).

General procedure for preparation of compounds 8–13. A mixture of compound **1** (50 mmol) and (50 mmol) cyclopentanone, cyclohexanon, thiazolidione, pyrazolone, barbaturic acid, or camphor in DMF in the presence of a few drops of hydrochloric acid as a catalyst was refluxed, and solid products were observed after 30 min. The reaction was proceeded with reflux for further 1 h. After cooling down, the solid crystalline products were filtered, washed, and recrystallized from ethanol.

2-Amino-4-cyclopentane-3,4-dihydro-6H-[1,3,5]triazino [2,1-b]quinazolin-6-one 8. Yield 91%, mp >360°C; IR: cm^{-1} 3382, 3257, 3187 (NH_2, NH), 1685 (CO); ^{1}H-NMR: δ 10.74 (s, 1H, NH), 8.08–7.57 (m, 4H, arom), 4.74 (br, 2H, NH_2), 2.35 (s, 4H, $2CH_2$), 1.87 (s, 4H, $2CH_2$); MS *m/z* (%): M^+ 269 (18.40), 253 (56.14), 237 (34.13), 119 (85.17), 76 (100); Anal. Calc. For $C_{14}H_{15}N_5O$ (269.30):C(62.44%) H(5.61%) N (26.01%). Found: C(62.69%) H(5.09%) N(25.95%).

2-Amino-4-cyclohexane-3,4-dihydro-6H-[1,3,5]triazino [2,1-b]quinazolin-6-one 9. Yield 82%, mp >360°C; IR: cm^{-1} 3385, 3260, 3177 (NH_2, NH), 1684 (CO); ^{1}H-NMR: δ 10.45 (s, 1H, NH), 8.08–7.17 (m, 4H, arom), 4.82 (br, 2H, NH_2), 1.91–1.36 (m, 10H, $5CH_2$); MS *m/z* (%): M^+ 283 (28.47), 251 (46.49), 161 (80. 16), 77 (100); Anal. Calc. For $C_{15}H_{17}N_5O$ (283.33):C(63.59%) H(6.05%) N(24. 72%). Found: C(63.24%) H(5.97%) N(24. 30%).

2-Amino-4-thiazolidin-4-one-3,4-dihydro-6H-[1,3,5]triazino [2,1-b]quinazolin-6-one 10. Yield 79%, mp 305°C ; IR: cm^{-1} 3380, 3261, 3167 (NH_2, 2NH), 1684 (CO), 1664 (CO); ^{1}H-NMR: δ 11.14 (s, 1H, NH), 8.28–7.49 (m, 4H, arom), 7.23 (s, 1H, NH), 4.81 (br, 2H, NH_2), 4.05 (s, 2H, CH_2); MS *m/z* (%): M^+ 302 (22.41), 286 (36.14), 158 (87.67), 105 (100); Anal. Calc. For $C_{12}H_{10}N_6O_2S$ (302.31): C(47.68%) H(3.33%) N(27.80%) S(10.21%). Found: C(47.29%) H (3.22%) N(27.19%) S(10.44%).

2-Amino-4-3-methyl-1-phenyl-1H-pyrazole-3,4-dihydro-6H-[1,3,5]triazino[2,1-b] quinazolin-6-one 11. Yield 78%, mp >360°C; IR: cm^{-1} 3381, 3272, 3181 (NH_2, NH), 1686 (CO); ^{1}H-NMR: δ 10.88 (s, 1H, NH), 8.28–6.87 (m, 9H, 2 arom), 4.61 (br,2H, NH_2), 3.35 (s,2H, CH_2), 2.47 (s,3H, $2CH_3$); MS *m/z* (%): M^+ 359 (15.88), 334 (10. 49), 203 (84.50), 119 (100), 77 (13.36); Anal. Calc. For $C_{19}H_{17}N_7O$ (359.38):C(63.50%) H(4.77%) N(27.28%). Found: C(63.39%) H(4.44%) N(27.03%).

2-Amino-4-barbaturic acid –3,4-dihydro-6H-[1,3,5]triazino [2,1-b] quinazolin-6-one 12. Yield 87%, mp 310°C; IR: cm^{-1} 3381, 3260, 3168 (NH_2, 3NH), 1685 (CO), 1673 (CO); ^{1}H-NMR: δ 10.88 (s, 1H, NH), 9.78 (s,2H, 2NH), 8.08–7.37 (m, 5H, arom), 4.96 (br,2H, NH_2), 3.25 (s,2H, CH_2); MS *m/z* (%): M^+ 313 (27.47), 132 (36.94), 107 (81.61), 67 (100); Anal. Calc. For $C_{13}H_{11}N_7O_3$ (313.27):C(49.84%) H(3.54%) N(31.30%). Found: C (49.92%) H(3.12%) N(31.03%).

2-Amino-4-camphor-3,4-dihydro-6H-[1,3,5]triazino[2,1-b]quinazolin-6-one 13. Yield 73%, mp >350°C; IR: cm^{-1} 3363, 3242, 3125 (NH, NH_2), 1685 (CO); MS *m/z* (%): M^+ 337 (27.47), 215 (31.14), 167 (71.92), 75 (100); Anal. Calc. For $C_{19}H_{23}N_5O$ (337.42): C(67.63%) H(6.87%) N(20.76%). Found: C(67.35%) H(6.32%) N(20.01%).

REFERENCES AND NOTES

[1] Inca, S. Z.; Selma, S.; Semra, C.; Kevser, E. Bioorg Med Chem 2006, 14, 8582.

[2] Zamanova, A. V.; Kurbanova, M. M.; Rzaeva, I. A.; Farzaliev, V. M.; Allakhverdiev, M. A. Russian J Appl Chem 2010, 83, 293.

[3] Hélio, A. S.; Carlindo, B. O.; Roberta, B. A.; Claudio, M. P. P.; Rodolpho, C. B.; Rodrigo, C.; Vanessa, C. B.; Lucielli S.; Cristina, W. N. Eur J Med Chem 2006, 41, 513.

[4] Prashantha Kumar, B. R.; Gopu, S.; Nasir Baig, R. B.; Srinivasan, C. Eur J Med Chem 2009, 44, 4192.

[5] Sushilkumar, S. B.; Devanand B. S. Bioorg Med Chem Lett 2004, 14, 1733.

[6] Nandakumar, A.; Prakasam, T.; Paramasivan T. P.; Vembu, P.; Ponnuswamy, M. N.; Ramesh, P. Bioorg Med Chem Lett 2010, 20, 4252.

[7] (a)Pratibha, S.; Nilesh, R.; Gurram, V. K.; Bioorg Med Chem Lett 2004, 14, 4185. (b)Kidwai, M.; Saxena S.; Khalilur, R. K. M.; Thukral, S. S. Eur J Med Chem 2005, 40, 816.

[8] Anil, K. C.; Pragya, A.; Chandrani, M.; Pankaj, K.; Yogesh, Y.; Ajendra, K. S.; Vibha, Y.; Jyotsana, G.; Rajesh, D.; Hirday, N. J.; Arthur C. W.; Virinder, S. P.; Ashok, K. P.; Gainda L. S. Bioorg Med Chem 2006, 14, 973.

[9] (a)Mithun, A.; Bantwal, S. H.; Nalilu, S. K. Eur J Med Chem 2007, 42, 380. (b)Atul, R. G.; Kiran, S. T.; Fazal, S.; Mukund, V. D.; Kumar, V. S. Tetrahedron 64, 10,214.

[10] (a)Chitra, S.; Devanathan, D.; Pandiarajan, K. Eur J Med Chem 2010, 45, 367. (b)Santosh, N. M.; Sandeep, S. S.; Rupali, D. E.; Jaiprakash N. S.; Devanand, B. S. Bioorg Med Chem Lett 2010, 20, 4424.

[11] Shishoo, C. J.; Ravikumar, T.; Jain, K. S.; Rathod, I. S.; Gandhi, T. P.; Satia, M. C. Ind J Chem 1999, 38, 1075.

[12] Papadakis, K. A.; Targan, S. R. Inflamm Bowel Dis 2000, 6, 303.

[13] Krishnamoorthy, S.; Honn, K. V. Cancer Metast Rev 2006, 25, 481.

[14] Jennifer, A. M.; Todd, A. B.; Michael, P. C.; Mark, S.; Adam, G.; Roger, G. B.; Matthew, J. L.; Steven, K. L.; John, C. V.; Biswanath, D.; Lily, C. H.; Kimberly, K. B.; Karen, J.; Richard, L. W.; Michael, J. J. Bioorg Med Chem Lett 2006, 16, 3514.

[15] Dominic, S. C.; Raj, M. D. Semin Arthrit Rheumat 2009, 38, 382.

[16] Todd, A. B.; Jennifer, A. M.; Michael, P. C.; Mark, S.; Adam, G.; Roger, G. B.; Matthew, J. L.; Steven, K. L.; John, C. V.; Biswanath,

D.; Lily, C. H.; Marlene, J. M.; Michael, J. J. Bioorg Med Chem Lett 2006, 16, 3510.

[17] Hiroshi, E.; Ayako, S.; Hiroshi, S.; Noriyoshi, Y.; Hiroyuki, I.; Chikako, S.; Fumio, T.; Masahiro, O.; Yoshimasa, S.; Masato, H.; Masakazu, B. Bioorg Med Chem Lett 2010, 20, 4479.

[18] El-Hiti, G. A.; Abdel-Megeed, M. F. Heterocycles 2005, 65, 3007.

[19] Connolly, D. J.; Cusack, D.; O'Sullivan, T. P.; Guiry, P. J. Tetrahedron, 2005, 61, 10,153.

[20] Sawada, M.; Furukawa, Y.; Takai, Y.; Hanafusa, T. Heterocycles 1984, 22, 501.

[21] Tietz, H.; Rademacher, O.; Zahn, G. Eur J Org Chem 2000, 2105.

[22] Kamal, A.; Sattur, P. B. Synthesis 1985, 892.

[23] Shaw, J. T.; Taylor, D. M.; Corbett, F. J.; Ballentine, J. D. J Heterocycl Chem 1972, 9, 125.

[24] Abdel-Megeed, M. F.; Teniou, A. Collect Czech Chem Commun 1988, 53, 329.

[25] Aly, A. A. M. J Chem Res 2006, 461.

[26] Aly, A. A. Z. Naturforsch 2006, 61B, 1012.

[27] Shaw, J. T.; Ballentine, J. J Chem Soc D Chem Commun 1969, 1040.

[28] Winter, R. A. E.; Villani, T. J. United State Patent 3,887,554, 1975; Winter, R. A. E.; Villani, T. J. Chem Abstr 1975, 83, 147,505.

[29] Balli, H.; Gunzenhauser, S.; Fletcher, I. J.; Bedekovic, D. German Patent 3,314,195, 1983; Balli, H.; Gunzenhauser, S.; Fletcher, I. J.; Bedekovic, D. Chem Abstr 1984, 100, 87,256.

[30] Part 9 in the series "Fused heterocyclic systems with s-triazine ring," for Part 8 see Dolzhenko, A. V.; Dolzhenko, A. V.; Chui, W. K. Tetrahedron, in press.

[31] Dolzhenko, A. V.; Chui, W. K.; Dolzhenko, A. V.; Chan, L.W. J. Fluorine Chem 2005, 126, 759.

[32] Dolzhenko, A. V.; Chui, W. K. J Heterocycl Chem 2006, 43, 95.

[33] Dolzhenko, A. V.; Chui, W. K.; Dolzhenko, A. V. J Heterocycl Chem 2006, 43, 1513.

[34] Dolzhenko, A. V.; Tan, G. K.; Koh, L. L.; Dolzhenko, A. V.; Chui, W. K. Acta Crystallogr 2007, E63, o2796.

[35] Dolzhenko, A. V.; Chui, W. K.; J Heterocyclic Chem 2008, 45, 173.

[36] Skowronska-Serafinowa, B.; Urbanski, T. Rocz Chem 1952, 26, 51.

[37] Sączewski, F.; Bułakowska, A.; Bednarski, P.; Grunert, R. Eur J Med Chem 2006, 41, 219.