FULL PAPER

Synthesis of Novel Isoindolo[2,1-*a*]quinazolinedione Derivatives Containing a 1,2,3-Triazole Ring System

by **Fatemeh Esmaeili-Marandi**[a]), **Mina Saeedi**[b])[c]), **Issa Yavari**[a]), **Mohammad Mahdavi**[d]), and **Abbas Shafiee***[d])

[a]) Department of Chemistry, College of Basic Science, Tehran Science and Research Branch, Islamic Azad University, Tehran, Iran

[b]) Medicinal Plants Research Center, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

[c]) Persian Medicine and Pharmacy Research Center, Tehran University of Medical Sciences, Tehran, Iran

[d]) Department of Medicinal Chemistry, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran (fax: +98-21-66461178; e-mail: shafieea@tums.ac.ir)

A synthesis of isoindolo[2,1-*a*]quinazolinedione derivatives, coupled with a 1,2,3-triazole ring system, *via* the reaction of isatoic anhydride, $HC{\equiv}CCH_2NH_2$, and 2-formylbenzoic acid is described, which led to the formation of the isoindolo[2,1-*a*]-quinazoline-5,11-dione scaffold having a C≡C bond that participated in a click reaction with various organic azides.

Introduction. – *N*-Heterocyclic compounds remain an attractive topic from both fundamental organic chemistry and medicinal chemistry points of view. They are an important class of heterocycles with various pharmaceutical applications existing in a wide range of synthetic and natural biologically active molecules. Among various *N*-heterocycles, quinazoline and its derivatives belong to the most important privileged scaffolds due to versatile medicinal properties. In this regard, condensed quinazolines have shown distinguished properties [1][2]. For example, isoindoloquinazolines have shown TNF-α inhibitory [3], sedative, analgesic, and antihypertensive activities [4]. Nevertheless, a literature survey indicated that there are only a few reports on the preparation of isoindoloquinazolines [5 – 7]. Some derivatives were synthesized *via* the reaction of oxo acids with anthranilic acid, anthranilamides, orthanilamides, or salicylamide [8]. Recently, isoindoloquinazolinediones have been synthesized *via* the reaction of isatoic anhydride, amines, and 2-formylbenzoic acid under different conditions [3][9][10].

1,2,3-Triazoles are known as a promising class of *N*-heterocycles. They have exhibited cytotoxic [11], anti-HIV-1 [12], anti-influenza [13], antiplatelet [14], acetylcholinesterase inhibitory [15], and antituberculosis [16] activities. The main method for the synthesis of the 1,2,3-triazole ring follows the click reaction described by *Sharpless et al.* [17] and modified procedures [18 – 20].

Considering the fact that combination of two or more pharmacophores has been a versatile tool for drug discovery developments, we focused on an isoindoloquinazoline-1,2,3-triazole hybrid which has not been reported in the literature. Herein, in continuation of our work on the synthesis of novel *N*-heterocycles [21 – 25], we report the design and synthesis of novel isoindolo[2,1-*a*]-quinazolines containing a 1,2,3-triazole ring system *via* a simple three-step reaction starting from isatoic anhydride (*Scheme 1*).

Results and Discussion. – The straightforward approach for the preparation of isoindolo[2,1-*a*]quinazoline-coupled 1,2,3-triazoles **9** is shown in *Scheme 1*. Based on our experience in the synthesis of a wide range of quinazolines, we chose isatoic anhydride as starting material [26 – 30]. Initially, isatoic anhydride (**1**) reacted with $HC{\equiv}CCH_2NH_2$ (**2**) in H_2O at room temperature to give 2-amino-*N*-(prop-2-yn-1-yl)benzamide (**3**). The reaction of **3** with 2-formylbenzoic acid (**4**) was conducted under various conditions using different solvents and reagents to obtain 6-(prop-2-yn-1-yl)-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (**5**). Some results are shown in *Table 1*. The tests revealed that using TsOH (20 mol-%) in EtOH under reflux afforded **5** in high yield (85%).

Next, compound **5**, possessing a potent C≡C bond, was readily converted to the desired product **9** *via* click reaction [17]. For this purpose, various organic azides, **8**, were prepared by the reaction of different benzyl chlorides/bromides, **6**, and NaN_3 (**7**) in the presence of Et_3N in a

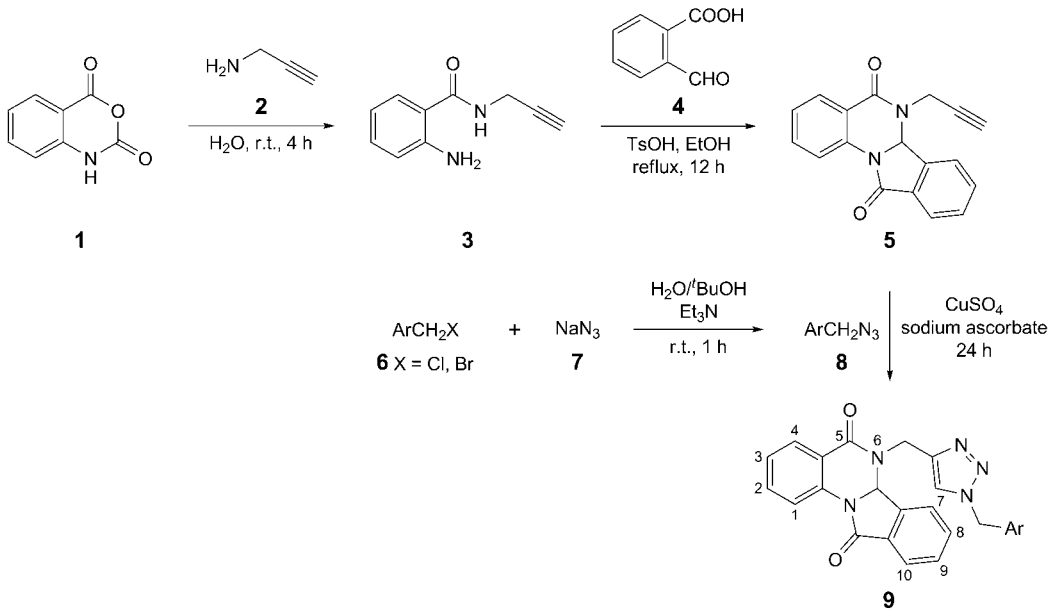
Table 1. *Investigation of Various Conditions for the Formation of* **5**

Entry	Solvent	Reagent	Yield [%][a])
1	EtOH	TsOH	85
2	EtOH	DABCO[b])	70
3	EtOH	K_2CO_3	75
4	MeCN	TsOH	65
5	MeCN	K_2CO_3	65
6	CH_2Cl_2	TsOH	30
7	Toluene	K_2CO_3	35

[a]) Yield of isolated product. [b]) DABCO, 1,4-diazabicyclo[2.2.2]octane.

DOI: 10.1002/hlca.201500122

Scheme 1. *Synthesis of Isoindolo[2,1-*a*]quinazoline-Coupled 1,2,3-Triazoles* **9**

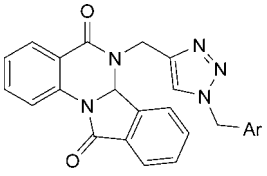


mixture of H_2O/^{t}BuOH at room temperature. Then, **5**, sodium ascorbate, and a catalytic amount of $CuSO_4$ (7 mol-%) were added to the freshly prepared azides **8** leading to the formation of different isoindolo[2,1-*a*]quinazolinedione-coupled 1,2,3-triazoles **9**.

The scope of the reaction was studied by varying azide derivatives **8** (*Table 2*). It was clear that all azide derivatives **8** possessing electron-donating and electron-withdrawing groups as well as halogens underwent a click reaction to afford products **9**. Also, the structures of products **9** were confirmed using IR and ^{1}H- and ^{13}C-NMR spectroscopy, as well as chemical analysis.

A plausible mechanism for the formation of product **9** is shown in *Scheme 2* [3][10]. Initially, reaction of isatoic anhydride (**1**) and HC≡CCH$_2$NH$_2$ (**2**) gives 2-amino-*N*-(prop-2-yn-1-yl)benzamide (**3**) by elimination of CO_2. Then, reaction of **3** and 2-formylbenzoic acid (**4**) in the presence of TsOH leads to the formation of imine intermediate **10** which undergoes nucleophilic addition of the NH N-atom to afford **11**. Next, nucleophilic attack of the ring N-atom on the activated C=O group of the carboxylic acid and loss of H_2O leads to the formation of five-membered intermediates **12** and **13**, respectively. Then, proton transfer gives 6-(prop-2-yn-1-yl)-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (**5**). Finally, Cu^{II}-catalyzed reaction of **5** and freshly prepared azide derivatives **8** affords products **9** *via* click reaction [17].

Table 2. *Synthesis of Isoindolo[2,1-*a*]quinazoline-Coupled 1,2,3-Triazoles* **9**



9

Entry	Ar	Product **9**	Yield [%][a])
1	Ph	**9a**	80
2	2-Me–C_6H_4	**9b**	85
3	4-F–C_6H_4	**9c**	80
4	2-Cl–C_6H_4	**9d**	90
5	2,3-Cl_2–C_6H_3	**9e**	85
6	3,4-Cl_2–C_6H_3	**9f**	70
7	2-Br–C_6H_4	**9g**	70
8	2-NO_2–C_6H_4	**9h**	65

[a]) Yield of isolated product.

Conclusions. – In summary, we described an operationally simple three-step procedure for the synthesis of novel isoindolo[2,1-*a*]quinazolinedione-coupled 1,2,3-triazoles starting from isatoic anhydride. Good yields (65 – 90%) and user-friendly procedures encourage organic and medicinal chemists to profit from both synthetic and biological aspects.

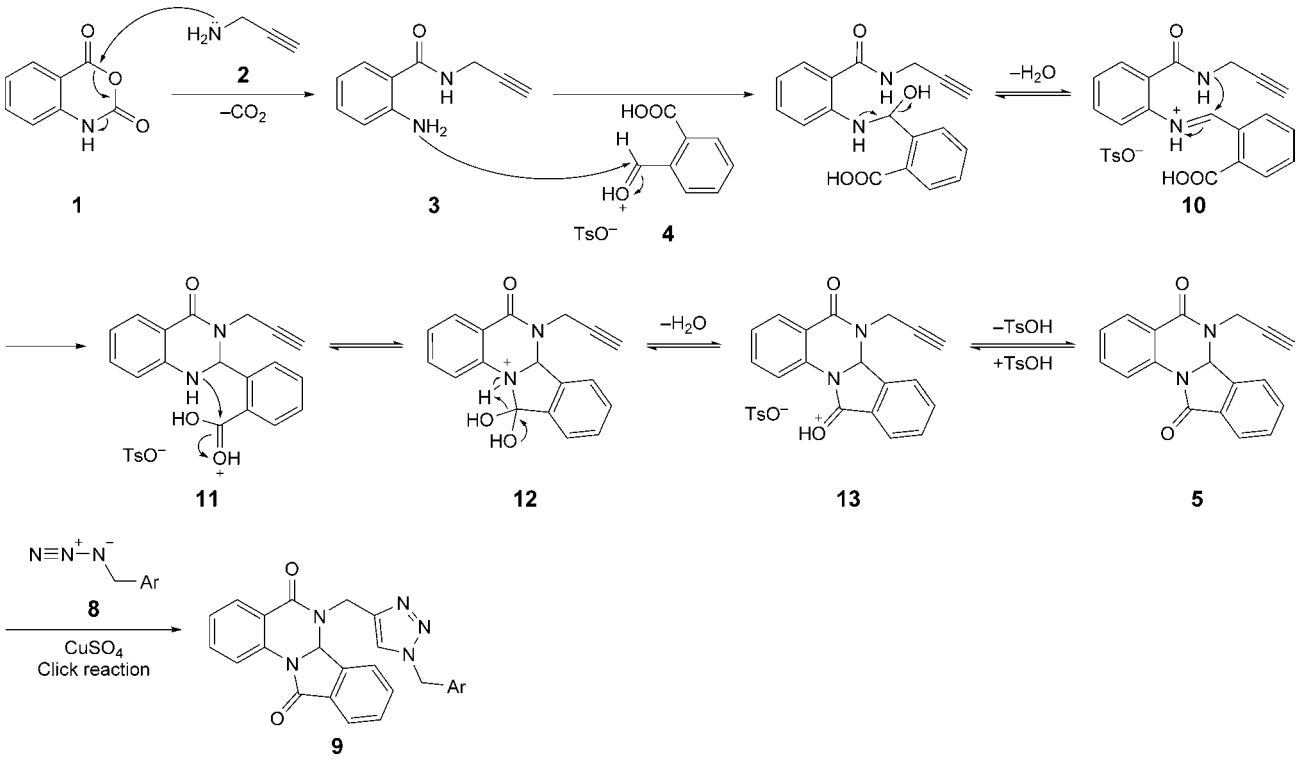
We gratefully acknowledge financial support from the Research Council of Tehran University of Medical Sciences and the *Iran National Science Foundation* (*INSF*).

Experimental Part

General. M.p.: *Kofler* hot stage apparatus; uncorrected. Thin layer chromatography (TLC): petroleum ether/AcOEt. IR Spectra: *Nicolet Magna FTIR 550* spectrophotometer; KBr; $\tilde{\nu}$ in cm^{-1}. ^{1}H- and ^{13}C-NMR spectra: *Bruker FT-500* (500 and 125 MHz, resp.); in (D_6)DMSO; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. Elemental analysis: *VarioEL* (*Elementar Analysensysteme GmbH*); CHNS mode; in %.

*Synthesis of 2-Amino-*N*-(prop-2-yn-1-yl)benzamide* (**3**). A mixture of isatoic anhydride (**1**; 10 mmol) and HC≡CCH$_2$NH$_2$ (**2**;

Scheme 2. *A Plausible Mechanism for the Formation of Products* **9**



10 mmol) in H_2O (20 ml) was stirred at r.t. for 4 h. After completion of the reaction (checked by TLC), the resulting off-colorless precipitate was filtered off and used for the next reaction steps without further purification.

*Synthesis of 6-(Prop-2-yn-1-yl)-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione* (**5**). A mixture of 2-amino-*N*-(prop-2-yn-1-yl)-benzamide (**3**; 1 mmol), 2-formylbenzoic acid (**4**; 1 mmol), and TsOH (20 mol-%) in EtOH (10 ml) was heated under reflux for 12 h. After completion of the reaction (checked by TLC), the mixture was cooled to r.t. and poured into cold H_2O. The precipitated product was filtered off, washed with H_2O, and used for the next reaction steps without further purification.

Synthesis of 1,2,3,4-Tetrahydroquinazolinone Derivatives (**9**). *Typical Procedure.* A soln. of benzyl chloride/bromide derivative **6** (1.1 mmol), NaN_3 (**7**; 0.9 mmol), and Et_3N (1.3 mmol) in H_2O (4 ml)/^{t}BuOH (4 ml) was stirred at r.t. for 1 h. Subsequently, a mixture of 6-(prop-2-yn-1-yl)-6,6*a*-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione (**5**; 1 mmol), sodium ascorbate (0.1 mmol), and $CuSO_4$ (7 mol-%) was added to the freshly prepared azide derivative **8** and the mixture was stirred at r.t. for 24 h. Upon completion of the reaction (monitored by TLC), the mixture was diluted with H_2O and poured into crushed ice. The precipitated product was filtered off and washed with cold H_2O. All products were recrystallized from petroleum ether/AcOEt 1:1 to give pure samples.

*6-[(1-Benzyl-1*H*-1,2,3-triazol-4-yl)methyl]-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione* (**9a**). Yield: 0.33 g (80%). Colorless crystals. M.p. 232 – 234°. IR: 3125, 3071, 2959, 1723, 1645, 1603. ^{1}H-NMR: 4.76 (*d*, *J* = 16.0, 1 H of CH_2); 5.19 (*d*, *J* = 16.0, 1 H of CH_2); 5.53 (*s*, 2 H of CH_2); 6.62 (*s*, CH); 7.19 – 7.20 (*m*, 1 H of Ph, H–C(3)); 7.35 – 7.36 (*m*, 4 H of Ph); 7.69 – 7.75 (*m*, H–C(7 – 9)); 7.91 (*d*, *J* = 6.5, H–C(1)); 8.00 – 8.04 (*m*, H–C(2,10), H of triazole); 8.14 (*d*, *J* = 6.5, H–C(4)). ^{13}C-NMR: 38.0; 52.7; 70.3; 119.8; 119.9; 123.6; 124.2; 125.0; 126.4; 127.7; 128.0; 128.5; 128.7; 130.6; 131.8; 133.0; 133.6; 136.0; 136.7; 138.1; 143.6; 163.2; 164.4. Anal. calc. for $C_{25}H_{19}N_5O_2$ (421.46): C 71.25, H 4.54, N 16.62; found: C 71.36, H 4.71, N 16.48.

*6,6a-Dihydro-6-{[1-(2-methylbenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}isoindolo[2,1-*a*]quinazoline-5,11-dione* (**9b**). Yield: 0.37 g (85%). Colorless crystals. M.p. 198 – 201°. IR: 3126, 3072, 2959, 1724, 1647, 1603. ^{1}H-NMR: 2.24 (*s*, Me); 4.78 (*d*, *J* = 16.0, 1 H of CH_2); 5.18 (*d*, *J* = 16.0, 1 H of CH_2); 5.53 (*s*, 2 H of CH_2); 6.62 (*s*, CH); 6.90 (*d*, *J* = 6.0, H–C(3′)); 7.16 – 7.21 (*m*, H–C(4′ – 6′)); 7.38 (*t*, *J* = 6.0, H–C(3)); 7.69 – 7.73 (*m*, H–C(7 – 9)); 7.86 (*s*, H of triazole); 7.91 (*d*, *J* = 6.0, H–C(1)); 7.99 – 8.04 (*m*, H–C(2,10)); 8.14 (*d*, *J* = 6.0, H–C(4)). ^{13}C-NMR: 18.6; 38.0; 50.9; 70.3; 119.8; 119.9; 123.5; 124.2; 125.0; 126.2; 126.4; 128.2; 128.4; 128.5; 130.3; 130.6; 131.8; 133.0; 133.6; 134.1; 136.2; 136.7; 138.1; 143.5; 163.1; 164.4. Anal. calc. for $C_{26}H_{21}N_5O_2$ (435.49): C 71.71, H 4.86, N 16.08; found: C 71.90, H 4.71, N 16.23.

*6-{[1-(4-Fluorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione* (**9c**). Yield: 0.35 g (80%). Colorless crystals. M.p. 220 – 221°. IR: 3125, 3055, 2959, 1726, 1642, 1603. ^{1}H-NMR: 4.76 (*d*, *J* = 16.0, 1 H of CH_2); 5.18 (*d*, *J* = 16.0, 1 H of CH_2); 5.52 (*s*, 2 H of CH_2); 6.62 (*s*, CH); 7.19 (*d*, *J* = 8.5, H–C(3′,5′)); 7.26 – 7.29 (*m*, H–C(2′,6′)); 7.38 (*t*, *J* = 7.5, H–C(3)); 7.68 – 7.76 (*m*, H–C(7 – 9)); 7.91 (*d*, *J* = 7.5, H–C(1)); 7.99 (*s*, H of triazole); 7.99 – 8.04 (*m*, H–C(2,10)); 8.13 (*d*, *J* = 7.5, H–C(4)). ^{13}C-NMR: 38.0; 51.9; 70.3; 115.5 (*d*, *J* = 21.2); 119.8; 120.0; 123.5; 124.2; 125.0; 126.4; 128.5; 130.1 (*d*, *J* = 8.7); 130.6; 131.8; 132.2; 133.0; 133.6; 136.7; 138.2; 143.7; 161.8 (*d*, *J* = 242.5); 163.2; 164.4. Anal. calc. for $C_{25}H_{18}FN_5O_2$ (439.45): C 68.33, H 4.13, N 15.94; found: C 68.50, H 4.22, N 16.18.

*6-{[1-(2-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione* (**9d**). Yield: 0.41 g (90%). Colorless crystals. M.p. 173 – 175°. IR: 3114, 3064, 2958, 1719, 1653, 1601. ^{1}H-NMR: 4.81 (*d*, *J* = 16.5, 1 H of CH_2); 5.20 (*d*, *J* = 16.5, 1 H of CH_2); 5.60 (*s*, 2 H of CH_2); 6.63 (*s*, CH); 7.30 (*t*, *J* = 7.5, H–C(3)); 7.36 – 7.40 (*m*, H–C(4′ – 6′)); 7.66 – 7.77 (*m*, H–C(7 – 9,3′)); 7.90 (*d*, *J* = 7.5, H–C(1)); 7.92 (*s*, H of triazole); 8.00 – 8.04 (*m*, H–C(2,10)); 8.13 (*d*, *J* = 7.5, H–C(4)). ^{13}C-NMR: 38.0; 52.8; 70.3; 119.9; 120.0; 122.8; 123.9; 124.2; 125.0; 126.4; 128.2; 128.5; 130.0; 130.3; 130.6; 131.9; 132.8; 133.0; 133.6; 134.9; 136.7; 138.2; 143.6; 163.2; 164.4. Anal. calc. for

$C_{25}H_{18}ClN_5O_2$ (455.90): C 65.86, H 3.98, N 15.36; found: C 65.70, H 4.18, N 15.41.

*6-{[1-(2,3-Dichlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione* (**9e**). Yield: 0.41 g (85%). Colorless crystals. M.p. 248 – 250°. IR: 3128, 3055, 2923, 2853, 1727, 1643, 1601. ^{1}H-NMR: 4.83 (*d*, *J* = 16.0, 1 H of CH_2); 5.19 (*d*, *J* = 16.0, 1 H of CH_2); 5.67 (*s*, 2 H of CH_2); 6.63 (*s*, CH); 6.91 (*d*, *J* = 7.5, H–C(6′)); 7.35 – 7.40 (*m*, H–C(3,5′)); 7.65 – 7.76 (*m*, H–C(7 – 9,4′)); 7.90 (*d*, *J* = 7.5, H–C(1)); 7.95 (*s*, H of triazole); 8.00 – 8.04 (*m*, H–C(2,10)); 8.13 (*d*, *J* = 7.5, H–C(4)). ^{13}C-NMR: 38.0; 51.0; 70.3; 119.8; 120.0; 124.0; 124.2; 125.0; 126.4; 128.5; 130.4; 130.5; 130.6; 131.8; 132.1; 133.0; 133.6; 135.9; 136.0; 136.7; 137.2; 138.2; 143.7; 163.2; 164.4. Anal. calc. for $C_{25}H_{17}Cl_2N_5O_2$ (490.34): C 61.24, H 3.49, N 14.28; found: C 61.42, H 3.28, N 14.18.

*6-{[1-(3,4-Dichlorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione* (**9f**). Yield: 0.34 g (70%). Colorless crystals. M.p. 220 – 222°. IR: 3126, 3056, 2959, 1726, 1642, 1603. ^{1}H-NMR: 4.79 (*d*, *J* = 16.5, 1 H of CH_2); 5.18 (*d*, *J* = 16.5, 1 H of CH_2); 5.54 (*s*, 2 H of CH_2); 6.62 (*s*, CH); 7.17 (*d*, *J* = 8.0, H–C(6′)); 7.39 (*t*, *J* = 7.5, H–C(3)); 7.56 (*s*, H–C(2′)); 7.67 (*d*, *J* = 8.0, H–C(5′)); 7.71 – 7.75 (*m*, H–C(7 – 9)); 7.89 (*d*, *J* = 7.5, H–C(1)); 7.96 – 8.04 (*m*, H–C(2,10), H of triazole); 8.12 (*d*, *J* = 7.5, H–C(4)). ^{13}C-NMR: 38.3; 51.3; 70.3; 119.9; 120.0; 123.7; 124.2; 125.0; 126.3; 128.3; 128.5; 130.1; 130.6; 131.0; 131.3; 131.8; 133.0; 133.6; 135.2; 137.0; 137.2; 138.2; 143.8; 163.1; 164.3. Anal. calc. for $C_{25}H_{17}Cl_2N_5O_2$ (490.34): C 61.24, H 3.49, N 14.28; found: C 61.11, H 3.60, N 14.33.

*6-{[1-(2-Bromobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-6,6a-dihydroisoindolo[2,1-*a*]quinazoline-5,11-dione* (**9g**). Yield: 0.35 g (70%). Colorless crystals. M.p. 170 – 171°. IR: 3115, 3062, 2959, 1721, 1656, 1602. ^{1}H-NMR: 4.81 (*d*, *J* = 16.0, 1 H of CH_2); 5.19 (*d*, *J* = 16.0, 1 H of CH_2); 5.60 (*s*, 2 H of CH_2); 6.63 (*s*, CH); 6.91 (*d*, *J* = 7.5, H–C(6′)); 7.29 – 7.38 (*m*, H–C(3,4′,5′)); 7.66 – 7.77 (*m*, H–C(7 – 9,3′)); 7.90 – 7.92 (*m*, H–C(1), H of triazole); 8.00 – 8.04 (*m*, H–C(2,10)); 8.13 (*d*, *J* = 7.5, H–C(4)). ^{13}C-NMR: 38.1; 52.8; 70.3; 119.8; 120.0; 122.7; 123.9; 124.2; 125.0; 126.4; 128.2; 128.5; 130.0; 130.3; 130.6; 131.9; 132.8; 133.0; 133.6; 134.9; 136.7; 138.2; 143.6; 163.2; 164.4. Anal. calc. for $C_{25}H_{18}BrN_5O_2$ (500.36): C 60.01, H 3.63, N 14.00; found: C 59.88, H 3.50, N 14.21.

*6,6a-Dihydro-6-{[1-(2-nitrobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl}-isoindolo[2,1-*a*]quinazoline-5,11-dione* (**9h**). Yield: 0.30 g (65%). Colorless crystals. M.p. 160 – 161°. IR: 3155, 3060, 2959, 1726, 1655, 1604. ^{1}H-NMR: 4.82 (*d*, *J* = 16.0, 1 H of CH_2); 5.21 (*d*, *J* = 16.0, 1 H of CH_2); 5.89 (*s*, 2 H of CH_2); 6.65 (*s*, CH); 6.91 (*d*, *J* = 7.5, H–C(6′)); 7.39 (*t*, *J* = 7.5, H–C(3)); 7.62 – 7.77 (*m*, H–C(7 – 9,4′,5′)); 7.91 (*d*, *J* = 7.5, H–C(1)); 7.97 (*s*, H of triazole); 7.99 – 8.05 (*m*, H–C(2,10)); 8.13 – 8.16 (*m*, H–C(2,3′)). ^{13}C-NMR: 38.0; 50.0; 70.1; 119.8; 120.0; 123.2; 124.6; 125.0; 126.5; 128.2; 128.5; 129.5; 130.0; 130.3; 130.6; 131.9; 132.7; 133.0; 133.5; 134.3; 138.2; 143.1; 150.0; 163.1; 164.1. Anal. calc. for $C_{25}H_{18}N_6O_4$ (466.46): C 64.37, H 3.89, N 18.02; found: C 64.25, H 3.71, N 18.18.

REFERENCES

[1] I. Khan, A. Ibrar, N. Abbas, A. Saeed, *Eur. J. Med. Chem.* **2014**, *76*, 193.

[2] I. Khan, A. Ibrar, W. Ahmed, A. Saeed, *Eur. J. Med. Chem.* **2015**, *90*, 124.

[3] K. S. Kumar, P. M. Kumar, K. A. Kumar, M. Sreenivasulu, A. A. Jafar, D. Rambabu, G. R. Krishna, C. M. Reddy, R. Kapavarapu, K. Shivakumar, K. K. Priya, K. V. L. Parsa, M. Pal, *Chem. Commun. (Cambridge, U.K.)* **2011**, *47*, 5010.

[4] W. J. Houlihan, *Sandoz Inc.*, U.S. Patent 3,509,147, 1970.

[5] M. Ghelardoni, V. Pestellini, *Ann. Chim. (Rome)* **1974**, *64*, 421.

[6] D. S. Goldfarb, U.S. Pat. Appl. Publ. 2009/0163545 A1, 2009.

[7] V. A. Kovtunenko, Z. V. Voitenko, *Russ. Chem. Rev.* **1994**, *63*, 997.

[8] P. Aeberli, W. J. Houlihan, *J. Org. Chem.* **1968**, *33*, 2402.

[9] G. R. Reddy, T. R. Reddy, R. G. Chary, S. C. Joseph, S. Mukherjee, M. Pal, *Tetrahedron Lett.* **2013**, *54*, 6744.

[10] K. V. Sashidhara, G. R. Palnati, R. P. Dodda, S. R. Avula, P. Swami, *Synlett* **2013**, *24*, 105.

[11] T. Ostrowski, P. Januszczyk, M. Cieslak, J. Kazmierczak-Baranska, B. Nawrot, E. Bartoszak-Adamska, J. Zeidler, *Bioorg. Med. Chem.* **2011**, *19*, 4386.

[12] R. Alvarez, S. Velázquez, A. San-Félix, S. Aquaro, E. De Clercq, C.-F. Perno, A. Karlsson, J. Balzarini, M. J. Camarasa, *J. Med. Chem.* **1994**, *37*, 4185.

[13] H. Cheng, J. Wan, M.-I Lin, Y. Liu, X. Lu, J. Liu, Y. Xu, J. Chen, Z. Tu, Y.-S. E. Cheng, K. Ding, *J. Med. Chem.* **2012**, *55*, 2144.

[14] A. K. Jordão, V. F. Ferreira, E. S. Lima, M. C. B. V. de Souza, E. C. L. Carlos, H. C. Castro, R. B. Geraldo, C. R. Rodrigues, M. C. B. Almeida, A. C. Cunha, *Bioorg. Med. Chem.* **2009**, *17*, 3713.

[15] M. Mohammadi-Khanaposhtani, M. Saeedi, N. S. Zafarghandi, M. Mahdavi, R. Sabourian, E. K. Razkenari, H. Alinezhad, M. Khanavi, A. Foroumadi, A. Shafiee, T. Akbarzadeh, *Eur. J. Med. Chem.* **2015**, *92*, 799.

[16] N. Boechat, V. F. Ferreira, S. B. Ferreira, M. de Lourdes G. Ferreira, F. de C. da Silva, M. M. Bastos, M. dos S. Costa, M. C. S. Lourenço, A. C. Pinto, A. U. Krettli, A. C. Aguiar, B. M. Teixeira, N. V. da Silva, P. R. C. Martins, F. A. F. M. Bezerra, A. L. S. Camilo, G. P. da Silva, C. C. P. Costa, *J. Med. Chem.* **2011**, *54*, 5988.

[17] H. C. Kolb, M. G. Finn, K. B. Sharpless, *Angew. Chem., Int. Ed.* **2001**, *40*, 2004.

[18] Y. Jiang, C. Kuang, Q. Yang, *Synlett* **2009**, 3163.

[19] A. Kolarovič, M. Schnürch, M. D. Mihovilovic, *J. Org. Chem.* **2011**, *76*, 2613.

[20] Y. M. A. Yamada, S. M. Sarkar, Y. Uozumi, *J. Am. Chem. Soc.* **2012**, *134*, 9285.

[21] S. Nahavandian, S. Allameh, M. Saeedi, S. Ansari, M. Mahdavi, A. Foroumadi, A. Shafiee, *Helv. Chim. Acta* **2015**, *98*, 1028.

[22] M. Mahdavi, M. Bialam, M. Saeedi, F. Jafarpour, A. Foroumadi, A. Shafiee, *Synlett* **2015**, *26*, 173.

[23] F. Goli-Garmroodi, M. Omidi, M. Saeedi, F. Sarrafzadeh, A. Rafinejad, M. Mahdavi, G. R. Bardajee, T. Akbarzadeh, L. Firoozpour, A. Shafiee, A. Foroumadi, *Tetrahedron Lett.* **2015**, *56*, 743.

[24] M. Saeedi, M. Mahdavi, A. Foroumadi, A. Shafiee, *Tetrahedron* **2013**, *69*, 3506.

[25] M. Mahdavi, R. Najafi, M. Saeedi, E. Alipour, A. Shafiee, A. Foroumadi, *Helv. Chim. Acta* **2013**, *96*, 419.

[26] M. Mahdavi, N. Foroughi, M. Saeedi, M. Karimi, H. Alinezhad, A. Foroumadi, A. Shafiee, T. Akbarzadeh, *Synlett* **2014**, *25*, 385.

[27] S. Farzipour, M. Saeedi, M. Mahdavi, H. Yavari, M. Mirzahekmati, N. Ghaemi, A. Foroumadi, A. Shafiee, *Synth. Commun.* **2014**, *44*, 481.

[28] B. Shafii, M. Saeedi, M. Mahdavi, A. Foroumadi, A. Shafiee, *Synth. Commun.* **2014**, *44*, 215.

[29] M. Asadi, M. Ebrahimi, M. Mahdavi, M. Saeedi, P. R. Ranjbar, F. Yazdani, A. Shafiee, A. Foroumadi, *Synth. Commun.* **2013**, *43*, 2385.

[30] M. Mahdavi, M. Asadi, M. Saeedi, Z. Rezaei, H. Moghbel, A. Foroumadi, A. Shafiee, *Synlett* **2012**, *23*, 2521.

Received May 18, 2015
Accepted September 30, 2015

