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ORIGINAL PAPER

Synthesis of novel 1,2,3-triazole derivatives of 2,3-dihydroquinazolin-4(1*H*)-one

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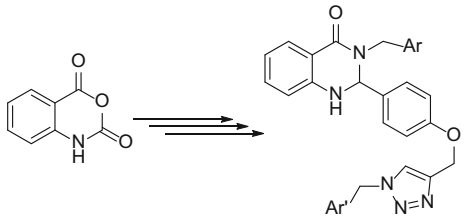
Abstract This work reports an efficient route for the synthesis of novel 1,2,3-triazole derivatives of 2,3-dihydroquinazolin-4(1*H*)-one starting from isatoic anhydride via a three-step reaction. The resulting 2-amino-*N*-substituted benzamides from the reaction of isatoic anhydride and benzylamines underwent coupling cyclization reaction with 4-(prop-2-yn-1-yloxy)benzaldehyde, and then click reaction with in situ prepared organic azides afforded the title compounds in good yields.

Graphical abstract



Keywords Quinazolin-4(1*H*)-one · 1, 2, 3-Triazole · Click chemistry · Isatoic anhydride

Introduction

N-Heterocyclic compounds are valuable synthetic targets and broadly found in various bioactive natural products and pharmaceuticals. At this juncture, quinazolinone and 1,2,3-triazole skeletons possess several valuable chemical, biological, and technical features [1, 2].

Quinazolinones have absorbed lots of attention due to antidiabetic [3], poly(ADP-ribose)polymerase-1 (PARP-1) inhibitory [4], antihypertensive [5], and cholinesterase inhibitory activities [6]. Also, 1,2,3-triazoles have been highly recognized for their cytotoxic [7], anti-HIV-1 [8], anti-influenza [9], anti-platelet [10], and anti-tuberculosis [11] activities. Therefore, it is not unexpected that a majority of research have been devoted to develop highly efficient synthetic strategies for preparing quinazolinone and 1,2,3-triazole derivatives. Recently, Saad et al. [12] and Ouahrouch et al. [13] investigated the synthesis and biological evaluation of some quinazolinone/1,2,3-triazole derivatives highlighting the demand for wide investigation

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of compounds bearing both quinazolinone and 1,2,3-triazole skeletons.

In the view of precious biological and pharmacological activities of quinazolinone and 1,2,3-triazole derivatives, in this paper, we focused on the synthesis of novel 1,2,3-triazole derivatives of 2,3-dihydroquinazolin-4(1*H*)-one due to lack of efficient synthetic procedures in the literature. With the aim of developing a general and practical method of synthesis, we concentrated on a trustworthy protocol for the construction of quinazolinone and triazole ring.

Focusing on isatoic anhydride as a versatile starting material for the preparation of quinazolinones [14–17], recently we have interested in the design and synthesis of novel routes to quinazolinone derivatives [18–21]. On the other hand, the "Click Chemistry" developed by Sharpless has been one of the most established methodologies for the construction of 1,2,3-triazole ring through the reaction of azides and propargyl compounds in the presence of Cu(I) [22]. Finally, as part of our ongoing investigations into the synthesis of *N*-heterocycles [23–25], we wish to report synthesis of a novel series of 1,2,3-triazole derivatives of quinazolin-4(1*H*)-one starting from isatoic anhydride (**1**) (Scheme 1).

Results and discussion

The first stage of our study involved the preparation of 2-amino-*N*-(arylmethyl)benzamide derivatives **3** from the reaction of isatoic anhydride (**1**) and benzylic amines **2** (Scheme 1). Equimolar amounts of **1** and amine **2** were reacted in water at room temperature to give compounds **3** in good yields. In the next step, compounds **3** reacted with 4-(prop-2-yn-1-yloxy)benzaldehyde (**4**) in the presence of K_2CO_3 in ethanol at reflux, affording the corresponding cyclized 3-substituted 2-[4-(prop-2-yn-1-yloxy)phenyl]-2,3-dihydroquinazolin-4(1*H*)-one derivatives **5**.

The presence of triple bond in compound **5** directed us toward click reaction to form 1,2,3-triazole ring. For this purpose, 3-benzyl-2-[4-(prop-2-yn-1-yloxy)phenyl]-2,3-dihydroquinazolin-4(1*H*)-one (**5a**) was reacted with in situ prepared (azidomethyl)benzene (**7a**) under the Sharpless-type click reaction conditions [21]. It was perceived that the reaction occurred in the presence of CuI (7 mol%) in H_2O/*t*-BuOH (1:1) at room temperature within 24 h, leading to the formation of the corresponding product, 3-benzyl-2-[4-[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methoxy]phenyl]-2,3-dihydroquinazolin-4(1*H*)-one (**8a**) in good yields (70 %).

Finally, the structure of compound **8a** was confirmed by ^{1}H NMR and ^{13}C NMR spectroscopy. The six protons of three methylene groups showed the chemical shift $\delta = 5.56$ (s, 2H), 5.18 (d, 1H), 5.10 (s, 2H), and 3.84 (d, 1H) ppm. The existence of CH proton was confirmed by the signal at 5.70 ppm. Eighteen protons of aromatic rings were found at 6.60–7.70 ppm and one proton of 1,2,3-triazole moiety was observed at 8.25 ppm as a singlet signal. Twenty-five distinct resonances were observed in ^{13}CNMR spectrum. Signals at $\delta = 45.9$, 52.3, 61.4, and 71.0 ppm confirmed the presence of three methylene and CH carbons

Scheme 1