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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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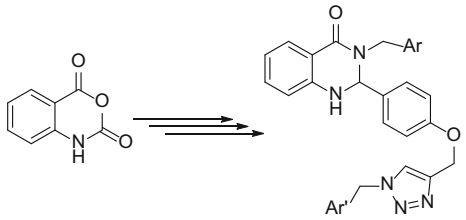
Abstract This work reports an efficient route for the synthesis of novel 1,2,3-triazole derivatives of 2,3-dihydroquinazolin-4(1*H*)-one starting from isatoic anhydride via a three-step reaction. The resulting 2-amino-*N*-substituted benzamides from the reaction of isatoic anhydride and benzylamines 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

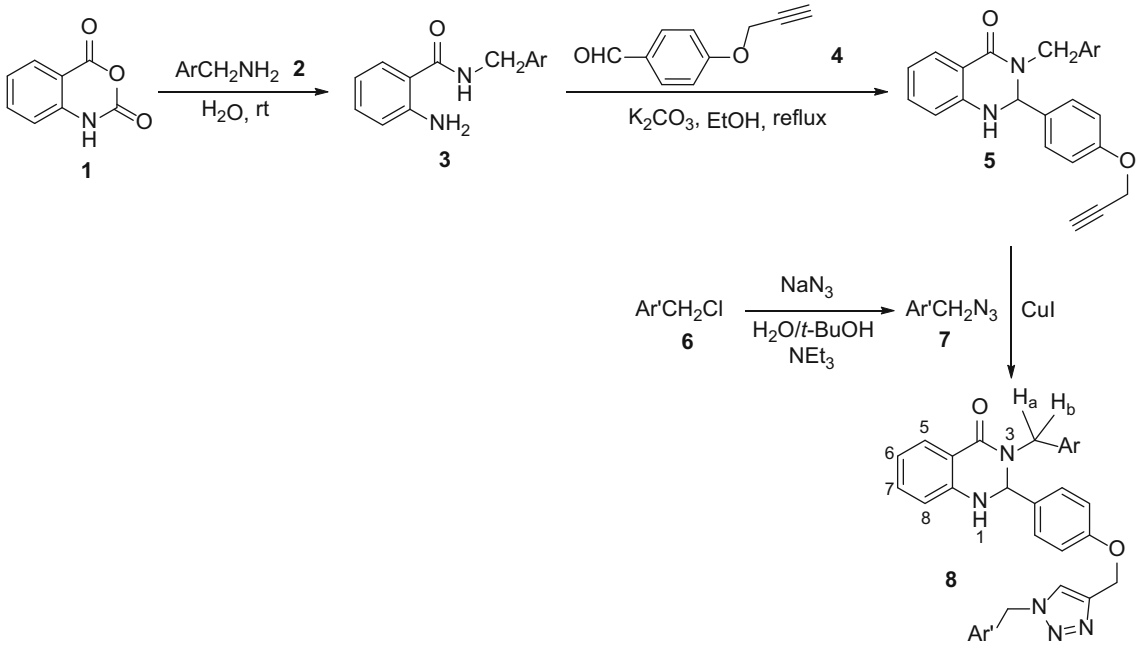

Table 1 Synthesis of 1,2,3-triazole derivatives of 2,3-dihydroquinazolin-4(1*H*)-one **8**

Entry	Ar	Ar′	Product **8**	Yield/%[a]
1	C_6H_5	C_6H_5	**8a**	70
2	C_6H_5	2-Me-C_6H_4	**8b**	75
3	C_6H_5	3-Me-C_6H_4	**8c**	70
4	C_6H_5	4-F-C_6H_4	**8d**	75
5	C_6H_5	4-Cl-C_6H_4	**8e**	80
6	C_6H_5	4-Br-C_6H_4	**8f**	80
7	4-F-C_6H_4	2-Me-C_6H_4	**8g**	75
8	4-F-C_6H_4	3-Me-C_6H_4	**8h**	75
9	4-F-C_6H_4	4-F-C_6H_4	**8i**	70
10	4-F-C_6H_4	2,4-diCl-C_6H_3	**8j**	80

[a] Yield of isolated product

in aliphatic region. Twenty different aromatic carbons were observed between 114.1 and 158.6 ppm and signal at 163.0 ppm belonged to the amide carbonyl group.

Also the structure was confirmed by mass spectrometry fragmentation pattern analysis. The peak at $m/z = 501.22$ was in accordance with the calculated mass for $C_{31}H_{27}N_5O_2$. The mass spectrum showed a strong peak at 424 which is related to elimination of phenyl. Another peak was observed at 263 resulting from loss of 3-benzyl-2,3-dihydroquinazolin-4(1*H*)-one moiety. The peak at 224 is associated with the formation of 2-amino-*N*-benzylidenebenzamide molecular ion and strongest peak was observed at 151 which is related to the formation of 2-amino-*N*-methylbenzamide ion.

The successful synthesis of **8a** inspired us to generate a library of compounds and explore the generality of this reaction. Next, using the above described method, various 1,2,3-triazole derivatives of 2,3-dihydroquinazolin-4(1*H*)-one involving different substituents on 1,2,3-triazole and quinazolinone rings were prepared (Table 1).

It is worth to mention that all reactions were conducted either with electron-withdrawing or electron-donating groups and the corresponding products were obtained in good yields.

Conclusion

In conclusion, we have successfully developed an expedient procedure for the preparation of 1,2,3-triazole derivatives of 2,3-dihydroquinazolin-4(1*H*)-one starting from isatoic anhydride. The isatoic anhydride reacted with benzylamine derivative and the obtained compound tolerated cyclization reaction with 4-(prop-2-yn-1-yloxy)benzaldehyde. Then, the latter compound reacted with in situ prepared organic azides to generate the corresponding final products in good yields. Notably, the design of our current synthetic route was based on biologically important scaffolds; quinazoloinone and 1,2,3-triazole rings.

Experimental

All the chemicals were purchased from Merck and Sigma-Aldrich and used without further purification. Melting points were taken on a Kofler hot stage apparatus. ^{1}H and ^{13}C NMR spectra were recorded on Bruker FT-400, using TMS as an internal standard. The IR spectra were obtained on a Nicolet Magna FTIR 550 spectrophotometer (in KBr). Mass spectra were determined on an Agilent Technology (HP) mass spectrometer operating at an ionization potential of 70 eV. The elemental analysis was performed with an Elementar Analysensystem GmbH VarioEL CHNS mode.

General procedure for the synthesis of 3-substituted 2-[4-(prop-2-yn-1-yloxy)phenyl]-2,3-dihydroquinazolin-4(1H)-one derivatives ***5***

A mixture of isatoic anhydride **1** (20 mmol) and amine **2** (20 mmol) in 50 cm^3 water was stirred for 2–3 h at room temperature. After completion of the reaction (checked by TLC), the resulting off-white precipitate **3** was filtered off, dried at 60 °C, and used for the next reactions without further purification [21]. Then, a mixture of 2-aminobenzamide **3** (1 mmol), 4-(prop-2-yn-1-yloxy)benzaldehyde **4** (1 mmol), and potassium carbonate (1 mmol) in 10 cm^3 EtOH was refluxed for 12–24 h. After completion of the reaction (checked by TLC), potassium carbonate was filtered off from the hot solution and pure product **5** was obtained as yellow crystals after the solution was cooled down to room temperature.

3-Benzyl-2-[4-(prop-2-yn-1-yloxy)phenyl]-2,3-dihydroquinazolin-4(1H)-one (**5a**, $C_{24}H_{20}N_2O_2$)

White solid; yield 0.29 g (80 %); m.p.: 145–147 °C; ^{1}H NMR (500 MHz, DMSO-d_6): $\delta = 7.70$ (dd, $J = 7.5$, 1.5 Hz, 1H, H_5), 7.35–7.20 (m, 9H, NH, Ph, H_7, $H_{2'}$, $H_{6'}$), 6.94 (d, $J = 8.5$ Hz, 2H, $H_{3'}$, $H_{5'}$), 6.69 (td, $J = 7.5$, 1.0 Hz, 1H, H_6), 6.66 (d, $J = 7.5$ Hz, 1H, H_8), 5.69 (s, 1H, CH), 5.30 (d, $J = 15.0$ Hz, 1H, CH_2), 4.76 (s, 2H, CH_2), 3.80 (d, $J = 15.0$ Hz, 1H, CH_2), 3.55 (t, $J = 2.5$ Hz, 1H, CH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): $\delta = 162.4$, 157.3, 146.4, 137.5, 133.4, 133.3, 128.5, 127.7, 127.5, 127.4, 127.1, 117.2, 114.8, 114.6, 114.4, 79.1, 78.3, 69.5, 55.3, 47.0 ppm; IR (KBr): $\bar{\nu} = 3300$, 2922, 2250, 1613, 1510 cm^{-1}.

3-(4-Fluorobenzyl)-2-[4-(prop-2-yn-1-yloxy)phenyl]-2,3-dihydroquinazolin-4(1H)-one (**5b**, $C_{24}H_{19}FN_2O_2$)

White solid; yield 0.25 g (65 %); m.p.: 120–121 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 8.01$ (d, $J = 7.5$ Hz, 1H, H_5), 7.28–7.12 (m, 6H, H_6, H_7, $H_{3'}$, $H_{5'}$, $H_{3''}$, $H_{5''}$), 6.96–

6.85 (m, 4H, $H_{2'}$, $H_{6'}$, $H_{2''}$, $H_{6''}$), 6.52 (d, $J = 7.5$ Hz, 1H, H_8), 5.59 (s, 1H, CH), 5.35 (d, $J = 15.5$ Hz, 1H, CH_2), 4.67 (s, 2H, CH_2), 4.42 (s, 1H, NH), 3.77 (d, $J = 15.5$ Hz, 1H, CH_2), 2.53 (s, 1H, CH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 163.4$, 162.1 (d, $J_{C\text{-}F} = 243.7$ Hz), 158.3, 145.3, 133.7, 132.7, 132.0, 129.6 (d, $J_{C\text{-}F} = 15.0$ Hz), 128.8 (d, $J_{C\text{-}F} = 7.5$ Hz), 128.2, 119.3, 115.7, 115.4, 115.2 (d, $J_{C\text{-}F} = 8.7$ Hz), 114.2, 78.2, 75.8, 71.1, 55.8, 46.2 ppm; IR (KBr): $\bar{\nu} = 3310$, 2925, 2255, 1622, 1525 cm^{-1}.

General procedure for the synthesis of 1,2,3-triazole derivatives of 2,3-dihydroquinazolin-4(1H)-one ***8***

A solution of an arylmethyl chloride **6** (1.1 mmol), 0.06 g sodium azide (0.9 mmol), and 0.13 g triethylamine (1.3 mmol) in 4 cm^3 water and 4 cm^3 *tert*-butyl alcohol was stirred at room temperature for 30 min. Then, the prepared compound **5** (0.5 mmol) and CuI (7 mol%) were added to the reaction mixture and the mixture was stirred for further 20-24 h. Upon completion of the reaction, monitored by TLC, the reaction mixture was diluted with 20 cm^3 water, poured in 20 g ice and the precipitated product was filtered of, washed with cold water, and purified by plate chromatography using silica gel and petroleum ether/ethyl acetate (3:1) as eluent.

3-Benzyl-2-[4-[(1-benzyl-1H-1,2,3-triazol-4-yl)methoxy]-phenyl]-2,3-dihydroquinazolin-4(1H)-one
(**8a**, $C_{31}H_{27}N_5O_2$)

White solid; yield 0.38 g (70 %); m.p.: 64–66 °C; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 8.25$ (s, 1H, triazole), 7.68 (d, $J = 7.6$ Hz, 1H, H_5), 7.29–7.27 (m, 3H, H_7, Ar), 7.25–7.21 (m, 5H, Ar), 7.16–7.09 (m, 5H, Ar), 6.98 (d, $J = 9.2$ Hz, 2H, Ar), 6.68 (t, $J = 7.6$ Hz, 1H, H_6), 6.64 (d, $J = 7.6$ Hz, 1H, H_8), 5.70 (d, $J = 1.6$ Hz, 1H, CH), 5.56 (s, 2H, CH_2), 5.18 (d, $J = 17.5$ Hz, 1H, CH_{2a}), 5.10 (s, 2H, CH_2), 3.84 (d, $J = 17.5$ Hz, 1H, CH_{2b}) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 163.0$, 158.6, 146.8, 145.9, 143.2, 139.3, 136.5, 135.3, 133.9, 133.3, 130.9, 130.4, 130.2, 130.0, 128.0, 125.6, 125.1, 118.7, 114.7, 114.5, 114.1, 71.0, 61.4, 52.3, 45.9 ppm; IR (KBr): $\bar{\nu} = 3391$, 3056, 2924, 2846, 1658, 1613 cm^{-1}; MS (70 eV): $m/z = 501.22$ ([M]$^+$, 37), 424 (34), 263 (15), 237 (28), 224 (40), 151 (100), 107 (34), 77 (31).

3-Benzyl-2-[4-[[1-(2-methylbenzyl)-1H-1,2,3-triazol-4-yl]methoxy]phenyl]-2,3-dihydroquinazolin-4(1H)-one
(**8b**, $C_{32}H_{29}N_5O_2$)

Yellow oil; yield 0.39 g (75 %); ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 8.25$ (s, 1H, triazole), 7.70 (d, $J = 6.8$ Hz, 1H, H_5), 7.47 (d, $J = 8.0$ Hz, 1H, NH), 7.32–7.23 (m, 12H, Ar, H_7), 6.99 (d, $J = 8.4$ Hz, 2H, Ar), 6.70–6.63 (m, 2H, H_6, H_8), 5.90 (s, 1H, CH), 5.70 (s, 2H, CH_2), 5.29 (d, $J = 15.2$ Hz, 1H, CH_{2a}), 5.11 (s, 2H, CH_2), 3.79 (d, $J = 15.2$ Hz, 1H, CH_{2b}), 2.50 (s, 3H, Me) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 162.9$, 158.6, 146.9, 143.2, 138.0, 134.5, 134.2, 133.9, 133.4, 132.8, 132.4, 129.6, 128.9, 128.4, 128.1, 127.9, 127.8, 127.6, 125.6, 117.6, 115.1, 115.0, 114.8, 69.9, 61.5, 50.5, 47.4, 21.9 ppm; IR (KBr): $\bar{\nu} = 3289$, 3068, 2916, 2842, 1622, 1595 cm^{-1}; MS (70 eV): $m/z = 515.23$ ([M]$^+$, 50), 438 (49), 410 (18), 385 (54), 307 (18), 225 (56), 107 (100), 65 (81).

3-Benzyl-2-[4-[[1-(3-methylbenzyl)-1H-1,2,3-triazol-4-yl]methoxy]phenyl]-2,3-dihydroquinazolin-4(1H)-one
(**8c**, $C_{32}H_{29}N_5O_2$)

White solid; yield 0.36 g (70 %); m.p.: 73–75 °C; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 8.25$ (s, 1H, triazole), 7.68 (d, $J = 7.5$ Hz, 1H, H_5), 7.29–7.27 (m, 3H, Ar, H_7), 7.25–7.21 (m, 4H, Ar), 7.16–7.09 (m, 5H, Ar), 6.98 (d, $J = 8.8$ Hz, 2H, Ar), 6.68 (t, $J = 7.5$ Hz, 1H, H_6), 6.63 (d, $J = 7.5$ Hz, 1H, H_8), 5.70 (d, $J = 2.0$ Hz, 1H, CH), 5.56 (s, 2H, CH_2), 5.18 (d, $J = 15.2$ Hz, 1H, CH_{2a}), 5.09 (s, 2H, CH_2), 3.85 (d, $J = 15.2$ Hz, 1H, CH_{2b}), 2.28 (s, 3H, Me) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 162.9$, 158.6, 146.9, 144.9, 143.3, 138.5, 136.3, 134.3, 133.9, 133.3, 130.0, 129.9, 129.3, 129.1, 129.0, 128.1, 128.0, 125.6, 125.1, 117.7, 115.1, 115.0, 114.8, 70.0, 61.5, 53.3, 46.8, 21.4 ppm; IR (KBr): $\bar{\nu} = 3293$, 3040, 2925, 2854, 1624, 1522 cm^{-1}.

3-Benzyl-2-[4-[[1-(4-fluorobenzyl)-1H-1,2,3-triazol-4-yl]methoxy]phenyl]-2,3-dihydroquinazolin-4(1H)-one
(**8d**, $C_{31}H_{26}FN_5O_2$)

Yellow solid; yield 0.39 g (75 %); m.p.: 80–82 °C; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 8.29$ (s, 1H, triazole), 7.71 (d, $J = 7.0$ Hz, 1H, H_5), 7.59 (bs, 1H, NH), 7.58–7.57 (m, 2H, Ar), 7.32–7.21 (m, 10H, Ar, H_7), 6.99 (d, $J = 8.8$ Hz, 2H, Ar), 6.69 (t, $J = 7.0$ Hz, 1H, H_6), 6.63 (d, $J = 8.4$ Hz, 1H, H_8), 5.69 (d, $J = 2.0$ Hz, 1H, CH), 5.60 (s, 2H, CH_2), 5.30 (d, $J = 15.5$ Hz, 1H, CH_{2a}), 5.11 (s, 2H, CH_2), 3.80 (d, $J = 15.5$ Hz, 1H, CH_{2b}) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 162.9$, 160.5 (d, $J_{C\text{-}F} = 240.0$ Hz), 158.6, 146.9, 143.4, 138.0, 135.8, 133.9, 133.4, 132.2, 130.7, 128.9, 128.1, 128.0, 127.9, 125.2, 117.6, 115.1, 115.0, 114.8, 114.7, 69.9, 61.5, 52.5, 47.4 ppm; IR (KBr): $\bar{\nu} = 3299$, 3066, 2920, 2849, 1637, 1616, 1520 cm^{-1}.

3-Benzyl-2-[4-[[1-(4-chlorobenzyl)-1H-1,2,3-triazol-4-yl]methoxy]phenyl]-2,3-dihydroquinazolin-4(1H)-one
(**8e**, $C_{31}H_{26}ClN_5O_2$)

Cream solid; yield 0.43 g (80 %); m.p.: 84–86 °C; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 8.28$ (s, 1H, triazole), 7.69 (d, $J = 8.0$ Hz, 1H, H_5), 7.45 (d, $J = 8.4$ Hz, 2H, Ar), 7.35–7.22 (m, 11 H, Ar, H_7, NH), 6.98 (d, $J = 8.8$ Hz, 2H, Ar), 6.69 (t, $J = 8.0$ Hz, 1H, H_6), 6.63 (d, $J = 8.0$ Hz, 1H, H_8), 5.68 (s, 1H, CH), 5.60 (s, 2H, CH_2), 5.29 (d, $J = 15.2$ Hz, 1H, CH_{2a}), 5.10 (s, 2H, CH_2), 3.79 (d,

J = 15.2 Hz, 1H, CH_{2b}) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.9, 158.6, 146.8, 143.4, 138.0, 135.4, 133.9, 133.4, 130.4, 129.2, 128.9, 128.1, 128.0, 127.9, 127.6, 126.7, 125.2, 117.6, 115.1, 115.0, 114.8, 69.9, 61.5, 52.5, 47.4 ppm; IR (KBr): $\bar{\nu}$ = 3278, 3064, 2928, 2854, 1636, 1527 cm^{-1}.

3-Benzyl-2-[4-[[1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl]methoxy]phenyl]-2,3-dihydroquinazolin-4(1H)-one (**8f**, $C_{31}H_{26}BrN_5O_2$)

Pale yellow solid; yield 0.46 g (80 %); m.p.: 94–97 °C; ^1H NMR (400 MHz, DMSO-d_6): δ = 8.28 (s, 1H, triazole), 7.69 (d, J = 8.0 Hz, 1H, H_5), 7.58 (d, J = 8.4 Hz, 2H, Ar), 7.35–7.20 (m, 11 H, Ar, H_7, NH), 6.99 (d, J = 8.8 Hz, 2H, Ar), 6.69 (t, J = 8.0 Hz, 1H, H_6), 6.64 (d, J = 8.0 Hz, 1H, H_8), 5.68 (d, J = 2.4 Hz, 1H, CH), 5.59 (s, 2H, CH_2), 5.29 (d, J = 15.6 Hz, 1H, CH_{2a}), 5.10 (s, 2H, CH_2), 3.79 (d, J = 15.6 Hz, 1H, CH_{2b}) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.9, 158.6, 146.9, 143.4, 138.0, 135.8, 133.9, 133.4, 132.2, 130.7, 128.9, 128.1, 127.9, 127.9, 127.6, 125.2, 121.9, 121.9, 117.6, 115.1, 115.0, 69.4, 61.5, 52.5, 47.4 ppm; IR (KBr): $\bar{\nu}$ = 3315, 3054, 2933, 2854, 1640, 1520 cm^{-1}.

3-(4-Fluorobenzyl)-2-[4-[[1-(2-methylbenzyl)-1H-1,2,3-triazol-4-yl]methoxy]phenyl]-2,3-dihydroquinazolin-4(1H)-one (**8 g**, $C_{32}H_{28}FN_5O_2$)

Cream solid; yield 0.40 g (75 %); m.p.: 63–64 °C; ^1H NMR (400 MHz, DMSO-d_6): δ = 8.17 (s, 1H, triazole), 7.68 (d, J = 6.8 Hz, 1H, H_5), 7.31–7.21 (m, 8H, Ar, H_7, NH), 7.17–7.06 (m, 4H, Ar), 6.98 (d, J = 8.4 Hz, 2H, Ar), 6.70–6.63 (m, 2H, H_6, H_8), 5.70 (d, J = 2.0 Hz, 1H, CH), 5.61 (s, 2H, CH_2), 5.18 (d, J = 15.5 Hz, 1H, CH_{2a}), 5.09 (s, 2H, CH_2), 3.84 (d, J = 15.5 Hz, 1H, CH_{2b}), 2.29 (s, 3H, Me) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.9, 161.5 (d, $J_{C\text{-}F}$ = 240.0 Hz), 158.6, 147.1, 143.3, 138.3, 136.8, 133.9 (d, $J_{C\text{-}F}$ = 136.2 Hz), 133.3, 130.9, 129.9 (d, $J_{C\text{-}F}$ = 8.1 Hz), 129.6, 129.3, 129.1, 128.8, 128.2, 128.0 (d, $J_{C\text{-}F}$ = 8.4 Hz), 125.5, 125.2, 117.7, 115.6 (d, $J_{C\text{-}F}$ = 21.3 Hz), 115.1, 115.0, 70.0, 61.5, 51.4, 46.1, 19.1 ppm; IR (KBr): $\bar{\nu}$ = 3391, 3056, 2924, 2846, 1658, 1613, 1590 cm^{-1}.

3-(4-Fluorobenzyl)-2-[4-[[1-(3-methylbenzyl)-1H-1,2,3-triazol-4-yl]methoxy]phenyl]-2,3-dihydroquinazolin-4(1H)-one (**8 h**, $C_{32}H_{28}FN_5O_2$)

Deep yellow oil; yield 0.40 g (75 %); ^1H NMR (400 MHz, DMSO-d_6): δ = 8.26 (s, 1H, triazole), 7.70 (dd, J = 7.7, 1.2 Hz, 1H, H_5), 7.31–7.20 (m, 6H, Ar, NH, H_7), 7.16–7.10 (m, 6H, Ar), 6.98 (d, J = 8.4 Hz, 2H, Ar), 6.69 (td, J = 7.7, 0.8 Hz, 1H, H_6), 6.65 (d, J = 7.7 Hz, 1H, H_8), 5.71 (d, J = 2.0 Hz, 1H, CH), 5.55 (s, 2H, CH_2), 5.19 (d, J = 15.2 Hz, 1H, CH_{2a}), 5.10 (s, 2H, CH_2), 3.85 (d, J = 15.2 Hz, 1H, CH_{2b}), 2.28 (s, 3H, Me) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.9, 161.8 (d, $J_{C\text{-}F}$ = 241.2 Hz), 158.6, 146.9, 143.3, 138.5, 136.3, 134.2 (d, $J_{C\text{-}F}$ = 134.5 Hz), 133.9, 133.3, 130.0, 129.9, 129.3, 129.1, 129.0, 128.1, 128.0, 125.6, 125.1, 117.7, 115.6 (d, $J_{C\text{-}F}$ = 21.2 Hz), 115.1, 115.0, 70.1, 61.5, 53.3, 46.8, 21.4 ppm; IR (KBr): $\bar{\nu}$ = 3390, 3054, 2928, 2850, 1650, 1590 cm^{-1}.

3-(4-Fluorobenzyl)-2-[4-[[1-(4-fluorobenzyl)-1H-1,2,3-triazol-4-yl]methoxy]phenyl]-2,3-dihydroquinazolin-4(1H)-one (**8i**, $C_{31}H_{25}F_2N_5O_2$)

Yellow solid; yield 0.37 g (70 %); m.p.: 68–70 °C; ^1H NMR (400 MHz, DMSO-d_6): δ = 8.27 (s, 1H, triazole), 7.69 (d, J = 8.0 Hz, 1H, H_5), 7.41–7.38 (m, 2H, Ar), 7.31–7.28 (m, 3H, Ar, H7), 7.24–7.19 (m, 5H, Ar, NH), 7.14 (t, J = 8.8 Hz, 2H, Ar), 6.98 (d, J = 8.4 Hz, 2H, Ar), 6.69 (t, J = 8.0 Hz, 1H, H_6), 6.65 (d, J = 8.0 Hz, 1H, H_8), 5.71 (d, J = 2.0 Hz, 1H, CH), 5.59 (s, 2H, CH_2), 5.19 (d, J = 15.2 Hz, 1H, CH_{2a}), 5.09 (s, 2H, CH_2), 3.85 (d, J = 15.2 Hz, 1H, CH_{2b}) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.3 (d, $J_{C\text{-}F}$ = 229.2 Hz), 162.9, 160.9 (d, $J_{C\text{-}F}$ = 222.0 Hz), 158.6, 146.9, 143.4, 134.3 (d, $J_{C\text{-}F}$ = 116.6 Hz), 133.9, 133.3, 132.7 (d, $J_{C\text{-}F}$ = 12.0 Hz), 130.8, 130.7, 129.9 (d, $J_{C\text{-}F}$ = 32.4 Hz), 128.1, 128.0, 125.0, 117.7, 116.1 (d, $J_{C\text{-}F}$ = 86.4 Hz), 115.6 (d, $J_{C\text{-}F}$ = 84.4 Hz), 115.0, 114.9, 70.0, 61.5, 52.5, 46.8 ppm; IR (KBr): $\bar{\nu}$ = 3290, 3055, 2928, 2842, 1652, 1597 cm^{-1}.

2-[4-[[1-(2,4-Dichlorobenzyl)-1H-1,2,3-triazol-4-yl]methoxy]-phenyl]-3-(4-fluorobenzyl)-2,3-dihydroquinazolin-4(1H)-one (**8j**, $C_{31}H_{24}Cl_2FN_5O_2$)

Yellow solid; yield 0.47 g (80 %); m.p.: 97–99 °C; ^1H NMR (400 MHz, DMSO-d_6): δ = 8.26 (s, 1H, triazole), 7.70 (dd, J = 7.5, 1.5 Hz, 1H, H_5), 7.68 (dd, J = 2.0 Hz, 1H, Ar), 7.48 (dd, J = 8.4, 2.0 Hz, 1H, Ar), 7.31–7.27 (m, 4H, Ar, H_7), 7.24–7.20 (m, 2H, Ar), 7.14 (t, J = 8.8 Hz, 2H, Ar), 6.99 (d, J = 8.8 Hz, 2H, Ar), 6.68 (td, J = 7.5, 1.2 Hz, 1H, H_6), 6.64 (d, J = 7.5 Hz, 1H, H_8), 5.71 (dd, J = 2.4 Hz, 1H, CH), 5.70 (s, 2H, CH_2), 5.19 (d, J = 15.2 Hz, 1H, CH_{2a}), 5.11 (s, 2H, CH_2), 3.84 (d, J = 15.2 Hz, 1H, CH_{2b}) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.9, 161.8 (d, $J_{C\text{-}F}$ = 241.1 Hz), 158.6, 146.9, 143.2, 134.5, 134.2 (d, $J_{C\text{-}F}$ = 2.9 Hz), 134.2, 133.9, 133.3, 132.8, 132.4, 129.9 (d, $J_{C\text{-}F}$ = 8.1 Hz), 129.6, 128.4, 128.1, 128.0, 125.6, 117.7, 115.6 (d, $J_{C\text{-}F}$ = 21.2 Hz), 115.1, 115.0, 114.8, 70.0, 61.4, 50.5, 46.8 ppm; IR (KBr): $\bar{\nu}$ = 3311, 3044, 2912, 2850, 1634, 1516 cm^{-1}.

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