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Original article

Synthesis and antifungal evaluation of novel triazole derivatives as inhibitors of cytochrome P450 14α-demethylase

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ABSTRACT

A series of 1-(1*H*-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-substituted-2-propanols (**1a**–**v**, **2a**–**w**), which are analogues of fluconazole, have been designed and synthesized as the potential antifungal agents by the click reaction. Click reaction approach toward the synthesis of two sets of novel 1,2,3-triazolyl linked triazole antifungal derivatives **1a**–**v**, **2a**–**w** was achieved by Cu(I)-catalyzed 1,3-dipolar cycloaddition of propargylated intermediate **8** with substituted azidomethyl benzene. The 1,2,3-triazolyl group was inserted into the side chain of the target molecule which can increase the antifungal activity of compounds.

1. Introduction

In recent years, life-threatening systemic fungal infections have become increasingly common in the immunocompromised hosts suffering from cancer, AIDS, and other diseases, or in organ-transplant patients [1,2]. Currently, there are three major clinical fungal infections caused by Candidosis, aspergillosis, and cryptococcosis, respectively [3,4]. Several clinical drugs, including azoles such as fluconazole, voriconazole and itraconazole (Fig. 1) [5], polyenes such as amphotericin B [6], echinocandins such as caspofungin [7] and micafungin [8], and allylamines such as naftifine [9] and terbinafine [10], have been developed to reduce the impact of fungal diseases. Among those antifungal drugs, azoles, especially triazole agents such as fluconazole, voriconazole and itraconazole, are proved to be more effective and thus are more widely used for the treatment of invasive fungal infections. These antigugal drugs act by inhibiting CYP51, a necessary enzyme in the biosynthesis of ergosterol, through a mechanism in which the heterocyclic nitrogen atom (N-4 of triazole) binds to the heme iron atom. However, the increasing administration of these antifungal agents has led to the development of fungal resistance. Survey reveals genetic mutations that result in resistance to clinically used drugs, especially to fluconazole, may also result in resistance to new structurally related azoles such as voriconazole and ravuconazole [11–13]. The emergence of resistance shows the necessity of discovering new antifungal agents with broader antifungal spectra, low toxicity, and higher therapeutic indexes. This report describes the design, synthesis and biological evaluation of a series of triazole derivatives that show promising antifungal properties.

It has been demonstrated that triazole antifungal drugs act through inhibiting cytochrome P450 14α-demethylase (CYP51), an enzyme involved in ergosterol biosynthesis, and that their functional mechanism is to have the N-4 of triazole interacting with the heme iron atom of CYP51 [14]. This binding pattern was further verified by our 3D computer modeling of the interaction between fluconazole and CYP51 of *Candida albicans* [15], as shown in Fig. 2. In addition, the difluorophenyl group of fluconazole is located in the hydrophobic cleft interacting with Gla114, Phe126, Leu139, Met140, Phe145, Ile304, Met306 and Gly307. Several residues, including Leu121, Thr122, Phe228, Thr311, Pro375, Leu376, His377, Ser378, Met508, Val509 and Val510 of CYP51, were further observed to form nonbonding interactions with the other triazolyl

Abbreviations: *C. alb.*, *C. albicans*; *C. neo.*, *C. neoformans*; *A. fum.*, *A. fumigatus*; *T. rub.*, *T. rubrum*; *C. tro.*, *C. tropicalis*; *C. par.*, *C. parapsilosis*; *C. kef.*, *C. kefyr*; ICZ, itraconazole; TRB, terbinafine; KCZ, ketoconazole; AMB, amphotericin B; VCZ, voriconazole; FCZ, fluconazole.

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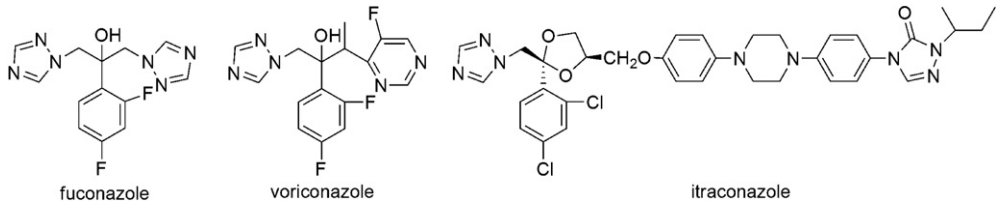


Fig. 1. Triazole antifungal agents used in clinical therapy.

ring [16]. These results, as well as literature structure–activity relationship studies [17], indicate that the triazole ring, the difluorophenyl group, the hydroxyl group, and potentially another heterocyclic group are important pharmacophores of this type of antifungal drugs. Moreover, the side chain located in the narrow hydrophobic cleft is also important.

Based on the above-discussed results and discoveries, we have designed a series of 1-(1*H*-1,2,4-triazole-1-yl)-2-(2,4-difluorophenyl)-3-substituted-2-propanols (**1**, **2** Fig. 3) as fluconazole analogues that contain a triazole ring, a difluorophenyl group, a hydroxyl group, and a side chain with another triazole group. While these compounds contain all the essential pharmacophores, the introduction of an additional triazole group was expected to enhance the interaction between these molecules and CYP51 to potentially result in systemic antifungal compounds that are less possible to develop drug resistance. Moreover, we systematically altered the side chain structure, which is oriented to interact with the narrow hydrophobic cleft, to explore how it may further affect the antifungal activity.

2. Chemistry

Compounds **1a**–**v**, **2a**–**w** were synthesized according to an efficient route based on click reaction, as outlined in Scheme 1. After the key intermediate **6** was prepared by a reported procedure [16], the title compound **7** was obtained by ring-open reaction of oxirane **6** with isopropylamine or cyclopropylamine. Then, compound **7** was transformed into **8** by reacting with propargyl bromide in the presence of KI and K_2CO_3 in acetonitrile. Synthesis of all the target triazole antifungal derivatives **1a**–**v**, **2a**–**w** was achieved using Cu(I)-catalyzed sharpless click chemistry [18] approach from propargylated intermediate **8** and substituted azidomethyl benzene. The addition of Cu(I) catalyst strongly activates terminal acetylenes toward 1,3-dipole in organic azides, exclusively forming the 1,4-disubstituted regioisomer.

3. Pharmacology

The *in vitro* antifungal activities of all the target compounds were evaluated against eight human pathogenic fungi, *Candida albican SC5314* and *Y0109*, *Cryptococcus neoformans*, *Candida parapsilosis*, *Candida tropicalis*, *Trichophyton rubrum*, *Candida kefyr*, and *Aspergillus fumigatus*, which are frequently encountered in clinic. The results were compared with positive controls itraconazole, terbinafine, ketoconazole, amphotericin B, voriconazole and fluconazole. *C. albican SC5314* and *C. neoformans*, purchased from ATCC, were provided by Shanghai Changzheng Hospital;

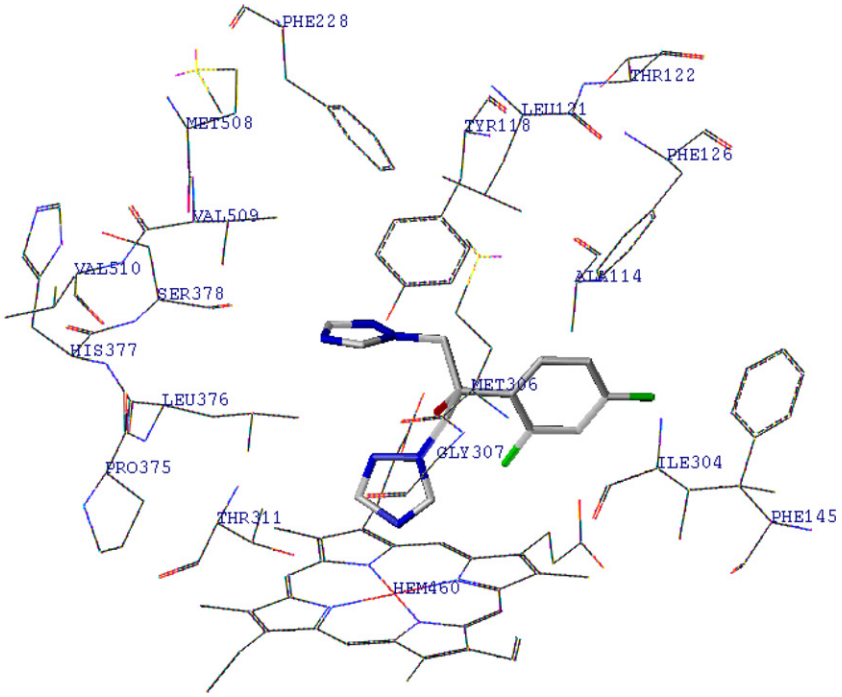


Fig. 2. Computed fluconazole binding to the heme iron atom at the active site of CYP51.

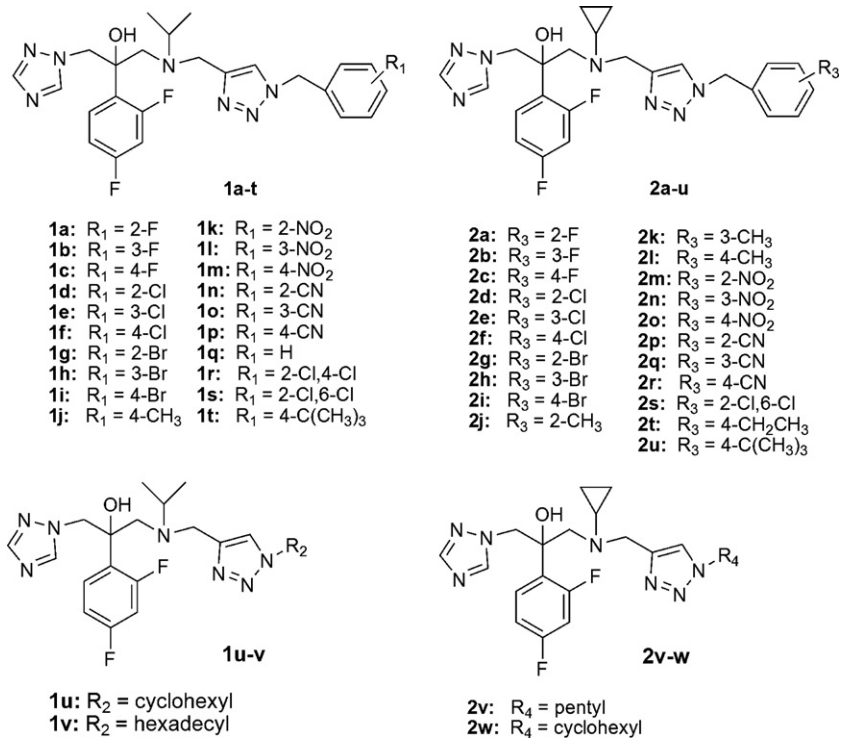


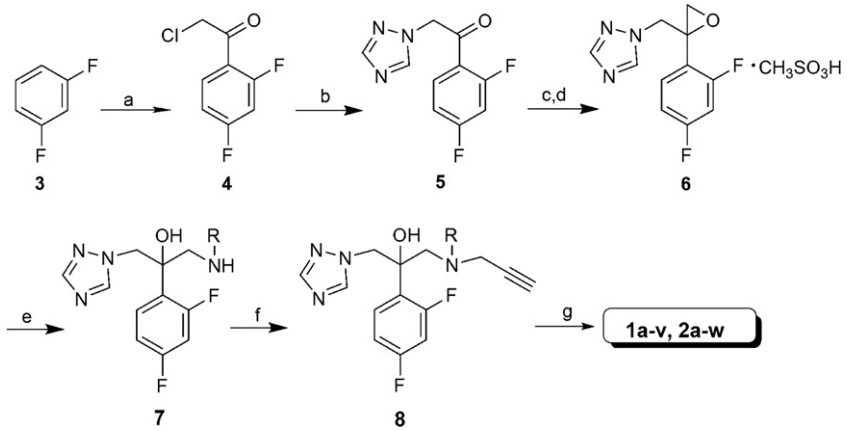
Fig. 3. Generic structure of the designed fluconazole analogues.

C. parapsilosis, *C. albican Y0109*, *C. tropicalis*, *T. rubrum*, *C. kefyr* and *A. fumigatus*, which are clinic isolates, were provided by Shanghai Changhai Hospital. Fluconazole, itraconazole, ketoconazole, voriconazole, amphotericin B and terbinafine served as the positive control were obtained from their respective manufacturers.

The *in vitro* minimal inhibitory concentrations (MICs) of the title compounds were determined by the micro-broth dilution method in 96-well microtestplates according to the methods defined by the National Committee for Clinical Laboratory Standards (NCCLS) [19]. The MIC_{80} was defined as the first well with an approximate 80% reduction in growth compared to the growth of the drug-free well. For assays, the title compounds to be tested were dissolved in dimethyl sulfoxide (DMSO), serially diluted in growth medium, inoculated and incubated at 35 °C. Growth MIC was determined at 24 h for *C. albican* and at 72 h for *C. neoformans*. The results of assays are summarized in Table 1. These data are the mean of three replicate tests performed with each antifungal agent.

4. Results and discussion

In our approach to synthesize title compounds, we have performed click reaction to connect the key intermediate **8** containing terminal alkynyl and the substituted azidomethyl benzene in the presence of Cu(I)-catalyst in dimethyl sulfoxide (DMSO) at room temperature to form the title compounds in good yields.



Scheme 1. Synthesis of the target compounds **1a**–**v**, **2a**–**w**. Conditions: (a) $ClCH_2COCl$, $AlCl_3$, 50 °C, 5 h, 80%; (b) 1*H*-1,2,4-triazole, $NaHCO_3$, toluene, reflux, 5 h, 42%; (c) $(CH_3)_3SOI$, NaOH, centylmethylammonium bromide, toluene, 60 °C, 3 h, 53%; (d) CH_3SO_3H, 0 °C, 1 h, 89%; (e) Et_3N, isopropylamine or cyclopropylamine, EtOH, reflux, 6 h, 80%; (f) propargyl bromide, KI, K_2CO_3, CH_3CN, rt, 5–6 h, 70%; (g) NaN_3, substituted benzyl bromide or alkyl bromide, DMSO, $CuSO_4 \cdot 5H_2O$, sodium ascorbate, rt, 12 h, 60–70%.

Table 1
Antifungal activities of the target compounds *in vitro*.

Compound no.	MIC[a] (μg/mL)							
	C. alb SC5314	*C. alb Y0109*	*C. neo*	*T. nru*	*C. tro*	*C. pra*	*C. kef*	*A. fum*
1a	<0.125	0.0156	2	0.25	<0.125	<0.125	0.0625	>64
1b	<0.125	0.0156	4	0.25	<0.125	<0.125	0.0625	>64
1c	0.25	0.25	8	4	1	2	0.25	>64
1d	<0.125	0.0039	16	2	1	<0.125	0.25	>64
1e	<0.125	0.0156	32	4	2	2	0.25	>64
1f	<0.125	0.0625	4	2	0.5	0.5	0.25	>64
1g	<0.125	0.0156	1	<0.125	<0.125	<0.125	0.0156	16
1h	0.25	1	1	0.0156	0.25	0.0625	0.0039	>64
1i	<0.125	0.0625	8	4	1	1	0.25	>64
1j	1	0.0625	8	2	0.25	0.25	1	>64
1k	<0.125	0.0625	32	8	2	1	0.0625	>64
1l	<0.125	0.0625	32	2	4	1	0.25	>64
1m	<0.125	0.0039	16	4	1	2	0.25	>64
1n	0.25	0.0156	64	8	1	2	1	>64
1o	<0.125	0.0625	64	16	16	16	0.25	>64
1p	1	0.0156	16	0.5	<0.125	<0.125	0.25	>64
1q	<0.125	0.0039	8	0.25	<0.125	<0.125	0.0625	64
1r	4	0.0156	8	0.5	0.25	0.25	0.25	>64
1s	0.0039	<0.125	0.0625	0.0625	0.0156	0.0156	0.0156	>64
1t	<0.125	0.25	32	1	2	1	0.25	>64
1u	<0.125	0.0625	16	2	0.5	1	0.25	>64
1v	<0.125	0.0625	2	0.5	<0.125	0.25	0.25	>64
2a	0.5	0.0625	8	1	0.5	0.25	0.0156	>64
2b	<0.125	0.0625	>64	<0.125	<0.125	<0.125	0.0156	64
2c	1	0.25	16	4	1	2	0.0625	>64
2d	<0.125	0.0625	4	0.25	<0.125	<0.125	0.0156	>64
2e	1	0.0156	64	8	4	4	0.0156	>64
2f	0.25	0.25	16	2	0.5	2	0.0156	>64
2g	0.25	16	64	2	2	2	0.0625	>64
2h	0.0156	0.0156	0.25	0.25	4	0.25	0.0625	>64
2i	0.25	0.0156	16	1	0.5	1	0.0156	>64
2j	0.0625	0.0156	0.0625	4	4	1	0.25	>64
2k	0.5	0.0156	2	<0.125	<0.125	<0.125	0.0156	64
2l	<0.125	0.0156	1	<0.125	<0.125	<0.125	0.0156	64
2m	16	0.0625	64	4	4	4	0.0625	>64
2n	4	0.0625	64	8	4	0.25	0.0156	>64
2o	<0.125	0.25	16	1	0.25	0.5	0.0039	>64
2p	0.25	16	64	2	1	2	1	>64
2q	4	4	64	4	1	4	1	>64
2r	1	0.0625	64	4	4	4	1	>64
2s	4	0.0625	64	4	4	1	0.25	>64
2t	4	0.25	1	4	2	2	0.25	>64
2u	0.0625	<0.125	4	0.25	16	4	1	>64
2v	<0.125	0.0625	32	0.5	0.25	<0.125	0.25	>64
2w	4	0.0625	2	1	1	2	0.25	32
ICZ	<0.0625	0.0625	0.125	0.0625	<0.0625	0.0625	0.0625	2
TBR	16	2	8	<0.125	<0.125	<0.125	0.0625	0.25
KCZ	<0.125	<0.125	0.5	<0.125	<0.125	<0.125	0.0625	0.125
AMB	8	4	4	0.125	0.25	1	0.25	32
VCZ	32	<0.125	<0.125	<0.125	<0.125	0.25	0.0039	<0.125
FCZ	0.5	0.5	8	2	<0.125	<0.125	1	>64

[a] Minimum inhibitory concentration for 80% inhibition of growth.

The results of Table 1 clearly show that the *in vitro* antifungal activities of all the target compounds **1a**–**v**, **2a**–**w** were active against nearly all fungi tested, except for *A. fumigatus*. Among the compounds tested, **1d**, **1h**, **1m**, **1q**, **1s**, **2h**, **2i**, **2j**, **2k** and **2o** showed higher activity against *C. albican SC5314*, *C. albican Y0109*, *C. parapsilosis* and *C. kefyr* than FCZ. Most of the target compounds exhibited higher activities against *C. albican SC5314* and *C. albican Y0109* than all six positive controls. Especially, the MIC values of compounds **1d**, **1m** and **1q** were 128 times lower than that of FCZ against *C. albican Y0109*, and the MIC value of compound **1s** was 128 times lower than that of FCZ against *C. albican SC5314*. The MIC values of compounds **2h**, **2i**, **2j**, **2k** and **2l** were 32 times lower than that of FCZ against *C. albican Y0109*, and the MIC value of compound **2o** was 256 times lower than that of FCZ against *C. kefyr*.

To explain the results, a likely binding mode of **2h** in the active site of CYP51 is proposed based on computational docking results (Fig. 4). As usual, the N(4) atom of the 1,2,4-triazole moiety of **2h** coordinates with the heme Fe-atom, while the 2,4-difluorophenyl group in the designed compound could be placed into the hydrophobic pocket formed by Phe126, Phe145, Met306, Gly307. The hydroxyl group and the vicinal His310 which is a highly conserved residue in the CYP51 family have been found to form a hydrogen bond. The 1,2,3-triazole group in the side chain would generate π–π stacking interactions with the Tyr118. Finally, the substituted benzyl could interact with a hydrophobic pocket formed by Ala114, Phe126, Gln142 and Phe145. In addition, the side chains were the pharmacophores, and the spatial orientations of the pharmacophores were just oriented in the hydrophobic pocket. The side chains of inhibitors were not the determinants for activity, but were very important.

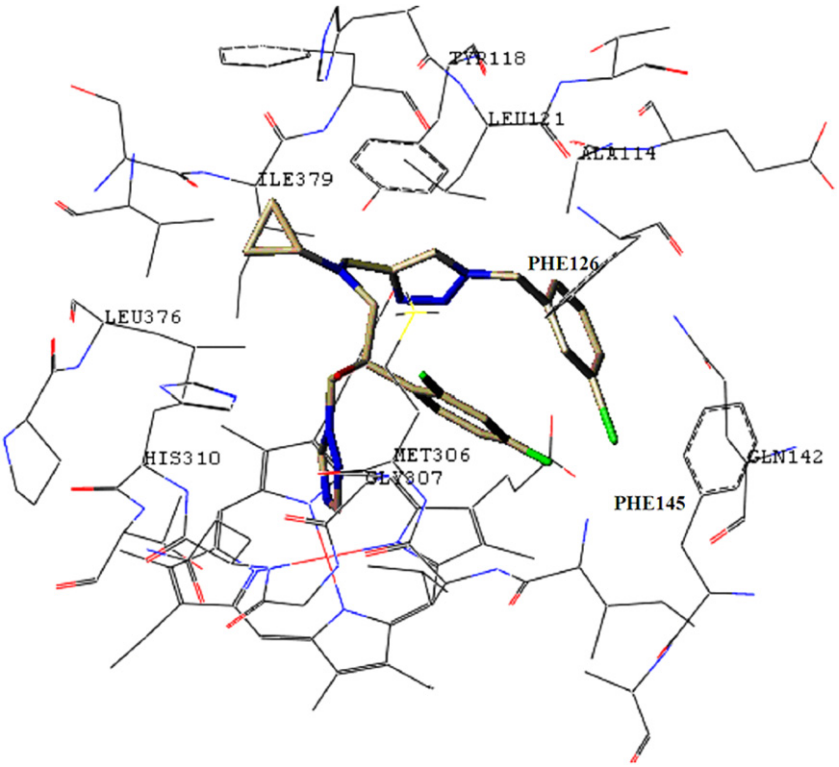


Fig. 4. Computed binding geometry of the new inhibitor **2h** in the active site of CYP51.

5. Conclusion

In conclusion, the current endeavor enables a practical, reliable and efficient synthesis of a series of 1-(1*H*-1,2,4-triazole-1-yl)-2-(2,4-difluorophenyl)-3-substituted-2-propanols as analogues of fluconazole by 'click chemistry' approach. Their antifungal activities were screened for eight human pathogenic fungi. Biological evaluations of the target compounds **1a**–**v**, **2a**–**w** showed that they had strong antifungal activities against nearly all the fungi tested, except for *A. fumigatus* and *C. neoformans*. The antifungal activities of compounds **1a**–**v** are just the same as compounds **2a**–**w**. The 1,2,3-triazole group was inserted into the side chain of the target molecule which can increase the antifungal activity of compounds. The obtained results indicated that for antifungal activity of these novel triazole derivatives it is very helpful to introduce the 1,2,3-triazole group and the substituted benzyl as side chains to generate a π–π stacking interactions with the Tyr118 and interact with a hydrophobic pocket. The research has led to the discovery of a series of compounds for further optimization.

6. Experimental part

In our studies, we constructed a 3D model of *C. albicans* CYP51 on the basis of *Ji et al.* [17]. All the molecular modeling calculations were performed using SYBYL 6.9 version. And the structures of the compounds were assigned with Gasteiger-Hückle partial atomic charges. Energy minimization was performed using the Tripos force field, Powell optimization method, and MAXIMIN2 minimizer with a convergence criterion 0.001 kcal/mol Å. Simulated annealing was then performed. The system was heated to 1000 K for 1.0 ps and then annealed to 250 K for 1.5 ps. The annealing function was exponential; 50 such cycles of annealing were run and the resulting 50 conformers were optimized using methods described above. The lowest energy conformation was selected. All the other parameters were default value.

Melting points were measured on a Yamato MP-21 melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ unless otherwise indicated with a Bruker AC-300P spectrometer or a Bruker Avance II 600 spectrometer, using TMS as internal standard. ESI mass spectra were performed on an API-3000 LC–MS spectrometer. The solvents and reagents were purchased from commercial vendors and were used either as received or dried prior to use as needed.

6.1. 1-(1H-1,2,4-triazole-1-yl)-2-(2,4-difluorophenyl)-3-isopropylamino-2-propanol (**7**)

A mixture of compound **6** (33.3 g, 0.10 mol), CH_3CH_2OH (500 mL) and Et_3N (50 mL), isopropylamine (9.0 g, 0.15 mol) was stirred and refluxed for 6 h. The reaction was monitored by TLC. After filtration, the filtrate was evaporated under reduced pressure. Water was added to the residue, extracted with ethylacetate twice, combinate the organic layer, washed with saturated NaCl solution twice, dried over anhydrous Na_2SO_4 and evaporated to get compound **7** (22.5 g, 80%). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.07 (1H, s, triazole-H), 7.77 (1H, s, triazole-H), 6.73–7.53 (3H, m, Ar-H), 4.35–4.51 (2H, d, $J = 14.0$ Hz, triazole-CH_2–), 2.83–3.06 (2H, d, $J = 14.0$ Hz, CH_2), 2.59–2.62 (1H, m, CH), 0.81–0.88 (6H, d, $J = 6.8$ Hz, $2 \times CH_3$); ^{13}C NMR(150 MHz, $CDCl_3$) δ: 160.2, 158.3, 151.2, 144.2, 131.5, 129.6, 110.2, 104.3, 68.9, 61.9, 57.4, 48.5, 23.5; MS (ESI) *m*/*z* calcd. for $C_{14}H_{18}F_2N_4O$ 296.1, found $[M - H]^+$ 296.5.

6.2. 1-(1H-1,2,4-triazole-1-yl)-2-(2,4-difluorophenyl)-3-(N-isopropyl-N-propargyl amino)-2-propanol (**8**)

A mixture of compound **7** (2.96 g, 0.01 mol), propargyl bromide (2.36 g, 0.02 mol), KI (166 mg, 0.001 mol), K_2CO_3 (3.45 g,

0.025 mol) and CH_3CN (100 mL) was stirred at room temperature for 6 h. The reaction was monitored by TLC. After reaction, filtrated off the solid, washed with CH_3CN, the filtrate was concentrated in a vacuum. Column chromatography of the residue afforded compound **8** as a white solid (2.0 g, 61%). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.05 (1H, s, triazole-H), 7.72 (1H, s, triazole-H), 6.77–7.51 (3H, m, Ar-H), 4.30–4.51 (2H, d, $J = 14.0$ Hz, triazole-CH_2–), 3.11–3.20 (2H, d, $J = 14.0$ Hz, CH_2), 2.81–3.02 (2H, d, $J = 14.0$ Hz, CH_2), 2.65 (1H, s, CH), 2.45–2.57 (1H, m, CH), 0.80–0.88 (6H, d, $J = 6.8$ Hz, $2 \times CH_3$); ^{13}C NMR(150 MHz, $CDCl_3$) δ: 160.0, 158.1, 151.5, 144.7, 131.4, 129.2, 110.1, 104.5, 78.2, 73.9, 68.4, 61.5, 57.3, 48.1, 44.5, 23.2; MS (ESI) m/z calcd. for $C_{14}H_{18}F_2N_4O$ 334.2, found $[M - H]^+$ 334.6.

The *1-(1H-1,2,4-triazole-1-yl)-2-(2,4-difluorophenyl)-3-cyclopropylamine-2-propanol* and *1-(1H-1,2,4-triazole-1-yl)-2-(2,4-difluorophenyl)-3-(N-cyclopropyl-N-propargyl amino)-2-propanol* were synthesized by the same procedure as the above respectively.

6.3. General procedure for the target compound **1a**

A mixture of NaN_3 (100 mg, 1.4 mmol), 2-fluorobenzyl bromide (200 mg, 1.2 mmol) and DMSO (15 mL) was stirred at room temperature for 6 h. Then added the compound **7** (200 mg, 0.6 mmol), sodium ascorbate (20 mg), $CuSO_4 \cdot 5H_2O$ (25 mg), H_2O (1 mL), were stirred at room temperature for 2 h, then put the reaction solution into $NH_3 \cdot H_2O$, extracted with ethylacetate, the organic layer was acidificated with dilute hydrochloric acid, then the aqueous layer was adjusted to pH about 7 by saturation sodium bicarbonate, extracted with ethylacetate, washed with water, dried with Na_2SO_4 concentrated in a vacuum to afford compound **1a** (189 mg, 65%).

The target compounds **1b**–**v** and **2a**–**w** were synthesized by same procedure as the compound **1a**.

6.4. The title compounds were characterized as follows

6.4.1. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(2-fluorobenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1a**)

Mp: 94.5–95.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.09 (1H, s, triazole-H), 7.77 (1H, s, triazole-H), 7.53–7.59 (1H, m, triazole-H), 6.72–7.38 (7H, m, Ar-H), 5.57 (2H, s, Ar-CH_2–), 4.47 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 4.43 (1H, d, $J = 14.1$ Hz, triazole-CH_2–), 3.53 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 3.41 (1H, d, $J = 14.1$ Hz, triazole-CH_2–), 2.83 (1H, d, $J = 14.1$ Hz, CH_2), 2.75 (1H, d, $J = 13.8$ Hz, CH_2), 2.59–2.61 (1H, m, CH), 0.83–0.92 (6H, m, $2 \times CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.32, 161.58, 159.60, 157.96, 150.74, 143.48, 140.40, 126.10, 122.20, 115.88, 111.06, 108.52, 103.78, 72.26, 60.10, 59.89, 58.52, 56.34, 53.04, 49.01, 48.67, 37.64, 20.97, 20.76. MS (ESI) m/z calcd. for $C_{24}H_{26}F_3N_7O$ 485.2, found $[M - H]^+$ 484.7.

6.4.2. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(3-fluorobenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1b**)

Mp: 78.5–79.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.08 (1H, s, triazole-H), 7.78 (1H, s, triazole-H), 7.54–7.60 (1H, m, Ar-H), 7.32–7.39 (1H, m, Ar-H), 6.74–7.09 (6H, m, Ar-H, triazole-H), 5.52 (2H, s, Ar-CH_2–), 4.52 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 3.37 (1H, d, $J = 14.1$ Hz, triazole-CH_2–), 3.52 (1H, d, $J = 14.8$ Hz, triazole-CH_2–), 3.47 (1H, d, $J = 14.1$ Hz, triazole-CH_2–), 3.14 (1H, d, $J = 14.1$ Hz, CH_2), 2.73 (1H, d, $J = 14.1$ Hz, CH_2), 2.55–2.60 (1H, m, CH), 0.84–0.92 (6H, m, $2 \times CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.76, 161.50, 158.63, 157.45, 150.43, 143.45, 140.31, 126.14, 122.67, 114.54, 111.87, 109.15, 103.08, 72.66, 60.25, 59.57, 58.52, 55.68, 52.37, 49.17, 48.04, 37.66, 20.77, 20.34. MS (ESI) m/z calcd. for $C_{24}H_{26}F_3N_7O$ 485.2, found $[M - H]^+$ 484.7.

6.4.3. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(4-fluorobenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1c**)

Mp: 119.3–120.7 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.09 (1H, s, triazole-H), 7.79 (1H, s, triazole-H), 7.54–7.58 (1H, m, Ar-H), 7.23–7.29 (3H, m, Ar-H), 7.03–7.11 (3H, m, Ar-H, triazole-H), 6.74–6.82 (3H, m, Ar-H), 5.49 (2H, s, Ar-CH_2–), 4.52 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 4.36 (1H, d, $J = 14.1$ Hz, triazole-CH_2–), 3.41–3.54 (2H, m, triazole-CH_2–), 3.13 (1H, d, $J = 14.4$ Hz, CH_2), 2.73 (1H, d, $J = 14.1$ Hz, CH_2), 2.56–2.60 (1H, m, CH), 0.84–0.87 (6H, m, $2 \times CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.06, 162.34, 157.65, 156.45, 150.41, 143.48, 140.22, 126.08, 122.51, 113.07, 111.41, 109.47, 103.33, 72.52, 60.33, 59.47, 57.72, 55.38, 52.14, 49.00, 47.79, 36.61, 20.50, 20.38. MS (ESI) m/z calcd. for $C_{24}H_{26}F_3N_7O$ 485.2, found $[M - H]^+$ 484.7.

6.4.4. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(2-chlorobenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1d**)

Mp: 104.2–105.1 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.12 (1H, s, triazole-H), 7.77 (1H, s, triazole-H), 7.51–7.56 (1H, m, Ar-H), 7.43–7.46 (1H, m, Ar-H), 7.15–7.36 (4H, m, Ar-H, triazole-H), 6.71–6.81 (2H, m, Ar-H), 5.64 (2H, s, Ar-CH_2–), 4.50 (1H, d, $J = 14.1$ Hz, triazole-CH_2–), 3.40 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 3.54 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.42 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.13 (1H, d, $J = 14.1$ Hz, CH_2), 2.76 (1H, d, $J = 14.1$ Hz, CH_2), 2.60–2.66 (1H, m, CH), 0.84–0.88 (6H, m, $2 \times CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.17, 160.79, 157.32, 156.33, 150.08, 145.27, 141.08, 124.69, 122.54, 113.10, 112.09, 109.52, 103.79, 72.82, 60.64, 59.28, 58.71, 55.27, 52.18, 50.15, 47.63, 36.14, 20.79, 20.54. MS (ESI) m/z calcd. for $C_{24}H_{26}ClF_2N_7O$ 501.2, found $[M - H]^+$ 500.7.

6.4.5. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(3-chlorobenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1e**)

Mp: 106.5–107.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.08 (1H, s, triazole-H), 7.78 (1H, s, triazole-H), 7.34–7.60 (1H, m, Ar-H), 7.18–7.32 (4H, m, Ar-H), 7.01 (1H, s, triazole-H), 6.75–6.81 (2H, m, Ar-H), 5.50 (2H, s, Ar-CH_2–), 4.53 (1H, d, $J = 14.1$ Hz, triazole-CH_2–), 4.36 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 3.42–3.55 (2H, m, triazole-CH_2–), 3.14 (1H, d, $J = 14.4$ Hz, CH_2), 2.73 (1H, d, $J = 14.1$ Hz, CH_2), 2.53–2.62 (1H, m, CH), 0.82–0.95 (6H, m, $2 \times CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.19, 160.82, 157.30, 156.21, 150.01, 145.45, 141.21, 124.54, 122.68, 113.10, 112.11, 109.52, 103.68, 72.87, 60.25, 59.39, 58.71, 55.68, 52.20, 50.26, 47.41, 36.03, 20.65, 20.59. MS (ESI) m/z calcd. for $C_{24}H_{26}ClF_2N_7O$ 501.2, found $[M - H]^+$ 500.7.

6.4.6. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(4-chlorobenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1f**)

Mp: 105.9–107.4 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.07 (1H, s, triazole-H), 7.78 (1H, s, triazole-H), 7.55–7.59 (1H, m, Ar-H), 7.20–7.23 (4H, dd, $J = 6.3$ Hz, Ar-H), 7.12 (1H, s, triazole-H), 6.73–6.82 (2H, m, Ar-H), 5.50 (2H, s, Ar-CH_2–), 4.53 (1H, d, $J = 14.1$ Hz, triazole-CH_2–), 4.38 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 3.43–3.55 (2H, m, triazole-CH_2–), 3.13 (1H, d, $J = 14.1$ Hz, CH_2), 3.13 (1H, d, $J = 14.1$ Hz, CH_2), 2.56–2.60 (1H, m, CH), 0.84–0.88 (6H, m, $2 \times CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.16, 161.57, 158.53, 157.05, 150.83, 143.05, 140.11, 126.14, 121.67, 114.34, 111.86, 109.13, 103.68, 72.16, 60.35, 59.52, 58.12, 55.28, 52.57, 49.11, 48.07,

37.16, 21.37, 20.44. MS (ESI) *m*/*z* calcd. for $C_{24}H_{26}ClF_2N_7O$ 501.2, found $[M-H]^+$ 500.7.

*6.4.7. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(2-bromobenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1g**)*

Mp: 101.9–103.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.14 (1H, s, triazole-H), 7.77 (1H, s, triazole-H), 7.53–7.64 (1H, m, Ar-H), 7.15–7.35 (4H, m, Ar-H, triazole-H), 6.72–6.81 (2H, m, Ar-H), 5.65 (2H, s, Ar-CH_2–), 4.51 (1H, d, J = 14.4 Hz, triazole-CH_2–), 4.44 (1H, d, J = 14.1 Hz, triazole-CH_2–), 3.60 (1H, d, J = 14.7 Hz, triazole-CH_2–), 3.54 (1H, d, J = 14.7 Hz, triazole-CH_2–), 3.18 (1H, d, J = 13.8 Hz, CH_2), 2.76 (1H, d, J = 14.1 Hz, CH_2), 2.04–2.40 (1H, m, CH), 0.85–0.98 (6H, m, 2 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.20, 160.82, 157.40, 156.52, 150.14, 14530, 141.08, 124.52, 122.43, 113.18, 112.04, 109.40, 103.63, 72.71, 60.57, 59.28, 58.57, 55.17 52.24 50.20, 47.52, 36.19, 20.58, 20.54. MS (ESI) *m*/*z* calcd. for $C_{24}H_{26}BrF_2N_7O$ 545.1, found $[M-H]^+$ 544.7.

*6.4.8. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(3-bromobenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1h**)*

Mp: 105.3–107.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.08 (1H, s, triazole-H), 7.79 (1H, s, triazole-H), 7.48–7.58 (3H, m, Ar-H), 7.17–7.28 (2H, m, Ar-H), 7.01 (1H, s, triazole-H), 6.75–6.81 (2H, m, Ar-H), 5.50 (2H, s, Ar-CH_2–), 4.53 (1H, d, J = 14.4 Hz, triazole-CH_2–), 4.36 (1H, d, J = 14.4 Hz, triazole-CH_2–), 3.47–3.55 (2H, m, triazole-CH_2–), 3.13 (1H, d, J = 14.1 Hz, CH_2), 2.73 (1H, d, J = 14.1 Hz, CH_2), 2.55–2.59 (1H, m, CH), 0.84–0.88 (6H, m, 2 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.14, 160.74, 157.45, 156.29, 150.04, 145.19, 141.15, 124.61, 122.48, 113.21, 112.11, 109.47, 103.65, 72.63, 60.58, 59.22, 58.52, 55.17, 52.14, 50.18, 47.63, 36.26, 20.62, 20.50. MS (ESI) *m*/*z* calcd. for $C_{24}H_{26}BrF_2N_7O$ 545.1, found $[M-H]^+$ 544.7.

*6.4.9. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(4-bromobenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1i**)*

Mp: 120.5–122.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.08 (1H, s, triazole-H), 7.79 (1H, s, triazole-H), 7.53–7.56 (1H, m, Ar-H), 7.13–7.52 (4H, dd, Ar-H), 7.03 (1H, s, triazole-H), 6.75–6.79 (2H, m, Ar-H), 5.51 (1H, s, OH), 5.48 (2H, s, Ar-CH_2–), 4.53 (1H, d, J = 14.1 Hz, triazole-CH_2–), 4.36 (1H, d, J = 14.4 Hz, triazole-CH_2–), 3.11–3.48 (2H, m, triazole-CH_2–), 3.13 (1H, d, J = 14.1 Hz, CH_2), 2.73 (1H, d, J = 14.1 Hz, CH_2), 2.50–2.59 (1H, m, CH), 0.84–0.88 (6H, m, 2 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.20, 160.57, 157.46, 156.42, 150.15, 145.27, 141.17, 124.45, 122.68, 113.10, 112.24, 109.01, 103.57, 72.38, 60.46, 59.18, 58.45, 55.16, 52.18, 50.21, 47.82, 36.24, 20.53, 20.49. MS (ESI) *m*/*z* calcd. for $C_{24}H_{26}BrF_2N_7O$ 545.1, found $[M-H]^+$ 544.6.

*6.4.10. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(4-methylbenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1j**)*

Mp: 133.5–135.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.08 (1H, s, triazole-H), 7.77 (1H, s, triazole-H), 7.52–7.57 (1H, m, Ar-H), 7.14–7.20 (4H, m, Ar-H), 7.03 (1H, s, triazole-H), 6.69–6.80 (2H, m, Ar-H), 5.57 (1H, s, OH), 5.46 (2H, s, Ar-CH_2–), 4.48 (1H, d, J = 13.8 Hz, triazole-CH_2–), 4.37 (1H, d, J = 14.1 Hz, triazole-CH_2–), 3.38–3.54 (2H, m, triazole-CH_2–), 3.11 (1H, d, J = 14.1 Hz, CH_2), 2.74 (1H, d, J = 14.1 Hz, CH2), 2.58–2.62 (1H, m, CH), 2.36 (3H, s, CH_3), 0.83–0.87 (6H, m, 2 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.87, 160.74, 157.09, 156.12, 151.07, 145.45, 141.39, 124.59, 122.02, 113.79, 112.12, 109.05, 103.48, 73.12, 60.23, 59.52, 58.09, 55.48, 52.14, 50.65, 47.18, 36.10, 20.94, 20.78, 20.17. MS (ESI) *m*/*z* calcd. for $C_{25}H_{29}F_2N_7O$ 481.2, found $[M-H]^+$ 480.6.

*6.4.11. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(2-nitrobenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1k**)*

Mp: 126.3–127.4 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.12–8.16 (1H, m, Ar-H), 8.10 (1H, s, triazole-H), 7.79 (1H, s, triazole-H), 7.36–7.66 (3H, m, Ar-H), 7.35 (1H, s, triazole-H), 6.76–7.19 (3H, m, Ar-H), 5.90 (2H, s, Ar-CH_2–), 4.56 (1H, s, OH), 4.54 (1H, d, J = 14.1 Hz, triazole-CH_2–), 4.40 (1H, d, J = 14.4 Hz, triazole-CH_2–), 3.56 (1H, d, J = 14.1 Hz, triazole-CH_2–), 3.47 (1H, d, J = 14.1 Hz, triazole-CH_2–), 3.15 (1H, d, J = 1.9 Hz, CH_2), 2.78 (1H, d, J = 14.1 Hz, CH_2), 2.58–2.67 (1H, m, CH), 0.84–0.89 (6H, m, 2 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.44, 161.78, 159.75, 158.11, 148.03, 144.14, 141.67, 129.75, 128.43, 126.24, 124.25, 122.66, 111.41, 104.20, 72.45, 65.75, 58.74, 56.43, 55.21, 52.97, 49.33, 37.90, 21.12, 20.56. MS (ESI) *m*/*z* calcd. for $C_{24}H_{26}F_2N_8O_3$ 512.2, found $[M-H]^+$ 511.6.

*6.4.12. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(3-nitrobenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1l**)*

Mp: 113.1–114.4 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.21–8.25 (2H, m, Ar-H), 8.07 (1H, s, triazole-H), 7.80 (1H, s, triazole-H), 7.56–7.63 (3H, m, Ar-H), 7.11 (1H, s, triazole-H), 6.76–6.83 (2H, m, Ar-H), 5.65 (2H, s, Ar-CH_2–), 5.45 (1H, s, OH), 4.56 (1H, d, J = 14.1 Hz, triazole-CH_2–), 4.34 (1H, d, J = 14.4 Hz, triazole-CH_2–), 3.47–3.52 (2H, m, triazole-CH_2–), 3.16 (1H, d, J = 14.1 Hz, CH_2), 2.71 (1H, d, J = 14.4 Hz, CH_2), 2.52–2.56 (1H, m, CH), 0.85–0.88 (6H, m, 2 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.16, 160.64, 157.03, 156.42, 150.15, 145.05, 141.16, 124.60, 122.53, 113.23, 112.08, 109.65, 103.48, 72.81, 60.25, 59.12, 58.56, 55.18, 52.06, 50.23, 47.68, 36.26, 20.80, 20.59. MS (ESI) *m*/*z* calcd. for $C_{24}H_{26}F_2N_8O_3$ 512.2, found $[M-H]^+$ 511.7.

*6.4.13. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(4-nitrobenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1m**)*

Mp: 134.1–135.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.10–8.15 (2H, d, Ar-H), 8.08 (1H, s, triazole-H), 7.79 (1H, s, triazole-H), 7.56–7.64 (1H, m, Ar-H), 7.39–7.42 (2H, d, Ar-H), 7.08 (1H, s, triazole-H), 6.77–6.83 (2H, m, Ar-H), 5.66 (2H, s, Ar-CH_2–), 5.43 (1H, s, OH), 4.57 (1H, d, J = 14.4 Hz, triazole-CH_2–), 4.35 (1H, d, J = 14.1 Hz, triazole-CH_2–), 3.47–3.52 (2H, m, triazole-CH_2–), 3.16 (1H, d, J = 14.1 Hz, CH_2), 3.16 (1H, d, J = 14.1 Hz, CH_2), 2.52–2.56 (1H, m, CH), 0.85–0.88 (6H, m, 2 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.26, 161.70, 158.64, 157.65, 150.43, 142.45, 141.31, 126.16, 122.17, 114.547, 111.86, 109.95, 103.28, 72.46, 60.21, 59.51, 58.51, 55.18, 52.37, 49.12, 48.05, 37.76, 21.34, 20.79. MS (ESI) *m*/*z* calcd. for $C_{24}H_{26}F_2N_8O_3$ 512.2, found $[M-H]^+$ 511.7.

*6.4.14. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(2-cyanobenzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1n**)*

Mp: 116.1–117.4 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.10 (1H, s, triazole-H), 7.80 (1H, s, triazole-H), 7.42–7.77 (5H, m, Ar-H), 7.34 (1H, s, triazole-H), 6.76–6.82 (2H, m, Ar-H), 5.72 (2H, s, Ar-CH_2–), 5.50 (1H, s, OH), 4.52 (1H, d, J = 14.4 Hz, triazole-CH_2–), 4.38 (1H, d, J = 14.1 Hz, triazole-CH_2–), 3.54 (1H, d, J = 14.1 Hz, triazole-CH_2–), 3.43 (1H, d, J = 14.4 Hz, triazole-CH_2–), 3.13 (1H, d, J = 14.4 Hz, CH_2), 2.75 (1H, d, J = 14.1 Hz, CH_2), 2.58–2.63 (1H, m, CH), 0.83–0.88 (6H, m, 2 × CH_3); ^{13}C NMR (75 MHz, CDCl3) δ: 162.15, 160.87, 157.46, 156.52, 150.16, 145.28, 141.20, 124.80, 122.65, 113.48, 112.24, 109.51, 103.16, 72.23, 60.72, 59.06, 58.69, 55.18, 52.26, 50.16,

47.35, 36.15, 21.68, 20.52. MS (ESI) *m*/*z* calcd. for $C_{25}H_{26}F_2N_8O$ 492.2, found $[M-H]^+$ 491.7.

*6.4.15. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(3-cyanobenzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1o**)*

Mp: 117.8–118.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.07 (1H, s, triazole-H), 7.80 (1H, s, triazole-H), 7.50–7.53 (4H, m, Ar-H), 7.07 (1H, s, triazole-H), 6.77–6.83 (2H, m, Ar-H), 5.58 (2H, s, Ar-CH_2–), 5.44 (1H, s, OH), 4.55 (1H, d, J = 14.4 Hz, triazole-CH_2–), 4.35 (1H, d, J = 14.4 Hz, triazole-CH_2–), 3.50 (2H, s, triazole-CH_2–), 3.16 (1H, d, J = 14.4 Hz, CH_2), 2.70 (1H, d, J = 14.1 Hz, CH_2), 2.51–2.56 (1H, m, CH), 0.86–0.88 (6H, m, 2 × CH_3); ^{13}C NMR (75 MHz, CDCl3) δ: 163.76, 161.52, 158.13, 157.75, 150.44, 143.65, 140.21, 126.54, 122.77, 114.84, 111.88, 109.95, 103.09, 72.46, 60.22, 59.57, 58.55, 55.63, 52.34, 49.87, 48.05, 37.26, 20.57, 20.35. MS (ESI) *m*/*z* calcd. for $C_{25}H_{26}F_2N_8O$ 492.2, found $[M-H]^+$ 491.7.

*6.4.16. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(4-cyanobenzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1p**)*

Mp: 75.1–76.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.06 (1H, s, triazole-H), 7.77 (1H, s, triazole-H), 7.67–7.70 (2H, d, Ar-H), 7.55–7.66 (1H, m, Ar-H), 7.32–7.35 (2H, d, Ar-H), 7.06 (1H, s, triazole-H), 6.76–6.82 (2H, m, Ar-H), 5.60 (2H, s, Ar-CH_2–), 5.44 (1H, s, OH), 4.55 (1H, d, J = 14.1 Hz, triazole-CH_2–), 4.34 (1H, d, J = 14.1 Hz, triazole-CH_2–), 3.45–3.52 (2H, m, triazole-CH_2–), 3.16 (1H, d, J = 14.1 Hz, CH_2), 2.70 (1H, d, J = 14.1 Hz, CH_2), 2.51–2.55 (1H, m, CH), 0.85–0.90 (6H, m, 2 × CH_3); ^{13}C NMR(75 MHz, CDCl3) δ: 162.83, 161.10, 158.65, 157.35, 150.42, 143.41, 140.37, 126.12, 122.47, 114.64, 111.84, 109.17, 103.05, 72.64, 60.25, 59.37, 58.22, 55.68, 52.34, 49.15, 48.54, 37.76, 20.78, 20.31. MS (ESI) *m*/*z* calcd. for $C_{25}H_{26}F_2N_8O$ 492.2, found $[M-H]^+$ 491.6.

*6.4.17. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]amino}-2-propanol (**1q**)*

Mp: 100.1–102.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.08 (1H, s, triazole-H), 7.75 (1H, s, triazole-H), 7.39–7.55 (1H, m, Ar-H), 7.37–7.40 (3H, m, Ar-H), 7.24–7.26 (2H, m, Ar-H), 7.05 (1H, s, triazole-H), 6.73–6.80 (2H, m, Ar-H), 5.52 (2H, s, Ar-CH_2–), 4.49 (1H, d, J = 14.1 Hz, triazole-CH_2–), 4.37 (1H, d, J = 14.4 Hz, triazole-CH_2–), 3.47–3.54 (2H, m, triazole-CH_2–), 3.12 (1H, d, J = 12.9 Hz, CH_2), 2.74 (1H, d, J = 14.1 Hz, CH_2), 2.58–2.62 (1H, m, CH), 0.83–0.88 (6H, m, 2 × CH_3); ^{13}C NMR (75 MHz, CDCl3) δ: 164.06, 161.30, 158.63, 157.75, 150.33, 143.25, 140.32, 126.24, 122.57, 114.14, 111.83, 109.17, 103.28, 72.67, 60.21, 59.55, 58.42, 55.38, 52.31, 49.27, 48.05, 37.66, 20.76, 20.34. MS (ESI) *m*/*z* calcd. for $C_{24}H_{27}F_2N_7O$ 467.2, found $[M-H]^+$ 466.8.

*6.4.18. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(2,4-dichlorobenzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1r**)*

Mp: 119.5–120.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.10 (1H, s, triazole-H), 7.79 (1H, s, triazole-H), 7.54–7.62 (1H, m, Ar-H), 7.46–7.48 (1H, m, Ar-H), 7.12–7.28 (3H, m, Ar-H), 6.74–6.83 (2H, m, Ar-H), 5.60 (2H, s, Ar-CH_2–), 4.53 (1H, d, J = 14.4 Hz, triazole-CH_2–), 4.38 (1H, d, J = 14.4 Hz, triazole-CH_2–), 3.45–3.56 (2H, m, triazole-CH_2–), 3.13 (1H, d, J = 14.1 Hz, CH_2), 2.75 (1H, d, J = 14.1 Hz, CH_2), 2.57–2.61 (1H, m, CH), 0.84–0.90 (6H, m, 2 × CH_3); ^{13}C NMR(75 MHz, CDCl3) δ: 162.06, 161.30, 158.53, 157.44, 150.43, 143.35, 140.33, 126.12, 122.65, 114.56, 111.86, 109.25, 103.28, 72.76, 60.35, 59.58, 58.32, 55.67, 52.39, 49.37, 48.05, 37.46, 20.77, 20.32. MS (ESI) *m*/*z* calcd. for $C_{24}H_{25}Cl_2F_2N_7O$ 535.2, found $[M-H]^+$ 534.9.

*6.4.19. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(2,6-dichlorobenzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1s**)*

Mp: 109.2–111.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.18 (1H, s, triazole-H), 7.81 (1H, s, triazole-H), 7.31–7.58 (3H, m, Ar-H), 7.18 (1H, s, triazole-H), 6.76–6.87 (2H, m, Ar-H), 5.83 (2H, s, Ar-CH_2–), 4.62 (1H, d, J = 14.1 Hz, triazole-CH_2–), 4.48 (1H, d, J = 14.1 Hz, triazole-CH_2–), 3.00–3.26 (2H, m, triazole-CH_2–), 2.80–2.95 (2H, m, CH_2), 2.57–2.60 (1H, m, CH), 0.83–0.90 (6H, m, 2 × CH_3); ^{13}C NMR (75 MHz, CDCl3) δ: 163.16, 161.30, 157.63, 157.45, 150.63, 143.46, 140.31, 126.34, 122.77, 114.94, 111.67, 109.95, 103.06, 72.65, 60.25, 59.57, 58.55, 55.67, 52.47, 49.14, 48.54, 37.67, 20.72, 20.54. MS (ESI) *m*/*z* calcd. for $C_{24}H_{25}Cl_2F_2N_7O$ 535.2, found $[M-H]^+$ 534.9.

*6.4.20. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(4-tertbutylbenzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1t**)*

Mp: 119.5–120.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.09 (1H, s, triazole-H), 7.77 (1H, s, triazole-H), 7.49–7.58 (1H, m, Ar-H), 7.18–7.41 (4H, dd, J = 8.1 Hz, Ar-H), 7.04 (1H, s, triazole-H), 6.68–6.80 (2H, m, Ar-H), 5.58 (1H, s, OH), 5.47 (2H, s, Ar-CH_2–), 4.51 (1H, d, J = 14.1 Hz, triazole-CH_2–), 4.37 (1H, d, J = 14.1 Hz, triazole-CH_2–), 3.38–3.54 (2H, m, triazole-CH_2–), 3.12 (1H, d, J = 14.1 Hz, CH_2), 2.74 (1H, d, J = 14.1 Hz, CH_2), 2.59–2.64 (1H, m, CH), 1.29–1.33 (9H, m, 3 × CH_3), 0.83–0.87 (6H, m, 2 × CH_3); ^{13}C NMR(75 MHz, CDCl3) δ: 162.74, 160.58, 157.35, 156.46, 151.36, 145.54, 141.31, 124.49, 121.11, 113.43, 112.64, 109.50, 103.72, 73.23, 61.12, 59.23, 57.78, 55.04, 52.27, 50.12, 47.33, 36.45, 33.25, 22.87, 22.70, 20.61, 20.49. MS (ESI) *m*/*z* calcd. for $C_{28}H_{35}F_2N_7O$ 523.3, found $[M-H]^+$ 522.8.

*6.4.21. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(4-cyclohexyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1u**)*

Mp: 84.1–85.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.13 (1H, s, triazole-H), 7.77 (1H, s, triazole-H), 7.58–7.76 (1H, m, Ar-H), 7.21 (1H, s, triazole-H), 6.76–6.84 (2H, m, Ar-H), 5.76 (1H, s, OH), 4.41–4.54 (2H, m, triazole-CH_2–), 4.38–4.39 (1H, m, triazole-CH–), 3.57 (1H, d, J = 14.4 Hz, triazole-CH_2), 3.43 (1H, d, J = 14.7 Hz, triazole-CH_2), 3.13 (1H, d, J = 13.8 Hz, CH_2), 2.67 (1H, d, J = 13.2 Hz, CH_2), 2.65–2.69 (1H, m, CH), 1.26–2.22 (10H, m, 5 × CH_2), 0.83–0.88 (6H, m, 2 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.47, 160.25, 156.29, 141.28, 124.37, 121.10, 113.44, 109.55, 73.20, 61.17, 59.28, 57.70, 55.06, 52.18, 50.26, 47.44, 36.95, 35.26, 34.17, 24.63, 23.58, 20.65, 20.43. MS (ESI) *m*/*z* calcd. for $C_{23}H_{31}F_2N_7O$ 459.3, found $[M-H]^+$ 458.7.

*6.4.22. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-isopropyl-N-[(1-(4-hexadecyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**1v**)*

Mp: 73.4–74.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.11 (1H, s, triazole-H), 7.78 (1H, s, triazole-H), 7.56–7.64 (1H, m, Ar-H), 7.14 (1H, s, triazole-H), 6.76–6.84 (2H, m, Ar-H), 5.65 (1H, s, OH), 4.39–4.57 (2H, m, triazole-CH_2–), 4.28–4.33 (2H, m, triazole-CH-), 3.41–3.58 (2H, m, triazole-CH_2), 2.63–3.16 (2H, m, CH_2), 2.60–2.65 (1H, m, CH), 1.00–1.90 (28H, m, 14 × CH_2), 0.84–0.98 (9H, m, 3 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 160.21, 158.32, 151.52, 143.82, 131.31, 130.73, 129.43, 122.59, 110.84, 104.45, 67.77, 65.57, 64.70, 55.67, 52.74, 40.73, 29.30, 29.24, 29.22, 28.67, 28.63, 26.12, 26.01, 24.23, 24.23, 23.12, 23.12, 22.45, 22.10, 21.12, 20.14 19.18, 14.15. MS (ESI) *m*/*z* calcd. for $C_{33}H_{53}F_2N_7O$ 601.4, found $[M-H]^+$ 600.8.

*6.4.23. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N- [(1-(2-fluorobe-nzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2a**)*

Mp: 71.0–72.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.08 (1H, s, triazole-H), 7.79 (1H, s, triazole-H), 7.44–7.52 (1H, m, Ar-H),

7.05–7.37 (5H, m, Ar-H, triazole-H), 6.64–6.74 (2H, m, Ar-H), 5.56 (2H, s, Ar-CH_2–), 4.45–4.58 (2H, m, triazole-CH_2–), 3.70 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.58 (1H, d, $J = 14.1$ Hz, triazole-CH_2–), 3.34 (1H, d, $J = 13.8$ Hz, CH_2), 2.87 (1H, d, $J = 13.8$ Hz, CH_2), 1.98–2.15 (1H, m, NCH), 0.15–0.41 (4H, m, 2*CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.06, 160.48, 157.20, 156.18, 150.64, 145.05, 141.18, 124.89, 122.44, 113.31, 112.02, 109.68, 103.99, 72.62, 60.64, 59.26, 58.48, 55.52, 52.38, 50.19, 47.48, 36.12, 21.80, 21.59. MS (ESI) m/z calcd. for $C_{24}H_{24}F_3N_7O$ 483.2, found $[M - H]^+$ 482.6.

*6.4.24. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N- [(1-(3-fluorobe-nzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2b**)*

Mp: 75.6–77.7 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.10 (1H, s, triazole-H), 7.72 (1H, s, triazole-H), 6.88–7.52 (6H, m, Ar-H, triazole-H), 6.65–6.77 (2H, m, Ar-H), 5.47 (2H, m, Ar-CH_2–), 5.15 (1H, s, OH), 4.44–4.50 (2H, m, triazole-CH_2–), 3.70 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.51 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.40 (1H, d, $J = 14.1$ Hz, CH_2), 2.87 (1H, d, $J = 14.1$ Hz, CH_2), 1.99–2.01 (1H, m, NCH), 0.15–0.35 (4H, m, $2 \times CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.31, 160.86, 157.16, 156.25, 150.18, 145.35, 141.24, 124.46, 122.62, 113.53, 112.14, 109.62, 103.24, 72.58, 60.68, 59.54, 58.49, 55.84, 52.15, 50.26, 47.37, 36.20, 20.81, 20.16. MS (ESI) m/z calcd. for $C_{24}H_{24}F_3N_7O$ 483.2, found $[M - H]^+$ 482.6.

*6.4.25. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(4-fluorobe-nzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2c**)*

Mp: 95.3–97.5 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.07 (1H, s, triazole-H), 7.68 (1H, s, triazole-H), 7.47–7.48 (1H, m, Ar-H), 7.18–7.20 (2H, m, Ar-H), 7.04 (1H, s, triazole-H), 7.00–7.01 (2H, m, Ar-H), 6.64–6.72 (2H, m, Ar-H), 5.41 (2H, dd, $J = 25.8$ Hz, 15.0 Hz, Ar-CH_2–), 5.15 (1H, s, OH), 4.42 (2H, dd, $J = 24.0$ Hz, 14.4 Hz, triazole-CH_2–), 3.49–3.70 (2H, dd, $J = 15.0$ Hz, triazole-CH_2–), 2.87–3.34 (2H, dd, $J = 14.4$ Hz, CH_2), 1.95–1.97 (1H, m, NCH), 0.12–0.30 (4H, m, $2 \times CH_2$); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 163.36, 161.52, 158.64, 157.44, 150.23, 143.65, 140.71, 126.15, 122.63, 114.54, 111.86, 109.13, 103.48, 72.26, 60.25, 59.67, 58.32, 55.68, 52.47, 49.67, 48.05, 37.66, 20.67, 20.36. MS (ESI) m/z calcd. for $C_{24}H_{24}F_3N_7O$ 483.2, found $[M - H]^+$ 482.8.

*6.4.26. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(2-chlorobe-nzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2d**)*

Mp: 124.1–126.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.11 (1H, s, triazole-H), 7.15 (1H, s, triazole-H), 7.14–7.51 (6H, m, Ar-H, triazole-H), 6.67–6.77 (2H, m, Ar-H), 5.60 (2H, s, Ar-CH_2–), 4.45–4.50 (2H, m, triazole-CH_2–), 3.72 (1H, d, $J = 15.0$ Hz, triazole-CH_2–), 3.50 (1H, d, $J = 15.0$ Hz, triazole-CH_2–), 3.36 (1H, d, $J = 13.8$ Hz, CH_2), 2.90 (1H, d, $J = 14.4$ Hz, CH_2), 2.00–2.16 (1H, m, NCH), 0.15–0.43 (4H, m, $2 \times CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 164.06, 161.50, 158.63, 157.45, 150.43, 143.45, 140.31, 126.14, 122.67, 114.54, 111.87, 109.15, 103.08, 72.66, 60.25, 59.57, 58.52, 55.68, 52.37, 49.17, 48.04, 37.66, 21.77, 21.34. MS (ESI) m/z calcd. for $C_{24}H_{24}ClF_2N_7O$ 499.2, found $[M - H]^+$ 498.6.

*6.4.27. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N- [(1-(3-chlorobe-nzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2e**)*

Mp: 104.4–106.7 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.22 (1H, s, triazole-H), 7.79 (1H, s, triazole-H), 7.22–7.66 (6H, m, Ar-H, triazole-H), 6.67–6.71 (2H, m, Ar-H), 5.62–5.68 (2H, dd, $J = 15.6$ Hz, Ar-CH_2–), 4.42–4.47 (2H, m, triazole-CH_2–), 3.48–3.69 (2H, dd, $J = 14.4$ Hz, triazole-CH_2–), 2.85–3.35 (2H, dd, $J = 13.8$ Hz, CH_2), 2.15–2.16 (1H, m, NCH), 0.12–0.31 (4H, m, $2 \times CH_2$); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 162.46, 160.18, 157.68, 156.53, 150.87, 145.19, 141.48, 124.29, 122.26, 113.11, 112.30, 109.68, 103.57, 72.61, 60.68, 59.35, 58.64, 55.30, 52.54, 50.24, 47.62, 36.16, 20.27, 20.41. MS (ESI) m/z calcd. for $C_{24}H_{24}ClF_2N_7O$ 499.2, found $[M - H]^+$ 498.6.

*6.4.28. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(4-chlorobe-nzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2f**)*

Mp: 105.2–107.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.13 (1H, s, triazole-H), 7.78 (1H, s, triazole-H), 7.44–7.53 (1H, m, Ar-H), 7.13–7.30 (4H, m, Ar-H), 7.06 (1H, s, triazole-H), 6.62–6.74 (2H, m, Ar-H), 5.43 (2H, s, Ar-CH_2–), 4.38–4.49 (2H, m, triazole-CH_2–), 3.70 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.50 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.33 (1H, d, $J = 14.4$ Hz, CH_2), 2.90 (1H, d, $J = 14.4$ Hz, CH_2), 1.93–2.00 (1H, m, NCH), 0.13–0.34 (4H, m, $2 \times CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.04, 162.50, 158.65, 157.35, 150.23, 143.75, 140.21, 126.13, 122.57, 114.53, 111.83, 109.13, 103.68, 72.56, 60.23, 59.52, 58.54, 55.28, 52.34, 49.15, 48.03, 37.64, 20.77, 20.32. MS (ESI) m/z calcd. for $C_{24}H_{24}ClF_2N_7O$ 499.2, found $[M - H]^+$ 498.6.

*6.4.29. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(2-bromobe-nzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2g**)*

Mp: 117.2–119.5 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.25 (1H, s, triazole-H), 7.85 (1H, s, triazole-H), 7.62–7.64 (1H, m, Ar-H), 7.22–7.45 (5H, m, Ar-H, triazole-H), 6.81–6.88 (2H, m, Ar-H), 5.56–5.63 (2H, m, Ar-CH_2–), 4.56–4.62 (2H, m, triazole-CH_2–), 3.88 (1H, d, $J = 15.0$ Hz, triazole-CH_2–), 3.69 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 3.50 (1H, d, $J = 13.8$ Hz, CH2), 3.06 (1H, d, $J = 13.8$ Hz, CH_2), 2.13–2.15 (1H, m, NCH), 0.29–0.48 (4H, m, $2 \times CH_2$); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 163.26, 161.53, 158.65, 157.15, 150.45, 143.45, 140.41, 126.12, 122.67, 114.64, 111.27, 109.16, 103.28, 72.61, 60.27, 59.51, 58.55, 55.68, 52.36, 49.11, 48.03, 37.61, 20.57, 20.31. MS (ESI) m/z calcd. for $C_{24}H_{24}BrF_2N_7O$ 543.1, found $[M - H]^+$ 542.6.

*6.4.30. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(3-bromobe-nzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2h**)*

Mp: 92.8–94.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.12 (1H, s, triazole-H), 7.75 (1H, s, triazole-H), 7.19–7.53 (5H, m, Ar-H), 7.11 (1H, s, triazole-H), 6.69–6.81 (2H, m, Ar-H), 5.48 (2H, dd, $J = 18.6$ Hz, 15.0 Hz, Ar-CH_2–), 5.16 (1H, s, OH), 4.52 (1H, d, $J = 14.1$ Hz, triazole-CH_2–), 4.45 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 3.76 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.56 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.39 (1H, d, $J = 14.1$ Hz, CH_2), 2.95 (1H, d, $J = 14.1$ Hz, CH_2), 2.01–2.06 (1H, m, NCH), 0.19–0.39 (4H, m, $2 \times CH_2$); ^{13}C NMR(75 MHz, $CDCl_3$) δ: 162.03, 161.10, 153.65, 157.35, 150.45, 143.41, 140.37, 126.12, 122.47, 114.74, 111.84, 109.17, 103.05, 72.62, 60.25, 59.37, 58.42, 55.68, 52.14, 49.15, 48.54, 37.56, 20.78, 20.31. MS (ESI) m/z calcd. for $C_{24}H_{24}BrF_2N_7O$ 543.1, found $[M - H]^+$ 542.6.

*6.4.31. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(4-bromobe-nzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2i**)*

Mp: 121.3–122.5 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.09 (1H, s, triazole-H), 7.72 (1H, s, triazole-H), 7.47–7.53 (3H, m, Ar-H), 7.09–7.10 (23H, m, Ar-H), 7.05 (1H, s, triazole-H), 6.66–6.76 (2H, m, Ar-H), 5.40–5.47 (2H, m, Ar-CH_2–), 5.16 (1H, s, OH), 4.42–4.51 (2H, m, triazole-CH_2–), 3.72 (1H, d, $J = 15.0$ Hz, triazole-CH_2–), 3.53 (1H, d, $J = 15.0$ Hz, triazole-CH_2–), 3.35 (1H, d, $J = 13.8$ Hz, CH_2), 2.90 (1H, d, $J = 13.8$ Hz, CH_2), 2.01–2.06 (1H, m, NCH), 0.19–0.39 (4H, m, $2 \times CH_2$); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 164.46, 161.52, 158.13, 157.75, 150.44, 143.65, 140.21, 126.54, 122.77, 114.84, 111.78, 109.95,

103.09, 72.46, 50.22, 59.57, 58.55, 55.63, 52.34, 49.87, 49.03, 37.26, 21.57, 21.25. MS (ESI) *m/z* calcd. for $C_{24}H_{24}BrF_2N_7O$ 543.1, found $[M-H]^+$ 542.8.

*6.4.32. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(2-methylbe-nzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2j**)*

Mp: 112.5–114.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.12 (1H, s, triazole-H), 7.74 (1H, s, triazole-H), 7.14–7.57 (5H, m, Ar-H), 6.86 (1H, s, triazole-H), 6.56–6.79 (2H, m, Ar-H), 5.55 (1H, d, $J = 14.7$ Hz, Ar-CH_2–), 5.46 (1H, d, $J = 15.0$ Hz, Ar-CH_2–), 5.20 (1H, s, OH), 4.46–4.47 (2H, m, triazole-CH_2–), 3.73 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.48 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.35 (1H, d, $J = 13.8$ Hz, CH_2), 2.91 (1H, d, $J = 13.8$ Hz, CH_2), 2.25 (1H, s, CH_3), 2.07–2.10 (1H, m, NCH), 0.18–0.39 (4H, m, $2 \times CH_2$); ^{13}C NMR(75 MHz, $CDCl_3$) δ: 163.07, 160.54, 157.21, 156.34, 151.31, 145.68, 141.50, 124.54, 121.98, 113.44, 112.54, 109.57, 103.35, 73.18, 60.29, 59.67, 57.93, 55.41, 52.18, 50.45, 47.28, 36.16, 20.77, 20.59, 20.21. MS (ESI) *m/z* calcd. for $C_{25}H_{27}F_2N_7O$ 479.2, found $[M-H]^+$ 478.6.

*6.4.33. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(3-methylbe-nzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2k**)*

Mp: 97.5–98.7 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.07 (1H, s, triazole-H), 7.68 (1H, s, triazole-H), 7.44–7.48 (1H, m, Ar-H), 7.08–7.25 (5H, m, Ar-H), 6.54–6.68 (2H, m, Ar-H), 5.40–5.50 (2H, m, Ar-CH_2–), 4.41–4.42 (2H, m, triazole-CH_2–), 3.68 (1H, d, $J = 15.0$ Hz, triazole-CH_2–), 3.45 (1H, d, $J = 15.0$ Hz, triazole-CH_2–), 3.29 (1H, d, $J = 13.8$ Hz, CH_2), 2.87 (1H, d, $J = 13.8$ Hz, CH_2), 2.20 (1H, s, CH_3), 2.00–2.03 (1H, m, NCH), 0.12–0.32 (4H, m, $2 \times CH_2$); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 163.14, 160.45, 157.65, 156.73, 151.57, 145.82, 141.50, 124.37, 121.98, 113.41, 112.54, 109.46, 103.77, 73.45, 60.23, 59.45, 57.86, 55.54, 52.24, 50.19, 47.33, 36.52, 20.82, 20.76, 20.25. MS (ESI) *m/z* calcd. for $C_{25}H_{27}F_2N_7O$ 479.2, found $[M-H]^+$ 478.8.

*6.4.34. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(4-methylbe-nzyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2l**)*

Mp: 93.6–95.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.13 (1H, s, triazole-H), 7.74 (1H, s, triazole-H), 7.48–7.57 (1H, m, Ar-H), 7.03–7.22 (3H, m, Ar-H), 7.01 (1H, s, triazole-H), 6.63–6.79 (2H, m, Ar-H), 5.40–5.52 (2H, m, Ar-CH_2–), 5.26 (1H, s, OH), 4.47–4.54 (2H, m, triazole-CH_2–), 3.74 (1H, d, $J = 15.0$ Hz, triazole-CH_2–), 3.52 (1H, d, $J = 14.70$ Hz, triazole-CH_2–), 3.38 (1H, d, $J = 15.0$ Hz, CH_2), 2.92 (1H, d, $J = 13.8$ Hz, CH_2), 2.36 (1H, s, CH3), 2.02–2.07 (1H, m, NCH), 0.18–0.39 (4H, m, $2 \times CH_2$); ^{13}C NMR(75 MHz, $CDCl_3$) δ: 163.44, 160.71, 157.23, 156.54, 151.57, 145.69, 141.38, 124.52, 121.14, 113.55, 112.62, 109.59, 103.73, 73.25, 60.28, 59.42, 57.86, 55.04, 52.27, 50.12, 47.43, 36.45, 20.87, 20.70, 20.21. MS (ESI) *m/z* calcd. for $C_{25}H_{27}F_2N_7O$ 479.2, found $[M-H]^+$ 478.7.

*6.4.35. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(2-nitrobenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2m**)*

Mp: 105.3–107.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.05–8.10 (2H, m, Ar-H, triazole-H), 7.67 (1H, s, triazole-H), 7.43–7.61 (4H, m, Ar-H), 7.36 (1H, s, triazole-H), 7.03–7.08 (1H, m, Ar-H), 6.66–6.73 (2H, m, Ar-H), 5.84 (2H, s, Ar-CH_2–), 5.14 (1H, s, OH), 4.39–4.49 (2H, m, triazole-CH_2–), 3.51–3.75 (2H, m, triazole-CH_2–), 2.87–3.43 (2H, m, CH_2), 1.96–1.98 (1H, m, NCH), 0.27–0.32 (4H, m, $2 \times CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.64, 161.30, 158.53, 157.44, 150.43, 143.35, 140.33, 126.12, 122.65, 114.56, 111.86, 109.25, 103.28, 72.76, 60.35, 59.58, 58.32, 55.67, 52.39, 49.37, 48.05, 37.46, 21.30, 20.98. MS (ESI) *m/z* calcd. for $C_{24}H_{24}F_2N_8O_3$ 510.2, found $[M-H]^+$ 509.8.

*6.4.36. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(3-nitrobenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2n**)*

Mp: 102.6–104.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.12–8.15 (2H, m, Ar-H), 8.11 (1H, s, triazole-H), 7.66 (1H, s, triazole-H), 7.21–7.52 (4H, m, Ar-H, triazole-H), 6.63–6.72 (2H, m, Ar-H), 5.58 (2H, s, Ar-CH_2–), 5.07 (1H, s, OH), 4.45 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 4.38 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 3.70 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.52 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.37 (1H, d, $J = 14.7$ Hz, CH_2), 2.86 (1H, d, $J = 14.1$ Hz, CH_2), 1.93–1.96 (1H, m, NCH), 0.06–0.29 (4H, m, $2 \times CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.16, 161.57, 158.53, 157.05, 150.83, 144.05, 140.11, 126.14, 121.67, 114.34, 111.73, 109.13, 103.68, 72.16, 60.35, 59.52, 54.12, 55.28, 52.57, 49.11, 47.07, 37.16, 21.37, 20.64. MS (ESI) *m/z* calcd. for $C_{24}H_{24}F_2N_8O_3$ 510.2, found $[M-H]^+$ 509.8.

*6.4.37. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(4-nitrobenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2o**)*

Mp: 114.3–116.1 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.22 (2H, d, $J = 8.4$ Hz, Ar-H), 8.10 (1H, s, triazole-H), 7.77 (1H, s, triazole-H), 7.53–7.55 (1H, m, Ar-H), 7.38 (2H, d, $J = 8.4$ Hz, Ar-H), 7.17 (1H, s, triazole-H), 6.72–6.80 (2H, m, Ar-H), 5.63 (2H, s, Ar-CH_2–), 4.44–4.53 (2H, m, triazole-CH_2–), 3.77 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 3.59 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 3.40 (1H, d, $J = 13.8$ Hz, CH_2), 2.93 (1H, d, $J = 13.8$ Hz, CH_2), 2.00–2.01 (1H, m, NCH), 0.15–0.38 (4H, m, $2 \times CH_2$); ^{13}C NMR(150 MHz, $CDCl_3$) δ: 163.04, 161.30, 158.63, 157.75, 150.33, 143.25, 140.32, 126.24, 122.57, 114.14, 111.83, 108.17, 103.28, 72.37, 60.21, 59.55, 58.42, 55.38, 52.31, 49.27, 48.05, 37.66, 20.76, 20.33. MS (ESI) *m/z* calcd. for $C_{24}H_{24}F_2N_8O_3$ 510.2, found $[M-H]^+$ 509.8.

*6.4.38. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(2-cyanoben-zyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2p**)*

Mp: 89.5.3–91.7 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.12 (1H, s, triazole-H), 7.71 (1H, s, triazole-H), 7.46–7.50 (1H, m, Ar-H), 7.39 (1H, s, triazole-H), 7.06–7.21 (4H, m, Ar-H), 6.66–6.73 (2H, m, Ar-H), 5.51–5.57 (2H, m, Ar-CH_2–), 5.14 (1H, s, OH), 4.41–4.47 (2H, m, triazole-CH_2–), 3.70 (1H, d, $J = 15.0$ Hz, triazole-CH_2–), 3.52 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 3.33 (1H, d, $J = 13.8$ Hz, CH_2), 2.89 (1H, d, $J = 13.8$ Hz, CH_2), 1.96–1.98 (1H, m, NCH), 0.14–0.33 (4H, m, $2 \times CH_2$); ^{13}C NMR (150 MHz, CDCl3) δ: 164.04, 162.50, 158.65, 157.35, 150.23, 143.75, 140.21, 126.13, 122.58, 114.53, 111.83, 109.33, 103.68, 72.56, 60.23, 59.52, 58.54, 55.28, 52.34, 49.15, 48.03, 37.64, 20.95, 20.12. MS (ESI) *m/z* calcd. for $C_{25}H_{24}F_2N_8O$ 490.2, found $[M-H]^+$ 489.7.

*6.4.39. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(3-cyanoben-zyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2q**)*

Mp: 97.5–98.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.05 (1H, s, triazole-H), 7.67 (1H, s, triazole-H), 7.40–7.59 (5H, m, Ar-H), 7.15 (1H, s, triazole-H), 6.6–6.73 (2H, m, Ar-H), 5.50 (2H, s, Ar-CH_2–), 5.06 (1H, s, OH), 4.36–4.47 (2H, m, triazole-CH_2–), 3.70 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.50 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.33 (1H, d, $J = 14.4$ Hz, CH_2), 2.87 (1H, d, $J = 14.1$ Hz, CH_2), 1.98–2.00 (1H, m, NCH), 0.15–0.36 (4H, m, $2 \times CH_2$); ^{13}C NMR (75 MHz, CDCl3) δ: 163.56, 161.52, 157.13, 157.75, 150.44, 143.65, 140.21, 126.54, 122.77, 114.84, 112.88, 109.95, 103.09, 72.46, 60.22, 59.67, 58.55, 55.63, 52.34, 49.87, 48.45, 37.26, 20.57, 20.37. MS (ESI) *m/z* calcd. for $C_{25}H_{24}F_2N_8O$ 490.2, found $[M-H]^+$ 489.6.

*6.4.40. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(4-cyanoben-zyl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2r**)*

Mp: 109.5–111.2 °C; ^{1}H NMR(600 MHz, $CDCl_3$) δ: 8.15 (1H, s, triazole-H), 7.81 (1H, s, triazole-H), 7.73 (2H, d, $J = 8.4$ Hz, Ar-H), 7.60–7.62 (1H, m, Ar-H), 7.40 (2H, d, $J = 8.4$ Hz, Ar-H), 7.27 (1H, s, triazole-H), 6.78–6.86 (2H, m, Ar-H), 5.66 (2H, m, Ar-CH_2–), 5.18 (1H, s, OH), 4.58 (1H, d, $J = 13.8$ Hz, triazole-CH_2–), 4.53 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 3.83 (1H, d, $J = 15.0$ Hz, triazole-CH_2–), 3.66 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 3.46 (1H, d, $J = 14.4$ Hz, CH_2), 3.01 (1H, d, $J = 14.4$ Hz, CH_2), 2.06–2.09 (1H, m, NCH), 0.23–0.44 (4H, m, $2 \times CH_2$); ^{13}C NMR(150 MHz, CDCl3) δ: 163.17, 161.30, 157.63, 157.45, 150.63, 143.56, 140.31, 126.34, 122.79, 114.94, 111.37, 109.95, 103.06, 72.64, 60.25, 59.54, 58.55, 55.67, 52.47, 49.12, 48.54, 37.67, 20.72, 20.67. MS (ESI) m/z calcd. for $C_{25}H_{24}F_2N_8O$ 490.2, found $[M - H]^+$ 489.7.

*6.4.41. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(2,6-dichlorobenzyl)-1H-1,2,3-triazol-4-yl) methyl]amino}-2-propanol (**2s**)*

Mp: 103.5–105.4 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.12 (1H, s, triazole-H), 7.80 (1H, s, triazole-H), 7.16–7.50 (4H, m, Ar-H), 7.08 (1H, s, triazole-H), 6.62–6.74 (2H, m, Ar-H), 5.78 (2H, s, Ar-CH_2–), 4.60 (2H, s, triazole-CH_2–), 3.68 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.44 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.33 (1H, d, $J = 13.8$ Hz, CH_2), 2.92 (1H, d, $J = 13.8$ Hz, CH_2), 1.93–2.02 (1H, m, NCH), 0.14–0.34 (4H, m, $2 \times CH_2$); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 164.37, 161.52, 158.64, 157.44, 150.23, 143.65, 140.71, 126.15, 122.63, 114.54, 111.86, 109.13, 103.48, 72.26, 60.25, 59.67, 58.32, 55.68, 52.47, 49.67, 48.05, 37.66, 21.65, 21.36. MS (ESI) m/z calcd. for $C_{24}H_{23}Cl_2F_2N_7O$ 533.1, found $[M - H]^+$ 532.8.

*6.4.42. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(4-ethylbenz-yl)-1H-1,2,3-triazol-4-yl)methyl] amino}-2-propanol (**2t**)*

Mp: 121.5–123.4 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.12 (1H, s, triazole-H), 7.71 (1H, s, triazole-H), 7.47–7.51 (1H, m, Ar-H), 7.12–7.28 (4H, m, Ar-H), 7.02 (1H, s, triazole-H), 6.60–6.75 (2H, m, Ar-H), 5.48 (2H, s, Ar-CH_2–), 4.44 (2H, s, triazole-CH_2–), 3.72 (1H, d, $J = 15.0$ Hz, triazole-CH_2–), 3.50 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.35 (1H, d, $J = 13.5$ Hz, CH2), 2.90 (1H, d, $J = 13.8$ Hz, CH2), 2.58–2.66 (2H, m, ph$CH^*_2CH_3$), 1.99–2.04 (1H, m, NCH), 1.19–1.24 (3H, m, ph$CH_2CH^*_3$), 0.17–0.35 (4H, m, $2 \times CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 164.35, 161.28, 157.41, 156.67, 151.32, 145.60, 141.45, 124.22, 121.05, 113.48, 112.83, 108.97, 103.55, 73.78, 61.39, 59.32, 57.55, 55.13, 52.14, 50.26, 47.25, 36.38, 34.50, 22.35, 20.97, 20.65. MS (ESI) m/z calcd. for $C_{26}H_{29}F_2N_7O$ 493.2, found $[M - H]^+$ 492.7.

*6.4.43. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-(4-tert-butyl-benzyl)-1H-1,2,3-triazol-4-yl) methyl]amino}-2-propanol (**2u**)*

Mp: 104.3–106.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.15 (1H, s, triazole-H), 7.76 (1H, s, triazole-H), 7.52–7.58 (1H, m, Ar-H), 7.42 (2H, d, $J = 1.8$ Hz, Ar-H), 7.20 (2H, d, $J = 1.8$ Hz, Ar-H), 7.03 (1H, s, triazole-H), 6.62–6.79 (2H, m, Ar-H), 5.51 (1H, d, $J = 14.7$ Hz, Ar-CH_2–), 5.43 (1H, d, $J = 14.7$ Hz, Ar-CH_2–), 5.24 (1H, s, OH), 4.51 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 4.45 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 3.74 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.53 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.38 (1H, d, $J = 14.1$ Hz, CH_2), 2.93 (1H, d, $J = 13.8$ Hz, CH_2), 2.03–2.10 (1H, m, NCH), 1.26–1.38 (9H, m, $3 \times CH_3$), 0.19–0.39 (4H, m, $2 \times CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.14, 160.25, 157.30, 156.29, 151.37, 145.64, 141.28, 124.37, 121.10, 113.44, 112.53, 109.55, 103.75, 73.20, 61.17, 59.28, 57.70, 55.06, 52.18, 50.26, 47.44, 36.95, 34.39, 22.94, 22.77, 20.65, 20.43. MS (ESI) m/z calcd. for $C_{28}H_{33}F_2N_7O$ 521.3, found $[M - H]^+$ 520.8.

*6.4.44. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-pentyl-1H-1,2,3-triazol-4-yl)methyl]amino}-2-propanol (**2v**)*

Mp: 71.2–73.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.17 (1H, s, triazole-H), 7.75 (1H, s, triazole-H), 7.55–7.61 (1H, m, Ar-H), 7.26 (1H, s, triazole-H), 6.76–6.85 (2H, m, Ar-H), 5.41 (1H, s, OH), 4.53–4.56 (2H, m, triazole-CH_2–), 4.31–4.36 (2H, t, trazole-$CH^*_2CH_2CH_2CH_2CH_3$), 3.79 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.62 (1H, d, $J = 14.7$ Hz, triazole-CH_2–), 3.43 (1H, d, $J = 13.8$ Hz, CH_2), 3.00 (1H, d, $J = 14.1$ Hz, CH_2), 1.94–2.04 (1H, m, NCH), 1.87–1.92 (2H, m, trazole-$CH_2CH^*_2CH_2CH_2CH_3$), 1.23–1.38 (4H, m, trazole-$CH_2CH_2CH^*_2CH^*_2CH_3$), 0.88–0.92 (3H, t, trazole-$CH_2CH_2CH_2CH_2CH^*_3$), 0.23–0.41 (4H, m, $2 \times CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 163.67, 161.09, 155.56, 141.24, 128.32, 121.57, 117.34, 115.20, 110.51, 74.21, 61.17, 59.37, 57.65, 55.29, 50.14, 47.44, 28.35, 24.80, 23.34, 20.39, 20.05, 14.68. MS (ESI) m/z calcd. for $C_{22}H_{29}F_2N_7O$ 445.2, found $[M - H]^+$ 444.7.

*6.4.45. 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-difluorophenyl)-3-{N-cyclopropyl-N-[(1-cyclohexyl-1H-1,2,3-triazol-4-yl)methyl]amino}-2-propanol (**2w**)*

Mp: 83.4–85.5 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.07 (1H, s, triazole-H), 7.65 (1H, s, triazole-H), 7.45–7.49 (1H, m, Ar-H), 7.16 (1H, s, triazole-H), 6.68–6.73 (2H, m, Ar-H), 5.34 (1H, s, OH), 4.43 (2H, s, triazole-CH_2–), 4.31–4.32 (1H, m, trazole-CH-), 3.68 (1H, d, $J = 14.4$ Hz, triazole-CH_2–), 3.51 (1H, d, $J = 15.0$, Hz, triazole-CH_2–), 3.33 (1H, d, $J = 14.4$ Hz, CH_2), 2.90 (1H, d, $J = 13.8$ Hz, CH_2), 1.93–1.94 (1H, m, NCH), 1.15–2.11 (10H, m, $5 \times CH_2$), 0.13–0.30 (4H, m, $2 \times CH_2$); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 165.13, 161.25, 155.20, 143.25, 124.17, 121.57, 113.34, 110.51, 74.21, 61.17, 59.37, 57.65, 55.29, 52.18, 50.14, 47.44, 36.82, 35.35, 34.28, 24.80, 23.34, 20.39, 20.05. MS (ESI) m/z calcd. for $C_{23}H_{29}F_2N_7O$ 457.2, found $[M - H]^+$ 456.8.

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