The Synthesis of Some New (*S*)-1-Aryl-*N*-(1-hydroxy-3-phenylpropan-2-yl)-5-methyl-1*H*-1,2,3-triazole-4-carboxamide

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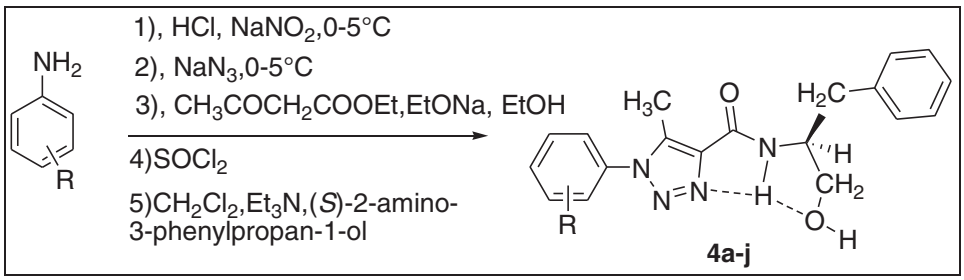

Some new (*S*)-1-aryl-*N*-(1-hydroxy-3-phenylpropan-2-yl)-5-methyl-1*H*-1,2,3-triazole-4-carboxamides **4a–j** have been synthesized and established by ^{1}H and ^{13}C NMR, IR, MS spectra, CHN analyses, and x-ray diffraction crystallography. The molecular conformation and packing is stabilized by interactions of intermolecular H-bond O2'-H2'···O1, O2-H2···O1' and intramolecular H-bond N4'-H4'N···N3', N4'-H4'N···O2', N4-H4N···N3, N4-H4N···O2. The two rings of five numbers were formed by H-bond in a molecular.

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INTRODUCTION

The (*S*)-2-amino-3-phenylpropan-1-ol, a surprising constituent was the peptide derivative, acid amide previously found in many natural products [1–3]. In recent years in various publications, certain compounds that 1-aryl-5-methyl-4-substituted-1,2,3-triazoles often exhibit broad spectrum biological actions [4,5], antibacterial [6], antifungal [7], antiviral [8], anti-inflammatory, and analgetic properties [9]. Some of 1,2,3-triazole derivatives had been reported to inhibit tumor proliferation, invasion, and metastasis [10]. Therefore, it is worthwhile to investigate these properties of 1,2,3-triazole. As a great deal of interest has been focused on it, we synthesized some new title compound.

The route of syntheses of the title compound is in Scheme 1.

RESULTS AND DISCUSSION

Title compound was obtained by the reaction of a chiral (*S*)-2-amino-3-phenylpropan-1-ol, triethylamine and 1-aryl-5-methyl-1,2,3-triazol-4-carboxylic acid acyl chloride in dichloromethane, which was from reaction of triazole carboxylic acid was treated with thionyl chloride in dichloromethane.

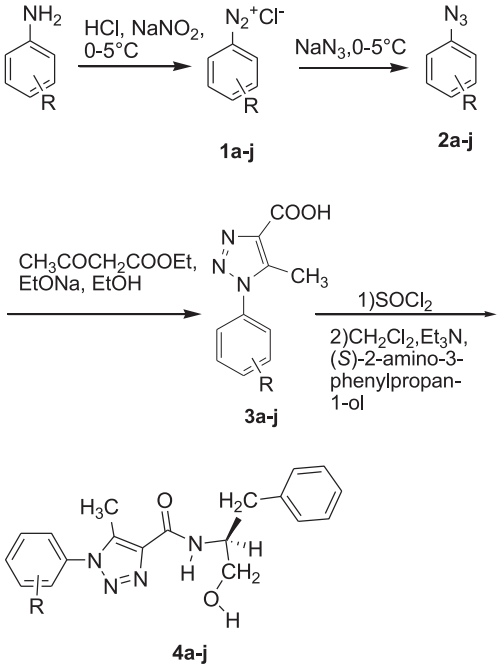
Our own interest in the development of some new (*S*)-1-aryl-*N*-(-1-hydroxy-3-phenylpropan-2-yl)-5-methyl-1*H*-1,2,3-triazole-4-carboxamides and in extending this type of one-pot reaction prompted us to examine potential applications and generalizations to the synthesis of substituted derivatives.

Identified as a compound, IR absorption of hydroxyl is showing at 3359 ~ 3478 cm^{-1} and amino at 3201 ~ 3416 cm^{-1} of **4a–j**, as a carbonyl compound showing strong IR absorption at 1642 ~ 1661 cm^{-1}. ^{1}HNMR, chemical shift range of triazole-5-CH_3 peak is at 2.464 ~ 2.647 ppm of **4a–i** and chemical shift range of -CO-NH- doublet peaks is show at 7.507 ~ 8.594 ppm, J = 8.0 ~ 8.8 Hz of **4a ~ j**, which are shifted to lower fields than the corresponding protons at 6.29 ppm [11] because of the hydrogen-bond and triazole ring induced. The chemical shift range of CH_2Ph peak is at 2.854 ~ 3.067 ppm, chemical shift range of CH_2O doublet peaks is show at 2.854 ~ 3.747 ppm, 2.958 ~ 3.849 ppm, chemical shift range of C*H*N peak is at 4.199 ~ 4.463ppm of **4a ~ i**. ^{13}CNMR, chemical shift range of triazole-5-CH_3 peak is at 9.29–10.34 ppm and chemical shift range of –CO- peaks is show at 161.02 ~ 162.08 ppm of **4a ~ i**.

An ORTEP diagram of the compound **4e** showing 50% thermal ellipsoids is shown in Figure 1. The X-ray structure analysis indicated that the compound **4e** consisted of two phenyl rings and one triazole ring. The *p*-chlorophenyl ring and a triazole ring do not share a common plane. The dihedral angles between the phenyl rings and triazole rings are 39.9–45.2° [C5-C6-N1-N2 -45.2(6)°, C1'-C6'-N1'-N2' 39.9(6)°].

In the crystal structure, there are two intermolecular O2'-H2'···O1, O2-H2···O1' hydrogen bond involving the hydroxyl group O-H bond and other molecular carbonyl group O. The bond length of Donor-H···Acceptor is 2.76 Å (O2'-H2' 0.82; H2'···O1 1.97 Å) and 2.71 Å (O2-H2 0.82; H2···O1' 2.00 Å), the bond angle is 162 and 143°. There are

Scheme 1. The synthesis route of compounds **4a–j**.



four intramolecular N4'-H4'N···N3', N4'-H4'N···O2', N4-H4N···N3, and N4-H4N···O2. Hydrogen bond involving the N-H bond and triazole ring 3 positions *N* or hydroxyl group O. The bond length of Donor-H···Acceptor is 2.75 Å (N4'-H 0.93; H···N3' 2.36Å), 2.67 Å (N4'-H 0.93; H···O2' 2.26Å), 2.79Å (N4-H 0.89; H···N3 2.46Å), and 2.61Å (N4-H 0.89; H···O2 2.16Å); the bond angle is 105, 106, 103 and 111°. The molecular conformation and packing is stabilized by interactions of two intermolecular and four intramolecular. The two rings of five numbers were formed by H-bond in a molecular. The H-bond structure of the compound **4e** is shown in Figure 2.

EXPERIMENTAL

The melting point was uncorrected and determined on an XT_4-100x microscopic melting point apparatus. IR spectra were obtained in KBr discs on a Shimadzu (American Pyroelectricity Corporation, USA) IR-435 spectrometer. MS was performed on a TRACED SQ instrument (EI at 70eV). ^{1}H NMR and ^{13}C NMR spectroscopy ($CDCl_3$) was recorded on Varian Mercury-400BB instrument H1 in 400.1370316 and C13 in 100.6127476 MHz with TMS as an internal standard. Elemental analyses were carried out on a Yanaco CHN Corder MT-3 analyzer. Optical rotatory power values were measured with an A21202-Tapiv automatic polarimeter at sodium D line 589 nm.

Preparation of the title compound. General procedure for the preparation of 1-aryl-5-methyl-1,2,3-triazol-4-carboxylic acid (3a–j). 1-Aryl-5-methyl-1,2,3-triazol-4-carboxylic acid **3a–j** was prepared following methods in the literature [12].

General procedure for the preparation of (*S*)-1-aryl-*N*-(1-hydroxy-3-phenylpropan-2-yl)-5-methyl-1 *H*-1,2,3-triazole-4-carboxamide (4a–j). (*S*)-1-Aryl-*N*-(1-hydroxy-3-phenylpropan-2-yl)-5-methyl-1 *H*-1,2,3-triazole-4-carboxamide **4a–j** was prepared following methods in the literature [13].

The 1-aryl-5-methyl-1,2,3-triazol-4-carboxylic acid **3a–j** (10.0 mmol) was treated with thionyl chloride (5 mL), then heated at 70°C for 8 h. The excess thionyl chloride was removed by evaporation under reduced pressure. Residual thionyl chloride was removed by co-evaporation with 30 mL of anhydrous benzene to afford the corresponding acid chloride.

To a cold (−5–0°C) solution of a chiral (*S*)-2-amino-3-phenylpropan-1-ol (1.51 mg, 10.0 mmol) and a solution of triethylamine (2.52 g, 25.0 mmol) in 20 mL of dichloromethane, a solution of 1-aryl-5-methyl-1,2,3-triazol-4-carboxylic acid acyl chloride (2.50 g, 9.8 mmol) in 30 mL dry dichloromethane over a period of 40 min was added. The reaction mixture was stirred at 0°C for 5 h and then at 25°C for 4 h. The product precipitated from the solution was collected by filtration, then washed with 1 M HCl (30 mL), saturated aqueous $NaHCO_3$ (30 mL), and distilled water. The crude product was either purified by recrystallization from EtOH or by column chromatography with silica gel as adsorbent and ethyl acetate/petroleum ether (1:2 volume ratios) as the eluent. The title compound **4a–j** was obtained.

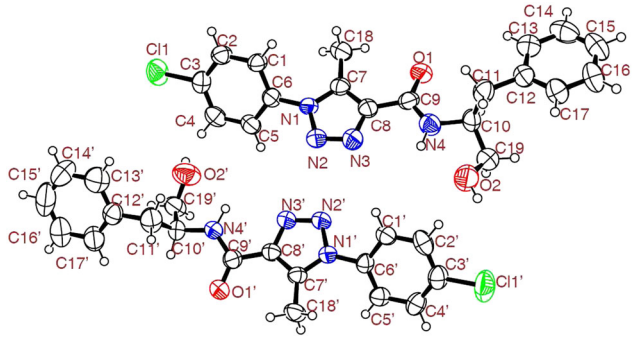


Figure 1. ORTEP diagram of the compound **4e** showing 50% thermal ellipsoids. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

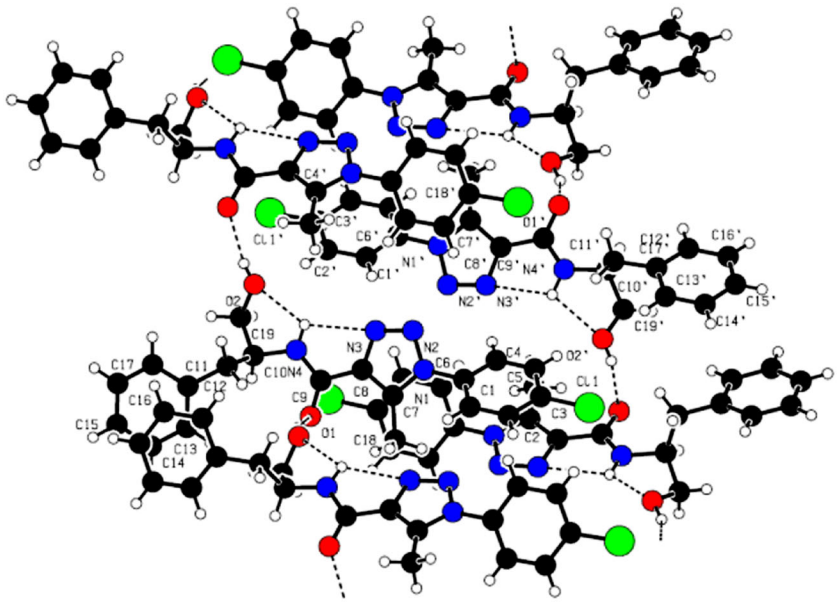


Figure 2. The H-bond structure of the compound **4e** (PWT drawing for the Platon). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

The purified product was dissolved in ethyl acetate and petroleum ether solvent. The crystal was obtained after 20d by evaporation of the solvent.

Single crystals were selected and mounted on the tip of a glass fiber. Data were collected on a SMART APEX II CCD using graphite monochromatized Mo*K*α radiation (λ = 0.71073 Å). The structure was determined by direct methods (SHELXS-97) and refined by full covariance matrix methods (SHELXL-97). The structure of the title compound is shown in Figure 1. The selected bond lengths are given in Table 1. The selected bond angles are given in Table 2. Hydrogen bonds (Angstrom, Deg) are given in Table 3. The geometric calculations were performed using the program SHELX-97.

(S)-1-(3-Bromophenyl)-N-(1-hydroxy-3-phenylpropan-2-yl)-5-methyl-1H-1,2,3-triazole-4-carboxamide (4a). Yield: 65%; white needle crystals; mp 115–117°C; $[\alpha]_D^{17.7} = -42.453$

Table 1

Selected bond lengths (Å).

Atoms length	Atoms length
C3 Cl-1 1.737(4)	C3’ Cl1’ 1.720(5)
C6 N1 1.427(5)	C6’ N1’ 1.440(5)
C7 N1 1.363(5)	C7’ N1’ 1.352(5)
C7 C8 1.368(6)	C7’ C8’ 1.377(6)
C7 C18 1.481(6)	C7’ C18’ 1.466(6)
C8 N3 1.364(6)	C8’ N3’ 1.352(5)
C8 C9 1.487(6)	C8’ C9’ 1.484(6)
C9 O1 1.241(5)	C9’ O1’ 1.224(5)
C9 N4 1.304(6)	C9’ N4’ 1.327(6)
C10 N4 1.478(5)	C10’ N4’ 1.448(5)
C10 C19 1.516(6)	C10’ C19’ 1.499(7)
C10 C11 1.535(7)	C10’ C11’ 1.529(8)
C11 C12 1.516(6)	C11’ C12’ 1.506(7)
C19 O2 1.410(7)	C19’ O2’ 1.348(5)

Table 2

Selected bond angles (°) and dihedral angle (°).

Atoms Angle	Atoms Angle
C2 C3 Cl1 119.4(4)	C1 C2 C3 Cl1 179.9(4)
C4 C3 Cl1 119.5(4)	C18 C7 C8 N3 -178.5(5)
C1 C6 N1 120.2(4)	N3 C8 C9 O1 174.1(5)
C5 C6 N1 118.7(4)	N3 C8 C9 N4 -4.6(7)
N1 C7 C8 103.4(4)	N4 C10 C11 C12 -159.7(4)
N1 C7 C18 124.5(4)	C19 C10 C11 C12 79.8(6)
C8 C7 C18 132.2(4)	N4 C10 C19 O2 -46.3(6)
N3 C8 C7 109.7(4)	C5 C6 N1 N2 -45.2(6)
N3 C8 C9 122.6(4)	C1’ C2’ C3’ Cl1’ 179.0(4)
C7 C8 C9 127.7(4)	C18’ C7’ C8’ N3’ 174.7(5)
O1 C9 N4 123.0(5)	N3’ C8’ C9’ O1’ 167.8(6)
O1 C9 C8 121.1(4)	N3’ C8’ C9’ N4’ -9.7(7)
N4 C9 C8 115.9(4)	N4’ C10’ C11’ C12’ 170.7(4)
N4 C10 C19 106.6(4)	C19’ C10’ C11’ C12’ 49.3(6)
N4 C10 C11 111.8(4)	N4’ C10’ C19’ O2’ -57.8(6)
C19 C10 C11 113.4(5)	C1’ C6’ N1’ N2’ 39.9(6)
C12 C11 C10 111.7(4)	
O2 C19 C10 107.9(5)	

Table 3

Hydrogen bonds (Å, °).

D	H	A	DH	HA	DA	DHA
O2’	H2’	O1	0.8200	1.9700	2.762(6)	162.00
N4’	H4’N	O2’	0.93(4)	2.26(4)	2.671(6)	106(3)
N4’	H4’N	N3’	0.93(4)	2.36(4)	2.754(5)	105(3)
O2	H2	O1’	0.8200	2.0000	2.706(6)	143.00
N4	H4N	O2	0.89(4)	2.16(4)	2.607(7)	111(3)
N4	H4N	N3	0.89(4)	2.46(4)	2.794(5)	103(3)

2-x,1/2 + y,1-z; 1-x,-1/2 + y,1-z

(c = 10.6 mg/mL, $CHCl_3$); ^{1}HNMR (δ ppm, $CDCl_3$): 2.611(s,3H), 2.997–3.022(dd, 2H, *J* = 2.8, 7.2 Hz; b, 1H, -OH), 3.685–3.726 (dd, 1H, *J* = 5.4, 11.0 Hz), 3.790–3.827(dd, 1H, *J* = 3.6, 11.2 Hz), 4.355–4.394(m, 1H), 7.200–7.257(b, 1H, N-H), 7.280–7.328 (m, 4H, *J* = 2.0, 8.0 Hz), 7.427–7.467(t, 2H, *J* = 8.0 Hz), 7.512–7.532(d, 1H, *J* = 8.0 Hz), 7.625–7.634(t, 1H, *J* = 1.8 Hz), 7.679–7.699(d, 1H, *J* = 8.0 Hz, CO-NH); ^{13}CHNR (δ ppm, $CDCl_3$): 9.95, 37.49, 53.11, 64.41, 123.33, 123.97, 126.84, 128.58, 128.85, 129.49, 131.08, 133.34, 136.75, 137.07, 137.82, 138.65, 161.74; MS M/z (%): 414 (M^+, 0.4) 416 (M + 2, 0.4), 385(2), 383(1), 355(1), 341(1), 325(6), 323(6), 307(2), 305(3), 295(3), 297(3), 281(3), 262(3), 247(4), 238 (5), 236(7), 223(7), 219(6), 210(6), 209(8), 208(7), 207(12), 205 (8), 191(9), 178(12), 165(13), 152(17), 151(17), 149(39), 138 (19), 129(29), 125(20), 124(26), 123(23), 111(34), 110(23), 105 (23), 97(48), 91(41), 84(76), 71(49), 69(59), 64(79), 57(100), 55 (84); IR(KBr, cm^{-1}): 543.0, 572.8, 681.1, 705.1, 754.8, 785.2, 864.9, 1044.3, 1074.7, 1143.8, 1263.0, 1429.4, 1460.3, 1490.0, 1512.5, 1590.2, 1661.5, 2869.8, 2931.6, 3022.6, 3083.6, 3393.5, 3478.2. *Anal*. Calcd. for $C_{19}H_{19}BrN_4O_2$: C, 54.95; H, 4.61; N, 13.49; Found: C, 55.06; H, 4.65; N,13.32.

(S)-1-(4-Bromophenyl)-N-(1-hydroxy-3-phenylpropan-2-yl)-5-methyl-1H-1,2,3-triazole-4-carboxamide (4b). Yield: 85%; white flaky crystals; mp 137–139°C; $[\alpha]_D^{16.8} = -46.535$ (c = 10.1 mg/mL, $CHCl_3$); ^{1}HNMR (δ ppm, $CDCl_3$): 2.611 (s, 3H), 2.956–3.051(dd, 2H, *J* = 3.2, 7.2 Hz; b, 1H, -OH), 3.678–3.720(dd, 1H, *J* = 5.6, 11.0 Hz), 3.785–3.822(dd, 1H, *J* = 3.6, 11.2 Hz), 4.354–4.433(m, 1H), 7.197–7.239(m, 1H, N-H), 7.290–7.333(m, 6H), 7.526–7.546(d, 1H, *J* = 8.0 Hz), 7.691–7.713(d, 2H, *J* = 8.8 Hz); ^{13}CHNR(δ ppm, $CDCl_3$): 9.94; 37.46; 53.07; 64.35; 124.38; 126.82; 126.86; 128.83; 129.48; 133.12; 134.64; 136.99; 137.82; 138.66; 161.74; MS M/z (%): 414 (M^+, 0.36) 416 (M + 2, 0.33), 385 (12), 383(13), 355(1), 325(93), 323(100), 307(5), 305(6), 289(2), 283(6), 281(7), 266(22), 264(25), 245(19), 243(26), 238(20), 236(19), 223(5), 210(17), 208(14), 198(44), 196 (40), 185(6), 157(76), 155(14), 149(31), 139(19), 129(39), 113(25), 111(66), 102(11), 91(36), 83(10), 75(20), 70 (14), 57(17), 55(14), 43(45), 40(54); IR(KBr, cm^{-1}): 597.7, 620.6, 697.1, 744.0, 816.1, 840.0, 980.9, 1002.7, 1041.7, 1067.1, 1135.8, 1246.3, 1281.8, 1398.4, 1426.9, 1449.5, 1494.3, 1513.1, 1572.2, 1589.6, 1658.2, 2920.6, 2952.7, 2989.2, 3023.9, 3061.3, 3390.1, 3395.2. *Anal*. Calcd. for $C_{19}H_{19}BrN_4O_2$: C, 54.95; H, 4.61; N, 13.49; Found: C, 54.86; H, 4.65; N, 13.55.

(S)-1-(2-Chlorophenyl)-N-(1-hydroxy-3-phenylpropan-2-yl)-5-methyl-1H-1,2,3-triazole-4-carboxamide (4c). Yield: 78%; white flaky crystals; mp 105–107°C; $[\alpha]_D^{17.0} = -48.696$ (c = 11.5 mg/mL, $CHCl_3$); ^{1}HNMR (δ ppm, $CDCl_3$): 2.464 (s, 3H), 2.975–3.067 (dd, 2H, *J* = 1.6, 7.6 Hz; b, 1H, -OH), 3.694–3.722(dd, 1H, *J* = 5.6, 11.2 Hz), 3.795–3.822(dd, 1H, *J* = 3.6, 11.2 Hz), 4.369–4.448(m, 1H), 7.209–7.266(m, 1H, N-H), 7.307–7.339(m, 4H), 7.398–7.417(dd, 2H, *J* = 1.2, 7.6 Hz), 7.464–7.502(t, 1H, *J* = 7.8 Hz), 7.533–7.587(m, 2H), 7.612–7.632 (d, 1H, *J* = 8.0 Hz, CO-NH); ^{13}CHNR (δ ppm, $CDCl_3$): 9.29, 37.49, 53.14, 64.41, 126.83, 128.22, 128.85, 129.35, 129.50, 130.88, 131.98, 132.26, 133.31, 137.83, 137.99, 138.84, 161.88; MS M/z (%): 370 (M^+, 0.31) 372 (M + 2, 0.1), 355(0.5), 341(1), 339(2), 281(3), 279(10), 259 (3), 241(4), 223(6), 205(6), 195 (5), 178(16), 168(7), 165(7), 149(88), 147(11), 141(10), 129 (40), 113(13), 112(17), 111(20), 105(10), 97(19), 91(11), 85(24), 83(37), 71(40), 57(100), 43(58). IR(KBr, cm^{-1}): 500.3, 530.4, 577.9, 660.0, 701.2, 746.1, 764.5, 851.9, 914.4, 1030.9, 1074.1, 1145.3, 1264.2, 1447.2, 1494.7, 1515.0, 1586.5, 1641.5, 2881.2, 2926.3, 3032.1, 3065.8, 3086.6, 3279.4, 3358.8. *Anal*. Calcd. for $C_{19}H_{19}ClN_4O_2$: C, 61.54; H, 5.16; N, 15.11; Found: C, 61.46; H, 5.21; N, 15.20.

(S)-1-(3-Chlorophenyl)-N-(1-hydroxy-3-phenylpropan-2-yl)-5-methyl-1H-1,2,3-triazole-4-carboxamide (4d). Yield: 41%; white needle crystals; mp 95–97°C; $[\alpha]_D^{17.5} = -47.664$ (c = 10.7 mg/mL, $CHCl_3$); ^{1}HNMR (δ ppm, $CDCl_3$): 2.613 (s, 3H), 2.964–3.058(dd, 2H, *J* = 3.2, 7.2 Hz; b, 1H, -OH), 3.686–3.728(dd, 1H, *J* = 5.6, 11.2 Hz), 3.791–3.828 (dd, 1H, *J* = 3.6, 11.2 Hz), 4.357–4.437(m, 1H), 7.199–7.255 (b, 1H, N-H), 7.281–7.308(m, 5H, *J* = 2.0, 8.0 Hz), 7.472–7.487 (dd, 1H, *J* = 1.6, 3.2 Hz), 7.507–7.533(m, 3H, Ar-H, CO-NH); ^{13}CHNR (δ ppm): 9.96, 37.49, 53.10, 64.41, 123.51, 125.73, 126.83, 128.84, 129.49, 130.41, 130.87, 135.67, 136.66, 137.06, 137.82, 138.66, 161.74; MS M/z (%): 370 (M^+, 0.52) 372 (M + 2, 0.14), 349(3), 341(6), 339(14), 289(40), 281(32), 279 (100), 271(5), 261(9), 237(7), 222(10), 220(29), 202(12), 194 (11), 192(26), 174(11), 166(15), 164(32), 154(20), 152(47), 149 (33), 146(11), 128(12), 113(10), 111(26), 105(9), 91(28), 83 (10), 71(11), 57(17), 43(22). IR(KBr, cm^{-1}): 551.8, 642.9, 682.4, 700.9, 745.0, 782.6, 868.2, 1035.3, 1075.6, 1145.2, 1268.0, 1425.1, 1492.7, 1524.8, 1586.8, 1648.5, 2928.2, 2947.1, 3023.8, 3056.9, 3080.3, 3304.9, 3412.4. *Anal*. Calcd. for $C_{19}H_{19}ClN_4O_2$: C, 61.54; H, 5.16; N, 15.11; Found: C, 61.43; H, 5.11; N, 15.02.

(S)-1-(4-Chlorophenyl)-N-(1-hydroxy-3-phenylpropan-2-yl)-5-methyl-1H-1,2,3-triazole-4-carboxamide (4e). Yield: 80%; white flaky crystals; mp 138–139°C; $[\alpha]_D^{16.5} = -44.231°$ (c = 0.1, $CHCl_3$); ^{1}H NMR δ(ppm, $CDCl_3$): 2.576 (s, 3H, CH_3), 2.991–3.015 (dd, 2H, *J* = 2.4, 7.2 Hz, Ph-CH_2-), 3.326 (b, 1H, OH), 3.675–3.716 (dd, 1H, *J* = 5.2, 11.0 Hz, -CH_2O-), 3.780–3.816 (dd, 1H, *J* = 3.6, 11.2 Hz, -CH_2O-), 4.359–4.438 (m, 1H, -CH-), 7.186–7.239 (m, 1H, -Ph-H), 7.284–7.294 (m, 4H, -Ph-H), 7.369–7.391 (d, 2H, *J* = 8.8 Hz, -C_6H_4-), 7.525–7.547 (d, 2H, *J* = 8.8 Hz, -C_6H_4-), 7.554–7.574 (d, 1H, *J* = 8 Hz, -CO-NH-); ^{13}C NMR δ(ppm, $CDCl_3$): 9.66, 37.21, 52.75, 63.91, 126.39, 126.52, 128.54, 129.24, 129.86, 133.87, 136.08, 136.78, 137.63, 138.38, 161.44. MS M/z (%): 370 (M^+, 2) 372 (M + 2, 0.65), 348(25), 271(100), 257(16), 244(10), 228(14), 221 (32), 195(66), 165(34), 149(28), 115(20), 105(60), 91(14), 77 (41), 43(74). IR(KBr, cm^{-1}): 533.0, 596.3, 694.7, 738.2, 835.0, 981.8, 1005.2, 1040.1, 1093.3, 1114.6, 1200.5, 1269.5, 1407.1, 1502.0, 1576.5, 1593.5, 1638.9, 1660.3(C = O), 2923.1, 2952.2, 3064.2, 3099.0, 3368.5(N-H), 3416.0(OH). *Anal*. Calcd. for $C_{19}H_{19}ClN_4O_2$: C, 61.54; H, 5.16; N, 15.11; Found: C, 61.59; H, 5.13; N, 15.20.

X-ray structure determination of **4e**. Colorless Block, C19H_{19}ClN4O_2, Mr = 370.83, CCDC 800563, Monoclinic, space group P2(1), a = 13.029 (7), b = 7.727(4), c = 18.954(10) Å, α = 90.00, β = 105.582(8), γ = 90.00 °, V = 1838.0(17) $Å^3$, Z = 4, D_x = 1.340 Mg m^{-3}, F_{000} = 776, μ = 0.229 mm^{-1}. Intensity data were collected using a Siemens SMART diffractometer at 296(2) K, graphite monochromator MoKα radiation (λ = 0.071073 nm), using the *ω-2θ* scan technique to a maximum of 0.981 ~ 25.50º. A total of 11896 reflections were collected with 8304 unique ones (*R* = 0.0339), of which 3133 reflections were observed with $I > 2\sigma(I)$. The final int *R* and *wR* values were 0.0536 and 0.1488, *s* = 0.978, (Δ/σ) max = 0.000. Flack = 0.06(9). The maximum peak and minimum peak in the final difference map is 0.428 and −0.194 e $Å^{-3}$.

(S)-N-(1-Hydroxy-3-phenylpropan-2-yl)-5-methyl-1-(4-methylphenyl)-1 H-1,2,3-triazole-4-carboxamide (4f). Yield: 97%; white flaky crystals; mp 136–138°C; $[\alpha]_D^{17.2} = -29.293$ (c = 9.9 mg/mL, $CHCl_3$); ^{1}H NMR δ(ppm, $CDCl_3$): 2.449 (s, 3H), 2.560 (s, 3H), 2.991–3.017(dd, 2H, *J* = 3.2, 6.8 Hz), 3.158(s,1H, OH), 3.679–3.721(dd, 1H, *J* = 5.6, 11.2 Hz), 3.782–3.819(dd, 1H, 1*J* = 4.0, 11.2 Hz), 4.365–4.463(m, 1H), 7.132–7.152 (m, 1H, *J* = 4.0 Hz), 7.186–7.357(m, 8H), 7.568–7.588(d, 1H, *J* = 8.0 Hz, CO-NH); ^{13}CHNR (δ ppm, $CDCl_3$): 9.89, 21.43, 37.48, 53.10, 64.42, 125.24, 126.76, 128.79, 129.49, 130.36, 133.20, 137.05, 137.90, 138.37, 140.45, 162.06; MS M/z (%): 350 (M^+, 0.24) 341(1), 319(2), 309(1), 289(2), 279(3), 259(17), 241 (6), 223(7), 205(9), 200(4), 178(4), 165(4), 149(100), 147 (15), 129(34), 128(10), 113(11), 112(16), 111(18), 105(8), 97 (14), 83(25), 70(27), 57(38), 43(60). IR(KBr, cm^{-1}): 512.4, 546.2, 625.4, 698.7, 746.1, 822.2, 1041.0, 1062.8, 1088.2, 1115.8, 1138.8, 1277.3, 1450.9, 1469.9, 1512.8, 1577.9, 1594.6, 1647.3, 2919.9, 2950.1, 3024.0, 3081.0, 3371.5, 3400.5. *Anal*. Calcd. for $C_{20}H_{22}N_4O_2$: C, 68.55; H, 6.33; N, 15.99; Found: C, 68.64; H, 6.43; N, 15.89.

(S)-1-(4-Ethoxyphenyl)-N-(1-hydroxy-3-phenylpropan-2-yl)-5-methyl-1 H-1,2,3-triazole-4-carboxamide (4g). Yield: 65%; white flaky crystals; mp 104–107°C; $[\alpha]_D^{17.6} = -49.153$ (c = 11.8 mg/mL, $CHCl_3$); ^{1}H NMR δ(ppm, $CDCl_3$): 1.442–1.477 (t, 3H, *J* = 7.0 Hz), 2.544 (s, 3H), 2.957–3.052(dd, 2H, *J* = 3.4, 7.4 Hz; b, 1H, OH), 3.680–3.721(dd, 1H, *J* = 5.2, 11.2 Hz), 3.785–3.822(dd, 1H, *J* = 3.6, 11.2 Hz), 4.070–4.122(q, 2H, *J* = 7.0 Hz), 4.355–4.414(m, 1H), 7.013–7.035(d, 2H, *J* = 8.8 Hz), 7.193–7.247(m, 1H), 7.292–7.322(m, 6H), 7.532–7.552(d, 1H, *J* = 8.0 Hz, CO-NH); ^{13}CHNR(δ ppm, $CDCl_3$): 9.86, 14.88, 37.51, 53.12, 64.17, 64.48, 115.41, 126.79, 126.83, 128.33, 128.82, 129.50, 137.18, 137.90, 138.28, 160.24, 162.08; MS M/z (%): 380 (M^+, 0.35) 350(3), 349(10), 323(1), 290(16), 289(100), 271(3), 247(4), 230(17), 203(5), 202(30), 175(7), 174(22), 162(8), 149(15), 146(20), 117(4), 111(2), 105(3), 91 (13), 83(3), 77(3), 65(5), 57(5), 43(6), 40(30); IR(KBr, cm^{-1}): 527.8, 655.1, 701.4, 745.3, 833.7, 865.9, 918.8, 1038.6, 1085.3, 1114.5, 1141.3, 1247.4, 1390.6, 1471.9, 1513.6, 1594.3, 1630.3, 1652.2, 2931.1, 2977.9, 3025.9, 3056.3, 3200.7, 3396.3. *Anal.* Calcd. for $C_{21}H_{24}N_4O_3$: C, 66.30; H, 6.36; N, 14.73; Found: C, 66.36; H, 6.29; N, 17.65.

(S)-N-(1-Hydroxy-3-phenylpropan-2-yl)-5-methyl-1-(3-nitrophenyl)-1 H-1,2,3-triazole-4-carboxamide (4h). Yield: 96%; white needle crystals; mp 179–182°C; $[\alpha]_D^{17.7} = -11.382$ (c = 6.15 mg/mL, $CHCl_3$); ^{1}HNMR (δ ppm, DMSO-d_6): 2.541(s, 3H), 2.854–2.910(dd, 1H, *J* = 8.8, 13.6 Hz), 2.958–3.006(dd, 1H, J = 5.6, 13.6 Hz), 3.436-3.556(m, 2H), 4.199–4.284(m, 1H), 4.937–4.965(t, 1H, *J* = 5.6 Hz, OH), 7.154–7.196(m, 1H), 7.274–7.287(m, 4H), 7.920–7.961 (t, 1H, *J* = 8.2 Hz), 8.123–8.144(d, 1H, *J* = 8.4 Hz), 8.298–8.321(d, 1H, *J* = 9.2 Hz, CON-H), 8.456–8.476(d, 1H, *J* = 8.0 Hz, CO-NH), 8.505–8.515(t, 1H, *J* = 2.0 Hz); ^{13}CHNR (δ ppm, DMSO-d_6): 10.34; 37.51; 53.26; 63.74; 121.63; 125.77; 127.03; 129.28; 130.18; 132.37; 132.89; 137.18; 138.39; 139.35; 140.41; 149.39; 161.28; MS M/z (%): 381 (M^+, 0.16) 369(0.12), 355(0.31), 343(0.23), 325(0.62), 295(1), 290(3), 241(2), 223(8), 205(5), 150(9), 149(100), 147(4), 129 (9), 121(4), 113(2), 112(4), 111(4), 105(4), 97(3), 83(4), 70 (7), 57(11), 43(25), 40(45). IR(KBr, cm^{-1}): 553.1, 602.6, 620.3, 674.2, 704.1, 753.1, 875.5, 897.7, 1045.4, 1100.2, 1149.5, 1266.3, 1288.0, 1349.5, 1420.9, 1452.8, 1493.4, 1536.8, 1586.1, 1664.3, 2867.0, 2918.6, 2944.9, 3024.6, 3057.6, 3090.4, 3109.4, 3195.6, 3377.5. *Anal*. Calcd. for $C_{19}H_{19}N_5O_4$: C, 59.84; H, 5.02; N, 18.36; Found: C, 59.96; H, 5.12; N, 18.20.

(S)-N-(1-Hydroxy-3-phenylpropan-2-yl)-5-methyl-1-(naphthalen-2-yl)-1 H-1,2,3-triazole-4-carboxamide (4i). Yield: 95%; white needle crystals; mp 178–179°C; $[\alpha]_D^{17.6} = -43.564$ (c = 10.1 mg/mL, $CHCl_3$); ^{1}H NMR δ(ppm, $CDCl_3$): 2.647(s, 3H), 3.019–3.043(dd, 2 H, *J* = 1.2, 7.6 Hz; b, 1 H, -OH); 3.705–3.747(dd, 1 H, *J* = 5.6, 11.2 Hz), 3.812–3.849(dd,1H, *J* = 3.6, 11.2 Hz), 4.384–4.462(m, 1H), 7.202–7.245(m, 1H), 7.285–7.317(m, 4H, *J* = Hz), 7.493–7.519(q, 1H, *J* = 2.0, 8.4 Hz), 7.493–7.519(m, 4H), 7.584–7.636(m, 3H), 7.903–7.954(m, 3H), 8.003–8.025(d, 1H, *J* = 8.8 Hz, CO-NH); ^{13}CHNR (δ ppm, $CDCl_3$): 10.07, 37.53, 53.17, 64.48, 122.73, 124.48, 126.82, 127.73, 127.92, 128.16, 128.58, 128.84, 129.52, 130.06, 133.04, 133.12, 133.53, 137.28, 137.90, 138.57, 162.02; MS M/z (%): 386 (M^+, 0.40) 368(0.51), 350 (0.53), 349(1.3), 290(3), 289(16), 274(1), 268(2), 250(2), 231 (5), 224(5), 210(7), 202(7), 174(7), 150(3), 149(19), 146(8), 129 (11), 127(4), 120(7), 113(5), 112(7), 111(11), 105(11), 97(14), 91 (13), 83(15), 69(18), 57(28), 45(47), 44(100), 43(59). IR(KBr, cm^{-1}): 477.4, 701.3, 749.3, 817.9, 867.0, 1050.7, 1086.4, 1269.9, 1425.6, 1450.3, 1461.3, 1509.5, 1585.8, 1653.6, 2924.5, 2943.7, 2981.2, 3002.1, 3030.1, 3052.3, 3403.7, 3456.8. *Anal*. Calcd. for $C_{23}H_{22}N_4O_2$: C, 71.48; H, 5.74; N, 14.50; Found: C, 71.56; H, 5.65; N, 14.36.

(S)-1-(4-Chlorophenyl)-N-(1-hydroxy-3-phenylpropan-2-yl)-5-methoxy-1 H-1,2,3-triazole-4-carboxamide (4j). Yield: 68%; white flaky crystals; mp 179–181°C; $[\alpha]_D^{17.2} = -129.66$ (c = 11.8 mg/mL, $CHCl_3$); ^{1}H NMR δ(ppm, $CDCl_3$): 2.782(s, 1H, -OH), 2.896–3.016(ddd, 2H), 3.638–3.679(dd, 1H, *J* = 5.4, 11.0 Hz), 3.745–3.779(dd, 1 H, *J* = 2.6, 11.0 Hz), 4.270–4.642 (m,1H; s, 3H, -OCH_3), 7.187–7.242(m, 1H), 7.268–7.314(m, 4H), 7.448–7.484(m, 2 H, *J* = 2.0, 7.2 Hz), 7.954–7.976(dd, 2H, *J* = 2.0, 7.2 Hz), 8.574–8.594(d, 1 H, *J* = 8.0 Hz, -CO-NH-); ^{13}CHNR (δ ppm): 37.69, 41.33, 53.20, 64.80, 112.52, 122.19, 126.79, 128.77, 129.51, 129.71, 133.92, 134.35, 137.92, 156.61, 158.81; MS M/z (%): 386 (M^+, 2.08) 388(M + 2, 0.5), 368(1.2), 355(4), 341(1), 307(6), 297(14), 295(24), 283(4), 277(3), 256(6), 238(14), 236(41), 223(9), 205(8), 198(12), 196(8), 169(6), 157 (15), 149(100), 129(14), 121(9), 111(24), 105(11), 97(19), 91(18), 83(22), 69(25), 57(38), 45(54), 44(68), 43(61). IR(KBr, cm^{-1}): 505.6, 526.4, 595.3, 627.8, 701.5, 751.1, 830.9, 868.0, 1010.9, 1034.9, 1083.1, 1184.1, 1259.6, 1304.7, 1415.9, 1449.2, 1491.1, 1541.8, 1632.7, 1679.9, 2936.6, 2958.0, 3025.7, 3056.0, 3079.2, 3102.5, 3290.1, 3474.7. *Anal*. Calcd. for $C_{19}H_{19}ClN_4O_3$: C, 58.99; H, 4.95; N, 14.48; Found: C, 58.86; H, 5.04; N, 14.31.

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