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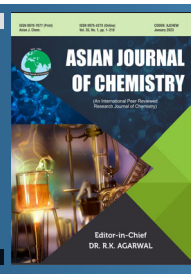

Synthesis of New Piperidine based N(2)-Alkylated 1,2,3-Triazole Hybrids in Basic Medium

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The nucleophilic reaction of 1*H*-triazole derivatives with piperidines under basic conditions is the essential step in the synthesis of a new series of dibenzyl N(2)-C-linked triazolyl piperidines. The triazole derivative was synthesized *via* the CuAAc reaction of 1-phenylprop-2-yn-1-ol (**1a-b**) with azidomethyl pivalate. Compound **3a-b** underwent dehydroxylation and deprotection reactions using TFA, triethyl silane and 1 M NaOH respectively, yielding monobenzyl 1*H*-1,2,3-triazole (**4a-b**). The N(2)-piperidinyltriazoles (**6a-j**) were synthesized in significant amounts by nucleophilically reacting 1*H*-triazole derivatives (**4a-b**) with 4-mesyl-1-*boc*-piperidine (**5**) under basic conditions using sodium hydride, which further on acidic deprotection followed by benzylation reaction furnished dibenzyl N(2)-C-linked triazolyl piperidines (**9a-j**).

Keywords: Click reaction, Propynol, Azidomethyl pivalate, 4-Mesyl-1-*boc*-piperidine, Sodium hydride, Piperidinyl triazole.

INTRODUCTION

Substituted 1,2,3-triazoles are one of the most significant *N*-heterocyclic compounds and have several applications in medicinal chemistry, agrochemicals and material science [1-5]. 1,2,3-Triazoles are employed as building blocks in the design of pharmaceutically valuable molecules. N(2)-Substituted triazoles have been shown to be effective binders in the coordination polymers exhibiting remarkable optical characteristics [6]. The N(1) and N(2) isomers may behave differently in the biological systems due to their differing basicity, which results in the opening of new areas for drug discovery [7]. Numerous biologically active molecules, which include a N(2)-substituted 1,2,3-triazole core, such as the dual orexin receptor antagonists used to treat insomnia [8], inhibitors of 2,3-oxidosqualene cyclase, α-glycosidase and serine hydrolase [9-11]. Some of the compounds of this regioisomer also exhibited antiasthma [12], anaesthetic [13] and antiarrythmic [14] activities.

Since the discovery of copper-catalyzed alkyne-azide-cycloaddition (CuAAC) reaction, which exclusively produces the 1,4-regioisomer in high yields, 1,2,3-triazole chemistry has received a lot of interest [15-17]. On the other hand, there is still no universal methodology capable of delivering the N2 substituted regioisomer. The N(2)-substituted 1,2,3-triazoles were reported in major yields recently using $FeCl_3$ catalyzed unsaturated substrates, DABCO mediated aza-Michael addition of cycloalkenones. Peddinti & Bhagat [18] reported that formation of N(2)-substituted 1,2,3-triazoles is enhanced compared to N(1)-substituted corresponding compound in the presence of basic medium due to the enhancement of N(2)-nucleophilicity. This was further supported by the report of Zhu *et al.* [19] stated in which copper bromide catalyzed reaction of azirines with aryl-diazonium salts leads to the formation of N(2)-substituted triazoles using DABCO as base.

Inspired by the biological applications of 2,4-substituted 1,2,3-triazoles and in view of the above facts in synthesizing these triazole derivatives, a new series of 2,4-disubstituted triazoles containing dibenzyl and piperidine moieties are undertaken to synthesize using azidomethyl pivalate and 4-substituted 1-phenylprop-2-yn-1-ol as key precursors.

EXPERIMENTAL

The melting points were determined in open capillaries and are uncorrected. ^{1}H NMR (300 MHz & 400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in Bruker AV instrument in $CDCl_3$, DMSO-d_6 solvents using TMS as internal standard. ESI-MS spectra were recorded Agilent 1100 LC-Q TOF instrument. TLC plates coated with Merck silica gel 60 F_{254} were used to monitor the reactions.

General procedure for the synthesis of (4-(hydroxy-(phenyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl pivalate (3a-b): To a stirred solution of chloromethyl pivalate (**2**) (66.6 mmol, 1.0 eq), acetylene compound **1a-b** (1.1 equiv.) in 400 mL of 1:1 mixture of *t*-BuOH/H_2O (30 vol.) at room temperature was added sodium azide (1.1 equiv.), followed by sodium ascorbate (30 mol%) and copper sulphate (10 mol%). The reaction mixture was heated to 90 ºC and continued for another 16 h at the same temperature. After completion of the reaction, ethyl acetate and water (1:1) added to the reaction mixture and the layers were separated. The organic layer was washed with 10% NH_4OH solution (50 mL) and brine solution (50 mL), dried and concentrated under reduced pressure to obtain the crude product, which was triturated with 5% ethyl acetate/hexanes (100 mL) to give hydroxy triazoles **3a-b** as an off-white solids.

Synthesis of (4-benzyl-1*H*-1,2,3-triazol-1-yl)methyl pivalate (4a-b): A stirred solution of hydroxy triazoles (**3a-b**) (27.66 mmol, 1.0 equiv.) in dry DCM (160 mL, 20 vol.) was added slowly triethyl silane (2.0 equiv.) at room temperature under nitrogen atmosphere and stirred for 15 min. Then cool to 0 ºC and added trifluoroacetic acid (4.0 equiv.) at 0-5 ºC, stirring for 2 h at room temperature. After completion of the reaction, the reaction mass was cooled to 0 ºC, neutralized with saturated $NaHCO_3$ and extracted with dichloromethane. The combined organic layer was dried and evaporated under reduced pressure. The obtained crude product dissolved in MeOH (15 mL) and then added 1 N NaOH (15 mL) at room temperature. Stirred the reaction mass for 3-4 h at room temperature, completion of the reaction was monitored by TLC. Then the reaction mixture was neutralized with 1 N HCl (25 mL) and the resulting precipitate was separated through filtration. After drying under vacuum, compound **4a-b** was obtained as off-white solid (**Scheme-I**).

4-Benzyl-1*H*-1,2,3-triazole (**4a**): White solid, yield: 55%, m.p.: 124-127 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 7.44 (s, 1H), 7.28 (t, *J* = 7.4 Hz, 2H), 7.23-7.20 (m, 3H), 4.09 (s, 2H). ESI-Mass *m/z*: 160.2 $[M+H]^+$.

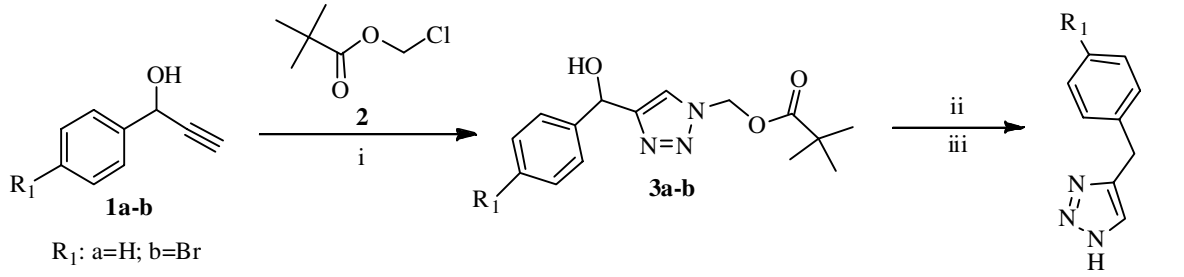
4-(4-Bromobenzyl)-1*H*-1,2,3-triazole (4b): Off-white solid, yield: 62%, m.p.: 132-136 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 7.47 (s, 1H), 7.46 (d, *J* = 7.5 Hz, 2H), 7.10 (d, *J* = 7.5 Hz, 2H), 4.04 (s, 2H). ESI-Mass *m/z*: 238.2 $[M+H]^+$; 239.09 $[M+2H]^+$.

General procedure for synthesis of 4-(4-(benzyl)-2*H*-1,2,3-triazol-2-yl)piperidines (7a-b): Compound **4a-b** (6.28 mmol, 1.0 equiv.) in DMF (10 mL) was added to sodium hydride (1.5 equiv.) at 0 ºC and stirred for 15 min at room temperature followed by the addition of compound **5** (O-mesylate) (1.5 equiv.). The reaction mixture was heated to 60 ºC and continued stirring for 16 h at 60 ºC. After the reaction was completed, the reaction mixture was left to cool to room temperature, quenched with cold water and extracted using ethyl acetate. The organic layer was washed with cold water (10 mL), followed by drying over Na_2SO_4 and evaporated under reduced pressure to obtain a crude product (1.0 equiv.), which was dissolved in dichloromethane (10 mL) and added trifluoroacetic acid (2.0 equiv.) at 0 ºC and allow to stir for 2 h at room temperature. The reaction mixture was then concentrated under reduced pressure and the crude product was mixed thoroughly with diethyl ether to yield compound **7a-b** (**Scheme-II**).

4-(4-Benzyl-2*H*-1,2,3-triazol-2-yl)piperidine (7a): Brown colour semi-solid, yield: 52%. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 7.32 (s, 1H), 7.11-7.09 (m, 2H), 7.08-7.01 (m, 3H), 4.82-4.72 (m, 1H), 4.02 (s, 2H), 3.38-3.32 (m, 2H), 3.27-3.25 (m, 2H), 2.64-2.55 (m, 4H). ESI-Mass *m/z*: 243.3 $[M+H]^+$.

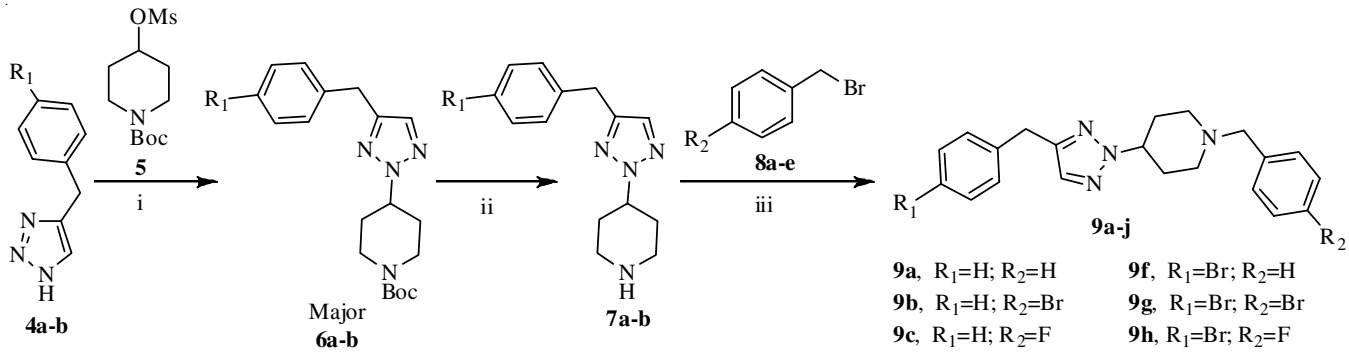
4-(4-(4-Bromobenzyl)-2*H*-1,2,3-triazol-2-yl)piperidine (7b): Brown colour semi-solid, yield: 52%. ^{1}H NMR (300 MHz, $CDCl_3$) δ, ppm: 7.62 (s, 1H), 7.49 (d, *J* = 7.5 Hz, 2H), 7.21 (d, *J* = 7.5 Hz, 2H), 4.82-4.72 (m, 1H), 3.99 (s, 2H), 3.19-3.05 (m, 4H), 2.74-2.72 (m, 2H), 2.28-2.23 (m, 4H). ESI-HRMS Mass *m/z*: 322.3244 $[M+H]^+$; 324.3244 $[M+2+H]^+$.

General procedure for synthesis of dibenzyl N2-linked triazolyl piperidines (9a-j): A stirred solution of compound **7a-b** (0.62 mmol, 1.0 equiv.) in DCM (10 mL) was added to triethylamine (2.0 equiv.) at 0 ºC and stirred for 15 min at room temperature. The reaction mixture was heated to reflux (40 ºC) for 16 h after benzyl bromide **8a-e** (1.5 equiv.) was added. The reaction mixture was then cooled with ice-water and extracted with dichloromethane. The organic layer was dried and concentrated under reduced pressure to obtain crude



(i) $CuSO_4{\cdot}5H_2O$ (10 mol%), NaN_3 (1.1 eq), sodium ascobrbate (30 mol%), *t*-BuOH:H_2O (1:1), 90 °C, 12 h, (ii) TFA (2 eq), TES (4 eq), 0 to rt, 1-2 h; (iii) 1 M NaOH, rt, 3-4 h

Scheme-I: Synthesis of 4-(4-substituted benzyl)-1*H*-1,2,3-triazole (**4a-b**)



(i) NaH (1.5 eq), DMF 60 °C, 16 h; (ii) TFA (2 eq), DCM, rt, 2-3 h; (iii) Et_3N (2 eq), DCM, reflux, 16 h

Scheme-II: Synthesis of 1-(4-substituted benzyl)-4-(4-(4-substiuted benzyl)-2*H*-1,2,3-triazol-2-yl)piperidine (**9a-j**)

title compounds **9a-j**, which was then purified by flash chromatography using 40-50% ethyl acetate and hexane as eluent (**Scheme-II**).

1-Benzyl-4-(4-benzyl-2*H*-1,2,3-triazol-2-yl)piperidine (9a): Pale yellow liquid, yield: 68%. ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.34 (s, 1H), 7.32-7.21 (m, 10H), 4.43-4.35 (m, 1H), 4.02 (s, 2H), 3.55 (s, 2H), 3.02-2.92 (m, 2H), 2.30-2.04 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 146.73, 138.87, 138.35, 132.5, 129.09, 128.68, 128.58, 127.08, 126.44, 62.73, 61.95, 50.84, 31.98, 31.75, 29.75, 22.69. HRMS (ESI, MeOH/CH_2Cl_2: 90/10): Exact mass calculated for $C_{21}H_{25}N_4$ $[M+H]^+$ 333.20737, found: 333.2077.

4-(4-Benzyl-2*H*-1,2,3-triazol-2-yl)-1-(4-bromobenzyl)-piperidine (9b): Light brown solid, yield: 59%. m.p.: 89-95 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.41 (d, *J* = 7.5 Hz, 2H), 7.34 (s, 1H), 7.33-7.23 (m, 5H), 7.12-7.08 (m, 2H), 4.40 (m, 1H), 3.96 (s, 2H), 3.55 (s, 2H), 3.00-2.92 (m, 2H), 2.20-2.10 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 146.67, 138.22, 134.58, 133.55, 132.57, 132.04, 128.81, 127.95, 126.54, 123.21, 63.65, 55.08, 50.84, 40.07, 30.83, 24.54. HRMS (ESI, MeOH/CH_2Cl_2: 90/10): Exact mass calculated for $C_{21}H_{23}N_4{}^{79}Br$ $[M+H]^+$: 411.11788, found: 411.1182.

4-(4-Benzyl-2*H*-1,2,3-triazol-2-yl)-1-(4-fluorobenzyl)-piperidine (9c): Light brown solid, yield: 63%. m.p.: 83-87 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.31 (s, 1H), 7.10-6.96 (m, 7H), 6.82 (t, *J* = 7.7 Hz, 2H), 4.90-4.78 (m, 1H), 3.91 (s, 2H), 3.71 (s, 2H), 2.56 (dd, *J* = 14.0, 8.9 Hz, 2H), 2.29-2.18 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 162.20,146.67, 138.22, 134.58, 133.55, 132.57, 132.04, 128.81, 127.95, 126.54, 123.21, 62.65, 54.90, 50.84, 40.07, 30.83. HRMS (ESI, MeOH/CH_2Cl_2: 90/10): Exact mass calculated for $C_{21}H_{24}N_4F$ $[M+H]^+$: 351.19795, found: 351.1982.

4-(4-Benzyl-2*H*-1,2,3-triazol-2-yl)-1-(4-methoxybenzyl)-piperidine (9d): Off-white semi-solid, yield: 59%. ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.29-6.96 (m, 7H), 7.34 (s, 1H), 6.82 (m, 2H), 4.90-4.78 (m, 1H), 3.99 (s, 2H), 3.81 (s, 3H), 3.71 (s, 2H), 2.56 (dd, *J* = 14.0, 8.9 Hz, 2H), 2.29-2.18 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 158.85, 147.46, 139.15, 130.19, 130.12, 128.76, 128.62, 126.48, 118.92, 113.69, 62.13, 58.29, 55.27, 52.10, 32.72, 32.40. HRMS (ESI, MeOH/CH_2Cl_2: 90/10): Exact mass calculated for $C_{22}H_{26}N_4ONa$ $[M+Na]^+$: 385.19988, found: 385.2001.

4-(4-Benzyl-2*H*-1,2,3-triazol-2-yl)-1-(4-nitrobenzyl)-piperidine (9e): Light brown solid, yield: 64%. m.p.: 92-95 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 8.18 (d, *J* = 7.5 Hz, 2H), 7.53 (d, *J* = 7.5 Hz, 2H), 7.33-7.22 (m, 6H, triazole proton also merged), 4.46-4.42 (m, 1H), 4.03 (s, 2H), 3.64 (s, 2H), 2.99-2.90 (m, 2H), 2.29-2.13 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 147.16, 146.92, 146.64, 138.79, 132.62, 129.25, 128.67, 128.58, 126.48, 123.59, 61.87, 61.64, 52.29, 31.97, 31.77, 29.70. HRMS (ESI, MeOH/CH_2Cl_2: 90/10): Exact mass calculated for $C_{21}H_{24}N_5O_2$ $[M+H]^+$: 378.19245, found: 378.1928.

1-Benzyl-4-(4-(4-bromobenzyl)-2*H*-1,2,3-triazol-2-yl)-piperidine (9f): Off-white solid, yield: 63%. m.p.: 102-110 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.42-7.39 (d, 2H), 7.35-7.25 (m, 6H, triazole H also merged with other aromatic protons), 7.11-7.08 (d, 2H), 7.18 (broad s, 1H), 7.13 (d, 2H), 4.40 (m, 1H), 3.99 (s, 2H), 3.54 (s, 2H), 3.01-2.91 (m, 2H), 2.28-2.09 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 146.13, 138.35, 137.85, 132.42, 131.61, 130.41, 128.97, 128.25, 127.08, 120.32, 62.49, 62.04, 52.11, 31.77, 31.39, 29.69. HRMS (ESI, MeOH/CH_2Cl_2: 90/10): Exact mass calculated for $C_{21}H_{24}N_4{}^{79}Br$ $[M+H]^+$: 411.11788, found: 411.1179; [M+H+2]: 413.1180.

1-(4-Bromobenzyl)-4-(4-(4-bromobenzyl)-2*H*-1,2,3-triazol-2-yl)piperidine (9g): Off-white solid, yield: 58%. m.p.: 126-131 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.42-7.39 (m, 4H), 7.23-711 (m, 5H, triazole H also merged with other aromatic protons), 4.41 (m, 1H), 4.40 (s, 2H), 3.54 (s, 2H), 3.01-2.91 (m, 2H), 2.28-2.09 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 146.79, 138.11, 137.24, 131.69, 131.43, 130.59, 130.51, 120.99, 120.38, 118.94, 61.96, 58.20, 52.16, 32.66, 31.77. HRMS (ESI, MeOH/CH_2Cl_2: 90/10): Exact mass calculated for $C_{21}H_{22}N_4{}^{79}Br_2Na$ $[M+Na]^+$: 511.01034, found: 511.0106; $[M+2H+Na]^+$: 513.0084, found: 513.0088; $[M+4H+Na]^+$: 515.0067, found: 515.0068.

4-(4-(4-Bromobenzyl)-2*H*-1,2,3-triazol-2-yl)-1-(4-fluorobenzyl)piperidine (9h): Off-white solid, yield: 60%. m.p.: 106.5-111.0 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.42 (d, 2H), 7.35-7.22 (broad m, 2H), 7.17 (broad s, 1H), 7.13 (d, 2H), 7.01 (d, 2H), 4.44 (tt, *J* = 11.4, 4.2 Hz, 1H), 4.02 (s, 2H), 3.51 (broad s, 2H), 3.07-2.89 (m, 2H), 2.26-2.09 (broad m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 162.13, 146.80, 138.10, 133.73, 131.71, 130.50, 130.43, 120.40, 118.95, 115.18, 61.85, 58.20, 52.08, 32.62, 31.78. HRMS (ESI, MeOH/CH_2Cl_2: 90/10):

Exact mass calculated for $C_{21}H_{23}N_4F^{79}Br$ $[M+H]^+$: 429.10846, found: 429.1088; exact mass calculated for $C_{21}H_{22}N_4F^{79}BrNa$ $[M+Na]^+$: 451.09041, found: 451.0905.

4-(4-(4-Bromobenzyl)-2*H*-1,2,3-triazol-2-yl)-1-(4-methoxybenzyl)piperidine (9i): Off-white solid, yield: 57%. m.p.: 101-105 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.42 (d, 2H), 7.22 (d, 2H), 7.29 (s, 1H), 7.13 (d, 2H), 6.86 (d, 2H), 4.45 (m, 1H), 4.02 (s, 2H), 3.80 (s, 3H), 3.48 (s, 2H), 3.04-2.94 (m, 2H), 2.19-2.02 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 158.82, 146.74, 138.11, 131.68, 130.49, 130.20, 120.37, 118.89, 113.67, 62.10, 58.33, 55.27, 52.06, 32.70, 31.77. HRMS (ESI, MeOH/CH_2Cl_2: 90/10): Exact mass calculated for $C_{22}H_{26}N_4O^{79}Br$ $[M+H]^+$: 441.12845, found: 441.1287; exact mass calculated for $C_{22}H_{25}N_4O^{79}BrNa$ $[M+Na]^+$: 463.11039, found: 463.1100.

4-(4-(4-Bromobenzyl)-2*H*-1,2,3-triazol-2-yl)-1-(4-nitrobenzyl)piperidine (9j): Off-white solid, yield: 68%. m.p.: 106-111 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 8.19-8.17 (d, 2H), 7.55-7.52 (d, 2H), 7.43-7.41 (d, 2H), 7.30 (s, 1H), 7.11-7.09 (d, 2H), 4.43 (m, 1H), 3.98 (s, 2H), 3.63 (s, 2H), 2.91-2.90 (m, 2H), 2.30-2.10 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 147.15, 146.61, 146.27, 137.79, 132.53, 131.63, 130.41, 129.24, 123.58, 120.36, 61.86, 61.72, 52.26, 31.76, 31.39. HRMS (ESI, MeOH/CH_2Cl_2: 90/10): Exact mass calculated for $C_{21}H_{22}N_5O_2{}^{79}BrNa$ $[M+Na]^+$: 478.08491, found: 478.0855, $[M+2H+Na]^+$: 480.0831, found: 480.0837.

RESULTS AND DISCUSSION

The synthesis of key intermediate 4-benzyl-1*H*-1,2,3-triazole (**4a**) is performed in two steps. The reaction of 1-phenylprop-2-yn-1-ol (**1a**) was carried out with azidomethyl pivalate (*in situ* generated from **2**), in presence of 10 mol% of $CuSO_4 \cdot 5H_2O$ and 30 mol% of sodium ascorbate at 90 ºC for overnight. After the usual workup, (4-(hydroxy(phenyl)methyl)-1*H*-1,2,3-triazol-1-yl)methyl pivalate (**3a**) was isolated. The removal of alcohol in **3a** was carried out under TFA and triethyl silane at 0-5 ºC for 2 h to obtain the crude product, which underwent deprotection of methyl pivalate group using 1 M NaOH in methanol gave the corresponding product 4-benzyl-1*H*-1,2,3-triazole (**4a**). Following the same protocol [20], prepared 4-bromobenzyl derivative **4b** from 4-bromophenylprop-2-yn-1-ol (**1b**) (**Scheme-I**).

1*H*-Triazole derivatives (**4a-b**) were treated independently with *tert.*-butyl 4-((methylsulfonyl)oxy)piperidine-1-carboxylate (**5**) in DMF at 60 ºC in presence of sodium hydride as base afforded the corresponding 4-(4-benzyl/4-bromobenzyl-2*H*-1,2,3-triazol-2-yl)piperidine (**6a-b**) as the major product and observed only ~5-8 % of other N(1)-alkylated triazolopiperidne derivatives.Products **6a-b** were used without any purification in the next deprotection step. Product **7a-b** was obtained on acid catalyzed deprotection of **6a-b** with 2 M trifluoroacetic acid in dichloromethane at room temperature for 2-3 h (**Scheme-II**). These compounds were confirmed on the basis of their spectral data. The ^{1}H NMR spectrum of compound **7b** showed the characteristic singlet signal at δ 7.62 ppm corresponds to 1,2,3-triazole proton and another singlet at δ 3.99 ppm integrated for two protons due to benzylic -CH_2 protons. The NH proton is merged with piperidine protons in the range δ 3.13-1.98 ppm (NH and eight protons of piperidine). The remaining proton multiplet signal related to piperidine is observed at δ 4.79 ppm. Its ^{13}C NMR spectrum of compound revealed the triazolyl carbon signals at δ 131.22 and 130.56 ppm. The benzylic CH_2 carbon resonated at δ 57.53 ppm, while the piperidine carbon signals are found at δ 60.74, 30.33, 28.76 and 28.16 ppm. The ESI-HRMS mass spectrum of compound **7b** showed the $[M+H]^+$ peak at *m/z* 322.3244 indicating the molecular formula $C_{14}H_{17}BrN_4$, which is correlated with the calculated value 322.3334 and also indicates the presence of bromine by showing the intensities of $[M+H]^+$ peak at *m/z* 322.3244 and $[M+2+H]^+$ peak at *m/z* 324.3244 in 1:1 ratio.

Monobenzyltriazolepiperidine derivative **7a** was benzylated in dichloromethane under reflux for 16 h in the presence of triethylamine with five typical benzyl bromide derivatives **8a-e**. After the usual workup, corresponding target compounds of dibenzyl N(2)-C linked triazolyl piperidines **9a-j** were obtained in 68 to 57% yield (**Scheme-II**). The spectral analysis of compound **9e** is discussed here. The presence of two doublet peaks and a singlet peak at δ 8.18, 7.53 and 3.64 ppm respectively, integrated each for two protons in the ^{1}H NMR spectrum of **9e** representing 4-nitrobenzyl group and the signal at δ 4.03 ppm integrated for two protons due to triazole attached CH_2 protons. The ^{13}C NMR spectrum of the compound revealed the triazolyl carbon signals at δ 132.62 and 129.25 ppm. The benzylic CH_2 carbon resonated at δ 52.29 ppm, while the piperidine carbon signals are found at δ 61.87, 31.97, 31.77 and 29.70 ppm. The ESI-HRMS mass spectrum of compound **9e** showed the $[M+H]^+$ peak at *m/z* 378.1928 indicating the molecular formula $C_{21}H_{24}N_5O_2$, which is correlated with the calculated value 378.19245

Conclusion

A new series of dibenzyl N(2)-C-linked triazolyl piperidines was synthesized using the nucleophilic reaction of 1*H*-triazole derivatives with piperidines under basic conditions as key step. The click reaction of 1-phenylprop-2-yn-1-ol (**1**) with azidomethylpivalate using CuAAC method results in the formation of triazole derivative. Compound **3** then underwent dehydroxylation followed by the deprotection using TFA, triethyl silane and 1 M NaOH, respectively to afford monobenzyl 1*H*-triazolyl piperidine (**4**). 1*H*-Triazole derivatives **4a-b** and 4-mesyl-1-bocpiperidine were nucleophilically reacted using sodium hydride as base furnished the N2-piperidinyl triazoles in major yields, which were then an acidic deprotection followed by benzylation reaction synthesized the titled dibenzyl N(2)-C-linked triazolyl piperidines.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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