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EFFICIENT MICROWAVE-ASSISTED BUCHWALD-HARTWIG COUPLING FOR THE SYNTHESIS OF 3- (SUBSTITUTED)BENZYL-7-BUT-2-YNYL-1-METHYL-8-(4METHYLENE-PIPERIDIN-1-YL)-3,4,5,7-TETRAHYDRO-PURINE-2,6-DIONE

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ABSTRACT:

Ten derivatives of 3-(Substituted)Benzyl-7-but-2-ynyl-1-methyl-8-(4-methylenepiperidin-1-yl)-3,4,5,7-tetrahydro-purine-2,6-dione was efficiently synthesized from simple available starting materials using two-step. 8-Bromo-7-but-2-ynyl-1-methyl3,4,5,7-tetrahydro-purine-2,6-dione was reacted with 4-Methylene-piperidine using Buchwald-Hartwig approach to give intermediate 7-But-2-ynyl-1-methyl-8-(4methylene-piperidin-1-yl)-3,4,5,7-tetrahydro-purine-2,6-dione, formed intermediate was reacted with substituted benzyl bromides using potassium carbonate in microwave gives aimed compounds. Synthetic Buchwald-Hartwig methodology was found great importance for the synthesis of reported derivatives.

Keywords: Synthesis, Buchwald-Hartwig, Purine, benzyl bromides, microwave.

1. INTRODUCTION

A compound containing a heterocyclic core has immense importance in drug discovery programs and drug synthesis due to its bioactivities[1,2]. The various studied heterocyclic compounds, purines and purine derivatives are the most present nitrogen-containing moiety available in nature[3]. Purines consisting of fused six-member pyrimidine types of rings with five-member imidazole ring systems and found in many important bio-molecules like cyclic adenosine monophosphate, nicotinamide adenine dinucleotide hydrogen, guanosine 5-triphosphate, adenosine triphosphate and coenzyme A[4].

Hydrogen bonding of purines makes it a more valuable scaffold to target a wide range of biosynthetic molecules and signal transduction proteins[5]. Purine rings containing drug molecules like theophylline, caffeine and methylxanthine are well known for their therapeutic uses as anti-asthmatic, analeptics, vasodilators, anti-HIV, antimicrobial, antihypertensive, diuretics, bronchodilators and anticancer agents[6,7,8].

Fused purines are considered the fundamental skeleton of the naturally occurring purine alkaloids[9,10]. Some substituted pyrimidine purine diones were reported as non-steroidal anti-inflammatory agent[11,12]. Recently 1,8-disubstituted purine-2,6-diones was reported to possess potent analgesic and anti-inflammatory activity through adenosine receptor antagonism[13,14,15,16]. The fusing of the pyrimidine ring to the imidazole ring is used for the synthesis of purine derivatives was reported by Traube[17].

The combination of multiple biological active sites in the synthesized single molecules is one of the most important approaches for designing new bioactive molecules[18,19,20]. In the view of above importance of Purine derivatives and the continuation of our research work[21,22,23,24] on the synthesis of heterocycles, we have decided to synthesize Purine derivatives. We mainly focus on the synthesis of Linagliptin kind of fused purine derivatives using simple synthetic strategies with good impact on the synthesis of this active pharmaceutical ingredient [25]. Linagliptin is a xanthine derivative and a highly potent, selective, long-acting and orally bioavailable DPP-4 inhibitor used for the treatment of type 2-diabetes[26].

Metal-catalyzed C-C and C-N bond formation reactions are the overgrowing and vastly used for the synthesis of new organic molecules[27,28]. Pd-catalyzed amination reactions (C-N bond formation) in between substituted amines and aryl, vinyl and hetero-aryl halides are well known and used in the synthesis of novel molecules[29,30].

The two most important amination name reactions are Pd metal catalyzed BuchwaldHartwig and Cu metal catalyzed Ullmann-Goldberg reactions are mostly used in organic and medicinal chemistry[31]. The discovery of the Buchwald-Hartwig reaction is a facile and efficient name reaction for the synthesis of aryl amines by replacing the tedious nucleophilic aromatic substitution[32]. A deep literature study on Buchwal-Hartwig coupling reactions showed that such C-N bond forming carried out using bases like NaOtBu[33], KOtBu[34], K_2CO_3[35], KOH[36], Na_2CO_3[37], Cs_2CO_3[38], various Pd metal complexes as catalyst and ligands like BINAP[39], dppf[40], XantPhos[41], SPhos[42], JosiPhos[43], JohnPhos[44], tri-alkylphosphines[45] etc.

Reported literature on Buchwald-Hartwig amination showed that researchers used such conditions for the amination using primary amines and secondary amines using different Pd metal catalysts, ligands and bases[46,47,48,49,50,51]. Modern methods like microwave irradiation, ultrasound sonication, and grinding techniques used for the synthesis of organic molecules have immense importance over the regular conventional methods due to their shorter time with a higher percent of isolated yields[52,53,54]. So we have used the microwave irradiation technique for the synthesis of 3(Substituted)Benzyl-7-but-2-ynyl-1-methyl-8-(4-methylene-piperidin-1-yl)-3,4,5,7tetrahydro-purine-2,6-dione.

Experimental

General

All the starting materials were purchased from BLD India and used without further purification. Anton Paar Monowave 400 microwave synthesizer was used for the synthesis. 1H NMR spectra were recorded on a Bruker Avance (400 MHz) spectrometer in DMSO. The 13C NMR spectra were recorded on the same instrument and chemical shifts were reported in parts per million relatives to tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded on an Agilent spectrometer and reported as M-1. Melting points of compounds were determined on the Labstar melting point apparatus.

Synthesis of 7-But-2-Ynyl-1-Methyl-8-(4-Methylene-Piperidin-1-Yl)-3, 4, 5, 7tetrahydro-Purine-2, 6-Dione (3).

Charged 300mg (1 mmole) of 8-Bromo-7-but-2-ynyl-3-methyl-3,4,5,7-tetrahydropurine-2,6-dione 1 and 146mg 4-Methylene-piperidine 2 (1.5 mmol) in 5mL of solvent at room temperature in 30mL microwave tube under purging of nitrogen. After well purging and stirring of reaction mass were added 10-20 mol % of first, second or third generation Buchwald-Hartwig catalyst and stirred reaction mass at room temperature with purging of nitrogen for the next 15 min. Then the tube was sealed placed in the microwave and irradiated it for 1-2 h at 100-120 OC. Progress of the reaction was monitored by using pre-coated TLC with 20% ethyl acetate in hexane. After completion of the reaction, the reaction mass was cooled to room temperature, diluted with ethyl acetate and filtered through celite pad and filtrate was washed with water. The organic layer was separated and dried over sodium sulphate and concentrated. The obtained solid was purified by silica gel chromatography. While using first and second-generation Buchwald-Hartwig catalysts potassium tert-butoxide (0.5 equiv.) and xantphos (0.05 equiv.) was used for this coupling reaction, scheme 1. Melting point: 190 - 191 ^{O}C. Reaction time: 1 h. Percent yield: 220 mg (70%). Mass: [ES]-: Calculated – 315.17, Found – 314.57.

General Procedure for the Synthesis of 3-(Substituted)Benzyl-7-But-2-Ynyl-1-Methyl8-(4-Methylene-Piperidin-1-Yl)-3,4,5,7-Tetrahydro-Purine-2,6-Dione (5a-J).

To a dried 30 mL microwave tube charged 1mmole of 7-But-2-ynyl-1-methyl-8-(4methylene-piperidin-1-yl)-3,4,5,7-tetrahydro-purine-2,6-dione **(3)** in 10 volume of acetonitrile at room temperature then 1.2mmol of substituted benzyl bromide **4a-j** was added under stirring. After 10 min 1.5mmol of potassium carbonate was added at room temperature and a microwave vial was placed in microwave and irradiated for 1-2h at 80 ^{O}C. Progress of the reaction was monitored by using pre-coated TLC with 35% ethyl acetate in hexane. After completion of the reaction, the reaction mass was cooled to room temperature poured on ice-cold water and extracted with ethyl acetate. The organic layer was washed with 20mL water and dried over anhydrous sodium sulphate. Concentrate and purify by flash chromatography eluting with 20% ethyl acetate in hexane scheme 1.

Spectral data

2-[7-But-2-ynyl-1-methyl-8-(4-methylene-piperidin-1-yl)-2,6-dioxo 1,2,4,5,6,7hexahydro-purin-3-ylmethyl]-benzonitrile (5a).

Melting point: 242 ^{O}C. Reaction time: 0.5 h. Percent yield: 83%. Mass: [ES]-: Calculated – 430.21, Found – 429.77. ^{1}H NMR (400 MHz, DMSO, δ ppm): 1.79 (s, 3H, -CH_3), 2.34 (d, 1H, -CH), 2.35 (t, 4H, -CH_2), 3.38 (s, 3H, -CH_3), 3.41 (d, 1H, CH_2), 3.42 (t, 4H, -CH_2), 4.81 (s, 2H, -CH_2), 4.91 (d, 2H, =CH), 5.21 (s, 2H, -CH_2), 7.25 (d, 1H, Ar-H), 7.44 (dd, 1H, Ar-H), 7.61 (dd, 1H, Ar-H), 7.82 (d, 1H, Ar-H). ^{13}C NMR (400 MHz, DMSO, δ ppm): 3.06, 29.54, 33.58,

35.61, 41.90, 50.71, 73.65, 81.32, 103.31, 109.56, 110.42, 117.26, 127.73, 132.80, 133.41, 141.33, 144.34, 147.85, 150.81, 153.05, 155.74.

7-But-2-ynyl-3-(3-methoxy-benzyl)-1-methyl-8-(4-methylene-piperidin-1-yl) 3,4,5,7 tetrahydro-purine-2, 6-dione (5b).

Melting point: 178 - 180 ^{O}C. Reaction time: 2.0 h. Percent yield: 75%. Mass: [ES]: Calculated – 435.23, Found – 434.70. ^{1}H NMR (400 MHz, DMSO, δ ppm): 1.78 (s, 3H, -CH_3), 2.35 (d, 1H, -CH), 2.36 (t, 4H, -CH_2), 3.37 (s, 3H, -CH_3), 3.40 (d, 1H, CH_2), 3.41 (t, 4H, -CH_2), 3.71 (s, 3H, -OCH_3), 4.80 (s, 2H, -CH_2), 4.91 (d, 2H, =CH), 5.00 (s, 2H, -CH_2), 6.79 – 7.22 (m, 4H, Ar-H). ^{13}C NMR (400 MHz, DMSO, δ ppm): 3.047, 29.49, 33.56, 35.53, 40.12, 50.77, 54.94, 73.73, 81.19, 103.32, 109.54, 111.99, 113.43, 119.46, 129.30, 139.40, 144.39, 147.55, 150.81, 153.21, 155.69, 159.59.

3-Benzyl-7-but-2-ynyl-1-methyl-8-(4-methylene-piperidin-1-yl)-3,4,5,7 tetrahydropurine-2,6-dione (5c).

Melting point: 215 ^{O}C. Reaction time: 1.0 h. Percent yield: 78%. Mass: [ES]-: Calculated – 405.22, Found – 404.77. ^{1}H NMR (400 MHz, DMSO, δ ppm): 1.79 (s, 3H, -CH_3), 2.34 (d, 1H, -CH), 2.36 (t, 4H, -CH_2), 3.37 (s, 3H, -CH_3), 3.38 (d, 1H, CH_2), 3.41 (t, 4H, -CH_2), 4.80 (s, 2H, -CH_2), 4.91 (d, 2H, =CH), 5.03 (s, 2H, -CH_2), 7.22 – 7.31 (m, 5H, Ar-H). ^{13}C NMR (400 MHz, DMSO, δ ppm): 3.04, 29.45, 33.56, 35.52, 43.34, 50.76, 73.71, 81.19, 103.32, 109.50, 126.91, 127.44, 128.19, 137.84, 144.37, 147.50, 150.79, 153.21, 155.64.

7-But-2-ynyl-3-(3-chloro-benzyl)-1-methyl-8-(4-methylene-piperidin-1-yl)3,4,5,7 tetrahydro-purine-2,6-dione (5d).

Melting point: 282 - 283 ^{O}C. Reaction time: 1.0 h. Percent yield: 76%. Mass: [ES]: Calculated – 439.18, Found – 438.68. ^{1}H NMR (400 MHz, DMSO, δ ppm): 1.79 (s, 3H, -CH_3), 2.33 (d, 1H, -CH), 2.36 (t, 4H, -CH_2), 3.34 (s, 3H, -CH_3), 3.39 (d, 1H, CH_2), 3.42 (t, 4H, -CH_2), 4.80 (s, 2H, -CH_2), 4.91 (d, 2H, =CH), 5.02 (s, 2H, -CH_2), 7.24 – 7.35 (m, 4H, Ar-H). ^{13}C NMR (400 MHz, DMSO, δ ppm): 3.06, 29.52, 33.57, 35.57, 40.12, 42.99, 50.77, 81.24, 103.34, 109.55, 126.22, 127.00, 127.31, 130.15, 132.88, 140.39, 144.37, 147.69, 150.81, 153.56, 155.72.

7-But-2-ynyl-3-(4-chloro-benzyl)-1-methyl-8-(4-methylene-piperidin-1-yl)3,4,5,7 tetrahydro-purine-2,6-dione (5e)

Melting point: 238 - 240 ^{O}C. Reaction time: 1.5 h. Percent yield: 80%. Mass: [ES]: Calculated – 439.18, Found – 438.68. ^{1}H NMR (400 MHz, DMSO, δ ppm): 1.70 (s, 3H, -CH_3), 2.30 (d, 1H, -CH), 2.32 (t, 4H, -CH_2), 3.32 (s, 3H, -CH_3), 3.38 (d, 1H, CH_2), 3.40 (t, 4H, -CH_2), 4.83 (s, 2H, -CH_2), 4.97 (d, 2H, =CH), 5.08 (s, 2H, -CH_2), 7.20 – 7.39 (m, 4H, Ar-H). 13C NMR (400 MHz, DMSO, δ ppm): 3.06, 29.50, 33.57, 35.57, 40.10, 42.99, 50.74, 81.28, 103.34, 109.55, 126.22, 127.05, 127.31, 130.13, 132.88, 140.39, 144.30, 147.69, 150.81, 153.56, 155.75.

7-But-2-ynyl-3-(2-chloro-benzyl)-1-methyl-8-(4-methylene-piperidin-1-yl)3,4,5,7 tetrahydro-purine-2,6-dione (5f)

Melting point: 231 - 232 ^{O}C. Reaction time: 1.5 h. Percent yield: 81%. Mass: [ES]: Calculated – 439.18, Found – 438.70. ^{1}H NMR (400 MHz, DMSO, δ ppm): 1.76 (s, 3H, -CH_3), 2.32 (d, 1H, -CH), 2.38 (t, 4H, -CH_2), 3.39 (s, 3H, -CH_3), 3.43 (d, 1H, CH_2), 3.46 (t, 4H, -CH_2), 4.84 (s, 2H, -CH_2), 4.92 (d, 2H, =CH), 5.25 (s, 2H, -CH_2), 7.28 (d, 1H, Ar-H), 7.42 (dd, 1H, Ar-H), 7.61 (dd, 1H, Ar-H), 7.80 (d, 1H, Ar-H). ^{13}C NMR (400 MHz, DMSO, δ ppm): 3.18, 29.51,

33.55, 35.61, 41.92, 50.78, 81.30, 103.32, 109.54, 110.45, 117.20, 127.70, 132.87, 133.45, 141.34, 144.36, 147.81, 150.88, 153.02, 155.70.

7-But-2-ynyl-3-(2,4-dichloro-benzyl)-1-methyl-8-(4-methylene-piperidin-1-yl)3,4,5,7-tetrahydro-purine-2,6-dione (5g)

Melting point: 260 - 261 ^{O}C. Reaction time: 2.0 h. Percent yield: 80%. Mass: [ES]: Calculated – 473.14, Found – 449.67.^{1}H NMR (400 MHz, DMSO, δ ppm): 1.70 (s, 3H, -CH_3), 2.34 (d, 1H, -CH), 2.38 (t, 4H, -CH_2), 3.37 (s, 3H, -CH_3), 3.38 (d, 1H, CH_2), 3.48 (t, 4H, -CH_2), 4.83 (s, 2H, -CH_2), 4.98(d, 2H, =CH), 5.09 (s, 2H, -CH_2), 7.21 – 7.39 (m, 3H, Ar-H). ^{13}C NMR (400 MHz, DMSO, δ ppm): 3.16, 29.53, 33.42, 35.52, 40.12, 42.99, 50.77, 81.24, 103.34, 109.55, 126.22, 127.00, 127.31, 130.15, 132.46, 140.39, 144.14, 147.69, 150.81, 153.56, 155.46.

7-But-2-ynyl-1-methyl-8-(4-methylene-piperidin-1-yl)-3-(3-nitro-benzyl)3,4,5,7 tetrahydro purine-2,6-dione (5h).

Melting point: 210 -211 ^{O}C. Reaction time: 1.0 h. Percent yield: 82%. Mass: [ES]-: Calculated – 450.20, Found – 449.67. ^{1}H NMR (400 MHz, DMSO, δ ppm): 1.79 (s, 3H, -CH_3), 2.33 (d, 1H, -CH), 2.36 (t, 4H, -CH_2), 3.38 (s, 3H, -CH_3), 3.41 (d, 1H, CH_2), 3.42 (t, 4H, -CH_2), 4.80 (s, 2H, -CH_2), 4.91 (d, 2H, =CH), 5.14 (s, 2H, -CH_2), 7.59 (d, 1H, Ar-H), 7.77 (d, 1H, Ar-H), 8.13 (dd, 2H, Ar-H), 8.11 (d, 1H, Ar-H). ^{13}C NMR (400 MHz, DMSO, δ ppm): 3.03, 29.52, 33.55, 35.59, 40.12, 42.96, 50.73, 73.65, 81.28, 103.30, 109.54, 122.31, 129.84, 134.41, 140.09, 144.34, 147.70, 147.76, 150.82, 153.13, 155.73.

7-But-2-ynyl-1-methyl-8-(4-methylene-piperidin-1-yl)-3-(2-nitro-benzyl)-3,4,5,7 tetrahydro-purine-2,6-dione (5i).

Melting point: 224-226 ^{O}C. Reaction time: 0.5 h. Percent yield: 85%. Mass: [ES]-: Calculated – 450.20, Found – 449.60. ^{1}H NMR (400 MHz, DMSO, δ ppm): 1.78 (s, 3H, -CH_3), 2.30 (d, 1H, -CH), 2.36 (t, 4H, -CH_2), 3.39 (s, 3H, -CH_3), 3.42 (d, 1H, CH_2), 3.44 (t, 4H, -CH_2), 4.82 (s, 2H, -CH_2), 4.90 (d, 2H, =CH), 5.23 (s, 2H, -CH_2), 7.24 (d, 1H, Ar-H), 7.43 (dd, 1H, Ar-H), 7.60 (dd, 1H, Ar-H), 7.83 (d, 1H, Ar-H). ^{13}C NMR (400 MHz, DMSO, δ ppm): 3.16, 29.50, 33.56, 35.60, 41.90, 50.75, 81.31, 103.30, 109.54, 110.40, 117.28, 127.71, 132.82, 133.40, 141.32, 144.30, 147.84, 150.80, 153.05, 155.70.

7-But-2-ynyl-1-methyl-8-(4-methylene-piperidin-1-yl)-3-(4-nitro-benzyl)-3,4,5,7 tetrahydro-purine-2,6-dione (5j).

Melting point: 2016-218 ^{O}C. Reaction time: 0.5 h. Percent yield: 85%. Mass: [ES]: Calculated – 450.20, Found – 449.62. ^{1}H NMR (400 MHz, DMSO, δ ppm): 1.77 (s, 3H, -CH_3), 2.35 (d, 1H, -CH), 2.34 (t, 4H, -CH_2), 3.32 (s, 3H, -CH_3), 3.37 (d, 1H, CH_2), 3.41 (t, 4H, -CH_2), 4.83 (s, 2H, -CH_2), 4.95 (d, 2H, =CH), 5.03 (s, 2H, -CH_2), 7.21 – 7.38 (m, 4H, Ar-H). ^{13}C NMR (400 MHz, DMSO, δ ppm): 3.04, 29.50, 33.55, 35.57, 40.10, 42.97, 50.75, 81.22, 103.32, 109.53, 126.20, 127.05, 127.30, 130.14, 132.89, 140.37, 144.34, 147.67, 150.82, 153.57, 155.70.

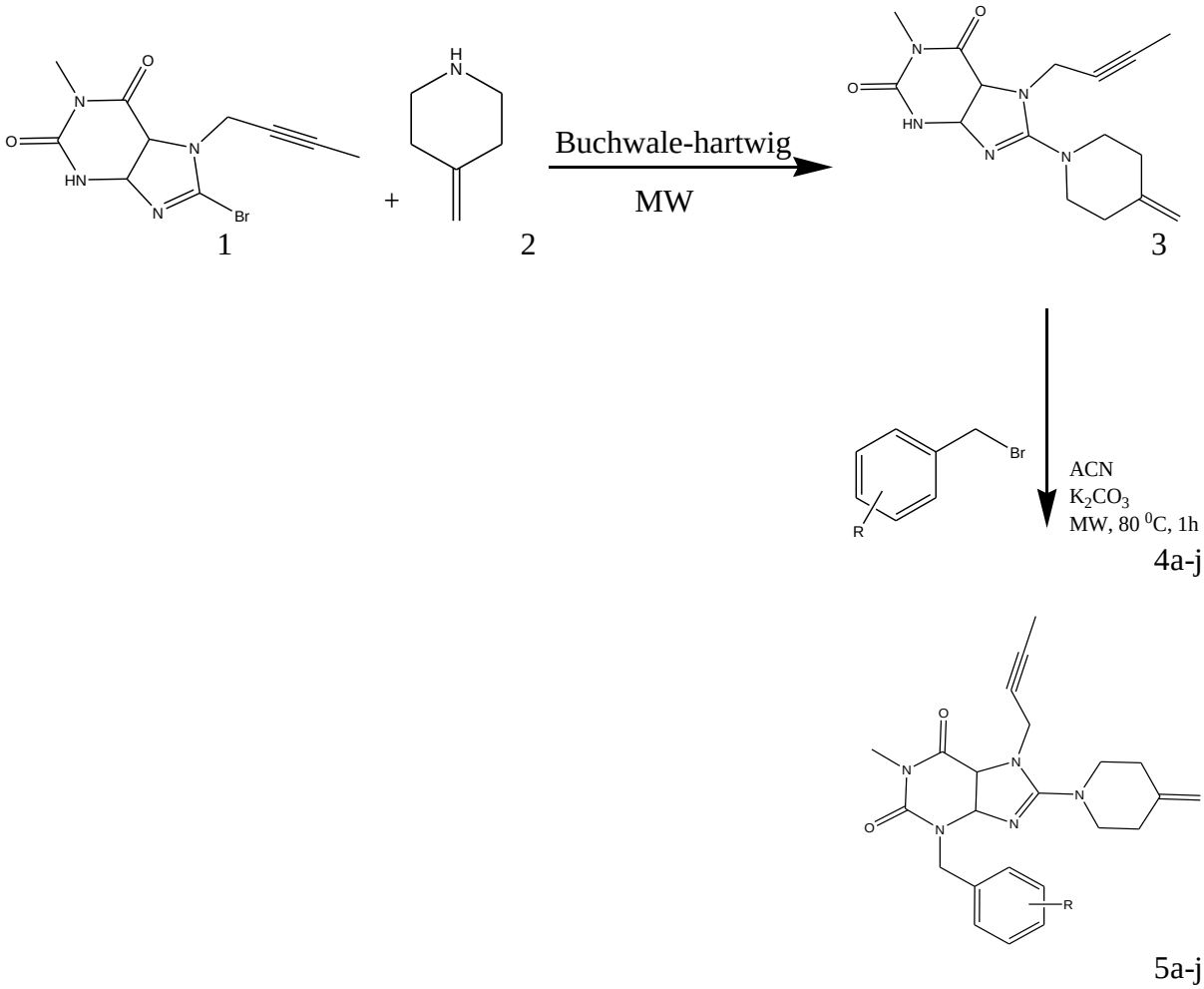
2. RESULT AND DISCUSSION

Successful two-step synthesis of 3-(Substituted)Benzyl-7-but-2-ynyl-1-methyl-8-(4methylene-piperidin-1-yl)-3,4,5,7-tetrahydro-purine-2,6-dione (5a-j) by reaction of 8Bromo-7-but-2-ynyl-1-methyl-3,4,5,7-tetrahydro-purine-2,6-dione 1 was treated with 4-Methylene-piperidine 2 by using Buchwald-Hartwig coupling to form intermediate 7-But-2-ynyl-1-methyl-8-(4-methylene-piperidin-1-yl)-3,4,5,7-tetrahydro-purine-2,6dione 3, once formed

intermediate 3 was reacted with substituted benzyl bromides (4a-j) using potassium carbonate gives aimed derivatives under microwave condition (Scheme 1, table 2).

For the synthesis of 7-But-2-ynyl-1-methyl-8-(4-methylene-piperidin-1-yl)-3,4,5,7tetrahydro-purine-2,6-dione 3 using Buchwald-Hartwig coupling solvent and catalyst optimization was done and observed results was enlisted in table 1.

During the optimization study, we found that first-generation, second-generation and third-generation catalysts were useful for the present synthesis with fluctuations in time yields Table 1. Mostly this study found that third third-generation catalyst for the amination reaction works better than other catalysts, so we have used the same for the synthesis of remaining derivatives. Also, during this study, we have found that electron-withdrawing substituent gives a good percent of yield within the short reaction time.



1 2 3 4a-j 5a-j

Scheme 1. Synthesis of 3-(Substituted)Benzyl-7-but-2-ynyl-1-methyl-8-(4methylene-piperidin-1-yl)-3,4,5,7-tetrahydro-purine-2,6-dione (5a-j).

Used synthetic strategy for the synthesis of 3-(Substituted)Benzyl-7-but-2-ynyl-1methyl-8-(4-methylene-piperidin-1-yl)-3,4,5,7-tetrahydro-purine-2,6-dione (5a-j) was very useful to produce a Purine based compounds. During the synthesis, we observed that the substitution of benzyl bromides adversely affected the rate of reaction and percentage of product. If electron withdrawing groups like –CN and $–NO_2$ present as substituents on benzyl bromide they make benzyl –CH2 more electrophilic due to resonance and help for SN^2 type of substitution faster. While electron-releasing substituent does its opposite and retards the rate of reaction. This

substitution effect not only affects the reaction time but also affects the per cent isolated yields of the synthesized derivatives. We observed fluctuation in the reaction time and percent isolated yield and mentioned.

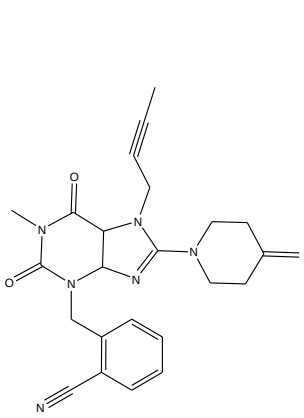
Table 1. Catalyst and solvent optimization study for Buchwald-Hartwig coupling to synthesis of 3.

Entry	Catalyst	Mol%	Solvent	Reaction time	% Yield
3	Pd G1	10	Toluene	1.5	30
3	Pd G2	10	Toluene	2.0	32
3	Pd G3	10	Toluene	0.5	25
3	Pd G1	10	t-butanol	1.0	20
3	Pd G2	10	t-butanol	0.5	43
3	Pd G3	10	t-butanol	1.0	70
3	Pd G1	10	DMF	3.0	45
3	Pd G2	10	DMF	2.0	42
3	Pd G3	10	DMF	2.5	38

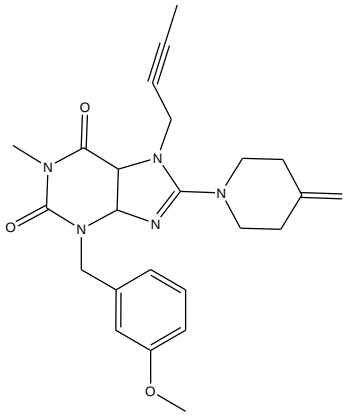
(Pd G1) = (Pd [P (o-Tolyl) $_{3-2}$) – First-generation catalyst
(Pd G2) = Pd (dba) $_2$ - Second generation catalyst
(Pd G3) = BrettPhos - Third-generation catalyst.

All the synthesized compounds were purified by flash column chromatography and confirmed by using spectral techniques Table 2. Mass spectral analysis of compound **5a** at negative mode shows 429.77 as molecular ion peak and its calculated mass is 430.21. ^{1}H NMR analysis of the same compound using DMSO solvent at 400 MHz, δ 1.79 (s, 3H, -CH_3), 2.34 (d, 1H, -CH), 2.35 (t, 4H, -CH_2), 3.38 (s, 3H, -CH_3), 3.41 (d, 1H, -CH_2), 3.42 (t, 4H, -CH_2), 4.81 (s, 2H, -CH_2), 4.91 (d, 2H, =CH), 5.21 (s, 2H, CH_2), 7.25 (d, 1H, Ar-H), 7.44 (dd, 1H, Ar-H), 7.61 (dd, 1H, Ar-H), 7.82 (d, 1H, ArH) number of protons and its splitting pattern also confirms the formation of compound. Carbon NMR of 5a at 400 MHz using DMSO solvent showing δ values at 3.06, 29.54, 33.58, 35.61, 41.90, 50.71, 73.65, 81.32, 103.31, 109.56, 110.42, 117.26, 127.73, 132.80, 133.41, 141.33, 144.34, 147.85, 150.81, 153.05, 155.74 these 21 different sets of carbons also confirmed formation of aimed compound.

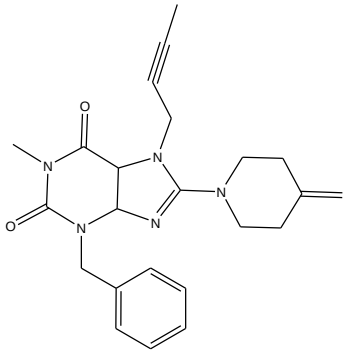
Table 2. Substrate scope for the synthesis of 5a-j.



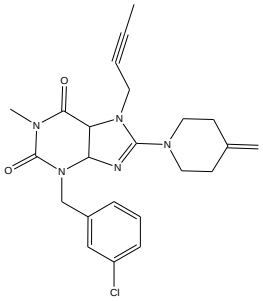
5a



5b



5c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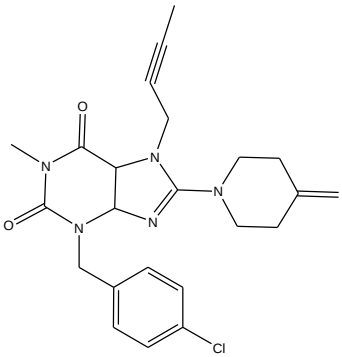
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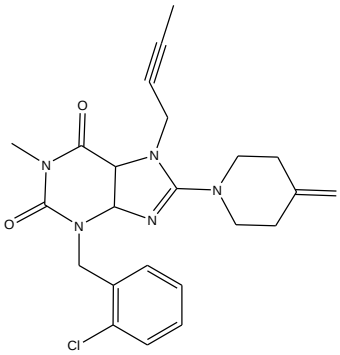
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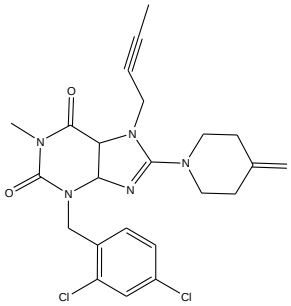
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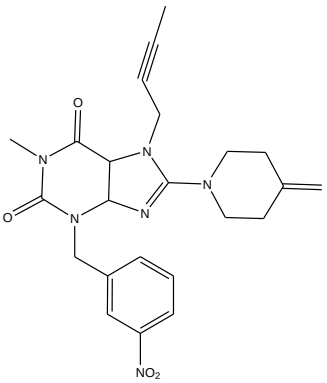
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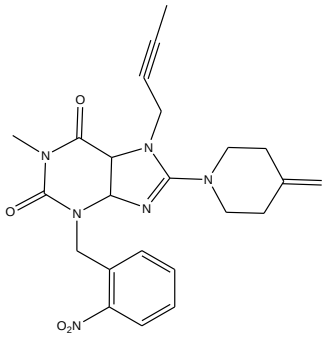
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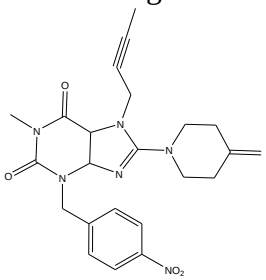
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3. CONCLUSION

In summary, by using simple and easily available material with strong two-step microwave irradiated synthetic pathway we have successfully synthesized ten derivatives of 3-(Substituted)Benzyl-7-but-2-ynyl-1-methyl-8-(4-methylenepiperidin-1-yl)-3,4,5,7-tetrahydro-purine-2,6-dione. We have found that BuchwaldHartwig in microwave irradiation for the amination reaction works potentially. The present synthetic route gives 75 to 85 percent of isolated yields.

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