Journal of Harbin Engineering University
ISSN: 1006-7043

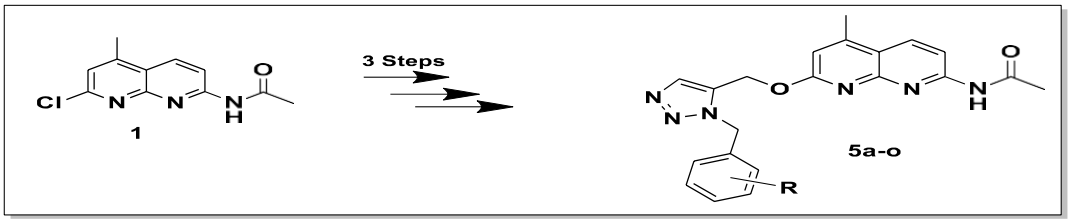
Vol 44 No. 7
July 2023

Design, Synthesis and Characterization of *N*-(7-((Substituted-1*H*-1,2,3-triazol-5-yl) methoxy)-5-methyl-1,8-naphthyridin-2-yl) acetamide Scaffolds

[1] Prashanth Raja Peddapyata, [1]*Jagadeesh Kumar Ega
Department of Chemistry, Chaitanya Deemed to be University, Hanumakonda, and Telangana 506001
*Email- jkjagadeeshkumare@gmail.com

Abstract- Herein, *N*-(7-chloro-5-methyl-1,8-naphthyridin-2-yl) acetamide **(1)** with Pd_2dba_3/Bippyphos catalytic amount, $CsOH{\cdot}H_2O$, and THF to give *N*-(7-hydroxy-5-methyl-1,8-naphthyridin-2-yl) acetamide **(2).** It is treated with propargyl bromide, K_2CO_3/DMF under reflux to yield *N*-(5-methyl-7-(prop-2-yn-1-yloxy)-1,8-naphthyridin-2-yl) acetamide **(3)** *viz O*- propargylation. Now compound 3 is reacted with NaN_3,TEA, various substituted benzyl bromides **(4a-o)** with sodium ascorbate,$CuSO_4.5H_2O$ namely Sharpless catalyst to give desired *N*-(7-((Substituted-1*H*-1,2,3-triazol-5-yl)methoxy)-5-methyl-1,8-naphthyridin-2-yl)acetamides **(5a-o)** with promising yields as shown in Scheme I and Fig:4. The structures of the products further confirmed by spectral analysis**.**

Keywords: Bippyphos, $Pd_2(dba)_3$, propargyl bromide, Sharpless catalyst, 1,2,3-triazole



Graphical Abstract

Introduction

Tris(dibenzylideneacetone)dipalladium(0) is a canonical precursor widely used to generate catalytically active palladium species for diverse applications. Typically, $Pd_2(dba)_3$ is considered as a source of soluble Pd(0) complexes formed upon interaction with suitable ligands and substitution of dba. Another important area is the usage of $Pd_2(dba)_3$ as a starting material for generation of more complex Pd-containing assemblies, cluster compounds,[1] potential catalysts, [2] and synthesis and study of plausible intermediates of the catalytic cycles. [3-4]

Phosphine ligands it was found that addition of excess phosphine to $Pd_2(dba)_3$ readily yields the complex Pd(dba)- $(PR_3)_2$. [5-6] This complex can either lose the remaining dba ligand (slow), furnishing a catalytically active low-ligated $Pd(PR_3)_2$ complex, or participate in oxidative addition, leading directly to catalytic intermediates fastly.

The ubiquitous utilization of $[Pd_2(dba)_3]$ in transition-metal catalysis on one hand has been governed by its simple preparation from readily available Pd(II) salts and on the other hand by its relative stability in air and convenient generation of desired PdLn species is depicted below in Fig: 1. [7]

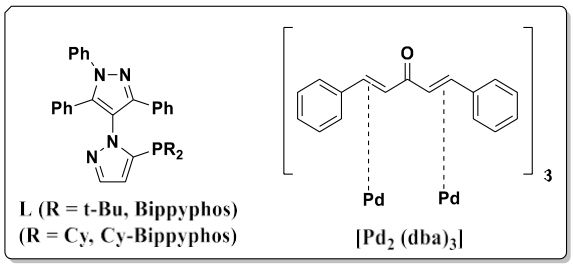


Fig: 1 Structures of Bippyphos and $[Pd_2(dba)_3]$

Aryl alcohols are among the most important synthons for the construction of a

variety of naturally occurring and biologically active products. [8-9] The metal-catalyzed cross-coupling of aryl halides and hydroxide anions represents a conceptually attractive method for the preparation of phenols. [10-11]

Difficult C-O bond reductive elimination owing to the small size of the hydroxide group; and uncontrolled arylation of the target phenol to afford the undesired diaryl ether. While copper catalysts have been identified for the hydroxylation of aryl halides, [12] the need for high metal/ligand loadings and harsh reaction conditions, as well as their typically poor performance with synthetically useful aryl chlorides, [13] represent important practical drawbacks. In this context, the use of palladium-based catalystsfor such transformations has been shown to offer significant reactivity advantages, including increased scope, lower catalyst loadings, and milder reaction conditions. [14]

Nevertheless these developments, the relative scarcity of palladium-based catalysts that have proven effective in promoting the hydroxylation of hetero - aryl halides provides motivation for further investigation. From a practical perspective, the development of alternative catalysts based on a single commercially available palladium precursor/ligand pair, which offers broad scope in the hetero aryl halide under mild conditions and without the need for microwave irradiation is of particular interest.

The identification of catalyst systems of this type that prove capable of operating under air using bench-top synthetic protocols would represent an important advance in terms of enabling the broader uptake of such hydroxylation protocols by synthetic chemists. Herein we report on such a catalyst system comprised of Pd_2dba_3 and Singer's Bippyphos [15] ligand (L, Fig.1).

The medicinal properties of naphthyridines and their derivatives are the majordriving forces to synthesize them on a large scale. Among naphthyridines, 1,8-naphthyridines (**1**) and their derivatives are used as drugs for antimicrobial activities (nalidixic acid, **2**), [16-18] HIV inhibitor (**3**) [19] shown in Fig: 2 below.

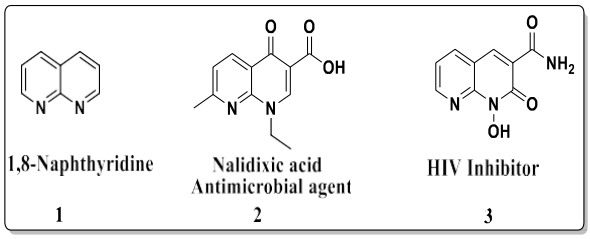


Fig: 2 Biologically active 1,8-naphthyridines

Triazole includes two carbon and three nitrogen atoms comprising a five membered heterocyclic ring. 1,2,3-Triazoles are of key importance in medicinal chemistry owing to its broad biological spectrum such as antimicrobial [22-25] , antioxidant [26-28] , anti- diabetic [29-30], anticancer [31–34] , anti-inflammatory [35], anti-tubercular [36-37], antiviral [38-39], antimalarial [40 -41] agents. Herein, we are going to report the naphthyridines fused Triazoles shown below.

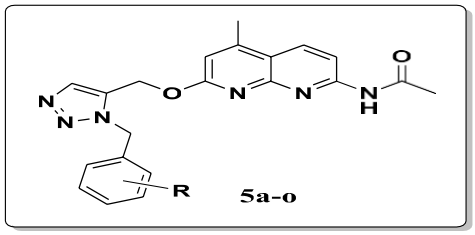
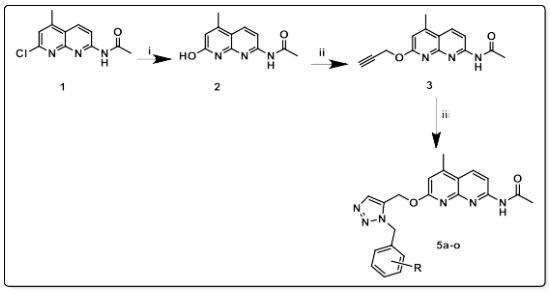


Fig: 3 Designed Target

Results and Discussions

At first *N*-(7-chloro-5-methyl-1,8- naphthyridin-2-yl) acetamide **(1)** Pd_2dba_3/Bippyphos, $CsOH{\cdot}H_2O$, and THF at 65^0C 8-12 h to give *N*-(7-hydroxy-5-methyl-1,8- naphthyridin-2-yl)acetamide **(2).** Compound 2 is treated with propargyl bromide, K_2CO_3/DMF at 70°C, up to 24 h, under reflux to yield *N*-(5-methyl-7-(prop-2-yn-1-yloxy)-1,8-naphthyridin-2- yl)acetamide**(3)** *viz* O-propargylation. Now compound 3 is reacted with NaN_3,TEA, various substituted benzyl bromides **(4a-o)** at room temperature at 24 h by means of Sharpless catalyst3+2 cyclo addition to give desired *N*-(7- ((Substituted-1*H*-1,2,3-triazol-5-yl)methoxy)-5-methyl-1,8-naphthyridin-2-yl)acetamides **(5a-o)** with promising yields as shown in **Scheme I** .The structures of the products

have been elucidated on the basis of ^{1}H NMR, ^{13}C NMR, MS data and elemental analysis are displayed in **Table II to IV.**



Reagents and conditions: (i) Pd_2dba_3, L, $CsOH{\cdot}H_2O$, aryl halide and THF (65^0C) or 1,4-dioxane ($110\ ^0C$); **(ii)** propargyl bromide, K_2CO_3, DMF, 70 °C, 24 h, reflux; **(iii)** NaN_3,TEA, various substituted benzyl bromides **(4a-o),** sodium ascorbate, $CuSO_4$.$5H_2O$, rt, 24 h, 70–88%.

Scheme 1

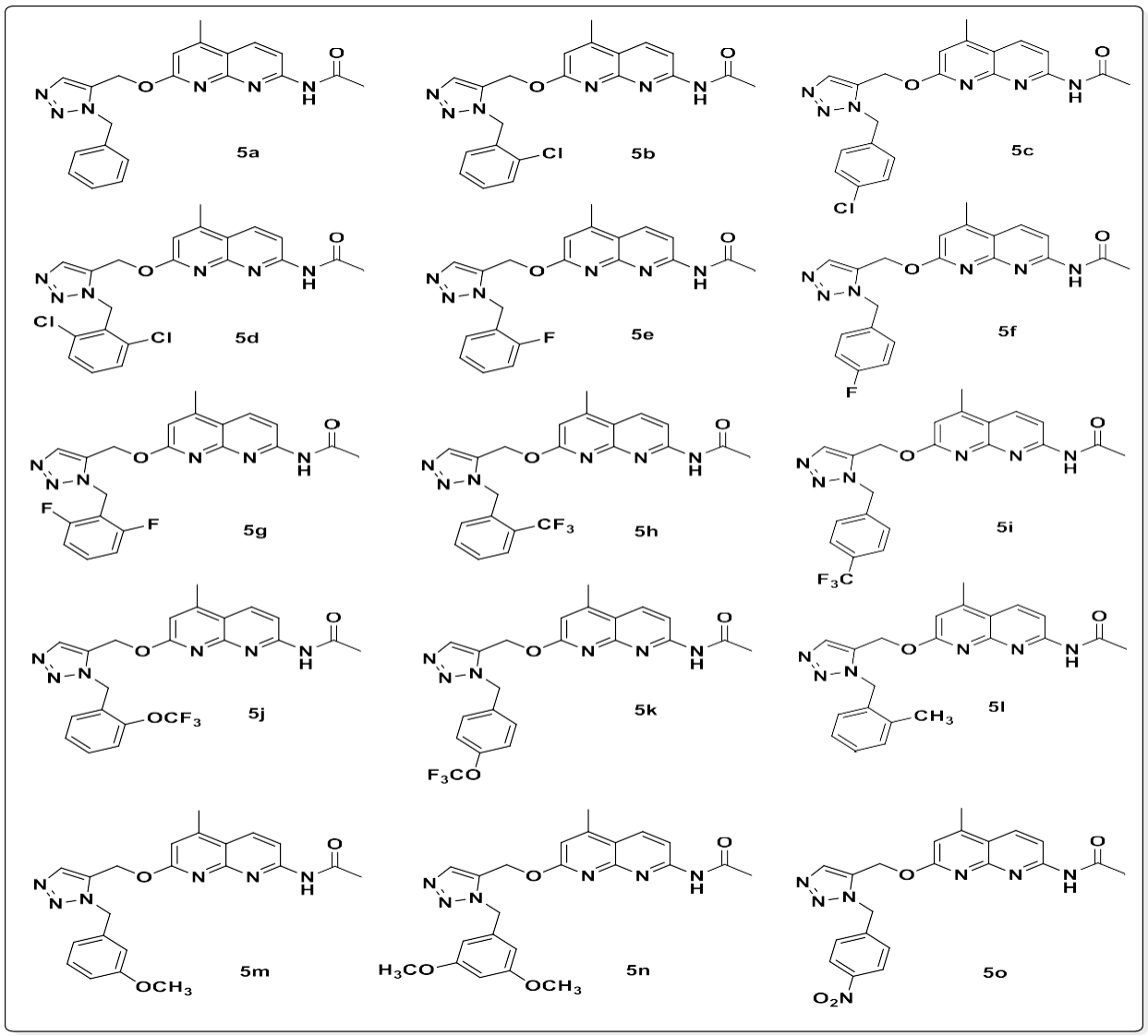


Fig: 4 Derivatives of target compounds 5a-o

Table I: IUPAC Names of compound 5a-o

Entry	IUPAC Name
5a	N-(7-((1-benzyl-1*H*-1,2,3-triazol-5-yl)methoxy)-5-methyl-1,8-naphthyridin-2-yl)acetamide
5b	*N*-(7-((1-(2-chlorobenzyl)-1*H*-1,2,3-triazol-5-yl)methoxy)-5-methyl-1,8-naphthyridin-2-yl)acetamide
5c	*N* -(7-((1-(4-chlorobenzyl)-1 *H* -1,2,3-triazol-5-yl)methoxy)-5-methyl-1,8-naphthyridin-2-yl)acetamide
5d	*N* -(7-((1-(2,6-dichlorobenzyl)-1 *H* -1,2,3-triazol-5-yl)methoxy)-5-methyl-1,8-naphthyridin-2-yl)acetamide
5e	*N* -(7-((1-(2-fluorobenzyl)-1 *H* -1,2,3-triazol-5-yl)methoxy)-5-methyl-1,8-naphthyridin-2-yl)acetamide
5f	*N* -(7-((1-(4-fluorobenzyl)-1 *H* -1,2,3-triazol-5-yl)methoxy)-5-methyl-1,8-naphthyridin-2-yl)acetamide
5g	*N* -(7-((1-(2,6-difluorobenzyl)-1 *H* -1,2,3-triazol-5-yl)methoxy)-5-methyl-1,8-naphthyridin-2-yl)acetamide
5h	*N* -(5-methyl-7-((1-(2-(trifluoromethyl)benzyl)-1 *H* -1,2,3-triazol-5-yl)methoxy)-1,8-naphthyridin-2-yl)acetamide
5i	*N* -(5-methyl-7-((1-(4-(trifluoromethyl)benzyl)-1 *H* -1,2,3-triazol-5-yl)methoxy)-1,8-naphthyridin-2-yl)acetamide
5j	*N* -(5-methyl-7-((1-(2-(trifluoromethoxy)benzyl)-1 *H* -1,2,3-triazol-5-yl)methoxy)-1,8-naphthyridin-2-yl)acetamide
5k	*N* -(5-methyl-7-((1-(4-(trifluoromethoxy)benzyl)-1 *H* -1,2,3-triazol-5-yl)methoxy)-1,8-naphthyridin-2-yl)acetamide
5l	*N* -(5-methyl-7-((1-(2-methylbenzyl)-1 *H* -1,2,3-triazol-5-yl)methoxy)-1,8-naphthyridin-2-yl)acetamide
5m	*N* -(7-((1-(3-methoxybenzyl)-1 *H* -1,2,3-triazol-5-yl)methoxy)-5-methyl-1,8-naphthyridin-2-yl)acetamide
5n	*N* -(7-((1-(3,5-dimethoxybenzyl)-1 *H* -1,2,3-triazol-5-yl)methoxy)-5-methyl-1,8-naphthyridin-2-yl)acetamide
5o	*N* -(5-methyl-7-((1-(4-nitrobenzyl)-1 *H* -1,2,3-triazol-5-yl)methoxy)-1,8-naphthyridin-2-yl)acetamide

Table II: Yield (%) and Mass values of compound 5a-o

Entry	R	MF	Yield (%)	ESI $[M+H]^+$
5a	H	$C_{21}H_{20}N_6O_2$	88	389.16
5b	2-Cl	$C_{21}H_{19}ClN_6O_2$	70	423.13
5c	3-Cl	$C_{21}H_{19}ClN_6O_2$	81	423.13
5d	2,6- di-Cl	$C_{21}H_{18}Cl_2N_6O_2$	71	457.09
5e	2-F	$C_{21}H_{19}FN_6O_2$	83	4076.16
5f	4-F	$C_{21}H_{19}FN_6O_2$	86	405.18
5g	2,6-di-F	$C_{21}H_{18}F_2N_6O_2$	82	425.15
5h	2-CF_3	$C_{22}H_{19}F_3N_6O_2$	87	457.15
5i	4-CF_3	$C_{22}H_{19}F_3N_6O_2$	72	457.15

5j	2-OCF_3	$C_{22}H_{19}F_3N_6O_3$	83	473.15
5k	4-OCF_3	$C_{22}H_{19}F_3N_6O_3$	84	473.15
5l	2-CH_3	$C_{22}H_{22}N_6O_2$	86	403.18
5m	3-OCH_3	$C_{22}H_{22}N_6O_3$	83	419.18
5n	3,5- di-OCH_3	$C_{23}H_{24}N_6O_4$	81	449.19
5o	4-NO_2	$C_{21}H_{19}N_7O_4$	85	434.15

Table III: ^{1}H NMR and ^{13}CNMR chemical shift values of compound 5a-o

Entry	^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm)	^{13}CNMR(100 MHz, $CDCl_3$) δ(ppm)
5a	8.34 (dd, *J* = 27.8, 7.5 Hz, 2H), 7.39 – 7.10 (m, 6H), 6.85 (d, *J* = 22.9 Hz, 2H), 5.48 (s, 1H), 5.25 (s, 2H), 4.97 (s, 1H), 2.76 (s, 3H), 2.23 (s, 3H).	170.47,167.92,157.66,151.67,148.11, 136.08, 132.84,128.91,128.53,127.80,121.00, 111.85, 111.07, 55.38, 48.11, 23.79, 21.50.
5b	8.37 (d, *J* = 7.5 Hz, 1H), 8.32 (d, *J* = 7.5 Hz, 1H), 7.39 – 7.01 (m, 5H), 6.84 (d, *J* = 29.9 Hz, 2H), 5.57 (s, 1H), 5.35 (s, 2H), 5.05 (s, 1H), 2.74 (s, 3H), 2.23 (s, 3H).	170.47,167.92,157.66,151.67,148.11,135.58,133.79,133.44,132.84,130.58,129.68,128.37, 127.77, 127.04, 121.00, 111.85, 111.07, 55.38 , 49.57 , 23.79, 21.50.
5c	8.36 (s, 2H), 7.37 – 7.07 (m, 5H), 6.89 (d, *J* = 63.6 Hz, 2H), 5.48 (s, 1H), 5.25 (s, 2H), 4.96 (s, 1H), 2.76 (s, 3H), 2.23 (s, 3H).	170.47,167.92,157.66,151.67,148.11, 135.58, 134.60,133.77,132.84,130.33,129.11,127.77,121.00,111.85,111.07,55.38,48.11,23.79, 21.50.
5d	8.43 (dd, *J* = 28.8, 7.5 Hz, 2H), 7.23 (s, 1H), 7.10 (dd, *J* = 27.9, 15.0 Hz, 4H), 6.90 (s, 1H), 5.51 – 4.93 (m, 4H), 2.75 (s, 3H), 2.25 (s, 3H).	170.47,167.92,157.66,151.67,148.11, 135.58, 134.82,132.84,131.68,129.12,127.77, 121.00, 111.85, 111.07, 55.38, 52.41, 23.79, 21.50.
5e	8.35 (dd, *J* = 22.9, 7.5 Hz, 2H), 7.14 (d, *J* = 7.3 Hz, 3H), 7.01 – 6.92 (m, 2H), 6.87 (s, 1H), 6.80 (s, 1H), 5.39 (s, 1H), 5.34 (s, 2H), 5.04 (s, 1H), 2.74 (s, 3H), 2.23 (s, 3H).	170.47,167.92,162.15,160.05,157.66,151.67, 148.11,135.58,132.84,131.81,128.51, 127.77, 125.92,124.97,121.00,117.79,111.85,111.07, 55.38, 49.60, 23.79, 21.50.
5f	8.36 (s, 2H), 7.31 – 7.23 (m, 2H), 7.16 (s, 1H), 7.02 – 6.93 (m, 3H), 6.83 (s, 1H), 5.47 (s, 1H), 5.25 (s, 2H), 4.95 (s, 1H), 2.76 (s, 3H), 2.23 (s, 3H).	170.47,167.92,162.98,160.89,157.66, 151.67, 148.11,135.58,132.84,130.70, 127.77, 121.00 ,115.06, 111.85, 111.07, 55.38 , 48.11, 23.79, 21.50.
5g	8.37 (d, *J* = 7.5 Hz, 1H), 8.27 (d, *J* = 7.5 Hz, 1H), 7.15 (d, *J* = 23.5 Hz, 2H), 6.82 (s, 4H), 5.42 – 5.12 (m, 4H), 2.74 (s, 3H), 2.23 (s, 3H).	170.47,167.92,165.58,163.42,157.66, 151.67, 148.11,135.58,132.84,130.17,127.77, 121.00, 119.16, 114.32, 111.85, 111.07, 55.38, 52.21, 23.79, 21.50.
5h	8.37 (d, *J* = 7.5 Hz, 1H), 8.30 (d, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 8.9 Hz, 1H), 7.25 (d, *J* = 7.4 Hz, 1H), 7.22 – 7.11 (m, 4H), 6.79 (s, 1H), 5.70 (s, 1H), 5.61 (s, 1H), 5.26 (s, 2H), 2.74 (s, 3H), 2.25 (s, 3H).	170.47,167.92,157.66,151.67,148.11, 135.58, 132.74,132.61,128.16,127.77,127.11, 126.34, 126.07,123.97,121.87,121.00,111.85, 111.07, 55.38, 45.83, 23.79, 21.50.
5i	8.37 (d, *J* = 4.8 Hz, 2H), 7.45 (d, *J* = 7.5 Hz, 2H), 7.25 (s, 2H), 7.16 (s, 1H), 6.89 (s, 1H), 6.83 (s, 1H), 5.48 (s, 1H), 5.25 (s, 2H), 5.00 (s, 1H), 2.76 (s, 3H), 2.23 (s, 3H).	170.47,167.92,157.66,151.67,148.11, 139.71, 135.58,132.84,130.59,127.77,127.60, 127.32, 125.51,123.41,121.32,121.00,111.85, 111.07, 55.38, 48.11, 23.79, 21.50.
5j	δ 8.37 (d, *J* = 7.5 Hz, 2H), 7.25 (s, 1H), 7.15 (t, *J* = 18.3 Hz, 3H), 6.99 (d, *J* = 9.6 Hz, 2H), 6.78	170.47,167.92,157.66,153.46, 151.67,148.11, 135.58,132.84,132.58,130.01,128.66, 127.77,

	(s, 1H), 6.07 (s, 1H), 5.18 (s, 3H), 2.74 (s, 3H), 2.23 (s, 3H)	126.47,125.71,123.61,121.52,121.00,119.42,118.89,111.85,111.07,55.38,47.09,23.79, 21.50.
5k	8.37 (d, *J* = 7.5 Hz, 1H), 8.29 (d, *J* = 7.5 Hz, 1H), 7.30 (d, *J* = 7.5 Hz, 2H), 7.16 (s, 1H), 6.98 (d, *J* = 7.5 Hz, 2H), 6.84 (d, *J* = 6.6 Hz, 2H), 5.50 (s, 1H), 5.25 (s, 2H), 4.99 (s, 1H), 2.76 (s, 3H), 2.23 (s, 3H).	170.47,167.92,157.66,151.67,148.11, 135.58, 135.08,132.84,128.71,127.77,125.02, 122.93, 122.18,121.00,118.74, 111.85, 111.07, 55.38, 48.11, 23.79, 21.50.
5l	8.37 (d, *J* = 7.5 Hz, 1H), 8.31 (d, *J* = 7.5 Hz, 1H), 7.18 (s, 1H), 7.12 (d, *J* = 4.3 Hz, 4H), 6.78 (s, 2H), 5.74 (s, 1H), 5.28 (s, 2H), 5.09 (s, 1H), 2.74 (s, 3H), 2.40 (s, 3H), 2.22 (s, 3H).	170.47,167.92,157.66,151.67,148.11,136.55,135.58,135.19,132.84,130.44,128.31,127.77,126.59,126.03,121.00,111.85,111.07,55.38,47.19,23.79,21.50, 19.44.
5m	8.36 (s, 2H), 7.23 – 7.14 (m, 2H), 7.04 (s, 1H), 6.94 (s, 1H), 6.84 (d, *J* = 10.4 Hz, 2H), 6.77 (d, *J* = 8.9 Hz, 1H), 5.49 (s, 1H), 5.26 (s, 2H), 4.99 (s, 1H), 3.94 (s, 3H), 2.76 (s, 3H), 2.23 (s, 3H).	170.47,167.92,159.91,157.66,151.67,148.11, 137.22,135.58,132.84,129.52,127.77,122.32, 121.00, 113.62, 112.08, 111.07, 56.03, 55.38, 48.47, 23.79, 21.50.
5n	8.45 (d, *J* = 7.5 Hz, 1H), 8.40 (d, *J* = 7.5 Hz, 1H), 7.25 (s, 1H), 6.96 (s, 2H), 6.49 (d, *J* = 16.2 Hz, 3H), 5.26 (s, 2H), 5.19 (s, 1H), 4.97 (s, 1H), 3.83 (s, 6H), 2.77 (s, 3H), 2.23 (s, 3H).	170.47,167.92,161.66,157.66,151.67, 148.11,137.05,135.58,132.84,127.77,121.00, 111.85, 111.07, 107.22, 96.53, 56.03, 55.38, 49.00, 23.79, 21.50.
5o	8.36 (q, *J* = 7.4 Hz, 2H), 8.13 (d, *J* = 7.5 Hz, 2H), 7.55 (d, *J* = 7.5 Hz, 2H), 7.16 (s, 1H), 6.92 (s, 1H), 6.83 (s, 1H), 5.54 (s, 1H), 5.25 (s, 2H), 5.02 (s, 1H), 2.77 (s, 3H), 2.24 (s, 3H).	170.47,167.92,157.66,151.67,147.94,142.67, 135.58,132.84,128.33,127.77,124.38,121.00, 111.85, 111.07, 55.38, 48.11, 23.79, 21.50.

Table IV: Physical constant and analytical data of Designed compounds 5a-o

Entry	m.p. °C	Found (%) (Calcd)		
		C	H	N
5a	177–178	79.33 (64.94	5.20 5.19	21.69 21.64)
5b	164–165	59.77 (59.65	4.54 4.53	19.92 19.87)
5c	198–199	59.77 (59.65	4.54 4.53	19.92 19.87)
5d	174–175	55.27 (55.15	3.98 3.97	18.43 18.38)
5e	182–183	62.18 (62.06	4.72 4.71	20.73 20.68)
5f	173–175	62.18 (62.06	4.72 4.71	20.73 20.68)
5g	179–180	59.55 (59.43	4.29 4.28	19.85 19.80)
5h	176–178	57.91	4.21	18.46

		(57.89	4.20	18.41)
5i	185–186	62.18	4.72	20.73
		(62.06	4.71	20.68)
5j	188–189	56.05	4.06	17.84
		(55.93	4.05	17.79)
5k	154–155	56.05	4.06	17.84
		(55.93	4.05	17.79)
5l	165–167	65.789	5.52	20.93
		(65.66	5.51	20.88)
5m	156–158	63.27	5.31	20.13
		(63.15	5.30	20.08)
5n	127–129	61.72	5.40	18.79
		(61.60	5.39	18.74)
5o	159–160	56.21	4.43	22.67
		(58.19	4.42	22.62)

Experimental Section

Melting points were determined using a Cintex melting point apparatus and are uncorrected. Thin-layer chromatography (TLC) was performed by using Merck silica gel 60 F254 precoated plates (0.25 mm) and column chromatography was performed by using Silica gel (particle size 100-200 mesh). ^{1}H NMR spectra were recorded on a Bruker AMX 400 MHz spectrometer. Chemical shift values were given in ppm (δ) with TMS as an internal standard. Mass spectra were determined on Agilent LC-1100 (LC-MS) series instrument. ^{13}C NMR spectra were recorded on a Bruker AMX 100 MHz spectrometer. Elemental analyses were performed on a Carlo Erba 106 and Perkin Elmer model 240 analyzers.

i) . Catalytic Hydroxylation of *N*-(7-chloro-5-methyl-1,8-naphthyridin-2-yl)acetamide (1):

To an oven-dried screw-capped vial was added a stir bar, Pd_2dba_3 (2 mol%), L (8%), $CsOH{\cdot}H_2O$ (3 mmol), aryl halide (1 mmol) and 2 mL of THF (65^{0}C) or 1,4-dioxane (110 ^{0}C). The vial was then sealed under dinitrogen with a cap containing a PTFE septum, removed from the glove-box and placed in a temperature-controlled aluminum heating block set at the required temperature and stirred vigorously. Reaction progress was monitored by use of TLC or GC methods and after complete consumption of the *N*-(7-chloro-5-methyl-1,8-naphthyridin-2-yl)acetamide **(1)** had been observed (8–12 h), the reaction mixture was allowed to cool, if necessary, and then acidified with 2N aqueous HCl and diluted with water. The resulting solution was extracted with either ethyl acetate or diethyl ether (3× 2 mL). The collected organic extractions were dried over sodium sulfate, filtered and concentrated to afford crude *N*-(7-hydroxy-5-methyl-1,8-naphthyridin-2-yl)acetamide **(2)** which was further purified by use of column chromatography.
$[Pd_2(dba)_3]$ is used as a source of soluble Pd(0), in particular as a catalyst for various reactions.

(ii). Propargylation of *N*-(7-hydroxy-5-methyl-1,8-naphthyridin-2-yl)acetamide (2)Hydroxyl Group:

The compound 2 (1 eq) was treated with K_2CO_3 (4 eq) in DMF for 30 min at 70 °C. After 30 min, propargyl bromide (1.5 eq) was added, and the reaction was continued for 24 h. After 24 h, the reaction was cooled and poured into ice-cold water to remove the DMF. The extraction was done with EtOAc (3 × 50 mL). The combined ethyl acetate layer was concentrated on a rotary evaporator, and the residue was purified over silica gel (solvent system: 40% EtOAc in hexane) to obtain corresponding propargylated compound namely *N*-(5-methyl-7-(prop-2-yn-1-yloxy)-1,8-naphthyridin-2-yl)acetamide **(3).**

(iii).Synthesis of *N*-(7-((Substituted-1*H*-1,2,3-triazol-5-yl)methoxy)-5-methyl-1,8-naphthyridin-2-yl)acetamides (5a-o):

To a RB flask, substituted benzyl bromide (**4a-o)** (1.5 eq), triethylamine (0.3 eq), and sodium azide (1.5 eq) were *taken in tert*-butanol/water (1:1). This mixture was stirred at RT for half an hour. After half an hour, propargylated 1,8-naphthyridin-2-yl)acetamide **(3)** (1.5 eq) was added along with sodium ascorbate (0.2 eq) and copper sulfate (0.1 eq), and the reaction was stirred for 24 h. Then, 30 mL water was added and extraction was done with EtOAc (3 × 50 mL). The three layers are combined and concentrated on a vacuum rotary evaporator. Thus, the residue was purified by column chromatography (solvent system: 40% EtOAc in hexane for desired 1,2,3-triazoles **(5a-o)** [20-21] under 70% EtOAc in hexane in 70-88% yields.

Conclusion

We have synthesized series of *N*-(7-((Substituted-1*H*-1,2,3-triazol-5-yl) methoxy)-5-methyl-1,8-naphthyridin-2-yl) acetamides had greater product yield and high purity. The structures of all the synthesized compounds were further confirmed by spectral analysis.

Acknowledgment

We, the authors, express our sincere gratitude to Department of Chemistry, Chaitanya Deemed to be University, Hanamakonda for the laboratory facilities provided to conduct this research work.

References

[1] (a) Mingos, D. M. P.; Vilar, R. *J. Organomet. Chem*. **1998**, 557, 131. (b) Herbst, K.; Rink,B.; Dahlenburg, L.; Brorson, M. *Organometallics.***2001**, 20, 3655.

[2] (a) Fuchita, Y.; Maruyama, H.; Kawatani, M.; Hiraki, K. *Polyhedron*. **1991**, 10, 561. (b)Vicente, J.; Chicote, M. T.; Martínez- Martínez, A.J.; Bautista, D. *Organometallics.* **2008**,27, 3254.

[3] (a) Vicente, J.; Abad, J.-A.; Förtsch, W.; Jones, P. G.; Fischer, A. K. *Organometallics.***2001**, 20, 2704. (b) Getty, A. D.; Goldberg, K. I. *Organometallics.* **2001**, 20, 2545.

[4] Ananikov, V. P.; Zalesskiy, S. S.; Kachala, V. V.; Beletskaya, I. P. *J. Organomet. Chem.***2011**, 696, 400.

[5] Amatore, C.; Jutand, A. Coord. *Chem. Rev.* **1998**,511.

[6] Jalón, F. A.; Manzano, B. R.; Gómez-de la Torre, F.; López- Agenjo, A. M.; Rodrıǵ uez, A.M.; Weissensteiner, W.; Sturm, T.;Maestro, M. *J. Chem. Soc, Dalton Trans*. **2001**, 2417.

[7] Sergey, S.; Zalesskiy and Valentine, P. *Organometallics.* **2012**, 31, 2302.

[8] a) S. Enthaler, A. Company, *Chem. Soc. Rev.* 2011, 40, 4912; b) D. A. Alonso, C. Najera, I.M. Pastor, M. Yus, *Chem. Eur. J.* **2010**, 16, 5274; c) Z. Rappoport, *The Chemistry of Phenols, Wiley*, Hoboken, NJ, 2003.

[9] a) C. Hoarau, T. R. R. Pettus, *Synlett.* **2003**, 127; b) T. George, R. Mabon, G. Sweeney, J. B.Sweeney, A. Tavassoli, *J. Chem. Soc.* PerkinTrans. 1 **2000**, 2529; c) J. B. Sweeney, Contemp.Org. Synth. **1997**, 4, 435.

[10] P. T. Anastas, *ChemSusChem.* **2009**, 2, 391.

[11] A. D. Chowdhury, S. M. Mobin, S. Mukherjee, S. Bhaduri, G. K. Lahiri, *Eur. J. Inorg.Chem.* **2011**, 3232.

[12] a) K. Yang, Z. Li, Z. Wang, Z. Yao, S. Jiang, *Org. Lett.* **2011**, 13, 4340; b) H.- J. Xu, Y.-F.Liang, Z.-Y. Cai, H.-X. Qi, C.-Y. Yang, Y. - S. Feng,*J. Org. Chem*. **2011**, 76, 2296.

[13] A. F. Littke, G. C. Fu, *Angew. Chem.* **2002**, 114, 4350.

[14] a) C.-W. Yu, G. S. Chen, C.-W. Huang, J.-W. Chern, *Org. Lett.* **2012**, 14, 3688; b) T. Schulz, C. Torborg, B. Schaeffner, J. Huang, A. Zapf, R. Kadyrov, A. Boerner, M. Beller, *Angew.Chem.* **2009**, 121, 936; *Angew. Chem*. Int. Ed.**2009**, 48, 918.

[15] G. J. Withbroe, R. A. Singer, J. E. Sieser, *Org. Process Res. Dev.* **2008**, 12, 480.

[16] Bisacchi, G. S. *J. Med. Chem*. **2015**, 58, 4874.

[17] Bao, J.; Marathe, B.; Govorkova, E. A.; Zheng, J. J. *Angew. Chem.,* Int. Ed. **2016**, 55, 3438.

[18] Ahmed, M.; Kelley, S. O. *ACS Chem. Biol.* **2017**, 12, 2563

[19] Pham, T. D. M.; Ziora, Z. M.; Blaskovich, M. A. T. *Med. Chem. Comm.* **2019**, 10, 1719.

[20] C.P. Kaushik, Jyoti Sangwan, Raj Luxmi, Devinder Kumar, Deepak Kumar, Ashutosh,Das, Ashwani Kumar, *Journal of Molecular Structure*. **2021,** 1226,129255.

[21] Ankita Sharma and Sandip B.Bharate,ACSOmega.2923,8,11162
[22] S.T. Harini, H.V. Kumar, J. Rangaswamy, N. Naik , *Bioorg. Med. Chem.* **2012,** 22, 7588.
[23] K. Ay , B. Ispartaloglu , E. Halay , E. Ay , I. Yasa , T. Karayıldırım *, Med. Chem. Res.* **2017**, 26, 1497.
[24] C.P. Kaushik, A. Pahwa, R. Thakur, P. Kaur, *Synth. Commun*. **2017**, 47, 368.
[25] C.P. Kaushik , A. Pahwa , D. Kumar , A. Kumar , D. Singh , K. Kumar , R. Luxmi , *J. Het. Chem.* **2018**, 55, 1720.
[26] N.J.P. Subhashini, E.P. Kumar, N. Gurrapu, V. Yerragunta, *J. Mol. Struct.* **2019**, 1180, 618.
[27] K.A. Kumar, S.M.Kumar, *Phosphorus Sulfur Silicon Relat. Elem.* **2018**, 193, 294.
[28] K. Padmavathy, K.G. Krishnan, C.U. Kumar, P. Sutha, R. Sivaramakarthikeyan, C.Ramalingan, *ChemistrySelect*. **2018**, 3, 5965.
[29] S.K. Avula , A. Khan , N.U. Rehman , M.U. Anwar Z. Al-Abri , A. Wadood , A. Al-Har-rasi, *Bioorg. Chem.* **2018** ,81,98.
[30] M. Saeedi, M. Mohammadi-Khanaposhtani, P. Pourrabia, N. Razzaghi, R. Ghadimi, S.Imanparast, H. Rastegar*, Bioorg. Chem.* **2019**,83, 161.
[31] M. Das, B. Das, A. Samantha, *J. Pharm. Pharmacol*. **2019**, 71, 1400.
[32] M. Gholampour, S. Ranjbar, N. Edraki, M. Mohabbati, O. Firuzi, M. Khosh- neviszadeh, *Bioorg. Chem.* **2019**, 88, 102967.
[33] R. Lakkakula , A. Roy , K. Mukkanti , G. Sridhar , *Russian J. Gen. Chem.* **2019**,89, 831.
[34] Y. Chinthala , S. Thakur , S. Tirunagari , S. Chinde , A.K. Domatti , N.K. Arigari , A.Tiwari, *Eur. J. Med. Chem.* **2015**, 93,564.
[35] P.S. Rao , C. Kurumurthy , B. Veeraswamy , G.S. Kumar ,Y. Poornachandra , C.G. Kumar,S.B. Vasamsetti , S. Kotamraju , B. Narsaiah , *Eur. J. Med. Chem.* **2014**,80, 184.
[36] M.H. Shaikh , D.D. Subhedar , B.B. Shingate , F.A. Khan , J.N. Sangshetti , V.M. Khedkar ,L. Nawale , D. Sarkar , G.R. Navale , S.S. Shinde ,*Med. Chem. Res.* **2016**,25,790.
[37] S.R. Patpi , L. Pulipati , P. Yogeeswari , D. Sriram ,N. Jain , B. Sridhar , R. Murthy, A. Devi, S.V.Kalivendi, S. Kantevari , *J. Med. Chem.***2012**,55,3911.
[38] O.I. Artyushin, E.V. Sharova, N.M. Vinogradova, G.K. Genkina, A .A. Moiseeva, Z.S.Klemenkova, I.R. Kadyrova, V.V. Brel, *Bioorg. Med. Chem. Lett.* **2017**,27,2181.
[39] I.E. Glowacka , J. Balzarini , G. Andrei , R. Snoeck , D. Schols , D.G. Pi- otrowska , *Bioorg.Med. Chem.* **2014***, 22*, 3629.
[40] C.P. Kaushik, A. Pahwa, *Med. Chem. Res.* **2018**, 27, 458.
[41] E.M. Guanta , K. Ncokazi , T.J. Egan , J. Gut , P.J. Rosenthal , P.J. Smith , K. Chibale ,*Bioorg. Med. Chem.* **2010**, 18, 8243.