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Hydrotalcite Catalyzed Synthesis of *N*-substituted 4-(4-Chlorophenethyl)-3-Methoxy Pyridin-2(1*H*)-Ones and their Anti-Proliferative Activity

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Abstract: An efficient and novel method has been developed for the synthesis of *N*-substituted 4-(4-chlorophenethyl)-3-methoxypyridin-2(1*H*)-ones **6a-j** by the reaction of 4-(4-chlorophenethyl)-3-methoxypyridin-2(1*H*)-one **5** with various alkyl bromides using catalytic amount of Hydrotalcite. Later, the anti-proliferative activity of synthesized molecules **6a-j** against cancer cell lines like A549, HeLa, HepG2, and MCF-7 revealed that compounds **6i** containing 2-methoxy-4-methylenepyrimidine group and **6j** containing 2-methoxy-6-methylenepyridine group had promising activity against all cell lines when compared with Doxorubicin. Besides, compound **6e** containing 4-nitro benzyl group had well activity against A549, HepG2, and MCF-7 as compared to positive control. Furthermore, compound **6h** containing 4-methoxy-2-methyleneoxazole group have shown promising activity against A549, HeLa and HepG2 as compared to Doxorubicin. Rests of the compounds were shown moderate to low activity against all cell lines when compared with Doxorubicin.

Keywords: Pyridin-2(1H)-one, Palladium catalyst, Hydrotalcite, Antiproliferative activity.

1. INTRODUCTION

The pyridine derivatives find significant roles in medicines, agriculture, and material science[1]. Predominantly, 2-Pyridone is one of the derivatives of pyridine which has gain keen attention by the research community, owing to its abundance in natural products of biological importance[2]. Recently, Huperzine A a genuinely isolated compound holding 2-pyridone skeleton has been validated for the treatment of Alzheimer's disease in China[3]. 2-Pyridone derivatives also have diverse biological activities

like antimicrobial[4], antiviral[5], sedative[6], antimalarial[7], antitumor[8], antiulcer[9], anticancer[10], anticoagulant[11], multiple sclerosis immunomodulators[12], insecticidal[13], antihypertensive[14], antiparasitic[15], and antagonist.[16.] On the other aspect, 2-pyridone scaffolds occur as a tenable synthons for the supramolecular chemistry[17-23] and as ligands[24] for organometallic chemistry.

It is well known that the Heck reaction is a Pd-catalyzed carbon–carbon cross-coupling reaction between aryl halides or vinyl halides and activated alkenes using base. Current developments in catalysis and reaction conditions have resulted in several donors and acceptors that acquiescent to the Heck reaction[25-31]. An innovative development of chemical pathway regarding *N*-alkylation reaction carried out by adding and recycling only catalytic amount of Hydrotalcite as solid base instead of stoichiometric amount, as per prior art techniques, has attempted[32].

Based on all the above findings, now, we are interested to make *N*-substituted 4-(4-chlorophenethyl)-3-methoxypyridin-2(1*H*)-ones **6a-j** and their anti -cancer evaluation.

2. RESULTS AND DISCUSSIONS

The synthetic approach to targeted compounds **(6a-6j)** was shown in **Scheme I.** At first**,** solution of 2,3-Dimethoxypyridine **1** in dry THF stirred and cooled to -78˚C. Later to this solution *N*-butyl lithium (1.6M in hexane) was added drop wise and stirred at room temperature for 40min. Then reaction mixture was cooled to -78˚C and solution of iodine in THF was added and the resulted reaction mixture was allowed to stirring at RT for 2.5 hr to produce compound **2**. The compound **2** was then subjected to $Pd(OAc)_2$ catalyzed Heck-cross coupling with 1-Chloro-4-styrene using potassium phosphate in DMF: water at room temperature to give internal alkene product **3**. The reduction of intermediate **3** using H_2 and Pd/C was produced compound **4.**The intermediate **4** was then treated with HBr/CH_3COOH to give amide intermediate **5.** Finally, Hydrotalcite catalyzed reaction between intermediate **5** and several alkyl/aryl bromides in CH_3CN solvent provided the targeted products **(6a-6j)** depicted below (Scheme I).

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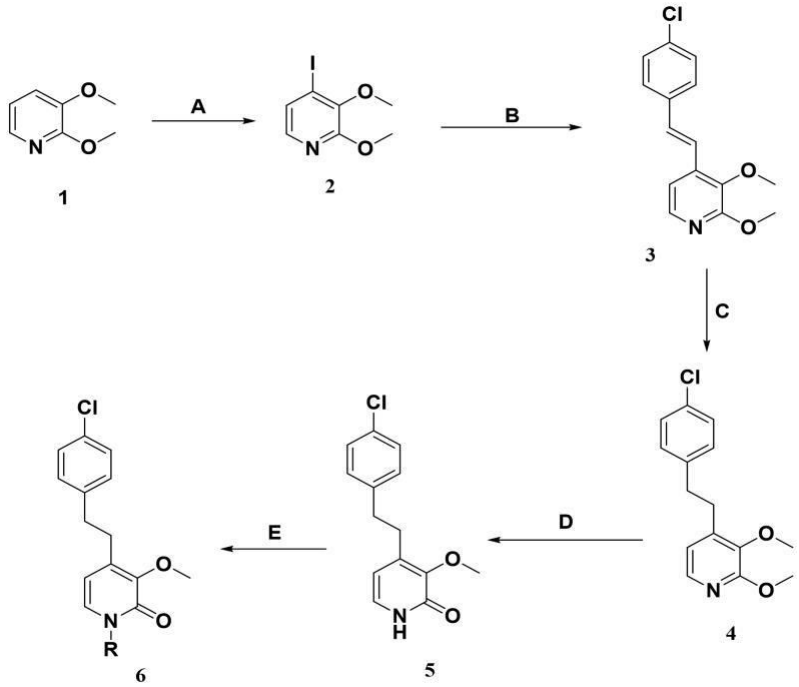
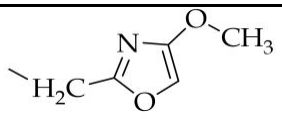
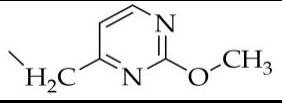
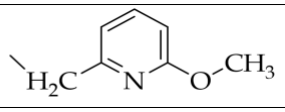


Scheme I. Synthetic path way for compounds **6a-6j**

Entry	R
6a :	C_2H_5
6b :	$-CH_2-C_6H_5$
6c :	$-CH_2-CH_2-C_6H_5$
6d :	$-CH_3$
6e :	$4-NO_2C_6H_4CH_2-$
6f:	$-CH_2CH=CH_2$
6g :	$-CH=CH_2$
6h :	
6i :	

6j :	

Reagents and Reaction conditions: (A) I_2, n-BuLi, THF (B) 1-Chloro-4-styrene, $Pd(OAc)_2$ (C) H_2, Pd/C (D) HBr/CH_3COOH (E) R-Br, Hydrotalcite , CH_3CN .

Antiproliferative activity

Later, the synthesized molecules at their µM concentration were assessed for anti-proliferative activity against cancer cell lines like A549, HeLa, HepG2, and MCF-7 and results were compared with the standard drug Doxorubicin. Out of all, compounds **6i** containing 2-methoxy-4-methylenepyrimidine group and **6j** containing 2-methoxy-6-methylenepyridine group have shown promising activity against all cell lines when compared with Doxorubicin. As well, compound **6h** containing 4-methoxy-2-methyleneoxazole group showed promising activity against A549, HeLa and HepG2 as compared to Doxorubicin. Furthermore, compound **6e** containing 4-nitro benzyl group had well activity against A549, HepG2, and MCF-7 as compared to positive control. On the other aspect, compound **6f** bearing allyl group displayed promising activity against HeLa only when compared with standard. Rests of the compounds were shown moderate to low activity against all cell lines when compared with Doxorubicin. In over all, compounds **6i** containing and **6j** were more active than all other synthesized compounds. The next better activity was shown by compound **6e**.

Table 1. Antiproliferative activity of compounds **(6a-6j)** in IC_{50} (µM)

Entry (R)	A549	HeLa	HepG2	MCF7
6a: C_2H_5	44.312	41.21	56.22	27.86
6b: $-CH_2-C_6H_5$	64.427	32.61	43.31	36.46
6c: $CH_2-CH_2-C_6H_5$	54.125	51.81	36.08	40.17
6d: CH_3	24.531	61.51	46.11	31.24
6e: $4-NO_2C_6H_4CH_2-$	**5.011**	21.41	**16.21**	**11.06**
6f: $CH_2CH=CH_2$	37.142	**6.41**	66.33	47.22
6g: $-CH=CH_2$	64.628	66.81	66.11	38.06

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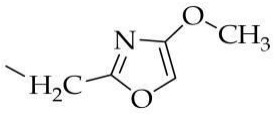
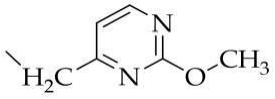
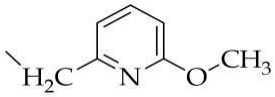
6h: 	**2.223**	**5.48**	**16.21**	17.86
6i: 	**3.213**	**4.61**	**13.33**	**13.06**
6j: 	**4.132**	**6.52**	**11.11**	**9.26**
Doxorubicin	**0.223**	**1.81**	**6.11**	**7.86**

3. CONCLUSION

In summary, a novel, cost-effective, eco-benign and practical method was developed to synthesize *N*-substituted 4 (4-chlorophenethyl)-3-methoxypyridin-2(1*H*)-ones as anti-proliferative agents. The advantages of this method include a simple reaction set-up not requiring specialized equipment's, low-toxicity of the reagent, less reaction times, and high product yields with excellent purity. Simple and efficient regeneration procedure of spent Hydrotalcite to have same characteristics. Amongst the series, compounds **6i** containing 2-methoxy-4-methylenepyrimidine group and **6j** containing 2-methoxy-6-methylenepyridine group had promising activity against A549, HeLa, HepG2, and MCF-7 as compared to Doxorubicin. Compound **6e** containing 4-nitro benzyl group have shown well activity against A549, HepG2, and MCF-7 when compared with positive control. Finally, compound **6h** containing 4-methoxy-2-methyleneoxazole group had promising potency against A549, HeLa and HepG2 as compared to Doxorubicin. Further mechanistic studies of anti-proliferative activity are under progress.

EXPERIMENTAL SECTION

General information

Electro thermal apparatus was used to record the melting point of synthesized compounds 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). IR spectra (KBr) were recorded on a Perkin-Elmer BX series FTIR spectrometer. ^{1}H NMR spectra were recorded on a Bruker AMX 400 MHz spectrometer. ^{13}C NMR spectra were recorded on a Bruker AMX 100 MHz spectrometer. Chemical shift values were given in ppm ( ) with TMS as an internal standard. Mass spectra were determined on Agilent LC-1100 (LC-MS) series instrument. Elemental analyses were performed on a Carlo Erba 106 and Perkin Elmer model 240 analyzers.

Synthesis of 4-Iodo-2, 3-dimethoxypyridine 2:

Solution of 2, 3-Dimethoxypyridine (5gm) **1** in dry THF (120mL) muddled and cooled to -78˚C. To this solution 2 equiv. of *N*-butyl lithium (1.6M in hexane) was added drop wise and trembled at room temperature for 45 min. Then chill the reaction mixture to -78˚C and solution of iodine (10g, 1.2eq.) in THF (250mL) was added and the resulted reaction mixture was allowed to RT and stirred for 2hr, TLC indicated consumption of starting material. The reaction mixture extricated with water(10mL)and pinched with saturated ammonium chloride solution and then extracted with ethyl acetate(3x40mL), the combined organic layer was laced with water (3 x 10 mL) followed by sodium thiosulfate (hypo) solution to remove the excess iodine. The organic layer was parched over anhydrous sodium sulphate, dribbled and intensive under reduced pressure, to afford the crude compound. The crude compound was further clarified by column chromatography (Silica gel: 100-200 mesh, eluent: ethyl acetate: n-hexane; 2:98) to get the pure compound **2** as yellow solid.

Synthesis of 4-(4-Chlorostyryl)-2, 3-dimethoxypyridine 3:

To a stirred solution of **2** (1eq.) and 1-chloro-4-styrene **3** in DMF: water (8:2**)** was added potassium phosphate (3eq.) at room temperature and degassed with argon for 10 min and then palladium acetate (0.05 eq.) was added and again degassed with argon for 10min. The reaction mixture was heated on oil-bath at 110˚C for about 10hr. The reaction mixture thinned with water (10mL) and then deracinated with ethyl acetate (3x40mL). The organic layer was scorch over anhydrous sodium sulphate, percolated and concentrated under reduced pressure, to obtain the crude compound **3**. The crude solid of **3** was

ISSN: 2366-1313

further purged by silica gel (100-200 mesh) column chromatography using ethyl acetate: hexane (3:7) as eluent to get the pure compound **3** as colour less oil.

Synthesis of 4-(4-Chlorophenethyl)-2, 3-dimethoxypyridine 4

To a stirred solution of compound **3** (6gm) in ethyl alcohol: ethyl acetate (1:1) was added 10% Pd/Charcoal. This reaction mixture was whipped in hydrogen atmosphere for 13hr. The reaction was monitored by TLC in *n*-hexane-ethyl acetate (9: 1). After fulfillment of the reaction, the reaction mixture was scoured with ethyl acetate. The insoluble solid was bleeded off and the filtrate was evaporated to give a color less oil **4**. The purification was clinched using a short column of silica gel eluted with *n*-hexane-ethyl acetate (9:1).

Synthesis of (4-Chlorophenethyl) - 3-methoxypyridin-2(1*H*)-one 5

The compound **4** (1 eq.) was dissolved in mixture of HBr and acetic acid (4:6) (40 mL), the solution was agitated at 90°C for 4.5hr. Reaction progress was monitored by TLC by using Ethyl Acetate: Heptane (1:1) as mobile phase. After reaction consummation, the reaction mixture was intensed under reduced pressure in a rota evaporator and the crude product was poured into ice, mopped with water purified by using Ethyl Acetete: Diethyl ether (20:80) to get White solid **5**

Synthesis of *N*-Substituted 4-(4-Chlorophenethyl)-3-methoxypyridin-2(1*H*)-ones 6

To a solution of compound **5**(1 eq.) in acetonitrile (25mL) was added catalytic amount of Hydrotalcite at RT. This reaction mixture was fluttered at 80˚C for 30min. After 30min alkyl bromides (1 eqv.) was tallied, the triggering reaction mixture was whisked at 80˚C for 1hr. On resolution of the reaction (monitored by TLC), the reaction mixture was cooled to RT and strenuous under reduced pressure in a rota evaporator and the formed product was sponged with water exorcised by using Ethyl Acetate: Diethyl ether (30:70) to get pale yellow oil **6a-j**

Charectirization data

1-Ethyl-4-(4-chlorophenethyl)-3-methoxypyridin-2(1*H*)-one 6a

IR (KBr) $_{max}$ (cm^{-1}): 3057, 2970, 1663, 1606, 1511, 1435, 1394, 1226, 1132, 1394, 1226, 1132, 1076,

1027; ^{1}H NMR (400 MHz, DMSO-d_6): 1.20 (t, 3H, -CH_3), 2.71 (t, 2H, -CH_2-), 2.77 (t, 2H, -CH_2-), 3.88 (q, 2H, -CH_2-), 6.12 (d, 1H, C_5-H of pyridone), 7.14-7.34 (m, 4H, Ar-H), 7.39 (d, 1H, C_6-H of pyridone); ^{13}C NMR (100 MHz, DMSO-d_6): 13.1, 29.1, 30.3, 48.2, 53.0, 114.2, 119.5, 121.0, 124.3, 128.9, 139.0, 140.2, 156.4, 160.0; LC-MS: *m/z* 292.14 $[M+H]^+$. Anal. Calcd for $C_{16}H_{18}ClNO_2$: C 65.86%, H 6.22%, N 4.80%. Found: C 65.97%, H 6.24%, N 4.85%.

1-Benzyl-4-(4-chlorophenethyl)-3-methoxypyridin-2(1*H*)-one 6b

IR (KBr) $_{max}$ (cm^{-1}): 3035, 2925, 2855, 1668, 1594, 1556, 1454, 1394, 1351, 1309, 1239, 1101, 1084, 1041; ^{1}H NMR (400 MHz, DMSO-d_6): 2.05 (t, 2H, -CH_2-), 2.07 (t, 2H, -CH_2-), 5.07 (s, 2H, -CH_2-), 3.61 (s, 3H, O-CH_3), 6.14 (d, 1H, C_5-H of pyridone), 7.14-7.34 (m, 9H, Ar-H), 7.48 (d, 1H, C_6-H of pyridone); LC-MS: *m/z* 353.2 $[M]^+$. Anal. Calcd for $C_{21}H_{20}ClNO_2$: C 71.28%, H 5.70%, N 3.96%. Found: C 71.39%, H 5.75%, N 3.99%.

4-(4-Chlorophenethyl)-3-methoxy-1-phenethylpyridin-2(1*H*)-one 6c

IR (KBr) $_{max}$ (cm^{-1}): 3024, 2971, 2947, 1648, 1599, 1552, 1434, 1408, 1368, 1223, 1161, 1081, 1031; ^{1}H NMR (400 MHz, DMSO-d_6): 2.68 (t, 2H, -CH_2-), 2.75 (t, 2H, -CH_2-), 2.90 (t, 2H, -CH_2-), 3.59 (s, 3H, O-CH_3), 4.05 (t, 2H, -CH_2-), 6.01 (d, 1H, C_5-H of pyridone), 7.16-7.29 (m, 10H, 9Ar-H, C_6-H of pyridone); LC-MS: *m/z* 367.1 $[M]^+$. Anal. Calcd for $C_{22}H_{22}ClNO_2$: C 71.83%, H 6.03%, N 3.81%. Found: C 71.93%, H 6.05%, N 3.83%.

4-(4-Chlorophenethyl)-3-methoxy-1-methylpyridin-2(1*H*)-one 6d

IR (KBr) $_{max}$ (cm^{-1}): 3024, 2970, 1649, 1586, 1557, 1426, 1370, 1299, 1223, 1145, 1116, 1087, 1032; ^{1}H NMR (400 MHz, DMSO-d_6): 2.70 (t, 2H, -CH_2-), 2.77 (t, 2H, -CH_2-), 3.38 (s, 3H, N-CH_3), 3.62 (s, 3H, O-CH_3), 6.09 (d, 1H, C_5-H of pyridone), 7.07 (t, 2H, Ar-H), 7.21 (t, 2H, Ar-H), 7.34 (d, 1H, C_6-H of pyridone); LC-MS: *m/z* 276.87 $[M]^+$. Anal. Calcd for $C_{15}H_{16}ClNO_2$: C 64.87%, H 5.81%, N 5.04%. Found: C 64.98%, H 5.83%, N 5.07%.

4-(4-Chlorophenethyl)-3-methoxy-1-(4-nitrobenzyl) pyridin-2(1*H*)-one 6e

IR (KBr) $_{max}$ (cm^{-1}): 3162, 3064, 2954, 2879, 2811, 1649, 1598, 1649, 1598, 1557, 1418, 1361, 1284, 1226, 1114, 1071, 1030; ^{1}H NMR (400 MHz, DMSO-d_6): 2.72 (t, 2H, -CH_2-), 2.80 (t, 2H, -CH_2-), 3.63 (s, 3H, O-CH_3), 5.21(s, 2H, -CH_2-), 6.18(d, 1H, C_5-H of pyridone), 7.08 (t, 2H, Ar-H), 7.22 (t, 2H, Ar-

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H), 7.47(d, 2H, Ar-H), 7.53 (d, 1H, C_6-H of pyridone); 8.22 (d, 2H, Ar-H), LC-MS: *m/z* 399.28 $[M+H]^+$. Anal. Calcd for $C_{20}H_{19}ClN_2O_4$: C 63.24%, H 4.80%, N 7.02%. Found: C 63.38%, H 4.81%, N 7.05%.

1-Allyl-4-(4-chlorophenethyl)-3-methoxypyridin-2(1*H*)-one 6f

IR (KBr) $_{max}$ (cm^{-1}): 3203, 3006, 2971, 2946, 1661, 1607, 1552, 1511, 1430, 1370, 1266, 1221, 1117; ^{1}H NMR (400 MHz, DMSO-*d*$_6$): 2.68 (t, 2H, -CH_2-), 2.75 (t, 2H, -CH_2-), 3.61 (s, 3H, O-CH_3), 4.47 (s, 2H, -CH_2-), 4.99(d,1H, olefinic-H), 5.16(d,1H, olefinic-H), 5.85-5.95(m, 1H, olefinic-H), 6.12 (d, 1H, C_5-H of pyridone), 7.07 (t, 2H, Ar-H), 7.21 (t, 2H, Ar-H), 7.30 (d, 1H, C_6-H of pyridone); LC-MS: *m/z* 303.82 $[M]^+$. Anal. Calcd for $C_{17}H_{18}ClNO_2$: C 67.21%, H 5.97%, N 4.61%. Found: C 67.34%, H 5.98%, N 4.63%.

4-(4-Chlorophenethyl)-3-methoxy-1-vinylpyridin-2(1*H*)-one 6g

IR (KBr) $_{max}$ (cm^{-1}): 3022, 1650, 1600, 1554, 1518, 1467, 1446, 1347, 1263, 1224, 1158, 1111, 1082, 1012; ^{1}H NMR (400 MHz, DMSO-*d*$_6$): 2.66 (t, 2H, -CH_2-), 2.73 (t, 2H, -CH_2-), 3.62 (s, 3H, O-CH_3), 4.97(d,1H, olefinic-H), 5.15(d,1H, olefinic-H), 5.84-5.97(m, 1H, olefinic-H), 6.14 (d, 1H, C_5-H of pyridone), 7.08 (t, 2H, Ar-H), 7.24 (t, 2H, Ar-H), 7.30 (d, 1H, C_6-H of pyridone); LC-MS: *m/z* 290.75

$[M+H]^+$. Anal. Calcd for $C_{16}H_{16}ClNO_2$: C 66.32%, H 5.57%, N 4.83%. Found: C 66.45%, H 5.57%, N 4.86%.

4-(4-Chlorophenethyl)-3-methoxy-1-((4-methoxyoxazol-2-yl) methyl) pyridin-2(1H)-one 6h

IR (KBr) $_{max}$ (cm^{-1}): 3072, 2729, 1632, 1587, 1556, 1477, 1434, 1380, 1300, 1264, 1243, 1199; ^{1}H NMR (400 MHz, DMSO-*d*$_6$): 2.94 (t, 2H, -CH_2-), 3.32 (s, 3H, O-CH_3), 3.54 (t, 2H,-CH_2-), 3.85 (s, 3H, O-CH_3), 5.00 (s, 2H, -CH_2-), 6.87 (d, 1H, Ar-H), 7.55-7.64 (m, 2H, Ar-H); 7.79(d, 1H, Ar-H), 8.10(d, 1H, Ar-H), 8.20(d, 1H, Ar-H), 9.29(s, 1H, oxazole-H); LC-MS: *m/z* 375.85 $[M+H]^+$. Anal. Calcd for $C_{19}H_{19}ClN_2O_4$: C 60.88%, H 5.11%, N 7.47%. Found: C 60.99%, H 5.13%, N 7.51%.

4-(4-Chlorophenethyl)-3-methoxy-1-((2-methoxypyrimidin-4-yl) methyl) pyridin-2(1*H*)-one 6i

IR (KBr) $_{max}$ (cm^{-1}): 3162, 3064, 2954, 2879, 2811, 1649, 1598, 1557, 1418, 1397, 1361, 1284, 1226, 1114; ^{1}H NMR (400 MHz, DMSO-*d*$_6$): 2.93 (t, 2H, -CH_2-), 3.45(s, 3H, O-CH_3), 3.52 (t, 2H, -CH_2-), 3.82 (s, 3H, O-CH_3), 5.02(s, 2H, -CH_2-), 6.88(d, 2H, Ar-H), 7.53-7.62(m, 2H, Ar-H), 7.75(d, 1H, Ar-H), 8.08(d, 1H, Ar-H), 8.15(d, 1H, Ar-H), 9.23(m, 2H, pyrimidine-H); LC-MS: *m/z* 386.12 $(M)^+$. Anal. Calcd for $C_{20}H_{20}ClN_3O_3$: C 62.26%, H 5.22%, N 10.89%. Found: C 62.39%, H 5.22%, N 10.92%.

4-(4-Chlorophenethyl)-3-methoxy-1-((6-methoxypyridin-2-yl) methyl) pyridin-2(1*H*)-one 6j

IR (KBr) $_{max}$ (cm^{-1}): 3035, 2925, 2855, 1668, 1594, 1556, 1454, 1394, 1351, 1309, 1239, 1168, 1131, 1101; ^{1}H NMR (400 MHz, DMSO-d_6): 2.94 (t, 2H, -CH_2-), 3.43(s, 3H, O-CH_3), 3.54 (t, 2H, -CH_2-), 3.81 (s, 3H, O-CH_3), 5.04(s, 2H, -CH_2-), 6.87(d, 2H, Ar-H), 7.51-7.60(m, 2H, Ar-H), 7.45(d, 1H, Ar-H), 8.07(d, 1H, Ar-H), 8.14(d, 1H, Ar-H), 8.68-8.71(m, 3H, pyridine-H); LC-MS: *m/z* 384.12 $(M)^+$. Anal. Calcd for $C_{21}H_{21}ClN_2O_3$: C 65.54%, H 5.50%, N 7.28%. Found: C 65.67%, H 5.54%, N 7.26%.

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References

1. S. Sangwan, Neelam Yadav, W.Pooja, Anil Duhan, *Eur. J. Med. Chem*, **2022**, 232,114199.
2. Li Q. Mitscher L. A., Shen L. L., *Med. Res. Rev.*, **2000**, 20 , 231.
3. L.Forlani, G.Gristoni, P. E. Todesco, E.Vechio, S. Salva, M. Monari, *Arkivoc*, **2002**, 11, 198.
4. I.Collins, C.Moyes, W.Davey, M.Rowley, F.Bromidge, K. Quirk, J. Atack, G.Dawson, A.Pike B.Sohal, Tsou N. Bull R., Castro J., *J. Med. Chem.*, **2002**, 45, 1887.
5. Fang Y.Q. Bio M.M. Hansen K.B. Potter M.S.,Clausen A., *J. Am. Chem. Soc.*, **2010**,132, 15525.
6. L.A. Hasvold, W.Wang, S. L. Gwaltney, T.W. Rockway L.T.J. Nelson, R.A.Mantei, J.Cohen, W. Z. Gu, J. Bauch, , *Bioorg. Med. Chem. Lett.*, **2003**, 13, 4001.
7. A. Patil, S. Ganguly Surana, *Rasayan J Chem*, **2008**, 1, 447.
8. Du W. *Tetrahedron*, **2003**, 59, 8649.
9. W.W.Mederski, D. Dorsch, S. Anzali, C.Tsaklakidis, *Bioorg. Med. Chem. Lett.*, **2004,** 14, 3763.
10. L.A. Sorbera, J.Castaner, *Drugs Future*, **2003** 28, 1059.
11. N.Sakamoto, T. Ishiwatari, N.Matsuo, *J. Pesticide Sci.*, **2000**, 25, 373.
12. P.Naik, P. Murumkar, R. Giridhar, R.M.Yadav, *Bioorg. Med. Chem.*, **2010**, 18, 8418.
13. I. C. Romero, N. G.Saravia, J.Walker, *J. Parasitol*, **2005** 91, 1474.
14. P.G. Nantermet, J.C.Barrow, H.G.Selnick, C.F. Homnick, R.M. Freidinger, R. S. L. Malley, T.P. Broten, R.W.Ransom, D.J. Pettibone, C. Forray, *Bioorg. Med. Chem. Lett.,* 2**000**, 10, 1625.
15. E.Zhang, J. Tang, Moses, K.B. Sharpless, *Chem. Eur. J.*, **2016**, 22, 5692-5697.
16. P.Pomaranski, Czarnocki Z., *Synthesis*, **2019**, 51, 587-611.
17. Li Y. Wang, G. Hao, J.P. Wang, *Tetrahedron Lett.* **2019**, 60, 219-222.
18. A.G. Fang, J. V. Mello, N. S. Finney, *Tetrahedron*, **2004**, 60, 11075-11087.
19. M. C. Petty, M. R. Bryce, *Oxford University Press*, New York, **1995**.

ISSN: 2366-1313

20. C. Doebelin, P. Wagner, I. Bertin, F. Simonin, M. Schmitt, F. Bihel, J. J.Bourguignon, *RSC Adv.,* **2013**, 3, 10296-10300.
21. K.J. Wilson, D. Bloomfield, A.M. MacLeod, *Biog. Med. Chem. Lett,* **2017**, 17, 2643-2648.
22. D.L. Bai, X. C. Tang, X.C.He, *Curr. Med. Chem.*, **2000**, **7**, 355.
23. J. M .Wilkinson, W. N. Leeuwen van, N. H. Reek, *J Org Biomol Chem.,* **2005**, 3, 2371.
24. L.B.Rai, H. Khodr, C.R.Hider, *Tetrahedron*, **1999**, 55, 1129.
25. Nadri S. Rafiee E. Jamali S., Joshaghani M., *Synlett*, **2015**, 26, 619-624.
26. Yu L. Huang Y. Wei Z. Ding Y. Su C. Xu Q., *J. Org. Chem.*, **2015**, 80, 8677-8683.
27. S.J. Sabounchi, .Ahmadi Azizi, Panahimehr M. *Synlett*, **2014**, 25, 336-342.
28. G.Z.Wang, R. Shang, M.W. Cheng, Y.Fu, *J. Am. Chem. Soc.*, **2017**, 139, 18307-18312.
29. C.Rossy, E. Fouquet, F.X. Felpin, *Synthesis*, **2012**, 44, 37-41.
30. W. B. Reid, J. J. Spillane, S.B. Krause Watson D.A., *J. Am. Chem. Soc.*, **2016,** 138, 5539- 5542.
31. G.Z. Wang, R. Shang, Y.Fu, *Org. Lett.*, **2018**, 20, 888-891.
32. S. Panel, Jitendra Vardia, *Sustainable Chemistry and Pharmacy*, **2017**, 6, 14-20.