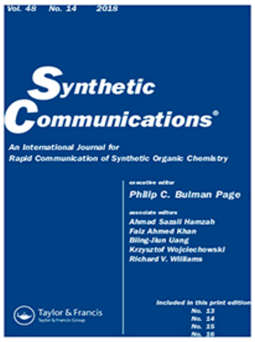

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A three component one-pot synthesis of N-amino-2-pyridone derivatives catalyzed by KF-Al_2O_3

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ABSTRACT

Synthesis of 1,6-diamino-4-phenyl-3,5-dicyano-2-pyridone derivatives *via* a one-pot, three-component reaction of aryl aldehydes, malononitrile, and cyanoacetic hydrazide at room temperature using KF-Al_2O_3 as a recyclable catalyst have been developed. The reaction proceeds through the initial Knoevenagel condensation between aldehyde and malononitrile in the presence of KF-Al_2O_3 to form the benzylidene derivative which then undergoes Michael addition with cyanoacetic hydrazide followed by intramolecular cyclization of the resulting intermediate to produce the N-amino-2-pyridones in good to excellent yields. The structure of the synthesized compounds were characterized and established on the basis of their spectral data analysis and single-crystal XRD analysis.

ARTICLE HISTORY
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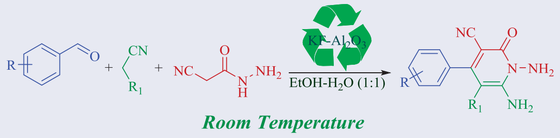
KEYWORDS
KF-Al_2O_3; multi-component reactions; N-amino-2-pyridones

GRAPHICAL ABSTRACT



Introduction

Multi-component reactions (MCRs) have become a powerful synthetic strategy in synthetic organic chemistry due to their flexibility, atomic economy, and convergence. They are usually favoured for development of environmentally benign synthetic methods in organic syntheses.[1] MCRs have also been successfully employed for the synthesis of diverse range of heterocyclic compounds having wide application in pharmaceutical industry and material science.[2,3] In recent years, MCRs have been used for the synthesis of N-heterocycles having structural diversity. The synthesis of 2-pyridone derivatives has attracted much attention as they are valuable building blocks in natural products synthesis. They are also known to possess pharmacological, antibacterial,[4] antifungal,[5] anti-inflammatory,[6] and anti-tumour[7,8] properties. Furthermore, 3,5-dicyanopyridine

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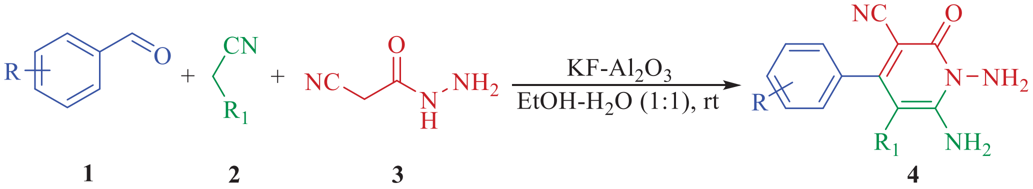


2a; R_1=CN, **2b**; R_1=COOMe, **2c**; R_1=COOEt

Scheme 1. Synthesis of N-amino-2-pyridone derivatives.

derivatives have been reported to possess a number of pharmacological properties and have been considered as useful anti-prion[9,10] and anticancer agents.[11] Likewise molecules bearing N-amino-2-pyridone moieties are also used as building blocks for the synthesis of biologically active natural products[12] and as well as a versatile synthon for the construction of biologically important heterocycles.[5,13–15]

A number of methods have been reported for the synthesis of N-substituted 2-pyridone derivatives. Generally, these methods employed heterogeneous catalysts such as Zirconium pyrophosphates (ZrP_2O_7) nano particles,[16,17] ZnO nanoparticles and magnesium oxide (MgO),[18] while bismuth (III) nitrate pentahydrate ($Bi(NO_3)_3{\cdot}5H_2O$)[18] and piperidine[19] have also been used for synthesis of the N-amino-2-pyridones. These methods, however, suffer from limitations such as long reaction time, harsh reaction conditions, use of toxic solvents and non-reusable catalysts. The development of an alternative protocol for an efficient, clean, and environmentally benign method for the synthesis of N-diamino-2-pyridone derivatives would therefore be of considerable interest. The use of solid heterogeneous catalysts in organic synthesis has been of great interest due to operational simplicity, high selectivity, and clean separation of the products.[20–22] Potassium fluoride impregnated over alumina (KF-Al_2O_3) has been recognized as an efficiently recyclable and useful green heterogeneous catalyst to promote a wide range of organic reactions.[23–29]

As part of our ongoing interest in the synthesis of some important heterocyclic compounds through MCRs,[30–32] we herein wish to report a rapid and green approach for the synthesis of highly substituted N-amino-2-pyridones *via* a three-component condensation of aromatic aldehydes **1**, active methylene compound **2**, and 2-cyanoacetohydrazide **3** in the presence of catalytic amount of KF-Al_2O_3 at room temperature to afford the required products **4** in excellent yields (Scheme 1).

Results and discussion

Optimization of reaction conditions

The reaction of 4-methoxybenzaldehyde **1b** (2 mmol) malononitrile **2a** (2.1 mmol) and cyanoacetic hydrazide **3** (2.1 mmol) was selected as model reaction to establish the best reaction conditions. The reaction was first performed without any catalyst at room temperature, and even after more than 3 h only trace amount of the product (<5%) was obtained. The reaction was then carried out in the presence of the prepared catalyst (KF-Al_2O_3) and the effect of different solvent systems for the synthesis of 1,6-diamino-4-(4-methoxyphenyl)-3,5-dicyano-2-pyridone **4b** was studied (summarized

Table 1. Synthesis of 1,6-diamino-4-(4-methoxyphenyl)-3,5-dicyano-2-pyridone 4b: Effect of solvent and catalyst loading.

t	Catalyst (mol%)	Solvent	Time (min)	Yield (%)[a]
1	No catalyst	EtOH	180	<5 (trace)
2	10	EtOH	45	89
3	10	CH_3CN	45	90
4	10	H_2O	45	65
5	5	EtOH-H_2O (1:1)	45	78
6	10	EtOH-H_2O (1:1)	40	89
7	15	EtOH-H_2O (1:1)	30	96
8	20	EtOH-H_2O (1:1)	30	96

[a] Isolated yield.

in Table 1). The reaction carried out using water, EtOH, EtOH-H_2O (1:1), and acetonitrile. From a greener approach in synthesis, 50% EtOH was chosen as a suitable solvent for the reaction. The model reaction was also optimized in terms of catalyst loading and addition of 5 mol% catalyst resulted in a sharp increase of yield within a short period of time. And the use of 15 mol% of catalyst was found to be most sufficient for good yield of the product. Further increase in addition of catalyst up to 20 mol% did not show any effective increase in the product yield.

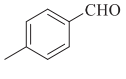
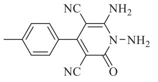
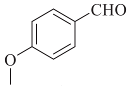
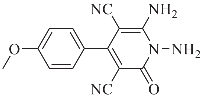
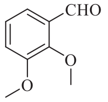
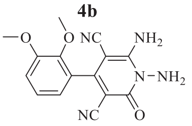
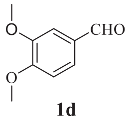
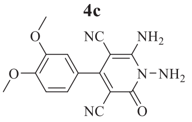
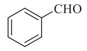
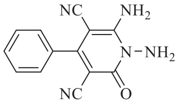
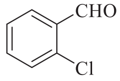
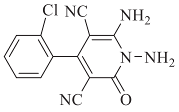
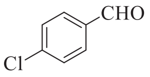
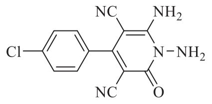
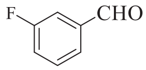
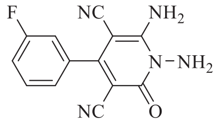
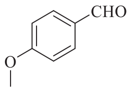
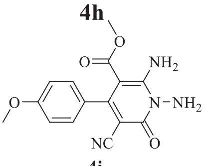
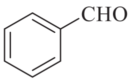
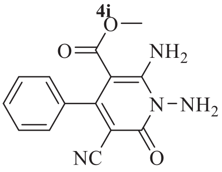
Under the optimized conditions, sets of controlled reactions in 50% ethanol of aromatic aldehydes, malononitrile or methyl cyanoacetate or ethyl cyanoacetate, and 2-cyanoacetohydrazide in the presence of catalytic amount of KF-Al_2O_3 (15 mol%) *via* a three component reaction generates the desired N-amino-2-pyridone derivatives in good yields. Substituted aldehydes with electron-withdrawing and electron-donating groups under the same reaction condition also resulted in excellent yield of the products (Table 2). Disubstituted aldehydes such as 2,3-dimethoxy benzaldehyde (**1c**) and 4,5-dimethoxy benzaldehyde (**1d**) with malononitrile **2a** and 2-cyanoacetohydrazide **3** gave **4c** and **4d** in 84–87% yields (Table 2, entry 3–4). This method also gave good yield of fluorinated N-amino-2-pyridone derivatives both at -*meta*, and -*para* positions (Table 2, entry 8,12–14). The present method was also carried out with aliphatic aldehydes under the optimized condition but failed to give the desired N-amino-2-pyridones.

The plausible mechanism is depicted in Scheme 2, which involves Knoevenagel condensation, Michael addition, and cyclization to form N-amino-2-pyridone derivatives. The reaction presumably proceeds through the initial Knoevenagel condensation between aldehyde **1** and malononitrile **2a** in the presence of KF-Al_2O_3 to form the intermediate **5**. The intermediate **5** then undergoes Michael addition with activated cyanoacetic hydrazide **3** followed by intramolecular cyclization of the resulting intermediate **6** which undergoes dehydration to produce N-amino-2-pyridones.

Recyclability of catalysts

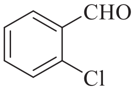
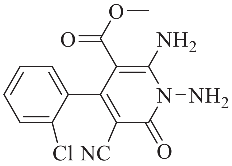
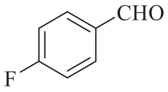
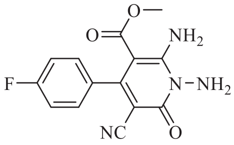
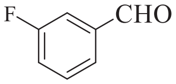
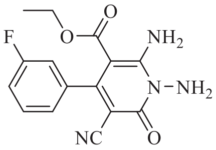
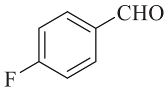
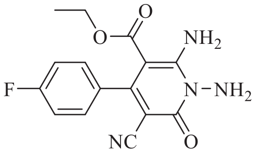
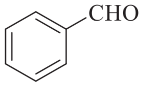
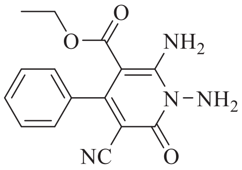
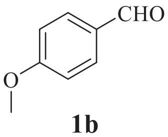
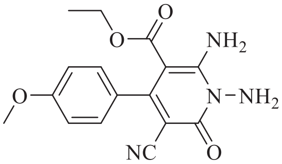
After first use, the catalyst was separated by filtration, washed with ethanol, ethyl acetate and then dried. The recovered catalyst was further used for the same reaction to check the catalytic activity and it was found out that the catalyst can be recycle and reused effectively up to five times, after which the yield start to decrease gradually (Fig. 1). A comparative study of the catalytic activity of KF-Al_2O_3 with reported catalysts was given in Table 3.

Table 2. Three-component one-pot synthesis of N-amino-2-pyridone derivatives.

Entry	Substrate 1	Substrate 2 (R_1)	Time (min)	Product	Yield^{a} (%)
1	 **1a**	CN	35	 **4a**	95
2	 **1b**	CN	30	 **4b**	96
3	 **1c**	CN	35	 **4c**	84^{b}
4	 **1d**	CN	40	 **4d**	87
5	 **1e**	CN	40	 **4e**	87^{b}
6	 **1f**	CN	30	 **4f**	93
7	 **1g**	CN	30	 **4g**	96
8	 **1h**	CN	35	 **4h**	92
9	 **1b**	COOMe	45	 **4i**	93
10	 **1e**	COOMe	45	 **4j**	82^{b}
11		COOMe	40		89

(*continued*)

Table 2. Continued

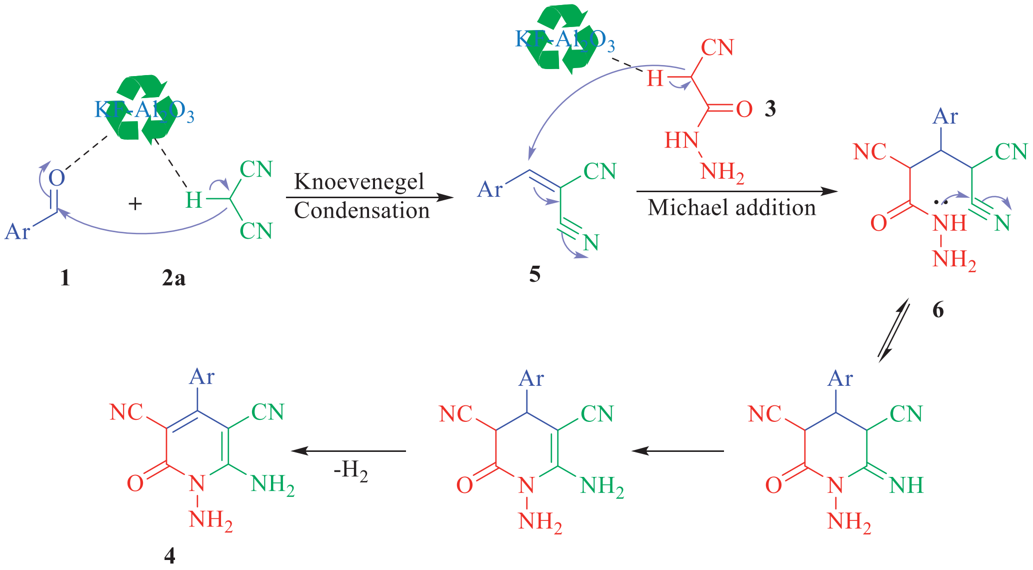
Entry	Substrate 1	Substrate 2 (R_1)	Time (min)	Product	Yield[a] (%)
	 **1f**			 **4k**	
12	 **1i**	COOMe	40	 **4l**	91
13	 **1h**	COOEt	35	 **4m**	87
14	 **1i**	COOEt	40	 **4n**	88
15	 **1e**	COOEt	40	 **4o**	85[b]
16	 **1b**	COOEt	35	 **4p**	89

[a] Isolated yield.
[b] Purified by column chromatography.

Experimental section

Materials and methods

All commercially available chemicals and reagents were purchased from Sigma Aldrich, Merck (St. Louis, MO) and were used without further purification. The synthesized compounds were characterized by FT-IR, ^1H NMR, ^{13}C NMR and mass spectrometry analyses. Melting points were recorded with open capillary tube method and are uncorrected.



Scheme 2. Mechanism for the synthesis of N-amino- 2- pyridine derivatives.

Table 3. Comparative study of catalytic activity of KF-Al_2O_3 with reported catalysts for the synthesis of N-amino-2-pyridones.

Catalyst	Reaction time	Solvent	Temperature	Yield (%)	References
ZrP_2O_7 NPs	35	EtOH	Reflux	84	[16]
$CdZr_4(PO_4)_6$ NPs	45	EtOH	Reflux	82	[17]
MgO	40	EtOH	Reflux	82	[18]
$Bi(NO_3)_3{\cdot}5H_2O$	10	EtOH	Reflux	90	[18]
Piperidine	5hrs	Dioxane	Reflux	42	[33]
KF-Al_2O_3	**30**	**EtOH-H_2O (1:1)**	**Rt**	**96**	**This work**

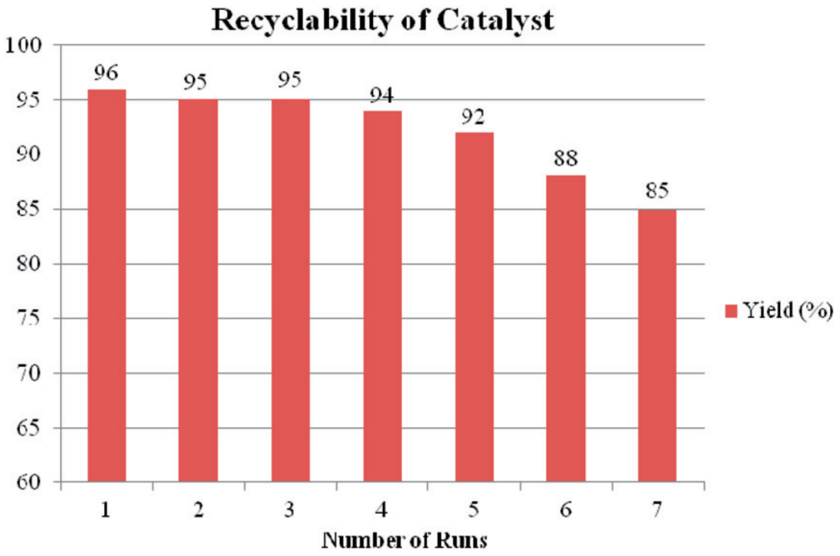


Figure 1. Recyclability results of KF-Al_2O_3 (15 mol%) with **4b**.

FT-IR spectra were recorded with KBr pellets using a Perkin-Elmer 400 Series FT-IR spectrometer (Waltham, MA). ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance II-400 instrument operating at 400 MHz for protons, 100 MHz for carbon in dimethylsulphoxide (DMSO-d_6) as solvent (chemical shifts in δ) with tetramethylsilane (TMS) as internal standard. Electrospray ionization (ESI) mass spectra were recorded on a Waters ZQ-4000 LC-MS spectrometer. The progress of the reaction was monitored by thin-layer chromatography (TLC) analysis on pre-coated silica gel 60 F_{254} aluminum sheets (Merck), visualized under UV light.

X-ray crystallography

The X-ray crystallography data of **4g** and **4i** (Table 4) was collected at 292.6(6) K with a Agilent Xcalibur (Eos, Gemini) diffractometer using graphite monochromated Mo-K_α radiation ($\lambda = 0.71073$ Å). The data was collected and refined in CrysAlis PRO (Rigaku, 2015) software[34] and data reduction was performed using the CrysAlisPro (Rigaku, 2015) software which corrects for Lorentz polarisation. A multi-scan absorption correction was performed using CrysAlisPro (Rigaku, 2015). Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm. Using Olex2,[35] the structure was solved with the ShelXS[36] structure solution program using Direct Methods and refined with ShelXL-2018[37] using full matrix least squares on F^2 minimisation. All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were calculated geometrically and refined using the riding model. An ORTEP view of **4g** and **4i** are illustrated by ORTEP-3[38] as shown in Figure 2. The crystal

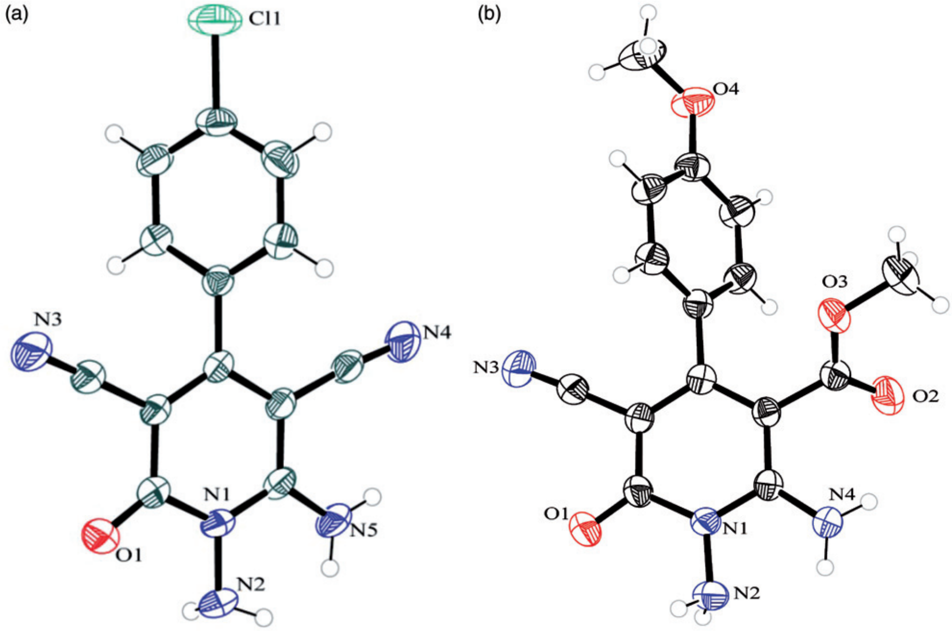


Figure 2. Ortep image of (a) **4g** (**CCDC 1824530**) and (b) **4i** (**CCDC 1824529**) showing thermal ellipsoids at 50% probability level.

Table 4. X-ray crystallography data for compound **4g** (**CCDC 1824530**) and **4i** (**CCDC 1824529**).

Empirical formula	$C_{13}H_8ClN_5O$ **(4g)**	$C_{15}H_{14}N_4O_4$ **(4i)**
Formula weight	285.69	314.30
Temperature (K)	292.6 (6)	295.7 (6)
Wavelength (Å)	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/n$
a (Å)	9.1112 (11)	9.3961 (7)
b (Å)	7.8131 (11)	14.2120 (9)
c (Å)	17.807 (2)	11.5460 (9)
α (°)	90	90
β (°)	94.076 (11)	99.299 (7)
γ (°)	90	90
Volume ($Å^3$)	1264.4 (3)	1521.56 (19)
Z	4	4
ρ (calc.) (g/cm^3)	1.501	1.372
Absorption coefficient (μ) (mm^{-1})	0.305	0.102
F(000)	584	656
2θ range for data collection (°)	6.638 to 52.73	6.738 to 52.74
Index ranges	$-5 \le h \le 11, -9 \le k \le 8, -22 \le l \le 21$	$-11 \le h \le 10, -17 \le k \le 16, -14 \le l \le 14$
Reflections collected	4883	5888
Independent reflections	2562 [$R_{int} = 0.0305$]	3109 [$R_{int} = 0.0294$]
Data/restraints/parameters	2562/0/182	3109/0/211
Goodness-of-fit on F^2	1.014	1.028
Final R indices [$I \ge 2\sigma(I)$]	$R_1 = 0.0532$, $wR_2 = 0.1334$	$R_1 = 0.0482$, $wR_2 = 0.1048$
R indices (all data)	$R_1 = 0.0823$, $wR_2 = 0.1526$	$R_1 = 0.0749$, $wR_2 = 0.1189$

structural data can be obtained free of charge on request from the Cambridge Crystallographic Data Center (https://www.ccdc.cam.ac.uk/structures/?).

Preparation of catalyst (KF-Al_2O_3)

The catalyst, KF-Al_2O_3 was prepared according to the method reported in the literature, with some modification.[39] A mixture of potassium fluoride (5.8 g, 10 mmol) and activated neutral alumina (10 g, 10 mmol) in water (10 mL) was stirred at room temperature for 12 h. The resulting suspension was concentrated on rotary evaporator at 60 °C, and then dried in a desiccator under vacuum for 6–8 h. After activation in hot oven at 140 °C for 4–6 h, KF-Al_2O_3 was used for catalysis.

General procedure

Synthesis of Cyanoacetic hydrazide (3)

Cyanoacetic acid hydrazide was obtained by careful addition of 22.62 g (0.20 mol) of ethyl cyanoacetate to hydrazine hydrate (10.01 g, 0.20 mol) with stirring at 0 °C.[40] The solid cyanoacetic acid hydrazide so formed was filtered, washed with Et_2O and dried, in which a yield of 95% is obtained.

Synthesis of N-amino-2-pyridone derivatives 4 (a-p)

A mixture of aromatic aldehydes **1** (2 mmol), active methylene compound **2** (2.1 mmol) and cyanoacetic hydrazide **3** (2.1 mmol), 15 mol% of KF-Al_2O_3 in EtOH-H_2O (1:1) was stirred at room temperature and the progress of the reaction was monitored by TLC. On completion, the reaction solution was filtered and washed with ethyl acetate and the catalyst was recovered and recycled. The solvent was evaporated and the solid which separated out was collected and recrystallized with ethanol to get the pure product. A few members of the synthesised products were purified by column chromatography. The synthesised products were characterised from their ^{1}H NMR, ^{13}C NMR, FT-IR and single crystal XRD analyses.

1,6-Diamino-4-(4-methoxyphenyl)-3,5-dicyano-2-pyridone 4(b)

White crystals; yield: 96%, mp 221–224 °C [Lit.[19], mp 225 °C] IR (KBr): ν_{max} 3479, 3343, 3229, 2218, 1637, 1610, 1243 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.42 (s, 2H, NH_2), 7.45 (d, $J = 8.4$ Hz, 2H, CH_{Ar}), 7.09 (d, $J = 8.4$ Hz, 2H, CH_{Ar}), 5.64 (s, 2H, NH_2), 3.83 (s, 3H, OCH_3) ppm; ^{13}C NMR (101 MHz, DMSO-d_6) δ 160.64, 159.35, 159.19, 156.62, 130.65, 129.80, 126.42, 116.65, 115.76, 113.87, 113.24, 86.06, 74.24, 55.27 ppm; MS (ES$^+$) calcd. for $C_{14}H_{11}N_5O_2$: 281.2, found m/z 282.1 $[M + H]^+$. Anal. Calcd. for $C_{14}H_{11}N_5O$: C 59.78, H 3.94, N 24.90%, found C 59.66, H 3.99, N 24.77%.

Conclusions

In summary, we have established a simple and efficient method for the synthesis of N-amino-2-pyridones following an environment friendly protocol using KF-Al_2O_3 as a recyclable catalyst. The method offers several advantages involving short reaction time, simple work-up procedure with little or no purification required affording good to excellent yields of the desired products. Due to its operational simplicity, this facile method is expected to have wider application for the preparation of N-amino-2-pyridone derivatives.

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References

[1] Dömling, A.; Ugi, I. Multicomponent Reactions with Isocyanides. *Angew. Chem. Int. Ed. Engl.* **2000**, *39*, 3168–3210. DOI:10.1002/1521-3773(20000915)39:18<3168::AID-ANIE3168>3.0.CO;2-U.

[2] Sunderhaus, J.D.; Martin, S.F. Applications of Multicomponent Reactions to the Synthesis of Diverse Heterocyclic Scaffolds. *Chemistry*. **2009**, *15*, 1300–1308. DOI:10.1002/chem.200802140.

[3] Sunderhaus, J. D.; Dockendorff, C.; Martin, S. F. Applications of Multicomponent Reactions for the Synthesis of Diverse Heterocyclic Scaffolds. *Org. Lett.* **2007**, *9*, 4223–4226. DOI:10.1021/ol7018357.

[4] Desai, N. C.; Rajpara, K. M.; Joshi, V. V. Synthesis of Pyrazole Encompassing 2-Pyridone Derivatives as Antibacterial Agents. *Bioorganic Med. Chem. Lett.* **2013**, *23*, 2714–2717. DOI:10.1016/j.bmcl.2013.02.077.

[5] Ibrahim, M. A.; Abdel-Rahman, R. M.; Abdel-Halim, A. M.; Ibrahim, S. S.; Allimony, H. A. Synthesis and Antifungal Activity of Novel Polyheterocyclic Compounds Containing Fused 1, 2, 4-Triazine Moiety. *Arkivoc.* **2008**, *2008*, 202–215. DOI:10.3998/ark.5550190.0009.g19.

[6] Ismail, M. M. F.; Ammar, Y. A.; El-Zahaby, H. S. A.; Eisa, S. I.; Barakat, E.-S. S. Synthesis of Novel 1-Pyrazolylpyridin-2-Ones as Potential anti-Inflammatory and Analgesic Agents. *Arch. Pharm. Chem. Life. Sci.* **2007**, *340*, 476–482. DOI:10.1002/ardp.200600197.

[7] Nagarajan, M.; Xiao, X.; Antony, S.; Kohlhagen, G.; Pommier, Y.; Cushman, M. Design, Synthesis, and Biological Evaluation of Indenoisoquinoline Topoisomerase I Inhibitors Featuring Polyamine Side Chains on the Lactam Nitrogen. *J. Med. Chem.* **2003**, *46*, 5712–5724. DOI:10.1021/jm030313f.

[8] Cocco, M. T.; Congiu, C.; Onnis, V. New Bis(pyridyl)methane Derivatives from 4-Hydroxy-2-Pyridones: Synthesis and Antitumoral Activity. *Eur. J. Med. Chem.* **2003**, *38*, 37–47. DOI:10.1016/S0223-5234(02)00002-8.

[9] Reddy, T. R. K.; Mutter, R.; Heal, W.; Guo, K.; Gillet, V. J.; Pratt, S.; Chen, B. Library Design, Synthesis, and Screening: Pyridine Dicarbonitriles as Potential Prion Disease Therapeutics. *J. Med. Chem.* **2006**, *49*, 607–615. DOI:10.1021/jm050610f.

[10] May, B. C. H.; Zorn, J. A.; Witkop, J.; Sherrill, J.; Wallace, A. C.; Legname, G.; Prusiner, S. B.; Cohen, F. E. Structure-Activity Relationship Study of Prion Inhibition by 2-Aminopyridine-3,5-Dicarbonitrile-Based Compounds: Parallel Synthesis, Bioactivity, and in Vitro Pharmacokinetics. *J. Med. Chem.* **2007**, *50*, 65–73. DOI:10.1021/jm061045z.

[11] Cocco, M. T.; Congiu, C.; Lilliu, V.; Onnis, V. Synthesis and Antiproliferative Activity of 2,6-Dibenzylamino-3,5-Dicyanopyridines on Human Cancer Cell Lines. *Eur. J. Med. Chem.* **2005**, *40*, 1365–1372. DOI:10.1016/j.ejmech.2005.07.005.

[12] Shojaei, H.; Li-Böhmer, Z.; von Zezschwitz, P. Iromycins: A New Family of Pyridone Metabolites from *Streptomyces* sp. II. Convergent Total Synthesis. *J. Org. Chem.* **2007**, *72*, 5091–5097. DOI:10.1021/jo070327j.

[13] Ibrahim, M. A.; Abdel-Rahman, R. M.; Abdel-Halim, A. M.; Ibrahim, S. S.; Allimony, H. A. Synthesis, Chemical Reactivity and Fungicidal Activity of Pyrido[1,2-b][1,2,4]Triazine Derivatives. *J. Braz. Chem. Soc.* **2009**, *20*, 1275–1286. DOI:10.1590/S0103-50532009000700012.

[14] Abdel-Monem, W. R. Synthesis and Biological Evaluation of Some New Fused Heterobicyclic Derivatives Containing 1,2,4-Triazolo/1,2,4-Triazinopyridinone Moieties. *Chem. Pap.* **2004**, *58*, 276–285.

[15] Harb, A. A. Reactions of Some Active Carbonyl Compounds with 4-Aryl-1,6-Diamino-2-Oxo-1,2-Dihydropyridine-3,5-Dicarbonitrile Derivatives. *Chem. Pap.* **2004**, *58*, 260–267.

[16] Safaei-Ghomi, J.; Hossein, S. -A.; Saberi-Moghadam, M. R.; Ziarati, A. ZrP2O7 NPs: A Recyclable, Efficient Heterogeneous Catalyst for the Synthesis of 1,6-Diamino-2-Oxo-4-Phenyl-1,2-Dihydropyridine-3,5-Dicarbonitrile Derivatives via a Multi-Component Reaction. *Iran. J. Catal.* **2014**, *4*, 289–294.

[17] Safaei-Ghomi, J.; Shahbazi-Alavi, H.; Ziarati, A. A Comparative Screening of the Catalytic Activity of Nanocrystalline MIIZr4(PO4)6ceramics in the One-Pot Synthesis of 1,6-Diamino-4-Aryl-2-Oxo-1,2-Dihydropyridine-3,5-Dicarbonitrile Derivatives. *Res. Chem. Intermed.* **2017**, *43*, 91–101. DOI:10.1007/s11164-016-2608-6.

[18] Seifi, M.; Rabori, M. K.; Sheibani, H. Highly Efficient Method for Synthesis of N-Amino-2-Pyridone Derivatives in the Presence of Catalysts Such as Magnesium Oxide (MgO) and Bismuth(III) Nitrate Pentahydrate (Bi(NO3)3·5H2O). *MRC*. **2013**, *02*, 8–12. DOI:10.4236/mrc.2013.22A002.

[19] Soto, J. L.; Seoane, C.; Zamorano, P.; Cuadrado, F. J. A Convenient Synthesis of N-Amino-2-Pyridones. *Synthesis (Stuttg)*. **1981**, *1981*, 529–530. DOI:10.1055/s-1981-29512.

[20] Climent, M. J.; Corma, A.; Iborra, S. Heterogeneous Catalysts for the One-Pot Synthesis of Chemicals and Fine Chemicals. *Chem. Rev*. **2011**, *111*, 1072–1133. DOI:10.1021/cr1002084.

[21] Daştan, A.; Kulkarni, A.; Török, B. Environmentally Benign Synthesis of Heterocyclic Compounds by Combined Microwave-Assisted Heterogeneous Catalytic Approaches. *Green Chem*. **2012**, *14*, 17–37. DOI:10.1039/C1GC15837F.

[22] Gao, W.; Hood, Z. D.; Chi, M. Interfaces in Heterogeneous Catalysts: Advancing Mechanistic Understanding through Atomic-Scale Measurements. *Acc. Chem. Res*. **2017**, *50*, 787–795. DOI:10.1021/acs.accounts.6b00596.

[23] Clark, J. H. Fluoride Ion as a Base in Organic Synthesis. *Chem. Rev*. **1980**, *80*, 429–452. DOI:10.1021/cr60327a004.

[24] Adams, D. J.; Clark, J. H. Nucleophilic Routes to Selectively Fluorinated Aromatics. *Chem. Soc. Rev*. **1999**, *28*, 225–231. DOI:10.1039/a808707e.

[25] Blass, B. E.; Drowns, M.; Harris, C. L.; Liu, S.; Portlock, D. E. A Facile KF/A1203 Mediated Method for the Synthesis of Substituted Oxazolidinones. *Tetrahedron Lett*. **1999**, *40*, 6545–6547. DOI:10.1016/S0040-4039(99)01310-6.

[26] Blass, B. E.; Burt, T. M.; Liu, S.; Portlock, D. E.; Swing, E. M. A Facile Kf/Al2O3 Mediated, Selective Alkylation of Benzodiazepin-2,5-Diones. *Tetrahedron Lett*. **2000**, *41*, 2063–2066. DOI:10.1016/S0040-4039(00)00115-5.

[27] Blass, B. E. KF/Al2O3 Mediated Organic Synthesis. *Tetrahedron*. **2002**, *58*, 9301–9320. DOI:10.1016/S0040-4020(02)00992-4.

[28] Blass, B. E.; Coburn, K.; Fairweather, N.; Sabat, M.; West, L. A Facile, KF/Al2O3 Mediated Method for the Preparation of Functionalized Pyrido[2,3-D]Pyrimidin-7(8H)-Ones. *Tetrahedron Lett*. **2006**, *47*, 3177–3180. DOI:10.1016/j.tetlet.2006.02.155.

[29] Basu, B.; Das, P.; Das, S. Recent Advances in KF/Alumina Promoted Organic Reactions. *Curr. Organic Chem*. **2008**, *12*, 141–158. DOI:10.2174/138527208783330046.

[30] Mecadon, H.; Rohman, M. R.; Kharbangar, I.; Laloo, B. M.; Kharkongor, I.; Rajbangshi, M.; Myrboh, B. L-Proline as an Efficicent Catalyst for the Multi-Component Synthesis of 6-Amino-4-Alkyl/Aryl-3-Methyl-2,4-Dihydropyrano[2,3-C]Pyrazole-5-Carbonitriles in Water. *Tetrahedron Lett*. **2011**, *52*, 3228–3231. DOI:10.1016/j.tetlet.2011.04.048.

[31] Rohman, M. R.; Mecadon, H.; Khan, A. T.; Myrboh, B. Synthesis of Important β-Functionalized 5-Methyl-1H-Pyrazol-3-Ol Derivatives in the Presence of γ-Alumina Catalyst in Aqueous Medium. *Tetrahedron Lett*. **2012**, *53*, 5261–5264. DOI:10.1016/j.tetlet.2012.07.073.

[32] Bhattacharjee, D.; Kshiar, B.; Myrboh, B. L-Proline as an Efficient Enantioinduction Organo-Catalyst in the Solvent-Free Synthesis of Pyrazolo[3,4-B]Quinoline Derivatives via One-Pot Multi-Component Reaction. *RSC Adv*. **2016**, *6*, 95944–95950. DOI:10.1039/C6RA22429F.

[33] Mahmoud, M. R.; Abu El-Azm, F. S. M.; Ali, A. T.; Ali, Y. M. Synthesis and Antimicrobial Evaluation of Some Novel Dithiolane, Thiophene, Coumarin, and 2-Pyridone Derivatives. *Synth. Commun*. **2017**, *47*, 1591–1600. DOI:10.1080/00397911.2017.1336776.

[34] CrysAlisPro Software System. CrysAlisPro: Single Crystal Diffraction Software. *Rigaku J*. **2016**, *32*, 31–34.

[35] Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; K, H. J. A.; Puschmann, H. OLEX2: A Complete Structure Solution, Refinement and Analysis Program. *J. Appl. Crystallogr*. **2009**, *42*, 339–341. DOI:10.1107/S0021889808042726.

[36] Sheldrick, G. M. A Short History of SHELX. *Acta Crystallogr. A Found. Crystallogr*. **2008**, *64*, 112–122. DOI:10.1107/S0108767307043930.

[37] Sheldrick, G. M. Crystal Structure Refinement with SHELXL. *Acta Crystallogr. C Struct. Chem*. **2015**, *71*, 3–8. DOI:10.1107/S2053229614024218.

[38] Farrugia, L. J. WinGX and ORTEP for Windows: An Update. *J. Appl. Crystallogr*. **2012**, *45*, 849–854. DOI:10.1107/S0021889812029111.

[39] Yamawaki, J.; Ando, T. Potassium Fluoride on Inorganic Solid Supports. A Search for Further Efficient Reagents Promoting Hydrogen-Bond-Assisted Alkylations. *Chem. Lett*. **1979**, *8*, 755–758. DOI:10.1246/cl.1979.755.

[40] Gorobets, N. Y.; Yousefi, B. H.; Belaj, F.; Kappe, C. O. Rapid Microwave-Assisted Solution Phase Synthesis of Substituted 2-Pyridone Libraries. *Tetrahedron*. **2004**, *60*, 8633–8644. DOI:10.1016/j.tet.2004.05.100.