ISSN 2321-807X

Poly (4-vinylpyridine) and polyaniline: As efficient and commercial available basic catalysts for the synthesis of *N*-amino-2-pyridones under thermal conditions or microwave irradiation

Tayebeh Sattaei Mokhtari[b], Hassan Sheibani[a*], Mohammad Ali Amrollahi [b] and Enayatollah Sheikh hosseini [c]

[a]Department of Chemistry, Shahid Bahonar University of Kerman, Kerman 76169, Iran
hsheibani@mail.uk.ac.ir
[b]Department of Chemistry, College of Science, Yazd University, P. O. Box 89195-741, Yazd, Iran
taybeh.mokhtari@gmail.com
[c]Department of Chemistry, Kerman Branch Islamic Azad University, Kerman, Iran
enayatsheikhhosseini@gmail.com

*Corresponding author: hsheibani@mail.uk.ac.ir

ABSTRACT

Poly (4-vinylpyridine) and polyaniline as highly effective base catalysts have catalyzed the three-component reaction of an appropriate aldehyde, cyanoacetic acid hydrazide and malononitrile to prepare of the corresponding *N*-amino-2-pyridone derivatives. These reactions occur in ethanol at reflux or under microwave heating, in the presence of the base catalysts, are inexpensive and easily obtained with consistent activity.

Keywords: Poly (4-vinylpyridine); polyaniline; cyanoacetic acid hydrazide; *N*-amino-2-pyridine; microwave irradiation

Council for Innovative Research

Peer Review Research Publishing System

Journal: Journal of Advances in Chemistry

Vol. 10, No. 1

editorjaconline@gmail.com

www.cirworld.org/journals

ISSN 2321-807X

1. INTRODUCTION

Heterocycles are ubiquitous in various compounds of interest, and among all heterocyclics, nitrogen-containing compounds have long been of interest to organic chemists and biochemists and are present in many types of pharmaceuticals. The six-membered ring systems having nitrogen atoms in their rings are found abundantly in nature[1].Among of these six-membered ring systems, polyfunctional pyridinones are highly reactive reagents that have been used extensively in heterocyclic synthesis[2]which possess biological as well as pharmacological activity [3]. *N*-amino-2-pyridoneshaveknown asusefulsynthetic intermediates and a versatile synthon for the synthesis of a variety of other nitrogen-containing heterocyclic compounds, such as β-lactams, piperidines, and indolizidine alkaloids[4]. The dienophiles have been reacted with diene portion of these molecules *via* Diels-Alder cycloaddition reactions, or one double bond of these molecules, may act as a dienophile and add to diene [5].There are few reported methods for the synthesis of *N*-amino-2-pyridones in the literature[6, 7].These compounds were usually prepared in low yields by condensation of hydrazine with 2-pyrones followed by the loss of water[8, 9]. The most common strategies involve the construction of arylidenemalononitriles, which are easily prepared by Knoevenagel condensation of aromatic aldehydes with malononitrile, and cyanoacetic acid hydrazide in the presence of piperidine as a base catalyst[7].Piperidine and pyridine were usually used as liquid base catalysts in condensation reactions[7, 10]. These liquid catalysts are highly flammable and toxic compounds and be absorbed through the skin mucous membranes. The replacement of liquid base by solid base catalysts would have the advantages to decrease corrosion and reduce environmental problems, accompanied by easier separation and recovery of the catalysts. A large number of solid base catalysts have been studied, including ion-exchange resins, zeolites, alkaline oxides, KNH_2/Al_2O_3 and KF/ Al_2O_3 [11]. Poly(4-vinylpyridine) (PVPy) and polyaniline (PANI) have been used as base catalysts in many organic reactions such as esterification of carboxylic acids with alcohols, convert iminodithiazoles into aryl isothiocyanates and quinazolines, and synthesis of chromene derivatives [12,13]. As part of our current studies on the development of new routes to the synthesis of heterocyclic compounds, by the condensation reaction of 1,3-bielectrophiles with binucleoplies in the presence of highly effective heterogeneous acid or base catalysts [14,15], we now turn our attention to the reactivity of heterogeneous base catalysts such as poly(4-vinylpyridine) and polyanilineon the three-component reaction of arylaldehydes, cyanoacetic acid hydrazide and malononitrile to synthesis of *N*-amino-2-pyridones under thermal conditions and microwave irradiation.

2. EXPERIMENTAL

Melting points were measured on an Electrothermal Enginering LTD apparatus and are uncorrected. IR spectrawere measured on a Mattson 1000 FT-IR spectrometer. The ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d6 as solvent at 400 and 100 MHz, respectively on BRUKER DRX-400 AVANCE spectrometer using TMS as internal standard. Microwave KMIC-1.5KW was used to carry out the reactions.

General procedure for compounds (4a-k)

*General procedure for the preparation of N-amino-2-pyridones (**4a-k**) via two or three-component reaction at reflux (Method I) and under microwave irradiation (Method II). **Method I:** A mixture of two component of cyanoacetic acid hydrazide **1**(2 mmol) and arylidenemalononitriles **I** (2 mmol) or three component of cyanoacetic acid hydrazide **1** (2 mmol), arylaldehydes **2** (2 mmol) and malononitrile **3**(2 mmol) in the presence a few drops pyridine or 0.1 gr poly(4-vinylpyridine) and polyaniline in ethanol (50 mL) was refluxed with stirring for the time reported in Table 2 (the progress of the reaction being monitored by TLC and unsing n-hexane/ethyl acetate as an eluent). The mixture of catalyst and product **4** after cooling, was filtered and separated. This product was placed into a dialysis tube and dialysed against 100 ml of dimethyl sulfoxide for 24h. After completion of dialysis, the solvent was distilled at low pressure. The final compounds 4 were obtained as a solid. **Method II:** the compounds 1, 2, 3 and catalysts were used same as method and placed in a 15 mL high pressure glass tube and situated in a 250 mL beaker. After microwave irradiation at 300 W in the microwave oven for the period of time shown in Table 2, the reaction mixture was allowed to cool to ambient temperature. The mixture of catalyst and product **4** were filtered and separated as described at method 1.*

1,6-Diamino-4-(4-chlorophenyl-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile (4d)

Withe crystals; mp. 243-245 ˚C .IR (KBr, v_{max}/cm^{-1}): 3455, 3265 ($2NH_2$), 2220, 2219 (2CN), 1645(C=O), 1596, 1523(C=C). ^{1}H NMR (400 MHz, DMSO-d_6, ppm): 8.54(broad, s, 2H, NH2), 7.63(d, 2H, Ar), 7.55 (d, 2H, Ar), 5.68 (broad, s, 2H, N-NH2). 13C NMR (100 MHz, DMSO-d6, ppm): 159.06, 158.26, 156.85, 135.49, 133.96, 129.63, 128.75, 115.64, 114.92, 86.91, 73.70.

1,6-Diamino-4-(3-nitrophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile (4j)

Yellow crystals; mp. 251-253 ˚C. IR (KBr, v_{max} /cm^{-1}): 3447, 3329 ($2NH_2$) ,2014, 2210 (2CN), 1676 (C=O), 1613, 1555 (C=C. ^{1}HNMR (400MHZ, DMSO-d_6): 8.63(s, 1H, Ar) , 8.44 (broad, 2H, NH2), 8.42-7.89 (m, 3H, Ar), 5.74 (s,2H,N- NH_2). ^{13}CNMR (100MHz, DMSO-d_6): 158.67, 157.14, 156.45, 146.86, 135.87, 134.37, 130.72, 125.51, 122.59, 116.72, 114.52, 85.81, 74.04

1,6-Diamino-4-(3-boromophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile (4f)

White crystals; mp. 249-250˚C. IR (KBr, v_{max} /cm^{-1}): 3395, 3273 ($2NH_2$), 2220, 2217 (2CN), 1651 (C=O), 1598, 1524 (C=C). ^{1}HNMR (400MHZ, DMSO-d_6): 8.67(s, 1H, Ar), 8.54(broad, 2H, NH2), 7.78-7.52 (m, 3H, Ar), 5.64 (s, 2H, N-NH_2). ^{13}CNMR (100MHz, DMSO-d_6): 159.06, 158.26, 156.86, 145.64, 135.49, 133.96, 130.87, 129.62, 128.75, 115.62, 114.92, 88.91, 74.70

1,6-Diamino-4-(2,4-dichlorophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile (4e)

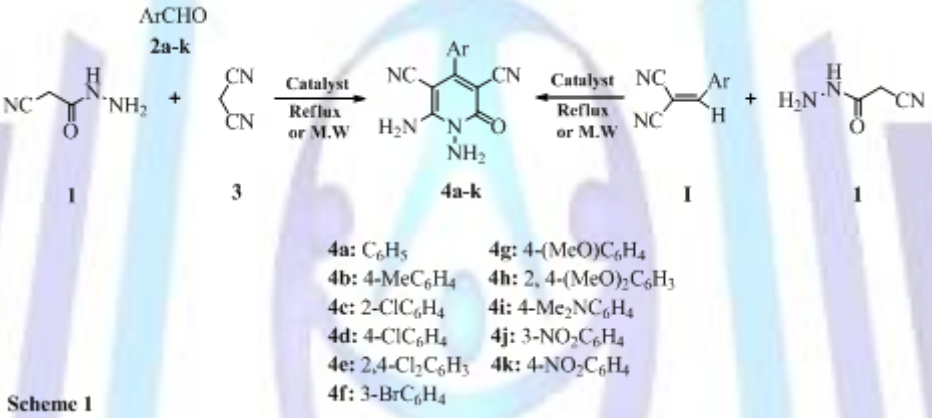
White crystals; mp .256-258 ˚C. IR (KBr, v_{max} /cm^{-1}): 3412, 3201 ($2NH_2$), 2222, 2219 (2CN), 1670(C=O), 1607, 1567(C=C). ^{1}HNMR (400MHZ, DMSO-d_6): 8.68(broad, 2H, NH2), 7.92(s, 1H, Ar), 7.69(d, 1H, Ar), 7.58 (d, 1H, Ar), 5.70 (s, 2H, N-NH_2). ^{13}CNMR (100MHz, DMSO-d_6):15 8.89, 156.51, 156.25, 135.54, 132.77, 131.86, 131.14, 129.45, 128.12, 116.74, 114.51, 87.31, 74.80

1,6-Diamino-4-(4-methoxyphenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile (4g)

Yellow crystals; mp. 225-226 ˚C . IR (KBr, v_{max} /cm^{-1}): 3457, 3269($2NH_2$), 2219, 2217 (2CN), 1643(C=O), 1597, 1513(C=C). ^{1}HNMR (400MHZ, DMSO-d_6): 8.44(broad, 2H, NH2), 7.48(d, 2H, Ar)-7.11(d, 2H, Ar), 5.65 (s, 2H, N- NH_2). ^{13}CNMR(100MHz, DMSO-d_6): 160.87, 159.37, 156.45,133.54, 129.24, 126.30, 116.74, 115.93, 113.80, 86.51, 74.02, 54,90

3. RESULTS AND DISCUSSION

Following our interest in the chemistry of pyridinones [16, 17], in this manuscript we describe our results that explore the potential of heterogeneous base catalysts such as pyridine, poly (4-vinylpyridine) and polyanilinein the synthesis of *N*-amino-2-pyridones. One-pot, two or three-component reaction of cyanoacetic acid hydrazide **1**, arylaldehydes **2** and malononitrile**3** have been proceeded to completion and produce pure product of *N*-amino-2-pyridone**4** derivatives in ethanol at reflux or under microwave heating in the presence of a base catalyst (Scheme 1).



Scheme 1

In recent years, several solid base and acid catalysts have been used as being effective in the reactions that involve the Michael addition and the Knoevenagel condensation. Since the three-component reaction of cyanoacetic acid hydrazide **1** arylaldehydes **2a-h** and malononitrile **3** involve both Knoevenagel condensation and Michael addition, we have studied the effect of the base catalysts such as pyridine, poly (4-vinylpyridine) and polyaniline on these reactions. The Knoevenagel condensations of malononitrile with aldehydes have been extensively studied, and the rate of these reactions are fast. So we have studied separately the Michael addition of cyanoacetic acid hydrazide **1**on arylidenemalononitriles **I**, which afforded the *N*-amino-2-pyridone derivatives**4** in the different conditions (Table 2). In order to optimize the reaction conditions, we used some polar and non-polar solvents in the two and three-component reactions of cyanoacetic acid hydrazide, benzaldehyde and malononitrile in the presence of catalysts such as pyridine, poly(4-vinylpyridine) and polyanilineas model reactions to investigate the effects of solvent for preparing compound **4a** at reflux. In each case, the substrates were mixed together with a few drops pyridine or 0.1 gr poly (4-vinylpyridine) and polyaniline with 10 mL solvent, under conventional heating. The results are shown in **Table 1**. It is noteworthy to mention that the polar solvents such as ethanol afford higher yields than non-polar solvents. We also optimized the quantity of catalysts. The best results were obtained when the reactions were carried out in the presence of 10 mgpoly (4-vinylpyridine) and polyaniline**.**

ISSN 2321-807X

Table1. Solvent and catalyst effects on the two or three-component reaction for the synthesis of **4a** at reflux**.**

Compd, No	Solvent	Base Catalysts	Two Component Time/ Yield (min) / (%)	Three Component Time/ Yield (min) / (%)
4a	Toluene	Py[a]	180/40	180/42
4a	Toluene	PVPy[b]	180/45	180/46
4a	Toluene	PANI[c]	180/47	180/49
4a	Acetonitrile	Py	180/53	180/56
4a	Acetonitril	PVPy	180/57	180/59
4a	Acetonitril	PANI	180/60	180/60
4a	Methanol	Py	60/60	60/62
4a	Methanol	PVPy	40/77	40/76
4a	Methanol	PANI	40/80	40/80
4a	Ethanol	Py	60/66	60/67
4a	Ethanol	PVPy	40/84	40/88
4a	Ethanol	PANI	40/88	40/90

a: Pyridine b: poly(4-vinylpyridine) **c:** polyaniline

As can be seen from Table **2**, the products of *N*-amino-2-pyridones were obtained in high yields and short reaction times in the presence of polyanilineas a base catalyst in ethanol at reflux and under microwave heating. Based on our previous studies on the use of microwave irradiation [16, 18], the effects of base catalyst such as pyridine, poly (4-vinylpyridine) and polyaniline for preparing compounds **4** under different reaction conditions and microwave irradiation were investigated. When polyaniline was employed as a base catalyst in these reactions, the *N*-amino-2-pyridones were obtained in high yield. The polyaniline has known as a conducting polymer. The high conductivity at microwave frequency makes it possible to be used as solid base catalyst in microwave assisted organic chemistry [19].

Table 2: Synthesis of compounds **4a-h** in the presence of base catalysts under thermal conditions and microwave irradiation:

Comp. No	Ar	Py Thermal Two comp. Three comp.] Time/ Yield (min) / (%)	Py M.W Two comp. [Three comp.] Time/ Yield (min) / (%)	PVPy Thermal Two Comp. [Three comp.] Time/ Yield (min) / (%)	PVPy M.W Two Comp. [Three comp.] Time/ Yield (min) / (%)	PANI Thermal Two Comp. [Three comp.] Time/ Yield (min) / (%)	PANI M.W Two Comp. [Three comp.] Time/ Yield (min) / (%)
4a	C_6H_5	60/ 66	10/74	40/84	10/83	40/88	10/92
		[60/67]	[10/73]	[40/83]	[10/85]	[40/90]	[10/90]
4b	4-MeC_6H_4	60/64	10/70	40/86	10/89	40/91	10/90
		[60/67]	[10/73]	[40/86]	[10/88]	[40/92]	[10/91]
4c	2-ClC_6H_4	60/35	10/36	40/69	10/70	40/80	10/84
		[60/39]	[10/39]	[40/72]	[10/72]	[40/79]	[10/85]
4d	4-ClC_6H_4	60/65	10/78	40/90	10/94	40/95	10/95
		[60/66]	[10/75]	[40/92]	[10/95]	[40/94]	[10/95]
4e	2,4-$Cl_2C_6H_3$	60/57	10/63	40/85	10/89	40/88	10/91
		[60/60]	[10/68]	[40/86]	[10/90]	[40/91]	[10/94]
4f	3-BrC_6H_4	60/55	10/68	40/86	10/90	40/90	10/93
		[60/59]	[10/75]	[40/90]	[10/88]	[40/91]	[10/93]

4g	4-$MeOC_6H_4$	60/62	10/71	40/89	10/91	40/90	10/94
		[60/65]	[10/75]	[40/94]	[10/95]	[40/94]	[10/96]
4h	2,4-$(MeO)_2C_6H_3$	60/60	10/66	40/88	10/89	40/89	10/90
		[60/65]	[10/69]	[40/89]	[10/92]	[40/90]	[10/91]
4i	4-$Me_2NC_6H_3$	60/58	10/60	40/80	10/84	40/83	10/88
		[60/61]	[10/66]	[40/84]	[10/89]	[40/85]	[10/91]
4j	3-$NO_2C_6H_4$	60/53	10/58	40/85	10/83	40/87	10/89
		[60/59]	[10/63]	[40/88]	[10/89]	[40/90]	[10/91]
4k	4-$NO_2C_6H_4$	60/54	10/58	40/85	10/87	40/88	10/91
		[60/58]	[10/61]	[40/89]	[10/88]	[40/90]	[10/90]

Malononitrile, aldehydes, pyridine and poly (4-vinylpyridine) were commercially available, obtained from Merck Chemical Co. and used without further purification. Cyanoacetic acid hydrazide was prepared according to a literature procedure [20].The lowmolecular weightpolyanilinewas prepared atroomtemperature according to a literature procedure [21]. Compounds **4a-j** are known in the literature [7, 8]. The structures of compounds **4d, e, f, g** and **j** were elucidated and assigned from their IR, ^{1}H NMR, ^{13}C NMR spectra [22]. Melting points were measured on an Electrothermal Enginering LTD apparatus and are uncorrected. IR spectra were measured on a Mattson 1000 FT-IR spectrometer. The ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d6 as a solvent at 400 and 100 MHz, respectively on BRUKER DRX-400 AVANCE spectrometer using TMS as an internal standard. Microwave KMIC-1.5KW was used to carry out the reactions.

ACKNOWLEDGMENTS

The authors express appreciation to the Shahid Bahonar University of Kerman, University of Yazd and Islamic Azad University of Kerman for supporting this investigation.

REFERENCES

[1] McKillop A.1996. In Comprehensive Heterocyclic Chemistry Katritzky, A. R., Rees, C. W., Scriven, E. F. V.,Eds., Pergamon: Oxford, 5 (1996).

[2] Asadov, Kh., Burangulova, R.N., Guseninov, F.H., Gilmanov, R.Z., Phaljachov, I. Ph. 2003.Regioselective Heterocyclization of Phosphoryl-α-chloroacetaldehydes with 2,3-Diaminopyridine.Chem. Heterocycl.Compounds 39 ,392-393.

[3] Rao, C.S., Venkaleswarlu, V., Achaiah, G. 2006. Quaternary salts of 4,3′ and 4,4′ bis-pyridinium monooximes. Part 2: Synthesis and biological activity**.**Bioorganic and Medicinal Chem. Let.16, 2134-2138

[4] Elbein, A.D., Molyneux, R.J.1981.In Alkaloids Chemical and Biological Perspectives. Pelletier, S.W., Ed., Wiley:New York.

[5] Chou, S.S.P., Chen, P.W. 2008. [4+2] Cycloaddition reactions of 4-sulfur-substituted 2-pyridones with electron-deficient dienophiles. Tetrahedron 64, 5291-97.

[6] Torres, M., Gil, S., Parra, M.C. 2005. New Synthetic Methods to 2-Pyridone Rings. Curr. Org. Chem. 9, 1757-1779.

[7] Soto, J.L., Seoane,C., Zamorano, P., Cuadrado, F.J. 1981. A convenient synthesis of N-amino-2-pyridones. Synthesis 2,529.

[8] Wiley R.H., Slaymaker, S. 1956. 2-Pyrones. XVIII. 5-Aroyl-2-pyrones and 5-Aroyl-2-pyridones. J. Am. Chern. Soc. 78,2393-2398.

[9] Rees,C.W., Yelland, M. 1972. Reactive intermediates. Part XVIII. An N-aminopyridone-to-pyridazine rearrangement, a new decarbonylation reaction. J. Chem. Soc. Perkin Trans. 1, 78-82

[10] Shaabani, A., Rezayan, A.H., Sarvary, A., Rahmati, A., Khavasi, H.R. 2008.Pyridine catalyzed reaction of tetracyanoethylene and activated 1, 3-dicarbonyl CH-acid compounds: A rapid and efficient synthesis of pyran annulated heterocyclic systems Catal. Commun**.** 9, 1082-1086.

[11] Ono, Y., Baba, T. 1997. Selective reactions over solid base catalysts**.** Catal.Today 38, 321-337.

[12] Palaniappan, S., Ram, M. 2002. Esterification of carboxylic acids with alcohols catalyzed by polyaniline salts. Green Chem. 4, 53-55.

[13] Albadi, J., Mansournezhad, A., Darvishi-Paduk, M. 2013.Poly (4-vinylpyridine): As a green, efficient and commercial available basic catalyst for the synthesis of chromene derivatives. Chin. Chem. Lett. 24, 208-210.

[14] Sheibani H., Seifi, M. 2008. High Surface Area MgO as a Highly Effective Heterogeneous Base Catalyst for Three-Component Synthesis of Tetrahydrobenzopyran and 3,4-Dihydropyrano[c]chromene Derivatives in Aqueous Media. Catal. Lett. 126, 275-279.

[15] Mohammadzadeh, I., Sheibani, H. A convenient one-pot synthesis of new chromeno[3,4-c]chromene and chromeno[3,4-c]pyridine derivatives in the presence of high surface area of magnesium oxide**.** Chin. Chem. Lett. 23 (2012) 1327-1330.

[16] Sheibani, H., Saljoogi, A.S., Bazgir, A. 2008. Three-component process for the synthesis of 4-amino-5-pyrimidinecarbonitriles under thermal aqueous conditions or microwave irradiation. Arkivoc**.** 2, 115-123.

[17] Abaszadeh, M., Sheibani H., saidi, K., MoordiniNejad R. 2008.. The condensation of (chlorocarbonyl) phenyl ketene with 1, 3-dinucleophiles. I. Synthesis of 4-hydroxy-2-(1H)-pyridinones and mesoionic 1, 3-oxazinium olates. Arkivoc**.** 2, 262-268.

[18] Cantillo, D.,Sheibani, H.,Kappe, C.O. 2012.Flash Flow Pyrolysis: Mimicking Flash Vacuum Pyrolysis in a High-Temperature/High-Pressure liquid-Phase Microreactor Environment**.** J. Org. Chem. 77, 2463-2473

[19] Chandrasekhar, P., Naishadham, K. 1999. Broadband microwave absorption and shielding properties of a poly(aniline). Synt. Met. 105,115.

[20] Gorobets, N.Y., Yousefi, B.H., Belaj, F., Kappe, C.O. 2004. Rapid microwave-assisted solution phase synthesis of substituted 2-pyridone libraries**.** Tetrahedron. 60, 8633-8644.

[21] Adams, P.N., Laughlin, P.J., Monkman, A.P., Kenwright, A.M. 1996. Low temperature synthesis of high molecular II; weight polyaniline. Polymer 37, 3411-3417