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A Rapid Solvent-Free Three Component Green Synthesis of 4, 6-Diaryl-3-Cyanopyridin-2(1H)-Ones

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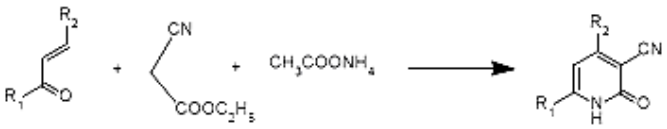
ABSTRACT

A rapid solvent-free green synthesis of versatile 4,6-diaryl-3-cyanopyridin-2(1H)-ones, the synthetically and biologically potent has been reported form 1,3-disubstitutedprop-2-en-1-one and ethyl cyanoacetate using ammonium acetate only by grinding in mortar at room temperature giving enhanced yield and purity.
Key wards: 2-Pyridone, 1,3-Disubstitutedpropen-2-One, Solvent Free Reaction, Green Synthesis

I. INTRODUCTION

A variety of significant biological activities have been associated with 2-pyridones and found to be a back-bone to many fused heterocycles of biological interests. [1,11]. This moiety is possessed by many natural origin[1-12].Synthesis of 2-(1H)-pyridone has been reported from active methylene compounds such as ethyl cyanoacetate, cyanoacetamide, malanonitrile or cynoacetic hydrazide and 1,3-diketones, benzylideneacetophenone or acetylenic ketones in presence of base like piperidine, sodium ethoxide, diethyl amine or ammonium acetate[13-17]. Synthesis of 2-pyridones from Cope-Knoevenagel products[18], 1,2-dithiolium[19] or 1,3-thiazinylium[20] perchlorate and aminovinyl ketones[21] have also been reported. The conventional synthesis of 2-pyridones involves the use of polar solvent such as alcohol and classical heating for a longer period of time[17]. The improved methodology includes the microwave[12, 22-25], infrared [26] or solvent-free classical heating[27]with shorter reaction time and increased reaction yield[12,22-26]. Dave et al reported microwave assisted synthesis of 4,6-diaryl-3-cyanopyridin-2(1H)-ones from the reaction between cyanoacetamide and 1,3-disubstituted-2-propen-1-one in presence of potassium hydroxide as a base[22]. Use of environmental benign techniques instead of conventional procedures always catches the attention of synthetic chemist. Growing interest our group to study the synthesis and reactions of pyridine derivatives and also the green methodologies like microwave irradiation and phase transfer catalysis[3-7,22,28-37], tempted us to employ newer strategy for the synthesis of 4,6-diaryl-3-cyanopyridin-2(1H)-ones **2** from the reaction between ethyl cyanoacetate and 1,3-disubstitutedprop-2-en-1-one 1 in presence of ammonium acetate as a base simply by grinding them in a mortar for a shorter period of time under solvent free condition at room temperature.

II. METHODS AND MATERIAL



1 2

Compound	R_1	R_2	Entry	R_1	R_2
2a	C_6H_5	C_6H_5	**2k**	4-$CH_3C_6H_4$	2-fuyl
2b	C_6H_5	4-$CH_3C_6H_4$	**2l**	4-$OCH_3C_6H_4$	C_6H_5
2c	C_6H_5	4-$OCH_3C_6H_4$	**2m**	4-$OCH_3C_6H_4$	4-CH_3 C_6H_4
2d	C_6H_5	4-ClC_6H_4	**2n**	4-$OCH_3C_6H_4$	4-$OCH_3C_6H_4$
2e	C_6H_5	2-fuyl	**2o**	4-$OCH_3C_6H_4$	4-ClC_6H_4
2f	C_6H_5	2-thienyl	**2p**	4-ClC_6H_4	C_6H_5
2g	4-$CH_3C_6H_4$	C_6H_5	**2q**	4-ClC_6H_4	4-$CH_3C_6H_4$
2h	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	**2r**	4-ClC_6H_4	4-$OCH_3C_6H_4$
2i	4-$CH_3C_6H_4$	4-$OCH_3C_6H_4$	**2s**	4-ClC_6H_4	4-ClC_6H_4
2j	4-$CH_3C_6H_4$	4-Cl C_6H_4	**2t**	4-ClC_6H_4	2-fuyl

Scheme 1

This method has found to be more simpler and advantageous as it omits the use of special assembly or microwave and infrared irradiation or polar solvent, rather the reaction has been done simply by grinding the reactants at room temperature for a shorter time (in minutes) in a mortar.

III. RESULTS AND DISCUSSION

A mixture of ethyl cyanoacetate, an active methylene compound, 1,3-diarylprop-2-en-1-ones[38], ammonium acetate, a base by was taken in a mortar and allowed to grind for 30-35 minutes to give compound **2**. The method avoids the use of special glass assembly, use of solvents which are often difficult to recover, classical, microwave or infrared heating, providing easy work up and reduced reaction time(30-35 minutes instead of 10-13 hr) with improved yield (80-86% instead of 64-74%) and purity of compound **3.** Identity of compound **2** was checked by tlc and attending the mixed melting point. The ir and nmr spectral analysis supported the structure elucidation of 4,6-diaryl-3-cyanopyridin-2(1H)-ones **2**. In ir(KBr) spectra of 2 absorption bands at near 1689-1672(√C=O), 2239-2228(√CN) and 3220-3150(√NH) supported the formation of 3-cyanopyridin-2(1H)-ones **2**. ^{1}H nmr spectra of **2** displayed NH proton at δ 12.88–12.42. Aromatic protons found to resonate at δ 7.92–6.57. Physical constants and spectral analysis of compound **2** are recorded in **Table 1.**

Experimental:

Melting points are uncorrected and were taken by electrothermal method in an open capillary tube. The IR spectra were recorded in cm^{-1} for KBr pellets on Brucker spectrophotometer. ^{1}H NMR spectra were recorded on Varian 300 MHz spectrometer using DMSO d^6 as a solvent and TMS as the internal reference standard. The chemical shifts are expressed in δppm. The purity of the compounds was routinely checked by TLC using Silica G and the spots were exposed in iodine vapour.

General procedure for the synthesis of 4,6-diaryl-3-cyanopyridin-2-(1H)-ones 2(a-t):

1,3-disubstituted-prop-2-en-1-one [30] (0.01 mole), ethyl cyanoacetate (0.01mole) and ammonium acetate (0.4 mole) were mixed in a mortar and allowed to grind at room temperature till the reaction mass was found to fuse as a yellow colored solid mass (30-35 minutes, tlc). Thus obtained solid was added the ice cold water, neutralized with dilute HCl, filtered, washed with water and recrystallized from DMF: ethanol (4:6) mixture.

Table 1: Physical constants, ir and ^{1}H nmr spectral analysis of 4,6-diaryl-3-cyanopyridin-2(1H)-ones 2a-t:

Entry	Yield %	Mp ^{0}C	ir(KBr) √cm^{-1}	^{1}H nmr(DMSO-d^6) δppm
2a	80	342-43	3150(NH) 2228(CN), 1672(C=O)	6.65-7.92(m,11H,ArH) 12.59(s,1H, NH)
2b	82	335-36	3155(NH), 2231(CN), 1677(C=O)	2.46(s,3H,CH_3), 6.63-7.9(m,10H,ArH) 12.62(s,1H, NH)
2c	81	331-32	3159(NH), 2230(CN), 1675(C=O)	3.9(s,3H,OCH_3), 6.62-7.82(m,10H,ArH) 12.60(s,1H, NH)
2d	80	312-13	3158(NH), 2232(CN), 1676(C=O)	6.77-7.92(m,10H,ArH) 12.61(s,1H, NH)
2e	81	298-99	3166(NH), 2229(CN),	6.63-7.90(m,8H,ArH) 12.42(s,1H, NH)

			1678(C=O)	
2f	84	274-75	3169(NH), 2230(CN), 1680(C=O)	6.64-7.98(m,8H,ArH) 12.73(s,1H, NH)
2g	81	289-90	3163(NH), 2231(CN), 1673(C=O)	2.43(s,3H,CH_3), 6.63-7.89(m,10H,ArH) 12.77(s,1H, NH)
2h	80	302-03	3175(NH), 2232(CN), 1674(C=O)	2.55(s,6H,CH_3), 6.65-7.91(m,9H,ArH) 12.71(s,1H, NH)
2i	80	309-10	3180(NH), 2230(CN), 1675(C=O)	2.5(s,3H,CH_3), 3.9(s,3H,OCH_3), 6.7-7.73,(m,9H,ArH) 12.76(s,1H, NH)
2j	82	310-11	3167(NH), 2233(CN), 1681(C=O)	2.51(s,3H,OCH_3), 6.67-7.92(m,9H,ArH) 12.49(s,1H, NH)
2k	82	300-01	3188(NH), 2236(CN), 1682(C=O)	2.43(s,3H,CH_3), 6.64-7.84(m,7H,ArH) 12.68(s,1H, NH)
2l	81	259-60	3190(NH), 2230(CN), 1685(C=O)	3.91(s,3H,OCH_3), 6.68-7.87(m,10H,ArH) 12.82(s,1H, NH)
2m	83	270-71	3154(NH), 2231(CN), 1680(C=O)	2.44(s,3H,CH_3), 3.93(s,3H,OCH_3), 6.68-7.93,(m,9H,ArH) 12.88(s,1H, NH)
2n	80	242-43	3140(NH), 2232(CN), 1675(C=O)	4.1(s,6H,OCH_3), 6.69-7.89,(m,9H,ArH) 12.85(s,1H, NH)
2o	83	253-54	3167(NH), 2234(CN), 1676(C=O)	3.9(s,3H,OCH_3), 6.57-7.82(m,9H,ArH) 12.65(s,1H, NH)
2p	80	294-95	3155(NH), 2235(CN), 1682(C=O)	6.57-.83(m,10H,ArH), 12.66(s,1H, NH)
2q	83	292-93	3210(NH), 2230(CN), 1686(C=O)	2.48(s,3H,CH_3), 6.69-7.83(m,9H,ArH) 12.74(s,1H, NH)
2r	82	270-71	3215(NH), 2238(CN), 1687(C=O)	3.9(s,3H,OCH_3), 6.67-7.82(m,9H,ArH) 12.8(s,1H, NH)
2s	85	257-58	3220(NH). 2239(CN), 1689(C=O)	6.78-7.92(m,9H,ArH), 12.82(s,1H, NH)
2t	80	>360	3170(NH), 2233(CN), 1684(C=O)	6.64-7.82(m,7H,ArH), 12.69(s,1H, NH)

IV.CONCLUSION

A simple and environment benign three component solvent free technique has been established for the widely studied 4,6-diaryl-3-cyanopyridin-2(1H)-ones of biological and synthetic importance under grinding at room temperature with improved yield, reduced reaction time and easy work up.

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VI.REFERENCES

[1] Jones, G.; Pyridines and their Benzo Derivatives: (V) Reactivity of Non-aromatics, Comprehensive Heterocyclic Chemistry, Vol. 2, edited by Katrizky A. R. & Rees C. W, (Pergamon Press, Oxford), 1984, 395.

[2] Youngdale, G. A.; Oglia, T. F.; J. Med. Chem. 28 1985 1790.

[3] Gorobets, N.; Yousefi, B. H.; Belaj, F.;Kappe, C. O.; Tetrahedron 60 2004 8633.

[4] Bharat, C.; Indian Chem. Soc. 7 1930 321.

[5] Basu, U.; Indian Chem. Soc. 7 1930 481.

[6] Basu, U.; Indian Chem. Soc. 7 1930 851.

[7] Basu, U.; Indian Chem. Soc. 7, 1930 119.

[8] Reid, W.; Meyer, A.; Chem Ber, 90 1957 2841.

[9] Soto, J. L; Seoana, C.; Mansilla, A.M.; Org Prep Proced Int 13, 1981 331.

[10] Kambe, S; Saito, K.; Sakurai, A.; Hayashi, T.; Synthesis, 1977, 841.

[11] Isao, S.; Bull. Chem. Soc. Jpn. 52 1979 1235.

[12] Isao S, Tokyo Kogyo Shikensho Hokoku, 76 1981 635.

[13] Alberola A, Andres C, Gonzalez O A, Pedrosa R & Vincente M, J Heterocycl Chem, 24, 1998 709.

[14] Dave, C. G.; D. A. Shah; Agrawal, Y, K.; Indian J. Chem, 43 2004 885.

[15] Mijin, D. Z.; Jelena M. Markovic, J. M.; Brkovic, D. V.; Marinkovic A. D.; Hem. Ind. 68 2014.

[16] Mijin, D. Z.; Marinkovic A. D.; Synthetic Commun. 36 2006 193.

[17] Schmid, H.; Process for the preparation of pyridone compounds, (Sandoz AG), DE 4314430 1994.

[18] Dostanic J. M.; D.R. Loncarevic, D. R.; P.T. Bankovic, P. T.; Cvetkovic, O.G.; Jovanovic, D. M.; Mijin, D. Z.; J. Environ. Sci. Health, A46 2011 70.

[19] Jia, R.; Zhang, S. T. Y.; Jiang, B.; Zhang, J.; Yao, C.; Shi, F.; J. Heterocycl. Chem. 44 2007 1177.

[20] Dave, C. G.; Shukla, M. C.; Indian J. Chem. 39B 2000 210.

[21] Dave, C. G.; Shukla, M. C., 34 19971805.

[22] Dave, C. G.; Augustin, C.; Indian J Chem, 39B, 2001, 403.

[23] Dave, C. G.; Shah. R. D.; Heterocycles, 51, 1999, 1819.

[24] Dave, C. G.; Joshipura, H. M.; Ind. J. Chem, 41B, 2002, 650.

[25] Shah, R. D.; Desai, N. D.; Synth, Commun. 2006 1343.

[26] Shah, R. D.; Desai, N. D.; Synthesis 19 2006 3225.

[27] Shah, R. D.; E. J. Chem. 11 2011 368.

[28] Shah, R. D.; Chem. for Sustain. Dev. 19 2011 321.

[29] Desai, N. D.; J. Heterocycl. Chem. 43 1999, 1819, 1999, 1819.

[30] Vogel, A. I.; Practical Organic Chemistry, 3rd Edn. 1962 718.