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NaCl: a facile, environmentally benign catalyst for the synthesis of pyrazole 4-carbonitrile in aqueous media

Amol Khandebharad[a], Swapnil Sarda[a], Mahesh Soni[a], Charansingh Gill[b], Pravin Kulkarni[a] and Brijmohan Agrawal[a*]

[a]*Department of Chemistry, J. E. S. College, Jalna,(MS), India*
[b]*Department of Chemistry, Dr. B.A.M.University, Aurangabad,(MS), India*

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A B S T R A C T

An ecofriendly methods for the synthesis of medicinally important class of heterocyclic scaffold, pyrazole 4-carbonitrile derivatives by one pot three component reaction of malononitrile, phenyl hydrazine and aromatic aldehyde has been achieved at room temperature. Greener protocols of reaction are followed by using sodium chloride to accelerate the reaction in aqueous media. Present methodology is a condition based divergence on synthesis of pyrazole by using simple salts, which offers several advantages like use of aqueous media and high yield of product along with short reaction time, simple work up procedure, no waste or by products, avoid the use of heavy metals or nanoparticles are the fascinating characteristics of reaction.

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1. Introduction

Organic chemists have been always demanded to mimic the principals of natural surroundings to develop new methodologies so as to achieve the aim of green chemistry. In this era of developing eco-friendly tools, chemists are on the way of maximizing the efficiency of reaction by using those raw materials which are produced by nature and whose use is in the favor of maintaining nature. Water is a distinctive solvent that plays an acute role in supporting life on earth. There are various discussions on the nature of water and its capability to associate with inorganic salts and organic molecules. The exceptional tendency of water to rapidly swap the protons between water molecules at a picoseconds time-scale referred to as hydrogen bonding.[1]

The use of salty water in organic synthesis gained an attention as a nontoxic, easily available, non-conventional and commonly available reaction medium. The making of salty water by using NaCl has been the useful way of performing domino multi component reaction.[2] With the growing impact of green chemistry, the use of NaCl in one pot reaction becomes a serious issue in recent years as it is

* Corresponding author. Tel./fax: +91-992156312/+91-02482230566
E-mail address: srsarda1@rediff.com (B. Agrawal)
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used as a promoter for the construction of various carbon-carbon and carbon-heteroatom bonds.[3] However, increased attention with regard to the constricted regulation on the maintenance of nature's harmony along with the novelty in the synthetic methodologies along with environmentally friendly strategies for the syntheses of heterocycles that gratify financial criteria is a major challenge.[4]

In last few years another criterion for the one pot multicomponent reactions (MCRs) is either by using solvent free reactions or use of eco compatible aqueous media which becomes an effectual and fascinating methodology for organic synthesis. Significant attention has been paid to MCRs in the aqueous phase.[5] A possible way of increasing the atom economy, time shortening and competence of synthesis and minimization of reaction steps with procedural simplicity are appealing the excellent way of executing one pot MCRs for drug discovery and the making of structurally complex molecules in a single stroke.

Nitrogen-containing five member heterocyclic rings, in particular the pyrazole ring, signifies the valuable choice for the synthesis of pharmaceutical compounds.[6] Densely substituted pyrazole derivatives are one of the most important modules of compounds owing to their importance in various Cyclooxygenase inhibitor [7] drugs to stop the synthesis of prostaglandins and thromboxanes from arachidonic acid. These pyrazole substituted structural subunits forms the class of NSAIDs (nonsteroidal anti inflammatory drugs) which finds the application in numerous biological activities.[8] In addition, these heterocyclic compounds found the variety of applications in medicinal and pharmaceutical sciences. Pyrazole scaffold is fundamental structure of a wide range of pharmaceuticals used as anti-inflammatory,[9] antibacterial antifungal,[10] anticancer,[11] hypoglycemic,[12] antiviral,[13] anti-hyperlipidemic,[14] inhibition of cyclooxigenase-2,[15] antiangiogenic [16] etc.

Generally synthesis of 5-amino-pyrazole-4-carbonitrile derivatives has been synthesized by three component reaction of aromatic aldehyde, malononitrile and phenylhydrazine in the presence of various catalyst like graphene oxide-TiO_2,[17] I_2,[18] ionic liquid (Bmim)OH,[19] $[HMIM]C(NO_2)_3$ as a nano structure ionic liquid,[20] glucose coated super magnetic Fe_3O_4 nano particles,[21] dioxo-molybdenum complex supported on silica-coated magnetite nanoparticles ,[22] CuO/ZrO_2,[23] atmospheric oxygen under visible light in presence of eosin Y dye,[24] water-ethanol,[25] nonconventional methods like ultrasonication in water-PEG media,[26] microwave irradiation,[27] and simple grinding method.[28]

With this goal in mind, our initial studies of the synthesis of amino cyanopyriden[29] took advantage of the promotion in the variety of green solvents. Herein, we report an efficient method for the synthesis of pyrazole-4-carbonitrile by using easily available table salt in aqueous media.

2. Results and Discussion

The study of reaction condition and performance of the reactant was observed by selecting 4-methoxyl benzaldehyde, malononitrile and phenyl hydrazine for model reaction in water as a solvent. Completion of the reaction takes place only by stirring the reactant component in the normal condition of pressure, temperature, and light.

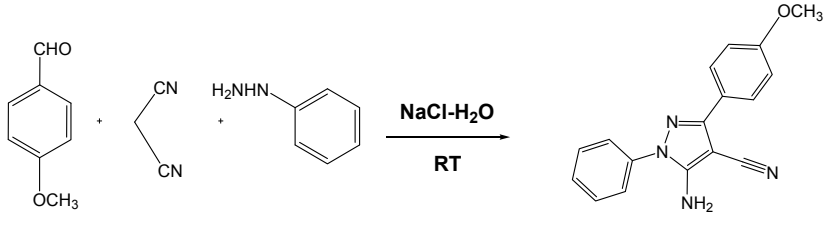

Fig. 1. Model reaction for the synthesis of pyrazole 4-carbonitrile

The involvement of catalyst in carrying out the reaction was studied in presence and absence of various catalysts. The selection of catalysts was carried out by applying different categories like simple salts, phase transfer type of catalyst and biocatalyst like vitamin B1 since literature survey reveals that such type of catalysts have been carrying out the condensation and cyclization type of reactions efficiently. The screening of catalyst was attempted in two categories (**Table 1**); In **part-A** catalysts reported in literature for such type of Knoevenagel and cyclization reactions. Initially, reaction performance was checked in the absence of catalyst which indicates that the product formation not take place easily; the only Knovenagel product was obtained after long reaction time in very trace quantity. By believing the necessities of reaction additive, we carried out the reaction by using mild base potassium carbonate, which was not found to be effectual to increase a reaction rate and yield. Bioorganic catalyst like Vitamine B1, Glycine gives 65% and 82% yield respectively. The effect of sulfonated zirconium oxide was not impressive in such reaction. One more criterion of phase transfer catalyst was applied to know the effect on the reaction by using p-toluene sulfonic acid gives a yield of 72%. Afterward, in part B the simple chloride salts of alkali group was selected in which HCl (Hydrochloric acid) and simple nonacidic salts like NaCl, NaBr and NaI were considered for this purpose. Best result was obtained in NaCl with maximum yield and short reaction time, while by using of bromide and iodide salt of sodium gives moderate yields of product. Finally, it conclude that NaCl was taken to be the best additive for completion of reaction within short duration along with outstanding yield. By using polar-nonpolar, protic-aprotic solvents, yield of product was found to be very low with long time. Polar aprotic solvents also gives inefficient yield (**Table** 1). Since polar protic solvents are favorable for Knovenagel condensation, we obtained the extremely improved results with these solvents. In the comparison of ethanol and methanol the appreciable yield was observed in water. In order to find the effectiveness of water quantitatively the reaction performed in different amount of of water and observed that 10 ml of water is sufficient to carry out the reaction.

Table 1. Screening of the catalysts at room temperature[a]

Entry	Catalyst	Solvents	Time (min)	Yield[b]
		Part-A		
1	-	Water	NR[c]	NR
2	K_2CO_3	Water	160	37
3	Vit.B1	Water	60	65
4	Glycine	Water	90	60
5	ZrO_2/SO_4	Water	180	55
6	PTSA	Water	70	72
		Part-B		
7	HCl	Water	90	NR
8	KCl	Water	120	78
9	NaBr	Water	60	85
10	NaI	Water	50	80
11	NaCl	Water	20	90
12	NaCl	DMF	180	72
13	NaCl	Ethanol	60	80
14	NaCl	Methanol	90	80
15	NaCl	Water	20	90

[a]*reaction condition:4-methoxy benzaldehyde(1 mmol),malanonitrile(1 mmol), phenylhydrazine (1 mmol), catalyst(10 mol%), 10 ml of solvent at room temperature*
[b] *isolated yields,* [c] *NR=No Reaction*

Further quantity wise screening of **NaCl** was achieved by performing the model reaction in 10 ml of water and 10 mol%, 5 mol% and 2 mol% of NaCl. It is observed that 10 mol% of NaCl is sufficient to give higher percentage of yield. It is observed that further increase in the catalytic amount of NaCl

did not affect the yield and time of reaction. To evaluate the appropriate temperature of reaction the reaction carried out at different temperatures, however, the increase of temperature lowers the yield since sticky product was obtained with partial incompletion of reaction. Whereas at room temperature reaction offered 92% yield **(Table 2, entry-4)**. Hence it conclude that the combination of 10 mol % NaCl and 10 ml of water at room temperature is an ideal condition for the synthesis of pyrazole 4-carbonitrile derivatives.

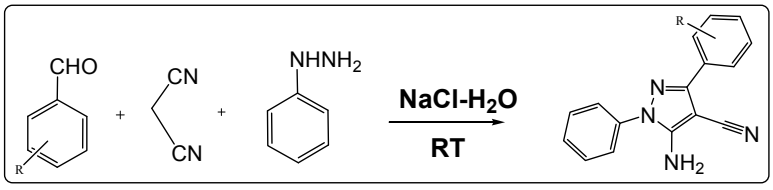

Fig. 2. NaCl catalysed synthesis of pyrazole 4-carbonitrile derivatives

Table 2. Effect of amount of catalyst and temperature[a]

Entry	Temperature	Catalyst (%)	Yield(%)[b]
1.	Reflux	10	35
2.	80	10	42
3.	60	10	65
4.	RT	10	92
5.	RT	15	90
6.	RT	05	72
7.	RT	20	88

[a] *reaction condition: 4-methoxy benzaldehyde(1 mmol),malanonitrile(1 mmol), phenylhydrazine(1 mmol), NaCl(10 mol%) in 10 ml water.*
[b] *isolated yields*

The selectivity of sodium salts due to smaller in size of sodium as compared with potassium ion. Smaller ions are good for enhancing the structure making property of water by forming the hydration sphere which increase the cohesive energy by interacting with water dipoles and ultimately the increase of structure affects the viscosity of medium.[30] Organic components in aqueous media shows the phobic nature towards the water molecules and increase the hydrophobic interaction,this phenomenon make the organic molecules close together to collide with each other , thereby incrasing the activation energy of reaction. The presence of NaCl in water makes the hydration sphere of Na^+ and Cl^- ions, resulting in to less availability of water molecule for organic components and solute-solute interaction will be stronger than solute-solvent interaction.The whole phenomenon is the salting out effect, which is more pronounced for NaCl.[31-32]

The reaction is proposed *via* formation of a Knoevenagel condensation product, a further cyclization of one with phenyl hydrazine leads to desired products likely according to the classical mechanisms. Because of formed hydration spheres of ions, hydrophobic interaction increase which leads to the collision of reactants and decreases the activation energy of reaction thereby completes the reaction within a short duration. The whole phenomenon was practically observed by pointing out the phases of reaction, initially the whole reaction mass was two layers of organic and aqueous phase afterward it changed to suspension and finally at the end of reaction time precipitate comes out.

It is observed that benzylidene-malononitrile intermediate remained unreacted even after stirring the reaction mass for a long time. To overcome this situation, excess amount of phenyl hydrazine (1.2 mmol) was used. However, the last step oxidation also not takes place easily in aprotic solvents but the water was found to be absolute media to cyclize and oxidized to get desired product. In order to demonstrate the superiority of this green methodology, the optimum condition was extended for the one-pot synthesis of pyrazole 4-carbonitrile derivatives. As mentioned in **(Table 3)**, the results clearly indicate that the reaction proceeded in high yields and produced the desirable product. It is worth mentioning that all the pyrazole 4-carbonitrile derivatives that synthesized by this method precipitated

from the reaction mixture and can be purified easily by recrystallization from the ethanol. All synthesized compounds were characterized by comparing the spectral data and melting point with the valid results. This comparative study shows that synthesized compounds are precisely matched with the reported compounds. Present methodology is another elegant example of one pot multi-component reaction in developing green tools of chemistry.

Table 3. Synthesis of pyrazole 4-carbonitrile derivatives [a]

Entry	R	Time (min)	Yield (%)[b]	mp (°C)	(Reported mp) [c] (°C)
4a	C_6H_5	18	95	164	(160-162)[17]
4b	4-Cl-C_6H_4	20	93	130	(132-134)[17]
4c	4-OMe-C_6H_4	20	92	116	(112-114)[17]
4d	4-NO_2-C_6H_4	18	90	160	(164-66)[17]
4e	3- NO_2-C_6H_4	20	90	126	(130-132)[17]
4f	2-OH-C_6H_4	22	92	158	(162-164)[17]
4g	4-N,N-dimethyl-C_6H_4	15	95	112	(108-110)[17]
4h	2-Thienyl	20	90	150	(150-152)[21]
4i	2-pyrole	22	92	255	(262-264)[21]
4j	2-Furyl	25	88	170	(170-172)[21]
4k	1-napthal	20	90	157	(162-164)[21]
4l	4-OH-C_6H_4	20	95	205	(212-214)[22]
4m	4-Br- C_6H_4	22	94	165	(166-168)[22]
4n	2-Cl- C_6H_4	20	92	140	(140-142)[22]
4o	2-NO_2-C_6H_4	18	90	164	(160-162)[24]

[a]reaction condition: aromatic benzaldehyde(1 mmol),malanonitrile(1 mmol), phenylhydrazine(1 mmol), catalyst(10 mol%) were stirred in 10 ml of solvent at RT
[b] isolated yields
[c]Reported melting point

3. Conclusions

Herein we developed a advance protocol for one pot multicomponent synthesis of highly functionalized pyrazole 4-carbonitrile derivatives using aldehydes, malononitrile and phenylhydrazine in the presence of sodium chloride as a easily available reaction promoter. The use of NaCl in aqueous solvent system act as a green reaction medium for carrying out this organic transformations. Present synthetic method includes several advantages such as operational simplicity, uncomplicated work up procedure, wide scope of substrate and higher product yields using simple salt NaCl.

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4. Experimental

4.1. Materials and Methods

All reagents were obtained from commercial sources Sigma Aldrich. The reaction was monitored on TLC using pre-coated plates (silica gel on aluminum, Merck).Melting points were measured in open glass capillaries and may be incorrect.[1] H NMR and [13] C NMR was recorded at room temperature on a 500 MHz and 125 MHz respectively in $CDCl_3$ using TMS as internal standard. The products were also characterized by comparison of their melting point with literature values.

4.2. General Experimental procedure the synthesis of pyrazole 4-carbonitrile derivatives

To a mixture of aromatic aldehyde (1 mmol), malononitrile (1 mmol) in 10 mL of water, 10 mol % of NaCl was added and the reaction mixture was stirred at room temperature. After 10 minutes solid

precipitate out this specified the formation of the Knoevenagel condensation product. To that reaction mass, phenylhydrazine (1 mmol) was added and the reaction mass was further stirred for a suitable time until the formation of pyrazole takes place **(Table 3).** Conversions of reactants to the product were screened by TLC. After complete conversion, a solid crude mass was filtered, washed with water and recrystallized by using absolute alcohol.

4.3 Spectral Data of selected compound

5-Amino-3-(4-methoxyphenyl)-1-phenyl-1H-pyrazole-4-carbonitrile **(4c):** ^{1}H NMR (500 MHz,$CDCl_3$): δ 7.66-7.56 (m, 3H), 7.28 (merged dd, J_1=J_2=8.1 Hz, 2H), 6.91(d, J=8.7Hz, 2H), 3.83(s, 3H);^{13}C NMR (125 MHz,$CDCl_3$): δ 164.9, 160.1, 145.1,137.5, 133.6, 129.4, 127.7 ,119.9, 115.2, 114.2, 112.7, 55.4; HRMS (ESI) (m/z): found 329.0796 $(M+K)^+$, calcd for $C_{17}H_{14}KN_4O$ 329.0799.

References

1. Bye J. W., and Falconer R. J. **(2015)** A study of the relationship between water and anions of the Hofmeister series using pressure perturbation calorimetry. *Phys Chem Chem Phys*, *17* (21) 14130–14137.
2. Dandia A., Gupta S. L., and Parewa V. **(2014)** An efficient ultrasound-assisted one-pot chemoselective synthesis of pyrazolo[3,4-b] pyridine-5-carbonitriles in aqueous medium using NaCl as a catalyst. *RSC Adv*, *4* (14) 6908-6915.
3. Gujar J. B., Chaudhari M. A., Kawade D. S., and Shingare M. S. **(2014)** Sodium chloride: A proficient additive for the synthesis of pyridine derivatives in aqueous medium. *Tetrahedron Lett*, *55* (50) 6939–6942.
4. Chanda A., and Fokin V. V. **(2009)** Organic synthesis "on water." *Chem Rev*, 109 (2) 725-748.
5. Tisseh Z. N., Dabiri M., Nobahar M., Khavasi H. R., and Bazgir A. **(2012)** Catalyst-free, aqueous and highly diastereoselective synthesis of new 5-substituted 1H-tetrazoles via a multi-component domino Knoevenagel condensation/1,3 dipolar cycloaddition reaction. *Tetrahedron*, *68* (6) 1769–1773.
6. Balbi A., Anzaldi M., MacCi C., Aiello C., Mazzei M., Gangemi R., and Viale M. **(2011)** Synthesis and biological evaluation of novel pyrazole derivatives with anticancer activity. *Eur J Med Chem*, *46* (11) 5293–5309.
7. El-Sayed M. A.-A., Abdel-Aziz N. I., Abdel-Aziz A. A.-M., El-Azab A. S., Asiri Y. A., and ElTahir K. E. H. (2011) Design, synthesis, and biological evaluation of substituted hydrazone and pyrazole derivatives as selective COX-2 inhibitors: Molecular docking study. *Bioorg. Med. Chem.*, 19 (11) 3416–3424.
8. Bandgar B. P., Chavan H. V., Adsul L. K., Thakare V. N., Shringare S. N., Shaikh R. and Gacche R. N. **(2013)** Design, synthesis, characterization and biological evaluation of novel pyrazole integrated benzophenones. *Bio Med Chem Lett*, *23* (3) 912–916.
9. Szabó G., Fischer J., Kis-Varga Á. and Gyires K. **(2008)** New celecoxib derivatives as anti-inflammatory agents. *J Med Chem*, *51* (1) 142–147.
10. Tanitame A., Oyamada Y., Ofuji K., Terauchi H., Kawasaki M., Wachi M., and Yamagishi J. **(2005)** Synthesis and antibacterial activity of a novel series of DNA gyrase inhibitors: 5-[(E)-2-arylvinyl]pyrazoles. *Bio Med Chem Lett*, *15* (19) 4299–4303.
11. Dias L. R. S., and Salvador R. R. S. **(2012)** Pyrazole carbohydrazide derivatives of pharmaceutical interest. *Pharmaceuticals*, *5* (3) 317–324.
12. Ismail N. S. M., Ali G. M. E., Ibrahim D. A., and Elmetwali A. M. **(2016)** Medicinal attributes of pyrazolo[1,5-a]pyrimidine based scaffold derivatives targeting kinases as anticancer agents. *Future J Pharm Sci*, *2* (2) 60–70.
13. Genin M. J., Biles C., Keiser B. J., Poppe S. M., Swaney S. M., Tarpley W. G. and Romero, D. L. **(2000)**. Novel 1,5-diphenylpyrazole nonnucleoside HIV-1 reverse transcriptase inhibitors with enhanced activity versus the delavirdine-resistant P236L mutant: Lead identification and SAR of 3- and 4-substituted derivatives. *J Med Chem*, *43* (5) 1034–1040.

14. Momose Y., Maekawa T., and Odaka H, K. H. **(2001)** 5-membered n-heterocyclic compounds with hypoglycemic and hypolipidemic activity.US patent 7179823
15. Penning T. D., Talley J. J., Bertenshaw S. R., Carter J. S., Collins P. W., Docter, S.,and Isakson P. C. **(1997)** Synthesis and biological evaluation of the 1,5-diarylpyrazole class of cyclooxygenase-2 inhibitors: identification of 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benze nesulfonamide (SC-58635, celecoxib). *J Med Chem*, *40* (9) 1347–1365.
16. Abadi A. H., Eissa A. A. H., and Hassan G. S. **(2003)** Synthesis of novel 1,3,4-trisubstituted pyrazole derivatives and their evaluation as antitumor and antiangiogenic agents. *Chem Pharm Bulletin*, *51* (7) 838–44.
17. Kumari S., Shekhar A. and Pathak D. D. **(2016)** Graphene oxide-TiO_2 composite: An efficient heterogeneous catalyst for the green synthesis of pyrazoles and pyridines. *New J Chem*, *40* (6) 5053-5060.
18. Srivastava M., Rai P., Singh J. and Singh J. **(2014)** Efficient iodine-catalyzed one pot synthesis of highly functionalised pyrazoles in water. *New J Chem*, *38* (1) 302–307.
19. Srivastava M., Rai P., Singh J., and Singh J. **(2013)** An environmentally friendlier approach—ionic liquid catalysed, water promoted and grinding induced synthesis of highly functionalised pyrazole derivatives. *RSC Adv*, *3* (38) 16994-16998.
20. Zolfigol M. A., Afsharnadery F., Baghery S., Salehzadeh S., and Maleki F. **(2015)** Catalytic applications of {[HMIM]C$(NO_2)_3$}: as a nano ionic liquid for the synthesis of pyrazole derivatives under green conditions and a mechanistic investigation with a new approach. *RSC Adv*, *5* (92) 75555–75568.
21. Esfandiary N., Nakisa A., Azizi K., Azarnia J., Radfar I., and Heydari A. **(2017)** Glucose-coated superparamagnetic nanoparticle-catalysed pyrazole synthesis in water. *App Org Chemistry*, *31* (7) https://doi.org/10.1002/aoc.3641
22. Rakhtshah J., Salehzadeh S., Godwini E., Maleki F., Baghery S., and Zolfigol M. A. **(2016)** Synthesis of pyrazole derivatives in the presence of a dioxomolybdenum complex supported on silica-coated magnetite nanoparticles as an efficient and easily recyclable catalyst. *RSC Adv*, *6* (106) 104875–104885.
23. Maddila S., Rana S., Pagadala R., Kankala S., Maddila S. and Jonnalagadda S. B. **(2015)** Synthesis of pyrazole-4-carbonitrile derivatives in aqueous media with CuO/ZrO_2 as recyclable catalyst. *Cat Comm*, *61* 26–30.
24. Yadav S., Rai P., Srivastava M., Singh J., Tiwari K. P., and Singh J. **(2015)** Atmospheric oxygen mediated synthesis of pyrazole under visible irradiation. *Tetrahedron Lett*, *56* (43) 5831–5835.
25. Hasaninejad A. and Firoozi S. **(2013)** Catalyst-free, one-pot, three-component synthesis of 5-amino-1,3-aryl-1- pyrazole-4-carbonitriles in green media. *Mol Diversity*, *17* (3) 459–469.
26. Nemati F., Nikkhah S. H. and Elhampour A. **(2015)** An environmental friendly approach for the catalyst-free synthesis of highly substituted pyrazoles promoted by ultrasonic radiation. *Chin Chem Lett*, *26* (11) 1397–1399.
27. Corradi A., Leonelli C., Rizzuti A., Rosa R., Veronesi P., Grandi R., Baldasari S., and Villa C. **(2007)** New "Green" Approaches to the Synthesis of Pyrazole Derivatives.*Moleecule*, 12 (7) 1482–1495.
28. Bhale P. S., Dongare S. B. and Chanshetti U. B. **(2014)** Simple Grinding, Catalyst-free, One-Pot, Three-Component Synthesis of Polysubstituted Amino Pyrazole. *Res J Chem Sci*, *4* (9) 2231–606.
29. Sarda S. R., Kale J. D., Wasmatkar S. K., Kadam V. S., Ingole P. G., Jadhav W. N. and Pawar R. P. **(2009)** An efficient protocol for the synthesis of 2-amino-4,6-diphenylpyridine-3-carbonitrile using ionic liquid ethylammonium nitrate. *Mol Diversity*, *13* (4) 545–549.
30. Bowen W. R. and Yousef H. N. S. **(2003)** Effect of salts on water viscosity in narrow membrane pores. *J Coll Int Sci*, *264* (2) 452–457.
31. Endo S., Pfennigsdorff A., and Goss K. U. **(2012)** Salting-out effect in aqueous NaCl solutions: Trends with size and polarity of solute molecules. *Environ Sci Technol*, *46* (3) 1496–1503.

32. Hasseine A., Meniai A. H., and Korichi, M. **(2009)** Salting-out effect of single salts NaCl and KCl on the LLE of the systems (water + toluene + acetone), (water + cyclohexane + 2-propanol) and (water + xylene + methanol). *Desalination*, *242* (1–3), 264–276.

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