RSC Advances

This article can be cited before page numbers have been issued, to do this please use: M. A. Zolfigol, F. Afsharnadery, S. Baghery, S. Salehzadeh and F. Maleki, *RSC Adv.*, 2015, DOI: 10.1039/C5RA16289K.

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/advances

Dynamic Article Links ►
View Article Online
DOI: 10.1039/C5RA16289K

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

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

Mohammad Ali Zolfigol,* Fatemeh Afsharnadery, Saeed Baghery, Sadegh Salehzadeh and Farahnaz Maleki

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

Catalytic applications of 1-methylimidazolium trinitromethanide {[HMIM]C(NO_2)$_3$}as a first nano ionic liquid (NIL) was studied. The described NIL was efficiently tested in the synthesis of 5-amino-pyrazole-4-carbonitrile derivatives in good to excellent yields on the three-component condensation of various aromatic aldehydes, malononitrile and phenylhydrazineat room temperature under solvent-free and ambient conditions. In the next study,1,4-dihydropyrano-[2,3-*c*]-pyrazole derivatives were also synthesized *via* a four-component condensation of a good range aromatic aldehydes, malononitrile, phenylhydrazine and ethyl acetoacetate in the presence of NIL under same reaction conditions. The described reactions were in good agreement with the green chemistry disciplines and their major advantages are short reaction times, good yields, ease of separation, recycle and reusability of NIL. A new mechanistic approach was proposed for the final step of the pyrazoles synthesis which was supported by theoretical studies.

Introduction

Ionic liquids (ILs) are commonly introduced as liquid electrolytes composed completely of ions, and occasionally a melting point criterion has been suggested to identify between molten salts and ionic liquids (m.p 100 °C). Though, both molten salts and ionic liquids are better defined as salts that show ionic covalent crystalline structures. Over the last few years, ionic liquids have effectively been useful as alternative solvents for homogeneous biphasic catalysis.[1-6] The increased interest in ionic liquids through chemists and technologists clearly is due to the efficiency of ionic liquids as solvents in chemical processes and counting catalytic reactions. The industrial for "green" solvents is more demand. Many chemists now understand that ionic liquids have dual roles and could be acts both as solvent and catalyst. Ionic liquids are materials that are entirely composed of ions and are liquid at or close to room temperature.[7] Attention in these compounds, frequently heralded as the green, their thermal stability,[8] is still increasing rapidly,[9] stems from their near-zero vapor pressure,[10] and their broadly harmonic properties as concerns polarity, hydrophobicity, and solvent miscibility behavior *via* suitable modification of the cation and the anion.

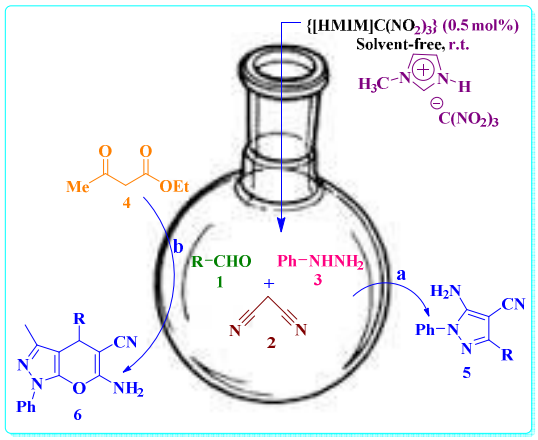
Multi-component reactions (MCRs) have occurred as a powerful tool for the construction of new and complex molecular structures because of their advantages over conventional multi-step synthesis. The major advantages of MCRs contain shorter reaction times, lower costs, high atom-economy, energy saving, the avoidance of time consuming and expensive purification procedures. It is recognized that MCRs are commonly much more eco-friendly, and suggestion rapid availability to large compound libraries with diverse functionalities.[11-14]

Pyrazoles are the significant kind of heterocyclic compounds that feature in several pharmaceutical targets and natural products of medicinal interest. Pyrazole derivatives have showed a wide variety of biological activities counting anti HIV,[15] anti-malarial,[16] antibacterial and antifungal,[17] anticancer,[18] anti-inflammatory,[19] antioxidant,[17, 20] and anti-depressant activities.[21] The prominence and importance of pyrazoles in drug discovery has frequently concerned the following for to improved methods.[22] Recent processes for the synthesis of 5-amino-pyrazole-4-carbonitrile and 1,4-dihydropyrano-[2,3-*c*]-pyrazole contain synthesis based on the procedure of $Ti(NMe_2)_2(PyPyr)_2$,[23] I_2,[24] $Sc(OTf)_3$,[25] water or ethanol media,[26-28] ZrO_2 nanoparticles,[29] LiOH,[30] CuO/ZrO_2,[31] [BMIM]OH[32] and triethylbenzylammonium chloride.[33]

Very recently, we have been reported the first nano ionic liquid (NIL) namely 1-methylimidazolium trinitromethanide {[HMIM]C(NO_2)$_3$} and its catalytic uses for Hantzsch four component condensation.[34] In continuation of our previously reported procedure for the preparation of 1,3,5-trisubstituted pyrazolines[35] and pyranopyrazoles,[36] here, we wish to describe an efficient and benign synthesis of 5-amino-pyrazole-4-carbonitrile (**5**) *via* one-pot three-component condensation of various aromatic aldehydes (**1**), malononitrile (**2**) and phenylhydrazine (**3**) at room temperature under solvent-free and ambient conditions (Scheme 1, **a**). Furthermore, synthesis of 1,4-dihydropyrano-[2,3-*c*]-pyrazole (**6**) by a one-pot four-component approach the reaction between several aromatic aldehydes (**1**), malononitrile (**2**),

View Article Online
DOI: 10.1039/C5RA16289K

phenylhydrazine (**3**) and ethyl acetoacetate (**4**) under same conditions, was studied (Scheme 1, **b**).



Scheme 1. The synthesis of 5-amino-pyrazole-4-carbonitrile derivatives (a) and 1,4-dihydropyrano-[2,3-*c*]-pyrazole (b) in the presence of {[HMIM]C$(NO_2)_3$} as nano structure ionic liquid catalyst.

Results and discussion

Development of task specific ionic liquids (TSILs) and their structural diversity could be achieved *via* designing and synthesis of novel cationic cores with suitable anionic counterparts. By considering the above-mentioned synthetic strategy, in the course of a decade of our investigation on designing and synthesis of TSILs lead to report a good range of TSILs.[34, 37]

Firstly, 1-methylimidazolium trinitromethanide {[HMIM]C$(NO_2)_3$} as a first reported nano ionic liquid (NIL), has been prepared according to our previously reported procedure. Then, optimization of the reaction conditions was followed. Finally, the influence of the nano ionic liquid catalyst in the synthesis of 5-amino-pyrazole-4-carbonitrile derivatives and 1,4-dihydropyrano-[2,3-*c*]-pyrazole derivatives was investigated (Scheme 1). For this intention, as a model, the condensation reaction of naphthalene-1-carbaldehyde, malononitrile and phenylhydrazine (in the synthesis of 5-amino-pyrazole-4-carbonitrile derivatives) and naphthalene-1-carbaldehyde, malononitrile, phenylhydrazine and ethyl acetoacetate (in the synthesis of 1,4-dihydropyrano-[2,3-*c*]-pyrazole derivatives) were considered using various amounts of the catalyst at range of 25–100 °C under solvent-free conditions (Table 1). As Table 1, show that, the best results were attained when the reaction was achieved in the presence of 0.5 mol% of NIL as a catalyst at room temperature (Table 1, entry 3). In the absence of catalyst a low yield of the products were achieved after 1 h (Table 1, entries 1 and 2). Increasing the reaction temperature and catalyst loading did not improve the rate of the reaction (Table 1, entries 4-14).

Table 1. Effect of amount of the catalyst and temperature under solvent-free conditions.[a]

Entry	Catalyst loading (mol%)	Reaction temperature (°C)	Reaction time (min)		Yield[b] (%)	
			Pathway **a**	Pathway **b**	Pathway **a**	Pathway **b**
1	Catalyst-free	r.t.	60	60	18	15
2	Catalyst-free	100	60	60	21	17
3	0.5	r.t.	10	12	95	94
4	0.5	50	10	12	95	94
5	0.5	75	10	12	95	94
6	0.5	100	10	12	95	94
7	1	r.t.	10	12	95	94
8	1	100	10	12	95	94
9	2	r.t.	10	12	95	94
10	2	100	10	12	95	94
11	5	r.t.	10	12	94	92
12	5	100	10	12	94	92
13	10	r.t.	15	15	93	90
14	10	100	15	15	93	90

Reaction conditions: [a] Pathway **a**: Naphthalene-1-carbaldehyde (1 mmol), malononitrile (1 mmol), phenylhydrazine (1 mmol); Pathway **b**: Naphthalene-1-carbaldehyde (1 mmol), malononitrile (1 mmol), phenylhydrazine (1 mmol), ethyl acetoacetate (1 mmol); [b] Isolate yield.

To compare the proficiency of the solution versus solvent-free conditions, a mixture of naphthalene-1-carbaldehyde, malononitrile and phenylhydrazine (in the synthesis of 5-amino-pyrazole-4-carbonitrile derivatives) and naphthalene-1-carbaldehyde, malononitrile, phenylhydrazine and ethyl acetoacetate (in the synthesis of 1,4-dihydropyrano-[2,3-*c*]-pyrazole derivatives) as model reaction, in the presence of 0.5 mol% of NIL as a catalyst in some several solvents such as H_2O, C_2H_5OH, CH_2Cl_2, CH_3CN, CH_3CO_2Et and toluene was considered at room temperature. The results are summarized in Table 2. As it can be realized in Table 2, solvent-free condition was the best conditions in this reaction.

Table 2. The effect of various solvents in the presence of 0.5 mol% of nano structure ionic liquid at room temperature.[a]

Entry	Solvent	Reaction time (min)		Yield[b] (%)	
		Pathway **a**	Pathway **b**	Pathway **a**	Pathway **b**
1	Solvent-free	10	12	95	94

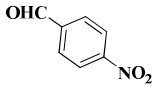
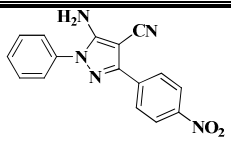
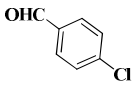
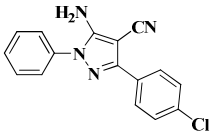
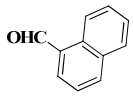
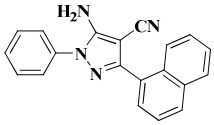
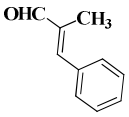
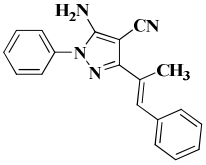
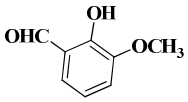
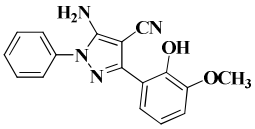
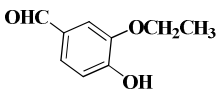
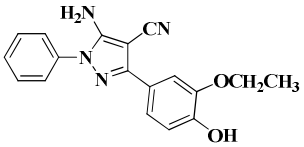
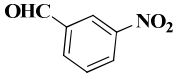
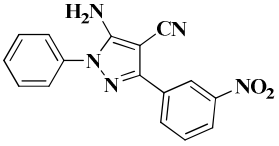
View Article Online
DOI: 10.1039/C5RA16289K

2	H_2O	15	20	95	94
3	C_2H_5OH	15	20	95	94
4	CH_3CN	20	25	94	92
5	CH_2Cl_2	30	30	88	85
6	CH_3CO_2Et	45	45	85	80
7	Toluene	60	60	75	70

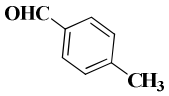
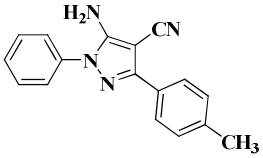
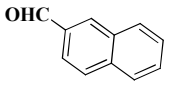
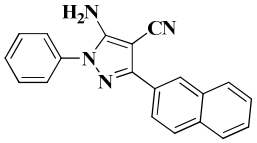
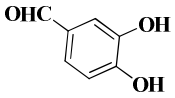
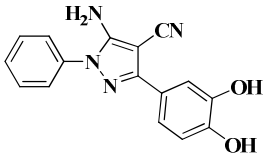
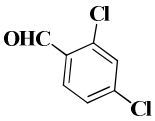
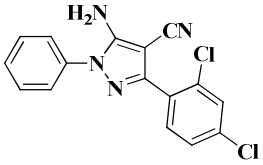
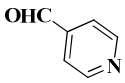
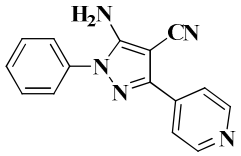
Reaction conditions: [a] Pathway **a**: Naphthalene-1-carbaldehyde (1 mmol), malononitrile (1 mmol), phenylhydrazine (1 mmol); Pathway **b**: Naphthalene-1-carbaldehyde (1 mmol), malononitrile (1 mmol), phenylhydrazine (1 mmol), ethyl acetoacetate (1 mmol); [b] Isolate yield.

Encouraged by the considerable results and with the aim of verification to overview the scope of this main process, several 5-amino-pyrazole-4-carbonitrile derivatives were synthesized from three-component condensation reaction of a range of aromatic aldehyde, malononitrile and phenylhydrazine under solvent-free conditions at room temperature in the presence of a catalytic amount of NIL as a catalyst. Consequently, various 1,4-dihydropyrano-[2,3-*c*]-pyrazole derivatives were synthesized *via* four-component condensation reaction of several aromatic aldehyde, malononitrile, phenylhydrazine and ethyl acetoacetate under same reaction conditions. The results have been represented in Table 3 and 4. The effect of substituents on the aromatic ring shows estimated strong effects in terms of yields under these reaction conditions. All aromatic aldehydes with electron-withdrawing and electron-releasing groups on their aromatic ring afforded the related products in high to excellent yields in short reaction times. The reaction times of aromatic aldehydes having electron withdrawing groups were rather faster than electron donating groups.

Table 3. The three-component synthesis of 5-amino-pyrazole-4-carbonitrile derivatives in the presence of 0.5 mol% of {[HMIM]C$(NO_2)_3$} as a nano structure ionic liquid catalyst.[a]

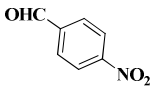
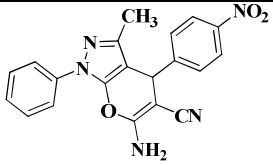
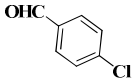
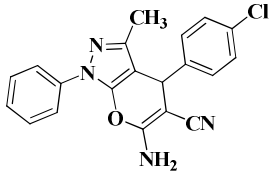
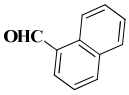
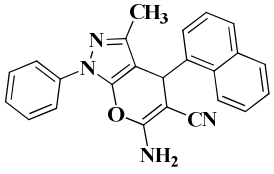
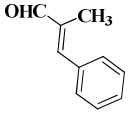
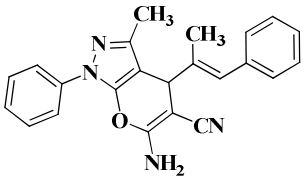
Entry	Aldehyde	Product	Time (min)	Yield[b] (%)	M.p (°C) [Lit.][Ref.]
1			8	97	172-174 [164-166][24]
2			10	95	227-229 [128-130][24]
3			10	95	162-164
4			20	91	237-239
5			20	92	281-283
6			20	92	221-223
7			12	94	178-180 [128-130][24]

View Article Online
DOI: 10.1039/C5RA16289K

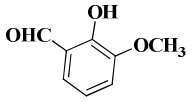
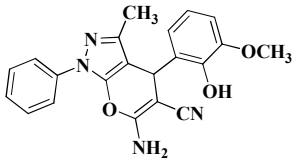
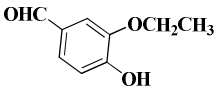
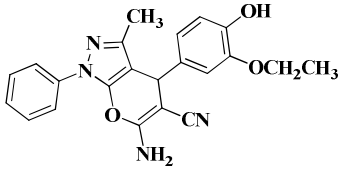
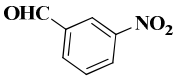
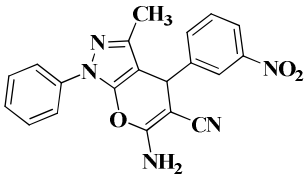
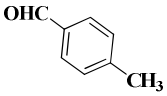
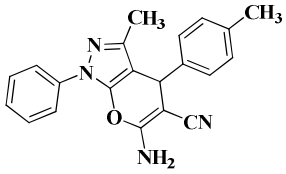
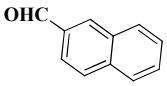
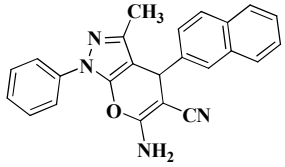
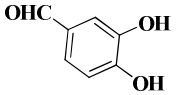
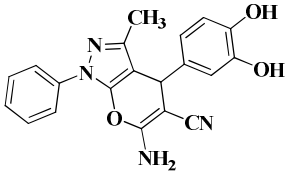
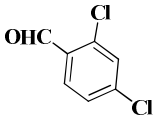
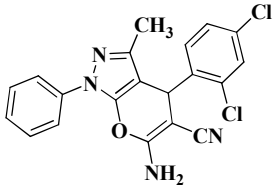
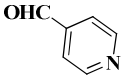
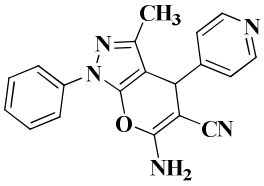
8			15	93	173-175 [118-120][24]
9			10	94	275-277
10			25	91	246-248 [212-213][31]
11			15	94	245-247
12			25	91	224-226

Reaction conditions: [a] Aldehyde (1 mmol), malononitrile (1 mmol), phenylhydrazine (1 mmol); [b] Isolate yield.

Table 4. The four-component synthesis of 1,4-dihydropyrano-[2,3-*c*]-pyrazole derivatives in the presence of 0.5 mol% of {[HMIM]C$(NO_2)_3$} as a nano structure ionic liquid catalyst.[a]

Entry	Aldehyde	Product	Time (min)	Yield[b] (%)	M.p (°C) [Lit.][Ref.]
1			10	95	204-206 [192-194][33]
2			15	93	183-185 [177-178][33]
3			12	94	235-237 [222-224][29]
4			25	89	267-269

View Article Online
DOI: 10.1039/C5RA16289K

5			30	90	297-299
6			30	89	175-177
7			15	93	207-209
8			18	91	179-181 [173-175][33]
9			15	93	206-208
10			35	88	189-191
11			17	91	231-233 [182-184][33]
12			30	88	249-251

Reaction conditions: [a] Aldehyde (1 mmol), malononitrile (1 mmol), phenylhydrazine (1 mmol), ethyl acetoacetate (1 mmol); [b] Isolate yield.

In Scheme 2 we introduce a possible mechanism for the synthesis of 5-amino-pyrazole-4-carbonitrile derivatives (**5**) in the presence of {[HMIM]C$(NO_2)_3$} as a nano structure ionic liquid catalyst. The reaction occurs *via* initial formation of arylidene malononitrile (**10**) in quantitative yield through the Knoevenagel addition of activated malononitrile (**2**) to the activated aromatic aldehyde (**1**) and followed by loss of water molecules. The formation of the 5-amino-pyrazole-4-carbonitrile derivatives (**5**) is suggested to include the reaction between arylidene malononitrile (**10**) and phenylhydrazine (**3**), followed by Michael addition, intermolecular cyclisation. Previously reported studies have been suggested aerobic auto oxidation of 5-amino-pyrazolidine-4-carbonitrile (**14**) to its corresponding 5-amino-pyrazole-4-carbonitrile (**5**). In contrast to the previously reported

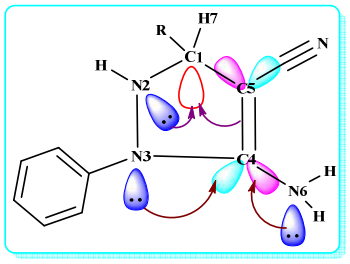
View Article Online
DOI: 10.1039/C5RA16289K

mechanistic description for the final step of the above described organic synthesis,[24, 25, 31] we believed that, this step might be proceed through unusual hydride transfer as well as Cannizzaro reaction (Fig. S98)[38] and H_2 releasing from tricyclic orthoamide (**16**) which presented in Scheme 3.[39] For improving of this idea, reaction was occurred under nitrogen atmosphere and in the absence of any molecular oxygen. It was observed that, the reaction proceeded under atmosphere of nitrogen as well as normal reaction condition in the presence of oxygen. By considering the above-mentioned evidence, conversion of 5-amino-pyrazolidine-4-carbonitrile (**14**) to its corresponding 5-amino-pyrazole-4-carbonitrile (**5**) might be occurred through unusual hydride transfer and releasing of molecular hydrogen (H_2). The C-H bond is so weakend by electron donation from the nitrogen lone pairs into the anti-bonding of C-H (σ^*_{C-H} orbital) which it can be broken via reaction with a proton to give molecular hydrogen. As we know, this phenomena has been named as anomeric effect.

To improvement a deeper kinetic and thermodynamic understanding of synthesis of 5-amino-pyrazole-4-carbonitrile derivatives DFT calculations were performed (Fig. 1). Starting from **13**, two different orientations of adjacent N-H and C-H groups on pyrazole ring with respect to each other give cis and trans like isomers. Our calculations show that the trans like isomer is about 2 kcal/mol more stable than cis one. Fig. 1 shows energy profile for more stable trans isomer. As can be seen, at first the intermediate **14** forms which are slightly more stable than **13**. Then through the formation of a logical transition structure and then removing the molecular hydrogen (H_2) the zwitterionic intermediate **15** will be formed. According to values of calculated Gibbs free energies this reaction is about -3.10 and -2.27 kcal/mol exothermic for cis and trans isomers, respectively. On the other hand, because of the delocalization of lone pair of adjacent nitrogen atom and π electrons to σ* C-H bond (the anomeric effect) the C-H bond in compound **14** is so weakened and the activation energy is relatively small. The NBO analysis of donor–acceptor interactions identified that the anomeric effect due to delocalization of lone pair of nitrogen atom to σ* C-H bond for cis and trans isomers of intermediate **14** is 3.84 and 3.82 kcal/mol, respectively. The delocalization from the π electron of adjacent double bond is 4.69 and 4.43 kcal/mol for cis and trans isomers, respectively. The main donor-acceptor interaction for pyrazole ring in intermediate **14** is shown in Table 5. In the final step of the reaction the zwitterionic intermediate **15** converts to 5-amino-pyrazole-4-carbonitrile (**5**) through an exothermic process (ΔG=-19.85 kcal/mol). In conclusion, the whole process of conversion of **13** to **5** through the releasing molecular hydrogen is exothermic (ΔG= -24.64 kcal/mol). Thus the above theoretical studies support our suggested mechanism and shows that releasing molecular hydrogen (H_2) is quite possible in such systems. The optimized structure of all compounds involved in our suggested mechanism is shown in Fig. 2.

Table 5. The main second order perturbation energies (kcal/mol) calculated for pyrazol ring in intermediate **14**.

Donor-acceptor interactions	14-cis	14-trans
nb N2 → σ* C1-H7	3.84	3.82
π C4-C5 → σ* C1-H7	4.69	4.43
nb N6 → π* C4-H5	38.53	39.79
nb N6 → σ* C4-H5	1.02	—
nb N3 → π* C4-H5	30.94	35.03
nb N3→ σ* C4-H5	—	0.52



The proposed catalytic method are recommend in Scheme 4, which are dependable with literature reports.[40, 41] The reaction happen through primary formation of arylidene malononitrile (**10**) in quantitative yield *via* the Knoevenagel addition of activated malononitrile (**2**) to the activated aromatic aldehyde (**1**) and followed by loss of water molecules. The formation of the 1,4-dihydropyrano-[2,3-*c*]-pyrazole (**6**) is proposed to contain the following tandem reactions: pyrazolone (**20**) formation by reaction between phenylhydrazine (**3**) and activated ethyl acetoacetate (**4**), Michael addition of pyrazolone (**20**) to arylidene malononitrile (**10**), followed *via* cyclization and tautomerization (Scheme 4).

Additionally, reusability of the NIL catalyst was corroborated aboard the condensation of naphthalene-1-carbaldehyde, malononitrile and phenylhydrazine (in the synthesis of 5-amino-pyrazole-4-carbonitrile derivatives) and naphthalene-1-carbaldehyde, malononitrile, phenylhydrazine and ethyl acetoacetate (in the synthesis of 1,4-dihydropyrano-[2,3-*c*]-pyrazole derivatives). At the end of the reaction, ethyl acetate was added to the reaction mixture and heated to extract product from remained starting materials. This solution was washed with water to separate catalyst from other materials (the product is soluble in hot ethyl acetate and NIL catalyst is soluble in water). The aqueous layer was decanted, separated and used for further reaction after removing of water. It have been detected that the catalytic activity of the catalyst was restored within the limits of the experimental errors for five continuous runs (Fig. 3). The deactivation of the nano

View Article Online
DOI: 10.1039/C5RA16289K

ionic liquid catalyst is low, while reactant was expected. The reaction was scaled up to 10 mmol of reactants in the presence of 5 mol% of NIL catalyst at room temperature. The yield of the reaction was 95% after 10 min and 91% after the fifth run (in the synthesis of 5-amino-pyrazole-4-carbonitrile derivatives) and 94% after 12 min and 89% after the fifth run (in the synthesis of 1,4-dihydropyrano-[2,3-*c*]-pyrazole derivatives). The results were summarized in Fig. 3.

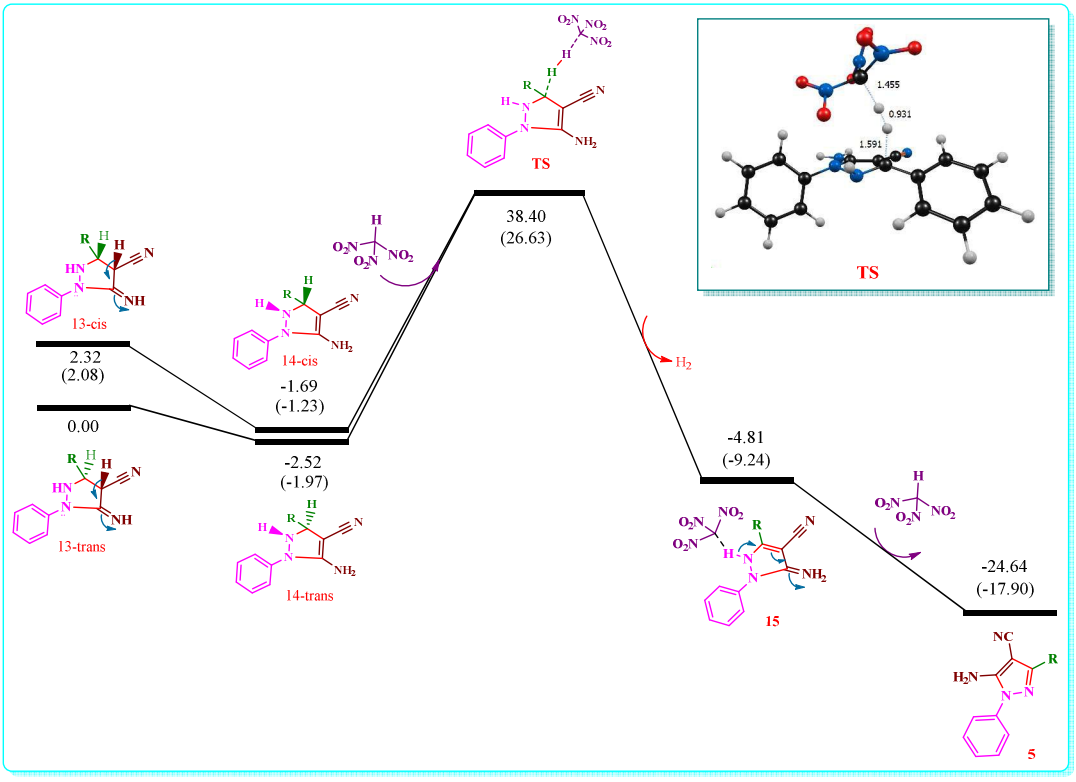
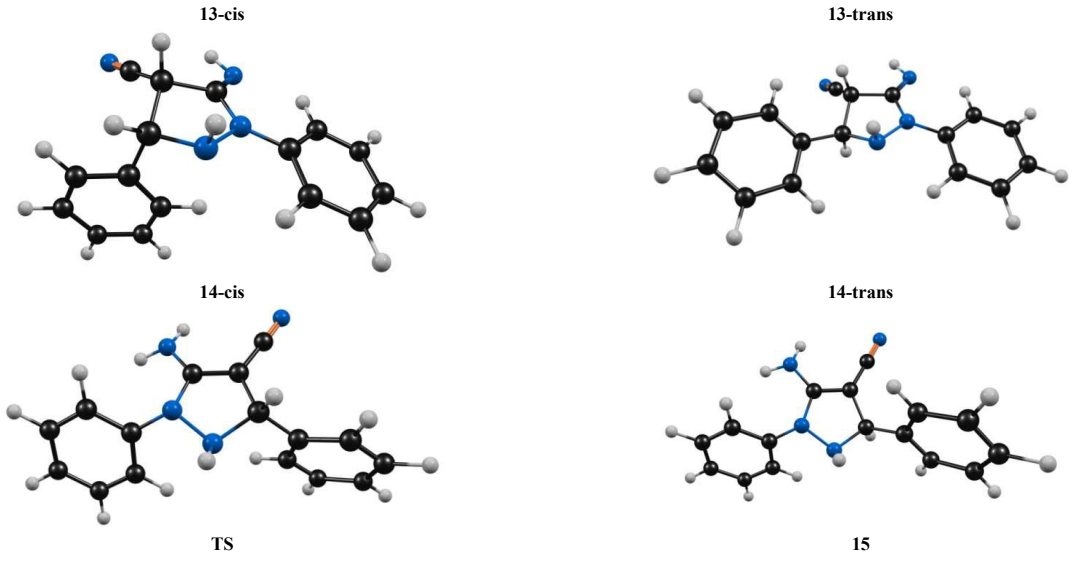


Fig. 1. Energy profile calculated for synthesis of 5-amino-pyrazole-4-carbonitrile derivatives (**5**) beginning from compound **13** (see Scheme 2). The relative Gibbs free energy and corrected electronic energies (Figures in parentheses) obtained from the B3LYP/TZVP calculations both are given in kcal/mol. The phenyl group is shown as R.



View Article Online
DOI: 10.1039/C5RA16289K

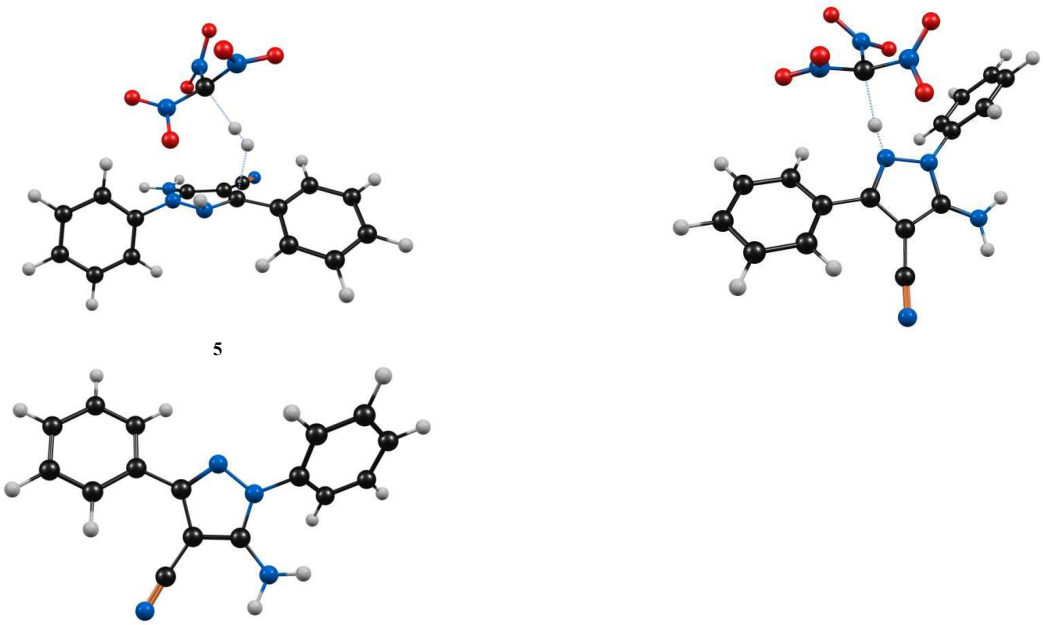
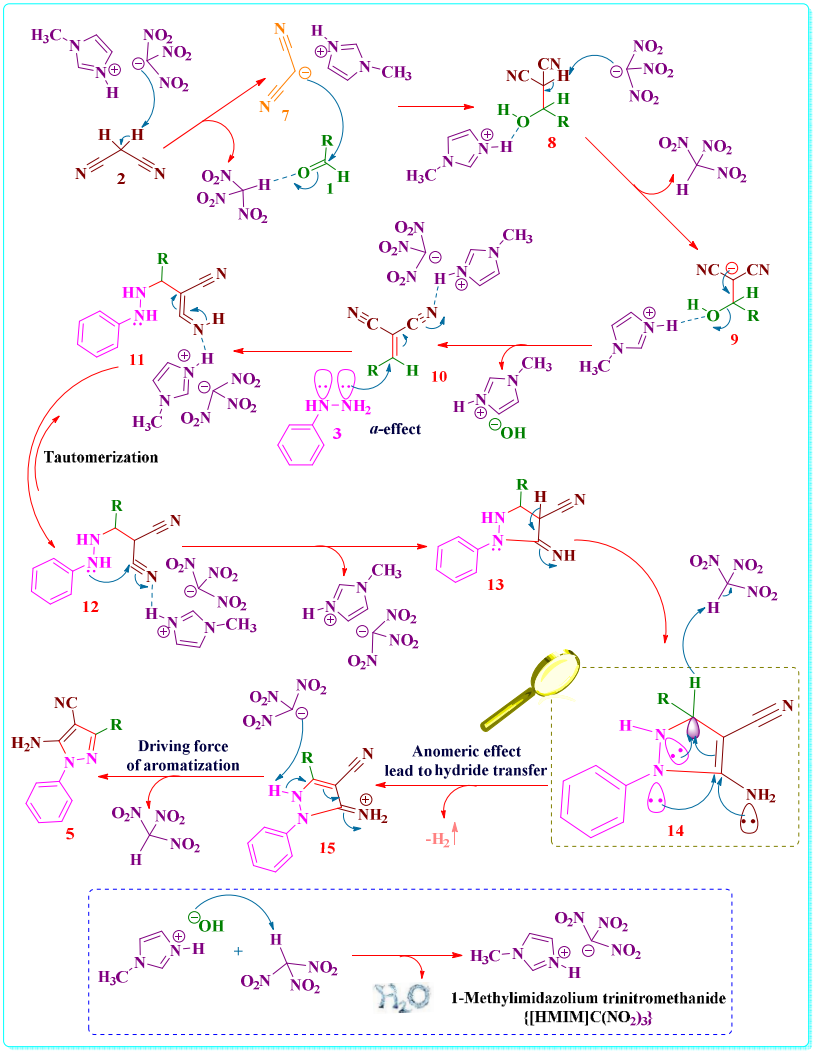
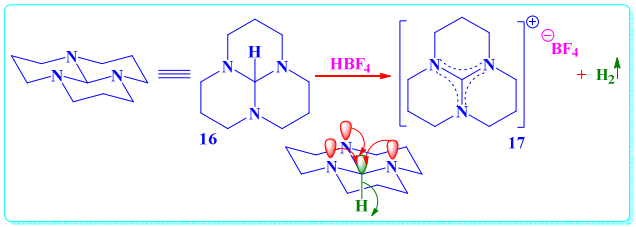


Fig. 2. The optimized structure of all compounds involved in conversion of **13** to **5** according to the mechanism suggested in Fig. 1.

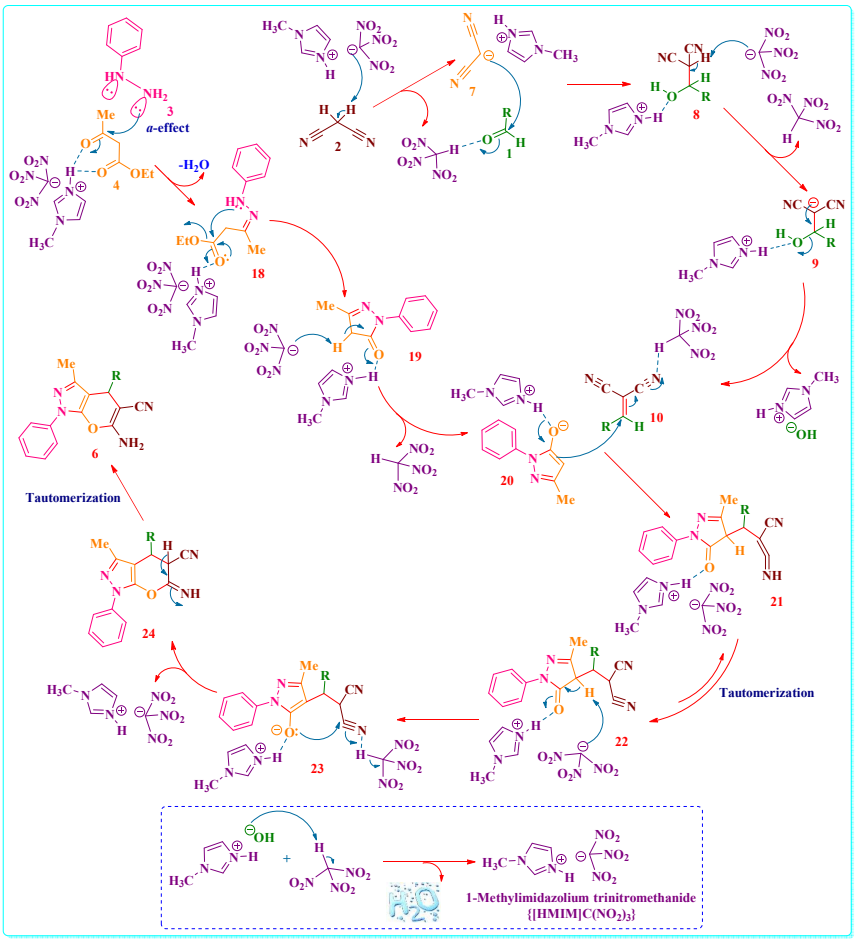


Scheme 2. The suggested mechanism for the synthesis of 5-amino-pyrazole-4-carbonitrile derivatives in the presence of {[HMIM]C$(NO_2)_3$} as a nano structure ionic liquid catalyst.

View Article Online
DOI: 10.1039/C5RA16289K



Scheme 3. A striking example which had been observed for an unusual hydride transfer from tricyclic orthoamide (16) through anomeric effect.[39]



Scheme 4. The proposed mechanism for the synthesis of 1,4-dihydropyrano-[2,3-*c*]-pyrazole derivatives in the presence of {[HMIM]C$(NO_2)_3$} as a nano structure ionic liquid catalyst.

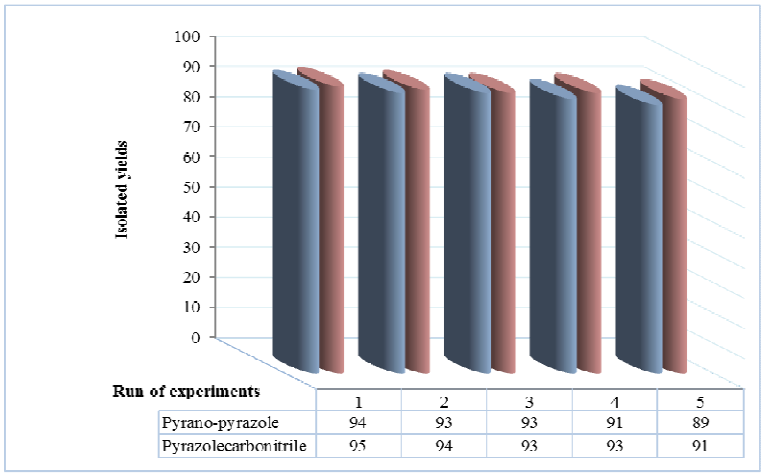


Fig. 3. Reusability of the nano structure ionic liquid catalyst in the synthesis of 5-amino-pyrazole-4-carbonitrile derivatives (in 10 minutes) and in the synthesis of 1,4-dihydropyrano-[2,3-*c*]-pyrazole derivatives (in 12 minutes).

View Article Online
DOI: 10.1039/C5RA16289K

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

In continuation of our study into the application of nano structure ionic liquid catalyst in the synthesis of 5-amino-pyrazole-4-carbonitrile derivatives, we studied the efficacy of this ionic liquid catalyst (an approval of suggested mechanism) is comparable with various catalysts. To optimize the reaction conditions, the reaction between 3-ethoxy-4-hydroxybenzaldehyde, malononitrile and phenylhydrazine under N_2 atmosphere at room temperature was used as a typical (Table 6).

Table 6. The synthsis of 5-amino-pyrazole-4-carbonitrile in the presence of different catalyst for an approval of suggested mechanism.[a]

Entry	Catalyst	Amount of catalyst (mol%)	Time (min)	Yield[b] (%)
1	{[HMIM]C(NO_2)$_3$}	0.5	20	92
2	HBF_4	10	30	85
3	$Ce(HSO_4)_3.7H_2O$	10	60	83
4	$Fe(HSO_4)_3$	12	60	79
5	NH_2SO_3H	10	60	85
6	[MSIM]Cl	1	60	87
7	$Zn(HSO_4)_2$	10	120	51
8	$Ca(HSO_4)_2$	15	120	47
9	$BiCl_3$	10	120	41
10	$H_3PW_{12}O_{40}$	1	180	—
11	$ZrOCl_2$	10	180	—
12	$B(OH)_3$	10	180	—
13	Oxone	5	180	—
14	$Bi(HSO_4)_3$	10	180	—
15	$Al(HSO_4)_3$	12	180	—

Reaction conditions: [a] 3-Ethoxy-4-hydroxybenzaldehyde (1 mmol), malononitrile (1 mmol), phenylhydrazine (1 mmol), under N_2 atmosphere, r.t.; [b] Isolate yield.

Conclusions

In summary, a green, effective and environmentally friendly NIL catalyst namely 1-methylimidazolium trinitromethanide {[HMIM]C(NO_2)$_3$} was used and considered in the synthesis of 5-amino-pyrazole-4-carbonitrile derivatives by three-component condensation reaction of various aromatic aldehydes, malononitrile and phenylhydrazine under solvent-free conditions at room temperature. Subsequently, 1,4-dihydropyrano-[2,3-*c*]-pyrazole derivatives were also synthesized *via* four-component condensation between several aromatic aldehydes, malononitrile, phenylhydrazine and ethyl acetoacetate under same reaction conditions. The presented mechanisms revealed that the buffer ability of nano ionic liquid, probably plays the key and dual catalytic roles in the described reactions. Finally, considerable advantages of the presented methodology and/or investigation are reasonably high yield, cleaner reaction profile, short reaction time, simple work up, recycle and reusability of the nano structure ionic liquid catalyst which makes it in close agreement with the green chemistry disciplines. A new mechanistic approach was also proposed for the final step of the pyrazoles synthesis which was supported by theoretical studies. Therefore, we thought that the suggested mechanism have potential for entering into the graduate text book in the future.

Experimental

General procedure for the preparation of nano structure ionic liquid catalyst: 1-methylimidazolium trinitromethanide

The nano ionic liquid {[HMIM]C(NO_2)$_3$} as a catalyst was synthesized according to our previously reported procedure.[34] A yellow solid was formed in high purity and then the physical data of these known nano structure ionic liquid was found to be identical. M.p: 54-56 ^oC; Yield: 97% (0.679 g); Spectral data: IR (KBr): υ 3433, 3144, 1584, 1383 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 3.87 (s, 3H, —CH_3), 7.68 (d, 1H, *J* = 3.2 Hz, —CH); 7.71 (d, 1H, *J* = 3.2 Hz, —CH), 9.08 (s, 1H, —CH), 14.23 (brs, 1H, —NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.8, 46.5, 120.2, 123.6, 136.3; MS: m/z = 233 $[M]^+$, 234 $[M+H]^+$.

General procedure for the synthesis of 5-amino-pyrazole-4-carbonitrile derivatives

A mixture of various aromatic aldehydes (1 mmol), malononitrile (1 mmol) and phenylhydrazine (1 mmol) in a round bottom flask, was added {[HMIM]C(NO_2)$_3$} as a nano structure ionic liquid catalyst (0.5 mol%; 0.117 g), and the subsequent mixture was firstly stirred magnetically under solvent-free conditions at room temperature. After completion of the reaction, as monitored by TLC *n*-hexane/ethyl acetate (5:3), ethyl acetate (10 mL) was added to reaction mixture, stirred and refluxed for 3 min, and then was washed with water (10 mL) and decanted to separate catalyst from the other materials (the reaction mixture was soluble in hot ethyl acetate and nano structure molten salt catalyst was soluble in water). The aqueous layer was decanted and catalyst separated after removing

View Article Online
DOI: 10.1039/C5RA16289K

of water. The remained catalyst was used for alternative reaction. The solvent of organic layer was evaporated and the crude product was purified by recrystallization from ethanol/water (10:1). In this study, nano structured ionic liquid catalyst was recycled and reused for five times without significant loss of its catalytic activity.

General procedure for the synthesis of 1,4-dihydropyrano-[2,3-c]-pyrazole derivatives

A mixture of various aromatic aldehydes (1 mmol), malononitrile (1 mmol), phenylhydrazine (1 mmol) and ethyl acetoacetate (1 mmol) in a round bottom flask, was added {[HMIM]C$(NO_2)_3$} as a nano structure ionic liquid catalyst (0.5 mol%; 0.117 g), and the subsequent mixture was firstly stirred magnetically under solvent-free conditions at room temperature. After completion of the reaction, as observed by TLC *n*-hexane/ethyl acetate (5:2), ethyl acetate (10 mL) was added to reaction mixture, stirred and refluxed for 3 min, and then was washed with water (10 mL) and decanted to separate catalyst from the other materials (the reaction mixture was soluble in hot ethyl acetate and nano structure ionic liquid catalyst was soluble in water). The aqueous layer was decanted and catalyst separated after removing of water. The remained catalyst was used for alternative reaction. The solvent of organic layer was evaporated and the crude product was purified by recrystallization from ethanol/water (10:1). In this work, nano structure ionic liquid catalyst was recycled and reused for five times without significant loss of its catalytic activity.

Spectral data analysis for compounds

5-Amino-3-(naphthalen-1-yl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table 3, entry 3): Yellow solid; M.p: 162-164 ^oC; Yield: 95%; IR (KBr): υ 3554, 3475, 3415, 3237, 3027, 2226, 1637, 1616, 1566, 1384, 1371 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_{ppm} 7.71 (t, 6H, J = 7.4 Hz, ArH), 8.11 (d, 2H, J = 7.2 Hz, ArH), 8.22 (d, 1H, J = 7.2 Hz, ArH), 8.28 (d, 2H, J = 8.4 Hz, ArH), 9.40 (s, 2H, —NH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ_{ppm} 85.5, 100.8, 101.5, 113.7, 114.5, 124.3, 125.9, 127.7, 128.6, 129.0, 129.4, 131.1, 133.5, 134.6, 160.8, 166.1, 167.3.

5-Amino-1-phenyl-3-(1-phenylprop-1-en-2-yl)-1H-pyrazole-4-carbonitrile (Table 3, entry 4): Yellow solid; M.p: 237-239 ^oC; Yield: 91%; IR (KBr): υ 3550m 3462, 3418, 3237, 2987, 2208, 1634, 1515, 1384, 1266 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_{ppm} 2.00 (s, 3H, —CH_3), 3.92 (s, 1H, —CH), 7.51 (t, 6H, J = 8.0 Hz, ArH), 7.66 (d, 4H, J = 7.6 Hz, ArH), 9.60 (s, 2H, —NH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ_{ppm} 33.9, 67.4. 114.7, 114.9, 126.1, 126.2, 126.7, 126.9, 127.4, 127.5, 129.0, 129.3, 129.4, 129.6, 137.4, 137.5, 137.6, 166.1.

5-Amino-3-(2-hydroxy-3-methoxyphenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table 3, entry 5): Orange solid; M.p: 281-283 ^oC; Yield: 92%; IR (KBr): υ 3545, 3483, 3412, 3237, 2217, 1638, 1618, 1498, 1347, 1246 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_{ppm} 3.37 (s, 3H, —OCH_3), 6.55 (s, 1H, —OH), 7.39 (t, 4H, J = 5.9 Hz, ArH), 7.48 (s, 2H, —NH_2), 7.77 (d, 4H, J = 5.9 Hz, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ_{ppm} 24.1, 63.9, 116.0, 116.1, 126.0, 126.1, 126.2, 126.8, 126.9, 127.1, 127.5, 127.8, 128.9, 129.3, 129.4, 129.5, 168.1.

5-Amino-3-(3-ethoxy-4-hydroxyphenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table 3, entry 6): Orange solid; M.p: 221-223 ^oC; Yield: 92%; IR (KBr): υ 3554, 3468, 3412, 3237, 2978, 2181, 1639, 1608, 1569, 1384, 1274 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_{ppm} 1.33 (t, 3H, J = 7.0 Hz, —CH_3), 4.04 (q, 2H, J = 6.8 Hz, —CH_2), 6.54 (d, 1H, J = 8.0 Hz, ArH), 6.70 (d, 2H, J = 8.4 Hz, ArH), 6.79 (d, 1H, J = 8.0 Hz, ArH), 6.86 (s, 1H, —OH), 7.01 (t, 1H, J = 8.4 Hz, ArH), 7.45 (t, 2H, J = 8.4 Hz, ArH), 7.54 (s, 1H, ArH), 7.95 (s, 2H, —NH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ_{ppm} 14.6, 28.5, 64.0, 114.9, 125.4, 125.6, 126.3, 126.4, 126.5, 126.6, 128.0, 131.1, 133.2, 147.1, 151.2, 151.3, 159.0, 159.1.

5-Amino-3-(naphthalen-2-yl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table 3, entry 9): Yellow solid; M.p: 275-277 ^oC; Yield: 94%; IR (KBr): υ 3550, 3470, 3411, 3358, 3237, 2983, 2219, 1638, 1559, 1384, 1283 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_{ppm} 7.33 (s, 1H, ArH), 7.52 (t, 5H, J = 9.2 Hz, ArH), 7.88 (d, 6H, J = 9.2 Hz, ArH), 8.87 (s, 2H, —NH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ_{ppm} 59.5, 144.6, 125.3, 125.4, 125.6, 126.0, 126.1, 126.3, 126.4, 126.9, 127.7, 127.8, 128.5, 131.7, 131.9, 132.0, 133.2, 133.3, 133.4, 167.4.

5-Amino-3-(2,4-dichlorophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table 3, entry 11): Yellow solid; M.p: 245-247 ^oC; Yield: 94%; IR (KBr): υ 3463, 3400, 3233, 2983, 2206, 1645, 1577, 1384 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_{ppm} 7.06 (s, 1H, ArH), 7.40 (t, 3H, J = 8.4 Hz, ArH), 7.45 (d, 1H, J = 8.4 Hz, ArH), 7.51 (d, 2H, J = 8.4 Hz, ArH), 7.61 (d, 2H, J = 8.4 Hz, ArH), 7.86 (s, 2H, —NH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ_{ppm} 65.0, 112.7, 112.8, 125.6, 125.7, 126.1, 127.4, 127.7, 127.8, 128.1, 132.0, 133.3, 145.3, 151.8, 152.0, 165.4.

5-Amino-1-phenyl-3-(pyridin-4-yl)-1H-pyrazole-4-carbonitrile (Table 3, entry 12): Brown solid; M.p: 221-223 ^oC; Yield: 92%; IR (KBr): υ 3550, 3462, 3416, 3229, 2987, 2194, 1639, 1615, 1384 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_{ppm} 7.05 (s, 2H, —NH_2), 7.21 (d, 2H, J = 6.0 Hz, ArH), 7.41 (t, 1H, J = 7.8 Hz, ArH), 7.82 (d, 2H, J = 7.2 Hz, ArH), 8.46 (t, 1H, J = 6.2 Hz, ArH), 8.53 (d, 2H, J = 6.0 Hz, ArH), 8.77 (t, 1H, J = 5.6 Hz, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ_{ppm} 60.8, 123.1, 125.5, 125.7, 126.2, 126.5, 126.6, 127.0, 128.0, 131.2, 133.4, 138.4, 145.4, 150.1, 165.6.

6-Amino-3-methyl-4-(naphthalen-1-yl)-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (Table 4, entry 3): Yellow solid; M.p: 235-237 ^oC; Yield: 94%; IR (KBr): υ 3550, 3470, 3415, 3241, 3062, 2197, 1600, 1498, 1370 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_{ppm} 2.27 (s, 3H, —CH_3), 5.42 (s, 1H, —CH), 7.09 (s, 2H, —NH_2), 7.35 (t, 2H, J = 8.0 Hz, ArH), 7.47 (t, 2H, J = 6.8 Hz, ArH), 7.53 (t, 2H, J = 8.0 Hz, ArH), 7.75 (d, 1H, J = 8.0 Hz, ArH), 7.86 (d, 3H, J = 7.6 Hz, ArH), 8.01 (d, 1H, J = 7.2 Hz, ArH), 8.23 (d, 1H, J = 7.6 Hz, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ_{ppm} 19.0, 31.7, 56.5, 103.8, 119.9, 120.4, 123.6, 124.1, 125.4, 125.8, 126.0, 126.2, 126.6,

View Article Online
DOI: 10.1039/C5RA16289K

126.7, 128.9, 129.2, 129.3, 129.9, 131.3, 134.1, 138.1, 140.2, 145.7.

6-Amino-3-methyl-1-phenyl-4-(1-phenylprop-1-en-2-yl)-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (Table 4, entry 4): Yellow solid; M.p: 267-269 °C; Yield: 89%; IR (KBr): υ 3545, 3470, 3414, 3333, 3061, 2925, 2204, 1599, 1499, 1383 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_{ppm} 1.87 (s, 3H, —CH_3), 2.10 (s, 3H, —CH_3), 6.41 (s, 1H, —CH), 6.84 (s, 1H, —CH), 7.06 (d, 2H, *J* = 7.2 Hz, ArH), 7.32 (t, 6H, *J* = 7.6 Hz, ArH), 7.96 (d, 2H, *J* = 7.2 Hz, ArH), 8.04 (s, 2H, —NH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ_{ppm} 21.1, 37.4, 69.4, 101.2, 111.7, 116.2, 122.9, 123.1, 125.3, 125.5, 125.6, 125.7, 126.1, 126.4, 126.6, 127.0, 128.1, 129.4, 131.1, 134.0, 138.4, 139.4, 145.9, 152.2.

6-Amino-4-(2-hydroxy-3-methoxyphenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (Table 4, entry 5): Pink solid; M.p: 297-299 °C; Yield: 90%; IR (KBr): υ 3462, 3420, 3333, 3231, 3062, 2945, 2201, 1640, 1599, 14971361 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_{ppm} 1.86 (s, 3H, —CH_3), 2.09 (s, 3H, —CH_3), 3.82 (s, 1H, —OH), 3.98 (s, 1H, —CH), 6.88 (d, 4H, *J* = 8.0 Hz, ArH), 7.30 (t, 2H, *J* = 7.8 Hz, ArH), 7.51 (s, 2H, —NH_2), 7.91 (t, 2H, *J* = 6.8 Hz, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ_{ppm} 21.1, 32.6, 37.2, 60.3, 100.4, 100.5, 101.4, 111.4, 116.0, 116.1, 126.1, 126.2, 126.7, 126.9, 127.5, 128.9, 129.3, 129.5, 137.3, 137.6, 140.8, 140.9, 145.0.

6-Amino-4-(3-ethoxy-4-hydroxyphenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (Table 4, entry 6): Orange solid; M.p: 175-177 °C; Yield: 89%; IR (KBr): υ 3420, 3331, 3229, 3195, 2984, 2186, 1647, 1597, 1516, 1494, 1395 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_{ppm} 1.32 (t, 3H, *J* = 7.0 Hz, —CH_3), 1.84 (s, 3H, —CH_3), 4.02 (q, 2H, *J* = 6.8 Hz, —CH_3), 4.58 (s, 1H, —OH), 6.44 (d, 1H, *J* = 8.0 Hz, ArH), 6.78 (d, 1H, *J* = 8.0 Hz, ArH), 6.82 (s, 1H, —CH), 7.07 (t, 1H, *J* = 7.4 Hz, ArH), 7.17 (s, 1H, ArH), 7.30 (t, 1H, *J* = 7.2 Hz, ArH), 7.50 (t, 1H, *J* = 8.0 Hz, ArH), 7.82 (d, 1H, *J* = 8.0 Hz, ArH), 7.89 (d, 1H, *J* = 7.6 Hz, ArH), 8.08 (s, 2H, —NH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ_{ppm} 27.0, 34.5, 36.8, 59.1, 64.3, 119.4, 120.1, 120.3, 120.7, 120.8, 124.1, 126.5, 128.9, 129.4, 129.8, 135.0, 138.1, 144.2, 145.0, 145.9, 146.3, 146.4.

6-Amino-3-methyl-4-(3-nitrophenyl)-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (Table 4, entry 7): Yellow solid; M.p: 207-209 °C; Yield: 93%; IR (KBr): υ 3462, 3411, 3328, 3249, 3195, 3057, 2920, 2195, 1661, 1597, 1519, 1385 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_{ppm} 1.82 (s, 3H, —CH_3), 4.80 (s, 1H, —CH), 7.35 (d, 2H, *J* = 7.2 Hz, ArH), 7.42 (s, 1H, ArH), 7.52 (t, 2H, *J* = 8.0 Hz, ArH), 7.69 7.30 (t, 2H, *J* = 7.6 Hz, ArH), 7.83 (d, 2H, *J* = 7.6 Hz, ArH), 8.18 (s, 2H, —NH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ_{ppm} 13.4, 26.6, 36.7, 57.5, 119.2, 119.8, 120.3, 120.6, 120.8, 122.3, 122.7, 122.8, 123.2, 123.9, 126.8, 128.9, 129.4, 129.7, 129.8, 130.8, 134.9.

6-Amino-3-methyl-4-(naphthalen-2-yl)-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (Table 4, entry 9): Yellow solid; M.p: 206-209 °C; Yield: 93%; IR (KBr): υ 3554, 3441, 3351, 3301, 3191, 3095, 2925, 2191, 1653, 1593, 1518, 1398 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_{ppm} 1.77 (s, 3H, —CH_3), 4.89 (s, 1H, —CH), 7.33 (d, 4H, *J* = 8.0 Hz, ArH), 7.53 (t, 5H, *J* = 8.4 Hz, ArH), 7.86 (d, 2H, *J* = 8.0 Hz, ArH), 7.90 (s, 1H, ArH), 7.92 (s, 2H, —NH_2); ^{13}C NMR (100 MHz, DMSO-d_6): δ_{ppm} 35.2, 37.5, 58.5, 124.9, 125.1, 125.2, 125.3, 125.4, 126.5, 126.6, 126.7, 126.8, 127.7, 1238.0, 128.1, 131.1, 131.2, 131.3, 133.4, 133.8, 134.0, 139.8, 142.9, 143.8.

6-Amino-4-(3,4-dihydroxyphenyl)-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (Table 4, entry 10): Orange solid; M.p: 189-191 °C; Yield: 88%; IR (KBr): υ 3413, 3329, 3237, 2186, 1655, 1598, 1496, 1384 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_{ppm} 1.90 (s, 3H, —CH_3), 4.14 (s, 1H, —OH), 4.49 (s, 1H, —OH), 6.58 (d, 1H, *J* = 8.4 Hz, ArH), 6.71 (d, 1H, *J* = 8.0 Hz, ArH), 6.83 (s, 1H, —CH), 6.86 (s, 1H, ArH), 7.10 (t, 1H, *J* = 6.8 Hz, ArH), 7.16 (s, 2H, —NH_2), 7.33 (t, 1H, *J* = 7.6 Hz, ArH), 7.51 (t, 1H, *J* = 8.0 Hz, ArH), 7.81 (d, 1H, *J* = 7.6 Hz, ArH), 7.90 (d, 1H, *J* = 7.6 Hz, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ_{ppm} 33.8, 36.6, 59.4, 99.6, 115.3, 115.5, 118.4, 119.1, 120.1, 120.3, 124.2, 126.6, 128.9, 129.9, 138.1, 145.9, 146.6, 157.7, 159.6.

6-Amino-3-methyl-1-phenyl-4-(pyridin-4-yl)-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (Table 4, entry 12): Red solid; M.p: 249-251 °C; Yield: 88%; IR (KBr): υ 3406, 3346, 3152, 3066, 2919, 2195, 1667, 1595, 1520, 1395 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_{ppm} 1.82 (s, 3H, —CH_3), 4.78 (s, 1H, —CH), 7.36 (d, 1H, *J* = 6.6 Hz, ArH), 7.41 (s, 2H, —NH_2), 7.51 (t, 3H, *J* = 8.0 Hz, ArH), 7.65 (d, 1H, *J* = 8.8 Hz, ArH), 7.81 (d, 2H, *J* = 7.6 Hz, ArH), 8.57 (d, 2H, *J* = 7.0 Hz, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ_{ppm} 30.6, 41.3, 57.9, 123.4, 124.2, 125.0, 125.4, 128.2, 128.3, 128.4, 129.3, 129.8, 130.0, 131.6, 133.6, 134.1, 134.6, 142.6, 145.4.

Computational detail

Computations were performed using the Gaussian09 program.[42] Density functional theory has been used to investigate the reactions of 5-amino-pyrazole-4-carbonitrile derivatives (**5**) in the presence of {[HMIM]$C(NO_2)_3$} as a nanostructure ionic liquid catalyst. All geometry optimizations were performed at B3LYP/TZVP level of theory and frequency calculations were carried out at the same level. All frequencies in the non-transition states are real. We have used the corrected electronic energy and Gibbs free energy for investigation of the mechanism of the synthesis of 5-amino-pyrazole-4-carbonitrile derivatives (**5**). The nature of transition structure was confirmed by intrinsic reaction coordinate (IRC)[43] searches and vibrational frequency calculations. The intramolecular interactions were calculated on the basis of natural bond orbital (NBO)[44] analyses.

Acknowledgements

We thank Bu-Ali Sina University and Iran National Science Foundation (INSF) for financial support to our research group.

Notes and references

View Article Online
DOI: 10.1039/C5RA16289K

Faculty of Chemistry, Bu-Ali Sina University, Hamedan 6517838683, Iran
**Corresponding Author: Fax: +988138257407*
E-mail: zolfi@basu.ac.ir and mzolfigol@yahoo.com (M.A. Zolfigol).
† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

1 P. Wasserscheid and W. Keim, *Angew. Chem., Int. Ed*., 2000, **39**, 3773.
2 K.R. Seddon, *In Molten Salt Chemistry*, G. Mamantov and R. Marassi, Eds., *Reidel Publishing Co*., Dordrecht, The Netherlands, 1987.
3 J.D. Holbrey and K.R. Seddon, *Clean Prod. Proc*., 1999, **1**, 223.
4 T. Welton, *Chem. Rev*., 1999, **99**, 2071.
5 J. Dupont, C.S. Consorti and J.J. Spencer, *Braz. Chem. Soc*., 2000, **11**, 337.
6 C.C. Tzschucke, C. Markert, W. Bannwarth, S. Roller, A. Hebel and R. Haag, *Angew. Chem., Int. Ed*., 2000, **41**, 3964.
7 J.S. Wilkes, *J. Mol. Catal. A: Chem*., 2014, **214**, 11.
8 M. Kosmulski, J. Gustafsson and J.B. Rosenholm, *Thermochim. Acta*., 2004, **412**, 47.
9 M. Deetlefs and K.R. Seddon, *Chim. Oggi*., 2006, **24**, 16.
10 M.J. Earle, J.M.S.S. Esperanca, M.A. Gilea, J.N. Canongia-Lopes, L.P.N. Rebelo, J.W. Magee, K.R. Seddon and J.A. Widegren, *Nature*., 2006, **439**, 831.
11 B.M. Trost, *Angew. Chem., Int. Ed. Engl*., 1995, **34**, 259.
12 P.A. Wender, S.T. Hanhdy and D.L. Wright, *Chem. Ind*., 1997, 765.
13 L. Weber, *Curr. Opin. Chem. Biol*., 2000, **4**, 295.
14 A. Dömling, *Curr. Opin. Chem. Biol*., 2002, **6**, 306.
15 J. Kim, D. Lee, C. Park, W. So, M. Jo, T. Ok, J. Kwon, S. Kong, S. Jo, Y. Kim, J. Choi, H.C. Kim, Y. Ko, I. Choi, Y. Park, J. Yoon, M.K. Ju, J. Kim, S-J. Han, T-H. Kim, J. Cechetto, J. Nam, P. Sommer, M. Liuzzi, J. Lee and Z. No, *ACS Med. Chem. Lett*., 2012, **3**, 678.
16 J. Bo, F. Wei, S. Mu-Yan, Y. Qin, W. Shu-Liang, T. Shu-Jiang and L. Guigen, *J. Org. Chem*., 2014, **79**, 5258.
17 R. Nagamallu and A.K. Kariyappa, *Bioorg. Med. Chem. Lett*., 2013, **23**, 6406.
18 I.M. El-Deeb and S.H. Lee, *Bioorg. & Med. Chem*., 2010, **18**, 3961.
19 S. Prekupec, D. Makuc, J. Plavec, L. Suman, M. Kralj, K. Pavelic, J. Balzarini, E.D. Clercq, M. Mintas and S. Raic-Malic, *J. Med. Chem*., 2007, **50**, 3037.
20 N.K. Piyush, P.S. Shailesh and K.R. Dipak, *New J. Chem*., 2014, **38**, 2902.
21 D.M. Bailey, P.E. Hansen, A.G. Hlavac, E.R. Baizman, J. Pearl, A.F. Defelice and M. E. Feigenson, *J. Med. Chem*., 1985, **28**, 256.
22 E. McDonald, J. Keith, A.B. Paul, M.J. Drysdale and P. Workman, *Curr. Topics in Med. Chem*., 2006, **6**, 1193.
23 A.A. Dissanayake and A.L. Odom, *Chem. Commun*., 2012, **48**, 440.
24 M. Srivastava, P. Rai, J. Singh and J. Singh, *New J. Chem*., 2014, **38**, 302.
25 K. Kumari, D.S. Raghuvanshi, V. Jouikov and K.N. Singh, *Tetrahedron Lett*., 2012, **53**, 1130.
26 Y. Peng, G. Song and R. Dou, *Green Chem*., 2006, **8**, 573.
27 G. Vasuki and K. Kumaravel, *Tetrahedron Lett*., 2008, **49**, 5636.
28 A.M. Shestopalov, Y.M. Emeliyanova, A.A. Shestopalov, L.A. Rodinovskaya, Z.I. Niazimbetova and D.H. Evans, *Org. Lett*., 2002, **4**, 423.
29 A. Saha, S. Payra and S. Banerjee, *Green Chem.*, 2015, **17**, 2859.
30 S. Aixue, Y. Jia-Hai, Y. Haitao, Z. Wenchao and W. Xiaolong, *Tetrahedron Lett*., 2014, **55**, 889.
31 S. Maddila, S. Rana, R. Pagadala, Sh. Kankala, S. Maddila and S.B. Jonnalagadda, *Catal. Commun*., 2015, **61**, 26.
32 M. Srivastava, P. Rai, J. Singh and J. Singh, *RSC. Advances*, 2013, **3**, 16994.
33 D. Shi, J. Mou, Q. Zhuang, L. Niu, N. Wu and X. Wang, *Synth. Commun*., 2004, **34**. 4557.
34 M.A. Zolfigol, S. Baghery, A.R. Moosavi-Zare, S.M. Vahdat, H. Alinezhad and M. Norouzi, *RSC. Adv*., 2014, **4**, 57662.
35 (a) M.A. Zolfigol, D. Azarifar, Sh. Mallakpour, I. Mohammadpoor-Baltork, A. Forghaniha, B. Maleki and M. Abdollahi-Alibeik, *Tetrahedron Lett*., 2006, **47**, 833; (b) D. Azarifar, M.A. Zolfigol and B. Maleki, *Bull. Korean Chem. Soc*., 2004, **25**, 1; (c) D. Azarifar, M.A. Zolfigol and B. Maleki, *Synthesis*., 2004, **11**, 1744; (d) M.A. Zolfigol, D. Azarifar and B. Maleki, *Tetrahedron Lett*., 2004, **45**, 2181.
36 (a) A.R. Moosavi-Zare, M.A. Zolfigol, E. Noroozizadeh, M. Tavasoli, V. Khakyzadeh and A. Zare, *New J. Chem*., 2013, **37**, 4089; (b) M.A. Zolfigol, M. Tavasoli, A.R. Moosavi-Zare, P. Moosavi, H.G. Kruger, M. Shiri and V. Khakyzadeh, *RSC Adv*., 2013, **3**, 25681.
37 (a) M.A. Zolfigol, A. Khazaeia, A.R. Moosavi-Zare and A. Zare, *Org. Prep. Proced. Int.* 2010, **42**, 95; (b) A. Khazaei, M.A. Zolfigol, A.R. Moosavi-Zare and A. Zare, *Scien. Iran.* 2010, **17**, 31; (c) M.A. Zolfigol, A. Khazaei, A.R. Moosavi-Zare, A. Zare and V. Khakyzadeh, *Appl. Catal. A: Gen.*, 2011**,** **400**, 1; (d) M.A. Zolfigol, V. Khakyzadeh, A.R. Moosavi-Zare, A. Zare, S.B. Azimi, Z. Asgari and A. Hasaninejad, *C. R. Chimie*, 2012, **15**, 719; (e) M.A. Zolfigol, A. Khazaei, A.R. Moosavi-Zare, A. Zare, H.G. Kruger, Z. Asgari, V. Khakyzadeh and M. Kazem-Rostami, *J. Org. Chem,* 2012, **77**, 3640; (f) A. Zare, A.R. Moosavi-Zare, M. Merajoddin, M.A. Zolfigol, T. Hekmat-Zadeh, A. Hasaninejad, A. Khazaei, M. Mokhlesi, V. Khakyzadeh, F. Derakhshan-Panah, M.H. Beyzavi, E. Rostami, A. Arghoon and R. Roohandeh, *J. Mol. Liq*., 2012**,** **167**, 69; (g) M.A. Zolfigol, A. Khazaei, A.R. Moosavi-Zare, A. Zare, Z. Asgari, V. Khakyzadeh and A. Hasaninejad, *J. Ind. Eng .Chem.* 2013, **19**, 721; (h) A.R. Moosavi-Zare, M.A. Zolfigol, M. Zarei, A. Zare and V. Khakyzadeh, *J. Mol. Liq.*, 2013, **186**, 63; (i) A.R. Moosavi-Zare, M.A. Zolfigol, M. Zarei, A. Zare, V.

View Article Online
DOI: 10.1039/C5RA16289K

Khakyzadeh and A. Hasaninejad, *Appl. Catal. A: Gen.*, 2013, **467**, 61; (j) M.A. Zolfigol, H. Vahedi, S. Azimi and A.R. Moosavi-Zare, *Synlett*, 2013, **24**, 1113; (k) A.R. Moosavi-Zare, M.A. Zolfigol, O. Khaledian, V. Khakyzadeh, M.D. Farahani and H.G. Kruger, *New J. Chem.*, 2014, **38**, 2342; (l) A.R. Moosavi-Zare, M.A. Zolfigol and M. Daraei, *Synlett*, 2014, **25**, 1173; (m) M.A. Zolfigol, A.R. Moosavi-Zare and M. Zarei, *C. R. Chim.*, 2014, **17**, 1264; (n) A.R. Moosavi-Zare, M.A. Zolfigol, V. Khakyzadeh, C. Böttcher, M.H. Beyzavi, A. Zare, A. Hasaninejad and R. Luque, *J. Mater. Chem. A.*, 2014, **2**, 770; (o) M.A. Zolfigol, S. Baghery, A. R. Moosavi-Zare and S.M. Vahdat, *RSC Adv.* 2015, **5**, 32933; (p) M.A. Zolfigol, S. Baghery, A.R. Moosavi-Zare, S.M. Vahdat, H. Alinezhad and M. Norouzi, *RSC Adv.* 2015, **5**, 45027.

38 M.A. Zolfigol, H. Gholami and V. Khakyzadeh, *Principles of organic synthesis with a new approach*, Third Ed., *Bu-Ali Sina University Publishers*, Hamedan, Iran, 2014, p. 26.

39 (a) J.M. Erhardt and J.D. Wuest, *J. Am. Chem. Soc.*, 1980, **102**, 6363; (b) T.J. Atkins, *J. Am. Chem. Soc.*, 1980, **102**, 6364; (c) J.M. Erhardt, E.R. Grover and J.D. Wuest, *J. Am. Chem. Soc*. 1980, **102**, 6365.

40 H. Sheibani and M. Babaei, *Synth. Commun*., 2010, **40**, 257.

41 H. Mecadon, Md. Rumum-Rohman, M. Rajbangshi and B. Myrboh, *Tetrahedron Lett*., 2011, **52**, 2523.

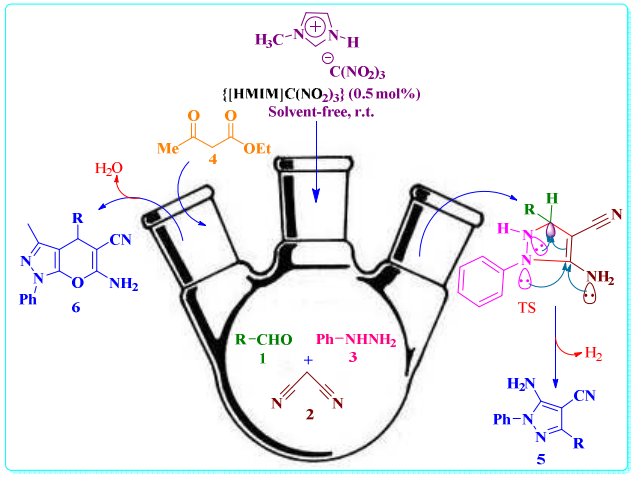
42 M.J. Frisch, *Gaussian 09*, revision A.02, Gaussian, Inc., Wallingford, CT, 2009.

43 (a) K.J. Fukui, *Phys. Chem*., 1970, **74**, 4161; (b) K. Fukui, *Acc. Chem. Res*., 1981, **14**, 363.

44 E.D. Glendening, A.E. Reed, J.A. Carpenter and F. Weinhold, NBO Version 3.1.

Graphical Abstract

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



Mohammad Ali Zolfigol,* Fatemeh Afsharnadery, Saeed Baghery, Sadegh Salehzadeh and Farahnaz Maleki

1-Methyl imidazoliumtrinitromethanide {[HMIM]C(NO$_2$)$_3$} as a nano structure ionic liquid was applied for the synthesis of 5-amino-pyrazole-4-carbonitrile and 1,4-dihydropyrano-[2,3-*c*]-pyrazole derivatives with high yields under mild and green conditions.

Faculty of Chemistry, Bu-Ali Sina University, Hamedan 6517838683, Iran
**Corresponding Author: Fax: +988138257407*
E-mail: zolfi@basu.ac.ir and mzolfigol@yahoo.com (M.A. Zolfigol).
† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/