J IRAN CHEM SOC
DOI 10.1007/s13738-017-1123-z

ORIGINAL PAPER

Application of novel nanostructured dinitropyrazine molten salt catalyst for the synthesis of sulfanylpyridines via anomeric based oxidation

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Received: 10 November 2016 / Accepted: 13 April 2017

Abstract 1,4-Dinitropyrazine-1,4-diium trinitromethanide {[1,4-pyrazine-NO_2][$C(NO_2)_3$]$_2$} as a novel nanostructured molten salt (NMS) catalyzed the synthesis of 2-amino-3,5-dicarbonitrile-6-sulfanylpyridine derivatives via the one-pot three-component condensation reaction between several aromatic aldehyde, malononitrile and benzyl mercaptan at room temperature under solvent-free conditions. The synthesized NMS catalyst was fully characterized by FTIR, ^{1}H NMR, ^{13}CNMR, mass, thermal gravimetric, X-ray diffraction patterns, scanning electron microscopy and transmission electron microscopy analysis. The major advantages of described methodology are mildness, ease of separation, good yields and short reaction times. A rational mechanism was suggested for the final step of the 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines synthesis. We think that the proposed mechanism has potential for entering into the graduate text book in the future.

Keywords Anomeric based oxidation · 2-Amino-3,5-dicarbonitrile-6-sulfanylpyridine · 1,4-Dinitropyrazine-1,4-diium trinitromethanide {[1,4-pyrazine-NO_2][$C(NO_2)_3$]$_2$} · Nanostructured molten salt · Theoretical study

Introduction

The pyridine ring plays a major role in various biological processes, most notably in the oxidation/reduction cofactors such as NADH, NADPH, NADH and NAD^+; the vitamin niacin is required for its biosynthesis [1, 2]. Pyridoxine (vitamin B6) plays a key role as the coenzyme in transaminases enzymatic behavior. Nicotine, a highly toxic alkaloid, is the major active component in tobacco and the most addictive drug known. To the best of our knowledge, heterocyclic derivatives with pyridine moiety display pharmacological activities such as isoniazide as an antituberculosis agent and sulfapyridine one of the sulfonamide antibacterials. Herbicides such as paraquat and fungicides (davicil) have also pyridine moieties in their structures (Fig. 1) [3].

3,5-Dicyanopyridines have been used as intermediates in the synthesis of pyrido[2,3-*d*]pyrimidines as antihistaminic agents [4], pyridothieno- and pyridodithienotriazines endowed with antihistaminic and cytotoxic activity [5], 3,4,6-triazabenz[*d*,*e*]anthracene and 3,4,6,9-tetrazabenz[*d*,*e*]anthracene that are DNA inserting agents [6] and acyclo-3-deazapyrimidine *S*-nucleosides that are active toward HIV [7]. Various kinds of reagent systems such as Et_2NH/C_2H_5OH/r.t. [8], microporous molecular sieves (zeolites)/H_2O [9], CaO NPs/50 °C [10], CuI NPs/C_2H_5OH/H_2O/reflux [11], Et_3N/C_2H_5OH/reflux [12, 13],

Electronic supplementary material The online version of this article (doi:10.1007/s13738-017-1123-z) contains supplementary material, which is available to authorized users.

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Published online: 25 April 2017

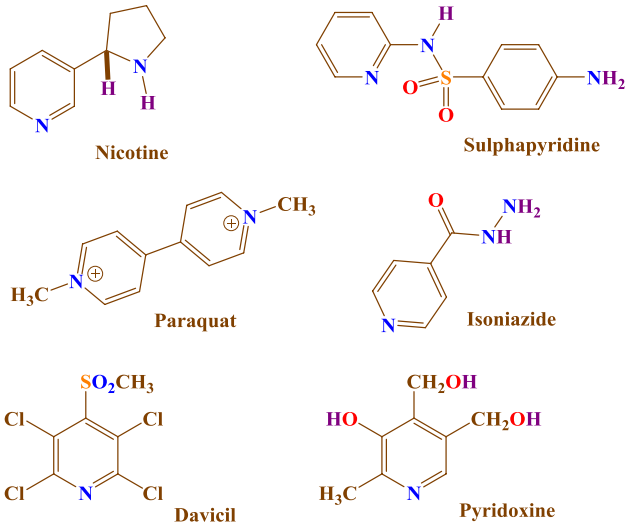


Fig. 1 Some bioactive compounds with pyridine moiety

SnO NPs/C_2H_5OH/reflux [14], borax/C_2H_5OH/reflux [15] and silica nanoparticle [16] have been used to catalyze these reactions.

Molten salts (MSs) and ionic liquids (ILs) are both liquids mainly composed of ions. Mainly, ILs and MSs are defined as those fused salts with a melting point less than 100 °C, with salts with higher melting points mentioned to as molten salts [17]. Combination of various cations and anions allows preparing a wide range of ILs and/or MSs for different purposes. Thus, the terms "designer" and "task-specific" ILs and MSs have been applied for these classes of compounds [18, 19]. Very recently, Atkin et al. [20] have extensively reviewed the chemical and physical properties of nanostructured ILs and MSs. Nowadays, energetic materials have attracted interest [21]; therefore, we decided to design and synthesize a novel, task-specific and bifunctional energetic salt. Thus, 1,4-dinitropyrazine-1,4-diium trinitromethanide{[1,4-pyrazine-NO_2][$C(NO_2)_3$]$_2$} as a unique and safe energetic nanostructured molten salt (NMS) was prepared (Scheme 1).

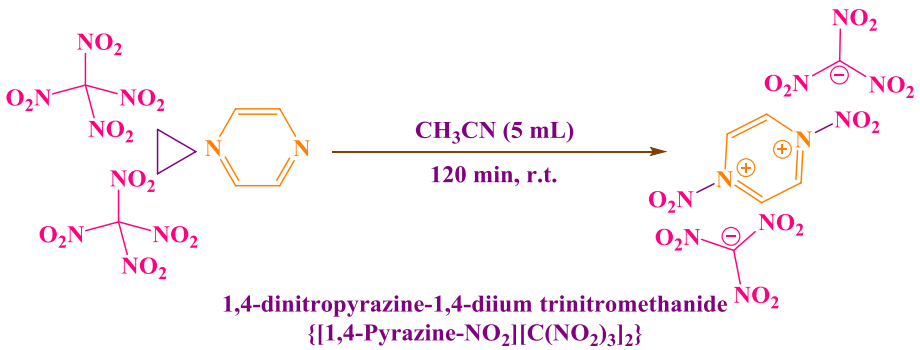
On the other hand, we know that the anomeric effect is a fundamental concept in organic chemistry. It includes an important interaction between the lone pair electrons of heteroatom and the antibonding orbitals of adjacent bonds, which can control reaction mechanism in appropriate systems [22, 23]. In this regard, we have introduced a new term entitled "anomeric based oxidation" (ABO) for unusual hydride releasing from carbon [24–27]. With this aim, we decided to join both of these research areas for the systematic development of ABO concept in organic synthesis.

Experimental

General

The materials were purchased from Merck, Fluka and Sigma-Aldrich companies and were applied without any additional purification. All reactions were checked out by thin-layer chromatography (TLC) on gel F254 plates. (^{1}H NMR 400 MHz and ^{13}C NMR 100 MHz) spectroscopy in pure deuterated DMSO with tetramethylsilane (TMS) as an internal standard. The prepared NMS catalyst was identified by FTIR, ^{1}H NMR, ^{13}CNMR, mass, X-ray diffraction patterns (XRD), scanning electron microscopy (SEM), transmission electron microscopy (TEM) and thermogravimetric (TG) analysis. X-ray diffraction (XRD) patterns of catalyst were achieved on a APD 2000, Ital structure with Cu K_ radiation (k = 0.1542 nm) operating at 50 kV and 20 mA in a 2-h range of 5°–90° with step size 0.01° and time step 1.0 s to assess the crystallinity of the catalyst. Fourier transform-infrared spectra of the samples were recorded on a Perkin-Elmer FTIR spectrometer 17,259 using KBr disks. Thermogravimetric analyses by a Perkin-Elmer TGA were attained on catalyst. The SEM analyses were done with a TESCAN/MIRA with a maximum acceleration voltage of the primary electrons between 10 and 15 kV. Transmission electron microscopy and TEM measurements were examined on a Philips CM10 analyzer.

Scheme 1 Synthesis of 1,4-dinitropyrazine-1,4-diium trinitromethanide {[1,4-pyrazine-NO_2][$C(NO_2)_3$]$_2$}



General procedure for the synthesis of 1,4-dinitropyrazine-1,4-diium trinitromethanide {[1,4-pyrazine-NO_2][$C(NO_2)_3$]$_2$} as nanostructured molten salt catalyst

To a round-bottomed flask (50 mL) containing a solution of pyrazine (3 mmol; 0.240 g) in CH_3CN (5 mL), was dropwise added tetranitromethane (6 mmol; 1.176 g) and stirred over a period of 120 min at room temperature. Then, the solvent was removed through distillation under reduced pressure and the product was dried under vacuum at 80 °C for 120 min. The orange solid product was filtered, washed with diethyl ether for three times and then dried under vacuum conditions. {[1,4-Pyrazine-NO_2][$C(NO_2)_3$]$_2$} was characterized by FTIR, ^{1}H NMR, ^{13}CNMR, mass, thermal gravimetry (TG), X-ray diffraction patterns (XRD), scanning electron microscopy (SEM) and transmission electron microscopy (TEM) analysis (Scheme 2).

1,4-Dinitropyrazine-1,4-diium trinitromethanide {[1,4-Pyrazine-NO_2][$C(NO_2)_3$]$_2$}: orange solid; M.p: 128–130 °C; Yield: 95% (1.346 g); IR (KBr): υ 3481, 3289, 3152, 1768, 1677, 1422, 1153 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ_{ppm} 8.68 (s, 4H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6): δ_{ppm} 122.8, 145.7; MS: $m/z = 472$ $[M]^+$.

General procedure for the synthesis of 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines

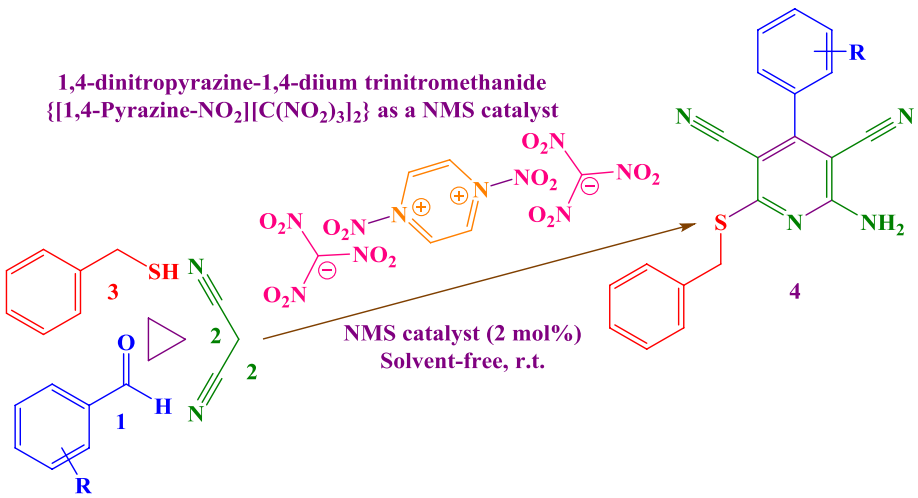
{[1,4-Pyrazine-NO_2][$C(NO_2)_3$]$_2$} (2 mol%; 0.009 g) was added and mixed to a mixture of aldehydes (1 mmol), malononitrile (2.5 mmol; 0.165 g) and benzyl mercaptan (1 mmol; 0.124 g) under solvent-free conditions and at room temperature for the appropriate time (Table 4). After completion of the reaction, which was monitored by TLC (*n*-hexane/ethyl acetate: 5/2), the resulting mixture was washed with water (10 mL) and filtered to separate catalyst from the other materials (the reaction mixture was insoluble in water and the catalyst was soluble in water). The organic layer was removed, and the crude product was purified by recrystallization from ethanol/water (10:1) to yield pure products. More purification can be happened by recrystallization in *n*-hexane. In this investigation, NMS catalyst was recycled and reused for five times without important loss of its catalytic activity (spectral data analysis for compounds refers to supplementary data).

Results and discussion

In continuation of our previous investigation related to the knowledge-based development of task-specific nanostructured ionic liquids (NILs), molten salts (NMSs) and their applications in multi-component reactions (MCRs) [28–33], we wish to report the synthesis of a novel task-specific nanostructured molten salt (NMS), namely 1,4-dinitropyrazine-1,4-diium trinitromethanide {[1,4-pyrazine-NO_2][$C(NO_2)_3$]$_2$} in acetonitrile at room temperature (Scheme 1). The catalytic application of the described NMS in the synthesis of 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines via the one-pot condensation reaction between aromatic aldehydes, malononitrile and benzyl mercaptan at room temperature and solvent-free conditions was examined (Scheme 2).

Characterization of 1,4-dinitropyrazine-1,4-diium trinitromethanide {[1,4-pyrazine-NO_2][$C(NO_2)_3$]$_2$} as nanostructured molten salt catalyst

Characterization of nanostructured molten salt catalyst was confirmed by using analytical approaches including FTIR, ^{1}H NMR, ^{13}C NMR, mass, TG, XRD, SEM and TEM analysis.



Scheme 2 Synthesis of 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines using {[1,4-pyrazine-NO_2][$C(NO_2)_3$]$_2$}

In the FTIR spectrum of {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$}, the absorption bond at 1677 and 1422 cm^{-1} is conformed to vibrational modes of $–NO_2$ bonds. Also, the peak identified at 3152 cm^{-1} linked to C–H stretching group on 1,4-dinitropyrazine-1,4-diium ring. The IR spectrum changes of {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} in comparison with pyrazine and tetranitromethane presented formation of described molten salt catalyst (Fig. 2).

The ^{1}H NMR spectrum of the {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} displays a singlet at 8.68 ppm linked to the aromatic hydrogen's of 1,4-dinitropyrazine-1,4-diium ring. The ^{1}H NMR chemical shift changes of {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} in comparison with pyrazine showed creation of nanostructured molten salt catalyst (Fig. 3).

Appearance of two signals in the ^{13}C NMR is in agreement with the {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} structure. Also the ^{13}C NMR chemical shift changes of {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} in comparison with pyrazine and tetranitromethane clearly displayed formation of nanostructured molten salt catalyst (Fig. 4).

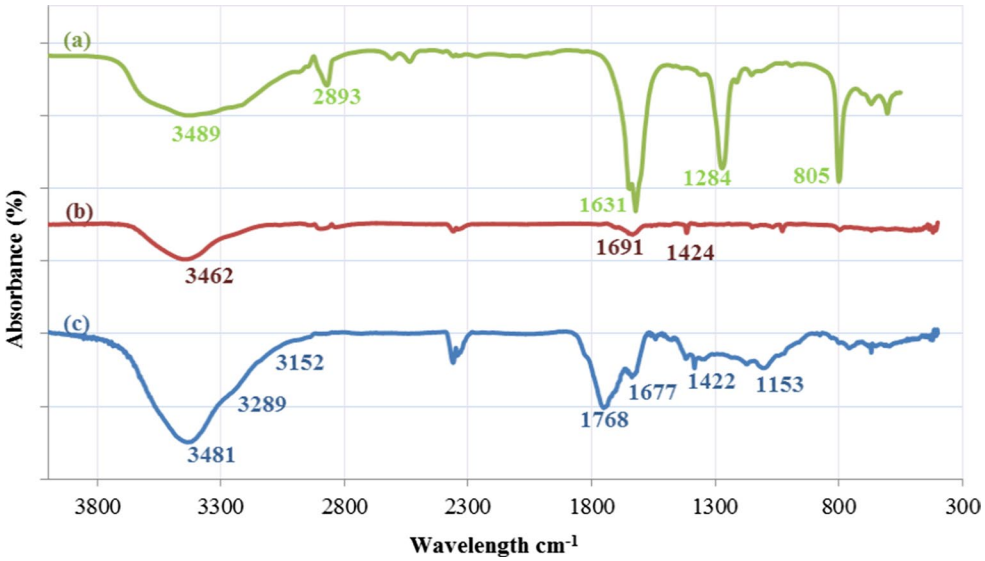


Fig. 2 The FTIR spectrum of tetranitromethane (*a*), pyrazine (*b*), {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} (*c*)

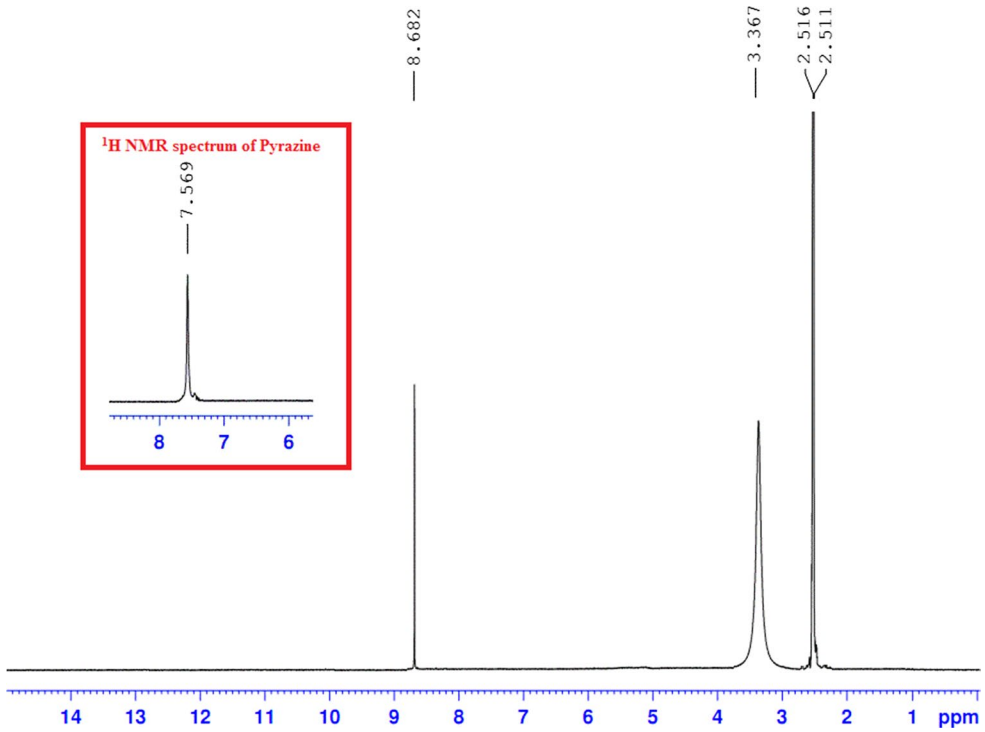


Fig. 3 The ^{1}H NMR spectrum of {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$}

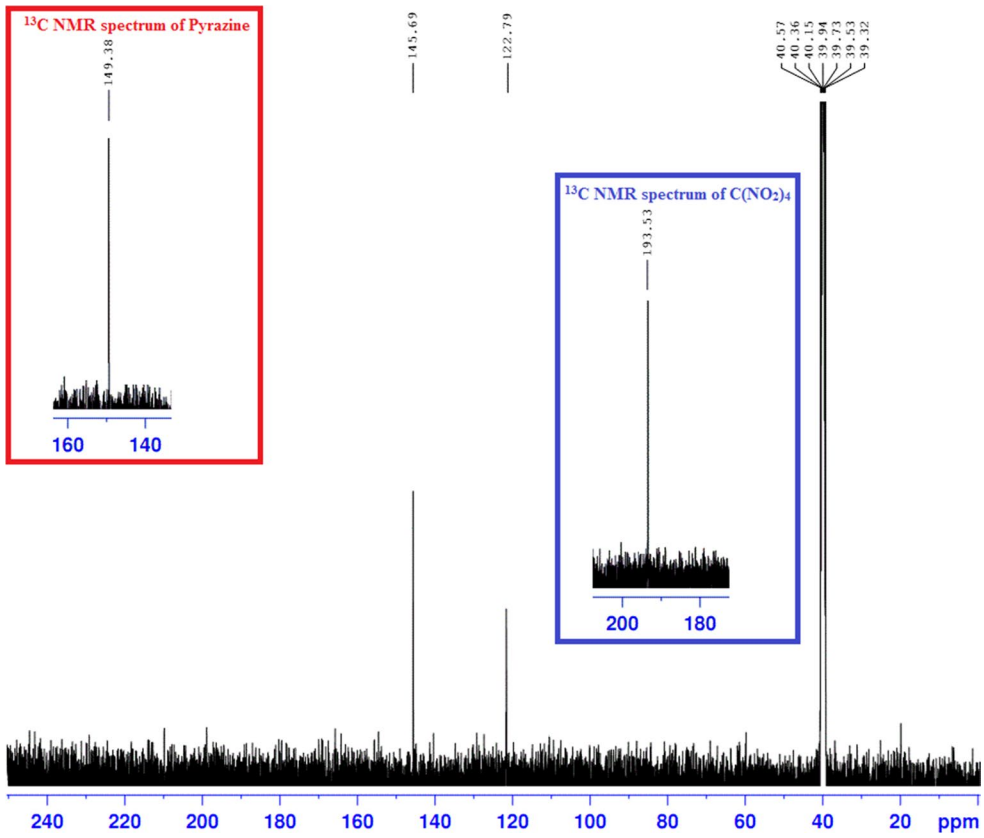


Fig. 4 The ^{13}C NMR spectrum of {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$}

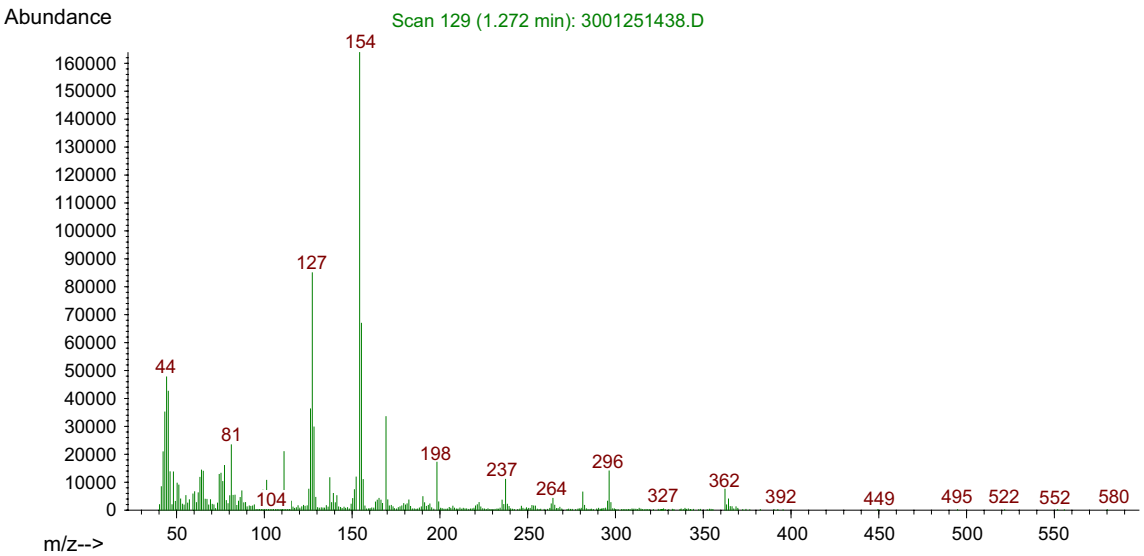


Fig. 5 The mass spectrum of {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$}

The mass spectrum of the {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} is in accordance with the structure of the catalyst. The significant peak of mass spectrum of nanostructured molten salt catalyst is related to trinitromethanide counter ion which is known at 300 m/z and connected peak at 172 m/z is related to 1,4-dinitropyrazine-1,4-diium ring (Fig. 5).

The thermal gravimetric analysis (TGA) curves of {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} display mass loss of organic materials as they decompose upon heating. The

TGA curve of catalyst (Fig. 6) shows an initial weight loss of 25% around 80–110 °C which is owing to residual physisorbed water and organic solvents, which were used in the course of catalyst synthesis. Thermal degradation of the catalyst occurred after 300 °C which reveal the high thermostability of catalyst. The second weight loss of 75% in the range of 110–300 °C was due to the thermal decomposition of the organic residues. The thermal gravimetric analysis of the described NMS catalyst offered significant loss in two steps and decomposed after 300 °C. Ionic chemical bonds afford the catalyst high thermal stability, so it is probable that the catalyst could be applied for high-temperature uses.

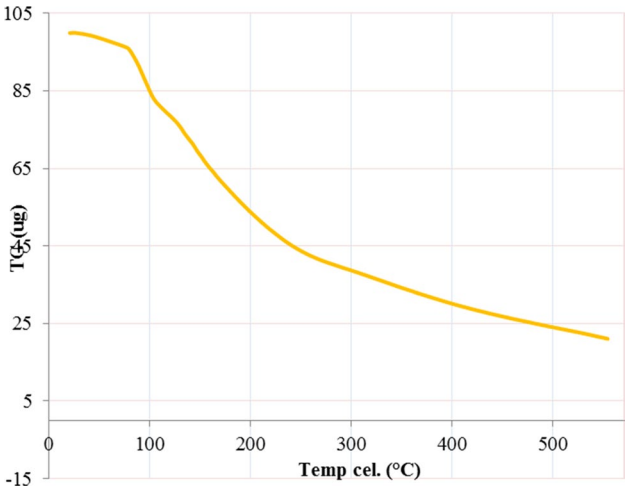


Fig. 6 The thermal gravimetric analysis (TGA) of {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$}

Described NMS catalyst was considered by X-ray diffraction (XRD) pattern (Fig. 7), scanning electron microscopy (SEM) and transmission electron microscopy (TEM) (Fig. 8). In this regard, to approve the structure of {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$}, firstly, its XRD pattern was studied. As shown in Fig. 7, the XRD patterns of NMS catalyst expose peaks at $2\theta \approx 18.30°$, 18.90°, 22.20°, 23.50°, 25.10°, 27.60°, 28.90°, 31.70°, 37.10°, 54.10°, 61.80° and 66.90°, correspondingly, which was confirmed through the described value of scanning electron microscopy (SEM) and transmission electron microscopy (TEM) (Fig. 8). Peak width (FWHM), size and interplanar distance related to XRD pattern of {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} were investigated in the 18.30°–66.90° degree, and the achieved results is summarized in Table 1. The average crystallite size D was studied using the Scherrer formula: $D = K\lambda/(\beta\cos\theta)$. The average size of the NMS catalyst, subsequently, attained from this equation was found to be about 5.88–71.22 nm, which is basically in a good agreement with the scanning electron microscopy and transmission electron microscopy (Fig. 8).

Application of 1,4-dinitropyrazine-1,4-diium trinitromethanide {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} as a nanostructured molten salt catalyst

The synthesis of 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines was attained by the one-pot, three-component condensation of aromatic aldehydes, malononitrile and benzyl mercaptan using {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} under solvent-free conditions at room temperature to give products in high yields (Scheme 2). For optimization of reaction conditions, the reaction

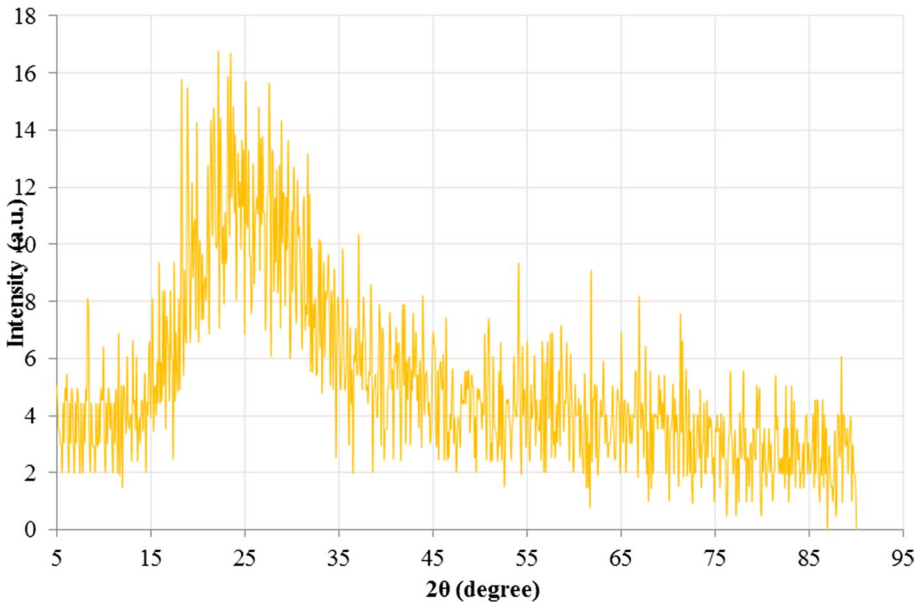


Fig. 7 The XRD pattern of {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$}

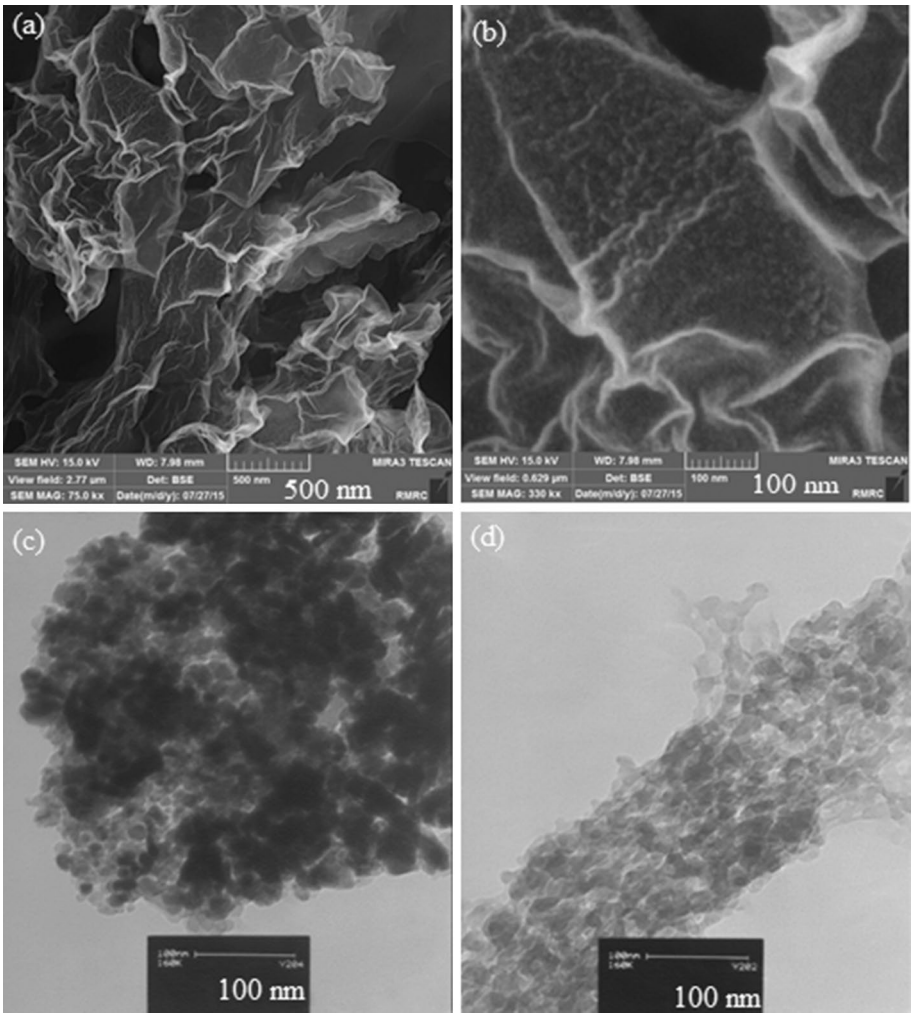


Fig. 8 Scanning electron microscopy (SEM) (**a**, **b**), transmission electron microscopy (TEM) (**c**, **d**) of {[1,4-pyrazine-NO_2][$C(NO_2)_3$]$_2$}

Table 1 The XRD data for the {[1,4-pyrazine-NO_2][$C(NO_2)_3$]$_2$}as a nanostructured molten salt catalyst

Entry	2θ	Peak width (FWHM) (degree)	Size (nm)	Interplanar distance (nm)
1	18.30	0.23	34.99	0.484216
2	18.90	0.13	61.95	0.468977
3	22.20	1.03	7.86	0.399954
4	23.50	1.38	5.88	0.378115
5	25.10	0.65	12.52	0.354362
6	27.60	0.50	16.07	0.322806
7	28.90	0.97	8.46	0.308574
8	31.70	0.87	9.49	0.281927
9	37.10	0.89	9.42	0.242038
10	54.10	0.27	33.04	0.169317
11	61.80	0.13	71.22	0.149939
12	66.90	0.23	41.40	0.139693

between 4-chlorobenaldehyde, malononitrile and benzyl mercaptan was selected as a model reaction for examining the effect of different solvents. As shown in Table 2, the solvent-free condition is the most effective conditions for this reaction. In this condition, the reaction was happened very fast. Although, for this reaction, studying the research in laboratory not in industry, the same results were achieved by carrying out the reaction at room temperature in ethanol for 25 min (yield of 91%) using 2 mol% of NMS catalyst.

Table 2 Solvent effect in the reaction between 4-chlorobenaldehyde, malononitrile and benzyl mercaptan

Solvent	Solvent-free	H_2O	C_2H_5OH	CH_2Cl_2	CH_3CN	CH_3CO_2Et
Reaction time (min)	25	60	25	45	45	60
Yield (%)[a]	91	53	91	81	87	75

Reaction condition: 4-chlorobenaldehyde (1 mmol), malononitrile (2.5 mmol) benzyl mercaptan (1 mmol), NMS catalyst (2 mol%), solvent (2 mL)

[a] Isolated yield

Table 3 Optimization reaction between 4-chlorobenaldehyde, malononitrile and benzyl mercaptan

Entry	Catalyst amount (mol%)	Temperature (°C)	Time (min)	Yield (%)[a]
1	–	r.t.	180	7
2	–	100	180	10
3	0.5	r.t.	60	25
4	0.5	100	60	27
5	1	r.t.	45	57
6	1	100	45	57
7	2	r.t.	25	91
8	2	50	25	91
9	2	75	25	87
10	2	100	25	87
11	5	r.t.	25	91
12	5	100	25	87

Reaction condition: 4-chlorobenaldehyde (1 mmol), malononitrile (2.5 mmol) benzyl mercaptan (1 mmol)

[a] Isolated yield

The scope of this procedure was extended to the synthesis of 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines. The three-component condensation reaction of 4-chlorobenaldehyde, malononitrile and benzyl mercaptan was selected as a model reaction, and the effect of different amounts of catalyst and temperature was studied under solvent-free conditions (Table 3). Table 3 clearly recognizes that in the absence of the catalyst, product was attained in low yield after 3 h (Table 3, entries 1 and 2). The good results were obtained in the presence of 2 mol% of NMS catalyst at 25 °C that affect temperature in terms of reaction time and obtained yield (Table 3, entry 7). Increasing the reaction temperature and catalyst loading did not improve the rate of the reaction (Table 3, entries 8–12).

Subsequently, a series of different 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines were synthesized successfully from different aldehydes bearing electron-withdrawing and electron-donating groups, malononitrile and benzyl mercaptan under solvent-free conditions at room temperature. Electron-withdrawing groups such as 3-nitro and 4-nitro reacted faster than electron-donating groups such as 4-Me and 4-OMe under optimized conditions. The results obviously show that reactions can tolerate a broad range of differently substituted aromatic aldehydes. Also, by using terephthaldehyde as a bifunctional aldehyde, bispyridine product was produced (Table 4, entry 9). A slight excess of the malononitrile was known to be favorable, and hence, the molar ratio of aromatic aldehyde and benzyl mercaptan to malononitrile was investigated at 1:1:2.5.

According to the previously reported process [22–26], an appropriate mechanism for the synthesis of 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines (4) by {[1,4-pyrazine-NO_2][$C(NO_2)_3$]$_2$} as a NMS catalyst was proposed (Scheme 3). Initially, we considered that the reaction happens via a Knoevenagel condensation between activated malononitrile (2) and aromatic aldehyde (1). Then, the consequent Michael-type addition of the second molecule of activated malononitrile (2) to the Knoevenagel adduct (5) causes the synthesis of the intermediate (6). In the other step by thiolate addition to cyanide group of the intermediate (6) and cyclization, dihydropyridine (7) was synthesized and tautomerized to dihydropyridine (8) [8–15]. Finally, dihydropyridine (8) via anomeric-based oxidation was converted to its corresponding 2-amino-3,5-dicarbonitrile-6-sulfanylpyridine (4). Previously reported investigations have proposed an aerobic auto-oxidation of intermediate (8) to its corresponding 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines (4). In contrast to the previously reported mechanistic description for the final step of the above-described organic synthesis, we proposed that this step might be progressed by unusual hydride transfer as well as Cannizzaro reaction (Scheme S1) [34] and H_2 releasing from tricyclic orthoamide (Scheme S2) [35–37]. As mentioned in Introduction part, we have suggested an anomeric-based oxidation (ABO) for the final step in mechanistic pathways in the synthesis of 1,4-dihydropyrano-[2,3-*c*]-pyrazole [24], 2,4,6-triarylpyridine derivatives [25], 2-amino-3-cyanopyridines [26] and 2-substituted benz-(imida, oxa and othia)-zole derivatives [27] (Schemes S3–S6). For approving of aforementioned idea, reaction was happened/done under nitrogen atmosphere and in the absence of any molecular oxygen. It was identified that the reaction proceeded under atmosphere of nitrogen as well as normal reaction condition (under air atmosphere). By considering the above-mentioned evidence, conversion of intermediate (8) to its corresponding 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines

Table 4 Synthesis of 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines using {[1,4-pyrazine-NO_2][$C(NO_2)_3$]$_2$} as a nanostructured molten salt catalyst under solvent-free conditions

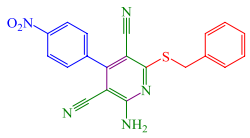
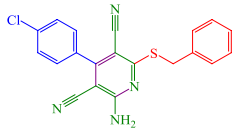
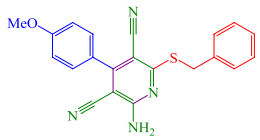
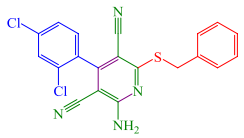
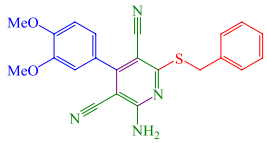
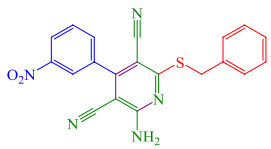
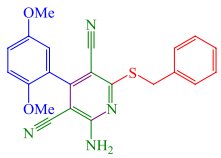
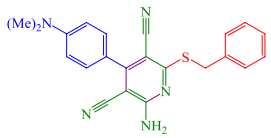
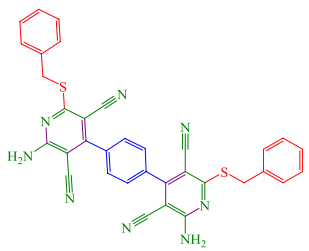
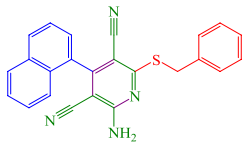
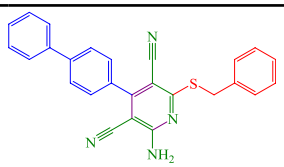
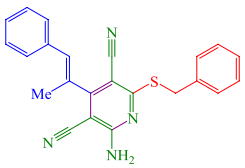
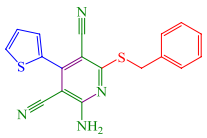
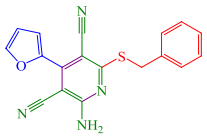
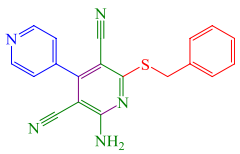
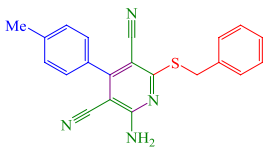
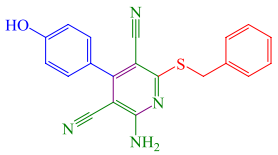
Entry	Product	Time (min)	Yield (%)[a]	M.p (°C) (Lit.) (Refs.) (color)
1		20	93	202–204 (210–212) [15] (red solid)
2		25	91	298–300 [15] (green solid)
3		30	89	249–251 [15] (yellow solid)
4		25	90	242–243 (brown solid)
5		30	89	166–168 (yellow solid)
6		25	91	223–225 (brown solid)
7		30	89	205–207 (214–215) [12] (brown solid)
8		30	89	202–204 (orange solid)
9		35	87	268–270 (cream solid)
10		25	90	197–199 (brown solid)

Table 4 continued

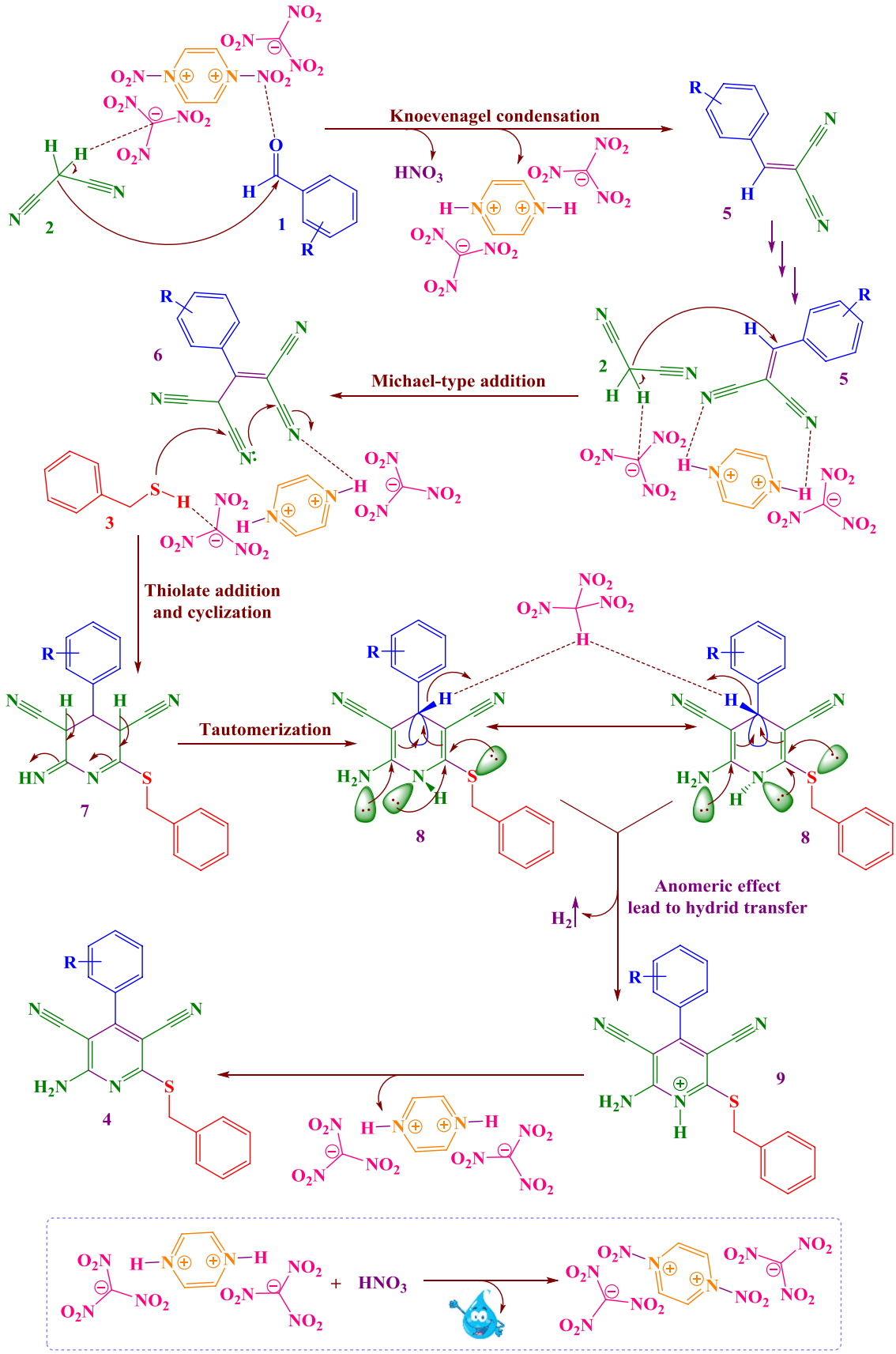
Entry	Product	Time (min)	Yield (%)[a]	M.p (°C) (Lit.) (Refs.) (color)
11		25	90	213–215 (brown solid)
12		35	85	218–220 (brown solid)
13		40	83	208–210 (224–226) [8] (brown solid)
14		40	83	214–216 (brown solid)
15		40	83	191–193 (brown solid)
16		30	89	255–257 [15] (yellow solid)
17		40	83	228–230 (cream solid)

Reaction condition: aldehyde (1 mmol), malononitrile (2.5 mmol) benzyl mercaptan (1 mmol), NMS catalyst (2 mol%)

[a] Isolated yield

(4) might be occurred through uncommon hydride transfer and releasing of molecular hydrogen (H_2). The C–H bond is so weaken via electron donation from the nitrogen lone pairs into the antibonding of C–H (σ^*_{C-H} orbital) which can be broken via reaction with a proton to provide molecular hydrogen. We have entitled this phenomenon "Anomeric Based Oxidation" (ABO). The major reason of ABO is driving force of aromatization which will be supported via stereoelectronic and/or anomeric effect (the experimental and theoretical study refers to supplementary data [38]).

The probability of recycling the {[1,4-pyrazine-NO_2][$C(NO_2)_3$]$_2$}as a NMS catalyst was investigated by the reaction between 4-chlorobenaldehyde, malononitrile and benzyl mercaptan under the optimized conditions. Upon completion of the reaction, the reaction mixture was washed with water and ethyl acetate to separate catalyst from other materials (the product is soluble in hot ethyl acetate and NMS catalyst is soluble in water). The recovered catalyst was dried and reused for consequent runs. The recycled catalyst could be reused fifth times without any additional treatment. There was no observation of any perceptible loss in the catalytic activity. The recycled catalyst was also characterized by FTIR spectrum after its application in the reaction. This spectrum was identical to those of the fresh catalyst. The deactivation of the NMS catalyst is low. The reaction was scaled up to 20 mmol of malononitrile and 10 mmol of 4-chlorobenaldehyde and benzyl mercaptan in the presence of 20 mol% of NMS catalyst at



Scheme 3 The suggested mechanism for the synthesis of 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines using {[1,4-pyrazine-NO_2][$C(NO_2)_3$]$_2$}

room temperature. The yield of the reaction was 91% after 25 min and 83% after the fourth run. The results are summarized in Fig. 9.

In addition to the usage of {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} as a NMS catalyst in the synthesis of 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines, we studied the efficiency of numerous catalysts for confirming ABO proposed mechanism. To optimize the reaction conditions, the reaction between 4-chlorobenaldehyde, malononitrile and benzyl mercaptan under N_2 atmosphere at room temperature was used as a model reaction (Table 5).

To compare the efficacy of {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} as a NMS catalyst with other reported catalysts for the synthesis of 3,5-dicarbonitrile-6-sulfanylpyridines, we have organized the results of these catalysts in Table 6. Table 6 shows that {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} has strangely improved the synthesis of 3,5-dicarbonitrile-6-sulfanylpyridines in different terms (reaction condition, time and yield). The reaction time was shorter, and the yields were higher with our described catalyst.

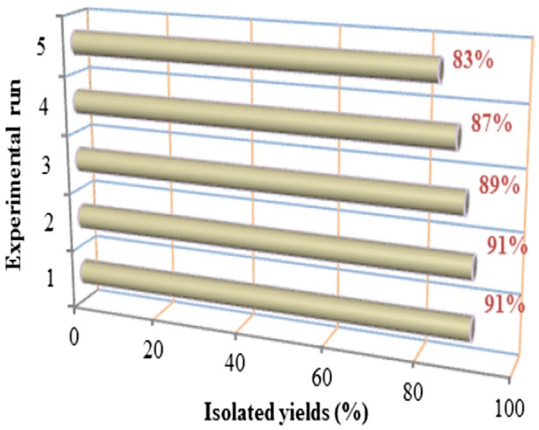


Fig. 9 Reusability studies of {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} as a nanostructured molten salt catalyst for the reaction between 4-chlorobenaldehyde, malononitrile and benzyl mercaptan in 25 min

Conclusion

In summary, a reusable 1,4-dinitropyrazine-1,4-diium trinitromethanide {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} as an energetic task-specific nanostructured molten salt (NMS) was designed and completely characterized by FTIR, ^{1}H NMR, ^{13}CNMR, mass, thermal gravimetric (TG), X-ray diffraction patterns (XRD), scanning electron microscopy (SEM) and transmission electron microscopy (TEM) analysis. Catalytic application of {[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$} was investigated in the synthesis of 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines via the three-component condensation reaction between aromatic aldehyde, malononitrile and benzyl mercaptan under solvent-free conditions at room temperature. Numerous noteworthy advantages of this study are relatively cleaner reaction profile, simplicity of product isolation, low cost, high yield, short reaction time, reusability of the NMS catalyst and agreement with the green chemistry disciplines. An anomeric based oxidation mechanistic process was also proposed for the final step of the 2-amino-3,5-dicarbonitrile-6-sulfanylpyridines synthesis which was supported

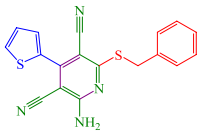
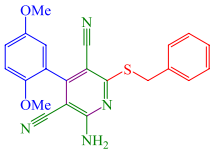
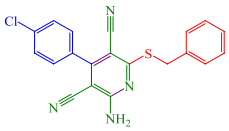
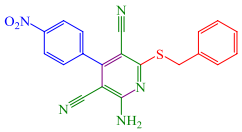
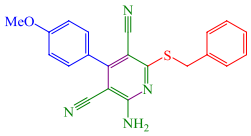
Table 5 The reaction between 4-chlorobenaldehyde, malononitrile and benzyl mercaptan using various catalysts for approving of ABO proposed mechanism

Entry	Catalyst	Catalyst loading (mol%)	Time (min)	Yield (%)[a]
1	{[1,4-pyrazine-NO_2][$C(NO_2)_3]_2$}	2	25	91
2	HBF_4	5	30	83
3	$Zn(HSO_4)_2$	5	45	65
4	Oxone	5	45	57
5	$Ce(HSO_4)_3{\cdot}7H_2O$	5	45	53
6	$Bi(HSO_4)_3$	10	45	50
7	CeO_2	10	45	48
8	PbO_2	10	45	45
9	$[MIMPS]_3PW_{12}O_{40}$	2	30	89
10	Nano-ZnO	2	30	85
11	[MSIM]Cl	2	30	88
12	$H_3PW_{12}O_{40}$	2	30	82

Reaction conditions: 4-chlorobenzaldehyde (1 mmol), malononitrile (2.5 mmol), benzyl mercaptan (1 mmol), under N_2 atmosphere, r.t.

[a] Isolated yield

Table 6 Comparison of the results in the synthesis of 1,4-dihydropyridines catalyzed by [3,6-DOMDA]OTf with those other reported catalysts

Entry	Reaction condition	Time (min)	Yield (%) (Refs.)
			
1	{[1,4-Pyrazine-NO_2][$C(NO_2)_3$]$_2$} (2 mol%), solvent-free, r.t.	40	83 (This work)
2	Diethylamine, ethanol, r.t.	270	77 [8]
			
3	{[1,4-Pyrazine-NO_2][$C(NO_2)_3$]$_2$} (2 mol%), solvent-free, r.t.	30	89 (This work)
4	Et_3N, ethanol, reflux, aldehyde/malononitrile/thiol in a ratio of 1:2:1	150–180	44 [12]
5	Et_3N, ethanol, reflux, aldehyde/malononitrile/thiol in a ratio of 1:1.5:0.5	150–180	88 [13]
			
6	{[1,4-Pyrazine-NO_2][$C(NO_2)_3$]$_2$} (2 mol%), solvent-free, r.t.	25	91 (This work)
7	Borax, ethanol, reflux	60	84 [15]
			
8	{[1,4-Pyrazine-NO_2][$C(NO_2)_3$]$_2$} (2 mol%), solvent-free, r.t.	20	93 (This work)
9	Borax, ethanol, reflux	150	81 [15]
			
10	{[1,4-Pyrazine-NO_2][$C(NO_2)_3$]$_2$} (2 mol%), solvent-free, r.t.	30	89 (This work)
11	Borax, ethanol, reflux	60	84 [15]

by theoretical investigations. Subsequently, we think that the suggested mechanism has potential for entering into the graduate text book in the future.

Acknowledgements We thank Bu-Ali Sina University, Iran National Science Foundation (INSF, Grant No: 95831207) and National Elites Foundation for financial support to our research group.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

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