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ORIGINAL PAPER

1,1′-Butylenebis(3-sulfo-3*H*-imidazol-1-ium) hydrogensulfate: a versatile task-specific ionic liquid catalyst for the synthesis of 4*H*-pyran scaffolds through non-conventional process

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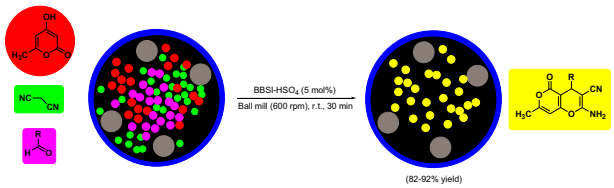
Abstract

In the present study, the catalytic efficiency of 1,1′-butylenebis(3-sulfo-3*H*-imidazol-1-ium) hydrogensulfate (BBSI-HSO_4) as a versatile sulfonic acid-functionalized ionic liquid was demonstrated for the one-pot mechanosynthesis of pyrano[4,3-*b*]-pyrans using planetary ball mill at room temperature under solvent-free conditions. This efficient mechanosynthesis approach to the 4*H*-pyran scaffolds displays a combination of the structure–activity relationship of ionic liquids with ecological benefits of a mechanocatalytic procedure. The ionic liquid was easily recycled and reused several times with no significant loss of its catalytic activity.

Graphical abstract



Keywords Sulfonic acid-functionalized ionic liquid · Ball milling process · 4*H*-Pyran · Structure–activity relationship · Recyclable catalyst · Mild conditions

Introduction

The synthesis and the application of ionic liquids (ILs) are continuing to grow exponentially in all fields of pure and applied chemistry due to their chemical tunability which allows different properties of ILs can be tailored by an appropriate selection of anion/cation components and functional groups [1–3].

Mechanochemistry has been developed as a clean and green approach to chemical transformations which minimize the use of toxic and volatile organic solvents and reduce environmental pollution [4]. The ball milling process plays a significant role in a solvent-free organic synthesis as a solid-state process which fits well with the principles of green chemistry. It can lead to improvements including the reduced amount of catalyst loading, shorter reaction time, and higher yield [5]. Planetary ball mills were broadly utilized

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in laboratories for the synthesis of catalysts [6], heterocycles [7], metal complexes [8], catenanes and rotaxanes [9], the formation of metal–organic frameworks (MOFs) [10], C–C bond formation reactions, protection functional groups, fullerenes, and redox processes [11].

The pyran moiety has received the broad attention of chemists both from the academic organizations and pharmaceutical industries due to a wide array of biological activities, particularly against cancer [12–14]. Based on the in vitro, in vivo, and in silico experiments, pyran derivatives could be heterocycle candidates with potentially exploitable structures and diverse biological properties for the development of new cytotoxic and anticancer agents [15]. Therefore, a variety of catalysts were developed for the synthesis of these versatile compounds as a valuable lead compound [16]; however, some of the reported methods have the drawbacks such as long reaction times, high temperature, moderate yields, expensive reagents, and use of:

- Toxic or volatile organic solvents,
- expensive catalysts,
- require safety measures in handling and storage of the catalysts,
- Lewis acids containing metals and transition metals.

The use of Lewis acids for the synthesis of pharmaceutical products is not desirable because of their toxicity [17]. Moreover, aldehydes bearing the coordinating functional groups, such as methoxy, nitro, or cyano groups, and heterocyclic aldehydes containing nitrogen or sulfur atom, are unsuitable for use as a substrate in a Lewis acid catalyzed because these functional groups could deactivate the acidic sites of Lewis acid catalyst by coordination. Hence, the development of an environment-friendly and sustainable catalytic protocol is a high demand for organic reactions. Furthermore, developing the novel reagents, catalysts and protocols provides a useful and wide range of selectivity.

In pursuit of our studies on the preparation of sulfonic-functionalized acidic ionic liquids and their applications as solvent, catalyst or dual solvent/catalyst in the various organic transformations [18–21], herein, the catalytic efficiency of 1,1′-butylenebis(3-sulfo-3*H*-imidazol-1-ium) hydrogensulfate (BBSI-HSO_4) as a versatile sulfonic acid-functionalized ionic liquid (SAIL) was demonstrated for the synthesis of the 4*H*-pyrans using planetary ball mill under solvent-free conditions. Easy separation and purification of product, a broad substrate-scope, handling and recycling of the SAIL as well as the possibility of continuous operation of the reactor are attractive features for the present protocol. Moreover, the catalytic effect of the functional groups and anions on this multi-component reaction was studied under optimal conditions.

Results and discussion

Synthesis of pyrano[4,3-*b*]pyrans in the presence of BBSI-HSO_4

Initially, the optimum conditions for the reaction were investigated using the condensation reaction of 4-chlorobenzaldehyde (**1a**), 4-hydroxy-6-methyl-2-pyrone (**A**), and malononitrile as a model reaction (Scheme 1).

The model reactants were ground using the planetary ball mill in the absence of catalyst and solvent at room temperature. No 2-amino-4-(4-chlorophenyl)-7-methyl-5-oxo-4*H*,5*H*-pyrano[4,3-*b*]pyran-3-carbonitrile (**2a**) was obtained after 4 h (Table 1, entry 1). Next, BBSI-HSO_4 was added to the model reactants, and the mixture was milled for 4 h at room temperature. Deionized water was added to this mixture and BBSI-HSO_4 was washed from the grinding beaker and separated by simple filtration. The SAIL was recovered through the evaporation of the water and used for the next run. The residue was washed from the grinding beaker with hot ethanol and was crystallized to afford the desired product **2a** in 86% yield (Table 1, entry 2). No significant difference in yield was observed when the reaction time was curtailed to 1 h (Table 1, entry 3), while the yield drop when the reaction time was reduced from 60 to 30 min (Table 1, entry 4). A small drop of the yield for **2a** was observed when the BBSI-HSO_4 loading was decreased to 5 mol% (Table 1, entries 5 and 6) but further decrease of SAIL loading to as

Scheme 1

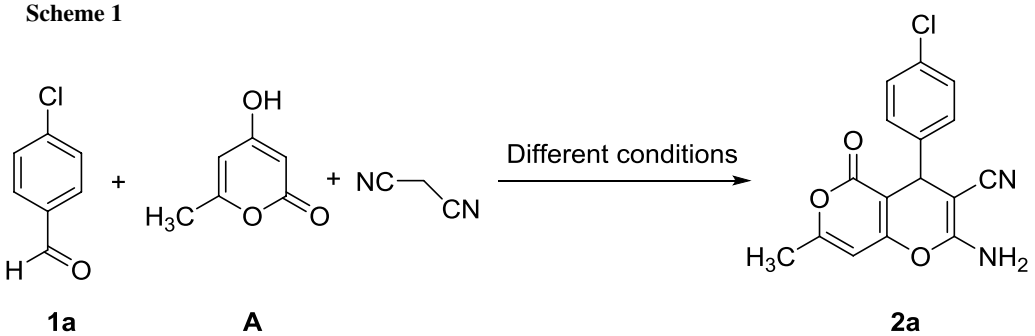


Table 1 Optimization of the synthesis of pyrano[4,3-*b*]-pyrans under a variety of reaction conditions

Entry	Loading BBSI-HSO_4/mol%	Number of ball mill	Speed/rpm	Ball mill diameter/mm	Milling time/min	Yield/%[a]
1	0	4	300	7	240	–[b]
2	20	4	300	7	240	86
3	20	4	300	7	60	84
4	20	4	300	7	30	65
5	10	4	300	7	60	84
6	5	4	300	7	60	82
7	2	4	300	7	60	55
8	5	4	600	7	60	90
9	5	4	600	7	30	92
10	5	4	600	7	20	76
11	5	4	500	7	30	88
12	5	4	400	7	30	67
13	5	4	600	5	30	48
14	5	2	600	7	30	46

Reaction conditions: 4-chlorobenzaldehyde (**1a**, 1.0 mmol), hydroxy-6-methyl-2-pyrone (**A**, 1.0 mmol), malononitrile (1.0 mmol), room temperature

[a]Isolated yield

[b]Monitored by GC–MS

low as 2 mol% decreased yield to 55% (Table 1, entry 7). Then, the influence of technical parameters such as revolution per minute (rpm), size and number of ball mill on performing the model reaction was investigated. As shown in Table 1, the experimental results revealed that rpm has a significant effect on the yield of the desired product, at which point the best yield for **2a** was observed at 600 rpm of the planetary ball mill within 30 min (Table 1, entries 8–12). Also, further decrease in the milling time to 20 min led to a lower yield of **2a** (Table 1, entry 10).

While the other parameters were kept constant, the size and the number of milling balls were changed. As reported in the literature [22], these parameters directly influence the active surface area and the total mass of the milling balls, which are important variables for the energy transfer and increase of internal temperature and pressure. As a consequence, the higher yields for **2a** were observed when the experiments were conducted with a larger size and higher number of mill balls (Table 1, entries 13 and 14).

The scope and generality of the present protocol for the preparation of pyrano[4,3-*b*]pyran derivatives was evaluated through the reaction of various aldehydes **1a–1m** and heteroaldehyde **1n** and 4-hydroxy-6-methyl-2-pyrone (**A**), and malononitrile under optimized reaction conditions based on entry 9 in Table 1 (Scheme 2).

A broad range of pyrano[4,3-*b*]pyrans was prepared in good to excellent yield under optimal reaction conditions (Table 2). Aldehydes bearing electron-withdrawing substituents afforded a slightly higher yield of pyrano[4,3-*b*]-pyran than electron-donating substituents at same position and conditions due to increasing the electrophilicity of carbonyl group. As shown in Table 3, the acid-sensitive aldehydes afforded the desired product in good yield with no decomposition under the optimized reaction conditions (Table 2, entries 9, 10).

The achieved experimental data for the synthesis of pyrano[4,3-*b*]pyrans showed that BBSI-HSO_4 could be an efficient catalyst for the one-pot multicomponent reactions.

Scheme 2

1a-1m **A** **2a-2m**

Table 2 The one-pot multicomponent synthesis of pyrano[4,3-*b*]pyran derivatives in the presence of BBSI-HSO_4 under optimized reaction conditions

Entry	Aldehydes **1a–1m**	Pyrano[4,3-*b*]-pyran	Yield/%[a]	Melting point/°C	
				Found	Reported
1	4-Cl–C_6H_4–	**2a**	92	219–221	228–230 [23]
2	C_6H_5–	**2b**	90	246–248	236 [23]
3	4-CH_3–C_6H_4–	**2c**	88	226–228	218–220 [23]
4	4-$(CH_3)_2CH$–C_6H_4–	**2d**	86	220–222	–
5	4-NO_2–C_6H_4–	**2e**	90	216–218	220–222 [23]
6	3,5-Cl_2–C_6H_3–	**2f**	87	212–214	–
7	4-(CH_3O)–C_6H_4–	**2g**	90	205–207	210–212 [24]
8	2-Cl–C_6H_4–	**2h**	89	258–260	270–272 [25]
9	2-(CH_3O)–C_6H_4–	**2i**	84	242–244	–
10	3,4,5-$(CH_3O)_3$–C_6H_2–	**2j**	82	227–229	235–237 [25]
11	4-Br–C_6H_4–	**2k**	90	219–221	217–219 [24]
12	4-CF_3–C_6H_4–	**2l**	91	217–219	–
13	4-F–C_6H_4–	**2m**	92	220–222	223–225 [26]

Reaction conditions: aldehyde **1a–1 m** (1.0 mmol), 4-hydroxy-6-methyl-2-pyrone (**A**, 1.0 mmol), malononitrile (1.0 mmol), BBSI-HSO_4 (0.05 mmol), four ball mill with diameter 7 mm, revolution rate 600 rpm, room temperature, milling time 30 min

[a]Isolated yield

Table 3 The comparison of the present protocol with other reported strategies for the synthesis of 2-amino-4-phenyl-7-methyl-5-oxo-4*H*,5*H*-pyrano[4,3-*b*]pyran-3-carbonitrile

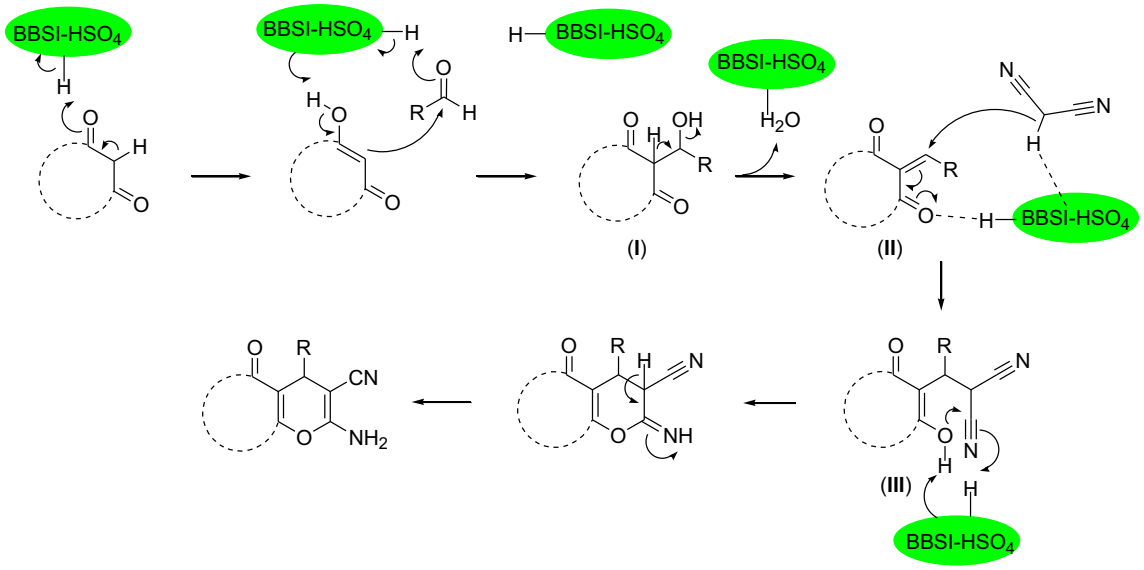
Entry	Catalyst	Calayst loading/mol%	Conditions	Time/min	Yield/%	References
1	Succinimide-*N*-sulfonic acid	10	Neat, 60 °C (Solar energy)	35	94	[23]
2	[BBMIm][HSO_4]	120.5	Neat, 60 °C	35	94	[24]
3	Urea	10	EtOH:H_2O (1:1 v/v), r.t.	420	81	[30]
4	TMGT	1.0	100 °C	60	77	[31]
5	Porcine pancreas lipase	120 U	*i*-Propanol, 60 °C	600	89	[32]
6	[BMIM][BF_4]	664	80 °C	180	85	[26]
7	Piperidine	1-2 drops per 1.0 mmol benzaldehyde	MeOH, reflux	60	79	[33]
8	–	–	H_2O, 80 °C	630	65	[34]
9	Thiurea dioxide	10	H_2O, 80 °C	40	92	[35]
10	4-(Succinimido)-1-butanesulfonic acid	4.2	Neat, 60 °C	60	88	[36]
11	KF-Al_2O_3	100 mg per 2.0 mmol 4-chlorobenzaldehyde	EtOH, reflux	480[a]	76	[37]
12	BBSI-HSO_4	5	Ball milling, r.t.	30	89	This work

[a]2-Amino-4-(4-chlorophenyl)-7-methyl-5-oxo-4*H*,5*H*-pyrano[4,3-*b*]pyran-3-carbonitrile

Based on the theoretical and experimental reports in the literature [27], a mechanism was postulated and illustrated in Scheme 3. The SAIL simultaneously activates aldehyde and 1,3-diketone to initiate the process through the increased electrophilicity of the aldehyde and the enhanced hydrogen bond network, respectively. A nucleophilic attack from 1,3-diketone to activated aldehyde gives intermediate **I**. Dehydration of the intermediate **I** could be promoted in the presence of the SAIL liquid as an efficient dehydrating agent [28, 29], and Knoevenagel intermediate **II** is produced. In the next step, the knoevenagel intermediate **II** acts as a Michael acceptor in the reaction with the activated malononitrile by hydrogen bond network of BBSI-HSO_4 which produces the intermediate **III**. Then, an intramolecular nucleophilic attack from the oxygen atom to nitrile group followed by tautomerization will give the desired product.

A comparison is made between the current protocol with some reported methods in the literature. For example, **2e** was obtained in 83% yield in the presence of 10 mol% urea in aqueous ethanol at room temperature after 7 h [30], whereas

Scheme 3



the same product was offered in 90% yield at room temperature within 30 min in the presence of 5 mol% BBSI-HSO_4 under solvent-free conditions by the present method.

The **2a** was obtained in 77% yield in the presence of 1 mol% of 1,1,3,3-*N*,*N*,*N*′,*N*′-tetramethylguanidinium trifluoroacetate (TMGT) at 100 °C within 1 h [31]. The same product was isolated in 92% yield through the current method.

Also, the product **2a** was obtained in 89.2% yield within 10 h in the presence of 120 unit of porcine pancreas lipase at room temperature [32], whereas the same reaction gave a 90% yield for **2a** after 30 min of stirring at room temperature in the presence of 5 mol% BBSI-HSO_4 under solvent-free conditions. In addition, in entries 2 and 6 use of a considerable amount of catalyst is unavoidable.

The commercially available catalysts such as thiourea dioxide (formamidinesulfinic acid) and piperidine are self-heating and highly flammable and toxic, respectively; therefore, it requires safe handling and storage (Table 3, entries 7 and 9).

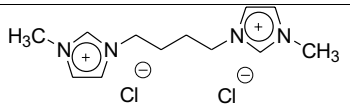
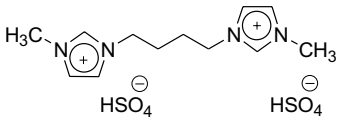
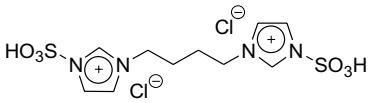
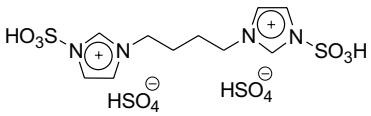
The feasibility of the present method on gram scaled experiment with 4-chlorobenzaldehyde (1.40 g, 10 mmol), malononitrile (0.66 g, 10 mmol), and 4-hydroxy-6-methyl-2-pyrone (1.26 g, 10 mmol) using 5 mol% BBSI-HSO_4 at room temperature under optimized reaction conditions which afforded the desired product, 2-amino-4-(4-chlorophenyl)-7-methyl-5-oxo-4*H*,5*H*-pyrano[4,3-*b*]pyran-3-carbonitrile in 81% isolated yield within 30 min, almost similarly in all respects with mmol scale entry. Therefore, the efficiency of the present protocol for large-scale production was demonstrated.

It is well known that the physical and chemical properties, effect, or catalytic activity associated with ionic liquids are related to the chemical structure of the cations and anions and their interaction with reactants, determine its catalytic efficiency. The chemists often change the chemical structure of catalysts to insert new functional groups and test the modifications for their catalytic efficiency in the model reaction under identical conditions [38]. This process can be one of attempting to understand and reveal how properties relevant to catalytic activity of ionic liquid are encoded within and determined by the chemical structure cation and anion. This can be particularly the case in the area of catalyst design, where ILs with desired physical and chemical properties and catalytic activities are sought. This allows modification of the catalytic effect or the potency of an ionic liquid by changing its functional groups.

Herein, we start to study on the determination of the functional group responsible for inducing a catalytic efficiency in this one-pot multi-component reaction. The catalytic efficiency of di-cationic ionic liquids including (BBMI) cation and (BBSI) along with nonacidic (Cl^-) and acidic (HSO_4^-) counter anion was compared under aforementioned optimized conditions (Table 4). The ionic liquids were prepared according to the literature [21, 24].

The initial results revealed that the catalytic efficiency of these SAILs is influenced by the functional groups on the cationic moiety and nature anion following the order: BBSI-HSO_4 > BBSI-Cl > BBMI-HSO_4 > BBMI-Cl. The best result was obtained with the BBSI-HSO_4 while much reduction of the catalytic effect was observed with BBMI-Cl. It seems that SAILs containing sulfonic acid moiety along with acidic anion are more efficient than that without acid groups and with a non-acidic anion.

Table 4 Comparison of the result obtained for the synthesis of **2a** in the presence of some sulfonic-functionalized ionic liquid containing a dicationic nucleus with four-carbon spacer

Entry	Ionic liquid	Abbreviation	Yield /%[a]
1		BBMI-Cl	58
2		BBMI-HSO_4	76
3		BBSI-Cl	86
4		BBSI-HSO_4	92

Reaction conditions: 4-chlorobenzaldehyde **1a** (1.0 mmol), 4-hydroxy-6-methyl-2-pyrone (**A**, 1.0 mmol), malononitrile (1.0 mmol), ionic liquid (0.05 mmol), four ball mill with diameter 7 mm, revolution rate 600 rpm, room temperature, milling time 30 min, solvent-free conditions

[a]Isolated yield

Table 4 displays an initial theme viz. sulfonic acid functionalized ionic liquids bearing counter anion HSO_4^- which is a most efficient catalyst to promote this one-pot multicomponent reaction under solvent-free conditions. More studies are conducting in our group to develop principals of the role sulfonic acid functional group and nature anion in the catalytic activity of SAILs.

Reusability of BBSI-HSO_4

Two routes were investigated to check the reusability of BBSI-HSO_4 under optimized reaction conditions. In the first route, the desired products were readily extracted using hot ethyl acetate, and the remained SAIL was concentrated under reduced pressure. Then, the reaction flask was recharged with new model reactants for another run. The **2a** was obtained in an average 92–90% yield for three subsequent runs in the presence of BBSI-HSO_4, respectively. Furthermore, the chemical structure of BBSI-HSO_4 showed no significant change under the present workup.

In the second route, the ionic liquid was separated by washing with deionized water after completion of the reaction followed by evaporation of water from an aqueous solution containing BBSI-HSO_4. The recovered ionic liquid was successfully reused for the subsequent runs without significant loss of catalytic activity. Therefore, the isolation of the product or the separation of ionic liquid was efficient for the recovering of BBSI-HSO_4 after reactions.

Conclusion

In summary, the catalytic efficiency of BBSI-HSO_4 was demonstrated for a one-pot multicomponent reaction under mild conditions. The structure–activity relationship (SAR) of the binuclear sulfonic-functionalized acid was studied in comparison with some previously reported sulfonic-functionalized ILs which proved the superiority of binuclear ionic liquids containing sulfonic-functionalized imidazolium moiety with an acidic counter anion. The current protocol has the advantages such as simple experimental and sustainable procedure, high yield of the desired products within short reaction times, a wide substrate-scope, and recyclable sulfonic acid-functionalized ionic liquid. The application of BBSI-HSO_4 in the one-pot multicomponent reactions has highlighted the importance of binuclear sulfonic acid-functionalized ionic liquids as an efficient and recyclable catalyst in organic chemistry, and we hope that our work will encourage further research in this area with promising results for future applications of BBSI-HSO_4.

Experimental

Unless specified, all chemicals were of analytical grade and purchased from Merck, Aldrich, and Fluka Chemical Companies and used without further purification. Products were characterized by their physical constant and IR, NMR, and elemental analysis. The purity determination of the substrates and reaction monitoring was accompanied by TLC

using silica gel SIL G/UV 254 plates. The FT-IR spectra were recorded on a Perkin Elmer 781 Spectrophotometer in the range of 4000–400 cm^{-1}. In all the cases, the ^1H and ^{13}C NMR spectra were recorded with Bruker Avance 400 MHz instruments. All chemical shifts are quoted in parts per million (ppm) relative to TMS using deuterated solvent. Microanalyses were performed on a Perkin-Elmer 240-B microanalyzer. Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes. The mass spectra of the products were recorded using an Agilent 6560 iFunnel Q-TOF LC–MS instrument. Ball milling was performed in a Retsch PM100 planetary ball mill using a 25 cm^3 stainless steel chamber and two or four stainless steel balls (diameter: 5 or 7 mm) with 300–600 revolution per minute (rpm).

Typical procedure for the synthesis of pyran-annulated derivatives in the presence of BBSI-HSO_4

The aldehyde (1.0 mmol), malononitrile (1.0 mmol), hydroxy-6-methyl-2-pyrone (**A**, 1.0 mmol), and BBSI-HSO_4 (5 mol%) were ground at 600 rpm using the planetary ball mill at room temperature for 30 min. The progress of the reaction was monitored by TLC. After completion of the reaction, the product was extracted by hot ethyl acetate, which after evaporation of solvent provided a solid crude product. The pure product was obtained by recrystallization from ethanol without tedious column chromatographic purification. The structure of each purified pyran annulated derivatives was confirmed by melting point and spectral studies including FT-IR, ^1H NMR, ^{13}C NMR, MS, and elemental analysis. All the known compounds had physical and spectroscopic data identical to the literature data.

2-Amino-4-(4-isopropylphenyl)-7-methyl-5-oxo-4*H*,5*H*-pyrano[4,3-*b*]pyran-3-carbonitrile (2d, $C_{19}H_{18}N_2O_3$) M.p.: 220–222 °C; FT-IR (KBr): $\bar{\nu}$ = 3365, 3300, 2200, 1715, 1670, 1640, 1615, 1375, 1265 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 7.20–7.18 (m, 4H), 7.10 (d, J = 8.8 Hz, 2H), 6.28 (s, 1H), 4.25 (s, 1H), 2.89–2.82 (m, 1H), 2.21 (s, 3H), 1.20 (s, 3H), 1.18 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.1, 161.7 (C=O), 158.5, 158.4 (C–NH_2), 147.3, 141.3, 127.7, 126.7, 119.8 (C≡N), 101.2, 98.2, 58.3, 36.1 (CH), 33.3 (CH_3–CH–CH_3), 24.2, 24.2, 19.6 ppm; MS: m/z = 323.14 ($[M+H]^+$).

2-Amino-4-(3,5-dichlorophenyl)-7-methyl-5-oxo-4*H*,5*H*-pyrano[4,3-*b*]pyran-3-carbonitrile (2f, $C_{16}H_{10}Cl_2N_2O_3$) Mp.: 212–214 °C; FT-IR (KBr): $\bar{\nu}$ = 3404, 3330, 2194, 1708, 1676, 1645, 1615, 1382, 1262 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 7.46 (t, J = 1.8 Hz, 1H), 7.20–7.18 (m, 2H), 6.98 (s, 2H), 6.30 (s, 1H), 4.46 (s, 1H), 2.28 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.1, 162.0 (C=O), 160.3, 158.7 (C–NH_2), 145.7, 134.6 (C–Cl), 127.4, 122.5, 117.3 (C≡N), 104.0, 98.4, 56.3, 39.5 (CH), 19.6 ppm; MS: m/z = 349.01 ($[M+H]^+$).

2-Amino-4-(2-methoxyphenyl)-7-methyl-5-oxo-4*H*,5*H*-pyrano[4,3-*b*]pyran-3-carbonitrile (2i, $C_{17}H_{14}N_2O_4$) Mp.: 242–244 °C; FT-IR (KBr): $\bar{\nu}$ = 3385, 3295, 2195, 1710, 1676, 1640, 1605, 1380, 1260 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 7.20–7.18 (m, 1H), 7.05–6.98 (m, 2H), 6.92–6.87 (m, 3H), 4.70 (s, 1H), 3.68 (s, 3H), 2.30 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.7, 162.0 (C=O), 158.8, 158.5 (C–NH_2), 155.7, 132.6, 130.6, 128.4, 120.5, 118.3 (C≡N), 112.0, 102.9, 98.4, 56.3 (O–CH_3), 55.7, 35.5 (CH), 19.7 ppm; MS: m/z = 311.10 ($[M+H]^+$).

2-Amino-4-[4-(trifluoromethyl)phenyl]-7-methyl-5-oxo-4*H*,5*H*-pyrano[4,3-*b*]pyran-3-carbonitrile (2l, $C_{17}H_{11}F_3N_2O_3$) Mp.: 217–219 °C; FT-IR (KBr): $\bar{\nu}$ = 3395, 3325, 2190, 1685, 1655, 1370, 1325, 1120 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 7.70 (d, J = 8.4 Hz, 2H), 7.51 (s, 2H), 7.46 (d, J = 8.4 Hz, 2H), 6.27 (s, 1H), 4.58 (s, 1H), 2.91 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.8, 162.4 (C=O), 159.0, 157.9 (C–NH_2), 143.8, 134.6 (q, $^2J_{C\text{-}F}$ = 28 Hz), 129.9, 125.6 (q, $^1J_{C\text{-}F}$ = 273 Hz), 125.1 (q, $^3J_{C\text{-}F}$ = 4 Hz), 118.3 (C≡N), 105.2, 98.4, 55.8, 39.5 (CH), 19.8 ppm; MS: m/z = 349.08 ($[M+H]^+$).

2-Amino-4-(4-fluorophenyl)-7-methyl-5-oxo-4*H*,5*H*-pyrano[4,3-*b*]-pyran-3-carbonitrile (2m, $C_{16}H_{11}FN_2O_3$) M.p.: 220–222 °C; FT-IR (KBr): $\bar{\nu}$ = 3398, 3322, 1688, 1648, 1368, 1329, 1117 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 7.25–7.12 (m, 6H), 6.28 (s, 1H), 4.31 (s, 1H), 2.22 (s, 3H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.4, 162.0 (C=O), 161.7 (d, $^1J_{C\text{-}F}$ = 267 Hz), 158.6, 158.5 (C–NH_2), 140.2, 129.9 (d, $^3J_{C\text{-}F}$ = 7 Hz), 119.8 (C≡N), 115.6, 115.4 (d, $^2J_{C\text{-}F}$ = 26 Hz), 100.9, 98.5, 58.2, 36.1 (CH), 19.7 ppm; MS: m/z = 299.08 ($[M+H]^+$).

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References

1. Amarasekara AS (2016) Chem Rev 116:6133
2. Sun X, Luo H, Dai S (2012) Chem Rev 112:2100
3. Koda-Földes R (2014) Molecules 19:8840
4. Do JL, Friščič T (2017) ACS Cent Sci 3:13
5. Martins MAP, Frizzo CP, Moreira DN, Buriol L, Machado P (2009) Chem Rev 109:4140

6. Kubias B, Fait MJG, Schlogl R (2008) In: Ertl G, Knozinger H, Schuth F, Weitkamp J (eds) Handbook of heterogeneous catalysis, 2nd edn. Wiley-VCH, Weinheim, p 571
7. M'hamed MO (2015) Synth Commun 45:2511
8. Garay AL, Pichon A, James SL (2007) Chem Soc Rev 36:846
9. Hsu CC, Chen NC, Lai CC, Liu YH, Peng SM, Chiu SH (2008) Angew Chem Int Ed 47:7475
10. Wilke M, Klimakow M, Rademann K, Emmerling F (2016) CrystEngComm 18:1096
11. Stolle A, Szuppa T, Leonhardt SES, Ondruschka B (2011) Chem Soc Rev 40:2317
12. Magedov IV, Manpadi M, Ogasawara MA, Dhawan AS, Rogelj S, Van Slambrouck S, Steelant MFA, Evdokimov NM, Uglinskii PY, Elias EM, Knee EJ, Tongwa P, Antipin MY, Kornienko A (2008) J Med Chem 51:2561
13. Saher L, Makhloufi-Chebli M, Dermeche L, Dermeche S, Boutemeur-Khedis B, Rabia C, Hamdi M, Silva AMS (2018) Tetrahedron 74:872
14. Banerjee B (2017) Ultrason Sonochem 35:15
15. Kumar D, Sharma P, Singh H, Nepali K, Gupta GK, Jaina SK, Ntie-Kang F (2017) RSC Adv 7:36977
16. Brimble MA, Gibson JS, Sperry J (2008) Pyrans and their benzo derivatives: synthesis. Comprehensive heterocyclic chemistry III, vol 7. Elsevier, Amsterdam, p 419
17. Rao RN, Talluri MVNK (2007) J Pharm Biomed 43:1
18. Khaligh NG (2016) Polycycl Aromat Compd 36:284
19. Khaligh NG (2015) Res Chem Intermed 41:5411
20. Khaligh NG (2014) Chin J Catal 35:1497
21. Khaligh NG, Mihankhah T, Johan MR, Ching JJ (2018) J Mol Liq 259:260
22. Schneider F, Stolle A, Ondruschka B, Hopf H (2009) Org Process Res Dev 13:44
23. Khaligh NG, Abd Hamid SB, Titinchi SJJ (2017) Polycycl Aromat Compd 37:31
24. Khaligh NG (2014) Monatsh Chem 145:1643
25. Abbaspour-Gilandeh E, Azimi SC, Rad-Moghadam K, Barkchai AM (2013) Iran J Catal 3:91
26. Fan X, Feng D, Qu Y, Zhang X, Wang J, Loiseau PM, Andrei G, Snoeck R, De Clercq E (2010) Bioorg Med Chem Lett 20:809
27. Dalessandro EV, Collin HP, Guimaraes LGL, Valle MS, Pliego JR Jr (2017) J Phys Chem B 121:5300
28. Flores AC, Flores EA, Hernández E, Castro LV, García A, Alvarez F, Vázquez FS (2014) J Mol Liq 196:249
29. Krannich M, Heym F, Jess A (2016) J Chem Eng Data 61:1162
30. Brahmachari G, Banerjee B (2014) ACS Sustain Chem Eng 2:411
31. Shaabani A, Samadi S, Badri Z, Rahmati A (2005) Catal Lett 104:39
32. Chen X, Zhang W, Yang F, Guo C, Zhao Z, Ji D, Zhou F, Wang Z, Zhao R, Wang L (2017) Green Chem Lett Rev 10:54
33. Stoyanov EV, Ivanov IC, Heber D (2000) Molecules 5:19
34. Shaabani A, Samadi S, Rahmati A (2007) Synth Commun 37:491
35. Ghashang M, Mansoor SS, Aswin K (2014) Chin J Catal 35:127
36. Khaligh NG (2015) Chin Chem Lett 26:26
37. Wang XS, Zhou JX, Zeng ZS, Li YL, Shi DQ, Tu SJ (2006) Arkivoc 11:107
38. Matuszek K, Chrobok A, Coleman F, Seddon KR, Swadźba-Kwaśny M (2014) Green Chem 16:3463