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Article

Ionic-liquid-catalyzed green synthesis of coumarin derivatives under solvent-free conditions

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ABSTRACT

Brönsted acidic ionic liquids, namely 2-pyrrolidonium hydrogen sulfate, *N*-methyl-2-pyrrolidonium hydrogen sulfate, *N*-methyl-2-pyrrolidonium dihydrogen phosphate, (4-sulfobutyl)tris(4-sulfophenyl)phosphonium hydrogen sulfate, and triphenyl(propyl-3-sulfonyl)phosphonium toluenesulfonate, catalyzed efficient Pechmann condensation of phloroglucinol with β-keto ethyl/methyl esters. 5,7-Dihydroxy-4-methylcoumarin and 5,7-dihydroxy-4-phenylcoumarin were prepared in good to excellent yields under mild, ambient, and solvent-free conditions. Pyrano[2,3-*h*]coumarins were then prepared by one-pot three-component reactions of 5,7-dihydroxy-4-subsituted coumarin, malononitrile, and aldehydes in the presence of catalytic amounts of Brönsted basic ionic liquids, namely 2-hydroxyethylammonium formate, 3-hydroxypropanaminium acetate, 1-butyl-3-methylimidazolium hydroxide, pyrrolidinium formate, and pyrrolidinium acetate, under thermal solvent-free conditions. The catalysts are environmentally benign and can be easily prepared, stored, and recovered without significant loss of activity.

1. Introduction

Ionic liquids (ILs) have generally been used as alternative reaction solvents, but are now being used as catalysts for various reactions [1]. The use of ILs as green solvents and catalysts is now attracting much attention in green chemistry [1,2]. ILs are of interest to researchers from a wide variety of fields, especially organic synthesis, and some ILs are used in the chemical and pharmaceutical industries [1]. ILs are classified as acidic ILs, basic ILs, metal-containing ILs, chiral ILs, guanidinium ILs, and ILs containing-OH groups [3].

In our continuing research on new synthetic methods in organic synthesis using ILs as green catalysts [4–7], we have developed the synthesis of 5,7-dihydroxy-4-methylcoumarin and 5,7-dihydroxy-4-phenylcoumarin via two-component condensation of phloroglucinol and β-keto ethyl/methyl esters (Scheme 1), using five Brönsted acidic ILs (BAILs), i.e., 2-pyrrolidonium hydrogen sulfate ([Hnmp][HSO_4]), *N*-methyl-2-pyrrolidonium hydrogen sulfate ([NMP][HSO_4]), *N*-methyl-2-pyrrolidonium dihydrogen phosphate ([NMP][H_2PO_4]), (4-sulfobutyl)tris(4-sulfophenyl)phosphonium hydrogen sulfate, and triphenyl(propyl-3-sulfonyl)phosphonium toluenesulfonate (Fig. 1), as catalysts under mild, ambient, and solvent-free conditions (Step 1).

In the second step, we used these products to synthesize pyrano[2,3-*h*]coumarin derivatives. The three-component reaction of 5,7-dihydroxy-4-substituted coumarins, malononitrile, and aromatic aldehydes (Scheme 2), using five basic ILs, i.e., 2-hydroxyethylammonium formate (2-HEAF), 3-hydroxypropanaminium acetate (3-HPAA), 1-butyl-3-methylimidazolium hydroxide ([Bmim]OH), pyrrolidinium formate ([Pyrr][HCOO]), and pyrrolidinium acetate ([Pyrr][CH_3COO]) (Fig. 2), as reusable catalysts, afforded the pyrano[2,3-*h*]coumarin derivatives under thermal solvent-free conditions.

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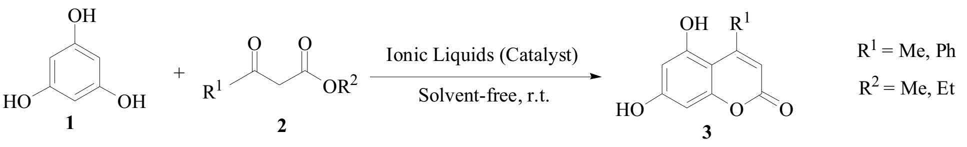


Ionic Liquids = [Hnmp][HSO_4], [NMP][HSO_4], [NMP][H_2PO_4], (4-sulfobutyl)tris(4-sulfophenyl)phosphonium hydrogensulfate and triphenyl(propyl-3-sulphonyl)phosphonium toluenesulfonate

Scheme 1. Synthesis of 5,7-dihydroxy-4-substituted coumarin derivatives.

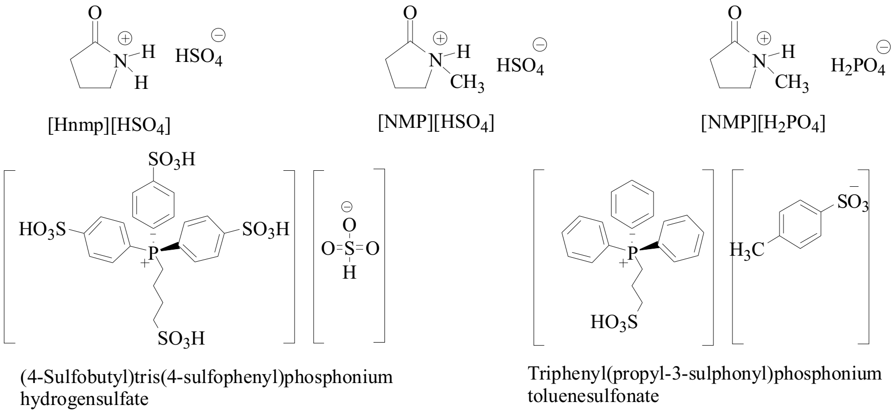


Fig. 1. Structure of [Hnmp][HSO_4], [NMP][HSO_4], [NMP][H_2PO_4], (4-sulfobutyl)tris(4-sulfophenyl)phosphonium hydrogen sulfate, and triphenyl(propyl-3-sulfonyl)phosphonium toluenesulfonate.

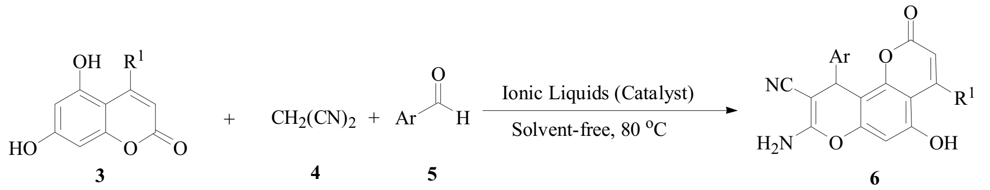
We attempted the one-pot synthesis of pyrano[2,3-*h*]coumarin derivatives with only one acidic or basic IL. The experimental results showed that the first step requires a BAIL, and the second step did not proceed in a one-pot manner with acidic ILs. We also performed the first step of the reaction using basic ILs as catalysts. The results showed that the all starting materials were intact and none of the desired products were obtained for the second step.

2. Experimental

2.1. Chemicals and materials

All reagents were purchased from Merck or Aldrich and used without further purification. All yields refer to isolated products after purification. ([Hnmp][HSO_4] [8], [NMP][HSO_4] [9], [NMP][H_2PO_4] [10], (4-sulfobutyl) tris (4-sulfophenyl) phosphonium hydrogen sulfate [11], triphenyl(propyl-3-sulfonyl)phosphonium toluenesulfonate [12], 2-HEAF [13], 3-HPAA [14], [Bmim]OH [15], [Pyrr][HCOO], and [Pyrr][CH_3COO] [16] were prepared according to literature procedures. Nuclear magnetic resonance (NMR) spectra were recorded using a Bruker Avance DPX 400 MHz instrument. The spectra were measured in DMSO-d_6 relative to tetramethylsilane (δ = 0.00). Melting points were determined in open capillaries using a BUCHI 510 melting point apparatus. Thin-layer chromatography was performed on silica-gel Poly Gram SIL G/UV 254 plates.

2.2. General procedure for synthesis of 5,7-dihydroxy-4-substituted coumarins (Step 1)



R^1 = Me, Ph; Ar = Ph, 4-$O_2NC_6H_4$, 3-$O_2NC_6H_4$, 4-MeC_6H_4, 4-$MeOC_6H_4$, 2-$MeOC_6H_4$, 3-BrC_6H_4, 4-ClC_6H_4, 2,4-$Cl_2C_6H_3$, 3-ClC_6H_4, 2-ClC_6H_4
Ionic Liquids = 2-HEAF, 3-HPAA, [Bmim][OH], [Pyrr][HCOO], and [Pyrr][CH_3COO]

Scheme 2. Synthesis of pyrano[2,3-*h*]coumarin derivatives.

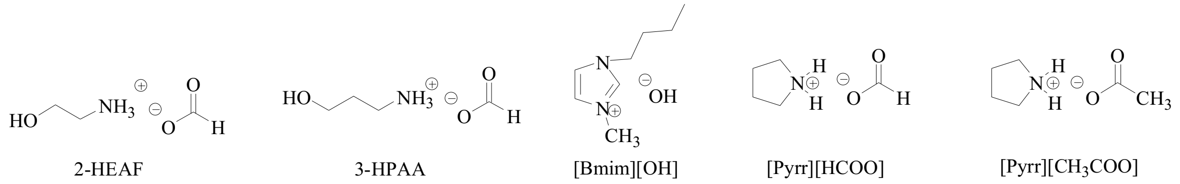


Fig. 2. Structure of 2-HEAF, 3-HPAA, [Bmim][OH], [Pyrr][HCOO], and [Pyrr][CH_3COO].

A mixture of phloroglucinol (1 mmol), β-keto ethyl/methyl ester (1 mmol), and one of [Hnmp][HSO_4] (0.009 g, 5 mol%, 0.05 mmol), [NMP][HSO_4] (0.0098 g, 5 mol%, 0.05 mmol), [NMP][H_2PO_4] (0.0098 g, 5 mol%, 0.05 mmol), (4-sulfobutyl) tris(4-sulfophenyl)phosphonium hydrogen sulfate (0.036 g, 5 mol%, 0.05 mmol), or triphenyl(propyl-3-sulfonyl)phosphonium toluenesulfonate (0.026 g, 5 mol%, 0.05 mmol) was stirred at room temperature for the appropriate time. After completion of the reaction, water (5 mL) was added to the mixture. The IL dissolved in the water, and the solid crude product was separated by filtration. The separated product was washed twice with water (5 mL). The solid product was recrystallized from hot EtOH to give the pure product **3**. After isolation of the insoluble products, the IL was recovered by evaporation of the water, washing the remaining viscous liquid with CH_2Cl_2 (5 mL), and drying under reduced pressure.

All the products have been reported in the literature and were characterized by comparing their melting points and infrared (IR) and NMR spectra with those of authentic samples [17–20].

2.3. *Typical procedure for synthesis of pyrano[2,3-h]coumarin derivatives (Step 2)*

A mixture of 5,7-dihydroxy-4-substituted coumarin **3** (1 mmol), malononitrile (**4**, 1 mmol), an aromatic aldehyde **5** (1 mmol), and one of 2-HEAF (0.0107 g, 10 mol%, 0.1 mmol), 3-HPAA (0.0135 g, 10 mol%, 0.1 mmol), [Bmim]OH (0.0139 g, 10 mol%, 0.1 mmol), [Pyrr][HCOO] (0.0117 g, 10 mol%, 0.1 mmol), or [Pyrr][CH_3COO] (0.0131 g, 10 mol%, 0.1 mmol) was stirred and heated in an oil bath at 80 °C for the appropriate time. After completion of the reaction, the mixture was cooled to room temperature. Water (5 mL) was then added to the mixture. The IL dissolved in the water, and the crude product was separated by filtration. The separated product was washed twice with water (5 mL). The solid product was recrystallized from hot EtOH to give the pure product **6**. After isolation of the insoluble products, the IL was recovered by evaporation of the water, washing the remaining viscous liquid with CH_2Cl_2 (5 mL), and drying under reduced pressure.

All the products have been reported in the literature and were characterized by comparing their melting points and IR and NMR spectra with those of authentic samples [21]. Spectroscopic data (^{1}H NMR, ^{13}C NMR, and IR) for two of the known compounds are given as examples.

Product **6a**. m.p. 254–256 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.27–7.23 (m, 2H), 7.18–7.13 (m, 3H), 6.88 (s, 2H), 6.10 (s, 1H), 5.80 (s, 1H), 4.61 (s, 1H), 2.55 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 163.69, 160.10, 160.05, 155.26, 153.51, 147.59, 145.81, 128.16, 127.01, 126.19, 120.53, 109.70, 107.89, 98.92, 98.57, 57.68, 36.31, 23.97; IR (KBr, cm^{-1}): 3460, 3390, 2191, 1652, 1617, 1399.

Product **6j**. m.p. 209–211 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 11.06 (s, 1H), 7.36–7.26 (m, 2H), 7.19 (s, 1H), 7.13–7.10 (m, 3H), 6.51 (s, 1H), 6.10 (s, 1H), 4.68 (s, 1H), 2.62 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 160.11, 159.80, 157.91, 155.00, 153.81, 148.11, 148.00, 133.39, 130.89, 127.33, 126.37, 120.36, 112.05, 108.16, 102.46, 99.10, 57.25, 36.56, 24.49; IR (KBr, cm^{-1}): 3401, 2194, 1728, 1661, 1390, 1095.

3. Results and discussion

To carry out the Pechmann condensation in a more efficient way, the reaction of phloroglucinol (1 mmol) and ethyl acetoacetate (1 mmol) under solvent-free conditions at room temperature was selected as a model system to optimize the conditions. The preparation of 5,7-dihydroxy-4-methylcoumarin was studied using different amounts of acidic ILs (5, 10, 15, and 20 mol%) as catalysts (Table 1). The best results were obtained using 5 mol% [Hnmp][HSO_4], 5 mol% [NMP][HSO_4], 5 mol% [NMP][H_2PO_4], 5 mol% (4-sulfobutyl)tris(4-sulfophenyl) phosphonium hydrogen sulfate, and 5 mol% triphenyl(propyl-3-sulfonyl)phosphonium toluenesulfonate at room temperature (Table 1).

Using these optimized reaction conditions, the scope and efficiency of the procedure were explored for the synthesis of 5,7-dihydroxy-4-methylcoumarin and 5,7-dihydroxy-4-phenylcoumarin via two-component condensation of phloroglucinol and β-keto ethyl/methyl esters at room temperature (Table 2, Entries 1, 2, and 3). As the data in Table 2 show, β-keto ethyl/methyl esters with phloroglucinol in the presence of a catalytic amount of [Hnmp][HSO_4] (5 mol%), [NMP][HSO_4] (5 mol%), [NMP][H_2PO_4] (5 mol%), (4-sulfobutyl)tris(4-sulfophenyl)phosphonium hydrogen sulfate (5 mol%), or triphenyl(propyl-3-sulfonyl)phosphonium toluenesulfonate (5 mol%) formed the corresponding 5,7-dihydroxy-4-substituted coumarins without the formation of any side products, in good to high yields. The results showed that steric hindrance plays a

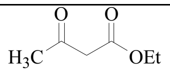
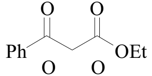
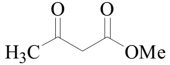
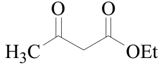
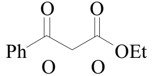
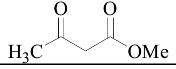
Table 1

Optimization of amounts of acidic ILs, [Hnmp][HSO_4] (A), [NMP][HSO_4] (B), [NMP][H_2PO_4] (C), (4-sulfobutyl)tris(4-sulfophenyl)phosphonium hydrogen sulfate (D), and triphenyl(propyl-3-sulfonyl)phosphonium toluenesulfonate (E) as catalysts for preparation of 5,7-dihydroxy-4-substituted coumarins (Scheme 1, Step 1).

Entry	Catalyst amount (mol%)	Time (min)					Yield^a (%)				
		A	B	C	D	E	A	B	C	D	E
1	—	720	720	720	720	720	—	—	—	—	—
2	5	45	18	39	12	15	88	90	87	91	90
3	10	38	15	53	9	10	90	89	92	91	89
4	15	32	10	53	7	8	89	93	92	90	88
5	20	30	10	50	6	8	92	91	90	93	93

^{a}Isolated pure products based on the reaction of phloroglucinol (1 mmol) and ethyl acetoacetate (1 mmol) at room temperature under solvent-free conditions. The reaction did not proceed in the presence of basic ionic liquids, which confirms observations in the literature [17–20].

Table 2
Synthesis of 5,7-dihydroxy-4-methylcoumarin and 5,7-dihydroxy-4-phenylcoumarin via Pechmann condensation using catalytic amounts of acidic ILs under solvent-free conditions at room temperature and at 80 °C (Scheme 1, Step 1).

Entry	β-Ketoester	*t*/°C	Time (min)					Yield [a] (%)					m.p. (°C) (Ref. [17])
			A	B	C	D	E	A	B	C	D	E	
1		r.t	45	18	39	12	15	88	90	87	91	90	282–285 (281–283)
2		r.t	62	48	68	24	20	90	89	89	91	88	243–245 (241–244)
3		r.t	40	15	37	10	12	88	85	89	90	90	282–285 (281–283)
4		80	9	11	12	8	9	95	93	90	96	85	282–285 (281–283)
5		80	48	38	42	35	37	88	87	91	88	81	243–245 (241–244)
6		80	8	10	10	6	6	93	92	94	93	90	282–285 (281–283)

[a] Isolated pure products based on the reaction of phloroglucinol (1 mmol) and β-keto ethyl/methyl esters (1 mmol).

major role in the reaction rates. Methyl esters are more reactive than ethyl esters (Table 2, Entries 1 and 3); ethyl acetoacetate is more reactive than ethyl benzoyl acetate (Table 2, Entries 1 and 2). We also studied the preparation of 5,7-dihydroxy-4-methylcoumarin and 5,7-dihydroxy-4-phenylcoumarin using the optimized amounts of ILs liquids at 80 °C (Table 2, Entries 4, 5, and 6). We observed that the reaction time was shorter at high temperatures than at room temperature. Furthermore, we observed that the effect of steric hindrance on the reaction was more important at 80 °C than the effect of temperature (Table 2, Entries 1 and 5). In the cases of methyl and ethyl esters, the effect of steric hindrance is not important (Table 2, Entries 1 and 6) and the temperature plays the major role in determining the reaction rate.

Reaction at room temperature under mild conditions, and a multi-steps synthesis, using ambient rather than thermal conditions, gave the best results. We therefore used mild and ambient conditions.

In the second step, i.e., the preparation of pyrano[2,3-*h*] coumarins, the reaction of 5,7-dihydroxy-4-methylcoumarin (**3**, 1 mmol), malononitrile (**4**, 1 mmol), and benzaldehyde (**5**, 1 mmol) was selected (Scheme 2, R^1 = Me, Ar = Ph) as a model system under solvent-free conditions to find the optimum conditions. The model was studied at different reaction temperatures (25, 60, 80, 100, and 120 °C) and with different amounts of basic ILs as catalysts (5, 10, 15, and 20 mol%; Table 3). The best results were obtained using 10 mol% 2-HEAF, 10 mol% 3-HPAA, 10 mol% [Bmim][OH], 10 mol% [Pyrr][HCOO], and 10 mol% [Pyrr][CH_3COO] at 80 °C (Table 3).

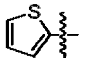
Using these optimized reaction conditions, the scope and efficiency of the procedure were explored for the synthesis of a wide range of pyrano[2,3-*h*]coumarins (Table 4). As the data in Table 4 show, aromatic aldehydes with both electron-withdrawing and electron-donating substituents reacted efficiently with 5,7-dihydroxy-4-substituted coumarins and malononitrile in the presence of catalytic amounts of 2-HEAF (10 mol%), 3-HPAA (10 mol%), [Bmim][OH] (10 mol%), [Pyrr][HCOO] (10 mol%), or [Pyrr][CH_3COO] (10 mol%), affording the corre-

Table 3
Optimization of amounts of basic ILs, i.e., 2-HEAF (F), 3-HPAA (G), [Bmim][OH] (H), [Pyrr][HCOO](I), and [Pyrr[[CH_3COO] (J), used as catalysts at different temperatures for preparation of pyrano[2,3-*h*]coumarins (Scheme 2, Step 2).

Entry	Catalyst amount (mol%)	Temperature (°C)	Time (min)					Yield [a] (%)				
			F	G	H	I	J	F	G	H	I	J
1	—	80	720	720	720	720	720	—	—	—	—	—
2	5	80	78	81	59	62	84	67	62	78	75	62
3	10	80	39	42	37	35	36	91	85	93	91	82
4	15	80	37	33	32	30	36	89	93	91	94	72
5	20	80	38	30	35	37	39	93	92	89	80	79
6	10	25	360	360	360	360	360	—	—	—	—	—
7	10	60	90	98	75	82	93	72	68	78	75	69
8	10	80	39	42	37	35	36	91	85	93	91	82
9	10	100	28	33	30	29	32	85	83	89	93	88
10	10	120	25	28	24	33	38	48	52	68	70	32

[a] Isolated pure products. Reaction conditions: 5,7-dihydroxy-4-methylcoumarin (1 mmol), malononitrile (1 mmol), benzaldehyde (1 mmol) under solvent-free conditions. The reaction did not proceed in the presence of acidic ILs, which confirms observations in the literature [21]. The pH values of these ILs were reported according to the literature: 2-HEAF (pH = 7.2) [14], 3-HPAA (pH = 7.14) [14], [Bmim][OH] (pH = 9.3) [15], [Pyrr][HCOO] (pH = 7.5) [16], and [Pyrr][CH_3COO] (pH = 7.7) [16].

Table 4
Synthesis of pyrano[2,3-*h*]coumarin derivatives (Scheme 2, Step 2).

Entry	Ar	R	Product	Time (min)					Yield [a] (%)					m.p. (°C) (Ref. [21])
				F	G	H	I	J	F	G	H	I	J	
1	C_6H_5	Me	**6a**	39	42	37	35	39	91	85	93	91	89	254–256 (255–256)
2	4-$O_2NC_6H_4$	Me	**6b**	27	38	48	39	43	88	90	91	90	92	246–248 (245–247)
3	3-$O_2NC_6H_4$	Me	**6c**	35	40	29	58	42	90	88	92	89	85	290–291 (293–295)
4	4-MeC_6H_4	Me	**6d**	58	68	52	65	70	91	84	90	91	88	224–226 (225–226)
5	4-$MeOC_6H_4$	Me	**6e**	52	45	58	61	68	89	91	93	87	84	267–268 (265–266)
6	2-$MeOC_6H_4$	Me	**6f**	42	35	48	51	32	91	90	89	88	88	302–304 (303–305)
7	3-BrC_6H_4	Me	**6g**	52	38	40	58	68	93	89	91	90	90	295–297 (295–296)
8	4-ClC_6H_4	Me	**6h**	48	55	34	39	45	85	81	89	87	82	240–242 (242–244)
9	2,4-$Cl_2C_6H_3$	Me	**6i**	65	68	58	70	50	87	89	85	88	80	321–323 (322–324)
10	3-ClC_6H_4	Me	**6j**	48	62	55	70	78	93	90	89	84	87	209–211 (208–210)
11	2-ClC_6H_4	Me	**6k**	38	31	42	33	35	90	85	93	93	89	319–321 (320–322)
12		Me	**6l**	89	97	78	82	140	88	85	89	87	80	249–251 (250–252)
13	2-ClC_6H_4	Ph	**6m**	180	165	172	148	195	66	61	70	69	73	244–246 (243–245)
14	*n*-Heptanal	Me	—	720	720	720	720	720	—	—	—	0	0	
15	*n*-Octanal	Me	—	720	720	720	720	720	—	—	—	0	0	

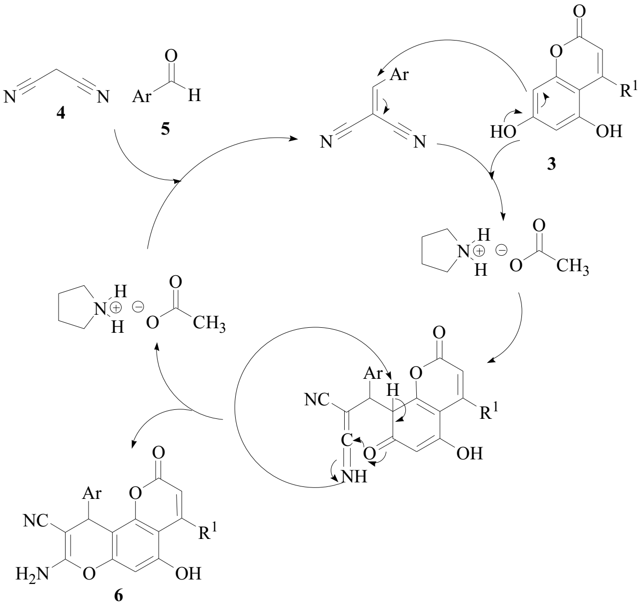
[a] Isolated pure products based on the reaction of 5,7-dihydroxy-4-substituted coumarin (1 mmol), malononitrile (1 mmol), and benzaldehyde (1 mmol) under solvent-free conditions at 80 °C.

sponding pyrano[2,3-*h*]coumarins, without the formation of any side products, in good to high yields. We also used aliphatic aldehydes such as *n*-heptanal and *n*-octanal instead of benzaldehydes in the reactions. Our attempts to synthesize pyrano[2,3-*h*]coumarin derivatives using aliphatic aldehydes were unsuccessful, even after 12 h (Table 4, Entries 14 and 15). In the case of aliphatic enolizable aldehydes, dehydrated and hydrated Knoevenagel products and also hydrated and dehydrated self aldol condensation products were formed, and some starting materials (aliphatic aldehyde and malononitrile) remained. In addition, 5,7-dihydroxy-4-methylcoumarin was intact under the reaction conditions.

A mechanism for the preparation of pyrano[2,3-*h*]coumarins is suggested based on mechanisms proposed in the literature [21]. Weak basic ILs are effective catalysts for the ready in situ formation of Knoevenagel products from aryl aldehydes and the malononitrile carboanion. Michael-type addition of C-8 of 5,7-dihydroxy-4-substituted coumarins to Knoevenagel products then occurs, followed by cyclization to give the desired cyclic product (Scheme 3).

We also compared the results using the present BAILs with the reported results obtained using other catalysts such as silica-gel-supported zirconyl chloride octahydrate ($ZrOCl_2{\cdot}8H_2O/SiO_2$) [17], 1-butanesulfonic acid-3-methylimidazolium tosylate ([BSMIm]Ts) [18], poly(4-vinylpyridine)-supported sulfuric acid (P_4VP-H_2SO_4) [19], and pentafluorophenylammonium triflate (PFPAT) [20] in the Pechmann condensation for the synthesis of 5,7-dihydroxy-4-substituted coumarins (Table 5). The data in Table 5 clearly demonstrate that [Hnmp][HSO_4], [NMP][HSO_4], [NMP][H_2PO_4], (4-sulfobutyl)tris(4-sulfophenyl) phosphonium hydrogen sulfate, and triphenyl(propyl-3-sulfonyl)phosphonium toluenesulfonate are effective catalysts in terms of reaction time and yields of obtained products compared with other reported catalysts. Among the ILs, (4-sulfobutyl)tris(4-sulfophenyl)phosphonium hydrogen sulfate is the best IL for the synthesis of 5,7-dihydroxy-4-substituted coumarins.

We also compared the results obtained using the present Brönsted basic ILs with the results for one catalyst reported in the literature [21] (Table 6). The data in Table 6 clearly demonstrate that 2-HEAF, 3-HPAA, [Bmim][OH], [Pyrr][HCOO], and [Pyrr][CH_3COO] are effective catalysts in terms of reaction time and yields of obtained products compared with potassium carbonate (K_2CO_3) as the catalyst [21]. As can be seen from Table 6, [Bmim][OH] is the best IL of those studied in this research. We also investigated the catalytic activity of different counter ions and examined their effects. We studied Brönsted



Scheme 3. Proposed mechanism of synthesis of pyrano[2,3-*h*]coumarin derivatives using [Pyrr][CH_3COO] as the IL catalyst.

Table 5

Comparison of results obtained using [Hnmp][HSO_4], [NMP][HSO_4], [NMP][H_2PO_4], (4-sulfobutyl)tris(4-sulfophenyl)phosphonium hydrogen sulfate, and triphenyl(propyl-3-sulfonyl)phosphonium toluenesulfonate with results obtained using other catalysts reported in the literature for the synthesis of 5,7-dihydroxy-4-substituted coumarins (Scheme 1, Step 1).

Entry	Catalyst (amount)	Condition	Time (min)	Yield [a] (%)	Ref.
1	$ZrOCl_2 \cdot 8H_2O/SiO_2$ (10 mol%)	90 °C	10	98	[17]
2	[BSMIm]Ts (10 mol%)	80 °C	90	70	[18]
3	P_4VP-H_2SO_4 (20 mol%)	65 °C / MW 560W	9	85	[19]
4	PFPAT (10 mol%)	Toluene / reflux, 110 °C	180	95	[20]
5	[Hnmp][HSO_4] (5 mol%)	Solvent-free, r.t	45	88	This work
6	[NMP][HSO_4] (5 mol%)	Solvent-free, r.t	18	90	This work
7	[NMP][H_2PO_4] (5 mol%)	Solvent-free, r.t	60	87	This work
8	(4-Sulfobutyl)tris(4-sulfophenyl)phosphonium hydrogensulfate (5 mol%)	Solvent-free, r.t	12	91	This work
9	Triphenyl(propyl-3-sulphonyl)phosphonium toluenesulfonate (5 mol%)	Solvent-free, r.t	15	90	This work
10	[Bmim]Br (5 mol%)	Solvent-free, r.t	180	—	This work
11	[Bmim]Cl (5 mol%)	Solvent-free, r.t	180	—	This work
12	[Hnmp][HSO_4] (5 mol%)	Solvent-free, 80 °C	9	95	This work
13	[NMP][HSO_4] (5 mol%)	Solvent-free, 80 °C	11	93	This work
14	[NMP][H_2PO_4] (5 mol%)	Solvent-free, 80 °C	12	90	This work
15	(4-Sulfobutyl)tris(4-sulfophenyl)phosphonium hydrogensulfate (5 mol%)	Solvent-free, 80 °C	8	96	This work
16	Triphenyl(propyl-3-sulphonyl)phosphonium toluenesulfonate (5 mol%)	Solvent-free, 80 °C	9	85	This work
17	[Bmim]Br (5 mol%)	Solvent-free, 80 °C	180	—	This work
18	[Bmim]Cl (5 mol%)	Solvent-free, 80 °C	180	—	This work

[a] Isolated pure products based on the reaction of phloroglucinol (1 mmol) and ethyl acetoacetate (1 mmol).

Table 6

Comparison of results obtained using 2-HEAF, 3-HPAA, [Bmim]OH, [Pyrr][HCOO], and [Pyrr][CH3COO] with those obtained using K_2CO_3 in the synthesis of pyrano[2,3-*h*]coumarin derivatives (Scheme 2, Step 2).

Entry	Catalyst (amount)	Condition	Time (min)	Yield [a] (%)	Ref.
1	K_2CO_3 (10 mol%)	MeOH / reflux	40	95	[21]
2	2-HEAF (10 mol%)	Solvent-free, 80 °C	39	91	This work
3	3-HPAA (10 mol%)	Solvent-free, 80 °C	42	85	This work
4	[Bmim][OH] (10 mol%)	Solvent-free, 80 °C	37	93	This work
5	[Pyrr][HCOO] (10 mol%)	Solvent-free, 80 °C	35	91	This work
6	[Pyrr][CH_3COO] (10 mol%)	Solvent-free, 80 °C	39	89	This work
7	[Bmim]Br (10 mol%)	Solvent-free, 80 °C	180	—	This work
8	[Bmim]Cl (10 mol%)	Solvent-free, 80 °C	180	—	This work

[a] Isolated pure products based on the reaction of 5,7-dihydroxy-4-methylcoumarin (1 mmol), malononitrile (1 mmol), and benzaldehyde (1 mmol).

and non-Brönsted counter ions. The results showed that non-Brönsted counter ions did not act as catalysts in the synthesis of pyrano[2,3-*h*]coumarin derivatives (Table 6, Entries 5, 7, and 8). The Brönsted counter ion is therefore important in substrate activation and product formation, and influences the formation mechanism and activation of reactive intermediates.

In green organic synthesis, catalyst recovery is important. The reusability of the ILs as catalysts was therefore studied in Step 1 and Step 2 of the reactions. After completion of the reaction, water (5 mL) was added to the cooled reaction mixture. The IL dissolved in the water and the crude product was separated by filtration. The separated product was washed twice with water (5 mL). The ILs were recovered by evaporation of the water, washing the remaining viscous liquid with CH_2Cl_2 (5 mL), and drying under reduced pressure. The catalytic activity of the recovered ILs was tested in subsequent runs without adding fresh catalyst. The ILs were tested in five runs. It was seen that the IL catalysts displayed very good reusability, without significant loss of their activity (Figs. 3 and 4).

4. Conclusions

We have developed a rapid and highly efficient method for the green synthesis of 5,7-dihydroxy-4-substituted coumarins (Step 1) at room temperature using BAILS as reusable catalysts under solvent-free conditions. In addition, pyrano[2,3-*h*]coumarin derivatives were prepared using Brönsted basic ILs as reusable catalysts under thermal solvent-free conditions. We

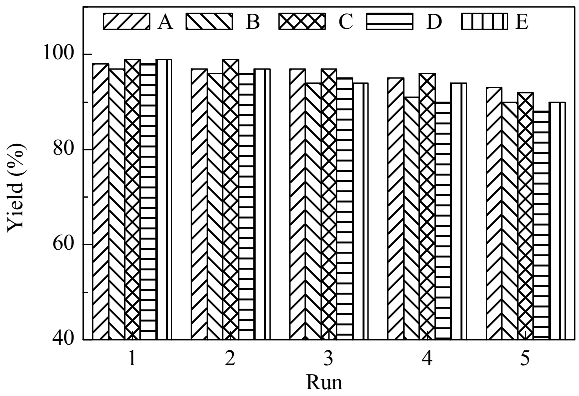


Fig. 3. Reusability of ILs as catalysts in synthesis of 5,7-dihydroxy-4-substituted coumarins (Step 1). A—[Hnmp][HSO_4]; B—[NMP][HSO_4]; C—[NMP][H_2PO_4]; D—(4-sulfobutyl)tris(4-sulfophenyl) phosphonium hydrogensulfate; E— triphenyl (propyl-3-sulphonyl) phosphonium toluenesulfonate.

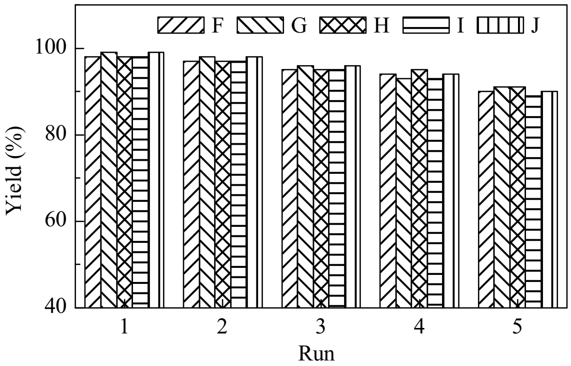


Fig. 4. Reusability of basic ILs as catalysts in synthesis of pyrano[2,3-*h*]coumarin derivatives (Step 2). F—2-HEAF; G—3-HPAA; H—[Bmim][OH]; I—[Pyrr][HCOO]; J—[Pyrr][CH_3COO].

showed that a number of ILs with different cores, different central atoms (P or N), different acidic functional groups, and different counter ions are good catalysts in the two steps of the reactions. This convenient and efficient protocol provides better alternatives to existing methods because the reactions are fast and clean, and high yields are obtained. Furthermore, the simple work-up procedure makes the present method useful and important for the synthesis of coumarin derivatives.

Acknowledgments

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Graphical Abstract

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Ionic-liquid-catalyzed green synthesis of coumarin derivatives under solvent-free conditions

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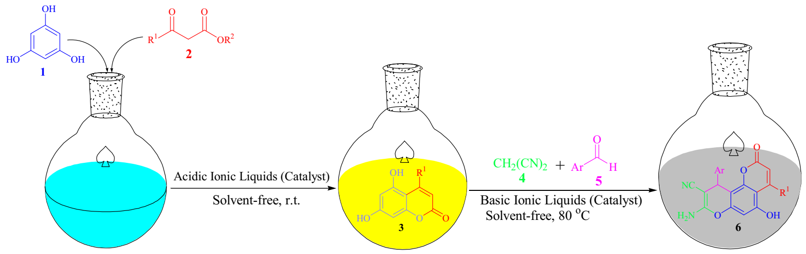

Brönsted acidic ionic liquids catalyzed efficient Pechmann condensations. The reaction of the Pechmann products, malononitrile, and aldehydes in the presence of Brönsted basic ionic liquids for synthesis of pyrano[2,3-*h*]coumarins was performed.