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Green synthesis of coumarin derivatives using Brønsted acidic pyridinium based ionic liquid [MBSPy][HSO_4] to control an opportunistic human and a devastating plant pathogenic fungus *Macrophomina phaseolina*†

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An eco-friendly simple protocol has been devised for the preparation of coumarin derivatives using doubly Brønsted acidic task specific ionic liquid (TSIL) as a catalyst. Solvent-free conditions were employed for the reaction of different substituted phenols with β-ketoester in TSIL to produce corresponding substituted coumarin derivatives in good to excellent yields at ambient conditions; at room temperature and with reduced reaction times. The ionic liquid catalyst can be recycled and reused up to five times. All the synthesized coumarins were evaluated for their antifungal activities against *Macrophomina phaseolina*, a plant as well as an opportunistic human pathogenic fungus affecting more than 500 plant species worldwide and with no registered commercial fungicide available against it, to date. Amongst all the coumarins tested, compounds **3f** and **3i** showed excellent antifungal activity comparable to reference fungicide mancozeb. The current methodology provides an easy and expedient way to access the coumarin core in search of potential fungicides for sustainable agriculture.

1. Introduction

Coumarins (2*H*-chromone-2-one) are considered a significant class of heterocyclic compounds due to their versatile biological and medicinal properties such as antihelmintic, antioxidant,[1] anticonvulsant,[2] antitumor and anti-inflammatory activities.[3] Broad range antimicrobial properties are also attributed to this core due to its distinct structural properties. Coumarins have important applications in cosmetics, fragrances, pharmaceuticals and food additives.[4] It is recognized to introduce resistance in plant tissues against microbial attack, which is evident by the presence of coumarin derivatives in commercially available pesticides.[5] The structures of some of the commercial coumarin based pesticides are depicted in Fig. 1, and include brodifacoum, dicoumarol, warfarin and difenacoum.[6]

One of the unique structural features of coumarin is the ease with which it could be assembled and modified using cheap and commercially available starting materials. During the past decades several methods used for the synthesis of coumarins include Knoevenagel,[9] Perkin,[8] Pechmann,[7] Wittig,[12] Claisen[11] and Reformatsky reactions.[10] Pechmann condensation is a widely used method in which phenols are reacted with β-ketoester to give 4-substituted coumarins in the presence of acid catalyst. Numerous Brønsted[13–15] and Lewis acidic[16–19] catalysts have been used like H_2SO_4, P_2O_5, H_3PO_4, $Bi(NO_3)_3$, $Cu(ClO_4)_2$ and others. The notability of the classical methods is significantly reduced due to the stoichiometric use of Brønsted acid and subsequent corrosion issues, water sensitivity of Lewis acids, high temperature requirements, poor selectivity and low yields.

Recently, ionic liquid (IL) became fascinating solvents and catalysis in organic synthesis owing to their unique properties like low volatility, non-inflammability, insignificant vapor pressure, high thermal stability and reusability.[20] Pechmann condensation was primarily reported using chloroaluminates of imidazolium and pyridinium based ILs, drawbacks of which are their moisture and air sensitivity.[21] Boroujeni *et al.* reported ionic liquid based catalyst [P_4VPy-$BuSO_3H$]Cl-X($AlCl_3$) possessing both Lewis and Brønsted acidic groups.[22] 1-Ethyl-3-(3-sulfopropyl)-benzimidazolium trifluoromethanesulfonate ([PSebim][OTf]) was also reported for the synthesis of biscoumarins.[23] In comparison, Brønsted acidic ionic liquids (BAILs) are superior due to their comparable acidity to inorganic acid, recyclability, thermal and moisture stability.[24] Amongst BAILs, the sulfonic acid

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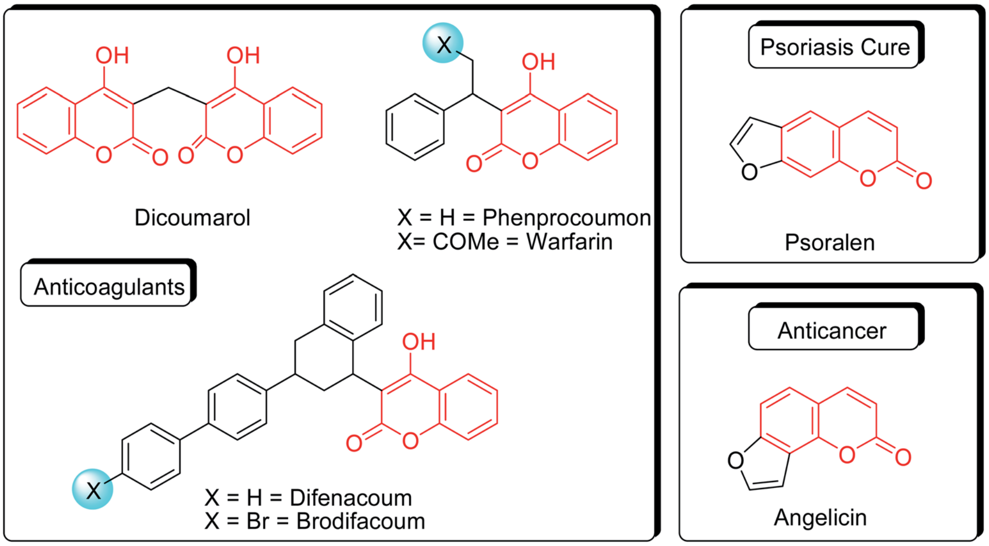


Fig. 1 Some commercially available coumarin drugs.

functionalized cations and hydrogen sulfate bearing anions have recently been found very efficient catalysts in acid catalyzed organic transformations. 2-Pyrrolidonium hydrogen sulfate ([Hnmp][HSO_4]), *N*-methyl-2-pyrrolidonium hydrogen sulfate ([NMP][HSO_4]), triphenyl(propyl-3-sulfonyl)phosphonium toluene sulfonate, (4-sulfobutyl)tris(4-sulfophenyl)phosphonium hydrogen sulfate and *N*-methyl-2-pyrrolidonium dihydrogen phosphate ([NMP][H_2PO_4]) were reported to catalyze the fabrication of derivatives of coumarin under solvent-free environment.[25] Similarly, Tiwari *et al.* reported triethylammonium hydrogen sulfate ([TEAN][HSO_4])[26] and Rezayati *et al.* reported 1,1′-butylenebispyridinium hydrogen sulfate (Bbpy)(HSO_4)$_2$ (ref. 27) for the synthesis of novel fungicidal coumarin derivatives. Research group of Mahato used 1-butane sulfonic acid-3-methylimidazolium tosylate ([BSMIM][OTs]) under solvent-free conditions for the regioselective production of pyrano[3,2-*c*] coumarins.[28] Same BAIL catalyst was also reported for the synthesis of pyrano[3,2-*c*]coumarins *via* tandem reaction between α,β-unsaturated carbonyl compounds and 4-hydroxycoumarin.[29] The previous reports of Pechmann condensation catalyzed by BAIL have acidic proton either on the cation or anion, therefore, requiring high catalyst loadings, elevated temperature and longer reaction times.[25–29] To the best of our knowledge, Pechmann condensation has not been tried so far with BAILs having acidic proton both on anion and cation of IL. Therefore a green synthetic protocol has been devised using task specific BAIL for the quick assembly of coumarin core and their subsequent antifungal potential was evaluated against *Macrophomina phaseolina*, an opportunistic human and a highly problematic plant pathogenic fungus affecting more than 500 plant species worldwide and with no registered commercial fungicide available against it to date.

2. Experimental

All the chemicals were purchased from Sigma Aldrich and Alfa-Aeser and used without any further treatment. Reported yields refer to pure crystallized products. [MBSPy][HSO_4] was synthesized following the previously reported procedure.[30] Pure coumarins were characterized by Fourier Transform Infrared (FTIR) analysis and proton nuclear magnetic resonance (^{1}H NMR) spectroscopy. ^{1}H NMR (300–400 MHz) spectra were run in D_2O and DMSO-d_6 relative to TMS (0.00 ppm). FTIR spectra were recorded on Agilent Cary 630 FTIR having scanning range of 400–4000 cm^{-1}. Melting points of pure crystallized products were taken on a Gallenkamp melting apparatus and were uncorrected.

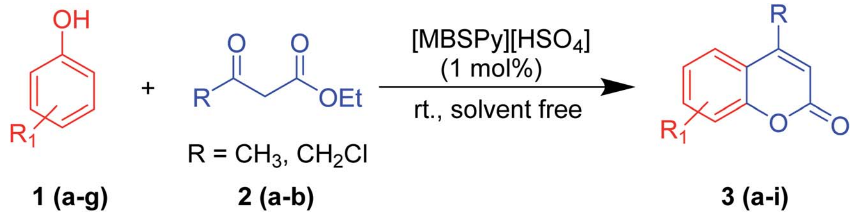
2.1. Synthesis of 1-butylsulfonic-3-methylpyridinium hydrogen sulfate [MBSPy][HSO_4]

A round bottom flask was charged with 3-methylpyridine (10 mmol) and 1,4-butanesultone (10 mmol) were added and refluxed at 80 °C with constant stirring until a white solid is formed. After that, sulfuric acid (10 mmol) is added to this white solid and refluxed at 80 °C. White solid began to react with sulfuric acid as apparent by formation of pale yellowish viscous liquid. Appropriate time was given to the reaction mixture until the completion of reaction.

Pale yellow viscous liquid, Yield (85%), ^{1}H NMR (300 MHz, D_2O) δ (ppm): 8.595 (s, 1H, HAr), 8.536 (d, 1H, $J = 6.3$ Hz, HAr), 8.236 (d, 1H, $J = 7.8$ Hz, HAr), 7.8 (t, 1H, $J = 6.5$ Hz, HAr), 4.466 (t, 2H, $J = 7.5$ Hz, CH_2), 2.814 (t, 2H, $J = 7.5$ Hz, CH_2), 2.425 (s, 3H, CH_3), 1.994 (m, 2H, CH_2), 1.621 (m, 2H, $J = 7.6$ Hz, CH_2).

2.2. General procedure for the synthesis of coumarins (3a–i)

A round bottom flask was charged with phenol (**1a–g**) (1 mmol), β-ketoester (**2**) (1.2 mmol) and [MBSPy][HSO_4] (0.01 mmol) and stirred at room temperature. Reaction progress was monitored *via* thin layer chromatography using 1 : 1 ethyl acetate and *n*-hexane. After the appearance of single spotted product on TLC, the reaction mixture was allowed to cool, and work-up was done by addition of distilled water and stirring for 5 to 10 min. The



Scheme 1 Synthesis of coumarin derivatives from different substituted phenols using [MBSPy][HSO_4] as a catalyst.

produced crystalline product was filtered, and recrystallized using ethanol (Scheme 1).

2.2.1 7-Hydroxy-4-methyl-2*H*-chromen-2-one (3a). Colorless solid, yield (92%), MP (182–184 °C), FTIR (cm^{-1}): 1395, 1595, 1677, 3129, ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 10.52 (s, 1H, OH), 7.55 (d, 1H, $J = 8.7$ Hz, HAr), 6.772–6.809 (dd, 1H, $J = 2.4$, 8.7 Hz, HAr), 6.69 (d, 1H, $J = 2.4$ Hz, HAr), 6.11 (s, 1H, CH), 2.34 (s, 3H, CH_3).

2.2.2 7-Hydroxy-4,5-dimethyl-2*H*-chromen-2-one (3b). Colorless solid, yield (80%), MP (189–190 °C), FTIR (cm^{-1}): 1362, 1513, 1619, 3325, ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 10.55 (s, 1H, OH), 6.56 (d, 2H, $J = 10.5$ Hz, HAr), 6.02 (s, 1H, CH), 3.44 (s, 3H, CH_3), 2.26 (s, 3H, CH_3).

2.2.3 5,7-Dihydroxy-4-methyl-2*H*-chromen-2-one (3c). White solid, yield (83%), MP (280–282 °C), FTIR (cm^{-1}): 1365, 1558, 1670, 3129, 3412, ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 10.53 (s, 1H, OH), 10.30 (s, 1H, OH), 6.25 (d, 1H, $J = 2.4$ Hz, HAr), 6.16 (d, 1H, $J = 2.4$ Hz, HAr), 5.84 (s, 1H, CH), 2.48 (s, 3H, CH_3).

2.2.4 7,8-Dihydroxy-4-methyl-2*H*-chromen-2-one (3d). White solid, yield (84%), MP (243–244 °C), FTIR (cm^{-1}): 1313, 1588, 1655, 3218, 3404, ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 10.0 (s, 1H, OH), 9.34 (s, 1H, OH), 7.05 (d, 1H, $J = 8.7$ Hz, HAr), 6.79 (d, 1H, $J = 8.7$ Hz, HAr), 6.10 (s, 1H, CH), 2.33 (s, 3H, CH_3).

2.2.5 4-(Chloromethyl)-2*H*-benzo[*h*]chromen-2-one (3e). Light yellow solid, yield (65%), MP (220–222 °C), FTIR (cm^{-1}): 1398, 1542, 1604, 3438, ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 8.517 (m, 1H, HAr), 7.845 (m, 1H, HAr), 7.70 (m, 1H, HAr), 7.60 (m, 3H, HAr), 6.62 (s, 1H, CH), 4.72 (s, 2H, CH_2).

2.2.6 4-(Chloromethyl)-7-hydroxy-5-methyl-2*H*-chromen-2-one (3f). Brown solid, yield (74%), MP (153–154 °C), FTIR (cm^{-1}): 1372, 1581, 1685, 3054, ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.0 (s, 1H, OH), 6.64 (d, 2H, $J = 14$, HAr), 6.59 (s, 1H, HAr), 6.40 (s, 1H, CH), 5.07 (s, 2H, CH_2), 2.28 (s, 3H, CH_3).

2.2.7 4-(Chloromethyl)-5,7-dihydroxy-2*H*-chromen-2-one (3g). Brown solid, yield (75%), MP (160–165 °C), FTIR (cm^{-1}): 1275, 1514, 1633, 3240, ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.87 (s, 1H, OH), 10.41 (s, 1H, OH), 6.27 (d, 1H, $J = 2.4$, HAr), 6.21 (d, 1H, $J = 2.4$, HAr), 5.02 (s, 2H, CH_2), 3.36 (s, 1H, CH).

2.2.8 4-(Chloromethyl)-7-hydroxy-2*H*-chromen-2-one (3h). Brown solid, yield (92%), MP (171–174 °C), FTIR (cm^{-1}): 1310, 1513, 1635, 3233, ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.63 (s, 1H, OH), 7.65 (d, 1H, $J = 8.8$ Hz, HAr), 6.81–6.84 (dd, 1H, $J = 2.4$ Hz, HAr), 6.74 (d, 1H, $J = 2$ Hz, HAr), 6.41 (s, 1H, CH), 4.94 (s, 2H, CH_2).

2.2.9 4-(Chloromethyl)-7,8-dihydroxy-2*H*-chromen-2-one (3i). Brown solid, yield (87%), MP (177–179 °C), FTIR (cm^{-1}): 1278, 1520, 1645, 3265, ^1H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.16 (s, 1H, OH), 9.36 (s, 1H, OH), 7.15 (d, 1H, $J = 7.2$ Hz, HAr), 6.82 (d, 1H, $J = 8.4$ Hz, HAr), 6.39 (s, 1H, CH), 4.92 (s, 2H, CH_2).

2.3. Antifungal bioassays

All the nine derivatives of coumarin (**3a–i**) were evaluated for their antifungal activity against *M. phaseolina* according to a reported procedure[31] with little modifications. Six milligrams of a reference fungicide mancozeb (active ingredients) and each of the nine coumarin derivatives were dissolved individually in 30 μL dimethyl sulfoxide (DMSO). Medium (3 mL) was then prepared by addition of autoclaved malt extract broth. This medium of 2 mg mL^{-1} concentration was divided into two 1.5 mL portions. One set was used in antifungal bioassays while the other was used for further serial double dilutions ranging from 1–0.0156 mg mL^{-1}. Bioassays were carried out with 0.5 mL growth medium taken in each 5 mL test tube in triplicate. Likewise, a set of control treatment was prepared to maintain the same amount of DMSO for comparison. *M. phaseolina* inoculum suspension (10 μL) was added to each test tube and incubated at 27 °C for 120 h. The fungal growth was observed with intervals of 24 h. After 120 h, fungal biomass from each test tube was collected on filter papers, dried at 60 °C and weighed.

2.4. Statistical analysis

Data regarding fungal biomass in different treatments were subjected to two-way ANOVA. The treatment means were separated by applying LSD Test at 5% level of significance using Statistix 8.1 software.

3. Results and discussion

3.1. Characterization of [MBSPy][HSO_4]

3.1.1 Thermogravimetric analysis (TGA). Thermal studies were carried out for [MBSPy][HSO_4] *via* thermogravimetric analysis (TGA) performed simultaneously with DSC. Percent weight loss by rise in temperature is recorded with high accuracy as provided in Fig. 2. The DSC was used to obtain the thermal critical points like melting point, glass transition temperature or enthalpy specific heat of substance.

The TGA and DSC curves depicted the catalyst potency towards weight gain or loss as a function of temperature with time. The TGA curve dictated that the mass loss is not so significant up to 300 °C, approving the thermal stability of the catalyst. A sharp mass loss is observed after the 300 °C. The water content was calculated 8%.

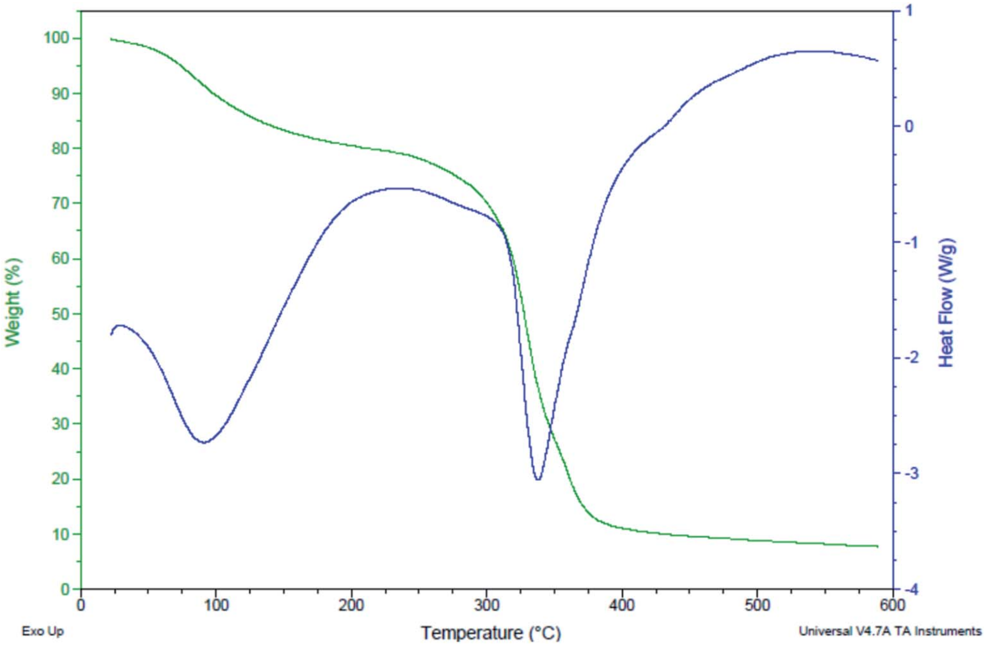


Fig. 2 TGA and DSC analysis of the catalyst.

DSC measured the catalyst energy change during the transformation as a function of temperature or time. We obtained very important quantities like the transition temperature of the material (melting point T_m, crystallization temperature T_c and glass transition temperature T_g). The water content was lost between the points 98.25 to 87.87. After that transition temperature was observed between the points 86.42 to 80.95 and the catalyst was decomposed at 300 °C (70.21 point). These data predicts the potential of synthesized catalyst with the temperature variations.

3.2. Optimization of synthesis of coumarin derivatives

Reaction of resorcinol (**1a**) and ethyl acetoacetate (**2a**) was carried out as a model reaction and the reaction conditions such as temperature, time and catalyst mol% were optimized for high yield of coumarin **3a** (Table 1). At first, reaction was carried out using 1 eq. of **1a** and 1.2 eq of **2a** under solvent-free conditions. 1 mol% [MBSPy][HSO_4] was used as catalyst at room temperature and 93% yield was obtained within one hour. Control reaction was also done without [MBSPy][HSO_4] under same conditions, but no yield was obtained even after four hours (Table 1; entry 1). When temperature was elevated from room temperature to 80 °C, time of the reaction was shortened but the yield was a little lower when compared to reaction done at room temperature; 82% yield was obtained in half an hour. Thus, temperature was observed to exhibit a little effect on reaction kinetics. So, all the reactions were performed next at room temperature in solvent-free environment. An increase in percentage of catalyst was not significant as it caused subsequent decrease in percentage yield of product. Increasing the catalysts loading from 1 to 5 mol% decreased the yield to 68%. Low catalytic activity of BAIL at higher concentrations is probably due to its high acidic strength and possibility to protonate the phenolic –OH, thus lowering its nucleophilicity. Therefore, the optimum dose of catalyst for this transformation was only 1 mol% of [MBSPy][HSO_4]. It demonstrated high catalytic proficiency of [MBSPy][HSO_4] due to its dual acidic sites.

After optimization of conditions of **3a**, eight other coumarin derivatives were prepared using different substituted phenols (**1a–g**) and β-ketoesters (**2a**, **2b**) under solvent-free, optimized conditions (Table 2). Yields of products and progress of reaction was affected by phenolic substitutions. Highest product selectivity was observed for reaction of resorcinol (**1a**) with ethylacetoacetate (**2a**) and ethyl chloroacetoacetate (**2b**). While high

Table 1 Optimization of reaction conditions

Entry	[MBSPy][HSO_4] (mol%)	Temperature (°C)	Time (h)	Yield of **3a** (%)
1	No catalyst	Room temp.	4	No reaction
2	1	Room temp.	1	93
3	1	80	0.5	82
4	2	80	0.5	81
5	2.5	80	0.5	75
6	5	80	0.5	68

Table 2 Synthesis of coumarin derivatives (**3a–i**) from phenols (**1a–g**) and ethyl acetoacetate (**2a**, **2b**) using [MBSPy][HSO_4] under solvent free conditions

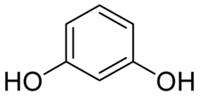
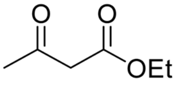
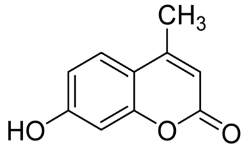
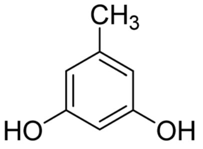
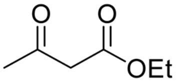
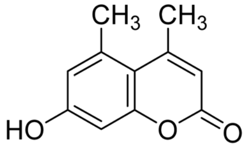
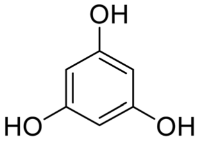
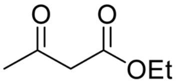
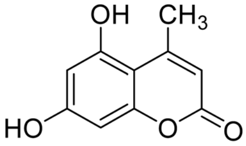
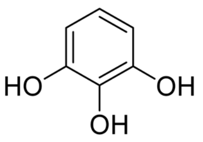
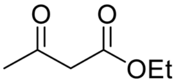
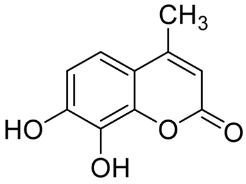
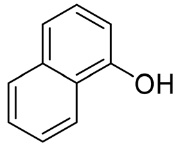
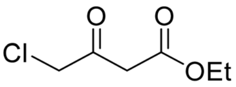
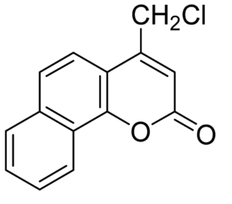
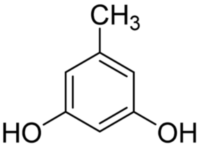
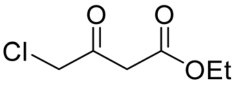
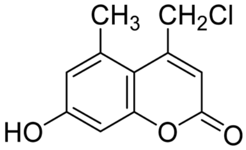
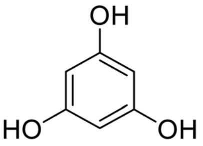
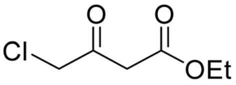
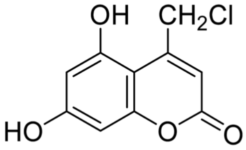
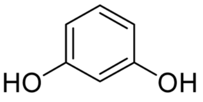
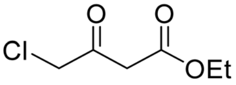
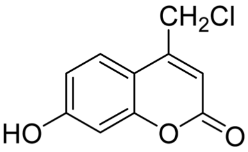
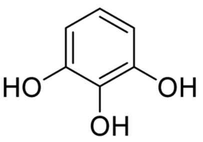
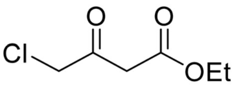
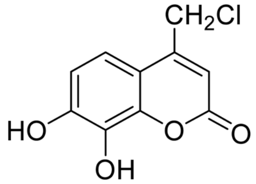
Sr. no.	Phenol	β-Keto ester	Product	Time (min)	Yield (%)
1	 (**1a**)	 (**2a**)	 (**3a**)	60	92
2	 (**1b**)	 (**2a**)	 (**3b**)	60	80
3	 (**1c**)	 (**2a**)	 (**3c**)	40	83
4	 (**1d**)	 (**2a**)	 (**3d**)	40	84
5	 (**1e**)	 (**2b**)	 (**3e**)	80	65
6	 (**1f**)	 (**2b**)	 (**3f**)	80	74
7	 (**1g**)	 (**2b**)	 (**3g**)	90	75
8	 (**1a**)	 (**2b**)	 (**3h**)	50	92

Table 2 (*Contd.*)

Sr. no.	Phenol	β-Keto ester	Product	Time (min)	Yield (%)
9	 (**1d**)	 (**2b**)	 (**3i**)	55	87

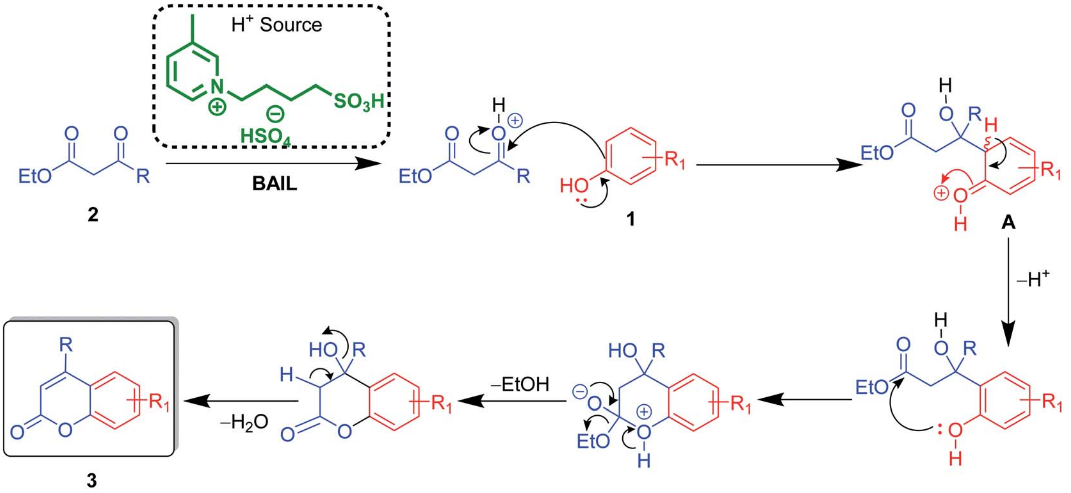


Fig. 3 Proposed Mechanism of the reaction.

reaction kinetics was for ethyl chloroacetoacetate (**2b**) from both β-ketoesters due to its inductive effect and high reactivity, in turn. Electron donating groups such as methyl and hydroxyl ones, substituted on *ortho*- or *para*- to both hydroxyls of resorcinol, also indicated best reaction rates and yields (>80%). Reaction of 1-naphthol (**1e**) took relatively longer time due to the adjacent benzene ring present in it. Consequently, the catalyst is efficient for the synthesis of coumarin derivatives starting from different phenols substituted with electron-donating groups. A plausible mechanism of the reaction is provided in Fig. 3. Pechmann condensation between substituted phenol **1** and ethyl acetoacetate **2** is proposed to happen by BAIL catalysis. Condensation followed by intramolecular cyclization of resultant intermediate **A**, elimination of ethanol from cyclized product and subsequent dehydration led to the final targeted product **3**.

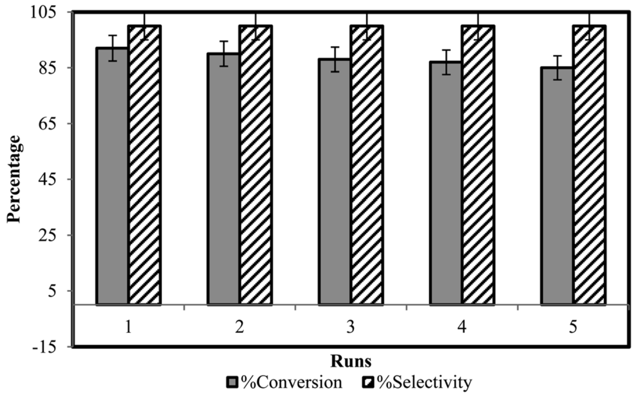


Fig. 4 Recycling of [MBSPy][HSO$_4$] catalyst.

3.3. Catalyst recycling

After completion of reaction and collection of coumarin derivatives *via* filtration, BAIL catalyst was regenerated by water

Table 3 Analysis of variance (ANOVA) for the effect of different concentrations of coumarin derivatives on biomass of *Macrophomina phaseolina*

Sources of variation	df	SS	MS	*F* values
Compounds (*P*)	10	4979	497.9	3098[a]
Concentration (*C*)	6	406	67.7	420[a]
$P \times C$	60	173	2.9	18[a]
Error	154	25	0.16	
Total	230	5584		

[a] Significant at $P \leq 0.001$.

Table 4 Minimum inhibitory concentrations of fungicide mancozeb and coumarine derivatives against *Macrophomina phaseolina*[a]

			Time (h)					
Treatments	Compound conc. (mg mL^{-1})	DMSO conc. (μL mL^{-1})	24	48	72	96	120	Fungal biomass (mg)
Control	0	10	+	+	+	+	+	16.8 ± 0.20 D
	0	5	+	+	+	+	+	17.7 ± 0.15 CD
	0	2.5	+	+	+	+	+	17.7 ± 0.25 CD
	0	1.25	+	+	+	+	+	18.6 ± 0.26 BC
	0	0.625	+	+	+	+	+	19.0 ± 0.26 A-C
	0	0.3125	+	+	+	+	+	19.5 ± 0.18 AB
	0	0.1562	+	+	+	+	+	20.5 ± 0.17 A
Mancozeb	2	10	−	−	−	−	−	0 ± 0.0 c
	1	5	−	−	−	−	−	0 ± 0.0 c
	0.5	2.5	−	−	−	−	−	0 ± 0.0 c
	0.25	1.25	−	−	−	−	−	0 ± 0.0 c
	0.125	0.625	−	−	−	−	−	0 ± 0.0 c
	0.0625	0.3125	−	−	−	−	−	0 ± 0.0 c
	0.0312	0.1562	−	−	−	−	−	0 ± 0.0 c
Compound **3a**	2	10	−	−	+	+	+	3.2 ± 0.23 S-W
	1	5	−	−	+	+	+	4.4 ± 0.15 Q-U
	0.5	2.5	−	−	+	+	+	4.5 ± 0.15 Q-T
	0.25	1.25	−	−	+	+	+	4.8 ± 0.20 M-R
	0.125	0.625	−	−	+	+	+	5.7 ± 0.17 K-Q
	0.0625	0.3125	−	−	+	+	+	6.3 ± 0.15 I-N
	0.0312	0.1562	−	−	+	+	+	6.9 ± 0.06 H-K
Compound **3b**	2	10	−	−	+	+	+	4.4 ± 0.19 Q-T
	1	5	−	−	+	+	+	4.4 ± 0.20 Q-T
	0.5	2.5	−	−	+	+	+	5.3 ± 0.18 L-Q
	0.25	1.25	−	−	+	+	+	6.2 ± 0.09 I-P
	0.125	0.625	−	−	+	+	+	6.3 ± 0.17 I-N
	0.0625	0.3125	−	−	+	+	+	7.2 ± 0.09 G-K
	0.0312	0.1562	−	−	+	+	+	7.4 ± 0.12 F-J
Compound **3c**	2	10	−	−	−	−	+	1.4 ± 0.12 YZa-c
	1	5	−	−	−	−	+	1.4 ± 0.18 YZa-c
	0.5	2.5	−	−	−	−	+	1.3 ± 0.06 Za-c
	0.25	1.25	−	−	+	+	+	3.6 ± 0.23 R-V
	0.125	0.625	−	−	+	+	+	4.3 ± 0.18 Q-U
	0.0625	0.3125	−	−	+	+	+	6.3 ± 0.09 I-O
	0.0312	0.1562	−	−	+	+	+	7.4 ± 0.12 G-J
Compound **3d**	2	10	−	−	−	−	+	2.3 ± 0.15 V-ZAB
	1	5	−	−	−	+	+	4.6 ± 0.13 P-S
	0.5	2.5	−	−	+	+	+	6.4 ± 0.12 I-M
	0.25	1.25	−	−	+	+	+	7.0 ± 0.12 H-K
	0.125	0.625	−	−	+	+	+	7.6 ± 0.44 E-I
	0.0625	0.3125	−	−	+	+	+	8.1 ± 0.20 E-H
	0.0312	0.1562	−	−	+	+	+	8.2 ± 0.19 E-H
Compound **3e**	2	10	−	−	−	−	+	0.7 ± 0.12 bc
	1	5	−	−	−	−	+	0.8 ± 0.27 a-c
	0.5	2.5	−	−	−	−	+	1.5 ± 0.20 X-Za-c
	0.25	1.25	−	−	−	−	+	2.9 ± 0.20 T-Y
	0.125	0.625	−	−	+	+	+	4.6 ± 0.18 O-S
	0.0625	0.3125	−	−	+	+	+	5.0 ± 0.15 M-R
	0.0312	0.1562	−	−	+	+	+	6.4 ± 0.29 I-N
Compound **3f**	2	10	−	−	−	−	+	1.4 ± 0.20 X-Za-c
	1	5	−	−	−	−	+	1.4 ± 0.12 X-Za-c
	0.5	2.5	−	−	−	−	+	1.4 ± 0.18 X-Za-c
	0.25	1.25	−	−	−	−	+	1.4 ± 0.09 X-Za-c
	0.125	0.625	−	−	−	−	+	1.7 ± 0.12 W-Zab
	0.0625	0.3125	−	−	+	+	+	1.8 ± 0.37 W-Zab
	0.0312	0.1562	−	−	+	+	+	2.5 ± 0.11 V-Z
Compound **3g**	2	10	−	−	−	−	+	3.0 ± 0.34 T-X
	1	5	−	−	+	+	+	5.0 ± 0.37 M-R
	0.5	2.5	−	−	+	+	+	5.2 ± 0.18 L-Q
	0.25	1.25	−	−	+	+	+	5.8 ± 0.17 J-Q
	0.125	0.625	−	−	+	+	+	6.7 ± 0.27 H-L

Table 4 (*Contd.*)

Treatments	Compound conc. (mg mL^{-1})	DMSO conc. (μL mL^{-1})	Time (h)					Fungal biomass (mg)
			24	48	72	96	120	
	0.0625	0.3125	−	−	+	+	+	8.8 ± 0.09 E-G
	0.0312	0.1562	−	−	+	+	+	9.2 ± 0.12 E
Compound **3h**	2	10	−	−	−	−	+	2.4 ± 0.23 V-Z
	1	5	−	−	−	−	+	2.5 ± 0.09 V-Z
	0.5	2.5	−	−	−	−	+	2.5 ± 0.18 V-Z
	0.25	1.25	−	−	−	+	+	4.2 ± 0.40 Q-U
	0.125	0.625	−	−	−	+	+	4.8 ± 0.22 N-S
	0.0625	0.3125	−	−	+	+	+	6.8 ± 0.12 H-L
	0.0312	0.1562	−	−	+	+	+	9.0 ± 0.12 EF
Compound **3i**	2	10	−	−	−	−	+	1.5 ± 0.18 X-Za-c
	1	5	−	−	−	−	+	1.6 ± 0.21 W-Za-c
	0.5	2.5	−	−	−	−	+	1.3 ± 0.12 YZa-c
	0.25	1.25	−	−	−	−	+	1.8 ± 0.12 W-Za-c
	0.125	0.625	−	−	−	−	+	1.9 ± 0.26 W-Za-c
	0.0625	0.3125	−	−	−	−	+	2.8 ± 0.19 U-Z
	0.0312	0.1562	−	−	−	−	+	3.0 ± 0.25 T-X
Critical value for comparison ($P \leq 0.001$)								1.6

[a] Values with different letters show significant difference as determined by LSD test at 5% level of significance. ± indicates standard errors of means of three replicates. − no fungal growth. + fungal growth appeared.

evaporation from the filtrate. It is washed with distilled ethyl acetate to eliminate the possibility of any impurities in it. The recovered catalyst was monitored for its activity up to five reaction cycles (Fig. 4). Recycling reactions show 100% selectivity of recovered catalyst for coumarins synthesis. For the first run carried out with freshly prepared ionic liquid catalyst, conversion rate is 92%, and it is reduced just to 85% for the fifth run (Table 3) thus exhibiting high recycling ability of the catalyst.

3.4. Antifungal activity against *Macrophomina phaseolina*

ANOVA presented in Table 3 clearly indicated the significant effect of compounds (P), concentration (C) as well as $P \times C$ for fungal biomass production at $P \leq 0.001$. Results regarding antifungal activity of different derivatives of coumarin are shown in Table 4. Different concentrations of DMSO in control also had significant effect on fungal growth. With an increase in DMSO concentration, a gradual decrease in biomass of the fungal pathogen was recorded. The reference fungicide mancozeb was found most effective in controlling the fungal growth. It's all concentrations completely inhibited the fungal growth throughout the experiment with MIC 0.0312 mg mL^{-1} after 120 h. None of the synthesized derivatives of coumarins completely controlled the fungal growth at the end of experiment (120 h). However, different derivatives delayed the fungal growth for variable time periods. Derivatives **6** and **9** proved more antifungal than rest of the synthesized compounds. All the concentrations of compound **3i** controlled fungal growth up to 96 h and the fungal growth was recorded after 120 h with 85–91% decrease in fungal biomass over different corresponding control treatments. Likewise, compound **3f** decreased fungal biomass by 90–92% over control. Other compounds were less effective than **3f** and **3i**. Compounds **3(a–e)**, **3g** and **3h** reduced fungal biomass by 66–81%, 64–74%, 64–92%, 60–86%, 69–96%, 55–82% and 56–86%, respectively.

4. Conclusion

Doubly Brønsted acidic task specific ionic liquid (TSIL) is utilized as effective catalyst for the production of potential fungicidal coumarin derivatives for sustainable agriculture. Nine different compounds were prepared using substituted phenol and ethyl acetoacetate or its chloro-derivative under ambient, solvent-free conditions in significantly high yields. The synthesis is highly green and benign due to recoverable and recyclable TSIL catalyst, ambient conditions like room temperature and short reaction times. 93% Yield was obtained at room temperature in just one hour with only 1 mol% catalyst. From all the tested compounds, compound **3f** and **3i** showed excellent antifungal activity comparable to reference fungicide mancozeb.

Conflicts of interest

There are no conflicts to declare.

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