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[BMIm]HSO_4 as a Green and Highly Efficient Catalyst for One-pot Synthesis of 3-Substituted Indoles under Ultrasound Irradiation

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A practical and green synthesis of 3-substituted indoles is reported *via* three-component coupling reaction of indoles, aldehydes and *N*-methylaniline in the presence of the acidic ionic liquid 1-butyl-3-methylimidazolium hydrogen sulfate ([BMIm]HSO_4) under ultrasound irradiation at room temperature. The significant features of this procedure are high yields of the products, simple work-up, operational simplicity and non-toxicity of the catalyst. Moreover, [BMIm]HSO_4 is successfully reused for four cycles without significant loss of activity.

Keywords: Indoles, *N*-methylaniline, Aldehyde, Ionic liquid

INTRODUCTION

Designing novel synthetic methodologies for preparation of biologically active molecules is one of the main challenges in the field of modern medicinal and combinatorial chemistry. Chemists are investigating new methods and reactions using molecular complexity and diversity in natural and biologically relevant systems [1,2].

Combining three or more different starting materials in a one-pot method, is a way to obtain this goal. Multicomponent reactions (MCRs) are synthetically appropriate organic reactions [3,4]. These reactions are of specific importance in modern organic synthesis to produce compound collections for screening purposes, simple procedures, convergence, facile execution and atom economy [3]. This methodology makes different molecular complexes by the facile formation of several new covalent bonds in a one-pot transformation which is particularly well adapted for combinatorial synthesis [5]. In addition, this procedure reduces time and saves both energy and raw materials because there is no need to isolate any intermediate substances during the processes [6]. Thus, extensive attention has been paid to the development of new and enhanced one-pot multicomponent reactions [7-14].

In this way, catalysts help the synthetic chemists to achieve many of these goals. Catalysts could be simple, complex, synthetic and natural. They are capable of creating an otherwise impossible reaction to occur in the mildest potential circumstances [15]. Ionic liquid family are important catalysts that has taken significant consideration of the synthetic chemists recently [16-22].

In recent years, ionic liquids (ILs) have been appealed increasingly in green organic synthesis [16]. Initially introduced as alternative green reaction media, ionic liquids marched today because of their unique chemical and physical features of negligible volatility, outstanding thermal stability, controlled miscibility, and the diversity of structures available [23-26].

Amongst which, organic salts that are liquid below 100 °C, also called as room-temperature ILs, have gained significant attention as substitutes for volatile organic solvents. They are categorized as green solvents due to their nonflammable, non-volatile and recyclable properties [27-29].

This agents can diminish the use of dangerous and polluting organic solvents as well. They have also increased interest because of their unique set of properties not reachable with any other materials [30-32]. Usually large

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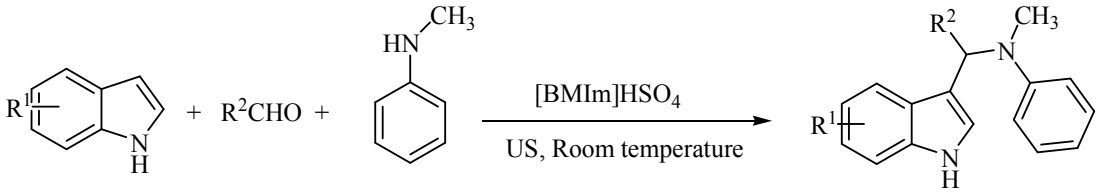


1 **2** **3** **4**

R^1= H, Br
R^2= C_6H_5, 4-Cl-C_6H_5,...

Scheme 1. Synthesis of 3-substituted indole derivatives in the presence of [BMIm]HSO_4

amounts of organic solvents are used in the pharmaceutical and fine chemical industries for the chemical reactions and separation processes. The fact is that these solvents often add to the environment burden and the cost of processing and recovery operations due to their volatile and also water-solubility to pollute air emissions and aqueous discharge streams [33].

The indole nucleus is undoubtedly the best recognized heterocycle with common and important feature of variety of natural products and medicinal mediators [34-36]. Indole derivatives are well known because of their high affinity to bind to many receptors. In particular, 3-substituted indoles are used to build blocks for the synthesis of many biologically active natural products [37]. The indole products act as a scaffold in a number of antibacterial [38], and antiviral [39] agents, and protein kinase inhibitors [40]. Indole-3-carbinols have been previously recognized to exhibit anticancer activities against a number of human cancers. They perform through different cellular signaling pathways [41]. So, synthesis and reactions of indoles have gained great importance in organic synthesis.

Although several methods have been reported in the literature for the synthesis of substituted indoles [42-48], only a few reports on the access of substituted 3-aminoalkylated indoles by multicomponent reaction protocols have been documented [49-59]. The synthesis of 3-aminoalkylated indole derivatives have been described in the presence of phosphomolybdic acid-silica (PMA-SiO_2) [51], 2,4,6-trichloro-1,3,5-triazine (TCT) [52], 3-chlorophenylboronic acid [53], Yb$(OTf)_3$-SiO_2 [35], zwitterionic-salt 4-(1-imidazolium)-butane sulfonate (IBS) [54], bromodimethylsulfonium bromide (BDMS) [55], silver triflate [56], $ZnCl_2$ [57] and $Fe(NO_3)_3.9H_2O$ [58]. So, a wide scope remains for the improvement of clean and efficient procedures for the preparation of these materials through a convenient and environmentally pleasant method.

In the last three decades, the benefits of ultrasounds in the field of organic chemistry have pronounced significant considerations [59]. Ultrasonic irradiation transfers activating energy to reacting molecules and provides a distinctive distribution of penetrating waves to accelerate numerous catalytic reactions in homogeneous and heterogeneous systems in a safe way [60]. With respect to the yields and reaction times, significant enhancements can be recognized in this way [61,62]. Ultrasound-assisted organic method is a green and clean synthetic method which seems to be a powerful technique to improve organic reactions and practical syntheses [63,64]. In this study, we describe the efficiencies of the ionic liquid [BMIm]HSO_4 for promoting the synthesis of 3-aminoalkylated indoles *via* rapid three-component coupling reaction between indoles, aldehydes, and *N*-alkylanilines under ultrasound irradiation at room temperature (Scheme 1).

EXPERIMENTAL

All chemicals and solvents were purchased from Merck or Fluka Chemical Companies and used without more purification. Also, products were illustrated by physical methods (mp), and spectral methods (IR, ^{1}H NMR, ^{13}C NMR). Melting points were determined on an Electrothermal 9200 apparatus. IR spectra were achieved on a Shimadzu FTIR-8400S spectrometer. ^{1}H NMR spectra was obtained on a BRUKER DRX-300 AVANCE

spectrometer at 300 MHz. Ultrasound promotted reactions were performed using a EUROSONIC®4D ultrasound cleaner with a frequency of 50 kHz and a nominal power of 350 W. The reaction flask was placed in the maximum energy area in the cleaner, where the surface of reactants (reaction vessel) is mildly lower than the level of the water. The temperature of the water bath was adjusted on the basis of room tempreature.

The Procedure for the Synthesis of [BMIm]HSO_4

1-Butyl-3-methylimidazolium hydrogen sulfate was synthesized due to the described method for 1-hexyl-3-methylimidazolium hydrogen sulfate [HMIm]HSO_4 [65]. A dropwise addition of one equivalent of concentrated sulfuric acid (97%) to a cooled solution of 1-butyl-3-methylimidazolium chloride (1 eq) in anhydrous methylene chloride made this reagent. The mixture of these materials were refluxed for 48 h. The HCl formed by this reaction was collected with dissolving it in deionized water at 0 ºC. Titration was performed to measure the acidity of the aqueous solution, using NaOH as a control for completion of the reaction. The solution was cooled to room temperature following completion of the reaction, and dichloromethane was ommitted in a rotary evaporator. The ionic liquid was dried under high vacuum at 60 ºC for 7 h.

General Procedure for the Preparation of 3-Substituted Indole

A catalytic amount of [BMIm]HSO_4 (1 ml) was added to mixture benzaldehyde (1 mmol, 0.106 g) and *N*-methylaniline (1.5 mmol, 0.142 g). The mixture was sonicated at room temperature. After 10 min, indole (1 mmol, 0.117 g) was admixed to the reaction and the mixture was allowed to be sonicated. About 25 ml cold distilled water was added to the mixture following completion of reaction as indicated by TLC (ethyl acetate/*n*-hexane) (3:1), and ethyl acetate (2 × 20 ml) was used to extract the product. Solvent was removed in vacuum to catch the crude product.

The Selected Spectral Data

N-[(1H-Indol-3-yl)-phenylmethyl]-N-methyl-phenyl-amine (4a). Brown solid, m.p.: 145-147 °C. IR (KBr) (ν_{max}/cm^{-1}): 3416, 3362, 2921, 2856, 1452, 739, ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.76 (s, 3 H), 5.54 (s, 1H), 6.51 (d, *J* = 8.3 Hz, 3H), 6.09-7.04 (m, 3H), 7.09-7.38 (m, 9H), 7.81 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.65, 47.92, 110.92, 112.36, 119.16, 120.47, 121.85, 123.92, 125.90, 127.04, 128.12, 128.89, 129.64, 132.90, 136.64, 144.68, 147.51.

N-[(4-Chlorophenyl)(1H-indol-3-yl)methyl]-N-methyl-phenyl-amine (4b). Brown solid, m.p.: 183-185 °C. IR (KBr) (ν_{max}/cm^{-1}): 3354, 3034, 2926, 2854, 1345, 758, ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.90 (s, 3H), 5.63 (s, 1H), 6.50 (d, 2H, *J* = 7.8 Hz), 6.90 (d, 4H, *J* = 7.8 Hz), 7.05-7.16 (m, 6H), 7.43 (d, 2H, *J* = 4.4 Hz), 7.86 (s, 1H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.31, 30.82, 43.50, 110.82, 115.03, 120.01, 121.13, 121.79, 124.58, 128.01.

N-[(1H-Indol-3-yl)-p-tolyl-methyl]-N-methyl-phenyl-amine (4c). Brown solid, m.p.: 160-161 °C. IR (KBr): 3408, 3376, 3215, 3041, 2861, 1875, 1613, 1512, 1451, 736, 519 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.29 (s, 3 H), 2.78 (s, 3H), 5.43 (s, 1H), 6.45 (d, *J* = 8.3 Hz, 2H), 6.82-7.31 (m, 11H), 6.98 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.97, 30.85, 47.44, 110.91, 112.30, 119.08, 119.96, 120.55, 121.77, 123.86, 127.02, 128.71, 128.78, 129.57, 133.02, 135.25, 136.61, 141.66, 147.45.

N-((1H-indol-3-yl)(3-nitrophenyl)methyl)-N-methyl-phenyl-amine (4d). Brown solid, m.p.: 189-191 °C. IR (KBr): 3415, 2925, 1613, 1516, 1611, 1344, 745, 425 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.84 (s, 3H), 5.68 (s, 1H), 6.66-6.57 (m, 3H), 7.02-7.06 (m, 3H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.45-7.37 (m, 2H), 7.58 (d, *J* = 8.0 Hz, 1H), 8.12-8.06 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 30.60, 47.61, 111.00, 112.31, 119.20, 119.52, 121.21, 123.50, 123.72, 126.51, 128.70, 129.51, 130.82, 134.85, 136.41, 146.43, 148.12, 147.80, 146.82.

N-((4-chlorophenyl)(5-methoxy-1H-indol-3-yl)-N-methyl)-phenyl-amine (4e). Brown solid, m.p.: 129-131 °C. IR (KBr): 3368, 3188, 2925, 2856, 1743, 1615, 1458, 1205, 1092, 925, 816, 467, 818, 925 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.84 (s, 3H), 3.66 (s, 3H), 5.43 (s, 1H), 6.45-6.54 (m, 4H), 6.74-6.76 (m, 2H), 6.94 (d, *J* = 8.3 Hz, 2H), 7.12-7.26 (m, 6H), 7.25 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.23, 31.12, 47.72, 55.98, 102.26, 111.76, 112.03, 112.57, 120.55, 124.87, 127.72, 135.49, 128.95, 129.01, 129.82, 132.02, 133.31, 141.85, 147.72, 153.78.

N-((1H-Indol-3-yl)(3-methoxyphenyl)methyl)-N-methyl)-phenyl-amine (4f). Brown solid, m.p.: 136-139

Table 1. Optimization of the Reaction Conditions[a]

Entry	Reaction conditions	Catalyst (X ml)	Time	Yield (%)[a]
1	Neat/rt	-	4 h	Trace
2	Neat/rt	[BMIm]HSO_4 (0.5 ml)	2:30 h	65
3	Neat/rt	[BMIm]HSO_4 (1 ml)	1:30 h	94
4	Neat/40 °C	[BMIm]HSO_4 (1 ml)	2 h	92
5	Neat/50 °C	[BMIm]HSO_4 (1 ml)	2:30 h	87
6	Neat/rt	[BMIm]HSO_4 (1.5 ml)	2:30 h	93
7	CH_3CN/rt	[BMIm]HSO_4 (1 ml)	4 h	45
8	DMF/rt	[BMIm]HSO_4 (1 ml)	4:30 h	43
9	EtOH/rt	[BMIm]HSO_4 (1 ml)	2:30 h	92
10	H_2O/rt	[BMIm]HSO_4 (1 ml)	2:30 h	89
11	H_2O-EtOH/rt	[BMIm]HSO_4 (1 ml)	2:30 h	90
12	Neat/rt/US[b]	-	3 h	Trace
13	Neat/rt/US	[BMIm]HSO_4 (0.5 ml)	2:30 h	69
14	Neat/rt/US	[BMIm]HSO_4 (1 ml)	50 min	98
15	Neat/40 °C/US	[BMIm]HSO_4 (1 ml)	1:30 h	93
16	Neat/50 °C/US	[BMIm]HSO_4 (1 ml)	2 h	88
17	Neat/rt/US	[BMIm]HSO_4 (1.5 ml)	2 h	94
18	CH_3CN/rt/US	[BMIm]HSO_4 (1 ml)	3:30 h	49
19	DMF/rt/US	[BMIm]HSO_4 (1 ml)	4:30 h	48
20	EtOH/rt/US	[BMIm]HSO_4 (1 ml)	2 h	93
21	H_2O/rt/US	[BMIm]HSO_4 (1 ml)	2:30 h	89
22	H_2O-EtOH/rt/US	[BMIm]HSO_4 (1 ml)	2 h	92

[a]A mixture of indole (1 mmol), benzaldehyde (1 mmol) and *N*-methylaniline (1.5 mmol). [b]Ultrasound irradiation.

°C. IR (KBr): 3365, 3185, 2915, 1756, 1635, 1463, 1187, 954, 816, 465, 815, 923 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.83 (s, 3H), 3.75 (s, 3H), 5.56 (s, 1H), 6.57 (d, J = 7.6 Hz, 2H), 6.84-6.81 (m, 2H), 7.08-6.86 (m, 2H), 7.20-7.17 (m, 3H), 7.43-7.22 (m, 3H), 7.94 (s, 2H). ^{13}C NMR (750 MHz, $CDCl_3$): δ 31.02, 48.02, 55.54, 110.12, 111.23, 112.52, 115.02, 120.03, 120.12, 121.63, 123.91, 127.12, 129.75, 132.92, 136.74, 145.82, 146. 54, 147.63, 148.52,

159.50.

N-((1H-Indol-3-yl)(4-hydroxyphenyl)methyl)-N-methyl)-phenyl-amine (4g). Brown solid, m.p.: 138-140 °C. IR (KBr): 3409, 2924, 1710, 1598, 1453, 1263, 745, 425 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.83 (s, 3H), 5.31 (s, 1H), 5.84 (s, 1H), 6.75-6.57 (m, 4H), 7.41-7.01 (m, 7H), 7.93 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 31.01, 39.52, 47.12, 112.12, 115.13, 119.32, 120.01, 122.01, 123.60, 123.98, 127.13, 129.93, 130.15, 130.52, 133.54, 136.87, 153.80.

N-((1H-Indol-3-yl)-(4-methoxy-phenyl)-methyl]-N-methyl-phenyl-amine (4h). Brown solid, m.p.: 175-177 °C. IR (KBr): 3362, 3416, 2856, 1615, 1453, 736, 602, 453 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 2.82 (s, 3H), 3.81 (s, 3H), 5.53 (s, 1H), 6.55 (d, J = 8.0 Hz, 3H), 6.82 (d, J = 7.6, 2H), 7.05-6.97 (m, 3H), 7.15 (d, J = 7.6 Hz, 3H), 7.43-7.25 (m, 3H), 7.92 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 30.95, 47.12, 55.23, 110.98, 112.43, 113.54, 119.26, 120.15, 121.97, 123.94, 127.13, 129.87, 133.97, 147.54, 157.93, 168.98.

N-((5-Bromo-1H-indol-3-yl)(phenyl)methyl)-N-methyl-phenyl-amine (4i). Brown solid, m.p.: 210-212 °C. IR (KBr): 3375, 3221, 3035, 2923, 1725, 1615, 1514, 1456, 1021, 745, 422 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.83 (s, 3H), 5.52 (s, 1H), 6.58 (d, J = 8.0 Hz, 3H), 7.02 (d, J = 8.0 Hz, 2H), 7.27-7.23 (m, 7H), 7.39 (s, 1H), 8.07 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 31.12, 47.71, 112.50, 112.71, 120.42, 122.51, 125.20, 126.21, 128.31, 128.92, 129.73, 132.73, 135.33, 143.42, 147.54.

N-[(5-Bromo-1H-indol-3-yl)(p-tolyl)methyl]-N-methyl-phenyl-amine (4j). Brown solid, m.p.: 195-197 °C. IR (KBr): 3412, 2923, 1713, 1605, 15117, 1257, 1043, 764, 695, 420 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.37 (s, 3H), 2.61 (s, 3H), 5.52 (s, 1H), 6.35 (d, 2H, J = 8.0 Hz), 6.53 (d, 2H, J = 4.0 Hz), 6.69 (d, 2H, J = 4.2 Hz), 7.03-7.11 (m, 4H), 7.21 (d, 2H, J = 4.2 Hz), 7.34 (d, 1H, J = 7.8 Hz), 10.32 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.40, 35.21, 49.42, 110.21, 114.62, 116.90, 120.11, 122.23, 124.41, 127.13, 128.91, 129.42, 129.69, 132.83, 136.17, 140.19, 144.48, 150.18.

RESULTS AND DISCUSSION

Herein, we described a novel and effective protocol for promoting the synthesis of 3-aminoalkylated indoles using [BMIm]HSO_4 ionic liquid as a catalyst-solvent under ultrasound irradiation (Scheme 1). A reaction between indole, aldehyde and *N*-methylaniline was studied at first by screening the reaction conditions. We examined the influence of the reaction temperature, choice of solvent, and amount of ionic liquid to recognize the optimum conditions (Table 1). Various solvents, such as C_2H_5OH, H_2O, CH_3CN, and C_2H_5OH/H_2O using [BMIm]HSO_4 as a catalyst were applied. The best result was obtained with [BMIm]HSO_4 in the lack of solvent at room temperature (Table 1, entry 14). The effect of the amount of the catalyst in the reaction was also examined. The best results were obtained using 1 ml of the catalyst. Using lower amounts of the catalyst resulted in lower yields. Also, the absence of the catalyst provided the trace yield of the product (Table 1, entry 1, 12). The conditions were enhanced for a 100% conversion. We also performed experiments in 25, 40, and 50 °C under ultrasonic irradiation to study the effect of temperature on this synthesis, (Table 1, entries 14-16).

After optimizing the settings, we examined the generality of the conditions to other substrates with the use of several aromatic aldehydes bearing electron-withdrawing and electron-donating groups (Scheme 1). The results revealed the effects of different groups on the aromatic ring on the time required and the yield of the reactions. Results showed that the presence of electron-donating, and electron-accepting substituents on the reacting aldehydes do not influence the general yield and rate of the reactions advisable. The reactions were performed within 50-80 min at room temperature, and the satisfactory yields were delivered (Table 2). As indicated in Table 2, in all cases, the reaction led to the products in good yields. To the best of our knowledge, this new procedure provides the first example of an eco-friendly and green approach for the synthesis of 3-substituted indoles in the presence of a catalytic amount of [BMIm]HSO_4 under ultrasound irradiation.

The efficiency of [BMIm]HSO_4 ionic liquid was compared with the previously reported catalysts in synthesis of 3-aminoalkylated indole derivatives. We have summarized the results obtained by the use of this ionic liquid and those reported on application of some other

Table 2. Synthesis of the 3-Substituted Indole Derivatives

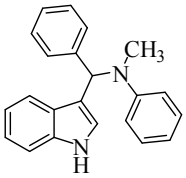
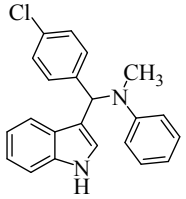
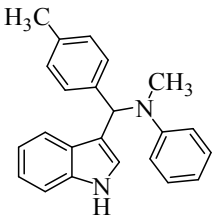
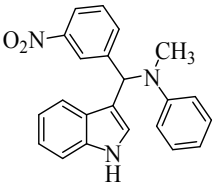
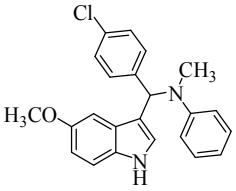
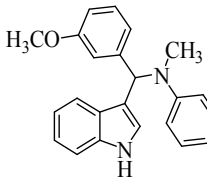
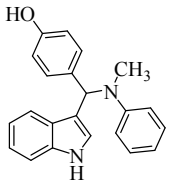
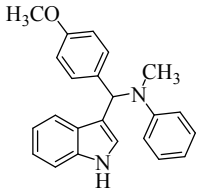
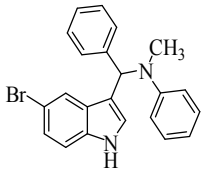
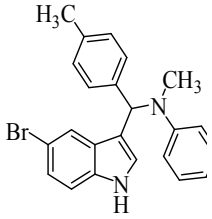
Entry	R^1	R^2	Product[a]	Time (min)	Yield (%)[b]	M.p. (°C) [Ref.]
1	H	C_6H_5	 4a	50	98	144-146 [51]
2	H	4-Cl-C_6H_4	 4b	55	94	181-183 [53]
3	H	4-H_3C-C_6H_4	 4c	50	92	160-161 [58]
4	H	3-NO_2-C_6H_4	 4d	75	93	189-191 [56]
5	5-OCH_3	4-Cl-C_6H_4	 4e	60	95	129-131 [51]

Table 2. Continued

6	H	3-OCH3-C6H4	 4f	70	94	134-136 [56]
7	H	4-HO-C_6H_4	 4g	75	92	138-140 [56]
8	H	4-H_3CO-C_6H_4	 4h	65	93	175-177 [58]
9	5-Br	C_6H_5	 4i	70	85	210-212 [56]
10	5-Br	4-H_3C-C_6H_4	 4j	80	93	195-197 [53]

[a]All products were characterized by ^{1}H NMR and IR spectral data and comparison of their melting points with those of authentic samples. [b]Isolated yield.

Table 3. Synthesis of 3-Substituted Indole 4a Using $[BMIm]HSO_4$ and Comparison with some other Reported Catalysts[a]

Entry	Reaction conditions	Catalyst (X mol%)	Time	Yield (%)[a]	Ref.
1	CH_3CN/rt	Phosphomolybdic acid-silica ($PMA\text{-}SiO_2$) (5 mol%)	3:30 h	80	[51]
2	Neat/rt	Phosphomolybdic acid-silica ($PMA\text{-}SiO_2$) (5 mol%)	1:45 h	90	[51]
3	CH_3CN/rt	2,4,6-Trichloro-1,3,5-triazine (TCT) (10 mol%)	2:30 h	87	[52]
4	CH_3CN/rt	3-Chlorophenylboronic acid (20 mol%)	14 h	80	[53]
5	CH_3CN/rt	$Yb(OTf)_3\text{-}SiO_2$ (5 mol%)	2 h	78	[35]
6	Neat/60 °C	4-(1-Imidazolium)-butane sulfonate (IBS) (20 mol%)	3 h	82	[54]
7	EtOH/rt	Bromodimethylsulfonium bromide (BDMS) (10 mol%)	2:30 h	96	[55]
8	CH_3CN/rt	AgOTf (10 mol%)	4 h	76	[56]
9	Neat/rt/US	$[BMIm]HSO_4$ (1 ml)	50 min	98	This work

[a]Isolated yield.

catalysts to the synthesis of *N*-[(1*H*-Indol-3-yl)-phenylmethyl]-*N*-methyl-phenyl-amine 4a in Table 3. Despite the own merit of each of these methods, some suffer from long reaction times, low yields, use of large quantities of volatile organic solvents, and tedious work-up. This reaction takes shorter time to complete and affords high yield in the presence of $[BMIm]HSO_4$ at room temperature under ultrasound irradiation.

In the next phase of study, the viability of catalysis by the recycled ionic liquid was evaluated. In this regard, preparation of 4a was chosen as the model. Following completion of the reaction, the ionic liquid was ommitted simply by dissolution in water added to the reaction mixture and then recovered by evaporation of water at 80 °C under reduced pressure. Even after five successive retrieval and reuse in the same synthesis, the catalytic activity of the ionic liquid system remained evidently unaltered (Fig. 1).

The possible mechanism for the synthesis of 3-substituted indole derivatives 4a-j is outlined in Scheme 2. Initially, $[BMIm]HSO_4$ protonated aryl aldehyde 2 and undergoes facile Mannich condensation with *N*-methylaniline to constitute an iminium ion intermediate 5. This imminium ion is then attacked by an electron rich indole to get the desired 3-substituted indoles 4.

CONCLUSIONS

In summary, we have demonstrated the efficacy and

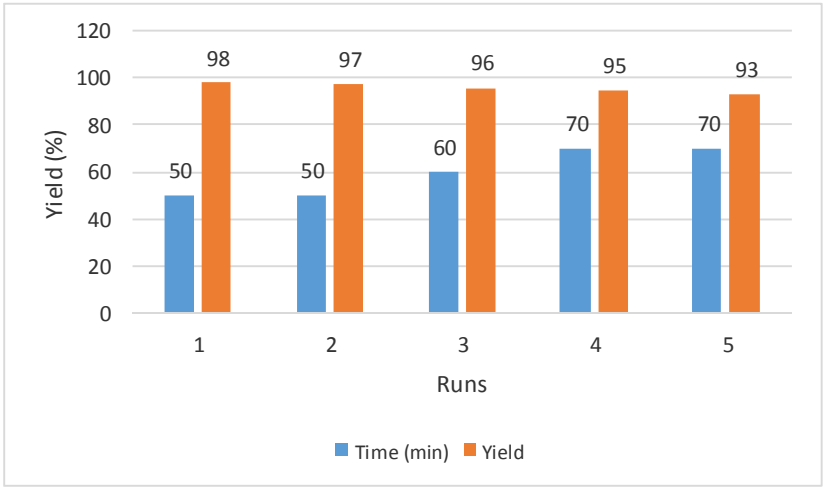
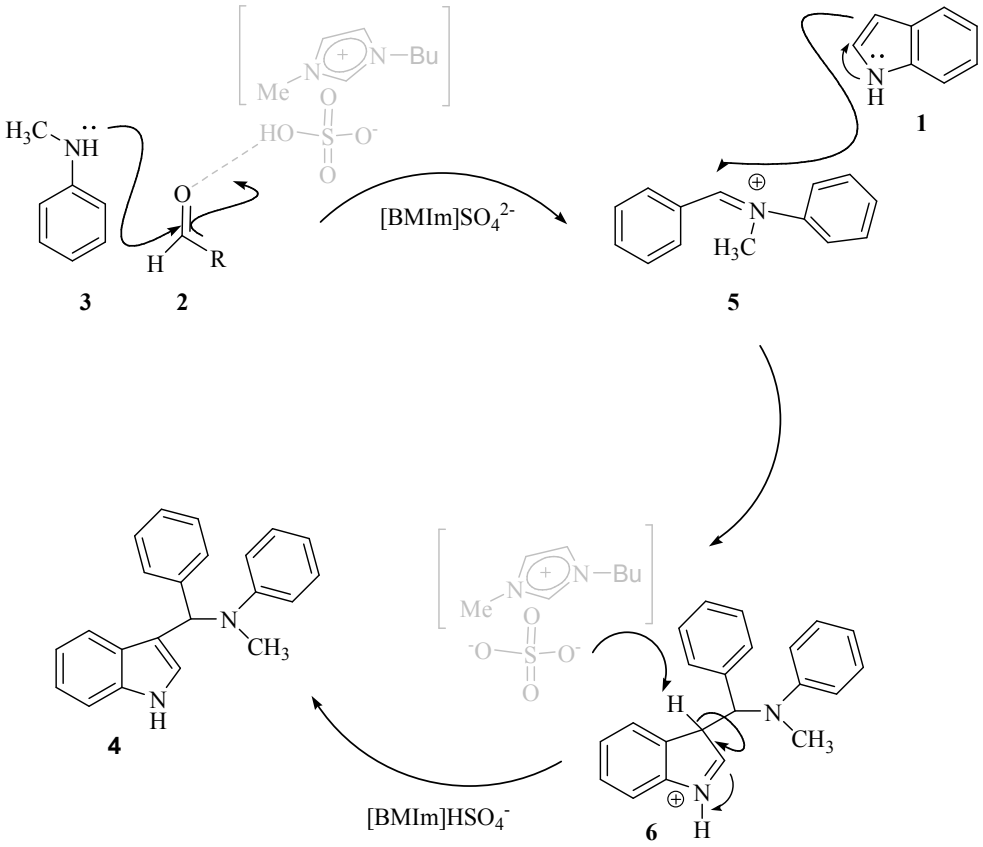


Fig. 1. Reusability of the catalyst in product 4a.



Scheme 2. Plausible mechanism for the synthesis of 3-substituted indoles in the presence of [BMIm]HSO_4

generality of [BMIm]HSO_4 as a green catalyst for the synthesis of 3-substituted indoles *via* an efficient and rapid three-component coupling reaction between indoles, aldehydes, and *N*-alkylanilines at room temperature under ultrasonic irradiation. This protocol offers several advantages such as mild reaction conditions, excellent yield, short reaction times, and simple experimental work-up.

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