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A Novel Synthesis and antimicrobial activity of Flavanone Using environmental friendly Catalyst H[bimBF$_4$]

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ABSTRACT

A high yielding and fast method for smooth conversion of substituted α-β-unsaturated carbonyl compounds (*E*) chalcones to corresponding substituted 2-phenylchroman-4-one i.e. flavanone by grinding at room temperature using ionic liquid H[bimBF4] .which is recyclable . Flavanone was synthesized and tested for antibacterial effects against Bacillus Subtalis, Escherichia coli, Staphylococcus aureus and Pseudomonas aeruginosa.. The antibacterial screening of the synthesized compounds were performed in vitro by the filter paper disc diffusion method.

Keywords: Dehydrate cyclization, Ionic liquid, Grinding, room temperature, α-β-unsaturated carbonyl compounds (*E)* chalcones compounds, antibacterial activity, Flavanone etc.

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INTRODUCTION

Flavanones are important naturally occurring organic compounds possessing a wide range of biological activities[1] used in the treatment of various diseases [2]. Different methods are used for the synthesis of flavones, includes Allan- Robinson synthesis [3], synthesis from chalcones [4] and via intramolecular witting reaction [5]. The most common method used involves Baker- Venkatramn arrangement. In this method 2- hydroxy acetophenone are converted to benzoyl ester, which in presence of base (pyridine/KOH) form 1,3 diketones. The diketones are further cyclized under strong acidic condition to afford the flavones [6]. In recent development of such dehydrative cyclization it includes the use of Amberlyst15 [7], Co^{III}(sulpr)OH [8], $FeCl_3$ [9], $Br_2/CHCl_3$ [10], EtOH/HCl [11], clay [12], NaOAc/AcOH [13] and H_2SO_4 under microwave irradiation [14]. Prenylated flavanone is a unique class of naturally occurring flavonoids characterized by the presence of a Prenylated side chain in the flavonoid skeleton. It was reported that one phenolic group and certain degree of lipophilicity are required for the activity of the flavonoids[10] Substitution of the flavonoid ring system with prenyl groups would increase their lipophilicity and consequently enhance their interaction with cellular membranes [15]. 4′,5,7-Trihydroxy-3′-prenylflavanone (1) has been isolated for the first time in 1989 from the chloroform extract of the stem bark of Erythrina eriotriocha [16] The chemical and pharmaceutical industries are always under the pressure to find out environmental friendly organic reaction methodologies. Microwave irradiation is used for a variety of organic reactions due to their use in a rapid and cleaner synthesis of organic compounds [17,18].

Ionic liquids are possible green catalyst acts as alternatives for several catalytic reactions. Ionic liquids attracted attention of researchers due to their mild reaction conditions, short reaction times and better yield, solvating ability and easy recyclibility [19]. Various reactions have been reported recently using ionic liquids as an catalyst, reaction media [20] and as rate enhancers [21].

RESULT AND DISCUSSION

Herein we wish to report for the first time a novel synthesis of flavanone **(2)** promoted by ionic liquid catalyst, **H[bimBF4**] at room temperature irradiation in excellent yield with shorter reaction time (**Scheme 1).** The ionic liquid can be recycled and reused several times. The ionic liquid H[bimBF4]was prepared as per literature method [22].

In a typical reaction, the α-β-unsaturated carbonyl compounds **(1)** in ionic liquid H[bimBF4] was grind into motor in a specified time. The progress of the reaction was monitor by TLC. After completion of the reaction, reaction mixture was directly extracted with 50% ethylacetate in petroleum ether. Compound comes in organic layer, was washed with water, brine & dried over MgSO4. Organic solvent is evaporated to afford pure flavanones (2).Ionic liquid was dried under reduced pressure & re used for another reaction gives same yield.

To evaluate the synthetic utility of the process, various substituted chalcones were prepared by the established procedure [6] and subjected to the reaction under rt grinding. The results are shown in **Table-1**.

The reaction proceeds cleanly without formation of any side product except water. The protocol of the process offers advantages in terms of simple procedure and work up, mild reaction conditions and excellent yields. The reactions are also carried out in presence of i[bbim]Br ionic liquid catalyst for comparison. The resulting flavanones are forms with same yield. The ionic liquid used for reaction was recovered and reused with identical results. Thus, the recylibility was confirmed as listed in a **Table-2.**

ANTIMICROBIAL ACTIVITY

The antibacterial activities of the synthesized compounds (d) and (f) were studied against four bacteria, viz. *Bacillus subtilis* (G+), *Escherichia coli* (G–),*Staphylococcus aureus* (G+) and *Pseudomonas aeruginosa* (G–). For the detection of antibacterial activities, the filter paper discs diffusion method was used [23]. Streptomycin sulphate was used as positive control. Nutrient agar (NA) was used as basal medium for test bacteria. The discs were prepared by impregnating them in methanol solution of each sample (1 mg/1 mL). Each culture was prepared to a turbidity equivalent to McFarland and spread on the test tube. The paper disc containing the compound were placed on the agar surface previously inoculated with suspension of each microbes to be tested. All determinations were made in duplicate. Inhibition diameter were determined after incubation at 37°C ± 1 for 24 h. The antimicrobial activity was indicated by the presence of the clear inhibition zones around each disc.

Minimum inhibition concentration

The determination of the minimum inhibitory concentration (MIC), the serial dilution technique were followed using nutrient broth medium. The MIC was defined as the lowest concentration of samples that had restricted the growth of microbial [24]. The MIC value of compound (c) were determined against *Escherichiacoli* (G–).

EXPERIMENTAL

The α-β-unsaturated carbonyl compounds **1** (1 mmol) was added in ionic liquid H[bimBF_4] (2 mmol) and grind into mortor for 10-15 min. The reaction was monitored on TLC. After completion on the reaction, the mixture was extracted 5 X 20 ml. of ethyl acetate:petrolium ether (50%+50%). Compound comes in organic layer, was again treated with water, brine & dried over MgSO4. Organic solvent is evaporated to afford pure flavones 2. Further, Ionic liquid was dried under reduced pressure & re used for another reaction gives same yield. The recovery percentage of ionic liquid is given in a Table-2.The obtained products **2a-h** were identified by comparison with authentic samples ^{1}H NMR and their melting points.

The antibacterial activity of compounds (d) and (f) has been assayed at the concentration 1000 µg/mL against four human pathogenic bacteria. Among them two were gram-positive and the other two were gram negative. The inhibitory effect of compounds (d) and (f) against these organisms are given in table 3.The screening results indicate that

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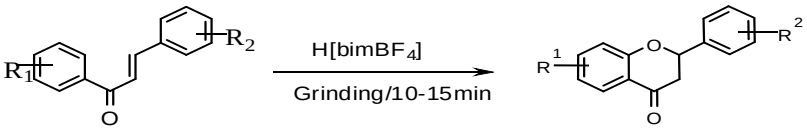
only compound (f) was active against a gram-negative bacteria, Escherichia coli with a mean zone of inhibition 12·5 ± 0·3 mm (table 3).

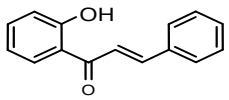
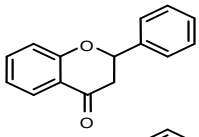
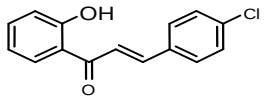
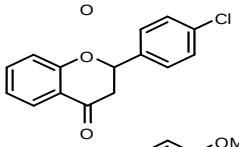
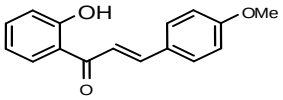
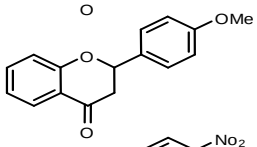
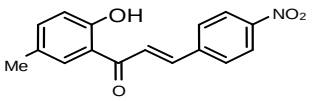
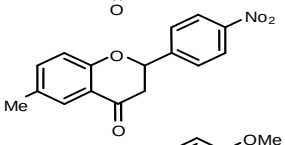
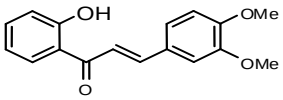
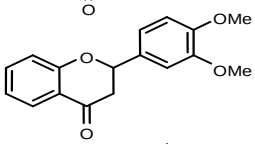
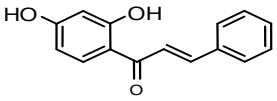
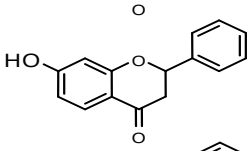
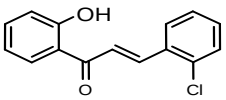
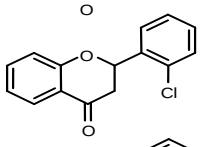
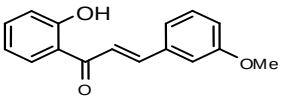
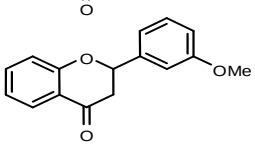
Determination of the minimum inhibitory concentration (MIC)

The active sample in the disc diffusion method was then tested for its activity by the serial dilution method to determine the minimum inhibition concentration (MIC-value). The MIC value obtained for flavanone (f) was 1000 µg/mL against Escherichia coli.



1 2

Table1: Synthesis of Flavones (2 a-h) using ionic liquid H[bimBF$_4$] grinding at room temperature

Entry	unsaturated carbonyl compounds **1(a-h)**	Product **2(a-h)**	Time(min.)	Yield(%)[a]	M.P.(^{0}C)[b]
a			10	81	97
b			12	90	185-187
c			10	83	155-156
d			14	88	277
e			12	89	154
f			10	80	240-241
g			13	87	118
h			15	90	128-129

[a] : Isolated yields.

b:Melting points of compounds are uncorrected and compared with reported compounds.

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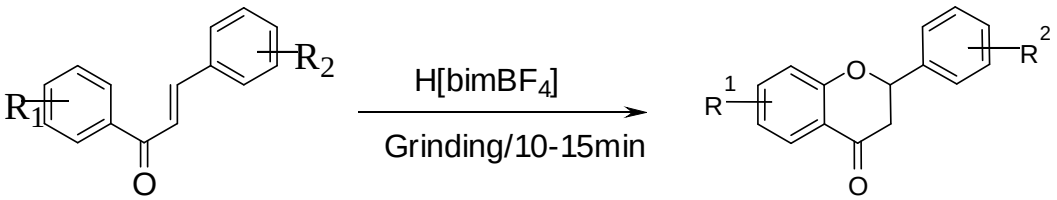
Table 2 :Synthesis of flavavanones **2(a-b)** with recovered ionic liquid H[bimBF4]

Entry	unsatured carbonyl compounds	product	Time(Sec)	Yield(%) Cycle 1	Recycle 1	Recycle 2
1	1a	2a	10	93	91	91
2	1b	2b	12	90	88	88

Table 3. Antibacterial screening for the compounds (d) and (f)

Diameter of the zone of inhibition (mm)

Organism	chalcones	flavanone	Streptomycin sulphate
Bacillus subtilis	–	–	22·0 ± 0·3
Staphylococcus aureus	–	–	22·5 ± 0·7
Escherichia coli	–	12·5 ± 0·3	22·0 ± 0·0
Pseudomonas aeruginosa	–	–	22·0 ± 0·0



1 **2**

Scheme 1

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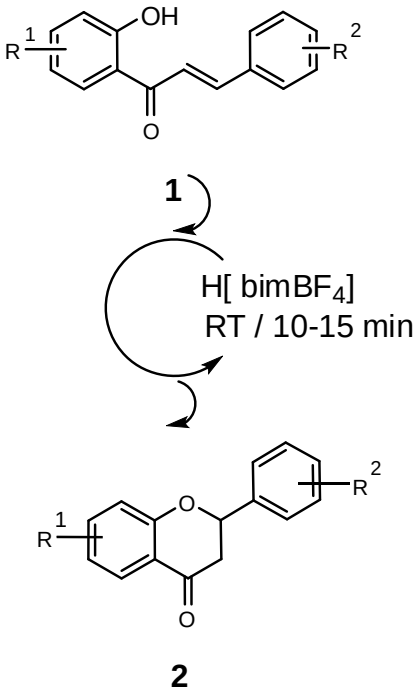

Scheme-2 Fig:Possible mechanism of (2) flavanone

SPECTRAL DATA

Melting points were determined in open glass capillaries and uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at room temperature on a varian Inova Spectrometer in $CDCl_3$ using TMS as internal standard.

The spectral data of some selected compounds:

Compound 2b: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.44 (s, 3*H*), 7.22 (s, 1*H*), 7.69 (dd, 1*H*, J = 8.9, 2.1 Hz), 7.74 (d, 1*H*, *J* = 8.6 Hz), 7.85 (m, 1*H*), 8.38 (s, 4*H*) ; ^{13}CNMR (125 MHz, CDCl3) 21.5, 109.9, 119.6, 125.1, 125.3, 128.8, 136.5, 136.8, 138.3, 149.7, 154.8, 160.6, 177.2.

Compound 2e: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.95 (s, 3*H*), 3.98 (s, 3*H*), 6.72 (s, 1*H*), 6.96 (d, 1*H*, *J* = 8.1Hz), 7.36 (d, 1*H*, J=1.8 Hz), 7.40 (dd, 1H, *J* = 7.2 Hz, *J* = 7.5 Hz), 7.51 (dd, 1H, *J* = 1.8 Hz, *J* = 8.1 Hz), 7.53 (d, 1H, *J* = 7.5 Hz), 7.67 (ddd, 1*H*, *J* = 1.5 Hz, *J* = 7.2, *J* = 7.8 Hz) 8.20 (dd, 1*H*, *J* = 1.5 Hz, *J* = 7.8 Hz); ^{13}CNMR (125 MHz, CDCl3) 56.1, 106.4, 108.8, 111.2, 118.0, 120.0, 123.9, 124.2, 125.6, 133.6, 149.3, 152.1, 156.1, 163.3, 178.3.

Compound 2f: ^{1}H NMR (300 MHz, CDCl3) δ 6.91 (s, 1*H*), 7.95 (dd, 1*H*, *J* = 1.8, *J* = 9.0 Hz), 7.02 (d, 1*H*, *J* = 1.8 Hz), 7.57-7.29 (m, 3*H*), 7.91 (d, 4*H*, *J* = 9.0 Hz), 8.05-8.08 (m, 2*H*); 10.8 (s, 1*H*); ^{13}CNMR (125 MHz, CDCl3) 102.6, 106.6, 115.1, 116.2, 126.2, 126.5, 129.1, 131.3, 131.5, 157.5, 161.2, 162.8, 176.4.

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REFRENCES

[1] AF Welton, LD Tobias, C Fiedler-Nagy, W Anderson, W Hope, K Middelton Jr; JB Harbirne and AR Liss, New York; 1986, 231.
[2] Havsteen. Biochem Pharmacol 1983; 32:1141.
[3] A Banerji and N Goomer. Synthesis 1980:874.
[4] Y Hoshino, T Oohinata and N Takeno. Bull Chem Soc Jpn 1986; 59: 2351.
[5] Y LeFloch'h and M LeFeuvre. Tetrahedron Lett 1986; 27: 2751.
[6] M Balogh and P Laszlo. Organic Chemistry Using Clays, Springer, Berlin, 1993. J Chisen, IC Chisen, JS Rafelt, DJ Macquarrie and JH Clark. Chem Commun 1997:2203.
[7] Y Hoshino and N Takino. Bull Chem Soc Jpn 1987; 60: 1919-1920.
[8] A Nishinaga, H Ando, K Maruyama and T Mashino. Synthesis 1982; 839.
[9] PK Zubaidha, AM Hashmi and RS Bhosale. Hetrocyclic Commun 2005; 11: 9100.
[10] S Garg, MPS Ishar, R Sarin, RP Gandhi. Indian J Chem Soc 1994; 33B:1123-1128.
[11] JC Jung, JP Min and OS Park. Synth Commun 2001; 31(12): 1837-
[12] RS Verma, R. K Saini and D Kumar. J Chem Res (S) 1998:348- 349.
[13] PE Kumar and KJR Prashad. Indian J Chem 1999; 38B:1277-1279.
[14] M Tsukayama, Y Kawamura, T Ishizuka, S Hayas and F Torii. Heterocycles 2003;60 (12), 2775.
[15] Baron D , Ragai K I. Phytochem 1989; 27: 87
[16] Nkengfack A E, Sanson D R , Tempesta M S. J Nat Prod 1989; 52: 320
[17] RS Varma, M Varma and AK Chatterjee. J Chem Soc Perkin Trans 1993; 1:999; RS Varma, AK Chatterjee and M Varma. Tetrahedron Lett 1993; 34: 3207; RS Varma, JB Lamture and M Varma. Tetrahedron Lett 1993; 34: 3029; RS Varma, AK Chatterjee, and M Varma. Tetrahedron Lett 1993; 34:4603.
[18] JM Lerestif, L Toupet, S Sinbandhit, F Tonnerd, JP Bazureaau and J Hanelin, Terahedron; 1997;53: 6351; AL Marrero-Terrero and A Loupy. Synlett 1996; 245: A Benalloum, B Labiad and D Villemin. Chem Commun 1998: 386.
[19] T Welton. Chem Rev 1999; 99:2071; P Wassercheid and W Keim. Angew Chem Int Ed 2000; 39: 3772; R Sheldon. Chem Commun 2001: 2399; D Zhao, M Wu, Y Kou and K Min. Catal Today 2002; 1: 2654.
[20] R Rajgopal, DV Jarikote, RJ Lahoti, D Thomas, KV Srinivasan. Tetrahedron Lett 2003; 44:1615; DV Jarikote, SA Siddiqui, R Rajgopal, D Thomas, RJ Lahoti and KV Srinivasan. Tetrahedron Lett 2003; 44: 1835; AR Gholap, K Venkatesan, D Thomas, RJ Lahoti and KV Srinivasan. Green Chem 2004; 6: 147-150; SP Panchgalle, UR Kalkote, PS Nipahadkar, PN Joshi, SP Chavan and GM Chaphekar. Green Chem 2004;6: 308-309.
[21] BR Madje, SS Shindalkar and MS Shingare. Indian J Hetro Chem 2004; 14:87-88.
[22] T Walton. Chem Rev 1999; 99:2071; P Walden. Bull Aced Imper Sci (St. Petersburg) 1914; 1800; S Sugden and H Wilkins. J Chem Soc 1929; 1291.
[23] Zavala MA, Perez GS and Perez GRM. Phytother Res 1997;11:368
[24] Arias ME, Gomez JD, Cudmani NM, Vattuone MA and Isla MI. Life Sci 2004 ;75: 191.