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# [BMIM] BF4: AN EFFICIENT IONIC LIQUID MEDIUM FOR THE SYNTHESIS OF 1, 2, 4-TRIAZINE DERIVATIVES

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**Abstract**

A series of new ( Z)-3-allkyl-5(benzylidene/substituted benzylidene)-2N-(carbothioamido)-6-oxo-1,2,5,6-tetrahydro-1-N*H*-1,2,4-triazine derivatives have been synthesized in [BMIM] BF4 as ionic liquid without catalyst for 30-40 min at 65-70 $^{o}$C with good yields. This method has the remarkable advantages of good yields, straightforward protocol, being environmentally friendly, short reaction times and mild reaction condition. Here the need for catalyst and solvent are avoided by using the catalytically active ionic liquid as medium.

**Keywords:** Green synthesis, MITC and [BMIM] BF4.

## Introduction

Ionic liquids (ILs) have become efficient and popular as novel and promising solvents for heterocyclic synthesis. They have chemical and physical properties make a careful choice of anion and cation and also have been used as desired reaction medium[i] . The main useful properties of ILs for their applications are negligible vapor pressure below their decomposition temperature. Due to this reason, ILs are measured as green chemistry solvents. The thermal stability of ILs is limited by the strength of their heteroatom– carbon and their hetero atom–hydrogen bonds, respectively [ii].

In recent, among the other ionic liquids 1-butyl-3-methyl imidazolium salts have most considerable attention as an environmentally sustainable and efficient media and immense uses in various heterocyclic transformations that include hydrogenations [iii], Heck reactions[iv], Friedel-craft reactions[v], Bishler-Napieral reactions[vi]. Among these, last decade has exposed marvelous applications of the ionic liquid 1-butyl-3-methyl imidazolium tetrafluoroborate ([bmim]$BF_4$) in various organic conversions [vii]. The weak electrostatic interactions of tetrafluoroborate with the imidazolium cation display good thermal and electrochemical stability of [BMIM]$BF_4$. The other favorable physical and chemical properties like mild and

lack of inflammability, neutral nature, commercial availability, volatility, environmentally sustainable and admirable solubility with many organic products make this ionic liquid greater than others [viii].

On the other hand, 1,2,4-triazin-6-ones are a very important class of heterocyclic compounds that show a wide variety of applications in both pharmaceutical and agrochemical fields. 1,2,4-triazin-6-ones have exhibited anticancer, antitumour, antibacterial and antifungal, antimicrobial, biological activities of cell lines cytotoxicity, antimalarials, antivirals and herbicides. 1,2,4-triazine ring system is very significant for its applications as corrosion inhibitors, additives to photographic development baths, uv absorbers for textiles, plastic resins and papers and indicators for volumetric analysis of NH-acids in acetonitriles [ix-xi].

This prompted us to synthesize derivatives of (Z)-3-allkyl-5(benzylidene/substituted benzylidene)-2N-(carbothioamido)-6-oxo-1,2,5,6-tetrahydro-1-NH-1,2,4-triazine in [BMIM] BF4 as ionic liquid without catalyst for 30-40 min at 65-70 $^{o}$C with good yields.

**Results and Discussion**

As illustrated in scheme-1, desired products (Z)-3-allkyl-5(benzylidene)-2N-(carbothioamido)-6-oxo-1,2,5,6-tetrahydro-1-NH-1,2,4-triazines **(5)** have been prepared by green approach. The tandem reaction of (Z)-4-benzylidene-2-methyloxazol-5(4H)-ones **1** (1mmol) with Hydrazinehydarte **2a** (1mmol) ) to from (Z)-N-(3-hydrazinyl-3-oxo-1-phenylprop-1-en-2-yl)acetamide **3a** in ionic liquid [BMIM]$BF_4$ as medium at 65-70 $^{o}$C for 10 min and then added MITC (1 mmol) at same temperature and maintained for 20 min to form (Z)-5-benzylidene-N,3-dimethyl-6-oxo-5,6-dihydro-1,2,4-triazine-2(1H)-carbothioamide with 85% yield **(Table-1 entry-1)**. The structure of the product was assigned on the basis of its spectral properties $^{1}$H & $^{13}$C-NMR & Mass. This one-pot reaction was done in different ionic liquids such as [BMIM]$BF_4$, [BMIM]Br, [BMIM]Cl and [BMIM]OH at different temperature with a view to optimise product formation **(Table-1)**. However, it has been found that the one-pot reaction of **1** with **2a** and **4** in the presence of BMIM]$BF_4$ as medium at 80-85$^{o}$C gave highest yield 85% and clean product **4a (Table-1 entry-1)**.

In order to examined the particular effect of temperature on the compound formation, the model three component reaction was performed at 60-65 $^{o}$C and 75-80 $^{o}$C. It was observed that the reaction was completed at 75-80 $^{o}$C for 25 min with 75% yield only and at 60-65$^{o}$C temperature the reaction was completed after prolonged time for 4 hr.

**Table 1.** Optimisation of Ionic liquids , solvents & Temperature to form **5a**.

| **Entry** | **Medium (6 eq)** | **Temp./$^{o}$ C** | **Time (min)** | **Yield (4a%)** |
|---|---|---|---|---|
| **1** | **[BMIM]$BF_4$** | **65-70** | **30** | **85** |
| 2 | [BMIM]Br | 65-70 | 120 | 81 |
| 3 | [BMIM]Cl | 65-70 | 240 | 72 |
| 4 | [BMIM]OH | 65-70 | 240 | 54 |
| 5 | [BMIM]$BF_4$ | 60-65 | 240 | 82 |
| 6 | [BMIM]$BF_4$ | 75-80 | 25 | 76 |

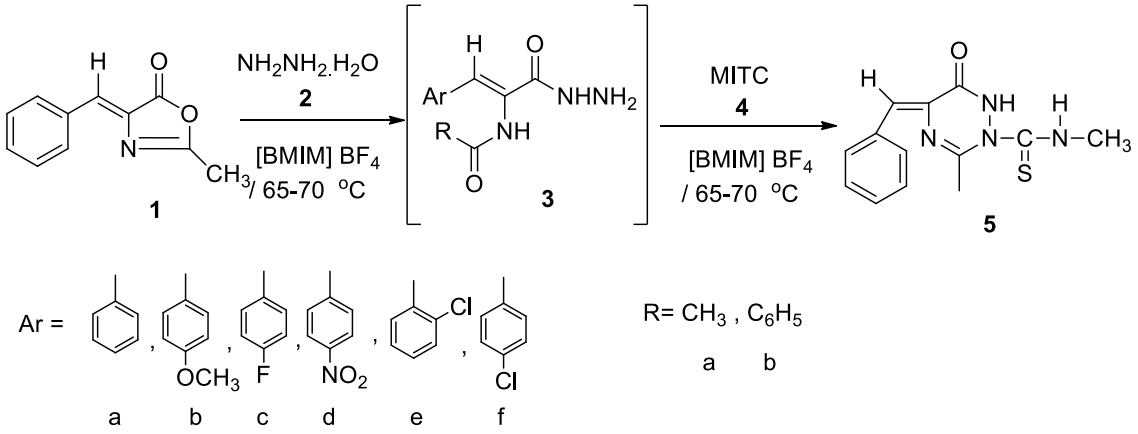
In continuations of optimisation reaction, amount of ionic liquid equivalence study was conducted with different amount of [BMIM] $BF_4$ at 65-70 $^{o}$C using **1** (1mmol), **2** (1mmol) and **4** (1mmol) to from desired **5a (Table-2).** However, the tandem reaction for the synthesis of **5a** gave excellent yield 85% in a relatively shorter time 30 min with 6 eq of [BMIM]$BF_4$ as medium at 65-70 $^{o}$C.

**Table 2.** Optimisation of amount of [BMIM]$BF_4$ at 65-70 $^oC$ to form **5a**.

| Entry | [BMIM]$BF_4$ (eq) | Temp./$^o$ C | Time (min) | Yield (4a%) |
|---|---|---|---|---|
| 1 | 4 | 65-70 | 240 | 78 |
| 2 | **6** | 65-70 | **90** | **85** |
| 3 | 8 | 65-70 | 80 | 79 |

Based on the above better optimized condition, the desired title compounds **5 (a-f)** were prepared in [BMIM]$BF_4$ as medium at 65-70 $^oC$ using **1 (a-b)** , **2(a-f)** and **4** for 30-40 min with 80-85% yield by tandem reaction.

**Scheme-1**




**Experimental:**

Melting points are determined on in open capillary tubes in sulphuric acid bath. FT-IR spectra are recorded on a VERTEX 70 Brucker by using KBr. A Bruker DRX-400 spectrometer 400 and 100 MHz was employed for recording 1H NMR and 13C NMR spectra respectively and DMSO-d6 was used as solvent and TMS as an internal standard. . Mass spectra were recorded on Agilent-LCMS instrument.

**Preparation of 5a-5l:**

Charged the mixture of **1(a-b)** (10 mmol) and **2** (a-f) (10 mmol) in [BMIM]$BF_4$ (6 eq) and heated at 65-70 $^oC$ for 10 min. After completion of the reaction as monitored by TLC. To this reaction mass added **4** and maintained for 20-30 min. After completion of the reaction as monitored by TLC. The reaction mass was cooled to 40-45$^oC$ and added water (50 ml). Then stirred for 15-20 min at the same temperature and cooled to 25-30 $^oC$. A colourless solid separated out from the reaction mixture which was collected by filtration. The isolated solid was washed with water (50 ml) and dried at 60-65 $^oC$ for 10 h. The crude product was recrystallized from a ethanol solvent to get **5**.

**Experimental section:**

Melting points are uncorrected and taken in open capillary tubes in sulphuric acid bath. TLC was run on silica gel – G and visualization was done using UV light. IR spectra were recorded using Perkin – Elmer 1000 instrument in KBr pellets. $^1H$ NMR spectra were recorded in CDCl3 using TMS as internal standard with 400 MHZ spectrometer. Mass

spectra were recorded on Agilent-LCMS instrument under CI conditions and given by Q+1 value only.

**(Z)-3-allkyl-5(benzylidene / substituted benzylidene)-2N-(carbothioamido)-6-oxo-1, 2, 5, 6-tetrahydro-1-NH-1,2,4-triazine derivatives 5a-5l:**

**5a:** IR (KBr) $cm^{-1}$: 3471 (broad, -NH-N), 3084 (broad, -NH), 1714 (-C=O), 1270 (C=S); $^1$H-NMR (400MHz, CDCl3/TMS): δ 2.1 (s, 3H, C-C**H₃**), δ 2.6 (s, 3H, N-C**H₃**), δ 6.8 (s, 1H, -N**H**-CH₃**, D₂O exchangeable**) 7.4-8.4 (m, 6H, Ar-**H** and s, 2H, =C**H**-Ar **),** 10.6 (s, 1H, **-NH, D₂O exchangeable).** $^{13}$C NMR **(**CDCl3): δ 24.66 (C-**CH₃**), 42.94 (N-**CH₃**), 116.79 (Ar-**C**=C), 120.14-137.69 (**Ar**), 147.79 (N-**C**-CH₃), 149.96 (Ar-C=**C**), 164.01 (**C**=S), 177. 70 (O=C-N). **Mass:** 239 (20%), 260 (10%). **M⁺·1 =** 275.

**5b:** IR (KBr) $cm^{-1}$ : 3313 (broad, -NH-N), 3249 (broad, -NH) 1656 (-C=O), 1263 (C=S); $^1$H-NMR (400MHz, CDCl3/TMS): δ 2.2 (s, 3H, C-C**H₃**), δ 2.6 (s, 3H, N-C**H₃**), δ 3.0 (s, 3H, -C**H₃**), δ 6.8 (s, 1H, -N**H, D₂O exchangeable**) 7.2-8.3 (m, 5H, Ar-**H** and s, 2H, =C**H**-Ar **),** 10.6 (s, 1H, **-NH, D₂O exchangeable).** $^{13}$C NMR **(**CDCl3): δ 23.62 (C-**CH₃**), 43.93 (N-**CH₃**), 53.93 (-O**CH₃**), 114.29 (Ar-**C**=C), 124.13-133.65 (**Ar**), 146.73 (N-**C**-CH₃), 149.94 (Ar-C=**C**), 163.31 (**C**=S), 176. 30 (O=C-N). **Mass:** 273 (10%). **M⁺·1 =** 305.

**5c:** IR (KBr) $cm^{-1}$: 3445 (broad, -NH), 3051 (broad, -NH), 1724 (-C=O), 1280 (C=S); $^1$H-NMR (400MHz, CDCl3/TMS): δ 2.4 (s, 3H, C-C**H₃**), δ 2.8 (s, 3H, N-C**H₃**), δ 6.6 (s, 1H, -N**H, D₂O exchangeable**) 7.4-8.4 (m, 5H, Ar-**H** and s, 2H, =C**H**-Ar **),** 10.4 (s, 1H, **-NH, D₂O exchangeable).** $^{13}$C NMR **(**CDCl3): δ 23.26 (C-**CH₃**), 42.24 (N-**CH₃**), 116.59 (Ar-**C**=C), 123.15-136. 69 (**Ar**), 144.49 (N-**C**-CH₃), 148.96 (Ar-C=**C**), 163.04 (**C**=S), 174. 60 (O=C-N). **Mass:** 239 (20%). **M⁺·1 =** 293.

**5d:** IR (KBr) $cm^{-1}$: 3283 (broad, -NH), 3251 (broad, -NH), 1726 (-C=O), 1257 (C=S); $^1$H-NMR (400MHz, CDCl3/TMS): δ 1.8 (s, 3H, C-C**H₃**), δ 2.3 (s, 3H, N-C**H₃**), δ 6.6 (s, 1H, -N**H, D₂O exchangeable**) 7.4-8.4 (m, 5H, Ar-**H** and s, 2H, =C**H**-Ar **),** 10.2 (s, 1H, **-NH, D₂O exchangeable).** $^{13}$C NMR **(**CDCl3): δ 23.63 (C-**CH₃**), 41.93 (N-**CH₃**), 115.39 (Ar-**C**=C), 121.13-136.62 (**Ar**), 146.74 (N-**C**-CH₃), 148.93 (Ar-C=**C**), 163.04 (**C**=S), 179.78 (O=C-N). **Mass:** 273 (10%). **M⁺·1 =** 320

**5e:** IR (KBr) $cm^{-1}$: 3307 (broad, -NH), 3198 (broad, -NH) 1729 (-C=O), 1255 (C=S); $^1$H-NMR (400MHz, CDCl3/TMS): δ 1.8 (s, 3H, C-C**H₃**), δ 2.4 (s, 3H, N-C**H₃**), δ 6.6 (s, 1H, -N**H, D₂O exchangeable**) 7.4-8.4 (m, 5H, Ar-**H** and s, 2H, =C**H**-Ar **),** 10.2 (s, 1H, **-NH, D₂O exchangeable).** $^{13}$C NMR **(**CDCl3): δ 23.26 (C-**CH₃**), 41.93 (N-**CH₃**), 113.29 (Ar-**C**=C), 121.24-135.66 (**Ar**), 146.76 (N-**C**-CH₃), 148.94 (Ar-C=**C**), 163.05 (**C**=S), 174. 60 (O=C-N). **M⁺·1 =** 309

**5f:** IR (KBr) $cm^{-1}$: 3300 (broad, -NH), 3280 (broad, -NH), 1710 (-C=O), 1280 (C=S); $^1$H-NMR (400MHz, CDCl3/TMS): δ 2.4 (s, 3H, C-C**H₃**), δ 2.6 (s, 3H, N-C**H₃**), δ 6.8 (s, 1H, -N**H, D₂O exchangeable**) 7.4-8.4 (m, 6H, Ar-**H** and s, 2H, =C**H**-Ar **),** 10.6 (s, 1H, **-NH, D₂O exchangeable).** $^{13}$C NMR **(**CDCl3): δ 23.56 (C-**CH₃**), 41.54 (N-**CH₃**), 114.69 (Ar-**C**=C), 122.24-137.65 (**Ar**), 146.69 (N-**C**-CH₃), 148.76 (Ar-C=**C**), 163.21 (**C**=S), 176. 40 (O=C-N). **M⁺·1 =** 309

**5g:** IR (KBr) $cm^{-1}$ : 2989 (broad, -NH), 3460 (broad, -NH), 1720 (-C=O), 1292 (C=S); $^1$H-NMR (400MHz, CDCl3/TMS): δ 2.3 (s, 3H, N-C**H₃**), δ 6.4 (s, 1H, -N**H, D₂O exchangeable**) 7.4-8.4 (m, 11H, Ar-**H** and s, 2H, =C**H**-Ar **),** 10.2 (s, 1H, **-NH, D₂O exchangeable).** $^{13}$C NMR **(**CDCl3): δ 39.34 (N-**CH₃**), 113.29 (Ar-**C**=C), 121.14-143.45 (**Ar**), 145.65 (N-**C**-CH₃), 148.46 (Ar-C=**C**), 162.11 (**C**=S), 173. 20 (O=C-N). **Mass:** 221 (20%), 318 (10%). **M⁺·1 =** 337.

**5h:** IR (KBr) $cm^{-1}$ : 3210 (broad, -NH), 3380 (broad, -NH),1750 (-C=O), 1280 (C=S); $^1$H-NMR (400MHz, CDCl3/TMS): δ 2.6 (s, 3H, N-C**H**$_3$), δ 6.9 (s, 1H, -N**H, D$_2$O exchangeable**) 7.4-8.4 (m, 10H, Ar-**H** and s, 2H, =C**H**-Ar **),** 10.3 (s, 1H, **-NH, D$_2$O exchangeable).** $^{13}$C NMR **(**CDCl3): δ 36.34 (N-**C**H$_3$), 115.35 (Ar-**C**=C), 120.34-139.65 (**Ar**), 146.69 (N-**C**-$CH_3$), 148.76 (Ar-C=**C**), 163.21 (**C**=S), 173.43 (O=C-N). **M$^{+\cdot}$1 =** 367

**5i:** IR (KBr) $cm^{-1}$: 3210 (broad, -NH), 3340 (broad, -NH), 1740 (-C=O), 1300 (C=S); $^1$H-NMR (400MHz, CDCl3/TMS): δ 2.4 (s, 3H, N-C**H**$_3$), δ 6.8 (s, 1H, -N**H, D$_2$O exchangeable**) 7.4-8.4 (m, 10H, Ar-**H** and s, 2H, =C**H**-Ar **),** 10.6 (s, 1H, **-NH, D$_2$O exchangeable).** $^{13}$C NMR **(**CDCl3): 42.54 (N-**C**H$_3$), 113.49 (Ar-**C**=C), 121.24-139.65 (**Ar**), 146.56 (N-**C**-$CH_3$), 147.76 (Ar-C=**C**), 164.21 (**C**=S), 175. 40 (O=C-N). **M$^{+\cdot}$1 =** 355

**5j:** IR (KBr) $cm^{-1}$: 3210 (broad, -NH), 3330 (broad, -NH), 1740 (-C=O), 1280 (C=S); $^1$H-NMR (400MHz, CDCl3/TMS): δ 2.6 (s, 3H, N-C**H**$_3$), δ 6.4 (s, 1H, -N**H, D$_2$O exchangeable**) 7.4-8.4 (m, 10H, Ar-**H** and s, 2H, =C**H**-Ar **),** 10.7 (s, 1H, **-NH, D$_2$O exchangeable).** $^{13}$C NMR **(**CDCl3): 40.35 (N-**C**H$_3$), 113.56 (Ar-**C**=C), 124.24-142.65 (**Ar**), 146.68 (N-**C**-$CH_3$), 148.74 (Ar-C=**C**), 162.22 (**C**=S), 174. 43 (O=C-N).**M$^{+\cdot}$1 =** 382

**5k:** IR (KBr) $cm^{-1}$ : 3210 (broad, -NH), 3350 (broad, -NH), 1720 (-C=O), 1270 (C=S); $^1$H-NMR (400MHz, CDCl3/TMS): δ 2.5 (s, 3H, N-C**H**$_3$), δ 6.8 (s, 1H, -N**H, D$_2$O exchangeable**) 7.4-8.4 (m, 10H, Ar-**H** and s, 2H, =C**H**-Ar **),** 10.6 (s, 1H, **-NH, D$_2$O exchangeable).** $^{13}$C NMR **(**CDCl3): 42.44 (N-**C**H$_3$), 115.65 (Ar-**C**=C), 120.24-139.65 (**Ar**), 146.60 (N-**C**-$CH_3$), 148.70 (Ar-C=**C**), 163.20 (**C**=S), 176. 49 (O=C-N). **M$^{+\cdot}$1 =** 371

**5l:** IR (KBr) $cm^{-1}$ : 3200 (broad, -NH), 3353 (broad, -NH) 1750 (-C=O), 1290 (C=S); $^1$H-NMR (400MHz, CDCl3/TMS): δ 2.3 (s, 3H, -C**H**$_3$), δ 6.5 (s, 1H, -N**H, D$_2$O exchangeable**) 7.4-8.4 (m, 10H, Ar-**H** and s, 2H, =C**H**-Ar **),** 10.4 (s, 1H, **-NH, D$_2$O exchangeable).** $^{13}$C NMR **(**CDCl3): δ 23.56 (C-**C**H$_3$), 41.54 (N-**C**H$_3$), 114.69 (Ar-**C**=C), 122.24-137.65 (**Ar**), 146.69 (N-**C**-$CH_3$), 148.76 (Ar-C=**C**), 163.21 (**C**=S), 176. 40 (O=C-N).**M$^{+\cdot}$1 =** 371

## Conclusion

Green synthesis of title compounds **5a-5l** has been developed by tandem method with excellent yields, short time and easy work up process.

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