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The Remarkable Cooperative Effect of a Brønsted Acidic Ionic Liquid in Cyclization between 2-Aminobenzamides with Ketones

Sudarshan Das,[a] Sougata Santra,[b] Sourav Jana,[a] Grigory V. Zyryanov,[b,c] Adinath Majee,[a] and Alakananda Hajra*[a]

Abstract: An unprecedented role of an imidazolium Brønsted acidic ionic liquid has been found in the formation of 2,2-disubstituted quinazolin-4(1*H*)-one derivatives where both C2-H of imidazolium moiety and acidic proton are necessary and simultaneously take part in catalysis. A library of quinazolin-4(1*H*)-ones was prepared from readily available ketones and 2-aminobenzamides in excellent yields through simple crystallization under solvent-free conditions with lower E factor. The catalyst can be reused for five consecutive runs without any significant loss of catalytic activities. This method produced only water as the byproduct and represents a green synthetic protocol. Clean reaction, non-chromatographic purification technique, easily accessible reactants, metal and solvent-free and environmentally friendly reaction conditions are the notable advantages of this procedure. The possible role of C2-H of imidazolium moiety in catalysis was studied by mass spectrometry.

Introduction

Room-temperature ionic liquids (RTILs) have been explored as greener alternatives to the volatile organic solvents due to their unique properties, such as negligible vapor pressure, high thermal stability, large liquid temperature range, easy recyclability, excellent chemical stability, and strong dissolving power for a wide range of organic and inorganic molecules.[1] However, their uses in large quantities as solvents are associated with limitations such as combustibility, biodegradability, toxicity, and high cost.[2] As a consequence, now a days ionic liquids have been used as effective catalysts rather than only as media for organic transformations.[3] By changing the cations and/or anions, the properties of ILs can be turned into many different ways. So far, a large number of functionalized ILs have been prepared for different applications by choosing the appropriate cations and anions.[4]

After the report by Forbes and Davis for the synthesis of the new class of phosphonium- and imidazolium ion-based ILs equipped with a pendant acidic sulfonic acid moiety,[5] Brønsted acidic ionic liquids (BAILs) have drawn a considerable attention in the field of catalysis.[6] BAILs are more preferable over the mineral acids as BAILs show strong acidity with usual properties of ionic liquids. As a result many transformations have been carried out involving acidic proton of these ILs.[6] However the specific role of cationic imidazole moiety with a pendant acidic sulfonic acid functionality has not been studied systematically.[7]

During the last few years we are actively engaged in the field of catalysis using BAILs as well as imidazole based zwitterions.[8] It is known that imidazolium motif provides an unconventional C–H bond for bonding.[9] Our previous study proves that C2-H of the imidazole moiety also plays a crucial role in catalyzing the reaction *via* electrophilic activations.[8e,f] In this regard, aldehydes are easily activated through the formation of hydrogen bond between the C2-H of imidazolium moiety and carbonyl oxygen atom of aldehyde. But this electrophilic activation is not sufficient to activate the ketones to react with nucleophiles and probably for this reason ketone has not been investigated as reaction partner catalyzed by imidazolium based ionic liquid under the guidance of hydrogen bonding. We therefore became interested to design such an ionic liquid which could serve as a Brønsted acid catalyst where both imidazolium C2-H and acidic proton could co-operatively activate ketone. In order to test this hypothesis, we applied 1-butanesulfonicacid-3-methylimidazolium tosylate [BSMIm][OTs] as a catalyst for the synthesis of 2,2-disubstituted quinazolin-4(1*H*)-one derivatives from ketones.

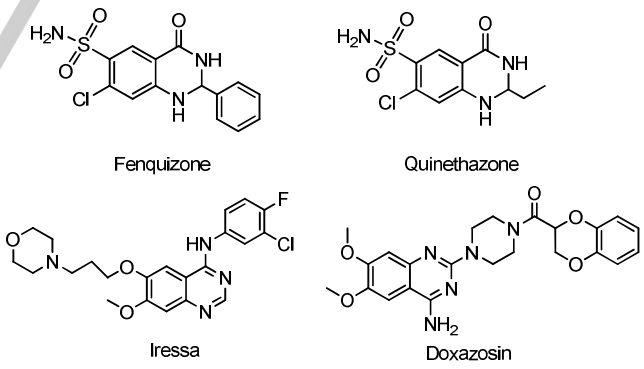

Figure 1. Quinazolinone containing drugs.

Quinazolinone and its derivatives are ubiquitous in many natural products such as vitamins, alkaloids and are also found to be as antagonists of various biological receptors, such as 5-HT5A related diseases, calcitonin gene-related peptide, and vasopressin V_3 receptors.[10] Quinazolinone scaffolds have also been used for designing various commercially available drugs such as Fenquizone (used in the treatment of oedema and hypertension), Quinethazone (used to treat hypertension), Iressa (clinically used against cell lung cancer with ever increasing popularity) and Doxazosin (used as antihypertensive

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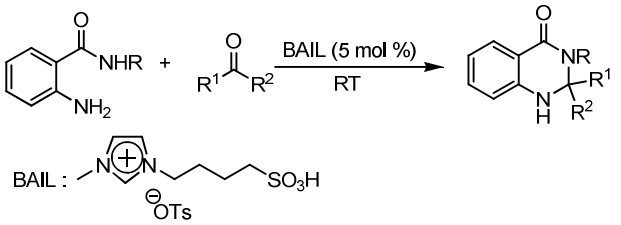
agent) (Figure 1).[11] Although several methods are available in literature for the synthesis of 2-arylquinazolinones,[12] only few methods are available for the synthesis of 2,2-disubstituted quinazolin-4(1*H*)-one derivatives.[13] However these methods were carried out in organic solvents using different catalysts. To the best of our knowledge, there is no report available so far for the synthesis of 2,2-disubstituted quinazolin-4(1*H*)-one derivatives by using the functionalized ionic liquid as a catalyst. As a part of our ongoing program on catalysis by IL,[8] herein we report a remarkable cooperative effect of both the acidic proton and the C2-H of the imidazole moiety on the cyclization reaction between 2-aminobenzamides and ketones for the formation of 2,2-disubstituted quinazolin-4(1*H*)-ones (Scheme 1).



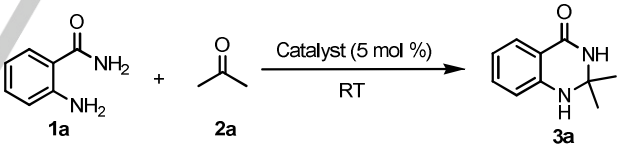
Scheme 1. BAIL-catalyzed cyclization between 2-aminobenzamides and ketones.

Results and Discussion

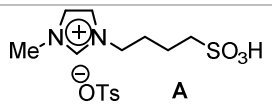
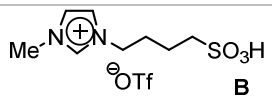
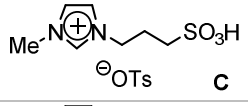
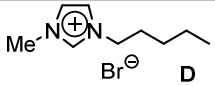
To study the factors which govern the catalytic activity of the IL in this reaction, we selected 2-aminobenzamide and acetone as model substrates employing various structurally diversified imidazolium based ILs, zwitterionic salt and BAILs. The reactions were carried out at room temperature and the results are summarized in Table 1. It made a clear distinction among various acidic ILs as catalysts in this reaction. Initially, we tested [BSMIm][OTs] (**A**) as a catalyst for the model reaction and gratifyingly 98% of the desired product was obtained within 5 min (entry 1, table 1). In the absence of catalyst no product was detected, even after 24 hour (entry 2, table 1). Another acidic IL [BSMIm][OTf] (**B**) gave the similar result with 96% yield (entry 3, Table 1). Chain length has significant role in controlling the reaction. When the chain length of IL was decreased the yield of the product decreased (entry 1 vs 4, Table 1). However, other ILs such as [PMIm][Br] (**D**) was found ineffective for this transformation (entry 5, table 1). This result implies that SO_3H group (acid) plays a crucial role in this reaction. In the presence of either only *para*-toluene sulfonic acid (PTSA) or the combination of PTSA and IL (entries 7 & 8, Table 1), no desired product was obtained within 5 min at room temperature. Aprotic imidazolium zwitterion (**F**) and imidazole could not catalyze the reaction also (entries 9 & 15, Table 1). The reactions did not proceed at all in the presence of ILs bearing counter anions SO_3H^- (**G**) (entry 10, table 1) and TsO^- (**I**) (entry 12, Table 1) without having pendant acidic SO_3H group on imidazolium part. No desired product was obtained when we used the combination of **I** with either HCl (entry 13, Table 1) or PTSA (entry 14, Table 1). Next we checked the effect of C2-H of the imidazole moiety by carrying out the reactions with [DMImB][OTs] (**E**) and [BDMIm][SO_3H] (**H**) (where C2-H is substituted by methyl group). But no formation of desired product was observed (entries 6 & 11, Table 1) which suggests the significant catalytic effect of C2-H on this reaction. These results strongly support that the reaction is influenced by both SO_3H and C2-H of imidazolium moiety. It is noteworthy to mention that the reaction did not proceed in the presence of acidic catalysts such as HCl, AcOH, TFA, TfOH and $NaHSO_3$ (Table 2). Furthermore, these results indicate that the presence of acidic proton is not the only factor to catalyze the reaction.

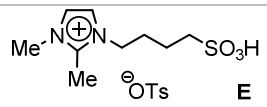
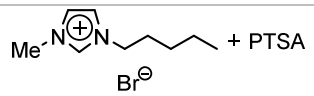
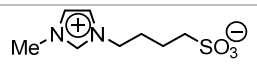
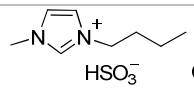
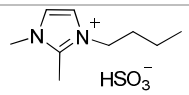
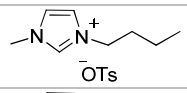
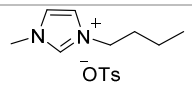
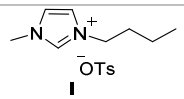
With the optimized reaction conditions (entry 1, table 1) in hand, we turned our attention towards examining the substrates scope with respect to ketones and the results are summarized in Table 3. Aliphatic ketones such as acetone and 4-methylpentan-2-one underwent the cyclization reaction smoothly to give the desired products in excellent yields (**3a** & **3b**). Aromatic ketones also afforded the corresponding products with excellent yields (**3c**-**3n**). Aryl ketones such as acetophenone and propiophenone reacted well under the present reaction conditions (**3c** & **3d**). Benzophenone also afforded the desired product (**3e**) with high yield in comparison to a previously reported method.[13a] Acetophenones bearing electron-donating groups such as –Me and –SMe and electron withdrawing groups like –Cl and –Br produced the desired products without any difficulty. Free hydroxy group on phenyl moiety in acetophenone also afforded the corresponding product (**3i**) with high yield. Acetophenone with strong electron-withdrawing group $–CF_3$ reacted well (**3k**). Hetero-aryl ketones afforded the desired products with excellent yields (**3l**-**3n**) without accompanying self-condensation or ring cleavage.

Table 1 Effects of different ILs as catalyst[a]



1a **2a** **3a**

Entry	Catalysts	Time	Yields[b] (%)
1	 **A**	5 min	98
2	None	24 h	0
3	 **B**	5 min	96
4	 **C**	5 min	84
5	 **D**	5 min	0

6	 E	5 min	0
7	PTSA	5 min	0
8	 + PTSA	5 min	0
9	 F	5 min	0
10	 G	5 min	0
11	 H	5 min	0
12	 I	5 min	0
13	 + HCl (5 mol%)	5 min	0
14	 + PTSA	5 min	0
15	Imidazole	5 min	0

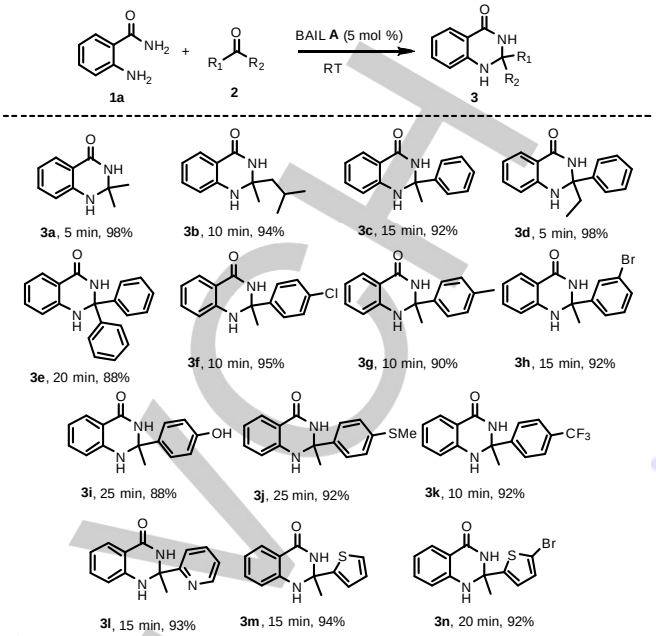
[a] **1a** (1 mmol) was treated with **2a** (1 mmol) in the presence of different catalysts (5 mol%) under neat condition at rt. [b] Isolated yields.

Table 2 Effects of different acidic catalysts[a]

Entry	Catalyst (5 mol %)	Time	Yield[b] (%)
1	HCl (12 N)	5 min	0
2	CH_3COOH	5 min	0
3	CF_3COOH	5 min	0
4	TfOH	5 min	0
5	PTSA	4 h	<10
6	$NaHSO_3$	6 h	0

[a] **1a** (1 mmol) was treated with **2a** (1 mmol) in the presence of different catalyst (5 mol %) under neat condition at rt. [b] Isolated yields.

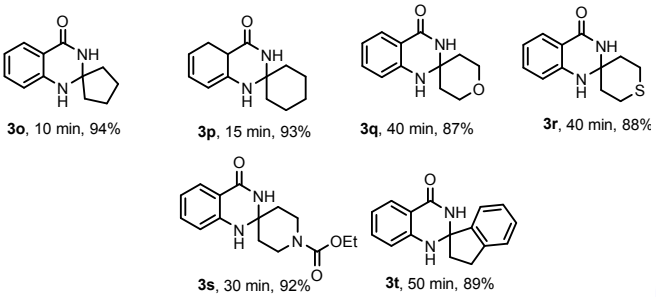
Table 3. Substrates scope [a]



[a] **1a** (1 mmol) was reacted with **2** (1 mmol) in the presence of BAIL **A** (5 mol %) at rt. All are isolated yields.

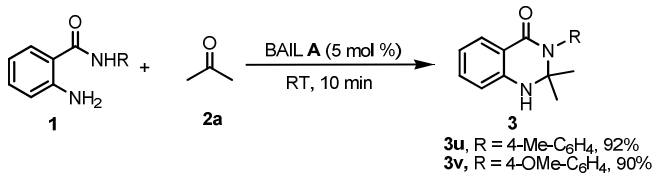
Recently spiroheterocyclic compounds present in many natural products and have attracted considerable interest in medicinal and pharmaceutical chemistry due to their unique structural array and highly pronounced pharmacological activities.[14] By virtue of our method various spiroquinazolin-4-(1*H*)-one derivatives were synthesized with high yields (Table 4). In addition, spiroheterocyclic quinazolin-4-(1*H*)-one derivatives were also obtained in excellent yields (**3q**-**3s**). Ethyl 4-oxopiperidine-1-carboxylate also reacted smoothly to afford the corresponding spiroheterocyclic quinazolin-4-(1*H*)-one derivative (**3s**).

Table 4 Synthesis of spiroheterocyclic quinazolin-4-(1*H*)-ones[a]



[a] **1a** (1 mmol) was reacted with **2** (1 mmol) in the presence of BAIL **A** (5 mol %) at rt. All are isolated yields.

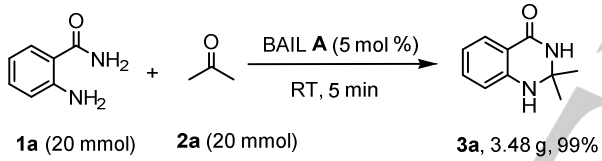
To further explore the scope of 2-aminobenzamide derivatives, *N*-substituted 2-aminobenzamides were investigated as depicted in Scheme 2. The desired products were obtained in high yields (**3u**-**3v**).



Scheme 2. Synthesis of 2,2,3-trisubstituted quinazolinone derivatives.

In the light of green chemistry, the concept of environmental factor (E-factor) and atom economy have been incorporated in conventional organic synthesis in both industry and academia.[15] Solvents are the main reason for an insufficient E-factor, especially in synthesis of fine chemicals and pharmaceutical industries. A greener reaction condition has been developed bearing lower E-factor of 0.12 and 0.16 in the cases of synthesizing **3a** and **3o** respectively (see Supporting Information).

This methodology is also applicable on a gram-scale synthesis (Scheme 3). We have successfully prepared the quinazolinone **3a** in 99% yield by the cyclization of 2-aminobenzamide (**1a**, 20 mmol) and acetone (**2a**, 20 mmol) using 5 mol% BAIL **A**.



Scheme 3. Gram-scale synthesis.

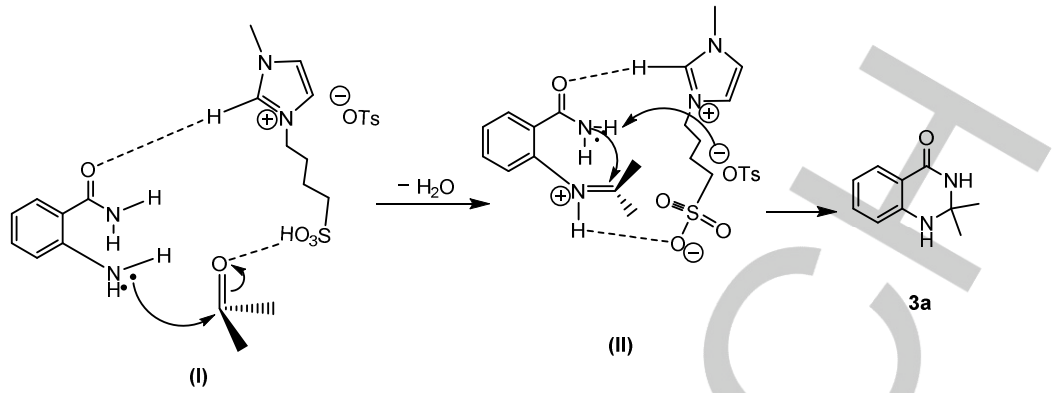
The reusability of the catalyst is also important from the viewpoint of commercial applications. Therefore the recovery and reusability of the catalyst were investigated for synthesis of **3a** (Table 5). The recovered catalyst can be recycled successfully without significant loss of catalytic activity. After third cycle, the catalyst still had a high activity and gave the desired product in excellent yield (96%).

Table 5 Recycling of the BAIL **A** for synthesis of **3a**[a]

Use/Cycle	Scale/mmol	Amount of the BAIL (**A**) used (g)	BAIL (**A**) recovery	Yield[b]
Fresh	20	0.078	0.076 g (97.4%)	99% (3.48 g)
1	19	0.076	0.073 g (96.1%)	98% (3.27 g)
2	18	0.073	0.070 g (95.8%)	97% (3.07 g)
3	17	0.070	0.067 g (95.7%)	97% (2.90g)
4	16	0.067	0.064 g (95.5%)	96% (2.70 g)

[a] Reactions were carried out with **1a (**1 equiv) and **2a** (1 equiv) in the presence of BAIL **A** (5 mol %) at rt for 5 min. All reactions were carried out in same reaction vessel. [b] Isolated yields.

A plausible mechanism for the synthesis of quinazolin-4-(1*H*)-one is depicted in Scheme 4. The crucial and distinct effect of BAIL on the overall reaction can be envisaged through domino catalysis involving an initial electrophilic activation of carbonyl oxygen of ketone through H-bond formation with SO_3H group. The additional H-bond involving the amidic carbonyl oxygen with the imidazolium C2-H[3c,d,16] further brings the reacting partners in close proximity favoring the formation of H-bonded supramolecular assembly.[16] The H-Bond interaction as well as charge-charge interaction cooperatively assist to form supramolecular assembly (**I**). Nucleophilic attack by amine at carbonyl carbon of ketone followed by dehydration gives the intermediate (**II**). The intermediate (**II**) also undergoes electrophilic-nucleophilic dual activation[4d] with the IL which facilitates intramolecular cyclization at this stage to afford the final product **3**. Mass spectrometry-based ion-fishing technique has appeared as vital tool in understanding mechanistic course of organic reactions.[3d,16c,17] Therefore, to identify the clusters and/or reactive intermediates (RI), the mass spectrometric ESI (+ve) ion-fishing studies have been carreid out (see Supporting Information). In a representative example, 2-aminobenzamide was treated with 4-chloroacetophenone in the presence of catalytic amount of **A** (5 mol%) and after 5 min the reaction mixture was subjected to the (+ve) ESI-MS analysis (see Supporting Information). Several peaks have appeared in the total ion chromatogram (TIC) spectra (see Supporting Information) which revealed the presence of ions at *m/z* 703.40 (m_1), 653.33 (m_2), 543.50 (m_3), 529.48 (m_4), 515.45 (m_5), 501.44 (m_6) and 459.17 (m_7) corresponding to $[RI\text{-}I + Na]^+$ (m_1), $[m_1 - Cl - CH_3]$ (m_2), $[(RI\text{-}I + H^{\cdot} + H^+) - ClC_6H_4CO]$ (m_3), $[(m_3 + H)^+ - CH_3]$ (m_4), $[(m_4 + H)^+ - CH_3]$ (m_5), $[(m_5 + H)^+ - CH_3]$ (m_6), and $[(m_6 + H^{\cdot} + H)^+ - CONH_2]$ (m_7) respectively, which suggests the formation of RI-I. The peaks at *m/z* 619.00, 567.34 and 551.17 correspond to $[RI–II + H^+ - CONH_2]$, $[RI–II + H^+ - CH_2SO_3H]$ and $[RI–II + H^+ - C_6H_4Cl]$ suggesting the formation of RI-II.



Scheme 4. Plausible reaction pathway.

Conclusions

In summary, we have demonstrated an unprecedented catalytic activity of an imidazolium based Brønsted acidic ionic liquid (BAIL) for the synthesis of 2,2-disubstituted quinazolin-4(1*H*)-one derivatives by the reaction of ketones with 2-aminobenzamides with excellent yields at room temperature under solvent-free conditions. To the best of our knowledge, this is the first report of activation of ketone for electrophilic addition by a BAIL where both C2-H and acidic-H are necessary. Our findings clearly demonstrate the necessity of C2-H of imidazolium cation and acidic proton for the activation of ketone. The notable advantages of the present methodology are clean reaction, ease of product isolation/purification (no need to use column chromatography), easily accessible reactants, metal and solvent-free and environmentally friendly reaction conditions and water is the only byproduct. The mass spectrometry studies support the formation of the supramolecular assembly from the interaction with amide, BAIL and ketone through H-bond formation. We hope that our new findings will be beneficial in the field of catalysis by IL.

Experimental Section

Materials and methods

^{1}H NMR spectra were determined on a Bruker 400 (400 MHz) spectrometer as solutions in DMSO-d_6. Chemical shifts are expressed in parts per million (δ) and are referenced to tetramethylsilane (TMS) as internal standard and the signals were reported as s (singlet), d (doublet), t (triplet), m (multiplet) and coupling constants *J* were given in Hz. ^{13}C NMR spectra were recorded at 100 MHz in DMSO-d_6 solution. TLC was done on silica gel coated glass slide (Merck, Silica gel G for TLC). Melting points were determined on a glass disk with an electric hot plate and are uncorrected. All solvents were dried and distilled before use. Commercially available substrates were freshly distilled before the reaction. Solvents, reagents and chemicals were purchased from Aldrich, Fluka, Merck, SRL, Spectrochem and Process Chemicals. All reactions involving moisture sensitive reactants were executed using oven dried glassware.

General procedure for the synthesis of 2,2-disubstituted quinazolin-4(1*H*)-one.

5 Mol% of BAIL (**A**) was added to a mixture of 2-aminobenzamide **1** (1 mmol) and ketone **2** (1 mmol) and the reaction mixture was stirred at room temperature for a certain period of time as indicated by TLC. After completion of the reaction, little amount of water (5 mL) was added to the reaction mixture and the crude product was isolated as solid by filtration. To get the analytically pure product, the solid was crystallized from ethanol. The catalyst left in the reaction vessel was dried by evaporating water under rotary vacuum evaporator and employed for subsequent four consecutive runs without significant loss of catalytic activity.

2,3-Dihydro-2,2-dimethylquinazolin-4(1*H*)-one (3a):[10c] White solid (172 mg, 98% yield); Mp 182-183 °C (Lit.[10c] 182-183 °C); IR (KBr): 1614, 1642, 3263, 3334 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.37 (s, 6H), 6.60-6.65 (m, 3H), 7.21 (t, *J* = 8.4 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.94 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 29.0, 66.8, 113.8, 114.2, 116.2, 127.1, 133.2, 147.0, 163.0.

2,3-Dihydro-2-(*iso*-butyl)-2-methylquinazolin-4(1*H*)-one (3b):[10c] White solid (204 mg, 94% yield); Mp 170-172 °C (Lit.[10c] 171-173 °C); IR (KBr): 1612, 1641, 3172, 3326 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.86-0.90 (m, 6H), 1.34 (s, 3H), 1.52-1.54 (m, 2H), 1.83-1.86 (m, 1H), 6.56-6.62 (m, 3H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.87 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 23.3, 24.2, 24.4, 28.6, 49.3, 69.3, 113.3, 113.9, 116.0, 127.0, 133.2, 147.1, 163.0.

2,3-Dihydro-2-methyl-2-phenylquinazolin-4(1*H*)-one (3c):[10c] White solid (218 mg, 92% yield); Mp 223-225 °C (Lit.[10c]: 224-225 °C); IR (KBr): 1615, 1671, 3047, 3404 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.65 (s, 3H), 6.58 (t, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 7.16-7.22 (m, 2H), 7.28 (t, *J* = 8.4 Hz, 2H), 7.50-7.52 (m, 3H), 7.65 (br, s, 1H), 8.81 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 30.7, 70.1, 114.3, 115.0, 116.8, 125.1, 127.0, 127.2, 127.9, 133.3, 147.2, 147.6, 163.8.

2,3-Dihydro-2-ethyl-2-phenyl-quinazolin-4(1*H*)-one (3d): White solid (246 mg, 98% yield); Mp 238-240 °C; IR (KBr): 1608, 1650, 3193, 3319 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.99 (t, *J* = 7.2 Hz, 3H), 1.83 (q, *J* = 7.2 Hz, 2H), 6.56 (t, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 8.0Hz, 1H), 7.15-7.22 (m, 2H), 7.28 (t, *J* = 8.0 Hz, 2H), 7.47-7.50 (m, 4H), 8.69 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 8.6, 35.0, 73.2, 114.1, 114.7, 116.5, 125.4, 126.9, 127.2, 127.9, 133.2, 147.5, 147.7, 164.2. Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10%; Found: C, 76.12; H, 6.31; N, 11.03%.

2,2-Diphenyl-2,3-dihydroquinazolin-4(1*H*)-one (3e):[10a] White solid (264 mg, 88% yield); White solid; Mp 139-141 °C (Lit.[10a] 138-142 °C); IR (KBr): 1612, 1648, 3187, 3321 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 6.59-6.60 (m, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 7.21-7.25 (m, 1H), 7.30-7.37 (m, 6H), 7.43 (d, *J* = 7.2 Hz, 4H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.86 (s, 1H), 8.98 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 75.4, 114.6, 114.8, 117.1, 127.2, 127.5, 127.8, 133.4, 144.7, 147.0, 163.7.

2,3-Dihydro-2-(4-chlorophenyl)-2-methylquinazolin-4(1*H*)-one (3f):[10c] White solid (258 mg, 95% yield); Mp 209-211 °C (Lit.[10c] 210-212 °C); IR (KBr): 1611, 1637, 3030, 3244 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 1.63 (s, 3H), 6.57-6.76 (m, 1H), 6.77 (d, *J* = 8 Hz, 1H), 7.19-7.23 (m, 1H), 7.36 (d, *J* = 8.8 Hz, 2H), 7.48-7.51 (m, 3H), 7.67 (s, 1H), 8.83 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 30.4, 69.8, 114.3, 115.0, 117.0, 127.1, 127.2, 127.9, 131.8, 133.4, 146.7, 146.9, 163.7.

2,3-Dihydro-2-methyl-2-*p*-tolylquinazolin-4(1*H*)-one (3g):[10c] White solid (226 mg, 90% yield); Mp 219-221 °C (Lit.[10c] 218-220 °C); IR (KBr): 1639, 3028, 3255 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 1.61 (s, 3H), 2.20 (s, 3H), 6.58 (t, *J* = 7.2 Hz,, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 7.17-7.21 (m, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H), 7.58 (s, 1H), 8.72(s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 20.4, 30.7, 70.0, 114.2, 115.0, 116.7, 125.1, 127.2, 128.4, 133.2, 136.1, 144.7, 147.2, 163.8.

2-(3-bromophenyl)-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (3h):[10c] White solid (290 mg, 92% yield); Mp 201-203 °C (Lit.[10c] 199-201 °C); IR (KBr): 1607, 1642, 3198, 3312 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 1.63 (s, 3H), 6.61 (t, *J* = 8.0 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 7.21-7.29 (m, 2H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.70 (d, *J* = 7.6 Hz, 2H), 8.84 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 30.5, 69.9, 114.3, 114.9, 117.1, 121.7, 124.2, 127.3, 128.1, 130.0, 130.2, 133.5, 146.8, 150.6, 163.7.

2,3-Dihydro-2-(4-hydroxyphenyl)-2-methylquinazolin-4(1*H*)-one (3i): White solid (223 mg, 88% yield); Mp 278-280 °C; IR (KBr): 1613, 1652, 3173, 3339 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) : δ 1.59 (s, 3H), 6.56 (t, *J* = 7.6 Hz, 1H), 6.63 (d, *J* = 8.8 Hz, 2H), 6.72 (d, *J* = 8.0 Hz, 1H), 7.18 (t, *J* = 8.4 Hz, 1H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.46-7.48 (m, 2H), 8.62 (s, 1H), 9.31 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 30.8, 69.9, 114.2, 114.5, 114.9, 116.6, 126.3, 127.1, 133.2, 137.8, 147.2, 156.3, 163.8. Anal. Calcd for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02%; Found: C, 70.76; H, 5.50; N, 11.01%.

2,3-Dihydro-2-methyl-2-(4-methylsulfanyl-phenyl)quinazolin-4(1*H*)-one (3j): White solid (261 mg, 92% yield); Mp 244-246 °C; IR (KBr): 1610, 1618, 3191, 3224 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 1.63 (s, 3H), 2.40 (s, 3H), 6.58 (t, *J* = 7.2 Hz, 1H), 6.7 (d, *J* = 8.0 Hz, 1H), 7.16-7.22 (m, 3H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 7.2 Hz, 1H), 7.62 (s, 1H), 8.76 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 14.5, 30.5, 69.9, 114.3, 115.0, 116.9, 125.5, 125.8, 127.2, 133.3, 136.9, 144.3, 147.1, 163.9. Anal. Calcd for $C_{16}H_{16}N_2OS$: C, 67.58; H, 5.67; N, 9.85%; Found: C, 67.52; H, 5.61; N, 9.78%.

2,3-Dihydro-2-methyl-2-(4-trifluoromethyl-phenyl)quinazolin-4(1*H*)-one (3k): White solid (281 mg, 92% yield); Mp 252-254 °C; IR (KBr): 1616, 3226, 3247 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 1.65 (s, 3H), 6.60 (t, *J* = 7.2 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.70 (s, 4H), 7.79 (s, 1H), 8.93 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 30.2, 70.0, 114.4, 114.9, 117.2, 124.1 (q, J_1 = 271 Hz), 125.1 (q, J_3 = 4.0 Hz), 125.2, 126.0, 127.3, 127.8 (q, J_2 = 31 Hz), 133.5, 146.9, 152.4, 163.7. Anal. Calcd for $C_{16}H_{13}F_3N_2O$: C, 62.74; H, 4.28; N, 9.15%; Found: C, 62.64; H, 4.22; N, 9.11%.

2,3-Dihydro-2-methyl-2-pyridin-2-yl quinazolin-4(1*H*)-one (3l): White solid (222 mg, 93% yield); Mp 242-244 °C; IR (KBr): 1616, 1654, 3201, 3265 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 1.66 (s, 3H) , 6.57 (t, *J* = 7.2 Hz, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 7.15-7.24 (m, 2H), 7.49 (d, *J* = 8.0 Hz, 3H), 7.75 (t, *J* = 7.6 Hz, 1H), 852 (s, 1H), 8.63 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 28.8, 71.0, 114.4, 114.6, 116.9, 119.4, 122.5, 127.1, 133.2, 136.7, 147.2, 148.7, 163.7, 164.5. Anal. Calcd for $C_{14}H_{13}N_3O$: C, 70.28; H, 5.48; N, 17.56%; Found: C, 70.22; H, 5.40; N, 17.48%.

2,3-Dihydro-2-methyl-2-thiophen-2-yl-quinazolin-4(1*H*)-one (3m): White solid (229 mg, 94% yield); Mp 208-210 °C; IR (KBr): 1614, 1633, 3201, 3234 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 1.78 (s, 3H), 6.64 (t, *J* = 7.6 Hz, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 7.00-7.01 (m, 1H), 7.23 (t, *J* = 8.4 Hz, 1H), 7.31 (d, *J* = 6.0 Hz, 1H), 7.53-7.57 (m, 2H), 8.77 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 30.8, 68.6, 114.4 114.6, 117.2, 123.8, 124.7, 126.6, 127.2, 133.4, 146.7, 153.0, 163.4. Anal. Calcd. for $C_{13}H_{12}N_2OS$: C, 63.91; H, 4.95; N, 11.47%; Found: C, 63.83; H, 4.87; N, 11.41%.

2,3-Dihydro-2-(5-bromo-thiophen-2-yl)-2-methylquinazolin-4(1*H*)-one (3n): White solid (296 mg, 92% yield); Mp 252-254 °C; IR (KBr): 1577, 1614, 3161, 3236 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 1.76 (s, 3H), 6.68 (t, *J* = 7.2 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 6.83 (d, *J* = 4.0 Hz, 1H), 6.99 (d, *J* = 4.0 Hz, 1H), 7.23-7.25 (m, 1H), 7.57-7.59 (m, 2H), 8.82 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 30.3, 68.6, 109.7, 114.6, 114.7, 117.7, 124.7, 127.3, 130.0, 133.6, 146.5, 154.9, 163.4. Anal. Calcd for $C_{13}H_{11}BrN_2OS$: C, 48.31; H, 3.43; N, 8.67%; Found: C, 48.25; H, 3.35; N, 8.61%.

1',3'-Dihydrospiro[cyclopentane-1,2'-quinazolin]-4'-one (3o):[10c] White solid (198 mg, 94% yield); Mp 265-267 °C (Lit.[10c] 265-267 °C); IR (KBr): 1616, 1639, 3163, 3292 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): 1.64-1.68 (m, 4 H), 1.77-1.79 (m, 4H), 6.63 (t, *J* = 7.6 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.74 (s, 1H), 7.21 (t, *J* = 8.4 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 8.10 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 22.4, 77.5, 114.8, 115.0, 117.0, 127.7, 133.4, 147.9, 163.9.

1',3'-Dihydrospiro[cyclohexane-1,2'-quinazolin]-4'-one (3p):[10c] White solid (200 mg, 93% yield); Mp 222-224 °C (Lit.[10c] 221-223 °C); IR (KBr): 1614, 1643, 3183, 3286 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 1.21-1.27 (m, 1H), 1.40-1.44 (m, 1H), 1.54-1.64 (m, 6 H), 1.73-1.76 (m, 2H), 6.61 (t, *J* = 7.6 Hz, 2H), 6.81 (d, *J* = 8.0 Hz, 1H), 7.21 (t, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 8.8 Hz, 1H), 7.94 (, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 20.8, 24.6, 37.1, 67.8, 14.4, 114.5, 116.4, 127.1, 133.1, 146.7, 163.2.

1',3'-Dihydrospiro[tetrahydropyran-4,2'-quinazolin]-4'-one (3q):[10c] White solid (189 mg, 87% yield); Mp 231-233 °C (Lit.[10c] 233-235 °C); IR (KBr): 1612, 1655, 2943, 3314 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 1.73-1.83 (m, 4H), 3.64-3.69 (m, 4H), 6.65, (t, *J* = 7.6 Hz, 1H), 6.79-6.84 (m, 2H), 7.24 (t, *J* = 7.2 Hz, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 8.16 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 37.6, 62.5, 65.5, 114.5, 114.7, 116.9, 127.2, 133.3, 146.4, 163.2.

1',3'-Dihydrospiro[tetrahydrothiopyran-4,2'-quinazolin]-4'-one (3r):[10c] White solid (205 mg, 88% yield); Mp 236-238 °C (Lit.[10c] 237-238 °C); IR (KBr): 1606, 1660, 2936, 3359 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 1.87-1.93 (m, 2H), 2.03-2.08 (m, 2H), 2.60-2.65 (m, 2H), 2.77-2.84 (m, 2H), 6.64 (t, *J* = 7.2 Hz, 1H), 6.76 (s, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 7.23 (t, *J* = 8.4 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 8.10 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ δ 23.2, 38.3, 66.9, 114.2, 114.6, 116.8, 127.1, 133.3, 146.2, 162.9.

1',3'-Dihydrospiro[(1-(ethoxycarbonyl)piperidine)-4,2'-quinazolin]-4'-one (3s):[10c] White solid (265 mg, 92% yield); Mp 216-218 °C (Lit.[10c] 217-219 °C); IR (KBr): 1620, 1656, 2938, 3293 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 1.17 (t, *J* = 7.2 Hz, 3H), 1.73 (s, 4H), 3.38-3.42 (m, 2H), 3.57-3.61 (m, 2H), 4. 03 (q, *J* = 7.2 Hz, 2H), 6.66 (t, *J* = 8.0 Hz, 1H), 6.79 (t, *J* =8.0 Hz, 2H), 7.25 (t, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 8.8 Hz, 1H), 8.13 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 14.6, 36.5, 60.7, 66.5, 114.3, 114.7, 117.0, 127.2, 133.4, 146.4, 154.6, 163.2.

1',3'-Dihydrospiro[indan-1,2'-quinazolin]-4'-one (3t):[10c] White solid (222 mg, 89% yield); Mp 224-226 °C (Lit.[10c] 222-223 °C); IR (KBr): 751, 1109, 1154, 1283, 1379, 1420, 1483, 1516, 1617, 1682, 2890, 2952, 3263, 3365 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 2.31-2.40 (m, 2H), 2.96 (t, *J* = 6.8 Hz, 2H), 6.66-6.71 (m, 2H), 7.14 (s, 1H), 7.16-7.19 (m, 1H), 7.23-7.31 (m, 4H), 7.66 (d, *J* = 6.8 Hz, 1H), 8.40 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): 27.7, 41.0, 78.5, 114.1, 114.2, 116.8, 122.4, 125.1, 126.7, 127.1, 128.8, 133.4, 141.5, 146.1, 146.9, 163.0.

2,3-Dihydro-3-(4-methylphenyl)-2,2-dimethylquinazolin-4(1*H*)-one (3u): White solid (244 mg, 92% yield); Mp 158-160 °C; IR (KBr): 1581, 1621, 2983, 3267 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 1.35 (s, 6H), 3.34 (s, 3H), 6.69-6.75 (m, 2H), 6.95 (s, 1H), 7.08 (d, *J* = 7.6 Hz, 2H), 7.22-7.32 (m, 3H), 7.64 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 20.6, 71.8, 114.5, 114.5, 117.1, 127.8, 129.3, 129.9, 133.4, 135.9, 136.8, 146.5, 162.6. Anal. Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52%; Found: C, 76.62; H, 6.75; N, 10.46%.

2,3-Dihydro-3-(4-methoxyphenyl)-2,2-dimethylquinazolin-4(1*H*)-one (3v):[10c] White solid (253 mg, 90% yield); Mp 166-168 °C (Lit.[10c] 164-165 °C); IR (KBr): 1582, 1622, 2986, 3263 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 1.35 (s, 6H), 3.78 (s, 3H), 6.74 (t, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 3H), 7.11 (d, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 6.4 Hz, 1H), 7.63 (d, *J* = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 27.5, 55.2, 71.9, 113.9, 114.4, 114.5, 117.0, 127.8, 131.1, 131.1, 133.4, 146.5, 158.3, 162.7..

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[1] a) P. Wasserscheid, T. Welton, *Ionic Liquids in Synthesis*, Wiley-VCH Verlag, **2008**; b) J. Ranke, S. Stolte, R. Stormann, J. Arning, B. Jastorff, *Chem. Rev*. **2007**, *107*, 2183; c) T. L. Greaves, C. J. Drummond, *Chem. Rev*. **2008**, *108*, 206; d) N. V. Plechkova, K. R. Seddon, *Chem. Soc. Rev*. **2008**, *37*, 123; e) J. P. Hallett, T. Welton, *Chem. Rev.* **2011**, *111*, 3508; f) L. Myles, R. G. Gore, N. Gathergood, S. J. Connon, *Green Chem.* **2013**, *15*, 2740; g) R. Sheldon, *Chem. Commun*. **2001**, 2399.

[2] D. Coleman, N. Gathergood, *Chem. Soc. Rev*. **2010**, *39*, 600.

[3] a) H. Xing, T. Wang, Z. Zhou, Y. Dai, *Ind. Eng. Chem. Res.* **2005**, *44,* 4147; b) Y. Leng, J. Wang, D. Zhu, X. Ren, H. Ge, L. Shen, *Angew. Chem. Int. Ed*. **2009**, *48*, 168; c) A. Sarkar, S. R. Roy, A. K. Chakraborti, *Chem. Commun*. **2011**, *47*, 4538; d) A. K. Chakraborti, S. R. Roy, D. Kumar, P. Chopra, *Green Chem*. **2008**, *10*, 1111; e) L. Myles, R. Gore, M. Spulak, N. Gathergood, S. J. Connon, *Green Chem.* **2010**, *12*, 1157.

[4] a) A. D. Sawant, D. G. Raut, N. B. Darvatkar, M. M. Salunkhe, *Green Chem. Lett. Rev*. **2011**, *4*, 41; b) B. C. Ranu, S. Banerjee, *Org. Lett*. **2005**, *7*, 3049; c) L. Myles, N. Gathergood, S. J. Connon, *Chem. Commun.* **2013**, *49*, 5316; d) A. Kumar, S. Srivastava, G. Gupta, P. Kumar, J. Sarkar, *RSC Adv.* **2013**, *3*, 3548; e) L. Zhang, S. Luo, X. Mi, S. Liu, Y. Qiao, H. Xu, J.-P. Cheng, *Org. Biomol. Chem*. **2008**, *6*, 567; f) D. Li, F. Shi, J. Peng, S. Guo, Y. Deng, *J. Org. Chem*. **2004**, *69*, 3582; g) R. Giernoth, *Angew. Chem. Int. Ed*. **2010**, *49*, 2834; h) J. H. Davis Jr., *Chem. Lett.* 2004, *33*, 1072; i) S.-G. Lee, *Chem. Commun.* **2006**, 1049; j) A. Winkel, P. V. G. Reddy, R. Wilhelm, *Synthesis* **2008**, *7*, 999; k) N. B. Darvatkar, A. R. Deorukhkar, S. B. Bhilare, D. G. Raut, M. M. Salukhe, *Synth. Commun.* **2008**, *38*, 3508.

[5] a) A. C. Cole, J. L. Jensen, I. Ntai, K. L. T. Tran, K. J. Weaver, D. C. Forbes, J. H. Davis, *J. Am. Chem. Soc*. **2002**, *124*, 5962; b) D. C. Forbes, K. J. Weaver, *J. Mol. Catal. A: Chem*. **2004**, *214*, 129.

[6] a) J. Guia, H. Bana, X. Cong, X. Zhang, Z. Hu, Z. Sun, *J. Mol. Catal. A: Chem*. **2005**, *225*, 27; b) A. Hubbard, T. Okazaki, K. K. Laali, *Aust. J. Chem*. **2007**, *60*, 923; c) D.-Q. Xu, J. Wu, S.-P. Luo, J.-X. Zhang, J.-Y. Wu, X.-H. Du, Z.-Y. Xu, *Green Chem*. **2009**, *11*, 1239; d) X. Liu, H. Ma, Y. Wu, C. Wang, M. Yang, P. Yana, U. Welz-Biermann, *Green Chem*. **2011**, *13*, 697; e) L. Myles, N. Gathergood, S. J. Connon, *Chem. Commun.* **2013**, *49*, 5316; f) L. Myles, R. G. Gore, N. Gathergood, S. J. Connon, *Green Chem.* **2013**, *15*, 2740.

[7] Y. W. Zhao, J. X. Long, F. G. Deng, X. F. Liu, Z. Li, C. G. Xia, J. J. Peng, *Catal. Commun*. **2009**, *10*, 732.

[8] a) M. Rahman, A. Sarkar, M. Ghosh, A. Majee, A. Hajra, *Tetrahedron Lett*. **2013**, *55*, 235; b) S. Santra, A. Majee, A. Hajra, *Tetrahedron Lett*. **2011**, *52*, 3825; c) S. Das, M. Rahman, D. Kundu, A. Majee, A. Hajra, *Canadian J. Chem*. **2010**, *88*, 150; d) D. Kundu, R. K. Debnath, A. Majee, A. Hajra, *Tetrahedron Lett.* **2009**, *50*, 6998; e) D. Kundu, A. Majee, A. Hajra, *Catal. Commun.* **2010**, *11*, 1157; f) D. Kundu, A. K. Bagdi, A. Majee, A. Hajra, *Synlett* **2011**, 1165; g) M. Rahman, A. K. Bagdi, D. Kundu, A. Majee, A. Hajra, *J. Heterocyclic Chem.* **2012**, *49*, 1224*;* h) M Rahman, A Roy, M Ghosh, S Mitra, A Majee, A Hajra, *RSC Adv.* **2014**, *4*, 6116; (i) A. K. Bagdi, A. Hajra, *RSC Adv*. **2014**, *4*, 23287; j) S. Mondal, S. Samanta, M. Singsardar, S. Mishra, S. Mitra, A. Hajra, *Synthesis* **2016**, ***48***, 4009; k) A. K. Bagdi, D. Kundu, A. Majee, A. Hajra, *Curr. Organocatal*. **2016**, *3*, 169; l) N. C. Ghosal, S. Santra, S. Das, A. Hajra, G. V. Zyryanov, A. Majee, *Green Chem.* **2016**, *18*, 565; m) S. Mahato, S. Santra, R. Chatterjee, G. V. Zyryanov, A. Hajra, A. Majee, *Green Chem*. **2017**, Accepted manuscript, doi.org/10.1039/C7GC01158J.

[9] a) G. R. Desiraju, T. Steiner, *The weak hydrogen bond in structural chemistry and biology.* Oxford University Press: Oxford, **1999**; b) K. J. Wallance, W. J. Belcher, D. R. Turner, K. F. Syed, J. W. Steed, *J. Am. Chem. Soc*. **2003**, *125*, 9699; c) K. Dong, S. Zhang, D. Wang, X. Yao, *J. Phys. Chem. A* **2006**, *110,* 9775; d) H.-C. Chang, J.-C. Jiang, W.-C. Tsai, G.-C. Chen, S. H. Lin, *J. Phys. Chem. B* **2006**, *110,* 3302; e) L. Zhang, X. Fu, G. Gao, *ChemCatChem* **2011**, *3*, 1359; f) K. Ghosh, S. S. Ali, S. Joardar, *Tetrahedron Lett*. **2012**, *53*, 2054; g) H.-C. Chang, J.-C. Jiang, W.-C. Tsai, G.-C. Chen, S. H. Lin, *J. Phys. Chem. B* **2006**, *110*, 3302; h) A. Aggarwal, N. L. Lancaster, A. R. Sethi, T. Welton, *Green Chem*. **2002**, *4*, 517; i) L. Cammarata, S. G. Kazarian, P. A. Salter, T. Welton, *Phys. Chem. Chem. Phys*. **2001**, *3*, 5192; j) A. R. Gholap, K.

Venkatesan, T. Daniel, R. J. Lahoti, K. V. Srinivasan, *Green Chem*. **2003**, *5*, 693; k) X. Fu, Z. Zhang, C. Li, L. Wang, H. Ji, Y. Yang, T. Zou, G. Gao, *Catal. Commun*. **2009**, *10*, 665.

[10] a) A. Alanine, L. C. Gobbi, S. Kolczewski, T. Luebbers, J.-U. Peters, L. Steward, U.S. Patent US 2006293350 A1, **2006**; *Chem. Abstr.* **2006**, *146*, 100721; b) P. V. Chaturvedula, L. Chen, R. Civiello, A. P. Degnan, G. M. Dubowchik, X. Han, X. J. Jiang, J. E. Macor, G. S. Poindexter, G. O. Tora, G. Luo, U.S. Patent US2007149503 A1 **2007**; *Chem. Abstr.* **2007**, *147*, 118256; c) J. Letourneau, C. Riviello, K.-K. Ho, J.-H. Chan, M. Ohlmeyer, P. Jokiel, I. Neagu, J. R. Morphy, S. E. Napier, PCT Int. Appl. WO 2006095014 A1 **2006**; *Chem. Abstr.* **2006**, *145*, 315012; d) M. Hour, L. Huang, S. Kuo, Y. Xia, K. Bastow, Y. Nakanishi, E. Hamel, K. Lee, *J. Med. Chem*. **2000**, *43*, 4479; e) J. F. Wolfe, T. L. Rathman, M. C. Sleevi, J. A. Campbell, T. D. Greenwood, *J. Med. Chem*. **1990**, *33*, 161; f) R. P. Maskey, M. Shaaban, I. Grun-Wollnu, H. Laatsch, *J. Nat. Prod*. **2004**, *67*, 1131.

[11] a) T. P. Selvam, P. V. Kumar, *Res. Pharmacy* **2011**, *1*, 1 and references cited therein; b) A. Camirand, M. Zakikhani, F. Young, M. Pollak, *Breast Cancer Res*. **2005**, *7*, R570; c) J. Baselga, S. D. Averbuch, *Drugs* **2000**, *60*, 33; d) R. Kim, T. Toge, *Surgery Today,* **2004**, *34*, 293.

[12] a) S. Santra, M. Rahman, A. Roy, A. Majee, A. Hajra, *Catal. Commun*. **2014**, *49*, 52 and references cited therein; b) M. Dabiri, P. Salehi, A. A. Mohammadi, M. Baghbanzadeh, *Synth. Commun.* **2005**, *35*, 279; c) M. Rueping, A. P. Antonchick, E. Sugiono, K. Grenader, *Angew. Chem. Int. Ed.* **2009**, *48*, 908; d) H. L. Yale, M. Kalkstein, *J. Med. Chem.* **1967**, *10*, 334.

[13] a) F. F. Li, Y. Feng, Q. Meng, W. Li, Z. Li, Q. Wang, F. Tao, *ARKIVOC* **2007**, *(i)*, 40; b) A. Maleki, H. Mofakham, *Synth. Commun*. **2008**, *38*, 3751; c) X.-S. Wang, K. Yang, J. Zhou, S.-J. Tu, *J. Comb. Chem.* **2010**, *12,* 417; d) D. Rambabu, S. K. Kumar, B. Y. Sreenivas, S. Sandra, A. Kandale, P. Misra, M. V. B. Rao, M. Pal, *Tetrahedron Lett*. **2013**, *54*, 495.

[14] a) J. F. M. Da Silva, S. J. Garden, A. C. Pinto, *J. Braz. Chem. Soc*. **2001**, 273; b) C. Fischer, C. Meyers, E. M. Carreira, *Helv. Chim. Acta* **2000**, *83*, 1175; c) P. B. Alper, C. Meyers, A. Lerchner, D. R. Siegel, E. M. Carreira, *Angew. Chem. Int. Ed.* **1999**, *38*, 3186; d) A. Ashimori, B. Bachand, L. E. Overmann, D. J. Poon, *J. Am. Chem. Soc*. **1998**, *120*, 6477; e) T. Matsuura, L. E. Overmann, D. J. Poon, *J. Am. Chem. Soc*. **1998**, *120*, 6500.

[15] a) R. A. Sheldon, *Chem. Commun.* **2008**, 3352; b) A. Kamal, V. Srinivasulu, B. N. Seshadri, N. Markandeya, A. Alarifi, N. Shankaraiah, *Green Chem*. **2012**, *14*, 2513.

[16] a) A. K. Chakraborti, S. R. Roy, *J. Am. Chem. Soc.* **2009**, *131*, 6902; b) A. Sarkar, S. R. Roy; N. Parikh, A. K. Chakraborti, *J. Org. Chem.* **2011**, *76*, 7132; c) S. R. Roy, A. K. Chakraborti, *Org. Lett.* **2010**, *12*, 3866.

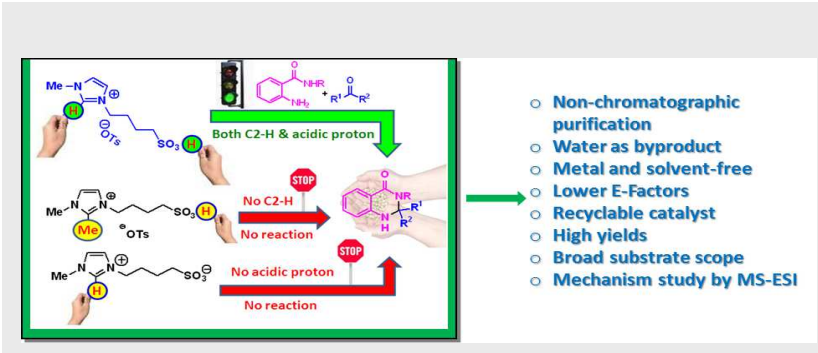
[17] L. S. Santos, *Eur. J. Org. Chem*. **2008**, 235.

Entry for the Table of Contents

Layout 2:

Ionic liquid-catalysis

FULL PAPER



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Page No. – Page No.

The Remarkable Cooperative Effect of a Brønsted Acidic Ionic Liquid in Cyclization between 2-Aminobenzamides with Ketones

An unprecedented role of an imidazolium Brønsted acidic ionic liquid has been found in the formation of 2,2-disubstituted quinazolin-4(1*H*)-one derivatives where both C2-H of imidazolium moiety and acidic proton are necessary and simultaneously take part in catalysis.