Tetrahedron Letters 55 (2014) 235–239

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Catalytic application of task specific ionic liquid on the synthesis of benzoquinazolinone derivatives by a multicomponent reaction

Matiur Rahman, Anirban Sarkar, Monoranjan Ghosh, Adinath Majee *, Alakananda Hajra *

Department of Chemistry, Visva-Bharati (A Central University), Santiniketan 731235, India

ARTICLE INFO

Article history:
Received 19 August 2013
Revised 31 October 2013
Accepted 2 November 2013
Available online 14 November 2013

Keywords:
Ionic liquid
Benzoquinazolin-2-one
Biginelli reaction
Hydrogen bond

ABSTRACT

Benzoquinazolin-2-one derivatives were synthesized by using a catalytic amount of task specific ionic liquid, [1-methyl-3-(4-sulfobutyl)imidazolium-4-methylbenzenesulfonate] through a one-pot multicomponent Biginelli reaction of α-tetralone, aldehyde, and urea/thiourea in excellent yields within a short reaction time. Mechanism studies suggest that the reaction proceeds through iminium intermediate and C2-H of the TSIL plays a major role on its catalytic activity. The catalyst has been reused four times without any significant loss in catalytic activity. Large scale reaction by using this TSIL suggests the applicability of this methodology for bulk synthesis of quinazolinone derivatives.

Multicomponent reactions (MCRs) have been proved to be a new tool in organic and medicinal chemistry as it provides rapid building of complex structure in a convergent and atom economical way.[1]

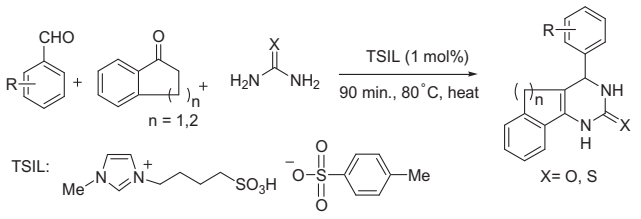
The quinazolinone moiety has a resourceful pharmacophoric feature and is present in many naturally occurring compounds. Thus it is of great importance to chemists and biologists. Compounds with this structural framework are also clinically useful and possess a wide range of biological activities such as antiviral, antimalarial, anticonvulsant, antibacterial, diuretic, hypnotic, hypoglycemic, antitumoral, and antihypertensive.[2] The Biginelli reaction, which was discovered more than a century ago is one of the most important reactions for the synthesis of dihydropyrimidinones by a three-component coupling of 1,3-dicarbonyl compounds, aldehydes, and urea.[3] Several improved procedures have been developed mainly based on 1,3-dicarbonyl compounds.[3c–f] However, only a few protocols have been reported using cyclic aryl ketones for the Biginelli condensation which produced quinazoline derivatives.[4] But these methodologies suffer from some stern drawbacks like use of TMSCl,[4a,e] HCl,[4b,d] $HClO_4$,[4g] $FeCl_3$,[4f] and other limitations such as narrow substrate scope and[4c] long reaction time.[4f] Thus, the quest remains for a practical and convenient method.

A new class of reaction medium has emerged–*ionic liquids* (ILs) that have been projected as green solvents. The tight legislation to maintain greenness in synthetic processes directs to prevent the generation of waste, avoid the use of auxiliary substances, and minimize the energy requirement.[5] The aspect of hazardness of the use of volatile organic solvents as auxiliary substances can be addressed by the use of *ionic liquids*[6] and the generation of waste and the consumption of energy can be minimized by the acceleration of reaction rates through the use of catalysts. However, there are some unresolved environmental, health, and safety issues in the use of ILs as solvents in large quantities.[7–9] Thus, its use in small quantities become an alternate choice to exploit the benefits of ILs.[10] The application of Brønsted acidic task-specific ionic liquids (TSILs) as catalytic materials is growing continuously in the field of catalysis.[11] Combining the useful characteristics of solid acids and mineral acids, TSILs have been applied to replace traditional mineral liquid acids, such as hydrochloric acid and sulfuric acid in chemical reactions. After the report by Forbes and Davis for the synthesis of a new class of phosphonium- and imidazolium ion-based ionic liquids equipped with a pendant acidic sulfonic acid moiety, Brønsted acidic ionic liquids (BAILs) have drawn considerable attention.[12] BAILs are more preferable over the traditional ionic liquids as these combine strong acidity with the use of nonvolatile ionic liquids. As a result many transformations have been carried out using this type of acidic IL.[11]

In continuation of our efforts toward the development of green methodologies using task specific ionic liquids (TSILs),[10b–f] we present in this study the use of 1-methyl-3-(4-sulfobutyl)imidazolium-4-methylbenzenesulfonate as a catalyst for the synthesis of benzoquinazolin-2-one and -2-thione in a one-pot, three-component reaction of α-tetralone, an aldehyde, and urea or thiourea (Scheme 1).

* Corresponding authors. Tel./fax: +91 3463 261526.
E-mail addresses: adinath.majee@visva-bharati.ac.in (A. Majee), alakananda.hajra@visva-bharati.ac.in (A. Hajra).

0040-4039/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetlet.2013.11.011



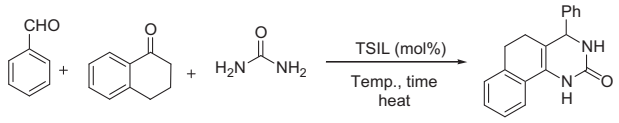
Scheme 1. Synthesis of quinazolinones catalyzed by TSIL.

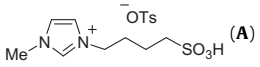
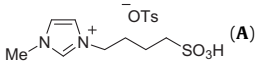
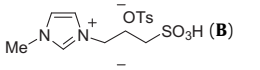
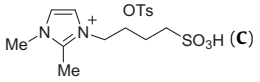
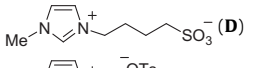
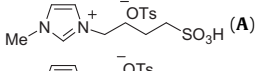
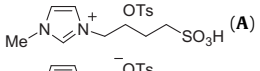
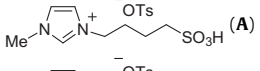
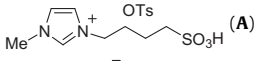
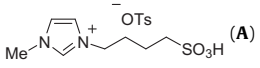
To find out a suitable TSIL, a model reaction was chosen by using benzaldehyde (1 mmol), α-tetralone (1 mmol), and urea (1 mmol) in the presence of different TSILs and the results are summarized in Table 1.

From Table 1 it is evident that TSIL **A** (Table 1, entry 2) was the most efficient catalyst which provided 85% yield within 90 min. It was also observed that catalytic efficiency depends on electronic environment and physiochemical properties of TSIL. With decreasing chain length of TSIL **B** catalytic properties decreased (Table 1, entry 3).[13] The poor catalytic effect was observed when C2-H was replaced by C2-Me (TSIL **C**) and afforded 56% yield in 90 min (Table 1, entry 4). It suggests that C2-H plays a crucial role to catalyze the reaction.[10g] Reaction without catalyst afforded very poor yield (<10%). It is worthy to mention that the Biginelli reaction for the synthesis of dihydropyrimidinones proceeded very well under catalyst and solvent-free conditions.[3f] It was also clear from Table 1 that the use of lower amount of catalyst decreased the yield, but use of higher quantity of catalyst did not improve the yield. Neither higher temperature (100 °C) nor longer reaction time (120 min) improved the yield of reaction (Table 1, entries 8 and 9). Moderate yield was obtained at lower temperature (Table 1, entry 10). Moreover, *p*-toluenesulfonic acid is not so effective like TSIL (**A**). Finally, the optimized condition for this reaction was chosen as use of 1 mol % catalyst (TSIL **A)** at 80 °C for 90 min (Table 1, entry 2).

To explore the generality and scope, several structurally diverse aldehydes were treated with α-tetralone (1 mmol) and urea/thiourea (1 mmol) under optimized reaction conditions and the results are summarized in Table 2. Both aromatic aldehydes substituted with electron donating group or electron withdrawing group underwent clean conversion to the desired products. The catalyst was compatible with various functional groups such as –Br (Table 2, entry 2) and $-NO_2$ (Table 2, entries 3 and 4). These reactions suggest the mildness of the catalyst. Acid sensitive aldehyde (piperonal) was also unaffected under these reaction conditions (Table 2, entries 7 and 8). The acid-sensitive heterocyclic substrate such as 2-thiophenecarboxaldehyde efficiently afforded the desired product without accompanying self-condensation (Table 2, entry 9). In general all the reactions were clean. No formation of undesired product was found. It is notable to mention that the pure product was isolated from the reaction mixture without use of any chromatographic method. Only ethanol was used for recrystallization to get the analytically pure products.

Table 1
Optimization of reaction conditions[a]



Entry	Catalyst	Mol (%)	Temp (°C)	Time (min)	Yield[b] (%)
1[c]	 (**A**)	0.5	80	90	49
2	 (**A**)	1	80	90	85
3	 (**B**)	1	80	90	68
4	 (**C**)	1	80	90	56
5	 (**D**)	1	80	90	52
6	 (**A**)	2	80	90	86
7	 (**A**)	5	80	90	86
8	 (**A**)	1	100	90	86
9	 (**A**)	1	80	120	85
10	 (**A**)	1	60	120	52
11	—	—	80	90	<10
12	*p*-Toluenesulfonic acid	1	80	90	24

[a] Reaction conditions: benzaldehyde (1 mmol), α-tetralone (1 mmol), and urea (1 mmol) in neat conditions.
[b] Isolated yield.
[c] Reaction was carried out on 5 mmol.