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An Expedient Synthesis of 2-Aryl-substituted 2,3-Dihydroquinazolin-4(1*H*)-ones in Low Transition Temperature Mixture (LTTM) containing $SnCl_2$ and L-Proline

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2,3-Dihydroquinazolin-4(1*H*)-ones were synthesized in excellent yield in a prepared low transition temperature mixture (LTTM) containing $SnCl_2$ and L-proline using either direct one-pot two-component cyclocondensation of anthranilamide and aldehydes or one-pot three-component cyclocondensation of isatoic anhydride, ammonium acetate and aldehydes. The prepared LTTM is a green solvent, inexpensive, non-toxic and serves a dual function as reusable catalyst and solvent with excellent reaction endorsing medium. The current protocol has several advantages including an easy work up, shorter reaction time, high yield with a higher atom economy and maximum reaction efficiency with excellent green chemistry metrics.

Keywords: Low transition temperature mixture, 2-Aryl-substituted 2,3-dihydroquinazolin-4(1*H*)-ones, Green chemistry, Quinazolinone.

INTRODUCTION

Quinazolinone skeletons are the important bicyclic aza-heterocycles with a wide range of pharmaceutical and biological applications. They possesses range of biological activities such as anti-inflammatory [1], antibacterial [2,3], anticancer [4,5], antifungal [6,7], antitumor [8,9], anticonvulsant [10], analgesic [11], antihypertension [12,13] and antidiabetes [14]. The researchers are therefore continuously engaged in development of simple and proficient rout for synthesis of quinazolinone.

A number of classical methodologies for the synthesis of 2,3-dihydroquinazolinones have been reported in the literature, including two-component condensation of anthranilamide with aldehyde and three-component condensation of isatoic anhydride, aldehyde and ammonium acetate with a variety of catalysts such as cerium(IV) sulfate [15], starch sulfate [16], SiO_2-$ZnCl_2$ [17], SiO_2-$FeCl_3$ [18], Al/Al_2O_3 nanoparticles [19], Co-CNTs [20], Amberlyst-15 [21], SPC [22], H_3BO_3-MCM-41 [23], trichloroacetic acid [24], aerosil silica-supported acidic ionic liquid [25], sulfamic acid [26], poly(4-vinylpyridine)-supported acidic ionic liquid [27], trifluoroethanol [28], supported N-propylsulfamic acid on magnetic nanoparticles [29], supramolecular synthesis [30], heteropoly acids [31], tetrabutylammonium bromide [32], $ZrCl_4$ [33] and heteropoly acid-clay nanocomposite [34]. Although each of these methods has advantages, some of them have drawbacks, such as low product yields, long reaction times, harsh reaction conditions, extractive product isolation with toxic organic solvents, time-consuming catalyst preparation procedures and use of toxic and expensive catalysts or media. Thus, scientific community appreciates the benign synthetic routes for synthesis of 2,3-dihydroquinazolinones. In view of this, a simple and efficient method is described for the synthesis of 2,3-dihydroquinazolinones *via* two-component condensation of anthranilamide with aldehyde and three-component condensation of isatoic anhydride, aldehyde and ammonium acetate using low transition temperature mixture (LTTM) as reaction medium and explored the study of green metric calculations.

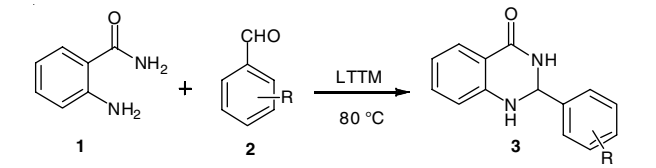
EXPERIMENTAL

All the solvents and reagents were commercially sourced and used without further purification. Melting points were taken on a melting point apparatus and are uncorrected. ^{1}H NMR

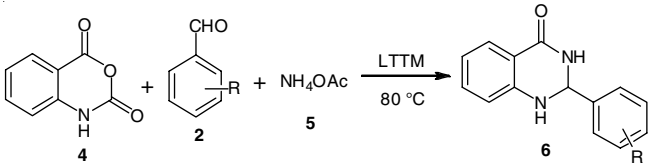
and ^{13}C NMR spectra were recorded on a Bruker 400 MHz instrument using tetramethylsilane (TMS) as an internal standard and DMSO-d_6 as the solvent at room temperature.

General synthetic procedure of $SnCl_2$:L-proline (1:1) (LTTM): The LTTM have been prepared by selecting hydrated stannous chloride as a hydrogen bond donor and L-proline as a hydrogen bond acceptor. A mixture of hydrated stannous chloride (10 mmol, 2.25 g) and L-proline (20 mmol, 2.3 g) in ratio 1:2 was heated at 80 ºC with continuous stirring for 30 min. The resulting LTTM forms whitish viscous liquid with an excellent atom economy was subsequently allowed to cool at room temperature and was used for the synthesis of 2-aryl-substituted 2,3-dihydroquinazolin-4(1*H*)-ones derivatives without further purification.

General procedure for synthesis of 3a-n and 6a-n: For two component condensation, a mixture of anthranilamide (1 mmol), LTTM (5 mL) and appropriate aldehyde (1 mmol) was stirred at 80 ºC for 30 min. For three component condensation a mixture of isatoic anhydride (1 mmol), LTTM (5 mL) and ammonium acetate (1.3 mmol) in reaction tube was stirred at 80 ºC for 5 min and then appropriate aldehyde (1 mmol) was added in reaction tube at 80 ºC for 30 min. The progress of the reaction was monitored by thin-layer chromatography (TLC). After completion, distilled water (15 mL) was added and the mixture was stirred for 2 min. The corresponding solid product was obtained through simple filtration, which was recrystallized from absolute ethanol (**Scheme-I**).



(A) Two component strategy



(B) Three component strategy

Scheme-I: Synthesis of 2-aryl-substituted 2,3-dihydroquinazolin-4(1*H*)-ones

2-Phenyl-2,3-dihydroquinazolin-4(1*H*)-one (3a/6a) [15]**:** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 5.57 (s, 1H), 6.59 (t, 1H), 6.66 (d, 1H), 7.13 (s, 1H), 7.44 (m, 3H), 7.29 (t, 1H), 7.54 (d, 1H), 7.55 (d, 2H), 8.35 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: 67.15, 114.18, 115.44, 117.69, 127.36, 127.53, 128.90, 128.94, 133.89, 142.15, 148.25, 164.18.

2-(4-Chlorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3b/6b) [23]**:** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 5.72 (s, 1H), 6.47 (s, 1H), 6.62-6.64 (m, 2H, *J* = 8 Hz), 7.15 (s, 1H), 7.25-7.25 (m, 2H, *J* = 8 Hz), 7.39-7.42 (m, 2H), 7.64-7.71 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): 66.96, 114.80, 115.01, 118.04, 127.83, 128.60, 128.80, 128.86, 133.75, 134.26, 139.67, 147.82, 164.72.

2-(4-Bromophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3c/6c) [15]**:** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 5.67 (s, 1H), 6.72-6.82 (m, 2H), 7.15 (s, 1H), 7.45 (d,, 1H, *J* = 7.8 Hz), 7.49 (d, 2H, *J* = 8.4 Hz), 7.60-7.68 (m, 3H), 8.32 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: 69.0, 113.15, 116.16, 117.22, 127.25, 128.35, 129.10, 129.24, 133.35, 143.40, 148.53, 167.67 ppm.

2-(4-Methylphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3d/6d) [15]**:** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 2.45 (s, 3H), 5.51 (s, 1H), 6.76 (d, 1H), 6.87 (t, 1H), 7.15 (s, 1H), 7.37-7.48 (m, 3H), 7.47 (m, 2H), 7.81 (d, 1H), 8.29 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: 21.39, 65.84, 114.57, 115.77, 117.83, 127.86, 127.57, 128.27, 133.52, 132.78, 138.57, 138.93, 147.98, 165.10 ppm.

2-(4-Methoxyphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3e/6e) [23]**:** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 3.70 (s, 3H), 5.67 (s, 1H), 6.37 (s, 1H), 6.60-6.67 (m, 2H, *J* = 8Hz), 6.80-6.82 (m, 2H, *J* = 8.2Hz), 7.17-7.32 (m, 1H), 7.61 (m, 3H, *J* = 6.9 Hz), 7.70 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: 55.36, 67.36, 113.83, 114.78, 115.07, 117.73, 127.76, 128.59, 132.94, 133.58, 148.30, 159.99, 164.76.

2-(4-Nitrophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3f/6f) [23]**:** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 5.35 (s, 1H), 6.75 (t, 1H), 6.88 (d, 1H), 7.17 (t, 1H), 7.36 (d, 1H), 7.44 (s, 1H), 7.65 (d, 2H), 8.45 (d, 2H), 8.63 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: 65.47, 115.92, 115.57, 117.54, 123.85, 123.87, 126.88, 127.525, 128.98, 134.25, 148.17, 146.49, 149.58, 162.96.

2-(2-Nitrophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3g/6g) [35]**:** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 6.46 (s, 1H), 6.66-6.73 (m, 2H), 7.11 (s, 1H), 7.22-7.26 (m, 1H), 7.61-7.66 (m, 2H), 7.72-7.82 (m, 2H), 8.09-8.12 (m, 1H), 8.23 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: 62.78, 115.13, 115.53, 117.11, 118.25, 125.29, 127.89, 129.47, 130.45, 134.07, 134.48, 136.46, 147.69, 148.19, 163.91.

2-(4-Cynophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3h/6h) [36]**:** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 5.91 (s, 1H), 6.66-6.72 (m, 1H), 6.79 (d, 1H, *J* = 8.1Hz), 7.23-7.33 (m, 2H), 7.65 (m, 1H, *J* = 7.7, 1.4 Hz), 7.69 (d, 2H, *J* = 8.2 Hz), 7.86-7.92 (m, 2H), 8.51 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: 66.30, 111.71, 115.11, 115.57, 117.81, 119.29, 127.87, 128.35, 132.77, 134.26, 147.78, 147.83, 163.77.

2-(4-Hydroxyphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3i/6i) [35]**:** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 6.97 (d, 3H, *J* = 8.3 Hz), 7.49 (t, 1H, *J* = 7.5 Hz), 7.63 (d, 1H, *J* = 8.2 Hz), 7.79 (t, 1H, *J* = 7.7 Hz), 8.13 (m, 4H, *J* = 12.0, 8.1 Hz), 10.17 (s, 1H), 12.09-12.34 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: 67.86, 113.33, 115.87, 121.15, 123.78, 126.29, 126.31, 127.66, 130.09, 134.91, 149.54, 152.62, 161.07, 162.83.

2-(Furan-2-yl)-2,3-dihydroquinazolin-4(1*H*)-one (3j/6j) [37]**:** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 5.82 (d, 1H, *J* = 3.2 Hz), 6.41 (s, 2H), 6.57 (bs, 1H), 6.75 (t, 2H, *J* = 8.1 Hz), 7.31 (t, 1H, *J* = 8.3 Hz), 7.59 (m, 1H, *J* = 7.7 Hz), 7.76 (bs, 1H), 8.19 (d, 1H, *J* = 2.5 Hz); ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: 60.28, 107.23, 109.79, 114.55, 117.46, 127.36, 133.23, 141.17, 142.43, 146.35, 152.29, 163.24.

2-(3,4-Dimethoxyphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3k/6k) [35]**:** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 3.76

(s, 6H), 5.66 (s, 1H), 6.52 (s, 1H), 6.60-6.64 (s, 1H), 6.67-6.69 (s, 1H), 6.78-6.81 (s, 1H), 6.95-6.98 (s, 1H), 7.09-7.16 (m, 2H), 7.62-7.64 (d, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: 55.89, 55.93, 67.68, 110.39, 110.91, 114.82, 115.07, 117.93, 119.74, 127.80, 133, 133.65, 148.24, 148.92, 149.41, 164.90.

2-(4-*N*,*N*-Dimethylaminophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3l/6l) [35]**:** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 2.81 (s, 6H), 5.63 (s, 1H), 6.77 (t, 1H, *J* = 8.2 Hz), 6.91 (d, 1H, *J* = 6.8 Hz), 7.21 (bs, 1H), 7.31-7.46 (m, 3H), 7.37 (d, 2H, *J* = 8.8 Hz), 7.69 (d, 1H, *J* = 7.8 Hz), 8.47 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: 41.39, 68.35, 113.13, 116.67, 117.88, 127.13, 128.15, 129.37, 129.49, 133.54, 142.17, 148.27, 166.39.

2-(4-Hydroxy-3-methoxyphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3m/6m) [23]**:** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 4.01 (s, 3H), 4.26 (s, 1H), 6.21 (s, 1H), 7.20-7.31 (m, 4H), 7.62 (s, 1H), 7.79 (d, *J* = 6.9 Hz, 1H), 8.17 (d, *J* = 7.2 Hz, 1H), 8.69 (s, 1H), 9.67 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: 56.57, 67.83, 112.05, 115.46, 115.93, 115.91, 118.16, 120.65, 128.38, 132.94, 143.27, 147.82, 148.47, 149.13, 164.82.

2-(Naphthalen-1-yl)-2,3-dihydroquinazolin-4(1*H*)-one (3n/6n) [36]**:** ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 6.12 (s, 1H), 6.63 (d, 1H, *J* = 8.3 Hz), 6.89 (t, 1H, *J* = 8.3 Hz), 7.16-7.19 (m, 3H), 7.26-7.37 (m, 3H), 7.49 (t, 1H, *J* = 8.3 Hz), 8.03 (d, 1H, *J* = 1.5 Hz), 8.07-8.13 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ ppm: δ 74.68, 114.85, 119.63, 126.77, 126.95, 128.43, 128.76, 128.94, 130.18, 133.89, 145.23, 163.16.

RESULTS AND DISCUSSION

Initially, low transition temperature mixture (LTTM) have been prepared from the reaction of hydrated stannous chloride and L-proline in the ratio 1:2 at 80 ºC with continuous stirring for 30 min. The prepared LTTM was then employed for synthesis of 2-aryl-substituted 2,3-dihydroquinazolin-4(1*H*)-ones *via* two component and three component strategies (**Scheme-I**).

The optimization of reaction conditions was then carried out selecting the model reaction of 4-chloro benzaldehyde (Table-1). Selecting LTTM catalytic medium (5 mL), we tested various solvents such as *n*-hexane, DCM, CH_3CN and ethanol at 80 ºC. Reaction in all mentioned solvents resulted moderate yield of desired products (Table-1, entries 1-4). The model reaction was also performed in water which gave good yields (Table-1, entry 5). Considering the above results we performed same reaction in LTTM without any solvent at 80 ºC. Interestingly, the reaction completed with excellent yields of desired products (Table-1, entry 6). To check the efficiency of LTTM, we examined the reaction at 2 mL and 10 mL of LTTM in the reaction (Table-1, entries 7-8). However, no positive yields were obtained. The model reaction was also carried out without LTTM catalytic medium and solvent which resulted no or lower yields (Table-1, entry 9). From the yields obtained at room temperature, it was confirmed that 80 ºC suitable reaction temperature (Table-1, entry 10).

The optimized reaction conditions employed to extend the generality of the present method. The synthesis of 2-aryl-substituted 2,3-dihydroquinazolin-4(1*H*)-ones have been carried out from two-component strategy (derivatives **3a** to **3n**) by reaction of anthranilamide with aldehyde and three-component strategy (derivatives **6a** to **6n**) by reaction of isatoic anhydride, ammonium acetate with aldehyde at 80 ºC in 30 min (**Scheme-I**). Variety of aldehydes possessing electron donating and electron withdrawing moieties have been reacted. All reactions resulted efficient yield of desired products (Table-2, entries 1-11). Highly functional 2,3-dihydroquinazolin-4(1*H*)-ones have also been synthesized in high yield under optimized reaction conditions (Table-2, entries 12-14). From the results, it is revealed that both strategies gave range of 2,3-dihydroquinazolin-4(1*H*)-ones with remarkable yields.

The efficiency of LTTM catalyst was evaluated form the comparison study with reported methodology at diverse conditions. From the study (Table-3), it is revealed that most of the reported methods performed at high temperature, required long reaction time and moderate yields. In conclusion, present method involving LTTM catalytic system at 80 ºC is proficient with respect to reaction time and yields.

Mechanism: A plausible mechanism for the synthesis of 2-aryl-2,3-dihydroquinazolin-4(1*H*)-one derivatives as shown in **Scheme-II**. Based on the experimental results, the mechanism of the reaction is thought to proceeded through condensation of aldehyde with isatoic anhydride or anthranilamide, which

TABLE-1
OPTIMIZATION OF REACTION CONDITIONS FOR SYNTHESIS OF 2,3-DIHYDROQUINAZOLIN-4(1*H*)-ONES[a]

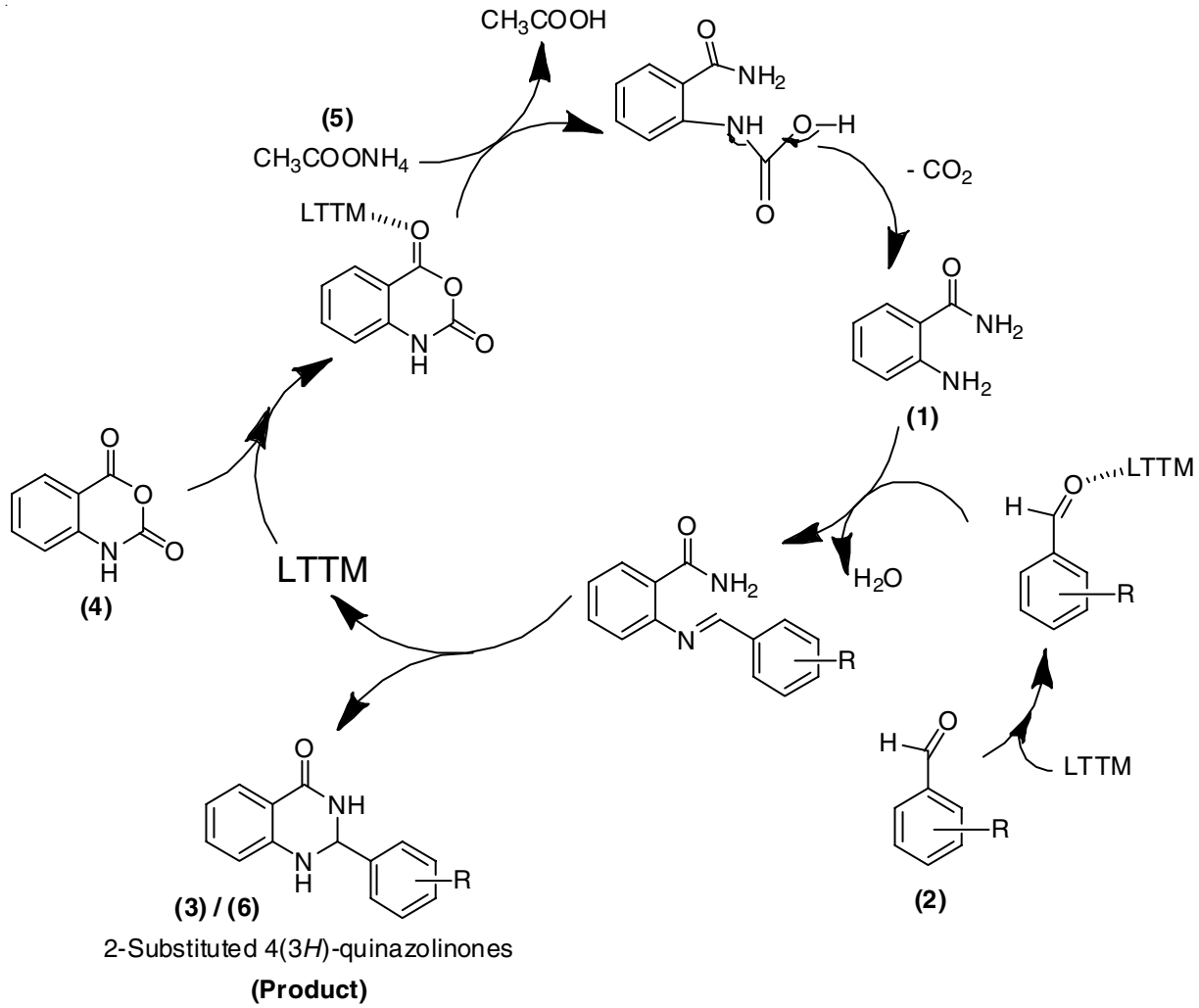
Entry	Catalyst (mL)	Solvent	Temp. (°C)	Time (min)	Isolated yields (%)	
					6b	**3b**
1	LTTM (5)	*n*-Hexane	80	60	30	34
2	LTTM (5)	CH_2Cl_2	80	60	35	39
3	LTTM (5)	CH_3CN	80	60	64	66
4	LTTM (5)	C_2H_5OH	80	60	78	82
5	LTTM (5)	H_2O	80	60	72	76
6	LTTM (5)	Solvent free	80	30	92	96
7	LTTM (2)	Solvent free	80	30	75	81
8	LTTM (10)	Solvent free	80	30	92	96
9	–	Solvent free	80	30	20	NR
10	LTTM (5)	Solvent free	RT	30	28	22

[a]Reaction conditions: [Anthranilamide (1 mmol), 4-Cl-benzaldehyde (1 mmol)] (**3b**) and [Isatoic anhydride (1 mmol), 4-Cl-benzaldehyde (1 mmol) and NH_4OAc (1.3 mmol)] (**6b**)

TABLE-2
SYNTHESIS OF 2-ARYL-SUBSTITUTED 2,3-DIHYDROQUINAZOLIN-4(1*H*)-ONES[a]

Entry	Product	Aldehyde R^2-CHO	Isolated yield (%)		Melting point (°C)	
			3	**6**	Found	Reported
1	**3a/6a**	C_6H_5-	90	89	217-218	218-219 [15]
2	**3b/6b**	4-(Cl)C_6H_4	92	91	205-206	206-208 [23]
3	**3c/6c**	4-(Br)C_6H_4	92	90	201-202	200-202 [15]
4	**3d/6d**	4-(CH_3)C_6H_4	87	86	233-234	234-236 [15]
5	**3e/6e**	4-(OCH_3)C_6H_4	89	89	188-190	190-192 [23]
6	**3f/6f**	4-(NO_2)C_6H_4	90	88	200-202	202-204 [23]
7	**3g/6g**	2-(NO_2)C_6H_4	86	84	186-189	186-188 [35]
8	**3h/6h**	4-(CN)C_6H_4	91	86	242-245	240-247 [36]
9	**3i/6i**	4-(OH)C_6H_4	88	88	276-277	275-277 [35]
10	**3j/6j**	2-Furyl	90	88	165-166	164-165 [37]
11	**3l/6l**	4-(NMe_2)C_6H_4	91	90	241-242	240-242 [35]
12	**3k/6k**	3,4-(OCH_3)$_2C_6H_3$	92	92	209-211	210-213 [35]
13	**3m/6m**	Vanillin	88	84	190-192	188-190 [23]
14	**3n/6n**	1-naphthaledehyde	92	90	209-210	208-210 [36]

[a]Reaction conditions: [Anthranilamide (1 mmol), aldehyde (1 mmol)] (**3a**) and [Isatoic anhydride (1 mmol), aldehyde (1 mmol) and NH_4OAc (1.3 mmol)] (**6a**), LTTM (5 mL), time 30 min.



Scheme-II: Plausible mechanism for synthesis of 2-substituted 4(3*H*)-quinazolinones

subsequently forms an imine intermediate that cyclizes to afford the corresponding 2-aryl-2,3-dihydroquinazolin-4(1*H*)-one as the desired product.

Reusability study: The reusability of catalyst is of important highly significant in view of green chemistry. In the present study, reusability of LTTM was evaluated by using the reaction

TABLE-3
COMPARISON STUDY WITH REPORTED METHODS

Entry	Catalyst	Temp. (°C)	Time (min)	Yield (%)	Ref.
1	Cerium(IV) sulfate	120	30-50	85-97	[15]
2	Starch sulfate	100	5-55	75-96	[16]
3	SiO_2-$ZnCl_2$	100	30-80	51-95	[17]
4	SiO_2-$FeCl_3$	80	9-120	45-91	[18]
5	Al/Al_2O_3 NPs	115	8-30	65-98	[19]
6	Co-CNTs	MW	10-35	75-98	[20]
7	Amberlyst-15	MW	3-7	69-87	[21]
8	SPC	70	150-210	78-86	[22]
9	H_3BO_3-MCM-41	80	18-60	76-94	[23]
10	LTTM (Sn-Pr 1:2)	80	30	86-96	Present work

of synthesis of **3b** or **6b** in presence of hydrated stannous chloride as a hydrogen bond donor and L-proline as a hydrogen bond acceptor in the ratio 1:2 under optimized conditions. After completion of the reaction, as indicated by TLC, 10 mL of water was added to the reaction mixture and the crude reaction product was separated by simple filtration. The LTTM was recovered by evaporating water under vacuum. The recovered LTTM was the employed for next reaction cycle. The LTTM catalyst can be recycled up to four reactions without significant loss in yield of the reaction (Fig. 1).

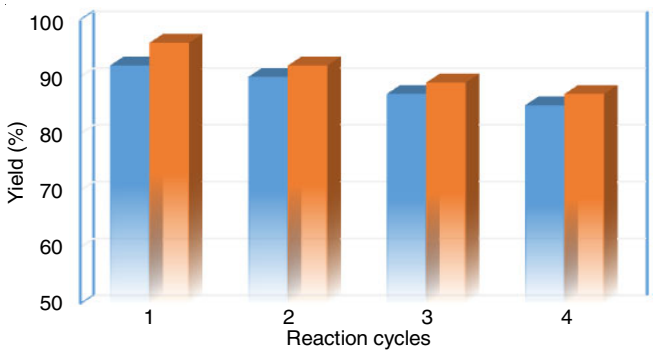


Fig. 1. Reusability study of LTTM catalyst

Green metric calculations for synthesis of 2-substituted 4(3*H*)-quinazolinones: In the context of green chemistry, the implementation of appropriate substrate, an efficient catalyst and an adequate solvent is thus planned. The goal of green chemistry in chemical research and engineering is to encourage the design of products and processes that minimize the use and generation of hazardous substances. Green metrics such as mass intensity (MI), reaction mass efficiency (RME), carbon efficiency (CE) and atom economy (AE) were used to evaluate the current protocol of two-component condensation of anthranilamide with aldehyde or ketones and three-component condensation of isatoic anhydride, aldehyde and ammonium acetate in accordance with green chemistry principles. The investigation of these green metrics revealed the greenness of reactions. In an ideal situation, it is expected that MI ≅ 1%, RME ≅ 100%, %CE ≅ 100 and %AE ≅ 100. The green metrics calculations for all the reactions are presented in Table-4. As compared to three-component system, results obtained from two-component system demonstrate that MI values for all compounds are quite excellent as well as excellent yields produced good values of RME while moderate yield produced moderate RME values (Fig. 2). Moreover, the present reactions show excellent CE because all the carbon atoms of the reactants are present in the product. Atom economy values ≅ 90% reveals that the present protocol is of high atom economy. The developed LTTM is a green solvent that is inexpensive, non-toxic and serves a dual function (reusable catalyst and solvent) and it has been discovered to be an excellent reaction endorsing medium.

Conclusion

In summary, hydrated stannous chloride and L-proline (1:2) low transition temperature mixture (LTTM) was successively reported and used as a biocompatible catalyst for two component and three component syntheses of 2-aryl-2,3-dihydro-quinazolin-4(1*H*)-ones. The LTTM exists to serve as a solvent as well as a catalyst with improved reusability. This

TABLE-4
GREEN METRIC CALCULATIONS FOR TWO COMPONENT AND THREE COMPONENT SYNTHESES OF 2-SUBSTITUTED 4(3*H*)-QUINAZOLINONES

Entry	Aldehyde R^2-CHO	Two component reaction						Three component reaction					
		Product	Yield (%)	AE (%)	CE (%)	RME (%)	MI (%)	Product	Yield (%)	AE (%)	CE (%)	RME (%)	MI (%)
1	C_6H_5-	**3a**	93	92.57	95.04	78.99	1.27	**6a**	88	64.75	78.27	55.16	1.81
2	4-(Cl)C_6H_4	**3b**	96	93.49	97.85	82.35	1.21	**6b**	92	67.94	77.44	57.37	1.74
3	4-(Br)C_6H_4	**3c**	96	94.39	96.35	81.88	1.22	**6c**	92	71.29	76.64	59.62	1.68
4	4-(CH_3)C_6H_4	**3d**	90	92.57	92.15	76.89	1.30	**6d**	87	66.12	59.20	44.42	2.25
5	4-(OCH_3)C_6H_4	**3e**	93	93.38	94.22	79.10	1.26	**6e**	89	70.56	60.51	48.46	2.06
6	4-(NO_2)C_6H_4	**3f**	94	93.73	96.08	81.14	1.23	**6f**	90	68.81	76.40	57.33	1.74
7	2-(NO_2)C_6H_4	**3g**	89	93.73	90.11	76.06	1.31	**6g**	86	68.81	72.56	54.45	1.84
8	4-(CN)C_6H_4	**3h**	95	93.26	97.02	81.30	1.23	**6h**	91	67.13	73.33	53.66	1.86
9	4-(OH)C_6H_4	**3i**	92	93.03	93.19	77.95	1.28	**6i**	88	66.31	74.07	53.52	1.87
10	2-Furyl	**3j**	93	92.24	93.45	77.59	1.29	**6j**	90	63.70	72.56	51.95	1.92
11	3,4-(OCH_3)$_2C_6H_3$	**3k**	96	94.04	98.24	83.11	1.20	**6k**	92	69.96	79.39	59.19	1.69
12	4-(NMe_2)C_6H_4	**3l**	95	93.69	96.76	81.49	1.23	**6l**	91	68.65	78.33	57.33	1.74
13	Vanillin	**3m**	92	93.75	92.83	78.32	1.28	**6m**	88	68.89	74.08	55.04	1.82
14	1-Naphthaledehyde	**3n**	96	93.84	98.00	82.52	1.21	**6n**	92	69.20	81.09	58.66	1.70

MI = mass intensity, RME = reaction mass efficiency, CE = carbon efficiency, AE = atom economy

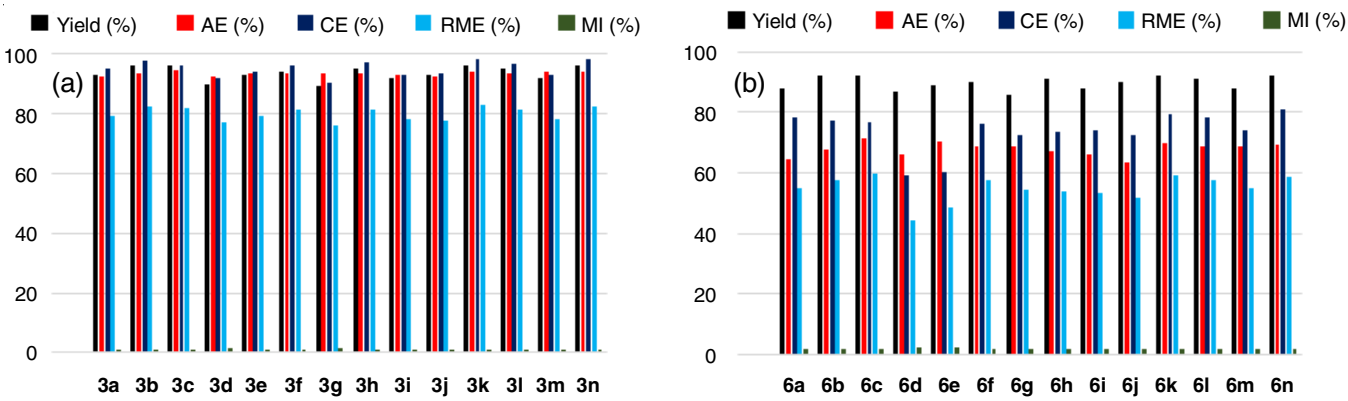


Fig. 2. Graphical illustration of green metric calculations for two (a) and three (b) component strategy

protocol has several advantages, including solvent-free green synthesis with operational simplicity, an easy work-up procedure, good to excellent yields, a column-free technique and an excellent correlation with green metrics calculations. As compared to three-component system, the high yield of products obtained in two-component system demonstrates that the significant RME values. Furthermore, all carbon atoms in the reactants are present in the product, resulting in excellent percent CE values. The reaction's MI values are extremely close to the ideal values. Each scaffold's percent atom economy indicates the maximum conversion of starting materials into product and the least amount of waste exclusion. The catalytic system can be recycled for at least four reaction cycles.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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