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Ionic liquid catalyzed reusable protocol for one-pot synthesis of 2,3-dihydroquinazolin-4(1*H*)-one under mild conditions

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An efficient protocol has been developed for the synthesis of 2,3-dihydroquinazolinone compounds from anthranilamide and aldehydes or ketones *via* ionic liquid catalyzed cyclization reaction. The reaction features high efficiency, shorter reaction duration, mild reaction conditions and inexpensive reagents. The catalyst was recovered and reused. The recyclability of ionic liquid resulted excellent yields of product without loss of any catalytic activity.

Introduction

Quinazolinones are important class of N-heterocycles, and often present in natural products, drug molecules and pharmaceutical compounds.[1] Initially, Bischler and Lang reported the first synthesis of quinazolinone in 1895. Later, in 1903, Gabriel prepared alternate approach *via* oxidation of 3,4-hydroxyquinazole to quinazolinone.[2] Moreover, 2,3-dihyroquinazolinones are associated with several important biological activities such as, anti-cancer,[3] anti-inflammation,[4] anti-bacterial,[5] anti-virus,[6] anti-tuberculosis,[7] anti-malarial,[8] anti-hypertensive,[9] anti-obesity, anti-psychotic, anti-diabetes,[10] etc. In this context, several synthetic methodologies have been developed employing metal-salts such as SmI_2,[11] Ru-salt,[12] $CuCl_2$,[13] $SnCl_2$,[14] $Sc(OTf)_3$,[15] $ZnCl_2$,[16] $[CpIrCl_2]_2$,[17] $Pd(OAc)_2$,[18] CuO,[19] $[Zr(DS)_4]$,[20] $Ga(OTf)_3$,[21] $TiCl_4$,[22] $KAl(SO_4)_2.12H_2O$,[23a] $Al(H_2PO_4)_3$,[23b] $[Ce(NH_4)_2.(NO_3)_6]$,[24] and metal nano-particles,[25] of Co, Cu, Ag, In, La and Fe. Transition metals are expensive, unstable and often produce considerable amount of metal wastes. Therefore series of non-metal catalysts has been developed for the preparation of molecules containing this motif, HCl,[26] p-TSA,[27] I_2,[28] TMSCl,[29] NH_4Cl,[30] trifluoroethanol,[31] acidic silica,[32] cyanuric chloride,[33] heteropoly acid,[34] Amberlyst-15,[35] montmorillonite K-10.[36]

The synthetic transformations employing non-toxic, eco-friendly catalyst have been received much attention in recent years. Particularly, utilizing organocatalyst and green catalyst, ionic liquids[37] are beneficial compared with the metal catalysts.

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The other reported green procedures for the synthesis of 2,3-dihydroquinazolinones have been employed using ionic liquids,[37a-g] and organocatalysts such as phosphoric acid,[38] T3P,[39] ^tBuOK,[40] β-cyclodextrine,[41] polyethylene glycol-400,[42] K_3PO_4,[43] *p*-sulfonic acid (calyx[4]arene)[44] and are known. Despite these synthetic protocols a practical, mild and green catalysts are still in great demand. In continuation of our efforts to develop eco-friendly protocols for multicomponent reaction,[45] here in, we wish to report a new efficient method employing ionic liquid catalyzed **1a-c** (Figure 1) one-pot synthesis of 2,3-dihydroquinazolinones under mild conditions (Scheme 1).

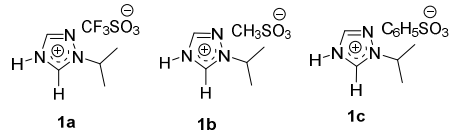
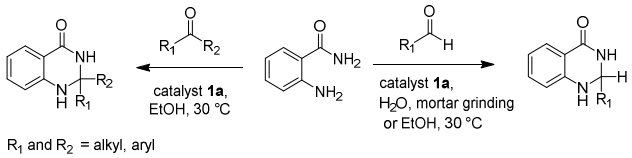


Figure 1. The structures of ILs examined in this paper

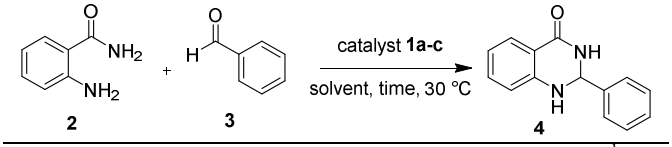


Scheme 1. IL-catalyzed synthesis of 2,3-dihydroquinazolinones

Results and discussion

The ionic liquids **1a-c** was prepared in large scale using our synthetic procedure.[45d] Our initial efforts focused on developing general, suitable and green reaction conditions and the results are summarized in Table 1. When anthranilamide **2** (1 equiv.) was allowed to react with benzaldehyde **3** (1 equiv.) in the presence of ionic liquid **1a** as catalyst (2 mol%) in H_2O at 25 °C, the traces of **4** was formed. The yield improved dramatically upon addition of 5 mol% of catalyst, resulted 70% yield of **4** (Table 1, entry 3). While increasing the amount of catalyst to 10 mol% 2,3- dihydroquinazolinone (**4**) was obtained in 85% yield (entry 4). Surprisingly, when the reaction was subjected to grinding using mortar for 2 minutes, quinazolinone was isolated as sole product in >95% yield. The product conversion proceeded slowly and in low yield (25%) under solvent-free condition (entry 6). A number of experiments were performed in an effort to extent the general/large-scale procedure to the preparation of 2,3-dihydroquinazolinone. The reaction proceeds in polar solvents (MeOH, EtOH) and afforded the product **4** in 40% and 88% yields, respectively (entries 7-8). To address, the need for enhanced yield, we added 10 mol% of catalyst **1a**, which resulted 92% of 2,3-dihydroquinazolinone in 10 minutes (entry 9). It was found that the use of 15-20 mol% **1a**, the reaction was faster and completed within a minute. However, the stoichiometric amount of catalyst **1a** (in absence of solvent) was resulted low yield of product (entry 12). The reaction improved efficiently, upon addition of a mixture of EtOH:H_2O (1:2) to the reaction (entry 13). Other screened solvents such as, THF, CH_2Cl_2, CH_3CN, DMF, toluene, EtOAc, led to a 80-94% yields of product **4** (entries 14-19). It was found that the other screened ionic liquids **1b** and **1c** were resulted product **4** in 85% and 80% yields, respectively. The reaction proceeds most efficiently with ionic liquid **1a**, probably due to strong C-F bonding enhance the rate of reaction. The excellent results were obtained with 10 mol% of ionic liquid **1a** at 30 °C, H_2O in mortar grinding (Table 1, entry 5) or at 30 °C, EtOH:H_2O stirring in sample vial (Table 1, entry 13).

Table 1 Evaluation of reaction parameters[a]

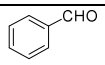
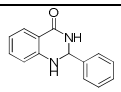


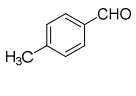
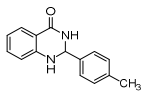
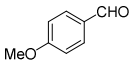
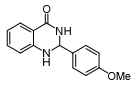
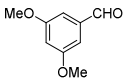
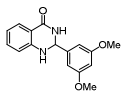
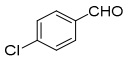
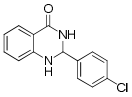
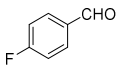
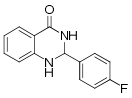
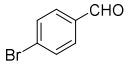
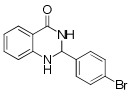
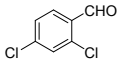
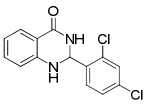
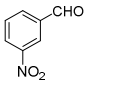
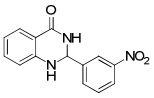
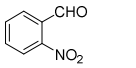
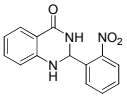
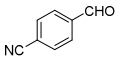
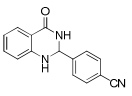
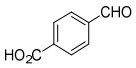
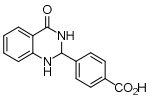
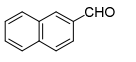
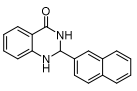
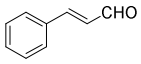
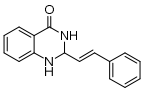
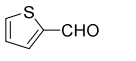
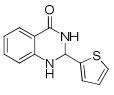
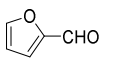
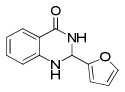
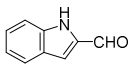
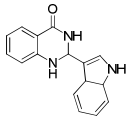
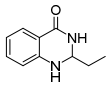
Entry	Catalyst (mol%)	Solvent (mL)	Time (min)	Yield[b] (%)
1	2	H_2O	10	traces
2	5	H_2O	10	35
3	5	H_2O	25	70
4	10	H_2O	4	85
5	10	H_2O	2	95[c] (85, 80)[d]
6	5	neat	120	10 (25)[e]
7	5	MeOH	2	40
8	5	EtOH	10	88
9	10	EtOH	5	92
10	15	EtOH	1	91
11	20	EtOH	1	91
12	100	nil	5	80
13	10	EtOH:H_2O	2	96
14	5	THF	5	90
15	5	CH_2Cl_2	10	94
16	5	CH_3CN	10	81
17	5	DMF	10	88
18	5	Toluene	10	80
19	5	EtOAc	20	82

[a]Reaction conditions: [a]anthranilamide (3.0 mmol), benzaldehyde (3.0 mmol), ionic liquid **1a**, solvent; [b]isolated yield; [c]reaction was carried out in mortar pestle; [d] catalyst **1b** and **1c** were employed, respectively; [e]stirred for overnight; solvent mixture of 2:1.

The versatility of this protocol was investigated by examining the reaction of anthranilamide (**2**) and scope of various aldehydes (**3**) to this cyclization using the optimized conditions, and the results are presented in Table 2. When we treated 4-methyl benzaldehyde (Table 2, entry 2) with anthranilamide, a desired product **4** was observed in 93% yield after a short reaction time of three minutes. Interestingly, high yield (93-95%) and selective cyclization were observed with all the electron-donating substrates (entries 3-8). Similarly, the consistency was observed in case of electron-withdrawing substrates (such as, NO_2, CN, CO_2H), which were smoothly afforded the corresponding 2,3-dihydroquinazolinone compounds (entries 9-12). The sterically encumbered aldehyde afforded the excellent yield of the corresponding quinazolinones (entries 13-14). The reaction with thiophene-2-carboxaldehyde resulted with 93% yield. However, the other hetero-carboxaldehyde such as 2-furaldehyde and indole-3-carboxaldehyde were resulted with low yield of the desired product (entries 15-17). These heterocycles are sensitive towards air and acid catalyst.[46] The reaction with propionaldeyde displayed a slightly slower reaction rate, reaching poor conversion at 6 hours (entry 18).

Table 2 Reaction of anthranilamide and aldehydes for the preparation of 2,3-dihydroquinazolinone[a]

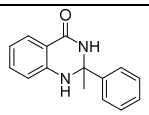
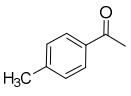
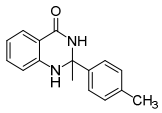
Entry	Substrate	Product	Time	Yield
	3	**4**	(min)	(%)[b,c]
1			2	96

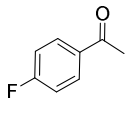
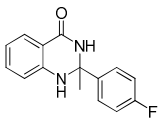
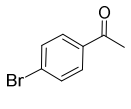
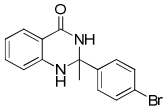
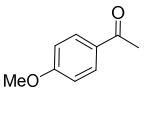
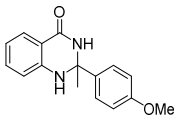
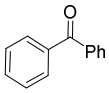
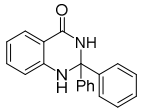
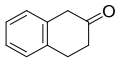
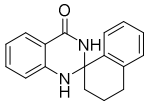
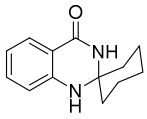
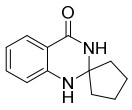
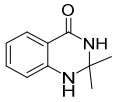
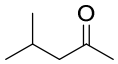
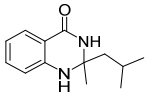
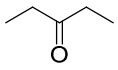
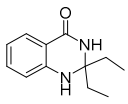
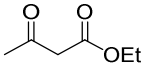
2			3	93
3			3	93
4			1	95
5			5	90
6			3	89
7			4	91
8			2	92
9			3	90
10			3	89
11			2	91
12			5	91
13			15	92
14			2	90
15			7	93
16			24	10
17			24	10
18			6	10

[a]Reaction conditions: anthranilamide (3.0 mmol), aldehyde (3.0 mmol), catalyst 1a (10 mol%), H_2O, 30 °C, mortar pestle; [b]products were characterized by m.p., FTIR, ^{1}H- and ^{13}C-NMR; [c]isolated yields.

We next explored the effect of ketones to this cyclization reaction. Initially, the treatment of acetophenone (**5**) with anthranilamide (**2**) and 10 mol% of ionic liquid **1a** in H_2O at room temperature resulted in the formation of low yield of 2,3-dihydroquinazolinone **6**. Therefore, the same reaction was performed in ethanol solvent; the product **6** was obtained in 93% yield in 3 hours stirring. Encouraged by these results, we evaluated other substituted acetophenones for example methyl, fluoro, bromo and methoxy, which smoothly transformed to the corresponding product in 88-92% yields, respectively (entries 2-5). Unfortunately, the sterically hindered benzophenone have shown poor reactivity and low yield of product under these conditions (entry 6). It is noteworthy that the reaction of cyclic and aliphatic ketones such as cyclohexanone, cyclopentanone, acetone and others were successfully yielded the corresponding quinazolinonone in excellent yield (89-93%) within 3-10 minutes (entries 7-12). However, in the case of β-keto ester (entry 13) no desired product was obtained.

Table 3 Reaction of anthranilamide and ketones for the preparation of 2,3-dihydroquinazolinone[a]

Entry	Substrate **5**	Product **6**	Time (min)	Yield (%)[b,c]
1			3	93
2			4	90

3			12	90
4			12	92
5			8	88
6			24	20
7			24	18
8			3[d]	91
9			3[d]	90
10			10[d]	89
11			10[d]	94
12			2[d]	93
13		nil	24	nr

[a]Reaction conditions: anthranilamide (3.0 mmol), ketone (3.0 mmol), catalyst 1a (10 mol%), EtOH, 30 °C, stirred in glass vial; [b]products were characterized by m.p., FTIR, ^{1}H- and ^{13}C-NMR; [c]isolated yields; [d]reaction time in minutes

We then studied the recyclability of the catalyst **1a** to this cyclization reaction. The ionic liquid **1a** was recovered after completion of the reaction and directly subjected to the cyclization reaction. To our surprise the reaction of recovered catalyst **1a** (10 mol%) with anthranilamide (**2**) and benzaldehyde (**3**) was resulted in the formation of 95% yield of quinazolinone (**4**). These results were consistent for the next four cycles without loss of efficiency of the catalyst **1a** (Figure 2). Similarly, when we subjected ketones (**5**) to our reusability studies, the results are excellent and afforded the corresponding 2,3-dihydroquinozolinone in >95% yield.

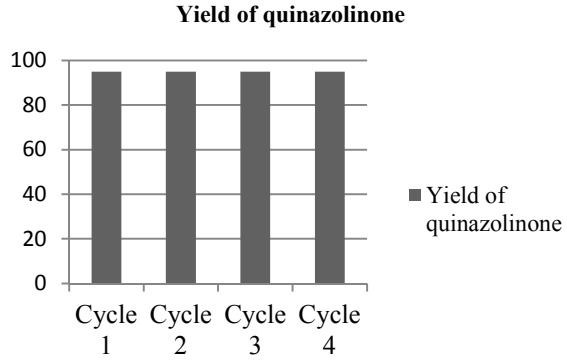


Figure 2. Catalyst 1a reusability study

Conclusions

In conclusion, we have described an efficient ionic liquid **1a** catalyzed multicomponent cyclization that allows the transformation of anthranilamide with aldehydes or ketones into their corresponding 2,3-dihyroquinazolinones in excellent yields. The C-N bond formation of aldehydes was achieved by two different conditions. It is important to note that the catalyst ionic liquid has been recycled after completion of the reaction. A novel feature of this catalytic reaction is that short reaction time, mild conditions and recoverable catalyst.

Experimental

General

Solvents were freshly distilled prior to use and glassware was dried in oven at 120 °C for 5 h. All the reagents were purchased from Merck and Sigma Aldrich. ^{1}H NMR spectra were recorded at 400 MHz and ^{13}C NMR spectra at 100 MHz on a Bruker AVANCE FT NMR instrument using $CDCl_3$ and DMSO-d_6 as standard solvents. Electrospray ionization mass spectrometry (ESI-MS) spectra were recorded on a Waters Q-TOF Premier mass spectrometer. LC/MS data were performed on a Agilent MSD mass spectrometer. Method info: A: 0.05 % HCOOH in H_2O, B: 0.04 % HCOOH in CH_3CN; flow rate: 2.0 ml/min; Column: Chromolith RP-18e, 100-3 mm, +ve

mode. Elemental analyses of the compounds were obtained from thermoquest CE instrument CHNS-O, EA/110 model. IR spectra were recorded using KBr pellets on a Bruker Vector 22 FT-IR spectrometer operating at 400-4000 cm^{-1}. Melting points were measured in DALAL melting point apparatus, India and corrected.

Synthesis of 1-isopropyl-1,2,4-triazolium triflate 1a.

To a solution of 1- isopropyl-1,2,4-triazoles (10 mmole) in toluene (10 ml) was added drop wise trifluromethanesulfonic acid (10 mmole). This reaction mixture was then heated to 80 $^{\circ}C$ for 12 h. After completion of the reaction, flask was cooled to room temperature (25 $^{\circ}C$) and excess of toluene was removed under reduced pressure. The resulting residue was thoroughly washed with hexane (20 mL x 2) and further dried over vacuum to afford pure catalyst **1a**.

Note: Syntheses of 1-isopropyl-1,2,4-triazolum methanesulfonate (**1b**) and 1-butyl-1,2,4-triazolium phenylsulfonate (**1c**) ionic liquids has been prepared similar to **1a**.

Syntheses of 2,3-dihydroquinazolinone (4)

Catalyst **1a** (10 mol %) was added to a solution of anthranilamide (3.0 mmole) and the corresponding aldehyde (3.0 mmole) in water (1 mL). The reaction mixture was mixed in a mortar and pestle at room temperature for designated time. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was quenched with mixture of water:ethanol (5:0.5 mL). The corresponding solid product was filtered, and washed with *n*-hexane (5 mL x 2), which afforded pure 2,3-dihydroquinazolinone.

Syntheses of 2,3-dihydroquinazolinone (6)

Catalyst **1a** (10 mol%) was added to a solution of anthranilamide (3.0 mmole) and the corresponding ketone (3.0 mmole) in ethanol (1 mL). The reaction mixture was stirred in 5 mL glass vial at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was quenched with mixture of water:ethanol (5:0.5 mL). The solid was filtered, and washed with *n*-hexane (5 mL x 2), which afforded pure 2,3-dihydroquinazolinone.

Procedure for the reusability of new triazolium based ionic liquids 1a

The catalyst was separated from the reaction mixture by simple filtration technique and the filtrate was concentrated to remove excess of water and small amount of ethanol. Then the crude residue was thoroughly washed with mixture of hexane: ethyl acetate (4:1) 5 mL and dried at 45 $^{\circ}C$ over vacuum for 1 h. This residue was subjected directly to catalyst reusable study.

Spectral data for selected compounds

1-Isopropyl 1, 2, 4-triazolium trifluoromethanesulfonate **(1a)**

Colorless liquid; yield 94%; elemental analysis: calcd. for C, 27.48; H, 4.23; N, 16.02, found: C, 27.24, H, 4.11, N, 16.01; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 12.9 (s, 1*H*, N*H*), 9.6 (s, 1*H*, 5-C*H*), 8.6 (s, 1*H*, 3-C*H*), 4.9 (m, 1*H*, C*H*(CH_3)$_2$), 1.6 (d, *J* = 8Hz, 6*H*, CH(C*H*$_3$)$_2$), ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 143.1 (*C*-5), 139.5 (*C*-3), 124.8, 121.6, 118.5 115.3, (CF_3SO_3), 55.7 *C*H(C*H*$_3$)$_2$), 21.4 CH(*CH*$_3$)$_2$) ES-MS *m/z* 112.1580; ^{19}F-NMR 78.9378.

1-Isopropyl 1, 2, 4-triazolium methanesulfonate **(1b)**

Colorless liquid; yield 91%; elemental analysis: calcd. for, C, 34.60; H, 6.78; N, 20.18; found, C, 34.54, H, 6.56, N, 20.10; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 12.4 (s, 1*H*, N*H*), 10.1 (s, 1*H*, 5-C*H*), 8.6 (s, 1*H*, 3-C*H*), 4.9 (m, 1*H*, C*H*(CH_3)$_2$), 2.8 (s, 3*H*, C*H*$_3$SO$_3$), 1.6 (d, 6H, CH(C*H*$_3$)$_2$); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 143.3 (*C*-5), 140.3 (*C*-3), 55.4 (*C*H(CH_3)$_2$), 39.6 (*C*H$_3$SO$_3$), 21.8 (CH(*C*H$_3$)$_2$).

1-Isopropyl 1, 2, 4-triazolium phenylsulfonate **(1c)**

White solid; yield 89%; elemental analysis: calcd. for, C, 48.87; H, 5.97; N, 15.54; found : C, 48.64, H, 5.85, N, 15.34; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 12.8 (brs, 1H, N*H*), 10.1 (s, 1*H*, 5-C*H*), 8.6 (s, 1*H*, 3-C*H*), 7.8 (m, 2*H*, C*H*), 7.3 (m, 3*H*, C*H*) 4.8 (m, 1H, C*H*(CH_3)$_2$), 1.5 (d, *J* = 6.6 Hz, 6H, CH(C*H*$_3$)$_2$); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 143.0 (*C*-5), 140.2 (*C*-3), 130.3, 128.3, 125.8 ($C_6H_5SO_3$), 55.5 (*C*H(CH_3)$_2$), 21.4 (CH(*C*H$_3$)$_2$).

2-phenyl-2, 3-dihydroquinazolin-4(1H)-one **(Table 2, entry 1)**

White solid; yield 96%; mp 217-219 $^{\circ}C$ (Lit.[33]: 218-220 $^{\circ}C$); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.2 (s, 1H), 7.6 (m, 1H), 7.5 (m, 2H), 7.3 (m, 3H), 7.2 (m, 1H), 7.1 (s, 1H), 6.7 (m, 2H), 5.7 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6); δ 163.5, 147.8, 141.6, 133.2, 128.4, 128.3, 127.3, 126.8, 117.0, 114.9, 114.3, 66.5; IR (KBr): 3305, 3180, 3059, 1665, 1615, 1535, 1450 cm^{-1}; LC/MS $[M+H]^+$ (m/z) 235.

2-(3,5-dimethoxyphenyl)-2,3-dihydroquinazolin-4(1H)-one **(Table 2, entry 4)**

White solid; yield 95 %; mp 139-140 $^{\circ}C$; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.2 (s, 1H), 7.5 (d, *J* = 12 Hz, 1H), 7.2 (m, 1H), 7.1 (s, 1H), 6.7 (d, *J* = 8 Hz, 1H), 6.6 (m, 3H), 6.4 (m, 1H), 5.6 (s, 1H), 3.7 (s, 6H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 163.5, 160.3, 147.7, 144.1, 133.2, 127.3, 117.1, 114.9, 114.3, 104.9, 99.7, 66.1, 55.2; FTIR (KBr): 3302, 3186, 3061, 2936, 2806, 1908, 1655, 1613, 1510, 1440, 1388, 1300, 1250, 1152, 1029 cm^{-1}; LC/MS $[M+H]^+$ (m/z) 285.

4-(4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl) benzoic acid **(Table 2, entry 12)**

White solid; yield 91%; mp 271-273 $^{\circ}C$; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.9 (s, 1H), 8.3 (s, 1H), 7.9 (d, *J* = 8 Hz, 2H), 7.6 (m, 3H), 7.2 (m, 2H), 6.7 (m, 2H), 5.8 (s, 1H); ^{13}C-NMR (100 MHz,

DMSO-d_6): δ 167.0, 163.4, 147.5, 146.4, 133.4, 130.8, 129.3, 127.3, 127.0, 117.2, 114.9, 114.4, 66.0; FTIR (KBr): 3300, 3179, 3127, 3063, 2934, 2865, 2677, 2551, 1698, 1656, 1610, 1584, 1509, 1431, 1385, 1291, 1155, 1015 cm^{-1}; LC/MS $[M+H]^+$ (m/z) 269.

2-(naphthalen-2-yl)-2, 3-dihydroquinazolin-4(1H)-one **(Table 2, entry 13)**

Colorless solid; yield 92%; mp 167-169 °C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.5 (m, 1H), 8.2 (s, 1H), 7.9 (t, *J* = 8 Hz, 2H), 7.7 (m, 2H), 7.5 (m, 3H), 7.2 (m, 1H), 7.1 (s, 1H), 6.7 (m, 1H), 6.5 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 164.0, 148.4, 135.1, 133.7, 133.2, 130.5, 129.3, 128.5,127.5, 126.0, 125.8, 125.1, 124.5, 117.2, 114.9,114.5, 65.9; IR (KBr): 3381, 3306, 3227, 3053, 2921, 1935, 1655, 1610, 1503, 1424, 1373, 1299, 1152 cm^{-1}; LC/MS $[M+H]^+$ (m/z) 275.

2-methyl-2-phenyl-2, 3-dihydroquinazolin-4(1H)-one **(Table 3, entry 1)**

Colorless solid; yield 93%; mp 225-226 °C (Lit.[28b]: 224-225 °C); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.7 (s, 1H), 7.6 (s, 1H), 7.5 (m, 3H), 7.2 (m, 2H), 7.1 (m, 2H), 6.7 (m, 1H), 6.5 (m,1H), 1.6 (s, 3H);^{13}C-NMR (100 MHz, DMSO-d_6) δ: 163.7, 147.6, 147.1, 133.2, 127.9, 127.2, 126.9, 125.1, 116.7, 115.0, 114.2, 70.1, 30.7; IR (KBr): 3400, 3045, 1667, 1618, 1510, 1599, 14420, 1395, 1330, 1275, 1220, 1191, 1153, 1120, 1082, 1030 cm^{-1}; LC/MS $[M+H]^+$ (m/z) 239.

1'H-spiro [cyclohexane-1,2'-quinazolin]-4'(3'H)-one **(Table 3, entry 8)**

White solid; yield 91%; mp 223-225 °C (Lit.[28b]: 224-225 °C); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.9 (s, 1H), 7.5 (m, 1H), 7.2 (m, 1H), 6.8 (s, 1H), 6.6 (m, 2H), 1.7 (m, 2H), 1.6 (m, 6H), 1.4 (m, 1H), 1.2 (m, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 163.1, 146.7, 133.0, 127.0, 116.4, 114.5, 114.4, 67.7, 37.1, 24.6, 20.8; IR (KBr): 3280, 3184, 3030, 2980, 2932, 2858, 1660, 1620, 1520, 1484, 1420, 1390, 1276, 1185, 1150 cm^{-1}; LC/MS $[M+H]^+$ (m/z) 217.

1'H-spiro[cyclopentane-1,2'-quinazolin]-4'(3'H)-one **(Table 3, entry 9)**

White solid; yield 90%; mp 258-260 °C (Lit.[30]: 257-260 °C); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.0 (s, 1H), 7.5 (d, *J* = 8 Hz, 1H), 7.2 (t, *J* = 12 Hz, 1H), 6.7 (s, 1H), 6.7 (m, 1H), 6.6 (m, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 163.9, 148.0, 133.4, 127.7, 117.0, 115.0, 114.8, 77.5, 22.4; IR (KBr): 3283, 3186, 3035, 2982, 2929, 2940, 2855, 1666, 1620, 1519, 1483, 1431, 1390, 1325, 1270, 1177, 1150 cm^{-1}; LC/MS $[M+H]^+$ (m/z) 203.

2, 2-dimethyl-2,3-dihydroquinazolin-4(1H)-one **(Table 3, entry 10)**

White solid; yield 89%; mp 183-184 °C (Lit.[28b]: 182-183 °C); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.9 (s, 1H), 7.6 (d, *J* = 8 Hz 1H), 7.2 (t, *J* = 8 Hz, 1H), 6.6 (m, 3H), 1.3 (s, 6H); ^{13}C-NMR (100 MHz, DMSO-d_6): 163.5, 147.5, 133.6, 127.6, 116.9, 114.7, 114.3, 67.3, 29.4; IR (KBr): 3330, 3261, 3033, 2991, 2969, 1655, 1620, 1515, 1484, 1388, 1361, 1335, 1278, 1197, 1180, 1140 cm^{-1}.

2-isobutyl-2-methyl-2,3-dihydroquinazolin-4(1H)-one **(Table 3, entry 11)**

White solid; yield 94%; mp 172-174 °C (Lit.[28b]: 171-173 °C); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.8 (s, 1H), 7.5 (d, *J* = 8Hz 1H), 7.2 (m, 1H), 6.6 (m, 3H), 1.9 (m, 1H), 1.8 (m, 1H), 1.5 (m, 3H), 0.9 (m, 6H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 163.5, 147.5, 133.6, 127.5, 116.4, 114.4, 113.8, 69.8, 49.8, 29.1, 24.8, 24.6, 23.8; IR (KBr): 3324, 3170, 2950, 2865, 1657, 1612, 1580, 1511, 1484, 1432, 1390, 1362, 1320, 1285, 1189, 1150, 1060, 825, 745 cm^{-1}.

2, 2-diethyl-2,3-dihydroquinazolin-4(1H)-one **(Table 3, entry 12)**

White solid; yield 93%; mp 189-190 °C; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.7 (s, 1H), 7.5 (m, 1H), 7.1 (m, 1H), 6.6 (d, *J* = 8Hz, 1H), 6.6 (m, 1H), 6.4 (s, 1H), 1.6 (m, 4H), 0.9 (m, 6H); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 163.8, 148.1, 133.5, 127.4, 115.9, 114.0, 113.4, 72.4, 33.2, 8.3; IR (KBr): 3320, 3167, 2870, 1665, 1600, 1570, 1521, 1479, 1428, 1385, 1323, 1285, 1178, 1090, 1050, 840, 739 cm^{-1}; LC/MS $[M+H]^+$ (m/z) 205.

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Notes and references

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Electronic Supplementary Information (ESI): scanned spectral data is available with this journal. See DOI: 10.1039/b000000x/

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Graphical abstract

Ionic liquid catalyzed reusable protocol for one-pot synthesis of 2,3-dihydroquinazolin-4(1*H*)-one under mild conditions

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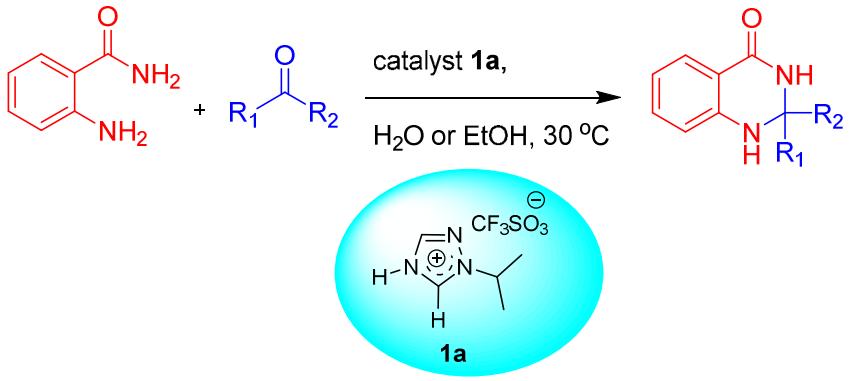

This article described an efficient protocol for the syntheses of 2,3-dihydroquinazolinones. The synthetic utility of this methodology has been demonstrated with 30 different substrates. The reaction showed good functional group tolerance and high levels of catalytic activity.