Received: 16 February 2021 | Revised: 25 April 2021 | Accepted: 17 May 2021

DOI: 10.1002/jhet.4321

ARTICLE

JOURNAL OF HETEROCYCLIC CHEMISTRY WILEY

Brønsted acid catalyzed synthesis of 2-aryl-quinazolinones via cyclization of 2-aminobenzamide with benzonitriles in PEG

Sowbhagya Lakshmi Matcha[1] | **Bharat Kumar Karasala**[2] | **Sathish Mohan Botsa**[3] | **Siddaiah Vidavalur**[2]

[1]Department of Chemistry, University college of Engineering, JNTUK, Vizianagaram, India

[2]Department of Organic Chemistry & FDW, Andhra University, Visakhapatnam, India

[3]National Centre for Polar and Ocean Research, Ministry of Earth Sciences, Goa, India

Correspondence
Sathish Mohan Botsa, National Centre for Polar and Ocean Research, Ministry of Earth Sciences, Goa-403804, India.
Email: bsathish401@gmail.com
Siddaiah Vidavalur, Department of Organic Chemistry & FDW, Andhra University, Visakhapatnam, India.
Email: sidduchem@gmail.com

Abstract

A simple and efficient Brønsted acid catalyzed synthesis of 2-aryl-quinazolinones via cyclization of 2-aminobenzamides with benzonitrile in PEG under metal and ligand-free condition. All substituted benzonitriles were also well participated with the formation of the corresponding products in moderate to good yields.

1 | INTRODUCTION

Quinazolinones represent one of the important fused six-membered heterocyclic compounds, and has assigned as a privileged structural component in several natural products, for example, 2-methyl-4(3H)-quinazolinone, tryptanthrin, luotonin F, luotonin A, rutaecarpine, and bouchardatine (Figure 1) [1]. Quinazolinones have an array of significant biological activities including anti-bacterial [2], anticancer [3], anti-inflammatory [4], anti-microbial [5], anti-tubercular [6], anti-ulcer, [7] and so on [8]. Besides, they are widely utilized in drug design, clinic medicines, material science, and used as inhibitors of several enzymes [9].

Based on their pharmacological activities, a variety of synthetic efforts have been developed for quinazolinones [1a,10–12]. Traditionally, oxidative condensation of *2*-aminobenzamide with aldehydes [13] or acid derivatives [14–16] followed by the oxidation of aminal intermediate is a most general synthetic procedure for the preparation of quinazolinones. However, these methods have associated with some limitations such as a large number of toxic oxidants were used like DDQ, $KMnO_4$, MnO_2, $CuCl_2$, and the usage of aldehyde is one of the major drawbacks because it was chemically unstable for the preparation and storage. To overcome these issues, several alternative protocols have been developed [17]. Thus, because of their great value, the development of eco-friendly and potential alternative methods for the quinazolinones was highly desirable.

In this context, in recent years acid-catalyzed reactions draw much attention in organic synthesis [18]. Especially, *p*-toluene sulfonic acid is widely used as an acid catalyst in several organic reactions with having several advantages such as feasibility and cheapness [19].

Besides that, instead of toxic, hazardous, and volatile organic solvents with an eco-friendly medium is one of the important challenging things from a green chemistry

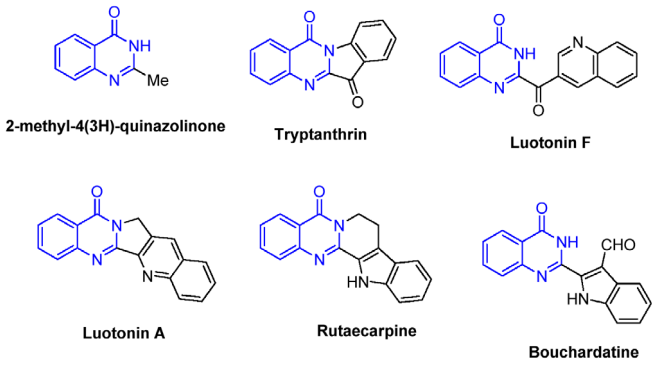
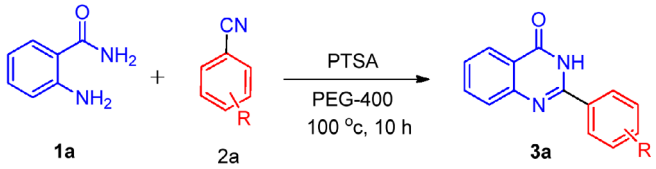


FIGURE 1 Selected examples of quinazolinones containing as scaffolds of naturally occurring alkaloids



SCHEME 1 Preparation of 2-aryl-quinazolinones

point of view [20]. In this regard, PEG-400 has found to emerge as an efficient and interesting eco-friendly solvent in various chemical transformations [21]. Because, it showed unique properties like inexpensive, nontoxicity, bio-compatibility, non-ionic liquid solvent of low volatility, etc.

Moreover, PEG acts as a safe, degradable, recyclable, and biologically ubiquitous green solvent [22]. In continuation of our research on the development of new methodologies for heterocyclic compounds [23], herein we reported a metal and ligand-free method for the 2-aryl-quinazolinones from cyclization of 2-aminobenzamide with benzonitrile in PEG as a solvent and PTSA used as a catalyst (Scheme 1).

2 | RESULTS AND DISCUSSION

Our investigation started with 2-aminobenzamide **1a** and benzonitrile **2a** chosen as model substrates for the synthesis of quinazolinones. Initially, 2-aminobenzamide **1a** reacts with benzonitrile **2a** in the presence of 10 mol% of AcOH as a catalyst under the solvent-free condition at 80°C for 10 h. The corresponding product **3a** was obtained with a moderate 51% yield (Table 1, entry 1). Hence, we have screened various acid catalysts to identify the suitable catalyst (Table 1, entries 2–5). PTSA was the best acid catalyst for this transformation with 68% yield of the corresponding **3a** (Table 1, entry 5). Next, the quantity of catalyst increase to 20 or 30 mol%, from 10 mol, the desired products were formed in unsatisfactory yields (Table 1, entries 6–7). Unfortunately, the corresponding **3a** was observed in a very low yield with 5 mol% of catalyst (Table 1, entry 8). Fortunately, with an increased reaction temperature up to 100°C (Table 1, entry 9), the reaction provided **3a** with 71% yields. However, at a higher temperature, the reaction did not show a positive effect on the reaction yield significantly (Table 1, entry 10). Next, we turn our focus on knowing the role of solvents on this reaction, various solvents were also screened (Table 1, entries 11–16). PEG-400 was the best and suitable solvent for this reaction with 88% excellent yield than remnants (Table 1, entry 12). The reaction could not proceed without the catalyst (Table 1, entry 17).

With optimized conditions in hand, we investigated the substrate scope of different benzonitriles; the resulted yields were shown in Table 2. Benzonitrile with electron-donating groups such as methyl, methoxy, and trimethoxy groups have well reacted with *o*-aminobenzamide (**1a)** to afford the desired products in good yields (Table 2, **3b–3e)**. Strong donating *N,N*-dimethyl substituted benzonitrile (**3f)** was well produced and the corresponding product in 82% yield (Table 2, **3f**). Furthermore, electron-withdrawing groups such as —Br, —Cl and —F on the aromatic ring of benzonitrile have well participated in the reaction, the corresponding products in moderate yields formed (Table 2, **3g–3k**). However, *ortho*-substituted benzonitrile gave a lower yield than *meta*- and *para*-substituted benzonitrile. These results clearly showed that the steric hindrance effect may on this reaction (Table 2, **3i**). Unfortunately, strong electron-withdrawing nitro substituted benzonitriles were affording the corresponding products in unsatisfactory yields (Table 2, **3l** and **3m**). To our delight, heteroaryl nitriles were well proceeded with **1a** under the standard reaction condition, the corresponding products in 84% and 86% good yields (Table 2, **3n–3o**). After, to expand the further scope of this reaction, various 2-aminobenzamides were also investigated. For example, 5-methoxy-2-aminobenzamides (**1b**) were reacted with simple benzonitrile (**2a**) and p-methoxybenzonitrile and (**2c**) under the optimized conditions, the desired products obtained in good yields (Table 1, **3p** and **3q**). 4-methyl-2-aminobenzamide (**1c**) underwent the reaction to give the corresponding 2-substituted-quinazolinone in good yields (Table 1, **3r**).

Based on the experimental results and literature [24], a plausible reaction mechanism was showed in (Scheme 2). Initially, benzonitrile (**2a)** was reacted with PTSA to form a nitrilium ion **A**, which underwent nucleophilic reaction with 2-aminobenzamide (**1a)** and provided the complex **B**. Tautomerism of B gives C, which

TABLE 1 Optimized conditions[a]

S.no	Acid catalyst (mol%)	Solvents	Temp (°C)	Yield[b] (%)
1	AcOH (10)	-	80	51
2	PhCOOH (10)	-	80	34
3	TfOH (10)	-	80	56
4	CF_3COOH (10)	-	80	42
5	PTSA (10)	-	80	68
6	PTSA (20)	-	80	64
7	PTSA (30)	-	80	62
8	PTSA (5)	-	80	35
9	PTSA (10)	-	100	71
10	PTSA (10)	-	120	68
11	PTSA (10)	MeOH	100	54
12	**PTSA (10)**	**PEG-400**	**100**	**88**
13	PTSA (10)	*n*-BuOH	80	60
14	PTSA (10)	DMSO	80	29
15	PTSA (10)	$PhCH_3$	80	23
16	PTSA (10)	THF	80	20
17	-	PEG-400	100	nd[c]

[a]Reaction conditions: 2-aminobenzamide **1a** (1.4 mmol), benzonitrile **2a** (1.4 mmol), acid catalyst (10 mol) in PEG (3 ml) at 100°C for 10 h.
[b]Isolated yield.
[c]nd, Not detected.

was further intramolecular nucleophilic addition to produce an adduct of **D**. Subsequently, **D** was tautomerized to **E,** further, which was eliminating NH_3 gas to gives an imide ion **F**. Finally, abstraction of **H** from **F,** and delivers the corresponding product **3a** in good to moderate yield.

3 | EXPERIMENTAL SECTION

3.1 | General information

All chemicals were purchase from Sigma Aldrich and AVRA synthesis Private Ltd. and used without further purification. The progress of the reactions were monitored by TLC and carried out on aluminum plates coated with silica gel (Silica gel 60 F254) using ethyl acetate and *n*-hexane as mobile phase. Chromatogram was visualized using UV light (254 nm). The products were purified by using column chromatography on silica gel (100–200 mesh). Melting points were determined in open capillary tube and are not corrected. ^1H and ^{13}C NMR spectra were recorded on 400 MHz spectrometer using TMS as internal standard. The chemical shifts were reported in (δ) ppm relative to tetramethylsilane(TMS) as internal reference. Data are reported as follows: (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). The coupling constant *J* is given in Hz.

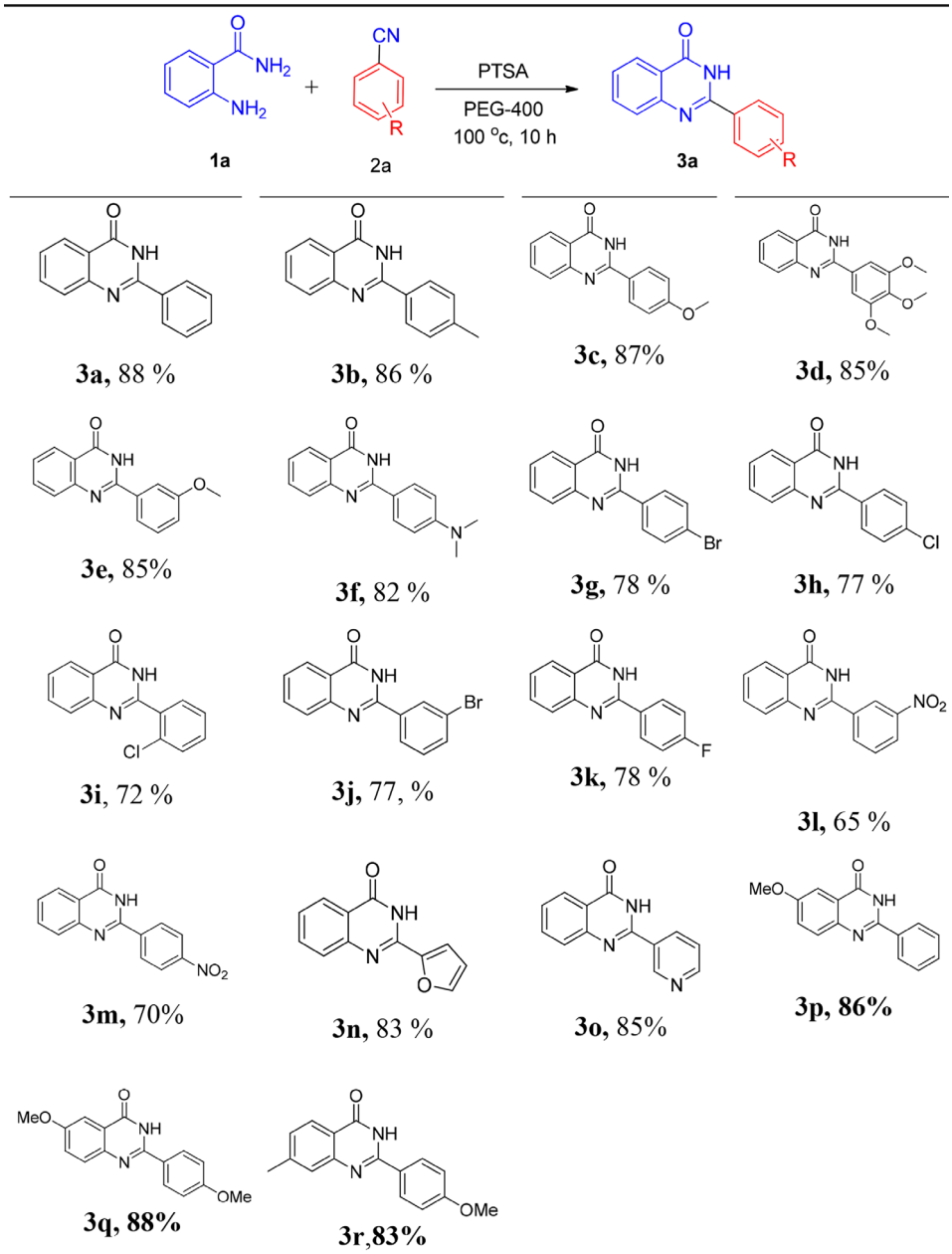
3.2 | General procedure for the synthesis of quinazolin-4(3H)-ones (3a–3n)

To an oven dried RB flask charged with a stir bar, 2-aminobenzamide (1.4 mmol), benzonitrile (1.4 mmol), PTSA (10 mol%) in 3 ml of PEG-400 and stirred on oil both at 100°C for 10 h. The progress of the reaction was monitored by TLC, the reaction mixture cooled at room temperature and aqueous Na_2CO_3 solution (10 ml) was added and extracted with ethyl acetate (2 × 15 ml). The organic phase was dried over with anhydrous Na_2SO_4, and solvent was removed under vacuum. The crude products was purified by column chromatography (ethyl acetate: hexane), to get corresponding pure products in 91%–71% good to moderate yields.

3.3 | Spectral data of synthetic compounds

2-Phenylquinazolin-4(3H)-one (3a). [1] White solid; Yield: 88%; Mp: 231–233°C;^1H NMR(400 MHz, $CDCl_3$) δ

TABLE 2 Synthesis of 2-aryl-quinazolinones[b]



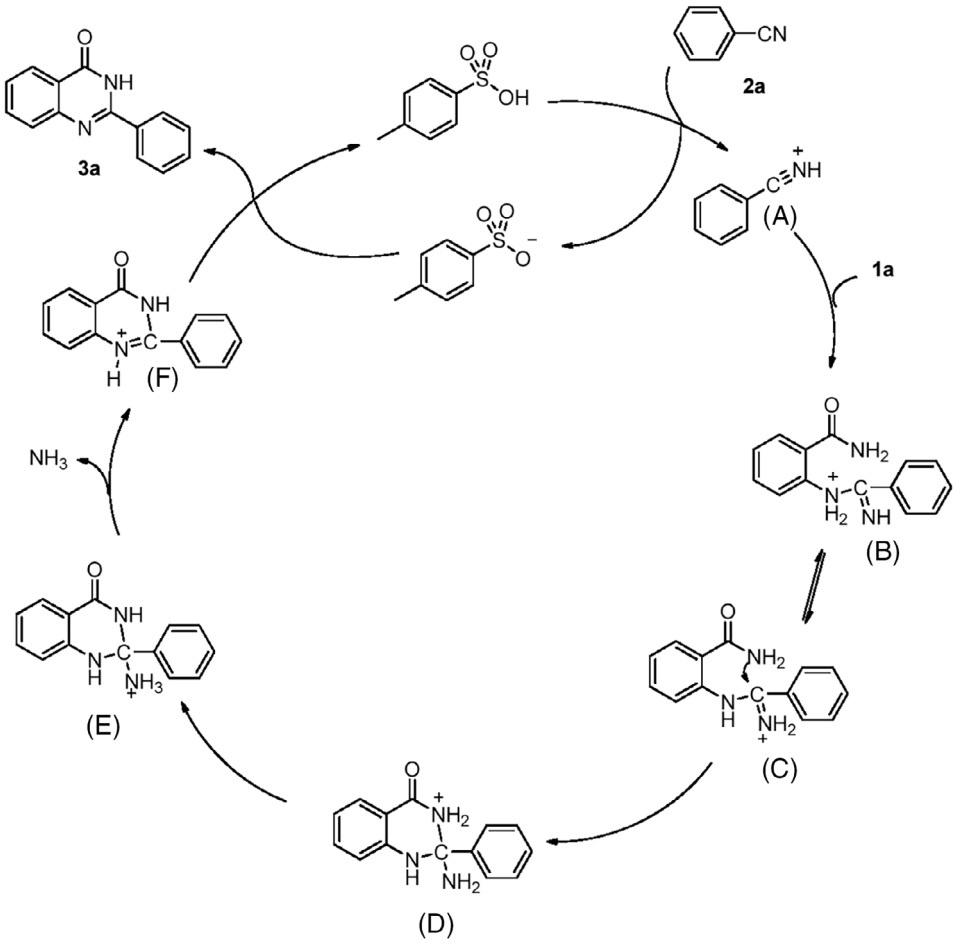
[a]Reaction conditions: 2-aminobenzamide **1a** (1.4 mmol), benzonitrile **2a** (1.4 mmol), acid catalyst (10 mol) in PEG (3 ml) at 100°C for 10 h.
[b]Isolated yield.
[c]nd, Not detected.

10.04 (s, 1H), 8.35 (d, J = 7.2 Hz, 1H), 8.12 (dd, J = 9.6, 2.8 Hz, 2H), 7.87–7.81 (m, 2H), 7.61 (t, J = 5.6, 2H), 7.55–7.51 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 151.4, 149.3, 134.9, 132.7, 131.7, 129.1, 128.0, 127.0, 126.9, 126.4, 120.9; LC–MS calcd for $C_{14}H_{10}N_2O$ $[M + H]^+$ 223.0826, found 223.0844.

2-(*p*-Tolyl)quinazolin-4(3H)-one (3b). [1] White solid; Yield: 86%; Mp: 240–242°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.48 (brs, 1H), 8.18 (d, J = 6.8 Hz, 1H), 8.09 (d, J = 8.0 Hz, 2H), 7.85 (t, J = 7.6 Hz,1H), 7.75 (d, J = 7.2 Hz, 1H), 7.47 (t, J = 7.2 Hz, 1H), 7.31 (d, J = 7.6 Hz, 2H), 2.31 (d, J = 7.6 Hz, 2H,) 2.35 (s, 3H); ^{13}C NMR (100 MHz,DMSO-d_6): δ 162.9, 152.8, 150.1, 141.9, 136.2, 130.0, 129.8, 128.1, 127.9, 126.7, 126.5, 121.3, 21.5; LC–MS calcd for $C_{15}H_{12}N_2O$ $[M + H]^+$237.0983, found, 237.0979.

2-(4-Methoxyphenyl)quinazolin-4(3H)-one (3c). [1] White solid; Yield: 87%; Mp: 245–247°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.46 (brs, 1H), 8.23 (dd, J = 6.8 Hz, 2H), 8.07–8.04 (m, 1H), 7.84–7.78 (m, 1H),

SCHEME 2 The plausible reaction mechanism for the synthesis of 2-aryl-quinazolinones



7.60 (d, J = 8.0 Hz, 1H), 7.48–7.43 (m, 1H), 7.13 (d, J = 8.0 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.4, 162.4, 153.3, 149.4, 136.0, 131.1, 129.6, 127.1, 126.6, 125.4, 122.4, 115.6, 57.0; LC–MS calcd for $C_{15}H_{12}N_2O_2$ $[M + H]^+$ 253.0938, found 253.0947.

2-(3,4,5-Trimethoxyphenyl)quinazolin-4(3H)-one (3d). [1] White solid; Yield: 85%; Mp 258–260°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.56 (brs, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.85 (t, J = 7.6 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.55 (s, 2H), 7.24 (t, J = 7.6 Hz, 1H), 3.93 (s, 6H), 3.71 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.5, 158.3, 156.8, 153.4, 145.3, 138.0, 132.7, 132.4, 130.7, 130.2, 126.5, 110.4, 65.4, 61.4; LC–MS calcd for $C_{17}H_{16}N_2O_4$ $[M + H]^+$ 313.1143, found 313.1127.

2-(3-Methoxyphenyl)quinazolin-4(3H)-one (3e). [3] White solid; Yield 85%; Mp: 181–182°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.55 (s, 1H), 8.18 (d, J = 7.2 Hz, 1H), 7.91–7.79 (m, 4H), 7.55 (d J = 8.0 Hz, 1H), 7.47 (t, J = 7.2 Hz, 1H), 7.17 (d, J = 7.6. Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.6, 159.4, 152.8, 148.2, 136.4, 135.1, 131.7, 128.2, 127.6, 126.6, 122.0, 121.2, 118.6, 112.6, 56.1; HRMS calcd for $C_{15}H_{12}N_2O_2$ $[M + H]^+$ 253.0938, found 253.0952.

2-(4-N,N-dimethylphenyl)quinazolin-4(*3H*)-one (3f). [2] White solid; Yield: 82%; Mp: 237–239; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.20 (brs, 1 H), 8.12 (t, J = 8.0 Hz, 1H), 7.78 (t, J = 7.5 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.43 (m, J = 7.5 Hz, 1H), 6.76 (d, J = 8.0 Hz, 2H), 3.07 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.9, 155.1, 153.9, 140.8, 140,1, 135.7, 132.4, 130.6, 129.2, 127.8, 124.5, 119.3, 46.8, 46.2; LC–MS calcd for $C_{16}H_{15}N_3O$ $[M + H]^+$ 266.1249, found 266.1253.

2-(4-Bromophenyl)quinazolin-4(3H)-one (3g). [1] White solid; Yield: 78%; Mp 293–295°C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.58 (brs, 1H), 8.16–8.12 (m, 3H), 7.85–7.82 (m, 1H), 7.76–7.72 (m, 3H), 7.53–7.50 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.1, 152.3, 151.3, 135.6, 133.8, 132.5, 131.2, 128.1, 127.4, 126.8, 126.1, 122.5; LC–MS calcd for $C_{14}H_9BrN_2O$ $[M + 2]^+$ 301.9878, found 301.9913.

2-(4-Chlorophenyl)quinazolin-4(3H)-one (3h). [3] White solid; Yield: 77%; Mp > 300°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.61 (brs, 1H), 8.19–8.12 (m, 3H), 7.82 (t, J = 8.0 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.54 (t, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.4, 152.3, 150.1, 137.2,

135.8, 132.6, 131.2, 130.0, 128.4, 127.8, 126.5, 122.2; LC–MS calcd for $C_{14}H_9ClN_2O$ [M + 2] 258.0374, found 258.0387.

2-(2-Chlorophenyl)quinazolin-4(3H)-one (3i). [3] White solid; yield: 72%; Mp: 195–198°C;^{1}H NMR (400 MHz, DMSO-d_6): δ 12.62 (brs, 1H), 8.17 (d, J = 8.0 Hz, 1H), 7.89–7.85 (m, 1H), 7.74–7.69 (m, 2H), 7.60–7.49 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.7, 152.6, 148.7, 135.4, 134.2, 131.7, 131.1, 130.6, 129.2, 127.5, 127.1, 126.8, 124.8, 121.6; LC–MS calcd for $C_{14}H_9ClN_2O$ [M + 2] 258.0374; found, 258.0393.

2-(3-Bromophenyl)quinazolin-4(3H)-one (3j). [4] White solid; Yield: 77% Mp: 294–296°C; ^{1}H NMR (400 MHz, DMSO-d_6,): δ 12.62 (brs, 1H), 8.37 (s, 1H), 8.18 (d, J = 8.0 Hz, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.85–7.74 (m, 3H), 7.57–7.51 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6,): δ 162.3, 150.2, 149.1, 135.1, 134.4, 134.1, 131.8, 131.1, 128.7, 127.3, 126.5, 125.3, 121.2, 120.0: LC–MS calcd for $C_{14}H_9BrN_2O$ [M + 2]$^+$ 301.9878, found 301.9913.

2-(4-Fluorophenyl)quinazolin-4(3H)-one (3k). [1] White solid; Yield: 78%; Mp 285–287°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.55(brs, 1H), 8.29–8.24 (m, 2H), 8.17 (d, J = 8.8 Hz, 1H), 7.86 (t, J = 7.6 Hz,1H), 7.76 (d, J = 7.6 Hz, 1H), 7.53 (t, J = 8.0 Hz, 1H), 7.42 (t, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 165.7 (d, JC =251.4 Hz) 163.0, 160.1, 149.4135.6, 131.4 (d, J C = 9.38 Hz), 129.3, 128.5, 127.5, 126.5, 122.4, 116.4 (d, JC = 21.96 Hz); LC–MS calcd for $C_{14}H_9FN_2O$ [M + H] $^+$ 241.0732, found 241.0745.

2-(3-Nitrophenyl)quinazolin-4(3H)-one (3l). [3] Brown solid; Yield: 65%;Mp: >300°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.83 (brs, 1H), 9.02 (s, 1H), 8.64 (d, J = 8.0 Hz, 1H), 8.45 (d, J = 8.0 Hz, 1H), 8.20 (d, J = 8.0 Hz, 1H), 7.91–7.82 (m, 3H), 7.56 (t, J = 8.0 Hz, 1H); ^{13}CNMR (100 MHz, DMSO-d_6): δ 162.8, 151.1, 148.7, 148.2, 135.5, 134.7, 133.6, 130.3, 128.3, 127.7, 125.9, 125.3, 123.1, 121.3; LC–MS calcd for $C_{14}H_{19}N_3O_3$ [M + H]$^+$ 268.0677, found, 268.0617.

2-(4-Nitrophenyl)quinazolin-4(3H)-one (3m). [3] Brown solid; Yield: 70%; Mp: > 300°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.48 (brs, 1H), 8.46–8.43 (m, 4H), 8.16 (d, J = 7.6 Hz, 1H), 7.86 (t, J = 8.0 Hz, 1H), 7.74 (d, J = 7.2 Hz, 1H), 7.56 (t, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.5, 151.1, 149.4, 148.6, 139.0, 135.1, 129.8, 128.3, 127.8, 126.5, 124.0, 120.5; LCMS calcd for $C_{14}H_9N_3O_3$ [M + H]$^+$ 268.0677; found, 268.0687.

2-(Furan-2-yl)quinazolin-4(3H)-one (3n). [4] White solid.; Yield: 83%; Mp: 276–277°C; **^{1}H NMR (400 MHz, DMSO-d_6)**: δ 12.45 (brs, 1H), 8.14 (d, J = 7.6 Hz, 1H), 7.95 (s, 1H), 7.82 (t, J = 7.6 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.61 (d, J = 8.0 Hz,1H), 7.44 (t, J = 8.0 Hz, 1H), 6.75 (t, J = 8.0 Hz, 1H), **^{13}C NMR (100 MHz, DMSO-d_6)**: δ 162.2, 149.6, 147.8, 146.5, 145.2, 135.4, 129.3, 127.6, 123.7, 114.4, 113.6; **LC–MS** calcd for $C_{12}H_8N_2O_2$ [M + H]$^+$ 213.0619, found 213.0623.

2-(Pyridin-3-yl)quinazolin-4(3H)-one (3o). [4] White solid; Yield: 85%; Mp: 281–283°C; **^{1}H NMR (400 MHz, DMSO-d_6)**: δ 12.73 (brs, 1H), 9.31 (s, 1H), 8.76 (d, J = 8.0 Hz, 1H), 8.52 (d, J = 8.0 Hz, 1H), 8.23 (d, J = 8.0 Hz, 1H), 7.85 (t, J = 7.6 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.60–7.51 (m, 2H); **^{13}C NMR (100 MHz, DMSO-d_6)**: δ 162.4, 152.0, 151.4, 149.1, 148.5, 136.0, 135.4, 130.6, 128.3, 127.4, 126.6, 125.2, 121.6; **LC-MS** calcd for $C_{13}H_9N_3O$ [M + H]$^+$ 224.0779, found 224.0789.

6-Methoxy-2-phenylquinazolin-4(3H)-one (3p). White solid; Yield: 85%; Mp: 247–249°C; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 12.33 (brs, 1H), 7.18 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.4 Hz, 1H), 7.56 (d, J = 7.2 Hz, 4H), 7.43 (dd, J = 8.0 Hz, 1H), 3.89 (s, 3H), 3.85(s, 3H), 3.80 (s, 3H);**^{13}C NMR (100 MHz, DMSO-d_6)**: δ 162.6, 158.1, 150.8, 142.9, 134.2, 132.2, 130.1, 129.1, 128.6, 124.5, 122.1, 105.9, 55.3, 31.0; **LC-MS** calcd for $C_{15}H_{12}N_2O_2$ [M + H]$^+$ 224.0972, found 253.0975.

6-Methoxy-2(4-methoxy)phenyl)quinazolin-4 (3H)-one (3q). White solid; Yield: 88%; Mp: 257–259°C; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 12.33 (brs, 1H), 7.16 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 8.8 Hz, 1H), 7.53 (s,1H), 7.44 (d, J = 7.6 Hz, 1H), 7.04 (d, J = 8.0 Hz, 2H); **^{13}C NMR (100 MHz, DMSO-d_6)**: δ 162.2, 161.3, 157.0, 149.5, 143.0, 129.0, 128.8, 124.9, 123.8, 121.7, 113.7, 105.3, 55.5, 55.3; **LC-MS** calcd for $C_{16}H_{14}N_2O_2$ [M + H]$^+$ 283.1077, found 283.1079.

6-Methoxy-2(4-methoxy)phenyl)quinazolin-4 (3H)-one (3s). Light yellow solid; Yield: 83%;Mp: 247–249°C; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 12.35 (brs, 1H), 7.16 (d, J = 8.0 Hz, 2H), 8.02 (d, J = 8.0 Hz, 1H), 7.53 (s,1H), 7.34 (d, J = 8.4 Hz, 1H), 7.09 (d, J = 8.8 Hz, 2H), 3.86 (s, 3H), 2.33(s, 3H); **^{13}C NMR (100 MHz, DMSO-d_6)**: δ 162.8, 162.5, 152.4, 149.5, 143.3, 129.2, 128.0, 127.3, 126.6, 125.0, 118.4, 114.3, 55.8, 21.3; **LC-MS** calcd for $C_{16}H_{14}N_2O_2$ [M + H]$^+$ 267.1128, found 267.1130.

4 | CONCLUSION

In conclusion, a simple and efficient method was disclosed for the construction of 2-aryl-quinazolin-4(3H)-ones via Brønsted acid-catalyzed cyclization reactions of 2-aminobenzamide with benzonitrile in PEG under metal and ligand-free condition. All substituted benzonitriles reacted significantly and afforded the corresponding products in moderate to good yields.

ORCID

Sathish Mohan Botsa https://orcid.org/0000-0003-2852-9187

REFERENCES

[1] (a) S. B. Mhaske, N. P. Argade, *Tetrahedron* **2006**, *62*, 9787; (b) S. Yoshida, T. Aoyagi, S. Harada, N. Matsuda, T. Ikeda, H. Naganawa, M. Hamada, T. J. Takeuchi, *Antibiotics* **1991**, *44*, 111; (c) J. P. Michael, *Nat. Prod. Rep.* **2007**, *24*, 223; (d) I. Khan, A. Ibrar, N. Abbas, A. Saeed, *Eur. J. Med. Chem.* **2014**, *76*, 193.

[2] K. Nanda, S. Ganguli, R. Chakraborty, *Molecules* **2007**, *12*, 2413.

[3] (a) P. M. Chandrika, T. Yakaiah, A. R. R. Rao, *Eur. J. Med. Chem.* **2008**, *43*, 846; (b) S. L. Cao, Y. P. Feng, Y. Y. Jiang, S. Y. Liu, G. Y. Ding, R. T. Li, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1915; (c) M. Dupuy, F. Pinguet, O. Chavignon, *Chem. Pharm. Bull.* **2001**, *49*, 1061; (d) Y. Takase, T. Saeki, N. Watanabe, *J. Med. Chem.* **1994**, *37*, 2106.

[4] O. Kenichi, Y. Yoshihisa, O. Toyonari, I. Toru, I. Yoshio, *J. Med. Chem.* **1985**, *28*, 568.

[5] S. Kuarm, Y. T. Reddy, J. V. Madhav, P. A. Crooks, B. Rajitha, *Bioorg. Med. Chem. Lett.* **2011**, *21*, 524.

[6] K. Waisser, J. Gregor, H. Dostál, J. Kunes, L. Kubicová, V. Klimesová, J. Kaustová, *Farmaco* **2001**, *56*, 803.

[7] K. Tereshima, H. Shimamura, A. Kawase, *Chem. Pharm. Bull.* **1995**, *43*, 2021.

[8] (a)H. Kikuchi, K. Yamamoto, S. Horoiwa, *J. Med. Chem.* **2006**, *49*, 4698; (b) N. Malecki, P. Carato, G. Rigo, *Bioorg. Med. Chem.* **2004**, *12*, 641; (c) K. Matsuno, J. Ushiki, T. Seishi, *J. Med. Chem.* **2003**, *46*, 4910.

[9] (a)J. Barluenga, F. Rodriguez, F. J. Fananas, *Chemistry – Asian J.* **2009**, *4*, 1036; (b) D. E. Stephens, O. V. Larionov, *Tetrahedron* **2015**, *71*, 8683; c) S. M. Prajapati, K. D. Patel, R. H. Vekariya, S. N. Panchal, H. D. Patel, *RSC Adv.* **2014**, *4*, 24463; (d) V. V. Kouznetsov, L. Y. V. Méndez, C. M. M. Gómez, *Curr. Org.Chem.* **2005**, *9*, 141; (e) B. Tanwar, A. Kumar, P. Yogeeswari, D. Sriram, A. K. Chakraborti, *Bioorg. Med. Chem. Lett.* **2016**, *26*, 5960; (f) G. Chelucci, A. Porcheddu, *Chem. Rec.* **2017**, *17*, 200; (g) N. J. Liverton, D. J. Armstrong, D. A. Claremon, D. C. Remy, J. J. Baldwin, R. J. Lynch, G. Zhang, R. J. Gould, *Bioorg. Med. Chem. Lett.* **1998**, *8*, 483.

[10] K. Upadhyaya, R. K. Thakur, S. K. Shukla, R. P. Tripathi, *J Org. Chem* **2016**, *81*, 5046.

[11] D. J. Connolly, D. Cusack, T. P. O'Sullivan, P. J. Guiry, *Tetrahedron* **2005**, *61*, 10153.

[12] Z. Zhe, W. Min, Z. Chaofeng, J. L. Zhixin Zhang, W. Feng, *Chem. Commun.* **2015**, *51*, 9205.

[13] (a) Y. Mitobe, S. Ito, T. Mizutani, T. Nagase, N. Sato, S. Tokita, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 4075; (b) C. Balakumar, P. Lamba, D. P. Kishore, B. L. Narayana, K. V. Rao, K. Rajwinder, A. R. Rao, B. Shireesha, B. Narsaiah, *Eur. J. Med. Chem.* **2010**, *45*, 4904; (c) D. Zhan, T. Li, H. Wei, W. Weng, K. Ghandi, Q. Zeng, *RSC Adv.* **2013**, *3*, 9325; (d) W. Ge, X. Zhu, Y. Wei, *RSC Adv.* **2013**, *3*, 10817; (e) N. Y. Kim, C. H. Cheon, *Tetrahedron Lett.* **2014**, *55*, 2340.

[14] T. M. Potewar, R. N. Nadaf, T. Daniel, R. J. Lahoti, K. V. Srinivasan, *Synth. Commun.* **2005**, *35*, 231.

[15] T. B. Nguyen, L. Ermolenko, A. Al-Mourabit, *Green Chem.* **2013**, *15*, 2713.

[16] H. Wei, T. Li, Y. Zhou, L. Zhou, Q. Zeng, *Synthesis* **2013**, *45*, 3349.

[17] (a) J. Sun, T. Tao, D. Xu, H. Cao, Q. Kong, X. Wang, Y. Liu, J. Zhao, Y. Wang, Y. Pan, *Tetrahedron Lett.* **2018**, *59*, 2099; (b) C. J. Feng, Z. Z. Wen, X. Cheng, Y. W. Dong, W. An-Xin, *Org. Lett.* **2016**, *18*, 2942; (c) S. Muhammad, O. Julita, L. Peter, B. Matthias, W. Xiao-Feng, *RSC Adv.* **2014**, *4*, 8; (d) T. Yellaiah, M. K. Lakshmi, S. Manda, A. Abdullah, K. Ahmed, *ChemistrySelect* **2016**, *1*, 2895.

[18] P. Sudipta, K. C. Majumdar, *RSC Adv.* **2016**, *6*, 37784.

[19] (a)J. Quiroga, S. Portillo, A. Perez, J. Galvez, R. Abonia, B. Insuasty, *Tetrahedron Lett.* **2011**, *52*, 2664; (b) R. Ghahremanzadeh, G. I. Shakibaei, S. Ahadi, A. Bazgir, *J. Comb. Chem.* **2010**, *12*, 191.

[20] (a) Y. L. Gu, F. Jerome, *Chem. Soc. Rev.* **2013**, *42*, 9550; (b) P. Liu, J. W. Hao, L. P. Mo, Z. H. Zhang, *RSC Adv.* **2015**, *5*, 48675; (c) H. C. Hu, Y. H. Liu, B. L. Li, Z. S. Cui, Z. H. Zhang, *RSC Adv.* **2015**, *5*, 7720.

[21] D. Sun, H. Zhai, *Catal. Commun.* **2007**, *8*, 1027.

[22] M. V. Reddy, J. S. Kim, K. T. Lim, Y. T. Jeong, *Tetrahedron Lett.* **2014**, *55*, 6459.

[23] I. Bhargavi, K. K. Bharat, V. Siddaiah, *ChemistrySelect* **2019**, *4*, 3290.

[24] X. Yu, Q. Yin, Z. Zhang, T. Huang, Z. Pu, M. Bao, *Tetrahedron Lett.* **2019**, *60*, 1964.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: S. L. Matcha, B. K. Karasala, S. M. Botsa, S. Vidavalur, *J Heterocyclic Chem* **2021**, 1. https://doi.org/10.1002/jhet.4321