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Efficient synthesis of novel quinazoline-4(1*H*)-one derivatives by *N*-halosulfonamides

Ramin Ghorbani-Vaghei[1] · Azadeh Shahriari[1] · Yaser Maghbooli[1] · Jafar Mahmoudi[1]

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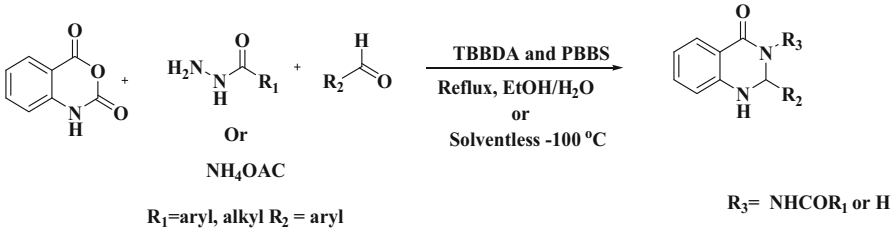
Abstract In this research, a facile, effective and one-pot synthesis of new quinazoline-4(1*H*)-one derivatives is reported. Isatoic anhydride, acid hydrazides or ammonium acetate and aromatic aldehydes in the presence of *N*-halosulfonamides; *N*,*N*,*N*′,*N*′-tetrabromobenzene-1,3-disulfonamide and poly(*N*-bromo-*N*-ethylbenzene-1,3-disulfonamide) are used to produce the above-mentioned compounds. In addition, the reaction medium is in agreement with green chemistry principles.

Graphical Abstract



Keywords *N*,*N*,*N*′,*N*′-tetrabromobenzene-1,3-disulfonamide · Poly(*N*-bromo-*N*-ethylbenzene-1,3,5-disulfonamide · Quinazoline-4(1H)-one · Isatoic anhydride · Acid hydrazide

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✉ Ramin Ghorbani-Vaghei
rgvaghei@yahoo.com

[1] Department of Organic Chemistry, Faculty of Chemistry, Bu-Ali Sina University, PO Box 65174, Hamedan, Iran

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Introduction

According to literature survey, quinazolin-4 (1*H*)-one derivatives are well known as important and valuable physiological compounds containing various medical properties. For example, they are active against bacteria, fungi, and tumors or they have a mono amine oxidase inhibitor trait [1]. Also, quinazolin-4(1*H*)-ones can be converted to quinazolin-4(3H)-one derivatives, which are biologically active heterocyclic materials and can also be found in some natural products. Specifically, the quinazolinone core scaffold has been extensively used as a drug-like template in medicinal chemistry [2]. For example, some novel nonpeptide antagonists for formyl peptide receptor-like1 with general structure 1 (Fig. 1) were synthesized when substitution on the para position of the 2-phenyl group of the quinazolinone backbone could alter the pharmacological properties of the compound [3]. Dihydroquinazolin-4-one with general structure 2 (Fig. 1) was identified as a thyroid-stimulating hormone receptor agonist [4]. Also, general structure 3 (Fig. 1) is well known as a TNKS inhibitor [5] and methaqualon structure 4 (Fig. 1) which has the antimalarial effect currently being used for the assessment of the abuse liability of sedative hypnotic drugs [6].

In recent years, this type of heterocyclic compound has attracted more attention due to a wide range of interesting properties; therefore, several techniques have been designed for their manufacture [7–11]. However, methods for the synthesis of this heterocycle include multi-step and low-yield reaction sequences.

An atom-efficient and more attractive procedure for the production of quinazolinones is through a three-component and one-pot reaction of isatoic anhydride, hydrazides and aldehydes. Until now, only a few strong acid catalysts such as montmorillonite K-10 [12], silica sulfuric acid [13, 14], zinc(II) perfluorooctanoate [15], [Zn(PFO)$_2$] [15], KAl(SO$_4$)$_2$·12H$_2$O [9], Al(H$_2$PO$_4$)$_3$ [9], gallium(III) triflate [16], molecular iodine [17], MCM-41-SO$_3$H [18], 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF$_4$) [19, 20], and Amberlyst-15 [21] have been applied to this reaction. Although most of those methods are accompanied by different limitations such as use of expensive reagents, strongly acidic conditions, longer reaction time, low yields and need of an additional microwave oven, still it is a requirement that we develop new procedures for the synthesis of quinazolinone derivatives [12].

N-halo sulfonamides have been widely used in organic synthesis; for example, *N*,*N*,*N*′,*N*′-tetrabromobenzene-1,3-disulfonamide [TBBDA] and poly(*N*-bromo-*N*-

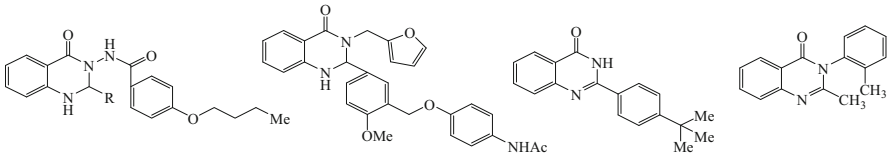


Fig. 1 Some examples of quinazolin-4-one derivatives with different properties

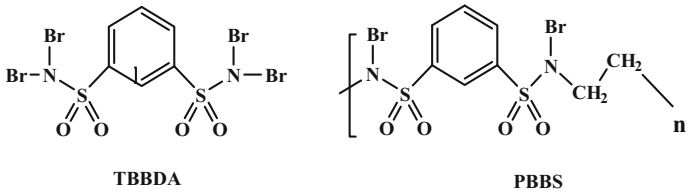
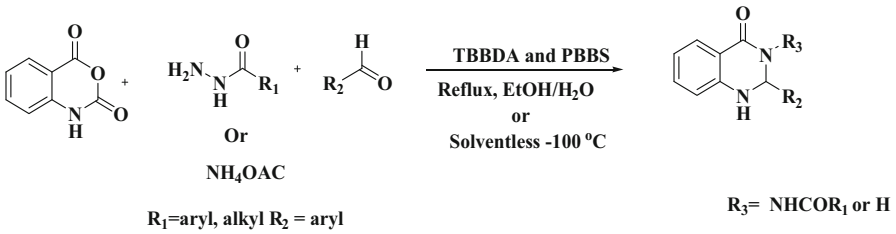


Fig. 2 The structure of TBBDA and PBBS



Scheme 1 Synthesis of quinazolin-4(1*H*)-one derivatives

ethylbenzene-1,3-disulfonamide) [PBBS] (Fig. 2)] as catalyst or reagent utilized in the synthesis of various compounds in our older research [22–27]. Some unique advantages of their applications include high stability, availability of the catalyst, a metal-free nature, low toxicity, neutral media and simple reaction conditions; thus, they are utilized in synthesis of diverse and new quinazoline-4(1*H*)-one derivatives, from the reaction of isatoic anhydride, aldehydes, *N*-halo sulfonamides (TBBDA and PBBS as reagent or catalyst) with acid hydrazides or ammonium acetate under reflux in ethanol/water or solvent-free conditions (Scheme 1).

Results and discussion

Preparation of TBBDA and PBBS is not difficult and they are unchanged even up to 2 months. TBBDA and PBBS are non-volatile, harmless, and low-cost reagents and they have not been used for quinazolin-4(1H)-one derivative synthesis before. In addition, products in this study have not been reported in previous literature except for a case rendered in Table 3, entry 10. However, the improvement in reaction time and yield from 3–6 h/64 % [32] to 2 h/95 % have been found in current research. Furthermore, the advancement of the reaction condition from a step-by-step synthesis to a one-pot reaction has occurred and the method of purification has been modified from column chromatography to purification with solvent (our research).

Considering the benefits such as time and resources preservation, avoiding a long separation process, purification of intermediates and increasing the efficiency of a chemical reaction, this reaction was carried out in one-pot condition with various amounts of reagents, while optimizing the conditions for the formation of *N*-(2-(4-

chlorophenyl)-1,2-dihydro-4-oxoquinazolin-3(4*H*)-yl)-3-methoxybenzamide using 3-methoxybenzhydrazide, isatoic anhydride, and 4-chlorobenzaldehyde (Table 1).

With attention paid to Table 1, due to the lack of proper results about using only water or ethanol and solvent-free conditions, a mixture of ethanol and water was chosen as the best solvent for these reactions (entry 4). This selection provides an environmentally safe method without any carcinogenic effect of common organic solvents.

Also, we test this one-pot reaction with ammonium acetate instead of acid hydrazide to study the effects of solvent, temperature and amount of catalysts in increments of yield of 2-(4-chlorophenyl)-2,3-dihydroquinazolin-4(1H)-one using ammonium acetate, isatoic anhydride, and 4-chlorobenzaldehyde (Table 2).

According to Table 2, solvent-free conditions in entry 7 were selected as the best choice for these reactions, which are in agreement with green chemistry principles as well.

After optimization of the reaction conditions, in order to study the generality of the procedure, isatoic anhydride was mixed with various aromatic aldehydes or salicylaldehyde derivatives and different acid hydrazides or ammonium acetate as a nucleophile. These reactants were subjected to the reaction conditions and provided correspondingly good to high yields (Table 3) and only in one case oxidation was occurred (Table 3, entry 14).

The possible mechanism shown in Scheme 2 may be suggested for the conversion of various aldehydes and acid hydrazides or ammonium acetate with isatoic anhydride into quinazolin-4(1*H*)-ones [28–30]. In the beginning, due to these *N*-sulfonamides focusing on liberating Br^+ as an electrophile and their capability of producing active carbonyl compounds [17–23], the reaction requires a Br^+ transfer from the reagents to isatoic anhydride to form (**A**). Afterward, nucleophilic attack of

Table 1 Optimization of reaction conditions for the synthesis of *N*-(2-(4-chlorophenyl)-1,2-dihydro-4-oxoquinazolin-3(4*H*)-yl)-3-methoxybenzamide using 3-methoxybenzhydrazide, isatoic anhydride, and 4-chlorobenzaldehyde

Entry	Solvent	[TBBDA (1–7)/PBBS (8–10) (g)]	Temperature (°C)	Time (h)	Yied[a] (%)
1	EtOH	0	25	3.5	–
2	EtOH–H_2O (4:1)	0	Reflux	3.5	Trace
3	EtOH–H_2O (4:1)	0.03	Reflux	2	80
4	EtOH–H_2O (4:1)	0.05	Reflux	1	95
5	Solvent-free	0.05	100	4	–
6	H_2O	0.05	100	4	–
7	Acetonitrile	0.05	Reflux	2.5	70
8	EtOH–H_2O (4:1)	0.05	Reflux	2.2	5
9	EtOH–H_2O (4:1)	0.08	Reflux	2.2	60
10	EtOH–H_2O (4:1)	0.10	Reflux	2.2	88

[a] Experimental conditions: Isatoic anhydride (1 mmol), 4-cholorobenzaldehyde (1 mmol) and 3-methoxybenzhydrazide (1 mmol)

Table 2 Optimization of reaction conditions for the synthesis of 2-(4-chlorophenyl)-2,3-dihydroquinazolin-4(1H)-one using ammonium acetate, isatoic anhydride, and 3,5-dichlorosalsiylaldehyde

Enty	Solvent	TBBDA	Temperature (°C)	Time (h)	Yied[a] (%)
1	EtOH	0	25	4	Trace
2	EtOH	0.05	Reflux	4	50
3	EtOH	0.1	Reflux	3	50
4	H_2O	0.1	Reflux	3	35
5	EtOH–H_2O (4:1)	0.1	Reflux	4	60
6	Solvent free	0.05	100	2	63
7	Solvent free	0.1	100	0.5	98
8	Acetonitrile	0.1	Reflux	3	55

[a] Experimental conditions: Isatoic anhydride (1 mmol), 4-cholorobenzaldehyde (1 mmol) and ammonium acetate (2 mmol)

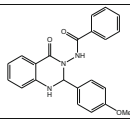
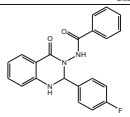
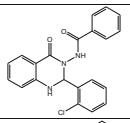
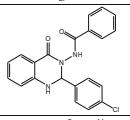
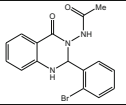
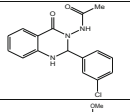
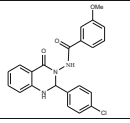
acid hydrazide or ammonium acetate to (**A**) produced (**B**). After the reaction of (**B**) with activated aldehyde via TBBDA followed by intramolecular cyclization and elimination of H_2O, quinazolin-4(1*H*)-one derivatives (**D**) were obtained. In order to find out the role of catalysts when we mixed isatoic anhydride with nucleophile species (hydrazide or ammonium acetate) without catalysts, not in this step for yielding (**B**) nor with addition of aldehyde, no product was observed. In a multicomponent reaction with free catalyst conditions, no product was obtained, as well (Tables 1, 2, entries 1). Furthermore, benzene-1,3-disulfonamide was recovered and then reused for preparation of TBBDA or, in another case (with ammonium acetate), catalyst was recovered as TBBDA.

Experimental

All commercially available chemicals were obtained from Merck Fluka and Aldrich companies, and used without further purification unless otherwise stated. Proton nuclear magnetic resonance (^{1}H NMR) and carbon-13 (^{13}C NMR) spectra were recorded on Bruker Evans 400 MHz FT NMR spectrometers (undertaken at the University of Isfahan and University of Urmia). Infrared (IR) spectroscopy was conducted on a Perkin Elmer GX Fourier transform (FT)-IR spectrometer followed by mass spectra recordation on a Shimadzu QP 1100 BX mass spectrometer (University of Tehran, Iran).

Typical procedure for the preparation of *N*-(2-(4-chlorophenyl)-1,2-dihydro-4-oxoquinazolin-3(4*H*)-yl)-3-methoxybenzamide (Table 2, entry 7): In a round flask, a mixture of isatoic anhydride (0.163 g, 1 mmol) and 3-methoxy benzhydrazide (0.16 g, 1 mmol) in 5 mL EtOH/H_2O (4:1) were heated and refluxed. Then, TBBDA (0.05 g, 0.10 mmol) or PBBS (0.1 g) and 4-chlorobenzaldehyde (0.14 g, 1 mmol) was added to the mixture and stirred for an appropriate time (Table 2, entry 7). After completion of the reaction, when bright blue spot appeared on thin

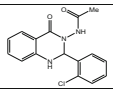
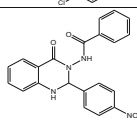
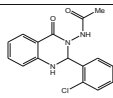
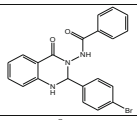
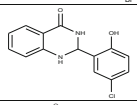
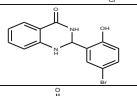
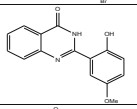
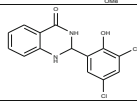
Table 3 Synthesis of quinazolin-4(1*H*)-one derivatives with aldehydes, hydrazides or ammonium acetate, isatoic anhydride using TBBDA and PBBS as reagents

Entry	Aldehyde	Nucleophile	Product[a]	Time(h)/Yield (%)[b]	
				TBBDA	PBBS
1				1.5/80	3.2/78
2				2.5/68	3.6/60
3				2/85	2.8/75
4				1/90	1.9/85
5				1.5/95	2.6/83
6				2.1/75	3.5/60
7				1/95	2.2/88

layer chromatography (TLC) [solvent ratio: acetone/*n*-hexane (8:20)], the solid was filtered and washed with ethanol (2 × 3 mL) and ether. The crude product was recrystallized in hot ethanol (to obtain sulfonamide, the solid was filtered; then, solvent was evaporated and CH_2Cl_2 (5 mL) was added, the precipitated sulfonamide was recovered by filtration. Furthermore, sulfonamide can be reused for preparation of TBBDA), the pure product (0.38 g, 95 %) was obtained as a cream powder. Mp: 199–200 °C; IR (KBr): υ (cm^{-1}) 3417, 3199, 1660, 1651, 1580, 1284, 804; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H (ppm) 3.75 (s, OCH_3, 3H), 4.65 (s, CH, 1H), 6.38 (s, NH, 1H), 6.69–7.95 (m, CH aromatic, 12H), 8.9 (s, NH, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm) 55.29, 74.35, 111.78, 114.66, 114.74, 118.96, 119.29, 119.84, 129.05, 129.14, 129.20, 129.34, 129.48, 131.49, 132.55, 134.63, 135.74, 135.85, 146.43, 159.46, 164.52, 166.35. MS: *m/z* 408 (M^+, 4 %), 257 (98), 242 (72), 214 (13), 180 (84), 151 (18).

N-(1,2-dihydro-2-(4-methoxyphenyl)-4-oxoquinazolin-3(4H)-yl) benzamide (Table 2, entry 1) Cream powder. Mp: 224–226 °C; IR (KBr): υ (cm^{-1}) 3390, 3312,

Table 3 continued

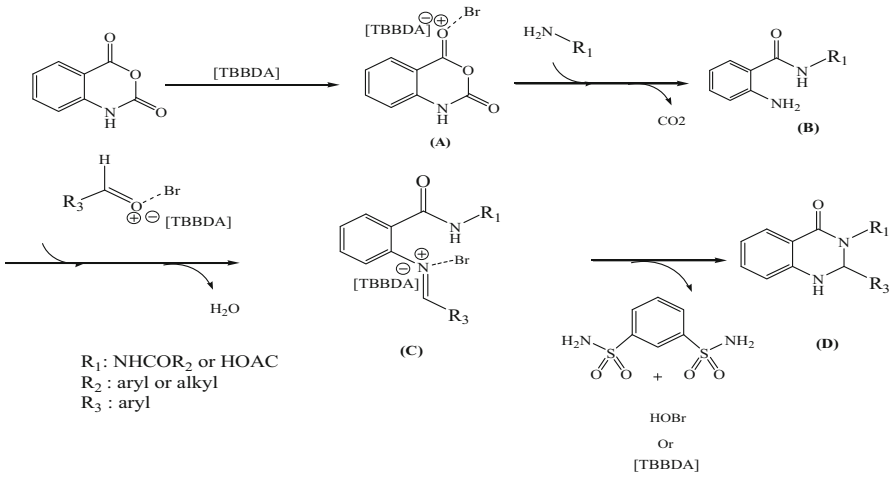
Entry	Aldehyde	Nucleophile	Product[a]	Time(h)/Yield (%)[b]	
				TBBDA	PBBS
8				2/85	3.5/70
9				1.5/94	2.5/80
10				2/95	3.5/82
11				1.5/96	2.4/88
12		NH_4OAC		1/95	1.5/83
13		NH_4OAC		1/93	1.5/88
14		NH_4OAC		1/98	1/ 95
15		NH_4OAC		1.5/93	2/90

[a] The known compounds were characterized from their physical properties, in comparison with authentic samples, and by spectroscopic methods

[b] Isolated yield

1685, 1653, 1610, 1252; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H (ppm) 3.74 (s, OCH_3, 3H), 6.14 (s, CH, 1H), 6.80–7.62 (m, CH aromatic, 13H), 7.29 (s, NH, 1H), 10.39 (s, NH, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm) 55.15, 74.02, 113.49, 113.73, 114.60, 117.74, 127.37, 127.66, 128.01, 128.30, 129.45, 129.80, 129.85, 131.77, 132.23, 132.28, 133.88, 148.03, 148.08, 159.87, 163.30, 165.47.MS: *m/z* 373 (M^+, 1.7 %), 371 (1.8), 321 (4), 295 (3.8), 280 (25), 253 (98), 238 (7), 210 (21).

N-(2-(4-fluorophenyl)-1,2-dihydro-4-oxoquinazolin-3(4H)-yl) benzamide (Table 2, entry 2) Cream powder. Mp: 243 °C; IR (KBr): υ (cm^{-1}) 3303, 3241, 1687, 1650, 1615, 1225; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H (ppm) 6.2 (s, CH, H), 6.80–7.61 (m, CH aromatic, 13H, 6.80 (s, NH, 1H), 10.44 (s, NH, 1H), ^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm) 73.77, 113.68, 114.63, 114.92, 115.13, 117.06, 117.93, 127.32, 128.02, 128.34, 130.27, 130.35, 131.85, 132.15, 134.01, 147.84, 147.89,



Scheme 2 Suggested mechanism for the synthesis of substituted quinazolin-4(1*H*)-ones

161.27, 163.11, 163.70, 165.50. MS: *m/z* 361 (M^+, 3 %), 360 (3), 319 (5), 295 (8), 280 (35), 241 (98), 226 (80), 210 (10), 198 (33).

N-(2-(2-chlorophenyl)-1,2-dihydro-4-oxoquinazolin-3(4H)-yl) benzamide (Table 2, entry 3) White powder. Mp: 223–224 °C; IR (KBr): υ (cm^{-1}) 3295, 3199, 1682, 1665, 1615, 1289; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H (ppm) 6.66 (s, CH, H), 6.79–7.90 (m, CH aromatic, 13H), 6.82 (s, NH, 1H), 10.51 (s, NH, 1H) ^{13}C NMR (100 MHz, DMSO-d_6): δ_c(ppm) 70.56, 113.17, 114.44, 117.78, 127.43, 127.97, 128.34, 129.27, 129.95, 130.64, 131.87, 132.16, 132.21, 132.97, 134.15, 135.74,135.78, 147.38, 147.43, 162.81, 165.55.MS: *m/z* 378 (M^+, 8 %), 360 (4), 257 (98), 242.(67), 214 (12).

N-(2-(4-chlorophenyl)-1,2-dihydro-4-oxoquinazolin-3(4H)-yl) benzamide (Table 2, entry 4) Cream powder. Mp: 267 °C; IR (KBr): υ (cm^{-1}) 3327, 3253, 1686, 1683, 1653, 1675, 1614; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H (ppm) 6.18(s, CH, H), 6.79–7.73 (m, CH aromatic, 13H), 7.34 (s, NH, 1H), 10.47 (s, NH, 1H).^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm), 73.76, 113.60, 114.61, 117.94, 127.35, 128.00, 128.23, 128.37, 129.94, 131.91, 132.03, 132.08, 133.67, 134.06, 137.05, 137.09, 147.70, 147.75, 162.95, 165.51. MS: *m/z* 378 (M^+, 1.6 %), 375 (4), 257 (88), 242 (41), 214 (10).

N-(2-(2-bromophenyl)-1,2-dihydro-4-oxoquinazolin-3(4H)-yl) acetamide (Table 2, entry 5) Cream powder. Mp: 271–273 °C; IR (KBr): υ (cm^{-1}) 3338, 3233, 3206, 1698, 1637, 1612, 1508; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H (ppm) 1.77 (s, CH_3, 3H), 6.42 (s, CH, H), 6.73–7.70 (m, CH aromatic, 8H), 6.77 (s, NH, 1H), 9.91 (s, NH, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm) 20.31, 73.05, 112.85, 114.32, 117.56, 122.85, 127.86, 128.16, 129.36, 130.88, 132.78, 134.10, 137.88, 146.86, 162.22, 168.30. MS: *m/z* 360 (M^+, 6 %), 301 (98), 286 (39), 218 (9), 180 (17).

N-(2-(3-chlorophenyl)-1,2-dihydro-4-oxoquinazolin-3(4H)-yl) acetamide (Table 2, entry 6) Cream powder. Mp: 200–203 °C; IR(KBr): υ (cm^{-1}) 3308, 3242.1, 1704, 1637, 1615, 1513; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H (ppm) 1.76 (s, CH_3, 3H), 6.02 (s, CH, 1H), 6.76–7.70 (m, CH aromatic, 8H), 7.32 (s, NH, 1H), 9.98 (s, NH, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm) 20.23, 73.32, 113.43, 114.51, 117.78, 126.22, 127.22, 127.90, 128.97, 130.27, 133.00, 134.04, 141.31, 147.13, 162.29, 168.36.MS: *m/z* 316 (M^+, 4 %), 303 (5), 291 (9), 257 (98), 242 (82), 214 (7), 180 (17).

N-(2-(2-chlorophenyl)-1,2-dihydro-4-oxoquinazolin-3(4H)-yl) acetamide (Table 2, entry 8) Cream powder. Mp: 269 °C; IR (KBr): υ (cm^{-1}) 3215, 3180, 1650, 1607, 1581, 1562;^{1}H NMR (400 MHz, DMSO-d_6): δ_H (ppm) 1.76 (s, CH_3, 3H), 6.45 (s, CH, 1H), 6.73–7.70 (m, CH aromatic, 8H), 7.31 (s, NH, 1H), 9.93 (s, NH, 1H) ^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm) 20.28, 70.45, 112.92, 114.30, 114.34, 117.61, 127.56, 127.86, 129.17, 129.55, 130.57, 134.09, 136.25, 146.92, 162.26, 168.30.MS: *m/z* 316 (M^+, 8 %), 298 (2), 257 (98), 242 (46), 214 (5), 180 (6).

N-(1,2-dihydro-2-(4-nitrophenyl)-4-oxoquinazolin-3(4H)-yl) benzamide (Table 2, entry 9) Cream powder. Mp: 260–261 °C; IR (KBr): υ (cm^{-1}) 3325, 3273, 1683, 1651, 1614; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H (ppm) 6.32(s, CH, H), 6.81–8.28 (m, CH aromatic, 13H), 6.84 (s, NH, 1H), 10.58 (s, NH, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm) 73.41, 86.47, 87.22, 102.59, 103.51, 104.55, 114.63, 114.66, 118.09, 123.34, 127.42, 127.95, 128.40, 129.43, 132.04, 134.20, 134.26, 135.32, 145.46, 147.32, 154.63. MS: *m/z* 388 (M^+, 5 %), 386 (10), 368 (11), 268 (98), 253 (51), 207 (23), 119 (17), 105 (88), 77 (65).

N-(2-(2,4-dichlorophenyl)-1,2-dihydro-4-oxoquinazolin-3(4H)-yl) acetamide (Table 2, entry 10) Cream powder. Mp: 238 °C (235 °C) [31]; IR (KBr): υ (cm^{-1}) 3260, 3243,1702, 1672, 1611, 1018; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H (ppm) 1.77 (s, CH_3, 3H), 6.42 (s, CH, H), 6.72–7.69 (m, CH aromatic, 7H), 7.31 (s, NH, 1H), 9.92 (s, NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm) 20.79, 70.92, 113.36, 115.54, 117.55, 118.94, 129.14, 130.17, 131.97, 134.23, 134.72, 135.89, 135.95, 147.32, 162.64, 168.83. MS: *m/z* 350 (M^+, 16 %), 332 (4), 291 (98), 276 (78), 248 (8), 214 (16).

N-(2-(4-bromophenyl)-1,2-dihydro-4-oxoquinazolin-3(4H)-yl) benzamide (Table 2, entry 11) Cream powder. Mp: 300 °C; IR (KBr): υ (cm^{-1}) 3313, 3244, 1686, 1649, 1614; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H (ppm) 6.15 (s, CH, 1H), 6.77–7.72 (m, CH aromatic, 13H), 6.77(s, NH, 1H), 10.45 (s, NH) .^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm) 74.31, 114.10, 115.80, 117.71, 119.13, 122.81, 127.10, 127.75, 127.81, 128.61, 129.61, 131.29, 132.40, 132.58, 133.61, 138.04, 148.18, 148.24,158.81, 163.39, 166.01.MS: *m/z* 422 (M^+, 2 %), 368 (5), 339 (8), 313 (12), 264 (14), 239 (14), 138 (25).

General procedure for preparation of 2-(3,5-dichloro-2-hydroxyphenyl)-2,3-dihydroquinazolin-4(1H)-one A mixture of isatoic anhydride (0.163 g, 1 mmol) and ammonium acetate (0.15 g, 2 mmol), TBBDA (0.1 g, 0.2 mmol) or PBBS (0.12 g)

and 3,5-dichlorosalsiylaldehyde (0.19 g, 1 mmol) was added to the mixture and stirred for an appropriate time (Table 3, entry 15). After completion of the reaction, when bright blue spot appeared on TLC [solvent ratio: acetone/n-hexane (8:20)], the solid was filtered and then washed with ethanol (2 × 3 mL) and water. The crude product was recrystallized in hot ethanol. The pure product (0.29 g, 93 %) was obtained as a white powder. Mp > 310 °C; IR (KBr): υ (cm^{-1}) 3395, 3295, 3197, 1655; ^{1}H NMR (400 MHz, DMSO-d6): δ_H (ppm) 6.12 (s, CH, 1H), 6.98 (s, NH, 1H), 6.77–7.59 (m, CH aromatic, 6H), 8.18 (s, OH, 1H). 10.12 (s, NH, 1H). ^{13}C NMR (100 MHz, DMSO-d6): δc (ppm) 61.43, 114.64, 114.68, 117.56, 122.10, 123.13, 126.09, 127.34, 128.78, 131.55, 133.43, 147.61, 149.45, 163.64. MS: m/z 309.

2-(5-chloro-2-hydroxyphenyl)-2,3-dihydroquinazolin-4(1H)-one (Table 3, entry 12) Cream powder. Mp > 300 °C; IR (KBr): υ (cm^{-1}) 3385, 3200, 3195, 1650; ^{1}H NMR (400 MHz, DMSO-*d6*): δ_H (ppm) 6.15 (s, CH, 1H), 6.81–7.72 (m, CH aromatic, 7H), 7.01 (s, NH, 1H), 8.21 (s, OH, 1H), 10.16 (s, NH, 1H) .^{13}C NMR (100 MHz, DMSO-*d6*): δ_c (ppm) 61.4, 114.64, 114.69, 117.56, 122.08, 123.12, 126.09, 127.34, 128.78, 131.53, 133.43, 147.62, 149.46, 163.64. MS: *m/z* 274.

2-(5-boromo-2-hydroxyphenyl)-2,3-dihydroquinazolin-4(1H)-one (Table 3, entry 13) Cream powder. Mp > 300 °C; IR (KBr): υ (cm^{-1}) 3390, 3285, 1667,1644; 1H NMR (400 MHz, DMSO-d6): δ_H (ppm) 6.01 (s, CH, 1H), 6.54–8.52 (m, CH aromatic, 7H), 6.82 (s, NH, 1H), 8.10 (s, OH, 1H), 10.32 (s, NH, 1H) .13C NMR (100 MHz, DMSO-d6): δ_c (ppm) 60.83, 109.80, 114.45, 117.22, 117.61, 120.07, 127.30, 129.66, 129.99, 131.83, 133.32, 147.77, 154.03, 163.74.

2-(2-hydroxy-5-methoxyphenyl) quinazolin-4(3H)-one : (Table 3, entry 14) Yellow powder. Mp > 300 °C; IR (KBr): υ (cm^{-1}) 3204, 3150, 1672, 1612; ^{1}H NMR (400 MHz, DMSO-*d6*): δ_H (ppm) 3.86 (s, CH_3, 3H), 6.99–8.21 (m, CH aromatic, 7H), 7.81 (s, OH, 1H), 13.53 (s, NH, 1H) .^{13}C NMR (100 MHz, DMSO-*d6*): δ_c (ppm) 55.81, 110.12, 112.98, 118.93, 120.627, 121.78, 126.01, 126.95, 128.08, 135.03, 146.08, 151.68, 153.65, 154.38, 161.51. MS: *m/z* 268.

Conclusions

We proposed a simple method and efficient procedure for the synthesis of quinazolin-4(1*H*)-one derivatives using TBBDA and PBBS as novel reagents utilizing an easy synthetic technique, low-cost reagents, a one-pot procedure, good to high yields, environmental friendliness (non-corrosive reagent and green solvent) and a facial isolation for synthesis of new quinazoline-4(1*H*)-one derivatives with probable pharmacological properties like similar compounds [32].

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