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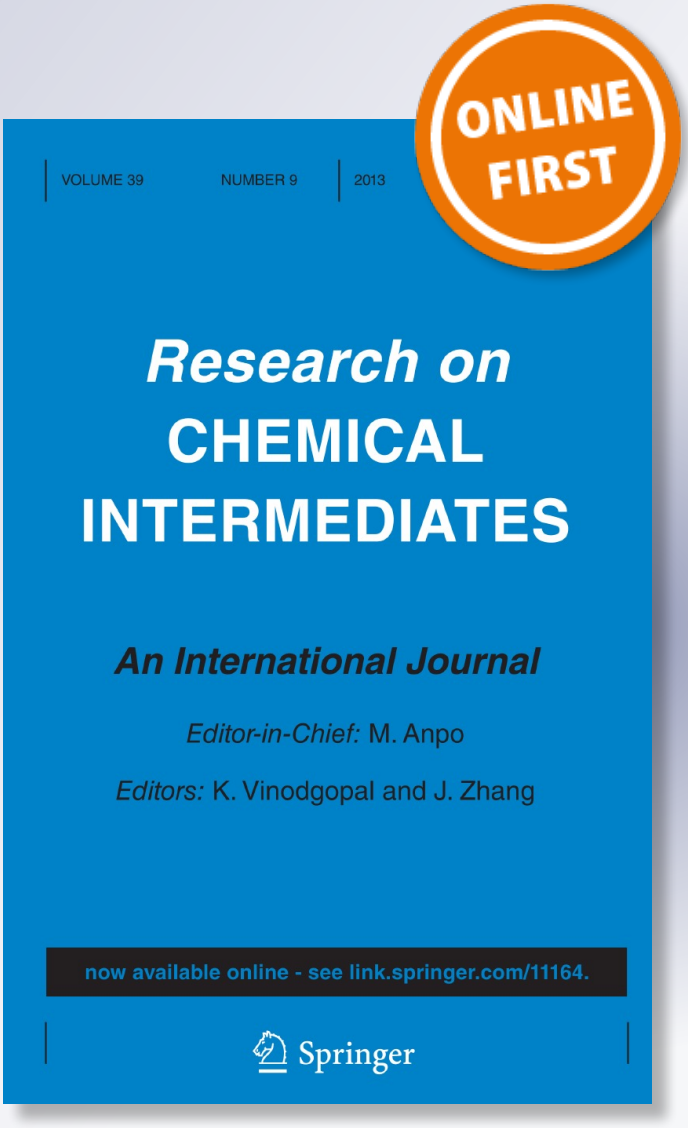

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Synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones catalyzed by succinimide-*N*-sulfonic acid as a mild and efficient catalyst

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Abstract A simple, green and environmentally benign procedure was developed for the synthesis of 2,3-dihydro-2-phenylquinazolin-4(1*H*)-ones using catalytic amounts of succinimide-*N*-sulfonic acid via the cyclocondensation of 2-amino-benzamide with an aldehyde. The present methodology offers several advantages such as high yields, simple procedure, low cost, short reaction times, mild reaction conditions, and use of a reusable catalyst.

Keywords 2,3-Dihydroquinazolin-4(1*H*)-one · Succinimide-*N*-sulfonic acid · 2-Amino benzamide · Catalyst recovery

Introduction

2,3-Dihydroquinazolin-4(1*H*)-ones are an important class of heterocyclic compounds that have attracted considerable attention. The natural quinazolinones and their synthetic analogous have been reported to possess a wide range of pharmacological and biological activities including antitumor [1], sodium/calcium exchanger inhibitors [2], tubulin polymerization inhibitors [3], α_1-adrenoreceptor antagonists [4], and antibacterial and antifungal activity [5]. Some novel 6,8-diiodo-2-methyl-3-substituted-quinazolin-4(3*H*)-ones bearing sulfonamide derivatives were synthesized in good yields and evaluated for their possible antibacterial

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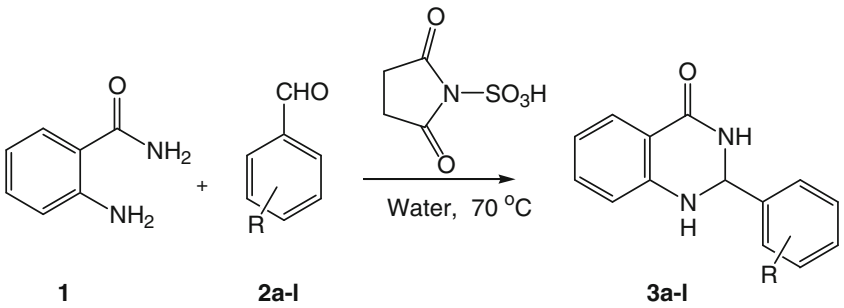
and anti-inflammatory activities and acute toxicity [6]. Novel quinazolinone library of 85 compounds were synthesized and the binding affinities of all the synthesized compounds were obtained by radio-ligand binding assay for the 5-HT_7 receptor. Among the 85 compounds, 24 compounds show very good binding affinities with IC_{50} values below 100 nM [7]. Therefore, considerable efforts have been made to explore new simple and direct approaches towards the construction of 2,3-dihydroquinazolin-4(1*H*)-ones skeletons.

In the past few years, several methods for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones have been reported. The typical procedure for the synthesis of this compound involves the condensation reaction of 2-aminobenzamide with aldehydes or ketones using various promoting agents, such as trichloroacetic acid [8], SiO_2–$FeCl_3$ [9], aerosil silica-supported acidic ionic liquid [10], sulfamic acid [11], poly(4-vinylpyridine)-supported acidic ionic liquid [12], trifluoroethanol [13], supported *N*-propylsulfamic acid on magnetic nanoparticles [14], supramolecular synthesis [15], heteropoly acids [16], tetrabutyl ammonium bromide [17], amberlyst-15 [18], $ZrCl_4$ [19], and heteropolyacid–clay nanocomposite [20]. Three-component reaction of isatoic anhydride, aldehyde, and amine are also reported for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones [21–26]. Many of these methods, however, suffer from drawbacks, such as low yields of products, the requirement of longer reaction time and high temperature, along with the use of non-recyclable catalysts. Moreover, preparation of required catalysts is cumbersome in some cases. Thus, development of a facile, atom-efficient, and eco-friendly method is highly desirable. In recent years, heterogeneous catalysis has played the central role in various organic transformations.

In recent years, succinimide-*N*-sulfonic acid (SuSA) has drawn much interest in different organic reactions due to its experimental simplicity. SuSA has shown considerable catalytic efficiency in different transformations, such as chemoselective trimethylsilylation of alcohols and phenols with hexamethyldisilazane (HMDS) [27], chemoselective conversion of amines to their corresponding *N*-Boc protected derivatives with $(Boc)_2O$ [28], and the synthesis of xanthene derivatives via three-component condensation of aldehydes with 2-naphthol, 1,3-cyclohexanedione and/or a mixture of 2-naphthol and 1,3-cyclohexanediones under solvent-free conditions [29], and also for the acetylation reactions in the absence of a solvent [30].

The use of water as a solvent has many advantages in organic synthesis from both economic and environmental points of view. Water has therefore become an attractive medium for many organic reactions, not only because one can avoid using drying reactants and expensive catalysts and solvents but also for rendering unique reactivity and selectivity [25].

In continuation of our efforts in the development of green synthetic methodologies [31–35], we report here a facile, efficient, and environmentally friendly procedure for the synthesis of 2,3-dihydro-2-phenylquinazolin-4(1*H*)-ones using catalytic amounts of SuSA via the cyclocondensation of 2-aminobenzamide with an aldehyde in water at 70 °C (Scheme 1).



Scheme 1 Preparation of various 2,3-dihydroquinazolin-4(1*H*)-ones

Experimental

Chemicals and apparatus

Chemicals were purchased from Merck, Fluka, and Aldrich. All yields refer to isolated products unless otherwise stated. ^{1}H-NMR (500 MHz) and ^{13}C-NMR (125 MHz) spectra were obtained using Bruker DRX-500 Avance at ambient temperature, using TMS as internal standard. FT-IR spectra were obtained as KBr discs on Shimadzu spectrometer. Mass spectra were determined on a Varion-Saturn 2000 GC/MS instrument. Elemental analysis were measured by means of Perkin Elmer 2400 CHN elemental analyzer flowchart.

General procedure for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones

To a solution of 2-aminobenzamide (1 mmol) and aromatic aldehyde (1 mmol) in water (3 mL), SuSA (5 mol%) was added. The mixture was stirred at 70 °C for an appropriate time. After completion of the reaction, as indicated by TLC (ethyl acetate: *n*-hexane 1:1), water was decanted, hot ethanol (5 mL) was added to the residue which was then filtered. The resulting solution was condensed under reduced pressure. Finally, the crude product was purified by recrystallization from EtOH to afford the corresponding 2,3-dihydroquinazolin-4(1*H*)-ones in 86–95 % yield.

*Spectroscopic data for synthesized compounds (**3a–l**)*

2,3-Dihydro-2-phenylquinazolin-4(1H)-one (3a) White solid; IR (KBr): 3,302, 3,166, 3,044, 1,662, 1,611, 1,501, 1,477 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 5.68 (s, 1H, CH), 6.72 (t, $J = 7.2$ Hz, 1H, Ar–H), 6.81 (d, $J = 8.0$ Hz, 1H, Ar–H), 7.13 (brs, 1H, NH), 7.29 (t, $J = 7.2$ Hz, 1H, Ar–H), 7.39–7.49 (m, 3H, Ar–H), 7.63 (d, $J = 7.0$ Hz, 2H, Ar–H), 7.72 (d, $J = 7.7$ Hz, 1H, Ar–H), 8.37 (brs, 1H, NH) ppm; ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 68.3, 113.3, 116.7, 117.8, 127.5, 128.7, 129.2, 129.7, 133.3, 142.7, 148.6, 166.9 ppm; MS (ESI): *m*/*z* 225 $(M + H)^+$. Anal.

Calcd. for $C_{14}H_{12}N_2O$ (%): C, 75.00; H, 5.36; N, 12.50. Found: C, 74.91; H, 5.31; N, 12.44.

2-(4-Fluorophenyl)-2,3-dihydroquinazolin-4(1H)-one (3b) White solid; IR (KBr): 3,296, 3,170, 3,052, 1,661, 1,611, 1,511, 1,473 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 5.79 (s, 1H, CH), 6.77 (t, $J = 8.1$ Hz, 1H, Ar–H), 6.92 (d, $J = 6.6$ Hz, 1H, Ar–H), 7.19 (brs, 1H, NH), 7.33–7.47 (m, 3H, Ar–H), 7.55 (d, $J = 8.8$ Hz, 2H, Ar–H), 7.77 (d, $J = 7.8$ Hz, 1H, Ar–H), 8.44 (brs, 1H, NH) ppm; ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 67.7, 112.6, 116.6, 117.4, 127.0, 128.5, 129.4, 129.6, 133.3, 142.6, 148.6, 167.2 ppm; MS (ESI): m/z 243 $(M + H)^+$. Anal. Calcd. for $C_{14}H_{11}FN_2O$ (%): C, 69.42; H, 4.55; N, 11.57. Found: C, 69.33; H, 4.46; N, 11.50.

2-(4-Bromophenyl)-2,3-dihydroquinazolin-4(1H)-one (3c) White solid; IR (KBr): 3,295, 3,172, 3,060, 1,659, 1,615, 1,513, 1,472 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 5.69 (s, 1H, CH), 6.73–6.81 (m, 2H, Ar–H), 7.17 (s, 1H, NH), 7.35 (d, $J = 7.8$ Hz, 1H, Ar–H), 7.47 (d, $J = 8.4$ Hz, 2H, Ar–H), 7.61–7.69 (m, 3H, Ar–H), 8.42 (s, 1 H, NH) ppm; ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 68.0, 113.1, 116.6, 117.2, 127.2, 128.5, 129.0, 129.4, 133.5, 143.0, 148.3, 167.7 ppm; MS (ESI): m/z 303.5 $(M + H)^+$. Anal. Calcd. for $C_{14}H_{11}BrN_2O$ (%): C, 55.46; H, 3.63; N, 9.24. Found: C, 55.35; H, 3.57; N, 9.19.

2-(3-Nitrophenyl)-2,3-dihydroquinazolin-4(1H)-one (3d) White solid; IR (KBr): 3,305, 3,174, 3,061, 1,658, 1,615, 1,505, 1,480 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 5.72 (s, 1H, CH), 6.79 (t, $J = 8.2$ Hz, 1H, Ar–H), 6.90 (d, $J = 6.4$ Hz, 1H, Ar–H), 7.16 (brs, 1H, NH), 7.29–7.42 (m, 3H, Ar–H), 7.58 (d, $J = 8.4$ Hz, 2H, Ar–H), 7.63–7.67 (m, 1H, Ar–H), 8.44 (brs, 1H, NH) ppm; ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 67.6, 112.7, 116.7, 117.0, 127.0, 128.3, 129.3, 129.7, 133.6, 143.2, 148.8, 166.8 ppm; MS (ESI): m/z 270 $(M + H)^+$. Anal. Calcd. for $C_{14}H_{11}N_3O_3$ (%): C, 62.45; H, 4.09; N, 15.61. Found: C, 62.40; H, 4.03; N, 15.63.

2-(4-Methylphenyl)-2,3-dihydroquinazolin-4(1H)-one (3e) White solid; IR (KBr): 3,299, 3,174, 3,055, 1,666, 1,612, 1,507, 1,481 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 2.17 (s, 3H, CH_3), 5.74 (s, 1H, CH), 6.81 (t, $J = 8.1$ Hz, 1H, Ar–H), 6.98 (d, $J = 6.4$ Hz, 1H, Ar–H), 7.12 (brs, 1H, NH), 7.31–7.44 (m, 3H, Ar–H), 7.54 (d, $J = 8.8$ Hz, 2H, Ar–H), 7.69 (d, $J = 7.8$ Hz, 1H, Ar–H), 8.39 (brs, 1H, NH) ppm; ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 20.9, 68.2, 113.0, 116.5, 117.8, 127.6, 128.4, 129.5, 129.9, 133.7, 142.9, 148.3, 167.5 ppm; MS (ESI): m/z 239 $(M + H)^+$. Anal. Calcd. for $C_{15}H_{14}N_2O$ (%): C, 75.63; H, 5.88; N, 11.76. Found: C, 75.60; H, 5.86; N, 11.77.

2-(4-Methoxyphenyl)-2,3-dihydroquinazolin-4(1H)-one (3f) White solid; IR (KBr): 3,304, 3,172, 3,056, 1,664, 1,616, 1,509, 1,475 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 3.57 (s, 3H, OCH_3), 5.75 (s, 1H, CH), 6.74–6.83 (m, 2H, Ar–H), 7.19 (s, 1H, NH), 7.32 (d, $J = 7.9$ Hz, 1H, Ar–H), 7.50 (d, $J = 8.5$ Hz, 2H, Ar–H), 7.66–7.72 (m, 3H, Ar–H), 8.46 (s, 1 H, NH) ppm; ^{13}C-NMR (125 MHz, DMSO-d_6) δ 54.4, 67.5, 112.5, 116.5, 117.7, 127.6, 128.4, 129.3, 129.8, 133.4, 143.3, 148.6, 166.9 ppm; MS (ESI): m/z 255 $(M + H)^+$. Anal. Calcd. for $C_{15}H_{14}N_2O_2$ (%): C, 70.87; H, 5.51; N, 11.02. Found: C, 70.79; H, 5.47; N, 11.01.

2-(3-Bromophenyl)-2,3-dihydroquinazolin-4(1H)-one (3g) White solid; IR (KBr): 3,301, 3,168, 3,060, 1,655, 1,614, 1,511, 1,475 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6) δ 5.68 (s, 1H, CH), 6.75 (t, $J = 8.2$ Hz, 1H, Ar–H), 6.88 (d, $J = 6.8$ Hz, 1H, Ar–H), 7.09 (brs, 1H, NH), 7.19–7.36 (m, 3H, Ar–H), 7.46 (d, $J = 8.4$ Hz, 2H, Ar–H), 7.63–7.71 (m, 1H, Ar–H), 8.48 (brs, 1H, NH) ppm; ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 68.1, 113.3, 116.7, 117.7, 127.4, 128.8, 129.3, 129.7, 133.5, 142.8, 148.9, 167.3 ppm; MS (ESI): *m/z* 303.5 $(M + H)^+$. Anal. Calcd. for $C_{14}H_{11}BrN_2O$ (%): C, 55.46; H, 3.63; N, 9.24. Found: C, 55.43; H, 3.60; N, 9.25.

2-(3-Fluorophenyl)-2,3-dihydroquinazolin-4(1H)-one (3h) White solid; IR (KBr): 3,294, 3,162, 3,061, 1,658, 1,609, 1,514, 1,478 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 5.83 (s, 1H, CH), 6.73 (t, $J = 8.4$ Hz, 1H, Ar–H), 6.91 (d, $J = 6.6$ Hz, 1H, Ar–H), 7.11 (brs, 1H, NH), 7.25–7.40 (m, 3H, Ar–H), 7.50 (d, $J = 8.6$ Hz, 2H, Ar–H), 7.60–7.72 (m, 1H, Ar–H), 8.42 (brs, 1H, NH) ppm; ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 67.5, 112.9, 116.4, 117.8, 127.2, 128.6, 129.0, 129.6, 133.4, 143.1, 148.9, 167.0 ppm; MS (ESI): *m/z* 243 $(M + H)^+$. Anal. Calcd. for $C_{14}H_{11}FN_2O$ (%): C, 69.42; H, 4.55; N, 11.57. Found: C, 69.39; H, 4.53; N, 11.55.

2-(4-N,N-Dimethylaminophenyl)-2,3-dihydroquinazolin-4(1H)-one (3i) White solid; IR (KBr): 3,308, 3,160, 3,057, 1,659, 1,606, 1,513, 1,480 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 2.87 (s, 6H, $N(CH_3)_2$), 5.65 (s, 1H, CH), 6.76 (t, $J = 8.2$ Hz, 1H, Ar–H), 6.91 (d, $J = 6.8$ Hz, 1H, Ar–H), 7.12 (brs, 1H, NH), 7.31–7.45 (m, 3H, Ar–H), 7.56 (d, $J = 8.8$ Hz, 2H, Ar–H), 7.67 (d, $J = 7.8$ Hz, 1H, Ar–H), 8.47 (brs, 1H, NH) ppm; ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 40.4, 68.3, 113.1, 116.9, 117.9, 127.2, 128.0, 129.2, 129.6, 133.3, 142.6, 148.4, 166.8 ppm; MS (ESI): *m/z* 268 $(M + H)^+$. Anal. Calcd. for $C_{16}H_{17}N_3O$ (%): C, 71.91; H, 6.37; N, 15.73. Found: C, 71.84; H, 6.30; N, 15.69.

2-(4-Hydroxyphenyl)-2,3-dihydroquinazolin-4(1H)-one (3j) White solid; IR (KBr): 3,304, 3,172, 3,059, 1,663, 1,612, 1,507, 1,481 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 5.70 (s, 1H, CH), 6.77–6.84 (m, 2H, Ar–H), 7.19 (s, 1H, NH), 7.33 (d, $J = 7.9$ Hz, 1H, Ar–H), 7.49 (d, $J = 8.6$ Hz, 2H, Ar–H), 7.62–7.75 (m, 3H, Ar–H), 8.45 (s, 1H, NH), 9.97 (s, 1H, OH) ppm; ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 67.9, 11292, 116.4, 117.2, 127.1, 128.1, 129.4, 129.7, 133.2, 143.0, 148.5, 166.9 ppm; MS (ESI): *m/z* 241 $(M + H)^+$. Anal. Calcd. for $C_{14}H_{12}N_2O_2$ (%): C, 70.00; H, 5.00; N, 11.67. Found: C, 69.88; H, 4.94; N, 11.64.

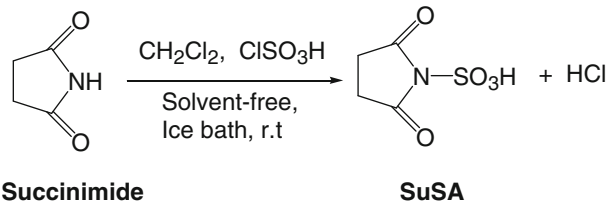
2-(4-Chlorophenyl)-2,3-dihydroquinazolin-4(1H)-one (3k) White solid; IR (KBr): 3,292, 3,175, 3,060, 1,662, 1,611, 1,506, 1,477 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 5.71 (s, 1H, CH), 6.79 (t, $J = 8.3$ Hz, 1H, Ar–H), 6.86 (d, $J = 6.5$ Hz, 1H, Ar–H), 7.07 (brs, 1H, NH), 7.27–7.39 (m, 3H, Ar–H), 7.48 (d, $J = 8.8$ Hz, 2H, Ar–H), 7.72 (d, $J = 7.8$ Hz, 1H, Ar–H), 8.49 (brs, 1H, NH) ppm; ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 67.8, 113.0, 116.6, 117.3, 127.8, 128.6, 129.5, 129.9, 133.4, 142.8, 148.5, 166.6 ppm; MS (ESI): *m/z* 259 $(M + H)^+$. Anal. Calcd. for $C_{14}H_{11}ClN_2O$ (%): C, 65.00; H, 4.26; N, 10.83. Found: C, 64.96; H, 4.23; N, 10.79.

2-(3-Hydroxyphenyl)-2,3-dihydroquinazolin-4(1H)-one (3l) White solid; IR (KBr): 3,298, 3,173, 3,063, 1,659, 1,614, 1,512, 1,472 cm^{-1}; ^{1}H-NMR (500 MHz,

DMSO-d_6) δ: 5.73 (s, 1H, CH), 6.81 (t, $J = 8.2$ Hz, 1H, Ar–H), 6.97 (d, $J = 6.6$ Hz, 1H, Ar–H), 7.09 (brs, 1H, NH), 7.20–7.38 (m, 3H, Ar–H), 7.55 (d, $J = 8.4$ Hz, 2H, Ar–H), 7.66–7.70 (m, 1H, Ar–H), 8.44 (brs, 1H, NH), 9.88 (s, 1H, OH) ppm; ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 68.1, 112.7, 116.7, 117.4, 127.9, 128.7, 129.4, 129.9, 133.7, 143.2, 148.3, 166.3 ppm; MS (ESI): m/z 241 $(M + H)^+$. Anal. Calcd. for $C_{14}H_{12}N_2O_2$ (%): C, 70.00; H, 5.00; N, 11.67. Found: C, 69.95; H, 5.01; N, 11.68.

Results and discussion

SuSA as a stable reagent was easily prepared by the reaction of succinimide with neat chlorosulfonic acid (Scheme 2) [27]. The prepared SuSA was assessed for its



Scheme 2 Preparation of succinimide-*N*-sulfonic acid

Table 1 Synthesis of 2,3-dihydro-2-phenylquinazolin-4(1*H*)-ones in the presence of SuSA as catalyst in different reaction conditions

Entry	Solvent	Catalyst (mol%)	Temperature (°C)	Time (h)	Yield (%)[a]
1	1,4-Dioxane	5	Reflux	4.0	44
2	$CHCl_3$	5	Reflux	5.0	42
3	DMF	5	Reflux	5.0	43
4	EtOH	5	Reflux	5.0	82
5	CH_3CN	5	Reflux	5.0	68
6	Water	5	70	1.0	94
7	Solvent-free	5	70	3.0	63
8	Water	2	70	1.0	53
9	Water	3	70	1.0	69
10	Water	4	70	1.0	83
11	Water	7	70	1.0	94
12	Water	8	70	1.0	93
13	Water	5	50	2.0	57
14	Water	5	60	1.5	76
15	Water	5	80	1.0	94

Reaction conditions: 2-aminobenzamide (1 mmol) and benzaldehyde (1 mmol)

[a] Isolated yield

Table 2 Synthesis of various 2,3-dihydro-2-phenylquinazolin-4(1*H*)-ones in the presence of SuSA (5 mol%)

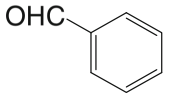
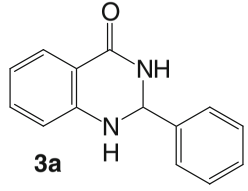
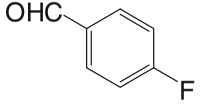
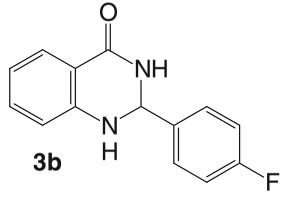
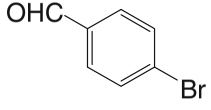
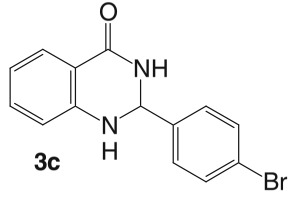
Entry	Aldehyde	Product	Time (h)	Yield (%)[a]	M.p. (°C)
1		 **3a**	1.0	94	220–222
2		 **3b**	0.8	95	202–204
3		 **3c**	0.8	95	196–198

Table 2 continued

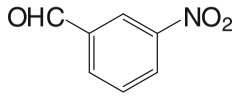
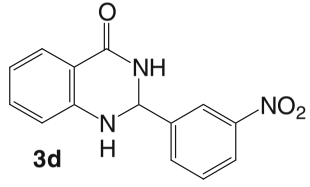
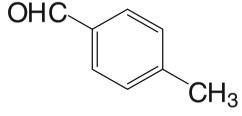
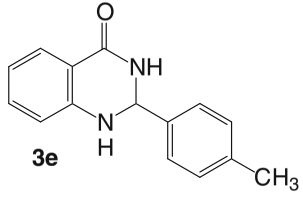
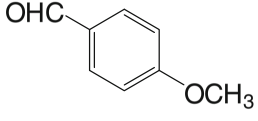
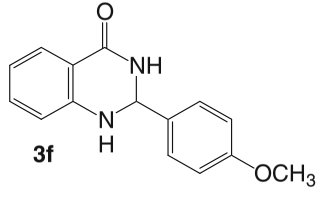
Entry	Aldehyde	Product	Time (h)	Yield (%)[a]	M.p. (°C)
4		 **3d**	0.8	90	216–218
5		 **3e**	1.0	87	232–234
6		 **3f**	1.0	86	180–182

Table 2 continued

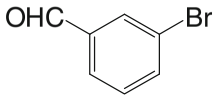
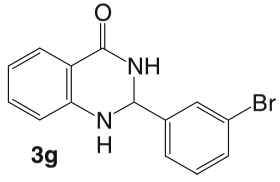
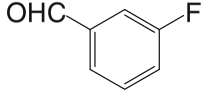
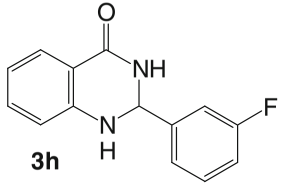
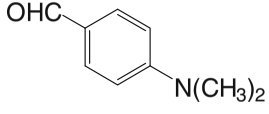
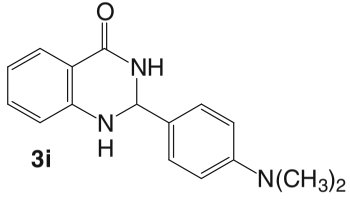
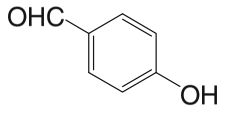
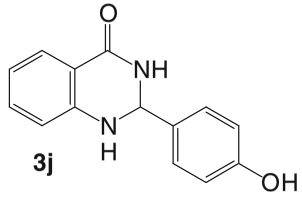
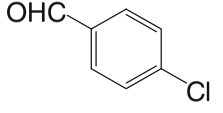
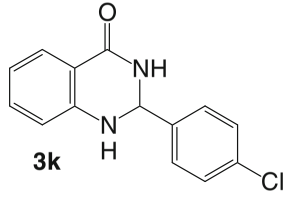
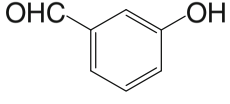
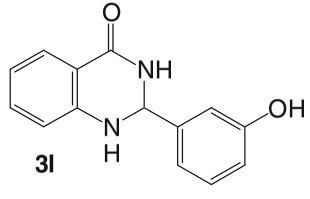
Entry	Aldehyde	Product	Time (h)	Yield (%)[a]	M.p. (°C)
7		 **3g**	0.8	91	227–229
8		 **3h**	0.8	92	266–268
9		 **3i**	1.0	89	226–228

Table 2 continued

Entry	Aldehyde	Product	Time (h)	Yield (%)[a]	M.p. (°C)
10		 **3j**	0.8	90	277–279
11		 **3k**	0.8	94	204–206
12		 **3l**	0.8	89	190–192

Reaction conditions: 2-aminobenzamide (1 mmol) and benzaldehyde (1 mmol) at 70 °C

[a] Isolated yield

catalytic activity in the synthesis of 2,3-dihydro-2-arylquinazolin-4(1*H*)-ones by studying the condensation reaction between 2-aminobenzamide and aromatic aldehydes. For the selection of the optimized condition, the cyclo-condensation reaction of 2-aminobenzamide (1 mmol) and benzaldehyde (1 mmol) to form 2,3-dihydro-2-phenylquinazolin-4(1*H*)-one was chosen as model of the reaction.

Initial studies addressed the effect of solvent and solvent-free condition on the reaction conversion using 5 mol% of SuSA as catalyst. Various solvents like 1,4-dioxane, $CHCl_3$, DMF, EtOH, CH_3CN, and water was examined. Among the various solvents (Table 1, entries 1–6) and solvent-free conditions (Table 1, entry 7), water was selected to be the best reaction media for its higher yielding and shorter reaction time (Table 1, entry 6). The results of the optimization experiments are summarized in Table 1.

With this result in hand, the effect of catalyst concentration on reaction conversion was investigated. The optimized amount of the catalyst was determined using 5, 2, 3, 4, 7, and 8 mol% of SuSA at 70 °C (Table 1, entries 6, 8–12). It was observed that 5 mol% of SuSA was the best of amount of the catalyst at 70 °C (Table 1, entry 6). Using lower amounts of catalyst resulted in lower yields, while higher amounts of catalyst did not affect the reaction times and yields (Table 1, entries 6, 8–12). Also, this reaction was checked under different temperatures including 70, and 50, 60, and 80 °C (Table 1, entry 6, 13–15). The greatest yield in the shortest reaction time was obtained in water at 70 °C in the presence of 5 mol% of SuSA.

Encouraged by this result, in order to build the generality of the reaction, our attention moved to the reactions of other aldehydes, and the results are summarized in Table 2. As expected, this reaction proceeded smoothly and the desired products were obtained in good to excellent yields. A series of aldehydes with either electron-

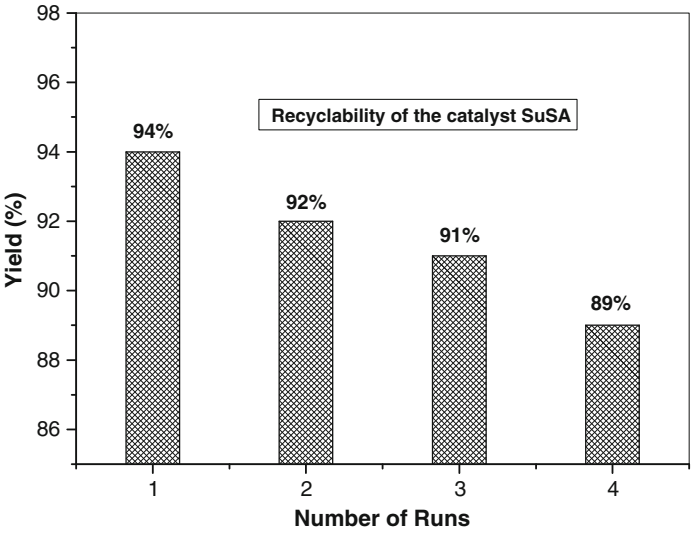
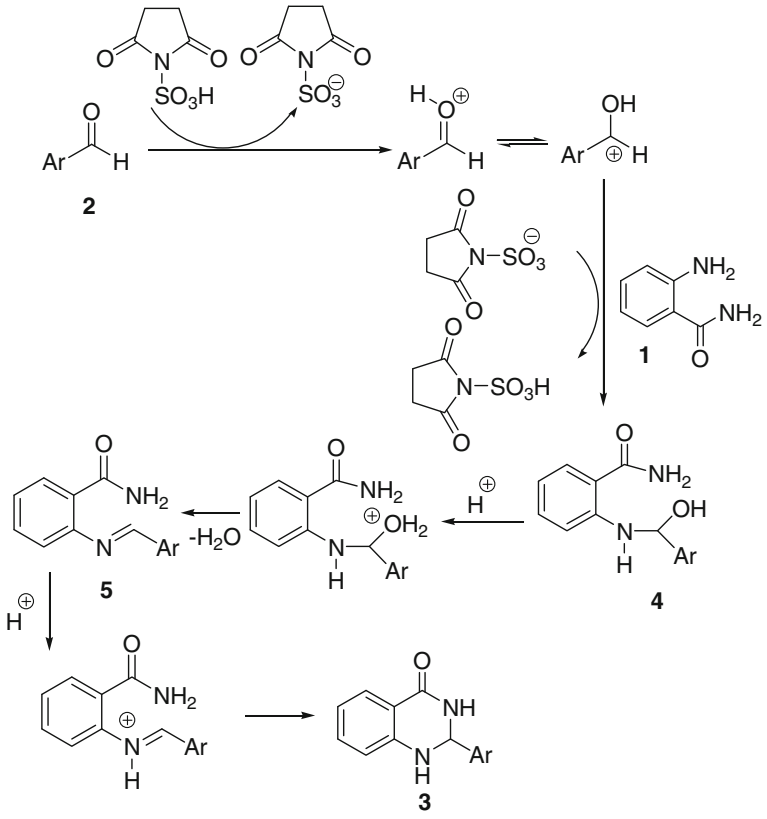


Fig. 1 Recycling of catalyst SuSA for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-one

donating or electron-withdrawing groups attaching to aromatic ring were investigated. The substitution groups on the aromatic ring had no obvious effect on the yield. From these experiments, it is clearly demonstrated that the synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones using SuSA as catalyst under thermal condition is indeed an effective method and is undoubtedly superior to other procedures with respect to reaction time, availability of catalyst, work-up procedure, and yields.

In the interests of green chemistry and developing an environmentally benign process, the recyclability of the catalyst was investigated using a model reaction between 2-aminobenzamide and benzaldehyde in the presence of 5 mol% of the catalyst in the presence of water. After the separation of product, the catalyst was washed with diethyl ether and vacuumed to remove diethyl ether, and the resulting catalyst was reused directly for the next run. As shown in Fig. 1, the recycled catalyst was used for further runs, and its activity did not show any significant decrease even after four runs, the yields ranging from 94 to 89 %.

A plausible mechanism for the formation of products **3** is shown in Scheme 3. The addition of nucleophiles to the aldehydes is promoted by protonation of the carbonyl group with the aid of SuSA and enhancing the electrophilicity of this



Scheme 3 Proposed mechanism for the formation of 2,3-dihydroquinazolin-4(1*H*)-ones

moiety. The proton from SuSA is donated to the oxygen atom of the aldehyde [29]. Therefore, it is proposed that, at first, the reaction starts through nucleophilic attack of the amino group in 2-aminobenzamide at the activated carbonyl group in arylaldehyde by SuSA. It seems that the reaction proceeds through intermediate **4**, such that, after dehydration, the imine intermediate **5** is produced. Then, the intermediate **5** undergoes protonation and heterocyclization to furnish the corresponding 2,3-dihydroquinazolin-4(1*H*)-ones (Scheme 3).

Conclusions

In summary, we have developed a direct and efficient method for the preparation of 2,3-dihydroquinazolin-4(1*H*)-ones using catalytic amount of SuSA via the cyclo-condensation of 2-aminobenzamide with an aldehyde. The simplicity of the procedure, eco-friendly, non-volatile, and easy handling are the advantages of these methods.

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