One-pot Synthesis and Antimicrobial Activities of some 2-Aryl/ Alkyl, 3-Aminoquinazolin-4(*3H*)-ones

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Summary: A simple, facile one-pot method for the synthesis of 2-aryl, 3-aminoquinazolin-4 (*3H*) one is described. The method was found more efficient and high yielding than the stepwise method reported in the literature. The synthesized compounds were characterized with the help of spectroscopic techniques including ^{1}H-NMR, EI-MS, FAB-MS and were tested against bacteria (*Bacillus pumis* and *Staphylococus aureus*) and a fungus (*Candida albicanus*).

Introduction

Derivatives of 4*H*-3,1-benzoxazin-4-one like other heterocyclic compounds share interesting properties *i.e.*, they are directly or indirectly involved in many industrial processes and also used as synthetic precursors in the synthesis of many heterocyclic compounds such as quinazolin-4(3*H*)-ones ring system [1-5].

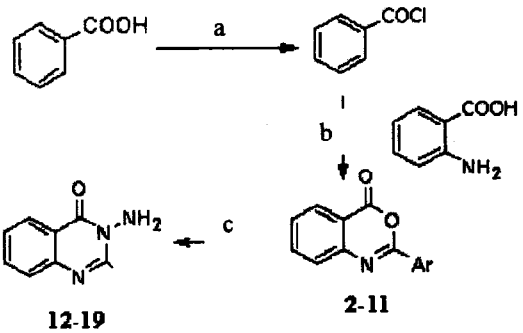
4*H*-3,1-Benzoxazin-4-one derivatives have shown antiphlogistic [6], antifungal, antibacterial [7-10], anti-muscular contractor and hypnotic activities [11-12]. Compounds possessing this heterocyclic nucleus are found to be serine protease inhibitors and are also reported for anti-inflamatory, antipyretic and analgesic activities [13-14]. On the other hand, quinazolin-4(3*H*)-ones have exhibited a wide range of bioactivities and for this reason is a class of organic compounds of active research interest. The chemistry and biological activates of quinazolin-4(3*H*)-ones and derivatives have been reviewed comprehensively in the literature [15-17].

In this paper, we report a simple, facile and traceless one-pot synthesis of position 2-substituted 3-aminoquinazolin-4(3*H*)-ones to attain better yields and develop easy synthetic methodology as well as synthesize new compounds having useful biological activities.

Results and Discussion

Literature describes the synthesis of benzoxazinone using cyclizing agents such as cyanuric chloride [18], reactants having heteroatom at suitable position [19]. In some other methods, benzoxazinone have been prepared using anthranyl-3, 1-benzisoxazole as a key intermediate [20]. Synthesis of benzoxazinones has also been accomplished by reacting acid halides and 2-aminobenzoic acid in basic solvent, which is the most widely, discussed literature method [21-23]. In the later method, substituted benzoyl chlorides were allowed to react with anthraxnillic acids, which upon further reaction with primary amines resulted in 2, 3-disubstituted quinazolinones. The method follows a stepwise experimental procedure which is a time consuming and laborious.

The target molecules, 2-Aryl/ alkyl, 3-aminoquinazolin-4(3*H*)-ones were synthesized *via* modification of the reported literature protocol. Here we report two ways in comparative manner for the synthesis of target quinazolinones **12-19** *i.e.*, a stepwise synthetic procedure (Scheme-1) and three components one-pot traceless synthesis with out isolating any of the resulting intermediate products. The later



12-19 **2-11**

Scheme-1. Stepwise synthesis of 2-aryl- 3-amino quinazolinones *via* benzoxazinones.

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method is a new synthetic method being reported here.

In the step wise method suitable substituted benzoic acid was converted into to its corresponding acid halide by refluxing in excess of thionyl chloride followed by cyclocondensation with 2-aminobenzoic acid to give the corresponding 2-substituted benzxo-azinones **2-11** (Table-1) Compounds **2-11** were then refluxed with hydrazine hydrate in boiling pyridine to obtain 2-substituted, 3-amino quinazolinones **12-19** Keeping in mind shortcomings of aforementioned stepwise method in which overall yield decrease during each step, we decided to develop a one-pot strategy for the synthesis of series of 4*H*-3,1-benzoxazin-4-ones (Table-1) and thus a suitable aromatic carboxylic acid was allowed to cyclize with 2-aminobenzoic acid by *in situ* preparation of the acid chloride using thionyl chloride and its spontaneous cyclization into benzoxazinones followed by hydrazine hydrate insertion reaction into the cyclic system to afford the target compounds (Scheme-2).

Table-1: List of 2-arylbenzoxazinane compounds synthesized (**2-11**).

Compounds	Ar	M.P. (°C)	Yield (%)
2	C_6H_5	108-110	93
3	p-$C_6H_4NO_2$	202-204	95
4	p-$C_6H_4CH_3$	140	92
5	p-C_6H_4Cl	158-160	90
6	p-C_6H_4Br	184	87
7	m-C_6H_4I	130	93
8	C_5H_4N	207	90
9	3,5-$(NO)_2.C_6H_3$	125-126	83
10	m-C_6H_4Br	118-120	61
11	m- C_6H_4Cl	128-130	76.6

12-19

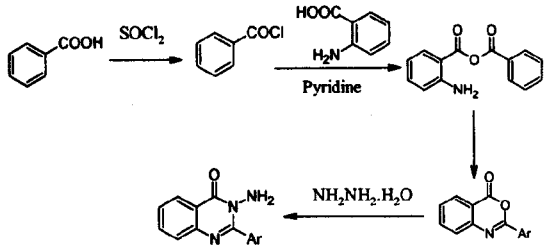
i.) substituted benzoic acid, thionyle chlorid reflux, 3-7 h

ii) anthranilic acid, dry pyridine, stirring, r.t. 1/2-1 h

iii) hydrazine hydrate, dry pyridine, reflux, 3-6 h

Scheme-2. Direct one post synthesis of 2-aryl,3-aminoquinazolin-4-one (**12-19**).

The chemical pathway of both methods is almost the same; we explain modification of stepwise method to one pot method (Scheme-2), the later method is less tedious and can be setup easily in the laboratory. The probable mechanism is believed to involve the initial formation of anhydride by reaction of substituted benzoyl chloride with anthranillic acid in dry pyridine followed by internal nucleophillic cyclization (Scheme-3).



Scheme-3. General mechanism of formation of 2-aryl- 3-amino-4-(3*H*)quinazolinone *via* benzoxazinone intermediate.

Microbial Activities

Today almost 60 % of the total prostatheses received from different clinical laboratories are contaminated with pathogenic microorganisms [24], moreover, resistant to the commonly used antibiotics have led the medicinal chemists to explore new and more potent antimicrobial compounds.

Antimicrobial activities including antibacterial and antifungal activities of the some of the synthesized compounds against selected microbes *i.e., Candida albicanas* (fungus), *Bacillus pumi* (bacteria), *Staphylococus aureus* (bacteria) were also assessed using the standard procedures. Antifungal activity of the synthesized compounds was evaluated by the agar tube dilution method as described in the literature [25], while the antibacterial activity was carried out by the agar well diffusion protocol [26].

Most of the tested compounds were found moderately active against fungus, *Candida albicans* and bacteria namely *Bacillus pumis* and *Staphylococcus aureus* compared to standard anti-fungal (Miconazole) and antibacterial (Imepenium and Gentamycine) (Table-2). Structural activity relationship revealed that substitution on position 2-phenyl group dramatically affects the activities and generally increased compared to compounds **2** and **12** where the phenyl group is not substituted. Among the benzoxazinones, 2-(3-bromophenyl)-4*H*-3,1-benzoxazin-4-one **10** was more potent which is due to the

Table-2: List of synthesized 2-aryl-3-aminoquinazolinones (**12-19**).

Compound	Ar	M.P (°C)	Yield (%)
12	Phenyl	238	86
13	4-methylphenyl	156°C	85
14	4-nitrophenyl	202	91
15	4-chlorophenuyl	189-190	90
16	4-bromohenyl	170-172	72
17	3,5-dinitrophenyl	225-226	72
18	Pyridinyl	207	72
19	3-iodophenyl	150	58

Table-3: Antimicrobial activities of the newly synthesized quinazolinones against the tested organisms

Compounds	Biological Activities (% Inhibition)		
	Antibacterial		Antifungal
	Bacillus pumis	*Staphylococus aureus*	*Candida albicanas*
3	NT	NT	NT
4	NT	NT	NT
5	NT	NT	NT
6	16	--	22
7	16	20	23
8	21	23	23
9	18	19	24
10	18	19	23
11	NT	NT	NT
12	12	16	NT
13	--	--	--
14	NT	NT	NT
15	--	--	NT
16	NT	NT	NT
17	NT	NT	NT
18	NT	NT	NT
19	19	22	27
SD 1	26	17	NT
SD 2	31	35	NT
SD 3	NT	NT	00

-- = No activity, NT = Not tested, SD = Standard drug, SD 1 = Imepenium (antibiotic)
SD 2 = Gentamycine (antibiotic), SD 3 = DMSO (negative control)

bromo group substituted on phenyl group, looking at the effect of other halogens we found complete loss of activity due to chlorosubstitution as in case of 3-amino-2-(4-chlorophenyl)quinazolin-4(3*H*)-one **15**, while on the other hand methyl substituent at position 2-phenyl ring was also responsible for complete loss of activities against both the fungi, and bacteria species. Dramatic increased was recorded when phenyl group was replaced with pyridinyl as in case of synthesis of 2-pyridin-3-yl-4*H*-3,1-benzoxazin-4-one **8** which was found more potent in the whole series.

Nitro group was also found to increase activity as was observed in case of 2-(3,5-dinitrophenyl)-4*H*-3,1-benzoxazin-4-one **9** A step ahead in search of more potent compounds it was found that in some cases 2-substituted, 3-aminoquinazolinones are more active then their corresponding 2-substituted benzoxazinones analogues as was observed in case of 3-amino-2-(3-iodophenyl)quinazolin-4(3*H*)-one **19** which is more potent then it its corresponding 2-(3-iodophenyl)-4*H*-3,1-benzoxazin-4-one 7.

Experimental

All the chemicals and solvents used were of synthetic grade and were purified before use according to standard methods. TLC analysis was done on alumina supported pre-coated TLC plates (Merck). Melting points were determined in open capillary using Gallenkamp melting point apparatus and are uncorrected. ^{1}H-NMR spectra were recorded on Bruker 300 MHz and 400 MHz in $CDCl_3$, CD_3OD or DMSO as solvent using TMS is internal standard while Mass spectra were recorded on MAT312 instrument.

2-Phenyl-4H-3, 1-benzoxazine-4-one (2)

To a well stirred solution of anthranilic acid (2 g, 6 mmol) in dry pyridine (20 mL), was added drop-wise benzoyl chloride (3.5 mL) with continuous stirring for next 30 min at room temperature. The mixture was then poured into saturated $NaHCO_3$ aqueous solution. The product precipitated out was filtered, washed with distilled water followed by saturated $NaHCO_3$ solution. Yield: 93 %, M.P.: 108-110 °C, EI-MS *m/z*: 223 (M^+, 100), 146 (15), 120 (13), 105 (100), 77 (83), 51 (18), ^{1}HNMR (400 MHz, $CDCl_3$): δ 8.26 (d, 1H, J = 8), 8.12 (d, 1H, J = 8.3), 7.82 (t,1H, J = 8.7), 7.67 (m, 2H), 7.5 (t, 1H, J = 8.6), 7.42 (m, 3H)

General Method for the Synthesis of Compounds (3-11)

Substituted benzoic acid(s) in freshly distilled thionylchloride catalyzed with 2-3 drops DMF was boiled under reflux for 2-5 h with continuous stirring, the mixture was allowed to cool below the room temperature and was then added portion wise to the well stirred solution of anthranilic acid in dry pyridine. The stirring was continued for next 30 min or till the precipitate appeared and was then poured into saturated $NaHCO_3$ solution, the solid precipitated was filtered, washed with $NaHCO_3$ solution followed by distilled water, dried and recrystallized from suitable solvent to give the corresponding benzoxazinone (**3-9**) in 83-95 % yield.

2-(4-Nitrophenyl)-4H-3,1-benzoxazin-4-one (3)

p-nitrobenzoic acid (1.2 g, 0.007 mol) in freshly distilled $SOCl_2$ (10 mL) was refluxed for 3 h the mixture was allowed to cool to room temperature and was then added to well stirred solution of anthranillic acid (0.5 g, 0.0036 mol) in dry pyridine (15 mL). The stirring was continued for the next 30 min till the solid precipitated out. The solid formed was washed with saturated $NaHCO_3$ solution followed by distilled water, dried and recrystallized from water ethanol. Yield: 95 %, M.P.: 202-204 °C, EI-MS *m/z*: 268 (M^+, 28), 253 (44), 236 (7), 235 (15), 207 (48), 179 (19), 178 (27), 167 (9), 105 (91), 104 (17), 102 (32), 92 (10), 77 (39), 76 (100), 63 (17), 51 (20), ^{1}HNMR (400 MHz, $CDCl_3$): δ 8.34 (d, 2H, J = 9, Ar-H's), 8.02 (d, 1H, J = 9, Ar-H's), 7.98 (m, 3H, Ar-Hs), 7.81(t, 1H, J = 8.7),7.39 (t,1H, J = 8.5).

2-(4-Methylphenyl)-4H-3,1-benzoxazin-4-one (4)

4-Methyl benzoic acid (3.9 g, 0.29 mol), thionylchloride (10 mL) and anthranillic acid (2 g, 0.0155 mol). Yield : 92 %, EI-MS *m/z*: 237 (M^+,92), 146 (21), 120 (18), 119 (100), 91 (38), 76 (10), 65 (10), ^{1}HNMR (300 MHz, $CDCl_3$): 8.21 (d, 1H, J = 8.6), 8.11 (d, 1H, J = 8.7), 7.97 (d, 2H, J = 8), 7.82 (t, 1H, J = 8.4), 7.44 (t, 1H, J = 8.0), 7.18 (d, 2H, J = 8.4), 2.36 (s, 3H, CH_3)

2-(4-Chlorophenyl)-4H-3,1-benzoxazin-4-one (5)

4-Chloro benzoic acid (3 g, 0.19 mol), thionylchloride (10 mL) and anthranillic acid (2 g, 0.0155 mol). Yield: 90 %, M.P.: 158-160 °C, EI-MS *m/z*: 259 (M^{+2}, 3), 257 (M^+, 8), 243 (10), 241 (61), 215 (2), 213 (5), 146 (24), 139 (5), 113 (4), 111 (13), (91), 50 (5); ^{1}HNMR (300 MHz, $CDCl_3$): δ 8.23 (d, 1H, J = 9), 8.15 (d, 1H, J = 9), 7.94 (d, 2H, J = 8), 7.8 (t, 1H, J = 8.5), 7.51-7.42 (m, 3H)

2-(4-Bromophenyl)-4H-3,1-benzoxazin-4-one (6)

4-Bromo benzoic acid (6 g, 0.029 mol), thionylchloride (10 mL) and anthranillic acid (2 g, 0.0155 mol). Yield: 87 %, M.P.: 184 °C, EI-MS *m/z*: 303 (M^{+2}, 48), 301 (M^+, 56), 287 (4), 285 (40), 259 (12), 257 (16), 182 (4), 181 (11), 180 (6), 168 (9), 166 (13), 146 (81), 120 (20), 118 (22), 105 (92), 92 (11), 76 (100), 63 (25), 57 (29), 51 (42); ^{1}HNMR (300 MHz, $CDCl_3$): δ 8.23 (d, 1H, J = 8.9), 8.12 (d, 1H, J = 8.7), 7.93 (dd, 2H, $J_{1,2}$ = 8.7, $J_{3,4}$ = 9.5), 7.81 (t, 1H, J = 9.2), 7.66 (m, 2H), 7.45 (d, 1H, J = 8.3)

2-(3-Iodophenyl)-4H-3, 1-benzoxazin-4-one (7)

3-Iodo benzoic acid (4 g, 0.016 mol), thionylchloride (10 mL) and anthranillic acid (2 g, 0.0155 mol). Yield: 93 %, M.P.: 130 °C, EI-MS *m/z*: 349 (M^+, 89), 335 (11), 307 (19), 222 (67), 204 (76), 131 (17), 120 (27), 119 (31), 105 (100), 104 (9), 92 (71), 80 (24), 76 (57), 67 (10), 54 (18); ^{1}HNMR (400 MHz, $CDCl_3$): 8.27 (d, 1H, J = 8), 8.17 (m, 2H), 8.1(d, 1H, J = 9.5), 7.89 (t, 1H, J = 8.4), 7.80 (d, 1H, J = 9), 7.45 (t, 1H, J = 8.5), 7.35 (t, 1H, J = 9.6).

2-Pyridin-3-yl-4H-3,1-benzoxazin-4-one (8)

Nicotinic acid (2 g, 0.106 mol), thionylchloride (10 mL) and anthranillic acid (2 g, 0.0155 mol). Yield: 90 %, M.P.: 207 °C, EI-MS *m/z*: 224 (M^+, 89), 209 (27), 182 (15), 147 (43), 132 (5), 120 (19), 105 (100), 92 (59), 79 (71), 76 (18), 63 (5), 54 (11); ^{1}HNMR (400 MHz, $CDCl_3$) δ: 9.31 (s, 1H, Ar-H), 9.14 (d, 1H, J = 8.9), 8.27 (d, 1H, J = 8), 8.19 (d, 2H, J = 8.2), 8.07 (t, 1H, J = 8), 7.93 (t, 1H, J = 8), 7.44 (t, 1H, J = 8.7).

2-(3,5-Dinitrophenyl)-4H-3,1-benzoxazin-4-one (9)

2,3-Dintrobenzoic acid (2 g, 0.016 mol), thionylchloride (10 mL) and anthranillic acid (2 g, 0.0155 mol). Yield: 82 %, M.P.: 125-126 °C, EI-MS *m/z*: 313 (94), 299 (35), 268 (7), 221 (5), 168 (12), 120 (18), 105 (100), 92 (37), 76 (11), 75 (3), 63 (7), 54 (3); ^{1}HNMR (300 MHz, $CDCl_3$) δ: 9.8 (s, 1H), 9.21 (s, 2H), 8.2 (d, 1H, J = 7.37), 8.10 (d, 1H, J = 8.09), 7.81 (t, 1H, J = 7.6), 7.47(t, 1H, J = 8.07).

2-(3-Bromophenyl)-4H-3,1-benzoxazin-4-one (10)

3-Bromobenzoic acid (4.65 g, 0.0235 mol), thionylchloride (10 mL) and anthranillic acid (2 g, 0.0155 mol) Yield: 61 %, M.P.: 118-120 °C, EI-MS *m/z*: 303(M^{+2}, 15), 301 (M^+, 62), 300 (4), 29 (46), 257 (44), 222 (10), 182 (4), 181 (11), 180 (6), 168 (10), 166 (13), 145 (79), 120 (18), 119 (14), 118 (25), 105 (92), 104 (4), 92 (11), 53 (7), 54 (34), 53 (7), 52 (14), 51 (42); ^{1}HNMR (400 MHz, $CDCl_3$) δ: 8.6 (s, 1H), 8.2 (d, 1H, J = 8), 8.15 (d, 1H, J = 8.2), 8.07 (d,1H, J = 8.2), 7.6 (d, 1H, J = 8.5), 7.46 (t, 1H, J = 8.2), 7.37 (t, 1H, J = 8.4).

2-(3-Chlorophenyl)-4H-3,1-benzoxazin-4-one (11)

3-Cholorobenzoic acid (3.6 g, 0.0235 mol). thionylchloride (10 mL) and anthranillic acid (2 g,

0.0155 mol). Yield: 77.6 %, M.P.: 128-130 °C, EI-MS *m/z*: 259 (M^{+2}, 86), 257 (100), 243 (21), 241 (12), 215 (2), 214 (4), 213 (5), 207 (24), 152 (4), 140 (6), 138 (36), 120 (6), 119 (13), 102 (7), 90 (4), 77 (5), 76 (48), 50 (4); ^{1}HNMR (300 MHz, $CDCl_3$): δ 8.31 (s, 1H), 8.25-8.20 (m, 2H), 8.15 (d, 1H, J = 9.7), 7.80-7.60 (t, 1H, J = 8.5), 7.48 (t, 1H, J = 9), 7.41-7.37 (m, 2H).

Synthesis of 2-Aryl/alkyl, 3-amino quinazolin-4(3H)-ones (12-19)

Method A:

General Rout to Synthesis from Benzoxazinones (2-11)

3-Amino-2-phenylquinazolin-4(3H)-one (12)

A mixture of 2-phenyl-4H-3,1-benzoxazine-4-one (**2**) (2 g, 0.00896 mol) and hydrazine haydrate 80 % (5 mL) in benzene (15 mL) was refluxed for 2 h. After completion of the reaction as indicated by TLC, the product precipitated upon cooling and was further digested dilute HCl solution for 1 h, and was then cooled to room temperature, the precipitate formed was filtered, washed with water and recrystallized from ethanol. Yield: 86 %, M.P: 238 °C, EI-MS *m/z*: 237 (M^+, 100), 136 (34), 222 (26), 208 (59), 180 (18), 152 (7), 119 (37), 105 (10), 77 (28), 63 (5), 50 (14); ^{1}HNMR (300 MHz, $CDCl_3$): δ 8.35 (d, 1H, J=8), 7.82 (m, 4H), 7.56 (m, 4H), 4.43 (s, 2H, NH_2)

3-Amino-2-(4-methylphenyl) quinazolin-4(3H)-one (13)

2-(4-methylphenyl)-4*H*-3,1-benzoxazin-4-one (**4**) (2 g, 0.00843 mol) and hydrazine hydrate 80 % (5 mL) in benzene (15 mL) were refluxed for 8 h as described compound **12**. Yield: 85 %, M.P: 156 °C EI-MS *m/z*: 251 (M^+, 4), 138 (100), 222 (2), 200 (5), 146 (19), 120 (96), 91 (38), 82 (10), 65 (18); ^{1}HNMR (300 MHz, $CDCl_3$): δ 8.35 (d, 1H, J = 8), 7.93 (d, 2H, J = 8), 7.64 (m, 3H), 7.45 (d, 1H, J = 8), 7.15 (q, 1H, J = 8),4.08 (s, 2H), 2.348 (s, 3H, CH_3)

3-Amino-2-(4-nitrophenyl) quinazolin-4(3H)-one (14)

2-(4-nitrophenyl)-4H-3,1-benzoxazin-4-one (**3**) (2 g), and hydrazine hydrate 80 % (5 mL) in 15 mL benzene. Yield: 91 %, M.P.: 202 °C : EI-MS *m/z*: 281 (M^+, 82), 180 (30), 253 (40), 236 (44), 207 (43), 179 (19), 177 (27), 105 (10), 92 (10), 90 (26), 76 (100), 65 (13), 51 (19), ^{1}HNMR (300 MHz, $CDCl_3$): δ 8.34 (d, 3H, J = 9), 8.02 (d, 2H, J = 9), 7.81 (s, 2H), 7.59 (m, 1H), 4.89 (b, s, 2H, N-H)

3-Amino-2-(4-chlorophenyl) quinazolin-4(3H)-one (15)

2-(4-chlorophenyl)-4H-3,1-benzoxazin-4-one (**5**) (2 g), and hydrazine hydrate 80 % (5 mL) in 15 mL benzene. Yield: 90 %, M.P.: 189-190 °C, EI-MS *m/z*: 273 (M^{+2}, 50), 272 (53), 271 (M^+, 100), 270 (86), 257 (4), 255 (13), 243 (100), 242 (61), 214 (4), 213 (5), 202 (24), 178 (73), 90 (3), 77 (5), 76 (8), 50 (4); ^{1}HNMR (300 MHz, $CDCl_3$): δ 8.30 (d, 1H, J = 6), 7.79-7.77 (m, 4H), 7.57-7.44 (m, 3H), 5.05 (b, s, 2H).

3-Amino-2-(4-bromophenyl) quinazolin-4(3H)-one (16)

2-(4-bromophenyl)-4H-3,1-benzoxazin-4-one (**6**) (2 g), hydrazine hydrate 80 % (5 mL) and benzene (15 mL). Yield: 72 %, M.P.: 170-172 °C, EI-MS *m/z*: 317 (M^{+2}, 99), 316 (63), 315 (92), 314 (49), 301 (6), 299 (4), 288 (46), 287 (46), 286 (40), 285 (40), 236 (12), 207 (44), 185(5), 183 (16), 182(4), 180 (10), 179 (27), 178 (19), 177 (8), 157 (8), 155 (13),152 (7), 150 (14), 120 (21), 119 (55),118 (22), 105 (12), 103 (15), 102 (39), 97 (8), 91 (11), 81 (18), 77 (49), 76 (100), 71 (11), 63 (25),56 (29), 51 (42); ^{1}HNMR (300 MHz, $CDCl_3$): δ 8.83 (D, 1H, J = 8), 7.93-7.87 (q, 2H, $J_{1,2}$=8, $J_{3,4}$ = 8, $J_{1,3}$ = 16, $J_{2,4}$ = 16), 7.64-7.43 (m, 3H), 7.15-7.1 (q, 1H, $J_{1,3}$ = 14, $J_{2,4}$ = 14, $J_{1,2}$ = 8), 4.08 (s, b, 2H, N-H).

3-Amino-2-(3, 5-dinitrophenyl) quinazolin-4(3H)-one (17)

2-(3,5-dinitrophenyl)-4*H*-3,1-benzoxazin-4-one (**9**) (2 g), hydrazine hydrate 80 % (5 mL) benzene (15 mL). Yield: 72 %, M.P.: 225-226 °C, EI-MS *m/z*: 327 (M^+, 82), 312 (91), 299 (71), 168 (7), 105 (100), 74 (4), 76 (12), 51 (19); ^{1}HNMR (300 MHz, $CDCl_3$): δ 9.4 (s, 1H), 8.91 (s, 2H), 8.41 (d, 1H, J = 8), 8.02 (t, 1H, J = 8), 7.63 (d, 1H, J = 9, 4), 7.51(t, 1H, J = 8)

3-Amino-2-(pyridin-3-yl) quinazolin-4(3H)-one (18)

2-pyridine-3-yl-4*H*-3, 1-benzoxazin-4-one (**8**) (2 g), hydrazine hydrate 80 % (5 mL) and benzene (15 mL). Yield: 72 %, M.P.: 207 °C, EI-MS *m/z*: 238 (M^+, 19), 223 (18), 222 (91), 209 (27), 146 (43), 120 (19), 105 (100), 102 (39), 90 (34), 79 (83), 76 (100), 81 (18), 51 (42); ^{1}HNMR (300 MHz, $CDCl_3$): 9.4 (s,

1H, Ar-H), 8.9 (d, 1H, J = 14.5), 8.53 (d, 1H, J = 14), 8.27 (d, 1H, J = 9), 7.81-7.78 (m, 2H), 7.71 (t, 1H, J = 14.5), 7.56 (m, 1H), 5.06 (br, s, 1H)

3-Amino-2-(3-iodophenyl) quinazolin-4(3H)-one (19)

2-(3-iodophenyl)-4H-3,1-benzoxazin-4-one (7) (2 g), hydrazine hydrate 80 % (5 mL) and benzene (15 mL). Yield: 58 %, M.P.: 150 °C, EI-MS *m/z*: 363 (M+, 13), 347 (100), 334 (19), 221 (5), 206 (43), 204 (79), 146 (27), 132 (5), 120 (19), 105 (100), 92 (73), 76 (57), 54 (3); ^{1}HNMR (300 MHz, $CDCl_3$): δ 8.3 (d, 1H, J = 7.6), 8.27 (s, 1H), 8.10 (t, 1H, J = 14.5), 7.8 (d, 1H, J = 8.5), 7.75 (m, 2H), 7.58 (t, 1H, J = 8), 7.4 (t, 1H, J = 15), 4.89 (b, s, 1H, NH_2)

Method B:

Direct One-Pot Synthesis of Compounds (12-19)

Substituted benzoic acid in excess of thionyl chloride was refluxed for 3-6 h and the reaction was catalyzed with few drops of DMF. After cooling to room temperature, the mixture was then added portion wise to vigorously stirred solution on anthranillic acid in dry pyridine at 0 °C and the stirring was further continued for 1-2 h at room temperature. Then 5-10 mL hydrazine hydrate was added to the same mixture and refluxed for 3-7 h. After completion of reaction, the reaction mixture was poured in ice cooled water congaing few drops of HCl, the product precipitated was filtered washed with water, dried and recrystallized from suitable solvent to get the target compounds **12-19**.

Antimicrobial Activities

Antimicrobial activities including antibacterial and antifungal activities of the synthesized compounds were also assessed using the standard procedures. Antifungal activity of the synthesized compounds was evaluated by the agar tube dilution method as described in the literature [25], while the antibacterial activity was carried out against various human pathogens by the agar well diffusion protocol [26].

Conclusions

A facile one pot method has been optimized for the synthesis of 3-aminoquinazolin-4(3*H*)-one, the method is easy, convenient and can be utilized for a range of aromatic carboxylic acids. Moreover, the percentage yield is better in this case then the stepwise strategy and other methods involving cyclizing agents. In addition to this, some of the compounds have been evaluated for their antimicrobial activities and the effect of substituents on their antimicrobial activities has been discussed.

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