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Article

Amberlite Infrared-120 Catalyzed Synthesis of 6-Aryl-5H-Quinazolino[4,3-b] Quinazolin8(6H)-one Derivatives as Anticancer Agents

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ABSTRACT

Amberlite infrared (IR)-120 catalyzed synthesis of 6-aryl-5H-quinazolino[4,3-b]quinazolin8(6H)-one derivatives was reported. 2-(2-aminophenyl)quinazolin-4(3H)-ones on reaction with aromatic aldehydes using Amberlite IR-120 resin yielded a variety of 6-aryl-5H-quinazolino[4,3-b]quinazolin-8(6H)-one derivatives in good to excellent yields. This method has the advantages of high yields, easy purification and having mild reaction condition. All the synthesized compounds were evaluated for their anti-proliferative properties *in vitro* against cancer cell lines, and several compounds were found to be active.

Key words: Amberlite IR-120, 2-(2-Aminophenyl)quinazolin-4(3H)-ones, Aromatic aldehydes, Synthesis, High yield.

1. INTRODUCTION

Quinazoline derivatives created great attention in medicinal chemistry due to their widely usage in biopharmaceutical activity. Quinazoline derivatives possess good anti-tumor activities [1-3]. Several quinazoline derivatives are existing as active drug molecules against cancer (Figure 1).

Further, quinazoline derivatives have shown remarkable biological activities, such as anti-inflammatory [4], antimicrobial [5], and anti-tubercular activities [6]. On the other hand, quinazolinoquinazolines contains a tetracyclic heterocycle core consisting of two quinazoline analogs. Quinazolinoquinazolines and their derivatives have significant anti-inflammatory agents [7] as well as hypnotic activity [8].

Therefore, many researchers want to develop a well suitable procedure for the synthesis of quinazolinoquinazolines and their derivatives. Only a few procedures were reported in literature for the synthesis of quinazolinoquinazolines [9-15].

In addition, to obtain these potentially bioactive quinazolino[4,3-b] quinazoline derivatives, 2-(2-aminophenyl)quinazolin4(3H)-one is usually used as a starting material to react with another active site such as Schiff bases [16], orthoesters [17], and anhydrides [18]. Despite several limitations still remain unresolved when we use above reaction conditions, for example, low yields or flammable organic solvents.

Use of acidic resin, either stoichiometric or in catalytic systems has gained importance in organic synthesis due to several advantages such as operational simplicity, reusability, low cost, and ease of isolation after completion of the reaction. For example, Amberlite-infrared (IR) 120 resin has emerged as an efficient heterogeneous catalyst for chemical transformations. Due to our continuous interest in the use of a recyclable solid catalyst and biologically active compounds [19-26,19-27], we now wish to report the use of Amberlite IR-120 resin as an extremely powerful useful catalyst for the synthesis of quinazoline moiety. After considering the advantages of Amberlite IR-120 resin, herein, we report the synthesis of 6-aryl-5H-quinazolino [4,3-b]quinazolin-8(6H)-one derivatives in acetonitrile catalyzed by Amberlite IR-120 resin.

2. EXPERIMENTAL

Melting points are uncorrected and were determined in open capillary tubes in a sulfuric acid bath. Thin-layer chromatography (TLC) was run on silica gel - G pre-coated plates and visualization was done using iodine or UV light. IR spectra were recorded using Perkin–Elmer 1000 instrument in KBr pellets. ^{1}H nuclear magnetic resonance (NMR) spectra were recorded in dimethyl sulfoxide (DMSO) - d_6 using TMS as an internal standard with 400 MH_Z Bruker instrument. Mass spectra were recorded on Agilent-liquid chromatography-mass spectrometry instrument under CI conditions and given by Q+1 values only.

2.1. General Procedure for the Synthesis of 3

Into a round bottom flask benzaldehyde (1 mmol.), 2-(2-aminophenyl) quinazolin-4(3H)-one (1 mmol.) and Amberlite IR-120 resin (10 mol %), in acetonitrile (10 vol.) were added and stirred at room temperature. The reaction mixture was heated to 60°C till the starting material disappears completely. The reaction was monitored by TLC, after completion of the starting material it was cooled to room temperature and filtered. The filtrate was evaporated to get the crude compound. The crude compound was purified by recrystallization from 95 % EtOH to give pure three as solid.

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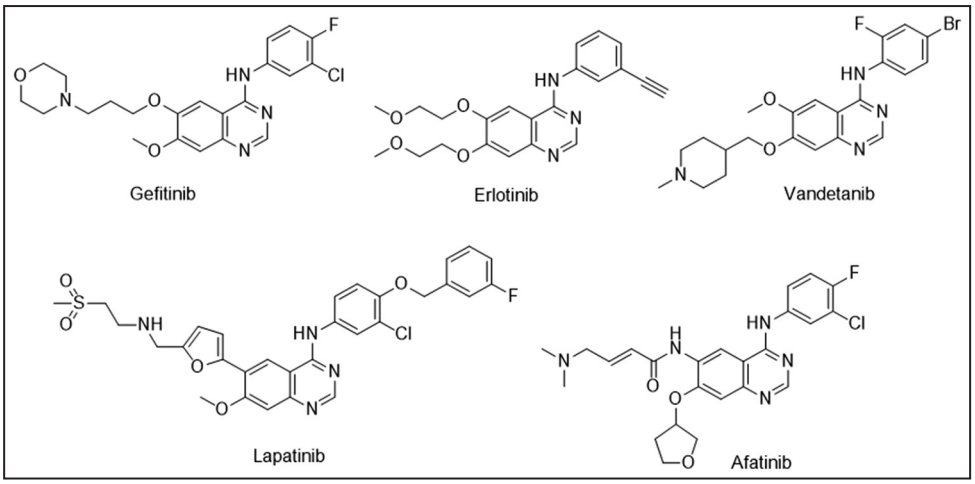


Figure 1: Quinazoline core containing active drug molecules in the market.

2.1.1. 6-Phenyl-5H-quinazolino[4,3-b]quinazolin-8(6H)-one (3a)
Pale yellow solid, m.p. 226–229°C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 8.21 (dd, J=8.0 Hz, 1H), 8.11–8.14 (m, 1H), 8.02 (d, J=3.6 Hz, 1H, NH), 7.86–7.91 (m, 1H), 7.76 (d, J=8.4 Hz, 1H), 7.52–7.55 (m, 1H), 7.33–7.37 (m, 1H), 7.23–7.28 (m, 4H), 7.17–7.19 (m, 2H), 6.94 (d, J=8.0 Hz, 1H), 6.81–6.86 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 160.8, 148.1, 147.2, 143.7, 139.1, 134.7, 133.6, 128.7, 128.5, 127.8, 127.5, 127.4, 127.2, 127.1, 126.3, 126.1, 120.6, 116.4, 64.7. Mass (ESI, m/z): 326.2 $[M+H]^+$.

2.1.2. 6-(4-Bromophenyl)-5H-quinazolino[4,3-b]quinazolin-8(6H)-one (3b)
Pale yellow solid, m.p. 267–269°C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 8.21 (dd, J=8.0 Hz, 1H), 8.14 (d, J=7.2 Hz, 1H), 7.98 (d, J=3.6 Hz, 1H, NH), 7.84–7.88 (m, 1H), 7.76 (d, J=8.4 Hz, 1H), 7.51–7.55 (m, 1H), 7.34–7.38 (m, 3H), 7.24 (d, J=3.6 Hz, 1H), 7.20 (d, J=8.4 Hz, 2H), 6.93 (d, J=8.0 Hz, 1H), 6.83–6.87 (m, 1H).^{13}C NMR (DMSO-d_6, 100 MHz): δ 160.2, 148.3, 147.6, 145.4, 139.5, 135.7, 134.4, 132.1, 128.6, 127.9, 127.5, 127.3, 126.7, 122.1, 120.2, 119.5, 116.4, 116.2, 62.6. Mass (ESI, m/z): 404.2 $[M+H]^+$.

2.1.3. 6-(4-Chlorophenyl)-5H-quinazolino[4,3-b]quinazolin-8(6H)-one (3c)
Pale yellow solid, m.p. 259–262°C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 8.20 (dd, J=8.0 Hz, 1H), 8.14 (d, J=7.2 Hz, 1H), 7.98 (d, J=3.6 Hz, 1H), 7.84–7.88 (m, 1H), 7.74 (d, J=8.4 Hz, 1H), 7.51–7.56 (m, 1H), 7.34–7.38 (m, 3H), 7.24 (d, J=3.6 Hz, 1H), 7.18 (d, J=8.4 Hz, 2H), 6.92 (d, J=8.0 Hz, 1H), 6.81–6.85 (m, 1H).^{13}C NMR (DMSO-d_6, 100 MHz): δ 160.2, 148.3, 147.4, 145.2, 138.8, 135.7, 134.4, 133.5, 129.2, 128.2, 127.7, 127.3, 127.1, 126.9, 120.2, 119.4, 116.4, 116.2, 62.4. Mass (ESI, m/z): 360.2 $[M+H]^+$.

2.1.4. 6-(2,4-Dichlorophenyl)-5H-quinazolino[4,3-b]quinazolin-8(6H)-one (3d)
Pale yellow solid, m.p. 249–252°C;^{1}H NMR (DMSO-d_6, 400 MHz): δ 8.26 (dd, J=8.0 Hz, 1H), 8.09 (dd, J=8.0 Hz 1H), 7.83–7.88 (m, 1H), 7.79 (d, J=7.6 Hz, 1H), 7.71–7.74 (m, 2H), 7.46–7.50 (m, 1H), 7.38 (d, J=3.6 Hz, 1H), 7.30–7.35 (m, 1H), 7.22 (dd, J=8.4 Hz, 1H), 6.85–6.90 (m, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 160.1, 148.2, 147.6, 142.9, 135.3, 134.8, 134.5, 133.6, 132.8, 130.4, 127.8, 127.7, 127.5, 127.2, 127.1, 126.7, 120.8, 120.4, 116.9, 115.9, 61.7. Mass (ESI, m/z): 392.2 $[M-H]^-$

2.1.5. 6-(3-Hydroxyphenyl)-5H-quinazolino[4,3-b] quinazolin-8(6H)-one (3e)
Pale yellow solid, m.p. 276–278°C;^{1}H NMR (DMSO-d_6, 400 MHz): δ 9.47 (s, 1H), 8.22 (d, J=8.0 Hz, 1H), 8.13 (d, J=8.0 Hz, 1H), 7.95 (d, J=3.6 Hz, 1H), 7.86–7.89 (m, 1H), 7.76 (d, J=8.0 Hz, 1H), 7.51–7.53 (m, 1H),7.32–7.37 (m, 1H), 7.16 (d, J=3.6 Hz, 1H), 7.04–7.08 (m, 1H), 6.92 (d, J=8.0 Hz, 1H), 6.81–6.85 (m, 1H), 6.58–6.63 (m, 2H),6.52 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 160.2, 157.8, 148.3, 147.9, 145.6, 141.3, 135.7, 134.4, 130.2, 127.8, 127.5, 127.4, 126.8, 120.5, 119.4, 116.8, 116.4, 116.1, 115.6, 113.3, 62.9. Mass (ESI, m/z):340.1 $[M-H]^-$.

2.1.6 6-(2,3-Dimethoxyphenyl)-5H-quinazolino[4,3-b]quinazolin-8(6H)-one (3f)
Pale yellow solid, m.p. 238–242°C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 8.22 (d, J=8.0 Hz, 1H), 8.09 (d, J=8.0 Hz, 1H), 7.84–7.88 (m, 1H), 7.77 (d, J=8.4 Hz, 1H), 7.45–7.49 (m, 1H), 7.42 (s, 1H), 7.37 (s, 1H), 7.26–7.29 (m, 1H), 6.97 (d, J=8.4 Hz, 1H), 6.81–6.84 (m, 3H), 6.32(d, J=7.6 Hz, 1H), 3.92 (s, 3H), 3.78 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 160.5, 152.8, 148.4, 148.2, 145.8, 144.3, 134.8, 133.5, 132.5, 127.7, 127.5, 127.1, 126.3, 124.1, 120.7, 120.1, 117.6, 116.6, 115.7, 112.8, 61.1, 60.9, 55.9. Mass (ESI, m/z): 386.2 $[M+H]^+$.

2.1.7. 6-(4-Fluorophenyl)-5H-quinazolino[4,3-b]quinazolin-8(6H)-one (3g)
Pale yellow solid, m.p. 234–236°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.35 (d, J=8.0 Hz, 1H), 8.32 (d, J=8.0 Hz, 1H), 7.76–7.79 (m, 2H), 7.44–7.48 (m, 1H), 7.35–7.39 (m, 2H), 7.27–7.31 (m, 2H), 6.99–7.04 (m, 1H), 6.85–6.90 (m, 2H), 6.83 (d, J=8.0 Hz, 1H), 5.02 (d, J=3.2 Hz, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 162.3, 160.2, 148.3, 147.7, 145.5, 136.4, 135.6, 134.4, 128.5, 127.8, 127.5, 127.2, 126.9, 120.5, 119.5, 116.5, 116.1, 115.8, 62.6. Mass (ESI, m/z): 342.2 $[M-H]^-$.

2.1.8. 6-(p-Tolyl)-5H-quinazolino[4,3-b]quinazolin-8(6H)-one (3h)
Pale yellow solid, m.p. 197–198°C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 8.18 (dd, J=8.0 Hz, J=1.2 Hz, 1H), 8.11 (dd, J=8.0 Hz, J=1.2 Hz, 1H), 7.97 (d, J=4.0 Hz, 1H),7.85–7.89 (m, 1H), 7.75 (d, J=8.0 Hz, 1H), 7.48–7.52 (m, 1H), 7.31–7.36 (m, 1H), 7.22 (d, J=4.0 Hz, 1H), 7.06 (s, 4H), 6.92 (d, J=8.0 Hz, 1H), 6.78–6.83 (m, 1H), 2.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 160.8, 148.3, 147.3, 143.8, 138.5, 136.5, 134.7, 133.6, 129.5, 127.8, 127.6, 127.2, 126.2, 125.8, 120.8, 120.7, 117.8, 116.4, 63.7, 21.2. Mass (ESI, m/z): 362.2 $[M+Na]^+$.

2.1.9. 6-(2-Fluorophenyl)-5H-quinazolino[4,3-b]quinazolin-8(6H)-one (3i)

Pale yellow solid, m.p. 203–206°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.36 (d, J=8.0 Hz, 1H), 8.29 (d, J=8.0 Hz, 1H), 7.79–7.83 (m, 2H), 7.59 (s, 1H), 7.45–7.48 (m, 1H), 7.26–7.28 (m, 1H), 7.19–7.23 (m, 1H), 7.07–7.12 (m, 1H), 6.93–6.96 (m, 1H), 6.87–6.94 (m, 1H), 6.66–6.73 (m, 2H), 5.14 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 160.4, 160.2, 148.3, 147.7, 143.6, 134.9, 133.6, 130.5, 127.7, 127.6, 127.3, 126.8, 126.5, 126.1, 124.3, 120.6, 120.5, 116.8, 116.1, 115.8, 59.9. Mass (ESI, m/z): 344.2 $[M+H]^+$.

2.1.10. 2-Chloro-6-(4-chlorophenyl)-5H-quinazolino [4,3-b] quinazolin-8(6H)-one (3j)

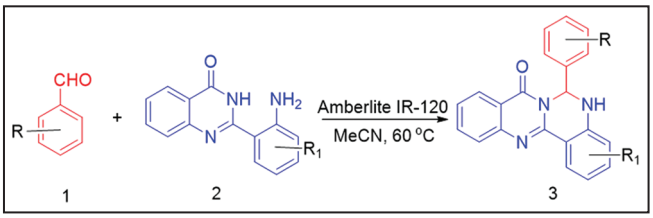
Pale yellow solid, m.p. 246–248°C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 8.18–8.20 (m, 2H), 8.06 (d, J=2.0 Hz, 1H), 7.88–7.92 (m, 1H), 7.79 (d, J=8.0 Hz, 1H), 7.52–7.58 (m, 1H), 7.35–7.39 (m, 3H), 7.29 (d, J=2.8 Hz, 1H), 7.19 (d, J=8.4 Hz, 2H), 6.98 (d, J=8.8 Hz, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 160.1, 147.8, 146.4, 144.3, 138.8, 135.8, 133.8, 133.6, 129.3, 128.2, 127.8, 127.2, 127.1, 126.3, 123.2, 120.6, 118.5, 117.2, 62.7. Mass (ESI, m/z): 394.1 $[M+H]^+$.

2.1.11. 6-(4-Bromophenyl)-2-chloro-5H-quinazolino [4,3-b] quinazolin-8(6H)-one (3k)

Pale yellow solid, m.p. 263–266°C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 8.19–8.21 (m, 2H), 8.06 (d, J=2.4 Hz, 1H), 7.88–7.92 (m, 1H), 7.79 (d, J=8.0 Hz, 1H), 7.52–7.55 (m, 1H), 7.48 (d, J=8.4 Hz, 2H), 7.39 (d, J=8.4 Hz, 1H), 7.25 (d, J=3.6 Hz, 1H), 7.12 (d, J=8.4 Hz, 2H), 6.97 (d, J=8.8 Hz, 1H);^{13}C NMR (DMSO-d_6, 100 MHz): δ 160.1, 147.8, 146.4, 144.3, 139.3, 135.8, 133.8, 132.2, 128.5, 127.8, 127.2, 127.1, 126.3, 123.2, 122.2, 120.6, 118.6, 117.2, 62.7. Mass (ESI, m/z): 438.1 $[M+H]^+$.

2.1.12. 2-Bromo-6-(p-tolyl)-5H-quinazolino[4,3-b]quinazolin-8(6H)-one (3l)

Pale yellow solid, m.p. 231–233°C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 8.16–8.20 (m, 3H),7.85–7.89 (m, 1H), 7.76 (d, J=8.0 Hz, 1H), 7.50–7.54 (m, 1H), 7.47 (dd, J=8.8 Hz, 1H), 7.23 (d, J=3.6 Hz, 1H), 7.02–7.08 (m, 4H), 6.84 (d, J=8.4 Hz, 1H), 2.18 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 160.1, 147.8, 146.6, 144.9, 138.3, 136.7, 136.6, 135.7, 129.8, 129.2, 127.8, 127.2, 126.1, 120.6, 118.8, 117.8, 110.3, 62.9, 21.1. Mass (ESI, m/z): 418.1 $[M+H]^+$.



Scheme 1: Synthesis of 5H-quinazolino[4,3-b]quinazolin-8(6H)-one derivatives

2.2. Biology

2.2.1. General methods

2.2.1.1. Antitumor screening

Human chronic myeloid leukemia cells, K562, human colon carcinoma cells, Colo-205, and breast cancer cells (MDA-MB 231) were procured from National Center for Cell Sciences, Pune, India. All cells were grown in RPMI-1640 supplemented with 10% heat-inactivated fetal bovine serum, 100 IU/ml penicillin, 100 mg/ml streptomycin, and 2 mM-glutamine. Cultures were maintained in a humidified atmosphere with 5% CO_2 at 37°C. The cells were subcultured twice each week, seeding at a density of about 2×10^3 cells/ml.

2.2.2. 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay

Cell viability was determined by MTT assay. Cells (5×10^3 cells/well) were seeded to 96-well culture plate and cultured with or without compounds at 1 µM and 10 µM concentration for 24 h in a final volume of 200 µL. After treatment, the medium was removed, and 20 µL of MTT (5 mg/ml in PBS) was added to the fresh medium. After 2 h incubation at 37°C, 100 µL of DMSO was added to each well and plates were agitated for 1 min. Absorbance was read at 570 nm on a multi-well plate reader (Victor3, Perkin Emler). Percent inhibition of proliferation was calculated as a fraction of control (without compound).

3. RESULTS AND DISCUSSION

3.1. Chemistry

To optimize and establish the reaction conditions, we started the synthesis by considering 2-(2-aminophenyl)quinazolin-4(3H)-one (2a) and benzaldehyde (1a) as substrates for the model reaction using Amberlite IR-120 resin. The results are summarized in Table 1.

When the reaction was carried out between 2-(2-aminophenyl) quinazolin-4(3H)-one (2a, 1 mmol) and benzaldehyde (1a, 1 mmol) in acetonitrile (10 vol) using 5 mol% of Amberlite IR-120 resin at RT only, a trace amount of the required product 6-Phenyl-5H-quinazolino[4,3-b]quinazolin-8(6H)-one (3a) was obtained (Table 1, entry 1). Surprisingly, the yield of the reaction was increased to 88% when the same reaction was stirred at 60°C for 2 h (Table 1, entry 2).

Table 1: Optimization of reaction conditions for the synthesis of 3a.

Entry	Catalyst (amount)	Solvent	Temp/Time	Yield (%)
1	Amberlite IR-120 (5 mol%)	MeCN	RT/3 h	5
2	Amberlite IR-120 (5 mol%)	MeCN	60°C/2 h	88
3	Amberlite IR-120 (5 mol%)	MeOH	60°C/2 h	68
4	Amberlite IR-120 (5 mol%)	DCM	40°C/2 h	74
5	Amberlite IR-120 (5 mol%)	THF	60°C/2 h	72
6	Amberlite IR-120 (5 mol%)	DMF	60°C/2 h	38
7	Amberlite IR-120 (10 mol%)	MeCN	60°C/2 h	95
8	Amberlite IR-120 (15 mol%)	MeCN	60°C/2 h	91
9	No catalyst	MeCN	60°C/2 h	Trace

Reagents and conditions: 2-(2-Aminophenyl) quinazolin-4 (3H)-one (2a, 1 mmol) benzaldehyde (1a, 1 mmol), Amberlite IR-120 (10 mol%), acetonitrile (10 vol) 60°C.

The use of other organic solvents, for example, MeOH, DCM, THF, and DMF did not improved the yield of the product 3a (Table 1, entry 3-6). When the reaction was carried out using Amberlite IR-120 resin from 5 mol% to 10 mol% increased the product yield to 95% in 2 h (Table 1, entry **7**). Further, the increase in the quantity of resin from 10 mol% to 15 mol% did not improve the product yield (Table 1, entry 8). The reaction did not progress in the absence of resin indicating its key role in accelerating the reaction (Table 1, entry 9).

The versatility of this transformation was examined under the above-optimized reaction conditions (Table 1, entry 7), and the results are summarized below. A wide array of diverse benzaldehydes (1) was tested to find the broad range of the present methodology.

In general, benzaldehydes containing both electron donating and electron withdrawing groups substituents such as Cl, F, Br, OMe, and Me (Figure 2) underwent the present methodology in good yields (85–95%). It was observed that a variety of substituents on the aromatic ring were well tolerated. The reaction was also compatible with different substituted aromatic quinazolines (Figure 2 compounds 3j, 3k, 3l).

Recyclability of the Amberlite IR-120 resin was examined. For this reason, the catalyst used was recovered from the reaction of 1a and 2a through filtration, dried, and reused for the same reaction. This procedure was repeated for 4 times, and results are summarized in Table 2. It is evident from Table 2 that the catalyst can be recycled successfully several times without significant loss of its catalytic activities.

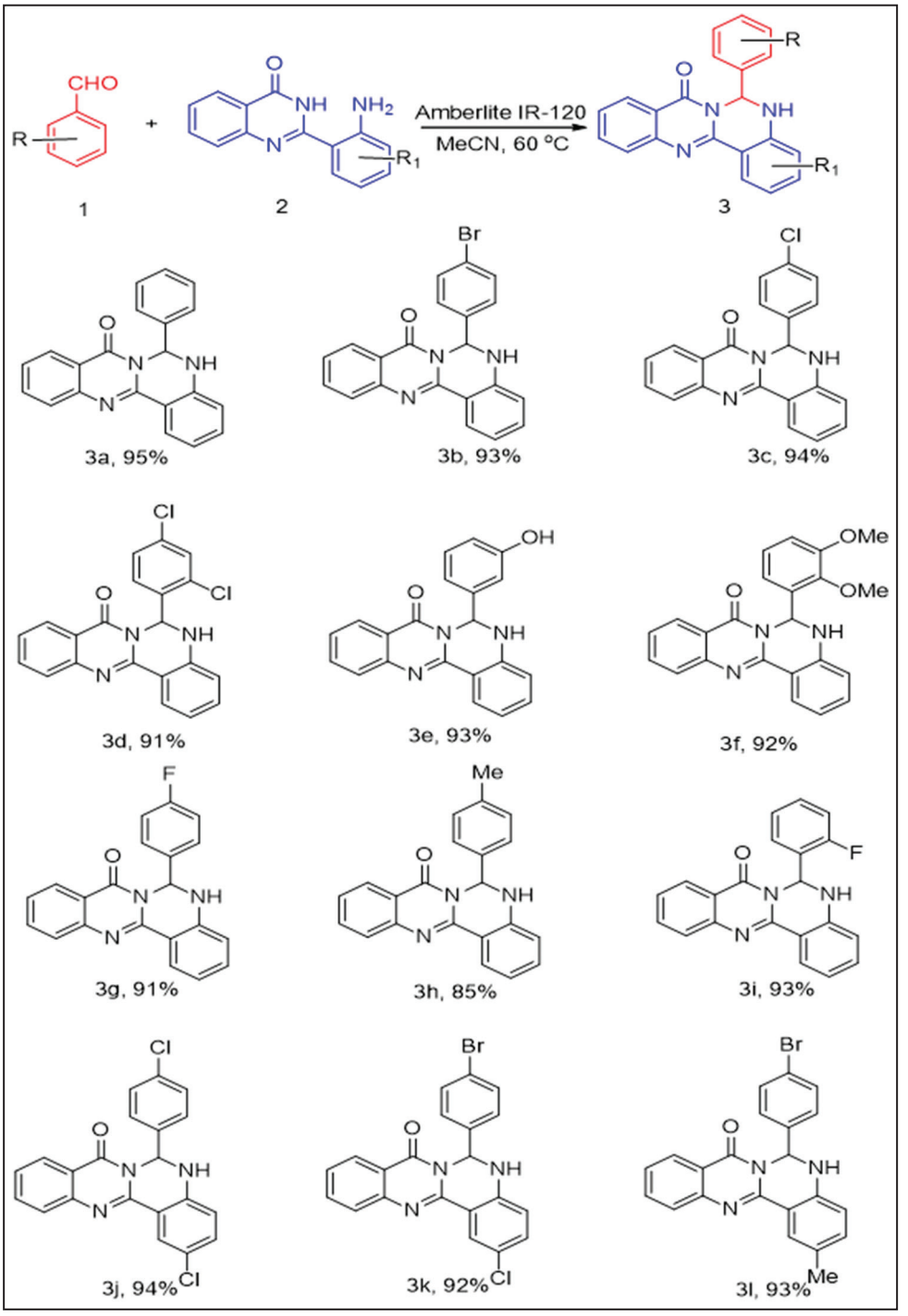


Figure 2: Synthetic results for compound 3.

Table 2: Recycle of the Amberlite IR-120 catalyst

Cycle	Amberlite IR-120 (mol%)	Yield (%)
1	10	95
2	10	93
3	9	92
4	9	90

IR: Infrared

Table 3: *In vitro* cytotoxic activity of the synthesized compounds 3a–l against leukemia cells, K562, human colon carcinoma cells, Colo-205, human breast cancer cell line (MDA-Mb 231)

Compound	IC_{50}[a,b] (μM)		
	K562	Colo-205	MDA-MB 231
3a	32	29	55
3b	24	37	34
3c	28	32	56
3d	16	15	38
3e	24	29	61
3f	35	40	37
3g	16	12	34
3h	39	34	54
3i	26	32	38
3j	36	45	59
3k	15	18	28
3l	29	26	39
Sunitinib	14	8	32

After synthesizing different molecules, we were interested to check the anticancer properties of the synthesized compounds *in vitro*. We tested the synthesized compounds against a number of cancer cell lines, for example, human chronic myeloid leukemia cells (K562), human colon carcinoma cells (Colo-205), and human breast cancer cell line (MDA-MB 231) for their anti-proliferative properties *in vitro*.

The anticancer activity of all the synthesized compounds was tested at different concentrations in an MTT assay, and the IC_{50} values obtained for each compounds are summarized in Table 2. Sunitinib, a receptor protein-tyrosine kinase inhibitor, a member of β-carboline family of compounds showed cytotoxicity against Colo-205 and K562 cell lines[20] was used as a reference compound. While most of these compounds showed inhibition of leukemia cell growth as reflected by their IC_{50} values; however, 3d, 3i, and 3 k showed good results (IC50 <20 μM, Table 3). Only 3d, 3i, and 3 k showed that good results were found active against colon cancer cells and breast cancer cells (IC_{50}~12–39 μM, Table 3).

4. CONCLUSION

We have developed a novel method for the construction of 6-aryl-5Hquinazolino[4,3-b]quinazolin-8(6H)-one derivatives catalyzed by Amberlite IR-120 resin in MeCN. The usage of acidic ion-exchange-resin as a catalyst could be readily separated from the products by simple filtration and directly reused at least 4 times without any reactivation. Few of the compounds shown good activity against cancer cell lines.

5. ACKNOWLEDGMENT

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