Original Article

Bulletin of Pure and Applied Sciences.
Vol.36 C (Chemistry), No.2, 2017: P.38-44
Print version ISSN 0970 4620
Online version ISSN 2320 320X
DOI 10.5958/2320-320X.2017.00005.X

A Facile One-Pot Synthesis of Series of 2-Aminoquinoline-3-Carbonitrile Derivatives by Using Magnetite Nanoparticle Catalyst

Dr. Shraddha Upadhyay

Author Affiliations:
Department of Chemistry, Swami Vivekanand Subharti University, Meerut, U.P., India, 250005.

Corresponding Author:
Dr. Shraddha Upadhyay, Department of Chemistry, Swami Vivekanand Subharti University, Meerut, U.P., India, 250005.

E-mail: dr.shrupa@gmail.com

Received on 07.11.2017,
Accepted on 25.12.2017

Abstract
2-Aminoquinoline-3-carbonitrile synthesized by one-pot condensation of aromatic 2-Choloro-3-Carboxyaldehyde, with aq. NH3, sublimed I2 and Fe2O3 nanoparticle catalyst. The C-N coupling reactions preceded much faster via simple SNAr displacement reactions of chlorine. The synthetic methods depended on functional group transformation, nucleophilic attack and/or intramolecular cyclization by the cyanoquinoline moiety. The competition of the reaction pathways including nucleophilic attack, and functional group transformation that leads to the synthesized product. This newly synthesized compound were characterized by elemental analysis and spectral data, and screened for their biological activity. The amination reactions using magnetite nanoparticle as catalyst gave the best yield of the products.

Keywords: Magnetite Nanoparticle, Catalyst, Nucleophilic.

1. INTRODUCTION

Although, quinoline derivatives are common in nature, and many of the derivatives exhibit various biological activities, such as antimalarial, antitumor, anthelmintic, antibacterial, antiasthamatic, and antiplatelet activities[1]. Ortho-aminocarbonitriles quinoline derivative is much more interesting because these have a wide scope of biological activities and applications as precursors for the synthesis of novel heterocyclic compounds[2]. 2-Aminoquinoline and its derivatives are pharmaceutically important alkaloids exhibiting various biological activities[3]. Recently, it has been revealed that 2-aminoquinolines possess sub-nano-molar potency for BACE1 (beta-site amyloid precursor protein cleaving enzyme 1)

and may serve as a small BACE inhibitor for Alzheimer's disease therapeutics[4]. Therefore, these compounds continue to be an attractive study target and are anticipated as potent leads in the medicinal chemistry community. There are several methods for the synthesis of aminoquinoline is reported. An early synthesis, beginning from 2-Chloroquinoline-3-carbonirile, has been described by Kamal M. El-Gaml[5]. As reported by Ali Khalafi-Nezhad et al[6] the compound has been synthesized by multi-component process batches by treating the readily available aniline, aldehyde with L-proline as catalyst. The drawbacks of the amination process of chloro-cyanoquinoline requires harsh reaction condition, excess of amine and high temperature starting from 3, 7 dichlorocyanoquinoline as described in US4511393 A, Patent[7], 1985 by Helmut Hagen et al. Another synthesis, comprising the amination along with intra molecular nitrogen insertion has been described by Bo Jiang et al [8] who report that the desired product was obtained under high temperature. A synthesis beginning with aminonapthiridine has been disclosed by Shujiang Tu[9].

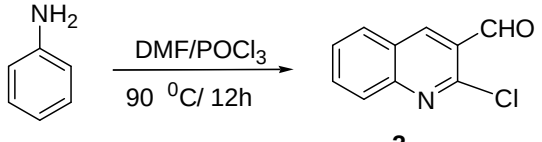
2. MATERIAL AND METHODS

2-Aminoquinoline-3-carbonitrile has been Synthesis by using 2-chloroquinoline-3-carboxyaldehyde 2 (1.0 equiv), added aq. NH_3 (30% solution, 5 ml) followed by adding sublimed I_2 (3 mmol) and Fe_2O_3 nanoparticle catalyst (0.5mmol) at room temperature for 2hr. Reaction were optimize by using different nanoparticles and quinolines derivatives.

Experiment was optimized at room temperature. Melting points of product are measured using Buchi Melting-point apparatus in an open capillary tube and are uncorrected. The product structure was characterized by different spectral analysis such as IR and NMR etc. IR spectra were recorded on VARIAN 3300 FTIR spectrophotometers. 1 H (300 MHz) and 13C (75 MHz) NMR spectra were recorded on JEOL AL 300 MHz spectrometer. The chemical shifts (d ppm) and coupling constants (Hz) are reported in the standard fashion with reference to either internal tetramethylsilane (for 1 H) or the central line (77.0 ppm) of CDCl3 / DMSO (for 13C). Elemental analyses were performed on Exter Analytical Inc. 'Model CE-400 CHN Analyzer' from Department of Chemistry, IIT, Delhi, and Mass spectral analyses were performed on Thermo LCQ Advantage Max (ESI and APCI) Ion Trap (LCeMS / MS) from IIT, Delhi. Reactions were monitored by Thin-layer chromatography. Thin-layer chromatography (TLC) was performed on glass plates (7.52.5 and 7.55.0 cm) coated with Loba Chemie's silica gel GF254 and various combinations of ethyl acetate and hexane were used as eluent. Visualization of spots was accomplished by exposure to UV light. Crud product was purified through column chromatography. Qualigen's silica gel (60-120 mesh) was used for column chromatography (approximately 15-20 g per 1 g of the crude product).

3. RESULTS AND DISCUSSION

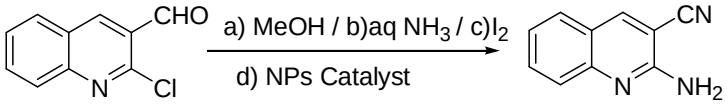
2-Chloroquinoline-3-carboxyaldehyde (2) is a prominent precursor for 2-Aminoquinoline-3-carbonitrile. 2-Chloroquinoline-3-carboxyaldehyde is synthesized from aniline (1) under V.H reaction condition DMF (1 eq.), $POCl_3$ (3 eq.) at 90 ^{0}C Fig 2. Reaction completed in 12 hrs as checked by TLC, and product obtained in 90% yield, purified by column chromatography and characterized via spectral analysis. Fig 1.



1 **2**

Fig 1:

Further, this synthesized 2-Chloroquinoline-3-carboxyaldehyde (1 eq.) (2) when treated with a) Methanol (1ml) / b) aqueous ammonia (3ml)/ c) Iodine (3 eq.) / and d) Magnetite nanoparticle as catalyst (0.05 eq) at room temperature converted into 2-Aminoquinoline-3-carbonitrile (3) in good yield. Reaction completed in 2 hrs as monitored by TLC techniques. Product recovers by simple extraction techniques and purified by column chromatography using 5% mixture of EtOAc/ Hexane solvent. Pure product obtained is yellow green solid and characterized by spectral analysis as 2-Aminoquinoline-3-carbonitrile (3) Fig 2. Scheme 1.

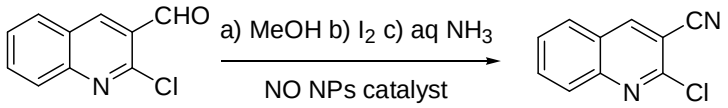


3

Fig 2:

Scheme: 1. Synthesis of 2-aminoquinoline-3-carbonitriles (3) from 2-choloroquinoline-3-carboxyaldehyde (2).

Alternatively, when 2-Chloroquinoline-3-carboxyaldehyde (1 eq.) (2) is treated with a) Methanol (1ml) / b) aqueous ammonia (3ml)/ c) Iodine (3eq.) under similar reaction condition but in absence of nanoparticle catalyst it is converted into 2-Chloroquinoline-3-carbonitrile (4) in good yield Fig 3. Reaction completed in 3 hrs as monitored by TLC techniques. Product recovers by simple work-up procedure, i.e reaction mixture neutralized by 10% aqueous solution of Sodium-thiosulphate followed by simple filtration. Formed product is white solid and are quite pure requires no any further purification. Pure product obtained is characterized by spectral analysis (4).



4

Fig 3:

It is nanoparticle catalyst which actually facilate nucleophilic property of ammonia and promote S_NAr as well as functional group transformation of 2-Chloroquinoline-3-carboxyaldehyde and synthesis 2-Aminoquinoline-3-carbonirile in one step. In presence of nanoparticle catalyst both organic reaction i.e functional group transformation and S_NAr was occurred in quick succession. Alternatively, when 2-Chloroquinoline-3-carboxyaldehyde (1 eq.) (2) was treated with a) Methanol (1ml) / b) aqueous ammonia (3ml)/ and c) Fe_2O_3 nanoparticle catalyst (0.05 eq) in absence of Iodine under similar reaction condition it was found that no reaction will occur Fig 4. This reaction provide an evidence that initially functional group transformation will occur (iodine acts as oxidant for the synthesis of nitrile from aldehyde) rather than S_NAr

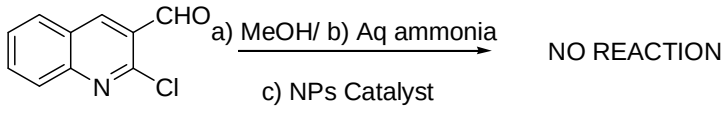


Fig 4:

Nanoparticle catalyst has been used for the first time ever for synthesis of this compound. It was used for functional-group transformation also promote S_NAr reaction.

Under similar reaction condition reaction is also performed with other different nanoparticles catalyst. Among the various nanopartical catalyst such as MnO, AgO, CuO, ZnO, MnO_2 (Table 1, entries 2-6).

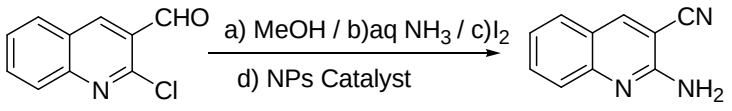
Fe_2O_3 nanopartical was found to be the best catalyst (Table 1, entries 1).

Table 1 Optimization of amination reaction conditions on 2-choloroquinoline-3-carboxyaldehyde (2a) with different nanoparticles[a]

Entry	Nanopartical Catalyst[a]	Product	Time (h)	Yield of 3a (i-vii)[b] (%)
1	Fe_2O_3	3a(i)	2	90.5
2	MnO	3a(ii)	3	58.7
3	ZnO	3a(iii)	2	75
4	CuO	3a(iv)	2	70
5	AgO	3a(v)	1.5	75
6	FeO	3a(vi)	2	20.8
7	MnO_2	3a(vii)	2	45

a) 2-Choloroquinoline-3-carboxyaldehyde (1 mmol), methanol (2 ml), aq. NH_3 (30% solution, 5 ml), sublimed I_2 (3 mmol) and nanoparticle catalyst (0.5mmol)

b) Isolated yields.



2a **3** 3a (i-vii)

3a(i): With catalyst Fe_2O_3
3a(ii): With catalyst MnO
3a(iii): With catalyst ZnO
3a(iv): With catalyst CuO
3a(v): With catalyst AgO
3a(vi): With catalyst FeO
3a(vii): With catalyst MnO_2

Further, reaction was Optimized with different Quinoline also (2b-g). It observed that electron donation substituents on quinoline moiety will increases the reaction rate. While, electron donating substituents decreses the reaction rate (entry 1-6)

Table 2: Optimization of amination reaction conditions on 2-choloroquinoline-3-carboxyaldehyde (2a) with differentQuinoline derivatives

Entry	R	Product	Time	Yields (%)
1	6Me (2b)	3b	3	80
2	7Me (2c)	3c	3.5	82
3	6MeO (2d)	3d	1	85
4	7MeO (2e)	3e	1	85
5	6Br (2f)	3f	1	78
6	7Cl (2g)	3g	1	80

2(b-g) **3(b-g)**

Reaction Reagent: MeOH / aq.NH_3 / I_2 / NPs Catalyst
Condition: Room Temperature
R= 6Me, 7Me, 6MeO, 7MeO, 6-Br, 7-Cl

4. CONCLUSIONS

In conclusion, we have developed novel conditions for synthesis of 2- Aminoquinoline-3-carbonitriles. A series of 2-Aminoquinoline-3-carbonitrile derivatives were synthesized by one-pot condensation of aromatic aldehyde, in methanol with aq NH3, sublimed I2 and Fe2O3 nanoparticle catalyst at room temperature. The reaction with magnetite nanoparticle proceeded with faster rates via simple alternatively functional group transformation and SNAr displacement reaction. This reaction reaction has the notable advantages of short route, high yield and convenient operation.

5. EXPERIMENTAL SECTION

5.1. General procedure for synthesis of 2-Aminoquinoline-3- carbonitriles with Fe_2O_3 (2) To a stirred solution of 2-Chloroquinoline-3-carboxyaldehyde (1 eq.) in methanol (1 ml) was added aq. NH_3 (30% solution, 3 ml) followed by adding sublimed I_2 (3 eq.) and Fe2O3 nanoparticle catalyst (0.05 eq) at room temperature for 2hr. The dark violet solution neutralized with aqueous solution of sodiumthiosulphate (5ml). The muddy yellow-green color reaction mixture extracted with ethyl acetate (3x5 ml) and washed with water (3x5 ml), dried over Na_2SO_4 and evaporated under vacuum to obtained yellow green solid. Product obtained purified by column chromatography using 5% mixture of EtOAc / Hexane solvent. Pure product obtained is yellow green solid and characterized by spectral analysis as 2-Aminoquinoline-3-carbonitrile

5.1.1 2-Aminoquinoline-3-carbonitrile (3a) M.P. 233-235°C, Yield(%) 90.5, IR (KBr) cm^{-1}: 3353, 2222. ^{1}HNMR (DMSO-d6) δ: 7.56(s, 2H, D_2O exchange), 7.20-7.24 (t, 1H), 7.41-7.45 (t, 1H), 7.61-6.64 (d, 1H), 7.76-7.80 (d, 1H), 8.38 (s, 1H), ^{13}C NMR (DMSO-d6): 166.9 (C), 148.6 (C), 141.4 (CH), 132.4 (CH), 126.4 (CH), 125.3 (CH), 123.7 (CH), 119.6 (C), 118.3 (C), 95.4 (C); ESI-MS *miz:* 169.15, Caled for $C_{10}H_7N_3$: 169.20

5.1.2 6-Methyl-2-Aminoquinoline-3-carbonitrile (3b) M.P. 253-255°C, Yield(%) 80, IR (KBr) cm^{-1}: 3360, 2220. ^{1}HNMR (DMSO-d6): δ2.45 (d, 3H), δ 7.42(s, 2H, D_2O exchange), 7.21-7.25 (t, 1H), 7.43-7.46 (t, 1H), 7.58-6.61 (d, 1H), 7.73-7.77 (d, 1H), 8.42 (s, 1H), ^{13}C NMR (DMSO-d6): 166.1 (C), 148.2 (C), 141.2 (CH), 132.3 (CH), 126.8 (CH), 125.5 (CH), 123.5 (CH), 119.6 (C), 118.1 (C), 95.3 (C), 25.1 (C). ESI-MS *miz:* 183.21, Caled for $C_{11}H_9N_3$: 183.41

5.1.3 7-Methyl-2-Aminoquinoline-3-carbonitrile (3c) M.P. 258°C, Yield(%) 82, IR (KBr) cm^{-1}: 3357, 2223. ^{1}HNMR (DMSO-d6): δ2.44 (d, 3H), δ 7.52(s, 2H, D_2O exchange), 7.22-7.27 (t, 1H), 7.44-7.48 (t, 1H), 7.56-6.60 (d, 1H), 7.72-7.76 (d, 1H), 8.39 (s, 1H), ^{13}C NMR (DMSO-d6): 166.3 (C), 148.1 (C), 141.3 (CH), 132.4 (CH), 126.9 (CH), 125.4 (CH), 123.4 (CH), 119.7 (C), 118.3 (C), 95.5 (C), 25.2 (C). ESI-MS *miz:* 183.21, Caled for $C_{11}H_9N_3$: 183.61

5.1.4 6-Methoxy-2-Aminoquinoline-3-carbonitrile (3d) M.P. 260 ℃, Yield(%) 85, IR (KBr) cm^{-1}: 3354, 2222. ^{1}HNMR (DMSO-d6): δ3.87 (d, 3H), δ 7.52 (s, 2H, D_2O exchange), 7.23-7.26 (t, 1H), 7.42-7.46 (t, 1H), 7.54-6.61 (d, 1H), 7.73-7.78 (d, 1H), 8.30 (s, 1H), ^{13}C NMR (DMSO-d6): 166.7 (C), 148.5 (C), 141.5 (CH), 132.6 (CH), 126.4 (CH), 125.8 (CH), 123.6 (CH), 119.5 (C), 118.3 (C), 95.5 (C), 45.1 (C). ESI-MS *miz:* 199.21, Caled for $C_{11}H_9N_3O$: 199.38

5.1.5 7-Methoxy-2-Aminoquinoline-3-carbonitrile (3e) M.P. 260-262 ℃, Yield(%) 85, IR (KBr) cm^{-1}: 3351, 2218. ^{1}HNMR (DMSO-d6): δ3.96 (d, 3H), δ 7.50 (s, 2H, D_2O exchange), 7.24-7.28 (t, 1H), 7.43-7.47 (t, 1H), 7.57-6.63 (d, 1H), 7.73-7.78 (d, 1H), 8.32 (s, 1H), ^{13}C NMR (DMSO-d6): 166.8 (C), 148.1 (C), 141.5 (CH), 132.7 (CH), 126.1 (CH), 125.3 (CH), 123.7 (CH), 119.3 (C), 118.5 (C), 95.8 (C), 45.1 (C). ESI-MS *miz:* 199.21, Caled for $C_{11}H_9N_3O$: 199.49

5.1.6 6-Br-2-Aminoquinoline-3- carbonitrile (3f) M.P. 278-279℃, Yield(%) 78, IR (KBr) cm^{-1}: 3355, 2223. ^{1}HNMR (DMSO-d6) δ: 7.57(s, 2H, D_2O exchange), 7.22-7.25 (t, 1H), 7.43-7.47 (t, 1H), 7.63-6.65 (d, 1H), 7.78-7.84 (d, 1H), 8.41 (s, 1H), ^{13}C NMR (DMSO-d6): 166.6 (C), 148.9 (C), 141.7 (CH), 132.1 (CH), 126.3 (CH), 125.7 (CH), 123.4 (CH), 119.8 (C), 118.1 (C), 95.7 (C); ESI-MS *miz:* 249.09, Caled for $C_{10}H_7N_3$: 249.11

5.1.7 7-Cl-2-Aminoquinoline-3-carbonitrile (3g) M.P. 252-255℃, Yield(%) 80, IR (KBr) cm^{-1}: 3359, 2220. ^{1}HNMR (DMSO-d6) δ: 7.53(s, 2H, D_2O exchange), 7.27-7.29 (t, 1H), 7.47-7.49 (t, 1H), 7.65-6.69 (d, 1H), 7.81-7.87 (d, 1H), 8.44 (s, 1H), ^{13}C NMR (DMSO-d6): 166.8 (C), 148.7 (C), 141.9 (CH), 132.6 (CH), 126.8 (CH), 125.4 (CH), 123.8 (CH), 119.4 (C), 118.8 (C), 95.9 (C); ESI-MS *miz:* 204.64, Caled for $C_{10}H_7N_3Cl$: 204.68

5.1.8 2-Aminoquinoline-3-carbonitrile 3a(ii) M.P. 233-235℃, Yield(%) 58.7, IR (KBr) cm^{-1}: 3353, 2222. ^{1}HNMR (DMSO-d6) δ: 7.56(s, 2H, D_2O exchange), 7.20-7.24 (t, 1H), 7.41-7.45 (t, 1H), 7.61-6.64 (d, 1H), 7.76-7.80 (d, 1H), 8.38 (s, 1H), ^{13}C NMR (DMSO-d6): 166.9 (C), 148.6 (C), 141.4 (CH), 132.4 (CH), 126.4 (CH), 125.3 (CH), 123.7 (CH), 119.6 (C), 118.3 (C), 95.4 (C); ESI-MS *miz:* 169.15, Caled for $C_{10}H_7N_3$: 169.20

5.1.9 2-Aminoquinoline-3-carbonitrile 3a(iii) M.P. 232℃, Yield(%) 75, IR (KBr) cm^{-1}: 3355, 2228. ^{1}HNMR (DMSO-d6) δ: 7.55(s, 2H, D_2O exchange), 7.19-7.24 (t, 1H), 7.41-7.46 (t, 1H), 7.59-6.63 (d, 1H), 7.77-7.81 (d, 1H), 8.38 (s, 1H), ^{13}C NMR (DMSO-d6): 166.7 (C), 148.9 (C), 141.5 (CH), 132.2 (CH), 126.2 (CH), 125.1 (CH), 123.2 (CH), 119.6 (C), 118.1 (C), 95.5 (C); ESI-MS *miz:* 169.15, Caled for $C_{10}H_7N_3$: 169.30

5.1.10 2-Aminoquinoline-3-carbonitrile 3a(iv) M.P. 230-233℃, Yield(%) 70, IR (KBr) cm^{-1}: 3355, 2228. ^{1}HNMR (DMSO-d6) δ: 7.56 (s, 2H, D_2O exchange), 7.19-7.22 (t, 1H), 7.41-7.45 (t, 1H), 7.60-6.61 (d, 1H), 7.77-7.80 (d, 1H), 8.37 (s, 1H), ^{13}C NMR (DMSO-d6): 166.6 (C), 148.8 (C), 141.1 (CH), 132.4 (CH), 126.5 (CH), 125.1 (CH), 123.3 (CH), 119.4 (C), 118.1 (C), 95.1 (C); ESI-MS *miz:* 169.15, Caled for $C_{10}H_7N_3$: 169.18

5.1.9 2-Aminoquinoline-3-carbonitrile 3a(v) M.P. 232-234℃, Yield(%) 75, IR (KBr) cm^{-1}: 3354, 2223. ^{1}HNMR (DMSO-d6) δ: 7.57(s, 2H, D_2O exchange), 7.21-7.24 (t, 1H), 7.45-7.48 (t, 1H), 7.60-6.63 (d, 1H), 7.72-7.75 (d, 1H), 8.40 (s, 1H), ^{13}C NMR (DMSO-d6): 166.5 (C), 148.7 (C), 141.8 (CH), 132.1 (CH), 126.4 (CH), 125.4 (CH), 123.3 (CH), 119.5 (C), 118.5 (C), 95.7 (C); ESI-MS *miz:* 169.15, Caled for $C_{10}H_7N_3$: 169.20

5.1.10 2-Aminoquinoline-3-carbonitrile 3a(vi) M.P. 230-232℃, Yield(%) 20.8, IR (KBr) cm^{-1}: 3352, 2222. ^{1}HNMR (DMSO-d6) δ: 7.53 (s, 2H, D_2O exchange), 7.17-7.21 (t, 1H), 7.42-7.45 (t, 1H), 7.63-6.66 (d, 1H), 7.79-7.82 (d, 1H), 8.40 (s, 1H), ^{13}C NMR (DMSO-d6): 166.4 (C), 148.7 (C), 141.2 (CH), 132.3 (CH), 126.1 (CH), 125.6 (CH), 123.5 (CH), 119.8 (C), 118.6 (C), 95.7 (C); ESI-MS *miz:* 169.15, Caled for $C_{10}H_7N_3$: 169.40

5.1.9 2-Aminoquinoline-3-carbonitrile 3a(vii) M.P. 231°C, Yield(%) 45, IR (KBr) cm^{-1}: 3358, 2221. ^{1}HNMR (DMSO-d6) δ: 7.58(s, 2H, D_2O exchange), 7.22-7.25 (t, 1H), 7.43-7.46 (t, 1H), 7.59-6.62 (d, 1H), 7.79-7.82 (d, 1H), 8.42 (s, 1H), ^{13}C NMR (DMSO-d6): 166.5 (C), 148.7 (C), 141.9 (CH), 132.3 (CH), 126.8 (CH), 125.6 (CH), 123.6 (CH), 119.8 (C), 118.8 (C), 95.2 (C); ESI-MS *miz:* 169.15, Caled for $C_{10}H_7N_3$: 169.25

REFERENCES

1. Daoud R , Desneves J , Deady L W , Tilley L , Scheper R J, Gros P , Georges V, (2000). The Multidrug Resistance Protein Is Photoaffinity Labeled by a Quinoline-Based Drug at Multiple Sites. *Biochemistry*, 39: 6094-6102.
2. Zhang Zhan-Hui, Lü Hong-Yan, Yang Shu-Hong, and Gao Jian-Wu (2010). Synthesis of 2, 3-Dihydroquinazolin-4(1*H*)-ones by Three-Component Coupling of Isatoic Anhydride, Amines, and Aldehydes Catalyzed by Magnetic Fe_3O_4 Nanoparticles in Water. *J. Comb. Chem.,* 12: 643-646
3. Inglis S. R. (2004). Identification and specificity studies of small molecules ligands for SH3 protein domains. *J. Med. Chem.,* 47: 5405-5417.
4. Cheng Yuan, Judd Ted C., Bartberger Michael D., Brown James, Chen Kui, Fremeau Robert T. Hitchcock Stephen A. , Jordan Brad, J. St. David, Wahl Robert C. Wen Paul H. and Wood Stephen (2011). From Fragment Screening to In Vivo Efficacy: Optimization of a Series of 2-Aminoquinolines as Potent Inhibitors of Beta-Site Amyloid Precursor Protein Cleaving Enzyme 1 (BACE1), *J. Med. Chem.,* 54: 5836-5857.
5. El-Gaml Kamal M.(2015). Synthesis and Antimicrobial Evaluation of New Polyfunctionally Substituted Heterocyclic Compounds Derived from 2-cyano-N-(3-cyanoquinolin-2-yl)acetamide. *American Journal of Organic Chemistry*, 5: 1-9.
6. Khalafi-Nezhad Ali, Sarikhani Samira, Shahidzadeh Elham Shaikhi and Panahi Farhad (2012). L-Proline-promoted three-component reaction of anilines, aldehydes and barbituric acids / malononitrile: regioselective synthesis of 5-arylpyrimido [4, 5-*b*] quinoline-diones and 2-amino-4-arylquinoline-3-carbonitriles in water. *Green Chem.,* 14: 2876-2884.
7. Hagen Helmut, Markert Juergen, Kohler Rolf-Dieter, Wuerzer Bruno (1985). 3-Chloro-8-cyanoquinolines and their use for controlling undesirable plant growth. US4511393 A, Patent.
8. Jiang Bo, Li Chao, Tu Shu-Jiang and Shi Feng (2010). Iodine-Promoted Domino Reaction Leading to N-Substituted 2-Aminoquinoline-3-carbonitriles under Microwave Irradiation. *Journal of Combinatorial Chemistry,* 12: 482-487.
9. Shujiang Tu Tu Shujiang, Jia Runhong, Zhang Junyong, Zhang Yan, Jiang Bo (2007). A facile one-pot synthesis of 2-amino-4-arylbenzo[h]quinoline-3-carbonitrile derivatives without catalyst. *Journal of Heterocyclic Chemistry 44: 735–738.*