*Available online www.jocpr.com*

**Journal of Chemical and Pharmaceutical Research, 2018, 10(11): 88-100**

**Research Article**

**ISSN : 0975-7384**
**CODEN(USA) : JCPRC5**

# Synthesis, Optimization and Evaluation of Substituted Quinolines by Solvent and Catalyst Free Conditions as a Green Protocol

**K Rama Devi[1*], D Ashok[1], KSK Rao Patnaik[2], Raju Bathula[3], and Vasudha Bhakshi[4]**

[1]*University College of Technology, Osmania University, Hyderabad, T.S. India*
[2]*Department of Chemical Engineering, School of Mechanical, Chemical and Materials Engineering, Adama Science and Technology University, Adama, Ethiopia*
[3]*Centre for Pharmaceutical Sciences, Institute of Science and Technology, JNTU-Hyderabad, TS, India*
[4]*School of Pharmacy, Anurag Group of Institutions, Venkatapur, Ghatkesar, Hyderabad. TS, India*

---

**ABSTRACT**

*A straightforward, exceedingly and environmentally method for the synthesis of quinolines have been developed by solvent free and catalyst free conditions as a green protocol. This method avoids environmentally destructive predictable organic solvents. Therefore; this Method provides a green and much enhanced protocol over the existing methods. We have developed an eco-friendly process for the synthesis of functionalized quinolines from imines with styrene. The proposed quinolines were synthesized and evaluated for their pharmacological activities like anti-helmenthic activity.*

**Keywords:** Catalyst free conditions; Eco-friendly synthesis; Quinolines; Anti-helmenthic activity

---

## INTRODUCTION

Quinoline is a heterocyclic aromatic organic compound with the chemical formula $C_9H_7N$. It is a colorless hygroscopic liquid with a strong odor. Aged samples, especially if exposed to light, become yellow and later brown. Quinoline is only slightly soluble in cold water but dissolves readily in hot water and most organic solvents [1]. Quinoline itself has few applications, but many of its derivatives are useful in diverse applications. A prominent example is quinine, an alkaloid found in plants. 4-Hydroxy-2-alkylquinolines (HAQs) are involved in antibiotic resistance. Quinolines and their derivatives take place in frequent natural products, and display a wide variety of biological activities [2] the skeleton is an important synthetic midway of many synthetic compounds with pharmacological properties. In addition, these compounds are well-known ligands for the preparation of OLED phosphorescent complexes [3]. In view of these points a great deal of attempt has been done to expand new and well-organized synthetic methods for quinoline derivatives in both synthetic organic and medicinal chemistry. now, various methods have been developed for the synthesis of these compounds, such as Skraup, Doebner- von Miller, Friedländer, Combes methods, and so on [4]. Among these methods, The most simple and uncomplicated method is

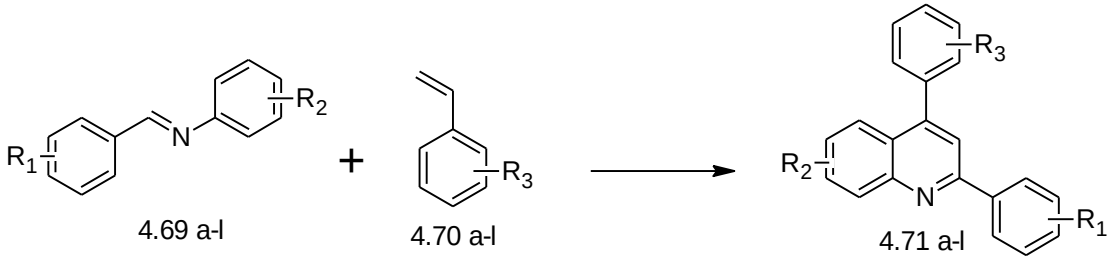
the Friedländer synthesis based on acid or base-catalyzed Aldol Quinoline derivative are important as functional materials [5] and medicines [6].

There have been several classical methods for the synthesis of quinolines for example, Skraup et al. [7] Doebner–von Miller [8], Friedlander, Combes [9] and Ciamician–Dennsted procedures. Recently, electrophilic cyclization using iodine [10] and metal-mediated catalysed [11] synthesis of quinoline derivatives are developed. Quinoline is used in the manufacture of dyes, the preparation of hydroxyquinoline sulphate and niacin. It is also used as a solvent for resins and terpenes.

Quinoline is mainly used as in the production of other specialty chemicals. Approximately 4 tonnes are produced annually according to a report published in 2005 [12]. Its principal use is as a precursor to 8-hydroxyquinoline, which is a versatile chelating agent and precursor to pesticides. Its 2- and 4-methyl derivatives are precursors to cyanine dyes. Oxidation of quinoline affords quinolinic acid (pyridine-2,3-dicarboxylic acid), a precursor to the herbicide sold under the name "Assert". The reduction of quinoline with sodium borohydride in the presence of acetic acid is known to produce Kairoline A [13].

**Materials Used**

Aldimines, Substituted Styrenes, Ethyl Acetate, Na2so4, Methanol, Petridishes ( purchased from Vijay Enterprises, Shop Number:149/A, Saidabad, Hyderabad), Reference Standard - Piperazine Citrate, Control - Normal Saline And Test Compounds:2,4-Di Phenyl Quinolines.




**Scheme**

**Procedure for the Synthesis of Quinolines by Using Different Solvents and Catalysts**

In a 50 mL round bottom flask substituted aldimines (1 mmol), substituted Styrenes (1 mmol) were heated with different catalysts and solvents (as mentioned in the table) at 110°C for 5 h. The movement of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was refrigerated to room temperature; water and ethyl acetate were added and stirred for a while. The organic layer was separated and dried with $Na_2SO_4$, and concentrated under reduced pressure. The crude solid obtained was recrystallized using methanol which afforded the products in the following yields (Table 1).

**Microwave**

In a 50 mL round bottom flask substituted aldimines (1 mmol), substituted Styrenes (1 mmol) were irradiated with different catalysts and solvents (mentioned in the table) at 110°C for 15-20 min. The movement of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was refrigerated to room temperature; water and ethyl acetate were added and stirred for a while. The organic layer was separated and dried with $Na_2SO_4$,

and concentrated under reduced pressure. The crude solid obtained was recrystallized using methanol which afforded the products in the following yields (Table 2).

**Procedure for the Synthesis of Quinolines without Solvent and Catalyst**

In a 50 mL round bottom flask substituted aldimines (1 mmol), substituted Styrenes (1 mmol) were heated without solvent and catalyst at 110°C for 5 h. The movement of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was refrigerated to room temperature; water and ethyl acetate were added and stirred for a while. The organic layer was separated and dried with $Na_2SO_4$, and concentrated under reduced pressure. The crude solid obtained was recrystallized using methanol which produced the products in the following yields (Tables 3 and 4).

**Microwave**

In a 50 mL round bottom flask substituted aldimines (1 mmol), substituted Styrenes (1 mmol) were irradiated at 110°C for 15Min. The movement of the reaction was monitored by TLC. After finishing of the reaction, the mixture was refrigerated to room temperature; water and ethyl acetate were added and stirred for a while. The organic layer was separated and dried with $Na_2SO_4$, and concentrated under reduced pressure. The crude solid obtained was recrystallized using methanol to afford the products in good yield.

**Table 1. Optimization of the yield with various catalyst and solvent**

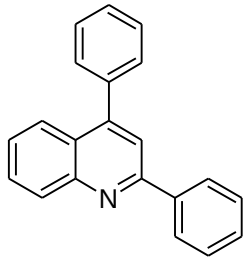
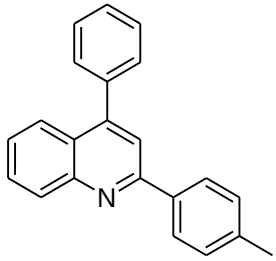
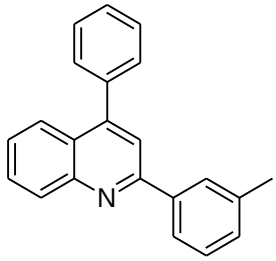
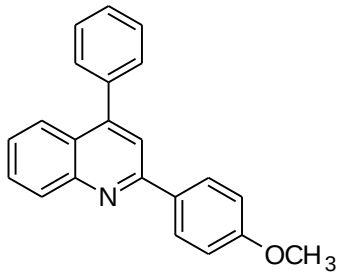
| S.NO | Catalyst | Solvent | Time (Hrs) | Yield % | Time (Min) | Yield % |
|---|---|---|---|---|---|---|
| 1 | M-K-1O | MeOH | 5 | 55 | 20 | 60 |
| 2 | L-PROLINE | MeOH/EtOH | 5 | 60 | 15 | 65 |
| 3 | PTSA | EtOH | 5 | 65 | 20 | 69 |
| 4 | Sulphamic acid | WATER | 5 | 58 | 20 | 62 |
| 5 | --- | -- | 4 | 75 | 15 | 85 |

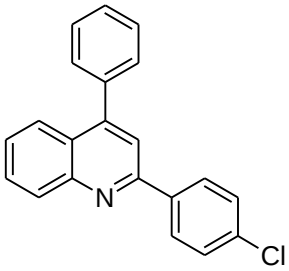
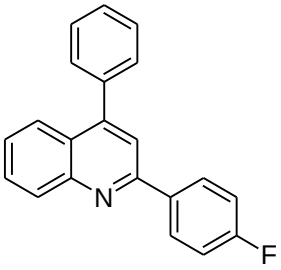
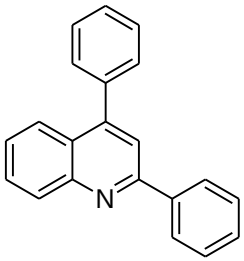
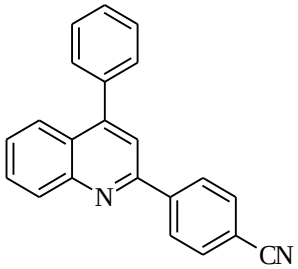
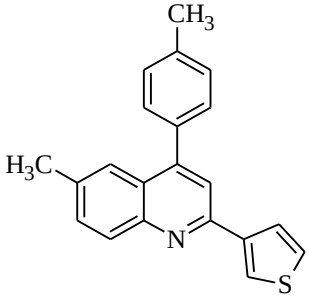
**Table 2. Synthesis of quinolines by condensations aldimines and arylstyrenes**

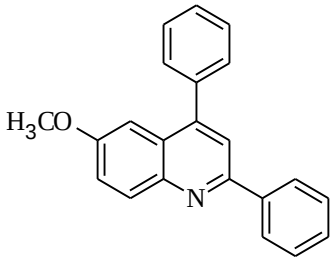
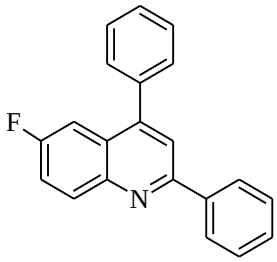
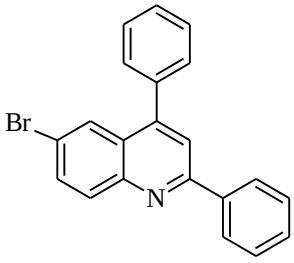
| PRODUCT | $R_1$ | $R_2$ | $R_3$ |
|---|---|---|---|
| 4.71a | H | H | H |
| 4.71b | H | H | 4-$CH_3$ |
| 4.71c | H | H | 3- $CH_3$ |
| 4.71d | H | H | 4-$OCH_3$ |
| 4.71e | H | H | 4-Cl |
| 4.71f | H | H | 4-F |
| 4.71g | H | H | 4-Br |
| 4.71h | H | H | 4-CN |

| | | | |
|---|---|---|---|
| 4.71i | SH-CHO | 4-$CH_3$ | H |
| 4.71j | H | 4-$OCH_3$ | H |
| 4.71k | H | 4-F | H |
| 4.71l | H | 4-Br | H |

**Table 3. Physical data**

| S.No | Structure | IUPAC | M.F | M.W | Yield in % | M.P |
|---|---|---|---|---|---|---|
| 4.71a |  | 2, 4-Diphenylquinoline | $C_{21}H_{15}N$ | 281 | 85.0 | 104-106 |
| 4.71b |  | 4-Phenyl-2-*p*-tolylquinoline | $C_{22}H_{17}N$ | 295 | 85.4 | 105-106 |
| 4.71c |  | 4-Phenyl-2-*m*-tolylquinoline | $C_{22}H_{17}N$ | 295 | 80.2 | 108-109 |
| 4.71d |  | 2-(4-Methoxyphenyl)-4-phenylquinoline | $C_{22}H_{17}NO$ | 311 | 84.8 | 110-112 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 4.71e |  | 2-(4-Chlorophenyl)-4-phenylquinoline | $C_{21}H_{14}ClN$ | 315 | 86.2 | 129-130 |
| 4.71f |  | 2-(4-Fluorophenyl)-4-phenylquinoline | $C_{21}H_{14}FN$ | 299 | 85.9 | 105-107 |
| 4.71g |  | 2-(4-Bromophenyl)-4-phenylquinoline | $C_{21}H_{14}BrN$ | 360 | 83.6 | 117-118 |
| 4.71h |  | 4-(4-Phenylquinolin-2-yl) benzonitrile | $C_{22}H_{14}N_2$ | 306 | 82.6 | 169-170 |
| 4.71i |  | 6-Methyl-4-phenyl-2-(thiophen-3-yl) quinoline | $C_{21}H_{17}NS$ | 315 | 84.0 | . 92-93 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 4.71j |  | 6-Methoxy-2, 4-diphenylquinoline | $C_{22}H_{17}NO$ | 311 | 85.1 | 112-114 |
| 4.71k |  | 6-Fluoro-2, 4-diphenylquinoline | $C_{21}H_{14}NF$ | 299 | 84.8 | 140-141 |
| 4.71l |  | 6-Bromo-2,4-diphenylquinoline | $C_{21}H_{14}BrN$ | 360 | 85.4 | 153-155 |

**Anthelmintic Activity**

The increasing prevalence of helminth parasites those are resistant to conventional anthelmintics have been the spur for different research programs exploring alternative approaches to parasite control.

Materials used: Petridishes

Reference standard- Piperazine citrate

Control- Normal Saline

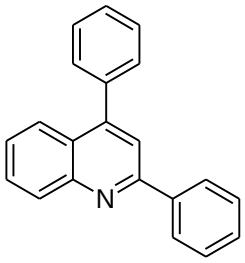
Test Compound: 2,4-di Phenyl Quinoline analogues.

**Method**

The synthesized compounds were evaluated for anthelmintic activity in *Pheretimaposthuma* (earth worms) of nearly equal size (6 ± 1 cm). *Pheretimaposthuma* is used due to its anatomical and physiological resemblance with the intestinal roundworm parasite of human being. The worms were acclimatized to the laboratory condition before experimentation. The earth worms were divided into groups of six earth worms in each. Piperazine citrate diluted with normal saline solution to obtained 0.1, 0.2, 0.5 and 1% m/*V* served as standard and poured into petri dishes. Test solutions were prepared in minimal quantity of ethanol and diluted to prepare four concentrations *i.e.*, 0.1, 0.2, 0.5 and 1% m/*V* for each compound. Normal saline serves as control. Six earth worms were nearly equal size (6 ± 1 cm) are taken for each concentration and placed in petriplates at room temperature. The time taken for complete paralysis and death are recorded. The mean paralysis time and lethal time for each sample was calculated (each reading were taken in a triplicate). The time taken for worms to become motionless was noted as paralysis time and

to ascertain death, each worm was frequently applied with external stimuli which stimulates and induce movement in the worms, if alive.

## RESULT AND DISCUSSION



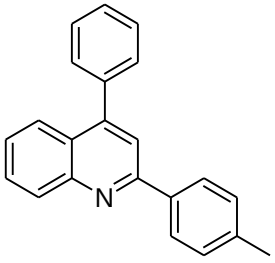
**2, 4-Diphenylquinoline : 4.71a**

Yellow solid; m.p. 104-106°C;

HRMS, C21H15N 281.1204, found 281.1

1H NMR: (400 MHz, CDCl3): δ 8.27 (d, J = 8.4 Hz, 1 H), 8.20 (d, J = 7.2 Hz, 2 H), 7.90 (dd, J = 1.2 Hz, J = 8.8 Hz, 1 H), 7.82 (s, 1 H), 7.72 (td, J =1.2 Hz, J = 7.4 Hz, 1 H), 7.57-7.47 (m, 9 H);

13C NMR: (100 MHz, CDCl3): δ 156.8, 149.2, 148.6, 139.5, 138.3, 130.0, 129.5, 129.3, 128.7, 128.5, 128.3, 127.5, 126.3, 125.7, 125.6, and 119.3.



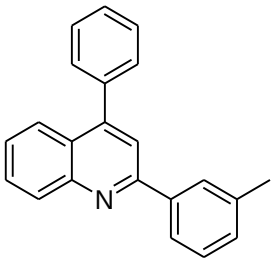
**4-Phenyl-2-p-tolylquinoline: 4.71b**

yellow solid; m.p. 105-106°C;

HRMS**,** $C_{22}H_{17}N$ 295.1361, found 295.1353.

$^{1}$H NMR: (400 MHz, CDCl3): δ 8.22 (d, *J* = 8.3 Hz, 1 H), 8.10 (d, *J* = 8.0 Hz, 2 H), 7.89 (d, *J* = 8.4 Hz, 1 H), 7.79 (s, 1 H), 7.74 (t, *J* = 7.2 Hz, 1 H), 7.55-7.52 (m, 5 H), 7.47 (t, *J* = 7.6 Hz, 1 H), 7.36 (d, *J* = 7.6 Hz, 2 H), 2.46 (s, 3 H);

$^{13}$CNMR: (100 MHz, CDCl3): δ 156.7, 149.0, 148.6, 139.4, 138.4, 136.6, 129.9, 129.5, 129.4, 128.5, 128.3, 127.4, 126.1, 125.6, 125.5, 119.1, 21.2.



**4-Phenyl-2-*m*-tolylquinoline: 4.71c**

Durty solid; m.p. 108-109°C;

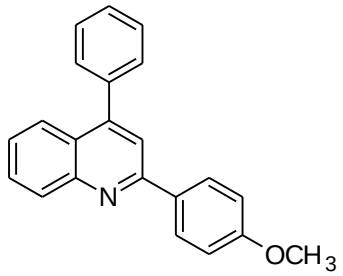
HRMS, $C_{22}H_{17}N$ 295.1361, found 295.1353.

$^1$H NMR: (400 MHz, CDCl3): δ 8.23 (d, *J* = 8.0 Hz, 1 H),

8.04 (s, 1 H), 7.96 (d, *J* = 8.0 Hz, 1 H), 7.90 (d, *J* = 8.4 Hz, 1 H), 7.88 (s, 1 H), 7.73 (td, *J* =

1.2 Hz, *J* = 8.0 Hz, 1 H), 7.47-734 (m, 7 H), 7.28 (d, *J* = 7.2 Hz, 1 H), 2.48 (s, 3 H);

$^{13}$C NMR: (100 MHz, CDCl3): δ 156.0, 148.0, 147.7, 138.5, 138.4, 137.3, 130.1, 130.0, 129.5, 129.4, 128.6, 128.5, 128.3, 128.2, 126.2, 125.7, 124.5, 124.7, 118.4, 21.5.



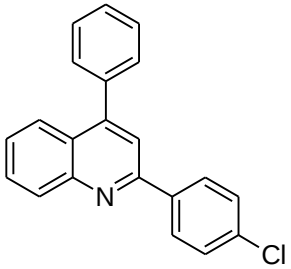

**2-(4-Methoxyphenyl)-4-phenylquinoline: 4.71d**

Yellow solid; m.p. 110-112°C;

HRMS $C_{22}H_{17}NO$ .311.1310, found 311.13

$^1$H NMR: (400 MHz, CDCl3): δ 8.20 (d, *J* = 8.4 Hz, 1 H), 8.15 (d, *J* = 8.8 Hz, 2 H), 7.76 (d, *J* = 8.3 Hz, 1 H), 7.72 (s, 1 H), 7.71 (t, *J* = 7.7 Hz, 1 H), 7.53-7.48 (m, 5 H), 7.42 (t, *J* = 8.0 Hz, 1 H), 7.06 (d, *J* = 8.5 Hz, 2 H), 3.85 (s, 3 H);

$^{13}$C NMR: (100 MHz, CDCl3): δ 160.8, 156.3, 149.1, 148.6, 138.4, 131.9, 129.7, 129.5, 128.9, 128.5, 128.3, 125.9, 124.6, 125.4, 118.8, 114.2, 55.3.



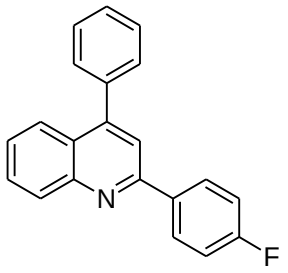

**2-(4-Chlorophenyl)-4-phenylquinoline: 4.71e**

White solid; m.p. 129-130°C;

HRMS, $C_{21}H_{14}ClN$ 315. found 315.08.

$^1$H NMR: (400 MHz, CDCl3): δ 8.20 (d, J = 8.4 Hz, 1 H), 8.11 (d, J= 8.4 Hz, 2 H), 7.82 (d, *J* = 8.4 Hz, 1 H), 7.71 (s, 1 H), 7.70 (t, J = 8.0 Hz, 1 H),7.44-7.35 (m, 8 H);

$^{13}$C NMR: (100 MHz, CDCl3): δ 155.4, 149.5, 148.5, 138, 137.8, 135.5, 129.9, 129.7, 129.4, 128.8, 128.6, 128.5, 128.4, 126.5, 125.7, 125.6, 118.8.



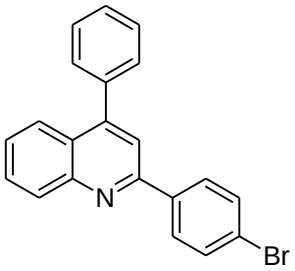

**2-(4-Fluorophenyl)-4-phenylquinoline: 4.71f**

Yellow solid; m.p. 105-107°C;

HRMS, $C_{21}H_{14}FN$ 299.1, found 299.11.

$^{1}$H NMR: (400 MHz, CDCl3): δ 8.22 (d, *J* = 8.4 Hz, 1 H), 8.19-8.16 (m, 2 H), 7.89 (dd, *J* = 1.0 Hz, *J* = 8.4 Hz, 1 H), 7.75 (s, 1 H), 7.74-7.70 (m, 1 H), 7.55-7.44 (m, 6 H), 7.21-7.17 (m, 2 H);

$^{13}$C NMR: (100 MHz, CDCl3): δ 165.0, 162.5, 155.6, 149.4, 148.6, 138, 135.6, 129.9, 129.6, 129.5, 129.3, 128.6, 128.4, 126.4, 125.6, 118.9, 115.8 ,115.6.




**2-(4-Bromophenyl)-4-phenylquinoline: 4.71g**

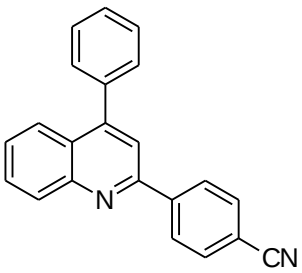
Pale yellow solid; m.p. 117-118°C;

HRMS, $C_{21}H_{14}BrN359$, found 359.03.

$^{1}$H NMR: (400 MHz, CDCl3): δ 8.22 (d, *J* = 8.4 Hz, 1 H),

8.06 (dd, *J* = 0.8 Hz, *J* = 6.8 Hz, 2 H), 7.89 (d, *J* = 8.4 Hz, 1 H), 7.75 (s, 1 H), 7.72 (td, *J* =1.2 Hz, *J* = 8.4 Hz, 1 H), 7.63 (dd, *J* = 0.8 Hz, *J* = 6.4 Hz, 2 H), 7.54-7.45 (m, 6 H);

$^{13}$CNMR: (100 MHz, CDCl3): δ 155.4 , 149.4 , 148.6 , 138.3 , 138.1 , 131.9 (2, 129.9 , 129.7 , 129.4, 129.0, 128.5 , 128.4 , 126.5, 125.8 , 125.6 , 123.9 , 118.7.




**4-(4-Phenylquinolin-2-yl) benzonitrile: 4.71h**

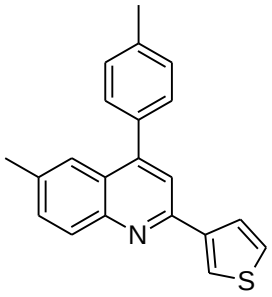
Pale yellow solid; m.p. 169-170°C;

HRMS, $C_{22}H_{14}N2$ 306, found 306.1.

$^{1}$H NMR: (400 MHz, CDCl3): δ 8.30 (d, *J* = 8.4 Hz, 2 H),

8.20 (d, *J* = 8.4 Hz, 1 H), 7.87 (d, *J* = 8.0 Hz, 1 H), 7.83 (S, 1 H), 7.72 (d, *J* = 8.4 Hz, 2 H),7.70(t, *J* = 8.0 Hz, 1 H), 7.45-7.41 (m, 6 H);

$^{13}$C NMR: (100 MHz, CDCl3): δ 152.4,147.8 , 147.7, 142.5, 136.9, 132.5, 130.1, 130.0, 129.4, 128.1, 128.0, 127.3, 126.3, 125.8, 117.9, 118.8,111.7.




**6-Methyl-4-phenyl-2-(thiophen-3-yl) quinoline: 4.71i**

Pale yellow solid; m.p. 92-93°C;

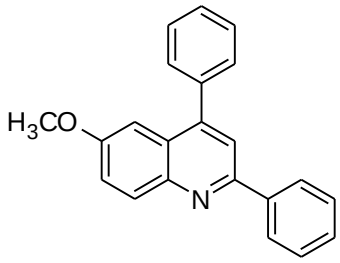
HRMS $C_{20}H_{15}NS$ 315, found 315.09.

$^{1}$H NMR: (400 MHz, CDCl3): δ 8.06 (d, *J* = 8.4 Hz, 1 H),

8.01 (s, 1 H), 7.86 (dd, *J* = 0.8 Hz, *J* = 5.2 Hz, 1 H), 7.65 (s, 1 H), 7.60 (s, 1 H), 7.54-7.52 (m,

6 H), 7.41 (dd, *J* = 3.2 Hz, *J* = 5.2 Hz, 1 H), 2.44 (s, 3 H);

$^{13}$C NMR: (100 MHz, CDCl3): δ152.0, 148.3, 147.2, 142.6, 138.4, 136.0, 131.7, 129.5,129.4, 128.5, 128.2, 126.7, 126.2, 125.6, 124.4 ,124.2, 119.4, 21.7.



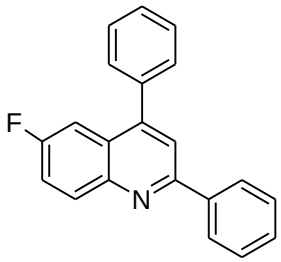

**6-Methoxy-2, 4-diphenylquinoline: 4.71j**

Yellow solid; m.p. 112-114°C;

HRMS $C_{22}H_{17}NO$ 311.1, found 311.13.

$^{1}$H NMR(400 MHz, CDCl3): δ8.11-8.12 (m, 3 H), 7.71 (s, 1 H), 7.48-7.51 (m, 7 H), 7.40 (d, J= 7.2 Hz, 1 H), 7.34 (dd, J= 2.8 Hz, J = 9.2 Hz, 1 H), 7.15 (s, 1 H), 3.78 (s, 3 H);

$^{13}$C NMR(100 MHz, CDCl3): δ155.7 , 153.5 , 146.7 , 144.8 , 138.6 , 138.6, 131.5 , 129.2 , 128.9, 127.7 , 127.6 , 128.2 , 126.2 , 125.5 , 120.7 , 118.5 , 103.6 , 55.3.



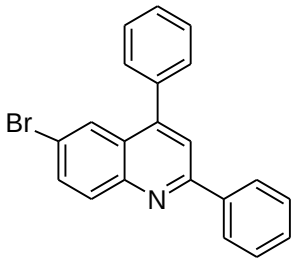

**6-Fluoro-2, 4-diphenylquinoline: 4.71k**

Pale Yellow solid; m.p. 140-141°C;

HRMS $C_{21}H_{14}FN$ 299.1, found 299.10.

$^{1}$H –NMR: (400 MHz, CDCl3): δ8.20 (dd, J= 5.6 Hz, J= 9.2 Hz, 1 H), 8.11 (d, J= 8.4 Hz, 2 H), 7.82 (s, 1 H), 7.47-7.42 (m, 10 H);

$^{13}$C NMR: (100 MHz, CDCl3): δ160.5 (d, JC-F= 246.0 Hz, C), 155.1 (d, JC-F= 2.2 Hz, C), 147.5 (d, JC-F= 5.8 Hz, 144.8, 138.2, 137.3, 132.4 (d, JC-F= 8.8 Hz, 128.3 , 129,128.6 , 128.4 , 127.5 , 127.3 , 118.7 (d, JC-F= 5.1 Hz, 119.4, 108.9 (d, JC-F= 93.6 Hz, );




**6-Bromo-2,4-diphenylquinoline: 4.71l**

Yellow solid; m.p. 153-155°C;

HRMS $C_{21}H_{14}BrN$ 359, found 359.03

$^{1}$H-NMR: (400 MHz, CDCl3): δ8.18-8.15 (m, 2 H), 8.08 (d, J=8.8 Hz, 1 H), 8.02 (s, 1 H), 7.81 (s, 1 H), 7.77 (dd, J= 2.0 Hz, J= 8.8 Hz, 1 H), 7.56-7.46 (m, 8 H);

$^{13}$C NMR: (100 MHz, CDCl3): δ157.1 , 147.3 , 147.3 , 139.1 , 138.6 , 132.9 , 131.3 , 129.6 , 129.4 , 128 , 128.2 , 127.2 , 127.4 , 126.7 , 120.2 , 119.5

**ANTHELMINTIC ACTIVITY OF 2,4-DI PHENYL QUINOLINE DERIVATIVES**

Among the series of compounds synthesized from 4.71a to 4.71l, 4.71a, 4.71d, 4.71j showed significant anti-helminthic activity. Compound 4.71a showed 0.92 min for paralysis of worms and the death time was recorded to be 3.09 min at a concentration of 1mg/ml. Compound 4.71d showed 0.62 min for paralysis of worms and the death time was recorded to be 2.19 min at a concentration of 1mg/ml. Compound 4.71j showed 0.59 min for paralysis of worms and the death time was recorded to be 2.15 min at a concentration of 1 mg/ml (Table 4).

| S. No | Compound | Conc. % | Time (min, Mean ± SEM) | |
|---|---|---|---|---|
| | | | For paralysis | For death |
| 1 | 4.71a | 0.1 | 2.63 ± 0.59 | 4.65 ± 0.85 |
| | | 0.2 | 2.12 ± 0.62 | 4.01 ± 0.25 |

| | | | | |
|---|---|---|---|---|
| | | 0.5 | 1.93 ± 0.25 | 3.72 ± 0.94 |
| | | 1 | 0.92 ± 0.85 | 3.09 ± 0.55 |
| 2 | 4.71b | 0.1 | 2.03 ± 0.07 | 4.42 ± 0.20 |
| | | 0.2 | 1.49 ± 0.09 | 4.27 ± 0.23 |
| | | 0.5 | 1.25 ± 0.06 | 3.45 ± 0.19 |
| | | 1 | 1.26 ± 0.03 | 3.28 ± 0.04 |
| 3 | 4.71c | 0.1 | 2.23 ± 0.14 | 4.55 ± 0.31 |
| | | 0.2 | 1.74 ± 0.74 | 4.01 ± 0.46 |
| | | 0.5 | 1.31 ± 0.25 | 3.46 ± 0.64 |
| | | 1 | 1.02 ± 0.91 | 2.37 ± 0.02 |
| 4 | 4.71d | 0.1 | 1.48 ± 0.98 | 4.41 ± 0.94 |
| | | 0.2 | 1.36 ± 0.99 | 4.12 ± 0.65 |
| | | 0.5 | 1.15± 0.46 | 3.26 ± 0.71 |
| | | 1 | 0.62 ± 0.04 | 2.19 ± 0.84 |
| 5 | 4.71e | 0.1 | 3.91 ± 0.75 | 5.01 ± 0.51 |
| | | 0.2 | 2.06 ± 0.49 | 4.86 ± 0.24 |
| | | 0.5 | 1.43 ± 0.34 | 4.22 ± 0.97 |
| | | 1 | 1.03 ± 0.82 | 3.04 ± 0.81 |
| 6 | 4.71f | 0.1 | 2.03 ± 0.56 | 4.52 ± 0.24 |
| | | 0.2 | 1.77 ± 0.54 | 4.27 ± 0.51 |
| | | 0.5 | 1.35 ± 0.18 | 3.55 ± 0.17 |
| | | 1 | 1.11 ± 0.47 | 3.14 ± 0.78 |
| 7 | 4.71g | 0.1 | 2.50 ± 0.64 | 5.18 ± 0.12 |
| | | 0.2 | 2.08 ± 0.07 | 4.47 ± 0.28 |
| | | 0.5 | 1.66 ± 0.09 | 4.23 ± 0.44 |
| | | 1 | 1.14 ± 0.47 | 3.02 ± 0.06 |
| 8 | 4.71h | 0.1 | 2.09 ± 0.74 | 4.75 ± 0.12 |
| | | 0.2 | 1.83 ± 0.58 | 4.85 ± 0.42 |
| | | 0.5 | 1.92 ± 0.06 | 3.22 ± 0.41 |
| | | 1 | 1.47± 0.64 | 2.47 ± 0.98 |
| 9 | 4.71i | 0.1 | 2.64 ± 0.29 | 5.80 ± 0.43 |
| | | 0.2 | 2.36 ± 0.18 | 5.21 ± 0.49 |
| | | 0.5 | 2.01 ± 0.17 | 4.75 ± 0.86 |
| | | 1 | 1.13 ± 0.09 | 3.47 ± 0.86 |
| 10 | 4.71j | 0.1 | 1.51 ± 0.11 | 4.29 ± 0.82 |
| | | 0.2 | 1.36 ± 0.70 | 4.06 ± 0.27 |
| | | 0.5 | 1.14± 0.41 | 3.86 ± 0.35 |
| | | 1 | 0.59 ± 0.88 | 2.15 ± 0.23 |
| 11 | 4.71k | 0.1 | 1.23 ± 0.22 | 4.31 ± 077 |
| | | 0.2 | 1.22 ± 0.56 | 4.12 ± 0.64 |
| | | 0.5 | 1.18 ± 0.86 | 3.26 ± 0.13 |

| | | | | |
|---|---|---|---|---|
| | | 1 | 1.06 ± 0.07 | 2.61 ± 0.71 |
| 12 | 4.71l | 0.1 | 2.59 ± 056 | 5.41 ± 086 |
| | | 0.2 | 2.19 ± 0.22 | 4.54 ± 0.73 |
| | | 0.5 | 1.47 ± 0.94 | 3.27 ± 0.11 |
| | | 1 | 1.36 ± 0.09 | 3.29 ± 0.73 |
| Piperazine citrate (Standard drug) | | 0.1 | 1.36 ± 0.06 | 4.11 ± 0.21 |
| | | 0.2 | 1.21 ± 0.09 | 4.02 ± 0.24 |
| | | 0.5 | 1.05 ± 0.03 | 3.58 ± 0.23 |
| | | 1 | 0.54 ± 0.02 | 2.16 ± 0.03 |

**Table 4. No paralysis or death was found with control group**

## CONCLUSION

In this study, we have prepared a small set of new nitrogen heterocycles displaying scaffold using a flexible chemistry. Five new derivatives cinnamic acid were prepared in good yield. The antimalarial activity of these compounds has been described. The compounds were tested against P. falciparum 3D7 strains and W2. The best result is obtained with compound 8 against 3D7.

## ACKNOWLEDGEMENTS

We thank Université de REIMS, Institut de chimie moléculaire de Reims (ICMR), France, for recording NMR, Université Jules Verne, Plate-Forme Analytique, Amiens for recording GC/MS and Université Paris XI, France, for bioactive tests.

## REFERENCES

[1] Chisholm H. Quinoline.Encyclopaedia Britannica, 11th edn. Cambridge University Press, London, **1911,** 759.
[2] Novotny A; Brezik Z; Pridal J; *Cesk Fam*. **1958,** 7, 517.
[3] Maffi G; Testa E; Fusco R; *Farmaco Ed Sci*. **1958,** 13, 629.
[4] Pohlemann H; Stassen A. German patent, **1958,** 1, 116.
[5] Hasegawa MJ. *Polymer Sci*. **1964**, 237.
[6] Weidinger H, Kranz J. French patent, 1,222,050, **1959**.
[7] Sarah JD; Francis G; O'shea PD. *J Org Chem*. **2006,** 71, 9548-9551.
[8] Wilder Smith AE; Brodhage H. *Nature*. **1961**, 1, 195.
[9] Guptha RR; Kumar M; Guptha V. *Heterocycl Chem*. **1999**, 540-543.
[10] Medvedev MN; Matveeva EN; Zhil'tstova Lya. *Izv Akad Nauk SSSR Ser Fiz*. **1958,** 22, 44.
[11] Ciba, French Patent, 1, 287, 017, **1961.**
[12] Gerd Collin; Hartmut Höke. Ullmann's Encyclopedia of Industrial Chemistry. **2000**.
[13] O'Loughlin EJ; Kehrmeyer SR; Sims GK. *Int Biodeterior Biodegradation*. **1996**, 38(2), 107.