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DOI: 10.2478/auoc-2025-0008

Ovidius University Annals of Chemistry Volume 36, Number 1, pp. 66 - 72, 2025

Microwave assisted synthesis and evaluation of antimalarial potencies of some 8-quinoline enones

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Abstract. Ten new chalcones of 8-quinoline were efficiently synthesized via a solvent-free cross-aldol condensation between 8-quinoline carbaldehyde and various substituted aryl ketones, catalyzed by nano fly-ash:H_3PO_4 under microwave irradiation. This method afforded over 82 % yield efficiency. The resulting 8-quinoline enones were characterized through their physicochemical properties, analytical, and spectroscopic techniques. The role of the catalyst and solvents in the reaction was examined, revealing the optimal catalyst amount to be 0.25 g for 0.01 mol of aldehydes. Additionally, the *in vitro* antimalarial activity of the synthetic compounds against the intra-erythrocytic development of *Plasmodium falciparum* was evaluated. The halo-substituted 8-quinoline enones were extremely dynamic in contraction with the antimalarial microbes among the other enones.

***Keywords*:** 8-quinoline enones; nano fly-ash:H_3PO_4; crossed-aldol condensation; microwave irradiation; IR spectra; NMR spectra; anti-malarial activity.

1. Introduction

Quinoline chalcones belong to α, β-unsaturated ketones. They play a significant role in medicinal pharmaceutical, synthetic organic, and natural product chemistry due to the presence of various biological activities and key intermediates [1-4]. Chalcones are a unique main kind of natural product with extensive dispersal in spices, vegetables, fruits, tea, and soy-based food products that possess pharmacological activities [5, 6]. The condensation of aryl ketones with aldehydes is significant, and crossed-aldol condensation is an efficient method for their synthesis. However, conventional acid-base catalyzed reactions are often affected by competing reverse processes [7]. Several catalysts, like Lewis's acids and bases [8, 9], metal oxides [10], bentonite [11], metal tungstates [12], fly-ash-based catalysts [13], phosphates [14], silica [15], and nanoparticles [16], were utilized for deriving aryl enones through the condensation of aryl carbonyl substrates under conventional heating or greener methods. Spectral analysis plays a key role in predicting the ground state equilibrium of α, β–unsaturated ketones [17, 18]. The *E* or *Z* configuration of the chalcones was determined based on the orientation of protons within the alkene segment and confirmed by the coupling constant 'J' values observed in their ^{1}H-NMR spectra [19]. Chalcones, on the other hand, hold a pivotal role in organic synthesis, serving as precursors to an array of synthetic heterocyclic compounds like isoxazoles [20], pyrazolines [21], pyrimidines [22], and thiazoles [23]. Enone derivatives exhibit a wide spectrum of bio-activities, such as antimicrobial [1], anti-inflammatory [24], antimalarial [25], anticancer [26], antileishmanial [27], antiplasmodial [28], and antimalarial [29]. Within these activities, the enones play a significant role in biological chemistry research [20-29]. All notorious quinoline substrate drugs possess the side chain in 4 or 8 carbons and they involve the synthesis of many quinoline derivatives. However, recently, it has been described that affecting a functionalized side chain around the quinolone core to the other position causes the retention of biological activity and provides new opportunities for the design of bioactive compounds [30]. Malaria is mainly caused by the *Plasmodium falciparum*. As per the WHO report, approximately 156 classes of plasmodium have been availed in the biological field. There are 5 Plasmodium parasite species that cause malaria in humans, and two of these species – *P. falciparum* and *P. vivax* – pose the greatest

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threat. *P. falciparum* is the deadliest malaria parasite and the most prevalent on the African continent. *P. vivax* is the dominant malaria parasite in most countries outside of sub-Saharan Africa. The other malaria species that can infect humans are *P. malariae*, *P. ovale*, and *P. knowlesi* [31]. Chemists and researchers were attracted by the simple structured, cheapest synthetic methodology for the synthesis of potent, anti-malarial chalcones. The *in vivo* and *in vitro* antimalarial activities of enones were deceptive due to the presence of antimalarial active pharmacophores such as quinolines and substituents [32, 33]. Quinoline-based cinchona alkaloids such as cinchonine, quinidine, and cinchonine were effective for malarial microbes. The essential factors in molecular design and the structure-activity relationship (SAR) influencing biological functions, including the antimalarial potency of quinoline enones, were minimally availed in the literature [31-33]. A literature survey indicated that no prior studies had reported the synthesis and in-vitro antimalarial evaluation of certain 8-quinoline enones. Thus, the authors wish to report the microwave-assisted greener synthesis and assessment of the *in vitro* antimalarial potential of 8-quinoline enones.

2. Experimental

2.1. General

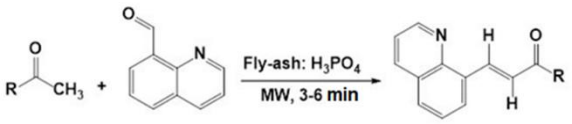
Entire chemical reagents employed in this investigation were obtained from Sigma-Aldrich Chemical Company, Bengaluru, India. The synthesized ketone's melting points were recorded using a Raga Tech electric melting point device and are reported without correction**.** IR spectra were obtained with an Agilent Cary-630N infrared spectrophotometer using KBr discs. NMR spectra were acquired using a Bruker AV-III 500 spectrometer, functioning at 400 MHz for ^{1}H and 100 MHz for ^{13}C nuclei. The deuterated chloroform ($CDCl_3$) was utilized as the solvent, and tetramethylsilane (TMS) was used as the internal reference standard. Elemental analysis (CHN) of the ketones was conducted using a Perkin Elmer 240C analyzer. Mass spectra of all synthesized 8-quinoline enones were recorded on a Shimadzu mass spectrometer in EI mode.

2.2. Formulation of nano fly-ash:H_3PO_4

Nano fly-ash:H_3PO_4 catalyst was formulated and analyzed by literature method [34, 35].

2.3. Synthesis of 8-quinonline enones

Equimolar quantities of 8-quinoline carbaldehyde (0.01 mol), various aryl aldehydes (0.01 mol), and 0.25 g (15.8 wt %) of nano fly-ash:H_3PO_4 catalyst were exposed to microwave radiation for 3–6 min in 30 s intervals using a Samsung Grill, GW73BD Microwave Oven (230 V AC, 50 Hz, 2450 MHz, 100–750 W, IEC–705) (Scheme 1). Thin Layer Chromatography (TLC) was utilized to screen the improvement of the reaction. Upon finalization, the compounds were separated by treatment with 10 mL of dichloromethane, the catalyst was recovered through simple filtration, and evaporation of dichloromethane yielded the target enones. The crude enones were further purified by recrystallization from ethanol afforded a glittering solid and these are kept in a desiccator. The heterogeneous catalyst was rinsed with 7 mL of ethyl acetate, dried in a hot air oven for 4 h, and reused for subsequent reactions.



R = 1. 4-Bromophenyl; 2. 4-Chlorophenyl; 3. 3,4-Dimethoxyphenyl
4. 4-Methylphenyl; 5. 3-Nitrophenyl; 6. 4-Biphenyl; 7. 2-Naphthyl
8. 2-(9H)-Fluorenyl; 9. 2-Phenothiazenyl; 10. 5-Benzodioxal

Scheme 1. Fly-ash:H_3PO_4 catalyzed solvent-free synthesis of 8-quinolinostyryl-substituted aryl ketones

2.2. Antimalarial activity of 8-quinonline enones

2.2.1. Procedure. Parasite culture: The *P. falciparum* Thailand strain Thai and strain K1 were used for this cell culture [36, 37]. Culture was grown in complete medium consisting RPMI1640 supplemented with 27.5 mmol medium hydrogen carbonate, 11 mmol glucose, each 100 µL/mL streptomycin, penicillin and 8% heat-inactivated human serum albumin. Parasite cultures were incubated on 37 °C, using A_+ red blood cells of humanoid with hematocrit of -3% CO_2, 6% oxygen, and 91% nitrogen atmosphere. The *in vitro* assays were performed cultures with a 3-6% parasitemia as determined by counting parasites on Giemsa-stained smears.

2.2.2. Inhibition tests. Increasing concentration of the different 8-quinoline enones and amines are dissolved in dimethyl sulfoxide (DMSO) and examined for their inhibitory level towards the *P. falciparum* intra-erythrocytic growth. Parasites were allowed to grow at 37 °C for 24 h in a candle jar, the 0.5 µCi ^{3}H-hypoxanthine was added per well. After an additional 24 h incubation period, plates are freeze thawed and harvested on filters. The scintillation liquid mixture was applied for moistened of dried filters and the total counts was gets from 1450 Micro beta counter.

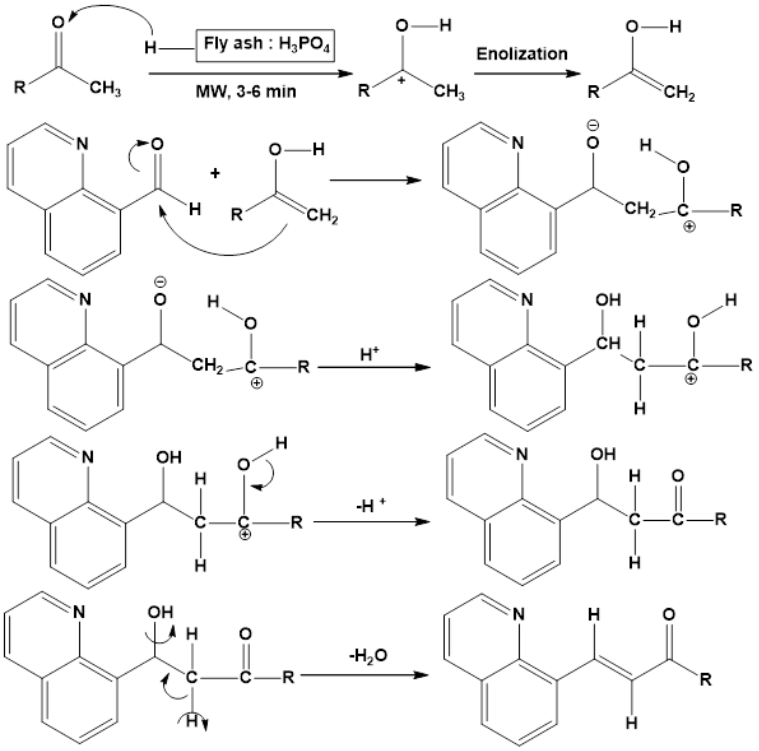
The evaluation of proportion of inhibiting development process was done by the parasite culture-associated radioactivity decay. A 100% assimilation of ^{3}H-hypoxanthine existence was identified from controlled development without 8-quinoline enones. The IC_{50} quantities were determined after each mean concentration was estimated from three different experiment sets.

3. Results and discussion

3.1. Synthesis of enones

As mentioned in the experimental section, we synthesized the 8-quinoline enones. In this condensation, the obtained yield was more than 83 %. The electron donating substituents gave more yield than electron-withdrawing substituents in the ketone moieties. This condensation undergoes well known acidic catalyzed crossed-aldol condensation. The proposed reaction mechanism was depicted in Scheme 2. The first step consists of the protonation of carbonyl group aryl ketones by supply of protons from the acidic site of nano fly-ash:H_3PO_4 catalyst and that carbon gets positive charge. The positive charge of carbon was

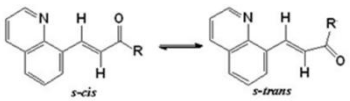
neutralized by loss of proton from methyl group and enol was formed. Secondly, the 8-quinoline carbaldehyde carbonyl carbon was attached by this enol to form oxonium ion and enol carbon gets positive charge. The third step consists of the loss of the proton from the enol group to neutralize the positive charge of the carbon, returning it as a carbonyl group, simultaneously with the protonation of the oxonium ion. The fourth step is the loss of water through β-elimination which leads to the formation of enones.



R= 1. 4-Bromophenyl, 2. 4-Chlorophenyl, 3. 3,4-Dimethoxyphenyl, 4. 4-Methylphenyl, 5. 3-Nitrophenyl, 6. 4-Biphenyl, 7. 2-Naphthyl, 8. 2-9H-Fluorenyl, 9. 2-Phenothiazenyl, 10.5- Benzodioxal

Scheme 2. The proposed mechanistic pathway for the synthesis of 8-quinolinostyryl substituted aryl ketones by nano fly-ash:H_3PO_4 catalyzed solvent-free microwave irradiated crossed-Aldol condensation method.

The synthesized 8-quinoline enones were characterized using their nature, physico-chemical, CHN elemental quantities, and spectroscopic data. In general, from infrared spectral studies, enones exhibit *s-cis* and *s-trans* conformers, but in this investigation, the *s-trans* conformer vibrations merged with CN vibrations, and the conformers are shown in Figure 1.



R = 1. 4-Bromophenyl; 2. 4-Chlorophenyl; 3. 3,4-Dimethoxyphenyl 4. 4-Methylphenyl; 5. 3-Nitrophenyl; 6. 4-Biphenyl; 7. 2-Naphthyl 8. 2-(9H)-Fluorenyl; 9. 2-Phenothiazenyl; 10. 5-Benzodioxal

Figure 1. The *s-cis* and *s-trans* conformers of 8-quinolinostyryl substituted aryl ketones

The complete characterization data of the synthesized 8-quinoline enones are as:

(2*E*)-8-Quinolinostryryl-4-bromophenyl ketone (1): Reaction time: 4 min. Pale yellow solid, Yield: 94%, M. P. 180-109 °C. FT-IR (KBr, cm^{-1}); ν = 1654 ($CO_{s\text{-}cis}$), 1592 ($CO_{s\text{-}trans}$ and CN), 1249 (CH_{ip}), 756 (CH_{op}), 987 ($CH{=}CH_{op}$), 674 ($C{=}C_{op}$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.937 (d, 1H, $H_α$), 8.925 (d, 1H, $H_β$), 7.609-8.210 (10H, m, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ=121.70 ($C_α$), 146.58 ($C_β$), 190.37 (CO), 150.44 (C=N), 124.80-146.58 (Ar-C). Anal. for M.F.: $C_{18}H_{12}BrNO$, Found (Calcd.): C 63.88 (63.92), H 3.59 (3.58), N 4.09 (4.14) %. M: 338. Mass (m/z) = 338[M^+], 340[M^{2+}].

(2*E*)-8-Quinolinostryryl-4-chlorophenyl ketone (2): Reaction time: 3.5 min. Pale brown solid, Yield: 89%, M. P. 130-144 °C. FT- IR (KBr, cm^{-1}); ν = 1654 ($CO_{s\text{-}cis}$), 1585 ($CO_{s\text{-}trans}$ and CN), 1252 (CH_{ip}), 758 (CH_{op}), 896 ($CH{=}CH_{op}$), 675 ($C{=}C_{op}$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.934 (d,1H, $H_α$), 8.945 (d,1H, $H_β$), 7.564 - 8.182 (10H, m, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 121.68 ($C_α$), 146.56 ($C_β$), 190.07 (CO), 150.40 (C=N), 124.77-146.56 (Ar-C). Anal. for M.F.: $C_{18}H_{12}C1NO$, Found (Calcd.): C 73.55 (73.60), H 4.13 (14.12), N 4.72 (4.77) %. MW: 293. Mass (m/z) = 293[M^+], 295[M^{2+}].

(2*E*)-8-Quinolinostryryl-(3,4-dimethoxyphenyl ketone (3): Reaction time: 3 min. Yellow solid, Yield: 88%, M. P. 85-90 °C. FT-IR (KBr, cm^{-1}); ν = 1648 ($CO_{s\text{-}cis}$), 1592 ($CO_{s\text{-}trans}$ and CN), 1148 (CH_{ip}), 762 (CH_{op}), 1020 ($CH{=}CH_{op}$), 706 ($C{=}C_{op}$). ^{1}H NMR (400 MHz, $CDCl_3$) δ =7.986 (d,1H, $H_α$), 8.911 (d, 1H, $H_β$), 3.883 (s, 6H, $(OCH_3)_2$), 7.588-8.910 (m, 9H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 121.61 ($C_α$), 146.61 ($C_β$), 189.62 (CO), 150.31 (C=N), 56.10 (OCH_3), 123.28-149.17 (Ar-C). Anal. for M.F.: $C_{20}H_{17}NO_3$, Found (Calcd.): C 75.18 (75.22), H 5.38 (5.37), N 15.01(15.03) %. M.W: 319. Mass (m/z) = 319[M^+].

(2*E*)-8-Quinolinostryryl-4-methylphenyl ketone (4): Reaction time: 3.5 min. Pale red solid, Yield: 87%, M. P. 80-85 °C. FT-IR (KBr, cm^{-1}); ν =1652 ($CO_{s\text{-}cis}$), 1592 ($CO_{s\text{-}trans}$ and CN), 1233 (CH_{ip}), 753 (CH_{op}), 1112 ($CH{=}CH_{op}$), 681 ($C{=}C_{op}$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.991(d, 1H, H_α), 8.911(d, 1H, H_β), 3.896(s, 3H, CH_3), 7.576-8.192 (10H, m, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 121.58 (C_α), 146.61 (C_β), 189.58 (CO), 150.30 (C=N), 29.70 (CH_3), 125.22-145.71 (Ar-C). Anal. for M.F.: $C_{19}H_{15}NO_2$, Found (Calcd.): C 78.85 (78.87), H 5.24(5.23) N 4.80 (4.84) %. MW: 289. Mass (m/z) = 289[M^+].

(2*E*)-8-Quinolinostryryl-3-nitophenyl ketone (5): Reaction time: 4.5 min. Pale brown solid, Yield: 87%, M. P. 70-80 °C. FT- IR (KBr, cm^{-1}): ν =1685 ($CO_{s\text{-}cis}$), 1663 ($CO_{s\text{-}trans}$), 1164 (CH_{ip}), 719 (CH_{op}), 1012 ($CH{=}CH_{op}$), 700 ($C{=}C_{op}$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.037 (d, 1H, H_α), 9.003 (d, 1H, H_β), 7.624-8.911 (10H, m, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ =121.80 (C_α), 143.56 (C_β), 187.89 (CO), 150.57 (C=N), 123-136 (Ar-C). Anal. for M.F.: $C_{18}H_{12}N_2O_3$, Found (Calcd.): C 72.13 (71.05), H 3.92 (3.97), N 9.18 (9.21) %. MW: 304. Mass (m/z) = 304 [M^+].

(2*E*)-8-Quinolinostryryl-4-biphenyl ketone (6): Reaction time: 4.5 min. Pale yellow solid, Yield: 84%, M. P. 130-140 °C. FT-IR (KBr, cm^{-1}); ν = 1681 ($CO_{s\text{-}cis}$), 1584 ($CO_{s\text{-}trans}$ and CN), 1222 (CH_{ip}), 820 (CH_{op}), 1118 ($CH{=}CH_{op}$), 693 ($C{=}C_{op}$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.028 (d, 1H, H_α), 8.972 (d, 1H, H_β), 7.597−8.210 (11H, m, Ar-H,). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 121.65(C_α), 145.35(C_β), 182.32(CO), 150.39 (C=N), 125.27-145.35 (Ar-C). Anal. for M.F.: $C_{26}H_{21}NO$, Found (Calcd.): C 85.70 (85.68), H 6.12 (6.16) %. MW: 196. Mass (m/z) = 196[M^+].

(2*E*)-8-Quinolinostryryl-2-naphthyl ketone (7): Reaction time: 4 min. Pale yellow solid, Yield: 83%, M. P. 130-140 °C. FT-IR (KBr, cm^{-1}); ν =1649 ($CO_{s\text{-}cis}$), 1618 ($CO_{s\text{-}trans}$ and CN), 1164 (CH_{ip}), 786 (CH_{op}), 1026 ($CH{=}CH_{op}$), 726 ($C{=}C_{op}$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.917 (d, 1H, H_α), 8.167 (d, 1H, H_β), 7.557-8.606 (m, Ar-H, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 121.65 (C_α), 146.61 (C_β), 191.13 (CO), 150.38 (C=N), 124.03-141.56 (Ar-C). Anal. for M.F.: $C_{22}H_{15}NO$, Found (Calcd.): C 84.84 (84.78), H 4.58 (4.62), N 4.88 (4.94) %. MW: 283. Mass (m/z) = 283[M^+].

(2*E*)-8-Quinolinostryryl-2-(9H)-Fluorenyl ketone (8): Reaction time: 5 min. Yellow solid, Yield: 82%, M. P. 70-80 °C. FT-IR (KBr, cm^{-1}); ν = 1671($CO_{s\text{-}cis}$), 1605 ($CO_{s\text{-}trans}$ and CN), 1131 (CH_{ip}), 769 (CH_{op}), 1017 ($CH{=}CH_{op}$), 686 ($C{=}C_{op}$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.452 (d, 1H, H_α), 7.758 (d, 1H, H_β), 7.557-8.201 (13H, m, Ar-H,). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 125.29 (C_α), 128.69 (C_β), 178.56 (CO), 145.78 (C=N), 120.91-128.69 (Ar-C). Anal. for M.F.: $C_{25}H_{17}NO$, Found (Calcd.): C 86.48 (86.43), H 4.87 (4.93), N 3.98 (4.03) %. MW: 347. Mass (m/z) = 347[M^+].

(2*E*)-8-Quinolinostryryl-2-phenothiazene (9): Reaction time: 4.5 min. Brown solid, Yield: 86%, M. P. 80-90 °C. IR (KBr, cm^{-1}); ν = 1643 ($CO_{s\text{-}cis}$), 1587 ($CO_{s\text{-}trans}$ and CN), 1244 (CH_{ip}), 756 (CH_{op}), 972 ($CH{=}CH_{op}$), 726 ($C{=}C_{op}$); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.923 (d, 1H, H_α), 8.979 (d, 1H, H_β), 7.582-8.990 (13H, m, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 121.67 (C_α), 146.62 (C_β), 190.47 (CO), 150.39 (C=N), 124.85-145.72 (Ar-C). Anal. for M.F.: $C_{24}H_{16}N_2OS$, Found (Calcd.): C 75.80 (75.77), H 4.19 (4.24), N 7.29 (7.36) %. MW: 380. Mass (m/z) = 380[M^+].

(2*E*)-8-Quinolinostryryl-5-Bezodioxal (10): Reaction time: 6 min. Pale yellow solid, Yield: 82%, M. P. 75-85 °C. IR (KBr, cm^{-1}); ν =1653 ($CO_{s\text{-}cis}$), 1612 ($CO_{s\text{-}trans}$ and CN), 1141 (CH_{ip}), 922 (CH_{op}), 1037 ($CH{=}CH_{op}$), 672 ($C{=}C_{op}$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.603 (d, 1H, H_α), 8.454 (d, 1H, H_β), 3.780 (s, 2H, CH_2), 7.585-8.068 (10H, m, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 125.45 (C_α), 147.38 (C_β), 188.13 (CO), 154.38 (C=N), 44.09 (CH_2), 125.45-138.71 (Ar-C). Anal. for M.F.: $C_{19}H_{13}NO_3$, Found (Calcd.): C 75.30 (75.24), H 6.57 (4.62), N 5.54 (4.62) %. MW: 303. Mass (m/z) = 303[M^+].

The consequence of catalyst was investigated in this condensation by the observed yields for 8-quilinostryryl 4-bromophenyl ketone (Entry 1). As mentioned in the experimental section, the equal molar quantities of 8-quinoline carbaldehyde and 4-bromophenyl methyl ketone were condensed with varying quantity of the catalyst increasing the catalyst amount from 0.05 to 0.3 g improved the yield from 83 to 94%. The optimum quantity of the catalyst needs for proceeding the condensation reaction is 0.25 g and the obtained yield was 94%. There is no increase the quantity of product beyond 0.25 g of the catalytic substance in the condensation. The obtained yields with the corresponding quantity of catalyst were illustrated in Figure 2.

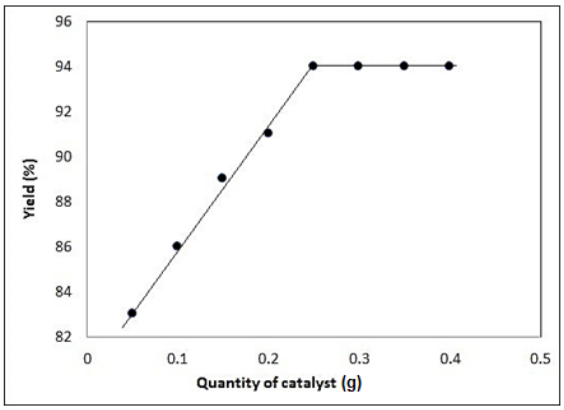


Figure 2. Effect of catalyst on the yield of 8-quilinostryryl-4-bromophenyl ketone (**1**)

3.2. Antimalarial activity

The measured antimalarial potencies of 8-quinolinestyryl substituted aryl ketones are shown in Table 1.

Table 1. The antimalarial inhibition of 8-quinolinostyryl substituted aryl ketones.

Entry	R	Antimalarial inhibition (%)
1	4-Bromophenyl	34±0.04
2	4-Chlorophenyl	38±0.04
3	3.4-Dimethoxyphenyl	34±0.05
4	4-Methylphenyl	35±0.07
5	3-Nitrophenyl	31±0.03
6	4-Biphenyl	29±0.07

Entry	R	Antimalarial inhibition (%)
7	2-Naphthyl	27±0.02
8	2-9H-Fluorenyl	28±0.06
9	10-Phenothiazene-2-yl	30±0.07
10	Benzodioxal-5-yl	33±0.02

All ketones are active in antimalarial activity. Among these, the halogen-substituted compound shows more antimalarial activity. The inductive effect of chlorine enhances the anti-malarial action higher than the bromo substituent. Then the +I effect of the methoxy substituent demonstrated similar antimalarial potential as that of the bromo substituent. The +I effect of the methyl group slightly improves the antimalarial activity. The electron-withdrawing -I effect of the nitro group has lesser antimalarial activity compared to the chloro substituent. The electronegativity of oxygen in the benzodioxol, nitrogen, and sulfur containing phenothiazine rings shows lesser antimalarial activity. The +I effect of biphenyl, fluorenyl, and 2-naphthyl rings shows the lowest antimalarial activity.

4. Conclusions

More than 80% of ten 8-quinoline enones were synthesized by nano fly-ash:H_3PO_4 catalyzed microwave-irradiated solvent-free crossed-aldol condensation of 8-quinoline carbaldehyde and substituted aryl ketones. The physico-chemical methods and spectroscopic data are fully supported for the synthesized enones. In this enone synthetic strategy, the catalytic effect of nano fly-ash:H_3PO_4 was investigated and the optimum quantity of the catalyst for proceeding with the condensation reaction was identified to be 0.25 g for 0.01 mol of aldehydes. Also, the *in-vitro* antimalarial potencies of these enones were studied using *P. falciparum* strain. All ketones show the inhibition of malarial activity. The halogen-substituted enones, such as **1** and **2**, exhibit better antimalarial potencies than other enones.

Acknowledgement

Two authors (P. Gayathri and Dr. G. Thirunarayanan) thank to RUSA-2, Field 1, Anti-Malarial Drug Synthesis, No. F3/RUSA/673/2022 dated 4-6-2022, Annamalai University, Annamalai nagar-608 002 for financial support.

Conflict of interest

The authors declare that there is no conflict of interest regarding this research article.

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Received: 06.04.2025
Received in revised form: 08.06.2025
Accepted: 11.06.2025