Indian Journal of Chemistry
Vol. 64, July 2025, pp. 670-681
DOI: 10.56042/ijc.v64i7.12246

Greener synthesis, molecular docking, antimicrobial and antimalarial activities of some unsaturated ketones

P Gayathri[a], J Divya[a], I Muthuvel[a,b], V Usha[c], Malar Retna[d] & G Thirunarayanan*[a]

[a] Department of Chemistry, Annamalai University, Annamalainagar 608 002, India

[b] Department of Chemistry, M. R. Government Arts College, Mannargudi 614 001, India

[c] Department of Chemistry, University College of Engineering Panruti, Panruti 607 106, India

[d] Department of Chemistry, Scott Christian College, Nagercoil 629 003, India

E-mail: drgtnarayanan@gmail.com, thirunarayanan.g.10313@annamalaiuniversity.ac.in

Received 3 July 2024; accepted (revised) 2 July 2025

A series of α,β-unsaturated ketones including isoquinoline enones have been synthesised by fly-ash:sulphated SnO_2 catalyzed Crossed-Aldol condensation of various aryl methyl ketones and aldehydes under solvent-free microwave irradiation technique. In this synthetic methodology, the obtained yield of the unsaturated ketones is more than 90%. The synthesised ketones have been characterized by their physical constants, micro analysis and spectroscopic data. The molecular docking and, *in vitro* antimicrobial and antimalarial activities of the synthesised ketones have been studied.

Keywords: Fly-ash:sulphated SnO_2, Aryl enones, Environmentally-benign reaction, Molecular docking, Antimicrobial activity, Antimalarial activity

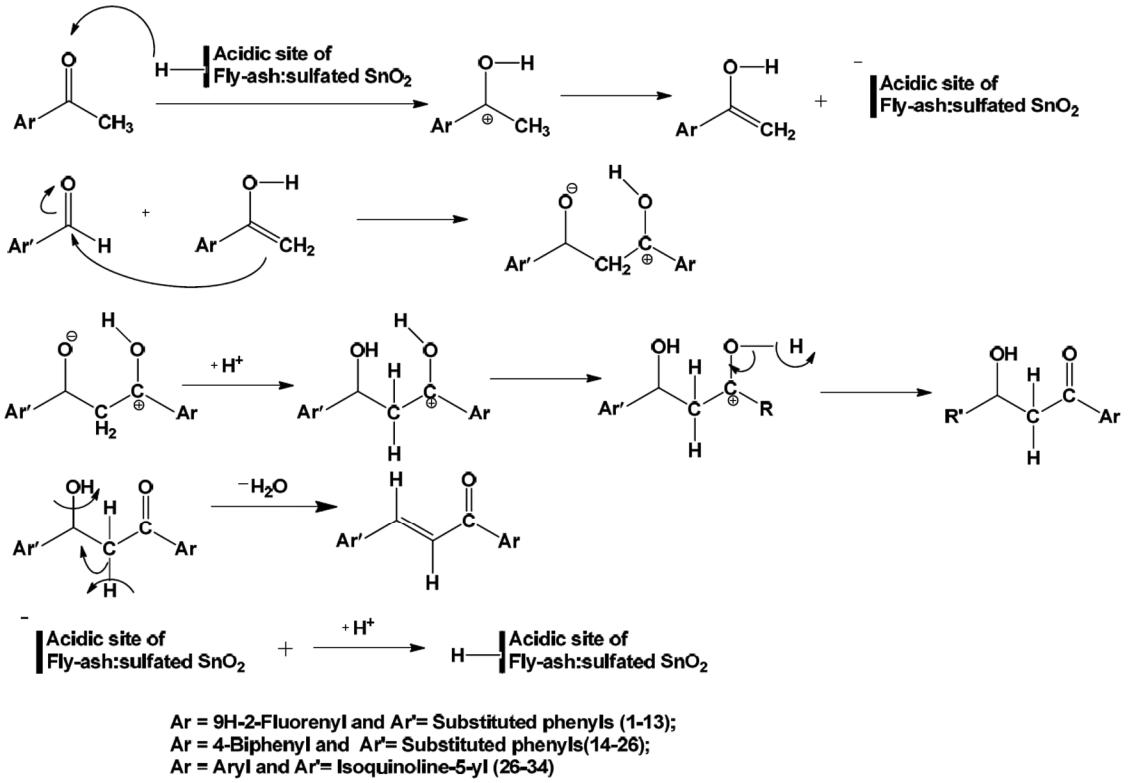
Chalcone is a unique, α,β-unsaturated carbonyl compound with vast biological properties and is a precursor for the synthesis of several beneficial therapeutic organic compounds such as flavonoids, iso flavonoids and heterocyclic. Earlier decades, researchers paid special consideration to chalcones due their pharmaceutical properties[1-3]. Various methods available for synthesizing chalcones such as Aldol, Crossed-Aldol, Claisen-Schmidt, Knoevenagel, greener methods-Grinding of reactants, solvent-free and oxides of nanoparticles with microwave heating [4-10]. Also microwave assisted solvent free Aldol and Crossed-Aldol condensation offers better yield of products in shorter reaction time[4,5]. Microwave strategy is fascinating for a variety of reactions such as cycloaddition, condensation, displacements, oxidation and coupling reactions to achieve wide-range of organic scaffolds and heterocyclic compounds[11-15]. Both the conventional and greener synthetic methods involve an appropriate quantity of acetylated aliphatic or aromatic compounds, substituted aromatic aldehydes and aqueous alcoholic alkali or greener catalysts[16,17]. Well-known Claisen-Schmidt condensation offers facile preparation of chalcones by reacting acetophenone and benzaldehyde. Numerous catalysts were employed for the enone synthesis such as fly-ash: sulphuric acid[18], anhydrous zinc chloride[19], grinding with sodium hydroxide at RT[8], aqueous alkali at lower temperatures[20], solid sulphonic acid from bamboo[21], barium hydroxide[22], anhydrous sodium bicarbonate[23], SiO_2-H_3PO_4[24], SiO_2–H_2SO_4[9], Cu^{2+}/Zeolite[12], NaOH[25], $Zn_3(PO_4)_2$[26], solid acidic SO_4^{2-}-SnO_2-fly ash peony flower[27], cadmium phosphate[28], $FeCl_3$/Bentonite[29], fly-ash:H_3PO_4[30], and KOH/EtOH[31]. Ultrasound assisted synthesis of aryl enones also more attunable to organic synthetic researchers[32,33]. Aryl enones are a key intermediate for synthesis of wide-range of heterocyclic derivatives of such as pyrazoline[34], imidazole's[35], pyrimidines[36], thiazoles[37], pyrroles[38] and oxazine amine[39]. Aryl enones are characterized by their spectroscopic data. From infrared spectral data, the *s-cis* and *s-trans* conformers were predicted and the NMR data provides the *E* and *Z* configurations[18,25,32]. Due to presence of enone moiety and substituents, they produce broad range of biological activities such as anti–bacterial, antifungal[40], anti–inflammatory[41], anti–cancer[42], anti-tubercular[43], anti–malarial[44], antitumor[45], anti-viral[46], anti-HIV[47] and antiplasmodial[48]. Molecular docking is one of the best tools for finding the molecular binding-interaction of lyophilic and lipophilic groups

of enone and various proteins based on the bio activities[49-51]. From this interaction, the best and fast activity of the enones may be predicted using various molecular dock proteins. When the enone combined with quinolines, that chalcones may be expected to exhibit high anti-plasmodial and anti-malarial activity[44,48]. The anti-malarial property of chalcone was first reported after an in-vitro evaluation of an oxygenated chalcone, "licochalcone A" exclusively obtained from Chinese licorice, as an antimalarial agent against chloroquine sensitive and chloroquine resistant Plasmodium strains[52-55]. Literature review reveals that there are no reports available for the solvent-free synthesis, molecular docking, antimalarial and microbial activities of some aryl enones including quinolino chalcones. Therefore, the authors have taken efforts to solvent-free synthesize and studied the bio-activities of enones.

Results and Discussion

Enone Chemistry

Fly-ash based sulfated SnO_2:fly-ash catalyst was employed for the synthesis of enones carbonyl compounds under solvent-free microwave irradiation conditions. Equal molar quantities of aryl aldehydes and aryl methyl ketones were condensed in the presence of fly-ash:sulfated SnO_2 catalyst. In this reaction the obtained yields were more than 90%. The electron donating substituents gave more yields than electron withdrawing substituents. This condensation follows well known acid catalyzed nucleophilic addition followed by elimination water reaction path way and it leads to afforded the corresponding imines. The plausible reaction mechanistic pathways are illustrated in Scheme 1. First step consists of the protonation of carbonyl oxygen from the acidic site of the fly-ash:sulfated SnO_2 catalyst and carbon cation was formed. Second step is the enolization formation. Third step is the attach of carbonyl carbon of aldehyde by ene nucleophile to form oxonium ion. Fourth step is the protonation. Fifth step is the removal of water by beta-elimination afforded the enone. In this study, the author examined the effect of catalyst on the synthesize of enone (**27**). The quantity of catalyst was increased from 0.05 to 0.5 g for each reaction, yields the product from 41 to 92%. The optimum quantity of the catalyst for this reaction is 0.3 g. The effect of catalyst on the yield of the reaction is illustrated in Fig. 1. The synthesized enones are exists in *s-cis* and *s-trans* conformers by



Scheme 1 — The mechanistic route for the synthesis of enones

infrared spectroscopy and the structures are illustrated in Fig. 2. The spectroscopic data of all compounds are confirmed for the formation of enones.

Molecular docking outcome

The molecular docking was carried out to investigated the binding of interaction between the synthesized compounds and the tested protein theoretically. The synthesized compounds were analyzed *via* Auto dock vina to interpret their binding activity relationship with protein structure PDB:3ERT was selected for molecular docking studies of due to good parameters for experimental resolution with the binding sites of protein receptor recognized as binding affinity which observed *via* hydrogen bonding π– π interaction, it consists van der wall interaction. The results of all the synthesized compounds and proteins with higher binding energies values were summarized in Table 1. The compounds stability of the best-docked pose was estimated by determining the protein's hydrogen bonding interactions with compounds. Based on these results, enones (2*E*)–1–(9*H*–fluoren –2–yl)–3–(3– nitrophenyl) prop–2–en–1–one (**12**) and 4-aminophenylstryl biphenyl ketone **(16)** are best docked (ΔG = – 8.01 and -7.92) with protein 1J3I. The highest binding energy observed for the compound (*E*)-1-(9*H*-fluoren-2-yl)-3-(isoquinolin-5-yl)prop-2-en-1-one ΔG -9.71 (kcal/mol) **(33)** with 3ERT protein. The docking score values and H- bonding interaction was done for all the synthesized compounds. Binding energy values were also calculated; it consists of H-bonding, π-π interactions, cation-π interactions, *etc*. The hydrogen bonding distance for (*E*)-1-(9H-fluoren-2-yl)-3-(isoquinolin-5-yl)prop-2-en-1-one **(33)** with proteins closet atom distance are 3.39 and 3.94. The interactions with various amino acid residues such as, ILED:403, ILED:379, PHED:375, ARGD:377, ARGD:402; ALAB:60, LYSB:56, METB:55, CYSB:59, ARGB:122 and GLU:323, GLU353, ARGA:394, META:357, PROA:324, ARGA:394, TRPA:393. The 2D and 3D Structures of good binded enones are shown in Fig. 3.

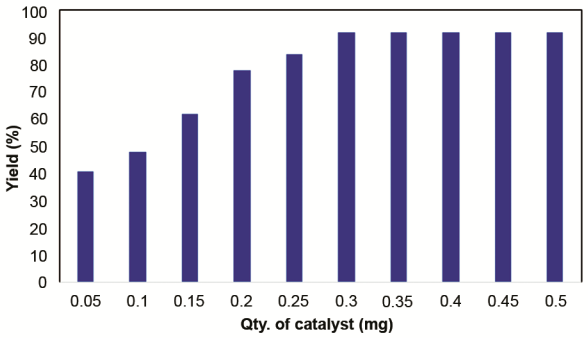


Fig. 1 — Effect of catalyst on the yield of enone **27**

Antimicrobial activity

Antibacterial activity

The measured antibacterial activities by means of the mm of zone of inhibition[2,33,40,51,56-66] values are presented in Table 2 and the mm of zone of inhibition in the petri-plates of chalcones is shown in Fig. 4. In general, all ketones possess antibacterial activity against their bacterial microbes. Enones **1-10, 12, 14-27, 29-34** are shown good antibacterial activity against *S. aureus* strain. Chalcones **1-7, 9, 10, 18-20, 22, 25** and **27-34** shows good antibacterial activity against *Enterococcus faecalis* microbe. All synthesized unsaturated ketones except **33** shows good antibacterial activity against *Escherichia coli* bacterial organism. The compounds **1-7, 9-26, 28-30, 32** and **33** where exhibits good antibacterial activity against *K. pneumonia strain.* The halogen substituted ketones shows significant antibacterial activity against

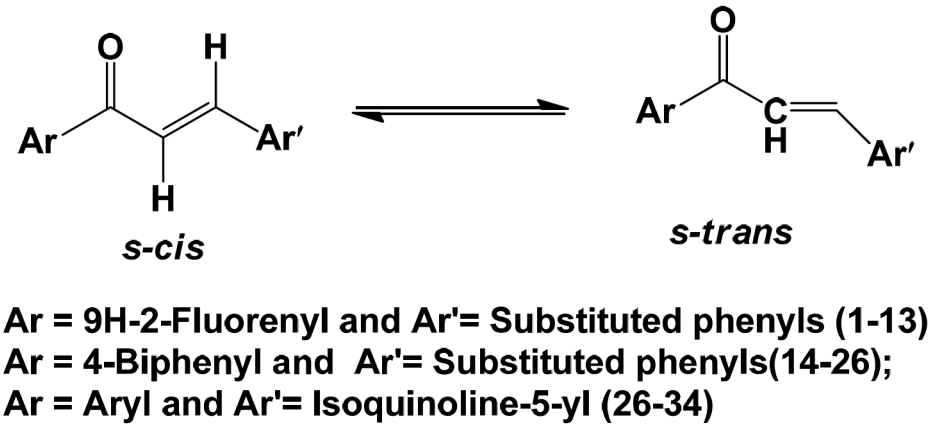


Fig. 2 — The *s-cis* and *s-trans* conformers of synthesized enones

Table 1 — The molecular docking protein-enone binding interaction results of ketones.

Entry	Ar	Ar′	PDB	Binding Energy(ΔG) kcal/mol
1	9*H*-Fluoren-2-yl	Phenyl	1J3I	–6.84
2	9*H*-Fluoren-2-yl	3-Aminophenyl	1J3I	–7.61
3	9*H*-Fluoren-2-yl	4-Aminophenyl	1J3I	–7.18
4	9*H*-Fluoren-2-yl	3-Bromophenyl	1J3I	–7.53
5	9*H*-Fluoren-2-yl	3-Chlorophenyl	1J3I	–7.47
6	9*H*-Fluoren-2-yl	4-Chlorophenyl	1J3I	–7.41
7	9*H*-Fluoren-2-yl	4-Dimethylaminophenyl	1J3I	–6.87
8	9*H*-Fluoren-2-yl	4-Hydroxyphenyl	1J3I	–7.27
9	9*H*-Fluoren-2-yl	4-Methoxyphenyl	1J3I	–7.61
10	9*H*-Fluoren-2-yl	4-Methylphenyl	1J3I	–7.58
11	9*H*-Fluoren-2-yl	2-Nitrophenyl	1J3I	–7.12
12	9*H*-Fluoren-2-yl	3-Nitrophenyl	1J3I	–8.01
13	9*H*-Fluoren-2-yl	4-Nitrophenyl	1J3I	–7.64
14	4-Biphenyl	Phenyl	1J3I	–6.21
15	4-Biphenyl	3-Aminophenyl	1J3I	–7.35
16	4-Biphenyl	4-Aminophenyl	1J3I	–7.92
17	4-Biphenyl	3-Bromophenyl	1J3I	–6.56
18	4-Biphenyl	3-Chlorophenyl	1J3I	–7.45
19	4-Biphenyl	4-Chlorophenyl	1J3I	–6.62
20	4-Biphenyl	4-Dimethylaminophenyl	1J3I	–6.73
21	4-Biphenyl	4-Hydroxyphenyl	1J3I	–6.76
22	4-Biphenyl	4-Methoxyphenyl	1J3I	–6.64
23	4-Biphenyl	4-Methylphenyl	1J3I	–6.56
24	4-Biphenyl	2-Nitrophenyl	1J3I	–7.53
25	4-Biphenyl	3-Nitrophenyl	1J3I	–7.68
26	4-Biphenyl	4-Nitrophenyl	1J3I	–7.24
27	4-Bromophenyl	Isoquinoline-5-yl	3ERT	–8.89
28	4-Chlorophenyl	Isoquinoline-5-yl	3ERT	–8.21
29	3,4-Dimethoxyphenyl	Isoquinoline-5-yl	3ERT	–7.64
30	4-Methoxyphenyl	Isoquinoline-5-yl	3ERT	–7.98
31	2-Thienyl	Isoquinoline-5-yl	3ERT	–7.64
32	4-Biphenyl	Isoquinoline-5-yl	3ERT	–8.86
33	9*H*-Fluorene-2-yl	Isoquinoline-5-yl	3ERT	–9.71
34	Benzdioxol-5-yl	Isoquinoline-5-yl	3ERT	–7.91

their strains then other substituted compounds. Here the inductive, hyper-cojnugative effects of the substituents of the ketones enhances the antibacterial activity.

Antifungal activity

The experimentally assessed *in vitro* antifungal activities of the synthesized chalcones by means of mm of zone of inhibitions[2,33,40,51,56-66] were shown in Table 3 and the statistical comparative column chart was shown in Fig. 5. In this study, all ketones active for showing their antifungal activity against their fungal microbes. Enones **1-7, 9-11, 14-21, 23, 25, 26, 28, 30** and **32** are exhibits their good antifungal activity against *C. albicans* fungal microbe. The unsaturated ketone **1-7, 14-20, 28** and **30** were shows good antifungal activities against *C. tropicalis* fungal strains. Comparatively, the halogen substituted ketones shows more antifungal activity then other substituted compounds. Here the inductive both (+I and –I) and hyperconjugation effects raises the antifungal activity against the fungal organism.

Antimalarial activity

The measured antimalarial activities of all synthesized aryl unsaturated ketones are shown in

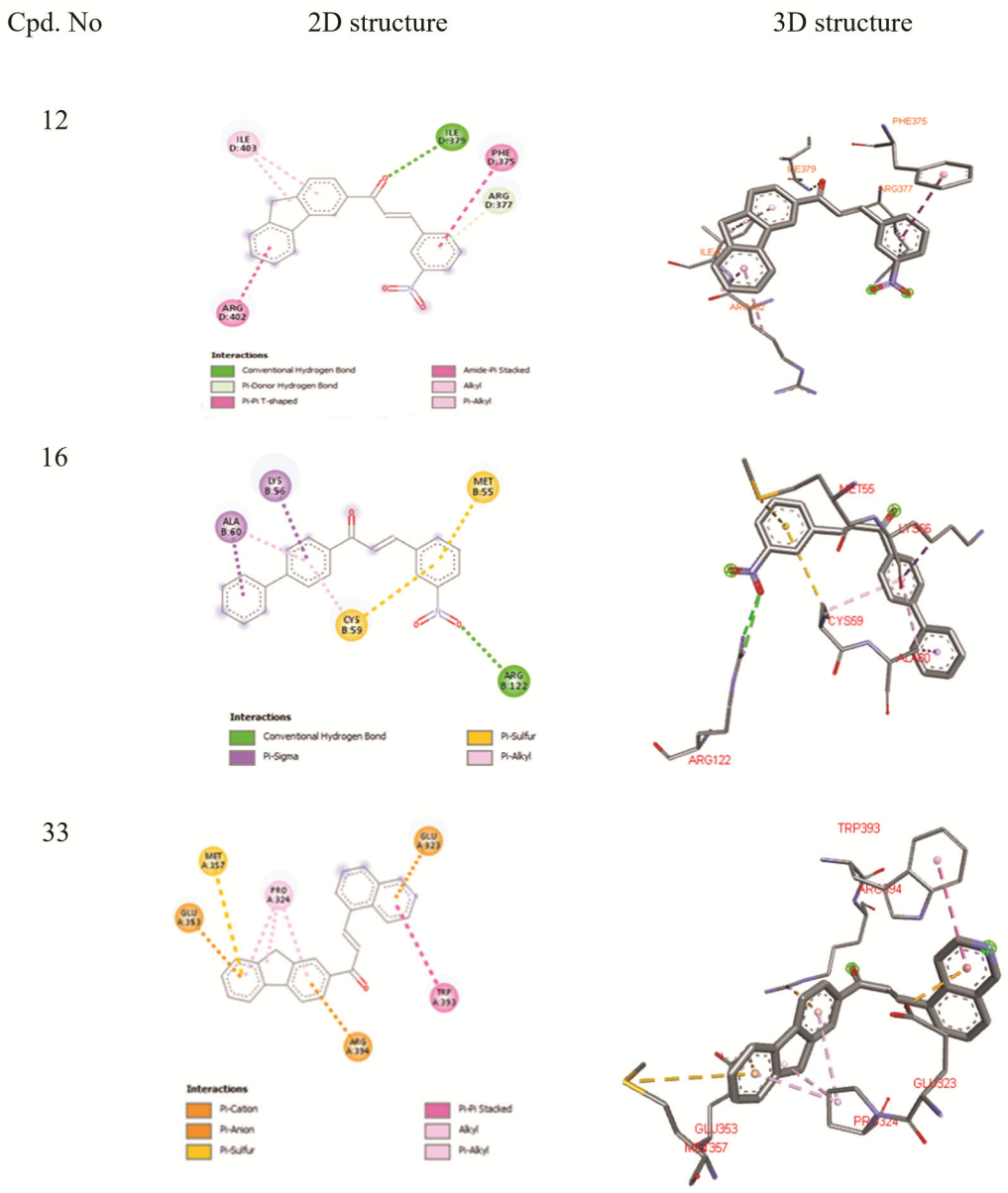


Fig. 3 — The 2D and 3D Structures of good binded enones with protein

Table 2 — The antimicrobial activities of synthesized enones

Entry	Substituents in Aldehyde/Ketone	Zone of inhibition (mm)					
		Antibacterial activity				Antifungal activity	
		S. aureus	*E. faecalis*	*E. coli*	*K. pneumonia*	*C. albicans*	*C. tropicalis*
		Substituted styryl 9*H*-fluorenyl ketones					
1	H	21	17	19	20	19	18
2	3–NH_2	20	16	21	19	18	15
3	4–NH_2	22	19	22	21	19	16
4	3–Br	24	21	23	23	21	20
5	3–Cl	25	22	24	22	22	19
6	4–Cl	25	23	26	25	22	20

(*contd.*)

Table 2 — The antimicrobial activities of synthesized enones *contd.*

Entry	Substituents in Aldehyde/Ketone	Zone of inhibition (mm)					
		Antibacterial activity				Antifungal activity	
		S. aureus	*E. faecalis*	*E. coli*	*K. pneumonia*	*C. albicans*	*C. tropicalis*
		Substituted styryl 9*H*-fluorenyl ketones					
7	4–$N(CH_3)_2$	19	18	17	18	16	17
8	4–OH	16	14	16	13	10	9
9	4–OCH_3	20	19	20	22	19	11
10	4–CH_3	19	18	20	19	17	13
11	2–NO_2	12	10	16	19	15	11
12	3–NO_2	16	14	17	20	12	9
13	4–NO_2	14	13	18	21	9	8
		Substituted styryl-4-biphenyl ketones					
14	H	19	18	21	17	18	16
15	3–NH_2	18	16	18	16	22	19
16	4–NH_2	21	22	21	23	21	20
17	3–Br	23	22	24	25	22	21
18	3–Cl	24	24	23	25	21	20
19	4–Cl	25	25	25	24	21	20
20	4–$N(CH_3)_2$	20	19	21	20	18	16
21	4–OH	16	14	19	17	15	14
22	4–OCH_3	19	16	18	19	12	11
23	4–CH_3	17	14	16	18	16	10
24	2–NO_2	16	12	17	17	14	9
25	3–NO_2	19	15	19	20	17	8
26	4–NO_2	18	14	20	21	16	9
		5-isoquinolinostyryl substituted aryl methyl ketones					
27	4–Br	19	15	15	13	11	09
28	4–Cl	15	16	21	17	15	16
29	3,4–$(OCH_3)_2$	18	16	20	16	14	13
30	4–OCH_3	22	23	22	20	17	15
31	2–Thienyl	19	15	19	13	09	09
32	4–Biphenyl	16	20	21	17	15	16
33	9*H*–Fluorene-2-yl	20	17	14	15	11	08
34	Benzdioxol-5-yl	16	19	17	14	13	11
	Standard	Chloramphenicol				Fluconazole	
		26	25	27	26	23	21

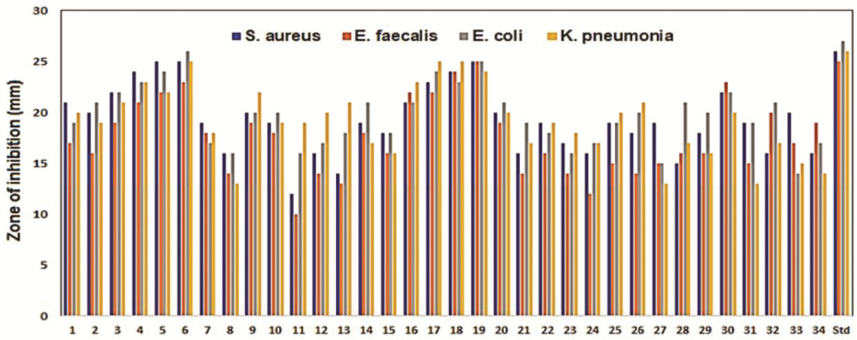


Fig. 4 — Clustered column chart for the antibacterial activities of synthesized enones

Table 3. All ketones are active in antimalarial activity. Among these the halogen substituted and isoquinoline enones **4-6, 12, 16-20, 27-34** shows good and moderate antimalarial activity. In halogen substituted system, the inductive effect of chlorine enhances the malarial activity and then bromo substituent. The electron withdrawing nitro group shows moderate antimalarial activity. The isoquinoline enones (**27-34**) shows good antimalarial activity. Here the bromo and chloro substituents show equal antimalarial activity.

Table 3 — The *in vitro* antimalarial activity of the synthesized enones

Entry	Ar	Ar′	Antimalarial activity
1	9*H*-Fluoren-2-yl	Phenyl	26±0.24
2	9*H*-Fluoren-2-yl	3-Aminophenyl	27±0.93
3	9*H*-Fluoren-2-yl	4-Aminophenyl	27±0.14
4	9*H*-Fluoren-2-yl	3-Bromophenyl	31±0.04
5	9*H*-Fluoren-2-yl	3-Chlorophenyl	33±0.04
6	9*H*-Fluoren-2-yl	4-Chlorophenyl	33±0.04
7	9*H*-Fluoren-2-yl	4-Dimethylaminophenyl	25±0.34
8	9*H*-Fluoren-2-yl	4-Hydroxyphenyl	23±0.21
9	9*H*-Fluoren-2-yl	4-Methoxyphenyl	25±0.65
10	9*H*-Fluoren-2-yl	4-Methylphenyl	29±0.62
11	9*H*-Fluoren-2-yl	2-Nitrophenyl	21±0.43
12	9*H*-Fluoren-2-yl	3-Nitrophenyl	31±0.94
13	9*H*-Fluoren-2-yl	4-Nitrophenyl	26±0.14
14	4-Biphenyl	Phenyl	23±0.12
15	4-Biphenyl	3-Aminophenyl	26±0.36
16	4-Biphenyl	4-Aminophenyl	31±0.84
17	4-Biphenyl	3-Bromophenyl	32±0.24
18	4-Biphenyl	3-Chlorophenyl	33±0.23
19	4-Biphenyl	4-Chlorophenyl	33±0.12
20	4-Biphenyl	4-Dimethylaminophenyl	30±0.92
21	4-Biphenyl	4-Hydroxyphenyl	26±0.25
22	4-Biphenyl	4-Methoxyphenyl	26±0.06
23	4-Biphenyl	4-Methylphenyl	26±0.54
24	4-Biphenyl	2-Nitrophenyl	23±0.29
25	4-Biphenyl	3-Nitrophenyl	24±0.94
26	4-Biphenyl	4-Nitrophenyl	29±0.95
27	4-Bromophenyl	Isoquinoline-5-yl	39±0.74
28	4-Chlorophenyl	Isoquinoline-5-yl	39±0.92
29	3,4-Dimethoxyphenyl	Isoquinoline-5-yl	36±0.21
30	4-Methoxyphenyl	Isoquinoline-5-yl	35±0.23
31	2-Thienyl	Isoquinoline-5-yl	36±0.12
32	4-Biphenyl	Isoquinoline-5-yl	33±0.05
33	9*H*-Fluorene-2-yl	Isoquinoline-5-yl	37±0.93
34	Benzdioxol-5-yl	Isoquinoline-5-yl	36±0.25

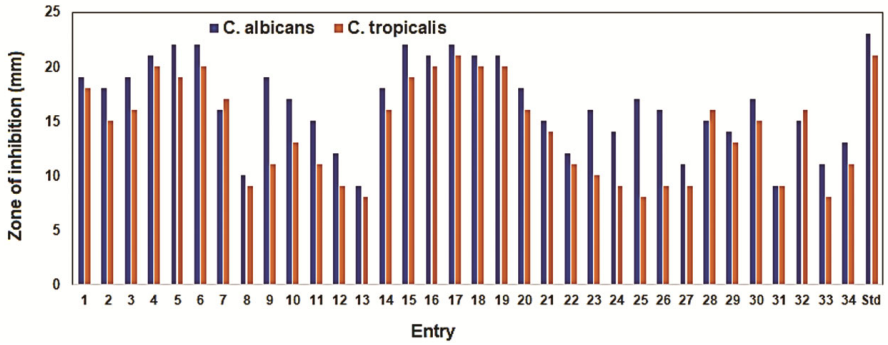
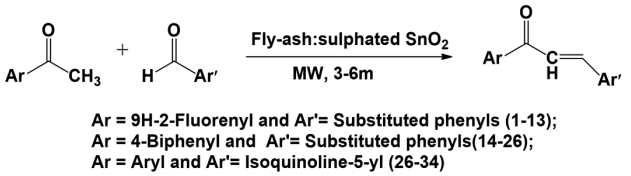


Fig. 5 — Clustered column chart for the antifungal activities of synthesized enones



Scheme 2 — Synthesis of various enones using fly-ash: sulphated SnO_2 catalyzed crossed aldol condensation under microwave irradiation

Then the –I effect of methoxy substituents shown lesser antimalarial activity as bromo substituent. The +I effect of methyl group slightly enhance the antimalarial activity. The electron-withdrawing +I effect of nitro group have lesser antimalarial activity comparatively chloro substituent except the enone **12**. The thienyl, electronegative oxygen atom containing the Benzodioxol and the +I effect of 9H fluorene ring system (**31, 33** and **34**) shows equal antimalarial activity.

Experimental Section

Materials and methods

All the chemicals used were purchased from Sigma-Aldrich and TCI chemical companies. Melting points of all chalcones were determined in open glass capillaries on Raga Tech electrical melting point apparatus and are uncorrected. Infrared spectra (KBr, 3000–800 cm^{-1}) were recorded, in Agilent Cary–630N infrared spectrophotometer. The NMR spectrometer was used for recording NMR spectra. The applied frequencies such as 400 and 100 MHz for ^1H and ^{13}C NMR spectra, deuterated chloroform and TMS as solvent and standard reference. Micro analysis of the ketones was performed in Perkin Elmer 240C CHN analyzer. The Mass spectra of all compounds recorded in Shimadzu Mass spectrometer using EI mode.

Synthesis of aryl enones

An appropriate equimolar quantity of aryl methyl ketones (2 mmol) aryl aldehydes (2 mmol), fly-ash: sulphated SnO_2 (0.35mg)[27] and 1 mL of water subjected to microwave irradiation for 3.5-6 minutes in a microwave oven in the period of 30 s (Samsung Grill, GW73BD Microwave oven, 230 V A/c, 50 Hz, 2450 Hz, 100–750 W(IEC–705) (Scheme 2). After completion of the reaction then cooled to RT, added 10 mL of dichloromethane, the organic layer had been separated which on evaporation yielded the solid product. The solid was recrystallized using ethanol to afforded pale-yellow glittering solids. The solid catalyst was washed with 7 mL of ethyl acetate, dried for 4h in a hot air oven and reused. The physiochemical constants, analytical and yields of all enones are summarized in Table 4.

Spectroscopic and analytical characterization data of the synthesized enones, 27-34

2(*E*)–5–Isoquinolinstryryl–4–bromophenyl ketone, 27: Mol. Formula $C_{18}H_{12}BrNO$. Mol. Wt. 338. IR (KBr): 1647 ($CO_{s\text{-}cis}$), 1580 ($CO_{s\text{-}trans}$ and CN), 1259 (CH_{ip}),756 (CH_{op}), 823 ($CH{=}CH_{op}$), 682 cm^{-1} ($C{=}C_{op}$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.616 (d, 1H, Hα), 8.559 (d,1H, Hβ), 7.613-8.137 (m, Ar-H, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 121.56 (Cα), 145.23 (Cβ), 188.74 (CO), 153.05 (C=N), 124.86-143.69 (Ar-C); MS: *m/z* 338[M^+] 27, 53, 103, 129, 128, 154, 186, 207, 208, 233, 283. Anal. Found (%) (Calcd): C, 63.88 (63.92); H, 3.59 (3.58); N, 4.09 (4.14).

2(*E*)–5–Isoquinolinstryryl–4–chlorophenyl ketone, 28: Mol. Formula $C_{18}H_{12}ClNO$. Mol. Wt. 293. IR (KBr): 1677 ($CO_{s\text{-}cis}$), 1587 ($CO_{s\text{-}trans}$ and CN), 1259 (CH_{ip}), 756 (CH_{op}), 820 ($CH{=}CH_{op}$), 682 cm^{-1} ($C{=}C_{op}$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.627 (d, 1H, Hα),8.560 (d, 1H, Hβ),7.608-8.120 (m, Ar-H, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 124.79(Cα),144.12(Cβ), 188.57 (CO),153.29 (C=N),126.82-143.46 (Ar-C); MS: *m/z* 293[M^+] 27, 52, 59, 77, 111, 128, 139, 154, 165, 233. Anal. Found (%) (Calcd): C, 73.55 (73.60); H, 4.13 (14.12); N, 4.72 (4.77).

2(*E*)–5–Isoquinolinstryryl–3,4–dimethoxyphenyl ketone, 29: Mol. Formula $C_{20}H_{17}NO_3$. Mol. Wt. 319. IR (KBr): 1651 ($CO_{s\text{-}cis}$), 1580 ($CO_{s\text{-}trans}$ and CN), 1241(CH_{ip}), 730 (CH_{op}), 823 ($CH{=}CH_{op}$), 670 cm^{-1} ($C{=}C_{op}$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.599(d, 1H, Hα), 8.455 (d, 1H, Hβ), 3.920 (s, 6H, $(OCH_3)_2$), 7.260-8.580 (m, Ar-H, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 123.25 (Cα), 143.78 (Cβ), 187.94 (CO), 153.35 (C=N), 56.11 (OCH_3), 125.09-153.55 (Ar-C); MS: *m/z* 319[M^+]27, 53, 112, 128, 137, 154, 165, 182, 191, 207, 263, 266. Anal. Found (%) (Calcd): C, 75.18 (75.22); H, 5.38 (5.37); N, 15.01(15.03).

2(*E*)–5–Isoquinolinstryryl–4-methoxyphenyl–ketone, 30: Mol. Formula $C_{19}H_{15}NO_3$. Mol. Wt. 289. IR (KBr): 1654 ($CO_{s\text{-}cis}$), 1595 ($CO_{s\text{-}trans}$ and CN),

Table 4 — The physiochemical constants, time and yields of the synthesized enones

Entry	Ar	Ar′	M.F.	M.W	Yield (%)	Time(m)	M.p. (˚C)
1	9*H*-Fluoren-2-yl	Phenyl	$C_{22}H_{16}O$	296	92	5	150-151(149-150)[67]
2	9*H*-Fluoren-2-yl	3-Aminophenyl	$C_{22}H_{17}NO$	311	95	4.5	97-98(95-96)[67]
3	9*H*-Fluoren-2-yl	4-Aminophenyl	$C_{22}H_{17}NO$	311	90	4	85-96(93-94)[67]
4	9*H*-Fluoren-2-yl	3-Bromophenyl	$C_{22}H_{15}BrO$	375	91	3.5	127-128(127-128)[67]
5	9*H*-Fluoren-2-yl	3-Chlorophenyl	$C_{22}H_{15}ClO$	331	95	4	43-44 (43-44)[67]
6	9*H*-Fluoren-2-yl	4-Chlorophenyl	$C_{22}H_{15}ClO$	331	95	5	84-85 (84-85)[67]
7	9*H*-Fluoren-2-yl	4-Dimethylaminophenyl	$C_{24}H_{21}NO$	339	90	5	89-90 (88-89)[67]
8	9*H*-Fluoren-2-yl	4-Hydroxyphenyl	$C_{22}H_{16}O_2$	312	93	4.5	91-92 (93-94)[67]
9	9*H*-Fluoren-2-yl	4-Methoxyphenyl	$C_{23}H_{18}O_2$	326	96	4	94-95 (94-95)[67]
10	9*H*-Fluoren-2-yl	4-Methylphenyl	$C_{23}H_{18}O$	310	95	4	104-104(103-104)[67]
11	9*H*-Fluoren-2-yl	2-Nitrophenyl	$C_{22}H_{15}NO_3$	341	90	5.5	91-92(90-91)[67]
12	9*H*-Fluoren-2-yl	3-Nitrophenyl	$C_{22}H_{15}NO_3$	341	91	6	77-78 (77-78)[67]
13	9*H*-Fluoren-2-yl	4-Nitrophenyl	$C_{22}H_{15}NO_3$	341	93	6	85-86 (85-86)[67]
14	4-Biphenyl	Phenyl	$C_{21}H_{16}O$	284	93	3.5	155-156 (156)[67]
15	4-Biphenyl	3-Aminophenyl	$C_{21}H_{17}NO$	229	93	4.5	116-117(115-116)[67]
16	4-Biphenyl	4-Aminophenyl	$C_{21}H_{17}NO$	229	91	5	85-87(85-86)[67]
17	4-Biphenyl	3-Bromophenyl	$C_{21}H_{15}BrO$	363	93	4.5	118-119(117-118)[67]
18	4-Biphenyl	3-Chlorophenyl	$C_{21}H_{15}ClO$	319	92	4	154-155(153-154)[67]
19	4-Biphenyl	4-Chlorophenyl	$C_{21}H_{15}ClO$	319	94	4.5	185-186(184-185)[67]
20	4-Biphenyl	4-Dimethylaminophenyl	$C_{23}H_{21}NO$	327	94	5.5	120121(118-119)[67]
21	4-Biphenyl	4-Hydroxyphenyl	$C_{21}H_{16}O_2$	300	93	5	110-111(109-110)[67]
22	4-Biphenyl	4-Methoxyphenyl	$C_{22}H_{18}O_2$	314	97	5.5	122-123 (123-124)[67]
23	4-Biphenyl	4-Methylphenyl	$C_{22}H_{18}O$	298	95	4	116-117 (117-118)[67]
24	4-Biphenyl	2-Nitrophenyl	$C_{21}H_{15}NO_3$	329	93	4.5	181-182(179-180)[67]
25	4-Biphenyl	3-Nitrophenyl	$C_{21}H_{15}NO_3$	329	93	4	183-184 (183-184)[67]
26	4-Biphenyl	4-Nitrophenyl	$C_{21}H_{15}NO_3$	329	94	3.5	189-190(190-191)[67]
27	4-Bromophenyl	Isoquinoline-5-yl	$C_{18}H_{12}BrNO$	338	92	4	180-110
28	4-Chlorophenyl	Isoquinoline-5-yl	$C_{18}H_{12}ClNO$	293	94	5.5	135-137
29	3,4-Dimethoxyphenyl	Isoquinoline-5-yl	$C_{20}H_{17}NO_3$	319	93	5	180-181
30	4-Methoxyphenyl	Isoquinoline-5-yl	$C_{19}H_{15}NO_2$	289	97	4	85-57
31	2-Thienyl	Isoquinoline-5-yl	$C_{16}H_{11}NOS$	265	93	5.5	98-100
32	4-Biphenyl	Isoquinoline-5-yl	$C_{24}H_{17}NO$	335	94	5	95-97
33	9*H*-Fluorene-2-yl	Isoquinoline-5-yl	$C_{25}H_{17}NO$	347	91	6	90-92
34	Benzdioxol-5-yl	Isoquinoline-5-yl	$C_{19}H_{13}NO_3$	303	93	5.5	75-77

1248 (CH $_{ip}$), 741 (CH $_{op}$), 827 (CH=CH $_{op}$), 682 cm^{-1} (C=C$_{op}$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.566(d, 1H, Hα),7.954 (d, 1H, Hβ),6.777- 9.189(m, Ar-H, 10H), 3.734 (3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 125.27ppm(Cα), 143.34(Cβ), 188.05(CO), 153.2(C=N), 55.54(OCH_3),113.99- 163.68(Ar-C); MS: *m/z* 289[M^+] 27, 53, 56, 77, 82, 107, 128, 132, 154, 161, 182, 207, 212, 233, 236. Anal. Found (%) (Calcd): C, 78.85 (78.87); H, 5.24(5.23); N, 4.80 (4.84).

2(*E*)–5–Isoquinolinstryryl–2–thiophenyl ketone, 31: Mol. Formula $C_{16}H_{11}NOS$. Mol. Wt. 265. IR (KBr): 1651 (CO$_{s\text{-}cis}$), 1513 (CO$_{s\text{-}trans}$ and CN), 1233(CH$_{ip}$), 723 (CH $_{op}$), 823 (CH=CH $_{op}$), 670 cm^{-1} (C=C$_{op}$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.544(d, 1H, Hα),8.574 (d, 1H, Hβ), 7.605-8.111 (m, Ar-H, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 125.10 (Cα),145.22 (Cβ),181.55 (CO),153.22 (C=N),126.84-144.01 (Ar-C); MS: *m/z* 265[M^+] 212, 188, 182, 162, 154, 137,128, 110, 103, 77, 53. Anal. Found (%) (Calcd): C, 72.43(72.47); H, 4.18(4.22); N, 5.28((5.25).

2(*E*)–5–Isoquinolinstryryl–4–biphenylketone, 32: Mol. Formula $C_{27}H_{17}NO$. Mol. Wt. 335. IR (KBr): 1654 (CO$_{s\text{-}cis}$), 1587 (CO$_{s\text{-}trans}$ and CN), 1218(CH $_{ip}$),

827(CH $_{op}$), (CH=CH $_{op}$), 678 cm^{-1} (C=C$_{op}$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.458 (d, 1H, Hα), 8.580 (d, 1H, Hβ), (m, Ar-H, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 125.39 (Cα),145.30 (Cβ), 189.35(CO), 153.30 (C=N),126.95-145.90 (Ar-C); MS: *m/z* 335[M^+] 27, 50, 55, 57, 77, 127, 153, 155, 182, 183, 207, 279, 283. Anal. Found (%) (Calcd): C, 85.70 (85.68); H, 6.12 (6.16).

2(*E*)–5–Isoquinolinstryryl–2(9*H*)–fluorenyl ketone, 33: Mol. Formula $C_{25}H_{17}NO$. Mol. Wt. 347. IR (KBr): 1669(CO$_{s\text{-}cis}$), 1602 (CO$_{s\text{-}trans}$ and CN), 1211(CH $_{ip}$), 734 (CH $_{op}$), 823 (CH=CH $_{op}$), 670 cm^{-1} (C=C$_{op}$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.952 (d, 1H, Hα),8.501 (d, 1H, Hβ), 2.104 (2H, Flu-ring)6.937-8.481 (m, Ar-H, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 124.16(Cα),143.03 (Cβ),182.32 (CO), 153.04(C=N), 29.71 (CH_2)121.28-153.11(Ar-C); MS: *m/z* 347[M^+] 27, 53, 77, 114, 128, 154, 165, 182, 193, 219, 234, 270, 294. Anal. Found (%) (Calcd): C, 86.48 (86.43); H, 4.87 (4.93); N, 3.98 (4.03).

2(*E*)–5–Isoquinolinstryryl–5–benzodioxal ketone, 34: Mol. Formula $C_{19}H_{13}NO_3$. Mol. Wt. 303. IR (KBr): 1654 (CO$_{s\text{-}cis}$), 1580 (CO$_{s\text{-}trans}$ and CN), 1259(CH $_{ip}$), 760(CH $_{op}$), 801 (CH=CH $_{op}$), 715 cm^{-1} (C=C$_{op}$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.564 (d, 1H, Hα), 8.450 (d, 1H, Hβ), 6.028 (2H, -CH_2), 6.851-8.584 (m, Ar-H, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 125.01 (Cα), 143.98 (Cβ), 187.51 (CO), 153.22(C=N), 29.69 (-CH_2), 124.88-151.97 (Ar-C); MS: *m/z* 303[M^+] 27, 53, 70, 77, 121, 128, 149, 155, 175, 182, 233, 226, 250. Anal. Found (%) (Calcd): C, 75.30 (75.24); H, 6.57 (4.62); N, 5.54 (4.62).

Molecular Docking

Molecular docking of the synthesized enones were performed by decrypt the chemical interaction and binding conformation of the compounds in the binding sites of biological drug target against breast cancer. The ligand target interaction was examined using Auto Dock Tools 1.5.6, software after receiving modeled three-dimensional structure of a protein form (PDB ID: 3ERT[68] and 1J3I[69] All the docked compounds were drawn using Chem Draw ultra 7.0 as mole file and the energies of compounds were minimized then converted into the PDB format using open Babel 2.3.1 software. Water molecules were removed and hydrogen atoms were added to the protein amino acids. All the ligands and receptor were prepared for docking simulation and protonated. The optimized structure to a protein through hydrogen adding by solvation and default Kollman charge parameters were designate to the macromolecule atoms. Addition of Gasteiger charges to molecule as a ligand atom. After adding hydrogen, the model was saved in the format (PDBQT). A grid box comprised of 60 × 60 × 60 points distance by 0.375 Å and was focused on the XYZ binding site (x = 30.282, y = −1.913, and z = 24.207). The bond strength of the atom in the ligand was calculated using an Auto grid[33] Auto Dock Vina 1.5.6 utilized for the molecular docking simulation. The parameters of the Lamarckian Genetic Algorithm (LGA) were: 100 runs, elitism of 1, the mutation rate of 0.02, the population size of 100, and a crossover rate of 0.08 band 10,000,000 energy evaluations. A root means square deviation was used for clustering the results of docked conformation, tolerance of 1.0 Å. The docking outcomes were imaged using Discovery Studio Visualizer 4.0.

Antimicrobial activity

Measurement of antibacterial activity

The Kirby-Bauer[70] disc diffusion technique was employed for measuring the antibacterial potential of all enones using each two of gram-positive microbes namely *Staphylococcus aureus*, *Enterococcus faecalis* and two-gram negative bacterial strains such as *Escherichia coli* and *Klebsiella pneumonia*. In each petri plate about 15 mL of the test bacterial sample was spread uniformly over the solidified Mueller Hinton agar using sterile glass spreader. The plates could solidify for 5 minutes and 0.1% inoculums suspension was swabbed uniformly, and the inoculums could dry for 5 min. Wells were cut and 20 µL of the different concentration of test drug were added. The plates were then incubated at 37°C for 24 hours. The antibacterial activity was assayed by measuring the diameter of the inhibition zone formed around disc was used as a positive control. The zones of mm of inhibition were measured after 24 h. Chloramphenicol disc was used as a positive control.

Measurement of antifungal activity

Antifungal activity was measured using methods of well diffusion plates on agar[70]. To test the antifungal activity, 20 mL of Sabouraud Dextrose Agar was poured into each 15 cm Petri dish. *C.* albicans and C. tropicalis were grown in sabouraud dextrose broth at 27°C for 48 h. Growth was adjusted to OD (600 nm) of 0.1 by dilution with sabouraud dextrose broth.

Then, Wells were cut and 20 µL of the different concentration of test drug were placed on agar to load 10 and 15 µL of each spice sample (1 mg/mL). 100 units of Fluconazole, obtained from a local pharmacy, were served as a positive control. Inhibition zones were determined after incubation at 27°C for 48 h.

Antimalarial activity

The *P. falciparum* Thailand strain Thai and strain K1 will be used for this cell culture[52,54,55]. Culture was grown in complete medium consisting RPMI1640 supplemented with 11mM glucose, 27.5 mM medium hydrogen carbonate, 100 UI/mL penicillin, 100 µL/mL streptomycin and 8% heat-inactivated human serum albumin. Parasites were grown at 37°C, in human A+ red blood cells (RBCs) at a 2% hematocrit, under 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. Increasing concentration of the different chalcones and amines were dissolved in dimethyl sulfoxide (DMSO) and tested for their inhibitory effect toward the *P. falciparum* intraerythrocytic development. Parasites were allowed to grow at 37°C for 24h in a candle jar, the 0.5µCi ^{3}H-hypoxanthine was added per well. After an additional 24 h incubation period, plates are freeze thawed and harvested on filters. Dried filters were moistened in scintillation liquid mixture and counted in a 1450 Micro-beta counter. Growth inhibition in percent was calculated from the parasite associated radioactivity. Hundred percent ^{3}H-hypoxanthine incorporation was determined from control growth in the absence of the retinoid-like chalcones. Values for the IC_{50} were determined. Each mean concentration was estimated from three different experiment sets.

Conclusions

There are three series of various substituted aryl enones were synthesized using greener Crossed-Aldol condensation method. In this method the obtained yields are more than 90%. The synthesized enones were analyzed by micro analysis and spectroscopic data. The molecular docking study, antimicrobial and antimalarial activity analysis of these enones were studied. From the docking analysis, the enones **12, 16** and **33** shows good protein-ligand interactions. In general, all enones shows antimicrobial activity against their microbes. Notably, the halogen substituted enones were shows more antimicrobial activity than other compounds. Regarding the measurement of in-vitro anti-malarial activity of enones, the isoquinolinyl styryl substituted aryl ketones (**27-34**) exhibits more antimalarial activity.

Acknowledgements

Authors thank to (i) DST-NMR facility, Department of Chemistry, Annamalai University, Annamalainagar-608002, India for recording NMR spectra of all compounds. (ii) RUSA-2, Field 1, Anti-Malarial Drug Synthesis, No. F3/RUSA/673/2022 dated 4-6-2022, Annamalai University, Annamalainagar 608 002, India for financial support.

References

1 Dinka Ma A, *Sci J Chem,* 10 (2022) 52.
2 Jung J C, Lee Y, Min D, Jung M & Oh S, *Molecules,* 22 (2017) E1872.
3 Verma S, Srivastava A K, Pandey O P, *Pharma Tutor,* 6 (2018) 2239.
4 Jayapal M R & Sreedhar N Y, *J Pharm sci Res,* 2 (2010) 647.
5 Venkat Reddy G, Maitraie G, Narsaiah D, Rambahu B & Rao R, *Synth Comm,* 31 (2001) 2884.
6 Mihir Ekanayaka U G, Weeratunga H, Weerasinghe J, Waclawik E R, Sun Z, Macleod J M O, Mullane A P & Ostrikov K, *Sustainable Mat Tech*, 32 (2022) e00394.
7 Christuraj P, Rajakumar P R, Geetha C, Vanangamudi G, Arulkumran R, Sundararajan R & Thirunarayanan G, *Int J Bioorg Chem,* 1 (2016) 31.
8 Palleros D R, *J Chem Edu,* 81 (2004) 1345.
9 Revathi R, Ratna Sree C, Jayakumar R, Visagaperumal D & Anbalagan N, *Pharmacopho* 4(2) (2013) 69.
10 Usha V, Thangaraj V & Thirunarayanan G, *Org Prep Procedures Int* (OPPI), 50 (2018**)** 463.
11 Marinozzi M, Tondi S, Marcelli G & Giorgi G, *Tetrahedron,* 50 (2014) 9491.
12 Ranganathan K Arulkumaran R, Kamalakkannan D, Sundararajan R, Sakthinathan S P, Vijayakumar P, Suresh S R, Vanangamudi G, Thirumurthy K, Mayavel P & Thirunarayanan G, *Int J Pharma Med Biol Sci,* 1 (2012) 85.
13 Swamy K M K, Yeh W B, Lin M J & Sun C M, *Curr Med Chem,* (2003) 2423.
14 Jharna M, Partha S B & Tanmoy K S, *Org Biomol Chem,* 22 (2024) 4528.
15 Younis B, *Catal*, 11 (2021) 46.
16 Adnan D, Singh B, Mehta S K, Kumar V & Kataria R, *Cur Res Green Sust Chem,* 3 (2020) 100041.
17 Alves Sobrinho R C M, De Oliveira P M, Montes D'Oca, C R, Russowsky D & Montes D'Oca M G, *R S C Adv,* 7 (2017) 3221.
18 Thirunarayanan G, Mayavel P & Thirumurthy K, *Spectrochim Acta*, 91A (2012) 22.
19 Shoreya S, Prakash C, Choudhary & Intodia K, *Chem Sci Trans,* 2 (2013) 348.
20 Basaif S A, Sobahi T R, Khalil A K & Hassan M A, *Bull Chem Soc,* 26 (2005)1677.

21 Xu Q, Yang Z, Yin D & Zhang F, *Cat Comm,* 9 (2008) 1582.
22 Blackwell H E, *Curr Opin Chem Biol,* 10 (2006) 212.
23 Kumar D, Suresh & Sandhu J S, *Green Chem Lette Rev,* 3 (2010) 286.
24 Thirunarayanan G, *Adv Appl Res* 6 (2014) 2104.
25 Kamalakkannan D, Senbagam R, Vanangamudi G & Thirunarayanan G, *J Mol Struc*, 1264 (2022) 133218.
26 Muthuvel I, Thirunarayanan G, Thangaraj V, Sundaramurthy N, Rajalakshmi S & Usha V, *Mater Today Proc,* 43 (2021) 2207.
27 Sekar K G, Janaki P, Muthuvel I, Usha V, Thirumurthy K & Thirunarayanan G, *Mater Today Proc,* (2021) 2214.
28 Rajasri S, Krishnakumar B, Sobral A J F N, Balachandran S, Swaminathan M & Muthuvel I, *Mat Today Proc,* 15 (2019) 480.
29 Balaji S, Manikandan V, Rajarajan M, Usha V, Rajalakshmi S, Venkatachalam P, Muthuvel I & Thirunarayanan G, *Mat Today Proc,* 22 (2020) 936.
30 John Joseph S, Ranganathan K, Suresh R, Arulkumaran R, Sundararajan R, Kamalakkannan D, Sakthinatha S P, Vanangamudi G, Dineshkumar S, Thirumurthy K, Muthuvel I, Thirunarayanan G & Viveksarathi K, *Mat Sci Appl Chem,* 34 (2017) 20.
31 Yan H, Huang D, Zhang J, Huang R, Fu Y & Wang W, *Adv Mat Res,* 1033-1034 (2014) 84.
32 Bhuiyan M M H, Hossain M I, Mahmud M M & Al-Amin M, *J Chem,* 1 (2011)7924.
33 Stefani, H A, Cella R, Do¨rr F A, Claudio M P, De Pereira P, Gomesa F P & Zenid G, *Tetrahedron Lett,* 46 (2003) 2001.
34 Munirajasekhar D, Himaja M & Mail S V, *J Hetero chem,* 51 (2014) 465.
35 Zhu Y, Li C, Zhang J, She M, Sun W, Wan K, Wang Y, Yin B, Liu P & Li J, *Org Lett,* 17 (2015) 3875.
36 Venkateshwarlu K, Chakradar Rao G, Reddy V M & Narasimha Reddy Y, *J Iranian Chem Soc*, 11 (2014) 1627.
37 Xu Z, Guo J, Yang Y, Zhang M, Ba M, Li Z, Cao Y, He R, Yu M, Zhou H, Li X, Huang X, Guo Y & Guo C, *Eur J Medi Chem,* 123 (2016) 316.
38 Kalmode H P, Vadagaonkar K S, Murugan K & Chaskar A C, *New J Chem,* 39 (2015) 4639.
39 Thirunarayanan G & Sekar K G, *Der Pharma Chem* 5 (2013) 148.
40 Duval A R, Carvalho P H, Soares M C, Gouvea D P, Siqueira G M, Lund R G & Cunico W, *Sci World J*, 11 (2011) 1489.
41 Rashid H U, Yiming X U, Ahmad N, Muhammad Y & Wang L, *Bioorg Chem,* 87 (2019) 365
42 Manikala V & Madhusudhan Rao V, *Chem Data Coll,* 28 (2020) 100423.
43 Lin Y M, Zhou Y, Flavin M T, Zhou L M, Nie W & Chen F C, *Bioorg Med Chem*, 10 (2002) 2802.
44 Tomar V, Bhattacharjee G, Kamaluddin G, Rajakumar S, Srivastava S K & Puri K, *Euro J Med Chem,* 45 (2010)751.
45 Sharma R, Kumar R, Kodwani R, Kapoor S, Khare A, Bansal R, Khurana S, Singh S, Thomas J, Roy B, Rajendra P, Shukla S & Sanjay K, *Anti-Cancer Agent Med Chem,* 16 (2016) 211.
46 Elkhalifa D, Al-Hashimi I, Moustafa A A & Khalil A, *J Drug Targeting,* 29 (2021) 419.
47 Turkovic N, Ivkovic B, Kotur-Stevuljevic J, Tasic M, Markovic B & Vujic Z, *Curr Pharma Design,* 26 (2020) 814.
48 Verhaeghe P, Azas N, Gasquet M, Bastien Hutter S, Ducros C M, Le Laget S, Rault, Rathelota P & Vanellea P, *Bioorg Med Chem Lett,* 18 (2008) 401.
49 Divya J, Gayathri P, Muthuvel I & Thirunarayanan G, *Indian J Chem,* 62 (2023)1185.
50 Muthuvel I, Manikandan S, Thirunarayanan G, Usha V & Sathiyendiran V, *Indian J Chem,* 62 (2023) 138.
51 Usha V, Thirunarayanan G & Manikandan S, *Indian J Chem,* 61 (2022) 527.
52 Vinindwa B, Akpeko Dziwornu G & Masamb W, *Molecules,* 26 (2021) 4093.
53 Liu M, Wilairat P & Go M L, *J Med Chem,* 44 (2001) 4452.
54 Narender T, Shweta, Tanvir K, Srinivasa Rao M, Srivastava K & Puri S K, *Bioorg Med Chem Lett,* 15 (2005) 2455.
55 Tadigoppula N, Korthikunta V, Gupta S, Kancharla P, Khaliq T, Soni A, Srivastava R K, Srivastava K, Puri S K, Raju K S R, Wahajuddin Sijwali P S, Vikash K & Mohammad I S, *J Med Chem,* 56 (2013) 45.
56 Sivakumar P M, Prabhakar P K & Doble M, *Med Chem Res*, 20 (2011) 492.
57 Hasan S A, Elias A N & Farhan M S, *Der Pharm Chem,* 7 (2015) 42.
58 Adibi H, Mojarrad J S, Asgharloo H & Zarrini G, *Med Chem Res,* 20 (2010) 1324.
59 Chlupacova M K, Tyllova V V, Finkova L R, Kunes J, Buchta V, Vejsova M, Paterova P, Semelkova L, Jandourek O & Opletalova V, *Drugs Mol,* 21 (2016) 1421.
60 Nalini S, Divya J, Gayathri P, Muthuvel I, Thirunaryanan G, Manikandan V & Usha V, *Indian J Chem,* 63 (2024) 557.
61 Patel R N & Piyush P V, *Euro J Exper Biol,* 2 (2012) 1496.
62 Thirunarayanan G, *World Sci News,* 118 (2019)16.
63 Sakthinathan S P, Suresh R, Kamalakkannan D, Mala V, Sathiyamoorthi K, Vanangamudi G & Thirunarayanan G, *J Chilean Chem Soc,* 63 (2018) 3923.
64 Usha V, Thangaraj V & Thirunarayanan G, *Indian J Chem,* 56 (2017) 1102.
65 Thirunarayanan G, *Macedonian J Chem Chem Eng,* 36 (2017) 14.
66 Thirunarayanan G, *Arabian J Chem,* 10 (2017) S643.
67 Thirunarayanan G & Vanangamudi G, *E. J. Chem*, 4 (2007) 90-96
68 Prasetiawati R, Zamri A, Barliana M I & Muchtaridi M, *J appl pharm sci,* 9 (2019) 028.
69 Syahri J, Rullah K, Armunanto R, Yuanita, E, Nurohmah B A, Aluwi M F F M, Kok Wai L & Purwono B, *J Asian Pacific Trop Dis,* 7 (2017) 13.
70 Bauer A W, Kirby W M M, Sherris J C & Truck M, *Am J Clin Pathol,*45 (1996) 498.