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ORIGINAL PAPER

Superfast synthesis, antibacterial and antifungal studies of halo-aryl and heterocyclic tagged 2,3-dihydro-1*H*-inden-1-one candidates

Rahul A. Shinde[1] · Vishnu A. Adole[1] · Bapu S. Jagdale[1] · Thansing B. Pawar[2]

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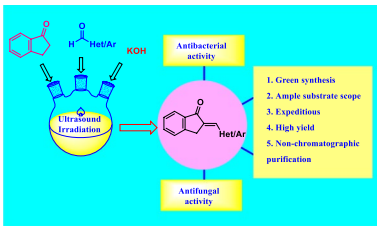
Abstract

We describe a successful synthesis of halo-aryl and heterocyclic labelled 2,3-dihydro-1*H*-inden-1-one derivatives, as well as their antibacterial and antifungal properties. A total of 15 derivatives from 2,3-dihydro-1*H*-inden-1-one were synthesized by grinding, stirring, and ultrasound irradiation methods. The findings revealed that the ultrasound technique is increasingly satisfactory in terms of time and synthetic performance. The synthesized compounds have been tested for their antimicrobial activities against two Gram-positive (*Staphylococcus aureus* and *Bacillus subtilis*) and two Gram-negative bacteria (*Escherichia coli* and *Proteus vulgaris*), and also two fungal agents (*Aspergillus niger* and *Candida albicans*). Most of the compounds were found to exert potent antibacterial action with broad-spectrum antibacterial activity. Likewise, few compounds were revealed to have potent antifungal properties against *A. niger* and *C. albicans*. The synthesized compounds were characterized by FT-IR, ^{1}H NMR, ^{13}C NMR, and HRMS spectral techniques.

Graphic abstract



Keywords 2,3-Dihydro-1*H*-inden-1-one · Antibacterial · Antifungal · Ultrasound irradiation

Introduction

Microorganisms are living things that have ability to replicate, flourish, and spread rapidly and productively. They can adjust to their environments and evolve in ways that ensure their long-term survival. The worldwide problem of antimicrobial resistance is rapidly becoming a major health problem [1–4]. It has been postulated that the resistance of microbes to current antimicrobials could be overcome by developing new synthetic organic compounds by updating the current antimicrobial concept, and discovering new agents with promising activity and structure [5–7]. 2,3-Dihydro-1*H*-inden-1-one is a fused molecule containing cyclopentanone and a benzene ring. A literature survey reveals that compounds containing a 2,3-dihydro-1*H*-inden-1-one structure exhibit the great profile of pharmacological properties [8]. Some noticeable examples include activities like anticancer [9, 10], anti-inflammatory [11, 12], antioxidant [13], anti-Alzheimer disease [14], etc. Likewise, the presence of a halogen atom

✉ Bapu S. Jagdale
dr.jagdalebs@gmail.com

[1] Department of Chemistry, Mahatma Gandhi Vidyamandir's Arts, Science and Commerce College, Manmad, (Affiliated to Savitribai Phule Pune University, Pune), Nashik 423 104, India

[2] Department of Chemistry, Mahatma Gandhi Vidyamandir's Loknete Vyankatrao Hiray Arts, Science and Commerce College Panchavati, (Affiliated to Savitribai Phule Pune University, Pune), Nashik 422 003, India

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in the drug molecule can change its properties dramatically. Especially, fluorinated compounds possess a broad range of medicinal properties. Some examples of biologically active compounds containing above said properties are depicted in Fig. 1. The excellent activities shown by them are anticancer, anaesthetics, antibacterial, antiviral, antimalarial, antidepressants, and many more [15, 16]. On the other hand, the applications of heterocyclic compounds have been expanded in the last decade. Heterocyclic compounds are known to display tremendous therapeutic applications [17, 18].

Green chemistry has carved out a distinct niche for itself in synthetic organic chemistry. The green chemistry fields like microwave [19, 20], ultrasound [21–24], grindstone chemistry [25, 26], benign reaction media [27–31], nanochemistry [32–37], and ionic liquids [38, 39] are tremendously used to develop environmental-friendly approaches. Antimicrobial agents become very interesting to research when looking at these important aspects of modern times. In light of all these crucial points, we would like to report the expeditious synthesis, antibacterial, and antifungal studies of halo-aryl and heterocyclic tagged 2,3-dihydro-1*H*-inden-1-one derivatives. To the best of our knowledge, this is the first report on combined investigation on green synthesis, antibacterial and antifungal screening of 2-arylideneindanones. In the present investigation, synthesized compounds have been tested for their biological activities against two Gram positive (*Staphylococcus aureus* and *Bacillus subtilis*) and two Gram negative bacteria (*Escherichia coli* and *Proteus vulgaris*), and two fungal agents (*Aspergillus niger* and *Candida albicans*).

Results and discussion

Chemistry

We began our investigation to determine the most effective method for synthesizing the titled compounds. Three environmentalfriendly synthetic methods were addressed; grinding, stirring, and ultrasound irradiation. The reaction of 2,3-dihydro-1*H*-inden-1-one with thiophene-2-carbaldehyde was selected as a standard reaction for the exploration of the better synthetic method. Ethanol and KOH were chosen as solvent and base, respectively. We performed three parallel reactions; grinding, stirring, and ultrasound strategies. To our credit, all three reactions yielded the corresponding (*E*)-2-(thiophen-2-ylmethylene)-2,3-dihydro-1*H*-inden-1-one in excellent yield within 15 minutes. More importantly, the ultrasound irradiation required less reaction time and furnished more yield of the product as compared to the other two methods. Then, we shifted our emphasis on solvent comparison (Table 1). For that, we varied the solvents from non-polar to polar solvents. The outcome revealed that the polar protic solvents are better at giving more yield and that with less reaction time except water (Table 1). The non-polar solvents required long reaction run and also resulted in lesser yields as compared to polar aprotic and polar protic solvents. To mark the importance of KOH as a base, we performed same

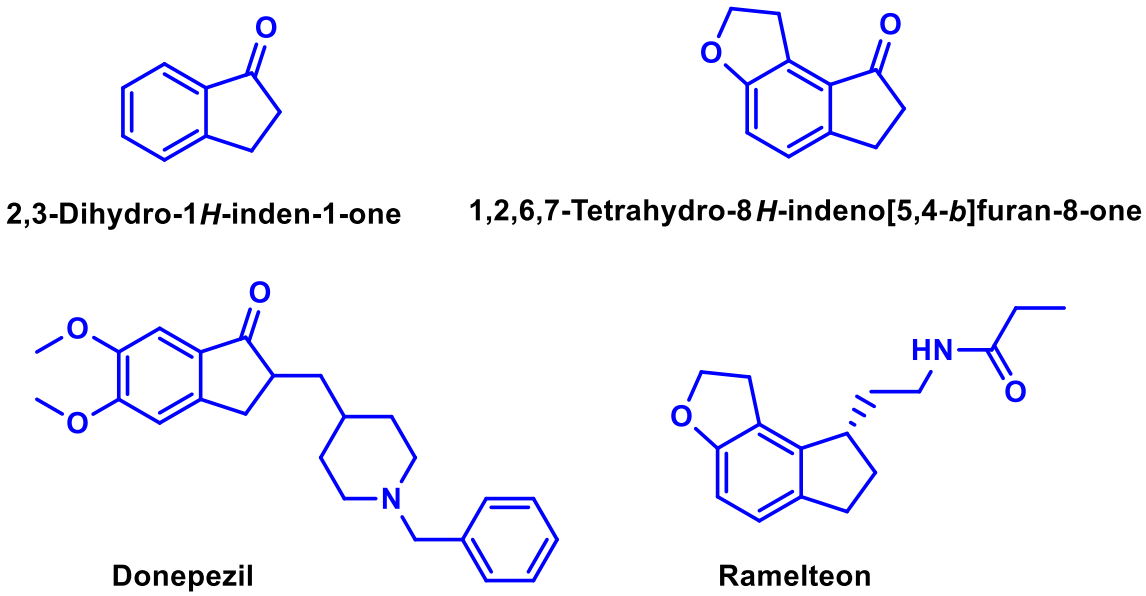
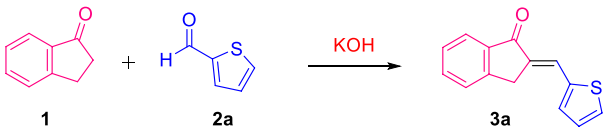


Fig. 1 Some biologically important intermediates and medicinal agents

Table 1 Solvent study for the synthesis of **3a**[a]

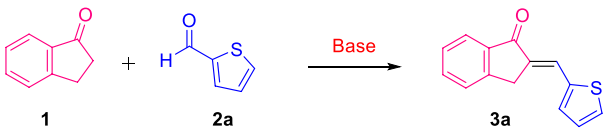


Entry	Solvent	Grinding		Stirring		Ultrasonic irradiation	
		Time/min	Yield/%[b]	Time/min	Yield/%[b]	Time/min	Yield/%[b]
1	$PhCH_3$	50	60	45	60	40	62
2	MeCN	35	70	32	75	30	75
3	CH_2Cl_2	40	70	42	72	38	75
4	THF	45	65	38	68	40	70
5	$CHCl_3$	40	72	40	76	30	78
6	H_2O	65	45	50	48	50	50
7	CCl_4	45	65	40	70	30	74
8	MeOH	18	80	15	82	12	88
9	AcOH	25	60	25	62	24	62
10	EtOH	15	85	10	86	09	97

[a]Reaction conditions: dihydro-1*H*-inden-1-one (10 mmol), thiophene-2-carbaldehyde (10 mmol), KOH (10 mmol), 5 cm^3 solvent at r.t

[b]Isolated yield of pure product

Table 2 Base study for the synthesis of **3a**[a]



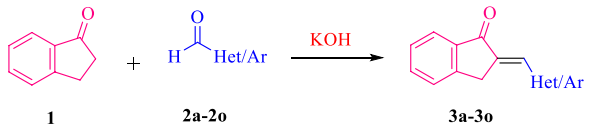
Entry	Base	Grinding		Stirring		Ultrasonic irradiation	
		Time/min	Yield/%[b]	Time/min	Yield/%[b]	Time/min	Yield/%[b]
1	K_2CO_3	45	60	40	60	38	70
2	Piperidine	50	65	50	67	40	70
3	NaOH	20	85	20	85	15	94
4	KOH	15	85	10	86	09	97

[a]Reaction conditions: dihydro-1*H*-inden-1-one (10 mmol), thiophene-2-carbaldehyde (10 mmol), base (10 mmol), 5 cm^3 ethanol, at r.t

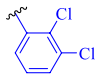
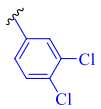
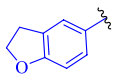
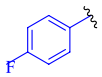
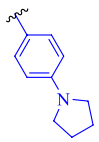
[b]Isolated yield of pure product

reaction using NaOH, piperidine, and K_2CO_3 (Table 2). However, none of the used bases could compete with KOH in terms of synthetic efficiency. Only NaOH came close to matching KOH's synthetic results, but KOH outperformed NaOH in terms of yield and reaction time. This affirmed that the best solvent is none other than ethanol and base as KOH. As all three methods were affording product formation within 15 minutes, we tested all three methods for all remaining reactions in ethanol solvent and KOH as a base. The scope and validity of the synthetic methods were tested for variety of heterocyclic and halogenated aromatic aldehydes (Table 3). All three methods were best at their task. In all instances the product yield was greater than 80%. The highest yield was recorded for the compounds **3g** and **3h** under ultrasound irradiation conditions. The ultrasound approach was more accomplished in terms of

Table 3 Substrate scope and physicochemical data of the synthesized compounds and comparison between grinding, stirring, and ultrasonic irradiation[a]



1 **2a-2o** **3a-3o**

Entry	Het/Ar	Grinding		Stirring		Ultrasonic irradiation		M.p. /°C
		Time/min	Yield/%[b]	Time/min	Yield/%[b]	Time/min	Yield/%[b]	
3a		15	85	10	86	9	97	122–124
3b		17	93	12	93	10	93	118–120
3c		20	92	17	92	15	92	110–112
3d		22	90	13	92	10	92	126–128
3e		12	91	10	90	08	95	153–155
3f		13	93	11	92	10	95	182–184
3g		15	95	08	96	08	97	154–158
3h		12	96	08	92	08	97	163–166
3i		13	90	13	91	12	94	132–134
3j		22	92	13	94	10	96	152–154
3k		15	85	10	87	07	88	163–165
3l		12	83	10	85	08	86	186–188
3m		13	89	11	92	10	94	162–164
3n		18	81	10	80	08	85	184–186
3o		15	90	10	91	10	94	120–122

[a]Reaction conditions: dihydro-1*H*-inden-1-one (10 mmol), thiophene-2-carbaldehyde (10 mmol), KOH (10 mmol), 5 cm^3 ethanol, at r.t

[b]Isolated yield of pure product

reaction yield and time by examining all reactions under three reaction conditions (Table 3).

Biological studies

Disc diffusion assay

Disc diffusion method were employed for the screening of the antibacterial and antifungal activities and the results are summarized in Table 4. The synthesized compounds were tested for their biological activities against two Gram-positive (*S. aureus* and *B. subtilis*) and two Gram-negative bacteria (*E. coli* and *P. vulgaris*), and also two fungal agents (*A. niger* and *C. albicans*). The compounds **3c**, **3d**, **3f**, and **3o** were found to apply strong antibacterial action with broad-spectrum antibacterial activity. The compounds **3b** and **3g** were exerted strong antifungal action against *A. niger* and *C. albicans*. Besides, other compounds have additionally shown great antimicrobial potential. The assays were performed in triplicate using Chloramphenicol and Amphotericin-B as standards. The compounds **3h**, **3l**, and **3n** have been found to exert null effect on both bacterial and fungal agents.

Resazurin microtiter plate assay

The resazurin microtiter plate assay (REMA) was used for checking the minimum inhibitory concentration (MIC) [29]. The REMA is a simple and inexpensive which is a routine method for checking cellular viability. The oxidation–reduction mechanism involves the reduction of blue color to pink by the metabolically active live cells. If blue color does not change, it indicates the absence of metabolically live cells. The MIC values of synthesized compounds were evaluated and the results are depicted in Table 5 which clearly stresses the differential sensitivity pathogens toward the synthesized compounds. The MIC results are expressed as the mean values of three independent experiments.

Structure–activity relationship studies

The various aromatic and hetero-aromatic aldehydes were exactly chosen to present diverse electronic condition to the molecules (Fig. 2 and Table 3). Therefore, various five membered and six membered hetero-aromatic aldehydes containing oxygen, nitrogen, and sulfur atoms were precisely selected. Besides, aromatic aldehydes containing chloro and fluoro substituents were also selected to test their antimicrobial action. Most of the synthesized compounds were exhibited wide range of antibacterial and antifungal activity. Amongst heterocyclic linked synthesized compounds; those containing sulfur and nitrogen atoms were exerted better antimicrobial activity. The compounds **3c**, **3d**, **3f**, and **3o** were found as strong antibacterial agents with broad-spectrum antibacterial activity. Especially the compound bearing 4-pyridyl ring (**3f**) was linked with the stronger antibacterial activity. It has exerted broad-spectrum antibacterial potential. Other compound which has exhibited nearly same antibacterial action is compound **3d** which contains thiazole system. The compound **3a** was active against three bacterial agents and inactive against *E. coli*. The heterocyclic linked

Table 4 Antibacterial and antifungal activity of synthesized compounds **3a–3o**

Entry	*E. coli*	*P. vulgaris*	*S. aureus*	*B. subtilis*	*A. niger*	*C. albicans*
3a	–	+++	+++	+++	++	–
3b	–	+++	–	++	+++	+++
3c	+++	+++	+++	++	–	–
3d	++++	++++	+++	+++	–	–
3e	+++	+++	–	++	–	–
3f	++++	++++	+++	++++	–	–
3g	–	++	–	++	+++	+++
3h	–	–	–	–	–	–
3i	–	–	–	++	–	–
3j	++	+++	++	++	++	–
3k	–	–	–	++	+++	–
3l	–	–	–	–	–	–
3m	+	+	–	+	++	++
3n	–	–	–	–	–	–
3o	++	+++	++	++	+++	–
Chloramphenicol	+++++	+++++	+++++	+++++	NA	NA
Amphotericin-B	NA	NA	NA	NA	++++	++++

+ ≤5 mm zone, ++ = 5–10 mm zone, +++ ≥ 10–15 mm zone, ++++ ≥ 15–20 mm, +++++ ≥ 20 mm, – = No inhibition, NA = Not applicable

Table 5 Minimum inhibitory concentration (MIC) of synthesized compounds **3a**–**3o**

Compounds	*E. coli*	*P. vulgaris*	*S. aureus*	*B. subtilis*	*A. niger*	*C. albicans*
3a	> 250	62.5	62.5	62.5	125	> 250
3b	> 250	62.5	> 250	125	62.5	125
3c	62.5	62.5	125	125	> 250	> 250
3d	62.5	31.25	62.5	31.25	> 250	> 250
3e	62.5	62.5	> 250	62.5	> 250	> 250
3f	31.25	31.25	31.25	62.5	> 250	> 250
3g	> 250	125	> 250	125	31.25	62.5
3h	> 250	> 250	> 250	> 250	> 250	> 250
3i	> 250	> 250	> 250	125	> 250	> 250
3j	> 250	> 250	> 250	125	> 250	> 250
3k	> 250	> 250	> 250	62.5	31.25	> 250
3l	> 250	> 250	> 250	> 250	> 250	> 250
3m	250	250	> 250	250	250	125
3n	> 250	> 250	> 250	> 250	> 250	> 250
3o	125	62.25	125	62.5	31.25	> 250
Chloramphenicol	1.95	1.95	1.95	3.9	NA	NA
Amphotericin-B	NA	NA	NA	NA	1.95	1.95

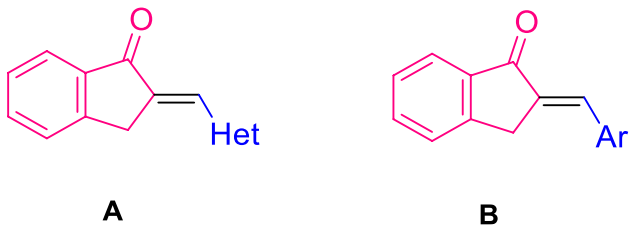


Fig. 2 General structures (A and B) for synthesized compounds

indanones were found to be less potent antifungal agents than simple aromatic linked indanones. On the contrary, former were more potent antibacterial agents than latter. Amongst aromatic aldehydes, the compound **3g** has exerted strong antifungal action against both fungal agents *A. niger* and *C. albicans*. The only heterocyclic linked synthesized compound to be active against both fungal agents was compound **3b**. The compounds containing chorine and fluorine atoms (**3g** and **3k**) were good against both fungal agents. Comparing the compounds **3j** and **3o**, the compound **3o** was far better in terms of antibacterial and antifungal activity. The presence of methyl group is linked with reduction in antimicrobial potential. The chorine substituents are powerful antibacterial and antifungal at C-2 and C-3 positions.

Conclusion

In summary, we presented eco-friendly synthesis and antimicrobial screening of fifteen halo-aryl and heterocyclic labelled 2,3-dihydro-1*H*-inden-1-one derivatives. Three synthetic methods grinding, stirring, and ultrasound method have been deliberately employed in which ultrasound irradiation method has been found to be more superior in terms of yield and reaction time. The ample substrate scope, simple reaction conditions, excellent yields, and high purity of the products are the key highlights of the present synthetic strategies. The antibacterial potential of the synthesized compounds was screened against against two Gram-positive bacteria namely *S. aureus* and *B. subtilis* and two Gram-negative bacteria namely *E. coli* and *P. vulgaris* whereas antifungal activity against two fungal agents namely *A. niger* and *C. albicans*. Most of the synthesized compounds were found as good antibacterial and antifungal agents. Especially, the compounds **3c**, **3d**, **3f**, and **3o** were found to apply strong antibacterial activity with a wide range of antibacterial action. On the other hand, the compounds **3b** and **3g** were applied solid antifungal activity against *A. niger* and *C. albicans*.

Experimental

The chemicals (Make—Sigma Aldrich, SD Fine Chemicals, and Avra synthesis) were purchased from Sigma laboratory, Nashik with a high purity and were used as such without any purification. The NMR experiment was performed on sophisticated multinuclear FT-NMR spectrometer model Advance-II (Bruker). The compounds were dissolved in chloroform-*d* or DMSO-d_6 and the chemical shifts were reported in ppm relative to tetramethylsilane (TMS). The reactions were monitored by thin-layer chromatography

using Merck Aluminum TLC plate, silica gel coated with fluorescent indicator F254. All the glass apparatus were cleaned and dried in oven prior to use.

Procedures for the synthesis of compounds 3a–3o

The general scheme for the synthesis of compounds **3a**–**3o** is depicted in Scheme 1.

Grinding method

A mixture of 2,3-dihydro-1*H*-inden-1-one (**1**, 10 mmol), and hetero-aromatic/aromatic aldehyde (**2**, 10 mmol), 0.5 cm^3 ethanol were taken in a mortar and pestle. To this reaction mixture, equimolar amount of KOH was added. The colour of the solution turned into dark yellow/brown after addition of KOH. The alkaline mixture was grinded at room temperature until the formation of products (checked by TLC). The reaction mass was allowed to cool at room temperature, then added into beaker containing ice-cold water, acidified, filtered, dried, and recrystallized using ethanol solvent.

Stirring method

A mixture of 2,3-dihydro-1*H*-inden-1-one (**1**, 10 mmol), and hetero-aromatic/aromatic aldehyde (**2**, 10 mmol), 5 cm^3 ethanol were taken in a 25 cm^3 Pyrex flask. To this reaction mixture, equimolar amount of KOH was added. The colour of the solution turned into dark yellow/brown after addition of KOH. The alkaline mixture was stirred on magnetic stirrer at room temperature until the formation of products (checked by TLC). The reaction mass was allowed to cool at room temperature, then added into beaker containing ice-cold water, acidified, filtered, dried and recrystallized using ethanol solvent.

Ultrasound method

A mixture of 2,3-dihydro-1*H*-inden-1-one (**1**, 10 mmol), and hetero-aromatic/aromatic aldehyde (**2**, 10 mmol), 5 cm^3 ethanol were taken in a 25 cm^3 Pyrex flask. To this reaction mixture, equimolar amount of KOH was added. The colour of the solution turned into dark yellow/brown after addition of KOH. The alkaline mixture was exposed to ultrasound irradiation at room temperature until the formation of products (checked by TLC). The reaction mass was allowed to cool at room temperature, then added into beaker containing ice-cold water, acidified, filtered, dried and recrystallized using ethanol solvent.

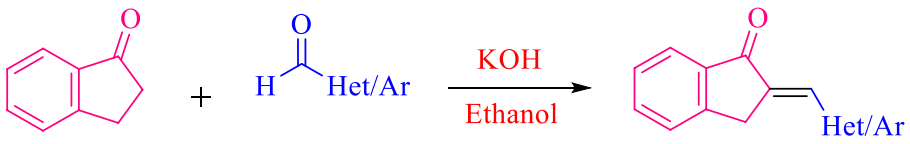
(Note: In all three methods, the reaction mixture was not acidified when one of the reactant was either 2-pyridinecarboxaldehyde or 4-pyridinecarboxaldehyde.)

(E)-2-(Thiophen-2-ylmethylene)-2,3-dihydro-1H-inden-1-one (3a, $C_{14}H_{10}OS$) Pale yellow colour; yield 97%; m.p.: 122–124 °C; FT-IR (KBr): $\overline{\nu}$ = 3059.10, 2873.94, 1672.28, 1469.76 1415.75, 1371.39, 1251.80, 1201.65, 1099.43, 1029.99, 952.84, 908.47, 831.32, 781.17, 725.23, 663.51, 524.64, 472.56, 424.34, 358.76 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.97–3.93 (m, 2H), 7.18 (dd, J = 5.0, 3.7 Hz, 1H), 7.47–7.40 (m, 2H), 7.61–7.55 (m, 2H), 7.66–7.61 (m, 1H), 7.92–7.87 (m, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 193.89, 149.07, 139.92, 138.56, 134.58, 133.16, 132.76, 130.57, 128.23, 126.62, 127.69, 126.26, 124.34, 32.35 ppm; HRMS (ESI): *m/z* calcd. 227.0530 ($[M+H]^+$), found 227.0531.

(E)-2-(Thiophen-3-ylmethylene)-2,3-dihydro-1H-inden-1-one (3b, $C_{14}H_{10}OS$) Pale yellow colour; yield 93%; m.p.: 118–120 °C; FT-IR (KBr): $\overline{\nu}$ = 3059.10, 2941.44, 1660.71, 1591.27, 1415.75, 1367.53 1313.52, 1244.09, 1199.72, 1109.07, 1068.56, 985.62, 904.61, 825.53, 775.38, 661.58, 570.93, 516.92, 385.76, 368.40 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.03–3.93 (m, 2H), 7.47–7.34 (m, 3H), 7.56 (td, J = 7.4, 1.2 Hz, 1H), 7.62 (td, J = 7.4, 1.2 Hz, 1H), 7.70 (m, 2H), 7.93–7.88 (m, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 194.44, 149.27, 138.43, 137.76, 134.58, 133.40, 129.64, 128.32, 127.70, 127.37, 126.70, 126.22, 124.37, 32.38 ppm.

(E)-2-[(3-Methylthiophen-2-yl)methylene]-2,3-dihydro-1H-inden-1-one (3c, $C_{15}H_{12}OS$) Yellow colour; yield 92%; m.p.: 110–112 °C; FT-IR (KBr): $\overline{\nu}$ = 3059.10, 1662.64, 1593.20, 1413.82, 1367.53, 1313.52, 1242.16, 1199.72, 1109.07, 1066.64, 983.70, 904.61, 825.53, 775.38, 719.45, 661.58, 570.93, 518.85, 381.91 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.48 (s, 3H), 3.96–3.90 (m, 2H), 7.00 (d, J = 5.1

Scheme 1



1 **2a-2o** **3a-3o**

Hz, 1H), 7.46–7.39 (m, 1H), 7.50 (d, $J = 5.1$ Hz, 1H), 7.65–7.54 (m, 2H), 7.90 (m, 1H), 7.97 (m, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 193.96$, 149.14, 143.20, 138.67, 134.38, 133.90, 131.68, 131.06, 129.12, 127.58, 126.20, 124.96, 124.27, 32.45, 14.58 ppm; HRMS (ESI): *m/z* calcd. 241.0687 ($[M+H]^+$), found 241.0682.

(E)-2-[(4-Methylthiazol-5-yl)methylene]-2,3-dihydro-1H-inden-1-one (3d, $C_{14}H_{11}NOS$) Pale yellow colour; yield 92%; m.p.: 122–128 °C; FT-IR (KBr): $\overline{\nu} = 3057.21$, 1668.98, 1610.51, 1413.82, 1387.45, 1319.51, 1267.53, 1202.70, 1135.50, 1064.99, 987.42, 906.13, 835.50, 782.35, 729.55, 663.51, 535.50, 466.71, 352.70 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 8.89$ (s, 1H), 7.94–7.88 (m, 2H), 7.64 (m, $J = 7.6$, 1.2 Hz, 1H), 7.57 (dt, $J = 7.6$, 1.2 Hz, 1H), 7.48–7.41 (m, 1H), 3.91–3.87 (m, 2H), 2.70 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 188.52$, 152.87, 149.31, 144.03, 133.68, 130.06, 129.82, 123.25, 123.11, 121.53, 119.77, 118.45, 27.37, 11.25 ppm.

(E)-2-(Pyridin-2-ylmethylene)-2,3-dihydro-1H-inden-1-one (3e, $C_{15}H_{11}NO$) White colour; yield 95%; m.p.: 153–155 °C; FT-IR (KBr): $\overline{\nu} = 3094.74$, 1669.64, 1596.27, 1417.46, 1367.26, 1317.38, 1245.74, 1215.75, 1117.38, 1069.46, 1026.64, 985.21, 956.64, 915.75, 817.38, 782.27, 729.24, 663.51, 527.46, 472.27, 370.63 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 8.59$–8.55 (m, 1H), 7.78–7.76 (m, 1H), 7.57 (m, 1H), 7.44 (m, 2H), 7.38 (td, $J = 7.7$, 1.9 Hz, 2H), 7.23 (m, 1H), 7.16 (m, 1H), 4.11–4.15 (m, 2H) ppm.

(E)-2-(Pyridin-4-ylmethylene)-2,3-dihydro-1H-inden-1-one (3f, $C_{15}H_{11}NO$) White colour; yield 95%; m.p.: 182–184 °C; FT-IR (KBr): $\overline{\nu} = 3101.65$, 1673.59, 1602.75, 1473.56, 1415.75, 1378.09, 1269.89, 1201.65, 1109.43, 1034.95, 950.84, 912.41, 839.32, 783.53, 731.33, 667.51, 531.34, 481.17, 425.23, 353.51 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 8.48$–8.41 (m, 2H), 8.41–8.35 (m, 2H), 7.80 (m, 1H), 7.62 (m, 1H), 7.52 (td, $J = 7.5$, 1.3 Hz, 1H), 7.45 (m, 1H), 7.33 (m, 1H), 4.06–4.08 (m, 2H) ppm.

(E)-2-(2,3-Dichlorobenzylidene)-2,3-dihydro-1H-inden-1-one (3 g, $C_{16}H_{10}Cl_2O$) Yellow colour; yield 97%; m.p.: 154–158 °C; FT-IR (KBr): $\overline{\nu} = 3248.13$, 1676.88, 1612.49, 1417.68, 1257.59, 1163.08, 1097.50, 972.12, 810.10, 732.95, 582.50, 534.28, 464.84, 441.70 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 3.94$ (d, $J = 2.3$ Hz, 2H), 7.29 (m, 1H), 7.69–7.38 (m, 5H), 7.92 (m, 1H), 7.99 (t, $J = 2.3$ Hz, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 193.56$, 149.55, 137.96, 137.83, 135.92, 134.99, 134.10, 134.03, 130.85, 129.88, 127.92, 127.88, 127.16, 126.21, 124.68, 31.69 ppm.

(E)-2-(3,4-Dichlorobenzylidene)-2,3-dihydro-1H-inden-1-one (3 h, $C_{16}H_{10}Cl_2O$) Pale yellow colour; yield 97%; m.p.: 163–166 °C; FT-IR (KBr): $\overline{\nu} = 3059.10$, 3008.95, 1662.64, 1593.20, 1413.82, 1369.46, 1315.45, 1242.16, 1199.72, 1109.07, 1068.56, 1020.34, 983.70, 906.54, 825.53, 777.31, 719.45, 661.58, 570.93, 516.92, 426.27, 383.83 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 4.03$ (d, $J = 2.2$ Hz, 2H), 7.47–7.42 (m, 1H), 7.49 (t, $J = 2.2$ Hz, 1H), 7.63–7.51 (m, 3H), 7.65 (dd, $J = 7.6$, 2.0 Hz, 1H), 7.75 (d, $J = 2.0$ Hz, 1H), 7.92 (d, $J = 7.6$ Hz, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 193.89$, 149.33, 137.70, 136.30, 135.41, 135.04, 133.69, 133.25, 131.81, 131.14, 130.93, 129.73, 127.94, 126.25, 124.63, 32.24 ppm; HRMS (ESI): *m/z* calcd. 289.0186 ($[M+H]^+$), found 289.0179.

(E)-2-[(2,3-Dihydrobenzofuran-5-yl)methylene]-2,3-dihydro-1H-inden-1-one (3i, $C_{18}H_{14}O_2$) Bright yellow colour; yield 94%; m.p.: 132–134 °C; FT-IR (KBr): $\overline{\nu} = 3059.10$, 1662.64, 1593.20, 1413.82, 1369.46, 1315.45, 1201.65, 1111.00, 1066.64, 983.70, 906.54, 825.53, 777.31, 719.45, 661.58, 379.98 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 3.28$ (t, $J = 8.7$ Hz, 2H), 3.99 (d, $J = 2.1$ Hz, 2H), 4.65 (t, $J = 8.7$ Hz, 2H), 6.86 (d, $J = 8.3$ Hz, 1H), 7.47–7.38 (m, 1H), 7.48 (dd, $J = 8.3$, 1.9 Hz, 1H), 7.58–7.51 (m, 2H), 7.60 (td, $J = 7.3$, 1.2 Hz, 1H), 7.64 (t, $J = 2.1$ Hz, 1H), 7.90 (m, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 194.45$, 161.81, 149.48, 138.33, 134.39, 134.29, 132.25, 131.76, 128.28, 128.19, 127.58, 127.54, 126.09, 124.28, 109.97, 71.95, 32.63, 29.40 ppm.

(E)-2-[(5-Methylfuran-2-yl)methylene]-2,3-dihydro-1H-inden-1-one (3j, $C_{15}H_{12}O_2$) Yellow colour; yield 96%; m.p.: 152–154 °C; FT-IR (KBr): $\overline{\nu} = 3315.63$, 3059.10, 2949.16, 1670.35, 1598.99, 1492.90, 1465.90, 1415.75, 1369.46, 1317.38, 1280.73, 1249.87, 1201.65, 1105.21, 1070.49, 1029.99, 981.77, 952.84, 908.47, 829.39, 781.17, 721.38, 663.51, 522.71, 470.63, 405.05 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.88$ (d, $J = 7.6$ Hz, 1H), 7.60 (m, 1H), 7.55 (m, 1H), 7.43–7.41 (m, 1H), 7.41–7.39 (m, 1H), 6.69 (d, $J = 3.4$ Hz, 1H), 6.17 (d, $J = 3.4$ Hz, 1H), 4.03–3.99 (m, 2H), 2.43 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 194.05$, 156.27, 150.93, 149.76, 138.74, 134.20, 131.00, 127.37, 126.13, 124.12, 120.26, 118.50, 109.36, 32.40, 14.20 ppm; HRMS (ESI): *m/z* calcd. 225.0915 ($[M+H]^+$), found 225.0916.

(E)-2-(4-Fluorobenzylidene)-2,3-dihydro-1H-inden-1-one (3 k,$C_{16}H_{11}FO$) Yellow colour; yield 88%; m.p.: 190–194 °C; FT-IR (KBr): $\overline{\nu} = 3057.17$, 1666.50, 1597.06, 1415.75, 1369.46, 1317.38, 1247.94, 1201.65, 1105.21, 1066.64, 1022.27, 981.77, 952.84, 906.54, 827.46, 779.24, 719.45, 663.51, 520.78, 470.63, 366.48 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 4.06$–4.01 (m, 2H), 7.20–7.12 (m, 2H), 7.48–7.41 (m, 1H), 7.57 (m, 1H), 7.76–7.60 (m, 4H), 7.92 (m, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 194.26$, 164.35, 162.35, 149.49, 137.97, 134.71, 134.29, 134.27, 132.71,

132.66, 132.60, 131.70, 131.67, 127.79, 126.19, 124.51, 116.25, 116.07, 32.34 ppm.

(E)-2-[(1-Methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-1H-inden-1-one (3l, $C_{15}H_{13}NO$) Yellow colour; yield 86%; m.p.: 186–188 °C; FT-IR (KBr): $\overline{\nu}$ = 3057.17, 1672.28, 1415.75, 1371.39, 1249.87, 1201.65, 1101.35, 1029.99, 950.91, 908.47, 831.32, 781.17, 723.31, 663.51, 522.71, 470.63, 381.91 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.88 (d, J = 7.8 Hz, 1H), 7.65 (m, 1H), 7.60–7.57 (m, 1H), 7.55 (m, 1H), 7.41 (m, 1H), 6.87 (m, 1H), 6.76 (m, 1H), 6.36–6.29 (m, 1H), 3.87–3.84 (m, 2H), 3.81 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 193.97, 149.03, 139.00, 134.02, 129.95, 129.93, 127.44, 126.08, 124.04, 120.90, 114.94, 110.06, 34.45, 32.76 ppm; HRMS (ESI): *m/z* calcd. 224.1075 ($[M+H]^+$), found 224.1072.

(E)-2-[4-(Pyrrolidin-1-yl)benzylidene]-2,3-dihydro-1H-inden-1-one (3m, $C_{20}H_{19}NO$) Yellow colour; yield 94%; m.p.: 162–164 °C; FT-IR (KBr): $\overline{\nu}$ = 3057.17, 1670.35, 1467.83, 1415.75, 1371.39, 1317.38, 1249.87, 1201.65, 1103.28, 1029.99, 952.84, 908.47, 829.39, 781.17, 723.31, 663.51, 522.71, 470.63, 358.76 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.90 (d, J = 7.6 Hz, 1H), 7.65 (m, 1H), 7.63–7.51 (m, 4H), 7.44–7.37 (m, 1H), 6.61 (m, 2H), 4.00 (d, J = 1.9 Hz, 2H), 3.41–3.33 (m, 4H), 2.10–2.01 (m, 4H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 194.33, 149.38, 148.79, 138.89, 135.36, 133.71, 133.01, 129.27, 127.35, 125.96, 124.05, 122.68, 111.89, 47.56, 32.80, 25.48 ppm; HRMS (ESI): *m/z* calcd. 290.1544 ($[M+H]^+$), found 290.1544.

(E)-2-[(1H-Pyrrol-2-yl)methylene]-2,3-dihydro-1H-inden-1-one (3n, $C_{14}H_{11}NO$) Yellow color; yield 85%; m.p.: 184–186 °C; FT-IR (KBr): $\overline{\nu}$ = 3059.10, 1668.43, 1597.06, 1415.75, 1369.46, 1317.38, 1247.94, 1201.65, 1107.14, 1068.56, 1026.13, 981.77, 908.47, 827.46, 779.24, 721.38, 663.51, 520.78, 470.63, 381.91 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 9.05 (s, 1H), 7.89 (ddd, J = 7.7, 1.3, 0.7 Hz, 1H), 7.67 (m, 1H), 7.63–7.53 (m, 2H), 7.47–7.39 (m, 1H), 7.08 (m, 1H), 6.76 (s, 1H), 6.46–6.40 (m, 1H), 3.92–3.88 (m, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 194.06, 148.87, 138.94, 134.14, 129.38, 129.25, 127.56, 126.11, 124.06, 123.66, 122.91, 114.89, 111.99, 32.37 ppm.

(E)-2-(Furan-2-ylmethylene)-2,3-dihydro-1H-inden-1-one (3o, $C_{14}H_{10}O_2$) Yellow color; yield 94%; m.p.: 120–122 °C; FT-IR (KBr): $\overline{\nu}$ = 3776.62, 3059.10, 2947.23, 1668.43, 1598.99, 1492.90, 1465.90, 1415.75, 1369.46, 1319.31, 1247.94, 1201.65, 1107.14, 1068.56, 1028.06, 981.77, 952.84, 908.47, 829.39, 781.17, 721.38, 663.51, 522.71, 472.56, 403.12, 360.69 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.89 (dt, J = 7.6, 1.0 Hz, 1H), 7.63 (m, 1H), 7.62–7.58 (m, 1H), 7.55 (m, 1H), 7.46 (t, J = 2.1 Hz, 1H), 7.44–7.38 (m, 1H), 6.78 (m, 1H), 6.56 (m, 1H), 4.06 (d, J = 2.1 Hz, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 194.02, 152.32, 149.80, 145.38, 138.50, 134.46, 132.58, 127.49, 126.20, 124.25, 120.07, 116.64, 112.67, 32.36 ppm; HRMS (ESI): *m/z* calcd. 211.0759 ($[M+H]^+$), found 211.0761.

Biological methods

Disk diffusion assay

The antibacterial and antifungal potential of synthesized compounds was evaluated as per the previous reported method. Briefly, each compound dried paper disk (Whatman filter paper No.1) contained synthesized compounds 50 mm^3 (0.001 mM) [29]. Each disk was then placed on the surface of the sterile solidified agar which was spread with inoculums of bacterial and fungal cultures (0.5 McFarland Standard). Chloramphenicol and Amphotericin-B was used as standard (0.001 mM) for antibacterial and antifungal activities respectively. The plates were kept in refrigerator for diffusion for 1 h and then transferred to the incubator at 37 °C for 24 h. After incubation, the zones around the discs were measured by the zone scale (Himedia Pvt. Ltd. Mumbai).

Resazurin microtiter assay

The resazurin microtiter assay (REMA) plate assay was carried out as described elsewhere [29]. Briefly, 100 mm^3 of 7H9-S (containing 0.1% casitone, and 0.5% glycerol and supplemented with oleic acid, albumin, dextrose, and catalase) broth was dispensed in each well of a sterile flat-bottom 96-well plate, and serial twofold dilutions of each synthesized compounds were prepared directly in the plate. One hundred micro liters of inoculums was added to each well. Sterile cold water was added to all perimeter wells to avoid evaporation during the incubation. The plate was covered, sealed in a plastic bag, and incubated at 37 °C for 24 h. After incubation, 30 mm^3 of resazurin solution (0.01% in sterile deionized water) was added to each well, and the plate was re-incubated for 4 h. A change in color from blue to pink indicated the growth of bacteria, and the MIC was defined as the lowest concentration of drug that prevented this change in color. The drug concentration ranges used were as follows: for synthesized compounds, 0.048–500 μg/cm^3 and for Chloramphenicol and Amphotericin-B, 0.048–500 μg/cm^3.

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