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Synthesis, Biological Evaluations and Molecular Docking of Novel Pyrazolyl, Dihydro-1*H*-inden-1-one Derivatives

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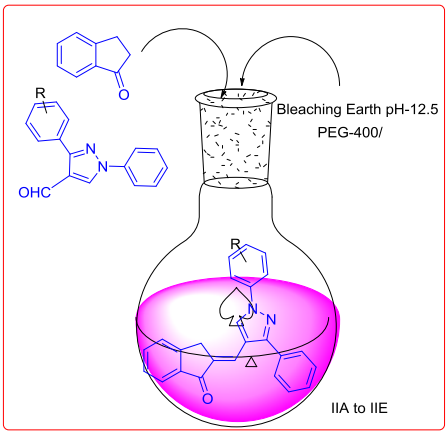
ABSTRACT

A series of novel pyrazol-4-yl- dihydro-1*H*-inden-1-one derivatives were synthesized by using greener catalyst pH 12.5 (Bleaching earth clay BEC) as an efficient catalytic and PEG-400 as a green, recyclable solvent. All the synthesized compounds are characterized with 1HNMR, 13CNMR, IR and Mass Spectroscopy techniques. The synthesized molecules are subjected for the molecular docking study with 6KZV-A enzyme, the compounds IIb (E)-2-((1-(4-bromophenyl)-3-phenyl-1*H*-pyrazol-4-yl)methylene)-2,3-dihydro-1*H*-inden-1-one, IIc(E)-2-((3-phenyl-1-(p-tolyl)-1*H*-pyrazol-4-yl)methylene)-2,3-dihydro-1*H*-inden-1-one, IId (E)-2-((1-(4-methoxyphenyl)-3-phenyl-1*H*-pyrazol-4-yl)methylene)-2,3-dihydro-1*H*-inden-1-one and IIe (E)-2-((1-(4- nitrophenyl)-3-phenyl-1*H*-pyrazol-4-yl)methylene)-2,3-dihydro-1*H*-inden-1-one shows the desired bonding interaction with 6KZV-A enzyme. The compounds further were evaluated for antimicrobial activities. Amongst these synthesized compounds, the mentioned compounds show good to moderate antimicrobial activities.

GRAPHICAL ABSTRACT



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Introduction

The heterocyclic compound with hetero atom has significant importance for preparing bioactive scaffolds. The chalcone and its analogs have a broad interest in the field of medicinal chemistry. The chemical simplicity and easy synthesis method for the preparation of α, β-unsaturated ketones are of high significance for several research groups and synthetic chemists. Based on the literature report and the biological activity of α, β-unsaturated ketones, the SAR indicates the chalcones with heterocyclic moiety have significant interest for their synthesis [1–3].

The chalcone with heterocyclic moiety has significant application in the field of medicinal chemistry with a broad range of biological activity including microbial activity like antifungal, antibacterial, anti-inflammatory, Antineoplastic, Antitubercular [4–6], high blood pressure [7], phagostimulatory [8], and antioxidant activities [9]. And such ketone chalcones possess anticancer, anti-inflammatory, analgesic, and antispasmodic properties [10,11]. The insertion of the heterocyclic compound instead of the phenyl/aryl has an important interest for the synthesis of heterocyclic α, β-unsaturated ketones. The SAR research proves that the introduction of heterocyclic compound s in α, β-unsaturated ketones leads to an increase in the pharmaceutical properties including their ADMET properties. Because of their wild range of application chalcones, the preparation of biologically active heterocyclic has great interest for the researchers and scientists.

The use of homogeneous greener catalysts has tremendous importance for preparing bioactive compounds, since the bleaching clay from nature has unique important includes there (pH 12.5), chemo selectivity, acidic and basic in properties, and heat stability. Among them, the catalyst BEC (pH 12.5) is a more coherent catalyst that is applied for numerous chemical organic transformations [12–14]. The huge surface area of clay is viscous because of its small-size (5 microns) particles and easy to solid support compared to the other catalysts like solid-supported ones.

The use of greener solvent is one of the alternative green solvents for preparing bioactive compounds because the greener solvent has unique properties including heat stability, solubility, availability, solubility with the various organic solvent, and easy recovering. The PEGs solvent is labeled under the greener category because it is nontoxic to the environment and easily available [15-18] to design novel methods and their antimicrobial property.

Herein, we have developed a novel method for preparing hybrids heterocyclic *α, β*-unsaturated ketones, and their biological activity. Our fundamental aim is to get the novel methodology for the synthesis of new heterocyclic moiety and its biological activity [19-24]. The main significance of this research is to find out the novel lead ligand molecule with active antimicrobial properties. The importance of medicinal applications is for discovering the novel derivatives of pyrazol-4-yl-dihydro-1*H*-inden-1-one, thus we have attempted to study docking for the novel multi-substituted α, β-unsaturated ketones derivatives by attractive targets 6KZV-A enzyme [25].

Material and Method

Experimental

All the melting points were uncorrected and determined in an open capillary tube. The chemicals and solvents used were of laboratory grade and purified. Completion of the reaction was monitored by thin layer chromatography on precoated sheets of silica gel-G (Merck, Germany) using iodine vapour for detection. IR spectra were recorded as KBr pellets on FTIR Shimadzu spectrophotometer (8400s). ^{1}H NMR and ^{13}C NMR (70 MHz) spectra were recorded in DMSO-d_6 with an Avance spectrometer (Bruker, Germany) at 400-MHz frequency using TMS as an internal standard. Mass spectra were recorded by an EI-Shimadzu QP 2010 PLUS GC-MS system (Shimadzu, Japan). Elemental analyses were performed using a Carlo Erba 106 Perkin-Elmer model 240 analyzer (Perkin-Elmer, USA).

General procedure for the synthesis of α, β-unsaturated ketones (IIa-e):

The mixture of substituted Het/Ar aldehyde (1 mmol), and bleaching earth (10 wt. % of pH 12.5) was taken in the 100 mL round bottom flask along with polyethyleneglycol-400 (20mL). The formed reaction mixture was heated at 60-80 °C for 2.5 to 3.5 h. The completion of the reaction was monitored by TLC, once it confirmed the complete utilization of starting substrate; the reaction mixture was filtered over Whitman filter paper to recover the bleaching clay earth. The liquid aliquot pours into the ice-cold water and the solid precipitate is formed, filter the ppt and wash with water for 3×2 (10 mL). The crude product was dried and purified by recrystallized from aqueous acetic acid to afford corresponding α, β-unsaturated ketones as products.

2-((3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl) methylene)-2,3-dihydro-1H-inden-1-one(IIA)

Yellow solid; mp.155°C; IR (KBr, ν, cm^{-1}): 3059, 2934, 1705, 1599, 1500-1542, 1230, 754; ^{1}HNMR (400 MHz, DMSO-d6) (δ,ppm): 4.2 (s, 2H) 7.0-9.1 (m,15H, aromatic)); ^{13}C-NMR (70 MHz, DMSO-d6) (δ,ppm): 33, 113-142, 141-152, EIMS (m/z): 396 (M+) ; Anal. Calcd. For $C_{25}H_{17}ClN_2O$: C, 75.66; H, 4.32; Cl, 8.93; N, 7.06; O, 4.03% Found; C, 75.63, H, 4.30, Cl, 8.95, N,7.07, O, 4.01%

2-((3-(4-bromophenyl)-1-phenyl-1H-pyrazol-4-yl) methylene)-2,3-dihydro-1H-inden-1-one (IIB)

Yellow solid; mp.140°C; IR (KBr, ν, cm^{-1}): 3057, 2932, 1708, 1598, 1500-1545 1235, 754; ^{1}HNMR (400 MHz, DMSO-d6) (δ,ppm): 4.2 (s, 2H), 6.8-9.0 (m,15H); ^{13}C-NMR (70 MHz, DMSO-d6) (δ,ppm): 34, 111-145, 140-153; EIMS (m/z): 441 (M+H) ; Anal. Calcd. For $C_{25}H_{17}BrN_2O$: C, 68.04; H, 3.88; Br, 18.11; N, 6.35; O, 3.63% Found; CC, 68.02; H, 3.90; Br, 18.12; N, 6.33; O, 3.61%

(E)-2-((3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl) methylene)-2,3-dihydro-1H-inden-1-one (IIE):

Yellow solid; mp.141°C; IR (KBr, ν, cm^{-1}): 3056, 2926, 1706, 1592, 1510-1546, 1230, 757; ^{1}HNMR (400 MHz, DMSO-d6) (δ,ppm): 4.1 (s, 2H), 6.8-9.1 (m,15H); EIMS (m/z): 407 (M+) ; Anal. Calcd. For $C_{25}H_{17}N_3O_3$: C, 73.70; H, 4.21; N, 10.31; O, 11.78% Found; C, 73.72; H, 4.20; N, 10.33; O, 11.80%

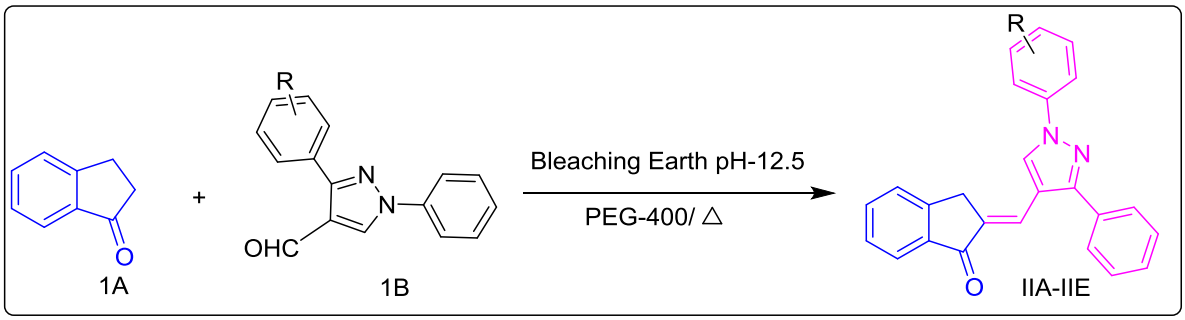
Recycle Bleaching Clay earth

Bleaching earth clay (pH 12.5) is readily available in India and the USA at very low cost (0.10 USD per kg) compared to the others, such as supported Zirconia, 12-tungstosilicicacid, bleaching earth clay (pH 12.5), etc. After completing the reaction, the solid catalyst was recovered in the resulting reaction mixture by filtration.

Results and Discussion

The chalcone can be synthesized by the Claisen–Schmidt condensation in presence of a base. The method has some limitations in regards to the selectivity, solubility, time duration, less yield, and use of the toxic reagent/solvent. Since form the last decade high awareness was developed regarding the use of greener techniques for generating important chemical intermediates, solid catalyst because of their easy handling, high storage capacity, and easy disposal with nontoxic to the environment. The significant aim of the study is to use greener catalysts in the greener methods for the synthesis of bioactive heterocyclic compounds. Herein, we have developed a greener eco-friendly method for the preparation of heterocyclic *α,β*-unsaturated ketones sing bleaching earth clay pH 12.5 as a heterogeneous catalyst and PEG-400 as a recyclable reaction solvent.

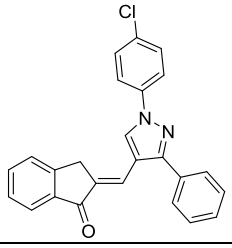
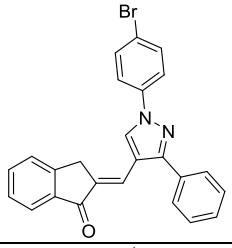
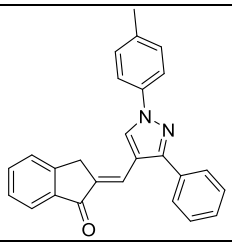
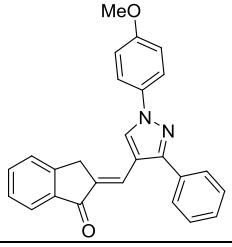
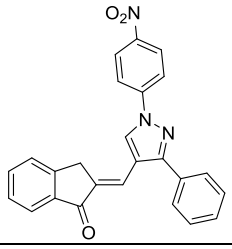
At the beginning of the research, we have treated the starting substrate with Indanone and hetero-aldehyde using heterogeneous base BEC with pH 12.5 and solvent PEG-400 at room temp. The reaction was performed at room temperature after 12 hours of reaction time. Then, we have increased the reaction temperature to 45 °C for the 6 to 10 hours of reaction time; there was 40% conversion of the product. At 60 °C for 10 hours, there was the formation of the product as observed with 60% yield. When the reaction mixture was treated at 80 °C for 4 hours with a catalytic amount of bleaching Clay catalyst, there was completion consumption of the starting substrate, and the product formation was observed with 85 to 90% yield.



Scheme 1: The new synthetic pathway for α, β-unsaturated ketones (IIa-e)

The formation of the desired product with very good form of the desired protocol, we moved to explore the catalyst selectivity with the range of electron donation and accepting substituent on the 1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde substrate. The halogen-substituted substrate gives a higher yield than the NO_2 groups. Table-1 indicates all the novel compounds elucidated by spectral data and analytical methods.

Table 1: Physico-chemicaldata of newly synthesized α, β-unsaturated ketones

Product Code	R	Time(min)	Yield (%)	MP(°C)
IIA		145	92	155
IIB		150	90	140
IIC		170	85	146
IID		160	90	163
IIE		155	84	141

The final compounds were confirmed by matching with literature spectroscopic data. The Infrared (IR) spectra of the compounds show the characteristic band at region 1690-1640 cm^{-1} due to >C=O stretching vibrations. Lowering stretching frequency of normal > C=O (1780-1710cm^{-1}) is attributed to the presence of *α, β*-unsaturated ketones.[1] H NMR spectra of compounds indicated a characteristic singlet of 1H near 8.1δppm due to olefinic proton and singlet of 1H proton near 8.6-9.1 δppm for pyrazoline ring. However, these singlets are coalesced (mixed) with aromatic protons. Singlet of three protons appeared near 3.8 δppm and due to-OCH_3 group. Singlet of two protons appears at4.1-4.6 δppm for–CH_2 of indanone ring. The aromatic protons appear as multiple around 7.0–8.5 δppm. The NMR data indicate the formation of the desired product and the peak shows the signal for pyrazole protons proton in the deshielded region, while the aromatic peak appears at the aromatic region as confirmed the formation of *α, β*-unsaturated ketones (chalcones). These spectral characterization and physicochemical data are helpful for confirming the formation of *α, β* -unsaturated ketones.

Antibacterial Activity

Method

The Agardiffusion protocol was used to carry out the antimicrobial activity of synthesized compound [26]. The results are summarized in the zone of inhibition (ZOI) and results were checked along with the (MICs) values and totally with the standard sample and blank sample. The DMSO solvent was used for the preparation and dilution of the sample by taking 0.001 gram of compound in the dimethyl sulfide solvent. The dissolved sample was allowed to study in the plates with seed agar. The final results of the compounds were compared to penicillin drug (Table 2), based on the result, the data indicate that the compounds IIC, IID, and IIE possess more antibacterial activity (Table 2).

Table 2: The zone of inhibition for indazole derivatives (IIA-IIE) against tested bacteria

Compounds	S. aureus	Bacillus subtilis	E. coli
IIA	9	10	11
IIB	8	14	14
IIC	10	11	11
IID	14	18	16
IIE	19	20	21
penicillin	32	34	35

The ligand molecules IIC, IID and IIE display moderate activity again the *Bacillus subtilis* (MTCC-441), (MTCC- 443) *Escherichia Coli* and (MTCC-96) *Staphylococcus aureus* (Table 1). All the other remaining molecules IIA and IIB possess less antibacterial activity. Based on the obtained results, when the percentage of scaffold increases from 0.001 g/mL to 0.002 mg/mL, the compounds' activity increases, as well. It is observed that the enhanced antibacterial activity of the synthesized compounds may be due to the presence of –OMe, Br, -Cl or -NO_2 groups presented in the *2-((3-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl) methylene)-2,3-dihydro-1H-inden-1-one* compounds. The ZOI and the related MICs shown in Table-1 for the present antimicrobial studies signifies the importance of synthesized pyrazole derivatives as potential antimicrobial agents.

Molecular Docking

Method

The molecular docking was performed by using Autodock software. The 3D structure of the ligand was generated from the 3D chem and saved in the PDB format. The protein molecules were extracted from the Protein Data Bank (https://www.rcsb.org/) [27]. The active sites/ binding sites of the protein were identified using

the Computed Atlas of Surface Topography of Proteins (Castro) program (http: //cast.engr.uic.edu) [28].

The molecular docking for the synthesized compounds was performed with the enzyme 1kzn DNA gyrase and 6kzv protein an Ecoli DNA gyrase enzyme with native ligand 2-oxo-1,2-dihydroquinoline. The synthesized compound shows the active potential against the antimicrobial activity. The DNA gyrase protein is a commonly studied enzyme. The DNA gyrase is an important protein, which is responsible for the bacterial biochemical mechanism. The enzyme involves in the transcription activity which helps to produce a new copy of the DNA strand. The antibacterial agent's DNA gyrase, the enzyme blocks the generation of another copy of DNA, therefore, resulting in bacterial death. Since the higher use of antibiotics and resistance is a high problem, therefore the development of a novel antimicrobial agent is essential to combat resistant strains of bacteria.

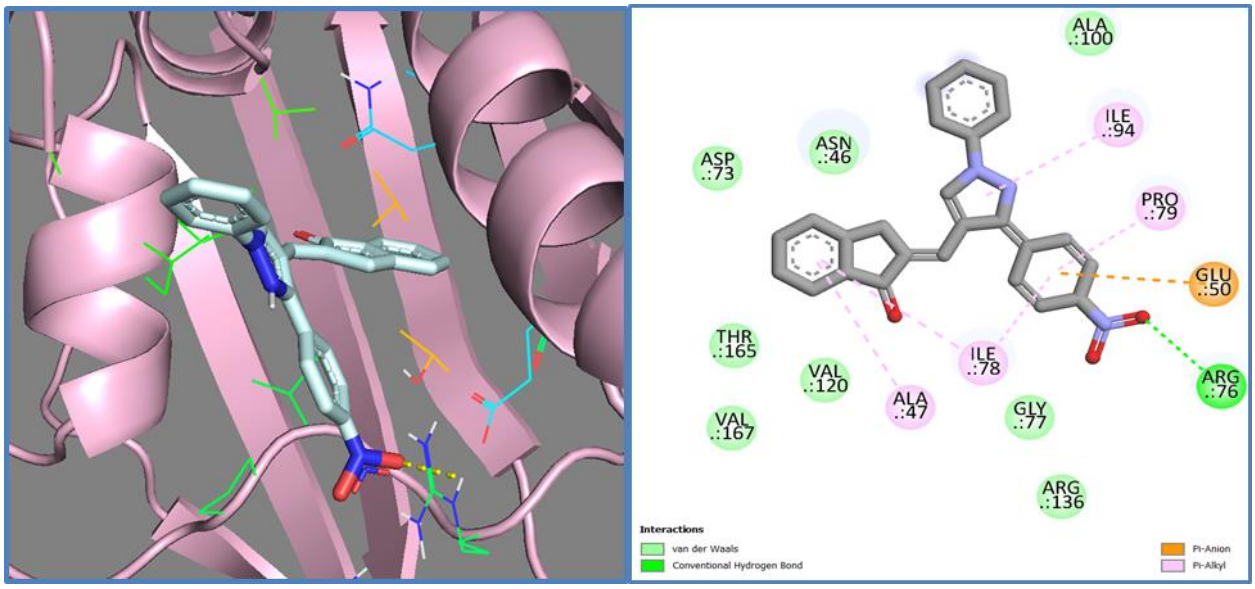


Figure 2: A). Binding interactions between IIE and DNA gyrase (PDB code 6kzv). B) 2D structure showing hydrogen bonding and hydrophobic interactions of 5F with 9 DNA gyrase (PDB code 6kzv) complex

The synthesized ligand IIA-IIE shows good docking results with the enzyme 1kzn and 6kzv protein. The molecule is docked in the active site of the enzyme indicating the hydrogen bonding interaction with the ARG-76 amino acids. The residues ARG-76 amino acids from H-bond with the NO_2 group of the ligand with 3.1Å bond distance. Similarly, the ligand shows van der Waals of interaction with amino acid residues like ASP-73, ASN-46, ALA100, THR-165, VAL-120, ALA-47, GLY-77, ARG-136 acids (Figure 2).

Conclusion

Finally, we have synthesized a series of synthesis of novel series of *2-((3-(4-methoxyphenyl)-1-phenyl-1H-pyrazol-4-yl) methylene)-2,3-dihydro-1H-inden-1-one derivatives* via a mild, rapid, and environmentally sustainable synthesis process. The compounds IIC, IID, and IIE display activity against the *S. aureus, Bacillus subtilis, and E. Coli* bacterial strain. Furthermore, the molecular docking results give information about the compound IIC and IIE as good candidate for further research with the targeted enzyme with DNA gyrase 1kzn and 6kzv protein.

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Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to responsible for all the aspects of this work.

Conflict of Interest

We have no conflicts of interest to disclose.

References

[1]. Modzelewska A., Pettit C., Achanta G., Davidson N.E., Huang P., Khan S.R., *Bioorg. Med. Chem*. 2006, **15**:3491 [Crossref], [Google Scholar], [Publisher]

[2]. Hsieh C.J., Xu K., Lee I., Graham T.J.A., Tu Z., Dhavale D., Kotzbauer P., Mach R.H., *ACS Omega*, 2018, **3**:4486 [Crossref], [Google Scholar], [Publisher]

[3]. Jasim H.A., Nahar L., Jasim M.A., Moore S.A., Ritchie K.J., Sarker S.D., *Biomolecules*, 2021, **11**:1203 [Crossref], [Google Scholar], [Publisher]

[4]. Narwal S., Kumar S., Verma K.P., *Res. Chem. Intermediates*, 2021, **47**:1625 [Crossref], [Google Scholar], [Publisher]

[5]. Salehi B., Quispe C., Chamkhi I., El Omari N., Balahbib A., Sharifi-Rad J., Bouyahya A., Akram M., Iqbal M., Docea A.O., Caruntu C., Leyva-Gómez G., Dey A., Martorell M., Calina D., López V., Les F., *Front. Pharmacol.* 2021, **11**:592654 [Crossref], [Google Scholar], [Publisher]

[6]. Shaik A.B., Bhandare R.R., Nissankararao S., Edis Z., Tangirala N.R., Shahanaaz S., Rahman M.M., *Molecules,* 2020, **25**:3188 [Crossref], [Google Scholar], [Publisher]

[7]. Ogawa H., Okada Y., Kamisako T., Baba K., *Clin. Exp. Pharmacol. Physiol.*, 2007, **34**:238 [Crossref], [Google Scholar], [Publisher]

[8]. Ogawa H., Okada Y., Kamisako T., Baba K., *Clin. Exp. Pharmacol. Physiol.*, 2007, **34**:238 [Crossref], [Google Scholar], [Publisher]

[9]. Higgs J., Wasowski C., Marcos A., Jukič M., Paván C. H., Gobec S., de Tezanos Pinto F., Colettis N., Marder M., *Heliyon*, 2019, **5**:E01376 [Crossref], [Google Scholar], [Publisher]

[10]. Lahsasni S.A., Al Korbi F.H., Aljaber N.A., *Chem. Cent. J.,* **2014**, **8**:32 [Crossref], [Google Scholar], [Publisher]

[11]. Gomes M.N., Muratov E.N., Pereira M., Peixoto C., Rosseto L., Cravo P.V.L., Andrade C.H., Neves B.J., *Molecules,* 2017, **22**:1210 [Crossref], [Google Scholar], [Publisher]

[12]. Nowakowska Z., *Eur. J. Med. Chem.*, 2007, **42**:125 [Crossref], [Google Scholar], [Publisher]

[13]. Acharya A.P., Kamble R.D., Patil S.D., Hese S.V., Yemul O.S., Patil S.G., Halale S.N., Dawane S.B., *Chem. Papers.*, 2014, **68**:719 [Crossref], [Google Scholar], [Publisher]

[14]. Kamble R.D., Jawadwar, G.V., Patil S.D., Hese S.V., Acharya A.P., Dawane, B.S., Pekamwar S.S., *Org. Commun.,* 2013, **6**:95 [Google Scholar], [Publisher]

[15]. Acharya A.P., Kamble R.D., Patil S.D., Hese S.V., Yemul O.S., Dawane B.S., *Res. Chem. Intermed.,* 2015, **41**:2953 [Crossref], [Google Scholar], [Publisher]

[16]. Chandrasekhar S., Narsihmulu C., Sultana S.S., *Org. Lett.*, 2002, **4**:4399 [Crossref], [Google Scholar], [Publisher]

[17]. Dawane B.S., Konda S.G., Mandawad G.G., Shaikh B.M., *Eur. J. Med. Chem*., 2010, **45**:387 [Crossref], [Google Scholar], [Publisher]

[18]. Dawane B.S., Shaikh B.M., Khandare N.T., Kamble V.T., Chobe S.S., Konda S.G., *Green Chem. Lett. Rev*., 2010, **3**:205 [Crossref], [Google Scholar], [Publisher]

[19]. Vafaeezadeh M., Hashemi M.M., *J. Mol. Liq.,* 2015, **207**:73 [Crossref], [Google Scholar], [Publisher]

[20]. Gaikwad M.V., Kamble R.D., Hese S.V., Kadam S.N., Ambhore A.N., gaikwad S.V., Acharya A.P., Dawane B.S., *Chem. Methodol.*, 2021, **5**:341 [Crossref], [Google Scholar], [Publisher]

[21]. Gaikwad S.V., Gaikwad M.V., Lokhande P.D., *Eurasian Chem. Commun.*, 2020, **2**:945 [Crossref], [Google Scholar], [Publisher]

[22]. Gaikwad M.V., Kamble R.D., Hese S.V., Acharya A.P., Mogle P.P., Kadam S.N., Dawane B.S., *Res. Chem. Intermed.*, 2015, **41**:4673 [Crossref], [Publisher]

[23]. Gaikwad M., Gaikwad S., Kamble R., *J. Med. Chem. Sci.,* 2022, **5**:239 [Crossref], [Google Scholar], [Publisher]
[24]. Gaikwad M., *J. Appl. Organomet. Chem.,* 2021, **1**:59 [Crossref], [Publisher]
[25]. Gaikwad S.V., Gaikwad M.V., Lokhande P.D., *J. Heterocycl. Chem.*, 2021, **58**:1408 [Crossref], [Google Scholar], [Publisher]
[26]. Ushiyama F., Hideaki Amada H., Takeuchi T., Yamamoto N.T., Kanazawa H., Nakano K., Mima M., Masuko A., Takata I, Hitaka K., Iwamoto K., Sugiyama H., Ohtake N., *ACS Omega,* 2020, **5**:10145 [Crossref], [Google Scholar], [Publisher]
[27]. Balouiri M., Sadiki M., Ibnsouda S.K., *J. Pharm. Anal.,* 2016, **6**:71 [Crossref], [Google Scholar], [Publisher]
[28]. Lafitte D., Lamour V., Tsvetkov P.O., Makarov A.A., Klich M., Deprez P., Moras D., Briand C., Gilli R., *Biochemistry*, 2002, **41**:721. [Crossref], [Google Scholar], [Publisher]
[29]. Binkowski T.A., Naghibzadeh S., Liang J., *Nucleic Acids Res.*, 2003, **31**:3352 [Crossref], [Google Scholar], [Publisher]

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