JSR Publications
Available Online
J. Sci. Res. **15** (3), 783-791 (2023)
JOURNAL OF SCIENTIFIC RESEARCH
www.banglajol.info/index.php/JSR

Insect Antifeedant Active Substituted Styryl 4-Ethoxyphenyl Ketones

S. Nalini[1], K. G. Sekar[2], S. Srinivasan[3], I. Muthuvel[4, 5], G. Thirunarayanan[4*]

[1]Department of Chemistry, Periyar Government Arts College, Cuddaloare-607 001, India
[2]Department of Chemistry, National College, Tiruchirappalli-620 001, India
[3]DDE Wing of Chemistry, Annamalai University, Annamalainagar-608 002, India
[4]Department of Chemistry, Annamalai University, Annamalainagar-608 002, India
[5]Department of Chemistry, MR. Government Arts College, Mannargudi-614 001, India

Received 29 November 2022, accepted in final revised form 21 May 2023

Abstract

About eleven substituted styryl 4-ethoxy phenyl ketones were synthesized by ultrasound-promoted greener solvent assisted Crossed Aldol condensation of 4-ethoxy acetophenone and various substituted benzaldehydes. In this method, the obtained yield was more than 85 %. These unsaturated ketones were characterized by their analytical and spectroscopic data. The insect antifeedant activity of these ketones was evaluated by castor leaf discs with the 4th instar larvae *Achoea Janata L*. All enones showed weak, moderate, and good insect antifeedant activity.

Keywords: Styryl 4-ethoxyphenyl ketone; Ultrasonication; Greener solvent; Environmentally benign condensation; Insect antifeedant activity; 4th Instar larvae.

doi: http://doi.org/10.3329/jsr.v15i3.63033 J. Sci. Res. **15** (3), 783-791 (2023)

1. Introduction

Enones possess a secondary metabolite, and they behave as insect repelling activity. More than one lakh secondary metabolite compounds occur in terrestrial plants, and they behave as herbivores in nature [1]. Due to the presence of all kinds of alkaloids, phenolics, and terpenoids in secondary metabolites, they act as insect-repellent agents [2]. Terpenoids are well insect repellents among the other compounds present in the secondary metabolites. Based on the carbon skeleton numbers, the compounds with more than 30 carbons (triterpenoids-limonin) possess antifeedant insect characters. Secondary clerodanes, the abietanes, sesquiterpenes lactones, and drimane polygodial also showed insect-repellent activity [1]. Numerous chemicals are used for insect antifeedant agents. Among synthetic organics, the chalcones and flavanones showed good antifeedant activities [3]. Numerous chalcones were employed for the inhibition of insect activity on agricultural plants. Halo-substituted keto compounds enhance insecticidal activities [4]. Numerous enones were

---

[*] *Corresponding author*: drgtnarayanan@gmail.com

synthesized using various methods, including crossed-aldol condensation. The crossed-aldol condensation consists of a reaction between methyl ketones and aldehydes in the presence of a Lewis kind of acid-base catalyst to yield the beta hydroxy carbonyl compounds, and the elimination of water gave an unsaturated carbonyl substrate [4,5]. This condensation was carried out with an ultrasonication process. This ultrasonication method offered short reaction time, high yields, applying greener solvents, and environmentally benign reactions. Chalcones are the key transitional species for organic building blocks. This is employed for the synthesis of pyrazolines, pyrimidines, thiopyrimidines, oxazine, [R] N-hydroxyethyl-piperidine, pyrrolidine homo aza sugars, bicyclic di-aza sugars, and 5-hydroxy substituted isofagomine analogs derivatives either using solvent-free or greener solvent assisted conventional heating or ground chemistry demonstrations [6-11]. The polar group, ene, and carbonyl segments are important for the insect antifeedant activities of enones. The insect antifeedant activity of various substituted naphthyl enones, 9H-fluorenyl chalcones [12], piper ribesioides wall extracts and alleleo chemicals [13], (+)-isofraxinellone [14], 2,5-dimethyl-3-thienyl enones [15] and substituted styryl 3,4-dichloro phenyl ketones [16] were investigated by Thirunarayanan and his co-workers. The Fluorinated methyl imine shows insect antifeedant activities against 4th instar larvae [17]. Subramanian *et al.* has studied the solvent-free synthesis and insect antifeedant character of 2, 5-dimethyl-3-furyl chalcones [18]. The essential oil and its derivatives possess insect antifeedant properties [19,20]. Researchers found to be that oxazine derivatives also showed antifeedant activities [21]. The bicyclo norbornyls, carbothioamides-based substrates, halogen-substituted enones, and Malagasy medicinal plant behaves as insect antifeedants [22, 23]. Keto oxirane, Troger bases, and 4-substituted naphthacyl ester substances reflect their well-insect antifeedant activities through castor leaf discs [24-26]. In the present and past, a literature survey against the synthesis and evaluation of insect antifeedant activities of the title compounds was not reported. Hence the authors enthusiastically studied the synthesis of the above-titled compounds in assessing their insect antifeedant activities against the 4th instar larva *Achoea Janata L* through castor leaf discs.

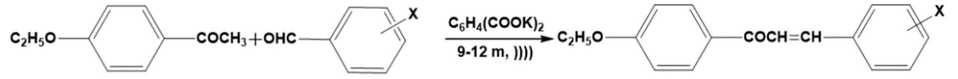
2. Experimental

2.1. *General*

Chemicals and solvents used in this study were procured from Sigma-Aldrich Chemical Company, Bengaluru, India. Melting points of all enones were measured from Raga Tech electrical melting point apparatus and are uncorrected. The purities of all enones were examined with the authentic sample data reported earlier in the literature.

2.2. *Synthetic procedure the synthesis of substituted styryl 4-ethoxy phenyl ketones*

An equimolar quantity of 4-ethoxy acetophenone and (1 mmol) substituted benzaldehydes (1 mmol) and 0.5 mL of 1 M potassium phthalate, and 10 mL of ethanol were ultrasonicated for 7-12 minutes (**Scheme 1**) (CITIZEN Ultra Sonicator, 120W, 40 Hz, 230V Ac).



Entry	1	2	3	4	5	6	7	8	9	10	11
X	H	3-Br	4-Br	3-Cl	4-Cl	4-F	2-OCH_3	4-OCH_3	2-CH_3	3-NO_2	4-NO_2

Scheme 1. Ultrasonicated Crossed Aldol condensation for the synthesis of substituted styryl 4-ethoxyphenyl enones.

The feasibility of the reaction was checked by a thin-layer chromatogram. The obtained crude (*E*)-4-ethoxyphenyl enones were filtered at the pump and washed with water dried. Further, it was recrystallized from rectified spirit to afford the glittering yellow color solids, which are kept in a desiccator. The yield, time, and physical constants are presented in Table 1. The IR and NMR spectral values of these substituted styryl 4-ethoxyphenyl enones are verified with the data reported in the literature earlier. These comparisons of spectral data were well in agreement with the reported data and are given in Table 2.

Table 1. Analytical, time, yield, and melting points of synthesized substituted styryl 4-ethoxyphenyl enones.

Entry	X	M.F.	M.W.	Time (m)	Yield (%)	M.P. (°C)
1	H	$C_{17}H_{16}O_2$	252	7	88	72-73(71-72) [26]
2	3-Br	$C_{17}H_{15}BrO_2$	330	8	87	90-91 (88-89) [26]
3	3-Br	$C_{17}H_{15}BrO_2$	330	8	90	133-134 (132-133) [26]
4	3-Cl	$C_{17}H_{15}ClO_2$	286	8	89	91-92 (89-90) [26]
5	4-Cl	$C_{17}H_{15}ClO_2$	286	7	88	127-128 (126-127) [26]
6	4-F	$C_{17}H_{15}FO_2$	270	10	85	102-103 (101-102) [26]
7	2-OCH_3	$C_{18}H_{18}O_3$	282	11	89	99-100 (98-99) [26]
8	4-OCH_3	$C_{18}H_{18}O_3$	282	8	91	92-93 (91-92) [26]
9	2-CH_3	$C_{18}H_{18}O_2$	266	9	86	98-99 (97-98) [26]
10	3-NO_2	$C_{18}H_{15}NO_4$	297	12	85	93-94 (91-92) [26]
11	4-NO_2	$C_{18}H_{15}NO_4$	297	10	85	119-120 (118-119) [26]

Table 2. The infrared and NMR characteristic spectral data of synthesized substituted styryl 4-ethoxyphenyl ketones.

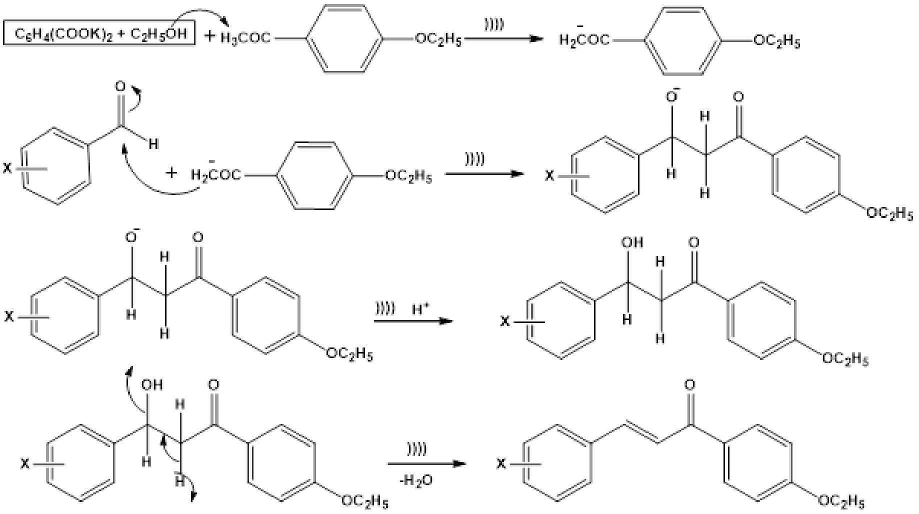
Entry	X	IR (ν, cm^{-1})		^1H (δ, ppm)			^{13}C NMR (δ, ppm)			
		$CO_{s\text{-}cis}$	$CO_{s\text{-}trans}$	Hα	Hβ	X	Cα	Cβ	CO	X
1	H	1657	1603	7.575	7.780	---	121.89	143.22	188.75	---
2	3-Br	1657	1608	7.275	7.710	---	123.02	142.15	188.19	---
3	3-Br	1658	1631	7.516	7.212	---	122.43	142.46	188.41	---
4	3-Cl	1660	1611	7.534	7.721	---	123.19	142.17	188.24	---
5	4-Cl	1663	1604	7.521	7.768	---	122.35	142.43	188.43	---
6	4-F	1656	1605	7.481	7.761	---	121.59	142.63	188.55	---
7	2-OCH_3	1652	1603	7.431	7.781	3.792	119.59	143.67	188.81	63.54
8	4-OCH_3	1651	1609	7.429	7.765	3.771	119.64	143.71	188.82	63.56
9	2-CH_3	1650	1600	7.512	7.767	2.381	120.01	144.13	188.77	23.43
10	3-NO_2	1659	1616	7.671	7.823	---	122.21	140.76	187.83	---
11	4-NO_2	1664	1623	7.763	7.715	---	123.82	146.56	187.89	---

2.3. *Insect antifeedant activity*

The multi-biological activities present in these different chalcones are intended to inspect their insect antifeedant activities against castor semi-looper. The larvae of *Achoea Janata L* were trained as pronounced on the leaves of castor Ricinus communis in the laboratory in the range of 26 ±1 °C temperature and a comparative humidity of 75-85 %. The leaf–disc bioassay method [27] was employed against the 4th instar larvae to evaluate the antifeedant activity. The 4th instar larvae were selected for examination because the larvae at this level fed very voraciously.

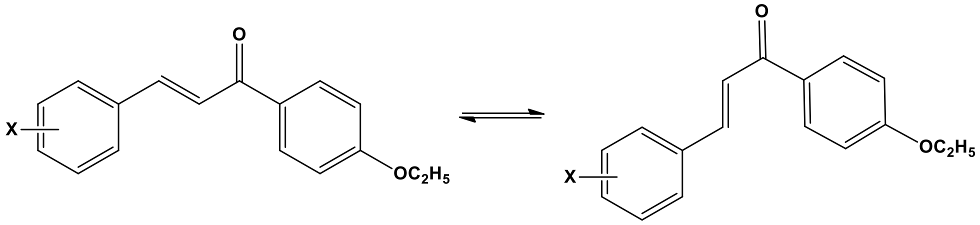
3. Results and Discussion

In our synthetic organic research laboratory, authors attempt to synthesize these enones by ultrasonication-assisted potassium phthalate-promoted Crossed Aldol condensation of 4-ethoxy acetophenone and various substituted benzaldehydes. This condensation gave more than 85 % yield and followed the well-known Lewis's acid-base catalyzed aldol condensation mechanism. The first step consists of the formation of carbanion of methyl ketone by loss of proton by the Lewis base catalyst. The second step consists of the attack of carbonyl carbon of the aryl aldehyde and carbonyl oxygen, getting a negative charge and then protonated to form a beta-hydroxy carbonyl compound. The third step consists of beta-elimination of water given the respective enone. These steps are shown in Scheme 2.



Scheme 2. Ultrasonicated Crossed Aldol condensation mechanistic synthetic route for the synthesis of substituted styryl 4-ethoxyphenyl enones.

The synthesized ketones existed in *s-cis* and *s-trans* conformers based on carbonyl and an alkene group orientation. These conformers are shown in Fig. 1.



s-cis *s-trans*

Fig. 1. The *s-cis* and *s-trans* conformers of substituted styryl 4-ethoxyphenyl enones.

The effect of this condensation was investigated using various solvents such as acetonitrile, dichloromethane, dioxane, ethanol, methanol, n-propanol, and tetrahydrofuran. Among these solvents, we found to be the ethanol solvent gave more yield than other solvents. Dioxane gave the least yield. In general, the electron-donating substituents yield a higher percentage of products than electron-withdrawing substituents in all solvents medium. The high electronegative fluorine substituted aldehyde gave lesser yields than the parent and electron-donating substituent methoxy group. The effect of solvent effect on this condensation is presented in Table 3.

Table 3. Influence of solvent effects on the ultrasonicated promoted potassium phthalate assisted Aldol condensation of 4-ethoxy acetophenone and substituted benzaldehydes.

Entry	Solvents→ X ↓	ACN	DCM	DO	EtOH	MeOH	n-Prop	THF
1	H	78	69	55	86	82	80	65
2	3-Br	76	64	54	85	79	75	64
3	4-Br	80	65	55	87	80	77	65
4	3-Cl	78	63	50	86	75	76	60
5	4-Cl	80	68	56	87	76	78	56
6	4-F	63	59	55	85	74	74	65
7	2-OCH_3	82	74	63	90	87	85	72
8	4-OCH_3	84	76	65	92	88	88	75
9	2-CH_3	85	73	62	88	76	86	70
10	3-NO_2	65	55	56	86	74	73	51
11	4-NO_2	68	56	53	85	75	73	52

ACN: Acetonitrile; DCM: Dichloromethane; DO: Dioxane; EtOH: Ethanol; MeOH: Methanol; n-Prop: n-Propanol; THF: Tetrahydrofuran

3.1. *Insect antifeedant activity*

Leaf discs of a span of 1.85 cm were perforated from castor leaves with the petioles intact. The 4-methoxyphenyl chalcones were dissolved in acetone at 200 ppm concentration and dipped for 5 min. The leaf discs were well dried and kept in a one-liter beaker holding little water to enable translocation of water. Therefore, the leaf discs will be fresh throughout the duration of the rest. The test insect 4th instar larvae were released on the leaf discs of all enones and permissible to feed on them for 24 h. The insect feed portion of the leaf discs consumed was measured by Dethler's' method [27]. The observed antifeedant activity of enones exists in Table 4. The consequences of the antifeedant activity of chalcones are presented in Table 5, and these data reveal that compounds 2-6 are found to reflect remarkable antifeedant among all other compounds. This test was performed with the insects, which took only a two-leaf disc soaked under the solution of this compound. Enones 2-6 also showed enough antifeedant activity, but their activities were lesser than 5. In other words, the +I effect of electron-withdrawing substituents such as halogens, including the high electronegative character of fluorine, showed good insect antifeedant activities other than nitro substituents. The electron-donating -I effect of substituents such as methoxy and methyl groups showed less insect antifeedant activities. It may be associated with the conjugative resonance structure, as shown in Fig. 2. The conjugation arises from either substituent in styryl moiety or ketone moiety.

Table 4. The measured insect antifeedant activities of synthesized substituted styryl 4-ethoxyphenyl ketones.

Entry	X	4-6 p.m.	6-8 p.m.	8-10 p.m.	10-12 p.m.	12-6 a.m.
1	H	1	2.5	2.5	1.5	1
2	3-Br	0.75	0.75	1.5	1	1.5
3	3-Br	0.75	0.75	1.5	1	1.5
4	3-Cl	0.5	0.5	1	0.5	1
5	4-Cl	0.25	0.25	0.5	0	0.5
6	4-F	0.75	1	1	1	1
7	2-OCH_3	1	3	3	2	1
8	4-OCH_3	1	3	3	2	1
9	2-CH_3	1.5	3	2.5	2.5	1.5
10	3-NO_2	3	3	3	3	2
11	4-NO_2	3	3	3	3	2

Entry	X	6-8 p.m.	8 a.m. –12 noon	12 noon – 2 p.m.	2-4 p.m.	Total leaf disc consumed in 24 h
1	H	1	0	0	0	1.05
2	3-Br	0.5	0	0	0	0.66
3	3-Br	0.5	0	0	0	0.66
4	3-Cl	0.25	0	0	0	0.41
5	4-Cl	0	0	0	0	0.15
6	4-F	0.75	0	0	0	1.02
7	2-OCH_3	1	0	0	0	1.20
8	4-OCH_3	1	0	0	0	1.20
9	2-CH_3	1.5	0	0	0	1.38
10	3-NO_2	1	0	0	0	1.66
11	4-NO_2	1	0	0	0	1.66

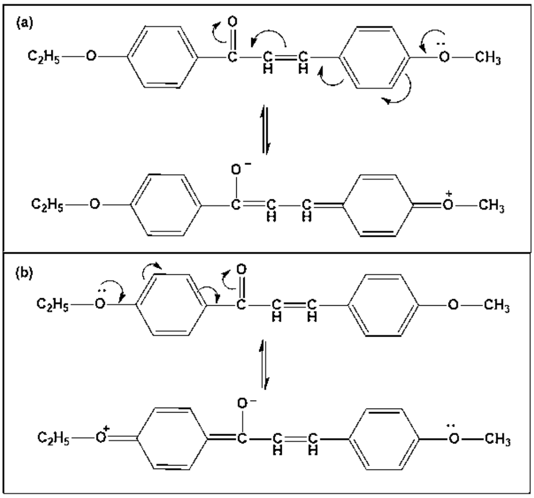


Fig. 2. The Resonance-conjugative structure of 4-methoxystyryl-4-methoxyphenyl ketone.

Further, compound 5 was subjected to measure the antifeedant activity at different 50, 100, and 150 ppm concentrations, and the observation was tabulated in Table 4. These data reveal that as the concentrations decrease, the activity also decreases. The results in Table 4 show that chalcone 5 showed considerable antifeedant activity at 150 ppm concentration.

Table 5. The measured insect antifeedant activities of 4-chlorostyryl-4-ethoxyphenyl ketone in 50, 100, and 150 ppm concentrations.

Entry	X	Concentration (ppm)	4-6 p.m.	6-8 p.m.	8-10 p.m.	10-12 p.m.	12-6 a.m.
5	4-Cl	50	0.75	0.50	0.25	0	0
		100	0.50	0.50	0.25	0.25	0.25
		150	0.25	0. 25	0	0	0
		Concentration (ppm)	6-8 p.m.	8 a.m. – 12 noon	12 noon – 2 p.m.	2-4 p.m.	Total leaf disc consumed in 24 h
		50	0	0	0	0	0.16
		100	0	0	0	0	0.19
		150	0	0	0	0	0.05

4. Conclusion

More than 85 % yields of various substituted 4-ethoxy phenyl enones were synthesized by ultrasound-assisted Crossed Aldol condensation method. These enones were characterized by their physical constants and spectroscopic data. The greener solvent, ethanol, affords higher yields in this condensation. The insect antifeedant activities of these enones were measured using castor leaf discs with the 4th instar larvae *Achoea Janata L*. All enones show insect antifeedant activity. Compound 5 shows good antifeedant activity than 2-4 and 6. The remaining compounds show moderate and weak insect antifeedant activity.

Acknowledgment

The authors thank the DST-NMR facility, Department of Chemistry, Annamalai University, Annamalainagar-608002, for recording the NMR spectra of all compounds.

References

1. M. Isman, Pesticide Outlook. **3**, 152 (2002). https://doi.org/10.1039/b206507j
2. J. L. Frazier, The Perception of Plant Allelochemicals that Inhibit Feeding, In: Molecular Aspects of Insect-Plant Associations, Edited by L. B. Brattsten and S. Ahmad (Plenum Press, New York, 1986) pp. 1-42. https://doi.org/10.1007/978-1-4613-1865-1_1
3. M. Morimoto, K. Tanimoto, S. Nakano, T. Ozaki, A. Nakano, and K. Komai, J. Agri. Food Chem. **51**, 389 (2003). https://doi.org/10.1021/jf025627a
4. R. Sundararajan, R. Arulkumaran, S. Vijayakumar, D. Kamalakkannan, *et al.* Q-science Connect. **13**, 1, (2013). https://doi.org/10.5339/connect.2013.30
5. G. Thirunarayanan and K. G. Sekar, J. Korean Chem. Soc. **57**, 599 (2013). https://doi.org/10.5012/jkcs.2013.57.5.599
6. G. Thirunarayanan and K. G. Sekar, Der Pharma Chemica. **5**, 142 (2013).
7. G. Thirunarayanan and V. Renuka, J. Chil. Chem. Soc. **59**, 2574 (2014). https://doi.org/10.4067/S0717-97072014000300011
8. S. P. Sakthinathan, G. Vanangamudi, and G. Thirunarayanan, Spectrochim. Acta Part A: Mol. Biomol. Spectro. **95**, 693 (2012). https://doi.org/10.1016/j.saa.2012.04.082
9. D. D. Dhavale, M. M. Matin, T. Sharma, and S. G. Sabharwal, Bioorg. Med. Chem. **11**, 3295 (2003). https://doi.org/10.1016/S0968-0896(03)00231-1
10. D. D. Dhavale and M. M. Matin, Tetrahedron **60,** 4275 (2004). https://doi.org/10.1016/j.tet.2004.03.034
11. M. M. Matin, T. Sharma, S.G. Sabharwal, and D. D. Dhavale, Org. Biomol. Chem. **3**, 1702 (2005). https://doi.org/10.1039/b418283a
12. G. Thirunarayanan and V. Sathiyendiran, Int. Lett. Chem. Phys. Astro. **49**, 1 (2015). https://doi.org/10.56431/p-g0r04d
13. A. Pengsook, V. Bullangpoti, O. Koul, S. Nobsathian, *et al.* Chem. Biol. Tech. Agric. **9**, 17 (2022). https://doi.org/10.1186/s40538-021-00270-3
14. Y. Okuno, S. Marumoto, J. Tsurumi, and M. Miyazawa, Natural Prod. Res. **23**, 1518 (2019). https://doi.org/10.1080/14786419.2017.1422180
15. G. Vanangamudi, M. Subramanian, and G. Thirunarayanan, Arabian J. Chem. **10**, S1254 (2017). https://doi.org/10.1016/j.arabjc.2013.03.006
16. G. Thirunarayanan, S. Surya, S. Srinivasan, G. Vanangamudi, and V. Sathiyendiran, Spectrochim. Acta Part A: Mol. Biomol. Spectro. **75**, 152 (2010). https://doi.org/10.1016/j.saa.2009.10.003
17. G. Thirunarayanan and G. Vanangamudi, Spectrochim. Acta Part A: Mol. Biomol. Spectro. **81**, 390 (2011). https://doi.org/10.1016/j.saa.2011.06.027
18. M. Subramanian, G. Vanangamudi, and G. Thirunarayanan, Spectrochim. Acta Part A: Mol. Biomol. Spectro. **110**, 116 (2013). DOI: http://dx.DOI.org/10.1016/j.saa.2013.03.023
19. F. Valcárcel, A. Sonia Olmeda, M. G. González, M. F. Andrés *et al.* Frontiers Agro. **3**, ID 662802 (2021). https://doi.org/10.3389/fagro.2021.662802
20. J. Brari and V. Kumar, Int. J. Pure Appl. Zoo. **7**, 41, (2019). https://doi.org/10.35841/2320-9585.7.41-45
21. G. Thirunarayanan, World Sci. News **118**, 1 (2019).

22. G. Thirunarayanan, Macidonian J. Chem. Chem. Engg. **36**, 1 (2017).
23. E. A. Inocente, B. Nguyen, P. K. Manwill, A. Benatrehina, *et al*., Insects **10**, 373 (2019). https://doi.org/10.3390/insects10110373
24. G. Thirunarayanan and G. Vanangamudi, Arabian J. Chem. **9**, S269, (2016). https://doi.org/10.1016/j.arabjc.2011.03.020
25. G. Thirunarayanan, Arabian J. Chem. **10(S1),** S636 (2017). https://doi.org/10.1016/j.arabjc.2012.10.025
26. P. Janaki, K. G. Sekar, and G. Thirunarayanan, Org. Chem. Indian J. **9**, 68 (2013).
27. V. G. Dethler, Chemical Insect Attractants and Repellents (Blackistan, Philadeciphia, 1947) pp. 210.