SYNTHESIS AND CHARACTERIZATION OF SOME NEW ODORANT SCHIFF BASES FOR FRAGRANCE COMPOSITION

THESIS

SUBMITTED TO THE
FOREST RESEARCH INSTITUTE (DEEMED) UNIVERSITY
DEHRADUN, UTTARAKHAND

FOR
THE AWARD OF THE DEGREE OF

DOCTOR OF PHILOSOPHY IN FORESTRY
(DISCIPLINE: CHEMISTRY OF FOREST PRODUCTS)

BY

PRASOON KUMAR KAUSHIK

CHEMISTRY DIVISION
(CENTRE FOR ADVANCED STUDIES IN CHEMISTRY OF FOREST PRODUCTS)
FOREST RESEARCH INSTITUTE
(INDIAN COUNCIL OF FORESTRY RESEARCH AND EDUCATION)
P.O. NEW FOREST, DEHRADUN-248 006 (INDIA)

2016
No.33/10PHD91/2011-FRIDU  
Forest Research Institute (Deemed) University  
P.O.I.P.E., Kaulagarh Road,  
Dehra Dun – 248 195

Dated 11/10/2011  
E-mail: tripathiak@icfse.org

To,  
Mr. Prasoon Kumar Kaushik  
Research Scholar  
Chemistry Division  
FRI, Dehradun

Sub:-  Registration for Doctor of Philosophy Degree in Forestry.

Dear Sir/Madam,

In response to your application dated 20.04.2010 for enrolment as Research Scholar for the Degree of Doctor of Philosophy in Forestry in this Institute, it is to inform you that the following decisions have been taken:-

1. You have been registered for Doctor of Philosophy w.e.f. 01.03.2011 to 28.02.2015.
2. Your Enrolment number is: 10PHD91  
   (For all further correspondence please quote your enrolment number.)
3. Name of Research Centre: FRI, Dehradun
4. The Topic of research approved by the FRI University: “Synthesis and characterization of some new odorant Schiff bases for fragrance composition”.
5. Name of Discipline: Chemistry of Forest Products  
   (As per clause 3.3 of the Ph.D. Ordinance)
6. (i) Name of Supervisor: Dr. V.K. Varshney  
   (ii) Name of Co-Supervisor: Dr. S.V. Shukla
7. (a) You are advised to deposit the next installment of Laboratory fee Rs. 3,000/- payable at FRIU/Research Centre concerned through bank draft in the month of March, 2012.
   (b) Library fee of Rs. 1,000/- per year payable at FRIU/Research Centre concerned in the month of March for each year of registration till submission of thesis.
   (c) Annual fee of Rs. 5,000/- payable every year in the month of March during the period of Registration at FRI University till submission of thesis.
   (d) The above mentioned fee should be deposited during the month of March every year failing which a late fee of Rs. 500/- (Bank Draft) will also have to be deposited in this office.
   (e) You are also required to deposit the thesis fee and viva-voce exam fee at the time of submitting the thesis and viva voce exam respectively to the University.
8. The research scholar is required to submit the six monthly progress report till the work is presented in the pre-thesis submission seminar and is approved by the committee for submission of thesis.

P.T.O.
The initial 4 progress reports may come through Chairman and Member Secretary R.A.C. The rest can come through Head of Division and Supervisor concerned. **The RAC shall consider the progress reports and forward the same with recommendations and comments, if any, to the Registrar, otherwise the progress report will not be counted.**

9. **Registration of a Ph.D. Scholar is liable to be cancelled by the Director at any time if:**
   i. Two consecutive six monthly progress reports are not submitted at all or are not satisfactory.
   ii. The attendance in case of Research Scholar is less than 75% in any term.

10. No Ph.D. Scholar shall accept during the period of research any paid assignment apart from Research Fellowships, Research Assistantship etc. unless in the opinion of the RAC such an assignment will not interfere with his/her research work.

11. A Ph.D. Scholar shall not be permitted to take any other degree course, but may be permitted by the RAC to take part-time Diploma or Certificate course(s) not affecting the scholars research work adversely.

12. **A Research Scholar is required to pursue research in the Institute/Research Centre under the Supervisor on the approved subject for not less than twenty-four months commencing from the date of his/her registration.**

13. The Research Scholar may not later than eight months from the date of Registration, modify the scheme of the research work or nature or scope of the subject, on the recommendation of the Supervisor and RAC with the approval of Director.

14. As per clause 6.14 of the Ph.D. Ordinance, the Ph.D. scholars shall publish at least one research paper in a peer reviewed journal before the submission of the thesis to the University for Evaluation, and produce evidence for the same in the form of acceptance letter or the reprint. The acceptance letter or the reprint should be attached along with the thesis in the annexure.

15. **The research scholar should normally submit the thesis within 4 calendar years from the date of registration. Further extension of the term on yearly basis is possible only on specific recommendation of R.A.C., if approved by the R.D.C. However no extension is possible beyond 6 years of registration. The recommendation of Research Advisory Committee for extension of term of registration of the scholar should reach this office before expiry of term of registration.**

16. Further the performance of the Research Scholar shall be evaluated at the end by the R.A.C. concerned in the pre-thesis submission seminar and R.A.C. shall send the minutes to Registrar, FRI University with full comments.

17. **Please ensure that the clause 7 of the Ph.D. Ordinance is fully complied with before submission of the thesis to University.**

18. **Please note that your Registration as Research Scholar is to be governed as per rules, regulation and ordinances of FRI University, with applicable amendments made by the University from time to time. For all further correspondence please quote your enrolment number.**

(Encl: 1. Fee receipt No. 9078 dated 07.09.2011 for Rs. 22,500/-
2. Format of progress report)

Copy to:
1. Dr. V.K. Varshney, Scientist -E, Chemistry Division, FRI, Dehradun, for information and necessary action.
2. Dr. S.V. Shukla, Dy. Director (Flavour & Fragrance), Flavour & Fragrance Development Centre, Kannauj for information and necessary action.
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FOREST RESEARCH INSTITUTE (DEEMED) UNIVERSITY
Under Section 3 of the UGC Act 1956
P.O.I.P.E. KAULAGARH ROAD
DEhra DUN

Enrollment Number 10PHD91

CERTIFICATE

This is to certify that
Sh./Smt. Km. Prasoon Kumar Kaushik Research Scholar
of Forest Research Institute (Deemed) University
has successfully completed the 6 monthly compulsory courses in
Basic Forestry,
Computer Application
Statistics and Research Methods in Forestry
And
Research Problem
as per the U.G.C. (minimum standard and procedure for Award of M.Phil/Ph.D. Degree) Regulations, 2009

Dehra Dun
Dated: 19.6.2013

Registrar
Knowledge gives humility, from humility, one attains character; From character, one acquires wealth; from wealth good deeds (righteousness) follow and then happiness.
Dedicated

to

My beloved parents...
ACKNOWLEDGEMENTS

I want to thank ‘God’, the Almighty, for my life through all tests in the past years and blessed me with health, courage and patience to carry on this work even when the going got tough.

A research work is never the work of anyone alone. The contributions of many different people, in their different ways, have made this possible. I would like to extend my appreciation especially to the followings.

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PRASOON KUMAR KAUSHIK
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<td>Description</td>
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<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>α</td>
<td>Alpha</td>
</tr>
<tr>
<td>β</td>
<td>Beta</td>
</tr>
<tr>
<td>b.p.</td>
<td>Boiling point</td>
</tr>
<tr>
<td>CO₂</td>
<td>Carbon dioxide</td>
</tr>
<tr>
<td>°C</td>
<td>Centigrade</td>
</tr>
<tr>
<td>cm⁻¹</td>
<td>Characteristic absorptions</td>
</tr>
<tr>
<td>δ</td>
<td>Delta (Chemical shift)</td>
</tr>
<tr>
<td>CDCl₃</td>
<td>Chloroform-d</td>
</tr>
<tr>
<td>cfu</td>
<td>Colony forming unit</td>
</tr>
<tr>
<td>CAGR</td>
<td>Compound annual growth rate</td>
</tr>
<tr>
<td>CM</td>
<td>Conventional method</td>
</tr>
<tr>
<td>DMSO</td>
<td>Dimethylsulfoxide</td>
</tr>
<tr>
<td>DSC</td>
<td>Differential scanning calorimetry</td>
</tr>
<tr>
<td>DTG</td>
<td>Derivative thermogravimetric analysis</td>
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<tr>
<td>$</td>
<td>Dollar</td>
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<tr>
<td>ε</td>
<td>Epsilon</td>
</tr>
<tr>
<td>E.U. Patent</td>
<td>European union patent</td>
</tr>
<tr>
<td>F&amp;F</td>
<td>Fragrance &amp; Flavor</td>
</tr>
<tr>
<td>FT-IR</td>
<td>Fourier Transform Infrared spectroscopy</td>
</tr>
<tr>
<td>&gt;</td>
<td>Greater than</td>
</tr>
<tr>
<td>H</td>
<td>Hydrogen</td>
</tr>
<tr>
<td>HCl</td>
<td>Hydrochloric acid</td>
</tr>
<tr>
<td>h</td>
<td>Hour</td>
</tr>
<tr>
<td>MPA</td>
<td>Megapascal</td>
</tr>
<tr>
<td>MHz</td>
<td>Megahertz</td>
</tr>
<tr>
<td>m.p.</td>
<td>Melting point</td>
</tr>
<tr>
<td>m</td>
<td>Meta</td>
</tr>
<tr>
<td>MA</td>
<td>Methylantranilate</td>
</tr>
<tr>
<td>MTCC</td>
<td>Microbial Type Culture Collection</td>
</tr>
<tr>
<td>Symbol</td>
<td>Definition</td>
</tr>
<tr>
<td>--------</td>
<td>------------</td>
</tr>
<tr>
<td>μg</td>
<td>Microgram</td>
</tr>
<tr>
<td>MW</td>
<td>Microwave</td>
</tr>
<tr>
<td>MWI</td>
<td>Microwave irradiation</td>
</tr>
<tr>
<td>ml</td>
<td>Millilitre</td>
</tr>
<tr>
<td>mm</td>
<td>Millimetre</td>
</tr>
<tr>
<td>MIC</td>
<td>Minimum Inhibitory Concentration</td>
</tr>
<tr>
<td>min.</td>
<td>Minutes</td>
</tr>
<tr>
<td>MW</td>
<td>Molecular weight</td>
</tr>
<tr>
<td>HHP</td>
<td>N (2-hydroxy benzylidine) 2-hydroxy phenyl</td>
</tr>
<tr>
<td>PHP</td>
<td>N-(1-phenyl-2-hydroxy-2-phynyl-ethylidine) 2-hydroxyphenyl</td>
</tr>
<tr>
<td>PDH</td>
<td>N-(1-phenyl-2-hydroxy-2-phynyl-ethylidine)2,4-dinitrophenyl hydrazine</td>
</tr>
<tr>
<td>NCCLS</td>
<td>National Committee for Clinical Laboratory Standards</td>
</tr>
<tr>
<td>NTCC</td>
<td>National type culture collection</td>
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<tr>
<td>–ve</td>
<td>Negative</td>
</tr>
<tr>
<td>N</td>
<td>Nitrogen</td>
</tr>
<tr>
<td>NMR</td>
<td>Nuclear magnetic resonance</td>
</tr>
<tr>
<td>NAM</td>
<td>Nutrient Agar Media</td>
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<tr>
<td>O</td>
<td>Oxygen</td>
</tr>
<tr>
<td>ppm</td>
<td>Parts per million</td>
</tr>
<tr>
<td>p</td>
<td>Pera</td>
</tr>
<tr>
<td>%</td>
<td>Percentage</td>
</tr>
<tr>
<td>+ve</td>
<td>Positive</td>
</tr>
<tr>
<td>KBr</td>
<td>Potassium bromide</td>
</tr>
<tr>
<td>PDA</td>
<td>Potato Dextrose Agar</td>
</tr>
<tr>
<td>ROS</td>
<td>Reactive oxygen species</td>
</tr>
<tr>
<td>Rs</td>
<td>Rupees</td>
</tr>
<tr>
<td>SBs</td>
<td>Schiff bases</td>
</tr>
<tr>
<td>SME’s</td>
<td>Small and medium enterprise</td>
</tr>
<tr>
<td>SOR</td>
<td>Structure odor relationships</td>
</tr>
<tr>
<td>TG</td>
<td>Thermo-gravimetric analysis</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
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<td>--------------</td>
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<tr>
<td>USD</td>
<td>United state dollar</td>
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<tr>
<td>U.S. Patent</td>
<td>United state patent</td>
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<tr>
<td>W</td>
<td>Watt</td>
</tr>
<tr>
<td>μl</td>
<td>Microlitre</td>
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<tr>
<td>π</td>
<td>Pi</td>
</tr>
<tr>
<td>ν</td>
<td>Nu</td>
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</tbody>
</table>
INTRODUCTION

Until the 1870s, perfumers worked with a relatively small number of materials, which were naturally derived, and they created a correspondingly small range of fragrance types, primarily in the citrus and floral families. Within this limited domain, perfumers could use an inefficient trial-and-error approach to create fragrances. The explosive growth of organic chemistry at the end of nineteenth century made innumerable new materials available to the perfumer, necessitating a rational method of fragrance creation (Rowe and Herman, 2005). The great world religions of Hinduism, Christianity, Islam, Budhism, Shintoism use fragrance in pursuance of their belief. Thus religious and pleasurable pursuits have been the main drives in the phenomenal growth of fragrance uses throughout the countries (Pybus and Sell, 2006). In fragrance industry, there is a lasting interest in the development of novel fragrances in order to create new odorant molecules in augmenting the aroma of fragrance composition for perfumery or for new extended applications. Schiff bases (or azomethines / anils / imines) are well known in the art of flavoring and perfumery.

A large number of odorant molecule have been produced since the dawn of organic chemistry 200 years ago, and vast database of odorants and their corresponding odor profiles has built up. The field of fragrance synthesis, though still small in comparison to say pharmaceuticals, is an 8-billion dollar industry. Odorant chemicals that are inexpensive, highly substantive, long lasting and non-toxic are highly desirable in the art of perfumery and flavoring. There is a global need to create perfumes that present much less hazard to human health in view of recent concerns over the safety of the perfumery materials. Many of the natural materials which contribute desired nuances to perfumery compositions are high in cost, vary in quality from one batch to another and /or are generally subject to the usual variations of natural products.

Aroma chemicals or fragrance compounds containing a carbonyl (aldehyde / ketone) functional group constitute an important group of raw materials for fragrance and flavor industry. However, most of such chemicals containing an aldehydic functional group are inherently unstable at the aldehyde moiety to oxidation to the corresponding
carboxylic acid, thereby losing their fragrance characteristics and hence limiting their use (McMurry, 1988). The ketone compounds of natural origin, except few cyclic terpene ketones and aromatic ketones are of minor importance as fragrance chemicals. The commercially used fragrant ketones are generally of synthetic origin. Ketones are generally much less reactive than aldehydes in the formation of Schiff bases. By using acid catalyst, higher reaction temperatures, longer reaction times, and removing the water as it forms, respectable yields of Schiff bases are obtained. Aromatic ketones are less reactive than aliphatic ketones. Recently the use of musk ketones has been stringently regulated due to their stability and consequently deleterious effect on the environment (Reeves, 1966; David, et al., 1984). The chemical transformation of carbonyl compounds into their novel derivatives, Schiff bases, therefore presents an innovative approach to overcome their above mentioned undesired attributes. Modern perfumers use an extensive palette of natural and synthetic chemicals. Thus, it will be of great scientific and technical interest to develop novel odorant Schiff bases from naturally occurring or nature identical reactant compounds.

### 1.1. Schiff bases

Schiff base is a nitrogen analog of an aldehyde or ketone in which the >C=O is replaced by RCH=NR’, where >C=N- is azomethine linkage. Schiff bases are typically prepared by the condensation of primary amines and aldehydes and less commonly ketones (Schiff, 1864; Patai, 1970). This condensation was first discovered by Hugo Schiff in 1864. The reaction is nucleophilic addition of the amine to the carbonyl compound followed by transfer of a proton from nitrogen to oxygen, water is lost and stable Schiff bases are formed. This removal is important as the conversion of aminal into the imine is reversible (Wenling, et al., 2013).

![Scheme 1: Condensation of primary amine with carbonyl compound to form Schiff base](image.png)
The experimental conditions depend on the nature of the amine and especially of the carbonyl compound which determine the position of the equilibrium. The general scheme of formation of a Schiff base is given in Scheme 1. Structurally these compounds are distinguished by the >C=N- linkage (Schiff, 1864; Reeves, 1966).

Where R, may be an alkyl or aryl group, Schiff base that contain aryl substituents are substantially more stable and more readily synthesized, while those which contain alkyl substituents are relatively unstable and readily polymerizable (Rauf, 2005). The formation is generally driven to the completion by removal of water, many Schiff base can be hydrolyzed back to their aldehyde and ketone and amine by aqueous acid or base, to avoid the reverse reaction some solvent is used in the water can be removed by azeotropic distillation. Sterically hindered carbonyl compounds are particularly unreactive. Aromatic aldehyde reacts smoothly under mild conditions and at relatively low temperature in a suitable solvent or without it. In condensation of aromatic amines with aromatic aldehyde, electron attracting substituents in the pera-position of amine decrease the rate of the reaction, while increasing it when on the aldehyde (Reeves, 1966). Aromatic ketones are less reactive than aliphatic ketones and harsh conditions such as higher reaction temperatures and longer reaction time are required to convert them into imines. Acid catalysis and water removal from the reaction mixture can significantly increase the reaction yields, from 80%-95%. Several new techniques of the synthesis of imines have been published, including solvent-free (Vass, et al., 1999; Gopalakrishnan, et al., 2007), K10 clay (Varma, et al., 1997), water suspension medium (Tanaka and Shiraishi, 2000), liquid crystals, molecular sieves (Andrade, et al., 2004; Taguchi and Westheimer, 1971), infrared and ultrasound irradiation (Wenling, et a., 2013; Vázquez, et al., 2004; Guzen, et al., 2007), Mg(ClO₄)₂ (Chakraborti, et al., 2001), P₂O₅/SiO₂ (Naeimi, et al., 2008), CaO under microwave power (Gopalakrishnan, et al., 2007), ethyl lactate as a tunable solvent (Bennett, et al., 2009), alumina (Boullet, 1985), CeC₁₃.7H₂O (Ravishankar, et al., 2010), polymer-supported (Annunziata, et al., 2002) and nanotube TiO₂ (in sunlight) (Sarvari, 2011).

Schiff bases are also known as ‘imines’, ‘azomethines’, ‘anils’ etc. When these compounds are prepared by ketones they are known as ‘kitimines’ and when prepared
by aldehydes they are known as the ‘aldimines’. Schiff bases called imines, anils, oximes, hydrazones, when H atom, phenyl group, OH group, NH$_2$ group attached respectively with nitrogen. Among the large number of synthetic and naturally occurring nitrogen donor molecules, Schiff bases are the greatest interest (Bheshadadia, 2007).

Schiff bases are well known in the art of flavoring and perfumery (Arctender, 1969). A great majority of Schiff bases are reported to possess floral and fruity odors, namely citrus type and, more particularly, reminiscent of the order of the orange flower (Baudin, 1993; Bauer, et al., 1997; Surburg and Panten, 2005; Mookherjee, et al., 1988; Mookharjee, et al., 1989(a); 1989(b); 1989(c); 1989(d); IFF, 2002; Firmenich, 1995). Schiff bases are also known to be useful as intermediates in producing other fragrance materials (Patai, 1970; Clercq, 2002). Several studies showed that the presence of a lone pair of electrons in a sp$^2$ hybridised orbital of nitrogen atom of the azomethine group is of considerable chemical and biological importance (Clercq and Verpoort, 2002; Rauf, 2005; Wenling, et al., 2013). Ligands containing sp$^2$ hybridized nitrogen atoms, particularly those in which the N-atom is a part of the aromatic system, show very extensive coordination chemistry (Adsule, et al., 2006; Bu, et al., 2005; Wenling, et al., 2013).

1.1.1. Formation of Schiff bases

The formation of a Schiff base (Scheme 2) is an equilibrium system. The reaction begins with a nucleophilic attack at the carbonyl carbon of the aldehyde/ketone by the lone pair on the N atom of the incoming primary amine. A proton is moved from the positively charged nitrogen to the negatively charged oxygen producing a neutral carbinolamine. The -OH group is then protonated by the reaction medium, forming OH$_2^+$, which is better leaving group than OH group. This dehydration step leads to the formation of an iminium ion. The next step is the deprotonation of the nitrogen of the iminium ion by water and the formation of the final product, an imine. As the formation of water is one of the driving forces of the reaction, its removal should push the reaction to the right and maximize yields (Tallon, 2010; March, 1985; McMurry, 1988).
The Schiff base formation is really a sequence of two types of reactions, i.e. _addition_ followed by _elimination_. Typically, the dehydration of the carbinolamine is the rate determining step of Schiff base formation and that is why the reaction is catalysed by acidic medium. Yet the acid concentration cannot be too high because amines are basic in nature. If the amine is protonated and becomes non nucleophile, equilibrium pulled to the left and carbinolamine formation cannot occur. Therefore, many Schiff bases synthesis are best carried out at mildly acidic pH. The formation is generally driven to the completion by separation of the product or removal of water, or both, many Schiff bases can be hydrolysed back to their aldehyde or ketones and amines by aqueous acid or base (Tallon, 2010; March, 1985; McMurry, 1988).

**1.1.2. Chemistry of Schiff bases**

German chemist Hugo Schiff developed a new class of organic compounds, Schiff bases. The preparation of these compounds is simple and smart. Because of the relative easiness of preparation, synthetic flexibility, and the special property of azomethine (\(>\text{C}=\text{N}<-\)) group, they show very interesting chemistry in fragrance compositions (Adsule, et al., 2006; Bu, et al., 2005; Sell, 2006).

When added to a carbonyl donor (aldehyde/ketone) in amino donor (primary amine), it forms the corresponding Schiff base. If the aldehyde carries an \(\alpha\)-hydrogen atom, the schiff base will be in equilibrium with the corresponding enamine. The relative proportions of Schiff base and enamine present will depend on the structure of the aldehyde, since the inductive and resonance effects will seek to minimise the total free energy of the molecule (Sell, 2006). Literature reveals that the importance of the Schiff bases to perfumery results from the fact that they increase aroma, chemical stability and tenacity of the aldehyde component. The Schiff bases are less reactive than the free aldehyde and, since the molecular weight is much higher, they are less volatile (Sell, 2006). Thus, loss of the aldehyde by both chemical reaction and evaporation is slowed down. Moreover, hydrolysis of the Schiff bases releases both the aldehyde and amine, both of has intense odors. Thus, use of a Schiff base generates a long-lived fragrance composition of the two ingredients. In general, the colour of the Schiff base is due to the presence of azomethine linkage. The color of reaction medium is darkened when a
Introduction

Scheme 2: Mechanism of Schiff base formation
Schiff base is formed from it. This is because of the hypsochromic shift in the ultraviolet absorption maximum resulting from the extension of conjugation (Sell, 2006).

1.1.3. Application of Schiff bases

Because of the special property of azomethine (>C=N-) group, Schiff bases have found extremely important applications, in Pharmacology, as a corrosion inhibitor, as a pesticide, as a disperse dye, as catalysts and also in miscellaneous applications, described briefly as below.

1.1.3.1. Pharmacological significance of Schiff bases

Biologically active molecules, Schiff bases, are known to show a variety of pharmacological activities (an account of which is given below) (Figure 1).

![Figure 1: Example of pharmacologically active Schiff bases](Murtaza, et al., 2014; Silva, et al., 2011)
1.1.3.1.1. Antimicrobial activities

1.1.3.1.1.1. Anti-plasmodium activity
Schiff bases are the potential molecules, which can be affective against the problem of drug resistance. In addition to synthetic derivatives, ancistrocladidine having iminium group moiety (Figure 2a), is a natural product produced by plant belonging to family Dioncophyllaceae and Ancistrocladiceae and is known as anti-malarial agent with activity against Plasmodium falciparum. Moreover, Schiff bases derived from aryl and ferrocyl group show activity against P. falciparum strain (Adams, et al., 2013). Schiff base obtained by the condensation of 2, 6-diarylsubstituted piperidin-4-one with 7-chloro-4-hydrazinoquinoline also showed antimalarial activity (Murtaza, et al., 2014; Kumar, et al., 2009).

1.1.3.1.1.2. Anti-fungal activity
Schiff bases have been reported to show promising anti-fungal activity (Nucci and Marr, 2005; Sahu, et al., 2012; Martins, et al., 2009; Khan, et al., 2013). Schiff bases of N-fluorosalicylaaldehyde are reported to show antifungal activity (Silva, et al., 2011; Shanmugam, et al., 2013). In addition, chitosan Schiff bases were found to stop the growth of many fungal strains including Colletotrichum humlagenarium and Botrytis cinerea (Figure 2b) (Silva, et al., 2011). Moreover, isatin based Schiff bases have been reported to show remarkable antifungal activity against various fungal strains like Microsporum gypseum, Microsporum audouinii, Cryptococcus neoformans, Epidermophyton floccosum and Candida albicans (Murtaza, et al., 2014; Silva, et al., 2011; Fadl, et al., 2010; Kumar, et al., 2009; Kumar, et al., 2013).

1.1.3.1.1.3. Anti-bacterial activity
Schiff bases are reported to be potent antibacterial agents (Silva, et al., 2011; Pradhan and Kumar, 2015; Sahu, et al., 2012). Schiff base synthesized from 2-hydroxy-1-naphthaldehyde and α-amino acids (L-tyrosine, L-arginine and L-lysine) and their manganese complexes have been reported to show excellent activity against the gram positive and gram negative strains of bacteria (Sakiyan, et al., 2014). Additionally, Schiff bases derived from salicylaldehyde show potent anti-bacterial activity (Figure 2c). N-(salicylidene)-2-hydroxy-aniline has been reported to show a prominent activity
against *Mycobaacterium tuberculosis* (Souza, et al., 2007; Murtaza, et al., 2014). While Schiff bases of 5-chlorosalicylalddehyde show enhanced anti-bacterial activity against bacterial strains (Shi, et al., 2007; Wang, et al., 2011; Panneerselvam, et al., 2009). However, some Schiff bases derivatives have also been reported to be bacteriostatic agent e.g. Schiff bases of 2, 4-dichloro-5-fluorophenyl are useful to stop the bacterial growth (Karthikeyan, et al., 2006; Silva, et al., 2011). Moreover, isatin-derived Schiff base or Schiff bases bearing nitroimidazole moiety show good antibacterial activities against various bacterial strains (Makawana, et al., 2013; Pandeya, et al., 1999; Patel, et al., 2006; Bhat, et al., 2013; Raparti, et al., 2009; Kulkarni, et al., 2009; Chohan, et al., 2012; Kumar, et al., 2009).

![Figure 2: Examples of bioactive Schiff bases, the imine or azomethine group present in each molecular structure with in a circle](Silva, et al., 2011)

1.1.3.1.4. Anti-viral activity

Schiff bases can play a vital role due to their reported antiviral nature. Schiff bases derived from isatin and bis-isatin are reported to show activities against different strains of viruses. Schiff base of gossypol show high antiviral activity (Silva, et al., 2011; Abbas, et al., 2013; Aliasghar, et al., 2013). Moreover, Schiff bases derived from prodrug abacavir (Ziagen) are reported to show good antiviral activity and trial revealed...
that they are potent lead molecule for further clinical use as anti-HIV therapy (Silva, et al., 2011; Clercq, 2002). Furthermore, Schiff bases of 2-phenylquinazoline-4(3)H-one are reported to show antiviral activity against some strains of viruses like feline corona virus, influenza viruses and herpes simplex virus type 1 and 2 (Murtaza, et al., 2014; Kumar, et al., 2010; Kumar, et al., 2009; Sahu, et al., 2012).

1.1.3.1.1.5. Anticancer activity
Cancer is a disease which leads to death. More than 200 cancer types have been reported in the human body. Schiff bases obtained from coumarin and pyrazole aldehyde has been tested against cancerous cell lines and showed mild anti-cancerous activity (Ali, et al., 2013). Moreover, in another study, mono and bis-schiff base have been reported effective against five cancer cell lines (Sondhi, et al., 2012; Ren, et al., 2002). Furthermore, Schiff bases can effectively form complexes with transition metal and these metal complexes are reported to show good anticancer activities; Cu-complexes with vaniline Schiff bases (Tabassum, et al., 2013) and 5-dimethyl-2-phenyl-4-[(pyridine-2-ylmethylene)-amino]-1,2-dihydro-pyrazol-3-one Schiff bases has been reported for their anti-cancerous activities (Sathiyaraj, et al., 2013). Extensive literature is available on the effectiveness of Schiff bases against cancer cell lines, therefore, a more systemic and extensive research both in-vitro and in-vivo is suggested to extend their therapeutic use to alleviate the disease (Murtaza, et al., 2014; Kumar, et al., 2009).

1.1.3.1.1.6. Antioxidant activity
Aging is a biological process of human beings. Production of reactive oxygen species (ROS) increases with the passage of time, in the human body and leads to many physiological disorders including cardiovascular disease. Schiff bases and their metal complexes play an important role in the production of ROS (Li, et al., 2013) and therefore, can show antioxidant properties. Recently, Schiff bases of natural phenylpropene derived methoxylated cinamaldehyde and tin metal complexes have been reported to have antioxidant activity (JimÈnez, et al., 2013). In a recent study on thymol and carvacrol Schiff base derivatives in 5µg/ml concentration showed 60-90% inhibition of free radicals (Beena and Rawat, 2013). Moreover, Schiff base of 2-oxoquinoline-3-carbaldehyde has been reported as excellent antioxidant and its activity was comparable
with the ascorbic acid used as standard (Murtaza, et al., 2014; Zhang, et al., 2013; Kumar, et al., 2009). Literature reveals effectiveness of Schiff bases in the antioxidant behavior; therefore, more targeted research can possibly lead to their use in the therapy of various ailments.

### 1.1.3.1.1.7. Anti-inflammatory activity
Schiff bases derived from 2-(2, 6-dichloroanilino) (Bhandari, et al., 2008) and 4-amino-1,5-dimethyl-2-phenylpyrazole-3-one have been reported to have excellent anti-inflammatory activity (Alam, et al., 2012). Transition metal complexes of Schiff bases containing aldose group have also been reported for anti-inflammatory activities (Murtaza, et al., 2014; Iqbal, et al., 2013; Kumar, et al., 2009; Kajal, 2013).

### 1.1.3.2. Catalysts

### 1.1.3.3. Disperse dyes
In the last 20 years important studies have been undertaken in the field of azomethine and some very interesting pigments have been found out. In 1950, Calico Printer’s Association patented polyterephthaldazine, which was result of polycondensation of terephthaldehyde with hydrazine. It is a lemon yellow pigment and used in paints, since it has good fastness with solvents, and heat resistance (Calico Printer’s, BP-694,451). Cobalt complex of Schiff base (Salicylaldehyde with diamine) has excellent light resistance ability and does not degrade even in acidic gases (CO₂). Novel tetra dentate Schiff base act as a chromogenic reagent for determination of Ni in some natural food samples (Fakhari, et al., 2005). Table 1 shows metal complex monoazomethine pigments obtained from orthoaminophenol derivatives and 2-hydroxy-1-naphthaldehyde. These pigments are distinguished by their high color strength, high resistance to solvents, good
light fastness, and good weather fastness. Due to these strengths they play a vital role in colouring paints, lacquers, printing inks, polymers, rubber, paper, and textiles industries (Kanetkar and Deulgaonkar, 2006).

Table 1: Examples of Schiff base’s pigments

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Schiff base</th>
<th>Color</th>
</tr>
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<tbody>
<tr>
<td>1.</td>
<td><img src="image1" alt="Schiff base" /></td>
<td>Brownish yellow</td>
</tr>
<tr>
<td>2.</td>
<td><img src="image2" alt="Schiff base" /></td>
<td>Orange red</td>
</tr>
<tr>
<td>3.</td>
<td><img src="image3" alt="Schiff base" /></td>
<td>Orange red</td>
</tr>
<tr>
<td>4.</td>
<td><img src="image4" alt="Schiff base" /></td>
<td>Brownish yellow</td>
</tr>
<tr>
<td>5.</td>
<td><img src="image5" alt="Schiff base" /></td>
<td>Golden yellow</td>
</tr>
<tr>
<td>6.</td>
<td><img src="image6" alt="Schiff base" /></td>
<td>Greenish yellow</td>
</tr>
<tr>
<td>7.</td>
<td><img src="image7" alt="Schiff base" /></td>
<td>Golden yellow</td>
</tr>
</tbody>
</table>

(Kanetkar and Deulgaonkar, 2006)
1.1.3.4. Synergistic action on insecticides

Schiff base derived from sulfane thiazole and salicylaldehyde or thiophene-2-aldehydes and their complexes show toxicities against insects. Ali, et al., 2013 reported three Schiff bases namely PDH [N-(1-phenyl-2-hydroxy-2-phenyl-ethylidene) 2,4-dinitrophenyldiazine], PHP [N-(1-phenyl-2-hydroxy-2-phenyl-ethylidene) 2-hydroxyphenyl imine] and HHP [N (2-hydroxy benzylidine) 2-hydroxy phenyl imine] derived from benzoin, salicylaldehyde, 2-aminophenol and 2,4-dinitrophenyl hydrazine, and evaluated against Tribolium castaneum. Flourination on aldehyde part of Schiff bases enhances insectoacaracacial activity. Schiff bases (thiadiazole derivatives with salicylaldehyde or o-vanillin) and their metal complexes with Mo (IV) show insecticidal activity against bollworm and promote cell survival rate of mung bean sprouts (Kumar, et al., 2009; Saddiqi, et al., 1988; Kozlov, et al., 1987; Dhar and Taploo, 1982). Kumar and Chaudhary, 2010 also reported pesticidal activity of some Schiff bases.

1.1.3.5. Corrosion inhibitors

An interesting application of Schiff bases is their use as an effective corrosion inhibitor which is based on their ability to spontaneously form a monolayer on the surface to be protected. Schiff bases have been found to possess more inhibitor efficiency than their constituent carbonyls and amines. Schiff bases derived from cinnamaldehyde with 2-aminophenol and cinnamaldehyde with phenylene diamine studied as inhibitor for corrosion of carbon steel in acidic media 0.5N HCl by Mohammad, 2011. The results indicated that these Schiff bases inhibited the corrosion efficiently. Some authors have attributed these considerably stronger inhibition efficiencies to the presence of unoccupied π*-orbitals in the Schiff base molecules, which enable electron back donation from the metal d-orbitals and thereby stabilize the existing metal-inhibitor bond, which is not possible with the constituent amines. Literature survey reveals that the corrosion behaviour of iron in 2M HCl solution at 298 K with three Schiff base compounds have the perfect inhibition efficiency (Adabiardakani, et al., 2012).
1.1.3.6. Miscellaneous applications

Schiff bases have recently assumed greater importance in photographic emulsion, heart resistant polymers, lubricating oils, antiknocking agents and liquid crystal display composition (Bheshadadia, 2007). Schiff base polymers with a system of conjugated -C=C- and -C=N- bonds in their main chain are of considerable interest due to their thermal stability similar to polyamides and their using as solid stationary phase for gas chromatography, their semiconductor properties, mechanical strength, electrochemical and nonlinear optical properties, and useful catenation ligand, where the coordination polymeric Schiff bases are extensively studies. Quinoxaline derivatives Schiff bases play vital role in dye, pharmaceuticals and in electrical/photochemical materials. Quinoxaline ring moiety is a part of the chemical structures of various antibiotics such as echinomycin, levomycin and actinoleutin, which are known to inhibit growth of gram positive bacteria and are active against various transplantable tumors. Naga and Anupama, 2014 reported that schiff base of veratraldehyde shows good anthelmenthic activity. Chromium and cobalt Schiff base complexes have been used as dyes which give fast colour to leather, food packages and wools. Cobalt complexes of a salen type Schiff base have excellent light resistance and storage ability and resist degradation even in acidic gases like CO₂. Tetridentate Schiff bases like salens and salophens act as chromogenic reagents for determination of nickel in natural food samples (Naga and Anupama, 2014; Xina and Yuan, 2012). Application of Schiff bases as an antituberculosis (Patole, et al., 2006; Hearn and Cynamon, 2004), analgesic (Bhandari, et al., 2008) and anticonvulsant (Sridhar, et al., 2002; Kaplan, et al., 1980) was also reported.

1.1.3.7. As intermediates in producing other fragrance materials

Schiff bases or oximes have also been reported to be useful as intermediates in producing other fragrance material such as odorant nitriles (Schreiber, et al., 1975; Kaiser, et al., 2002; Ochsner, 1985; Narula, 1991; Sprecker, et al., 1989; Dahill and Robert, 1972; Strub, et al., 2016; Narula, et al., 2006). U.S. Patent 3,898,283 (Schreiber, et al., 1975) discloses novel Schiff base intermediates (I) used in producing 4 or 5 phenylpentenals having the structure.

Introduction
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Synthesis and characterization of some new odorant Schiff bases for fragrance composition

(1) (Schreiber, et al., 1975)

Wherein ‘x’ is consisting group

1.2. Microwave (MW) irradiation in organic synthesis

Before and during World War II, microwave radiation was widely used for telecommunication purposes such as radar, navigation, and sensing (Peiris, 2014). The heating ability of microwaves was accidently discovered in 1947 by Dr. Percy Spencer, a self-taught engineer, while building magnetrons for radar sets with the company Raytheon. He was working on an active radar set when he noticed that a peanut chocolate bar he had in his pocket started to melt. The radar had melted his chocolate bar with microwaves. The first food to be deliberately cooked with Spencer's microwave was popcorn, and the second was an egg, which exploded in the face of one of the experimenters. The first microwave oven was introduced by Tappan in 1955 but the widespread use of domestic microwave ovens occurred during the 1970s and 1980s. The first application of microwaves irradiation in chemical synthesis was published in 1986 (Clark and Sutton, 1996; Katz, 1992; Surati, et al., 2012).

Microwave ovens for the home were introduced in the early 1950s and by the mid-1970s they became more popular in domestic kitchens for cooking (Katz, 1992). However, the oil shock or natural gas crisis in the 1970s promoted research on microwaves in western countries, due to political pressures to make use of electrical heating methods such as microwaves rather than oil or gas (Oda, 1992). Since then many researchers have used microwave radiation as an alternative energy source in the synthesis and processing of polymers, ceramics, glass and other organic and inorganic materials (Peiris, 2014). Now day’s technique is considered as an important approach toward green chemistry.
1.2.1. Microwave (theory and fundamentals)

Electromagnetic radiation is a form of energy that exhibits wave-like behaviour as it travels through space. It has both electric and magnetic field components, which oscillate in phase perpendicular to each other and perpendicular to the direction of energy propagation as in Figure 3. The electromagnetic theory was first presented by James Clerk Maxwell in 1864 (Maxwell, 1865; Peiris, 2014).

![Figure 3: Electric and magnetic field components of electromagnetic radiation](Peiris, 2014)

Electromagnetic radiation is classified by the wavelength into radio waves, microwaves, infrared radiation, visible light, ultraviolet radiation, X-rays and gamma rays as shown in Figure 4.

![Figure 4: The electromagnetic spectrum](Peiris, 2014)

In the electromagnetic spectrum, the microwave radiation region lies between infrared radiation and radio waves. Microwaves have wavelengths of 1mm to 1m, corresponding
to frequencies between 300 MHz to 300 GHz. Microwaves travel in matter in the same manner as light waves, they are reflected by metals, absorbed by some dielectric materials and transmitted without significant losses through other materials. All domestic microwave ovens, microwave reactors and other laboratory and industrial systems usually work at 12.2 cm, corresponding to a frequency of 2.450 (±0.050) GHz. The microwave photon corresponding to 2.45 GHz has energy close 0.0016 eV (~1 kJ/mol) (Lidstrom, et al., 2001).

1.2.2. Principle of microwave irradiation

The basic principle behind the heating in microwave oven is due to the interaction of charged particle of the reaction material with electromagnetic wavelength of particular frequency. The phenomena of producing heat by electromagnetic irradiation are either by collision or by conduction, some time by both (Bhatre and Phadke, 2015). The electric field of commonly used irradiation frequency (2450 MHz) oscillates $4.9 \times 10^9$ times per second. Thus, microwave heating is directly dependent on dielectric properties of a substance, dielectric constant ($\varepsilon'$) and dielectric loss ($\varepsilon''$). The ability of a material to convert electromagnetic energy into heat energy at a given frequency and temperature, is calculated using

$$\frac{\varepsilon''}{\varepsilon'} = \tan \delta$$

(1)

where $\delta$ is the dissipation factor of the sample, $\varepsilon''$ is the dielectric loss, which measures the efficiency with which heat is generated from the electromagnetic radiation and $\varepsilon'$ is the dielectric constant which gives the ability of a molecule to be polarized by an electric field. The high value of dissipation factor $\delta$ indicates large susceptibility to microwave energy (Surati, et al., 2012)

The conduction mechanism leads, due to the much stronger interaction of ions with electric field, to the generation of heat. The ions will move under the influence of an electric field, resulting in expenditure of energy due to an increased collision rate, converting kinetic energy into heat. The heat generated by both mechanisms adds up resulting in a higher final temperature (Surati, et al., 2012).
1.2.3. Advantages and disadvantages of microwave (MW) irradiation in organic synthesis

The use of microwave irradiation in organic synthesis has become increasingly popular within the industrial, academic or research arenas, because it is a new enabling technology for thermal driven research and development. By taking advantage of this efficient source of energy and optimization can be assembled in a fraction of the time required by classical thermal methods (Hayes, 2004).

Presently, thermally driven organic transformations take place by either of two ways: conventional heating or microwave accelerated heating. In the conventional heating, reactants are slowly activated by a conventional external heat source. Heat is driven into the substance, passing first through the walls of the vessel in order to reach the solvent and reactants. This is a slow and inefficient method for transferring energy into the reacting system. In the microwave accelerated heating, microwaves couple directly with the molecules of the entire reaction mixture, leading to a rapid rise in temperature. Since the process is not limited by the thermal conductivity of the vessel, the result is an instantaneous localized superheating of any substance that will respond to either dipole rotation or ionic conduction - the two fundamental mechanisms for transferring energy from microwaves to the substance(s) being heated (Hayes, 2004). Due to its ability to couple directly with the reaction molecule and by passing thermal conductivity leading to a rapid rise in the temperature, microwave irradiation has been used to improve many organic synthesis. Important advantage of this technology include highly accelerated rate of the reaction, reduction in reaction time with an improvement in the yield and quality of the product. Now day’s technique is considered as an important approach toward green chemistry, because this technique is more environmentally friendly (Bhusnure, et al., 2015; Gawande, et al., 2014). Advantages and disadvantages are given below.

Advantages

➢ Rapid reactions
➢ High purity of products
➢ Less side-products
Introduction

➢ Improved yields
➢ Simplified and improved synthetic procedure
➢ Wider usable range of temperature
➢ Higher energy efficiency
➢ Sophisticated measurement and safety technology
➢ Modular systems enable changing from mg to kg scale

Disadvantages

➢ Heat force control is difficult
➢ Water evaporation
➢ Closed container is dangerous because it could be burst
➢ In microwave synthesis sudden increase in temperature may lead to the distortion of molecules which may lead to distortion of the reaction
➢ Many other things like, temperature sensitive reactions, reactions involving bumping of material, and reaction in which effervescences and colour reaction are not be done in microwave reactor

(Surati, et al., 2012; Bhatre and Phadke, 2015)

1.3. Fragrance

A fragrance is not a single material of clearly defined properties, but rather mixture of individual chemicals, each behaving according to its own unique attributes. Characterizing these chemicals separately, and then combining their effects, allows the behaviour of the complete fragrance composition in diverse media to be understood (Rowe and Herman, 2005). Fragrances give a social expression to a purely functional product and provide emotional feeling of satisfaction for good health and well-being. It is interesting to know that countries where fragrance sales are high have the least cases of malaria, plague and typhoid (Rowe and Herman, 2005).

1.3.1. The basic structure of fragrances

The characteristic odor of a single material is called a ‘note’. Mixtures of two or more materials, having a unified olfactory theme, are called ‘accords’. Very volatile materials, which disappear first, comprise the “top notes” of a finished perfume, those
of intermediate volatility and tenacity are the “modifiers” or “middle notes”, and those with the lowest volatility, tenacious products constitute the “base notes”. If individual chemicals are like words, accords are short phrases, the top, middle and base notes are sentences, and the finished fragrance is a paragraph. The ratio of 25% top notes, 20% modifiers and 55% base notes is typical of a well-balanced blend (Rowe and Herman, 2005). In 1983, Michael Edwards designed a fragrance wheel (Figure 5) to know the relationships between each individual fragrance family of a perfume. The fragrance wheel is the only complete, accurate and industry respected fragrance classification system. The main purpose of the wheel is to allow a retailer to suggest different fragrances in a similar category to ones that their customers may prefer, which has been put into use by perfumer (Edwards, 1983).

![Figure 5: The fragrance wheel](Edwards, 1983)

**1.3.2. Degree of freedom in perfumery**

At first sight there would appear to be hundreds of ingredients to choose from, but in practice there are a number of restricting factors. This concept of freedom of choice of ingredients can be described by employing the analogy of Degrees of Freedom as used in chemistry in which a system is constrained by a number of factors. The eight degrees of freedom in perfumery are as follows:

i. Skin safety
Introduction

ii. Environmental safety
iii. Acceptable odor
iv. Cost
v. Stability
vi. Performance
vii. Physical properties (e.g. solubility, color)
viii. Added value (e.g. mal odor counteractancy, insect repellency)

(Sell and Small, 2006)

1.3.3. The structure of fragrance & flavour industry
The top five companies, Givaudan, Firmenich, IFF, Symrise and Takasago each have a turnover in excess of $1 billion. Most interesting is the geographical distribution of sales: North America 32%, Asia-Pacific 26% and Western Europe 25%, with ‘the rest’, Eastern Europe, South America, the Middle East and Africa, constituting less than 20%.

Table 2: Demand sector of aroma chemicals

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Sector</th>
<th>Large consumer group</th>
<th>Key area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Fragrance</td>
<td>Givaudan, Firmenich, IFF, Symrise and Takasago</td>
<td>Toiletries, Cream, Perfume, Hair oil, Agarbatti, Talcum powder, Room Freshner</td>
</tr>
<tr>
<td>2.</td>
<td>Food &amp; Flavor</td>
<td>Kerry, Danisco and Nestle</td>
<td>Beverages, Snacks, Dairy products, Toothpaste, Bakery products, Ice-cream, Chwingums /Tobaco</td>
</tr>
<tr>
<td>3.</td>
<td>Pharmaceutical</td>
<td>Proctor &amp; Gamble, Unilever, L’Oreal</td>
<td>Cough, Cold, Headache, Skincare, Haircare, Burn</td>
</tr>
<tr>
<td>(Aromatherapy)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Traditional uses</td>
<td>In-house blenders</td>
<td>Mass fragrances - Small and Medium Enterprise (SME’s)</td>
</tr>
</tbody>
</table>

Here we can see again the principle that the flavour and fragrance industry is a consequence and a measure of ‘disposable income’; the developed world accounts for 80% of the sales. Market growth is fuelled by demand from emerging markets and consumer lifestyle trends, in particular the importance of luxury and status. The
structure of the flavor and fragrance industry is based on four key sectors, described in Table 2 (Jose, 2012).

1.3.4. Global fragrance market scenario
The future of the flavor and fragrance market looks good with opportunities in the dairy, soap & detergents, fine fragrance and cosmetic & toiletries industries. The global market for fragrance ingredients was valued at $12,383.25 million in 2013. This market is projected to grow at a compound annual growth rate (CAGR) of 5.6% from 2014 to reach $17,104.21 million by 2020. Europe dominated the market in 2013, which was followed by North America. Latin America is projected to be the fastest-growing market between 2014 and 2019 (The NPD Group, 2015). The world F&F market today is estimated to be about 19.8 billion USD of which the top ten players account for 69% of the market. The remaining 31% is spread over all other F&F houses, both multinational and regional players (Table 3).

Table 3: Market of top global companies

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>USD</th>
<th>Market Share %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Givaudan</td>
<td>3,647.0</td>
<td>18.4</td>
</tr>
<tr>
<td>2</td>
<td>Firmenich</td>
<td>2,512.8</td>
<td>12.7</td>
</tr>
<tr>
<td>3</td>
<td>IFF</td>
<td>2,276.6</td>
<td>11.5</td>
</tr>
<tr>
<td>4</td>
<td>Symrise</td>
<td>1,860.8</td>
<td>9.3</td>
</tr>
<tr>
<td>5</td>
<td>Takasago</td>
<td>1,112.0</td>
<td>5.6</td>
</tr>
<tr>
<td>6</td>
<td>Sensient Technologies</td>
<td>572.0</td>
<td>2.9</td>
</tr>
<tr>
<td>7</td>
<td>Mane SA</td>
<td>448.7</td>
<td>2.3</td>
</tr>
<tr>
<td>8</td>
<td>T Hasegawa</td>
<td>448.1</td>
<td>2.3</td>
</tr>
<tr>
<td>9</td>
<td>Frutarom</td>
<td>368.3</td>
<td>1.9</td>
</tr>
<tr>
<td>10</td>
<td>Robertet SA</td>
<td>352.1</td>
<td>1.8</td>
</tr>
<tr>
<td></td>
<td><strong>Top Ten Totals</strong></td>
<td><strong>13,598.4</strong></td>
<td><strong>68.7</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Remaining Others</strong></td>
<td><strong>6201.6</strong></td>
<td><strong>31.3</strong></td>
</tr>
<tr>
<td></td>
<td><strong>(US $$)</strong></td>
<td><strong>19,800.00</strong></td>
<td></td>
</tr>
</tbody>
</table>

(IAL Consultants, 2015)
This statistics depicts (Figure 6) the estimated size of the global fragrance market from 2012 to 2021. In 2016, the global fragrance market is estimated to be worth about USD 40.1 billion (NPD Group, 2015).

![Figure 6: Estimated size of global fragrance market from 2012 to 2021](image)

**1.3.5. The Indian F&F market**

The Indian F&F market is highly fragmented with both purchasers and suppliers ranging from multinational companies and large Indian industrial houses to small-scale industrial units, and local manufacturers. It is estimated that the total global market size of F & F and allied industry is of the order of USD 20 billion. Indian share is about 10% of the globe, which is USD 2000 Millions. Indian population is 17.8% of the globe which indicates potential growth. The fragrance turnover is arrived at based on the data available from various sources. Soaps and detergents: Rs 950 Crores, Cosmetics and toiletries: Rs 400 Crores, Household products: Rs 200 Crores, Traditional products: Rs 1450 Crores (Ranade, 2014). This is particularly applicable to the flavor industry and more particularly to savory, bakery and confectionary segments where the manufacturing process is relatively simple in comparison to others. In this case, even local eateries and individual homes contribute significantly to the increase in market. In comparison, there is better consolidation in the fragrance market, with larger players...
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like Unilever, Godrej, Dabur, Reckitt Benkeiser, Wipro, Henkel, ITC, etc., generating most of the sales (Dixit, 2015).

1.4. Scope of present investigation

Aroma chemicals or fragrance compounds containing a carbonyl (aldehyde / ketone) functional group constitute an important group of raw materials for fragrance and flavor industry. However, most of such chemicals containing an aldehydic functional group are inherently unstable at the aldehyde moiety to oxidation to the corresponding carboxylic acid, thereby losing their fragrance characteristics and hence limiting their use. The ketone compounds of natural origin, except few cyclic terpene ketones and aromatic ketones are of minor importance as fragrance chemicals. The commercially used fragrant ketones are generally of synthetic origin. Recently the use of musk ketones has been stringently regulated due to their stability and consequently deleterious effect on the environment. When the individual materials are pooled into perfume compositions further change can transpire. Very few chemical reactions occur between perfume materials to a significant degree, but Schiff bases, are an important exception. The chemical transformation of carbonyl compounds into their novel derivatives, Schiff bases, therefore presents an innovative approach to overcome their above mentioned undesired attributes. Schiff bases play an important role in ‘art of perfumery and flavoring’. There have been numerous researches on novel odorant Schiff bases and their use in formulations disclosed in patents and research papers (Mookherjee, et al., 1988; 1989(a); 1989(b); 1989(c); 1989(d); Blanc and Aschiers, 1992; Baudin, 1993; Koshino, et al., 1990; Firmenich, 1995).

Many of the natural materials provide novel fragrances and contribute desirable nuances to fragrance compositions as well as aroma articles including personal care products, soaps and detergents, industrial and pharmaceutical products and are high in cost, vary in quality from one batch to another and/or are generally subjects to the usual variations of natural products (Mookherjee, et al., 1988; 1989(a); 1989(b); 1989(c); 1989(d)). There is a global need to create perfumes that present much less hazard to human health in view of recent concerns over the safety of the perfumes and the relationship of
modern societies to the environment that requires reinventing the manufacture and use of materials. Another point should be in spotlight that natural cosmetics are high on the agenda of marketers for some years. Terms like ‘Bio’, ‘Natural’, ‘Eco’, ‘Herbal’, ‘Wonder Ingredient’, etc., have become common. Beauty products made from naturally occurring substances or nature identical ones that promise natural goodness effects are increasing in the market (Surburg and Panten, 2005). Natural compounds are obtained directly from natural sources by physical, enzymatic, or microbial procedures. Nature identical compounds are produced synthetically, but are chemically identical to their natural counterparts. Artificial flavor substances are compounds that have not yet been identified in plant or animal product for human consumption. Alcohols, aldehydes, ketones, esters, and lactones are classes of compounds that are represented most frequently in natural and artificial fragrances (Surburg and Panten, 2005). There is an ongoing need in the fragrance industry to provide new odorant eco-affable chemicals for their use in compositions.

Present study is in tune with the above desired traits and introduces some odorant Schiff bases which are prepared from natural or natural identical compounds with a specificity of green and facile method alternative to the classical method for synthesizing the odorant Schiff bases.
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Organic chemists have carried on fiction with fragrant chemicals from the early days of organic chemistry. In the beginning the challenge was to isolate and identify the fragrant chemicals from natural products. Subsequently, effort was directed toward the synthesis and commercial production of natural identical chemicals for the growing perfume industry. Finally, new chemicals were designed and synthesized for their valuable odor properties. Progress in this field has been amply recorded in scientific journals, patents, several books, reports and industrial compendiums. Researches and reviews reported in the literature usually treat the chemistry of each material individually or group the material according to structure or functionality (Dorsky, et al., 1991).

2.1. Odorant Schiff bases

Careful survey of the literature reveals that a large number of Schiff bases have been synthesized and a wide range of their applications are reported. Schiff bases play an important role in ‘art of perfumery and flavoring’ and much interested to the chemists not only for their chemical composition but also their biological or pharmaceutical possessions (Silva, et al., 2011). There have been numerous researches on novel odorant Schiff bases disclosed in patents and research papers (Arctander, 1969; Blanc and Aschiers, 1992; Baudin, 1993; IFF, 2002; Koshino, et al., 1990; Mookherjee, et al., 1988; 1989(a); 1989(b); 1989(c); 1989(d); 1989(e); Well, 1948) Being a classical fragrance raw material having an orange flower note, methyl 3,7-dimethyl-7-hydroxyoctylidene anthranilate, a Schiff base derived from hydroxycitronellal and methylanthranilate, has been recognized as an indispensable aroma chemical that is compounded for manufacturing perfumes within the class of floral family (Arctander, 1969; Pybus and Sell, 2006; Firmenich, 1995)

The book “Flavor & Fragrance Materials” discloses on page 154 the commercial availability of the following Schiff bases (Computer Sources Association, 1987; Bauer,
et al., 1997; Baudin, 1993; Mookherjee, et al., 1988; 1989(a); 1989(b); 1989(c); 1989(d); 1989(e)).

❖ Methyl anthranilate and amyl cinnamic aldehyde

❖ Methyl anthranilate and hydroxyl citronellal

❖ Methyl anthranilate and lilial

❖ Methyl anthranilate and anisic aldehyde
Review of literature

❖ Methyl anthranilate and decanal

(E)-methyl 2-(decylideneamino)benzoate

❖ Methyl anthranilate and lyral

(E)-methyl 2-((4-(4-hydroxy-4-methylpentyl)cyclohex-3-enyl)methyleneamino)benzoate

❖ Methyl anthranilate and phenylacetaldehyde

methyl 2-(2-cyclohexylethylideneamino)benzoate

Flavoring of foodstuffs with α, β-keto-imine having a nutty corn, cereal aroma and the use of aldimines as chocolate-like flavors, resulted from the reaction of methyl anthranilate and aldehydes such as N-isobutylidene furfurylamine, N-isopentylidenefurffurylamine, N-isopentylidene-isopentylamine are reported (Parliament, 1986; Rizzi, 1971). Synthesis of odorant Schiff bases from some aldehydes or ketones (bergamal, pinoacetalddehyde, pino isobutyaldehyde, melonal, canthoxal, myrtenal, 2-decanal, floralozone, Alpha-methylisioionone) and alkyl anthranilate, and their organoleptic uses have been disclosed in different patents (Mookherjee, et al., 1988; Mookherjee, et al., 1989; 1989(a); 1989(b)). Preparation of some Schiff bases of isophorone and dihydro-isophorone with various amines has been described and the aroma properties of the new ketimines were discussed (Buchbauer, et al., 1999).
Abiding efforts are made to find odorant molecules which will replace, enhance or augment the essential fragrance and flavor notes for perfumery compositions. Unfortunately, many of the synthetic materials either have the desired nuances only to a relatively small degree or else contribute undesirable or unwanted odor to the compositions. The search for materials which provide, for example, a more refined grape-like flavor or more refined lemon flavor or more refined watermelon flavor, has been difficult and relatively costly in the areas of both natural products and synthetic products (Mookherjee, et al., 1989(a)).

Natural materials contribute desirable nuances to fragrance compositions for cosmetic or household formulations are high in cost, vary in quality from one batch to another and generally subjects to the usual variations of natural products. By same token, odorant Schiff bases, which can provide intense floral, oriented, citrus, lemony, meloney, watermelon, green and concord grapes aromas with floral, oriental, citrus, lemony, meloney, green, raspberry and concord grapes tastes are highly useful and well known in the art of flavoring for foodstuffs, toothpastes, chewing gums, medicinal products and chewing tobaccos (Mookherjee, et al., 1989(a)).

Synthetic flavoring agents for foodstuffs have received rising attentions for many years. These food flavoring agents have been preferred over natural flavoring agents at least in part due to their diminished costs and their reproducible flavor qualities. For examples, natural food flavoring agents such as extracts, concentrates are often subject to extensive variations due to changes in quality and type and treatment of the raw materials. Such variations can be reflected in the end products and results in unfavorable flavor characteristics in the end product. Additionally the presence of the natural products in the ultimate food may be undesirable because of increasing tendency to spoil. This is particularly troublesome in food and food uses where such products as dips, soups, chips, sausages, gravies and desserts and the like are apt to stored prior to use. Thus, U.S. Patent 4,618,501 issued on 1986 discloses the flavoring of foodstuff with \textit{alpha, beta}-keto-amines (1) having a nutty corn, cereal aroma may be used for flavoring compositions for foods having the structure.
Wherein, $R_1$, $R_2$ and $R_3$ are selected from the group consisting of a saturated or unsaturated alkyl straight or branched chain hydrocarbons having from 1-3 carbon atoms. U. S. Patent 3,625,710 issued in 1971 disclosed the use of aldimines as chocolate-like flavors, resulting from the reaction product of amines and aldehydes for example, N-isobutylidenefururylamine, N-isopentylidene furfurylamine, N-isopentylideneidopentylamine, Schiff base derived from canthoxal and methyl anthranilate, showed a quality of flavoring as a grape and mandarin flavored beverages (Mookharjee et al., 1989(b)).

Chemical Abstracts volume 103, 1985, No. 123134, disclosed Schiff bases 2-5 have been used in perfumery. Steffen Arctander’s in 1969 documented a number of odorant Schiff base with their organoleptic properties in the book “Perfume and flavor chemicals (Aroma chemicals)”, volume II. One of the examples is the Schiff base of MA and vanillin (6) which is Viscous, dark-yellowish liquid, occasionally with an orange-reddish tint or an olive green color, Insoluble in water, soluble in alcohol and oils.
Synthesis and characterization of some new odorant Schiff bases for fragrance composition

Organoleptic properties of the odorant Schiff base (7) of vanillin ethyl carbonate and peraphenetidine have been described (Arctander, 1969).

Compound (3) having yellowish needle like crystals m.p. 88°C, was developed many decades ago for pharmaceutical purposes, but was also introduced to perfumery sector (Mookherjee, et al., 1989(b)). It has no longer significance to fragrance and flavors industry but is still used in pharmacy.

Schiff bases of $p$- and $m$-aminostyrenes with perfume aldehydes such as citral, cinnamaldehyde, piperonal, vanillin, and ethyl vanillin were synthesized in more than 50% yield. Water-soluble copolymers of these Schiff bases with $N$-vinyl-2-pyrrolidone or with $N$, $N$-dimethylacrylamide were obtained. The hydrolytic behavior of Schiff base monomers and copolymers to liberate perfume aldehydes was structure dependent, thereby affording chemical release control (Lewis, et al., 1975; Kamogawa, et al., 1982).

45, 03 and 01 odorant Schiff bases of methyanthranilate (8), ethylanthranilate (9) and linalylanthranilate (10), respectively with several carbonyl compounds (Bergamal,
Floralzone, Pino-acetaldehyde, Lyral, Canthoxal, Helional, Pino-isobutyraldehyde, Myrtenal, Alpha-methylisoionone, 2-decal, Ethyl vanillin, 2-cyclohexylpropanal, Acetophenone, Alpha-amylcinnamic aldehyde, Anisaldehyde, Citral, Citronellal, Cyclamenaldehyde, Heptylidene, Hexenyldiene, Hydroxy-citronellal, Alpha-methyl cinnamylidene, Methyl naphthyl ketone, Methyl Nonyl Acetaldehyde, Iso-nonylaldehyde, Musk Ketone, Ocean propanal, 2,4-ivy carbaldehyde and Anisyl-propanal) along with their odor profile have been reported (Table 4). Many of these compounds were not isolated in a pure state (shown in italics in Table 4).
Table 4: Schiff bases of methylantranilate, ethylantranilate and linalyl anthranilate, and their odor profile

<table>
<thead>
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<tbody>
<tr>
<td></td>
<td><strong>Methylantranilate derived Schiff bases</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td><em>Methyl anthranilate and Bergamal</em></td>
<td>A lemony and floral aroma profile</td>
<td>11</td>
<td>29</td>
</tr>
<tr>
<td>2.</td>
<td><em>Methyl anthranilate and Floralozone</em></td>
<td>A green, floral and ozoney aroma anisic topnotes</td>
<td>12</td>
<td>29</td>
</tr>
<tr>
<td>3.</td>
<td><em>Methyl anthranilate and Pino-acetaldehyde</em></td>
<td>A melony and floral aroma profile</td>
<td>13</td>
<td>29</td>
</tr>
<tr>
<td>4.</td>
<td><em>Methyl anthranilate and Lyral</em></td>
<td>A citrus, green floral aroma profile with fresh air and ozoney topnotes</td>
<td>14</td>
<td>29</td>
</tr>
<tr>
<td>5.</td>
<td><em>Methyl anthranilate and Canthoxal</em></td>
<td>A sweet, floral fruity and ozoney aroma with anisic topnotes and a grape flavor at 0.1 ppm causing it to be useful in grape and mandarin flavoured beverages</td>
<td>15</td>
<td>29</td>
</tr>
<tr>
<td>6.</td>
<td>Methyl anthranilate and Helional</td>
<td>Green, orange flower, fruity, ozoney, sweet and anisic aroma with grape, fruity, green, floral, anisic and ozoney topnotes</td>
<td>16</td>
<td>32</td>
</tr>
<tr>
<td>7.</td>
<td>Methyl Anthranilate and Pino-isobutyraldehyde</td>
<td>A walnut, green, melony and ozoney aroma with floral, woody, animalic, walnut, green and ozoney topnotes</td>
<td>17</td>
<td>32</td>
</tr>
<tr>
<td>8.</td>
<td><em>Methyl anthranilate and Myrtenal</em></td>
<td>Odor Hay-like, coumarinic ,tonka absolute and honey topnotes</td>
<td>18</td>
<td>28</td>
</tr>
<tr>
<td>9.</td>
<td><em>Methyl anthranilate and Alpha-methylisoionone</em></td>
<td>An intense rose aroma with coumaric topnotes</td>
<td>19</td>
<td>28</td>
</tr>
<tr>
<td>10.</td>
<td><em>Methyl anthranilate and 2-decnal</em></td>
<td>Intense animalic aroma with fatty topnotes</td>
<td>20</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Chemical Structure</td>
<td>Aroma Profile</td>
<td>References</td>
<td></td>
</tr>
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<td>----------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
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<td></td>
</tr>
<tr>
<td>11.</td>
<td>Methyl anthranilate and Ethyl vanillin</td>
<td>A sweet, vanilla bean like and sassafras aroma profile with sweet topnotes</td>
<td>21 28</td>
<td></td>
</tr>
<tr>
<td>12.</td>
<td>Methyl 2-(octylideneamino) benzoate</td>
<td>Orange flower, Neroli, Petitgrain, green</td>
<td>22 5 &amp; 14</td>
<td></td>
</tr>
<tr>
<td>13.</td>
<td>Methyl 2-(6-hydroxy-2,6-dimethylheptylideneamino) benzoate</td>
<td>Orange flower, Neroli, White flower</td>
<td>23 1 &amp; 5</td>
<td></td>
</tr>
<tr>
<td>15.</td>
<td>Methyl 2-(3-(4-tert-butylphenyl)-2-methylpropyldieneamino) benzoate</td>
<td>Orange flower, Green, Powder</td>
<td>25 1 &amp; 5</td>
<td></td>
</tr>
<tr>
<td>16.</td>
<td>Methyl 2-((2,4-dimethylcyclohex-3-enyl)methyleneamino) benzoate</td>
<td>Orange flower, Petitgrain, Green</td>
<td>26 5 &amp; 14</td>
<td></td>
</tr>
<tr>
<td>17.</td>
<td>Methyl, 2-(3-(4-methoxyphenyl)-2-methylpropyldieneamino) benzoate</td>
<td>Neroli, Powdery</td>
<td>27 5 &amp; 32</td>
<td></td>
</tr>
<tr>
<td>18.</td>
<td>Methyl 2-(3-(benzo [d][1,3]dioxol-5-yl)-2-methylpropyldieneamino) benzoate</td>
<td>Orange, white flower, powdery</td>
<td>28 5 &amp; 32</td>
<td></td>
</tr>
<tr>
<td>19.</td>
<td><em>Methyl-N</em>-{(1,1,4,4-tetramethyl-tetralin-6-yl)methlidene]-anthranilate</td>
<td>Honey like,”orange” flower (orange blossom), musky, powerful and soft</td>
<td>29 2</td>
<td></td>
</tr>
<tr>
<td>20.</td>
<td><em>Methyl –N</em>-{(1,1,4,4,7-pentmethyl-tetralin-6-yl)methyldiene]-anthranilate</td>
<td>Powdery, polycyclic must-like, floral (oranger flower).</td>
<td>30 2</td>
<td></td>
</tr>
<tr>
<td>21.</td>
<td><em>Methyl-N</em>-{(1,1,3,4,4-pentamethyl-tetralin-6-yl)methyldiene]-anthranilate</td>
<td>Flowery, musky, woddy, oranger</td>
<td>31 2</td>
<td></td>
</tr>
<tr>
<td>22.</td>
<td><em>Methyl-N</em>-{(1,1,2,4,4,7-hexamethyl-tetralin-6-yl)methyldiene]-anthranilate</td>
<td>Musky, powdery, floral, oranger flower</td>
<td>32 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Odorant Schiff Bases</td>
<td>Notes</td>
<td></td>
<td></td>
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<td>---</td>
<td>------------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------</td>
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</tr>
<tr>
<td>23.</td>
<td>methyl-N-[(1,1,2,3,3-pentamethyl-indian-5-yl)methylidene]-anthranilate and methyl-N-[(3-ethyl-1,1,3-trimethlindian)-anthranilate</td>
<td>Musky, flora, oranger flower</td>
<td>33</td>
<td>2</td>
</tr>
<tr>
<td>24.</td>
<td>Methyl-N-[(1,1,4,4-tetramethyl-tetralin-6-yl)methylmethylidene]-anthranilate</td>
<td>Flowery, oranger flower</td>
<td>34</td>
<td>2</td>
</tr>
<tr>
<td>25.</td>
<td>Methyl-N-[(1,1,2,4,4,7-hexamethyl-tetralin-6-yl)methylmethylidene]-anthranilate</td>
<td>Floral, oranger flower, fresh</td>
<td>35</td>
<td>2</td>
</tr>
<tr>
<td>26.</td>
<td>Methyl-N-[(1,1-dimethyl-6-teri-butyl-indian-4yl)methylmethylidene]-anthranilate</td>
<td>Intensity sweet, orange blossom-acacia like</td>
<td>36</td>
<td>2</td>
</tr>
<tr>
<td>27.</td>
<td>Methyl-N-[(1,1,3,4,4-pentamethyl-tetralin-6-yl)-methylidene]-anthranilate</td>
<td>Flowery, musky, slightly woody</td>
<td>37</td>
<td>2</td>
</tr>
<tr>
<td>28.</td>
<td>2-cyclohexylpropanal methyl anthranilate enamine</td>
<td>Soft, sweet floral, weak green</td>
<td>38</td>
<td>23</td>
</tr>
<tr>
<td>29.</td>
<td>Methyl anthranilate and Acetophenone</td>
<td>Heavy, sweet-floral, somewhat animal odor</td>
<td>39</td>
<td>1</td>
</tr>
<tr>
<td>30.</td>
<td>Methyl anthranilate and Alpha-amylcinnamic aldehyde</td>
<td>Oily -herbaceous, somewhat green-balsamic</td>
<td>40</td>
<td>1</td>
</tr>
<tr>
<td>31.</td>
<td>Methyl anthranilate and Anisaldehyde</td>
<td>Heavy-sweet, intensely floral odor with fruity undertones</td>
<td>41</td>
<td>1</td>
</tr>
<tr>
<td>32.</td>
<td>Methyl anthranilate and Citral</td>
<td>Sweet Orange-blossom, fresh Orange peel-like with citrus undertone</td>
<td>42</td>
<td>1</td>
</tr>
<tr>
<td>33.</td>
<td>Methyl anthranilate and Citronellal</td>
<td>Sweet-floral, Orange-peel and Orange-blossom complex odor</td>
<td>43</td>
<td>1</td>
</tr>
<tr>
<td>34.</td>
<td>Methyl anthranilatre and Cyclamenaldehyde</td>
<td>Intensely sweet, fresh-floral odor of great tenacity</td>
<td>44</td>
<td>1</td>
</tr>
<tr>
<td>35.</td>
<td>Methyl anthranilate and Heptylidene</td>
<td>Very sweet, green-floral, herbaceous-Orangeblossom</td>
<td>45</td>
<td>1</td>
</tr>
<tr>
<td>36.</td>
<td>Methyl anthraniite and Hexenylidene</td>
<td>Very sweet, but refreshingly citrusy, floral</td>
<td>46</td>
<td>1</td>
</tr>
</tbody>
</table>
### Ethylanthranilate derived Schiff bases

<table>
<thead>
<tr>
<th>No.</th>
<th>Reactants</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>46</td>
<td>Ethyl anthranilate and Hydroxy-citronellal</td>
<td>Very sweet, heavy-floral and extremely tenacious</td>
</tr>
<tr>
<td>47</td>
<td>Ethyl-N-[(1,1,4,4-tetramethyl-tetralin-6-yl)methylidene]-anthranilate</td>
<td>Honey-like, orangr –flower, musky</td>
</tr>
<tr>
<td>48</td>
<td>Ethyl-N-[(1,1,3,4,4-pentamethyl-tetralin-6-yl)methylidene]-anthranilate</td>
<td>Vanilla-like, slightly musky</td>
</tr>
</tbody>
</table>

### Linalylanthranilate derived Schiff base

<table>
<thead>
<tr>
<th>No.</th>
<th>Reactants</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>49</td>
<td>Linalyl anthranilate and Hydroxy-citronellal</td>
<td>Sweet, floral odor of great tenacity</td>
</tr>
</tbody>
</table>
Synthesis and characterization of some new odorant Schiff bases for fragrance composition
Synthesis and characterization of some new odorant Schiff bases for fragrance composition
Synthesis and characterization of some new odorant Schiff bases for fragrance composition
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Synthesis and characterization of some new odorant Schiff bases for fragrance composition
Another class of Schiff base “oxime” identified by >C=NOH, also plays a vital role in perfumery. The oximes are also known for their value as intermediates in preparing other fragrance compounds. Several oximes have been reported in literature (Kaiser, et al., 2002; Ochsner, P. A., 1985). Narula, 1991, reported an oxime (60) namely 3, 5, 5-Trimethylhexanal in U.S. Patent 5,066,641, has a green, vertivert, woody, earthy, orris, minty, camphoraceous, cassis and grapefruit aroma profile with minty, camphoraceous, green, herbaceous, vertivert and galbanum topnotes. The applications of this oxime in Chypre formulation, Hair Spray Formulation, Cosmetics Powder Composition, Soap Composition, Solid Detergents Composition, Perfumed Liquid Detergents, Colognes and Handkerchief Perfumes, Conditioning Shampoos were also discussed. Sprecker, et al., 1989 reported the genus of compound (61), which is useful as perfumery ingredient. U.S. Patent No. 3,637,533 (Dahill and Robert, 1972) discloses the use of 3, 7-dimethyloctanal oxime (62) in perfumery compositions. However, Koshino, et al. 1990, introduced 2-cyclohexylpropanal oxime (63) having minty, woody, green odor profile.

![Diagram of oximes]

Narula, et al. 2006, disclosed odorant oxime ethers 64-67 of following structures in U.S. Patent 7,015,189 B2:
Oxime ethers are important odoriferous compounds. Fragrant oxime ethers are not commonly found in nature. Marine sponges have been found to produce many of these compounds. Examples include, niphatesines E-H from *Niphates* sp., (Kobayashi, et al., 1992) Hemibastadin 1 and 2 from *Ianthanella basta* (Butler, et al., 1991) ikimines A and D from an unidentified Micronesia sponge (Carroll and Scheuer, 1990) and lobatamides A-F, from Aplidium lobatum. The only example of plant derived oxime ether is phenylacetaldoxime O-methyl ether which is a minor constituent of the essential oils of *Gardenia taitensis*, *Citrus aurantium*, *Spartium junceum* (Muller and Lamparsky, 1994; Johnson, et al., 2009; Sell, 2014).

Very recently, manuscript on synthesis and olfactory properties of a homologous series of 18 oxime ethers from (+)- and (-)-carvone, the commonly found monoterpenes in nature and used as flavouring agent in food and beverages have been published by Strub, et al., 2016. A homologous series of noval semi-synthetic fragrant carvone oxime ethers were prepared from both isomers of carvone, and also discussed their olfactory ranged from vegetable-like (pickled cucumber, leaves of horseradish and carrot, scallion and onion) and herbaceous to sulphuric, floral (lily) and fruity (blackcurrant and pear) in this manuscript.

Literature published in relevance of Schiff bases derived from anthranilic acid and carbonyl compounds. Thangadurai et al., 2002, reported new hexa-coordinated ruthenium (III) complexes of the type [RuX₂ F(L)(EPh₃)₂] (X=Cl or Br; L=monobasic bidentate Schiff base ligand; E=P or As) were synthesised by the reactions of
[RuCl₃(PPh₃)₃], [RuCl₃(AsPh₃)₃], [RuBr₃-(AsPh₃)] or [RuBr₃(PPh₃)₂(MeOH)] with the appropriate ligands such as anthranilic acid cinnamaldehyde (Hanthcin), anthranilic acid p-toluualdehyde (Hanth-p-tol) and anthranilic acid p-anisaldehyde (Hanth-p-ans). The antibacterial activities of ligands and their complexes have also been determined (Thangadurai, et al., 2002). Sharma, et al., 1988, also reported some iridium (III) complexes with Schiff bases derived from amino carboxylic acids. In view of this research, reactions of iridium(III) chloride with different Schiff bases gave complexes of types [Ir(SB)₃], [Ir(SB')Cl(H₂O)]₂, [Ir(SB'')Cl₂]n, [Ir(SB'')Cl(H₂O)]n, commencing Schiff bases derived from anthranilic acid with benzaldehyde, acetophenone, vanillin, salicylaldehyde, cinnamaldehyde or m-hydroxyacetophenone, o-hydroxyacetophenone and Schiff base derived from p-aminobenzoic acid with benzaldehyde, acetophenone, vanillin, salicylaldehyde, cinnamaldehyde or m-hydroxyacetophenone and o-hydroxyacetophenone. These complexes were been characterized on the basis of elemental analyses, conductance, magnetic moment, and spectral (Electronic, IR, and ¹H NMR) data. The thermal behavior of these complexes has also been studied by TG, DTG, and DSC techniques. The different kinetic parameters, viz., order of reaction, activation of energy, and heat of reaction were calculated. The antifungal and antiviral activities of these complexes with Schiff bases derived from anthranilic acid have also been investigated by Sharma, et al., 1988. Rehina and Parameswaran, 1999 reported Cobalt(II), nickel(II), copper(II) and zinc(II) complexes of two new Schiff-bases, citronellal anthranilic acid and citronellal-5-bromoanthranilic. Thermal spectral and magnetic studies of citral-anthranilic acid and citral-5-bromo-anthranilic acid complexes of Co(II), Ni(II) and Cu(II) were published by Devi and Parameswaran, 1999. Suresh and Prakash, 2010 reported Cr⁺³, Co⁺², Ni⁺², Cu⁺², Zn⁺² and Cd⁺² chelates of Schiff base derived from vanillin and anthranilic acid. Analgesic, antipyretic and CNS activities of 2-(4-hydroxy-3-methoxybenzylidene amino) benzoic acid Schiff base were studied using albino rats of both the sexes by Valli, et al., 2012.

2.2. Microwave-assisted organic synthesis

The organic synthesis is one of the major role of research in chemistry, from plastics to medication it participates in the improvements of everyone’s life. Over the past few
Review of literature

decades, many significant advances in practical aspects of organic chemistry have included novel synthetic strategies and methods as well as advent of a vast array of analytical techniques (Surati, et al., 2012; Lidstram, et al., 2001). In these environmentally conscious days, the developments in the technology are directed towards environmentally sound and cleaner procedures. Hence, the present day chemists are no longer confined to using only thermal energy for driving chemical reactions. With increasing complexity of the problems and the availability of newer methods of activation of chemical reactions, chemist have restored to using wide variety of techniques such as photochemical, electrochemical, sonochemical, microwave and enzymatic methods. The first method used as old as chemistry itself, their use by synthetic chemist has gained importance only in the past decade. With easy availability of ultrasound and microwave sources, their use in chemistry has gained momentum recently (Surati, et al., 2012; Lidstram, et al., 2001).

Microwave irradiation has gained popularity in the past decade as a powerful tool for rapid and efficient synthesis of a variety of compounds because of selective absorption of microwave energy by polar molecules. This emerging environmentally benign technique belongs to the upcoming area of green chemistry. The microwave-assisted organic reactions have been broadly classified into two categories:

(a) Microwave-assisted reactions using solvents

Examples: Hydrolysis, Oxidation, Esterification, Decarboxylation, Cycloaddition, N-Acylations etc.

(b) Microwave-assisted reactions using solvent-free conditions

Examples: Aromatic Nucleophilic Substitutions, Deacetylation etc.

(Surati, et al., 2012)

2.2.1. Microwave-assisted synthesis of Schiff bases

Recent developments in microwave-accelerated solventless organic synthesis are summarized. This expeditious and solvent-free approach involves the exposure of neat reactants to microwave (MW) irradiation in conjunction with the use of supported reagents or catalysts. The salient features of these high yield protocols are the enhanced reaction rates, greater selectivity and the experimental ease of manipulation (Verma,
1999). Among other reagents recently described in the literature on this eco-friendly green approach. Verma, 1999, disclosed MW-induced acceleration of such dehydration reactions using montmorillonite K10 clay26 (66) to facile preparation of imines and enamines via the reactions of primary and secondary amines with aldehydes and ketones, respectively.

Bhusnure et al., 2015 reported microwave assisted solvent free synthesis of Schiff bases (68) of aromatic aldehydes and aromatic amines (ethyl 4-aminobenzoate) by using wetting reagent β-ethoxyethanol. Microwave-assisted organic efficient Synthesis of Schiff Base (69) of Isatin Derivatives using and their antibacterial activities were disclosed by Panda, et al., 2013. Naglah, et al., 2015 introduced a coupling reaction of nicotinic acid with certain L-amino acid methyl esters including valine, leucine, and phenylalanine was done by the use of acid chloride method. The products were reacted with hydrazine hydrate 99% to give the corresponding hydrazides that were reacted with indoline-2, 3-dione (isatin) to get Schiff base (70) under the application of microwave irradiation technique.

Aldehyde based Schiff bases (71) were synthesized using salicyladehyde with different substituted amines and ketone based Schiff bases (72) were synthesized from different substituted aromatic ketone and phenyl amine by Chakraborty, et al., 2012.
Schiff bases are important intermediates for the synthesis of various bioactive products (Prajapati and Chourasia, 2011; Kamaria, et al. 2011). On the other hand, they are fundamental materials for synthesis of various Schiff base ligands which are used as chiral auxiliaries in asymmetric synthesis. Metal complex Schiff bases have also been used as catalyst in many reactions (Gagieva, et al., 2005). Microwave based synthesis depends on many factors such as amount of solvent, temperature and microwave power (Somani, et al., 2010; Peng, et al., 2014). Yang, et al., 2002 reported microwave-assisted preparation of a series of Schiff-base via efficient condensation of salicylaldehyde and aryl amines without solvent. Gao and Zheng, 2002 synthesized three optically active Schiff-base ligands derived from condensation of 2-hydroxyacetophenone and chiral diamines. Yang and Sun, 2006 compared the three ways of synthesis of simple Schiff base and microwave irradiation was found to be the simplest way of synthesis. Naqvi, et al., 2009 reported the non classical methods (water based reaction, microwave and grindstone chemistry) for the preparation of Schiff bases Rawal, et al., 2009; Kulshrestha and Baluja, 2010; Somani, et al., 2010; Prajapati and Chourasia, 2011; Chakraborty, et al., 2012; Srivastava, et al., 2014; Venugopala and Jayashree, 2008).

Careful survey of the literature reveals that a large number of odorant Schiff bases or their derivatives have been synthesized and a wide range of their applications in soap composition, conditioning shampoos, hair spray formulation, a fabric washing deodorants, solid detergents composition, perfumed liquid detergents, colognes, handkerchief perfumes, pharmaceutical formulations are reported. (Arctander, 1969; Mookherjee, et al., 1988; 1989(a); 1989(b); 1989(c); 1989(d); 1989(e); Blanc and Aschiers, 1992; Baudin, 1993; IFF, 2002; Kaiser, et al., 2002; Ochsner, 1985; Narula, 1991; Sprecker, 1989; Dahill and Robert, 1972; Strub, et al., 2016; Narula, et al., 2006).
2.3. Rationale of the study

Consequent upon detailed review of literature, inference were drawn and rationale made is given as under

❖ Review of literature reveals that interest in development of odorant molecules including Schiff bases as novel ingredient for fragrance and flavor composition is high and global efforts made in this direction are well reported.

❖ Schiff bases of acetophenone, anisaldehyde, benzaldehyde, cinnamaldehyde, citral, and citronellal with anthranilic acid have been prepared by condensation method for their use as ligands for synthesis of metal complexes, however have not been characterized and examined for their odoriferous properties.

❖ Preparation of Schiff bases of acetophenone, anisaldehyde, benzaldehyde, cinnamaldehyde, citral, citronellal, cuminaldehyde, vanillin and alpha-ionone with methylanthranilate using classical condensation method and their odor attributes are reported in literature.

❖ Schiff bases including the odorant ones previously reported in the literature have been synthesized using classical condensation method which has limitations of long reaction time, increased thermal exposure of the reactants to the heated surface for a longer time and consequently decomposition of the thermolabile compounds, consumption of solvent and energy, tedious work up affecting thereby the reaction efficiency, yield and quality of the product. Thus, an improved method overcoming these limitations for synthesizing the Schiff bases was desired.

❖ MW irradiation technique has not been attempted previously for synthesis of the Schiff bases envisaged in the present investigation.

2.4. Objective of the present work

The proposed study aimed at the production of new odorant Schiff bases for their utilization in fragrance composition. The objective of the study was the synthesis and characterization of some new odorant Schiff bases from naturally occurring or natural identical reactant compounds for their use in fragrance composition. It was also envisaged to study the odor properties of the synthesized Schiff bases.
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MATERIALS AND METHODS

Details of the general reagents used, preparation of the Schiff bases, various analytical and physico-chemical methods employed for characterization of synthesized Schiff bases are described in this chapter.

3.1. Solvent and reagents

The solvent and reagents (Table 5) used in this investigation were of highest purity available from commercial source and used without further purification.

**Table 5: Reactants/reagents, purity and their source**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Reagents</th>
<th>Purity %</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Acetophenone</td>
<td>99.0</td>
<td>Himedia</td>
</tr>
<tr>
<td>2.</td>
<td>α-ionone</td>
<td>98.0</td>
<td>Merck</td>
</tr>
<tr>
<td>3.</td>
<td>Anisaldehyde</td>
<td>98.0</td>
<td>Loba chemie</td>
</tr>
<tr>
<td>4.</td>
<td>Anthranilic acid</td>
<td>98.0</td>
<td>Sigma Aldrich</td>
</tr>
<tr>
<td>5.</td>
<td>Benaldehyde</td>
<td>99.0</td>
<td>Merck</td>
</tr>
<tr>
<td>6.</td>
<td><em>trans</em>-Cinnamaldehyde</td>
<td>98.0</td>
<td>Himedia</td>
</tr>
<tr>
<td>7.</td>
<td>Ciprofloxacin</td>
<td>98.0</td>
<td>Cipla Limited</td>
</tr>
<tr>
<td>8.</td>
<td>Citral</td>
<td>96.0</td>
<td>Himedia</td>
</tr>
<tr>
<td>9.</td>
<td>Citronellal</td>
<td>95.0</td>
<td>Merck</td>
</tr>
<tr>
<td>10.</td>
<td>Cuminaldehyde</td>
<td>98.0</td>
<td>Sigma Aldrich</td>
</tr>
<tr>
<td>11.</td>
<td>Ethanol</td>
<td>95.0</td>
<td>-</td>
</tr>
<tr>
<td>13.</td>
<td>Methylanthranilate</td>
<td>98.0</td>
<td>Himedia</td>
</tr>
<tr>
<td>14.</td>
<td>Nutrient Agar Media</td>
<td>-</td>
<td>Himedia</td>
</tr>
<tr>
<td>15.</td>
<td>Potato Dextrose Agar</td>
<td>-</td>
<td>Himedia</td>
</tr>
<tr>
<td>16.</td>
<td>Vanilllin</td>
<td>99.0</td>
<td>SD-Fine chem.</td>
</tr>
<tr>
<td>17.</td>
<td>Veratraldehyde</td>
<td>98.0</td>
<td>Hi-media</td>
</tr>
</tbody>
</table>
3.2. Scientific microwave reactor/oven

Microwave assisted synthesis of the Schiff bases was performed in a scientific microwave oven (SRL-Milestone Start-S Labstation) operating between 140-1600W. All the reactions were carried out at 300-500W.

3.3. Details of reactants

Name: [CAS No.], chemical name (structure no.)

3.3.1. Amines

(i) Anthranilic acid: [118-92-3], 2-aminobenzoic acid (73)

C₇H₇NO₂; MW: 137.14; b.p.: 200°C, m.p.: 146-148°C; Odor: odorless. It is white to pale yellow crystalline powder. Oats is the natural source for anthranilic acid. Owing to the occurrence of anthranilic acid in the major biochemical pathways of bacteria, plants and animals, anthranilic acid is also the starting material for several other types of compounds in nature. Anthranilic acid, amino group substituted benzoic acid at ortho position, is used as an intermediate for production of fragrant molecule (Surburg and Panten, 2005). It has amino and carboxylic group attached in ring structure and its esters are used in preparing perfumes (Wiklund, 2004).

(ii) Methyl anthranilate: [134-20-3], Methyl 2-aminobenzoate (74)

C₈H₉NO₂; MW: 151.16; b.p.: 256°C; m.p.: 24°C; Odor: Musty, fruity and dry floral reminiscent of concord grapes. It occurs as white crystals, or a yellowish liquid, that show blue fluorescence. Occurs in a large number of blossom essential oils (e.g., orange, neroli, ylang-ylang, strawberry and jasmine oils), grapes, and citrus oils, Methyl anthranilate is prepared by esterification of anthranilic acid with methanol or by reaction of isatoic anhydride with methanol.

It is used in a large number of blossom fragrances. However, its use in perfumes for soap and cosmetics is limited because it causes discoloration. It is used in aroma compositions (e.g., in grape and citrus flavors) (Bauer, et al., 1997; Surburg and Panten, 2005; Arctander, 1969).
3.3.2. Carbonyl compounds

3.3.2.1. Aldehydes

(i) Anisaldehyde: [123-11-5], 4-methoxybenzaldehyde (75)

C_8H_8O_2; MW: 136.15; b.p.: 248°C; Odor: Sweet, mimosa, hawthorn, mild, floral. It is a colorless to slightly yellowish liquid. Anisaldehyde occurs in star anise, fennel, vanilla, cranberry, black currant and also in many essential oils. p-Anisaldehyde is frequently used in sweet blossom compositions (e.g., in lilac and hawthorn types) as well as in flavor compositions for confectioneries and beverages. p-Anisaldehyde is an intermediate in many industrial processes (Bauer, et al., 1997; Surburg and Panten, 2005; Arctander, 1969).

(ii) Benzaldehyde: [100-52-7], Benzoic aldehyde (76)

C_7H_6O; MW: 106.12; b.p.: 178.1°C; Odor: Powerful sweet odor of freshly cut bitter almonds. It is a colorless or yellowish liquid strongly refractive. Naturally it occurs in apricot, apples, cherry, kemels, peach and in many other essential oils.

It is a component of bitter almond oil. In the absence of inhibitors, benzaldehyde undergoes autoxidation to perbenzoic acid, which reacts with a second molecule of benzaldehyde to yield benzoic acid. Benzaldehyde is used in aroma compositions for its bitter almond odor. It is the starting material for a large number of araliphatic fragrance and flavor materials (Bauer, et al., 1997; Surburg and Panten, 2005; Arctander, 1969).

(iii) Cinnamaldehyde: [104-55-2], 3-phenyl, 2 propenal (77)

C_9H_8O; MW: 132.16; b.p.: 248-252°C; Odor: Powerful warm spicy. It is a pale yellow, viscous liquid. It is the main component of cassia oil (up to 90%), Sri Lanka cinnamon
bark oil (up to 75%), and bark of *Cinnamomum aromaticum* (min. 80%). Smaller quantities are found in many other essential oils. In nature, the *trans* isomer is predominant. On an industrial scale, cinnamaldehyde is prepared almost exclusively by alkaline condensation of benzaldehyde and acetaldehyde. Cinnamaldehyde is used in many compositions for creating spicy and oriental notes (e.g., soap perfumes) (Bauer, et al., 1997; Surburg and Panten, 2005; Arctander, 1969).

**(iv) Citral:** [5392-40-5], 3,7-dimethylocta-2,6-dienal (78)

C$_{10}$H$_{16}$O; MW: 152.24; b.p.: 229°C; Odor: Strong green lemony. It is a pale yellow liquid. Occurs as *cis* and *trans* isomers (citral a and b, respectively) analogous to the corresponding alcohols, geraniol and nerol: citral a [141-27-5] (geranial), citral b [106-26-3] (neral). Natural citral is nearly always a mixture of these two isomers. It occurs in lemon myrtle (*Backhousia citriodora*) (up to 90-98%), lemon-grass (*Cymbopogon citrates*) oil (up to 85 %), in *Litsea cubeba* oil (up to 75 %), Mandarin Petitgrain (up to 45%), and in small amounts in many other essential oils. The citrals are colorless to slightly yellowish liquids, with an odor reminiscent of lemon (Bauer, et al., 1997; Surburg and Panten, 2005; Arctander, 1969).

**(v) Citronellal:** [106-23-0], 3, 7-dimethyloct-6-enal (79)

C$_{10}$H$_{18}$O; MW: 154.25; b.p.: 207°C; Odor: Fresh green, citrusy. Pure citronellal is a colorless liquid. Occurs in citronella oil at a concentration of up to 45 %; *Backhousia citriodora* oil contains up to 80% citronellal. Racemic citronellal occurs in a number of *Eucalyptus citriodora* oils at a concentration of up to 85% (Bauer, et al., 1997; Surburg and Panten, 2005; Arctander, 1969).

**(vi) Cuminaldehyde:** [122-03-2], 4-isopropylbenzaldehyde (80)

C$_{10}$H$_{12}$O; MW: 148.21; b.p.: 235.5°C. Odor: spicy. It is a colorless liquid and occur in the essential oils of eucalyptus, myrrh, cassia, cumin (ca. 45-58%) and others. It is used as a flavoring additive in various foods and also in perfumes and cosmetics (Bauer, et al., 1997; Surburg and Panten, 2005; Arctander, 1969).
(vii) Vanillin: [121-33-5], 4-hydroxy-3-methoxybenzaldehyde (81)

C₈H₈O₃; MW: 152.15; b.p.: 285°C; m.p.: 82-83°C; Odor: Intensely sweet and very tenacious creamy vanilla. Vanillin is a white, crystalline solid. It is found in many essential oils and foods, but is often not essential for their odor or aroma. However, it does determine the odor of essential oils and extracts from *Vanilla planifolia* and *V. tahitensis* pods, in which it is formed during ripening by enzymatic cleavage of glycosides. The main application of vanillin is the flavoring of foods (e.g., ice cream, chocolate, bakery products, and confectioneries). Small quantities are used in perfumery to round and fix sweet, balsamic fragrances (Bauer, et al., 1997; Surburg and Panten, 2005; Arctander, 1969).

(viii) Veratraldehyde: [120-14-9], 3, 4-dimethoxybenzaldehyde (82)

C₉H₁₀O₃; MW: 166.18; b.p.: 281°C; m.p.: 44-45°C; Odor: Woody, vanilla-like. It is a crystalline solid, occurs in a few essential oils such as *Cymbopogon microstachys*, *C. juvanensis* and *Eryngium poterium*. Veratraldehyde can be prepared by methylation of vanillin. It is used in oriental and warm-woody fragrances, as well as in flavor compositions for vanilla notes. It is also an intermediate in, for example, the synthesis of pharmaceuticals (Bauer, et al., 1997; Surburg and Panten, 2005; Arctander, 1969).
3.3.2.2. Ketones

(i) Acetophenone: [98-86-2], Phenyl methyl ketone (83)

C₈H₈O; MW: 120.15; b.p.: 202.0°C; m.p.: 20.5 °C; Colorless liquid; Odor: Sweet odor, reminiscent of orange blossom. It is a naturally occurring component of a large number of foods including apples, cheese, apricot, banana, beef and cauliflower. Acetophenone is used for perfuming detergents and industrial products and is an intermediate in the synthesis of other fragrance materials (Bauer, et al., 1997; Surburg and Panten, 2005; Arctander, 1969).

(ii) Alpha-Ionone: [127-41-3], 4-(2,6,6-trimethylcyclohex-2-enyl)but-3-en-2-one (84)

C₁₃H₂₀O; MW: 192.30; b.p.: 121-122°C; Odor: Floral, heavy, sweet, reminiscent of violets. Alpha-ionone is a slightly viscous, yellowish orange liquid and occurs in the rose oil, in the leaf of *Iryingia barter* or *Klainedoxa gabonensis*, in the roots of *Orris* species. Alpha-Ionone is a highly valued fragrance material (Bauer, et al., 1997; Surburg and Panten, 2005; Arctander, 1969).
3.4. Characterization of the synthesized Schiff bases

3.4.1. Melting point

Melting points were measured on Buchi Melting Point (b-540) apparatus using open glass capillary method and are uncorrected.

3.4.2. Elemental analysis

Elemental analysis of the synthesized Schiff bases for carbon, hydrogen and nitrogen content were carried out on Thermo Scientific, Flash-2000, CHNS/O analyser.

3.4.3. Fourier Transform Infrared (FT-IR) spectroscopy

FT-IR spectra were recorded at room temperature from 4000 cm\(^{-1}\) to 500 cm\(^{-1}\) with KBr pellets at a resolution of 4cm\(^{-1}\), using Thermo-Nicolet 8700, Research Spectrophotometer (Thermo Scientific).

3.4.4. \(^1\)H NMR and \(^{13}\)C NMR spectra

\(^1\)H NMR (500 MHz) and \(^{13}\)C NMR (125 MHz) spectra were recorded on Bruker Avance-II instrument using CDCl\(_3\) and TMS as an internal standard. Chemical shifts (\(\delta\)) are reported in ppm.

3.5. Olfactory evaluation

Olfactory properties of the synthesized Schiff bases were studied employing standard olfactory method (IS: 2284-1988, 1988). Sample solutions (10 wt. % in ethyl alcohol) were used to evaluate their odor properties. The test was done in an odorless environment with temperature control at 27°C. Smelling strips of 15 cm long, 1 cm wide and length of dip was about 0.5 to 1 cm.
3.6. Antimicrobial activity

Antimicrobial activity of Schiff bases was evaluated according to the guidelines of National Committee for Clinical Laboratory Standards (NCCLS, 1997) using disc diffusion method. The bacterial cultures for *Staphylococcus aureus* (ATCC 259235) and *Escherichia coli* (ATCC 27853) were obtained from Microbial Type Culture Collection (MTCC), Chandigarh and fungal cultures of *Aspergillus niger* (NTCC 17) and *Penicillium chrysogenum* (NTCC 52) were obtained from National Type Culture Collection (NTCC), Forest Research Institute, Dehradun.

3.6.1. Disc diffusion method

Exponentially grown cultures of bacteria and fungi were mixed with sterile 0.85% saline solution to make the final volume upto $10^5$- $10^6$ cfu/ml. Petri plates containing 15 ml of Nutrient Agar Media (NAM) and Potato Dextrose Agar (PDA) were used for bacteria and fungi respectively. The inoculum of bacterial and fungal cultures was spread separately on the surface of their respective solidified media. Schiff bases (40 µg/ml) were dissolved in dimethylsulfoxide (DMSO) and Whatman no. 1 filter paper discs (5mm in diameter) impregnated with the test compound (5 µl/disc) were placed on the plates. Ciprofloxacin (10µg/disc) was used for bacteria and griseofulvin was used for the fungi as positive control. A paper disc impregnated with DMSO was used as negative control. Plates inoculated with the bacteria were incubated for 24h at 30±2 ºC and the fungal cultures were incubated for 5-6 days at 27±2ºC. The inhibition zone diameters were measured in millimeters. All the tests were performed in triplicate and the average was taken as final reading.

3.6.2. Determination of Minimum Inhibitory Concentration (MIC)

MIC values were determined according to the guidelines of NCCLS (Tuite, 1969). Solutions of the test compounds, ciprofloxacin and griseofulvin were prepared in DMSO at different concentrations of 10, 20, 30, 40, 50, 60 µg/ml to determine the MIC. All determinations were done in triplicate and presented as mean of three values.
Materials and Methods

3.6.3. Determination of percent activity index

\[
\text{Activity index (\%)} = \frac{\text{Zone of inhibition by test compound (diameter)}}{\text{Zone of inhibition by standard (diameter)}} \times 100
\]

(Pradeep, et al., 2013)

3.7. General protocol for synthesis of odorant Schiff bases

Twenty Schiff bases namely 2-(4ʹ-methoxybenzylideneamino) benzoic acid (Sb1), 2-(benzylideneamino) benzoic acid (Sb2), 2-(3ʹ-phenylallylideneamino) benzoic acid (Sb3), 2-(3ʹ,7ʹ-dimethyloct-2ʹ,6ʹ-dienylideneamino) benzoic acid (Sb4), 2-(3ʹ,7ʹ-dimethyloct-6ʹ-enylideneamino) benzoic acid (Sb5), 2-(4ʹ-isopropylbenzylideneamino) benzoic acid (Sb6), 2-(4ʹ-hydroxy-3ʹ-methoxybenzylideneamino) benzoic acid (Sb7), 2-(3ʹ,4ʹ-dimethoxybenzylideneamino) benzoic acid (Sb8), 2-(1ʹ-phenylethylideneamino) benzoic acid (Sb9), 2-[4ʹ-(6ʹ,10ʹ,10ʹ-trimethylcyclohex-6ʹ-enyl)-but-3ʹ-en-2ʹ-enylidene amino] benzoic acid (Sb10), methyl 2-(4ʹ-methoxybenzylideneamino) benzoate (Sb11), methyl 2-(benzylideneamino) benzoate (Sb12), methyl 2-(3ʹ-phenylallylideneamino) benzoate (Sb13), methyl 2-(3ʹ,7ʹ-dimethyloct-2ʹ,6ʹ-dienylideneamino) benzoate (Sb14), methyl 2-(3ʹ,7ʹ-dimethyloct-6ʹ-enylideneamino) benzoate (Sb15), methyl 2-(4ʹ-isopropyl benzylideneamino) benzoate (Sb16), methyl 2-(4ʹ-hydroxy-3ʹ-methoxybenzylidene amino) benzoate (Sb17), methyl 2-(3ʹ,4ʹ-dimethoxybenzylideneamino) benzoate (Sb18), methyl 2-(1ʹ-phenylethylideneamino) benzoate (Sb19) and methyl 2-[4ʹ-(6ʹ,10ʹ,10ʹ-trimethylcyclohex-6ʹ-enyl)-but-3ʹ-en-2ʹ-enylideneamino] benzoate (Sb20) were prepared (Scheme 4-13 and Scheme 15-24) by condensation of anthranilic acid and methyl anthranilate separately with corresponding naturally occurring carbonyl compounds represented by six aromatic aldehydes - anisaldehyde, benzaldehyde, cinnamaldehyde, cuminaldehyde, vanillin, vertraldehyde; two acyclic terpene aldehydes - citral, citronellal; an aromatic acetophenone, and a cyclic terpenoid ketone- α-Ionone employing conventional and MW assisted methods. Protocols used for these syntheses are shown in Figure 7 and Figure 8.
3.7.1. Conventional method

![Diagram of conventional method](image)

**Figure 7:** Reaction protocol for synthesis of Schiff bases by conventional method

3.7.2. Microwave assisted synthesis

![Diagram of microwave assisted method](image)

**Figure 8:** Reaction protocol for synthesis of Schiff bases by microwave assisted method
3.8. Synthesis of odorant Schiff bases

3.8.1. General procedure for preparation of Schiff bases of anthranilic acid

(Scheme 3)

3.8.1.1. Conventional method

To a solution of 0.1 mol (13.71g) of anthranilic acid in ethanol was added (0.1mol) of ethanolic solution of carbonyl compound(s) and the reaction mixture was refluxed under inert atmosphere on a water bath for 4-13h, concentrated under vacuum and purified by vacuum distillation [2-(3'-phenylallylideneamino) benzoic acid (Sb3), 2-(3',7'-dimethyloct-2',6'-dienyldeneamino) benzoic acid (Sb4) and 2-[4'-(6',10',10'-trimethyl cyclohex-6'-enyl)-but-3'en-2'-enyldeneamino] benzoic acid (Sb10)] or kept refrigerated overnight. Solid product [2-(4'-methoxybenzylideneamino) benzoic acid (Sb1), 2-(benzylideneamino) benzoic acid (Sb2), 2-(3',7'-dimethyloct-6'-enyldiene amino) benzoic acid (Sb5), 2-(4'-isopropylbenzylideneamino) benzoic acid (Sb6), 2-(4'-hydroxy-3'-methoxybenzylideneamino) benzoic acid (Sb7), 2-(3',4'-dimethoxy benzylideneamino) benzoic acid (Sb8), 2-(1'-phenylethylideneamino) benzoic acid (Sb9)] were filtered under reduced pressure, crystallized with ethanol and dried. All the compounds were stored at 4ºC.

Reaction condition: [i] = CM: 4-13h, reflux at 98-100ºC / MWI: 4-14 min. 300-500W, molar ratio = 1:1,

\[
R = \text{C}_9\text{H}_{10}\text{O} / \text{C}_8\text{H}_8 / \text{C}_{10}\text{H}_{10} / \text{C}_{11}\text{H}_8 / \text{C}_{11}\text{H}_{13} / \text{C}_8\text{H}_{13} / \text{C}_9\text{H}_{10}\text{O}_2 / \text{C}_{10}\text{H}_{12}\text{O}_2 / \text{C}_9\text{H}_{10} / \text{C}_{14}\text{H}_{22} \\
[\text{(-)}\text{R'}\text{(-)} = \text{alkyl/aryl group attached with carbonyl carbon in case of ketone}]
\]

MWI: Microwave irradiation method; CM: Conventional method

Scheme 3: General reaction of anthranilic acid derived Schiff bases
3.8.1.2. Solvent free MW irradiation method

The equi-molar ratio of anthranilic acid (0.1mol) and carbonyl compound (0.1mol) were mixed in a reaction flask and irradiated with MW at 300-500W for 4-14min. After completion of the reaction, the mixture was either purified by vacuum distillation (Sb3, Sb4 and Sb10) or cooled in a refrigerator overnight. The solid (Sb1, Sb2, Sb5, Sb6, Sb7, Sb8 and Sb9) separated was filtered under reduced pressure, crystallized with ethanol and dried. All the products were stored at 4ºC.
Materials and Methods

Scheme 4: Synthesis of 2-(4'-methoxybenzylideneamino) benzoic acid (Sb1)

Reaction condition: [i] = CM: 5h. reflux at 98-100ºC, MWI: 6 min./300W, molar ratio - (1:1)

Scheme 5: Synthesis of 2-(benzylideneamino) benzoic acid (Sb2)

Reaction condition: [i] = CM: 4h. reflux at 98-100ºC, MWI: 4 min./300W, molar ratio - (1:1)

Scheme 6: Synthesis of 2-(3’-phenylallylideneamino) benzoic acid (Sb3)

Reaction condition: [i] = CM: 5h. reflux at 98-100ºC, MWI: 6 min./300W, molar ratio - (1:1)
Scheme 7: Synthesis of 2-(3',7'-dimethyloct-2',6'-dienylideneamino) benzoic acid (Sb4)

Reaction condition: [i] = CM: 7h. reflux at 98-100°C, MWI: 7min./300W, molar ratio - (1:1)

Scheme 8: Synthesis of 2-(3', 7'-dimethylct-6'-enylideneamino) benzoic acid (Sb5)

Reaction condition: [i] = CM: 6h. reflux at 98-100°C, MWI: 5min./300W, molar ratio - (1:1)

Scheme 9: Synthesis of 2-(4'-isopropylbenzylideneamino) benzoic acid (Sb6)

Reaction condition: [i] = CM: 5h. reflux at 98-100°C, MWI: 4min./300W, molar ratio - (1:1)
Materials and Methods

Scheme 10: Synthesis of 2-(4′-hydroxy-3′-methoxybenzylideneamino) benzoic acid (Sb7)

![Scheme 10]

Reaction condition: \([i] = \text{CM: 4h. reflux at 98-100°C, MWI: 4 min./300W, molar ratio} - (1:1)\)

Scheme 11: Synthesis of 2-(3′,4′-dimethoxybenzylideneamino) benzoic acid (Sb8)

![Scheme 11]

Reaction condition: \([i] = \text{CM: 6h. reflux at 98-100°C, MWI: 5 min./300W, molar ratio} - (1:1)\)

Scheme 12: Synthesis of 2-(1′-phenylethylideneamino) benzoic acid (Sb9)

![Scheme 12]

Reaction condition: \([i] = \text{CM: 8h. reflux at 98-100°C, MWI: 11 min./400W, molar ratio} - (1:1)\)
Scheme 13: Synthesis of 2-[4’-(6’,10’,10’-trimethylcyclohex-6’-enyl)-but-3’-en-2’-enylideneamino] benzoic acid (Sb10)

**Reaction condition:** [i] = CM: 13h. reflux at 98-100ºC, MWI: 14 min./500W, molar ratio - (1:1)
3.8.2. General procedure for preparation of Schiff bases of methylantranilate

(Scheme 14)

3.8.2.1. Conventional method

To a solution of 0.1mol of methylantranilate in ethanol was added to 0.1mol of ethanolic solution of carbonyl compound and the reaction mixture was refluxed under inert atmosphere on a water bath for 4-12h, concentrated under vacuum and purified by vacuum distillation. All the compounds were stored at 4ºC.

**Scheme 14:** General reaction of methylantranilate derived Schiff bases

3.8.2.2. Solvent free MW irradiation method

The equi-molar ratio of methylantranilate (0.1mol) and carbonyl compound (0.1mol) were mixed in a reaction flask and irradiated with MW at 300-500W for 4-13min. After completion of the reaction, the mixture was purified by vacuum distillation and stored at 4ºC.
**Scheme 15:** Synthesis of methyl 2-(4'-methoxybenzylideneamino) benzoate (Sb11)

\[
\text{methylantranilic acid} + \text{anisaldehyde} \xrightarrow{\text{MWI} / \text{CM}} \text{Sb11}
\]

**Reaction condition:** [i] = CM: 5-6h. reflux at 98-100°C, MWI: 4 min./300W, molar ratio - (1:1)

**Scheme 16:** Synthesis of methyl 2-(benzylideneamino) benzoate (Sb12)

\[
\text{methylantranilic acid} + \text{benzaldehyde} \xrightarrow{\text{MWI} / \text{CM}} \text{Sb12}
\]

**Reaction condition:** [i] = CM: 5-6h. reflux at 98-100°C, MWI: 4 min./300W, molar ratio - (1:1)

**Scheme 17:** Synthesis of methyl 2-(3'-phenylallylideneamino) benzoate (Sb13)

\[
\text{methylantranilic acid} + \text{cinnamaldehyde} \xrightarrow{\text{MWI} / \text{CM}} \text{Sb13}
\]

**Reaction condition:** [i] = CM: 7h. reflux at 98-100°C, MWI: 4 min./300W, molar ratio - (1:1)
Scheme 18: Synthesis of methyl 2-(3',7'-dimethyloct-2',6'-diénylideneamino) benzoate (Sb14)

\[
\begin{align*}
\text{methylantranilate} & \quad + \quad \text{citral} \quad \text{MWI/CM} \quad [i] \quad \text{Sb14} \\
\text{methylantranilate} & \quad + \quad \text{citral} \quad \text{MWI/CM} \quad [i] \quad \text{Sb14}
\end{align*}
\]

*Reaction condition:* \([i] = \text{CM: 7h. reflux at 98-100ºC, MWI: 6min./300W, molar ratio - (1:1)}\)

Scheme 19: Synthesis of methyl 2-(3',7'-dimethyloct-6'-énylideneamino) benzoate (Sb15)

\[
\begin{align*}
\text{methylantranilate} & \quad + \quad \text{citronellal} \quad \text{MWI/CM} \quad [i] \quad \text{Sb15} \\
\text{methylantranilate} & \quad + \quad \text{citronellal} \quad \text{MWI/CM} \quad [i] \quad \text{Sb15}
\end{align*}
\]

*Reaction condition:* \([i] = \text{CM: 6-7h. reflux at 98-100ºC, MWI: 5min./300W, molar ratio - (1:1)}\)

Scheme 20: Synthesis of methyl 2-(4'-isopropylbenzylideneamino) benzoate (Sb16)

\[
\begin{align*}
\text{methylantranilate} & \quad + \quad \text{cuminaldehyde} \quad \text{MWI/CM} \quad [i] \quad \text{Sb16} \\
\text{methylantranilate} & \quad + \quad \text{cuminaldehyde} \quad \text{MWI/CM} \quad [i] \quad \text{Sb16}
\end{align*}
\]

*Reaction condition:* \([i] = \text{CM: 4h. reflux at 98-100ºC, MWI: 6min./300W, molar ratio - (1:1)}\)
**Scheme 21:** Synthesis of methyl 2-(4'-hydroxy-3'-methoxybenzylideneamino) benzoate (Sb17)

\[
\text{methylantranilate} \quad \text{vanillin} \quad \xrightarrow{\text{MWI/CM}} \quad \text{Sb16}
\]

**Reaction condition:** [i] = CM: 5h. reflux at 98-100ºC, MWI: 5 min./300W, molar ratio - (1:1)

**Scheme 22:** Synthesis of methyl 2-(3',4'-dimethoxybenzylideneamino) benzoate (Sb18)

\[
\text{methylantranilate} \quad \text{veratraldehyde} \quad \xrightarrow{\text{MWI/CM}} \quad \text{Sb18}
\]

**Reaction condition:** [i] = CM: 6h. reflux at 98-100ºC, MWI: 4 min./300W, molar ratio - (1:1)

**Scheme 23:** Synthesis of methyl 2-(1'-phenylethylideneamino) benzoate (Sb19)

\[
\text{methylantranilate} \quad \text{acetophenone} \quad \xrightarrow{\text{MWI/CM}} \quad \text{Sb19}
\]

**Reaction condition:** [i] = CM: 9h. reflux at 98-100ºC, MWI: 6 min./400W, molar ratio - (1:1)
**Scheme 24:** Synthesis of methyl 2-[4’-(6’,10’,10’-trimethylcyclohex-6’-enyl)-but-3’-en-2’-enyldieneamino] benzoate (Sb20)

Reaction condition: [i] = CM: 12h. reflux at 98-100°C, MWI: 13 min./500W, molar ratio - (1:1)
3.9. References

8. Tuite, J., 1969, Plant Pathological Methods, Fungi and Bacteria, Burgess Publishing Company: Minneapolis, MN, USA, 93
RESULTS AND DISCUSSION

Conventional method employed for preparation of Schiff bases involving condensation of a carbonyl compound with a primary amine. Though it is used extensively, but has many limitations including long reaction time, increased thermal exposure of the reactants to the heated surface, consequently decomposition of the thermolabile compounds, consumption of solvent and energy, tedious work up affecting the reaction efficiency, yield and quality of the product. Microwave (MW) assisted synthesis of organic compounds has acquired significant importance over conventional organic synthesis in terms of reduced solvent and energy consumption and reaction duration, instantaneous and uniform heating, easier workup, improved product purity and yield matching with green chemistry approach (Venugopala and Jayashree, 2008; Shah and Krishnapriya, 2014; Jacob, 2012). MW irradiation has been widely used for preparation of a large number of Schiff bases (Naqvi, et al., 2009; Rawal, et al., 2009; Kulshrestha and Baluja, 2010; Lidstram, et al., 2001; Chakraborty, et al., 2012; Bhusnure, et al., 2015; Satyanarayana, et al., 2008; Srivastava, et al., 2014; Naglah, et al., 2015; Peng, et al., 2014; Panda, et al., 2013). Therefore, feasibility of using MW irradiation for synthesis of the odorant Schiff bases of naturally occurring carbonyl compounds was carried out in the present study.

Twenty odorant Schiff bases namely 2-(4’-methoxybenzylideneamino) benzoic acid (Sb1), 2-(benzylideneamino) benzoic acid (Sb2), 2-(3’-phenylallylideneamino) benzoic acid (Sb3), 2-(3’,7’-dimethyloct-2’,6’-dienylideneamino) benzoic acid (Sb4), 2-(3’,7’-dimethyloct-6’-enylideneamino) benzoic acid (Sb5), 2-(4’-isopropylbenzylideneamino) benzoic acid (Sb6), 2-(4’-hydroxy-3’-methoxybenzylideneamino) benzoic acid (Sb7), 2-(3’,4’-dimethoxybenzylideneamino) benzoic acid (Sb8), 2-(1’-phenylethylideneamino) benzoic acid (Sb9), 2-[4’-(6’,10’,10’-trimethylcyclohex-6’-enyl)-but-3’-en-2’-enylidene amino] benzoic acid (Sb10), methyl 2-(4’-methoxybenzylideneamino) benzoate (Sb11), methyl 2-(benzylideneamino) benzoate (Sb12), methyl 2-(3’-phenylallylideneamino) benzoate (Sb13), methyl 2-(3’,7’-dimethyloct-2’,6’-dienylideneamino) benzoate (Sb14),
methyl 2-(3',7'-dimethyloct-6'-enylideneamino) benzoate (Sb15), methyl 2-(4'-isopropyl benzylideneamino) benzoate (Sb16), methyl 2-(4'-hydroxy-3'-methoxybenzylidene amino) benzoate (Sb17), methyl 2-(3',4'-dimethoxybenzylideneamino) benzoate (Sb18), methyl 2-(1'-phenylethylideneamino) benzoate (Sb19) and methyl 2-[4'-(6',10',10'-trimethylcyclohex-6'-enyl)-but-3'-en-2'-enylideneamino] benzoate (Sb20) (Scheme 4-13 and Scheme 15-24) were prepared from naturally occurring eight aldehydes (anisaldehyde, benzaldehyde, cinnamaldehyde, citral, citronellal, cuminaldehyde, vanillin and veratraldehyde) and two ketones (acetophenone and α-ionone) with anthranilic acid and methyl anthranilate, separately, by conventional (CM) and microwave (MW) assisted methods. A large number of experiments were performed to optimize the irradiation power and its duration and the optimized conditions are reported. MW irradiation resulted in no solvent consumption, reduced reaction time from 4 to 14 minutes, and increment in yields from 53% to 89% over conventional method requiring 4 to 13 hours and affording 42% to 71% yield. Altogether there was an improvement of 7% to 21% in the yield of these Schiff bases.

The Schiff bases were characterized by analysis of the elements (C, H and N), FT-IR, $^1$H NMR and $^{13}$C NMR spectral data. Elemental analysis of the Schiff bases was in agreement to their molecular formula assigned.

4.1. Spectral analysis of the Schiff bases

Schiff base wise FT-IR, $^1$H NMR and $^{13}$C NMR spectra are shown in Figure 9-68.

4.1.1. FT-IR spectral analysis

IR spectra of the free aldehydes (anisaldehyde, benzaldehyde, cinnamaldehyde, citral, citronellal, cuminaldehyde, vanillin and veratraldehyde), and ketones (acetophenone and α-ionone) have a strong band at 1690-1700 cm$^{-1}$ (due to carbonyl stretch), two bands of moderate intensity in the region 2700-2800 cm$^{-1}$ (due to H-C=O stretch in aldehydes only), while two moderate bands at 3500 and 3580 cm$^{-1}$ corresponding to N-H stretch were observed in the IR spectrum of anthranilic acid and methyl anthranilate. In the IR spectra of the Schiff bases, these bands disappeared and a new band appeared in the
range of 1613-1662 cm⁻¹ attributed to the ν (C=N) mode of azomethine linkage showing the condensation between the -CHO / >C=O group of the carbonyl compounds and amino group of anthranilic acid / methyl anthranilate resulting in the formation of the respective Schiff base. The OH absorption of –COOH group in the Schiff bases of antharinilic acid (Sb1- Sb6 and Sb9, Sb10) was observed around 3478-3331 cm⁻¹ while in Sb7 it appeared at 3120 cm⁻¹. A broad band around 3408 and 3310 cm⁻¹ observed in the IR spectrum of Sb7 and Sb17 was attributed to the phenolic hydroxy group.

4.1.2. ¹H NMR spectral analysis

¹H NMR spectra of the Schiff bases exhibit singlet of integration intensity equivalent to one hydrogen at 7.84-8.78 ppm and three hydrogens at 8.33-8.39 ppm attributed to (-CH=N-) and to (-CH₂-C=N-) protons, respectively. A singlet at 9.78-9.98 ppm due to hydroxyl proton of carboxylic group was observed in the spectra of the Schiff bases, Sb1-Sb10. A singlet at 3.73-3.91 ppm due to ester protons was observed in the spectra of the Schiff bases, Sb11-Sb20. A broad signal at 8.3-8.4 ppm and 5.74 ppm due to free NH₂ protons in the spectra of anthranilic acid and methyl anthranilate, respectively was absent in the observed spectra of all the Schiff bases which indicated the formation of the azomethine linkage. The multiplets within the 6.54-7.93 ppm range were assigned to protons belonging to aromatic rings. The spectra of Sb1, Sb7, Sb8, Sb11, Sb17 and Sb18 (two methoxyl groups) showed a singlet with an integration equivalent to three hydrogens at 3.90, 3.98, 3.98, 3.89, 3.83, 3.83 and 3.87 ppm, respectively corresponding to the methoxyl protons. A doublet integrating one hydrogen at 6.59-6.65 ppm observed in the spectra of Sb7 and Sb17 was assigned to phenolic proton in these compounds. Vinylic protons in compounds Sb3 and Sb13 were assigned at 5.89-6.68 and 5.79-6.62 ppm, respectively. Proton and methyl protons of the isopropylidene moiety in Sb4, Sb5, Sb14 and Sb15 were inferred from the singlet and doublet appeared at 4.99-5.09, and 1.68 ppm integrating to one and six protons, respectively in their spectra. Spectra of Sb6 and Sb16 displayed doublet with an integration equivalent to 6 protons of isopropyl group at 2.98 and 3.19 ppm, respectively. Singlets in the spectra of Sb10 and Sb20 integrating three protons observed at 1.27, 1.28, 1.16 and 1.18 were assigned to gem dimethyl protons.
4.1.3. $^{13}$C NMR spectral analysis

$^{13}$C NMR spectra of the synthesized Schiff bases (Sb1-Sb20) demonstrate that azomethine carbons in these compounds appeared between 155.0-165.2 ppm. Carboxyl carbons of the Schiff bases Sb1-Sb10 and ester carbons of the Schiff bases Sb11-Sb20 were observed between 167.7-169.7 ppm and 166.4-168 ppm, respectively. Methoxy carbons of Sb1, Sb7, Sb8, Sb11, Sb17 and Sb18 were observed at 55.6, 56.3, 56.2, 54.8, 55.2 and 55.2 ppm, respectively. Vinylic carbons of Sb3 and Sb13 emerged at 119.7, 138.5 and 119.9, 144.1 ppm, respectively. Methyl carbons of the isopropylidene moiety in Sb4, Sb5, Sb14, Sb15 were found at 19.6, 25.6, 20.3, 25.3 and 17.6, 27.6 ppm, respectively while those for isopropyl group in Sb6 and Sb16 were detected at 23.4, 22.9, respectively. Isopropylidene carbons of Sb4, Sb5, Sb14, Sb15 and isopropyl carbons of Sb6 and Sb16 were inferred from the signals at 133.4, 131.4, 132.2, 131.8 ppm, and 36.7, 39.9 ppm, respectively. Methyl carbons attached to azomethine carbon of Sb9, Sb10, Sb19 and Sb20 were found at 48.3, 16.8, 16.0, 16.8 ppm, respectively. Signals at 25.6 ppm observed in the spectra of Sb10 and Sb20 were assigned to their gem dimethyl carbons. Aromatic carbons in all the Schiff bases were observed in their characteristic range.

The NMR spectral assignments of the Schiff bases supported the inferences drawn from their elemental and IR studies.
4.2. Physico-chemical and spectroscopic data of synthesized odorant Schiff bases

**Compound Sb1: 2-(4’-methoxybenzylideneamino) benzoic acid**

Light yellow solid; C\textsubscript{15}H\textsubscript{13}NO\textsubscript{3}; Yield: 64% (conventional method) / 83% (MW irradiation method); m.p. 188 °C; Solubility: C\textsubscript{2}H\textsubscript{5}OH, CH\textsubscript{3}OH, CDCl\textsubscript{3}, DMSO; IR (KBr, cm\textsuperscript{-1}): 3431, 1721, 1658, 1490, 1243, 1165; \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}, (δ) ppm): 9.87 (1H, s, carboxylic OH), 8.63 (1H, s, HC=N); 6.66-7.91 (8H, m, Ar-H), 3.91 (3H, s, OCH\textsubscript{3}); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}, (δ) ppm): 55.6 (C8’), 114.1 (C5’), 116.4 (C1), 122.2 (C3), 126.1 (C1’), 127.2 (C5), 130.1 (C2’), 131.2 (C6), 135.3 (C4), 154.4 (C2), 160.1 (C7’), 163.3 (C4’), 169.4 (C7); Anal. Calc. for C\textsubscript{15}H\textsubscript{13}NO\textsubscript{3}: (%) calculated: 70.56, 5.13, 5.48, 18.81, found: 70.58, 5.16, 5.59, 18.85; MW: 255.08

![FT-IR spectrum of compound Sb1](image-url)
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition

Figure 10: $^1$H NMR spectrum of compound Sb1

Figure 11: $^{13}$C NMR spectrum of compound Sb1
Compound Sb2: 2-(benzylideneamino) benzoic acid

Yellow solid; C\textsubscript{14}H\textsubscript{11}NO\textsubscript{2}; Yield: 69\% (conventional method) / 89\% (MW irradiation method); m.p. 148°C; Solubility: C\textsubscript{2}H\textsubscript{5}OH, CH\textsubscript{3}OH, CDCl\textsubscript{3}, DMSO; IR (KBr, cm\textsuperscript{-1}): 3418, 1714, 1615, 1512, 1279, 1181; \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}, (δ) ppm): 9.97 (1H, s, carboxylic OH), 8.78 (1H, s, HC=\texttext{N}); 6.66-7.82 (9H, m, Ar-H); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}, (δ) ppm): 116.6 (C1), 122.4 (C3), 127.2 (C5), 128.6 (C3', C5'), 129.3 (C2', C6'), 131.1 (C4'), 131.5 (C6), 133.8 (C1'), 135.3 (C4), 154.1 (C2), 160.1 (C7'), 169.7 (C7); Anal. Calc. for C\textsubscript{14}H\textsubscript{11}NO\textsubscript{2} (%) calculated: 74.64, 4.92, 6.22, 14.21, found: 74.66, 4.90, 6.27, 14.17; MW: 225.07

![Figure 12: FT-IR spectrum of compound Sb2](image-url)
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition

Figure 13: $^1$H NMR spectrum of compound Sb2

Figure 14: $^{13}$C NMR spectrum of compound Sb2
Results and Discussion

**Compound Sb3: 2-(3’-phenylallylideneamino) benzoic acid**

Amber orange viscous liquid; C_{16}H_{13}NO_2; Yield: 57% (conventional method) / 72% (MW irradiation method); Fraction condition: 140-142 °C (0.0079MPa); Solubility: C_2H_5OH, CH_3OH, CDCl_3, DMSO; IR (KBr, cm^{-1}): 3478, 1718, 1638, 1482, 1218, 1132; ^1H NMR (500 MHz, CDCl_3, (δ) ppm): 9.89 (1H, s, carboxylic OH), 8.57 (1H, s, HC=N); 6.99-7.93 (9H, m, Ar-H), 6.68 (1H, s, Vinylic H), 5.89 (1H, s, Vinylic H); ^13C NMR (125 MHz, CDCl_3, (δ) ppm): 116.6 (C1), 119.7 (C2’), 122.6 (C3), 126.2 (C5’, C9’), 128.0 (C7’), 128.4 (C5), 128.9 (C6’, C8’), 131.1 (C6), 135.0 (C4’), 135.3 (C4), 138.5 (C3’), 149.9 (C2), 163.7 (C1’), 168.7 (C7); Anal. Calc. for C_{16}H_{13}NO_2 (%) calculated: 76.46, 5.21, 5.57, 12.74, found: 76.44, 5.28, 5.61, 12.81; MW: 251.09

![FT-IR spectrum of compound Sb3](image-url)
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition

Figure 16: $^1$H NMR spectrum of compound Sb3

Figure 17: $^{13}$C NMR spectrum of compound Sb3
Results and Discussion

Compound Sb4: 2-(3′,7′-dimethyloct-2′,6′-diienylideneamino) benzoic acid

Dark amber viscous liquid; C_{17}H_{21}NO_{2}; Yield: 64% (conventional method) / 84% (MW irradiation method); Fraction condition: 140-142 °C (0.0079MPa); Solubility: C_{2}H_{5}OH, CH_{3}OH, CDCl_{3}, DMSO; IR (KBr, cm^{-1}): 3411, 1738, 1624, 1513, 1249, 1188; ^{1}H NMR (500 MHz, CDCl_{3}, (δ) ppm): 9.79 (1H, s, carboxylic OH), 8.73 (1H, s, HC=N); 6.62-7.90 (4H, m, Ar-H), 6.45 (1H, s, C2′), 4.99 (1H, s, -CH=C(CH_{3})_{2}), 2.15 (3H, s, C4′ methyl), 2.0 (2H, m, C5′), 1.68 (6H, d, C8′, C9′ methyls), 1.38 (2H, s, C10′); ^{13}C NMR (125 MHz, CDCl_{3}, (δ) ppm): 17.3 (C10′), 19.6 (C9′), 25.6 (C8′), 26.1 (C5′), 39.6 (C4′), 116.0 (C2′), 116.8 (C1), 122.2 (C3), 123.5 (C6′), 127.2 (C5), 130.8 (C6), 133.4 (C7), 135.7 (C4), 149.1 (C2), 150.5 (C3′), 163.7 (C1′), 168.2 (C7); Anal. Calc. for C_{17}H_{21}NO_{2} (%) calculated: 75.23, 7.80, 5.16, 11.79, found: 75.22, 7.84, 5.25, 11.86; MW: 271.15

Figure 18: FT-IR spectrum of compound Sb4
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition

Figure 19: $^1$H NMR spectrum of compound Sb4

Figure 20: $^{13}$C NMR spectrum of compound Sb4
Compound Sb5: 2-(3',7'-dimethyloct-6'-enyldeneamino) benzoic acid

Greenish yellow solid; C_{17}H_{23}NO_2; Yield: 63% (conventional method) / 73% (MW irradiation method); m.p. 172 °C; Solubility: C_2H_5OH, CH_3OH, CDCl_3, DMSO; IR (KBr, cm^{-1}): 3388, 1728, 1628, 1488, 1248, 1154; ^1H NMR (500 MHz, CDCl_3, (δ) ppm): 9.79 (1H, s, carboxylic OH), 8.78 (1H, s, HC=N); 6.66-7.91 (4H, m, Ar-H), 5.08 (1H, s, -CH=C(CH_3)_2), 2.20 (2H, s, C2'), 2.10 (1H, s, C3'); 2.0 (2H, m, C5'), 1.68 (6H, d, C7' methyls), 1.32 (2H, s, C4'), 0.89 (3H, s, C3' methyl); ^13C NMR (125 MHz, CDCl_3, (δ) ppm): 19.6 (C9'), 20.9 (C10'), 24.1 (C5'), 25.6 (C8'), 31.8 (C3'), 35.2 (C2'), 37.8 (C4'), 116.4 (C1), 122.2 (C3), 126.8 (C6'), 127.2 (C5), 131.4 (C7'), 131.6 (C6), 134.3 (C4), 149.6 (C2), 163.7 (C1'), 168.6 (C7); Anal. Calc. for C_{17}H_{23}NO_2 (%) calculated: 74.67, 8.48, 5.12, 11.71, found: 74.71, 8.52, 5.18, 11.75; MW: 273.17

Figure 21: FT-IR spectrum of compound Sb5
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition

**Figure 22:** $^1$H NMR spectrum of compound Sb5

**Figure 23:** $^{13}$C NMR spectrum of compound Sb5
Compound Sb6: 2-(4’-isopropylbenzylideneamino) benzoic acid

Dark greenish brown solid; C_{17}H_{17}NO_{2}; Yield: 58% (conventional method) / 77% (MW irradiation method); m.p. 156 °C; Solubility: C_{2}H_{5}OH, CH_{3}OH, CDCl_{3}, DMSO; IR (KBr, cm\textsuperscript{-1}): 3331, 1712, 1617, 1496, 1243, 1165; \textsuperscript{1}H NMR (500 MHz, CDCl_{3}, (δ) ppm): 9.96 (1H, s, carboxylic OH), 8.76 (1H, s, HC=N); 6.66-7.81 (8H, m, Ar-H), 2.98 (6H, d, Isopropyl methyl group), 1.28 (3H, s, methyl); \textsuperscript{13}C NMR (125 MHz, CDCl_{3}, (δ) ppm): 23.4 (C9', C10'), 36.7 (C8'), 116.4 (C1), 122.2 (C3), 126.1 (C3', C5'), 126.8 (C5), 129.3 (C2', C6'), 130.4 (C1'), 133.6 (C6), 137.4 (C4), 150.4 (C4'), 154.1 (C2), 160.4 (C7'), 168.8 (C7); Anal. Calc. for C_{17}H_{17}NO_{2} (%) calculated: 76.37, 6.41, 5.24, 11.97, found: 76.43, 6.47, 5.29, 11.91; MW: 267.12

Figure 24: FT-IR spectrum of compound Sb6
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition

Figure 25: $^1$H NMR spectrum of compound Sb6

Figure 26: $^{13}$C NMR spectrum of compound Sb6
Compound Sb7: 2-(4'-hydroxy-3'-methoxybenzylideneamino) benzoic acid

Intense yellow solid; C_{16}H_{15}NO_{4}; Yield: 71% (conventional method) / 86% (MW irradiation method); m.p. 205°C; Solubility: C_{2}H_{5}OH, CH_{3}OH, CDCl_{3}, DMSO; IR (KBr, cm^{-1}): 3408, 3120, 1711, 1618, 1511, 1253, 1165; ^1H NMR (500 MHz, CDCl_{3}, (δ) ppm): 9.83 (1H, s, carboxylic OH), 8.64 (1H, s, HC=N); 6.45-6.65 (1H, Ar-OH), 3.98 (3H, s, OCH_{3}); ^13C NMR (125 MHz, CDCl_{3}, (δ) ppm): 160.1 (C7'), 151.5 (C2), 151.8 (C2'), 167.7 (C7); Anal. Calc. for C_{16}H_{15}NO_{4} (%) calculated: 66.40, 4.83, 5.16, 23.60, found: 66.48, 4.86, 5.18, 23.57; MW: 271.08

Figure 27: FT-IR spectrum of compound Sb7
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition

Figure 28: $^1$H NMR spectrum of compound Sb7

Figure 29: $^{13}$C NMR spectrum of compound Sb7
Compound Sb8: 2-(3',4'-dimethoxybenzylideneamino) benzoic acid

Light yellow solid; \( \text{C}_{16}\text{H}_{15}\text{NO}_4 \); Yield: 66% (conventional method) / 79% (MW irradiation method); m.p. 206°C; Solubility: \( \text{C}_2\text{H}_5\text{OH}, \text{CH}_3\text{OH}, \text{CDCl}_3, \text{DMSO} \); IR (KBr, cm\(^{-1}\)): 3441, 1711, 1632, 1496, 1255, 1140; \(^1\text{H NMR}\) (500 MHz, \( \text{CDCl}_3 \), (δ) ppm): 9.84 (1H, s, carboxylic OH), 8.64 (1H, s, HC=N); 6.98-7.60 (7H, m, Ar-H); 3.98 (3H, s, OCH\(_3\) ); \(^1^3\text{C NMR}\) (125 MHz, \( \text{CDCl}_3 \), (δ) ppm): 56.2 (C8', C9'), 114.4 (C2'), 115.4 (C5'), 116.4 (C1), 122.2 (C3), 122.5 (C6'), 126.3 (C5), 129.6 (C6), 133.3 (C4), 148.8 (C3'), 150.4 (C4'), 153.5 (C2), 160.3 (C7'), 168.4 (C7); Anal. Calc. for \( \text{C}_{16}\text{H}_{15}\text{NO}_4 \) (%) calculated: 67.34, 5.30, 4.91, 22.44, found: 67.37, 5.35, 4.97, 22.48; MW: 285.10

**Figure 30:** FT-IR spectrum of compound Sb8
Results and Discussion

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Figure 31: $^1$H NMR spectrum of compound Sb8

Figure 32: $^{13}$C NMR spectrum of compound Sb8
Compound Sb9: 2-(1’-phenylethylideneamino) benzoic acid

Light yellow solid; C_{15}H_{13}NO_{2}; Yield: 59% (conventional method) / 73% (MW irradiation method); m.p. 127 ºC; Solubility: C_{2}H_{5}OH, CH_{3}OH, CDCl_{3}, DMSO; IR (KBr, cm\(^{-1}\)): 3471, 1711, 1613, 1527, 1247, 1124; \(^1\)H NMR (500 MHz, CDCl_{3}, (\delta) ppm): 9.94 (1H, s, carboxylic OH), 8.73 (3H, s, CH_{3}-C=N); 7.32-7.92 (9H, m, Ar-H), 1.29 (3H, d, methyl); \(^1\)C NMR (125 MHz, CDCl_{3}, (\delta) ppm): 48.3 (C7'), 116.8 (C1), 124.2 (C3), 127.3 (C5), 128.0 (C3’, C5’), 129.8 (C2’, C6’), 132.1 (C4’), 132.6 (C6), 134.0 (C1’), 135.1 (C4), 154.1 (C2), 165.2 (C7’), 168.4 (C7); Anal. Calc. for C_{15}H_{13}NO_{2} (%) calculated: 75.28, 5.47, 5.85, 13.37, found: 75.30, 5.51, 5.83, 13.45; MW: 239.09

Figure 33: FT-IR spectrum of compound Sb9
Results and Discussion

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Figure 34: $^{1}$$\text{H}$ NMR spectrum of compound Sb9

Figure 35: $^{13}$$\text{C}$ NMR spectrum of compound Sb9
Compound Sb10: 2-[4’-(6’,10’,10’-trimethylcyclohex-6’-enyl)-but-3’en-2’-enylidene amino] benzoic acid

Dark orange viscous liquid; C_{20}H_{25}NO_2; Yield: 46% (conventional method) / 64% (MW irradiation method); Fraction condition: 152-154°C (0.0053MPa); Solubility: C_2H_5OH, CH_3OH, CDCl_3, DMSO; IR (KBr, cm^{-1}): 3408, 1747, 1617, 1498, 1251, 1177; ^1H NMR (500 MHz, CDCl_3, (δ) ppm): 9.97 (1H, s, carboxylic OH), 8.37 (3H, s, CH_3-C=N); 7.37-7.81 (4H, m, Ar-H); 5.93 (1H, d, 4’ H); 5.11 (1H, s, C7’ H); 2.99 (3H, s, C1’ methyl); 1.66 (3H, s, C13’ methyl); 1.28 (3H, s, C11’ methyl); 1.27 (3H, s, 12’ methyl); ^13C NMR (125 MHz, CDCl_3, (δ) ppm): 16.8 (C1’), 19.6 (C13’), 20.4 (C8’), 25.6 (C11’, C12’), 34.3 (C10’), 37.2 (C9’), 54.9 (C5’), 114.0 (C3’), 116.4 (C1), 123.2 (C3), 124.4 (C7’), 127.3 (C5), 131.7 (C6), 133.8 (C6’), 135.4 (C4), 142.3 (C4’), 150.6 (C2), 164.6 (C2’), 169.4 (C7); Anal. Calc. for C_{20}H_{25}NO_2 (%) calculated: 77.12, 8.09, 4.50, 10.28, found: 77.15, 8.06, 4.58, 10.25; MW: 311.18

Figure 36: FT-IR spectrum of compound Sb10
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition

Figure 37: $^1H$ NMR spectrum of compound Sb10

Figure 38: $^{13}C$ NMR spectrum of compound Sb10
Compound Sb11: Methyl 2-(4’-methoxybenzylideneamino) benzoate

Shine yellow viscous liquid; C₁₆H₁₅NO₃; Yield: 58% (conventional method) / 69% (MW irradiation method); Fraction condition: 153-155°C/0.0079MPa; Solubility: C₂H₅OH, CH₃OH, CDCl₃, DMSO; IR (KBr, cm⁻¹): 1727, 1621, 1492, 1236, 1140; ¹H NMR (500 MHz, CDCl₃, (δ) ppm): 8.45 (1H, s, HC=N), 6.66-7.91 (8H, m, Ar-H), 3.91 (3H, s, OCOCH₃), 3.89 (3H, s, OCH₃); ¹³C NMR (125 MHz, CDCl₃, (δ) ppm): 50.8 (C₈), 54.8 (C₈’), 113.8 (C₃’, C₅’), 116.2 (C₁), 119.9 (C₃), 124.1 (C₁’), 127.3 (C₅), 130.7 (C₂’, C₆’), 131.3 (C₆), 134.2 (C₄), 153.0 (C₂), 161.9 (C₇’), 164.0 (C₄’), 167.9 (C₇); Anal. Calc. for C₁₆H₁₅NO₃: (%) calculated: 71.34, 5.61, 5.20, 17.83, found: 71.39, 5.67, 5.18, 17.76; MW: 269.10

Figure 39: FT-IR spectrum of compound Sb11
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition
Compound Sb12: Methyl 2-(benzylideneamino) benzoate

Intense pale yellow viscous liquid; C\textsubscript{15}H\textsubscript{13}NO\textsubscript{2}; Yield: 67\% (conventional method) / 79\% (MW irradiation method); Fraction condition: 130-132\^{\circ}C/0.0079MPa; Solubility: C\textsubscript{2}H\textsubscript{5}OH, CH\textsubscript{3}OH, CDCl\textsubscript{3}, DMSO; IR (KBr, cm\textsuperscript{-1}): 1714, 1610, 1504, 1253, 1160; \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}, (\delta) ppm): 8.49 (1H, s, HC=N), 6.92-7.89 (9H, m, Ar-H), 3.89 (3H, s, OCOCH\textsubscript{3}); \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}, (\delta) ppm): 50.8 (C8), 116.3 (C1), 126.2 (C3), 128.0 (C5), 129.1 (C3', C5'), 129.6 (C2', C6'), 131.1 (C4'), 131.3 (C6), 133.9 (C1'), 135.9 (C4), 150.4 (C2), 162.8 (C7'), 168.0 (C7); Anal. Calc. for C\textsubscript{15}H\textsubscript{13}NO\textsubscript{2} (\%) calculated: 75.28, 5.47, 5.85, 13.37, found: 75.33, 5.46, 5.84, 13.46; MW: 239.09

Figure 42: FT-IR spectrum of compound Sb12
Results and Discussion

Figure 43: $^1$H NMR spectrum of compound Sb12

Figure 44: $^{13}$C NMR spectrum of compound Sb12
Compound Sb13: Methyl 2-(3'-phenylallylideneamino) benzoate

Intense yellow viscous liquid; C_{17}H_{15}NO_{2}; Yield: 48% (conventional method) / 69% (MW irradiation method); Fraction condition: 153-155°C/0.0079MPa; Solubility: C_{2}H_{5}OH, CH_{3}OH, CDCl_{3}, DMSO; IR (KBr, cm\(^{-1}\)): 1717, 1613, 1488, 1228, 1139; \(^1\)H NMR (500 MHz, CDCl\(_3\), (δ) ppm): 7.84 (1H, s, HC=N), 6.64-7.36 (9H, m, Ar-H), 6.62 (1H, s, vinylic H), 5.79 (1H, s, vinylic H), 3.82 (3H, s, OCOCH\(_3\)); \(^{13}\)C NMR (125 MHz, CDCl\(_3\), (δ) ppm): 51.3 (C8), 116.6 (C1), 119.9 (C2'), 122.7 (C3), 126.2 (C5', C9'), 127.2 (C5), 128.0 (C7'), 128.9 (C6', C8'), 131.0 (C6), 133.9 (C4), 142.5 (C4'), 144.1 (C3'), 149.9 (C2), 161.0 (C1'), 168.4 (C7); Anal. Calc. for C_{17}H_{15}NO_{2} (%) calculated: 76.94, 5.70, 5.28, 12.06, found: 76.93, 5.79, 5.31, 11.98; MW: 265.11

Figure 45: FT-IR spectrum of compound Sb13
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition

Figure 46: $^1$H NMR spectrum of compound Sb13

Figure 47: $^{13}$C NMR spectrum of compound Sb13
Compound Sb14: Methyl 2-(3’, 7’-dimethyloct-2’,6’-dienylideneamino) benzoate

Dark orange viscous liquid; C_{18}H_{23}NO_2; Yield: 56% (conventional method) / 71% (MW irradiation method); Fraction condition: 145-147°C/0.0079MPa; Solubility: C_2H_5OH, CH_3OH, CDCl_3, DMSO; IR (KBr, cm\(^{-1}\)): 1714, 1620, 1483, 1222, 1151; \(^1\)H NMR (500 MHz, CDCl_3, (\(\delta\) ppm)): 7.92 (1H, s, HC=N), 7.14-7.56 (4H, m, Ar-H), 6.45 (1H, s, C\(^1\)'), 5.09 (1H, t, -CH=C(CH_3)_2), 3.73 (3H, s, OCOCH_3), 2.15 (3H, s, C\(^{10}\)' methyl), 1.68 (6H, d, C\(^{8}\)', C\(^{9}\)' methyl), 0.89 (3H, s, C\(^{3}\)' methyl); \(^1^3\)C NMR (125 MHz, CDCl_3, (\(\delta\) ppm): 17.3 (C\(^{10}\)'), 20.3 (C\(^9\)'), 25.3 (C\(^8\)'), 26.1 (C\(^5\)'), 40.2 (C\(^4\)'), 51.0 (C\(^8\)), 115.6 (C\(^2\)'), 116.4 (C\(^1\)), 122.8 (C\(^3\)), 123.2 (C\(^6\)), 127.2 (C\(^5\)), 131.8 (C\(^6\)), 132.2 (C\(^7\)), 134.4 (C\(^4\)), 149.6 (C\(^2\)), 150.5 (C\(^3\)'), 163.6 (C\(^1\)'), 168.2 (C\(^7\)); Anal. Calc. for C_{18}H_{23}NO_2 (%) calculated: 75.74, 8.12, 4.91, 11.21, found: 75.77, 8.19, 4.93, 11.12; MW: 285.17

*Figure 48: FT-IR spectrum of compound Sb14*
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition

Figure 49: $^1$H NMR spectrum of compound Sb14

Figure 50: $^{13}$C NMR spectrum of compound Sb14
Compound Sb15: Methyl 2-(3',7'-dimethyloct-6'-enylideneamino) benzoate

Greenish yellow viscous liquid; C_{18}H_{25}NO_{2}; Yield: 61% (conventional method) / 74% (MW irradiation method); Fraction condition: 140-142°C/0.0079MPa; Solubility: C_{2}H_{5}OH, CH_{3}OH, CDCl_{3}, DMSO; IR (KBr, cm^{-1}): 1745, 1650, 1483, 1233, 1149; ^1H NMR (500 MHz, CDCl_{3}, (δ) ppm): 7.91 (1H, s, HC=N), 7.14-7.55 (4H, m, Ar-H), 5.09 (1H, s, -CH=C(CH_{3})_{2}), 3.73 (3H, s, OCOCH_{3}), 1.68 (6H, d, C7' methyl), 0.89 (3H, s, C3' methyl); ^13C NMR (125 MHz, CDCl_{3}, (δ) ppm): 17.6 (C9'), 19.7 (C10'), 25.6 (C5'), 27.6 (C8'), 29.3 (C3'), 34.3 (C2'), 37.1 (C4'), 51.3 (C8), 116.0 (C1), 122.8 (C3), 124.3 (C6'), 124.4 (C5), 131.7 (C6), 131.8 (C7'), 133.9 (C4), 149.5 (C2), 155.0 (C1'), 168.7 (C7); Anal. Calc. for C_{18}H_{25}NO_{2} (%) calculated: 75.21, 8.77, 4.87, 11.13, found: 75.28, 8.68, 4.91, 11.14; MW: 287.18

Figure 51: FT-IR spectrum of compound Sb15
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition

Figure 52: $^1$H NMR spectrum of compound Sb15

Figure 53: $^{13}$C NMR spectrum of compound Sb15
Compound Sb16: Methyl 2-(4'-isopropylbenzylideneamino) benzoate

Yellow viscous liquid; $\text{C}_{18}\text{H}_{19}\text{NO}_2$; Yield: 58% (conventional method) / 72% (MW irradiation method); Fraction condition: 148-150°C/0.0079MPa; Solubility: $\text{C}_2\text{H}_5\text{OH}$, $\text{CH}_3\text{OH}$, CDCl$_3$, DMSO; IR (KBr, cm$^{-1}$): 1762, 1651, 1501, 1261, 1180; $^1$H NMR (500 MHz, CDCl$_3$, (δ) ppm): 8.32 (1H, s, HC=N), 6.92-7.84 (8H, m, Ar-H), 3.83 (3H, s, OCOCH$_3$), 3.19 (6H, d, -C(CH$_3$)$_2$), 1.27 (3H, s, methyl), $^{13}$C NMR (125 MHz, CDCl$_3$, (δ) ppm): 22.9 (C9'), 39.9 (C8'), 50.7 (C8), 116.3 (C1), 122.2 (C3), 126.5 (C3', C5'), 127.5 (C5), 128.8 (C2', C6'), 130.7 (C1'), 130.9 (C6), 133.5 (C4), 148.6 (C4'), 150.4 (C2), 155.5 (C7'), 168.0 (C7); Anal. Calc. for $\text{C}_{18}\text{H}_{19}\text{NO}_2$ (%) calculated: 76.83, 6.81, 4.98, 11.37, found: 76.86, 6.88, 4.93, 11.33; MW: 281.14

Figure 54: FT-IR spectrum of compound Sb16
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition

Figure 55: $^1$H NMR spectrum of compound Sb16

Figure 56: $^{13}$C NMR spectrum of compound Sb16
Compound Sb17: Methyl 2-(4’-hydroxy-3’-methoxybenzylideneamino) benzoate

Intense yellow viscous liquid; C_{16}H_{15}NO_4; Yield: 59% (conventional method) / 69% (MW irradiation method); Fraction condition: 153-155°C/0.0053MPa; Solubility: C_2H_5OH, CH_3OH, CDCl_3, DMSO; IR (KBr, cm\(^{-1}\)): 3310, 1702, 1642, 1479, 1221, 1150; \(^1\)H NMR (500 MHz, CDCl_3, (δ) ppm): 8.29 (1H, s, HC=N), 6.89-6.64 (7H, m, Ar-H), 6.59-6.46 (1H, Ar-OH), 3.89 (3H, s, OCOCH_3), 3.83 (3H, s, OCH_3); \(^{13}\)C NMR (125 MHz, CDCl_3, (δ) ppm): 50.6 (C8), 55.2 (C8’), 115.1 (C2’), 116.3 (C1), 117.7 (C5’), 122.1 (C3), 122.3 (C6’), 127.2 (C5), 127.4 (C1’), 132.1 (C6), 134.1 (C4), 148.9 (C4’), 150.3 (C3’), 153.8 (C2), 158.3 (C7’), 167.8 (C7); Anal. Calc. for C_{16}H_{15}NO_4: (%) calculated: 67.34, 5.30, 4.91, 22.43, found: 67.37, 5.34, 4.89, 22.41; MW: 285.10

Figure 57: FT-IR spectrum of compound Sb17
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition

Figure 58: $^1$H NMR spectrum of compound Sb17

Figure 59: $^{13}$C NMR spectrum of compound Sb17
Compound Sb18: Methyl 2-(3', 4'-dimethoxybenzylideneamino) benzoate

Pale purple viscous liquid; C_{17}H_{17}NO_{4}; Yield: 61% (conventional method) / 68% (MW irradiation method); Fraction condition: 153-155°C/0.0053MPa; Solubility: C_{2}H_{5}OH, CH_{3}OH, CDCl_{3}, DMSO; IR (KBr, cm^{-1}): 1743, 1661, 1482, 1236, 1148; ^1H NMR (500 MHz, CDCl_{3}, (δ) ppm): 8.28 (1H, s, HC=N); 6.58-7.82 (7H, m, Ar-H); 3.89 (3H, s, OCOCH_{3}); 3.87 (3H, s, OCH_{3}); 3.83 (3H, s, OCH_{3}); ^13C NMR (125 MHz, CDCl_{3}, (δ) ppm): 50.7 (C8), 55.2 (C8'), 114.4 (C2'), 115.4 (C5'), 116.3 (C1), 122.1 (C3), 122.2 (C6'), 127.2 (C1'), 127.3 (C5), 132.0 (C6), 134.2 (C4), 148.9 (C3'), 150.3 (C4'), 153.9 (C2), 160.8 (C7'), 167.9 (C7); Anal. Calc. for C_{17}H_{17}NO_{4} (%) calculated: 68.20, 5.72, 4.68, 21.39, found: 68.26, 5.75, 4.71, 21.28; MW: 299.11

Figure 60: FT-IR spectrum of compound Sb18
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition

Figure 61: $^1$H NMR spectrum of compound Sb18

Figure 62: $^{13}$C NMR spectrum of compound Sb18
Compound Sb19: Methyl 2-(1'-phenylethylideneamino) benzoate

Intense yellow viscous liquid; C_{16}H_{15}NO_{2}; Yield: 51% (conventional method) / 61% (MW irradiation method); Fraction condition: 138-140°C/0.0079MPa; Solubility: C_{2}H_{5}OH, CH_{3}OH, CDCl_{3}, DMSO; IR (KBr, cm\(^{-1}\)): 1744, 1652, 1473, 1257, 1157; \(^{1}\)H NMR (500 MHz, CDCl_{3}, (\delta) ppm): 8.33 ((3H, s, CH_{3}-C=N), 6.93-7.84 (9H, m, Ar-H), 3.83 (3H, s, OCOCH_{3}), 0.95 (3H, d, methyl); \(^{13}\)C NMR (125 MHz, CDCl_{3}, (\delta) ppm): 16.0 (C8'), 51.5 (C8), 116.6 (C1), 122.2 (C3), 127.7 (C5), 128.9 (C3', C5'), 129.2 (C2', C6'), 131.1 (C4'), 131.3 (C6), 134.0 (C1'), 134.6 (C4), 153.3 (C2), 164.5 (C7'), 166.7 (C7); Anal. Calc. for C_{16}H_{15}NO_{2} (%) calculated: 75.85, 5.97, 5.53, 12.63 found: 75.89, 5.99, 5.56 12.56; MW: 253.11

Figure 63: FT-IR spectrum of compound Sb19
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition

Figure 64: $^1$H NMR spectrum of compound Sb19

Figure 65: $^{13}$C NMR spectrum of compound Sb19
Compound Sb20: Methyl 2-[4-(6',10',10'-trimethylcyclohex-6'-enyl)-but-3’-en-2'-enylideneamino) benzoate

Reddish orange viscous liquid; C_{42}H_{56}N_{2}O_{5}; Yield: 42% (conventional method) / 53% (MW irradiation method); Fraction condition: 148-150°C/0.0053MPa; Solubility: C_{2}H_{5}OH, CH_{3}OH, CDCl_{3}, DMSO; IR (KBr, cm^{-1}): 1717, 1662, 1487, 1238, 1144; \textsuperscript{1}H NMR (500 MHz, CDCl_{3}, (δ) ppm): 8.39 ((3H, s, CH_{3}-C=N), 6.93-7.85 (4H, m, Ar-H), 5.58 (1H, d, 2' vinylic H), 4.95 (1H, d, 3’ vinylic H), 3.83 (3H, s, OCOCH_{3}), 2.59 (3H, d, C1' methyl), 1.71 (3H, d, C13' CH_{3}), 1.18 (1H, s, C11' methyl), 1.16 (3H, s, C12' methyl); \textsuperscript{13}C NMR (125 MHz, CDCl_{3}, (δ) ppm): 16.8 (C1’), 19.8 (C13’), 20.4 (C8’), 25.6 (C11’, C12’), 32.1 (C10’), 38.7 (C9’), 51.5 (C8), 54.8 (C5’), 114.1 (C3’), 116.3 (C1), 122.4 (C3), 123.2 (C7’), 127.2 (C5), 131.3 (C6), 133.8 (C6’), 135.4 (C4), 142.5 (C4’), 149.5 (C2), 162.3 (C2'), 166.4 (C7); Anal. Calc. for C_{42}H_{56}N_{2}O_{5} (%) calculated: 75.40, 8.44, 4.18, 11.96, found: 75.48, 8.48, 4.23, 11.81; MW: 668.41

Figure 66: FT-IR spectrum of compound Sb20
Results and Discussion

Synthesis and characterization of some new odorant Schiff bases for fragrance composition
4.3. Olfactory evaluation of Schiff bases

Odorant chemicals that are inexpensive, highly substantive, long lasting and non-toxic which can provide lemony, floral, green, ozoney, fruity, citrus, piney, grape like, melony, sweet and muguet aromas with anisic, fresh cut wood, ozoney, fresh air, floral and orange floral top notes, and anisic, woody, floral, green and citrus undertones are highly desirable in the art of perfumery. Many of the natural materials which contribute desired nuances to perfumery compositions as well as perfumed articles including personal care products, household and industrial cleaning compositions, disinfectants, pharmaceutical and medicinal compositions are high in cost, vary in quality from one batch to another and/or are generally subject to the usual variations of natural products. Thus there is a continuing effort to find synthetic materials which will replace, enhance or augment the essential fragrance notes provided by the natural essential oils or compositions thereof.

Odor related properties can be set into three types: odor quality, odor intensity and odor fondness, the latter being strictly a personal attribute. There exists a significant relationship of odor of the aroma compounds with their chemical structures. Structure odor relationships (SOR) are key issues for (i) the synthesis of new odorant molecules (Korichi, et al., 2006; Boelens, 1974) (ii) understanding their application to a variety of compositions (in soap composition, conditioning shampoos, a fabric washing deodorants, solid or liquid detergents composition, handkerchief perfumes, pharmaceutical formulations); and (iii) mechanisms of human olfaction (Turin and Yoshii). SOR of aroma and odor compounds have been described in the literature (Chastrette, et al., 1995; Cherqaoui, et al., 1998; Gorbachov and Rossiter, 1999; Korichi, et al., 2006; Rossiter, 1996). Schiff bases are well known in flavoring and perfumery due to their odor characteristics (Arctander, 1969). Olfactory characteristics of several Schiff bases have been examined which demonstrated them to exhibit floral, fruity odors, namely of the citrus type and, more particularly, reminiscent of the odor of the orange-flower (Baudin, 1993; Bauer, et al., 1997; Blanc and Aschiers, 1992; Buchbauer, et al., 1999). Schiff bases are also known to be useful as intermediates in producing other fragrance materials (Patai, 1970; Clercq and Verpoort, 2002.; Mookherjee, et al., 1988). SOR of the Schiff bases have not been studied much. Some studies regarding SOR of simple cyclic and acyclic oxime ethers have been reported (Strub, et al., 2016). Synthesized Schiff bases were examined for their olfactory properties in terms of their odor profile and odor strength and the results are shown in Table 6.
Table 6: Olfactory properties of synthesized Schiff bases

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Schiff base</th>
<th>Odor profile</th>
<th>Odor strength</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Schiffs of anthranilic acid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A.</td>
<td>Aldehyde and Anthranilic acid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>Sb1</td>
<td>Sweet, floral with fruity undertones</td>
<td>medium</td>
</tr>
<tr>
<td>2.</td>
<td>Sb2</td>
<td>Bitter almond</td>
<td>medium</td>
</tr>
<tr>
<td>3.</td>
<td>Sb3</td>
<td>Sweet, floral, honeysuckle</td>
<td>medium</td>
</tr>
<tr>
<td>4.</td>
<td>Sb4</td>
<td>Sweet floral, orange blossom to fresh orange peel</td>
<td>intense</td>
</tr>
<tr>
<td>5.</td>
<td>Sb5</td>
<td>Very tenacious, sweet floral, fruity</td>
<td>intense</td>
</tr>
<tr>
<td>6.</td>
<td>Sb6</td>
<td>Herbaceous sweet very tenacious</td>
<td>medium</td>
</tr>
<tr>
<td>7.</td>
<td>Sb7</td>
<td>Intense sweet vanilla</td>
<td>intense</td>
</tr>
<tr>
<td>8.</td>
<td>Sb8</td>
<td>Sweet-floral</td>
<td>low</td>
</tr>
<tr>
<td></td>
<td>B. Ketone and Anthranilic acid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>Sb9</td>
<td>Heavy, sweet-floral</td>
<td>medium</td>
</tr>
<tr>
<td>10.</td>
<td>Sb10</td>
<td>Heavy and very sweet-floral</td>
<td>intense</td>
</tr>
</tbody>
</table>
### Results and Discussion

Schiff bases of methyl anthranilate

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td><strong>C. Aldehyde and Methylantranilate</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11.</td>
<td>Sb11</td>
<td>Strong sweet floral with fruity undertone</td>
<td>Medium</td>
</tr>
<tr>
<td>12.</td>
<td>Sb12</td>
<td>Bitter almond with mild floral fruity tone</td>
<td>Medium</td>
</tr>
<tr>
<td>13.</td>
<td>Sb13</td>
<td>Spicy, sweet, cinnamon like</td>
<td>Medium</td>
</tr>
<tr>
<td>14.</td>
<td>Sb14</td>
<td>Fresh, sweet, orange blossom, citrusy</td>
<td>Intense</td>
</tr>
<tr>
<td>15.</td>
<td>Sb15</td>
<td>Sweet, floral, reminiscent of orange blossom and peel</td>
<td>Intense</td>
</tr>
<tr>
<td>16.</td>
<td>Sb16</td>
<td>Herbaceous sweet tenacious, orange blossom like</td>
<td>Medium</td>
</tr>
<tr>
<td>17.</td>
<td>Sb17</td>
<td>Strong sweet vanilla odor reminiscent of orange blossom</td>
<td>Intense</td>
</tr>
<tr>
<td>18.</td>
<td>Sb18</td>
<td>Woody vanilla with floral undertone</td>
<td>Low</td>
</tr>
<tr>
<td><strong>D. Ketone and Methylantranilate</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19.</td>
<td>Sb19</td>
<td>Heavy sweet floral, somewhat animalic</td>
<td>Medium</td>
</tr>
<tr>
<td>20.</td>
<td>Sb20</td>
<td>Sweet, woody, reminiscent of orange blossom</td>
<td>Intense</td>
</tr>
</tbody>
</table>
A smaller odor diversity was observed between the Schiff bases of the aldehydes and ketones. The Schiff bases (Sb1-Sb10) possessed interesting odor profile, maintaining fragrance characteristics of respective carbonyl compounds, described as sweet floral differed in the notes and the strength, except Sb2 and Sb6 which had bitter almond and herbaceous sweet very tenacious profile, respectively. Schiff bases Sb8 and Sb9 derived from the ketones exhibited similar odor profile differed, however, in the strength. Though Sb1 of benzaldehyde and Sb7 of veratraldehyde had similar odor profile but differed in the notes (Sb1 with fruity undertone and Sb 7 with intense sweet vanilla) and the strength (Sb1 of medium and Sb7 of low strength) which could be linked to the presence of another methoxy group in Sb7.

The Schiff bases (Sb11-Sb20) also possessed interesting odor profile having contributions of the characteristic aroma of methyanthranilate and respective carbonyl compounds which differed in the notes and the strength. Sb11, Sb14, Sb15 and Sb16 had similar odor profile of varied odor strength (Sb11 and Sb16 being of medium and Sb14, Sb15 being of intense odor strength). Odor of Sb17 and Sb18 had common vanilla character but differed in the strength which could be attributed to presence of an additional methoxyl group of veratraldehyde in Sb18.

Though citral and citronellal had similarity in their chemical structures, the perceived difference in the odor of their respective Schiff bases (Sb4, Sb5, Sb14 and Sb15) was observed which could be explained due to the presence of a double bond and a methyl group in close proximity of the azomethine linkage in citral moiety than in the citronellal moiety. The differed odor profile of citral and citronellal attributed to this subtle difference in their chemical structures has been reported (Osada, et al., 2013).

The synthesized Schiff bases possessed improved olfactory properties than their respective reactants which can primarily be linked to the conversion of carbonyl group in to azomethine linkage. The chemical instability of anisaldehyde, benzaldehyde, cinnamaldehyde, citral, citronellal, cuminaldehyde, vanillin, veratraldehyde largely due to the presence of an aldehyde group was also removed after transformation into their Schiff bases which would result into their improved useful life times. Odor notes of the
synthesized Schiff bases were natural and relative to those of these Schiff bases, except Sb18, reported earlier. Odor profile of Sb1 to Sb10 and Sb18 is reported for the first time. The olfactory properties of these Schiff bases indicated their possible use in varied fragrance compositions. Low molecular weight of these compounds showed their suitability to be perceived by the olfactory receptors (Turin and Yoshii). Odor profile of these Schiff bases prepared by MW irradiation and conventional method were also compared, and MW irradiation was not found to influence their olfactory attributes.

4.4. Antimicrobial activity

Antimicrobial activity of Schiff bases has widely been reported (Amer, et al., 2013; Mitu, et al., 2012; Chhajed and Padwal, 2010). In search of new and effective antimicrobial agents of natural origin, natural product derived Schiff bases have shown promise (Silva, et al., 2011). Madurahydroxy lactones, occurring in Actinomadura rubra, derived Schiff bases have effectively inhibited Bacillus subtilis, Micrococcus flavus, Sarcina lutea and Staphylococcus aureus with MIC values ranged from 0.2 to 3.1µg/mL (Heinisch, et al., 1999). Chitosan, isatin and nystatin-dextran-derived Schiff bases reported to exhibit antifungal activity against Botrytis cinerea, Colletotrichum lagenarium and Microsporum audouinii (Guo, et al., 2007), respectively.

Antimicrobial activity of the synthesized Schiff bases was, therefore, examined against two bacteria - Staphylococcus aureus (gram +ve) and Escherichia coli (gram –ve), and two fungi- Aspergillus niger and Penicillium chrysogenum using disc diffusion method. All the Schiff bases (Sb1-Sb20) showed moderate to good activity against the pathogenic microorganisms. The solvent used for the preparation of test solutions (DMSO) did not show inhibition against the tested microorganisms (negative control). Compared to the positive control, compounds showing the zones of inhibition between 9-16 mm and > 17 mm were considered to be moderate and highly active (Gupta, et al., 2013; Kaushik, et al., 2016(a); 2016(b)). Percent of activity index of the tested compounds against the microorganisms was also determined and are shown in Table 7.
Table 7: Zone of inhibition, MIC (%) and activity index (%) of odorant Schiff bases

<table>
<thead>
<tr>
<th>Schiff base</th>
<th>Zone of inhibition (MIC) (bacteria)</th>
<th>Zone of inhibition (MIC) (fungi)</th>
<th>* % Activity index (bacteria)</th>
<th>% Activity index (fungi)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>E. coli</strong></td>
<td><strong>S. aureus</strong></td>
<td><strong>A. niger</strong></td>
<td><strong>P. chrysogenum</strong></td>
</tr>
<tr>
<td>Sb1</td>
<td>14.0 (40)</td>
<td>15.0 (40)</td>
<td>12.0 (40)</td>
<td>12.0 (40)</td>
</tr>
<tr>
<td>Sb2</td>
<td>11.0 (40)</td>
<td>11.0 (40)</td>
<td>9.5 (40)</td>
<td>10.0 (40)</td>
</tr>
<tr>
<td>Sb3</td>
<td>20.0 (40)</td>
<td>19.0 (40)</td>
<td>17.0 (30)</td>
<td>17.0 (30)</td>
</tr>
<tr>
<td>Sb4</td>
<td>19.0 (40)</td>
<td>18.5 (40)</td>
<td>18.5 (40)</td>
<td>18.0 (40)</td>
</tr>
<tr>
<td>Sb5</td>
<td>19.0 (20)</td>
<td>20.0 (20)</td>
<td>19.0 (20)</td>
<td>20.0 (20)</td>
</tr>
<tr>
<td>Sb6</td>
<td>15.0 (20)</td>
<td>16.0 (20)</td>
<td>18.5 (30)</td>
<td>18.0 (30)</td>
</tr>
<tr>
<td>Sb7</td>
<td>19.0 (30)</td>
<td>19.5 (30)</td>
<td>16.5 (20)</td>
<td>16.0 (20)</td>
</tr>
<tr>
<td>Sb8</td>
<td>19.5 (30)</td>
<td>20.0 (30)</td>
<td>16.0 (20)</td>
<td>16.5 (20)</td>
</tr>
<tr>
<td>Sb9</td>
<td>20.5 (30)</td>
<td>20.0 (30)</td>
<td>18.0 (40)</td>
<td>18.5 (40)</td>
</tr>
<tr>
<td>Sb10</td>
<td>19.0 (20)</td>
<td>19.0 (20)</td>
<td>19.0 (30)</td>
<td>20.0 (30)</td>
</tr>
</tbody>
</table>
Ciprofloxacin
Griseofulvin
DMSO

1 - 8 mm = less active; 9 - 16 mm = moderate active; >17 mm = highly active

* % Activity index - 3.7.3.
All the synthesized Schiff bases showed varied antimicrobial activity against the microbes tested. The MIC values (Table 7) of the highly active compounds ranged between 20-30 μg/ml with 57.40-83.33% activity index while those for moderately active compounds were 40μg/ml with 39.58-77.08% activity index. Compounds Sb5, Sb6, Sb7, Sb8, Sb10, Sb13, Sb16, Sb17 and Sb19 found highly active, while compound Sb1, Sb2, Sb4, Sb11 and Sb12 found moderate active against all four microorganisms tested. Compound Sb3 and Sb18 were highly fungitoxic against the fungi with 70.83-70.83% and 77.08-79.16% activity index at 30μg/ml and moderately active against the bacteria with 70.37-80% and 53.70-56% activity index at 40μg/ml, however compound Sb9, Sb14, Sb15 and Sb20 were moderately active against the fungi with 54.16-77.08%, activity index at 40μg/ml and highly active against bacteria with 66.66-82% activity index at 30μg/ml. Our findings indicated that the synthesized Schiff bases could be developed into effective antimicrobial agents against the bacteria - *Staphylococcus aureus* (gram +ve) and *Escherichia coli* (gram –ve), and fungi - *Aspergillus niger* and *Penicillium chrysogenum*. 
4.5. References

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CONCLUSION

Microwave irradiation technique proved to be advantageous for preparation of twenty odorant Schiff bases namely 2-((4’-methoxybenzylideneamino) benzoic acid (Sb1), 2-(benzylideneamino) benzoic acid (Sb2), 2-(3’-phenylallylideneamino) benzoic acid (Sb3), 2-(3’,7’-dimethyloct-2’,6’-dienylideneamino) benzoic acid (Sb4), 2-(3’,7’-dimethyloct-6’-enylideneamino) benzoic acid (Sb5), 2-(4’-isopropylbenzylideneamino) benzoic acid (Sb6), 2-(4’-hydroxy-3’-methoxybenzylideneamino) benzoic acid (Sb7), 2-(3’,4’-dimethoxybenzylideneamino) benzoic acid (Sb8), 2-(1’-phenylethylideneamino) benzoic acid (Sb9), 2-[4’-(6’,10’,10’-trimethylcyclohex-6’-enyl)-but-3’-en-2’-enylideneamino] benzoic acid (Sb10), methyl 2-(4’-methoxybenzylideneamino) benzoate (Sb11), methyl 2-(benzylideneamino) benzoate (Sb12), methyl 2-(3’-phenylallylideneamino) benzoate (Sb13), methyl 2-(3’,7’-dimethyloct-2’,6’-dienylideneamino) benzoate (Sb14), methyl 2-(3’,7’-dimethyloct-6’-enylideneamino) benzoate (Sb15), methyl 2-(4’-isopropylbenzylideneamino) benzoate (Sb16), methyl 2-(4’-hydroxy-3’-methoxybenzylideneamino) benzoate (Sb17), methyl 2-(3’,4’-dimethoxybenzylideneamino) benzoate (Sb18), methyl 2-(1’-phenylethylideneamino) benzoate (Sb19) and methyl 2-[4’-(6’,10’,10’-trimethylcyclohex-6’-enyl)-but-3’-en-2’-enylideneamino] benzoate (Sb20) in terms of no solvent consumption, reduced reaction time 4 to 14 minutes, and increased yield (53% to 89%) over conventional method requiring 4 to 13 hours and affording 42% to 71% yield. Altogether there was an improvement of 7% to 21% in the yield of these Schiff bases. Structures of the synthesized Schiff bases were confirmed by their elemental analysis, and spectroscopic (FT-IR, $^1$H NMR and $^{13}$C NMR) data. MW assisted synthesis of the above Schiff bases is reported for the first time.

These Schiff bases possessed interesting odor profile, having contributions from respective reactants, which differed in the notes and strength. Odor notes of the Schiff bases were natural. Low molecular weight of these compounds showed their suitability to be perceived by the olfactory receptors. Olfactory attributes of the Schiff bases were not influenced by the microwave irradiation and indicative of their use in various fragrance compositions. Olfactory characteristics of the Schiff bases Sb1-Sb10 and
Sb18 have not been reported previously. Synthesized Schiff bases also exhibited, moderate to good antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli*, *Aspergillus niger* and *Penicillium chrysogenum* for the first time. Schiff bases Sb3, Sb4, Sb5, Sb9, Sb10, Sb13 and Sb19 were found more effective among the tested compounds against all the pathogenic microorganisms.

A greener approach for facile synthesis of Schiff bases, which not only are useful as important ingredients of various fragrance compositions but also hold promise to be used by pharmaceutical industry for antimicrobial applications, is demonstrated.
Title: Synthesis and characterization of some new odorant Schiff bases for fragrance composition

The thesis has been organized into four chapters as summarized below:

Chapter I: Introduction

This chapter gives an overview of Schiff bases, their chemistry and applications; microwave irradiation technique, its principles, advantages and disadvantages, and applications in organic synthesis. An account of the fragrance, structure of the fragrance and flavor (F&F) industry, domestic and international market scenario of F&F industry is also mentioned. Scope of the present investigation in light of the current knowledge on the subject is also defined here.

Chapter II: Review of literature

This chapter presents an account of the detailed literature survey on synthesis, olfactory attributes and applications of Schiff bases including odorant ones, followed by microwave assisted synthesis of Schiff bases. Literature review was done by regular screening of various published literature (research and review papers, patents, books, reports and industrial compendiums). Need of the present work based on the inferences drawn from review of literature was brought out and objectives were made. Present study was aimed at production of new odorant Schiff bases for their utilization in fragrance composition. The objective of the study was the synthesis and characterization of some new odorant Schiff bases from naturally occurring or natural identical reactant compounds for their use in fragrance composition. It was also envisaged to study the odor properties of the synthesized Schiff bases.

Chapter III: Materials and Methods

This chapter embodies experimental part including (i) chemicals and reagents including reactants, (ii) methods and techniques used for characterization of Schiff bases, (iii)
Synthesis and characterization of some new odorant Schiff bases for fragrance composition

methods employed for determining olfactory properties and antimicrobial activities of the synthesized Schiff bases, (iv) General protocol for synthesis of odorant Schiff bases-conventional and microwave assisted, and (v) physico-chemical and spectroscopic data of each of the synthesized Schiff bases.

All chemicals obtained from commercial suppliers were of highest purity grade and used without further purification. These include acetophenone (Himedia), anisaldehyde (Loba chemie), anthranilic acid (Sigma aldrich), benzaldehyde (Merck), cinnamaldehyde (Himedia), citral (Himedia), citronellal (Merck), cuminaldehyde (Sigma aldrich), α-ionone (Sigma Aldrich), methylantranilate (Himedia), vertraldehyde (Himedia), Nutrient Agar Media (Himedia) and Potato Dextrose Agar (Himedia). Melting points were measured on open glass capillary method on Buchi Melting Point (b-540) and are uncorrected. Elemental analysis of carbon, nitrogen and hydrogen were carried out on CHN elemental analyser (Thermo Scientific). Infrared (IR) spectra were recorded at room temperature from 4000 cm\(^{-1}\) to 500 cm\(^{-1}\) with KBr pellets at a resolution of 4cm\(^{-1}\), using Thermo-Nicolet 8700, Research spectrometer (Thermo Scientific). \(^1\)H NMR (500 MHz) and \(^{13}\)C NMR (125 MHz) spectra were recorded on Bruker Avance-II instrument using CDCl\(_3\) as solvent and tetramethylsilane (TMS) as an internal slandered. Chemical shifts (δ) are reported in ppm. The microwave assisted synthesis was performed in scientific microwave oven, (SRL-Milestone Start S Labstation for synthesis, (Operating between 140-1600W). All the reactions were carried out at power 300-500W.

In conventional method employed for preparation of Schiff bases, equi molar mixture of carbonyl compound and anthranilic acid / methyl anthranilate, separately, in ethanol was refluxed under inert atmosphere on a water bath for 4-13h; concentrated under vacuum and, wherever applicable, purified by vacuum distillation or kept refrigerated overnight, filtered under reduced pressure, washed with ethanol and dried. Solvent free MW irradiation method involved mixing of the equi-molar mixture of carbonyl compound and anthranilic acid / methyl anthranilate, separately in a reaction flask and its irradiation with MW at 300-500W for 4-14min. After completion of the reaction, the mixture was, wherever applicable, purified by vacuum distillation or kept refrigerated
overnight, filtered under reduced pressure, washed with ethanol and dried (Scheme 1 and Scheme 2). These Schiff bases were characterized by analysis of the elements (C, H and N), FT-IR, $^1$H NMR and $^{13}$C NMR spectral data.

**Scheme 1:** General reaction of anthranilic acid derived Schiff bases

**Scheme 2:** General reaction of methylanthranilate derived Schiff bases

Olfactory properties of the synthesized Schiff bases were studied employing standard olfactory method (IS: 2284-1988, 1988). Sample solutions (10 wt. % in ethyl alcohol) were used to evaluate their odor properties. The test was done in an odorless environment with temperature control at 27°C. Smelling strips of 15 cm long, 1 cm wide and length of dip was about 0.5 to 1 cm.
Antimicrobial activity of the Schiff bases was evaluated according to the guidelines of the National Committee for Clinical Laboratory Standards (NCCLS, 1997) using the disc diffusion method. The bacterial cultures for *Staphylococcus aureus* (ATCC 259235) and *Escherichia coli* (ATCC 27853) were obtained from Microbial Type Culture Collection (MTCC), Chandigarh and fungal cultures of *Aspergillus niger* (NTCC 17) and *Penicillium chrysogenum* (NTCC 52) were obtained from National Type Culture Collection (NTCC), Forest Research Institute, Dehradun. MIC values were determined according to the guidelines of NCCLS, and % activity index was ascertained from the MIC value and zone of inhibition. All the experiments were done in triplicate and the values determined, were presented as means of three measurements.

**Chapter IV: Results and Discussion**

Twenty odorant Schiff bases (I&II) namely 2-(4′-methoxybenzylideneamino) benzoic acid (Sb1), 2-(benzylideneamino) benzoic acid (Sb2), 2-(3′-phenylallylideneamino) benzoic acid (Sb3), 2-(3′,7′-dimethyloct-2′,6′-dienylideneamino) benzoic acid (Sb4), 2-(3′,7′-dimethyloct-6′-enylideneamino) benzoic acid (Sb5), 2-(4′-isopropylbenzylidene amino) benzoic acid (Sb6), 2-(4′-hydroxy-3′-methoxybenzylideneamino) benzoic acid (Sb7), 2-(3′,4′-dimethoxybenzylideneamino) benzoic acid (Sb8), 2-(1′-phenylethylidene amino) benzoic acid (Sb9), 2-[4′-(6′,10′,10′-trimethylcyclohex-6′-enyl)-but-3′-en-2′-enylideneamino] benzoic acid (Sb10), methyl 2-(4′-methoxybenzylideneamino) benzoate (Sb11), methyl 2-(benzylideneamino) benzoate (Sb12), methyl 2-(3′-phenyl allylideneamino) benzoate (Sb13), methyl 2-(3′,7′-dimethyloct-2′,6′-dienylideneamino) benzoate (Sb14), methyl 2-(3′,7′-dimethyloct-6′-enylideneamino) benzoate (Sb15), methyl 2-(4′-isopropyl benzylideneamino) benzoate (Sb16), methyl 2-(4′-hydroxy-3′-methoxybenzylidene amino) benzoate (Sb17), methyl 2-(3′,4′-dimethoxybenzylidene amino) benzoate (Sb18), methyl 2-(1′-phenylethylideneamino) benzoate (Sb19) and methyl 2-[4′-(6′,10′,10′-trimethylcyclohex-6′-enyl)-but-3′-en-2′-enylideneamino] benzoate (Sb20) were prepared from naturally occurring eight aldehydes (anisaldehyde, benzaldehyde, cinnamaldehyde, citral, citronellal, cuminaldehyde, vanillin and veratraldehyde) and two ketones (acetophenone and α-ionone) with anthranilic acid and methylanthranilate, separately, by conventional (CM) and microwave (MW) assisted
methods. A large number of experiments were performed to optimize the irradiation power and its duration and the optimized conditions are reported. MW irradiation resulted in no solvent consumption, reduced reaction time from 4 to 14 minutes, and increment in yields from 53% to 89% over conventional method requiring 4 to 13 hours and affording 42% to 71% yield. Altogether there was an improvement of 7% to 21% in the yield of these Schiff bases. Elemental analysis, FT-IR $^1$H NMR and $^{13}$C NMR data of these compounds supported their structures. MW assisted synthesis of the above Schiff bases is reported for the first time.

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A greener approach for facile synthesis of Schiff bases, which not only are useful as important ingredients of various fragrance compositions but also hold promise to be used by pharmaceutical industry for antimicrobial applications, is demonstrated.
Synthesis and characterization of some new odorant Schiff bases for fragrance composition
(II) Molecular structures of the Schiff bases (Sb11-Sb20)

Synthesis and characterization of some new odorant Schiff bases for fragrance composition
PUBLICATIONS


- **Kaushik, P. K.,** Varshney, V. K., Kumar, P., Bhatia, P. and Shukla, S. V., 2016, Microwave assisted synthesis, characterization and antimicrobial activity of some odorant Schiff bases derived from naturally occurring carbonyl compounds and anthranilic acid, Synthetic Communications, 46(24), 2053-2062

PAPERS PRESENTED IN THE CONFERENCE/WORKSHOP/SYMPOSIA


- **Kaushik, P. K.,** Varshney, V. K. and Shukla, S. V., 2014, Microwave-assisted synthesis of Schiff bases: A literature appraisal in National conference on Recent Advances in Biosciences & Drug Discovery (RABDD) held at Gurukula Kangri University, Haridwar on March 03-04th, 2014

- **Kaushik, P. K.,** Varshney, V. K. and Shukla, S. V., 2013, Comparative studies on synthesis of some odorant Schiff bases using conventional and microwave irradiation process, in 8th Uttarakhand State Science and Technology Congress at Doon University, Dehradun on December 26-28th, 2013

- **Kaushik, P. K.**, Varshney, V. K. and Shukla, S. V., 2012, Microwave-assisted synthesis of odorant Schiff bases, presented in 7th Uttarakhand State Science and Technology Congress held at Graphic Era University, Dehra Dun from November 21-23\textsuperscript{rd}, 2012

- **Kaushik, P. K.** and Varshney, V. K., 2011, Utilization of tree derived carbonyl compounds as Schiff bases for fragrance and flavor composition: a literature appraisal, presented in 1\textsuperscript{st} Indian Forestry Congress held at New Delhi from November 22-25\textsuperscript{th}, 2011