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Synthesis and Olfactory Characterization of New Fragrant Materials through Chemical Modification of Methyleugenol Molecular Framework by Introducing Ester Functional Groups

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ABSTRACT: There is a continuing search for materials having desirable fragrance properties. Such materials are sought either to replace costly natural materials or to provide new fragrances or perfume types, which have not heretofore been available. Hence, the objective of this paper is the synthesis and olfactory characterization of new fragrant materials through chemical modification of methyleugenol (ME) molecular framework by introducing Ester functional groups using appropriate standard procedures. ME is a common phenylpropanoid found in many plant species, particularly in spices and medicinal plants. It is used as a flavouring agent in food and as a fragrance in cosmetics. In this research, methyleugenol was modified to obtain esters. The transformations involve the opening of 2-(4-ethyl-3-methoxybenzyl) oxirane (epoxide ring) to yield 3-(3,4-dimethoxyphenyl)propane-1,2-diol (Dihydroxy). 1-(3,4-dimethoxyphenyl)-3-hydroxypropan-2-yl acetate (53.33% yield) derivatives, was synthesized from the Dihydroxy. The results showed that the odour characteristic of 3-(3,4-dimethoxyphenyl)propane-1,2-diol [floral, pungent, Caramel and sweet] compounds, is clearly different from the odours of the 1-(3,4-dimethoxyphenyl)-3-hydroxypropan-2-yl acetate [fresh, pungent, lime-like, sweet]. Our findings show that double bond substitution and functional alterations to methyl eugenol modify the perceived odour of methyl eugenol derivatives. Thus, overall structural alteration increased odour potency.

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The demand for new fragrance and flavour compounds is driven by today's consumers, who are always on the lookout for something different. Fragrance chemistry is constantly searching for new molecules to meet these demands for materials that have desirable fragrances. Fragrance materials are used in a wide variety of consumer products ranging from perfumes to skin care products such as creams, lotions, detergents and various other personal and household products. These materials are either to

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fortify weak natural materials, to improve the weaknesses of natural materials, or to provide new fragrance or perfume types which have not existed. The supply of natural fragrance compounds and the numbers of these natural fragrance are limited. For many years, scientists have been very successful in synthesising fragrances. The fragrance activities of these oils are related to functional groups (osmophores). Such groups include OH, O, CHO, CO, CH_3, OCH_3; hetero atoms such as nitrogen (NO_2, CN, N_3.) and/or sulphur (Ernest, 2007). Their activities are dependent upon the nature and position of the functional groups and molecular configuration of the molecules (Ohloff, 1994; Weyerstahl and Licha 1996; Sell, 2004; Schwab *et al.*, 2008; Muna *et al.*, 2013).

Swapping the positions of functional groups on a molecule or changing the functional group entirely may have a significant impact on the odour. For instance, as shown in Fig 1, a simple rearrangement of β-ionone into "roseketone", changed from the typical violet (*Viola odorata*) odour character to a fruity and camphoraceous odour.

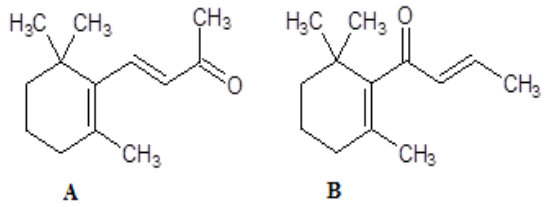
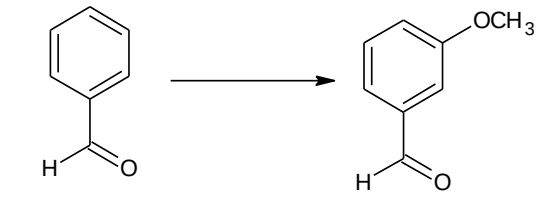


Fig 1: Structures of β-ionone [A] and Roseketone [B]

Adding a methoxyl group to benzaldehyde changes its smell from bitter almonds to aniseed (Anisaldehyde).



Scheme 1: Conversion of benzaldehyde to anisaldehyde.

For instance (Fig 2), substances with very similar molecular structures (stereoisomers) may give rise to odours that are quite different from each other, as in the case of (S)- (–)-limonene smells like turpentine (pine) but (R)- (+)-limonene has the odour of oranges.

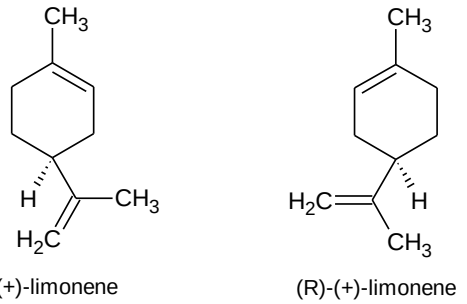


Fig 2: Structure of S)-(+) and (R)-(+) Carvone and (S)- (–) and (R)- (+)-limonene

It is therefore possible to improve the olfactory quality of a fragrant material by chemical modification. The modification can be in the form of greater intensity and/or greater chemical stability without change in odour character, it's odour influence to a fragrance, and performance in the products to be perfumed or it's safety in use and it's cost of production.

Methyleugenol (Fig 3) is an allylbenzene compound that occurs naturally in a variety of spices, herbs and essential oils, including nutmeg, clove oil, allspice, basil, citronella, pimento, hyacinth, anise, mace, pixuri seeds, cinnamon leaves, and laurel fruits and leaves. It also has been found in black pepper, blackberry essence, walnuts, bananas, and bilberries (Keng and Ritsou, 2012).

Methyleugenol has been used extensively: (a) as a flavouring agent in many types of processed food, soft drinks, and sauces; (b) in perfumery; and (c) as an essential oil in aromatherapy (Council of Europe, 1999). It has two electrons donating methoxy groups, a benzene ring and an alkene moiety giving many possibilities to use it as a starting material for the synthesis of more advanced valuable compounds.

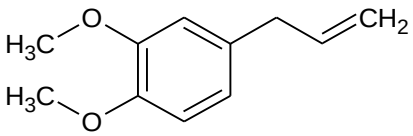
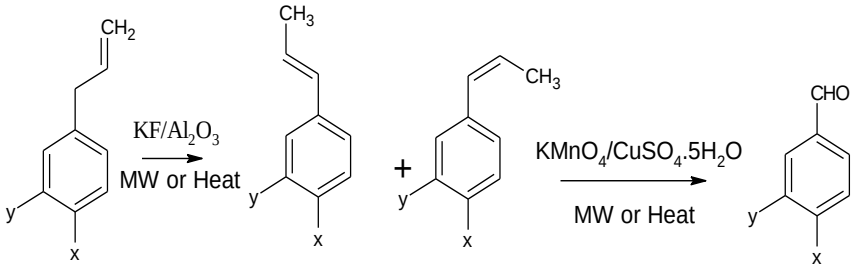


Fig 3: Structure of methyl eugenol (1,2-dimethoxy-4-(prop-2-en-1-yl)benzene)

Recently, Okopi and Affiku (2020) have demonstrated the chemical modification of methyleugenol to yield different fragrance chemicals when they successfully converted the alkene moiety in methyleugenol (a cheap and abundant essential oil) to Hydroxyether and alcohol functional group. Chemical modification of the methyleugenol result in changes in odour and olfactory properties of a fragrant entity. Therefore, introduction of alcohol

(Diol) and/or ester functional group into the molecular framework of methyleugenol may lead to a new compound with enhanced odour characteristics and better olfactory properties. It is well documented in literature that esters are sweet smelling (Pardo *et al.,* 2015; Keller and Vosshall, 2016). Also, Xuan *et al.* (2006) reported the preparation of vanillin from four allylbenzenes, a-d, through isomerisation by KF/Al_2O_3 under solvent free reaction conditions (scheme 2).



Scheme 2: Conversion of allylbenzene into their corresponding benzaldehyde under solvent free condition

	X	Y
Eugenol	$-OCH_3$	-OH
Methyleugenol	$-OCH_3$	$-OCH_3$
Estragole	$-OCH_3$	-H
Safrole	O- CH_2 – O -	

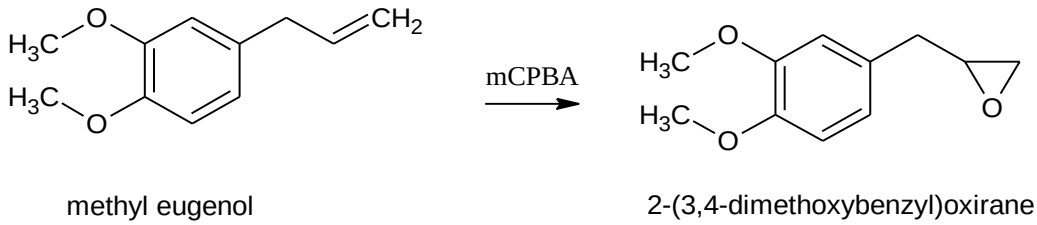
Hence, the objective of this paper is the synthesis and Olfactory characterization of new fragrant materials through chemical modification of methyleugenol molecular framework by introducing Ester functional groups.

MATERIALS AND METHODS

Materials: Methyl eugenol was purchased from Sigma Aldrich Company, USA. Solvents (n-hexane, acetone, ethyl acetate) were purchased from Fab Laboratory Nigeria Enterprise, Jos. 3-Chloroperbenzoic acid (mCPBA) was purchased from Acros Organics, USA. Other solvents and chemicals (Hydrogen peroxide, methanol, ethanol, dichloromethane, diethyl ether, hydrochloric acid, sodium hydroxide, sodium acetate, sodium bicarbonate, anhydrous sodium sulphate and sodium metal) were obtained from the Chemical Store, Nasarawa State University, Keffi. All chemicals were used as received. Silica gel and Thin-layer chromatography (TLC) plates were purchased from Fab Laboratory Nigeria Enterprise, Jos.

Instrumentation: The instrumentation used in this research was Nuclear Magnetic Resonance spectrometer (BRUKER TOPSPIN 300 MHz), located in Bioscience and Biotechnology Division, Los Alamos National Laboratory, Los Alamos, New Mexico, USA.

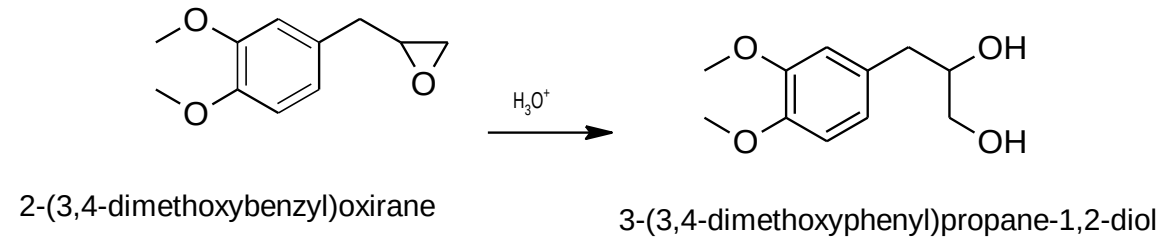
Epoxidation of Methyl Eugenol: Epoxidation of Methyl Eugenol were prepared as previously described (Okopi and Affiku, 2020).



Scheme 3: Conversion of methyl eugenol to 2-(4-ethyl-3-methoxybenzyl) oxirane (Methyl eugenol epoxide)

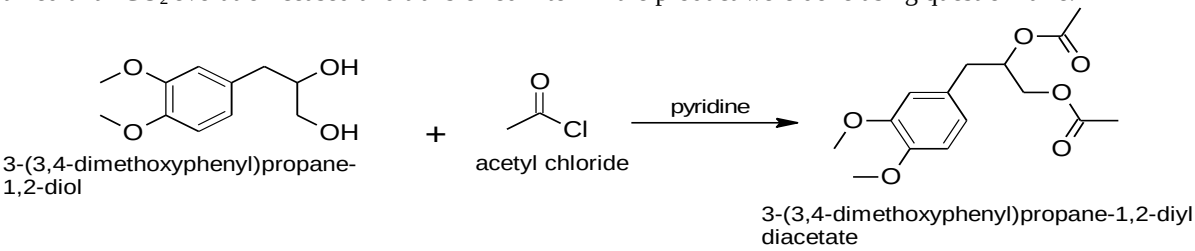
Synthesis of 3-(3,4-dimethoxyphenyl)propane-1,2-diol: Into 250 cm^3 round-bottomed flask equipped with a magnetic stir bar, 2-(3,4-dimethoxybenzyl) oxirane (7.7 g, 39.6 mmol) and dichloromethane (30 cm^3) were placed. Hydrochloric acid (3M. 50 cm^3) was added and the mixture was allowed to stir at room temperature and the progress of the reaction was monitored by TLC (Silica gel, EtOAc : Hexane, 3:7 v/v). The reaction was allowed to run overnight. After 22 hours TLC indicated complete reaction. Ethyl acetate (100 cm^3) and 5 % $NaHCO_3$ (200 cm^3) were added to the reaction mixture and transferred

into a separatory funnel. The upper organic phase was removed into an Erlenmeyer flask. The aqueous phase was back-extracted with EtOAc (50 cm^3). The organic phase was washed successively with 5 % $NaHCO_3$ (100 cm^3) and brine (20 cm^3). It was dried (anhydrous Na_2SO_4), filtered and solvent removed under reduced pressure (ROTOVAP) to give the crude diol as a yellow oily liquid. The product was purified by column chromatography. The fractions corresponding to product were pooled. Solvent was removed from the pooled fraction under reduced pressure (ROTOVAP) to give a yellow liquid product in 5.7 g (65.4 % yield). The TLC (Silica gel, EtOAc : Hexane, 3:7 v/v) conducted shows an R_f value of 0.54. ^{1}H-NMR spectrum of the compound was obtained. Odour characterizations of the product were done using questionnaire.



Scheme 4: Showing the opening of the oxirane

Synthesis of 1-(3,4-dimethoxyphenyl)-3-hydroxypropan-2-yl acetate: The diol, 3-(3,4-dimethoxyphenyl)propane-1,2-diol (0.7 g, 0.329 mmol) and dichloromethane (20 cm^3) were placed in a 250 cm^3 round-bottom flask equipped with magnetic stir bar. Acetyl chloride (10.0 cm^3) followed by pyridine (5.0 cm^3) were added to the mixture. The reacting mixture was allowed to stir for an hour at room temperature while samples were taken at intervals to monitor the progress of the reaction by TLC. After 1hour, TLC (Silica gel, EtOAc : Hexane, 3:7 v/v) showed complete reaction. Ethyl acetate (50 cm^3) and 5 % $NaHCO_3$ (100 cm^3) were added to the reaction mixture. The reaction was stirred until CO_2 evolution ceased and transferred into a separatory funnel. The upper organic phase was removed into a conical flask. The aqueous phase was back-extracted with EtOAc (30 cm^3). The combined organic phase was washed with brine (20 cm^3) and dried (anhydrous Na_2SO_4). The crude product was purified by column chromatography. The fractions corresponding to product were pooled. Solvent was removed from the pooled fraction under reduced pressure (ROTOVAP) to give a yellow liquid product in 0.40 g (53.33 % yield). TLC (Silica gel, EtOAc: Hexane, 3:7 v/v) shows an R_f value of 0.69 for the product which is higher than that of the starting diol (0.54). Analysis of the Product was performed using 1H-NMR spectrometers. Odour characterizations of the product were done using questionnaire.



Scheme 5: Esterification with acetyl chloride

RESULTS AND DISCUSSION

Synthesis of 2-(4-ethyl-3-methoxybenzyl) oxirane: The epoxidation reaction to synthesise the 2-(4-ethyl-3-methoxybenzyl) oxirane compound (Scheme 3) yielded 68.8%. The NMR data matches the simulated spectrum, confirming the successful formation of the target compound. Additionally, TLC analysis shows that the starting material, methyl eugenol, has an Rf value of 0.83, while the product has an Rf value of 0.60. This decrease in Rf is consistent with the introduction of the polar oxygen atom in the epoxide, as epoxides generally have lower Rf values compared to their alkene precursors. These observations further support the successful synthesis of the compound. The structural characterization of the product was conducted using ^{1}H (Fig 4**).** The chemical shift and multiplicity were in agreement and fully matched spectra of the compound simulated using nmrdb.org simulator (Fig 5**)**. Based on the questionnaire analysis (**Table 1**), was characterized by floral (30 %), fresh (40 %), slight lime (10 %) and sweet (20 %) qualities. Based on odour scale, 60 % agreed that 2-

(4-ethyl-3-methoxybenzyl) oxirane has a medium strong odour, while 40 % agree with strong odour.

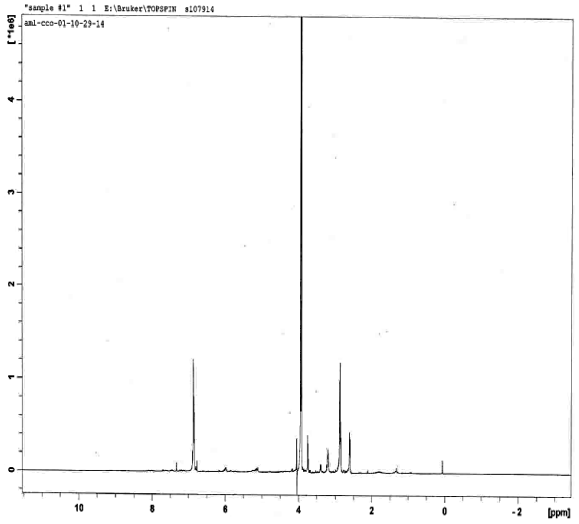


Fig 4: [1]H-NMR spectrum of 2-(3,4-dimethoxybenzyl) oxirane

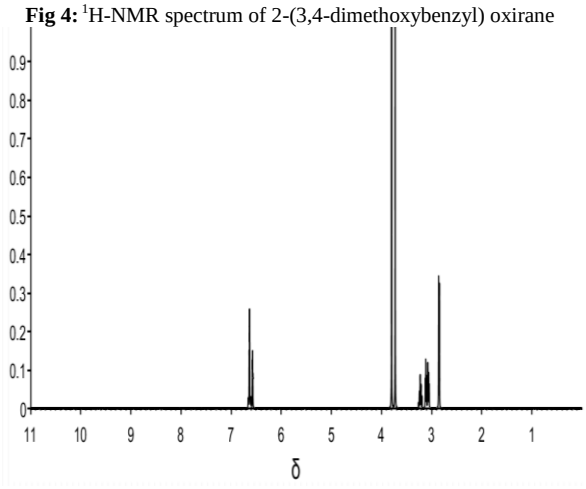


Fig 5: Simulated[1]H-NMR spectrum of 2-(3,4-dimethoxybenzyl) oxirane from nmrdb.org

Table 1: Odour Test Results for 2-(3,4-dimethoxybenzyl) oxirane

2-(3,4-dimethoxybenzyl)oxirane				
Smell Test			**Odour concentration**	
Floral	30 %		Medium strong odour	60 %
Fresh	40 %		Strong Odour	40 %
Slight lime	10 %			
Sweet	20 %			

Synthesis of 3-(3,4-dimethoxyphenyl)propane-1,2-diol: The synthesis of 3-(3,4-dimethoxyphenyl)propane-1,2-diol (Scheme 4) yielded 65.4%. NMR data matched the simulated spectrum, confirming the compound's formation. TLC analysis showed an Rf of 0.60 for 2-(3,4-dimethoxybenzyl)oxirane and 0.54 for the product, consistent with the expectation that the diol has a lower Rf than the epoxide. This supports the successful synthesis of the compound. The structural characterization of the product was conducted using [1]H NMR (Fig 6**)**. The chemical shift and multiplicity were in reasonable agreement with the spectra of the compound simulated using nmrdb.org simulator (Fig 7**)** with a number of exceptions. The data from the nmrdb.org did not show proton peaks for hydroxyl (OH) group. However, the rest of the proton chemical shifts are in good agreement with the observed data. Beside hydroxyl group, the rest of the chemical shift appears up field with the majority of shifts being within 0.2 ppm.

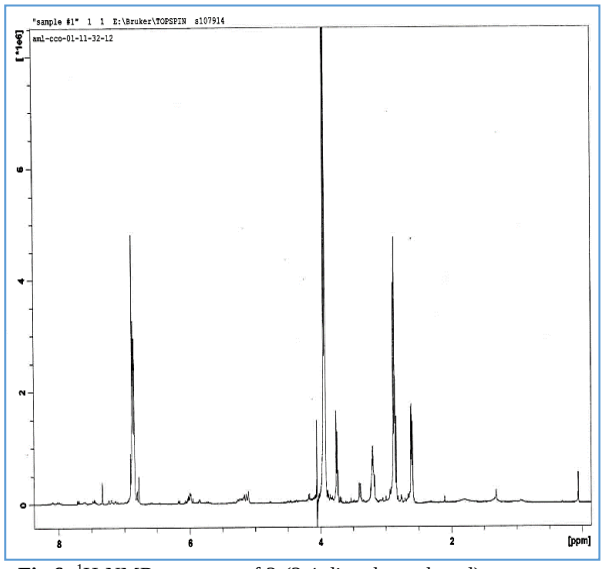


Fig 6: [1]H-NMR spectrum of 3-(3,4-dimethoxyphenyl) propane-1,2-diol

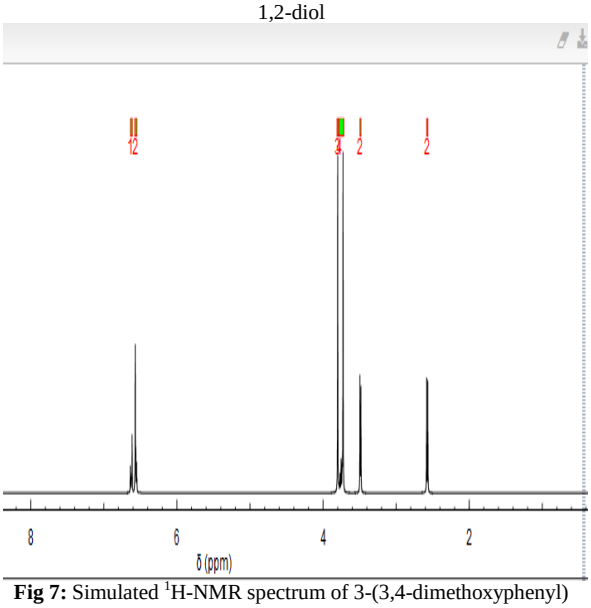


Fig 7: Simulated [1]H-NMR spectrum of 3-(3,4-dimethoxyphenyl) propane-1,2-diol from nmrdb.org

Odour characterizations of the product were done using questionnaire (Table 2). Based on the analysis of the questionnaires, 3-(3,4-dimethoxyphenyl) propane-1,2-diol was characterized by floral (10 %), pungent (50 %), Caramel (30 %) and sweet (10 %)

qualities. On the odour scale, 50 % agreed that the has a medium strong odour, while 50 % agree with strong odour.

Table 2: Odour Test Results for 3-(3,4-dimethoxyphenyl)propane-1,2-diol

3-(3,4-dimethoxyphenyl)propane-1,2-diol			
Smell Test		**Odour concentration**	
Floral	10 %	Medium strong odour	50 %
Pungent	50 %	Strong Odour	50 %
Caramel	30 %		
Sweet	10 %		

1-(3,4-dimethoxyphenyl)-3-hydroxypropan-2-yl acetate: The synthesis of 1-(3,4-dimethoxyphenyl)-3-hydroxypropan-2-yl acetate yielded a 53.33% yield. The NMR data confirmed the structure of the synthesized compound by matching the simulated spectrum.

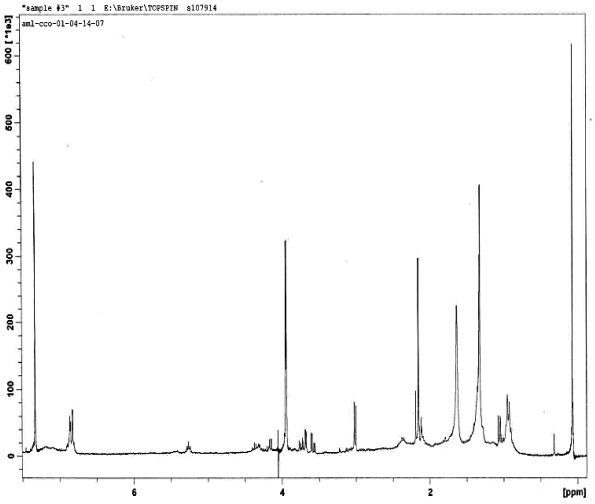


Fig 8: ^{1}H-NMR spectrum of 1-(3,4-dimethoxyphenyl)-3-hydroxypropan-2-yl acetate

Additionally, TLC analysis showed that the Rf value of the product (0.69) was higher than that of the starting diol (0.54), as expected for an ester. This further supports the successful synthesis of the target compound. Structural characterization of the product was done using ^{1}H NMR (Fig 8). Strong evidences for the success of the reaction are the disappearance of hydroxyl proton peak from the reactant at (δ) 2.6 ppm. Chemical shift and multiplicity were in reasonable agreement with the spectra of the compound simulated using nmrdb.org simulator (Fig 9) with a number of exceptions. However, the general picture is reasonably well reproduced. Odour characterizations of the product were done using questionnaire (Table 3). Based on the questionnaire analysis, the Ester was characterized by fresh (40 %), pungent (30 %), lime-like (10 %) and sweet (20 %) qualities. On the odour scale, 60 % agreed that the Ester has a medium strong odour, while 40 % agree with strong odour.

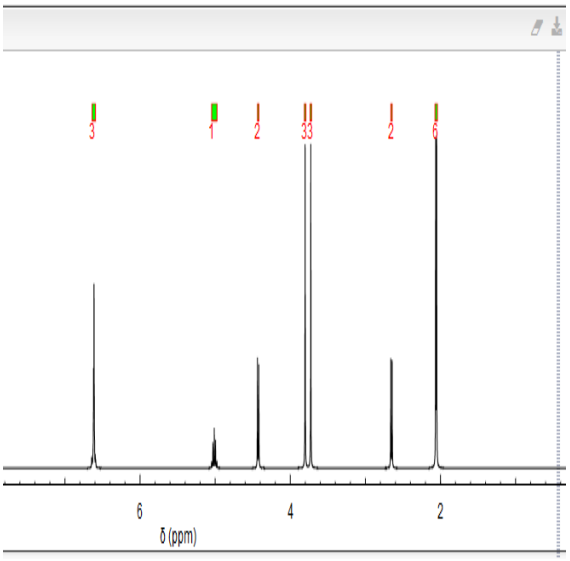


Fig 9: Simulated^{1}H-NMR spectrum of 1-(3,4-dimethoxyphenyl)-3-hydroxypropan-2-yl acetate from nmrdb.org

Table 2: Odour Test Results for 1-(3,4-dimethoxyphenyl)-3-hydroxypropan-2-yl acetate

1-(3,4-dimethoxyphenyl)-3-hydroxypropan-2-yl acetate			
Smell Test		**Odour concentration**	
Fresh	40 %	Medium strong odour	60 %
Pungent	30 %	Strong Odour	40 %
Lime-like	10 %		
Sweet	20 %		

Conclusion: This study successfully enhancement of the olfactory properties of methyleugenol by chemical transformation of its olefin bond to generate alcohol and ester functions in the molecule. The research show that the four synthesised compounds have different odour which make them readily distinguishable from each other. The results clearly show that changing the functional group in an odorant molecule could result in change of odour.

Declaration of Conflict of Interest: The authors declare no conflict of interest.

Data Availability Statement: Data are available upon request from the first author or corresponding author or any of the other authors

REFERENCES

Council of Europe - Committee of Experts on Flavouring Substances (2000). Use levels of datasheet on Methyleugenol. Document RD 4.14/2-45 submitted by the delegation of Italy for the 45th meeting in Zurich, October 1999.

Ernest, JP (2007). The chemistry of essential oils and artificial perfumes. 4th (ed). Scott Greenwood And Sons. Ludgate, London,

Keller, A; Vosshall, LB (2016). Olfactory perception of chemically diverse molecules. *BMC Neuroscience*, BMC series. 17: 55.

Keng, HT; Ritsuo, N (2012). Methyleugenol: its occurrence, distribution, and role in nature, especially in relation to insect behaviour and pollination. *J. Insect Sci.* 12(56): 1-60.

Luu, TXT; Lam, TT; Le, TN; Duus, F (2009). Fast and Green Microwave-Assisted Conversion of Essential Oil Allylbenzenes into the Corresponding Aldehydes via Alkene Isomerization and Subsequent Potassium Permanganate Promoted Oxidative Alkene Group Cleavage. *Molecules*, 14(9), 3411–3424. https://doi.org/10.3390/molecules14093411

Muna, AM; El Hadi; Feng-Jie, Z; Fei-Fei, W; Chun-Hua, Z; Jun, T (2013). Advances in fruit aroma volatile research. *Molecules* 18: 8200-8229.

Ohloff, G. (1994). Scent and fragrances. *Springer-Verlag*, Heidelberg 9, IX.

Okopi, SO; Affiku, LM (2020). Synthesis and Olfactory Characteristics of Hydroxyether Derivatives of Methyl Eugenol. *J. Appl. Sci. Environ. Manage*. 24(9): 1503-1507. DOI: https://dx.doi.org/10.4314/jasem.v24i9.3

Pardo, E; Rico, J; Gil, JV; Orejas, M (2015). De novo production of six key grape aroma monoterpenes by a geraniol synthase - engineered S. cerevisiae wine strain. *Microbial Cell Factories*. 14: 136.

Schwab, W; Davidovich-Rikanati, R; Lewinsohn, E (2008). Biosynthesis of plant-derived flavour compounds. *Plant J.* 54: 712–732.

Sell, CS (2010). Chemistry of essential oils. In Handbook of Essential Oils: Science, Technology, and Applications; Başer, KHC; Buchbauer, G; Eds.; CRC Press, Taylor and Francis Group: London,UK.

Weyerstahl, P; Licha, K; (1996). Structure-odour correlation. 24. Synthesis and olfactory properties of damascene and damascenone analogs. *Liebiegs Ann*., 5: 809–814.