Relationships between smell, carbon number, and molecular structure of acetate esters

Shoya Inoue[1]

[1] *Waseda junior and senior high school, Shinjuku, Babasitamachi 162-8654, Japan.*

Contact information:

Shoya Inoue

Adress: Waseda senior high school, Shinjuku, Babasitamachi 162-8654, Japan.

Tel: 090-8102-5358

Email: kagaku89daisuki5@gmail.com

Abstract:

Acetate esters, a group of substances found in natural fragrances and perfumes, are formed by the dehydration-condensation of acetic acid and alcohol and are known to have a variety of good smells. However, the regularity with which these smells change depending on the combination with the raw alcohol is not well understood yet. In order to investigate this, six alcohols with carbon numbers between 2 and 4 and phenol were used to synthesize and classify the smells, and the relationship between the smell of acetate esters, carbon number and molecular structure was compared. The results showed that the smell of acetate esters changes with changes in carbon number and with changes in molecular structure. These findings are discussed with respect to molecular polarization and human olfaction mechanisms.

Introduction:

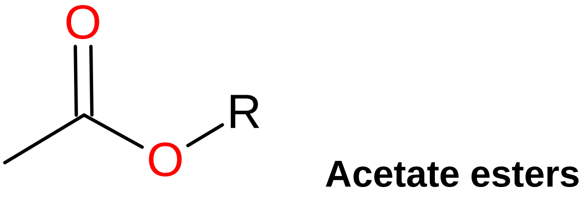
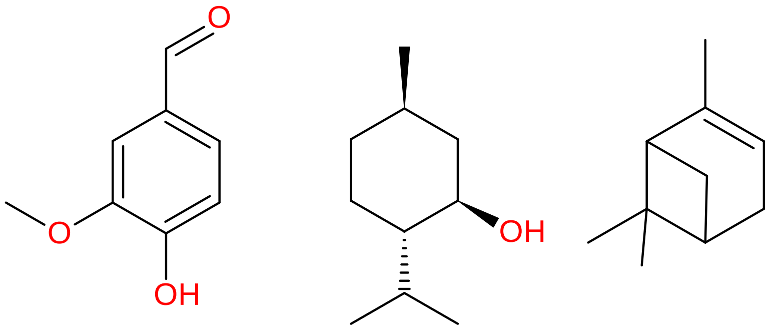


Figure 1. Structural formula of acetate esters

Some of the various organic molecules have great smells. Examples include vanillin, menthol and so on. Among them, acetate esters, which are formed by the dehydration-condensation of acetic acid and alcohols, are known to exhibit a variety of smells）1. However, there are only two reports on the smell of acetate esters and the carbon number of acetate ester, although the structure is relatively clear. The first article reports on ethyl acetate and butyl acetate, which have the same linear side-chain structure）2. It also

https://doi.org/10.26434/chemrxiv-2024-9t1d3 **ORCID:** https://orcid.org/0009-0003-3212-1421

describes the different smells of acetate esters. The second report)3 compared the smells of four Acetate esters with the same branched structure and 5-8 carbons in the side chain, and again suggested that the smells of acetate esters with different carbons were different. However, the discussions in these two reports make no mention of what physical properties change and smell of acetate esters differ as the carbon number of acetate esters changes. In addition, only the comparison of smells of acetate esters with similar molecular structures is carried out, and there is no research on acetate esters with the same number of carbons but different molecular conformation (structural isomers). In order to investigate these issues, this study hypothesized that the smell of acetate esters depends only on their carbon number and that the smell of acetate esters with different structural isomers will be the same. The results of this experiment were used to classify the smells. Using the results of these experiments, the polarity and other physical properties of the synthesized molecules and the human olfactory mechanism, we attempted to discuss the factors responsible for the differences in the smell of acetate esters.



Vanillin **(l)- Menthol** **Pinene**

Figure02. examples of famous smell molecules

Method of this study:

In this study, we concentrated on acetate esters consisting of six alcohols (2-4 carbons), synthesized them by the approach of Fig03, smelled them and classified them using expressions from the Ref [4].

We tried considerations of synthesis conditions first. A total of three patterns were performed with amounts of raw materials: acetic acid and alcohols of 0.03mol,0.05mol, and 0.07mol. Furthermore, we used a very small amount of concentrated sulfuric acid as a catalyst of these reactions.

Consequently, we gained results show that conditions at acetic acid and alcohols of 0.05 mol are most suitable, therefore Acetate esters were synthesized using 0.05 mol of acetic acid and alcohol used in the synthesis as the standard in this research.

We conducted the synthesis of phenyl acetate as process for reacting acetic anhydride with phenol.

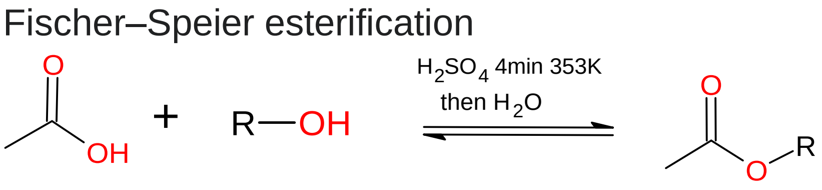


Figure03. Synthetic approach to Acetate ester in this study

	Alcohol\`s quantity	Acetic acid\`s quantity	Overall Results
Entry1	0.03mol	0.03mol	Little acetate ester produced
Entry2	0.05mol	0.05mo1	Much acetate ester produced
Entry3	0.07mol	0.07mol	A bit ingredient remained

Table1 The discussions of synthesized conditions

Representations of smell classification in the Ref [4]:

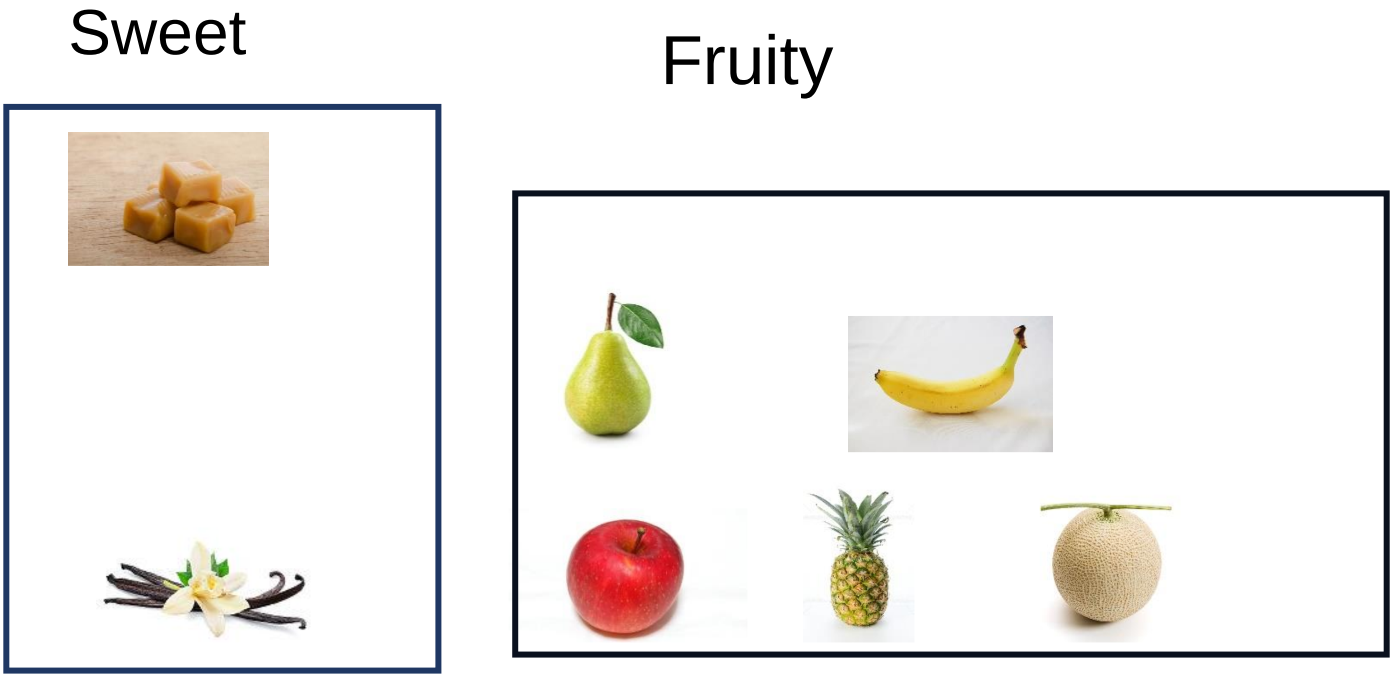


Figure04. representations of smell classification

Discussion of results:

Firstly, we conducted acetate ester synthesis respectively. As for quantities, take into account the previous description (Method of this study), with **0.05 mol** of acetic acid and alcohol. For the ester synthesis reactions, the corresponding acetate ester was obtained for all six alcohols used in the experiments. Here, the boiling points and solubility in water of the six Acetate esters synthesized in this study and what they smelled like during the experiment are shown in Figure 5. Also, we Denote the number of carbons in the alcohol as n, e.g. **Cn**. For example, we represent the case of ethanol with two carbons, **C2**.

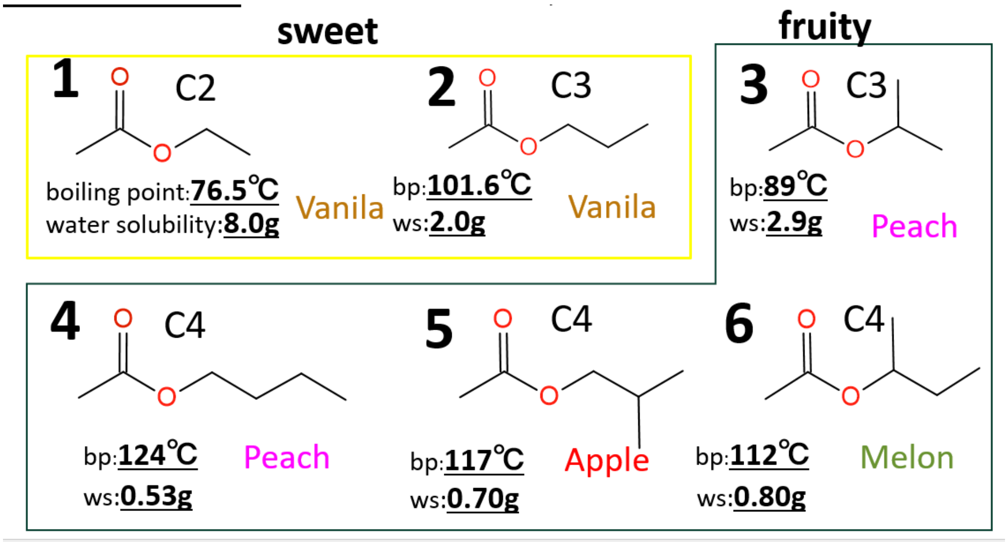


Fig.05 synthesis with 0.05 mol of acetic acid and alcohol

Here, there are two trends revealed by these results. First of all, Comparing Acetate esters with linear structures, In the linear structure, the longer the carbon chain, **the lower the water solubility**, **the higher the boiling point**, and the **more "fruity"** the smell tends to be.

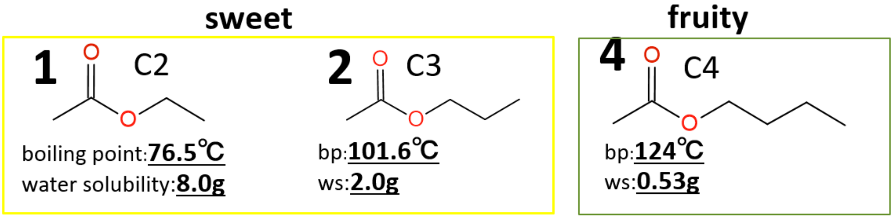
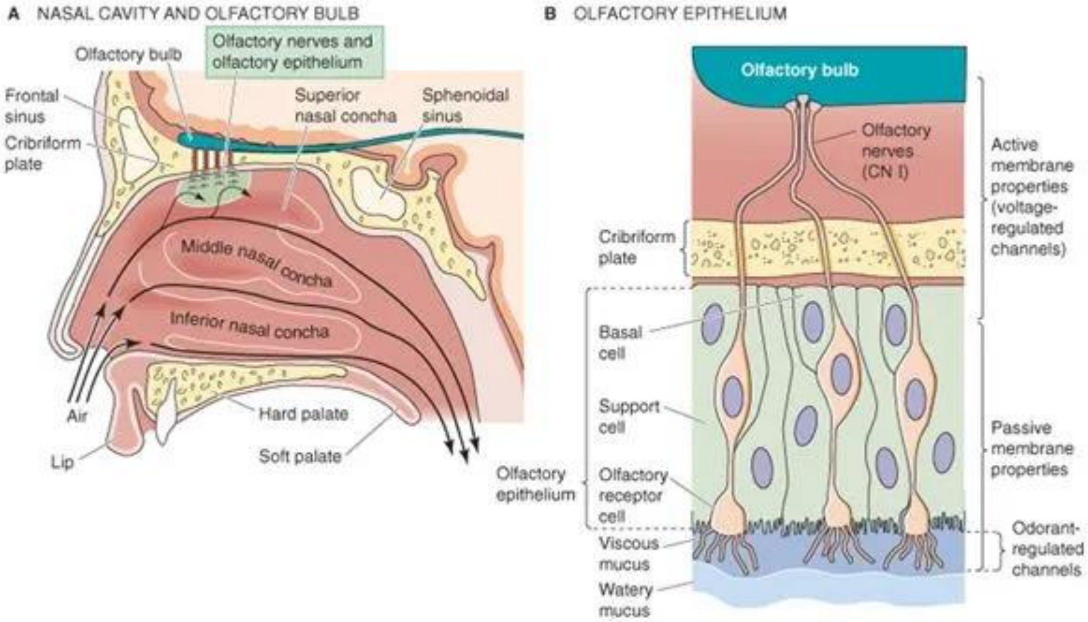


Fig.06 Comparing of smells of acetate esters with linear structures.

Then, making compression of smells of acetate esters between structural isomers, we will pick up two features about this. First, Esters **2** and **3** with C3 alcohols had quite different smells, whereas **4**, **5** and **6** with C4 alcohols had almost identical smells. Secondly, the Comparison the bp and ws of esters 1-3, ester 3 is located around the middle of esters 1 and 2, but it did not have a sweet aroma. Ws are expressed water solubility in this thesis.

In view of the above, we think that the fact is a key to find the relationship between smells and molecular structure of acetate esters. Specifically, it is suggested that bp and ws are not the only factors that determine the smell of acetate esters.

Herein, we will indicate the generally known figure of the structure of the olfactory epithelium 5). Considering human olfactory pathway4) 6) and this picture described the olfactory epithelium, this mechanism is as follows signals are transmitted when smell molecules first dissolve in the mucus of the nose and subsequently interact with olfactory receptors in the olfactory epithelium.



Boron & Boulpaep: Medical Physiology, 2nd Edition.
Copyright © 2009 by Saunders, an imprint of Elsevier, Inc. All rights reserved.

Fig.07 Structure of human olfactory epithelium from Ref. [5]

Based on this figure, a discussion on the fact that in the linear chain structure of Acetate esters, the smell of acetate esters changes to a fruity smell as the carbon chain gets longer.

As an additional experiment to verify the accuracy of this fact, Acetate ester synthesis with a 5-carbon linear alcohol and a similar experiment with a 6-carbon linear alcohol were carried out to verify the smell of acetate esters and the smell of acetate esters of the respective products. The results are shown in Fig08. In this figure, the results of previous experiments other than the additional experiments are also shown at the same time for comparison.

The results confirmed a similar trend (Fig.08). In this diagram, amyl acetate is designated as **Ester7** and hexyl acetate as **Ester8**.This can be considered using the human olfactory mechanism (Fig.07) presented earlier, whereby as the carbon number of the alcohol increases, the water solubility of the ester molecule decreases, and the smell changes on account of the decrease in solubility in the first step of the olfactory mechanism - dissolution into the mucous membranes.

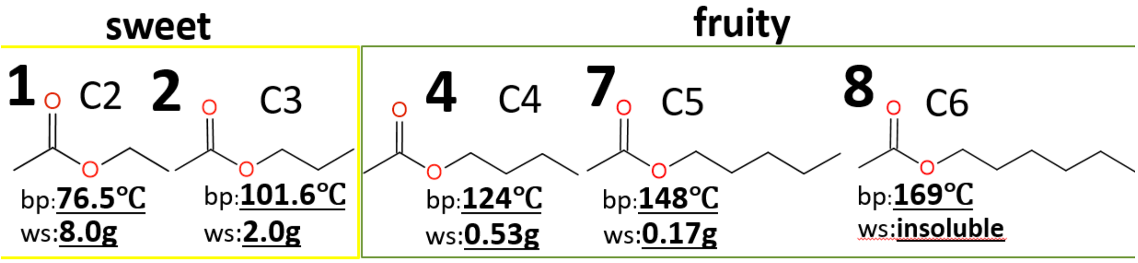


Fig.08. The outcomes of additional tries

In addition, we will talk about the smell of esters between structural isomers. There is a dispensable point concerning the discussion between structural isomers that we would like to mention here: Solubility in nasal mucus is not that different between structural isomers. Therefore, Differences in smell are largely dependent on differences in reactivity with olfactory receptors, the second step in the olfactory mechanism, i.e. on differences in the electron-donating capacity of the esters.

The relationship between the key and the keyhole. Namely, this is how the second step response is supposed to work.

Then, we will demonstrate some approaches to the reason why do esters of different structural isomers smell differently from each other: HOMO Energy, the charge of the carbon attached to the oxygen in the side chain, Spread of occupied orbitals.

Both approaches are due to differences in the magnitude of hyperconjugation caused by changes in the steric structure of the side chain. Here, it is the donation of electrons from the σC-H orbital to the π*C=O orbital.

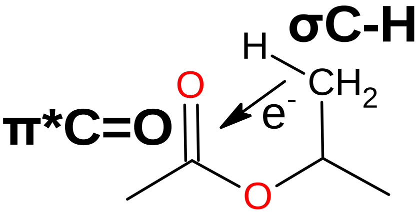
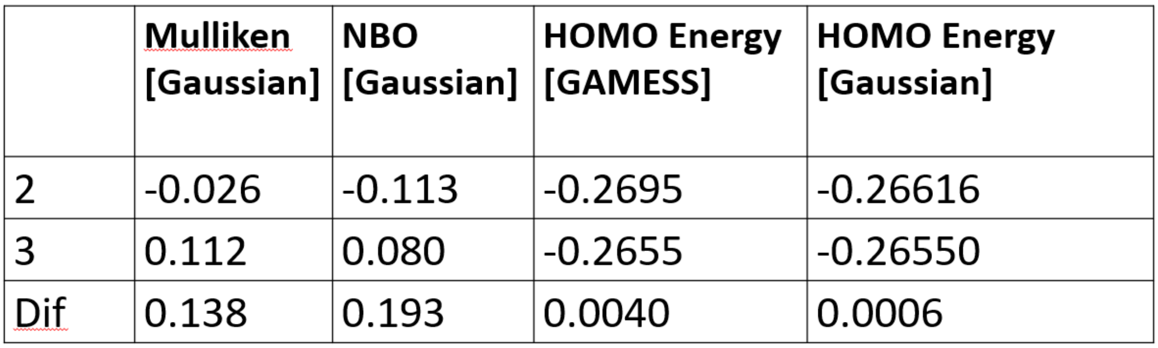


Fig09. The imagine of hyperconjugation of acetate esters (ester2 and ester3)

Herein, we will indicate the results of the verification of reasons. First, we will show the calculate consequence about comparing ester2 and ester3 with Gaussian16[7)] and GAMESS. All the calculation condition is B3LYP/6-31(d). The charge density and HOMO Energy are shown in Table 2 below. Difference is denoted here as Dif.

Then, we are going to present Spread of occupied orbitals, HOMO, and HOMO-1~HOMO-4. Seeing these orbitals, Ester3 is a little **more spread** out in HOMO, Ester3 is considerably more spread out in HOMO-1, HOMO-3, HOMO-4.



	Mulliken [Gaussian]	**NBO [Gaussian]**	**HOMO Energy [GAMESS]**	**HOMO Energy [Gaussian]**
2	-0.026	-0.113	-0.2695	-0.26616
3	0.112	0.080	-0.2655	-0.26550
Dif	0.138	0.193	0.0040	0.0006

Table2 The charge density and HOMO Energy (ester2 and ester3)

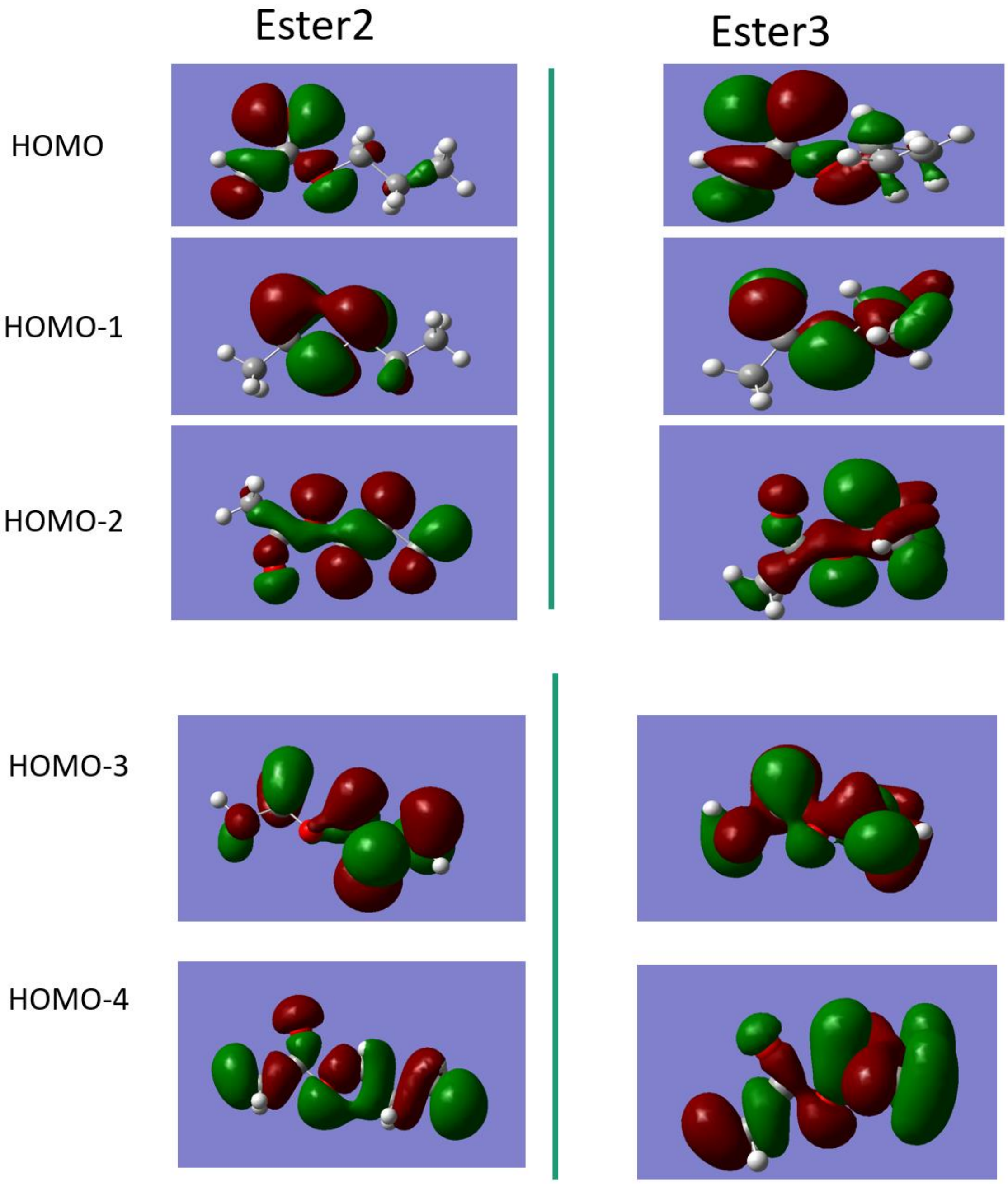
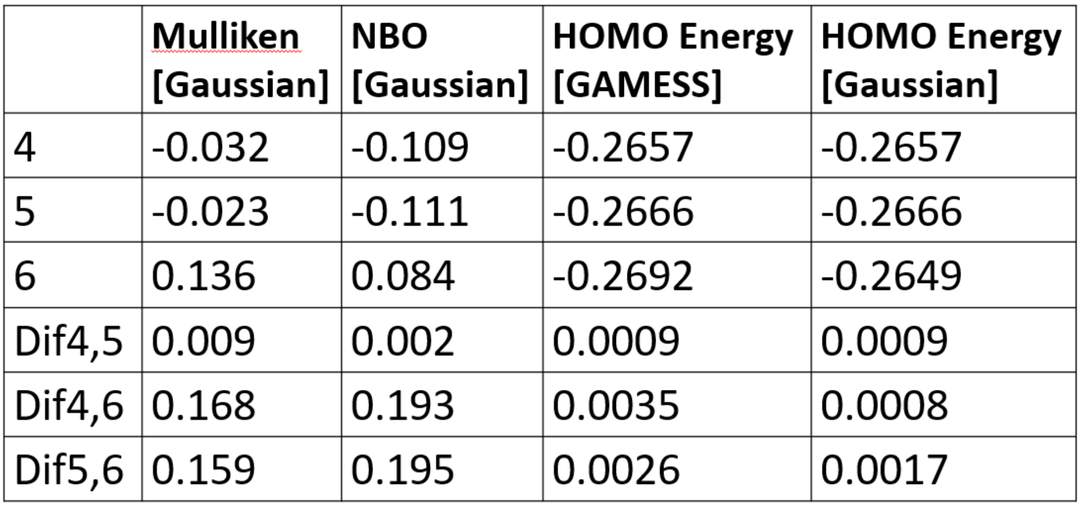


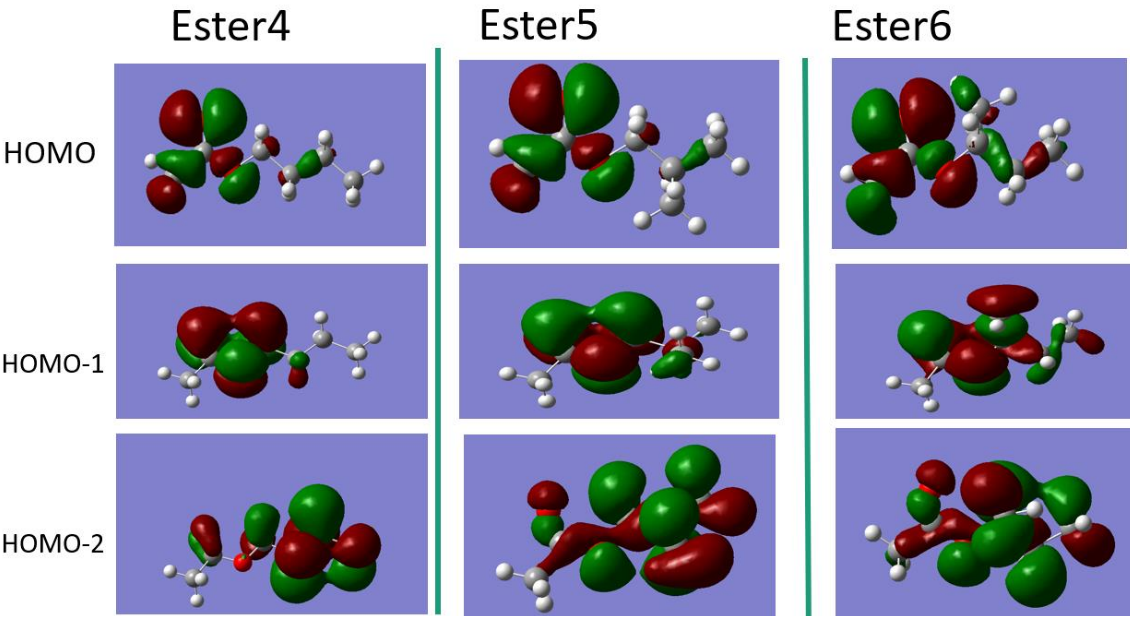
Fig10. Spread of occupied orbitals (ester2 and ester3)

Next, we will discuss the calculate outcomes about comparing ester4, ester5 and ester6 with Gaussian16 and GAMESS as in the previous section. The charge density and HOMO Energy are given in Table 3 below. Then, we are going to present Spread of occupied orbitals, HOMO, and HOMO-1~HOMO-4. Compering these orbitals, the extent of these occupied orbits does not vary much between the three esters. Also, in acetate esters, the presence of a methyl group in the adjacent position of the ester bond can change the phase.



	Mulliken [Gaussian]	NBO [Gaussian]	HOMO Energy [GAMESS]	HOMO Energy [Gaussian]
4	-0.032	-0.109	-0.2657	-0.2657
5	-0.023	-0.111	-0.2666	-0.2666
6	0.136	0.084	-0.2692	-0.2649
Dif4,5	0.009	0.002	0.0009	0.0009
Dif4,6	0.168	0.193	0.0035	0.0008
Dif5,6	0.159	0.195	0.0026	0.0017

Table3 The charge density and HOMO Energy (ester4,ester5, and ester6)



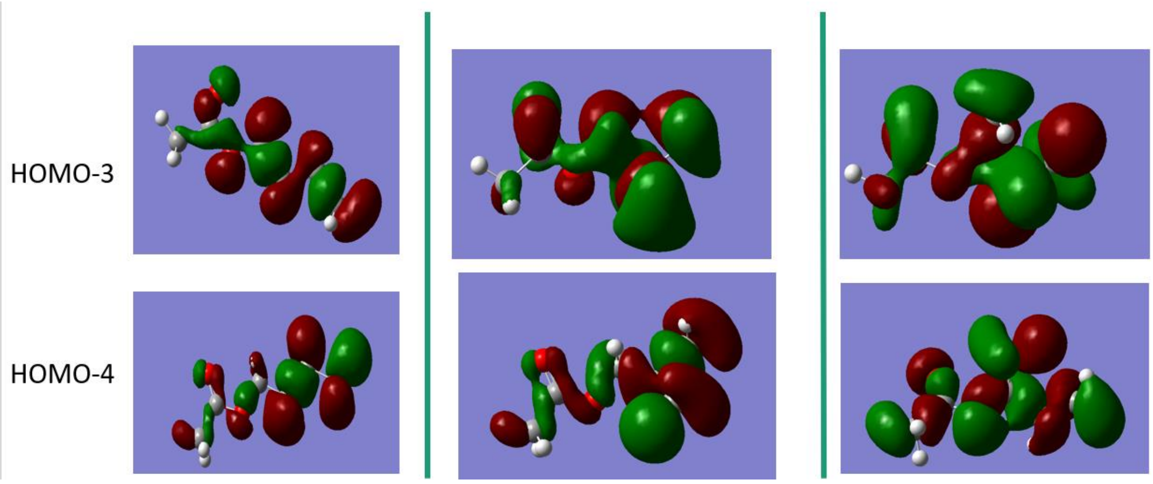


Fig11. Spread of occupied orbitals (ester4 ester5, and ester6)

Then, we will indicate what the calculations results show. The results of the extent of occupied orbitals show that the difference between esters 2 and 3 tends to be greater than the differences between esters 4, 5 and 6. On the other hand, the consequences of the electron density analysis and HOMO Energy were not necessarily similar to the results of the Extent of occupied orbitals. In view of the above, we guessed that factors determining smell of acetate esters are solubility of water and effect of hyperconjugation of side chain. The overall effect of these two factors makes a difference in smells.

Conclusion and further prospects:

The smell of low molecular weight acetate esters was found to have a certain relationship to both carbon number and molecular structure. The change in smell of acetate esters could be explained by the combined action of two factors: the 'solubility in water' and the 'effect of hyperconjugation of side chains'. However, consideration of the super-conjugation part is still insufficient and there is a great possibility that factors other than super-conjugation may be involved.

In the future, we intend to investigate the effects of hyperconjugation in more detail in terms from bond lengths and NMR spectra and report back. A similar investigation of Acetate esters formed from alcohols with a carbon number of 5 or more is currently underway and will be reported.

References:

1. K. Kimura., Flavouring chemistry. Kyoritsu Publishing (1969)
2. T. Hasegawa., Flavouring chemistry - The world of smells created by odour molecules -. Corona Corp. (2020)
3. Y. Oosuga; T.Hasegawa; E.Kuraya., Structure and Aroma of γ-Lactones Journal of Japan Association on Odor Environment vol. 51 issue 3 (2020) pp: 205-208
4. R. Hirayama., The science of smells, from what they are to what they do. Bluebacks (2017)
5. Schipke JD, Lemaitre F, Cleveland S, Tetzlaff K. Effects of Breath-Hold Deep Diving on the Pulmonary System. 2019;97(5):476-483
6. Gregory N. Bratman *et al.*, Nature and human well-being: The olfactory pathway.*Sci. Adv.***10**, eadn3028(2024).
7. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. Gaussian 16 Rev. B.01, Wallingford, CT, 2016.
8. Barca, Giuseppe M. J. and Bertoni, Colleen and Carrington, Laura and Datta, Dipayan and De Silva, Nuwan and Deustua, J. Emiliano and Fedorov, Dmitri G. and Gour, Jeffrey R. and Gunina, Anastasia O. and Guidez, Emilie and Harville, Taylor and Irle, Stephan and Ivanic, Joe and Kowalski, Karol and Leang, Sarom S. and Li, Hui

and Li, Wei and Lutz, Jesse J. and Magoulas, Ilias and Mato, Joani and Mironov, Vladimir and Nakata, Hiroya and Pham, Buu Q. and Piecuch, Piotr and Poole, David and Pruitt, Spencer R. and Rendell, Alistair P. and Roskop, Luke B. and Ruedenberg, Klaus and Sattasathuchana, Tosaporn and Schmidt, Michael W. and Shen, Jun and Slipchenko, Lyudmila and Sosonkina, Masha and Sundriyal, Vaibhav and Tiwari, Ananta and Galvez Vallejo, Jorge L. and Westheimer, Bryce and Wloch, Marta and Xu, Peng and Zahariev, Federico and Gordon, Mark S., Recent developments in the general atomic and molecular electronic structure system *J. Chem. Phys.* 152, 154102 (2020)