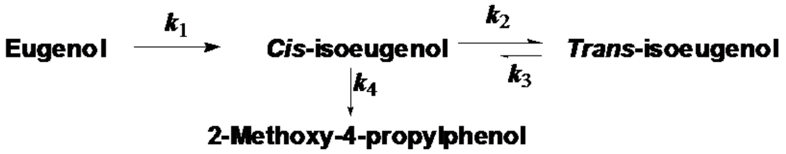
[1,3] SIGMATROPIC REARRANGEMENT OF *CIS*-ISOEUGENOL FORMATION IN EUGENOL ISOMERIZATION REACTION

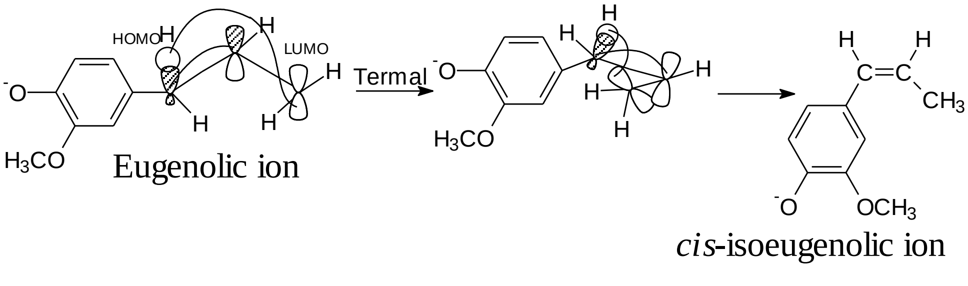
by Asep Kadarohman*)

Abstract

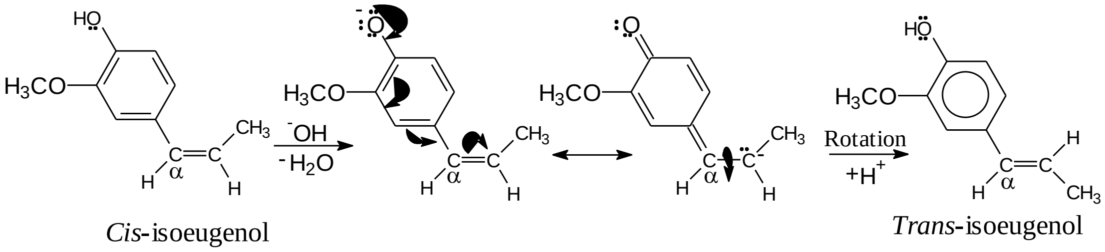
The purpose of this study to investigate the mechanism of eugenol isomerization reaction. Isomerization mechanism of eugenol to isoeugenol in basic condition was proposed similar to the isomerization mechanism of allylbenzene to prophenylbenzene through cabanion ion as intermediate. Isomerization reactions were carried out in basic condition by deuterium labeling, the variation of water, solvent, time, and temperature. Products were analyzed by GC and GC-MS. There were five experimental data that indicated the isomerization mechanism of eugenol that was different from the isomerization mechanism of allylbenzene. (1) The reaction pathway of eugenol isomerization to *cis*- and *trans*-isoeugenol was a consecutive, whereas the reaction pathway of allylbenzene isomerization was a parallel;



(2) the solvent and temperature of eugenol isomerization reaction was different from allylbenzene isomerization; (3) water inhibited isoeugenol formation; (4) the resulted of 2-methoxy-4-propylphenol and (5) isoeugenol were labeled by deuterium atom insignificant. All the data above mention, it indicates that the the mechanism of eugenol isomerization is not through cabanion ion as intermediate. To describe the reaction mechanism of eugenolic ion to *cis*-isoeugenolic ion was proposed by frontier orbital theory, namely through antarafacial [1,3] sigmatropic rearrangement.



The reaction mechanism of *cis*- to *trans*-isoeugenol was initiated by *cis*-isoeugenolic ion formation that will be followed by resonance process to form single bond at C_1-C_2. The next step of the C_1-C_2 single bond will rotate to form stable compound (*trans*-isoeugenolic ion).



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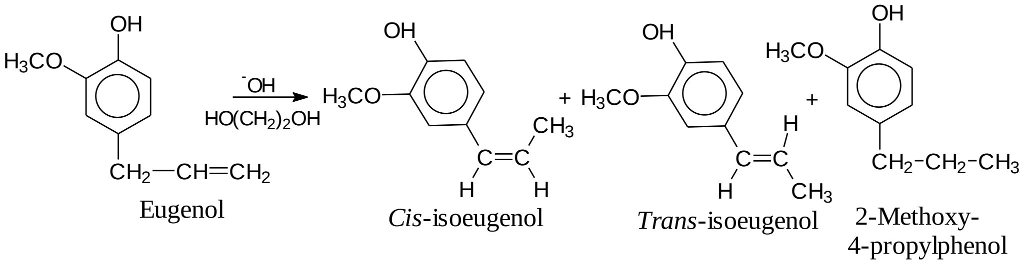
1. Introduction

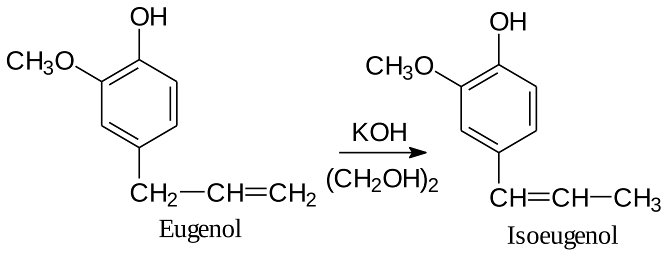
Clove leaf oil is an export material that is large enough from Indonesia. However, its derivative that is imported to Indonesia is more expensive than the oil (Sastrohamidjojo, 2000). Therefore, the conversion of clove leaf oil components to a more valuable substance is an important research. Eugenol is a major component in clove leaf oil. Eugenol isomerization is the first step in the conversion to a more valuable substance, such as vanillin.

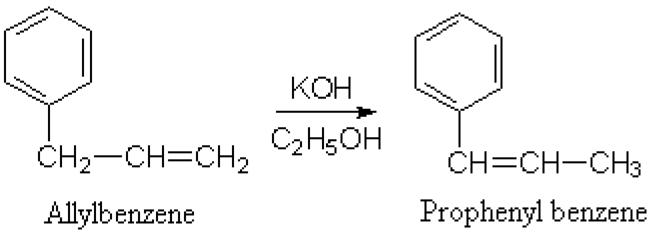
Eugenol isomerization reaction ordinarily used base catalyst (Sastrohamidjojo, 1981; Cerveny, *et.al.*, 1987; Peterson *et.al.*, 1993; Zucco, 1997). Sastrohamidjojo (1981) mentioned that eugenol isomerization reaction resulted *cis*- and *trans*-isoeugenol. In the beginning the ratio of *cis* to *trans*-isoeugenol was greater than in the end (changed from 1/5 to 1/20 approximately). Kadarohman (2000) reported that 2-methoxy-4-propilphenol was resulted as a side product on eugenol isomerization reaction by base catalyst and ethylene glycol solvent. Reaction of eugenol isomerization can be written as the following.



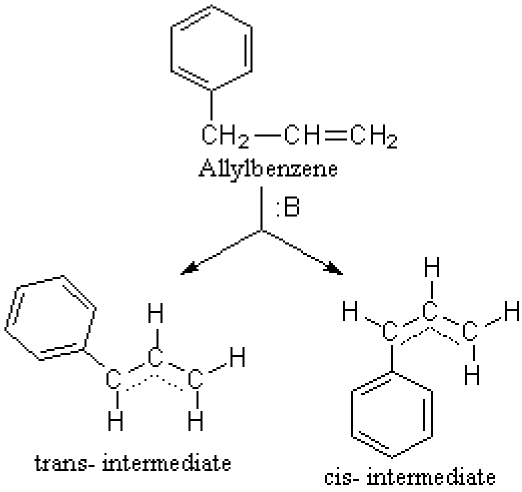
Peterson, *et.al.* (1993) and Kadarohman (1994) found that the formation of *cis*-isoeugenol was kinetically controlled and the formation of *trans*-isoeugenol was thermodynamically controlled. The rate of reaction was found to be pseudo first order. Frost and Pearson (1961) stated that there were two possibilities of the first order complex reaction, i.e. parallel and consecutive reactions.

The mechanism of eugenol isomerization to isoeugenol was proposed similar to the isomerization mechanism of allylbenzene to prophenylbenzene (Wheland, 1954).



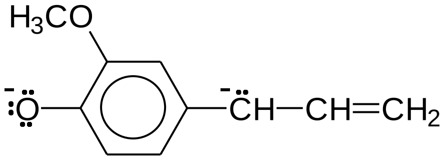


Cram dan Ela (1966) mentioned that the mechanism of allylbenzene to prophenylbenzene with KO-tBu in HO-tBu at 25° C through cabanion ion as intermediate. The impact of steric stability, *trans*-prophenylbenzene is resulted more than *cis*-prophenylbenzene

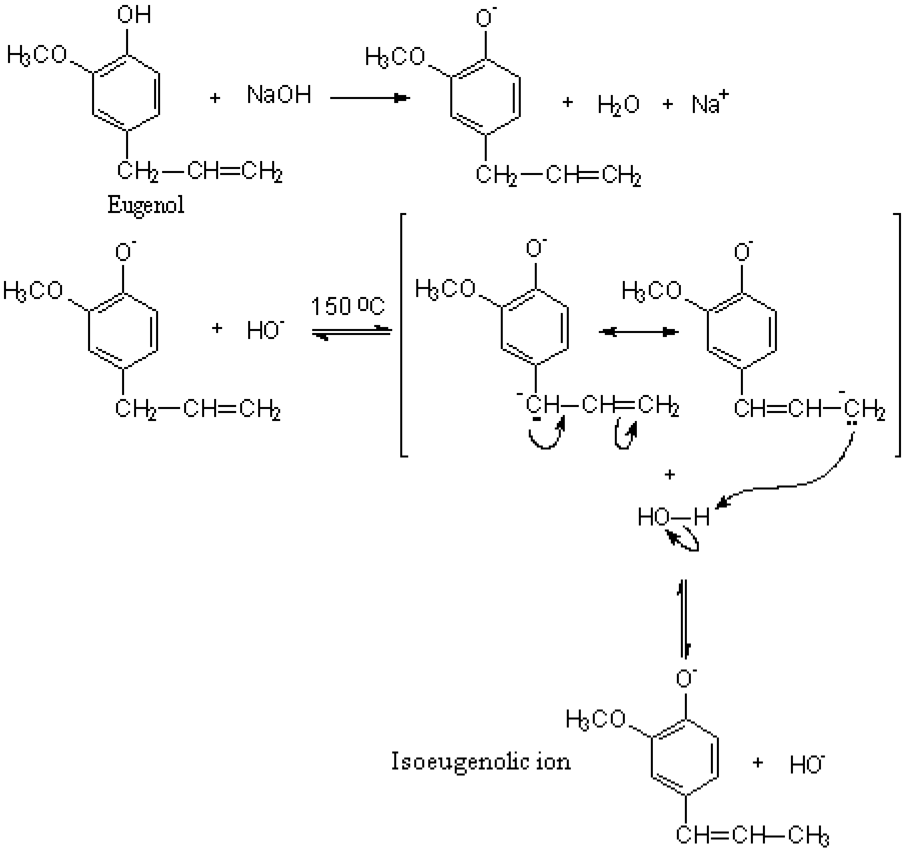


The formation of cabanion ion as intermediate in allylbenzene isomerization has proved by experiment through deuterium (D) labeling (Isaacs, 1974).

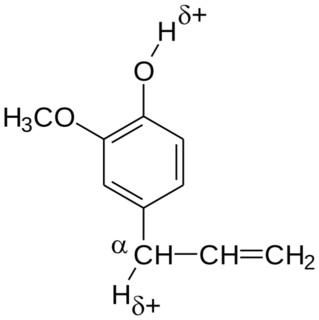
Based on the mechanism of allylbenzene isomerization, Sastrohamidjojo (1981) and Peterson *et al.* (1993) have proposed that the mechanism of eugenol isomerization to isoeugenol in basic condition through two anion as intermediate.



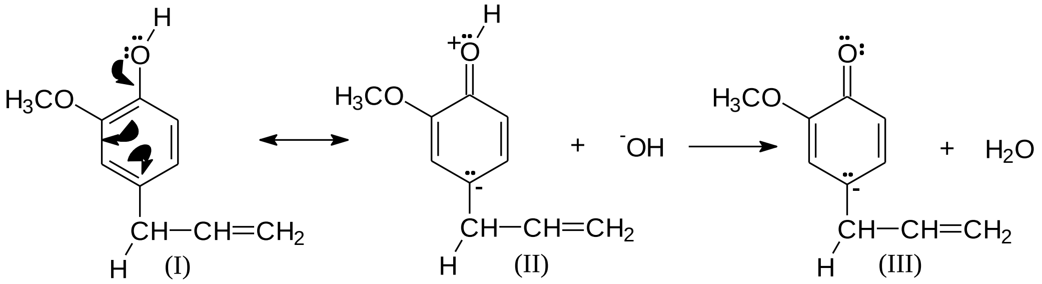
Sastrohamidjojo (1981) proposed that the mechanism of eugenol isomerization as follow.



The idea of this mechanism is the H atom that is bonded by O and C_α has positive relative charge, so it will be easy to attack by $^{-}$OH ion (base).

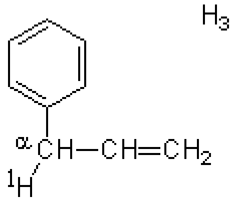


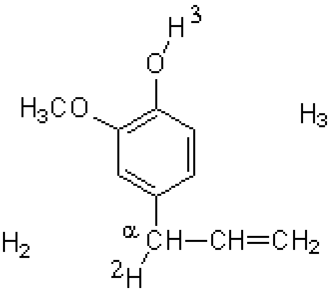
That the idea is needed to investigate. H atom with positive relative charge at C_α is possible based on induction, hyperconyugation, and carbanion stability effect. Anwar (1994) mention that the characteristic of proton benzilyc at methyl eugenol dan eugenol are less acidity than proton at allylbenzene. OH group that is bonded by phenyl at eugenol has para potition to allyl group. Therefore OH group will have resonance effect than induction effect.

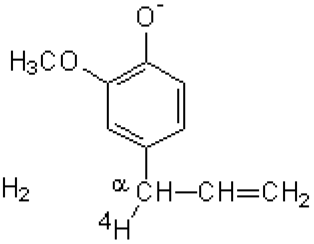


The form of resonance structure II indicated that H is bonded at O is easier to attack by $^{-}$OH ion. The form of resonance structure III indicated that C at benzene ring that bond C_{α}□ has negative charge. It will reduce the electronegativity properties of C_{α}□ to electron at C-H bond. So, it will reduce electropositive properties of H_{α}. Therefore, the H_{α} will be difficult attacked by $^{-}$OH ion.

The strength of hydrogen acidity at C_{α}□ allylbenzene, eugenol, and eugenolic ion is $H^1 > H^2$, $H^3 > H^1$, $H^3 >>> H^2$, $H^2 >>> H^4$. So, the acidity $H^3 > H^1 > H^2 > H^4$.

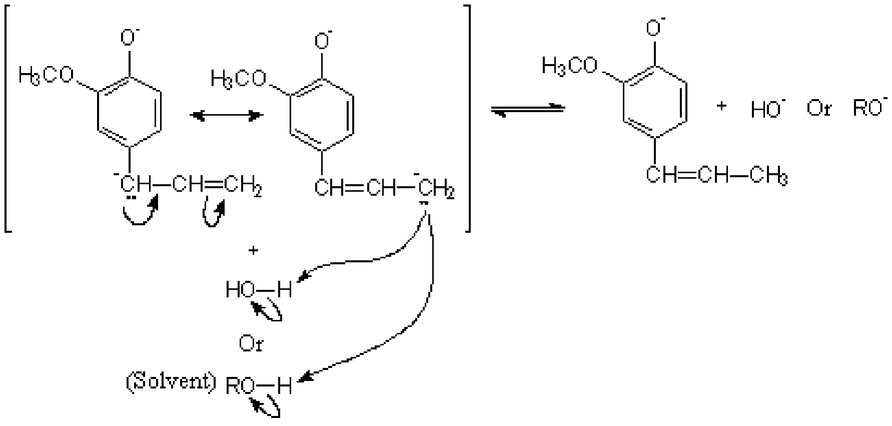

Allylbenzene


Eugenol


Isoeugenolic ion

The C atom at benzene ring to donate of electron to C_{α}□ was supported by –O-CH_3 group at meta position to allyl group, that has positive resonance effect.

Based on the condition of reaction, there are two possibities source of hydrogen, i.e. H_2O that is resulted from reaction system and ethylene glycol as a solvent. To study the reaction mechanism has investigated the water involvement, reaction condition, deuterium labeling, and reaction pathway.



2. Experiment

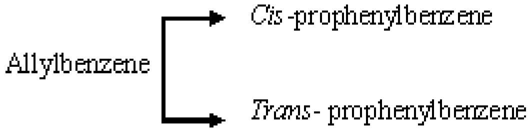
Eugenol and *cis*-isoeugenol were procured from Indesso Aroma Inc. Indonesia and it was analyzed by GCMS and FTIR spectroscopy for the characterization. Ethylene glycol, DMSO, ethanol, D_2O, KOH, HCl, diethylether, universal indicator, and vaseline for vacuum from Merck.

Procedure: Ten grams of KOH *p.a* and 40 mL of ethylene glycol were put into three necks round bottom flask that was fitted with thermometer and vacuum distillation. The reaction system was heated and stirred until all the base (KOH) dissolved. After cooling, 9.4 g of eugenol was added into the system. Reaction system was heated and stirred with vacuum distillation until the temperature of system 125^{o} C. Water as destilate was collected. Reaction system was refluxed at a 150^{o} C for 6 hours. The reaction mixture was cooled, added by 100 mL of aquades, and HCl 25% until pH of reaction mixture was about 2-3. The reaction mixture was extracted with diethyl ether, and washed with water, and then air dried using $MgSO_4$ anhidrous. The solvent was evaporated using Buchi evaporator, and the product was analyzed by GC and GCMS. The experiment was repeated with the variation of kind of solvent, times, temperatures, concentration of water, D_2O, and replace eugenol with *cis*-isoeugenol or trans-isoeugenol.

3. Result and discussion

There were five experimental data that indicated the mechamism of eugenol isomerization that was different from the mechanism of allylbenzene.

The first, reaction pathway of allylbenzene isomerization was a parallel reaction.



Three compounds were resulted in eugenol isomerization. Hence, there were three complex reaction possibilities of eugenol isomerization i.e. parallel, consecutive, and the combination of parallel and consecutive. To determine a model of complex reaction occurred, an investigation on isomerization reaction of eugenol, *cis*- and *trans*-isoeugenol have been done. The raw material of eugenol consists of 100% eugenol. The raw material of *cis*-isoeugenol consists of 5.37% of eugenol, 0.60% of 2-methoxy-4-propylphenol, 74.85% of *cis*-isoeugenol, and 18.73 of *trans*-isoeugenol. The raw material of *trans*-isoeugenol consists of 7.08% of *cis*-isoeugenol and 92.92% of *trans*-isoeugenol. Eugenol, c*is*- and *trans*-isoeugenol were refluxed respectively with KOH in ethylene glycol medium at 150^{o}C for 6 hours. The product was analysed by GC. The product of eugenol isomerization was indicated at Figure 1.

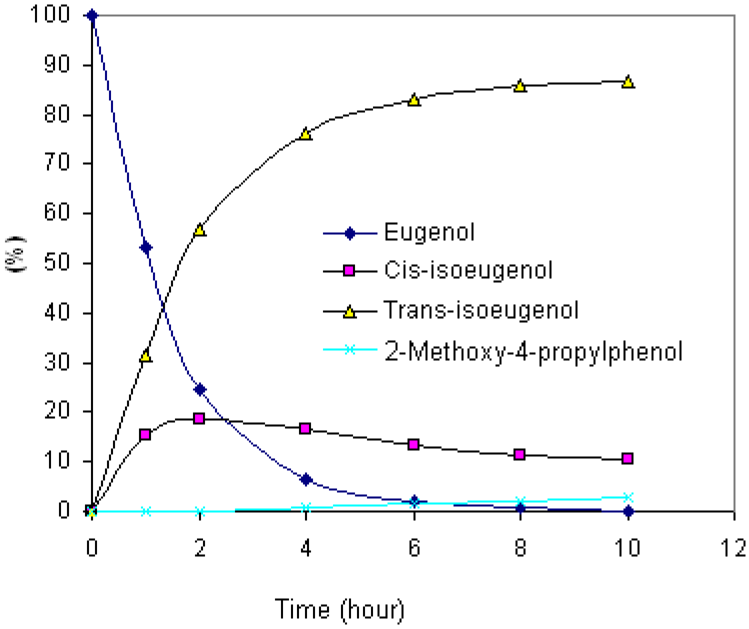
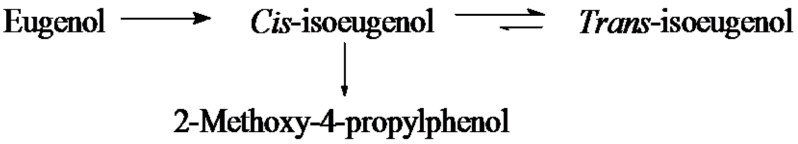


Figure 1. The influence of time to product concentration of eugenol isomerization at 150^{o}C for 6 hours

Figure 1 indicate that eugenol decrease, *trans*-isoeugenol dan 2-methoxy-4-propylphenol increase, and *cis*-isoeugenol increase and than decrease. This figure predict that the conversion of eugenol to cis- and trans-isoeugenol is consecutive. Chromatogram of GC showed that the product of *cis*-isoeugenol isomerization consists of 2.25% of eugenol, 3.77% of 2-methoxy-4-propylphenol, 11.05% of *cis*-isoeugenol, and 82,37% of *trans*-isoeugenol. By increasing 63.64% of *trans*-isoeugenol product (from 18.73 to 82,37%) it indicates that it is impossible all *trans*-isoeugenol products come from eugenol that decreases from 5.37% to 2.25% (3.12% reduction). Therefore, *trans*-isoeugenol came from *cis*-isoeugenol.

Kadarohman (1994) mentioned that 2-methoxy-4-propylphenol formations was thermodynamically controlled. To determine of 2-methoxy-4-propylphenol source is better than to carry out the isomerization reaction of *cis*- and *trans*-isoeugenol at high temperature. *Cis*-isoeugenol resulted 2-methoxy-4-propylphenol more than *trans*-isoeugenol at 165^{o}C for 6 hour. The difference was 2.78%. It mean 2-methoxy-4-propylphenol came from *cis*-isoeugenol.

Isomerization reaction product of *trans*-isoeugenol at 150^{o}C for 6 hours indicated that the amount of *trans*-isoeugenol decrease (92.92% to 85.88%) and the amount of *cis*-isoeugenol increase (7.08% to10.43%). It mean the conversion of *cis*- to *trans*-isoeugenol was reversible reaction. The reaction pathway of eugenol isomerization was a combination of parallel and consecutive.



The second, the condition of eugenol isomerization reaction is different from the condition of allylbenzene isomerization. To examine the possibilities of eugenol isomerization working at the same condition of allylbenzene isomerization reaction, eugenol isomerization reaction with KOH using ethanol solvent, oil batch temperature 158^oC and system temperature 83,5^oC (maximum temperature of reaction system) has been done for 6 hours. Chromatogram GC indicated that the eugenol isomerization did not take place.

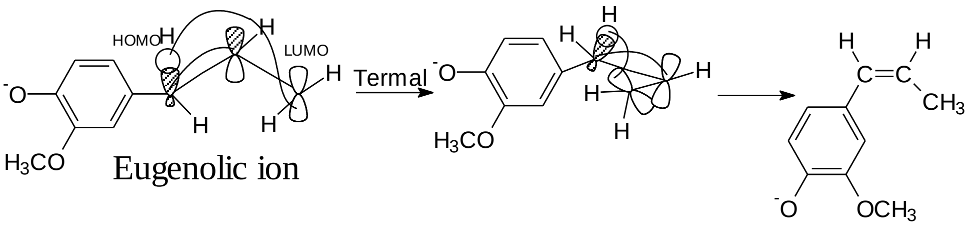
The third, water should be involved in the reaction system, if the mechanism via carbanion (dianoin). The study on the involvement of water molecule in the isomerization reaction of eugenol showed that the increase of water content in reaction system decreases isoeugenol product, but the decrease of water content in the reaction system increases isoeugenol product.

The fourth, the resulted of 2-methoxy-4-propylphenol indicates that there was hydride ion involved in eugenol isomerization reaction. It means hydrogen atom that is bonded at C_α atom has high electron density.

The fifth, to examine the water involvement, H_2O produced in reaction system was replaced with D_2O. After refluxing the reaction system for six hours at 150^oC, the reaction product were characterized by GC-MS. GC-MS spectra showed that the increase of abundance at *m/z* of 165 was relatively low, namely *cis*-isoeugenol 11,84% and *trans*-isoeugenol 10,11%. Ethylene glycol supposed to cause the abundance of *m/z* of 165 was low. To examine ethylene glycol involvement, the DMSO was used as the medium instead of ethylene glycol and H_2O produced in reaction system was replaced with D_2O. GC-MS spectra showing that the increase in abundance at *m/z* of 165 in DMSO medium was low too, namely *cis*-isoeugenol 5,63% and *trans*-isoeugenol 3,43% (1 g D_2O was added on) and *cis*-isoeugenol 19,12% and *trans*-isoeugenol 11,94% (2 g D_2O was added on). Based on these experiments, eugenol isomerization reaction to isoeugenol did not pass through carbanion intermediate. It means the conversion of eugenolic ion to *cis*-isoeugenolic ion was concerted.

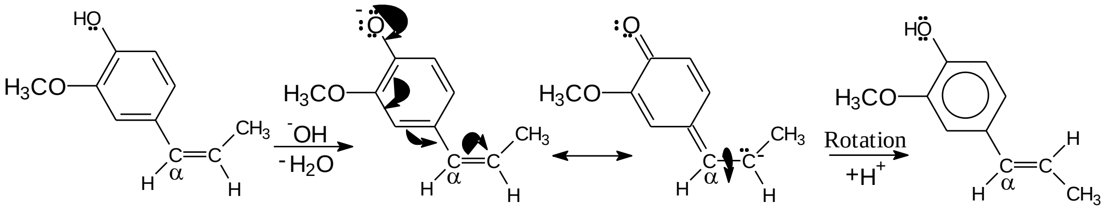
The reaction pathway of eugenol isomerization in basic condition and ethylene glycol solvent indicated there were three mechanisms that took place, namely eugenol to *cis*-isoeugenol, *cis*-isoeugenol to *trans*-isoeugenol, and *cis*-isoeugenol to 2-methoxy-4-propylphenol.

Sigmatropic rearrangement can be used to explain the concerted reaction with stereo selectivity. Fleming (1989) and Hardjosudirdjo (tt) mentioned that sigmatropic rearrangement would take place on *cis* position. Therefore, to describe the reaction mechanism of eugenolic ion to *cis*-isoeugenolic ion, it was proposed that the mechanism can be explained by frontier orbital theory, namely through antarafacial [1,3] sigmatropic rearrangement.



cis-isoeugenolic ion

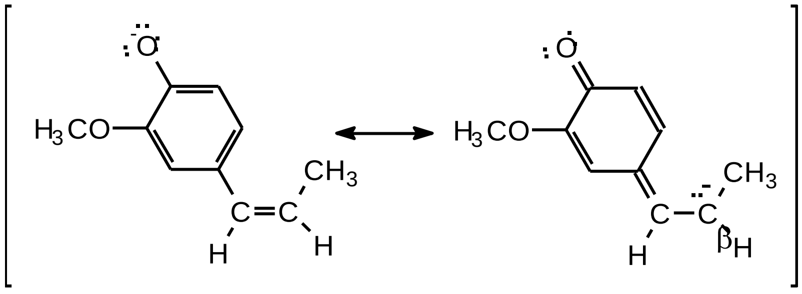
There were two mechanisms of the conversion *cis*- to *trans*-isoeugenol. *The first* was phisically mechanism by heating and *the second* was chemically mechanism as a result of adding KOH on the reaction system. Isomerization reaction of *cis*-isoeugenol using KOH in ethylene solvent and heating of *cis*-isoeugenol has been done to examine the mechanism. The products were analyzed by GC. Chromatogram GC indicated that the conversion *cis*-isoeugenol to t*rans*-isoeugenol was more easily done in basic condition than by heating. So, the reaction mechanism of *cis*- to *trans*-isoeugenol was initiated by *cis*-isoeugenolic ion formation that will be followed by resonance process to form single bond at C_1-C_2. The next step of the C_1-C_2 single bond will rotate to form stable compound (*trans*-isoeugenolic ion).



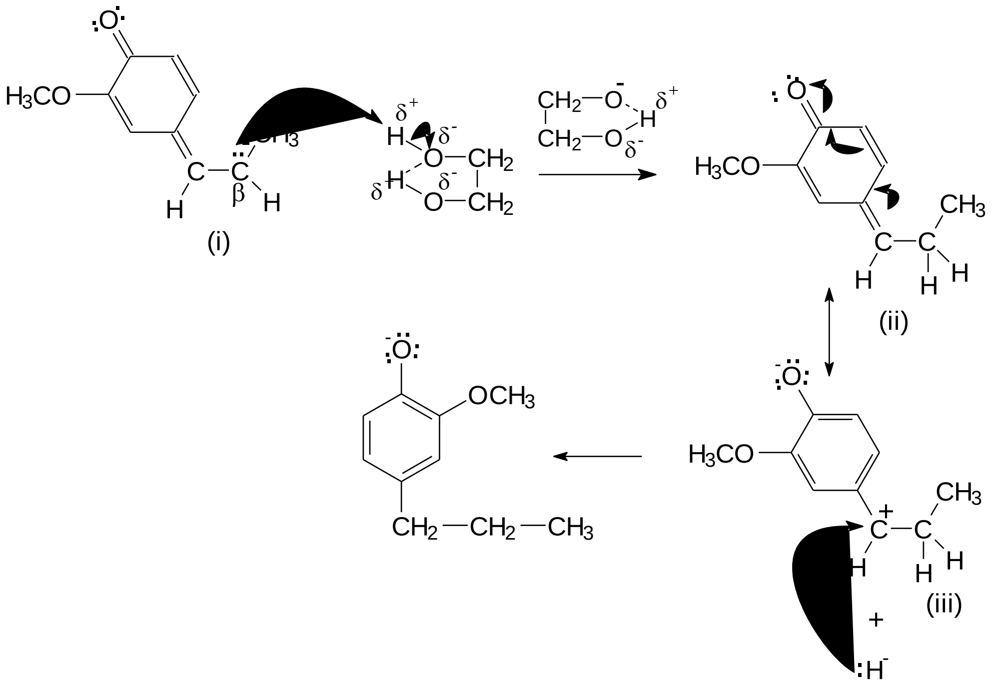
Cis-isoeugenol *Trans*-isoeugenol

The isomerization reaction of eugenol with variation of solvent (ethylene glycol, dimethyl sulfoxide, or without solvent) indicated that 2-methoxy-4-propilphenol was resulted if the reaction used ethylene glycol as solvent. The proportion of eugenol : KOH : ethylene glycol was 1 : 3 : 12.5. The amount of mol of ethylene glycol was greater than the rest of KOH. So there was still free ethylene glycol molecule in the reaction system. Unlike DMSO, ethylene glycol contains H protic as a source of proton.

2-Methoxy-4-propilphenol was not formed in the isomerization reaction if DMSO was used as solvent or the reaction did not contain solvent. This indicated that H protic atom at ethylene glycol had a role in the forming 2-methoxy-4-propilphenol. *Cis*-isoeugenol as the forming source of the 2-methoxy-4-propilphenol compound was on its ion form that was *cis*-isoeugenolic ion. The existence of free electron pairs on the phenolic group could cause resonance.



Cis-isoeugenolic ion



The electron pair, which is on C_β (i) would attack hydrogen atom with positive charge at ethylene glycol. The carbocation (iii) that was formed as the result of resonance would be attacked by hydride ion to form 2-methoxy-4-propilphenolic ion. The involvement of hydride ion in the forming 2-methoxy-4-propilphenol compound was possibly because the reaction system occured at high temperature and a very strong basic condition.

4. Conclusion

There were five experimental data that indicated the mechanism of eugenol isomerization is not through cabanion ion as intermediate, i.e. (1) The reaction pathway of eugenol isomerization to *cis*- and *trans*-isoeugenol was a consecutive, whereas the reaction pathway of allylbenzene isomerization was a parallel; (2) the solvent and temperature of eugenol isomerization reaction was different from allylbenzene isomerization; (3) water inhibited isoeugenol formation; (4) the resulted of 2-methoxy-4-propylphenol and (5) isoeugenol were labeled by deuterium atom insignificant.

To describe the reaction mechanism of eugenolic ion to *cis*-isoeugenolic ion was proposed by frontier orbital theory, namely through antarafacial [1,3] sigmatropic rearrangement. The reaction mechanism of *cis*- to *trans*-isoeugenol was initiated by *cis*-isoeugenolic ion formation that will be followed by resonance process to form single bond at C_1-C_2. The next step of the C_1-C_2 single bond will rotate to form stable compound (*trans*-isoeugenolic ion). The reaction mechanism of *cis*-isoeugenol to 2-methoxy-4-propilphenol was initiated by resonance of free electron pairs on the phenolic group, attack hydrogen atom with positive charge at ethylene glycol and hydride ion.

Acknowledgement

INDESSO AROMA Inc. Indonesia

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