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DIRECT OXIDATION OF EUGENOL USING A PERMANGANATE

Reinner Ishaq Lerrick
Chemistry Department, Faculty of Sciences and Techniques Nusa Cendana University,
Kupang, Indonesia 85112
Telp: +6285239025326
Email: i_lerrick@yahoo.com.sg

ABSTRACT

Direct oxidation of eugenol has been done using potassium permanganate. This research attempts to produce benzyl carboxylic acid, an important intermediate reactant for isoflavone synthesis, directly by breaking the π bond of allillic group attached to eugenol. The oxidation procedures were adopted from Wahyuningsih and Kusumaningsih anetol oxidation reactions. There were three modifications done i.e. one polar system of the oxidation environment, variation of time of reflux and temperature. Eugenol was firstly diluted in water by converting to its salt type and then oxidized using $KMnO_4$ at 75 ^oC for 4 hours. The expected acid was separated by acidifying using sulfuric acid.

The result showed that direct oxidation of eugenol using modified method of Wahyuningsih gave only a vicinal diol which undergoes polymerization into product in 80% yield with 83% purity. However, variation of time of reflux of Wahyuningsih method showed the same result with Kusumaningsih method as brown oily viscous liquid. The product was only 38% purity.

Keywords**: eugenol, potassium permanganate, direct oxidation**

INTRODUCTION

Isoflavone is one of secondary metabolic compounds paying attention intensively from researchers. This is because of wide and important use of this compound especially related to human health. Many research showed that soy isoflavones could decrease heart diseases by dropping blood cholesterol off, prevent breast and prostate cancer and reduce hot flash symptoms suffered by women menopausal phase (Alekel, 2000, Hillman *et al*, 2001, Naaz *et al*, 2003). Proven by *in vitro* assay, isoflavones inhibit formation of tyrosine kinase enzyme which triggers cancer cells growth. Nowadays, Daidzein and Genistein, two major constituens of soy isoflavone have been used as a medical treatment for anti-osteoporosis and prostate cancer drug, respectively (Hu *et al*, 2003, Ullmann *et al*, 2005).

Generally, retro-synthesis analysis of daidzein structure gives resorcinol and benzyl carboxylic acid derivate as the precursors (Figure 1.). Several researches followed this way. Faria *et al* (2005), in the attemp to synthesis 7,2′-dihydroisoflavone, used methoxyphenyl actate and resorcinol as the reactants. This research was even done in a one pot rection producing moderate yield percentage (83%).

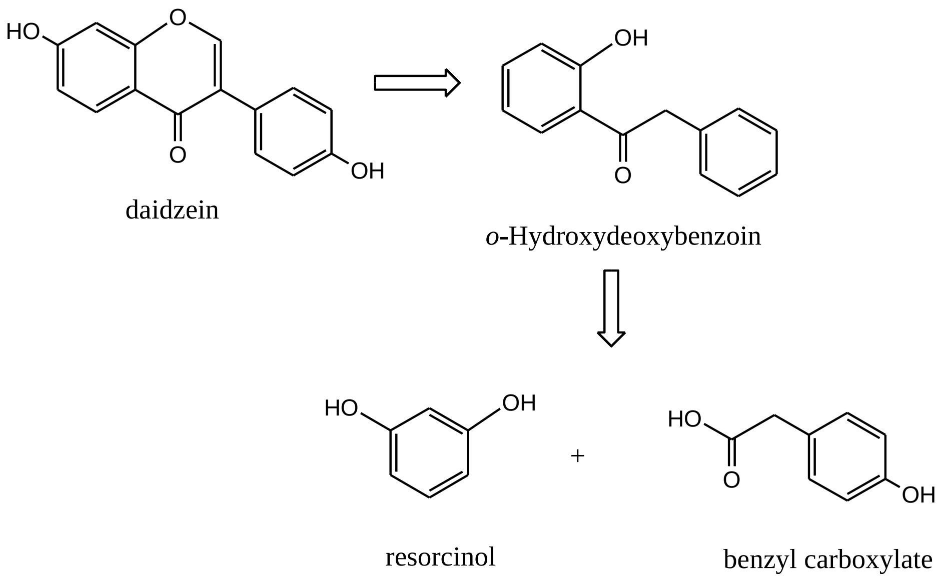

Figure 1. Retro-synthesis of daidzein

According to benzyl carboxylate structure, clove oil (one of the Indonesian essential oils) is possible to be used for dadzein derivative synthesis by converting its major constituent, Eugenol, to become an acid (Figure 2.). The conversion can be done by oxidation of the terminal alkenes group of eugenol. This method will be the simplest way for the synthesis of important intermediate compound of daidzein derivate inasmuch as many researcher follow long steps of synthesis i.e. involving three additional steps, halidation, nitrilation and hydrolysis (Whalley, 2000). Several methods have involved permanganate as an oxidizing agent such as Brown *et al* (1982), Wahyuningsih (1996) and Kusumaningsih (1999). However, all the three methods above are for different alkenes sample not for eugenol specifically.

This research was attempted to modify Wahyuningsih method of oxidation of the olephinic side chain functional group in order to change alillic functional group of eugenol to become carboxyl group. Wahyuningsih's oxidizing method was especially done for anetol. This method involve two steps of π bond breaking attached directly into the aromatic system of benzene i.e. step of synthesis of *p*-anis aldehyde and then oxidation to produce *p*-anisat. Both methods include organic solvent i.e. dichloromethane and phase transfer catalyst. According to solubility properties of eugenol in water as its salt, oxidation of the alillic functional group of eugenol is expected to be happened in polar system (water). The hypothesis is assumed that when the oxidation carried out in neutral or quite basic environment the hydroxyl ions were produced along the reaction makes eugenol dilute easily in polar system.

RESEARCH METHODOLOGY

Equipment:

Glass apparatus, three-necked round bottom flask, condenser, magnetic stirrer, exhaust gas, thermometer, vacuum rotary evaporator (Büchii R-124), analytical balance (Mettler AE-200), separator funnel, ice bath, water bath, FT-IR spectrometer (Shimadzu FTIR-820 PC), GCMS spectrometer (Shimadzu QP 5000) and ^{1}H-NMR spectrometer (Jeol JNM-MY 60).

Reagents

Eugenol, NaOH, $KMnO_4$, dichloromethane, KBr disc, $CDCl_3$, H_2SO_4. All reagents utilized were pro analysis quality from Merck except aquadest.

Method

In a 100 ml of Beaker glass was placed 0.03 mole of 97% eugenol, 10 ml of water and several mililiter of 10% sodium hydroxide was added drop wise while the solution is being stirred. This mixture was then placed in 250 ml three-neck flask equipped with a magnetic stirrer. Thermometer and dropping funnel was charged with a solution of 0.02 mole of potassium permanganate solution. After completion of the permanganate addition, the solution was refluxed for 4 hours at 75 ^{o}C. The stirring was discontinued and the product was filtered while hot. The solution was acidified using 10 M of sulphuric acid until pH = 1-2. The solution was placed into a separation funnel and then was shaked with 20 ml of dichloromethane. The organic layer was separated and the water part was extracted two times using dichloromethane. All the organic collection were placed on a rotary evaporator and the dichloromethane was removed under reduced pressure. The residue was analyzed using GCMS, FT-IR (KBr disc) and ^{1}H-NMR spectroscopy (60 MHz, $CDCl_3$).

RESULT AND DISCUSSION

Oxidation of eugenol according to Wahyuningsih method is carried out in two steps of reaction. In the first step, the addition of the permanganate was done at room temperature and the rising temperature as an excess of reaction was controlled tightly so that it does not up to 30 ^{o}C. The second step was re-oxidation of the product yielded from step one. At this condition (step 1), the direct oxidation of eugenol gives only brown oily liquid where the residue of dichloromethane is still contained as a contaminant of the product as shown in peak 1.

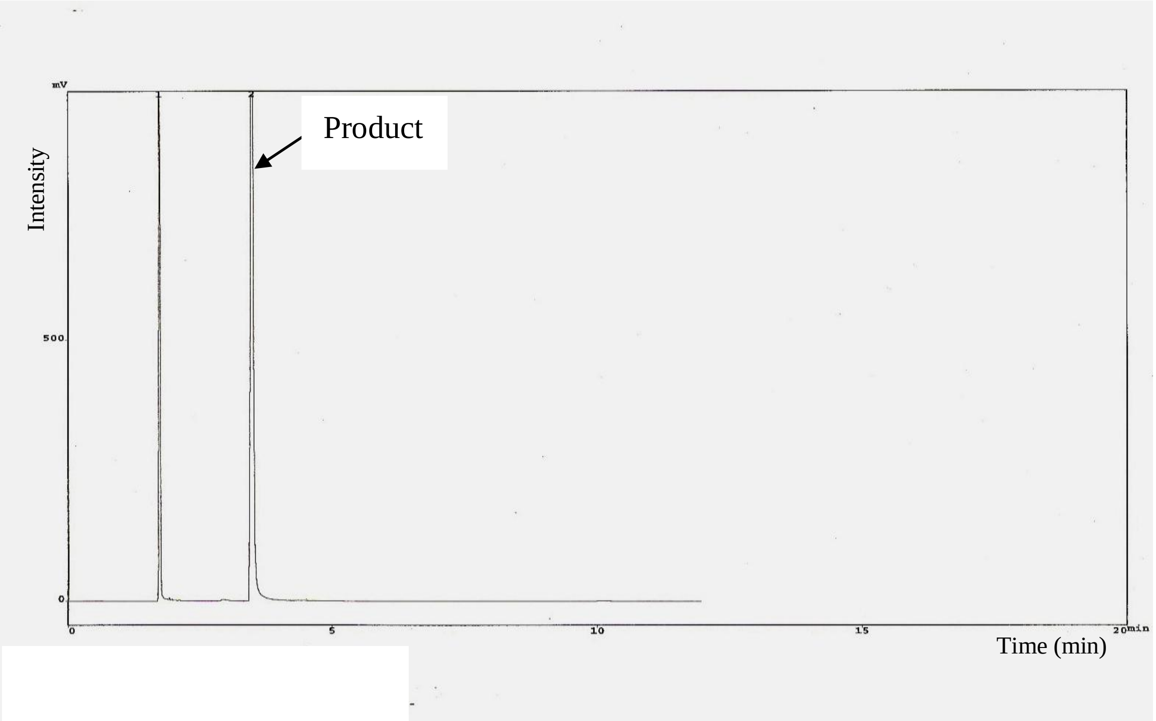

Figure 2. GC chromatogram of the oxidized eugenol

Gas chromatogram of the product showed that the compound is quite pure with 84% yield. Peak 1 (at Rt = 1.7 min) is the peak of the solvent and peak 2 (Rt = 3.5 min) is the peak of the product. This data is strengthened by comparison to GC chromatogram of Kusumaningsih oxidation method.

Infrared absorption of the product showed that the product is not the expected acid. The lack of acid carbonyl group vibration at ~1700 cm^{-1} indicates this reason strongly, even though broad absorption of hydroxyl group (O-H) at 3448.5 cm^{-1} emerge. In comparison to the IR absorption of eugenol, the absence of C=C alkenes stretching at around 1650 cm-1 presumes that the addition of π bond was occurred. The presence of IR absorption at around 1100-1200 cm^{-1} indicates that the product contains ether functional group.

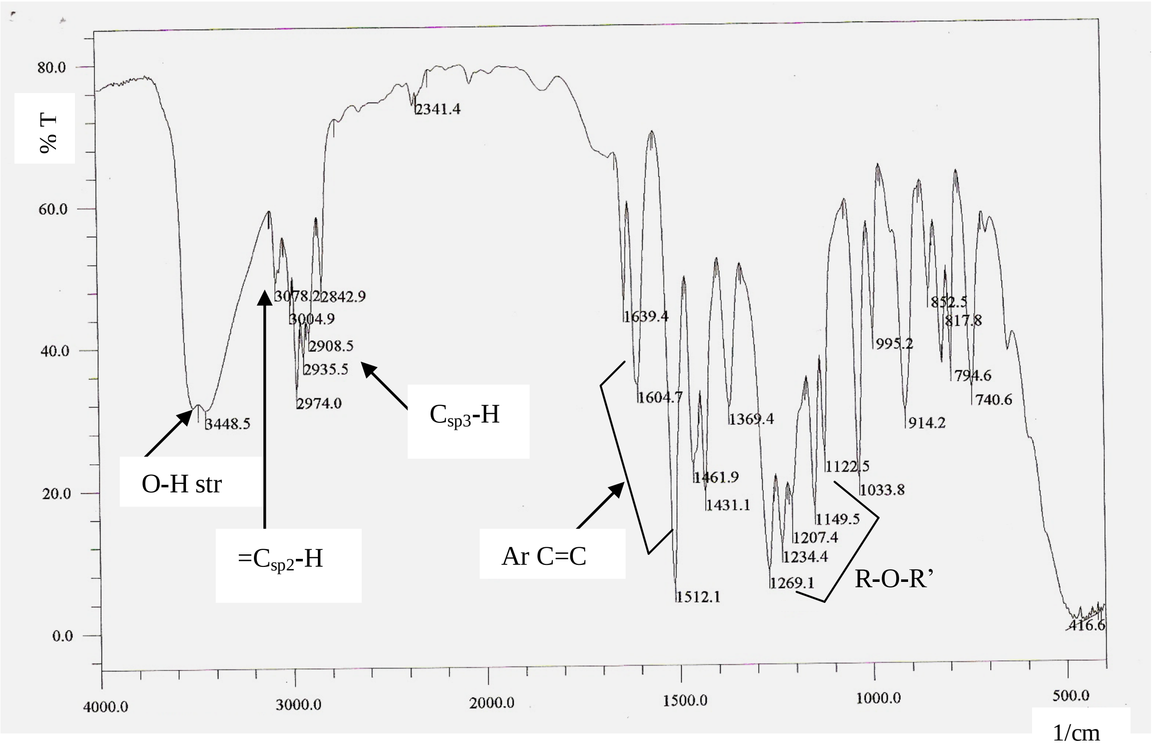

Figure 3. IR spectra of the oxidized eugenol

To confirm the assumption structure of the product, analysis using ^{1}H-NMR (in $CDCl_3$) was conducted. The spectrum showed that there are multiplex patterns of aromatic proton at their characteristic chemical shift (6.5-8.5 ppm), singlet pattern at 3.75 ppm belongs to the methylene group and chemical shift at 3.25 ppm indicates of the methoxy group which absorb more upfiled then the methylene group.

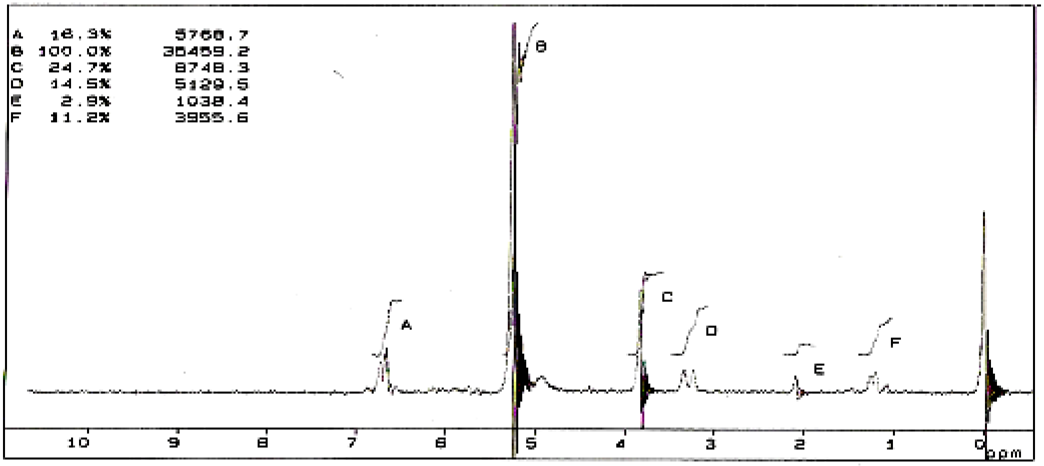

Figure 4. ^{1}H-NMR of the oxidized product

At the figure 5, the appearent of peak B may be because of solvent contamination. This is considered to the GC's purity result. The lack of magnetic resonance of phenolic proton at *ca* 7-8 ppm along with the absence of twin peaks at around 5-6 ppm due to alkene protons absoprtion indicates that the product is neither eugenol nor the desired product. The product may be diol according to the viscous oil property of the product and the presence of two magnetic absorption at 1.2 and 2.1 ppm that usually belongs to alkane.

CONCLUSION

Direct oxidation of eugenol using Wahyuningsih modified method gave only a vicinal diol which undergo polymerization as a product in 80% yield with 83% purity.

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