SYNTHESIS OF PIPERONYL ESTERS FROM COMMERCIAL ESSENTIAL OIL OF *CINNAMOMUM CULLILAWAN*, BLUME

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ABSTRACT

5-(Prop-2-enyl)benzo[*d*][1,3]dioxole as a major component of commercial essential oil of *Cinnamomum cullilawan*, Blume was separated subsequently by reaction with sodium hydroxide solution, extraction, and distillation under reduced pressure. Isomerization of 5-(Prop-2-enyl)benzo[*d*][1,3]dioxole under basic conditions furnished 5-(prop-1-enyl)benzo[*d*][1,3]dioxole which on oxidation afforded benzo[*d*][1,3]dioxole-5-carbaldehyde in good yield. Sodium borohydride reduction of benzo[*d*][1.3]dioxole-5-carbaldehyde gave benzo[*d*][1,3]dioxol-5-ylmethanol, which on reaction with carboxylic acid anhydride or acyl chloride furnished piperonyl esters in good yields. Aroma intensity of the esters is also discussed.

Key words: essential oil; synthesis; fragrances; *Cinnamomum cullilawan*, Blume

1. INTRODUCTION

Cinnamomum cullilawan, Blume originally comes from Papua, and distillation of its bark provides essential oil which has been used traditionally in Indonesia as ointment. The major components of *Cinnamomum cullilawan*, Blume are 2-methoxy-4-(prop-2-enyl)phenol and 5-(prop-2-enyl)-benzo[*d*][1,3]dioxole[1]. 2-Methoxy-4-(prop-2-enyl)phenol which is also the major component of clove oil has been transformed into various compounds such as 4-formyl-2-methoxyphenyl isobutyrate with commercial name Isobutavan®. The isobutyrate of vanillin has a sweet and creamy vanilla odor reminiscent of white chocolate, and plays an important part in the base note of commercial fragrances[2-9]. This paper reports the utility of the commercial essential oil of *Cinnamomum cullilawan*, Blume as renewable resource for the synthesis of piperonyl esters as Isobutavan® analogues. The synthesis was carried out in five steps. The first step involved separation of 5-(prop-2-enyl)benzo[*d*][1,3]dioxole from the oil, followed by isomerization in the second step to gave 5-(1-prop-1-enyl)benzo[*d*][1,3]dioxole. The third step was the oxidation of 5-(prop-1-enyl)benzo[*d*][1,3]dioxole to furnished benzo[*d*][1,3]dioxole-5-carbaldehyde, which on reduction yielded benzo[*d*][1,3]dioxol-5-ylmethanol. Reaction of the alcohol in the last step with corresponding carboxylic acid anhydride or acyl chloride afforded piperronyl esters.

2. EXPERIMENTAL

General: Commercial essential oil of *Cinnamomum cullilawan*, Blume was obtained from Ambon, Indonesia. All reagents and solvents were obtained from purchase and used without further purification. Melting points were measured using a Fisher-Johns melting point apparatus, and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a JNM-ECA300 spectrometer using TMS as the internal standard for ^{1}H and deuterated chloroform as the reference for ^{13}C. Monitoring reaction and mass spectra measurement were carried out by an Agilent 6890 series with the Agilent 5973 Plus N Mass Selective Detector. Infrared spectra were recorded with a Shimadzu 8400 S FTIR spectrometer using KBr discs. Odor intensity of the esters was examined by trained panelist from research and development department of PT. Gelora Djaja Indonesia.

Separation of 5-(prop-2-enyl)benzo[*d*][1,3]dioxole. Commercial essential oil of *Cinnamomum cullilawan*, Blume was treated thrice with 10% sodium hydroxide solution in an orbital shaker for fifteen minutes at room temperature. The water phase was combined and extracted thrice with diethyl ether. The extract was combined and mixed with the organic phase, washed with distilled water until neutral, dried over magnesium sulfate, evaporated under reduced pressure, and the remaining was distilled under reduced pressure to yield 5-(2-propenyl)benzo[*d*][1,3]dioxole as a colourless oil. Mass spectrum (EI): *m/z* 163 (M+1, 10%), 162 (M, 100), 161 (25), 135 (25), 131 (40), 104 (35), 91 (5), 77 (20), 63 (5), 51(10).

Isomerization of 5-(prop-2-enyl)benzo[*d*][1,3]dioxole. 5-(Prop-2-enyl)benzo[*d*][1,3]dioxole (2.00 g, 12.33 mmol) and potassium hydroxide (4.00 g, 71.29 mmol) in absolute ethanol (50 mL) was refluxed for fifteen hours. After cooling, the mixture was evaporated under reduced pressure. The remaining was added with water and extracted twice with diethyl ether. The extract was combined, dried over magnesium sulfate, and evaporated under reduced pressure to afford a mixture of (*E*)-5-(prop-1-enyl)benzo[*d*][1,3]-dioxole and (*Z*)-5-(prop-1-enyl)benzo[*d*][1,3]dioxole as a colourless oil (1.95 g, 98%). Mass spectrum of (*E*)-5-(prop-1-enyl)benzo[*d*][1,3]dioxole (EI): *m/z* 163 (M+1, 10%), 162 (M, 100), 161 (25), 135 (10), 131 (35), 104 (30), 91 (5), 77 (15), 63 (5), 51(5). Mass spectrum of (*Z*)-5-(prop-1-enyl)benzo[*d*][1,3]dioxole (EI): *m/z* 163 (M+1, 10%), 162 (M, 100), 161 (30), 135 (15), 131 (45), 104 (35), 91 (5), 77 (20), 63 (5), 51(10).

Oxidation of 5-(prop-1-enyl)benzo[*d*][1,3]dioxole. 5-(Prop-1-enyl)benzo[*d*][1,3]dioxole (1.90 g, 11.72 mmol), potassium hydroxide (4.75 g, 84.66 mmol), nitrobenzene (10 mL, 97.43 mmol) in dimethyl sulfoxide (20 mL) and water (10 mL) was refluxed for ten hours. After cooling, water and diethyl ether were added, and the mixture was shaken with orbital shaker for 45 minutes and filtered. The ether phase was separated and treated with sodium bisulfite solution 1.92 M; the aqueous phase was subsequently separated, acidified with concentrated sulfuric acid, heated at 50-60 °C for 40 minutes, allowed to cool at room temperature, and extracted thrice with diethyl ether. The extract was combined, dried over magnesium sulfate, and evaporated under reduced pressure. The remaining was recrystallized from cyclohexane to furnish benzo[*d*][1,3]dioxole-5-carbaldehyde as a white solid (1.53 g, 87%), mp 38-39 °C (Lit. 37 °C)[10]. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.04 (s, 2H), 6.88-7.36 (m, 3H), 9.77 (s, 1H). Mass spectrum (EI): *m/z* 151 (M+1, 10%), 150 (M, 80), 149 (100), 121 (20), 91 (10), 78 (20), 63 (40).

Benzo[*d*][1,3]dioxole-5-carbaldehyde reduction. Benzo[*d*][1,3]dioxole-5-carbaldehyde (0.99 g, 6.59 mmol) and sodium borohydride (0.41 g, 10.25 mmol) in absolute ethanol (10 mL) was refluxed for thirty minutes. After cooling, the mixture was evaporated under reduce pressure. The remaining was suspended in 10% aqueous sodium hydroxide (10 mL), and extracted with diethyl ether. The extract was dried over magnesium sulfate, evaporated under reduced pressure, and the residue was recrystallization from methanol to give benzo[*d*][1,3]dioxol-5-ylmethanol as a white solid (0.96 g, 96%), m.p. 53-55 °C (Lit. 49-51 °C)[11]; ν_{max} (KBr): 3310, 2908, 1442, 1249, 1041, 810 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.36 (bs, 1H), 4.51 (s, 2H), 5.91 (s, 2H), 6.74-6.82 (m, 3H). Mass spectrum (EI): *m/z* 153 (M+1, 10%), 152 (M, 100), 135 (50), 121 (25), 110 (5), 93 (40), 65 (30).

Synthesis of piperonyl esters. Benzo[*d*][1,3]dioxol-5-ylmethanol was treated with carboxylic acid anhydride or acyl chloride in pyridine and the reaction was monitored by gas chromatography-mass spectrometer. The mixture was then acidified with 3% hydrochloric acid, added with cold water, and extracted with diethyl ether. The extract was dried over magnesium sulfate, evaporated under reduced pressure to furnish piperonyl esters:

Benzo[*d*][1,3]dioxol-5-ylmethyl acetate (1): a yelowish oil (yield: 77%); ν_{max} (KBr): 3075, 2955, 1740, 1447, 1242; 1037, 810 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.01 (s, 3H); 4,93 (s, 2H); 5,86 (s, 2H); 6.70-6.78 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 20.70, 66.00, 101.02, 107.99, 108.84, 122.07, 129.63, 147.46, 147.65, 170.55. Mass spectrum (EI): *m/z* 195 (M+1, 7%), 194 (M, 64), 152 (57), 135 (100), 122 (11), 104 (11), 93 (10), 77 (23), 65 (11), 51 (10).

Benzo[*d*][1,3]dioxol-5-ylmethyl propanoate (2): a yelowish oil (yield: 72%); ν_{max} (KBr): 3075, 2982, 1736, 1447, 1041, 810 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.08 (t, *J*=8.0 Hz, 3H); 2.30 (q, *J*=8.0 Hz, 2H); 4.95 (s, 2H); 5.87 (s, 2H); 6.69-6.78 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.66, 27.26, 66.07, 101.09, 108.07, 108.87, 122.09, 129.82, 147.53, 147.74, 174.35. Mass spectrum (EI): *m/z* 209 (M+1, 5%), 208 (M, 40), 152 (50), 135 (100), 122 (10), 105 (7), 93 (5), 77 (15), 65 (5), 51 (7).

Benzo[*d*][1,3]dioxol-5-ylmethyl 2-methylpropanoate (3): a yelowish oil (yield: 66%); ν_{max} (KBr): 3075, 2974, 1732, 1447, 1041, 810 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.15 (d, 6H); 2.53-2.54 (m, 1H); 4,99 (s, 2H); 5,91 (s, 2H); 6.74-6.81 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 18.99, 34.09, 66.11, 101.21, 108.26, 108.88, 122.06, 130.14, 147.63, 147.89, 177.02. Mass spectrum (EI): *m/z* 223 (M+1, 5%), 222 (M, 35), 152 (25), 135 (100), 122 (2), 105 (5), 93 (3), 77 (13), 65 (5), 51 (6).

3. RESULTS AND DISCUSSION

Separation of 5-(prop-2-enyl)benzo[*d*][1,3]dioxole. Analysis of commercial essential oil of *Cinnamomum cullilawan*, Blume by gas chromatography-mass spectrometer showed the presence of sixteen components. The major components of the oil were 5-(prop-2-enyl)benzo[*d*][1,3]dioxole (25%) and 2-methoxy-4-(2-propenyl)phenol (61%). 5-(Prop-2-enyl)benzo[*d*][1,3]dioxole was separated from the oil following slight modification of 4-allyl-2-methoxyphenol separation from clove leaf oil[4]. The oil was treated with sodium hydroxide solution to separate phenolic compounds, and the remaining non phenolic compounds after extraction were distilled under reduced pressure to yield 5-(prop-2-enyl)benzo[*d*][1,3]dioxole as a colourless oil. The mass spectrum (EI) showed a molecular ion peak at *m/z* 162, which was also the base peak, corresponded to the relative mass of 5-(prop-2-enyl)benzo[*d*][1,3]dioxole, and elimination of a vinyl radical gave a peak at *m/z* 135.

Isomerization of 5-(prop-2-enyl)benzo[*d*][1,3]dioxole. Isomerization was carried out by refluxing 5-(prop-2-enyl)benzo[*d*][1,3]dioxole in absolute ethanol under basic condition, following isomerization procedure of 2-methoxy-4-(2-propenyl)phenol[12]. GCMS analysis showed the isomerization product as (*Z*)-5-(prop-1-enyl)benzo[*d*][1,3]dioxole in 76% and (*E*)-5-(prop-1-enyl)benzo[*d*][1,3]dioxole in 24%. Mass spectra of the two isomers quite similar, only relative abundance of fragments were slightly difference.

Oxidation of 5-(prop-1-enyl)benzo[*d*][1,3]dioxole. 5-(Prop-1-enyl)benzo[*d*][1,3]dioxole was oxidized in the mixture of nitrobenzene, potassium hydroxide, dimethyl sulfoxide and water; following the oxidation of of 2-methoxy-4-(2-propenyl)phenol[4,12]. The oxidation product was purified in two steps as sodium bisulfite adduct and by recrystallization from cyclohexane to yield benzo[*d*][1,3]dioxole-5-carbaldehyde as a white solid. The ^{1}H NMR spectrum of benzo[*d*][1,3]dioxole-5-carbaldehyde (in $CDCl_3$) exhibited singlet signal at 6.04 ppm assignable to the methylene group protons, multiplet signal at 6.88-7.36 ppm for the three aromatic protons, and singlet signal at 9.77 ppm for aldehyde group proton. The mass spectrum fitted with the formula mass of benzo[*d*][1,3]dioxole-5-carbaldehyde by indicating a molecular ion at *m/z* 150, and a base peak at *m/z* 149 obviously resulted from

expulsion of hydrogen atom of aldehyde group. Elimination of aldehyde group furnished a fragment with a peak at *m/z* 121.

Reduction of Benzo[*d*][1,3]dioxole-5-carbaldehyde. Reduction of benzo[*d*][1,3]dioxole-5-carbaldehyde was carried out by following the sodium borohydride reduction 4,6-dimethoxy-1-methylindol-3-carbaldehyde to 4,6-dimethoxy-3-hydroxymethyl-1-methylindole procedure[13]. The most significant feature of ^{1}H NMR of benzo[*d*][1,3]dioxol-5-ylmethanol (in $CDCl_3$) was the presence of two signals at 2.36 and 4.51 ppm corresponding to hydroxymethyl protons of benzo[*d*][1.3]dioxol-5-ylmethanol, and a singlet signal for aldehyde proton at 9.77 ppm for benzo[*d*][1,3]dioxole-5-carbaldehyde has disappeared. IR spectrum of benzo[*d*][1,3]dioxol-5-ylmethanol clearly exhibited a stretching vibration band 3310 cm^{-1} for the hydroxy group. Mass spectrum indicated a molecular ion which was also the base peak at *m/z* 152, corresponded to the relative mass of benzo[*d*][1,3]dioxol-5-ylmethanol. Expulsion of hydroxyl group and hydroxymethyl group gave rise to peaks at *m/z* 135 and 121 respectively.

Synthesis of piperonyl esters. Synthesis of piperonyl esters ware performed by adapting the synthesis procedure of 4-formyl-2-methoxyphenyl isobutyrate[4]. The comparison of spectral data of piperonyl esters can be seen in Table 1-3. Aroma intensity was evaluated by eleven trained panelits of Research and Development, PT Gelora Djaja Indonesia, in six grade: exellent [6], extremely good [5], very good [4], good [3], fair [2] and poor [1][14]. Table 4 exhibited that benzo[*d*][1,3]dioxol-5-ylmethyl propanoate has an exellent aroma, and benzo[*d*][1,3]dioxol-5-ylmethyl acetate and benzo[*d*][1,3]dioxol-5-ylmethyl 2-methylpropanoate have extremelly good aroma.

Table 1. The comparison of NMR spectral data of piperonyl esters

Protons	^{1}H NMR (in ppm)			Carbons	^{13}C NMR (in ppm)		
	(1)	**(2)**	**(3)**		**(1)**	**(2)**	**(3)**
$-CH_3$	2.01 (s, 3H)			$-CH_3$	20.70		
CH_3CH_2-		1.08 (t, 3H)		CH_3CH_2-		8.66	
CH_3CH_2-		2.30 (q, 2H)		CH_3CH_2-		27.26	
$(CH_3)_2CH-$			1.15 (d, 6H)	$(CH_3)_2CH-$			18.99
$(CH_3)_2CH-$			2.53-2.58 (m, 1H)	$(CH_3)_2CH-$			34.09
$-CH_2O-$	4.93 (s, 2H)	4.95 (s, 2H)	4.99 (s, 2H)	$-OCH_2-$	66.00	66.07	66.11
$-OCH_2O-$	5.86 (s, 2H)	5.87 (s, 2H)	5.91 (s, 2H)	$-OCH_2O-$	101.02	101.09	101.21
ArH	6.70-6.78 (m, 3H)	6.69-6.78 (m, 3H)	6.74-6.81 (m, 3H)	ArCH	107.99	108.07	108.26
					108.84	108.87	108.88
					122.07	122.09	122.06
				ArC	129.63	129.82	130.14
					147.46	147.53	147.63
					147.65	147.74	147.89
				$-CO_2-$	170.55	174.35	177.02

Table 2. The important fragments of mass spectral data of piperonyl esters

Compounds	*m/z* (Relative Abundance in %)										
(1)			194 (35)	152 (57)	135 (100)	122 (11)	105 (11)	93 (10)	77 (23)	65 (11)	51 (10)
(2)		208 (40)		152 (50)	135 (100)	122 (10)	105 (7)	93 (5)	77 (15)	65 (5)	51 (7)
(3)	222 (64)			152 (25)	135 (100)	122 (2)	105 (5)	93 (3)	77 (13)	65 (5)	51 (6)

Table 3. The comparison of IR mass spectral data of piperonyl esters

Compounds	IR vibration (in cm^{-1})					
	C-H_{Ar}	C-H_{Alk}	C=O	C-O	C=C	C-H_{Ar}
(1)	3075 (w)	2955 (w)	1740 (m)	1037 (s)	1447 (s)	810 (m)
(2)	3075 (w)	2982 (w)	1736 (m)	1041(s)	1447 (s)	810 (m)
(3)	3075 (w)	2974 (w)	1732 (m)	1041(s)	1447 (s)	810 (m)

Table 4. The aroma intensity data of piperonyl esters

Compounds	Scales	Category
(1)	4.7	Extremely good aroma
(2)	6.0	Excellent aroma
(3)	5.1	Extremely good aroma

4. CONCLUSIONS

Piperonyl esthers have been synthesized in five steps from commercial essential oil of *Cinnamomun cullilawan*, Blume. Aroma intensity of the piperonyl esters is in the range of extremely good to excellent, and aroma intensity of benzo[*d*][1,3]dioxol-5-ylmethyl propanoate is the highest one. Various benzo[*d*][1,3]dioxole-5-carbaldehyde derivatives are being synthesized in order to optimize the role of the oil as renewable starting material for the synthesis of various fragrances.

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