

toluene (18.5mg,0.5mM) and the solution was evacuated in order to remove the moisture by azeotropic distillation until it became anhydrous. To this solution was added camphorsulfonic acid (50mg, 5%), and this mixture was heated in a boiling water bath for 30 min. The consumption of sesamol (1) and simultaneous formation of sesaminol (2abc) were monitored by analyzing aliquot of the reaction mixture with HPLC (Develosil ODS-10) (MeOH:H₂O 7:3). It showed that the latter was produced in 78.8% yield, which was isolated by preparative TLC. Its ¹H-nmr spectrum actually showed the presence of three diastereoisomers of sesaminol in both fractions by the industrial acid clay process and from the model acidic treatment, though proportion of the isomers were different*. However, HPLC could not completely separate the theoretically possible four diastereoisomers. One of the three sesaminol isomers (2b) was analyzed by X-ray crystallographic analysis of its 3,5-dinitrobenzoate derivative (it will be reported elsewhere soon). When the ethanol solution of sesamol in a buffer (1 M HCl-CH₃COONa at pH 1.0) was heated in a boiling water bath for 30 min, all the amount of sesamol was hydrolysed into sesamol (4), samin (8)⁴⁾ and an ethanolsate (7)⁵⁾ but no sesaminol was produced (see Fig. 2). Formation of sesaminol (2abc) from sesamol (1) proceeded under an anhydrous condition in the presence of an acid as catalyst with

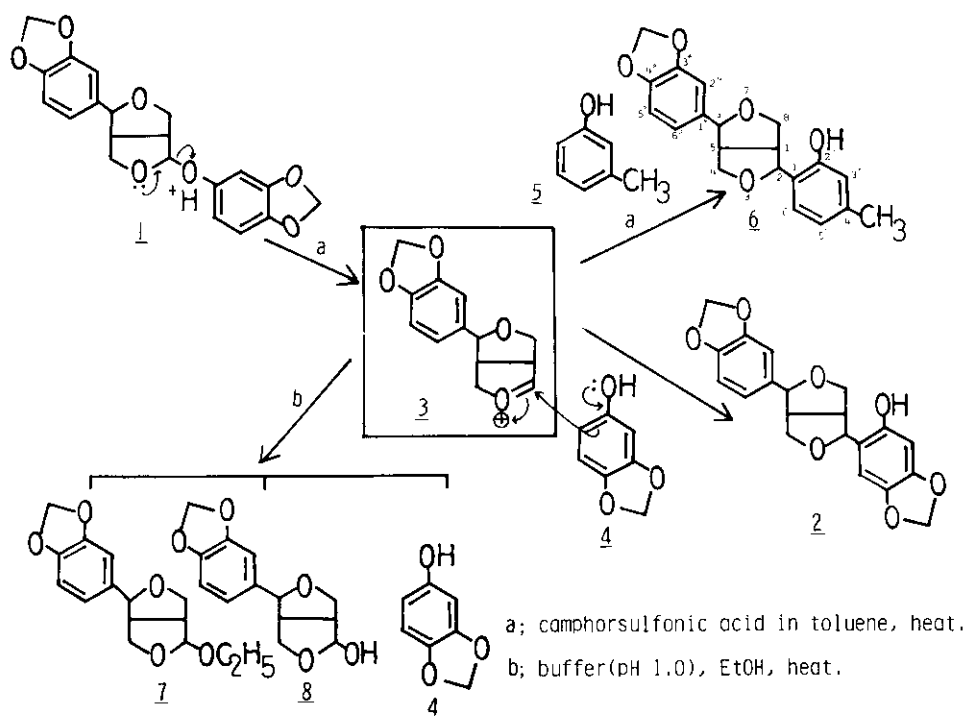


Fig. 2. Scheme for the mechanism of formation of sesaminol from sesamol.

*The ratio of sesaminol : 6 alpha-isomer : 2alpha-isomer was 1:1:1 in industrial process, while in the model acidic treatment it was found to be 1:0.3:1.

heating as shown in Fig. 3. Under this condition, it was postulated that sesamol was first decomposed into sesamol by protonolysis to form the oxonium ion (3) and then the carbon-carbon bond was formed at the indicated position in Fig. 2. The product sesaminol in fact existed as a mixture of the three diastereoisomers. In order to support the above mechanism, the following scrambling test was examined by addition of *m*-cresol (5) as a competitor in case of intermolecular mechanism to the acidic reaction mixture of sesaminol. The expected new compound (6)⁶ was formed, when *m*-cresol was added to the reaction mixture containing camphorsulfonic acid in toluene. The amounts of sesaminol (2), sesamol (4) and 6 were analyzed by HPLC to show that amount of 6 was increased according to the increasing amount of *m*-cresol in the reaction mixture as shown in Fig. 4. In the ¹H-nmr spectrum of 6, the sharp singlet at δ 2.3 was due to the aromatic methyl, while chemical shifts of H-6, H-1/5, H-4a/8a and H-4e/8e in the fused tetrahydrofuran ring were

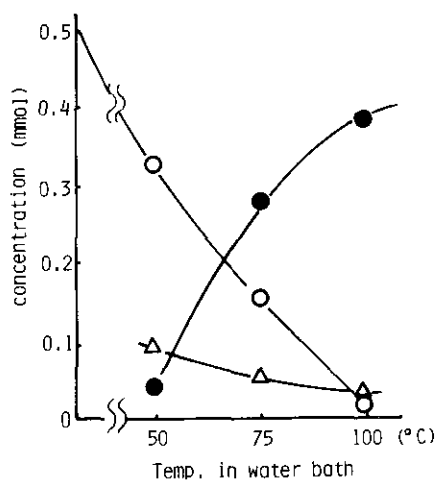


Fig. 3. Effect of reaction temperature on the formation of sesaminol from sesaminol.
 -○- sesaminol, -●- sesaminol, -△- sesamol

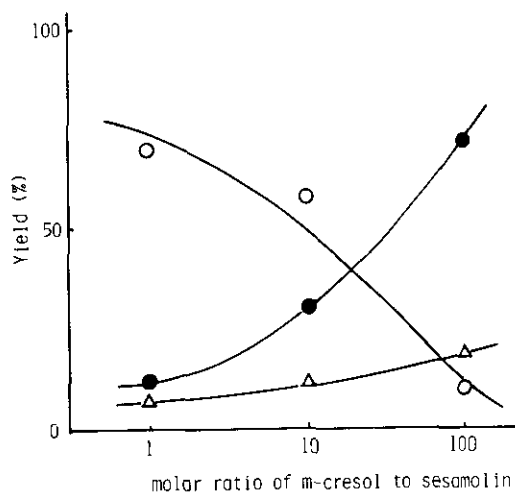


Fig. 4. Effect of the amount of *m*-cresol on sesaminol, sesamol and 6 yields.
 -○- sesaminol, -●- 6, -△- sesamol

very similar to those of sesaminol (2). But H-2 was found downfield because of the cresol ring and the singlet at δ 5.96 ppm was assigned to the dioxy-methylene protons suggesting the presence of only one methylenedioxy group (Table 1). The substitution pattern of the cresol fragment should be either 1', 2', 4', or 1', 2', 6'. In ¹H-nmr spectrum (500 MHz), aromatic six protons located between δ 6.64 and δ 6.94 and H-5' was observed at δ 6.67 (1H, broad doublet) to couple with doublet (1H, $J=7.4$) at δ 6.91 and broad singlet (1H) at δ 6.72 due to H-6' and H-3', respectively. Three aromatic protons at 6.79 (2H, s) and 6.84 (1H, s) were ascribable to methylenedioxyphenyl group³⁾ then its substitution pattern was confirmed to be 1', 2', 4'.

The results of above scrambling experiments and the reaction in a buffer medium suggested involve-

Table 1 $^1\text{H-NMR}$ data of Sesaminol(2) and 6.

	sesaminol(2)	6
H-1/5	3.14(2H,m)	3.18(2H,m)
H-2/6	4.76(2H,d, J=3.8)	4.80(1H,d, J=4.0) 4.90(1H,d, J=6.8)
H-4a/8a	3.86(2H,m)	3.88(2H,m)
H-4e/8e	4.14,4.36(2H,m)	4.16(1H,d,d, J=6.8, 9.7) 4.38(1H,d,d, J=7.4, 9.7)
-OCH ₂ O-	5.90, 5.97(4H,s)	5.96(2H,s)
Ar-CH ₃		2.3(3H,s)
Ar-OH	7.6(1H,s)	7.9(1H,s)

δ (ppm), J(Hz), TMS, solutions in CDCl_3 , 200MHz spectra

ment of intermolecular process in sesaminol formation from sesamolin. Biosynthetically, lignans were known to be constructed by oxidative coupling of two molecules of phenylpropanoid units¹⁾(for example, sesamin was thought to be formed by two molecules of coniferyl alcohol). Above mechanism implies the retro-process of the oxidative bio-degradation to form the original C-C bond which affords antioxidants back.

REFERENCE AND NOTE

1. Y.Fukuda, T.Osawa, M.Namiki and T.Ozaki, *Agric. Biol. Chem.*, 1985, 49, 301.
2. T.Osawa, M.Nagata, M.Namiki and Y.Fukuda, *Agric. Biol. Chem.*, 1985, 49, 3351.
3. Y.Fukuda, M.Nagata, T.Osawa and M.Namiki, *J. Am. Oil Chem. Soc.*, 1986, in press.
4. Samin (8): Samin does not appear to have been investigated since its isolation by Adriani (mp 106°C, $[\alpha]_D^{20}=+103^\circ$, *Untersuch Lebensm.*, 1928, 56, 187). This is the first success in the characterization to confirm the structure of samin although its structure was postulated by Budowski (*J. Am. Oil Chem. Soc.*, 1964, 41, 280). Instrumental analyses: ms (m/e) 249 (M^+), 203, 194, 175, 149, 135. uv (95%EtOH) $_{\lambda}$ max nm (log ϵ): 236 (4.06), 288 (4.04). $[\alpha]_D^{20}=+81.4^\circ$ (c=0.5, CHCl_3). $^1\text{H-nmr}$ δ (CDCl_3): 2.87 (1H, m, H-5), 3.09 (1H, m, H-1), 3.58 (1H, d,d, J=9.0 and J=7.6, H-8a), 3.92 (1H, d,d, J=9.0 and J=1.0, H-4a), 4.05 (1H, d,d, J=9.0 and J=6.3, H-4e), 4.34 (1H, d, J=7.0, H-6), 4.38 (1H, t, J=9.0, H-8e), 5.39 (1H, s, H-2), 5.96 (2H, s, -OCH₂O-), 6.71-7.37 (3H, m, Ar-H). Acetylation of 8: ms (m/e): 292 (M^+), 233, 203, 150, 149, 135.
5. Ethanolysate: ms (m/e) 278 (M^+), 248, 233, 203, 150, 149, 135. uv (95%EtOH) $_{\lambda}$ max nm : 238, 285, $[\alpha]_D^{20}=+82.7^\circ$ (c=0.5, CHCl_3).
6. 6: $\text{C}_{20}\text{H}_{20}\text{O}_5$, Found 340.1328, Calcd. 340.1311, ms (m/e), 340 (M^+), 322, 308, 279, 203, 194, 149, 135, 121, uv (95%EtOH) $_{\lambda}$ max nm (log ϵ): 222 (3.98), 284 (3.77), $[\alpha]_D^{20}=+42.60^\circ$ (c=0.33, CHCl_3).
7. Kurt B.G. Torssell, "Natural Product Chemistry," Wiley, NY, 1983, pp101-108.

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