Title	Dehydrogenative Polymerization of 3,5-Disubstituted p-Coumaryl Alcohols
Author(s)	TANAHASHI, Mitsuhiko; TAKEUCHI, Hideo; HIGUCHI, Takayoshi
Citation	Wood research : bulletin of the Wood Research Institute Kyoto University (1976), 61: 44-53
Issue Date	1976-10-30
URL	http://hdl.handle.net/2433/53378
Right	
Type	Departmental Bulletin Paper
Textversion	publisher

Dehydrogenative Polymerization of 3, 5-Disubstituted *p*-Coumaryl Alcohols*

Mitsuhiko TANAHASHI**, Hideo TAKEUCHI**
and Takayoshi HIGUCHI**

Abstract——3, 5-Disubstituted *p*-coumaryl alcohols (3-methoxy-5-iodo-, 3, 5-diiodo-, 3-methoxy-5-nitro-, 3, 5-dinitro-, 3, 5-dimethoxy- and 3, 5-dimethyl-*p*-coumaryl alcohols) were synthesized and dehydrogenated to their dimeric compounds with ferric chloride in dioxane (nonpolar solvent) and acetone-water (polar solvent), respectively. Yields of the β-ethers were, for example, 85 % (sinapyl alcohol) and 86 % (3, 5-diiodo-*p*-coumaryl alcohol) in dioxane, and 27 % (the former) and 80 % (the latter) in acetone-water, respectively. These results suggest that the most effective factor in the radical coupling of these alcohols is the electronic effects of the substituent groups, but not the steric hindrance. Syringylglycerol-β-sinapyl ether was obtained in a high yield from sinapyl alcohol when dioxane was used as a solvent.

Introduction

FREUDENBERG[1] reported that a mixture of coniferyl and sinapyl alcohols in equal amounts is dehydrogenated to a polymer similar to angiosperm lignin, but sinapyl alcohol alone does not form a lignin-like polymer but yields mainly syringaresinol. From these results, FREUDENBERG doubted the occurrence of syringyl lignin in nature. However, FERGUS and GORING[2] proposed on the basis of spectral analysis of lignin in cell walls with a UV microscope that birch lignin deposited in the secondary layers of wood fibers and parenchyma cell walls is composed of mostly syringyl component. Furthermore YAMASAKI, HATA and HIGUCHI[3,4] recently found that a considerable amount of DHP was formed from sinapyl alcohol alone with peroxidase and H_2O_2 in water.

In the "Zulauf" method, dehydrogenative dimerization of coniferyl and *p*-coumaryl alcohols with peroxidase and H_2O_2 in water gave 54 % and 48 % of phenylcoumaranes, 19 % and 20 % of arylglycerol-β-aryl ethers, and 27 % and 32 % of resinols, respectively[5]. However the dehydrogenation of sinapyl alcohol gives only a limited number of products because 5-position of the aromatic ring of sinapyl alcohol is unavailable for coupling, and β-β-coupling is the almost exclusive dehydrogenation reaction which gives syringaresinol in 80 to 90 % yields in the same Zulauf condition. The difference of the radical coupling reactions between coniferyl and

* Presented partly at the 20th Symposium on Lignin Chemistry, Nagoya, Oct. 1975.
** Division of Lignin Chemistry.

sinapyl alcohols has been so far ascribed by FREUDENBERG to the steric hindrance of two methoxyl groups of sinapyl alcohol, which was believed to give no syringylglycerol-*β*-sinapyl ether.

However, racemization rate of optically active *o*-substituted biphenyls[6] and the van der Waals radius of the substituted groups are concerned, the methoxyl group belongs to a class of relatively smaller bulkiness. Since syringylglycerol-*β*-syringylglycerol ether was isolated as a degradation product of Yachidamo (*Fraxinus mandshurica*) lignin[8], *β*-0-4 coupling is considered to be formed even between two molecules of sinapyl alcohol. Therefore, in the present investigation, 5-position of coniferyl alcohol and 3- and 5-positions of *p*-coumaryl alcohol were substituted by iodine, nitro or methyl groups which are more bulky than methoxyl group, and their reactivities in dehydrogenations were compared to that of sinapyl alcohol.

Experimental

Synthesis of 3, 5-disubstituted *p*-coumaryl alcohols

Sinapyl, coniferyl and p-coumaryl alcohols were synthesized by the methods of FREUDENBERG[9].

5-Iodo vanillin and 3, 5-diiodo p-hydroxybenzaldehyde were synthesized from vanillin and *p*-hydroxybenzaldehyde by the method of ERDTMAN[10].

5-Nitro vanillin was synthesized from vanillin by the method of ACERBO, SCHUBERT and NORD[11].

3, 5-Dinitro p-hydroxybenzaldehyde was synthesized by nitration of *p*-cresol according to the reference 11 and subsequent oxidation of 3, 5-dinitro *p*-cresol with anhydrous cromic acid by the method of LIEBERMAN and CONNOR[12].

○ 3, 5-Dinitro *p*-cresol

NMR ($CDCl_3$) δ: 2.44 (3H, s), 8.13 (2H, s), 11.19 (1H, broad).

○ 3, 5-Dinitro *p*-hydroxybenzaldehyde

NMR ($CDCl_3$) δ: 8.80 (2H, s), 10.01 (1H, s).

3, 5-Dimethyl p-hydroxybenzaldehyde was synthesized from 2, 6-dimethylphenyl according to the method of SMITH[13].

NMR ($CDCl_3$) δ: 2.22 (6H, s), 5.78 (1H, broad), 7.53 (2H, s), 9.78 (1H, s).

3, 5-Disubstituted ethyl p-coumarates were synthesized from the corresponding aldehydes according to the method of FREUDENBERG[9].

○ 5-Iodo ethyl ferulate

NMR ($CDCl_3$) δ: 1.20 (3H, t, J=6), 3.86 (3H, s), 4.11 (2H, q, J=6), 6.33 (1H, d, J=16), 7.16 (1H, d, J=2), 7.57 (1H, d, J=16), 7.59 (1H, d, J=2).

○ 3, 5-Diiodo ethyl *p*-coumarate

NMR (CD_3COCD_3) δ: 1.27 (3H, t, J=7), 4.24 (2H, q, J=7), 6.33 (1H, d, J=16), 7.48 (1H, d, J=16), 7.94 (2H, s).

○ 5-Nitro ethyl ferulate

NMR ($CDCl_3+CD_3OD$) δ: 1.17 (3H, t, J=7), 3.79 (3H, s), 4.16 (2H, q, J=7), 6.22 (1H, d, J=16), 6.89 (1H, d, J=2), 7.42 (1H, d, J=2), 7.45 (1H, d, J=16).

○ 3, 5-Dinitro ethyl *p*-coumarate

NMR ($CDCl_3+CD_3OD$) δ: 1.33 (3H, t, J=8), 4.29 (2H, q, J=8), 6.50 (1H, d, J=15), 7.61 (1H, d, J=15), 8.44 (2H, s).

○ 3, 5-Dimethyl ethyl *p*-coumarate

NMR ($CDCl_3$) δ: 1.15 (3H, t, J=7), 2.16 (6H, s), 3.67 (2H, q, J=7), 6.25 (1H, d, J=16), 7.08 (2H, s), 7.53 (1H, d, J=16).

5-Iodo coniferyl alcohol, 3, 5-diiodo p-coumaryl alcohol and 3, 5-dimethyl p-coumaryl alcohol were synthesized by the same method as in sinapyl alcohol, using anhydrous ether as a solvent.

○ 5-Iodo coniferyl alcohol

NMR ($CDCl_3$) δ: 3.78 (3H, s), 4.28 (2H, d, J=5), 6.20 (1H, d, t, J=15, 5), 6.44 (1H, d, J=15), 6.83 (1H, d, J=2), 7.29 (1H, d, J=2).

○ 3, 5-Diiodo *p*-coumaryl alcohol

NMR (CD_3COCD_3) δ: 4.24 (2H, d, J=3), 6.34 (1H, d, t, J=16, 3), 6.46 (1H, d, J=16), 7.86 (2H, s).

○ 3, 5-Dimethyl *p*-coumaryl alcohol

NMR ($CDCl_3$) δ: 2.16 (6H, s), 4.22 (2H, d, J=5), 6.11 (1H, d, t, J=16, 5), 6.40 (1H, d, J=16), 6.91 (2H. s),

5-Nitro coniferyl alcohol and 3, 5-dinitro p-coumaryl alcohol were synthesized by the same method, using anhydrous THF as a solvent.

○ 5-Nitro coniferyl alcohol

NMR ($CDCl_3$) δ: 3.96 (3H, s), 4.34 (2H, d, J=4.5), 6.31 (1H, d, t, J=16, 4.5), 6.40 (1H, d, J=16), 6.91 (2H, s).

Dehydrogenation of 3, 5-disubstituted *p*-coumaryl alcohols

Enzymic dehydrogenalion

Each alcohol (I, II, III) was dehydrogenated with peroxidase and H_2O_2 by Zulauf method, and the dilignols were extracted with ethyl acetate.

Dehydrogenation by $FeCl_3$ in dioxane-water (5:2)

Each alcohol (I~VIII) 100 mg was dissolved in 7 ml of dioxane-water (5;2) and 60 mg of $FeCl_3$ in 0.7 ml of water was added into the solution under stirring. Stirring was continued for one hour, and then the reaction mixture was extracted with chloroform.

Dehydrogenation by $FeCl_3$ in acetone-water (3:40)

Each alcohol (I～VIII) 100 mg was dissolved in 3 ml of acetone and 40 ml of water was added. $FeCl_3$ solution (0.7 ml) was added to the solution under stirring and then the reaction mixture was treated as described above.

Analysis of the dilignols by NMR spectrometry

The reaction products were dissolved in $CDCl_3$ or CD_3COCD_3 and analyzed by a R-22 HITACHI high resolution NMR spectrometer (90 MHz) with TMS as internal standard.

Separation and identification of dilignols

These reaction mixtures were separated by preparative TLC and identified by NMR and Mass spectrometries.

○ Syringylglycerol-*β*-sinapyl ether

NMR ($CDCl_3$) *δ*: 3.50 (1H, m), 3.6～3.9 (2H, m), 3.82 (6H, s), 3.84 (6H, s), 4.29 (2H, d, J=5), 4.96 (1H, d, J=3), 6.27 (1H, d, t, J=16, 5), 6.53 (1H, d, J=16), 6.56 (2H, s), 6.63 (2H, s).

^{13}C-NMR (CD_3CODC_3) *δ*: 56.5 (OCH_3), 60.9 (*γ*), 63.1 (*γ'*), 73.6 and 74.2 (*α*), 88.0 (*β*), 104.8 (arom. 2-C and 6-C), 105.4 (arom. 2'-C and 6'-C), 129.7 (*β'*), 130.8 (*α'*), 132,5 (arom. 1 and 1'-C), 136.2 (arom. 4 and 4'-C), 148.3 (arom. 3 and 5-C), 153.9 and 154.1 (arom. 3' and 5'-C).

○ 5-Iodo-guaiacylglycerol-*β*-5'-iodo coniferyl ether

NMR ($CDCl_3$) *δ*: 2.85 (2H, broad), 3.20 (1H, broad), 3.87 (6H, s), 4.10 (1H, m), 4.30 (2H, d, J=4.3), 4.40 (1H, m), 5.09 (1H, d, J=4), 6.24 (1H, d, t, J=6, 4.3), 6.47 (1H, d, J=16), 6.89 (1H, d, J=2), 6.96 (1H, d, J=2), 7.26 (1H, d, J=2), 7.39 (1H, d, J=2).

○ 5, 5'-Diiodo pinoresinol

NMR ($CDCl_3$) *δ*: 2.99 (2H, m), 3.79 (6H, s), 3.7～3.9 (2H, m), 4.05～4.30 (2H, m), 4.70 (2H, d, J=5), 6.48 (2H, broad s), 6.88 (2H, d, J=2), 7.28 (2H, d, J=2).

○ 3, 5-Diiodo *p*-hydroxyphenylglycerol-*β*-3', 5'-diiodo *p*-coumaryl ether (tetra acetate)

NMR ($CDCl_3$+CD_3OD) *δ*: 1.84 (3H, s), 2.10 (3H, s), 2.20 (3H, s), 2.38 (3H, s), 3.38 (1H, m), 4.31 (2H, m), 4.70 (2H, d, J=5), 5.31 (1H, d, J=5), 6.20 (1H, d, t, J=17, 5), 6.44 (1H, d, J=17), 7.44 (2H, s), 7.92 (2H, s).

○ 3, 5, 3', 5'-Tetra iodo *p*-coumaryl resinol (diacetate)

NMR (CD_3COCD_3) *δ*: 2.38 (6H, s), 3.01 (2H, m), 3.90 (2H, d, d, J=9, 4), 4.23 (2H, d, d, J=9, 7), 4.92 (2H, d, J=4), 7.76 (4H, s).

○ 5-Nitro guaiacylglycerol-*β*-5'-nitro coniferyl ether (tetra acetate)

NMR ($CDCl_3$) *δ*: 1.39 (3H, s), 2.07 (3H, s), 2.10 (3H, s), 2.33 (3H, s), 3.82 (3H, s), 3.91 (3H, s), 4.14 (1H, d, d, J=12, 4), 4.44 (1H, d, d, J=12, 5), 4.70 (2H, d, J=5), 5.05 (1H, m), 6.07 (1H, d, J=6), 6.24 (1H, d, t, J=16, 5), 6.53 (1H, d, J=16), 7.34

(4H, s).

○ 3, 5-Dimethyl *p*-hydroxyphenylglycerol-*β*-3′, 5′-dimethyl *p*-coumaryl ether

NMR ($CDCl_3$) δ: 2.15 (12H, s), 3.67~3.95 (2H, m), 4.02~4.20 (1H, m), 4.18 (2H, d, J=5), 4.88 (1H, d, J=4), 6.19 (1H, d, t, J=16, 5), 6.44 (1H, d, J=16), 6.92 (2H, s), 6.97 (2H, s).

○ 3, 5, 3′, 5′-Tetra methyl *p*-coumaryl resinol (diacetate)

NMR ($CDCl_3$) δ: 2.15 (12H, s), 3.00 (2H, m), 3.65~3.80 (2H, m), 4.05~4.20 (2H, m), 4.58 (2H, d, J=4), 6.27 (4H, s).

Results and discussion

NMR spectra of the dilignols formed from sinapyl alcohol are shown in Fig. 1. According to NAKATSUBO[4], *α*-methine protones of the three main dilignols, phenylcoumarane, arylglycerol-*β*-aryl ether and resinol give peaks at 5.50, 4.96 and 4.68, which are not interfered with other peaks. Therefore, the ratio of the amounts of these dilignols can be determined by integration of their *α*-methine peaks. This method was used for the determination of the ratio of dilignols in this paper. Fig. 2 shows the peaks of about 6.00 to 4.30 ppm in the NMR spectra of dehydrogenation products from the respective alcohols. The peaks of *α*-methine of phenylcoumarane, *β*-ether and resinol appeared at 5.7 to 5.5 ppm, at 5.1 to 4.9 ppm and at 4.7 to 4.5 ppm, respectively. The amonts of *β*-ether and resinol were calculated from the corresponding peak areas and the result is given in Table 1.

p-Coumaryl and coniferyl alcohols gave 38 % and 41 % of *β*-ether and 62 %

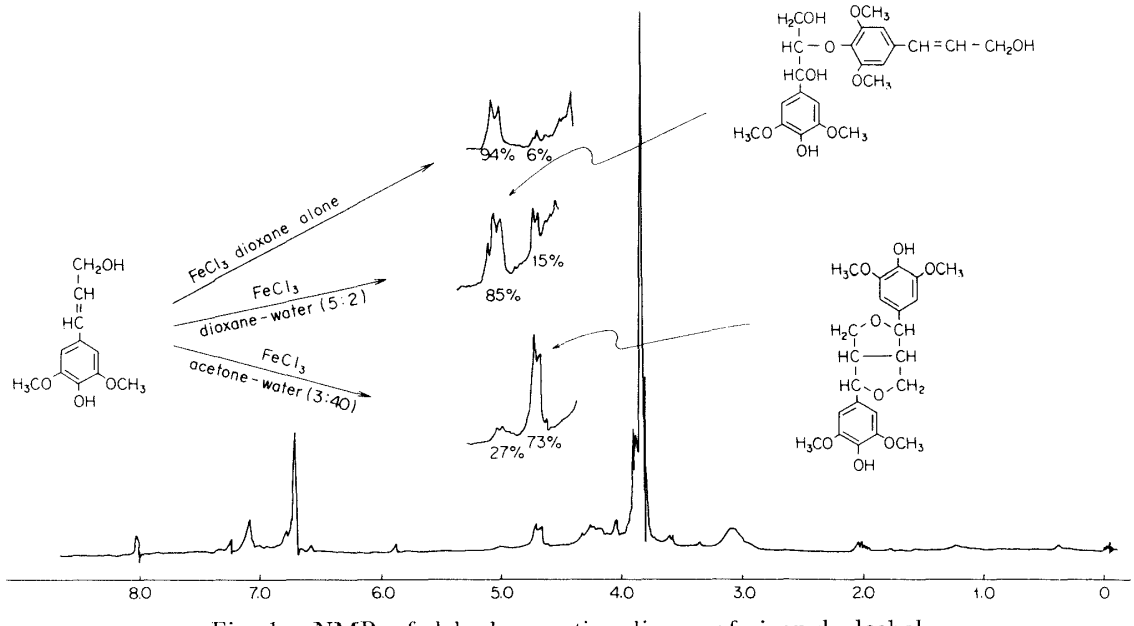

Fig. 1. NMR of dehydrogenative dimers of sinapyl alcohol.

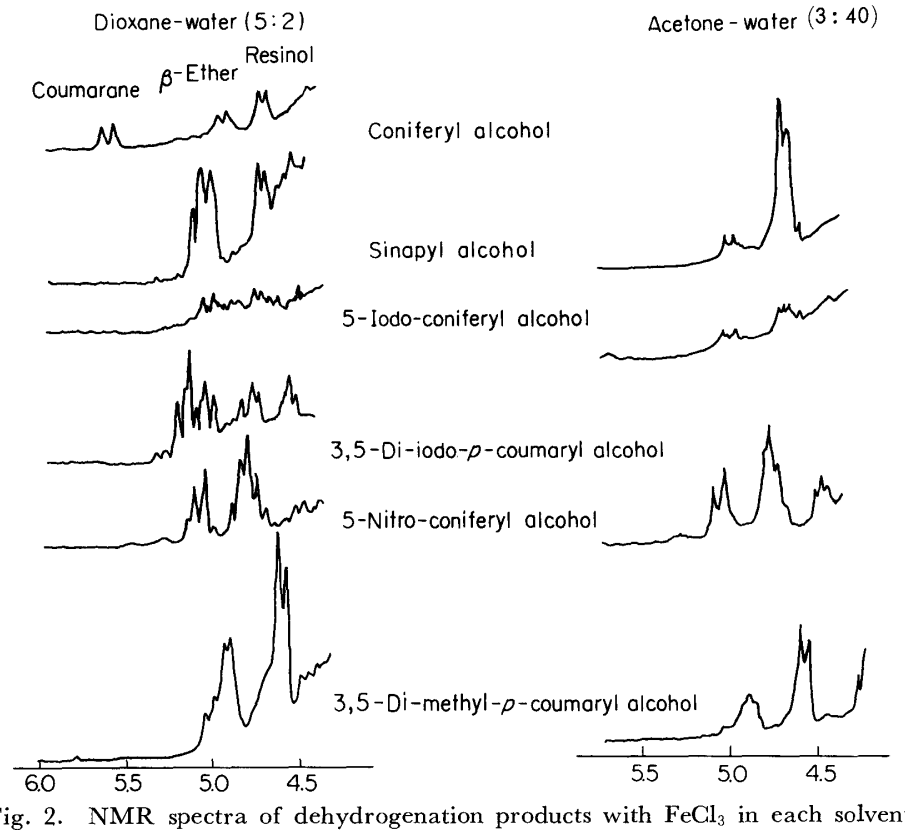

Fig. 2. NMR spectra of dehydrogenation products with $FeCl_3$ in each solvent.

and 59 % of resinol, respectively, and the amount of phenylcoumarane was negligible. On the other hand, sinapyl alcohol gave syringaresinol in 91 % yield. A preferential formation of syringaresinol from sinapyl alcohol has been ascribed to a steric hindrance of two methoxyl groups located at 3 and 5 positions of the aromatic ring by FREUDENBERG. If this assumption is correct, resinols should be mainly formed also from the 3, 5-disubstituted *p*-coumaryl alcohols with other large substituents. However, 5-iodo coniferyl alcohol and 3, 5-diiodo *p*-coumaryl alcohol gave β-ethers in the yields of 80 % and 86 %, respectively. Steric effects of iodine, nitro and methyl groups are evidently larger than that of methoxyl group (see Table 2, Fig. 3 and Fig. 4). Fig. 3, depicted from the data of Table 2, shows the methyl group in methoxyl at the most remote position from phenoxyl radical, which is considered to be the most stable position. It is recognizable from Fig. 3 that the methoxyl group must not be so large substituent to prevent β-0-4 coupling for a phenoxyl radical. Fig. 4 shows the level of the bulky effects of the *o*-substituents determined from racemization rate of substituted biphenyls. The racemization rate of the biphenyls substituted with methoxyl group should be faster than those of biphenyls substituted with iodine, nitro or methyl group indicating that methoxyl is the least hindered substituent among the four groups. In spite of the least bulky methoxyl substituent, sinapyl alcohol gives syringaresinol in high yields in dehydrogenation in polar solvent.

Table 1. Ratio of β-ethers and resinols formed by dehydrogenation of 3, 5-disubstituted *p*-coumaryl alcohols.

		Coumarane	β-Ether	Resinol
Peroxidase H_2O_2	*p*-Coumaryl alcohol	(48)*	(20)38**	(32)62**
	Coniferyl alcohol	(54)	(19)41**	(27)59**
	Sinapyl alcohol		9	91
$FeCl_3$ in dioxane-water (5:2)	Coniferyl alcohol	(39)	(39)64**	(22)36**
	Sinapyl alcohol		85	15
	5-Iodo coniferyl alcohol		80	20
	3, 5-Diiodo *p*-coumaryl alcohol		86	14
	5-Nitro coniferyl alcohol		100***	+
	3, 5-Dinitro *p*-coumaryl alcohol		100***	+
	3, 5-Dimethyl *p*-coumaryl alcohol		58	42
$FeCl_3$ in acetone-water (3:40)	Coniferyl alcohol	(27)	(27)37	(46)63
	Sinapyl alcohol		27	73
	5-Iodo coniferyl alcohol		50	50
	3, 5-Diiodo *p*-coumaryl alcohol		80***	20***
	5-Nitro coniferyl alcohol		100	+
	3, 5-Dinitro *p*-coumaryl alcohol		100	+
	3, 5-Dimethyl *p*-coumaryl alcohol		55	45

* The values in parentheses are the ratio of three main dilignols, coumaranes, resinols and β-ethers. ** The values are the ratio of resinol and β-ether in the dimers from which the amount of coumarane was excluded. *** The values are the yields of β-ethers and resinols separated by preparative TLC. Determination of dilignols from the peak areas of α-methins on NMR spectra was difficult for overlapping of α-methine peaks of resinols and γ-hydroxymethyl peaks of the starting materials.

Table 2. Radii of covalent bonds and of van der Waals.

Atom	Radius of covalent bond	Radius of van der Waals
H	0.30 (Å)	1.20 (Å)
C	0.77	1.85
N	0.70	1.50
O	0.66	1.40
I	1.33	2.15
CH_3	—	2.00

However, 3, 5-diiodo *p*-coumaryl alcohol having the most bulky iodine atoms gives a large amount of β-ether both in polar and nonpolar solvents. These results suggest that the most effective factor in these radical couplings may not be a steric effect but electronic effects.

Then, the substituents which have different inductive and electromeric effects and are more bulky than methoxyl group were chosen and synthesized in the present

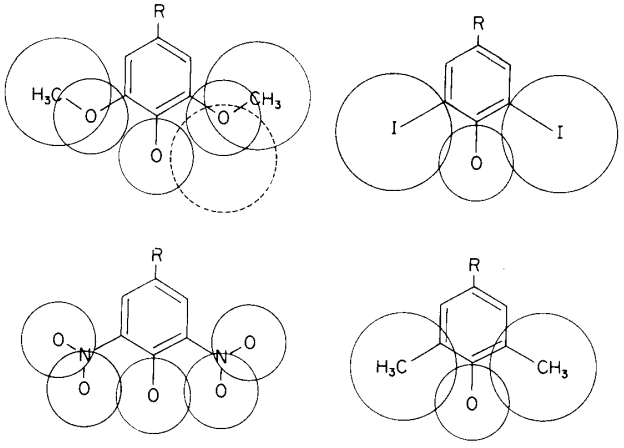

Fig. 3. Diagrams of steric hindrance of dual *o*-substituted phenoxy radicals. Fields of van der Waals of iodine, methyl and nitro groups are fixed because of only one single bond (the formers) and the resonanced π-electrones (the latter). However, methoxyl group has two single bonds which can rotate around the aromatic C-O bond. Dashed circle shows the nearest position of methoxyl group to the phenoxy radical but that position is less possible.

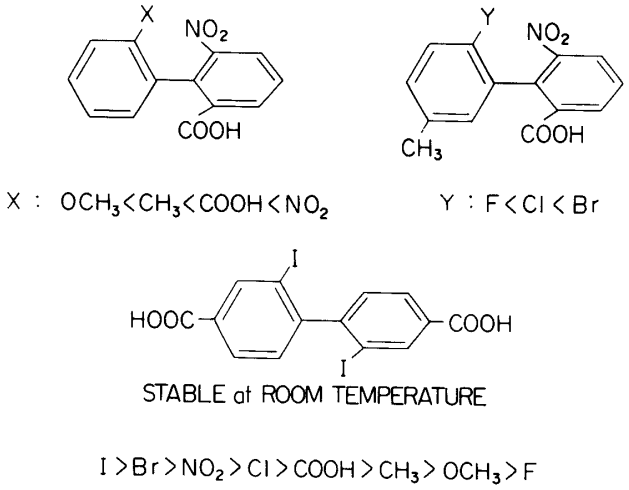

Fig. 4. Bulky effects determined from racemization rate of substituted biphenyls. The order of X or Y shows the facility of racemization of optical active biphenyl. The more bulky the substituent is, the slower the rate of racemization is. Iodine is the most bulky substituent among them, and then 2, 2′-diiodo-4, 4′-dicarboxy biphenyl is known to be stable at the room temperature. Methoxyl group belongs to a smaller class for the steric hindrance as indicated

investigation. Table 3 shows the HAMMETT substituent constants[14] of these groups. In a nonpolar solvent, only I effect acts on the reaction, whereas in a polar solvent, both I and E effects would be effective. Under these supposition dehydrogenation of these alcohols was carried out by using $FeCl_3$ in a relatively nonpolar solvent (dioxane-water 5: 2) and a polar solvent (acetone-water 3: 40), respectively. When

Table 3. Hammett substituent constants (σ).

Substituent group	Position		Electronic effect	
	meta I	*para* I+E	Inductive	Electromeric
CH_3	−0.08	−0.16	+ I	+ E
OCH_3	+0.11	−0.27	− I	+ E
I	+0.35	+0.18	− I	+ E
NO_2	+0.71	+0.78	− I	− E

nonpolar solvent is used, *meta* value of HAMMETT substituent constant is effective to the reaction and in polar solvent, *para* value should be effective. The results are shown in Table 1 which definitely indicates that the higher the HAMMETT substituent constant (σ-value), the more the ratio of β-ether increase in the same solvent. Moreover, this relation between the ratio of β-ether and σ-value was kept in constant even in the change of the polarity of solvents for the same 3, 5-substitued *p*-coumaryl alcohol. For example, the yields of β-ether from 5-iodo coniferyl alcohol changed from 50 % to 80 % when solvent was changed from polar to nonpolar (from $\sigma_{para}=-0.27$ (OCH_3) $+0.18$ (I) $=-0.09$ to $\sigma_{meta}=0.11$ (OCH_3) $+0.35$ (I) $=+0.46$). In particular, the relation is clearly found in the dehydrogenation of sinapyl alcohol (Fig. 1). When acetone-water (3 : 40) was used as a solvent syringaresinol was formed in a 73 % yield of dilignols by a stronger E effect of methoxyl ($\sigma_{para}=-0.27$), and the result is approximately same as that carried out with peroxidase-H_2O_2 system. When the polarity of solvent decreased, the amount of resinol decreased and that of β-ether increased. When dioxane alone was used as solvent, the amount of β-ether reached to 94 %, because of the only +I effect of methoxyl group ($\sigma_{meta}=+0.11$). From these results it is clear that the most effective factor in the mode of dehydrogenative polymerization of *p*-coumaryl alcohols is electronic effect.

The fact that syringylglycerol-β-sinapyl ether can be formed mainly in nonpolar solvent suggests that syringyl lignin is formed in cell wall matrix which may control the electronic effect of methoxyl groups of sinapyl alcohol in protoplasmic membrane and cell organelles.

Acknowledgment

This innestigation was supported in part by the Ministry of Educations Scientific Fund (No. 176105).

References

1) K. FREUDENBERG and A. C. NEISH, Constitutions and biosynthesis of lignin, Springer-Verlag, p. 34–37 (1968).

2) B. J. FERGUS and D. A. I. GORING, Holzforschung, **24**, 113 (1970).
3) T. YAMASAKI, K. HATA, and T. HIGUCHI, Mokuzai Gakkaishi, **19**, 299 (1973).
4) T. YAMASAKI, K. HATA, and T. HIGUCHI, Mokuzai Gakkaishi, in press.
5) F. NAKATSUBO and T. HIGUCHI, Wood Research **58**, 12 (1975).
6) T. SUAMI, Gendai Kagaku Shiriizu, **38**, Tokyo Kagaku Dojin p. 48 (1968).
7) J. A. DEAN, Lange's Handbook of Chemistry, **3**-118 (1973).
8) S. OMORI and A. SAKAKIBARA, Mokuzai Gakkaishi, **18**, 577 (1972).
9) K. FREUDENGERG, Chem. Ber., **85**, 1181 (1952).
10) H. ERDTMAN, Svensk. Kem. Tid., **47**, 223 (1935).
11) S. N. ACERBO, W. L. SCHUBERG, and F. F. NORD, J. Am. Chem. Soc. **82**, 735 (1960).
12) S. V. LIEBERMAN and R. CONNOR, Org. Syn., Coll. Voll. **2**, 441 (1943).
13) W. E. SMITH, J. Org. Chem., **37**, 3972 (1972).
14) D. H. MCDANIAL and H. C. BROWN, J. Org. Chem., **23**, 420 (1958).