The Reduction of Lignin Model Compounds and Spruce Dioxane Lignin by the Birch Reaction

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Several phenyl methyl ethers and spruce dioxane lignin were reduced by treatment with sodium in liquid ammonia in the presence of ethanol (Birch reduction). The product mixtures were resolved by vapor phase chromatographic techniques and the reduction products identified using combinations of NMR, IR, UV and mass spectrometric methods.

The aromatic moiety in 3,4-dimethoxyphenyl (veratryl) structures was reduced to a mixture of the corresponding unconjugated dihydro and tetrahydro derivatives. In addition, a methoxyl substituent was replaced by hydrogen, giving rise to 4-substituted di- and tetrahydroanisoles. In this instance both conjugated and unconjugated dienes were present with the latter greatly predominating. By contrast, reduction of a syringyl derivative, 3,4,5-trimethoxytoluene, resulted in the formation of the 1,4-dihydro derivative in 80 % yield as the only major product. With phenyl ethers containing a benzyl alcohol, α -keto or an α - or β -aryl ether substituent, reduction of these groups to the corresponding hydrocarbon took place and generally preceded reduction of the aromatic ring.

Reduction of spruce dioxane lignin with sodium in liquid ammonia under similar conditions resulted in the isolation of a material whose spectral properties were consistent with those of 2,5-dihydro-4-propylanisole.

Metal-liquid ammonia treatment of isolated lignins and softwood and hardwood meal has been used by Freudenberg,^{1,2} Shorygina,³⁻⁶ and Yamaguchi^{7,8} and their co-workers, primarily as a means of studying lignin structure. As a consequence of this type of treatment, inter-unitary ether linkages were found to undergo hydrogenolysis yielding a variety of guaiacyl

and syringylpropane monomeric fragments in which the propyl substituent exhibited varying degrees of reduction. The commonly observed net effect of the overall reaction is an increase in the hydroxyl content and a decrease in the methoxyl content of the lignin.

The discovery of Wooster,⁹ subsequently exploited by Birch,¹⁰⁻¹² that the presence of a suitable proton source in the liquid ammonia solution promotes the reduction of benzenoid and other aromatic ring systems was particularly significant in the development of dissolving metal chemistry. In the application of dissolving metal reductions to lignin reported to date, no external proton source appears to have been added. There is, however, the strong possibility that lignin (in particular the phenolic hydroxyl and terminal methylol groups) may function as its own proton source in such reductions.

The extensive changes occurring when lignin is subjected to a dissolving metal reduction makes such a process theoretically attractive from a chemical modification viewpoint.¹³ An examination of the literature indicates, however, a lack of systematic studies designed to describe the complete scope of possible transformations occurring when lignin is reacted under Birch reduction conditions. In attempting to fill this void, studies utilizing lignin model compounds appear to offer the best approach for isolating and subsequently cataloging the various reaction types in view of the complexity of the overall process.

Accordingly, the present investigation consisted mainly of an examination of the reactions of comparatively simple lignin model com-

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Table 1. Model compounds reacted with sodium in liquid ammonia.

Com- pound	R ¹	R ²	R ³
I	H	H	H
V	H	OCH ₃	H
VIII	H	OCH ₃	CH ₃
XV	OCH ₃	OCH ₃	CH ₃
XVII	H	OCH ₃	CH ₃ - O - (<i>o</i> -methoxyphenyl)
XVIII	H	OCH ₃	CH(OH)CH ₃
XXIII	H	OCH ₃	CH(OH)CH ₃ - O - (<i>o</i> -methoxyphenyl)
XXIV	H	OCH ₃	COCH ₃
XXVI	H	OCH ₃	COCH ₃ - O - (<i>o</i> -methoxyphenyl)
XXVII	H	H	O - (<i>p</i> -methoxyphenyl)

pounds with sodium-liquid ammonia solutions in the presence of an external proton source, ethanol; *i.e.*, with a Birch reduction system. The models selected for study (see Table 1) consisted solely of compounds whose phenolic rings were completely etherified. This arbitrary structural

restriction was made on the basis of results from a previous study¹⁰ where it was shown that with few exceptions^{10,14,15} unetherified phenolic units were not reduced by metals in liquid ammonia.

The model compound study was augmented by a brief examination of the behavior of Norway spruce dioxane lignin in the same reduction system.

RESULTS AND DISCUSSION

Products formed from the reactions of the various models with sodium in liquid ammonia in the presence of ethanol are summarized in Table 2. Spectrometric data essential to the identification of the various products are compiled in Table 3.

Anisole (I). The reduction of anisole with Na/NH₃ in the presence of ethanol was previously reported by Birch¹⁰ to yield 2,5-dihydroanisole (II) as the principal product. In a subsequent investigation, Benkeser *et al.*¹⁶ presented evidence indicating the probable formation of two additional compounds, 2,3-dihydroanisole (III) and 3,4,5,6-tetrahydroanisole (IV). The yields of reaction products recorded in Table 2 agree closely with those reported by Benkeser¹⁶ using either sodium or lithium as the

Table 2. Reaction products and product yields.

Starting material	Products	Yield, %
Anisole (I)	2,5-dihydroanisole (II)	74
	2,3-dihydroanisole (III)	4
	2,3,4,5-tetrahydroanisole (IV)	14
	phenol ^a	Trace
Veratrole (V)	3,6-dihydroveratrole (VI)	19
	2,5-dihydroanisole (II)	37
	2,3-dihydroanisole (III)	3
	3,4,5,6-tetrahydroveratrole (VII)	24
	2,3,4,5-tetrahydroanisole (IV)	9
	guaiacol ^a	7
4-Methylveratrole (VIII)	2,5-dihydro-4-methylanisole (IX)	25
	2,3-dihydro-4-methylanisole (X)	0.4
	3,6-dihydro-4-methylveratrole (XI)	57
	2,3,4,5-tetrahydro-4-methylanisole (XII)	1.9
	3,4,5,6-tetrahydro-4-methylveratrole (XIII)	6.6
	5-methylguaiacol (XIV)	3.3

Table 2. Continued.

Starting material	Products	Yield, %	
3,4,5-Trimethoxytoluene (XV)	1,4-dihydro-3,5-dimethoxytoluene (XVI)	80	
	di- and tetrahydroveratroles	Trace	
3,4-Dimethoxy- α -(<i>o</i> -methoxyphenoxy)toluene (XVII)		0.5 h	4 h
	2,5-dihydro-4-methylanisole (IX)	25	27
	2,3-dihydro-4-methylanisole (X)	< 0.1	< 0.1
	3,6-dihydro-4-methylveratrole (XI)	68	62
	2,3,4,5-tetrahydro-4-methylanisole (XII)	0.9	1.9
	3,4,5,6-tetrahydro-4-methylveratrole (XIII)	2.4	6.8
	5-methylguaiaicol	^b	1.9
	guaiaicol ^a	^b	~ 100
1-(3,4-Dimethoxyphenyl)ethanol (XVIII)	2,5-dihydro-4-ethylanisole (XIX)	46	
	3,6-dihydro-4-ethylveratrole (XX)	41	
	2,3,4,5-tetrahydro-4-ethylanisole (XXI)	1.7	
	3,4,5,6-tetrahydro-4-ethylveratrole (XXII)	3.7	
1-(3,4-Dimethoxyphenyl)-2-(<i>o</i> -methoxyphenoxy)ethanol (XXIII)	2,5-dihydro-4-ethylanisole (XIX)	50	
	3,6-dihydro-4-ethylveratrole (XX)	47	
	2,3,4,5-tetrahydro-4-ethylanisole (XXI)	1.3	
	3,4,5,6-tetrahydro-4-ethylveratrole (XXII)	5.6	
	guaiaicol ^a	50	
Acetoveratrone (XXIV)	2,5-dihydro-4-ethylanisole (XIX) }	50	
	2,5-dihydro-3-ethylanisole (XXV) }		
	3,6-dihydro-4-ethylveratrole (XX)	16	
	2,3,4,5-tetrahydro-4-ethylanisole (XXI)	1.0	
	3,4,5,6-tetrahydro-4-ethylveratrole (XXII)	1.7	
	polymer-like material	8.0	
3,4-Dimethoxyphenyl-2- <i>o</i> -methoxyphenoxy acetophenone (XXVI)	2,5-dihydro-4-ethylanisole (XIX) }	57	
	2,5-dihydro-3-ethylanisole (XXV) }		
	3,6-dihydro-4-ethylveratrole (XX)	29	
	2,3,4,5-tetrahydro-4-ethylanisole (XXI)	1.1	
	3,4,5,6-tetrahydro-4-ethylveratrole (XXII)	2.9	
	guaiaicol ^a	89	
4,4'-Dimethoxydiphenyl ether (XXVII)	2,5-dihydroanisole (II)	0.9	
	2,2',5,5'-tetrahydro-4,4'-dimethoxydiphenyl ether (XXVIII)	87 ^c	

^a Identified by comparison of gas chromatographic retention time with that of authentic material (anisole, phenol, or guaiaicol) and estimated by comparison with peak areas corresponding to known amounts of the corresponding authentic substance. ^b Not measured. ^c Yield based on weight of neutral fraction which was almost pure XXVIII.

metallic component. The principal steps in the overall reaction are outlined below.

The comparatively low yield of 2,3-dihydroanisol (III) undoubtedly reflects the facile reduction of the conjugated diene system to the tetrahydro derivative.

As indicated by the data in Table 2, reductive cleavage resulting in the formation of phenol occurred to less than 0.1 %. In the absence of ethanol under otherwise identical conditions, the yield of phenol was 27 %. Partial conversion (isomerization) of II to III probably from the action of the amido ion formed in the equilibrium reaction

on the former structure.^{17,18}

Veratrole (V). Veratrole was previously reported by Birch¹⁸ to yield a mixture of 2,5-dihydroanisol (II) and 3,6-dihydroveratrole (VI) with the former predominating. In the present study, the same two products were obtained together with other compounds listed in Table 2. The total yield of products (~99 %) accounts essentially for all of the starting material.

The nature of the products indicates that two main competing reactions occur: (1) replacement of one methoxyl group with a hydrogen resulting ultimately in the formation of anisole reduction products and (2) reduction to di- and tetrahydroveratrole. The fact that the ratios of the three anisole derivatives parallel those of the corresponding products resulting from direct treatment of anisole indicates that the methoxyl group is replaced by a hydrogen before the aromatic nucleus is reduced.

The detection of a significant amount (7 %) of

guaiacol indicates the occurrence of a competing ether cleavage reaction. The high yield of guaiacol compared to that of phenol is consistent with the substituent effect noted by Birch.¹²

4-Methylveratrole (VIII). The two principal products detected in the reaction mixture, 2,5-dihydro-4-methylanisole (IX) and 3,6-dihydro-4-methylveratrole (XI), together account for 82 % of the starting material (Table 2).

The position of the methoxyl group relative to the methyl group in the anisole derivatives was established by comparison of the IR and NMR spectra of 2,3,4,5-tetrahydro-4-methylanisole with those of the isolated products. The NMR spectrum of the conjugated compound 2,3-dihydro-4-methylanisole (X), which shows two vinyl protons as two doublets (*cf.* Table 3), further reinforces the validity of the structure assignment.

Spectra of the phenolic compound (XIV) suggested the presence of a methylguaiacol. Comparison of the IR and NMR spectra of this compound with those of authentic 4- and 5-methylguaiacol (XIV) clearly indicated that it was the latter isomer.

3,4,5-Trimethoxytoluene (XV). The reaction mixture consisted of only one major product, 1,4-dihydro-3,5-dimethoxytoluene (XVI), formed in 80 % yield and of trace amounts of di- and tetrahydroanisoles and veratroles. Failure of the 1,4-dihydro derivative to undergo further reduction is attributed to the difficulty in conjugating double bonds which involves displacement of one double bond from a position in which it is conjugated with the unshared electron pair of the oxygen of a methoxyl group. Benzoic acid derivatives typically give rise to 1,4-dihydro compounds under Birch conditions, and the previously reported¹⁹ conversion of 3,4,5-trimethoxybenzoic acid to 1,4-dihydro-3,5-dimethoxybenzoic acid by such treatment is particularly relevant to the case at hand.

In an attempt to form a bromo derivative, 1,4-dihydro-3,5-dimethoxytoluene was reacted with bromine in CCl_4 . The isolated product, 2,6-dibromo-3,5-dimethoxytoluene, ostensibly arose from a series of bromine additions and hydrogen bromide eliminations.

3,4-Dimethoxy- α -(*o*-methoxyphenoxy)toluene (XVII). Because of the small amount of material available for reaction, none of the products were isolated but were identified and estimated

by comparing retention times and peak areas with those of authentic materials isolated from the reduction of 4-methylveratrole (VIII). The yields of the various products obtained in the reduction of this ether are very nearly identical to those of the corresponding compounds resulting from the reduction of 4-methylveratrole (see Table 2). This suggests that the benzyl aryl ether linkage undergoes rapid hydrogenolysis generating guaiacol and 4-methylveratrole, which subsequently undergoes reduction to di- and tetrahydro anisoles and veratroles.

di- and tetrahydroanisoles and veratroles

That the hydrogenation of the benzyl aryl ether linkage is complete is indicated by the essentially quantitative recovery of guaiacol. The results in Table 2 also reveal that the overall reaction is virtually complete in 30 min or less and that the products thereafter undergo little additional change.

1-(3,4-Dimethoxyphenyl)ethanol (XVIII). Inspection of Table 2 indicates that the two dihydro products, XIX and XX, account for nearly 90 % of the starting material. While these two products were recovered from the product mixture, the tetrahydro compounds XXI and XXII were identified solely on the basis of similarities in the gas chromatographic patterns of the product mixture with those of veratrole and 4-methylveratrole. Quantitative analysis of XXI and XXII was accomplished by comparing their peak areas with that corresponding to a specified quantity of 3,6-dihydro-4-ethylanisole.

The general similarity of the product distribution to that noted above for veratrole and 4-methylveratrole leads to the conclusion that the starting material undergoes a stepwise reaction involving first hydrogenolysis of the benzyl alcohol group followed by reduction of the product, 4-ethylveratrole, by the usual pattern. The

total absence of hydroxyl group characteristics in the various product fractions supports the conclusion that reduction of this alcohol to the corresponding hydrocarbon is essentially quantitative.

1-(3,4-Dimethoxyphenyl)-2-(o-methoxyphenoxy)ethanol (XXIII). The distribution of reaction products replicates in general the now familiar pattern observed for other veratryl derivatives in which the dihydroanisole and dihydroveratrole derivatives account for the bulk of the starting material. The observed reductive cleavage of the β -aryl ether group is especially significant since linkages of this type comprise a major portion of the interunitary linkages in lignin. In this regard, treatment of lignin with sodium in liquid ammonia has, in fact, resulted in the formation of monomeric fragments in which the β -carbon of the side chain was completely reduced as would be expected if hydrogenolysis of the β -aryl ether linkage had occurred.

The less-than-theoretical recovery of guaiacol (50 %) probably has no fundamental significance since the other cleavage product can be fully accounted for in terms of the partially reduced 4-ethylanisoles and 4-ethylveratroles. Failure to achieve the expected near-quantitative recovery of guaiacol is ascribed to mechanical losses (*e.g.*, volatilization) in the workup.

As in the previous instance, the reduction products were identified by their relative positions in the gas chromatogram of the product mixture and were estimated by comparing their areas with the peak area produced by injection of a known amount of 3,6-dihydro-4-ethylveratrole (XX).

Acetoveratrone (XXIV). Acetoveratrone reacted more vigorously and was converted to products which collectively had sustained a greater loss of methoxyl groups than the models discussed heretofore. These observations can be logically rationalized on the basis of the electron-withdrawing property of the aceto group which would have the effect of activating the ring toward attack by a solvated electron.

Chromatography of the product mixture on an OV-1 column (maintained at 90 °C) resulted in the collection of a fraction whose NMR spectrum indicated the presence of a nonconjugated dihydroanisole with the methoxyl group situated either *meta* or *para* to the side chain.

When the chromatographic separation was repeated on a preparative size Carbowax column maintained at a considerably higher temperature (160 °C), the NMR spectrum (vinyl proton region) of the fraction corresponding to the same peak suggested the presence of a mixture consisting of 2,5- and 2,3-dihydro-4-ethylanisole. Evidently isomerization of the unconjugated to the conjugated compound had occurred as a result either of the higher column temperature or as the result of reaction with the column itself.

Additional peaks in the NMR spectrum of the material isolated from the Carbowax column, and in particular a signal at δ 1.65 (doublet), suggest the presence of 2,3-dihydro-3-ethylanisole. If this compound was indeed present in the product mixture, it most probably can be considered as an artifact resulting from isomerization of 2,5-dihydro-3-ethylanisole on the chromatographic column. If 2,5-dihydro-3-ethylanisole is a product in the Birch reduction of acetoveratrone, the increased tendency for replacement of methoxyl at the *para* position would accord with the activating effect of the aceto group on this position. This would further imply that some replacement of the *para* methoxyl group occurred prior to reduction of the α -carbonyl group.

The foregoing observations cannot be taken as providing incontrovertible evidence for the presence of 2,5-dihydro-3-ethylanisole in the product mixture. Nevertheless, if present, this compound was not separated from the corresponding 4-ethyl isomer under the imposed chromatographic conditions. Accordingly, the value reported in Table 2 is the combined yield of both isomers.

3,4-Dimethoxyphenyl-2-(*o*-methoxyphenoxy)-acetophenone (XXVI). The reductive pattern of this compound was similar to that of acetoveratrone in that more than 50 % of the starting material was accounted for by the dihydroanisole derivatives (Table 2). The yield of 3,6-dihydro-4-ethylveratrole was, however, nearly double the value obtained for acetoveratrone. The reduction of the veratryl (3,4-dimethoxyphenyl) moiety was accompanied by the near quantitative cleavage of the β -aryl ether linkage as indicated by an 89 % recovery of guaiacol (Table 2). It is also noteworthy that, whereas reduction of acetoveratrone was accompanied by

the formation of what appeared to be polymeric substances, material of this type was absent in the case at hand. This observation probably accounts for the difference in the total yield of recovered products in each instance.

4,4'-Dimethoxydiphenyl ether (XXVII). The diaryl ether linkage represented by the title compound was not extensively cleaved under Birch reduction conditions, and the sole cleavage product detected was 2,5-dihydroanisole in 0.9 % yield. The only other product identified was the tetrahydrodiphenyl ether (XXVIII) which accounted for nearly 90 % of the starting material.

The effect of *para* substituents on the cleavage of diaryl ether linkage in Na/NH₃ solutions has been studied by Sartoretto and Sowa.¹⁰ These authors found that methoxyl groups situated *para* to the ether linkage retarded the cleavage reaction. Further reduction of partially reduced diaryl ether XXVIII in all likelihood is retarded since both double bonds in each ring contain oxygen-bearing (electron-releasing) substituents.

Dioxane lignin. In order to enhance the probability of obtaining monomeric fragments with partially reduced phenolic rings, the dioxane lignin was pretreated with borohydride to remove carbonyl groups followed by methylation with diazomethane to convert the phenolic hydroxyl groups to methyl ethers. The modified lignin was dissolved in liquid ammonia and reacted with sodium (Na/phenylpropane, ~20/1) in the presence of ethanol. The reaction mixture was fractionated into neutral, acidic and dioxane-soluble components as described in the Experimental section.

The neutral fraction was separated by vapor phase chromatography into two components which were collected and subjected to spectroscopic analysis. The NMR and mass spectra of the component with the longer retention time were consistent with the patterns expected for 2,5-dihydro-4-propylanisole (see XXIX in Table 3). The assignment of the methoxyl *para* to the propyl group is arbitrary but considered justifiable in the light of the results of the model studies and since the influence of the α -carbonyl groups on cleavage of the *para*-situated methoxyl had been eliminated by prior reduction.

The amount of 2,5-dihydro-4-propylanisole (XXIX) was estimated from peak area measure-

Table 3. NMR, IR, UV and mass spectral properties of reaction products.

Product	NMR, δ^a	IR ^b , cm ⁻¹	Other (UV or mass spectra)
II	(CDCl ₃) 5.71 (s, 2 H), 4.67 (bs, 1 H), 3.53 (s, 3 H), 2.76 (s, 4 H)	3010(m), 2920(m), 2810(m), 1680(s), 1210(s), 1175(s), 1160(s)	UV: $\lambda_{\max}$, 211 nm
III	(CCl ₄) 5.82(q ^c , 1 H, $J=6.0$ Hz), 5.17–5.53 (m, 1 H), 4.86 (d, 1 H, $J=6.0$ Hz), 3.52 (s, 3 H), 2.21 (s, 2 H), 2.19 (s, 2 H)	3030(m), 2930(s), 2810(s), 1640(s), 1580(s), 1250(s), 1210(s), 1155(s),	UV: $\lambda_{\max}$, 269 nm
IV	(CDCl ₃) 4.54–4.73 (m, 1 H), 3.47 (s, 3 H), 1.90–2.03 (m, 4 H), 1.40–1.80 (m, 4 H)	2920(s), 2820(m), 1660(s), 1200(s), 1170(s), 1155(s)	—
VI	(CDCl ₃) 5.63(s ^d , 2 H), 3.62(s, 2 H), 2.87(s, 4 H)	3020(m), 2920(m), 2810(s), 1700(3), 1210(s), 1150(m), 1115(m)	—
VII	(CDCl ₃) 3.57(s, 6 H), 1.97–2.28 (m, 4 H), 1.47–1.73(m, 4 H)	2910(s), 2820(m), 1680(m), 1210(s), 1150(m), 1110(m)	—
IX	(CCl ₄) 5.27–5.46(m, 1 H), 4.42–4.63 (m, 1 H), 3.54(s, 3 H), 2.59(s, 4 H), 1.69(bs, 3 H)	2980(m), 2920(m), 2800(s), 1690(m), 1660(s), 1220(s), 1170(s), 1130(s)	—
X	(CCl ₄) 5.51(bd, 1 H, $J=6.0$ Hz), 4.77(d, 1 H, $J=6.0$ Hz), 3.50(s, 3 H), 2.18(s, 4 H), 1.72(bs, 3 H)	2920(m), 2810(m), 1650(s), 1600(s), 1240(s), 1215(s), 1160(s)	UV: $\lambda_{\max}$, 271 nm
XI	(neat) 5.15–5.36(m, 1 H), 3.54 (s, 3 H), 3.51(s, 3 H), 2.69(s, 4 H), 1.64(bs, 3 H)	2920(s), 2810(s), 1700(m), 1670(w), 1210(s), 1150(s), 1100(s),	—
XII	(CDCl ₃) 4.38–4.62(m, 1 H), 3.48 (s, 3 H), 1.80–2.33(m, 2 H), 1.45–1.80(m, 4 H), 0.96(d, 3 H, $J=4.5$ Hz)	2910(s), 2820(m), 1720(m), 1660(s), 1220(s), 1200(s), 1170(s), 1150(s)	UV: $\lambda_{\max}$, 209 nm
XIII	(CCl ₄) 3.51(s, 6 H), 1.71–2.30 (m, 4 H), 1.47–1.71(m, 2 H), 0.92–1.10(m, 3 H)	2910(s), 2820(m), 1680(m), 1210(s), 1120(m)	UV: $\lambda_{\max}$, 209 nm
XIV	(CDCl ₃) 6.5–7.0(m, 3 H), 5.84 (s, 1 H; exchanges with D ₂ O), 3.71(s, 3 H), 2.20(s, 3 H)	3500(s), 2920(m), 2820(m), 1590(s), 1500(s), 1230(s), 1205(s), 1170(m), 1140(m), 1125(s), 790(s), 760(s)	—
XVI	(neat) 4.45–4.62(m, 2 H), 3.46 (s, 6 H), 2.80–2.36(m, 1 H), 2.75 (bs, 2 H), 1.06(d, 3 H, $J=6.5$ Hz)	2940(s), 2810(m), 1685(s), 1660(m), 1230(s), 1200(s), 1140(s), 1125(s)	—
XIX	(CCl ₄) 5.27–5.52(m, 1 H), 4.47–4.65(m, 1 H), 3.50(s, 3 H), 2.50–2.88(m, 4 H), 2.03(q, 2 H, $J=6.0$ Hz), 1.04(t, 3 H, $J=6.0$ Hz)	2945(s), 2860(m), 2805(s), 1690(m), 1660(m), 1215(s), 1170(m), 1135(m),	Mass spectrum: Base peak m/e 109; parent peak, m/e 138 (75 %)
XX	(CCl ₄) 5.18–5.38(m, 1 H), 3.57 (s, 3 H), 3.55(s, 3 H), 2.70(s, 4 H), 1.99(q, 2 H, $J=6.0$ Hz), 1.02 (t, 3 H, $J=6.0$ Hz)	2945(s), 2860(m), 2805(s), 1700(m), 1210(s), 1150(m), 1095(s)	Mass spectrum: Base peak m/e 139; parent peak, m/e 172 (10 %)

Table 3. Continued.

Product	NMR, δ	IR, ^b cm ⁻¹	Other (UV or mass spectra)
XXVIII	(CDCl ₃) 4.87–5.18(m, 2 H), 4.40–4.70(m, 2 H), 3.50(s, 6 H), 2.81(s, 8 H)	2920(m), 2880(m), 2820(m), 1670(s), 1210(s), 1160(s)	Mass spectrum: Base peak <i>m/e</i> 111; parent peak, <i>m/e</i> 234 (53 %)
XXIX	(CCl ₄) 5.30–5.50(m, 1 H), 4.44–4.67(m, 1 H), 3.54(s, 3 H), 2.50–2.80(m, 4 H), 1.75–2.30(m, 2 H), 1.25–1.75(m, 2 H), 0.78–1.13(m, 3 H)	—	Mass spectrum: Base peak <i>m/e</i> 109; parent peak, <i>m/e</i> 152 (78 %)
XXX	(CCl ₄) 6.70–6.90(m, 3 H), 3.89(s, 3 H), 2.30–2.86(m, 2 H), 1.40–2.00(m, 2 H), 0.74–1.12(m, 3 H)	(CCl ₄), 3550(s), 2945(s), 2920(s), 1605(m), 1505(s), 1275(s), 1245(m), 1220(m), 1165(m), 1140(m)	Mass spectrum: Base peak <i>m/e</i> 137; parent peak, <i>m/e</i> 166 (91 %)

^a bs=broad singlet, bd=broad doublet. ^b Spectra measured as films except as otherwise indicated. ^c Further splitting observed. ^d Shoulders present.

ment to be ~1 % using 2-methoxy-4-propylphenol as a standard. This low yield is consistent with the expectation that the dihydro compound would arise only from those lignin monomer units which originally possessed free phenolic hydroxyl groups and which had no carbon-carbon bonds linking either the aromatic ring or the side chain to the adjoining unit. Based on the lignin structural scheme proposed by Freudenberg,²¹ approximately only 5 % of the units in the polymer network meet these requirements.

The NMR spectrum of the neutral component with the lower retention time did not correspond to any of the spectra of the products identified in the model compound reductions.

The acidic fraction was several fold larger than the neutral fraction and may be accounted for by the hydrogenolytic conversion of phenolic ether groups to phenols which are stable to reduction under Birch conditions. Gas chromatographic analysis of the acidic fraction revealed the presence of only one peak. The material corresponding to this peak was collected (200 mg or 1.6 %) and subjected to IR, NMR, and mass spectroscopic analysis. Collectively, these spectra suggested that the material was a phenol with methoxyl and propyl groups attached to the ring. Since the IR spectrum did not correspond to that of authentic 4-propylguaiacol, the compound has been tentatively identified as 2-methoxy-5-propylphenol (XXX, Table 3). If this assignment is correct, the formation of this

compound would be analogous to and consistent with the previously noted detection of 2-methoxy-5-methylphenol in the reduction of 4-methylveratrole.

Lignin-derived structures, such as the above, which contain a methoxyl substituent *para* to side chain, would necessarily have as their origin phenolic units which subsequently were converted to methyl ethers in the methylation pretreatment. This structural restriction accounts in part for the low recovery of XXX.

An NMR spectrum of the dioxane-soluble fraction displayed a broad band in the aromatic proton region but no pronounced signal in the vinyl proton region. This fraction appeared therefore to consist mainly of phenolic oligomers and was not investigated further.

Summary

1. Veratrole and its derivatives were reduced under Birch conditions to mixtures of di- and tetrahydroanisoles and veratroles. The dihydro-derivatives consisted mainly of the unconjugated type (1,4-addition) with much smaller amounts of conjugated cyclohexadiene derivatives being formed, either by 1,2-addition or from isomerization of unconjugated diene systems.

2. The relative proportion of the products varied somewhat from reaction mixture to reaction mixture in a manner which appeared to reflect differences in the electron-donating or electron-withdrawing characteristics of the sub-

stituent at the 1-position (*i.e.*, the side chain). The side chain substituent gave evidence of influencing not only the sites and degree of ring reduction but also the relative extents of replacement of the *meta*- and *para*-situated methoxyl groups as well.

3. Unlike the veratryl derivatives whose reduction gave rise to complex mixtures of partially reduced anisoles and veratroles, Birch reduction of 3,4,5-trimethoxytoluene afforded a comparatively simple product mixture consisting essentially of one product hydrogenated at the 1- and 4- positions with concomitant loss of the 4-methoxyl group.

4. Model compounds having α - and β -aryl ether substituents on the side chain were reduced in a stepwise fashion with cleavage of ether linkage preceding ring reduction. Hydrogenolysis in such cases was rapid and produced essentially quantitative yields of the phenol corresponding to the aryl substituent. Under the same conditions, methyl aryl ether groups were hydrogenolyzed to the corresponding phenols only to a slight extent, and the diphenyl ether linkage in 4,4'-dimethoxydiphenyl ether appeared entirely resistant to cleavage. In this latter case, the individual rings were each reduced to the dihydro stage in high yield.

5. Birch reduction of spruce dioxane lignin led to the formation of a neutral material in approximately 1 % yield which the available evidence strongly indicated to be 2,5-dihydro-4-propylanisole. Other evidence suggested that phenolic fragments in the monomer to oligomer range were produced as a consequence of hydrogenolysis of alkyl aryl ether linkages.

Conclusion

The present model compound study has shown that phenol ethers are extensively converted to cyclohexene and cyclohexadiene derivatives by reduction with sodium in liquid ammonia in the presence of a proton donor. Reduction of the aromatic ring is largely preceded by reduction of α -carbonyl groups and hydrogenolysis of benzyl alcohol and α - and β -aryl ether groups.

With respect to lignin itself, results of the current study lead to the conclusion that Birch reduction of phenolic ether moieties will occur only to a very limited extent since phenolic

structures, preferentially formed through hydrogenolysis of phenyl alkyl ether units, generally are not reduced under Birch conditions. Some Birch reduction can be expected to take place, however, on those units having ether units more resistant to hydrogenolysis (*e.g.*, diphenyl ether units) and on phenolic units converted to methyl ethers prior to reduction as demonstrated by the present study.

EXPERIMENTAL

Synthesis of reactants. 3,4-Dimethoxy- α -(*o*-methoxyphenoxy)toluene (XVII) was prepared as described by Mikawa,²² m.p. 77–78°C [lit.²² 78–79°C]. 3,4,5-Trimethoxytoluene (XV) was obtained by a Clemmensen reduction²³ of syringaldehyde²⁴ followed by methylation with dimethyl sulfate and alkali,²⁵ b.p. 95–98°C at 2–3 mmHg. NMR (neat): δ 6.43 (s, 2 H), 3.78 (s, 3 H), 3.73 (s, 6 H), 2.26 (s, 3 H).

Acetoguaiacone was methylated with dimethyl sulfate and alkali to produce acetoveratrone (XXIV), b.p. 135–136°C at 2–3 mmHg. NMR (CDCl₃): δ 7.37–7.70 (m, 2 H), 6.76–7.00 (m, 1 H), 3.90 (s, 3 H), 2.55 (s, 3 H). Reduction of XXIV with sodium borohydride afforded 1-(3,4-dimethoxyphenyl)ethanol (XVIII), b.p. 105–110°C at 2–3 mmHg. NMR (CCl₄): δ 6.82 (bs, 1 H), 6.70 (s, 2 H), 4.64 (q, 1 H, J =5.5 Hz), 3.67 (s, 6 H), 3.59 (s, 1 H), 1.32 (d, 3 H, J =5.5 Hz).

1-(3,4-Dimethoxyphenyl)-2-(*o*-methoxyphenoxy)ethanol (XXIII) was prepared by reduction of the corresponding ketone,²⁶ m.p. 133.5–134.0°C [lit.²⁴ 133–134°C]. 4,4'-Dihydroxydiphenyl ether was converted to the corresponding dimethyl ether (XXVII) by methylation with dimethyl sulfate and alkali, m.p. 100–102°C [lit.²⁸ 102°C].

Anisole, veratrole, and 4-methylveratrole were obtained commercially and used without further purification.

Synthesis of products. 2,3,4,5-Tetrahydroanisole (IV) was prepared by reaction of cyclohexanone with trimethyl orthoformate in the presence of mesitylene sulfonic acid as described by Lindsay and Reese.²⁹ Distillation of the product mixture through a Vigreux column yielded a fraction boiling at 139–142°C [lit.²⁹ 138–142°C] whose NMR and IR spectral characteristics (Table 2) were consistent with those expected for the compound. The same procedure was used to prepare 2,3,4,5-tetrahydro-4-methylanisole (XII) from 4-methylcyclohexanone; b.p. range of XII, 159–161.5°C.

2,3-Dihydroanisole was obtained by two methods. The first consisted of treatment of 2-cyclohexen-1-one with 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid as outlined by Nussbaum *et al.*³⁰ The product mixture was distilled through a Vigreux column

and the fraction boiling at 146–147°C collected. Gas chromatographic analysis indicated that the product was approximately 80 % pure.

2,3-Dihydroanisole was also obtained by reacting a fraction comprised of a mixture of 2,3-dihydroanisole and 2,5-dihydroanisole with potassium *t*-butoxide³¹ to isomerize the non-conjugated component. The fraction boiling at 142–145 °C was approximately 70 % pure as indicated by gas chromatographic analysis. This fraction was further purified by preparative gas chromatography (see Table 3 for NMR and IR characteristics).

3-Hydroxy-4-methoxytoluene (5-methylguaiacol) was prepared by subjecting isovanillin (3-hydroxy-4-methoxybenzaldehyde) to a Clemmensen reduction. The product was distilled under reduced pressure yielding an oil which solidified on cooling, m.p. 32–33 °C [lit.¹² 33 °C]. NMR (CDCl₃): δ 6.56–6.80 (bd, 3 H), 5.60 (s, 1 H), 3.67 (s, 3 H), 2.18 (s, 3 H).

4-Propylanisole was prepared by the catalytic hydrogenation of isoeugenol methyl ether.

Other products were obtained by preparative gas chromatography of the product mixtures and subsequently purified.

Bromination of 1,4-dihydro-3,5-dimethoxytoluene. 1,4-Dihydro-3,5-dimethoxytoluene (200 mg) was dissolved in CCl₄ and reacted at room temperature with a solution of bromine in the same solvent. After removal of solvent, a solid was obtained which after recrystallization from methanol/water melted at 170 °C. Yield, 88 mg, mass spectrum (70 eV): parent ion (p) and base peak at *m/e* 312, *p* + 2 and *p* – 2 peaks are 54 % of parent peak; NMR (CDCl₃): 6.46 (s, 1 H), 3.89 (s, 6 H), 2.62 (s, 3 H).

Reduction of model compounds. Approximately 400 ml of liquid NH₃ was distilled from a cylinder through a glass filter and condensed in a 1 l, three-necked, round-bottomed flask by means of a dry ice/acetone-cooled cold finger. The flask was immersed in a dry ice/acetone bath and fitted with a dropping funnel to which was attached a CaCl₂ drying tube.

The aromatic compound (0.2 mol) in ethanol* (1.0 mol) was added to the ammonia through the dropping funnel and the mixture heated to its reflux temperature by removal of the dry ice/acetone bath. Sodium (1.0 mol) was then added carefully in 0.5–1.0 g amounts; and when the addition was completed, the mixture was allowed to reflux for 4 h. Some additional ammonia was distilled into the flask during this period to maintain the level constant. Under these conditions, the starting compound was for all practical considerations completely consumed in all instances.

The reaction was quenched after replacing the cold finger with a stopper, by the slow addition of 100 ml of methanol through the dropping

funnel. After most of the excess sodium had reacted (~30 min), 100 ml of water was added and the mixture was extracted with 5 × 50 ml of ether (neutral fraction); the water phase was acidified with concentrated HCl and extracted with 5 × 50 ml ether (acidic fraction).

Small samples of the neutral and acidic fractions were set aside for quantitative VPC analysis. The remaining portions of the two fractions were concentrated by distilling off the solvent through a Vigreux column at atmospheric pressure.

Preparation and modification of dioxane lignin. Dioxane lignin was prepared from 150 g of ethanol-benzene (1:1) extracted Norway spruce wood meal by treatment with a solution of 1,4-dioxane/water (9:1) containing 0.2 N HCl as described by Browning.³² Yield, 22.8 g. Anal.: C 59.45; H 5.67; OCH₃, 14.27.

To maximize the possibility of obtaining Birch reaction products, the dioxane lignin was first modified by reducing the carbonyl groups with NaBH₄ and etherifying the phenolic hydroxyl groups with diazomethane. Dioxane lignin (10.5 g) in 440 ml of EtOH/H₂O (1:1) and 120 ml of 0.1 M NaOH was reacted with 6.4 g of NaBH₄ overnight.³³ The reaction mixture was acidified to pH 4 with hydrochloric acid and concentrated. Water was added and the resulting precipitate was centrifuged off and washed twice with water. Yield, 9.3 g. An IR spectrum of the product indicated that all but a trace of carbonyl had been removed.

The borohydride-reduced lignin (9.1 g) was partially dissolved in 200 ml of 1,4-dioxane and reacted twice with diazomethane over a 2 h period. The solution was concentrated to 200 ml and after removal of a small portion for IR and elemental analysis, was reacted directly with Na/NH₃ in the presence of ethanol. Anal.: C 62.08; H 5.90; OCH₃, 16.51.

Birch reduction of modified dioxane lignin. Modified dioxane lignin dissolved in 1,4-dioxane (see previous section) was reacted for 4 h in the standard way using 400 ml of liquid ammonia, 23.0 g of sodium, and 46.0 g of ethanol. After the addition of methanol and water and evaporation of the ammonia, a brownish-yellow liquid remained which contained no undissolved material.

The reaction mixture was extracted with 5 × 50 ml of ether (neutral fraction) following which the water phase was acidified with concentrated hydrochloric acid. A brown precipitate formed upon acidification which did not dissolve when the mixture was extracted with 5 × 50 ml of CHCl₃ (acidic fraction). The polymer-like precipitate was filtered off and dissolved in 1,4-dioxane (dioxane-soluble fraction).

The amount of material in each fraction in solution was obtained by evaporating an aliquot of each solution to dryness and weighing the residue: neutral fraction, 0.35 g; acidic fraction, 1.85 g; and dioxane-soluble fraction, 3.45 g.

Separation of reaction products. Preliminary

* Dioxane (50 ml) was employed as a co-solvent to dissolve compounds XVII, XXIII, XXVI, and XXVII.

attempts to separate the product mixtures into their individual components by distillation through Vigreux and spinning band columns were generally unsuccessful. Chromatography on a silver nitrate-silica gel column²⁴ was similarly unproductive, seemingly as a result of reaction between the products and the column.

Satisfactory separation of the product mixtures was ultimately obtained using preparative-scale gas chromatography. The retention time data in these analyses were diagnostically useful for classifying peaks as corresponding to dihydro unconjugated, dihydro conjugated, and tetrahydro cyclohexyl ring systems.

Preparative-scale gas chromatography was performed on an F & M Model 776 gas chromatograph. A 220 × 1.8 cm stainless steel column was filled with 3 % Carbowax 20M-TPA on Chromosorb G (30/60). Column conditions: oven, 90–150 °C (isothermal); detector, 190 °C; injector, 170 °C; manifold, 180 °C; flow rate, 200 ml N₂/min. A 300–400 μl amount of 50 % (by volume) ether solution was injected.

The collected samples were injected on an analytical column to confirm purity and, if necessary, reinjected on the preparative column to effect greater purification. After separation and purification, the components in the product mixture were subsequently characterized by various combinations of IR, UV, NMR and mass spectrometry. In other instances (compounds XVII, XXIII, XXIV, and XXVI), identification and estimation were based solely on comparison of the retention time and peak area of the component with the corresponding parameters of a known standard.

The analytical instrumentation consisted of Varian Aerograph models 1520 and 1700 fitted with a 180 × 0.3 cm stainless steel column filled with 3 % Carbowax 20M-TPA on Chromosorb G (45/60). Column conditions: oven, 90–130 °C (isothermal); detector, 195–250 °C; injector, 150–200 °C; flow rate, 25 ml N₂/min. Products in the acetoveratrone and dioxane lignin reaction mixtures were separated and collected using an F & M Model 720 (thermal conductivity) instrument fitted with a 180 × 0.6 cm stainless steel column filled with 3 % OV-1 on Chromosorb G (45/60). Column conditions: oven, 90–160 °C (isothermal); detector, 120–200 °C; 110–180 °C; flow rate, 40 ml He/min.

For quantitative gas chromatographic analysis, standards were prepared from the collected or synthesized samples whenever possible and peak heights were compared to those of the corresponding peaks in the reaction mixture. Otherwise, peak areas were compared to those of a closely related compound with a similar structure. The column support in these cases was coated with Carbowax 20M-TPA (3 %).

Spectrometric analysis. Infrared spectra were recorded on a Perkin-Elmer grating infrared spectrophotometer. Liquid samples were measured as films; solids were either mixed with KBr and made into pellets or dissolved in chloroform

or carbon tetrachloride. Mass spectra were obtained using a Perkin-Elmer Hitachi Model RMU-6E single-focusing spectrophotometer. Ultraviolet spectra were obtained on samples dissolved in 95 % ethanol using a Unicam Model SP-800A recording spectrophotometer.

NMR spectra were recorded on a Varian A-60 spectrometer using trimethylsilane as an internal standard. The spectra were obtained with the samples in the neat condition whenever possible, but usually the amount of collected sample was too small and the sample was dissolved in a solvent. The instability of some of the products in CDCl₃ resulted in the use of CCl₄ which, after first being washed with base, obviated this problem.

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