Insoluble Lignin Models (1): Synthesis of Lignin Dimers Containing Propyl Alcohol Appendages

Patrick B. Apfeld[a]; Donald R. Dimmel[a]

[a] The Institute of Paper Chemistry, Appleton, Wisconsin

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INSOLUBLE LIGNIN MODELS (1): SYNTHESIS OF LIGNIN DIMERS
CONTAINING PROPYL ALCOHOL APPENDAGES

Patrick B. Apfeld and Donald R. Dimmel
The Institute of Paper Chemistry
P.O. Box 1039, Appleton, Wisconsin 54912

ABSTRACT

Three lignin model dimers have been synthesized. The models
contain propyl alcohol appendages on C5 of ring A (12), C4 of ring
B (15), and Cβ of the side chain (21), respectively. The propyl
alcohol appendages will serve as "handles" for bonding the models
to a polymer matrix. Model 21 has also been used to diagnostically
examine the delignification efficiences of pulping chemicals.

INTRODUCTION

The random, crosslinked, polymeric structure[1] of lignin makes
studying its reactions difficult, primarily because the starting
material cannot be well characterized and there are a multitude of
products formed. Consequently, researchers have resorted to
studying reactions of well-defined lignin models.[2-5] The models
generally are patterned after a lignin dimer unit which is
believed to be present in the polymer. However, these models are
generally water soluble and their reactions may not accurately
reflect the chemistry occurring with water insoluble lignin
materials. Therefore, we have begun studying the synthesis and
reactions of heterogeneous (insoluble) lignin models.

This report describes the synthesis of three lignin model dimers
which have propyl alcohol appendages ("handles"). The primary

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alcohol handle will provide the site of bonding to the polymer.[5]
The precedence for polymer binding to a primary alcohol, in the
presence of other hydroxyl groups, is provided in several synthetic
carbohydrate studies. For example, monosaccharides can be bound
to polymers at the C_6-primary alcohol groups with triphenylmethyl
(trityl) linkages.[6] Selective reactions can then be performed on
secondary hydroxyl groups of the immobilized carbohydrates, and
the modified carbohydrates can be released from the polymers by
acid treatment.[7,8] Similar reactions should be possible for a
lignin model compound.[9,10]

    The principal considerations which need to be addressed when
designing a model with a primary alcohol handle are (1) the model
type, (2) the location of the handle, and (3) the length of the
handle. The most desirable model is a β-aryl ether type. A large
number of mechanistic studies have been done with this model type,
and direct comparison of homogeneous vs. heterogeneous reactions
would be very informative.

    The length of the primary alcohol handle was chosen to be
three carbons (propyl) because of the ease of synthesis and to
provide sufficient distance between the reactive parts of the
model and the bonding site. Reasonable distances are needed to
ensure that steric inhibition to reaction is not a factor.

    The location of the handle (and thus the polymer linkage)
plays a role in product analysis. Equation 1 illustrates a typi-
cal lignin model fragmentation reaction. The extent of fragmen-
tation is generally determined by the amount of simple phenol 3

$$\text{(1)}$$

1   2   3
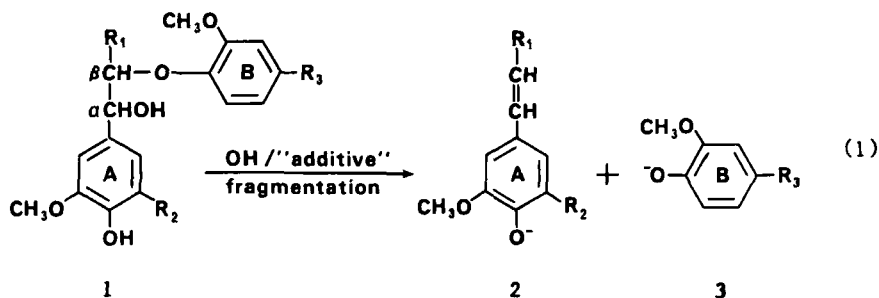
released and not the amount of the styrene product **2**.[11] The
latter is prone to polymerize; consequently, its observed yields
are often low and do not accurately reflect the extent of reaction.

A polymer attachment through ring B (i.e., **1**, R_3-attachment)
would liberate, upon fragmentation, a styrene product into the
solution phase which may be difficult to quantitate accurately. A
better attachment would be through ring A (i.e., **1**, R_2-attachment)
or the side chain (i.e., **1**, R_1-attachment) so that fragmentation
would liberate into solution an easily-analyzable phenol (**3**). We
describe here the synthesis of three models in which there is a
propyl alcohol "handle" on the ring A, ring B, and C_β positions,
respectively.

RESULTS AND DISCUSSION

A-Ring Handle Model

We sought a "generic" procedure, one which would start with
any of a variety of already conventional lignin dimers and add a
propyl alcohol handle to it. Portions of a recently described
coumarin synthesis appeared suitable. Panetta and Rapoport[12]
report that 2,2-diethoxychroman is formed when guaiacol is reacted
with triethylorthoacrylate. We have found that a diethoxychroman
can also be prepared from a para-acyl phenol and can be converted
into a propyl alcohol handle (Fig. 1).

Placing a propyl handle on the A-ring was first attempted with
the readily available acetoguaiacone (**4**). The diethoxychroman **6**
was formed in excellent yield (ca. 74%) and was subsequently
hydrolyzed with HCl to give the ester **7**. The simultaneous reduc-
tion of the α-carbonyl and ethyl ester of **7** was effected with
LiAlH$_4$, giving compound **8**, a lignin model monomer with a primary
alcohol handle.

Similarly, the phenacyl β-aryl ether **9**, which can be prepared
by several techniques,[13,14] was subjected to the identical synthe-
tic sequence. The desired compound **12** was successfully prepared
in an overall yield of 58% (3-steps, from **9**). This synthetic
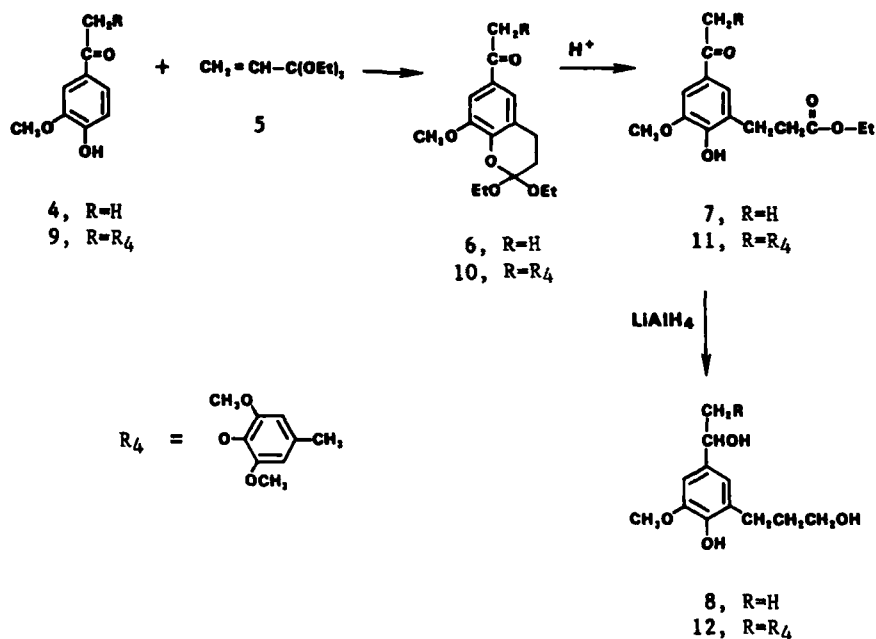
Figure 1. Adaptation of Panetta and Rapoport's[12] coumarin
           synthesis for the introduction of a propyl alcohol
           handle to acetoguaiacone (4) and lignin dimer **9**.

sequence should be applicable for introducing a primary alcohol
handle to a variety of other lignin dimers with different β-aryl
groups and/or β-alkyl substituents.   However, problems in deriva-
tizing[5] the A-ring propanol model **10** led us to seek alternative
functionalized models.

B-Ring Handle Model

     As mentioned previously, the alkaline fragmentation of a
polymer-bound model based on B-ring attachment would liberate a
styrene product which may be difficult to analyze quantitatively.
Alternatively, a B-ring handle model which has an α-carbonyl rather

than an α-hydroxyl could be a useful model; the alkaline degrada-
tion of phenacyl aryl ethers has been studied.[15] The alkaline
fragmentation of **15** bound to a polymer at the propyl alcohol site
should liberate acetoguaiacone (**4**), a product which should be
easily quantified.

Ketone **15** was obtained in roughly 60% yield from the coupling
of β-bromoketone **13**[13] with the sodium salt of 3-(3-methoxy-4-
hydroxyphenyl)-1-propanol (**14**) [Eq. (2)]. The latter was prepared
by (a) hydrogenation of ferulic acid over palladium on carbon, (b)
reduction of the resulting dihydroferulic acid with borane-THF or
LiAlH$_4$, and (c) treating with NaOH. Compound **15** was tritylated in
a modest yield (35% after chromatography) with trityl pyridinium
tetrafluoroborate[16] to give **15-Tr**. This latter reaction
demonstrated that the propyl OH can be selectively functional-
ized in the presence of a phenolic OH group and that **15** could
possibly be bound to a polymer _via_ a trityl ether linkage.

13   14-Na salt   15, R=H
                                              15-Tr, R=CPh$_3$

Beta-Position Handle Model

One way to functionalize the side chain of a lignin model is
alkylation of the β-carbon of an α-keto structure. For example,
16 can be alkylated with methyl iodide or formaldehyde to give **17**
or **18**, respectively; however, the alkylation failed with ethyl,
propyl, and benzyl halides.[17] We were gratified to find that **16**
was alkylated with allyl bromide to give ketone **19** in 68% yield.
Apparently, a highly reactive substrate, such as allyl bromide,[18]
is needed for a successful alkylation of ketone **16**.

16, R=H
17, R=CH$_3$
18, R=CH$_2$OH
19, R=CH$_2$CH=CH$_2$
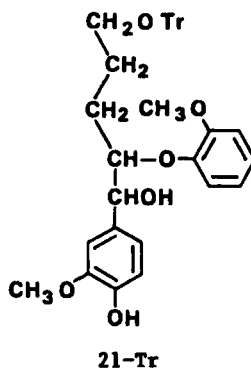
21-Tr

The β-allyl ketone **19** was transformed to the desired β-propanol alcohol **21** in two ways. The two routes (Fig. 2) differ in the order in which following steps were performed: (1) hydroboration of terminal olefin with disiamylborane (DSB) followed by an oxidative work-up with hydrogen peroxide (O)[19] to give a terminal alcohol and (2) sodium borohydride reduction of the α-carbonyl group to a benzyl alcohol. Either route involves the introduction of a second asymmetric carbon (step A$_2$ or B$_1$) and the likelihood of producing mixtures of erythro/threo diastereomers.

Route A afforded a mixture of diastereomers of **21** which could not be separated by chromatographic techniques. Route B, on the other hand, gave a mixture of isomers after the first step, which could be chromatographically separated; hydroboration of the major isomer of alcohol **22** afforded one diastereomer of **21** as a crystalline product. Both routes gave the same diastereomer as the major product. The yield of the three-step conversion of **16** to **21** was 28% (roughly 66% for each step).

The NaBH$_4$ reduction steps on either ketone **19** (step B$_1$) or ketone **20** (step A$_2$) might be expected to show a preference for one diastereomer product over the other, since the carbon adjacent to the carbonyl group under reduction is asymmetric.[20] Steric differences in the substituents on the asymmetric carbon can sometimes produce high selectivities for a particular diastereomer
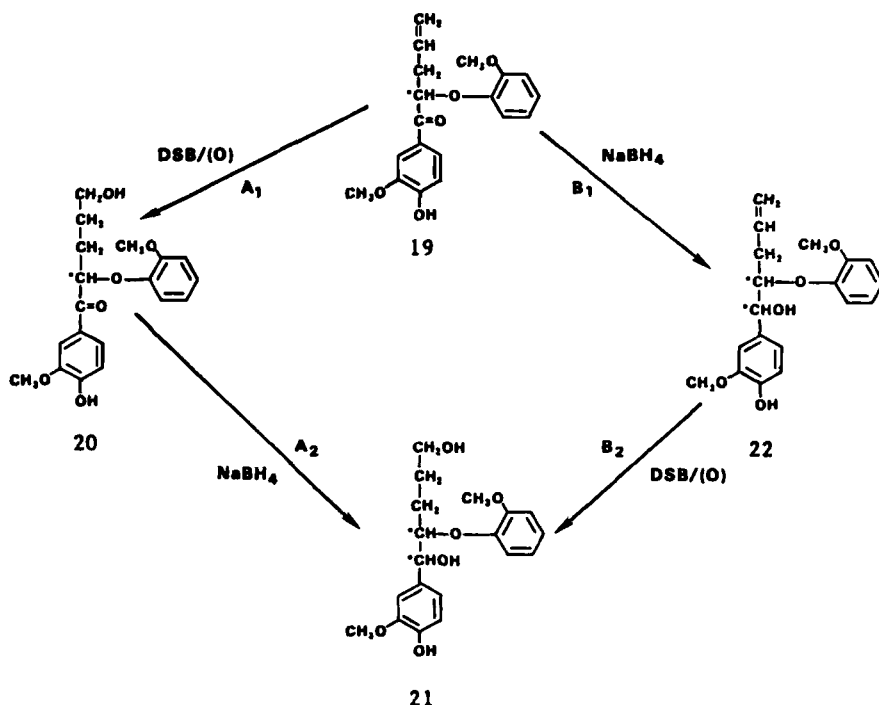
Figure 2.   Two routes (A and B) used to reduce the α-carbonyl
            group and convert the allyl substituent to a propanol
            substituent.

product.[21,22] The major isomer for **21** must be the same as for **22**
(a precursor of **21**). Sodium borohydride reduction of **19**, giving
22, would be expected to have a stereoselectivity similar to that
observed for reduction of **17**, which gives principally erythro-1
(R_1=CH$_3$, R_2=R_3=H).[23] Based on this analogy and the observed chem-
ical shifts,[24] the major isomers for both **21** and **22** appear to be
of the erythro-type.

The fact that the propyl alcohol handle can be functionalized
selectively in the presence of secondary benzyl OH group and
phenolic OH group was demonstrated by treating **21** with trityl
chloride/pyridine[25] and observing the production of a primary

trityloxy product, **21-Tr**, in 64% yield. Such a result suggests
that **21** could be bound to a polymer _via_ a trityl ether linkage.[5]

SUMMARY

Three unique lignin model dimers have been prepared. Each new
model is similar to lignin models which have been routinely studied,
but unique in that they all incorporate a propyl alcohol handle
onto their respective dimer, each at a different position. The
synthetic routes leading to β-aryl ethers **12** and **21** might possibly
be used to introduce a propyl alcohol handle to a variety of avail-
able lignin models. The third synthesis, leading to a B-ring handle
model is specific in that it does not involve adding a propyl
alcohol side-chain to an already prepared lignin model dimer.

Studies on the degradation reactions of models **21**, **21-Tr**, and
22 have provided interesting data on the efficiency by which
pulping chemicals (HO^-, HS^-, and AHQ^{-2}) fragment these models.[26]

EXPERIMENTAL

General Information - Proton and ^{13}C-NMR were recorded on a
Jeol FX-100 spectrometer using $CDCl_3$ or d_6-DMSO as a solvent and
TMS as an internal reference. Infrared spectra were recorded on a
Perkin-Elmer Model 700 infrared spectrometer and standardized with
polystyrene. Electron impact mass spectra were obtained at 70 eV
using a direct insertion probe (DIP) with a Hewlett-Packaged 5985
mass spectrometer. Elemental analyses were performed by Micro-
Tech Laboratories, Skokie, Illinois.

All solvents employed, unless indicated otherwise, were A.C.S.
reagent grade. Reagents and starting materials were obtained from
Aldrich Chemical Co., Milwaukee, Wisconsin. All melting points
recorded are uncorrected.

**4-Hydroxy-3-methoxy-β-(2,6-dimethoxy-4-methylphenoxy)aceto-
phenone (9)** - The phenacyl β-aryl ether **9** was prepared according
to the general method of Miksche;[14] its specific preparation is
detailed elsewhere.[26]

6-Acetyl-2,2-diethoxy-8-methoxychroman (6) - Into 150 mL of
toluene was dissolved 15.0 g (90.4 mmol) of acetoguaiacone (4),
9.2 g (90.4 mmol) of pivalic acid, and 31.5 g (180.8 mmol) of
triethylorthoacrylate (5).[27] The mixture was refluxed for 24 hr,
cooled, diluted with 30 mL of ether, washed with 1N NaOH, water,
and saturated aqueous NaCl, dried (Na_2SO_4), and concentrated in
vacuo to give a gold oil which crystallized upon standing.
(Acidification and ether extraction of the NaOH resulted in the
recovery of ca. 0.9 g of starting material.) Recrystallization
of the gold solid from hexane gave 19.8 g (74.2%) of light yellow
crystals of 6: mp 81.0-84.0°C; IR (mull) cm^{-1} 1680 (C=O); ^{1}H-NMR
($CDCl_3$) δ 1.19 (t, J = 7 Hz, 6, OCH_2CH_3), 2.12 (t, J = 7 Hz, 2,
$ArCH_2CH_2$), 2.55 (s, 3, $COCH_3$), 2.91 (t, J = 7 Hz, 2, $ArCH_2$), 3.72
(q, J = 7 Hz, 2, OCH_2CH_3), 3.74 (q, J = 7 Hz, 2, OCH_2CH_3), 3.85
(s, 3, OCH_3), and 7.35 (s, 2, aryl).

Ethyl 5-acetyl-2-hydroxy-3-methoxydihydrocinnamate (7) - Into
200 mL of ether was dissolved 12.0 g (40.5 mmol) of 6. To this
mixture was added 200 mL of 10% aqueous HCl and the two phase mix-
ture was stirred for 2.25 hr. The phases were separated and the
aqueous layer extracted with ether. The combined organic layers
were washed with water and saturated aqueous NaCl, dried (Na_2SO_4),
and evaporated to give 11.5 g of an oil which hardened upon
standing to orange-gold crystals of 7: mp 64.0-65.0°C; IR (mull)
cm^{-1} 3350 (OH), 1730 (ester C=O), 1670 (ketone C=O), and 1600
(aryl); ^{1}H-NMR ($CDCl_3$) δ 1.22 (t, J = 7 Hz, 3, CH_2CH_3), 2.54 (s,
3, $ArCOCH_3$), 2.67 (t, 2, $ArCH_2$), 3.08 (t, 2, $ArCH_2CH_2$), 3.92 (s,
3, OCH_3), 4.13 (q, 2, J = 7 Hz, $COOCH_2CH_3$), 6.59 (s, 1, OH), and
7.43 (s, 2, aryl).

1-(3-Methoxy-4-hydroxy-5-[γ-hydroxypropyl]phenyl) ethanol (8) -
A slurry of 0.86 g (22.7 mmol) of $LiAlH_4$ in 35 mL of dry, freshly
distilled THF was stirred while a solution of 2.0 g (8.8 mmol) of
7 in 35 mL THF was dripped in over 1 hr. The mixture was brought
to and kept at reflux for 1.5 hr and then allowed to come to room
temperature with stirring overnight. The reaction was quenched by

the addition of saturated aqueous Na_2SO_4, until effervescing
stopped and a nearly colorless granular solid was obtained. The
mixture was filtered and the collected residue rinsed with dry
ether. The organic filtrate was reduced in vacuo to give 0.5 g of
8 as an oil: IR (neat) cm^{-1} 3350 (broad, OH), no carbonyl absor-
bances, and 1600 (aryl); ^{1}H-NMR (d_6-DMSO) δ 1.28 (d, J = 6 Hz, 3,
CH_3), 1.64 (m, 2, $ArCH_2CH_2$), 2.53 (t, J = 8 Hz, 2, $ArCH_2$), 3.40
(t, J = 7 Hz, 2, CH_2OH), 3.76 (s, 3, OCH_3), 4.58 (q, J = 6.5 Hz,
1, ArCHOH), 5.38 (broad s, 3, three OH), 6.64 (s, 1, aryl), and
6.75 (s, 1, aryl).

The solid (aluminum salts) residue from above was dissolved in
$1\underline{N}$ H_2SO_4, and the acidic mixture was extracted with ether. The
ether extracts were washed with water, dried (Na_2SO_4), and reduced
in vacuo to give ca. 0.3 g of an oil with spectra identical to the
product 8 described above.

6-(2,6-Dimethoxy-4-methylphenoxyl)acetyl-2,2-diethoxy-8-
methoxychroman (10) - Compound 9 was subjected to the identical
procedure for preparing diethoxychromans (as described above) with
the following quantities: 12.0 g (32.1 mmol) of 8, 1.64 g (6.05
mmol) of pivalic acid, and 11.2 g (64.2 mmol) of triethyl ortho-
acrylate. The diethoxychroman 10, 17.5 g, was obtained as an oil
and used without further purification: IR (neat) cm^{-1} 1690 (C=O),
and 1590 (aryl); ^{1}H-NMR ($CDCl_3$) δ 1.19 (t, J = 7 Hz, 6, CH_2CH_3),
2.11 (t, J = 7 Hz, 2, $ArCH_2CH_2$), 2.32 (s, 3, $ArCH_3$), 2.89 (t, J =
6.5 Hz, 2, $ArCH_2CH_2$), 3.44 (m, 4, OCH_2CH_3), 3.79 (s, 6, $ArOCH_3$),
3.88 (s, 3, $ArOCH_3$), 5.09 (s, 2, $ArCOCH_2$), 6.4 (s, 2, aryl), 7.22
(s, 1, aryl), and 7.50 (s, aryl).

Ethyl 5-(2,6-dimethoxy-4-methylphenoxyacetyl)-2-hydroxy-3-
methoxydihydrocinnamate (11) - All of the crude product 10, from
the previous procedure, was dissolved in 100 mL ether and stirred
for 3 hr with 100 mL of 10% HCl. While the reaction proceeded, a
fine white powder crystallized out of the ether phase. The entire
reaction mixture was chilled; the white powder was collected on
a fine porosity filter funnel and washed with cold water and

ether to give 7.1 g of 11. The filtrate was separated and the
ether layer washed with water and saturated aqueous NaCl, dried
(Na_2SO_4), and concentrated on a steam cone until slightly cloudy;
upon cooling another 3.0 g of product was collected, to give a
total of 10.1 g (72.7% two-step yield from 9) of 11: mp 111.5-
113.0°C; IR (mull) cm^{-1} 3400 (OH), 1590 (aryl), 1660 (ketone C=O),
and 1710 (ester C=O); ^{1}H-NMR ($CDCl_3$) δ 1.22 (t, J = 7 Hz, 3,
CH_2CH_3), 2.32 (s, 3, $ArCH_3$), 2.64 (t, J = 6 Hz, 2, CH_2COO), 2.99
(t, J = 6 Hz, 2, CH_2CH_2COO), 3.80 (s, 6, $ArOCH_3$), 3.93 (s, 3,
$ArOCH_3$), 4.11 (q, J = 7 Hz, 2, CH_2CH_3), 5.08 (s, 2, CH_2OAr), 6.40
(s, 3, two aryl-H and OH), and 7.21 (d, 2, aryl); ^{13}C-NMR ($CDCl_3$)
ppm 14.2 (q, CH_2CH_3), 21.8 (q, $ArCH_3$), 25.4 (t, CH_2CH_2COO), 33.8
(t, CH_2COO), 55.9 (q, two $ArOCH_3$), 56.1 (q, $ArOCH_3$), 60.3 (CH_2CH_3),
75.1 (t, CH_2OAr), 105.8 (d, aryl C-3,5), 108.6 (d, aryl C-6), 124.0
(d, aryl C-2), 125.6, 126.9, 133.8, 133.9 (all d, aryl CH), 146.2,
148.3, 152.5 (all s, aryl C), 172.7 (s, COO), and 193.2 (s, ArCO);
MS (DIP) $\underline{m/z}$ (%) 432 (16, M^+), 251 (38), 167 (100), and 77 (14).

1-(4-Hydroxy-3-methoxy-5-[γ-hydroxypropyl]phenyl)-2-(2,6-di-
methoxy-4-methylphenoxyl)ethanol (12) - The $LiAlH_4$ reduction pro-
cedure used in the reduction of 7 was repeated with the following
quantities and conditions: 5.0 g (11.6 mmol) of 11 and 1.2 g
(32.4 mmol) of $LiAlH_4$; the mixture was refluxed for 21.5 hr. The
reaction was quenched by the addition of saturated aqueous Na_2SO_4
giving a suspension of grey-white solid in the THF. The mixture
was filtered and rinsed with copius quantities of ether. Additional
product was recovered by rinsing the aluminum salts with CH_2Cl_2.
The filtrates were washed with water and dried (Na_2SO_4) and con-
centrated in vacuo to give oils which were crystallized from ether
to give a total of 3.7 g (82%) of 12: mp 110.0-111.0°C; IR (mull)
cm^{-1} 3223, 3450 (OH), 1595 (aryl), and no C=O absorbances; ^{1}H-NMR
(d_6-DMSO) (60°C) δ 1.69 (m, 2, $CH_2CH_2CH_2$), 2.25 (s, 3, $ArCH_3$),
2.56 (t, J = 7 Hz [with further fine splitting], 2, $ArCH_2$), 3.42
(t, J = 7 Hz, 2, CH_2OH), 3.6-4.1 (broad signal, 1, OH), 3.75, 3.77
(2 s, 6 + 3, $ArOCH_3$), 3.79 (d of d, J = 7.5 and 10 Hz, 1,

CH$_A$CH$_B$OAr), 3.96 (d of d, J = 4.5 and 10 Hz, 1, CH$_A$CH$_B$OAr),
4.5-4.9 (broad signal, 1, OH), 4.71 (d of d, J = 4.5 and 7.5 Hz,
1, CHOH), 5.6-7.2 (broad signal, 1, OH), 6.47, 6.48 (2 s, 1 + 1,
aryl), 6.70 (d, J = 2 Hz, 1, aryl), and 6.82 (d, J = 2 Hz, 1,
aryl); ^{13}C-NMR (d$_6$-DMSO) ppm 21.3 (q, ArCH$_3$), 26.2 (t, CH$_2$CH$_2$CH$_2$),
32.8 (t, ArCH$_2$), 55.6 (q, ArOCH$_3$). 55.8 (q, two ArOCH$_3$), 60.5 (t,
CH$_2$OH), 71.5 (d, CHOH), 78.5 (t, CH$_2$OAr), 106.3, 107.6, 119.7,
134.5 (all d, aryl CH), and 127.9, 131.9, 132.8, 142.9, 146.8,
152.3, (all s, aryl C); MS (DIP) m/z (%) 392 (2, M$^+$), 182 (5), 168
(100, ArOH$^+$), and 77 (5).

Anal. calcd. for C$_{21}$H$_{28}$O$_7$(%): C, 64.27; H, 7.19; O, 28.54.
Found: C, 63.50; H, 7.17; O, 28.46.

3-(3-Methoxy-4-hydroxyphenyl)-1-propanol (14) - Into 700 mL of
absolute ethanol was dissolved 50.0 g of ferulic acid, after which
ca. 1.5 g of 10% Pd on carbon was added. The mixture was stirred
while hydrogen was supplied to the reaction mixture from a balloon
(attached to a 3-way stopcock), which could be periodically
recharged with the gas; the reaction was allowed to proceed until
no more hydrogen was consumed. The solution was filtered through
CELITE, concentrated in vacuo to give a light brown oil, and crystal-
lized from CH$_2$Cl$_2$/hexane to give 42.8 g (84.8%) of dihydroferulic
acid as light-brown needles: mp 88.0-90.5°C (Lit.^{28} 89-90°C).

Dihydroferulic acid, 40.0 g (20.4 mmol), was dissolved into
200 mL of dry, freshly distilled THF; all glassware was oven-dried
and all operations, until the workup, were under dry nitrogen. To
the dihydroferulic acid solution was added (in 5 portions using a
syringe) a total of 245 mL (24.5 mmol) of 1.0M BH$_3$-THF complex.
After ca. 75% of the reagent had been added, the reaction mixture
formed an unstirrable gel. The mixture was heated at reflux for 1
hr, allowed to cool, and diluted with 400 mL water to give a
clear, yellow-brown solution. This quenched reaction mixture was
extracted with ether and the ether extracts were washed with 5%
aqueous NaHCO$_3$, saturated aqueous NaCl, dried (Na$_2$SO$_4$) and con-
centrated in vacuo to give 31.3 g crude 14 (84% yield, ca. 100%

conversion). From the bicarbonate wash was recovered ca. 8 g
dihydroferulic acid.

Vacuum distillation of 18.9 g of crude **14** yielded 13.2 g of
purified **14**: bp 178-180°C (1 mm Hg); IR (neat) cm^{-1} 3400 (OH) and
1520, 1600 (aryl); ^{1}H-NMR (CDCl$_3$) δ 1.82 (m, 2, C**H**$_2$CH$_2$OH), 2.59
(t, J = 7 Hz, 2, ArC**H**$_2$), 3.62 (t, J = 7 Hz, 2, C**H**$_2$OH), 3.76 (s, 3,
ArOC**H**$_3$), and 6.5-6.9 (multiplets, 3, aryl).

The sodium salt of **14** was prepared by dissolving 5.6 g (30.6
mmol) of the phenol in 30.6 mL of 1.00N aqueous NaOH; the water
was removed in vacuo. Two 50 mL portions of 1,2-dichloroethane
were added and evaporated in vacuo to remove residual moisture;
the vacuum was always purged with nitrogen, and the contents
chilled to ca. 0°C between 1,2-dichloroethane additions. The
residual sodium salt of **14** was a fluffy off-white solid which was
desiccated for 24 hr over fresh P$_2$O$_5$ before its subsequent use.

**4-Hydroxy-3-methoxy-β-(2-methoxy-4-[γ-hydroxypropyl]phenoxy)-
acetophenone (15)** - The dimer **15** was prepared by the general
coupling technique of Hosoya, et al.,[13] as modified by Dimmel, et
al.[17] Three equivalents of the sodium salt of **14** (30.6 mmol)
were dissolved in 25 mL dry DMF (dried over molecular sieves) and
stirred under nitrogen while 2.5 g (10.2 mmol) of β-bromoaceto-
guaiacone (**13**) in 25 mL DMF was added dropwise over 1 hr, while
the reaction mixture was kept at 50°C. Stirring was continued for
1 hr after complete addition of **13**; the mixture was then diluted
with 250 mL water, acidified with HCl, and extracted with CHCl$_3$.
The organic layer was washed with large amounts of water to remove
excess DMF. The chloroform layer was concentrated in vacuo; the
residual syrup was diluted with two 50 mL portions of xylenes and
concentrated under high vacuum (ca. 1 mm Hg) leaving 6.8 g of
organic material.

A portion of the above material (4.1 g), which was a mixture
of product **15** and excess **14**, was subjected to column chromatography
(silica gel 60, hexane/acetone 1:1) to give a 2.6 g portion of **15**,
as a syrup. The syrup was crystallized from i-PrOH to give 1.3 g

(61%) of **15** as light-yellow needles: mp 94.5-96.0°C; IR (mull)
cm^{-1} 3400 (OH), 1665 (C=O), and 1590 (aryl); ^{1}H-NMR (CDCl$_3$) δ
1.65 (broad s, 1, CH$_2$OH), 1.84 (m, 2, CH$_2$CH$_2$OH), 2.64 (t, J = 7
Hz, 2, ArCH$_2$), 3.66 (t, J = 6.5 Hz, 2, CH$_2$OH), 3.85, 3.92 (2 s, 6,
ArOCH$_3$), 5.25 (s, 2, CH$_2$OAr), 6.36 (broad s, 1, ArOH), 6.6-7.0 (m,
4, aryl), and 7.58 (m, 2, aryl); ^{13}C-NMR (CDCl$_3$) ppm 31.7 (t,
CH$_2$CH$_2$OH), 34.2 (t, ArCH$_2$), 56.1 (q, two ArOCH$_3$), 62.1 (t, CH$_2$OH),
72.6 (t, CH$_2$OAr), 110.6, 113.2, 114.1, 115.6, 120.4, 123.3 (all d,
aryl CH), 127.6, 136.2, 145.9, 146.8, 149.7, 151.1 (all s, aryl
C), and 193.2 (s, C=O); MS (DIP) m/z (%) 346 (26, M^{+}), 151 (100),
and 137 (14).

   **4-Hydroxy-3-methoxy-β-(2-methoxy-4-[δ-trityloxypropyl]phenoxy)
acetophenone (15-Tr)** - Tritylpyridinium tetrafluoroborate reagent
(TPFB) was prepared according to the method of Hanessian and
Straub.[16]   Into 25 mL of spectroscopic grade acetonitrile was
dissolved 0.5 g (1.44 mol) of **15** and 0.9 g (1.5 equiv.) of TPFB.
The solution was kept at 55-60°C and after 24 hr the reaction
progress seemed sluggish (by tlc); two more 0.5 g portions of TPFB
were added on successive days.   After 5 days the entire reaction
mixture was evaporated to dryness in vacuo and the solid residue
was extracted with CHCl$_2$.   The chloroform extracts were washed
with water, dried (Na$_2$SO$_4$), and concentrated in vacuo to give an
oily residue which was visually contaminated with trityl alcohol
crystals.   This crude product was chromatographed on alumina
(Alumin-AR CC-10, CH$_2$Cl$_2$/methanol 40:1 to 20:1) to give a 0.3 g
fraction (35%) of **15-Tr** as a colorless oil: IR (neat) cm^{-1} 1690
(C=O), and 1595 (aryl); ^{1}H-NMR (CDCl$_3$) δ 1.87 (m, 2, CH$_2$CH$_2$OTr),
2.66 (t, J = 7 Hz, 2, ArCH$_2$), 3.10 (t, J = 6 Hz, 2, CH$_2$OTr), 3.80,
3.90 (2 s, 6, ArOCH$_3$), 5.21 (s, 2, CH$_2$OAr), 6.5-7.0 (m, 2, aryl),
and 7.2-7.6 (m, 19, aryl).

   **2-(2-Methoxyphenoxy1)-1-(3-methoxy-4-hydroxyphenyl)-4-penten-
1-one (19)** - The following alkylation procedure[17] employed oven-
dried glassware, freshly distilled anhydrous solvents, and
nitrogen atmospheres.   To 150 mL of ice-cooled THF was added 224

mL (0.347 mol) of 1.55$\underline{M}$ n-BuLi in hexane and 35.1 g of diisopropyl-
amine. After stirring 15 min, the solution was cooled to -70°C
and 25.0 g (86.7 mmol) of 3-methoxy-4-hydroxy-β-(2'-methoxy-
phenoxy)acetophenone (**16**)[17] dissolved in 150 mL THF was added
dropwise. The stirred mixture was then allowed to warm to room
temperature for 1 hr, followed by cooling again to -70°C; to this
mixture, 42.0 g (0.347 mol) of allyl bromide (dissolved in 100 mL
THF) was added dropwise. After complete addition of the allyl
bromide, the mixture was allowed to warm to room temperature and
stirred for several hours. The reaction mixture was quenched by
the addition of 0.5$\underline{N}$ H_2SO_4. The organic layer was separated, and
the aqueous layer was extracted with ether. The combined THF/ether
extracts were extracted with 1$\underline{N}$ NaOH; these NaOH extracts were
acidified and extracted with CH_2Cl_2. The CH_2Cl_2 extracts were
washed with water and saturated aqueous NaCl, dried (Na_2SO_4), and
concentrated _in vacuo_ to give ca. 30 g of a brown oil. The oil
was chromatographed (silica gel 60, $CHCl_3$/EtOAc 6:1) to give 19.4
g (68.1%) of **19** as a gold oil: IR (neat) cm^{-1} 3400 (OH), 3190,
and 1635 (CH=CH_2), 1670 (C=O), and 1590 (aryl); ^{1}H-NMR ($CDCl_3$) δ
2.81 (t, J = 7 Hz [with further fine splitting], 2, CH_2CH=),
3.77, 3.87 (2 s, 6, ArOCH_3), 5.0-5.4 (m, 3, CHOAr and =CH_2),
5.8-6.2 (m, 1, -CH=), 6.39 (s, 1, OH), 6.85 (m, 5, aryl), and
7.70 (m, 2, aryl); ^{13}C-NMR ($CDCl_3$) ppm 37.7 (t, CH_2CH=), 55.6
(q, ArOCH_3), 81.4 (d, CHOAr), 113.9 (t, =CH_2), 132.7 (d, CH=CH_2),
110.7, 112.4, 116.1, 117.6, 120.5, 122.1, 123.8 (all d, aryl CH),
126.9, 146.5, 146.8, 149.5, 150.8 (all s, aryl C), and 196.1 (s,
C=O); MS (DIP) $\underline{m/z}$ (%) 328 (24, M$^+$), 205 (10), 177 (15), 151
(100), 123 (15) and 77 (11),

    **2-(2-Methoxyphenoxy)-1-(3-methoxy-4-hydroxyphenyl)-4-penten-
1-ol (22)** - Into 300 mL of absolute EtOH was dissolved 20.0 g
(60.9 mmol) of **19**. Six equivalents (13.8 g) of $NaBH_4$ were quickly
dissolved in 150 mL water/50 mL EtOH and added dropwise to the
substrate solution. After 1 hr, the solution was quenched by the
dropwise addition of 3$\underline{N}$ HCl, diluted with more water, and

extracted with CH_2Cl_2. The organic extracts were dried (Na_2SO_4) and concentrated in vacuo to leave 20.4 g of an oil. The crude product was chromatographed (silica gel 60, CH_2Cl_2/EtOAc 20:1 to 5:1) to give a major fraction of 13.0 g (64.7%) of **22**, as a colorless oil: IR (neat) cm^{-1} 3100 (OH), 1650 (C=C), no C=O absor- bance, and 1600 (aryl); ^{1}H-NMR ($CDCl_3$) δ 2.0-2.2, 2.4-2.7 (2 m, 1 + 1, nonequiv $CH_2CH=CH_2$), 3.8-3.9 (broad signal, 1, OH), 3.87 (s, 6, $ArOCH_3$), 4.1-4.3 (m, 1, CHOAr), 4.80 (d, J = 3 Hz, 1, CHOH), 4.9-5.1 (m, 2, $=CH_2$), 5.74 (s, 1, ArOH), 5.7-6.0 (m, 1, -CH=), and 6.67-7.13 (m, 7, aryl); ^{13}C-NMR ($CDCl_3$) ppm 32.8 (t, $CH_2CH=$), 55.7 (q, two $ArOCH_3$), 72.8 (d, CHOH), 86.4 (d, CHOAr), 116.7 (t, $=CH_2$), 131.3 (d, $CH=CH_2$), 109.0, 112.0, 114.0, 119.0, 119.7, 121.1, 123.1 (all d, aryl CH), and 134.8, 144.6, 146.3, 146.9, 151.1 (all s, aryl C); MS (DIP) m/z (%) 330 (10, M$^+$), 206 (15), 178 (52), 177 (20), 153 (100), 124 (52), and 137 (19).

The chromatography fractions preceding the main component (**22**) collectively weighed 1.0 g and, based on NMR analysis, were mixtures of starting material **19** and product **22**. The fractions after the main component collectively weighed 3.0 g and were a mixture of two isomers of **22**. A small amount of the minor isomer was isolated: ^{1}H-NMR ($CDCl_3$) δ 2.1-2.4 (m, 2, -$CH_2CH=$), 3.84 and 3.88 (s, 3 + 3, $ArOCH_3$), 4.0-4.2 (m, 1, -CHOAr), 4.73 (d, 1, J = 7 Hz, -CHOH), 4.9-5.3 (m, 2, $=CH_2$), 5.7-6.1 (m, 1, -CH=), 5.76 (s, 1, ArOH) and 6.8-7.1 (m, 7, aryl); ^{13}C-NMR ($CDCl_3$) ppm 35.4 (t, $CH_2CH=$), 55.7 (q, $ArOCH_3$), 75.8 (d, CHOH), 86.5 (d, CHOAr), 117.5 (t, $=CH_2$) 133.5 (d, $CH=CH_2$), 109.7, 112.0, 114.2, 118.7, 120.3, 121.0, 122.7 (all d, aryl CH) and 131.7, 145.4, 146.5, 148.0, 150.4 (all s, aryl C).

Based on analogies to the stereoselectivities obsersed for the NaBH$_4$ reduction of **17**[23] and the lower chemical shift value for erythro-C$_\alpha$ vs. threo-C$_\alpha$,[24] the major isomer (> 80%) of **22** is most likely erythro and the minor isomer threo.

2-(2-Methoxyphenoxy)-1-(3-methoxy-4-hydroxyphenyl)-1,5-pent-anediol (21) - All procedures, until workup, employed oven-dried

glassware, freshly distilled anhydrous solvent, and nitrogen
atmospheres. Into 100 mL of THF was dissolved 12.0 g (36.3 mmol)
of **30**; the mixture was chilled in an ice bath and 600 mL (8.2
equiv) of 0.5$\underline{M}$ diisamylborane (DSB)[29] in THF was added to the
solution over 1 hr. The mixture was kept at ca. 0°C for 3 hours,
after which 130 mL water was added to decompose residual hydride.
The organoborane was oxidized <u>in situ</u> at room temperature by
adding 200 mL of 3$\underline{N}$ NaOH, followed by the dropwise addition of 183
mL of 30% H_2O_2. The aqueous phase was saturated with K_2CO_3 and
the THF layer was separated. The aqueous layer was then extracted
with additional THF and the combined THF was washed with saturated
aqueous NaCl, dried (Na_2SO_4), and concentrated under high vacuum
(ca. 1 mm Hg) to leave 14.7 g of a crude yellow oil. The crude
product was subjected to three successive column chromatographies
(silica gel 60, CH_2Cl_2/MeOH 50:1 to 20:1) to give 11.4 g of a
colorless oil which crystallized upon standing for several days;
the product was recrystallized from benzene to yield 8.1 g (64.3%)
of compound **21**: mp 108.5-109.0°C; IR (mull) cm^{-1} 3450, 3225 (OH),
and 1590 (aryl); ^{1}H-NMR (CDCl$_3$) δ 1.5-2.1 (m, 5, **CH$_2$CH$_2$** and OH),
3.55 (broadened t, J = 6 Hz, 3, CH$_2$OH and OH), 3.81, 3.82 (2 s, 6,
ArOCH$_3$), 4.25 (m, 1, CHOAr), 4.80 (d, J = 3 Hz, 1, CHOH), 5.74 (s,
1, ArOH), and 6.7-7.1 (m, 7, aryl) [the ^{1}H-NMR assignments were
verified with homonuclear decoupling experiments]; ^{13}C-NMR ppm
(CDCl$_3$) 24.5, 29.3 (2 t, **CH$_2$CH$_2$**), 56.1 (s, 2, ArOCH$_3$), 62.8 (t,
CH$_2$OH), 73.1 (d, CHOH), 86.4 (d, CHOAr), 109.5, 112.7, 114.2,
119.2, 119.4, 121.4, 123.1 (all d, aryl CH), and 132.0, 145.0,
146.6, 147.4, 151.4 (all s, aryl C); MS (DIP) $\underline{m/z}$ (%) 348 (14,
M$^+$), 224 (16), 196 (27), 153 (68), 137 (15), 124 (75), and 71
(100).

<u>Anal</u>., calcd. for C$_{19}$H$_{24}$O$_6$ (%): C 65.50; H 6.94; O 27.55.
Found: C 65.78; H 6.96; O 27.26 (by difference).

**2-(2-Methoxyphenoxy)-1-(3-methoxy-4-hydroxyphenyl)-5-tri-
phenylmethoxy-1-pentanol (21-Tr)** - Into 75 mL freshly distilled,
anhydrous pyridine was dissolved 1.53 g (4.39 mmol) of **21** and 2.41

g (2 equiv.) of trityl chloride. The reaction mixture was main-
tained at ca. 50°C for 5 days, and then diluted with 75 mL water.
The aqueous pyridine solution was extracted with toluene, which
was in turn washed repeatedly with water (until the wash was
neutral), washed with saturated aqueous NaCl, dried (Na$_2$SO$_4$), and
concentrated in vacuo to leave 4.7 g of an oil. The crude product
was chromatographed on alumina (AluminAR CC-10, CH$_2$Cl$_2$/MeOH, pure
CH$_2$Cl$_2$ to 20:1) to give 2.17 g of a colorless oil, which was
crystallized from warm MeOH to yield 1.67 g (64.5%) of 21-Tr:
mp 109.5-111.0°C; IR (mull) cm^{-1} 3450, 3270 (OH) and 1600, 1580
(aryl); ^{1}H-NMR (CDCl$_3$) δ 1.4-2.1 (m, 4, CH$_2$CH$_2$), 3.04 (t, J = 6
Hz, 2, CH$_2$OTr), 3.66 (d, J = 3 Hz, 1, OH), 3.77, 3.84 (2 s, 6,
ArOCH$_3$), 4.13 (m, 1, CHOAr), 4.76 (t, J = 3 Hz [d after D$_2$O wash],
1, CHOH), 5.65 (s, 1, ArOH), 6.6-7.0 (m, 7, aryl), and 7.0-7.4 (m,
15, trityl); ^{13}C-NMR (CDCl$_3$) ppm 24.2, 26.3 (2 s, CH$_2$CH$_2$), 55.8
(q, two ArOCH$_3$), 62.9 (t, CH$_2$OH), 72.6 (d, CHOH), 86.1 (s, CAr$_3$),
86.7 (d, CHOAr), 108.7, 111.9, 114.0, 118.8, 119.9, 121.3, 123.2
(all d, aryl CH), 126.6, 127.5, 128.4 (all d, trityl aryl CH),
144.0 (s, trityl aryl C), and 131.4, 144.5, 146.4, 146.8, 151.4
(all s, aryl C); MS (DIP) m/z (%) 244 (22), 243 (100, Tr$^+$), 223
(17), 165 (25), and 153 (36).

Anal., calcd. for C$_{38}$H$_{38}$O$_6$ (%): C 77.26; H 6.48; O 16.25.
Found: C 76.87; H 6.54; O 16.59 (by difference).

5-Hydroxy-2-(2-methoxyphenoxy)-1-(3-methoxy-4-hydroxyphenyl)-
1-pentanone (20) - The DSB procedure described above was repeated
with compound 19, using the following quantities: 4.8 g (14.6
mmol) of 19, 88 mL (3 equiv.) of 0.5M DSB, and the appropriate
amounts of NaOH and H$_2$O$_2$ during the workup. The crude product,
5.5 g, was chromatographed (silica gel 60, CH$_2$Cl$_2$/MeOH 30:1 to
10:1) to yield 1.8 g (36%) of 20 as an oil: IR (neat) cm^{-1} 3400
(OH), 1670 (C=O), 1590 (aryl), and no C≡C absorbances; ^{1}H-NMR
(d$_6$-DMSO) δ 1.65, 1.89 (2 m, 4, CH$_2$CH$_2$), 3.46 (t, J = 6 Hz, 2,
CH$_2$OH), 3.76, 3.93 (2 s, 6, ArOCH$_3$), 4.48 (broad s, 1, OH), 5.63
(t, J = 5 Hz, 1, CHOAr), 6.94 (m, 4, aryl), 7.62 (m, 2, aryl), and

10.15 (broad s, 1, ArOH); ^{13}C-NMR (d_6-DMSO) ppm 28.2, 29.7
(CH_2CH_2), 55.8 (ArOCH$_3$), 60.4 (CH$_2$OH), 80.3 (CHOAr), 112.3, 113.3,
115.0, 115.4, 120.5, 121.4, 123.1, 126.4, 147.1, 147.3, 149.4,
151.9 (aryl), and 195.5 (C=O).

Compound 21 (Alternate Preparation) - The NaBH$_4$ reduction pro-
cedure described above was repeated with compound 20, using the
following quantities: 2.9 g (8.4 mmol) of 20 and 1.9 g (6 equiv.)
of NaBH$_4$. The crude product, 2.8 g, was chromatographed (silica
gel 60, CH$_2$Cl$_2$/MeOH 50:1 to 30:1) to yield 1.4 g (48%) of 21 as an
oil which was a mixture of diastereomers: IR (neat) cm^{-1} 3400
(OH), no C=O absorbance, and 1595 (aryl); ^{1}H-NMR (CDCl$_3$) 1.4-2.0
(m, 4, CH$_2$CH$_2$), 2.10 (s, 1, OH), 3.60 (t, J = 6 Hz, 2, CH$_2$OH),
3.83, 3.85 (2s, 6, ArOCH$_3$), 4.1-4.2 (m, 1, CHOAr), 4.74 (d, J = 8
Hz, 0.3, CHOH), 4.82 (d, J = 3 Hz, 0.7, CHOH), 5.29 (s, 1, OH),
5.77 (broad s, 1, ArOH), and 6.6-7.1 (m, 7, aryl); ^{13}C-NMR (CDCl$_3$)
ppm 24.2, 29.1 (CH$_2$CH$_2$, major), 27.4, 28.1 (CH$_2$CH$_2$, minor), 55.7
(2 ArOCH$_3$), 62.5 (CH$_2$OH), 72.6 (erythro-CHOH, major), 76.1
(threo-CHOH, minor), 86.5 (CHOAr), 108.8, 112.0, 114.0, 118.7,
119.1, 121.2, 123.0 (aryl CH, major), 109.4, 117.8, 119.4, 120.7,
121.0, 122.4 (aryl CH, minor), 131.5, 144.5, 146.3, 146.7, 151.0
(aryl C, major), and 131.8, 145.2, 148.2, 148.1, 150.0 (aryl C,
minor); MS (DIP) m/z (%) 348 (2, M$^+$), 224 (10), 196 (16), 153
(46), 137 (13), 124 (51), and 71 (100). The major isomer here
matches the one obtained by reduction of 22, except the ^{13}C-NMR
signals here are all lower by roughly 0.3-0.5 ppm (indicative of
an instrument instability problem).

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REFERENCES

1. Sarkanen, K. V., and Ludwig, C. H., ed., Lignins - Occurrence,
    Formation, Structure, and Reactions, Wiley Interscience, New
    York, Chapter 17, p. 695 (1971).

2.   Gierer, J., Svensk Papperstidn., 73, 571 (1970).

3.   Gierer, J. and Noren, I., Holzforschung, 34, 197 (1980).

4.   Gierer, J., Ljunggren, S.; Ljungquist, P., and Noren, I.,
     Svensk Papperstidn., 83, 75 (1980).

5.   Apfeld, P. B. and Dimmel, D. R., J. Wood Chem. Technol.,
     paper to follow.

6.   Helferich, B., Advan. Carbohyd. Chem., 3, 80 (1948).

7.   Kawana, M. and Emoto, S., Tetrahedron Lett., 13, 4855 (1972).

8.   Hodge, P. and Sherrington, D. C., ed. Polymer-Supported
     Reactions in Organic Chemistry, Wiley-Interscience, New
     York, Chapters 6 and 8, pp. 293 and 407 (1980).

9.   Fyles, T. M. and Lesnoff, C. C., Can. J. Chem., 54, 935
     (1976).

10. Frechet, J. M. J. and Nuyens, L. J., Can. J. Chem., 54, 926
     (1976).

11. Dimmel, D. R. and Schuller, L., J. Wood Chem. Technol., 6, 345
     (1986).

12. Panetta, J. A. and Rapoport, H., J. Org. Chem., 47, 946 (1982).

13. Hosoya, S., Kanazawa, K., Kaneko, H., and Nakano, J., J.
     Japan Wood Res. Soc., 26, 118 (1980).

14. Miksche, G. E., Acta Chem. Scand., 27, 1355 (1973).

15. Gierer, J. and Ljunggren, S., Svensk Papperstidn., 82, 71
     (1979).

16. Hanessian, S. and Staub, A. P. A., Methods Carb. Chem., VII,
     63 (1976).

17. Dimmel, D. R. and Shepard, D., J. Wood Chem. Technol., 2, 297
     (1982).

18. March, J. Advanced Organic Chemistry: Reactions, Mechanisms,
     and Structures, 2nd Ed., McGraw-Hill, New York, Chapter 10,
     p. 316 (1977).

19. Zweifel, G. and Brown, H. C., Org. Reactions, 13, 1 (1963).

20. Cram, D. J. and Abd Elhafez, F. A., J. Org. Chem., 74, 5828
     (1952).

21. Eliel, E. L., Asymmetric Synthesis II(A), Academic Press,
     New York, J. D. Morrison, ed., (1983), p. 125.

22. Ibid., Chapter 3, p. 106.

23. Adler, E., Delin, S., and Miksche, G. E., Acta Chem. Scand.
     20, 1035 (1966).

24. Ralph, J. and Young, R. A., Holzforschung, 35, 39 (1981);
     personal communications with J. Ralph.

25. Fieser, L. F. and Fieser, M., Reagents for Organic Synthesis.
     John Wiley and Sons, New York, 1967, 1254.

26. Dimmel, D. R., Schuller, L., and Apfeld, P. B., J. Wood
     Chem. Technol., 7, 97 (1987).

27. Stetter, H. and Uerdingen, W., Synthesis, 207 (1973).

28. CRC Handbook of Chemistry and Physics, 56th Ed., p. C-450
     (1975/76).

29. Aldrich Technical Information Bulletin No. Al-109.