of 11-ketopregnane-3α,17α,20β-triol 3,20-diacetate, m.p. 240–246°. Recrystallization from methanol gave the diacetate, m.p. 243–245.5°; $[\alpha]_D^{26}$ +72.1°; reported m.p. 244–246°; $[\alpha]_D^{24}$ +71.9°[19]; m.p. 249–250°.[20] Saponification and recrystallization from acetone gave 11-ketopregnane-3α,17α,20β-triol, m.p. 218–220.5°; reported m.p. 179° and 220°.[20] A small amount (50 mg.) of pregnane-3α,11β,17α,20β-tetrol 3,20-diacetate was eluted from the chromatogram. The reduction of 3α,17α-dihydroxypregnane-11,20-dione with sodium borohydride under the same conditions gave essentially the same result.

Acknowledgment. We wish to express our appreciation to Dr. T. F. Gallagher for his interest throughout this investigation and to Dr. G. Roberts and Friederike Herling for the determination and interpretation of the infrared spectra. We are indebted to Merck and Co., Inc., Rahway, N. J. and Schering Corp., Bloomfield, N. J., for their generous gifts of steroids.

NEW YORK, N. Y.

(19) M. Finkelstein, J. v. Euw and T. Reichstein, *Helv. Chim. Acta*, **36**, 1266 (1953).

(20) L. H. Sarett, *J. Am. Chem. Soc.*, **71**, 1169 (1940).

[CONTRIBUTION FROM THE INSTITUTE OF PAPER CHEMISTRY]

Liriodendrin, a New Lignan Diglucoside from the Inner Bark of Yellow Poplar (*Liriodendron tulipifera* L.)

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A new di-β-D-glucoside was isolated from an alcohol extract of the inner bark of yellow poplar, *Liriodendron tulipifera* L., in yields of 0.05–0.08% of the fresh bark. The glucoside was colorless, odorless, tasteless, crystalline, m.p. 269–270°, and was hydrolyzed by dilute acids to D-glucose and a new lignan. The name "liriodendrin" is suggested for the glucoside and "lirioresinol" for the lignan. Liriodendrin octaacetate and octamethyl ether were prepared as crystalline substances. Lirioresinol was obtained in two forms, lirioresinol-*A* and -*B* from which the corresponding crystalline dimethyl and dibromodimethyl ethers were prepared. The dibromodimethyl ethers were degraded to 4-bromo-5,6-dinitropyrogallol trimethyl ether and bis-(hydroxymethyl)succinic acid dilactone to establish lirioresinol as a tetrahydro-1,4-bis(4-hydroxy-3,5-dimethoxyphenyl)-furo[3,4-*c*]furan, stereoisomeric with syringaresinol, and liriodendrin the corresponding di-β-D-glucoside. A diastereoisomeric form, lirioresinol-*C*, was obtained upon hydrolysis of liriodendrin with crude almond emulsin.

Introduction. The yellow poplar or tulip tree, *Liriodendron tulipifera* L., is ranked among the most beautiful and valuable of the hardwoods which are native to the North American continent.[1] The Indians made canoes from its strong, light wood. The colonists used the tree extensively for lumber, and developed the use of its bark for medicinal purposes. Morel and Totain[2] stated that without extracts of yellow poplar bark as a substitute for quinine, the War of Independence might have been lost!

During the 19th century, European scientists studied the extractives of the yellow poplar's wood and bark, but the isolation of specific substances was rarely reported.[3] In 1831, Emmet[4] isolated 2–3% of a bitter principle, from the fresh, winter-gathered root bark. He named the substance "liriodendrine," but it has not been reported by later investigators. Bouchardat[5] isolated a crystalline material which was alkaloidal in character but which was not further described. The Lloyds[6] named a material "tulipiferin" which, though not crystalline, was apparently an alkaloid. Since then the extractives of this tree have remained essentially uninvestigated, but the increasing utilization of yellow poplar along with other hardwoods for pulp and paper has renewed interest in its chemistry.

Studies in progress at The Institute of Paper Chemistry indicate that alcoholic extracts of fresh yellow poplar bark consist largely of sugars, and of lesser amounts of unknown phenolic substances, coloring matter, and an essential oil with a distinctive pleasant odor. In addition to these materials, a new colorless substance was crystallized from the extracts in amounts of 0.05–0.08% based on the fresh bark. This substance has been characterized as a di-β-D-glucoside of a new lignan built on a nucleus of tetrahydrofurofuran. *Liriodendrin* is proposed for the name of the glucoside, and *lirioresinol* for the lignan.

Lignans derived from tetrahydrofurofuran. A group of naturally occurring phenylpropane dimers which are linked through the beta-carbon atoms of the side chains are known as lignans, a compre-

(1) C. D. Mell, *Textile Colorist*, **63**, 349 (1941).

(2) P. Morel and P. Totain, *Assoc. franc. avance. sci. Congrés Nîmes, 41 Session*, 810 (1912).

(3) C. Wehmer, *Die Pflanzenstoffe*, p. 336, Jena, G. Fischer, 1929; J. von Wiesner, *Die Rohstoffe des Pflanzenreichs*, Vierte auflage, p. 146. Leipzig, W. Engelmann, 1927.

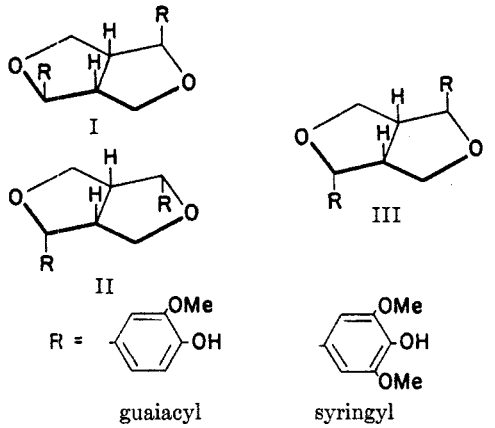
(4) J. P. Emmet, *J. pharm. chim.*, **17**, 334, 400 (1831).

(5) A. Bouchardat, *Bull. de therapeut.*, **19**, 243 (1842).

(6) J. U. Lloyd and C. G. Lloyd, *Pharm. Rundsch.*, **4**, no. 8, 169–72 (1886); *Jahresber. Pharm.*, **46**, 61 (1886); *Am. Druggist*, **15**, no. 6, 101 (June, 1886).

hensive review of which was prepared in 1955 by Hearon and MacGregor.[7]

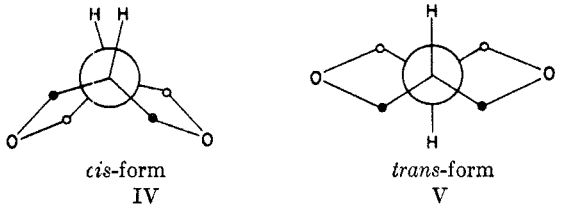
Among the several types of lignans, one group is built on a tetrahydrofuro[3,4-*c*]furan nucleus. (+)-Pinoresinol (I or II), tetrahydro-1,4-bis(4-hydroxy-3-methoxyphenyl)furo[3,4-*c*]furan, was the first guaiacyl type to be elucidated,[8,9] and several others with the same nucleus are now known. The first syringyl derivative of this type, syringaresinol, tetrahydro-1,4-bis(4-hydroxy-3,5-dimethoxyphenyl)furo[3,4-*c*]furan, I, II, or III, was described by Freudenberg and Dietrich.[10] It was synthesized from syringin in the presence of a crude almond emulsin, possibly through the action of accompanying dehydrogenases. The lignan analyzed as a dehydrodisinapyl alcohol and was found to be optically inactive.[10] The procedure was repeated in our laboratory and the product was also optically inactive. Freudenberg and Schraube[11] obtained



Pinoresinol (R = guaiacyl), and Syringaresinol and Lirioresinol (R = syringyl).

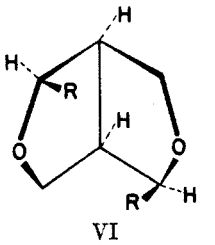
amorphous syringaresinol by a chemical synthesis and possibly identified the product through crystalline derivatives.

The central nucleus, tetrahydrofurofuran, on which these lignans are built, may be satisfactorily represented by the projection formulas, IV and V, as adapted from Newman.[12] The comparatively



Tetrahydrofurofuran nucleus

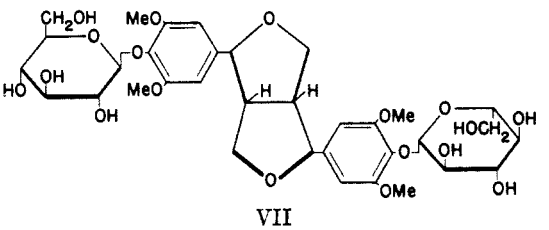
strainless *cis*-form (IV) would appear to be more probable than the puckered and very strained *trans*-form (V). This probability is strongly supported by the fact that all tetrahydrofurofuran lignans thus far elucidated have been derived from the *cis*-form. The spatial character of the *cis*-form may be even more realistically shown by the perspective formula VI (corresponds to formula II above), adapted from Cope and Shen.[13]



Tetrahydrofurofuran nucleus, *cis*-form

When the tetrahydrofurofuran nucleus is diagonally substituted, four asymmetric centers result which furnish two possible *meso*-structures and one *d,l*-pair for the *trans*-form (not shown), and three *d,l*-pairs for the *cis*-form (I, II, III).

The structure of liriodendrin. The new diglucoside was isolated from yellow poplar bark as a colorless, tasteless, crystalline solid. It was hydrolyzed in aqueous acid to D-glucose and the optically active aglucon, lirioresinol, which was diastereoisomeric with syringaresinol. Also the glucoside was hydrolyzed in the presence of a β-D-glucopyranosidase (crude almond emulsin) but not α- or β-anylase to establish that liriodendrin was probably a β-D-glucopyranoside. Liriodendrin was Mäule-positive,[14] and formed a crystalline octa-



Liriodendrin

acetate and a crystalline octamethyl ether. Hydrolysis of the ether and chromatography of the products on paper indicated the presence of a tetramethylglucose and unmethylated lirioresinol. Oxidation of the glucoside with nitrobenzene in alkali followed by chromatographic analysis yielded 13.2%

(7) W. M. Hearon and W. S. MacGregor, *Chem. Revs.*, **55**, 957–1068 (1955).

(8) H. Wedtman, *Svensk Kem. Tidskr.*, **48**, 236–41 (1936).

(9) H. Erdtman and J. Gripenberg, *Acta Chem. Scand.*, **1**, 71–75 (1947).

(10) K. Freudenberg and H. Dietrich, *Chem. Ber.*, **86**, 4–10 (1953).

(11) K. Freudenberg and H. Schraube, *Chem. Ber.*, **88**, 16–23 (1955).

(12) M. S. Newman, *J. Chem. Educ.*, **32**, 344–347 (1955).

(13) A. C. Cope and T. Y. Shen, *J. Am. Chem. Soc.*, **78**, 5912, 5916 (1956).

(14) The chlorination of pyrogallol derivatives followed by treatment with alkali results in the formation of a red to purple color; C. Mäule, *Beitr. wiss. Botanik*, **4**, 166 (1900).

TABLE I

STUDIES ON THE HYDROLYSIS OF THE DIGLUCOSIDE IN ACID

Acid	Time and Temp.	Crude Lirioresinol Yield, %	Crude Lirioresinol Melting Range, °C.
		1st crop	
10% Aqueous formic acid	25 min., steam bath	51	170–197
		2nd crop	
		19.5	173–195
		Total	
		70.5	
10% Aqueous formic acid	25 min., steam bath	55	173–175
Diglucoside dissolved in concd. hydrochloric acid, 0°; then diluted to 7% acid	2 min., steam bath	89	175–195
Diglucoside dissolved in concd. hydrochloric acid, diluted after 3 min. to 7% acid	10 min., room temp.	93	180–200
5% Sulfurous acid	30 min., steam bath	—	174–190
0.5*N* Hydrochloric acid	30 min., steam bath	82	168–197
0.5*N* Hydrochloric acid in 40% aq. ethanol	30 min., steam bath	75	168–202

of syringaldehyde and established the presence of syringyl groups.[15]

In an effort to improve the yield and quality of aglucon from the hydrolysis of the diglucoside, several different acids were tried. The results are summarized in Table I. The lirioresinol from the several hydrolyses melted over a considerable range and varied in yield.

By fractional crystallization of the crude lirioresinol from mixtures of ethanol and chloroform, two purified materials were obtained. The properties of these forms and some of their derivatives are summarized in Table II. To differentiate these forms, the higher melting one was designated as lirioresinol-*A* and the other, lirioresinol-*B*. The variations in yield and melting point of the crude lignan and the subsequent isolation of two forms are consistent with the known lability of such lignans in acid.[1]

TABLE II

SOME PROPERTIES OF LIRIORESINOL AND RELATED COMPOUNDS

	M.P., °C.	$[\alpha]_D$ (In Chloroform), Degrees	Molecular Rotation, [M], Degrees
Lirioresinol-A	210–211	+127	+53,100
Dimethyl ether	118–120	+119	+52,800
Dibromodimethyl ether	124–126	+ 64.4	+38,900
Lirioresinol-B	172–177	+ 62.2	+26,000
Dimethyl ether	121–123	+ 46.2	+20,300
Dibromodimethyl ether	152–155	− 61.9	−39,600
Lirioresinol-C	185–186	+ 48.9	+20,200
D-*Pinoresinol*[a]	120–121	+ 84.4	+30,200
Dimethyl ether	107–108	+ 64.5	+24,900
Dibromodimethyl ether	172–173	− 69.1	−35,700
Epipinoresinol	—	—	—
Dimethyl ether[b]	130–131	+141.1	+54,400

[a] Ref. 9. [b] J. Gripenberg, *Acta Chem. Scand.* **2**, 82 (1948).

Because of the acid sensitivity of lirioresinol, an attempt was made to hydrolyze liriodendrin in the presence of crude almond emulsin. After 23 days at 37°, a product, lirioresinol-*C*, was obtained in a yield of 55% (Table II).

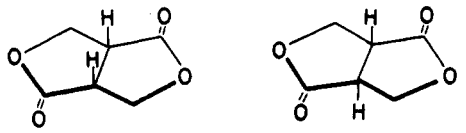
Through an elegant series of reactions Erdtman and Gripenberg[9] determined the structure of the central carbon skeleton of pinoresinol, and in a similar way syringaresinol was established by Freudenberg and Dietrich[10] as a bis(syringyl) tetrahydrofurofuran. Through the same series of reactions, the lirioresinols were converted to their dimethyl ethers from which the dibromodimethyl ethers were readily formed upon direct bromination in chloroform (Table II). The dibromolirioresinol dimethyl ethers were then cleaved in nitric acid to yield 34% of 4-bromo-5,6-dinitrotrimethyl pyrogallol and a very small amount of bis(hydroxymethyl)succinic acid dilactone; their properties are summarized in Table III. The isolation of the optically active dilactone (VIII), rather than the *meso*-form (IX), establishes the presence of the *cis*-form of the diagonally substituted tetrahydrofurofuran ring in lirioresinol. The new lignan is, therefore, tentatively identified as a diastereoisomer of syringaresinol, and its di-β-D-glucoside, liriodendrin, may be represented by formula VII.

(15) J. E. Stone and M. J. Blundell, *Anal. Chem.*, **23**, 771–774 (1951).

TABLE III

DEGRADATION PRODUCTS OF PINORESINOL, SYRINGARESINOL, AND LIRIORESINOL

	Yield, %	M.P., °C.	$[\alpha]_D$, Degrees
4-Bromo-5,6-dinitropyrogallol trimethyl ether			
Freudenberg[10]	38	134–135	—
This work	34	133–134	—
Bis(hydroxymethyl)succinic acid dilactone			
Erdtman[8,9]	—	137–138	Racemic
	65	160–161	+206 (water)
Freudenberg[10]			
From syringaresinol	63	136–137	Racemic
From pinoresinol	48	161	+203 (water)
This work	Very small	158–160	+253 (water)



VIII IX

cis-form *d,l* — *trans*-form *meso*

bis(hydroxymethyl)-succinic acid dilactone

From the relative values of the molecular rotations as listed in Table II it would appear that lirioresinol-*B* may have the same configuration as (+) pinoresinol, and that lirioresinol-*A* dimethyl ether may possibly correspond with *epi*-pinoresinol dimethyl ether.[16]

As shown in Fig. 1, the infrared spectra of the optically active lirioresinol-*C* and the inactive syringaresinol, both prepared in the presence of the same enzyme, are nearly identical which indicates no significant difference in structure. Syringaresinol, therefore, may be a single *d,l* pair and lirioresinol-*C* may be the dextrorotatory form. Proof of these possible relationships must await further chemical evidence, and a comparison of infrared spectra and other properties of the appropriate guaiacyl and syringyl compounds. Also, because of the acid sensitivity of lirioresinol, the stereoisomeric form of the lignan present in liriodendrin (VII) cannot yet be fixed.

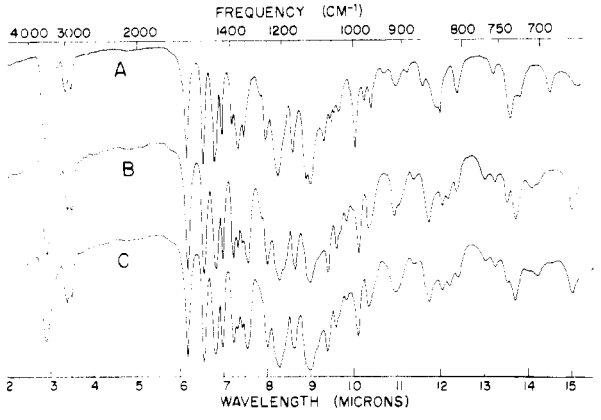


FIG. 1. INFRARED SPECTRA OF SYRINGYL LIGNANS. A. LIRIORESINOL-*A* AND -*B*. B. LIRIORESINOL-*C*. C. SYRINGARESINOL.

The work on liriodendrin and the lirioresinols is being continued.

EXPERIMENTAL

Isolation of liriodendrin. An amount of 20 kg. of fresh whole bark was peeled in 1-inch strips from saplings, 2–3 inches in diameter,[17] and was covered with 95% ethanol. After standing at room temperature for 4–6 weeks, the alcoholic extract, 30 l., was evaporated at reduced pressure, the aqueous concentrate was mixed with filter aid, filtered, and the combined filtrate and washings were extracted with chloroform. An excess of basic lead acetate was added and the heavy yellow precipitate was removed by filtration. The excess lead was then precipitated with hydrogen sulfide, the solution was filtered, and the filtrate was concentrated to a thin sirup at reduced pressure. After standing at room temperature for several days, a heavy deposit of colorless crystals of liriodendrin formed. The crystals were separated by filtration and washed on the funnel with water and absolute ethanol; yield of crude liriodendrin, 10 g. or about 0.05% based on the fresh bark, m.p. 262–265°.[18] The crude diglucoside was recrystallized from hot 50% aqueous ethanol; yield of purified material, 8.1 g., m.p. 269–270°. Liriodendrin was slightly soluble in hot ethanol, acetone, and ethyl acetate, and somewhat more soluble in water, glacial acetic acid, and quite soluble in hot 50% aqueous ethanol (3 g./100 ml. of boiling solvent).

Anal. Calcd. for $C_{34}H_{46}O_{18}$: C, 54.98; H, 6.24; CH_3O, 16.71. Found: C, 54.54; H, 6.35; CH_3O, 16.2.

Liriodendrin octaacetate. Liriodendrin, 1.02 g., was dissolved in a mixture of 5 ml. of pyridine and 10 ml. of acetic anhydride after heating on a steam bath for 45 min. After standing overnight, the clear, colorless reaction mixture was poured into 150 ml. of ice and water. The gummy precipitate gradually became friable, was collected on a tared funnel, and dried; yield 1.53 g. (103%). The acetate was crystallized from 30 ml. of boiling 95% ethanol; yield, 1.37 g. (92%), m.p. 124–125° to form a very viscous melt, $[\alpha]_D^{20}$ +7.2° (*c*, 4.7, chloroform).

Anal. Calcd. for $C_{50}H_{62}O_{26}$: C, 55.65; H, 5.79; CH_3O,

(16) J. Gripenberg, *Acta Chem. Scand.*, 2, 82 (1948).

(17) The yellow poplar saplings were obtained through the courtesy of Dr. J. G. Leech, West Virginia Pulp and Paper Co., Luke, Md.

(18) All melting points were observed in Pyrex capillaries and are uncorrected.

TABLE IV

HYDROLYSIS OF LIRIODENDRIN AND THE RECOVERY OF LIRIORESINOL

Amount of Liriodendrin, G.	Yield of Lirioresinol						
	Crystalline Precipitate			Chloroform Extract		Total Recovered	
	G.	%	M.P., °C.	G.	%	G.	%
1.056	0.349	58.6	185–202	0.234	39.4	0.583	98
1.000	0.407	74.6	168–202	—	—	—	—
2.000	0.672	59.7	—	0.468	—	1.140	101
3.000	1.389	82.2	168–197	—	—	—	—

11.50; CH_3CO, 31.91; mol. wt., 1079. Found: C, 55.46; H, 5.80, CH_3O, 11.38; CH_3CO, 32.1; mol. wt. (Rast), 938.

Liriodendrin octamethyl ether. An amount of 2.0 g. of liriodendrin was suspended in 30 ml. of dioxane in a 1-l. 3-necked flask under efficient mechanical stirring. Sodium hydroxide, 160 ml. of 30%, and 80 ml. of dimethyl sulfate were each added in ten equal portions at 10-min. intervals. The temperature was held at 30° with a water bath. When half the reagents had been added, white crystalline material began to form. It was partly dissolved by the addition of 20 ml. of acetone. After the alkali and dimethyl sulfate were added, the temperature was raised to 75° for 30 min. The mixture was quickly cooled and the crystalline, partly methylated product was collected by filtration. To complete the methylation the general procedure of Freudenberg and Dietrich[10] was used. The material was dissolved in 150 ml. of boiling methanol and 20 ml. of dimethyl sulfate and 40 ml. of 40% potassium hydroxide were added in five portions over a period of 30 min. The heating was continued for an additional 30 min. After dilution with a liter of water, the reaction mixture was allowed to stand overnight and the crystalline precipitate was collected by filtration and dried; yield, 1.23 g., m.p. 165–169°. Two crystallizations from methanol yielded pure material, m.p. 177–178°, $[\alpha]_D^{20}$ +8.6°. Paper chromatograms of an acid hydrolyzate indicated the presence of a tetramethylglucose and the aglucon as the only products.

Anal. Calcd. for $C_{42}H_{62}O_{18}$: C, 59.00; H, 7.32; CH_3O, 43.56. Found: C, 59.05; H, 7.27; CH_3O, 43.48.

Preliminary hydrolysis of liriodendrin. An amount of 50 mg. of liriodendrin was suspended in 5 ml. of 0.25*N* hydrochloric acid and the mixture was heated on a steam bath. Samples were withdrawn at intervals and chromatographed on paper in a developer of ethyl acetate–acetic acid–water (9:2:2 v/v) for 3 hr. The sugar was located by the aniline hydrogen phthalate spray reagent,[19] and the syringyl substances were located on a separate paper by the Mäule test.[20]

The unchanged glucoside, R_f 0.2, disappeared after five minutes' heating; another spot, R_f 0.6, appeared at the 2-min. interval, passed through a maximum, and disappeared after 15 minutes. The aglucon, lirioresinol, R_f 0.9, appeared at 2 min. and was the only Mäule-positive spot after 25 min. The only sugar spot was glucose which appeared at 2 min. and followed the same pattern as lirioresinol.

Hydrolysis of liriodendrin (VII). (A) *Preparation of lirioresinol* (*I*, *II*, or *III*). An amount of 5.28 g. of the glucoside was suspended in 400 ml. of hot water, 80 ml. of 1.0*N* hydrochloric acid was added, and the mixture was heated on a steam bath. Within 10 min. the solution was clear and colorless, and after 12 min., the aglucon began to crystallize. The heating was stopped at 20 min., the mixture was cooled and stored at 5° overnight. The crystalline precipitate was collected by filtration, washed, and dried; yield, 2.114 g. (66.8%), m.p. 170–200°. This material was triturated with 2–3 ml. of chloroform and the slurry was filtered, washed with chloroform and dried; yield, 1.767 g. (55.8%), m.p. 204–207°. After standing overnight, the hydrolysis filtrate yielded an additional 0.313 g., m.p. 164–170°, for a combined yield of 2.427 g. (76.6%). The aqueous filtrate was then extracted with chloroform, amount recovered, 0.5815 g., for a total yield of 3.008 g. (95%). Fractional crystallization from chloroform-ethanol (1:1) yielded two materials in purified form designated as lirioresinol-A, m.p. 210–211°, $[\alpha]_D^{20}$ +127° (chloroform) and lirioresinol-B, m.p. 172–177°, $[\alpha]_D^{21}$ = +62.2° (chloroform).

Anal. Calcd. for $C_{22}H_{26}O_8$: C, 63.15; H, 6.26; CH_3O, 29.67; Mol. wt. 418. Found: C, 63.30 (A), 63.16 (B); H, 6.26 (A), 6.23 (B); CH_3O, 29.68 (A), 29.46 (B); Mol. wt. (Rast) 362 (A). [(A) and (B) refer to lirioresinol-*A* and -*B*, respectively.]

(B) *Identification of* D-*glucose.* The aqueous solution from part (A) was deionized with Amberlite IR-4B (acetate form), and concentrated at reduced pressure to a thin sirup. After standing for several days, a colorless crystalline deposit formed. The substance was crystallized from aqueous alcohol and identified as anhydrous α-D-glucose, m.p. 146–150° upon very slow heating, $[\alpha]_D^{20}$ +52.3 (*c*, 5, water) constant after 24 hr., and by the preparation of *N*-*p*-nitrophenyl-D-glucosylamine, m.p. (dec.) 186–187°. An authentic specimen of anhydrous α-D-glucose melted at 146–150°, and the corresponding *p*-nitroaniline derivative melted (dec.) at 186–187°; the accepted equilibrium rotation of D-glucose in water is $[\alpha]_D^{20}$ = +52.6°.

Derivatives of lirioresinol. The procedures reported by Freudenberg and Dietrich[10] in their studies on syringaresinol were used with lirioresinol without significant modification. Although we have described experiments in the lirioresinol-*B* series only, analyses are given for derivatives in both the *A* and *B* series.

(A) *Methylation.* Lirioresinol-*B*, 1.093 g., m.p. 172–177°, was dissolved in 125 ml. of boiling methanol under a reflux condenser. The solution was treated portionwise with 15 ml. of dimethyl sulfate and 30 ml. of 40% potassium hydroxide over a period of thirty minutes. The mixture was boiled for an additional thirty minutes and was poured into 800 ml. of cold water. After standing for thirty minutes, colorless crystals formed in the cloudy solution. The product was extracted from the mixture with chloroform, and crystallized from methanol; the purified lirioresinol dimethyl ether was recovered as glistening, colorless plates, 0.534 g., m.p. 121–123°, $[\alpha]_D^{22}$ = 46.2°. A less pure lot of material was obtained from tailings, m.p. 117–119°, $[\alpha]_D^{25°}$ +44.4°.

Anal. Calcd. for $C_{24}H_{30}O_8$: CH_3O, 41.71. Found: CH_3O, 41.89 (A), 40.85 (B).

(B) *Bromination.* Lirioresinol-*B* dimethyl ether, 0.1973 g., was treated with an excess of bromine dissolved in chloroform (1:10) at room temperature. The reaction mixture was washed once with water and then with an excess of aqueous sodium sulfite. The product was crystallized from 95%

(19) The spray reagent was composed of 1.67 g. of *o*-phthalic acid and 1.02 g. of aniline dissolved in 100 ml. of water-saturated 1-butanol [S. M. Partridge, *Nature*, **164**, 443 (1949)].

(20) The air-dry chromatogram was placed in an atmosphere of chlorine gas for ten minutes and then sprayed with 10% aqueous sodium sulfite. Syringyl substances form cerise or purple spots.

ethanol in tufts of colorless needles; m.p. 152–155°, $[\alpha]_D^{25°}$ −61.9°.

Anal. Calcd. for $C_{24}H_{28}O_8Br_2$: C, 47.70; H, 4.67; Br, 26.45; CH_3O, 30.81. Found: C, 47.64 (A), 47.65 (B); H, 4.64 (A), 4.60 (B); Br, 26.42 (A), 26.02 (B); CH_3O, 30.76 (A), 30.46 (B).

(C) *Oxidation with nitric acid.* Dibromodimethyl lirioresinol-*B*, 140 mg., was added in small portions to 1.4 ml. of nitric acid (d. 1.42) at room temperature. The solution became dark violet in color and turned to an orange red after one hour. The mixture was then heated for an hour on a steam bath. Upon cooling, crystalline material separated, 2 vol. of water were added, and the mixture was filtered; yield of crude material, 53.3 mg. (34%) of 4-bromo-5,6-dinitropyrogallol trimethyl ether, m.p. 126–129°. After crystallization from 95% ethanol, the very light yellow needles melted at 133–134°.

The aqueous filtrate was combined with a corresponding filtrate obtained from lirioresinol-*A*, was neutralized with sodium bicarbonate, the solution was evaporated to dryness and extracted with ether to recover the bis(hydroxymethyl)-succinic acid dilactone. A very small yield was obtained, m.p. 158–160°, $[\alpha]_D^{26}$ +253° (water). The rotation was observed on 0.0029 g. of material in 3.0 ml. of solution and must be regarded as an approximation.

Preparation of syringaresinol. (A) *Crude almond emulsin.* Using the general procedure of Bourquelot,[21] 10.6 g. of crude emulsin was prepared from 340 g. of sweet almonds.

(B) *Enzymic synthesis of syringaresinol from syringin.* Using the general procedure of Freudenberg and Dietrich[10] 2.5 g. of syringin[22] was dissolved in 125 ml. of water, 0.1 g. of thymol and 0.25 g. of crude enzyme were added, and the mixture was incubated at 37°. An additional amount of 0.25 g. of the enzyme was added daily until a total of 2.0 g. had been added. Colorless crystals, m.p. 172–174°, began to form after five days, and the reaction was stopped after eleven days. The mixture was treated with 2–3 g. of "Fibra-Flo-C"[23] and filtered, the filter cake was washed with water, air dried, and extracted with chloroform at room temperature. Upon evaporation of the chloroform, crude syringaresinol was obtained; yield, 0.85 g. (60.2%). After two crystallizations from 95% ethanol, 0.57 g. of purified material was obtained, the main portion melted at 170–172° with a small amount melting at 176–178°. The product was optically inactive. In a second experiment the yield of crude syringaresinol after 17 days was 0.958 g. (68%). Freudenberg and Dietrich[10] obtained syringaresinol, m.p. 174–175° in a 66% yield after seven weeks.

The aqueous filtrate from the reaction mixture was extracted three times with chloroform; yield of oily material believed to be crude sinapyl alcohol, 0.46 g. (32.6%). The combined yield of syringaresinol and sinapyl alcohol was 92.8%.

Syringaresinol diacetate. The acetate was prepared from the lignan, acetic anhydride, and pyridine; colorless crystals m.p. 179–181°, from 95% ethanol. Freudenberg and Dietrich[10] reported the m.p. 181–183° for this derivative.

Hydrolysis of liriodendrin with crude almond emulsin. Using the above procedure, 0.5 g. of liriodendrin was dissolved in 125 ml. of water, 0.1 g. of thymol and 0.25 g. of the crude enzyme were added, and the mixture was incubated at 37°. More enzyme, 0.25 g., was added on the second, third, sixth, and fifteenth days; the reaction was stopped after twenty-three days. Filter aid was added, the filter cake was air dried and extracted with chloroform; yield of crude lirioresinol-*C*, 0.1565 g. (55%). After two crystallizations from 95% ethanol the lirioresinol-*C* melted 185–186°, $[\alpha]_D^{28}$ +48.9° (in chloroform). The infrared spectrum was nearly identical with that of syringaresinol (Fig. 1).

APPLETON, WIS.

(21) E. Bourquelot, *Archiv. Pharm.*, **245**, 172–180 (1907).

(22) Syringin was isolated from the bark of the common lilac by the general procedure of K. Freudenberg, R. Kraft, and W. Heimberger, *Chem. Ber.*, **84**, 472–476 (1951).

(23) Filter aid manufactured by Johns-Manville.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DE PAUL UNIVERSITY]

Racemic 2-Hydroxymethyl-2,3-dihydro-4*H*-pyran, a Model Carbohydrate[1]

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2-Hydroxymethyl-2,3-dihydro-1*4H*-pyran, a racemic dideoxyglucal, has been converted to 2,3,4-trideoxyaldohexose and its derivatives.

It has been demonstrated that 2,3-dihydro-4*H*-pyran can readily be converted to polydeoxyaldopentoses by hydration[3] and hydroxylation.[4] In similar manner, these glycal-like properties have now been extended to the formation of polydeoxyaldohexoses from 2-hydroxymethyl-2,3-dihydro-4*H*-pyran (II) with the ultimate, but as yet unrealized object, of synthesizing these in optically active forms of the D- or L-series.

The preparation of the precursor II, a racemic 3,4-dideoxyglucal, by reduction of 2,3-dihydro-4*H*-pyran-2-carboxaldehyde (I)[5] with aluminum alk-

(1) Abstracted from the senior thesis of Anthony Verbiscar (1951) and the master's thesis of Herman J. Eichel (1956). Part of this material has been reported at the Student Affiliate Symposium of the American Chemical Society, Chicago Section, in May 1951.

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(3) L. E. Schniepp and H. H. Geller, *J. Am. Chem. Soc.*, **68**, 1646 (1946).

(4) C. D. Hurd and C. D. Kelso, *J. Am. Chem. Soc.*, **70**, 1484 (1948); C. D. Hurd and O. E. Edwards, *J. Org. Chem.*, **14**, 680 (1949); and C. D. Hurd, J. Moffat, and L. Rosnati, *J. Am. Chem. Soc.*, **77**, 2793 (1955).

(5) K. Alder and E. Rüden, *Ber.*, **74**, 320 (1941); K. Alder, H. Offermans and E. Rüden, *Ber.*, **74**, 905 (1941). A sample of this compound, acrolein dimer, was generously supplied by the Shell Development Co., Emoryville, Calif.