17. *The Constituents of Natural Phenolic Resins. Part XXII. Reduction of Some Lactonic Lignans with Lithium Aluminium Hydride.*

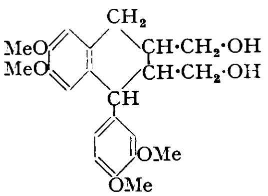
By Robert D. Haworth and Leslie Wilson.

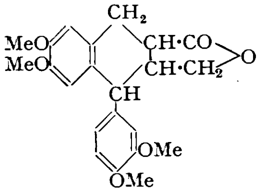
The "trans-"configuration previously assigned to (—)-matairesinol and (—)-hinokinin has been confirmed by reduction with lithium aluminium hydride to optically active diols; (+)-*iso*matairesinol has a " cis-"configuration and gives a *meso*diol on reduction. (—)-Conidendrin dimethyl ether has been reduced to (+)-*iso*lariciresinol dimethyl ether.

The introduction of lithium aluminium hydride as a reagent for the conversion of lactones into diols (Nystrom and Brown, *J. Amer. Chem. Soc.*, 1948, **70**, 3738) suggested several applications in the lignan field, and the present communication describes a number of stereochemical relations which have been established or confirmed by the use of this reagent.

The conversion of (+)-*iso*lariciresinol dimethyl ether (I) into (—)-conidendrin dimethyl ether (II) was reported in an earlier paper (*J.*, 1937, 384), and the reverse change has now been realised by the use of lithium aluminium hydride in ether–benzene, thereby confirming the close stereochemical relation of the two lignans.

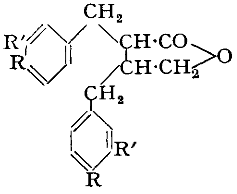
(I.)



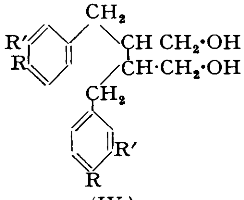


(II.)

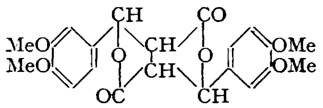
In earlier communications (*J.*, 1938, 797, 1985; 1939, 154, 1054; 1940, 1098), evidence was brought forward suggesting that (—)-matairesinol (III; R = OH, R′ = OMe) has a "trans-" configuration, and the corresponding " cis-"arrangement was assigned to (+)-*iso*matairesinol. These conclusions have now been confirmed by the reduction of (—)-matairesinol dimethyl ether (III; R = R′ = OMe) and (+)-*iso*matairesinol dimethyl ether into the (—) and ***meso***-forms of 1 : 4-*di*-(3 : 4-*dimethoxyphenyl*)-2 : 3-*di*(*hydroxymethyl*)*butane* (IV; R = R′ = OMe), respectively. In the same way (—)-hinokinin (III; RR′ = CH_2O_2) has been reduced to (—)-1 : 4-*di*-(3 : 4-*methylenedioxyphenyl*)-2 : 3-*di*(*hydroxymethyl*)*butane* (IV; RR′ = CH_2O_2), identical with " dihydrocubebin " (Bruchhausen and Gerhard, *Ber.*, 1939, **72**, 830), thus confirming the " trans-"configuration previously advanced for (—)-hinokinin.



(III.)



(IV.)



(V.)

Several attempts to reduce the synthetic dilactone (V) (*J.*, 1944, 535) have been made; so far we have failed to isolate crystalline material, but this synthetical route to pinoresinol dimethyl ether is still under investigation.

Experimental.

(+)-iso*Lariciresinol Dimethyl Ether* (I).—Cold solutions of (—)-conidendrin dimethyl ether (1 g.) in benzene (40 c.c.) and of lithium aluminium hydride (0·5 g.) in ether (40 c.c.) were mixed and allowed to react for 2 hours, during which a white gelatinous precipitate separated. The bulk of the solvent was reduced to about 40 c.c. by distillation under reduced pressure, and the precipitated metal alkoxide decomposed by careful addition of dilute hydrochloric acid. The benzene layer was washed twice with water, dried ($CaCl_2$), and evaporated to dryness. The product (0·85 g.) separated from aqueous methyl alcohol in colourless needles, m. p. 167—168°, $[\alpha]_D^{20}$ + 18° (*c*, 1·8272 in chloroform) (cf. *J.*, 1937, 384; m. p. 166—167°, $[\alpha]_D^{14}$ + 20° in chloroform). Anhydro*iso*lariciresinol dimethyl ether, obtained by heating the above diol (I) (0·2 g.) with potassium hydrogen sulphate (0·4 g.) at 180° for ½ hour, crystallised from methyl alcohol in colourless prisms (0·13 g.), m. p. 147—148°, $[\alpha]_D^{23}$ − 33·9° (*c*, 0·3840 in acetone) (cf. *J.*, 1937, 384; m. p. 146—147°, $[\alpha]_D^{16}$ − 33·4° in acetone).

(—)-1 : 4-*Di*-(3 : 4-*dimethoxyphenyl*)-2 : 3-*di*(*hydroxymethyl*)*butane* (IV; R = R′ = OMe).—(—)-Matairesinol dimethyl ether (1 g.) in benzene (30 c.c.) and lithium aluminium hydride (0·5 g.) in ether (30 c.c.) were allowed to react for 2 hours. The volume of the solvent was reduced by distillation, dilute hydrochloric acid was added, and the product from the washed and dried benzene layer was crystallised from methyl alcohol containing a little ether in colourless prisms (0·88 g.), m. p. 119—120°, $[\alpha]_D^{20}$ — 29·6° (*c*, 0·4380 in chloroform) (cf. *J.*, 1939, 1054; m. p. 121—122°, $[\alpha]_D^{17}$ — 26·2° in chloroform). (—)-3 : 4-Di-(3 : 4-dimethoxybenzyl)tetrahydrofuran, obtained by heating the above diol (0·15 g.) with potassium hydrogen sulphate (0·3 g.) at 180° for ½ hour, separated from methyl alcohol in colourless prisms (0·11 g.), m. p. 117—118°, $[\alpha]_D^{25}$ — 54·5° (*c*, 0·0928 in chloroform) (cf. *J.*, 1939, 1054; m. p. 118—119°, $[\alpha]_D^{17}$ — 58·9° in chloroform).

meso-1 : 4-*Di*-(3 : 4-*dimethoxyphenyl*)-2 : 3-*di*(*hydroxymethyl*)*butane*.—(+)-iso*Matairesinol* dimethyl ether (0·1 g.) in benzene (5 c.c.) was treated with cold lithium aluminium hydride (0·05 g.) in ether (5 c.c.). After 2 hours the volume was reduced by distillation under reduced pressure, and dilute hydrochloric acid was added. The product, isolated from the benzene layer, crystallised from methyl alcohol in colourless prisms (0·079 g.), m. p. 94—95°, $[\alpha]$ 0° (*c*, 0·1861 in chloroform) (Found: C, 67·5; H, 7·5. $C_{22}H_{30}O_6$ requires C, 67·7; H, 7·7%).

meso-3 : 4-*Di*-(3 : 4-*dimethoxybenzyl*)*tetrahydrofuran*, obtained by heating the *meso*-diol (0·06 g.) with potassium hydrogen sulphate (0·12 g.) at 180° for 0·5 hours, separated from methyl alcohol in colourless prisms (0·05 g.), m. p. 114—115°, $[\alpha]$ 0° (*c*, 0·0884 in chloroform) (Found: C, 70·8; H, 7·7. $C_{22}H_{28}O_5$ requires C, 70·9; H, 7·6%).

(—)-1 : 4-*Di*-(3 : 4-*methylenedioxyphenyl*)-2 : 3-*di*(*hydroxymethyl*)*butane* (IV; RR′ = CH_2O_2).—(—)-Hinokinin (1 g.) in benzene (50 c.c.) was mixed with a solution of lithium aluminium hydride (0·5 g.) in ether (50 c.c.). After 2 hours, dilute hydrochloric acid was added, and the diol, isolated from the benzene layer, separated from ether–light petroleum (b. p. 60—90°) in colourless needles (0·93 g.), m. p. 102—103°, $[\alpha]_D^{20}$ — 34° (*c*, 0·8476 in chloroform) (Bruchhausen and Gerhard, *loc. cit.*, give m. p. 104°, $[\alpha]_D^{18}$ — 30·6° in chloroform). (—)-3 : 4-*Di*-(3 : 4-*methylenedioxybenzyl*)*tetrahydrofuran*, formed by heating the above diol (0·2 g.) with potassium hydrogen sulphate (0·4 g.) at 180° for ½ hour, was distilled at 0·5 mm. (bath temperature, 280—300°) and crystallised from ether–light petroleum (b. p. 60—90°) in colourless prisms (0·14 g.), m. p. 52—52·5° $[\alpha]_D^{22}$ — 58·3° (*c*, 0·1716 in chloroform) (Found: C, 70·6; H, 6·2. $C_{20}H_{20}O_5$ requires C, 70·6; H, 5·9%).

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