ACTA CHEMICA SCANDINAVICA 8 (1954) 1827—1829

Constitution of Resin Phenols and their Biogenetic Relations. XVIII *. Conversion of α-Conidendrin to Galbulin

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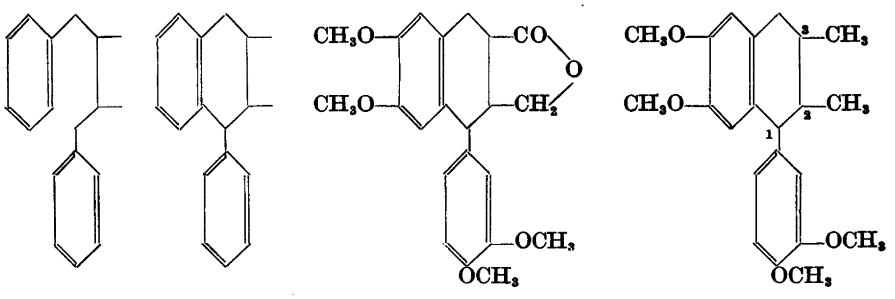
The dimethylethers of α- and β-conidendrin (III) have been converted to the corresponding fully reduced compounds (IV) which differ according to the configuration at carbon atom 3. The reduction product from the α-isomer is identical with galbulin — a new lignan isolated from *Himantandra baccata* Bail.

The lignans are dimerides of phenylpropanes characterized by the closely related carbon skeletons (I) or (II).



I II III IV; V All rings aromatic

The nonaromatic portion of the molecules frequently contains hydroxyl, ether, aldehyde or carboxylic (lactone) groups. The structure elucidation of the lignans has mainly been accomplished by means of oxidative degradations. Several interesting stereochemical relations between the various lignans have also been demonstrated. It is sometimes a matter of some difficulty to ascertain

*) Part XVII *Acta Chem. Scand.* 8 (1954) 806.

whether a natural product belongs to the lignan series or not. A simple method would be the reductive conversion to fully reduced compounds of the *d*- and *l*-dihydroguaiaretic acid and meso-dihydroguaiaretic acid types or to the corresponding cyclised analogues. It would therefore be of value to possess a series of such compounds for reference purposes.

In the present paper the reduction of the α- and β-conidendrin dimethylethers to compounds of the structure (IV) is reported. The work was initiated due to the paper chromatographic observation that guaiacum resin apparently contains a series of unknown compounds some of which may well be lignans. The facile conversion of guaiaretic acid dimethylether into dehydroguaiaretic acid dimethylether[1—2] and the recent isolation in these laboratories of dehydroguaiaretic acid from the products obtained by dehydrogenation of *iso*eugenol[3] would make the possible occurrence of phenylnaphthaline or phenyltetraline derivatives in guaiacum resin an attractive hypothesis.

The dimethylethers of α- and β-conidendrin (III) were reduced with lithium aluminium hydride to the previously-described, corresponding diols[4—5]. After esterification with *p*-toluenesulphonyl chloride the diol esters were subjected to another reduction with the same reagent[6] which resulted in formation of the desired compounds (IV). Since no optical inversion is likely to occur during these processes the fully reduced compounds retain the configuration of the original lactones — α- and β-conidendrin dimethylether — and hence differ only in respect to the configuration at carbon atom 3 (IV). Their structure was confirmed by catalytic dehydrogenation to dehydroguaiaretic acid dimethylether (V).

When this work was in progress we learned by the good services of Professor Birch (Sydney, Australia) that Hughes and Ritchie had isolated four new lignans from *Himantandra* species, one of which, galbulin, possesses the structure (IV). Their work has now been published[7]. Our compound from α-conidendrin was found to be identical with galbulin by mixed melting point and optical rotation. This constitutes a confirmation of the structure proposed by these authors and moreover connects galbulin stereochemically with α-conidendrin.

Quite recently we learned from Dr. Schrecker, National Cancer Institute, Bethesda, USA, that he has also converted α-conidendrin to galbulin[8].

EXPERIMENTAL *

p-Toluenesulphonates. 1. The diol (2 g) from α-conidendrin dimethylether was dissolved in dry pyridine (30 ml) and *p*-toluene-sulphonylchloride (6 g) added in one lot at a temperature of 5—10° and the mixture then allowed to attain room temperature slowly. Two hours after mixing, water (1.5 ml) was added dropwise with cooling and half an hour later the mixture was poured on to ice and hydrochloric acid (conc. 35 ml). The precipitated ester was collected, washed and dried in a vacuum desiccator, yield 2.8 g. Crystallization from ethanol gave a product melting at 158.5—159.5°, $[\alpha]_D^{20}$ +4.1° (*c* 1.95 in chloroform). (Found: OCH_3 17.2. Calc. for $C_{36}H_{40}O_{10}S_2$ (696.8): OCH_3 17.8).

2. The diol (2 g) from β-conidendrin dimethylether was treated similarly to the α-product above. Yield of dried crude β-ester 2.9 g. After several crystallizations from

*) All melting points uncorrected.

methanol it melted at 117.5—118.5°, $[\alpha]_D^{20}$ +53.8°. (*c* 1.80 in chloroform). (Found: OCH_3 17.5. Calc. for $C_{36}H_{40}O_{10}S_2$ (696.8): OCH_3 17.8).

Reduction of the p-toluenesulphonates. 1. A solution of the α-tosylester (1 g) in absolute benzene (20 ml) was added to a slurry of lithium aluminium hydride (1 g) in absolute ether (20 ml) and the mixture boiled for 3 h. Excess of the hydride was destroyed with ethyl-acetate, hydrochloric acid added and the product extracted with ether. The extract was then washed with sodium carbonate solution and water, dried over sodium sulphate and evaporated. The residue (0.45 g) was crystallized from methanol. M. p. 129.5—130.5°, $[\alpha]_D^{20}$ −7.6° (*c* 2.6 in chloroform). For analysis the substance was distilled *in vacuo*. (Found: C 73.94; H 8.01; OCH_3 34.12; C—CH_3 5.15. Calc. for $C_{23}H_{28}O_4$ (356.4): C 74.13; H 7.92; OCH_3 34.8; C—CH_3 8.4).

2. The β-tosylester treated as above gave after crystallization from methanol a product melting at 85—85.5°, $[\alpha]_D^{20}$ +45° (*c* 2.0 in chloroform). Distilled for analysis. (Found: C 73.80; H 8.01; OCH_3 34.0. Calc. for $C_{23}H_{28}O_4$ (356.4): C 74.13; H 7.92; OCH_3 34.8).

Dehydrogenation experiments. 1. The fully reduced α-compound (IV) (100 mg) was heated under reflux with palladized charcoal (10 %, 25 mg) in diethylene glycol (1 ml) for 4 h. The catalyst was then filtered off by suction and the colorless solution poured into water. After washing with water the precipitate (90 mg) was crystallized from glacial acetic acid and melted then at 176—177° undepressed by mixing with an authentic sample of dehydroguaiaretic acid dimethylether.

2. Using the same procedure the β-isomer of (IV) was also converted to dehydroguaiaretic acid dimethylether.

The author is indebted to *Statens Tekniska Forskningsråd* for financial support, to Dr. Hughes for determination of mixed melting point with galbulin and to Professor Erdtman for his interest in this work.

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Received July 17, 1954.