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DEOXYSCHIZANDRIN - STRUCTURE AND TOTAL SYNTHESIS

N.K. Kochetkov, A. Khorlin and O.S. Chizhov

Institute for Chemistry of Natural Products, Academy of Sciences, Moscow

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WE have discovered[1] six substances, related to schizandrin, in Schisandra chinensis Baill. seed oil. Structure (I) was proposed[2] for schizandrin. This report concerns the isolation and synthesis of a new substance from this group, named deoxyschizandrin.

Thin layer chromatography on alumina with heptane-ethyl acetate 7:3 mixture indicated the presence of a new substance in mother liquors after crystallization of γ-schizandrin.[1] This substance had an R_f-value somewhat lower than that of γ-schizandrin. The substance - deoxyschizandrin - was isolated from the mother liquor by adsorption chromatography on an alumina column as colourless crystals of composition $C_{24}H_{32}O_6$ (Found: C, 69.11, 69.05; H, 7.66, 7.54; OCH_3, 44.72, 44.93. Calc.: C, 69.22; H, 7.75; 6 OCH_3, 44.70%), m.p. 116°-117°, $[\alpha]_D$ +107° (c 5.7 in $CHCl_3$). The I.R. spectrum of deoxyschizandrin possesses no O-H band nor peaks in the 1800-1600 cm^{-1} region. The U.V. spectrum of this compound is practically identical with that of schizandrin[1] (λ_{max} 248 mμ, ε_{max} 16500, λ_{infl} 273 and 283 mμ, ε_{infl} 3100 and 2400 respectively). Deoxyschizandrin must therefore be a derivative of dibenzocycloöctadiene. The NMR spectrum*

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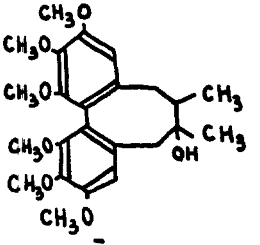
* The NMR spectrum was obtained in $CHCl_3$-soln. at 40 mc with benzene as external reference.

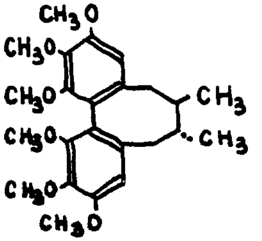
[1] N.K. Kochetkov, A. Khorlin and O.S. Chizhov, J. Gen. Chem. U.S.S.R. 31, 3454 (1961).

[2] N.K. Kochetkov, A. Khorlin, O.S. Chizhov and V.I. Sheichenko, Tetrahedron Letters 730 (1961).

of deoxyschizandrin displays maxima at 18 c.p.s. (aromatic hydrogens), 123 and 135 c.p.s. (OCH_3-groups), 177 and 192 c.p.s. (CH_2-groups in α-position to the aromatic ring), 236, 242, 247 and 253 c.p.s. (CH_3-groups) and no peaks, corresponding to other groups. These data are sufficient to propose structure (II) for deoxyschizandrin, which is thus 2',3',4',1",2",3"-hexamethoxy-1:2,3:4-dibenzo-6,7-dimethylcycloöcta-1,3-diene.



I



II

Optically active 6,7-cis-substituted 1:2,3:4-dibenzocycloöcta-1,3-dienes readily racemize,[3] owing to rotation about the aryl-aryl bond, relatively small substituents such as methoxy-groups retard this rotation only to a small extent.[4] On the other hand, 6,7-trans-substituted 1:2,3:4-dibenzocycloöcta-1,3-dienes are completely incapable of racemization at all.[3] Bearing this in mind, one may conclude, that in the case of deoxyschizandrin the methyls at C_6 and C_7 must be trans-orientated, since the compound has a specific rotation as high as +107° despite the fact that the above mentioned mother liquors before chromatography were stored for one and a half years and occasionally heated.

The structure of deoxyschizandrin was proved by synthesis of the racemic compound. Dimethyl trans-2',3',4',1",2",3"-hexamethoxy-1:2,3:4-dibenzocycloöcta-1,3-diene-6,7-dicarboxylate* yields the corresponding diol

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* The synthesis will be described in detail elsewhere.

[3] L.V. Dvorken, R.B. Smith and K. Myslow, J. Amer. Chem. Soc. 80, 486 (1958).

[4] L.A. Wiles, Chem. Rev. 56, 329 (1956).

when reduced with $LiAlH_4$ in tetrahydrofuran. The diol without further purification was transformed to the bis-p-toluenesulphonate (p-toluenesulphochloride in pyridine at 0°, cf.[5]). The product was reduced ($LiAlH_4$ in tetrahydrofuran) to give racemic deoxyschizandrin, m.p. 131°-133° (Found: C, 69.22, 69.39; H, 7.79, 7.93%). The substance obtained was indistinguishable from natural deoxyschizandrin on thin layer chromatography with the above mentioned solvent system and exhibited an I.R. spectrum, coinciding with that of the natural compound.

With the synthesis of deoxyschizandrin the structure of compounds of the schizandrin group may be considered to be fully established. These compounds may be regarded as a new and peculiar type of lignans.

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[5] A.W. Schrecker and J.L. Hartwell, J. Amer. Chem. Soc. **77**, 432 (1955).