Tetrahedron Letters No.9, pp. 781-785, 1967. Pergamon Press Ltd. Printed in Great Britain.

CONSTITUENTS OF CALIFORNIAN REDWOOD
THE STRUCTURES OF SEQUIRIN B AND C

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(Received 22 December 1966)

Serious chemical investigations into the phenolic constituents of Sequoia sempervivens heartwood have previously been reported on two occasions. Sherrard and Kurth[1] described a crystalline material, m.p. 214°, named sequoyin and more recently Balogh and Anderson[2], using their "chromatostick" technique[3] separated three products, Sequirin-A, Sequirin-B, and Sequirin-C, from the expressed extract of fresh green redwood. No structures were suggested. We now report the results of our studies on extractives from seasoned heartwood.

Concentrated aqueous extract of redwood was extracted with ether, and the ether soluble material was crystallised from acetone-benzene, and then from ethanol to give sequirin-B*, m.p. 212-213°, $C_{17}H_{18}O_5$, tetra-acetate m.p. 108°, trimethyl ether m.p. 135-136°, and monoacetyl trimethyl ether m.p. 152-3°. No phenol corresponding sequirin-A or -C has yet been isolated, but from the methylation of crude solid extractive, trimethyl sequirin-C was obtained by preparative thin-layer chromatography (m.p. 121° from benzene-ethyl acetate, $C_{20}H_{24}O_5$).

Sequirin-B contains three phenolic hydroxyls, and forms a trimethyl ether; the presence of one alcoholic hydroxyl is shown by formation of mono esters of the trimethyl derivative. It is shown to be secondary by the downfield shift of a one-proton signal in the n.m.r. spectrum on acetylation (see below). Oxidation of trimethyl sequirin-B with chromium trioxide in acetic acid yielded anisic and veratric acids, identified by t.l.c. and g.l.c. comparisons of their methyl esters with authentic samples.

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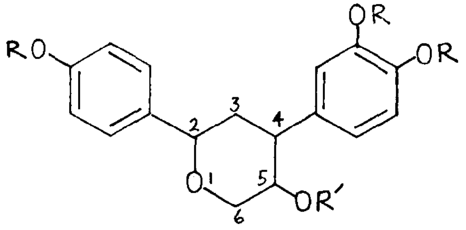
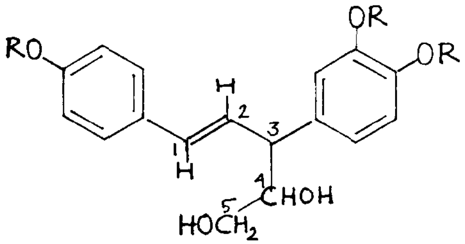
*Although our work had commenced prior to Balogh and Anderson's publication[2], we have adhered to their nomenclature to avoid confusion.

Trimethyl sequirin-C forms a diacetate, and thus contains two alcoholic hydroxy groups; that one is primary and the other secondary is shown by the downfield shift of both a one proton signal and a two proton signal in the n.m.r. spectrum after acetylation (see below). Trimethyl sequirin-C also contains one double bond. This is suggested by the signal (2H) in the n.m.r. spectrum due to olefinic protons. On hydrogenation over palladium-barium sulphate, one mol. of hydrogen was absorbed, and a new compound, trimethyl dihydrosequirin C was formed, m.p. 148-150°C. This product forms an amorphous diacetate, and affords formaldehyde on periodate oxidation. The same product is also formed on hydrogenolysis of trimethyl sequirin B over palladium-barium sulphate, 1 mol. of hydrogen being used.

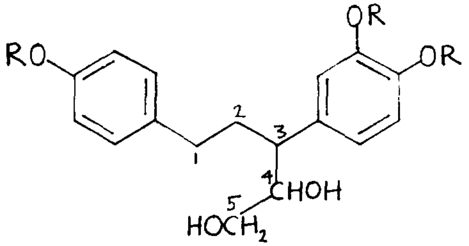
This information, together with n.m.r. spectra, lead us to structures (I), (II), and (III) for sequirin-B (R=R'=H), sequirin-C (R=R'=H) and trimethyl dihydrosequirin-C (R=Me, R'=H) respectively.



(I)



(II)



(III)

The n.m.r. spectrum of trimethyl sequirin-C (II; R=Me,R'=H) shows 3 methoxyl groups, at τ 6.22, 6.26 and 6.33. The anisyl ring protons appear as 2 superimposed AB quartets (4H), with J_{AB} = 9 c/s and centre at τ 3.01; the veratryl group hydrogens show as a broad singlet (3H), τ 3.25. Two hydroxylic protons can be identified at τ 7.31, disappearing on shaking the sample with deuterium oxide. A multiplet extending from τ 3.4 - τ 4.1 is assigned to the two olefinic hydrogens. This multiplet can be analysed as the AB part of an ABX spectrum; coupling constants calculated on this basis are $J_{AB} = -17$ c/s, J_{AX} and J_{BX} = 14 c/s and 5 c/s. The magnitude of the coupling between the two olefinic protons demonstrate a trans-configuration for this double bond. The remaining protons appear as a broad signal (4H), τ 6 - 6.8 partly obscured by methoxyl absorption. The acetate (II, R=Me, R'=Ac) has a similar spectrum, but shows in addition two acetate methyls τ 8.6, 8.23. Further the 4-H moves downfield to τ 4.54; the non-equivalent C-5 methylene protons shift to τ 5.64 and 6.03. This pair appear as an AB spectrum (J_{AB} = 12 c/s), each arm being further split by coupling to the adjacent methine proton with J = 4 c/s and J = 7 c/s. The benzylic 3-hydrogen signal is hidden by the methoxyl absorption.

The n.m.r. spectrum of trimethyldihydrosequirin-C acetate (III; R=Me, R'=Ac) is closely related to the spectrum just discussed, the signals of all protons, except the C-1 and C-2 hydrogens being very similar in chemical shift and coupling constants. The absorptions due to olefinic protons in trimethylsequirin-C acetate (II; R=Me, R'=Ac) are now replaced by a wide multiplet (4H) extending from τ 6.7 - 8.3.

Trimethylsequirin-B (I; R=Me, R'=H) shows three methoxy groups at τ 6.13, 6.16, and 6.23. Anisyl ring protons are displayed as two superimposed AB quartets, with centre at τ 2.87, J_{AB} = 10 c/s; the veratryl ring protons absorb together at τ 3.16. One alcoholic proton can be seen at τ 8.07, and is removed by deuterium exchange. In the tetrahydropyran ring, the 5-H is obscured by methoxyl signals; the C-3 methylene protons appear as a multiplet near τ8, 4 and the benzylic 4-proton is centred at τ 7.6. The axial and the equatorial 6-hydrogens are displayed at τ 6.59 and 5.75 respectively. The C-2 methine proton is apparent at τ 5.6 (benzylic, and adjacent to oxygen). The spectrum of trimethyl sequirin-B acetate is similar, but shows an acetate methyl at τ 8.14, and the 5-H shifts to τ 4.82.

The only possible ambiguity remaining in structure (II) is in the arrangement of aromatic groups: the disposition shown (1-anisyl 3-veratryl) is established by ozonolysis to give ansialdehyde (2,4-dinitrophenylhydrazone). As sequirin-B (I; R=R'=H) is structurally related to sequirin-C (II; R=R'=H) by conversion of both to the dihydro-compound (III; R=Me, R'=H), the same ambiguity is resolved also for sequirin-B.

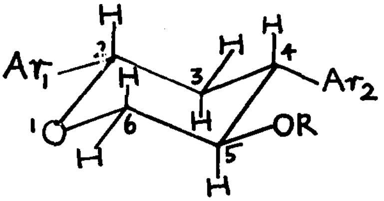
The complete relative stereochemistry of sequirin-B can be deduced from a consideration of the n.m.r. coupling constants of trimethyl sequirin-B acetate (I; R=Me, R'=Ac). The

*2-proton appears as a quartet, split by 10 c/s and again by 3 c/s, suggesting an axial dis*position, and is coupled to adjacent axial and equatorial hydrogens at C-3. The C-6 methylene absorption is basically an AB system (J_{AB} 10 c/s); coupling to an axial neighbour is shown by further splitting (J = 10 c/s) of the higher field (axial) arm (which thus appears as a triplet), and additional splitting (J = 4 c/s) of the equatorial branch. The adjacent 5-hydrogen appears as 6 lines (4 c/s and 10 c/s couplings to $C\underline{H}_2$-6, supplemented by a further 10 c/s coupling to 4-H). This 4-proton shows a similar 6 line spectrum, with coupling constants $J_{4,5}$ = 10 c/s, $J_{4,3\,eq}$ = 4 c/s, and $J_{4,3\,ax}$ = 10 c/s.,(Table I). Assuming that constants of 10 c/s can only represent coupling between trans-diaxial hydrogens, the smaller couplings being appropriate to axial-equatorial pairs, the stereochemistry shown in cipher (IV; Ar_1 *= anisyl,* Ar_2 *= veratryl, R = Ac) must follow.*

Table I

$J_{2,3\,eq}$	3	$J_{4,5}$	10
$J_{2,3\,ax}$	10	$J_{5,6\,eq}$	4
$J_{4,3\,eq}$	4	$J_{5,6\,ax}$	10
$J_{4,3\,ax}$	10		

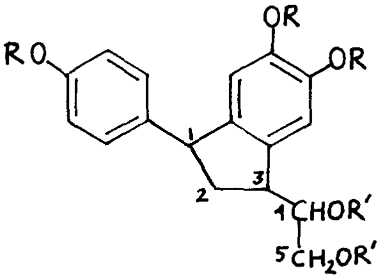
Coupling Constants (c/s) for trimethyl sequirin-B acetate.



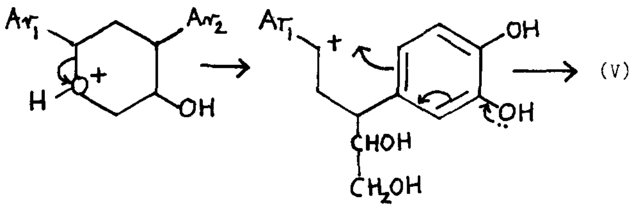
(IV)

All substituents are seen to be equatorial to the tetrahydropyran ring.

The treatment of sequirin-B (I; R = R' = H), or of sequirin-C[2] (II; R=R'=H) with acids yields a new compound, isosequirin $C_{17}H_{18}O_5$, m.p. 195° from ethanol-benzene. This forms a penta-acetate, m.p. 111°, and a trimethyl ether m.p. 117°, which affords formaldehyde on periodate oxidation. Structure (V) has been suggested for isosequirin by Balogh and Anderson[4] largely on the grounds of the isolation of 2-anisoyl-4,5-dimethoxybenzoic acid from the oxidation products of trimethylisosequirin. We support this proposal. The n.m.r. spectrum of trimethylisosequirin (V; R=Me, R'=H) shows 5 aromatic hydrogens as a group near τ 3.0, and one isolated aromatic hydrogen at τ 3.42. Three methoxyl absorptions at τ 6.08, 6.12 and 6.28 are observed. The dibenzylic proton at C-1 appears at τ 5.57 as a broad triplet; the signal from three C-4 and C-5 protons is partly obscured by the methoxyl peaks. The remaining protons, at C-2 and C-3, show as multiplet near τ 7.7.



(V)



The suggested mechanism of this rearrangement is outlined above. The intermediate carbonium VI might be envisaged as cyclizing to a position *ortho* to a phenolic hydroxyl rather than *para* as shown. The product from this alternative reaction would have no isolated aromatic hydrogens, and must be dismissed after consideration of the n.m.r. spectrum.

Adequate carbon and hydrogen analyses have been determined for all compounds described. Mass spectra have also been obtained for the principal compounds; as well as confirming the molecular formulae, fragmentation patterns are in accord with the structures presented here, and will be discussed in a fuller communication. Further degradative and synthetic work continues to test the present structural conclusions.

The sequirins belong to the small non-lignan group, which includes agatharesinol[5], sugiresinol[6], and hinokiresinol[7]. The properties of sequirin-A, reported by Balogh and Anderson[2] closely resemble those of sugiresinol, to which it may be identical.

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