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β'- DIHYDRODIOSPYRIN - THE FIRST REDUCED BISNAPHTHAQUINONE

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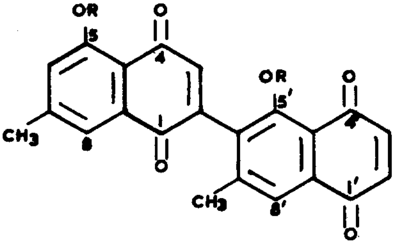
We have earlier established the structure of diospyrin, a bisnaphthaquinone with a benzene-quinone linkage.[1,2] We are currently interested in finding out how bisnaphthaquinones are elaborated in plants. It has been postulated that such bisnaphthaquinones may arise either by the oxidation of a bisnaphthol formed by the radical coupling of two naphthol units or by the condensation of a naphthaquinone unit with a naphthol (or quinol) unit and subsequent oxidation. No experimental evidence has, however, yet been offered in support of either of the above theories. We thought it, therefore, worthwhile to look for reduced compounds which may be involved as biointermediates in such syntheses in established plant sources of bisnaphthaquinones.

Petroleum ether extract of the fresh wood of D. montana yielded, in addition to diospyrin, 4 mg of a compound much more polar than diospyrin, red crystals m.p. 182°; M.W. 378, showing it to have four hydrogen atoms more than diospyrin.

A fresh sample of wood and bark was then collected from Kakinada Forests of Andhra Pradesh and put immediately in chloroform to prevent oxidation and brought to Hyderabad for working up in the hope of isolating more of the tetrahydro compound. Removal of triterpenoids by boiling with ether left a dark red residue. TLC did not show the presence of the tetrahydro compound but did show the presence, along with diospyrin, of another compound slightly more polar than diospyrin in the bark extract only. It polymerised on a silica gel column and was isolated by preparative TLC on deactivated silica gel plates coated in $CHCl_3/CH_3OH$ (4:1) and using chloroform as eluent. This was crystallised from chloroform/petroleum ether; m.p. 226 (decomp.), M.W. 376 by mass spectrometry, showing that the compound is a dihydrodiospyrin.

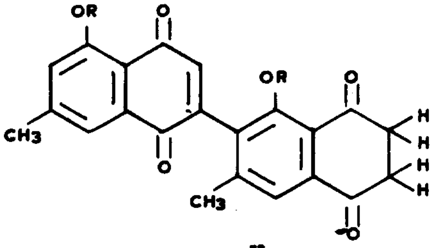
Methyl and ethyl ethers of this compound were prepared by alkylating the dark red residue with the alkyl iodide and silver oxide in chloroform and separating the ether from the corresponding diospyrin ether by TLC on deactivated silica gel plates with chloroform; the methyl ether crystallised from methylene chloride/petroleum ether in brown red hexagonal crystals m.p. 228° (M.W. 404 by mass spectrometry), ethylether, yellow crystals m.p. 78°.

A comparison of the PMR spectra of this dihydrodiospyrin and its methyl and ethyl ethers with those of diospyrin and its dimethyl and diethyl ethers shows it to have structure II (R=H).



I

DIOSPYRIN. R=H.



II

β'-DIHYDRODIOSPYRIN. R=H.

Table 1*

Compound	3-H	5-	5'-	6-H	7-	7'-	8-	8'-	2'- and 3'-
		OH or OCH$_3$			CH$_3$		H		H or H$_2$
I. R=H	6.90	Not seen		7.17	2.50	2.32	7.51	7.58	6.97
II. R=H	6.91	11.90	12.43	7.17	2.48	2.31	7.52	7.52	3.11
I. R=CH$_3$	6.76	4.04	3.71	7.16	2.52	2.32	7.60	7.82	6.89
II. R=CH$_3$	6.75	4.00	3.67	7.17	2.46	2.25	7.60	7.75	3.01
I. R=C$_2$H$_5$	6.60	expected		6.96	2.35	2.20	7.39	7.55	6.68
II. R=C$_2$H$_5$	6.65	CH$_3$CH$_2$ signals seen		7.05	2.35	2.15	7.47	7.61	3.10

*PMR spectra are recorded in CDCl$_3$. Chemical shifts are expressed in δ (ppm) relative to external TMS.

The PMR spectrum of diospyrin dimethylether has signals for one vinylic proton at 6.76 and two vinylic protons at 6.89, whereas in the case of the methylether of the new compound, only one vinylic proton is seen at 6.75 and one sees a new four proton singlet at 3.01 assignable to methylene protons; the other signals are comparable to corresponding signals of diospyrin dimethylether. It is thus obvious that the terminal quinone moiety of diospyrin dimethylether has been reduced to a β'-dihydro compound in the new ether which by integration and molecular weight is a dimethylether. Similarly the PMR spectra of diospyrin diethylether and the ethylether of the new substance differ only in the former having signals for three vinylic protons and the latter for one vinylic and four methylene protons at 3.10. This is also a diethylether as signals for two $-O-CH_2-$ (3.70 and 4.10) groups are seen. A comparison of the PMR spectra of diospyrin and the new dihydrodiospyrin also leads to the same conclusion.

The IR and UV spectra of the dihydrodiospyrin also support structure II (R=H); bands for aliphatic C-H stretching are seen at 2920 and 2850 cm^{-1}; in the carbonyl region there are three bands at 1690 (w), 1670 and 1640 cm^{-1} assignable to tetralone carbonyl, unbonded and bonded carbonyls respectively. The dimethyl and diethylethers also have bands for the tetralone carbonyls at 1690 and 1695 cm^{-1} respectively. The peaks at 235 $m\mu$ in the UV spectra in ethanol of dihydrodiospyrin, its dimethyl and diethylether ($\log \varepsilon$ 4.46, 4.60 and 4.48 respectively) are also assignable to the tetralone chromophore.

To confirm the above structure, specially the linkage between two halves, we decided to reduce diospyrin and diospyrin dimethylether. Diospyrin (40 mg.) on reduction with Wilkinson[3] homogeneous catalyst for 30 mts at room temperature in excess benzene gave a compound (23 mg.) m.p. 228° identical with that isolated from D. montana bark. The β'-dihydrodiospyrin was separated from unreduced diospyrin by preparative TLC with chloroform. It oxidises fairly quickly to diospyrin. Similarly diospyrin dimethylether (50 mg.) on reduction gave β'-dihydrodiospyrin dimethylether (34 mg.) m.p. 228° identical with the dimethylether prepared by the methylation of natural β'-dihydrodiospyrin. Hence selective hydrogenation of the C-2' double bond has taken place in both cases, as expected, without any reduction taking place at the hindered C-2 double bond. The continued shielding of the C-7' methyl group in dihydrodiospyrin and its ethers and the C-5' methoxymethyl and oxymethylene group in dihydrodiospyrin dimethyl and diethyl ethers respectively also points to the C-2 double bond remaining unreduced.

In diospyrin on electron impact the initial loss of methyl radical is dominant and this is followed by two successive losses of carbon monoxide whereas in dihydrodiospyrin, though the M-15 fragment is also quite prominent (21%), there are five successive losses of 28 mass units from the molecular ion. These losses could probably be assigned to losses of 4 molecules of carbon monoxide and one of ethylene. Fragments at m/e 163, 135, 134 and 106 are seen in the lower mass region. These are diagnostic of the 7-methyl juglone moiety. The tetrahydro compound referred to earlier also gives the same fragments in the lower mass region and may, therefore, possibly be reduced in the terminal quinone ring to a tetralone derivative like shinanolone.[4] Its resistance to oxidation by ferric chloride lends support to this speculation.

R.H. Thomson and A.F.Fallas[5] have earlier suspected the contamination of their diospyrin with a quinol, as on mass fragmentation the M+2 peak had an abundance of 72%. Our purified diospyrin shows an abundance of only 7% for the M+2 ion. Though 7-methyl β-dihydrojuglone is known[6], the β'-dihydrodiospyrin obtained by us is probably the first recorded isolation of a reduced bisnaphthaquinone derivative and diospyrin may be formed in nature by the oxidation of this in the tautomeric quinol form.

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