275. *Lignans from* Myristica otoba. *The Structures of Hydroxyotobain and Iso-otobain.*

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Proton magnetic resonance studies have been made on hydroxyotobain and on iso-otobain, and their structures have been shown to be (II) and (VI), respectively. The conformations of the molecules and the configurations at the asymmetric centres have been obtained. The conformations and configurations in otobain, hydroxyotobain, iso-otobain, and galcatin are identical.

Baughman *et al.*[1] reported that the expressed oil from the fruits of *Myristica otoba* contained two compounds which were named otobite and iso-otobite and formulated as $C_{20}H_{20}O_4$. Recently [2] the structure of otobite, now renamed otobain, was shown to be (I). When otoba fat is hydrolysed with ethanolic potassium hydroxide, and the neutral water-insoluble products are chromatographed on alumina, the less polar fragments yield otobain and the more polar fragments yield a hydroxy-otobain ($C_{20}H_{20}O_5$) along with a mixture of isomeric phenolic ethers ($C_{19}H_{19}O_3$·OMe). Methylation of these ethers yields [3] only one compound, $C_{19}H_{18}O_2(OMe)_2$, which has physical constants identical with those reported [1] for iso-otobite. Despite the different empirical formula and the lack of a methoxyl group previously reported for this compound,[1] we believe that this last phenolic ether *is* iso-otobite. The compound is renamed iso-otobain to conform with accepted lignan nomenclature.

The hydroxyotobain obtained by the above procedure readily undergoes acid-catalysed dehydration, yielding didehydro-otobain,[2] although it is stable to the alkaline hydrolysis involved in its isolation. It therefore contains the same phenyl-tetrahydronaphthalene skeleton as otobain, in which the methylenedioxy-groups span positions 5, 6 and 3′, 4′, with the addition of one tertiary hydroxyl group at position 2, 3, or 4.

The proton magnetic resonance absorption spectrum of hydroxyotobain is shown in Fig. 1, and the τ values of the groups giving rise to the observed spectrum are given in Table 1. The O*H* proton resonance is ascribed to peak 24 because that peak disappears during the dehydration to didehydro-otobain.

Table 1.

Assignments for hydroxyotobain.

Peaks	Assignment	τ Value	Peaks	Assignment	τ Value
1	C*H*Cl$_3$	2·81	24	O*H*	7·62
2—13	Aromatic protons		26—35	*H*(2),*H*(3)	H_2 = 8·19, H_3 = 8·44
14	O·C*H*$_2$·O (ring C)	4·20	36—37	C*H*$_3$(2)	9·01
15—18	O·C*H*$_2$·O (ring A)	4·43, 4·57	38—39	C*H*$_3$(3)	9·15
19—25	C*H*$_2$(1)	H_α = 7·25, H_β = 7·49			

The absence of absorption in the region $\tau = 6{\cdot}6$, which is very characteristic of a doubly benzylic proton,[2] shows that this hydroxyotobain is 4-hydroxyotobain (II). The conformation of ring B and the relative configurations at carbon atoms 1—4 are also defined by this spectrum. This follows from reasoning similar to that used in analysing the spectrum of otobain.[2] The AB quartet, peaks 15—18, observed for that part of the spectrum due to the O·CH$_2$·O group on ring A (J 1·5 c./sec.) shows that the 4,1′-bond is equatorial and that the hydrogen atoms of this methylenedioxy-group are not symmetrically arranged with respect to the aromatic ring C. Furthermore, when that part of

[1] Baughman, Jamieson, and Brauns, *J. Amer. Chem. Soc.*, 1921, **43**, 199.
[2] Gilchrist, Hodges, and Porte, *J.*, 1962, 1780.
[3] Karplus, *J. Chem. Phys.*, 1959, **30**, 11.

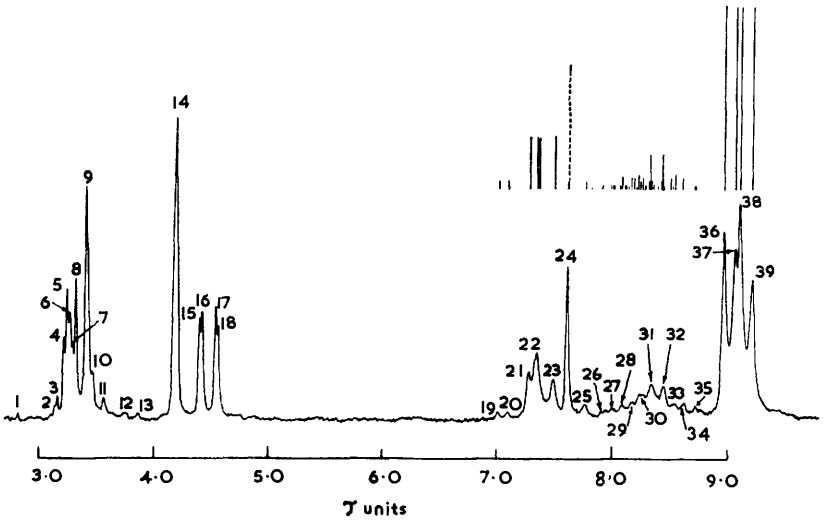
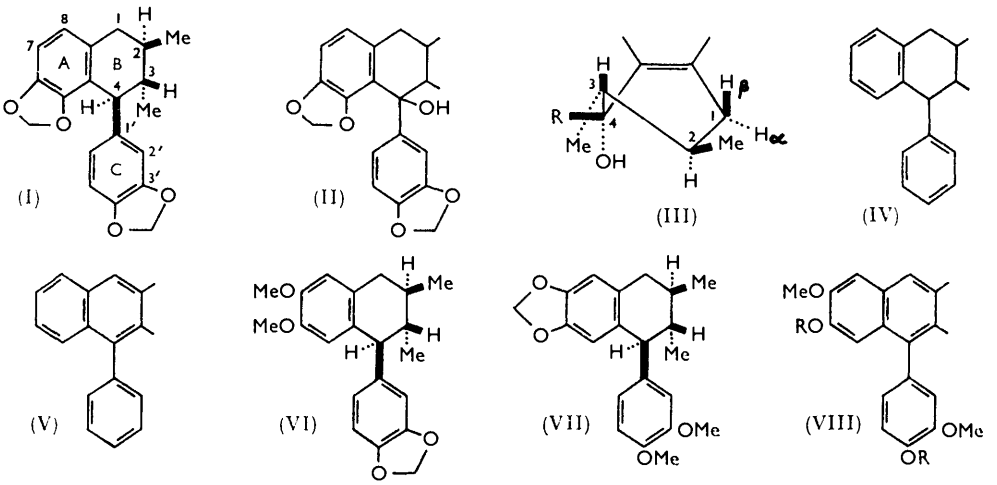


FIG. 1. Proton magnetic resonance spectrum of hydroxyotobain.

the spectrum arising from the $-CH_\alpha H_\beta \cdot CHMe \cdot CHMe-$ fragment is analysed, the following spin–spin coupling constants (c./sec.) are obtained:

$J[H(1)_\alpha–H(1)_\beta] = 16{\cdot}0$;	$J[H(1)_\beta–H(2)] = 9{\cdot}0$;	$J[H(2)–H(3)] = 9{\cdot}5$;
$J[H(1)_\alpha–H(2)] = 5{\cdot}0$;	$J[H(2)–CH_3] = 6{\cdot}0$;	$J[H(3)–CH_3] = 6{\cdot}5$.

The first-order line spectrum calculated for this fragment by using the chemical shifts quoted in Table 1 along with these coupling constants is shown on Fig. 1.



When the coupling constants obtained from the observed spectrum are compared with those predicted by Karplus's equation [3] for each of the possible conformations of ring B and for each of the possible configurations at carbon atoms 2—4, it follows that ring B is in the pseudo-chair form (III) with the phenyl and the two methyl substituents all equatorial and *trans-trans* to one another, *i.e.*, the conformation of ring B and the configurations at carbon atoms 2—4 of hydroxyotobain are identical with those of otobain.[2]

The proton magnetic resonance spectra of iso-otobain and its dehydrogenation product, tetradehydroiso-otobain, are shown in Figs. 2A and B, respectively, and the groups which give rise to the spectra are listed in Tables 2 and 3.

TABLE 2.

Assignments for iso-otobain.

Peaks	Assignment	τ Value	Peaks	Assignment	τ Value
1—4	Aromatic protons		11, 12	$Ph{\cdot}CH_2{\cdot}CH<$	7·35
5	Aromatic *H*	3·83		[Average $J[CH_2–CH)$ = 6 c./sec.]	
6	$O{\cdot}CH_2{\cdot}O$	4·13	13	Two $>CH–CH_3$	~8·5
7	$O{\cdot}CH_3$	6·20	14, 15	$>CH–CH_3$	8·94
8	$O{\cdot}CH_3$	6·42		[$J(CH–CH_3)$ = 4·8 c./sec.]	
9, 10	$Ph{\cdot}CH(CH<){\cdot}Ph$	6·63	16, 17	$>CH–CH_3$	9·12
	[J(CH–CH) = 9 c./sec.]			[$J(CH–CH_3)$ = 5·4 c./sec.]	

TABLE 3.

Assignments for tetradehydroiso-otobain.

Peaks	Assignment	τ Value	Peaks	Assignment	τ Value
1	Aromatic *H*	2·52	10	$O{\cdot}CH_3$	5·99
2	$CHCl_3$	2·78	11	$O{\cdot}CH_3$	6·21
3—8	Aromatic protons		12	$Ph{\cdot}CH_3$	7·54
9	$O{\cdot}CH_2{\cdot}O$	3·95	13	$Ph{\cdot}CH_3$	7·84

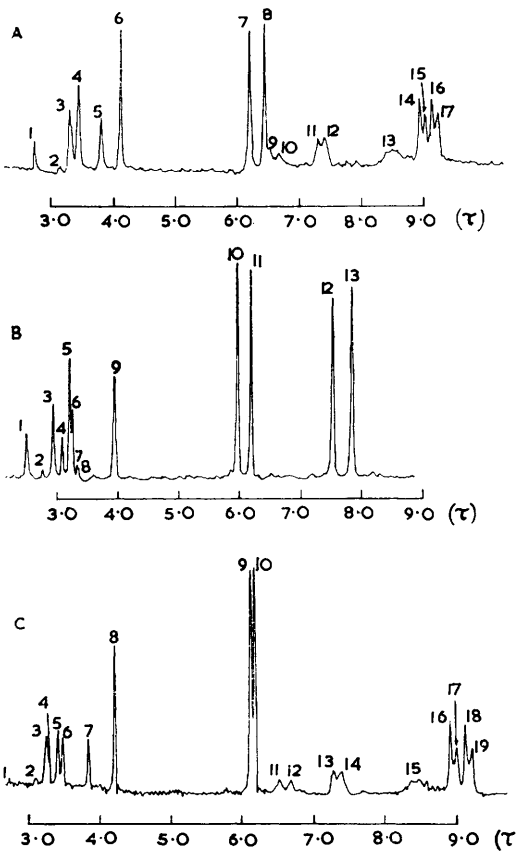


FIG. 2. Proton magnetic resonance spectra of iso-otobain (A), tetradehydroiso-otobain (B), and galcatin (C).

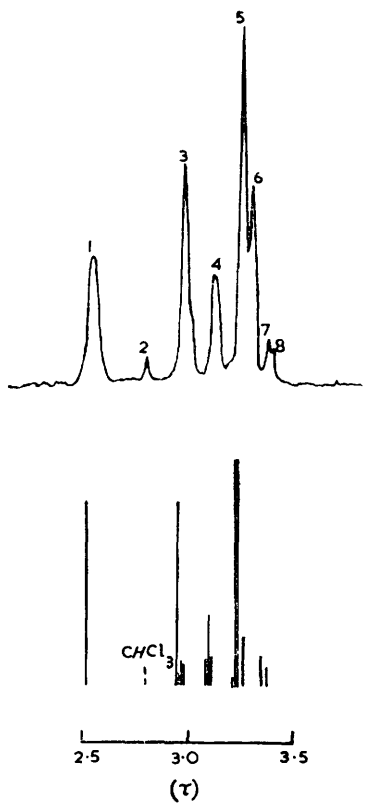


FIG. 3. Observed and calculated proton magnetic resonance spectra arising from the aromatic protons in tetradehydroiso-otobain.

It follows from these spectra that iso-otobain contains the phenyl-tetrahydronaphthalene fragment (IV) with further substitution of rings A and C by one methylenedioxy- and two methoxy-groups. The positions of substitution can also be obtained from the spectra. In iso-otobain the methylenedioxy-resonance is a single sharp peak and one of the aromatic resonances, peak 5 on spectrum 2A, appears at a τ value rather higher than that usually assigned [4] to aromatic protons, suggesting that H(5) is not replaced in the iso-otobain molecule and that peak 5 on spectrum 2A arises from H(5) of fragment (IV). Furthermore, no coupling of H(5) with any other proton is observed and so ring A is substituted at positions 6 and 7. These deductions are further substantiated by a complete analysis of the aromatic region, peaks 1—8, of the spectrum of tetradehydroiso-otobain, which shows that six protons forming three systems of types A, A'B', and A''B''C'' contribute to that region. There are no interactions between these systems. System A'B' consists of two protons in *para*-positions on a benzene ring, and the system A''B''C'' consists of three protons at positions 1, 2, and 4 in another benzene ring. The assignments of the six protons A, · · ·, C'' to the phenyl-naphthalene fragment (V), along with their τ values and associated coupling constants, are listed in Table 4, and the line spectrum calculated for these six protons by using the parameters in that Table is compared with the observed spectrum in Fig. 3.

TABLE 4.

Aromatic-proton assignments for tetrahydroiso-otobain.

Proton	τ	Assignment	Proton	τ	Assignment	Proton	τ	Assignment
A	2·52	H(1)	B'	2·95	H(8)	B''	3·05	H(5')
A'	3·23	H(5)	A''	3·24	H(2')	C''	3·29	H(6')

J(B''–C'') = 7·8 c./sec. J(A''–C'') = 1·4 c./sec.
All other coupling constants <0·5 c./sec.

The analysis of the proton magnetic resonance spectra 2A and B, therefore, shows that the structure of iso-otobain is either (VI) or (VII). Structure (VII) is that of a known compound, galcatin,[5] which is not identical with iso-otobain. Therefore, iso-otobain has structure (VI). Further, the coupling constants listed in Table 2 show that the conformation of ring B and the configurations at carbon atoms 2—4 are identical with those of otobain and hydroxyotobain.

TABLE 5.

Tetradehydroiso-otobain							
$\lambda_{max.}$ (mμ)	238	275i	285	290	315	323i	330
log ε	4·79	3·88	4·005	4·01	3·56	3·39	3·70
Dehydroguaiaretic acid dimethyl ether							
$\lambda_{max.}$ (mμ)	236	275i	284	291	315	323 (max.)	331
log ε	4·70	3·93	4·02	4·03	3·60	3·52	3·80

i = Inflexion.

Further support for structure (VI) for iso-otobain comes from the ultraviolet spectrum of tetradehydroiso-otobain. This (Table 5) is almost identical with that of dehydroguaiaretic acid dimethyl ether (VIII; R = Me), but it is different from that of tetradehydro-otobain.[2]

The similarities in the structures of iso-otobain and galcatin are reflected in their proton magnetic resonance spectra. That for galcatin is shown on Fig. 2C and the spectral parameters giving rise to it are listed in Table 6.

Spectrum 2C shows that the conformation of ring B and the configurations at carbon

[4] Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, London, 1959, p. 62.
[5] Hughes and Ritchie, *Austral. J. Chem.*, 1954, **7**, 104.

TABLE 6.

Assignments for galcatin.

Peaks	Assignment	τ Values	Peaks	Assignment	τ Values
1	$CHCl_3$	2·73	13, 14	$Ph{\cdot}CH_2{\cdot}CH<$	7·35
2—6	H(8),H(2′),H(5′),H(6′)			[Average $J(CH_2{-}CH)$ = 5·7 c./sec.]	
7	H(5)	3·85	15	Two $>CH{-}CH_3$	8·4
8	$O{\cdot}CH_2{\cdot}O$	4·21	16, 17	$>CH{-}CH_3$	8·95
9	$O{\cdot}CH_3$	6·15		[$J(CH{-}CH_3)$ = 6 c./sec.]	
10	$O{\cdot}CH_3$	6·20	18, 19	$>CH{-}CH_3$	9·16
11, 12	$Ph{\cdot}CH(CH<){\cdot}Ph$	6·63		[$J(CH{-}CH_3)$ = 5·4 c./sec.]	
	[$J(CH{-}CH)$ = 9·6 c./sec.]				

atoms 2—4 in galcatin are identical with those of otobain,[2] hydroxyotobain, and isootobain, thereby confirming the stereochemical relations derived for galcatin from other evidence.[6,7]

EXPERIMENTAL

Tetradehydroiso-otobain.—Iso-otobain (450 mg.) was heated under reflux with 5% palladium–charcoal (200 mg.) and diphenyl ether (3 g.) for 3 hr. After removal of the diphenyl ether in steam the product was adsorbed from benzene–light petroleum (1 : 1) on alumina and eluted with benzene, forming plates (210 mg.) (from ethanol–chloroform), m. p. 188—190° (Found: C, 74·85; H, 6·2. $C_{21}H_{20}O_4$ requires C, 75·0; H, 6·0%).

Spectra.—Proton magnetic resonance spectra were recorded, at 23° for ~0·3M-deuterochloroform solution, on an A.E.I. R.S.2 spectrometer operating at an applied radiofrequency of 60 Mc./sec. The calculation of the line spectrum in Fig. 3 was performed by the University of Glasgow's DEUCE computer

The authors thank Professor R. A. Raphael for advice, the Tropical Products Institute for supplying the otoba fat, and Dr. Ritchie of the University of Sydney for providing a sample of galcatin. One of us (R. W.) is indebted to the Carnegie Trust for the Universities of Scotland for the award of a Carnegie Scholarship.

CHEMISTRY DEPARTMENT, THE UNIVERSITY, GLASGOW, W.2. [*Received, August 20th,* 1962.]

[6] Birch, Milligan, Smith, and Speake, *J.*, 1958, 4471.
[7] Schrecker and Hartwell, *J. Amer. Chem. Soc.*, 1955, **77**, 432.