2β-Methyl-3β-acetamidomethyl-5α-isopropenylcyclohexanone (XV).[24]—To a vigorously stirred and ice-cold solution of 626 mg. of the 2β-methyl-3β-aminomethyl-5α-isopropenylcyclohexanol mixture (VI) in 200 cc. of pyridine and 30 cc. of dry benzene, 349 mg. of acetic anhydride in 150 cc. of benzene was added dropwise over a period of 4 hr. After one additional hour at ice-bath temperature, the mixture was poured into water, the product isolated in the usual manner with ether, then chromatographed on 10 g. of neutral alumina (activity III), elution being effected first with 250 cc. of methylene chloride, followed by 150 cc. of ethyl acetate. The desired acetamido alcohol mixture (XIV) was obtained as a colorless oil (135 mg.), which crystallized spontaneously; m.p. 70–96.5°. R.D. in methanol (*c* 0.12): $[\alpha]_{589}$ −21°, $[\alpha]_{500}$ −29°, $[\alpha]_{400}$ −50°, $[\alpha]_{300}$ −134°, $[\alpha]_{260}$ −183°. This material was directly oxidized with chromium trioxide in acetone solution[11,12] and recrystallized from acetone–hexane to give the desired, chromatographically homogeneous ketone XV, m.p. 98–99°, $\lambda_{max}^{CHCl_3}$ 2.90, 5.87, 6.00 and 11.20 μ. R.D. (Fig. 2) in methanol (*c* 0.105): $[\alpha]_{589}$ −48°, $[\alpha]_{308}$ +704°, $[\alpha]_{240}$ −2280°.

Anal. Calcd. for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48. Found: C, 69.72; H, 9.58.

Dipole Moment Measurements.—The dipole moments were measured in benzene solution at 25°, using the previously described[27] apparatus, the data being summarized in Table III. References to the method of calculation are given in the Discussion. The molar refractivity (50.25 cc.) was calculated from tables[28] and atomic polarization was neglected.

(27) N. L. Allinger, H. M. Blatter, M. A. DaRooge, and L. A. Freiberg, *J. Org. Chem.*, **26**, 2550 (1961).

(28) A. I. Vogel, W. T. Cresswell, G. J. Jeffrey, and J. Leicester, *Chem. Ind.* (London), 358 (1950).

The Constitution of Otobain

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A new lignan, otobain, for which the structure 5,6-methylenedioxy-2,3-dimethyl-4-(3′,4′-methylenedioxyphenyl)-1,2,3,4-tetrahydronaphthalene (VI) is proposed, has been isolated from the fruit of *Myristica otoba*.

The fat expressed from the fruit of *Myristica otoba* is reputedly used in Colombia as a medicament for skin diseases of domestic animals. It was first examined over one hundred years ago by Uricoechea,[2] who isolated a product which he named "otobite" and to which he attributed the empirical formula $C_{24}H_{26}O_5$. A more extensive examination was performed by Baughman and co-workers,[3] who reported the isolation of isomers, $C_{20}H_{20}O_4$, which they named otobite and isootobite, and suggested that the previously isolated product was a mixture. From a sample of otoba fat collected in 1960 in the Departmento of Tolima, Colombia,[4] we have isolated a lignan for which the name otobain was proposed in a preliminary communication.[5] Gilchrist, Hodges, and Porte[6] since have described work on the isolation and structure elucidation of the same product to which they have fortunately assigned the same name in conformance with lignan nomenclature. The assumption that otobite and otobain are identical[6] we regard as questionable on the basis of reported differences of behavior (*e.g.*, Zeisel determination, action of bromine).[3,5]

Empirical analyses and molecular weight determination established that otobain had a molecular formula, $C_{20}H_{20}O_4$. The absence of absorption bands in the infrared spectrum characteristic of hydroxyl and carbonyl groups indicated that all four oxygen atoms were present as ether functions. The absence of methoxyl groups, established by Zeisel determination, suggested the likelihood that the oxygen functions were two methylenedioxy groups. That at least one such group was present was apparent from the infrared spectrum (potassium bromide disk) which showed a strong band at 928 cm.$^{-1}$, with a weak overtone at 1850 cm.$^{-1}$, considered most characteristic for methylenedioxy groups[7]; the presence of strong bands at 1362, 1242, 1130, and 1045 cm.$^{-1}$, particularly in the demonstrated absence of aromatic methoxyl groups, supports this assignment. Chemical evidence for the presence of two methylenedioxy groups was obtained by treatment of otobain with phosphorus pentachloride followed by sodium carbonate. The isolated product, $C_{20}H_{16}O_6$, had an infrared absorption band at 1830 cm.$^{-1}$ characteristic of five-membered ring strained carbonyl systems[8] of which the derived benzenoid cyclic carbonate is typical.

Kuhn–Roth C-methyl determination indicated the presence of two such groups, leaving unaccounted only two carbon atoms to be incorporated in a ring. This preliminary characterization strongly suggested that otobain is a lignan[9,10] of the phenyltetralin class, of which structure I based on unexceptional biogenetic considerations,[11–13] is the most obvious possibility. Integration of the nuclear magnetic resonance spectrum of otobain established the presence of five aromatic protons, and the ultraviolet absorption spectrum was also consistent with this formulation. Closely related to I are the lignans, isolated from *Himantandra* species by Hughes and Ritchie,[14] named galbulin (II) and galcatin (III), the absolute stereochemical assignments being proposed by two independent groups.[15,16]

(1) Present address, Varian Associates, Palo Alto, Calif.

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(3) W. F. Baughman, G. S. Jamieson, and D. H. Brauns, *J. Am. Chem. Soc.*, **43**, 199 (1921).

(4) We wish to acknowledge our indebtedness to Dr. Alvaro Fernandez-Pérez of the Instituto de Ciencias Naturales, Universidad Nacional de Colombia, through whose kind efforts the material was supplied.

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(6) T. Gilchrist, R. Hodges, and A. L. Porte, *J. Chem. Soc.*, 1780 (1962). We wish to thank Drs. Hodges and Porte for communicating their findings after the appearance of our communication and prior to their publication.

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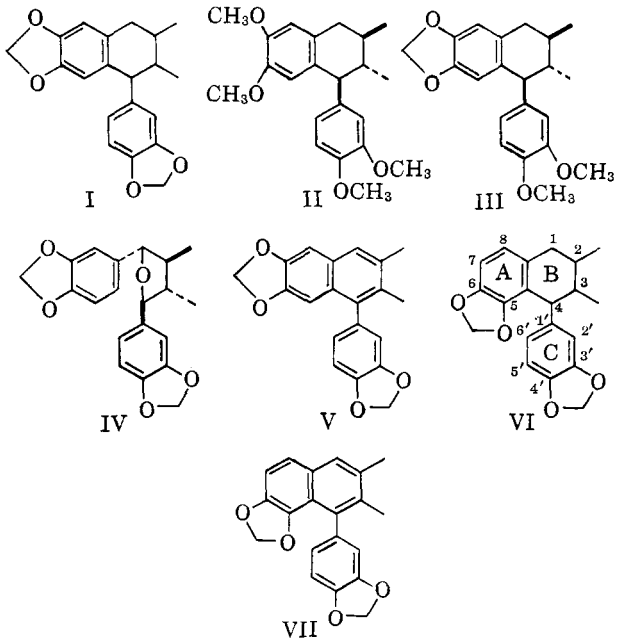
TABLE I[a]

ASSIGNMENTS OF PROTON MAGNETIC RESONANCE DATA (LIGNAN NUMBERING)

Compounds	H_1	H_2	H_3	H_4	H_5	H_7	H_8	$H_{2'}$	$H_{5'}$	$H_{6'}$	$-OCH_2O-$ ring A	$-OCH_2O-$ ring C	Methyl on C-2	Methyl on C-3
Otobain	2.63	*ca.* 1.44	*ca.* 1.44	3.43	..	6.65	6.65	6.58	6.58	6.58	5.58 and 5.64	5.88	0.96 or 1.04	0.96 or 1.04
Dehydrootobain	7.48	...	...	..	..	7.02	7.24	6.68	6.63	6.78	5.78	6.05	2.42	2.08
Dehydroepigalbacin	7.43	...	...	..	6.68	..	7.00	6.68	6.63	6.89	5.89	6.00	2.40	2.08
Dinitrootobain	2.93	*ca.* 1.57	*ca.* 1.57	4.77	..	7.33 or 7.37	..	6.48	7.33 or 7.37	..	5.72 and 5.80	6.03	0.98 or 1.09	0.98 or 1.09
Dibromootobain	2.76	*ca.* 1.45	*ca.* 1.45	4.23	..	6.95 or 7.02	..	6.43	6.95 or 7.02	..	5.62 and 5.68	5.89	0.92 or 1.06	0.92 or 1.06

[a] Tabulation of chemical shifts are indicated in parts per million of the respective protons.

Galbulin and galcatin were unaffected by bromination in carbon tetrachloride solution, and no pure nitro derivatives could be prepared by treatment with nitric acid in glacial acetic acid under a variety of conditions,[14] the latter behavior being regarded as characteristic of the phenyltetralin class of lignans.[9] In contrast, otobain readily gave in our hands crystalline dibromo and dinitro derivatives. At this juncture, we considered that this difference in behavior could be explained by otobain differing in configuration from II and III at one or more of the three asymmetric carbon atoms, particularly since the specific rotation of otobain (−40°) differed from the values for II (−8°) and III (−9°) more than would be expected by replacement of *ortho* dimethoxy groups by methylenedioxy groups. From the sequel, it is now evident that the behavior of phenyltetralin lignans on nitration cannot be regarded as diagnostic unless the ether substitution pattern is known.



Dehydrogenation of otobain with palladium–carbon yielded an optically inactive product, dehydroötobain, $C_{26}H_{16}O_4$, m.p. 185–187°. A compound to which structure (V) had been assigned,[14,16] prepared by acid isomerization of galbacin (IV) followed by dehydrogenation, had been reported with melting point, 168°. Since a comparison specimen was unavailable, we have

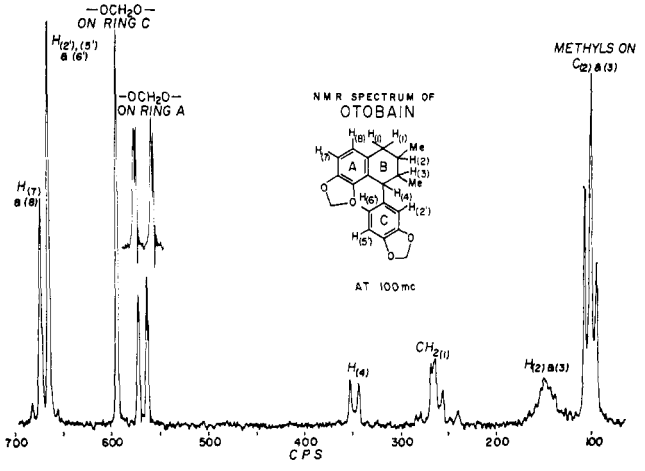


Figure 1

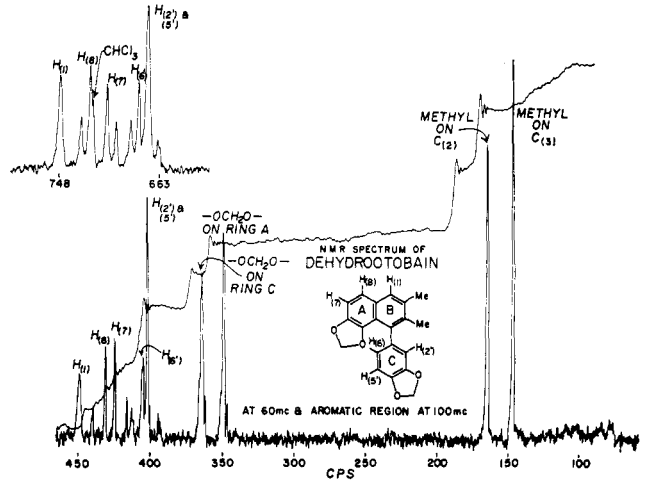


Figure 2

repeated the isomerization and dehydrogenation of galbacin[17] to give a product, m.p. 171–172°, referred to as dehydroepigalbacin, presumably the same as that previously reported. Since we find that dehydrootobain and dehydroepigalbacin differ and the structure (II) of dehydroepigalbacin has recently been confirmed by an independent synthesis,[6] otobain cannot have structure I.

Of alternative formulations in agreement with the above physical and chemical data and consistent with the theory of biogenesis, that represented by VI, in

(17) We wish to thank Professor A. J. Birch, Manchester University, England, for a generous sample of galbacin.

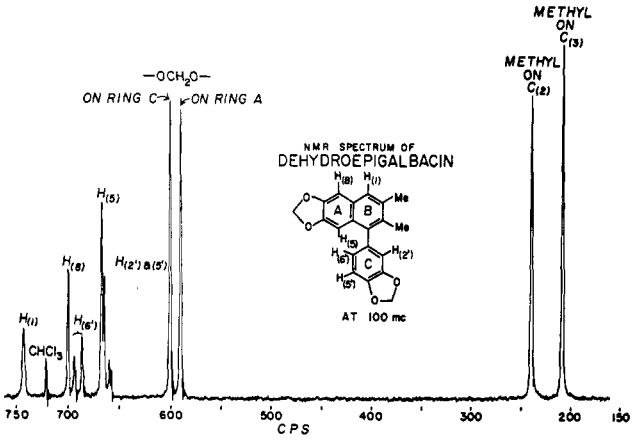


Figure 3

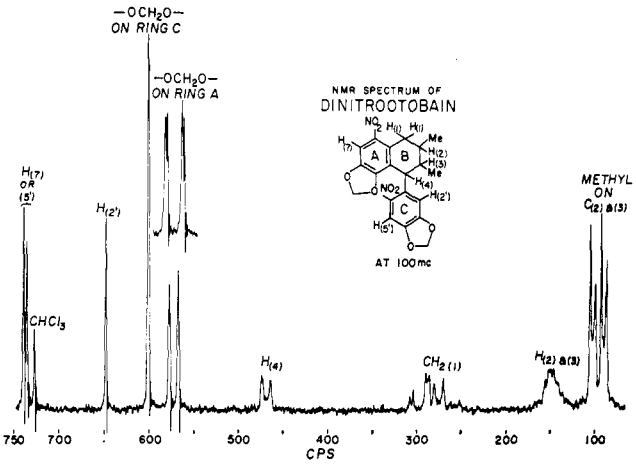


Figure 4

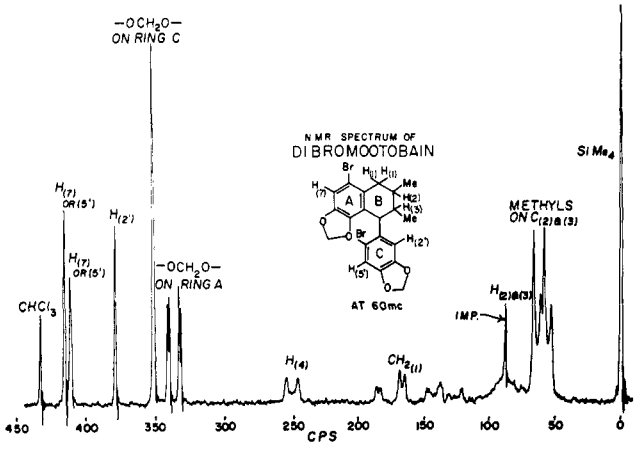


Figure 5

which the ring A methylenedioxy group is located at C-5 and C-6 rather than C-6 and C-7 of I, was considered most probable. A study of the nuclear magnetic resonance spectra of otobain (Fig. 1), dehydrootobain (Fig. 2), dehydroepigalbacin (Fig. 3), dinitrootobain (Fig. 4), and dibromootobain (Fig. 5) confirmed this conclusion. The assignments of the observed peaks to functional groups are summarized in Table I.[18]

In the spectrum of otobain, the pair of overlapping doublets at δ 0.96 and 1.04 with 5 c.p.s. coupling are assigned to the ring B secondary methyl groups. The broad unresolved signal at δ 1.44 can be attributed to the $H_{(2)}$ and $H_{(3)}$ protons which couple with each other, with the 2- and 3-methyl groups and with the $H_{(1)}$ and $H_{(4)}$ protons. As expected, the integral intensity of the signals due to these two sets of protons adds to eight protons. The peaks at δ 2.63, representing two protons, are characteristic of a benzylic methylene group, the corresponding function in α-tocopherol[19] displaying a chemical shift at δ 2.62. The multiplicity of the signals, which show an ABM pattern would strongly indicate the nonequivalence of the methylene protons. The doublet signal at δ 3.43 can be attributed to the dibenzyl methine proton at C-4. The pair of doublets at δ 5.58 and 5.64 indicates the nonequivalence of the two protons of a methylenedioxy group. They exhibit a chemical shift of 0.06 p.p.m. and a spin-coupling of 1.5 c.p.s. A similar case of nonequivalence of methylenedioxy protons was observed in dicentrine and bulbocapnine methyl ether.[20,21] This observation is consistent with the location in ring A of the methylenedioxy group at C-5 and C-6 where the methylene protons are unsymmetrically distributed with regard to ring C and inconsistent with any of the other two possible ring A locations. The second methylenedioxy group on ring C shows a normal singlet at δ 5.88, the same shift value as reported for safrole.[22]

Integration of the aromatic proton region confirmed the presence of five aromatic protons, the two signals showing respectively the intensities of three protons and two protons located at δ 6.58 and 6.65. Comparison with the spectrum of safrole[22] indicates by analogy that the peak at δ 6.58 can be assigned to the ring C aromatic protons, a degenerate ABC resonance pattern being exhibited in both cases. The two remaining ring A aromatic protons must consequently be responsible for the peak at δ 6.65. The absence of observable coupling is unusual for *ortho* protons; this ambiguity is resolved, however, by examination of the spectra of dehydrootobain (VII) and dehydroepigalbacin (V) from which it may be concluded that the $H_{(7)}$ and $H_{(8)}$ protons of otobain must have the same chemical shift and hence do not exhibit any spin–spin coupling. An analogous situation exists in the spectrum of protopine[23] where two similarly situated aromatic protons show a single peak at δ 6.69.

The n.m.r. spectra of dehydrootobain (Fig. 2) and dehydroepigalbacin (Fig. 3) are rather similar, although the few differences can be used to advantage in supporting structure VI of otobain. In accordance with the empirical formulas, integration data of both compounds account for sixteen protons, six from two aromatic methyl groups, four from two methylenedioxy groups, and six aromatic protons. The sharp signals at δ 2.08 and 2.42 (or 2.40) of both are characteristic of aromatic methyl protons. The resonance at δ 2.42 is slightly broader, indicating that these protons are slightly spin coupled to the adjacent $H_{(1)}$ proton, and is consequently assigned to the 2-methyl group; the 3-methyl group, closer to ring C, has the higher field

(18) The numbering system used for otobain (VI), conventional for lignan nomenclature, is also used for comparison purposes with the dehydrogenated phenylnaphthalene derivatives (V and VII).

(19) N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "NMR Spectra Catalog," no. 366, Varian Associates, 1962.

(20) S. Goodwin, J. N. Shoolery, and L. F. Johnson, *Proc. Chem. Soc.*, 306 (1958).

(21) Ref. 19, no. 333 and 342.

(22) Ref. 19, no. 253.

(23) Ref. 19, no. 339.

signal. In contrast to otobain, both methylenedioxy groups in the spectrum of dehydroötobain give single resonances at δ 5.78 and 6.05. This is as anticipated, since formation of the naphthalene A/B rings imparts planarity to the system and therefore equivalence of the ring A methylenedioxy protons with regard to the benzenoid C-ring. Again, the higher field aromatic resonance can be attributed to the ring A methylenedioxy protons.

The peaks shown by dehydrootobain at δ 6.68, 6.63, and 6.78 are the resonances of $H_{(2')}$, $H_{(5')}$, and $H_{(6')}$, respectively. They present an ABC pattern with $H_{(5')}$ and $H_{(6')}$ coupled to each other with 8 c.p.s. *ortho*-coupling, while $H_{(6')}$ is further coupled to $H_{(2')}$ with a *meta*-coupling of about 1.5 c.p.s. This ABC pattern is very similar to that exhibited in the spectrum of dehydroepigalbacin. The chemical shifts from $H_{(2')}$ and $H_{(5')}$ in both spectra are virtually identical. The resonance at δ 6.78 from $H_{(6')}$ in VII is at a higher field than the similar resonance of V at δ 6.89. This shift is conceivably due to the proximity of the oxygen atom of the ring A methylenedioxy group and supports formulation VII for dehydrootobain. The resonances at δ 7.02 and 7.24 of dehydrootobain present a typical AB pattern, with a characteristic 8 c.p.s. *ortho*-spin coupling, due to $H_{(7)}$ and $H_{(8)}$. In the spectrum of V, the ring A protons have their resonances at δ 6.68 due to $H_{(5)}$ and δ 7.00 due to $H_{(8)}$, the upfield shift of the $H_{(5)}$ peak being caused by the proximity of the benzenoid ring C. The remaining resonances at δ 7.48 and 7.43 in VII and V, respectively, are attributable to the $H_{(1)}$ proton.

The spectrum of dinitrootobain (Fig. 4) is consistent with the formula proposed for otobain and leads to the tentative conclusion that the nitro groups are located at C-8 and C-6′. Of the three aromatic protons, two resonate at considerably lower field (δ 7.33 and 7.37) suggesting that they are *ortho* to nitro groups. The observed downfield shift of the $H_{(1)}$ and $H_{(4)}$ protons is also consonant with nitro groups being located at C-8 and C-6′. The spectrum of dibromootobain (Fig. 5) is similar, except that the shifts are less pronounced with reference to otobain.

A stereochemical interpretation of the nuclear magnetic resonance spectrum of otobain has been presented.[6]

A cell culture cytotoxicity test[24] carried out on otobain gave an ED_{50} value of 1.0×10^2 μg./ml. The constitution of some minor constituents which we have isolated from *Myristica otoba* will be reported later.

Experimental[25]

Isolation of Otobain (VI).—Otoba fat (100 g.) was steam distilled for 4 hr. to yield a steam-volatile fraction (5.9 g.). The residue was suspended in water (1000 ml.), potassium hydroxide (30 g.) was added, followed by methanol (500 ml.) and the mixture heated under reflux for 5 hr. and allowed to stand overnight at room temperature. Most of the methanol was then removed by distillation, the cooled mixture extracted with ether, the extract well washed with water, dried (sodium sulfate), and the ether removed to give a dark oil (19.5 g.). Otobain crystallized from an ethanol solution of this oil as fibrous needles (6.0 g.), m.p. 125–128°, raised to m.p. 132–134° on one recrystallization. An analytical sample was prepared by filtration of a petroleum ether (b.p. 30–60°) solution through Merck alumina and crystallization of the eluate from ethanol, yielding otobain (VI) as long needles, m.p. 137–138°, $[\alpha]_D$ −40.5° (*c* 3.2), λ 234 (ε 9300) and 287 mμ (ε 6700).

Anal. Calcd. for $C_{20}H_{20}O_4$: C, 74.05; H, 6.22; O, 19.73; 2-CMe, 9.27. Found: C, 74.16; H, 6.14; O, 19.77; —OMe, 0.00; —CMe, 7.06. λ 3.41, 3.49, 6.21, 6.65, 6.75, 6.90, 7.36, 7.76, 8–8.4 (broad), 8.87, 9.13, 9.23, 9.48, 9.63, 9.83, 10.65 (broad), 10.78 (broad), 11.59 μ.

Dibromootobain.—A solution of bromine (640 mg.) in ether (4 ml.) was added to a solution of otobain (257 mg.) in ether (10 ml.). The mixture was allowed to stand at room temperature for 2 hr., then shaken with sodium thiosulfate solution, water, dried (sodium sulfate), and evaporated to give a pale yellow gum (410 mg.) which yielded a solid (147 mg.). Crystallization from chloroform–methanol gave dibromootobain as hard prisms, m.p. 197–199°, $[\alpha]_D$ + 64° (*c*, 2.7).

Anal. Calcd. for $C_{20}H_{18}O_4Br_2$: C, 49.82; H, 3.76; O, 13.27; Br, 33.15. Found: C, 49.74; H, 4.02; O, 13.48; Br, 33.49. λ 3.45, 3.51, 6.18, 6.27, 6.73, 6.78, 6.92, 7.15, 7.26, 7.37, 8–8.4 (broad), 8.79, 9.04, 9.19, 9.46, 9.65, 10.18, 10.76, 11.67, 11.89 μ.

Dinitrootobain.—Concentrated nitric acid (0.2 ml.) was added to a solution of otobain (90 mg.) in acetic acid (2.5 ml.), warmed on the steam bath for 1 min., allowed to stand at room temperature for a further 30 min., and diluted with water. Crystallization of the precipitate twice from chloroform–methanol gave dinitrootobain as pale yellow felted needles, m.p. 234–236° dec., $[\alpha]_D$ −170° (*c* 2.45).

Anal. Calcd. for $C_{20}H_{18}O_8N_2$: C, 57.97; H, 4.38; N, 6.76; 2-CMe, 7.26. Found: C, 58.12; H, 4.60; N, 6.62; —CMe, 6.56. λ 3.43, 3.50, 6.19, 6.60, 6.75, 6.89, 7.08, 7.30, 7.53, 7.72, 7.9–8.35 (broad), 8.71, 9.08, 9.44, 9.70, 10.70, 11.50 μ.

Otobain Biscarbonate.—Phosphorus pentachloride (5 g.) was added to a solution of otobain (1.0 g.) in dry toluene (10 ml.). The solution turned orange and hydrogen chloride was immediately liberated. The mixture was heated under reflux for 4 hr., during which the color faded to yellow, concentrated to *ca.* 5-ml. volume, cooled, and aqueous sodium carbonate solution added until effervescence ceased. It was extracted with ether, the extract washed with water, dried (sodium sulfate), and the solvent removed to give a yellow gum which solidified on trituration with methanol. Three recrystallizations of this solid (504 mg., m.p. 169–172°) from chloroform–methanol yielded 5,6-carbonyldioxy-2,3-dimethyl-4-(3′,4′-carbonyldioxyphenyl)-1,2,-3,4-tetrahydronaphthalene[26] as dense prisms, m.p. 178–180°, $[\alpha]_D$ −19° (*c* 2.1).

Anal. Calcd. for $C_{20}H_{16}O_6$: C, 68.18; H, 4.58. Found: C, 68.17; H, 4.74. λ 3.52, 5.47, 6.12, 6.73, 6.93, 7.44, 7.62, 7.78, 7.9–8.4 (broad), 8.60, 8.78, 9.13, 9.30, 9.71, 10.08, 10.42, 10.55, 10.83, 11.55 μ.

Dehydrogenation of Otobain.—A solution of otobain (932 mg.) in diethylene glycol (25 ml.) was heated under reflux with palladium on carbon (10%, 462 mg.) for 2 hr., filtered, diluted with water, and the resultant precipitate crystallized from methanol to give a solid (470 mg.), m.p. 111–114°, $[\alpha]_D$ −29° (suggesting 75% unchanged otobain). This was dissolved in petroleum ether (b.p. 30–60°, 60 ml.) and chromatographed on alumina (Merck, acid washed). Elution with light petroleum (480 mg.), and light petroleum–benzene (3:1, 130 ml.) gave no residue. The same eluent mixture (390 ml.) gave a semisolid (340 mg.), yielding crude otobain (m.p. 125–127°) on crystallization from chloroform–methanol, and the following 260 ml. eluted a solid (73 mg.) which on two recrystallizations from chloroform–methanol gave dehydrootobain [2,3-dimethyl-3′,4′,7,8-bismethylenedioxy-1-phenylnaphthalene (VII)] as spiky needles, m.p. 185–187°, $[\alpha]_D$ ±0° (*c* 2.0).

Anal. Calcd. for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03. Found: C, 74.64; H, 5.17. λ 352 (ε 3800), 311 (7800), 297 (9200), 243 (52,000), 220 mμ (43,500). λ 3.45, 3.58, 6.07, 6.22, 6.35, 6.64 (sh), 6.71, 6.87 (sh), 6.95, 7.32, 7.55, 7.78, 7.9–8.4 (broad), 8.80, 8.98, 9.13, 9.29, 9.65, 10.22, 10.7 (broad), 11.42 μ.

Acid Rearrangement and Dehydrogenation of Galbacin (IV).—Perchloric acid (70–72%, 0.5 ml.) added to a solution of galbacin (600 mg.) in acetic acid (20 ml.) caused an immediate pink → yellow color change. The mixture, after standing at room temperature for 3 days, was poured into 50% aqueous sodium

(24) C. G. Smith, W. L. Lummis, and J. E. Grady, *Cancer Res.*, **19**, 843 (1959).

(25) Melting points were determined on a Gallenkamp melting point apparatus. Specific rotations and infrared spectra were determined in chloroform solution. Ultraviolet absorption spectra were determined in ethanol solution.

(26) In systematic nomenclature, numbering is based on nayhthalene and consequently differs from lignan numbering.

hydroxide solution (40 ml.), and extracted with chloroform. Removal of the chloroform gave a residual gum which was heated under reflux in diethyleneglycol (20 ml.) for 1 hr. The mixture was filtered, the filter washed with methanol, and the combined filtrate diluted with water, extracted with ether, and worked up in the usual way. The product was dissolved in light petroleum–benzene (3:1) and chromatographed on alumina (Merck, acid-washed). Elution with the same solvents (300 ml.) gave an oil (9 mg.) followed by a solid (160 mg.), eluted with the next 600 ml. solvent. Recrystallization of this product from chloroform–methanol gave 2,3-dimethyl-3′,4′,6,7-bismethylenedioxy-1-phenylnaphthalene [dehydroepigalbacin (V)] as prisms, m.p. 171–172°.

Anal. Calcd. for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03; O, 19.98. Found: C, 75.40; H, 5.04; O, 19.63. λ 332 (ϵ 4900), 325 (2800), 318 (3300), 292 (10,200), 284 (9900), 234 mμ (48,500). λ 3.45, 3.58, 6.20, 6.65, 6.71, 6.85, 7.37, 7.50, 8.1–8.4 (broad), 8.59, 8.90, 9.09, 9.68, 10.5–10.8 (broad), 11.34 μ.

Nuclear Magnetic Resonance Spectra.—All samples were run in deuteriochloroform solution with tetramethylsilane added as an internal reference. The peak positions are relative to this standard and were obtained directly from a Varian A-60 spectrometer. The spectra reproduced in Fig. 1–5 were obtained, however, from Varian HR-60 and HR-100 spectrometers. The chemical shifts were measured in the following manner. For sharp lines, the shifts are rounded off to the nearest c.p.s. and converted to p.p.m. In the case of multiplets, the centers of the appropriate multiplets were located within a c.p.s. and also converted to p.p.m. When higher order perturbation was evident in the intensity distribution of a multiplet, the center of gravity was estimated to the nearest c.p.s. and converted to p.p.m.

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Chemistry of Carbon Diselenide. I. Reactions with Primary Amines[1]

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Carbon diselenide has been treated with primary amines to give good yields of seleno-2-benzimidazolinone, seleno-2-benzoxazolinone, seleno-2-benzothiazolinone, seleno-2-imidazolidinone, selenotetrahydro-2(1*H*)-pyrimidinone, and several substituted selenoureas. The diselenocarbamate salts and isoselenocyanates appear to be intermediates in the reaction.

Carbon diselenide has been prepared by the reaction of hydrogen selenide with carbon tetrachloride[2,3] and, more satisfactorily, by the reaction of selenium with methylene chloride.[4] In many respects carbon diselenide behaves like carbon disulfide. It reacts with alcohols to form diselenocarbonates,[2,3] with secondary alkyl amines to form diselenocarbamates,[5] and with chlorine to form perchloromethylselenol.[4] However, carbon diselenide differs from carbon disulfide in that it polymerizes readily,[3,5] especially in the presence of ammonia or amines. This polymerizability, along with the disagreeable odor frequently obtained when working with selenium compounds, apparently has discouraged a more complete study of the chemistry of carbon diselenide. However, with the potential commercialization of carbon diselenide in mind, we have undertaken such a study. In our initial work, we have found that carbon diselenide can react smoothly with primary amines to form the expected products. Most of the products reported are new compounds.

Barnard and Woodbridge[5] studied the reaction of carbon diselenide with secondary amines, and found that it was essential to avoid a localized excess of the diselenide in order to prevent polymer formation. By the slow addition of a 10% solution of carbon diselenide in dioxane to an alkaline solution of the secondary amine at −10°, they obtained high yields of dialkyldiselenocarbamates. The only work previously reported on reactions of carbon diselenide with primary amines is that of Grimm and Metzger[3] who prepared 1,3-diphenylselenourea in low yield by the addition of a dilute solution of carbon diselenide to an excess of aniline.

We have treated carbon diselenide with aniline in refluxing carbon tetrachloride and obtained 1,3-diphenylselenourea in essentially quantitative yield. The reaction of carbon diselenide with the dibasic *o*-phenylenediamine gave the cyclic selenourea, namely, seleno-2-benzimidazolinone.[6] Reactions with *o*-aminophenol and *o*-aminothiophenol gave the cyclic products, seleno-2-benzoxazolinone and seleno-2-benzothiazolinone, respectively. The primary aliphatic amines, benzylamine, ethylamine, *n*-butylamine, ethylenediamine, and 1,3-diaminopropane also gave analogous products in good yield.

Polymer formation was eliminated by maintaining extremely low concentrations of carbon diselenide in most cases. This was done by slowly adding a dilute solution of carbon diselenide to the vigorously stirred amine solution held usually at about 80° to ensure immediate reaction of the added carbon diselenide. Such precautions were not necessary in reactions with *o*-aminophenol and *o*-aminothiophenol, because these amines were not basic enough to promote polymerization of the carbon diselenide.

The reaction of carbon diselenide with a primary amine apparently proceeds in a manner similar to that of carbon disulfide.[7] Thus, the amine salt of the diselenocarbamate forms first, and, upon heating, decomposes with the evolution of hydrogen selenide and the formation of the isoselenocyanate and amine. The isoselenocyanate then reacts with the amine to form a selenourea.

(1) This work was supported by a research contract with The Selenium and Tellurium Development Committee.

(2) B. Rathke, *Ann.*, **152**, 181 (1869).

(3) H. G. Grimm and H. Metzger, *Ber.*, **69B**, 1356 (1936).

(4) D. J. G. Ives, R. W. Pittman, and W. Wardlaw, *J. Chem. Soc.*, 1080 (1947).

(5) D. Barnard and D. T. Woodbridge, *ibid.*, 2922 (1961).

(6) Infrared spectra and n.m.r. spectra were obtained in an attempt to establish the keto-enol equilibria of the products. However, several reference compounds must be studied before a sound interpretation of the spectra can be made. This work, coupled with alkylation studies, is in progress and will be reported later.

(7) D. C. Schroeder, *Chem. Rev.*, **55**, 189 (1955).