The Constituents of Natural Phenolic Resins. Part XXIII. The Constitution of Sesamolin.*

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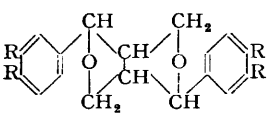
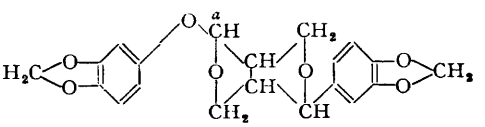
The structure (II), proposed by Boeseken and Cohen (*Rec. Trav. chim.*, **1936**, **55**, 815), for sesamolin has been substantiated by degradation of the natural product to the naphthalenes (III) and (VI; RR = CH_2O_2), and the nitro-lactone (VIII; RR = CH_2O_2). Structures (VI; RR = CH_2O_2) and (VIII; RR = CH_2O_2) were established by conversion of the substances into the corresponding dimethoxy-derivatives (VI; R = OMe), identical with pyroguaiacin methyl ether, and (VIII; R = OMe), identical with the compound obtained by the action of concentrated nitric acid on bromonitropinoresinol dimethyl ether (XI; R = OMe). The compound (VIII; RR = CH_2O_2) was also prepared from bromonitrosesamin (XI; RR = CH_2O_2) by the action of concentrated nitric acid.

SESAME oil is obtained from the seeds of several species of *Sesamum*, and *Sesamum indicum* cultivated in China, India, and Japan gives a seed containing 50—57% of oil, which has been used as a table oil, in the perfumery and pharmaceutical industries, and particularly in the manufacture of margarine and soap. The oil is frequently detected by the Badouin or Villavecchia test, which consists of the development of a deep red colour in the aqueous phase when the oil is shaken with concentrated hydrochloric acid and a 2% furfuraldehyde solution. The non-saponifiable fraction contains sterols, sesamin (I; RR = CH_2O_2) and



(I)



(II)

sesamolin, the last having been shown to be responsible for the Badouin reaction. Whilst the lignan structure (I) is well established for sesamin (Bruchhausen and Gerhard, *Ber.*, 1939, **72**, 830), much of the chemistry of sesamolin is discussed in inaccessible papers and its constitution remains unsettled. Villavecchia and Fabris (*Z. angew. Chem.*, 1893, **17**,

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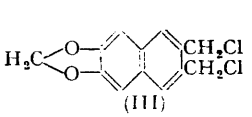
505), Bomer (*Z. Untersuch. Nahr. u. Genussm.*, 1899, **2**, 705), and Heiduschka (*Chem. Ztg.*, 1912, **36**, 1272) were unable to isolate sesamolin in a crystalline state. Kreis (*Chem. Ztg.*, 1903, **27**, 1030) showed that the compound responsible for the Badouin test was phenolic and although he was unable to purify the substance he called it sesamol. Canzoneri and Perciabosco (*Gazzetta*, 1903, **33**, II, 253) obtained a crystalline substance, m. p. 92°, which Adriani (*Z. Lebensm.-Untersuch.*, 1928, **58**, 157) later named sesamolin. Malagnini and Armanni (*Rend. Soc. chim. ital.*, 1907, **5**, 133), isolated both sesamolin and sesamol in crystalline forms, and showed that the latter was 4 hydroxycatechol methylene ether. Adriani (*loc. cit.*) showed sesamolin to have a molecular formula of $C_{20}H_{18}O_7$ and $[\alpha]_D$ +218°, confirmed the formation of sesamol, and showed that a neutral compound, samin, $C_{13}H_{14}O_5$, m. p. 106°, $[\alpha]_D$ +103°, was also produced during the hydrolysis of sesamolin. The constitution of sesamol is well established by three syntheses (Malagnini and Armanni, *loc. cit.*; Boeseken and Cohen, *Rec. Trav. chim.*, 1936, **55**, 815—820; Takata and Matsuda, *J. Pharm. Soc. Japan*, 1954, **74**, 693—694). Boeseken and Cohen also prepared the β-glucoside of sesamol, which, like sesamolin, slowly gave the red colour in the Badouin test, as distinct from sesamol which gave an immediate reaction. Boeseken and Cohen (*loc. cit.*) concluded that sesamolin was a type of glucoside of sesamol and suggested a structure (II), presumably on the basis of a hypothetical relation with sesamin (I; RR = CH_2O_2). This structure (II) contains two points of outstanding interest which encouraged a further investigation of the problem. It represents the first occurrence of a 4-hydroxycatechol methylene ether derivative in natural products and, secondly, it represents a unique variant of the lignan skeleton, which in all other cases is derived by union of two C_6C_3 units at the middle carbon atom in the C_3 system.

Two new methods were developed for the isolation of sesamolin from sesame oil, both depending in the first place on the removal of sesamin and sesamolin from the large quantities of glycerides in the oil. This was achieved either by adsorption of the aromatic constituents on a column of alumina, or by cooling to −50° an acetone solution of the oil, whereupon the glycerides separated; the latter method has also been developed during the course of our work by Budowski (*J. Amer. Oil Chemists' Soc.*, 1950, **27**, 164). The sesamin–sesamolin mixture was then separated by fractional crystallisation, and sesamin and sesamolin were obtained in yields of 0·6 and 0·15% respectively from sesame oil.

Our first approach aimed at a repetition of Adriani's hydrolysis of sesamolin to sesamol and samin and then structural investigation of the latter product. Although no difficulty was experienced in the isolation of the phenol sesamol, many attempts, using a wide variety of conditions, to obtain the neutral component, samin, in a crystalline form were unsuccessful. Hydrolysis of sesamolin with concentrated hydrochloric acid in ether–ethanol gave sesamol, and a pale yellow oil which was converted by further treatment with hydrochloric acid into a compound, $C_{13}H_{10}O_2Cl_2$. This dichloro-compound did not react with aldehydic reagents; the halogen atoms were readily removed by treatment with aqueous or alcoholic potassium hydroxide, potassium cyanide, or especially thiourea, which gave a chlorine-free product isolated as its picrate. Catalytic hydrogenation of the dichloro-compound gave a substance, $C_{13}H_{12}O_2$, showing an ultra-violet absorption spectra characteristic of a naphthalene structure. On the basis of structure (II) for sesamolin, the dichloro-compound could be (III), (IV), or (V), of which structure (III) is preferred on account of the rapid reaction with thiourea (see Campbell and Levy, *J.*, 1939, 1442). The compound, $C_{13}H_{12}O_2$, m. p. 186—187°, would then be 2 : 3-dimethyl-6 : 7-methylenedioxynaphthalene (VI; RR = CH_2O_2). This interpretation has been confirmed by conversion of (VI; RR = CH_2O_2) into the known dimethoxy-analogue (VI; R = OMe) (Haworth and Mavin, *J.*, 1932, 1485) by treatment with phosphorus pentachloride, hydrolysis of the resulting dichloromethylenedioxy-derivative (VI; RR = CCl_2O_2) to the 6 : 7-dihydroxy-compound (VI; R = OH), and finally methylation.

Whilst these observations are consistent with formula (II; RR = CH_2O_2) for sesamolin, they by no means establish it, and further interesting results have been obtained from a study of the action of bromine on sesamolin. Bromosesamol (5-bromo-4-hydroxycatechol methylene ether) was readily identified, and a crystalline neutral component, $C_{26}H_{26}O_9$, was also isolated. Attempted dehydration of the latter, dehydrogenation, mild

oxidation, and catalytic reduction were unsuccessful, hydrochloric or sulphuric acid in acetic acid did not affect it, and the infra-red and chemical examinations suggested that all the oxygen atoms were ethereal. On the basis of (II), structure (VII) is suggested for the substance $C_{26}H_{26}O_9$. As this compound is also obtained, with sesamol, when concentrated hydrochloric acid is added to an ice-cooled solution of sesamolin in ether or acetic acid, it is probable that its formation by the action of bromine is due to the liberation of hydrogen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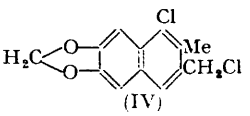
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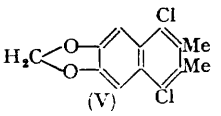
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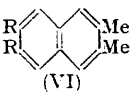
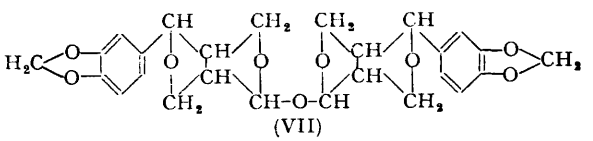

(VI)

bromide during the production of bromosesamol. When this ether (VII) was treated with nitric acid it was converted into a nitro-compound, $C_{13}H_{11}O_7N$, containing a lactone group, the presence of which was confirmed both by the action of sodium hydroxide and by infra-red measurements. Structure (VIII; RR = CH_2O_2) assigned to the nitro-compound is derived from the ether (VII) by nuclear nitration, hydrolysis of the ether linkage, and subsequent oxidation to the γ-lactone. In agreement with this view the ether (VII) is readily hydrolysed and converted into the bischloromethylnaphthalene (III) by warm hydrochloric acid; a similar cyclisation, however, was not realisable in the case of the nitro-compound.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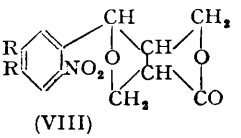
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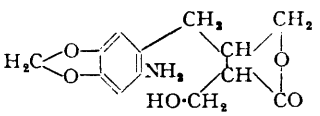
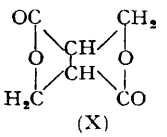
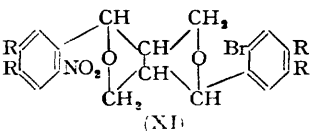

(IX)

The nitro-lactone (VIII; RR = CH_2O_2) was reduced by hydrogen in the presence of palladium–charcoal to an amine (IX), which gave a crystalline *N*-acetyl compound and a well defined Schiff's base with *p*-nitrobenzaldehyde. The analyses of these derivatives indicated that the benzyl ether linkage has also been reduced, as would be expected, and the presence of a hydroxyl group was supported by the infra-red spectrum of the Schiff's base.

Attempts to prepare the un-nitrated parent of (VIII; RR = CH_2O_2) were unsuccessful because of the ease of nitration of the ether (VII) which took place with dilute (0·5N) nitric acid. The nitro-lactone was not attacked by concentrated nitric acid but a small yield of 4 : 5-dinitromethylenedioxybenzene was obtained on treatment with fuming nitric acid, although we were unable to isolate the dilactone of 2 : 3-bishydroxymethylsuccinic acid (X) which Erdtmann (*Acta Chem. Scand.*, 1947, **1**, 71) had prepared from dibromopinoresinol dimethyl ether (XI; R = OMe; Br for NO_2) by the action of concentrated nitric acid and which we have prepared in a similar manner from dibromosesamin (XI; RR = CH_2O_2; Br for NO_2) and also in small yield by the action of fuming nitric acid on sesamin. In view


(X)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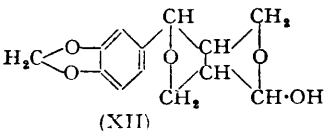
(XII)

of these experiments it appeared feasible that, if bromonitrosesamin (XI; RR = CH_2O_2) could be prepared, degradation with concentrated nitric acid should lead to (VIII; RR = CH_2O_2) and thus provide confirmatory evidence of the structure assigned to the nitration product of sesamolin. Early attempts to prepare bromonitrosesamin were unsuccessful but fortunately an alternative but similar approach was made possible by the ready

conversion of the nitro-compound (VIII; RR = CH_2O_2) into the dimethoxy-analogue (VIII; R = OMe). It was shown that 4-nitrocatechol methylene ether, 4 : 5-dinitrocatechol methylene ether, and the nitrated lactone (VIII; RR = CH_2O_2) were readily hydrolysed by warm aqueous sodium hydroxide to the corresponding catechols, although dinitrosesamin was unaffected under similar conditions (possibly owing to its relative insolubility in an aqueous medium). Methylation of the phenolic hydrolysis product (VIII; R = OH) with diazomethane yielded the dimethoxy-lactone (VIII; R = OMe). Erdtmann (*Svensk Kem. Tidskr.*, 1938, **50**, 161) has described the preparation of bromonitropinoresinol dimethyl ether (XI; R = OMe) and we have now shown that this compound is decomposed with concentrated nitric acid to give 4-bromo-5-nitroveratrole and the dimethoxy-lactone (VIII; R = OMe) identical with the compound obtained from sesamolin.

When these experiments had been completed it was found possible to prepare nitrosesamin and thence bromonitrosesamin (XI; RR = CH_2O_2); degradation of the latter with concentrated nitric acid at 50° gave 4-bromo-1 : 2-methylenedioxy-5-nitrobenzene and the nitro-lactone (VIII; RR = CH_2O_2).

From these experiments it can be deduced that in sesamolin the sesamol is united to the carbon atom represented by the carbonyl group in the nitrated lactone (VIII; RR = CH_2O_2). Welcome confirmation of formula (II), suggested by Boeseken and Cohen (*loc. cit.*), has consequently been obtained and it may also be concluded that in sesamolin the asymmetric centres have the same configuration as in (+)-pinoresinol (see Erdtmann, *Svensk Kem. Tidskr.*, 1936, **48**, 230), although more rigid proof of the configuration of the asymmetric centre (*a*) in formula (II) is desirable. Our failure to isolate Adriani's samin which should be represented by (XII) * remains unexplained, but the only crystalline product we have isolated from these reactions is the ether (VII).

Experimental

Isolation of Sesamolin.—(*a*) A column of alumina (75 g.; 4″ in length, 1½″ diameter) was set up in light petroleum (b. p. 60—80°). Sesame oil (100 c.c.) was passed down the column (1 day), and the fat was removed by washing with further solvent until the eluate gave a slight Badouin test. The portion immediately below the strong yellow band in the column was removed, and continuously extracted with ether (Soxhlet) for 6 hr. Removal of the solvent gave a yellow oil, which was saponified with 5% alcoholic potassium hydroxide (25 c.c.) for 1 hr. Water (100 c.c.) was added and the soap solution thrice extracted with ether (60 c.c.). Removal of the ether gave a yellow resin (approx. 2 g.) which was dissolved in ether (10 c.c.) and overnight yielded crystals of sesamin (0·5 g.). The filtrate, after removal of the ether, was dissolved in chloroform (1 c.c.), and light petroleum (b. p. 90—120°) was added until the onset of cloudiness. Sesamolin separated as a white solid which crystallised from ethanol in white plates (0·10—0·15 g.), m. p. 93—94°.

(*b*) Sesame oil (200 c.c.) was dissolved in acetone (1500 c.c.) and cooled overnight in acetone and solid carbon dioxide. The glyceride crystals were separated by filtration and removal of the acetone from the filtrate gave a yellow oil which was saponified and separated into its constituents as in (*a*). The sesamolin (0·3—0·35 g.) had m. p. 93—94° (Found: C, 64·7, 65·0; H, 4·8, 4·8. Calc. for $C_{20}H_{18}O_7$: C, 64·9; H, 4·9%).

Zerewitinoff determinations showed no active hydrogen to be present in sesamolin. Infrared analysis of sesamin and sesamolin showed no hydroxyl or carbonyl band.

Hydrolysis of Sesamolin.—Sesamolin (0·25 g.) was dissolved in a mixture of ether (15 c.c.), ethanol (2 c.c.), and concentrated hydrochloric acid (5 c.c.), and shaken for ½ hr. The ethereal layer was separated and washed twice with 2N-sodium hydroxide (5 c.c.) and with water. Removal of the ether gave a pale yellow oil (A) (0·15 g.). The alkaline extracts were acidified with 2N-sulphuric acid, and sesamol, isolated with ether and distilled at 70° (bath)/0·01 mm., was obtained in fine white needles (0·02 g.), m. p. 59—61°, giving an immediate Badouin test and a violet colour with ferric chloride. Recrystallisation from chloroform–light petroleum (b. p. 40—60°) raised the m. p. to 62—63°, and the product gave no depression on admixture with a synthetic specimen of sesamol (Boeseken and Cohen, *loc. cit.*). The *toluene*-p-*sulphonate* crystallised from methanol in needles, m. p. 86—87° (Found: C, 57·4; H, 3·9. $C_{14}H_{12}O_5S$

* After discussion with the Editor, it is proposed to refer to structures (XII) and (VII) as samino and disaminyl ether respectively.

requires C, 57·5; H, 4·1%). The oil (A) (0·15 g.) was heated on a water bath at 60—70° for ½ hr. with concentrated hydrochloric acid (5 c.c.). The light yellow solid which gradually separated was extracted with ether and purified by filtration in benzene (5 c.c.) through alumina. Recovery gave a white solid which crystallised from ethanol in needles, m. p. 146—147° (Found: C, 57·5, 58·3; H, 3·7, 4·0. $C_{13}H_{10}O_2Cl_2$ requires C, 58·0; H, 3·7%). 2 : 3-*Bischloromethyl*-6 : 7-*methylenedioxynaphthalene* (III) did not form a picrate and its ultra-violet absorption curve possessed no characteristic maxima, although its general shape conformed to that expected from a naphthalene derivative.

After the substance (III) had been boiled with thiourea (0·1 g.) in ethanol (3 c.c.) for 10 min., picric acid (0·1 g.) was added and the mixture heated until dissolution was complete. On cooling, a yellow crystalline *picrate* separated, which crystallised from ethanol in yellow needles (0·15 g.), m. p. 236—237° (Found: C, 40·4; H, 2·9; S, 8·6. $C_{27}H_{22}O_6N_{10}S_2$ requires C, 40·2; H, 2·8; S, 8·0%).

2 : 3-*Dimethyl*-6 : 7-*methylenedioxynaphthalene* (VI; RR = CH_2O_2).—Substance (III) (0·10 g.) was hydrogenated in glacial acetic acid (10 c.c.) with 15% palladium–charcoal (0·015 g.) for 2 hr. (uptake of H_2, 18·5 c.c.). Removal of the solvent gave 2 : 3-*dimethyl*-6 : 7-*methylenedioxynaphthalene* (VI; RR = CH_2O_2) which crystallised from ethanol in white plates (0·06 g.), m. p. 186—187° (Found: C, 77·7; H, 5·9. $C_{13}H_{12}O_2$ requires C, 78·0; H, 6·0%). Ultra-violet absorption in EtOH: max. at 2650, 2780, and 2885 Å (log ε 3·71, 2·69, 3·52), min. at 2975 Å (log ε 3·05). The picrate, m. p. 162—163°, decomposed on crystallisation from alcohol.

2 : 3-*Dimethyl*-6 : 7-*dimethoxynaphthalene* (VI; R = OMe).—A solution of phosphorus pentachloride (0·2 g.) in benzene (2 c.c.) was added to the substance (VI; RR = CH_2O_2) (0·1 g.) dissolved in five drops of dry benzene, and after 3 hours' refluxing the mixture was decomposed with ice. The benzene layer was dried ($CaCl_2$) and removal of the solvent gave a blue solid which was dissolved in methanol (2 c.c.) and methylated during 2 hr. with sodium hydroxide (20%; 1·5 c.c.) and methyl sulphate (0·6 c.c.). The product, isolated with ether and purified by filtration in benzene through a very short column of alumina, was a colourless oil which crystallised first from ethanol and then from light petroleum (b. p. 60—80°) in colourless plates (0·015 g.), m. p. 149—150°, which gave no depression with a synthetic specimen of 6 : 7-dimethoxy-2 : 3-dimethylnaphthalene (Haworth and Mavin, *loc. cit.*). Ultra-violet absorption in ethanol: max. at 2580, 2685, and 2750 Å (log ε 3·67, 3·68, 3·62) and min. at 3000 Å (log ε 3·07). The picrate was prepared in ethanol and crystallised from the same solvent in red needles, m. p. 132—133° (Found: C, 53·9; H, 4·6; N, 9·0. Calc. for $C_{20}H_{19}O_9N_3$: C, 53·9; H, 4·3; N, 9·4%).

Action of Bromine on Sesamolin.—A 20% solution of bromine in glacial acetic acid (0·5 c.c.) was added with stirring to an ice-cooled solution of sesamolin (0·25 g.) in glacial acetic acid (0·8 c.c.). After 10 min., the solution was diluted with chloroform (10 c.c.) and ether (20 c.c.) and washed twice with 2N-sodium hydroxide (10 c.c.) (B) and then water. Removal of the solvents gave *disaminyl ether* (VII), which crystallised from ethanol in plates (0·07 g.), m. p. 191—192°, $[\alpha]_D$ +143° (*c* 1·74 in $CHCl_3$) [Found: *M*, 466 (Rast), 481 (cryoscopic in benzene); C, 64·9, 64·7, 64·7; H, 5·6, 5·7, 5·4. $C_{26}H_{26}O_9$ requires *M*, 482; C, 64·8; H, 5·4%). Ultra-violet absorption in EtOH: max. at 2865 and 2355 Å (log ε 3·90, 3·94) and min. at 2555 Å (log ε 2·99). Zerewitinoff determinations did not show the presence of active hydrogen in the compound. The alkaline washings (B above) gave on acidification (2N-sulphuric acid) a brown oil, which after extraction with ether was sublimed at 80° (bath)/0·01 mm.; *bromosesamol* was obtained as white needles (0·03 g.), m. p. 82—83° (Found: C, 38·6; H, 2·4. $C_7H_5O_3Br$ requires C, 38·8; H, 2·3%), identical with the compound prepared by bromination of sesamol in acetic acid solution.

Action of Hydrochloric Acid on Sesamolin.—Concentrated hydrochloric acid (3 drops) was added to an ice-cooled solution of sesamolin (0·1 g.) in glacial acetic acid (5 c.c.). After 10 min. dilution and extraction with chloroform–ether, followed by washing with 2N-sodium hydroxide (the washings gave sesamol on acidification), yielded disaminyl ether (VII) (0·03 g.).

Hydrolysis of Disaminyl Ether (VII).—A mixture of disaminyl ether (VII) (0·04 g.), glacial acetic acid (1 c.c.), and concentrated hydrochloric acid (5 c.c.) was warmed at 60—70° for 10 min. and the pale yellow solid, which was precipitated, collected and purified by filtration in benzene (5 c.c.) through a layer of alumina. Removal of the solvent gave a solid which crystallised from alcohol in needles (0·02 g.), m. p. 146—147°, undepressed on admixture with a specimen of (III).

Action of Nitric Acid on Disaminyl Ether (VII).—Disaminyl ether (VII) (0·04 g.) was dissolved in glacial acetic acid (0·5 c.c.), and concentrated nitric acid (1·0 c.c.) added. After 1½ hr. at

30—40°, the mixture was diluted with water (15·0 c.c.) and the solid (0·035 g.) collected and crystallised from ethanol, giving yellow needles (0·030 g.), m. p. 154—155°, $[\alpha]_D$ −9·7° (*c* 3·39 in $CHCl_3$) (Found: C, 53·2, 53·4; H, 3·8, 4·0; N, 4·5. $C_{13}H_{11}O_7N$ requires C, 53·3; H, 3·8; N, 4·8%). This *tetrahydro-2-hydroxymethyl-1-(3 : 4-methylenedioxy-5-nitrophenyl)furan-3-carboxylic lactone* (VIII; RR = CH_2O_2) was insoluble in sodium hydrogen carbonate solution but gave a deep red solution in warm 2N-sodium hydroxide. Ultra-violet absorption in EtOH: max. at 2460 and 2950 Å (log ε 4·07, 3·50) and min. at 2700 Å (log ε 3·25). Infra-red analysis of the compound in a Nujol mull showed a strong band at 1782 cm.$^{-1}$ indicative of a γ-lactone.

Action of 2N-*Sodium Hydroxide on* 4-*Nitrocatechol Methylene Ether.*—This ether (1·0 g.) was warmed with 2N-sodium hydroxide (10 c.c.) on a water-bath. A blood-red solution was formed, which was extracted with ether after 30 min. to remove unchanged starting material, acidified, and extracted with ether to yield 4-nitrocatechol, which crystallised from water in pale yellow needles (0·6 g.), m. p. 175—176° (Kempf, *J. pr. Chem.*, 1908, **78**, 257, gives 175·5°). The *dibenzoate* crystallised from ethanol in white needles, m. p. 157—158° (Found: C, 65·9; H, 3·4. Calc. for $C_{20}H_{13}O_6N$: C, 66·1; H, 3·6%).

Action of 2N-*Sodium Hydroxide on* (VIII; RR = CH_2O_2) *and Methylation of the Product.*—A mixture of the compound (VIII; RR = CH_2O_2) (0·05 g.) and 2N-sodium hydroxide (5 c.c.) was heated on a steam-bath for ½ hr. After extraction with ether to remove unchanged material, the deep red solution was acidified with 2N-sulphuric acid and thrice extracted with ether to give a pale yellow solid, which gave a blue ferric chloride test. This phenol (VIII; R = OH) was dissolved in ether (5 c.c.), and an excess of ethereal diazomethane solution added. After 2 hr., the solvent was removed and *1-(3 : 4-dimethoxy-5-nitrophenyl)tetrahydro-2-hydroxymethylfuran-3-carboxylic lactone* (VIII; R = OMe) separated from ethanol in pale yellow clusters (0·02 g.), m. p. 157—158°, $[\alpha]_D$ −67·7° (*c* 3·4 in $CHCl_3$) (Found: C, 54·4; H, 4·4. $C_{14}H_{15}O_7N$ requires C, 54·4; H, 4·9%). Ultra-violet absorption in EtOH: max. at 2440 and 3020 Å (log ε 3·98, 3·62) and min. at 2665 Å (log ε 3·08).

Reduction of the Compound (VIII; RR = CH_2O_2).—The nitro-compound (VIII; RR = CH_2O_2) (0·04 g.) was hydrogenated in glacial acetic acid (5 c.c.) in the presence of 15% palladium–charcoal (0·02 g.). Hydrogen uptake (11·0 c.c. Calc.: 12·3 c.c.) was complete in 2 hr. The catalyst and solvent were removed and the residual brown oil 2-(5-amino-3 : 4-methylenedioxybenzyl)-1-hydroxymethylbutyrolactone (IX), which was easily oxidised in air, gave with acetic anhydride (0·1 c.c.) the N-*acetyl derivative*, which crystallised from ethanol in fine white needles, m. p. 222—223° (Found: C, 58·9, 58·8; H, 5·9, 5·7. $C_{15}H_{17}O_6N$ requires C, 58·7; H, 5·7%). The *N*-acetyl derivative was soluble in warm 2N-sodium hydroxide and was recovered after prolonged boiling with alkali. The p-*nitrobenzylidene derivative*, prepared from the crude amine (IX) in acetic acid, crystallised from the same solvent in orange needles, m. p. 219—220° (Found: C, 48·5; H, 3·4. $C_{20}H_{18}O_7N_2$ requires C, 48·2; H, 3·2%). Infra-red analysis of this compound on a potassium bromide disc showed bands at 1770 (γ-lactone) and at 2860 and 3382 cm.$^{-1}$ probably indicative of a free hydroxyl group.

Action of Concentrated Nitric Acid on Dibromosesamin.—Dibromosesamin (1·5 g.) was added portionwise to nitric acid (*d* 1·4) (20 c.c.) with efficient mechanical stirring. Brown fumes were evolved and the dibromosesamin gradually passed into solution, after which stirring was continued for a further ½ hr. Addition of water (40 ml.) gave 4-bromo-5-nitromethylenedioxybenzene which crystallised from alcohol in yellow plates, m. p. 89—90°. The filtrate was exactly neutralised with potassium hydrogen carbonate and evaporated to dryness and the residue extracted overnight (Soxhlet) with ether. Removal of the ether gave a brown gum which was dissolved in hot water. Filtration and evaporation gave a residue which when extracted with hot benzene (20 c.c.) gave 2 : 3-bis(hydroxymethylsuccinic) dilactone (X), white plates (from ethanol), m. p. 159—160° (Found: C, 50·7; H, 4·2. Calc. for $C_6H_6O_4$: C, 50·7; H, 4·2%). Erdtmann (*Acta Chem. Scand.*, 1947, **1**, 71) gives m. p. 160°.

Action of Concentrated Nitric Acid on Bromonitropinoresinol Dimethyl Ether (XI; R = OMe).—Bromonitropinoresinol dimethyl ether (0·1 g.) (Erdtmann, *loc. cit.*) was slowly added to nitric acid (*d* 1·4) (2 c.c.) with mechanical stirring. The mixture was warmed slightly, brown fumes being evolved, and after ½ hr., the mixture was diluted with water (20 c.c.) and the products were isolated with chloroform as a yellow gum, which was warmed for ½ hr. with 2N-sodium hydroxide (10 c.c.) and extracted with chloroform. The chloroform extract gave 4-bromo-5-nitroveratrole, m. p. 123°, on crystallisation from ethanol. The alkaline extract was acidified and extracted with chloroform to give a brown oil, which, after two crystallisations from ethanol, yielded pale yellow needles (0·02 g.), m. p. 157—158°, identical with (VIII; R = OMe), obtained as described above.

Nitrosesamin.—A solution of nitric acid (*d* 1·4; 0·5 c.c.) in acetic acid–acetic anhydride (2 : 1; 5 c.c.) was added during ¼ hr. to a solution of sesamin (2 g.) in the same solvent (15 c.c.) and the temperature kept at 15—20°. Dilution with water (25 c.c.) gave a yellow gum which crystallised from dioxan–methanol, to give pale yellow needles of *mononitrosesamin* (0·8 g.), m. p. 139—140°, $[\alpha]_D$ −70° (*c* 2·6 in $CHCl_3$) (Found: C, 59·8; H, 4·3; N, 3·6. $C_{20}H_{17}O_8N$ requires C, 60·1; H, 4·3; N, 3·5%).

Bromonitrosesamin (XI; RR = CH_2O_2).—Nitrosesamin (0·5 g.) was mixed on a watch-glass with a solution of bromine in chloroform (1 : 10; 8 c.c.). Hydrogen bromide was evolved and as the solvent evaporated *bromonitrosesamin* separated. Crystallisation from dioxan–acetic acid gave lemon-coloured needles (0·5 g.), m. p. 199—200°, $[\alpha]_D$ −37° (*c* 2·7 in $CHCl_3$) (Found: C, 50·5; H, 3·5; N, 2·9. $C_{20}H_{16}O_8NBr$ requires C, 50·2; H, 3·3; N, 2·9%).

Action of Nitric Acid on Bromonitrosesamin (XI; RR = CH_2O_2).—Bromonitrosesamin (0·3 g.) was added portionwise to nitric acid (*d* 1·4; 5 c.c.). Brown fumes were evolved at 50° during ½ hr. and, on cooling, needles of 5-bromo-1 : 2-methylenedioxy-4-nitrobenzene separated. The filtrate gave on dilution with water a yellow solid (0·1 g.) which crystallised from ethanol in yellow needles (0·02 g.), m. p. 153—154°, undepressed on admixture with the nitro-lactone (VIII; RR = CH_2O_2), prepared as described on p. 832.

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