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Synthesis and Reactions of α-(3-Methoxy-4-hydroxyphenyl)-glycerol ("Guaiacylglycerol"). II. Synthesis

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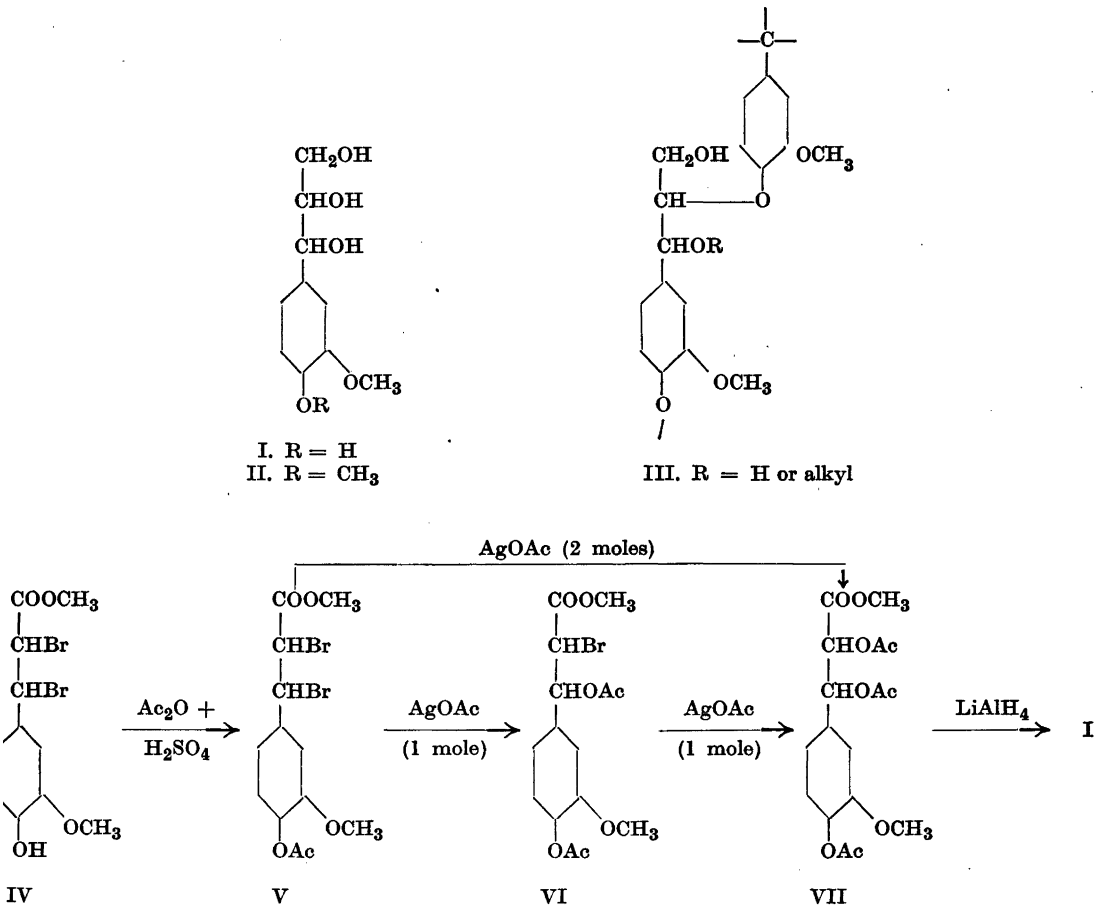
Guaiacylglycerol (I) has been considered to represent the basic structure of at least some of the building stones of lignin [1,2,3]. In lignin, guaiacylglycerol monomers may be assumed to be linked to adjacent monomers by aryl ether linkages in the β-(or γ-)position, and in addition, the hydroxyl group in the α-position may be etherified with a similar benzyl alcohol group or another aliphatic carbinol group belonging to another lignin unit. A possible structure of this kind is presented in the schematic formula III [4,5,6].

The synthesis of "veratrylglycerol" (II) [3] and its behaviour in some reactions related to lignin chemistry [7] have been reported earlier, and in the preceding paper [8], some preliminary experiments concerning the preparation of guaiacylglycerol have been described. The present communication deals with the synthesis of this substance.

This synthesis followed a route (Scheme 1) very similar to that used in the preparation of veratrylglycerol (II) [3].

α,β-Dibromohydroferulic acid methyl ester (IV), prepared according to the directions given in the preceding paper [8], was acetylated, and the bromine atoms in V were replaced by acetoxyl groups, either in a two-stage reaction (*via* VI), or directly, yielding the triacetate VII.

The reduction of the triacetate VII with lithium aluminium hydride yielded a water-soluble, colourless syrup which could not be distilled without decomposition. The identification of this product as guaiacylglycerol (I) was carried out as follows:



Scheme 1.

1. *General properties.* The ultraviolet absorption curve of the product (Fig. 1) is similar to that of phenols with no double bond in conjugation to the aromatic nucleus. The aqueous solution of the product is neutral, and treatment with alkali does not liberate any acidic groups. Hence, all three acetoxyl groups and the carbomethoxyl group in VII must have reacted with the lithium aluminium hydride.

In the absence of solvents, or in neutral solution, the product appears to be rather stable. On treatment with mineral acids, however, carbonyl compounds which yield orange-coloured precipitates with 2,4-dinitrophenylhydrazine, are formed. In this respect, the product behaves like veratrylglycerol

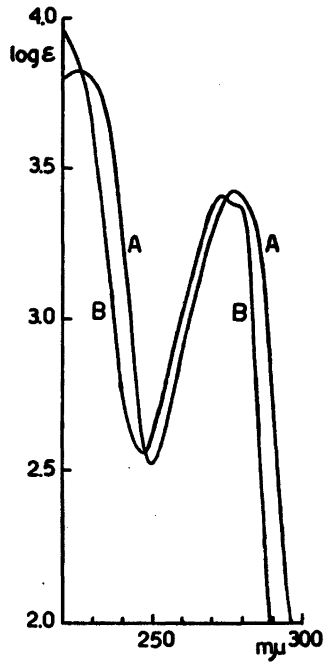


Fig. 1. Ultraviolet absorption of

A: Guaiacylglycerol (I) in water, based on methoxyl concentration,

B: Guaiacylglycerol tetraacetates (VIII, 1 and 2) in 96 per cent ethanol.

(II) [7]. Contrary to veratrylglycerol, however, it is also unstable in alkaline solution. (The mechanism of the alkaline breakdown is being further investigated.)

2. *Tetraacetates.* On treatment with acetic anhydride in pyridine, the syrupy product (I) yielded two crystalline tetraacetates, m.p. 84—85° (VIII, 1) and m.p. 113—114° (VIII, 2) respectively, of which the first-mentioned represented the major product (*cf.* scheme 2). Both tetraacetates distilled without decomposition and the distillates crystallized readily on treatment with suitable solvents such as ether. The ultraviolet absorption spectra of both tetraacetates proved to be identical (Fig. 1).

These results indicate that the syrupy guaiacylglycerol (I) is a mixture of the two possible D,L-forms, one of them being present in excess.

3. *Periodate oxidation.* Treatment of guaiacylglycerol with periodate should result in the following breakdown of the side-chain:

guaiacylglycerol $\xrightarrow{+\ 2\ HIO_4}$ formaldehyde + formic acid + vanillin.

However, this reaction may be complicated by the fact that, according to Pennington and Ritter [9], certain phenolic nuclei are also attacked by periodate. These authors have reported that, during a reaction period of two hours, about 3 moles of periodic acid are consumed by one mole of guaiacol, vanillylalcohol,

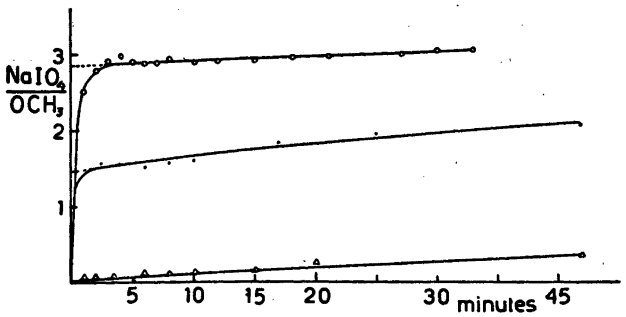


Fig. 2. Consumption of periodate by
O—O—O *guaiacylglycerol (I)*
●—●—● *guaiacol*
△—△—△ *vanillin*

and other guaiacyl derivatives, respectively. Vanillin, however, was practically stable under the same conditions. Therefore, provided that the nuclear oxidation proceeds sufficiently fast compared with the oxidation of the side-chain, it will interfere with the reaction scheme presented above. The periodate consumption will become higher than 2 moles, and the yield of vanillin less than 1 mole per mole of guaiacylglycerol. Due to the fact that vanillin is practically stable towards periodate, the yield of vanillin will essentially depend on the ratio of the rate of the α,β-cleavage in the side-chain to the rate of the nuclear oxidation.

Veratrylglycerol (II, m.p. 109—110°) [3] reacted with periodate in a normal way, consuming 2 moles of the oxidant and yielding 1 mole of formaldehyde, formic acid, and veratric aldehyde, respectively, the veratryl nucleus being stable towards periodate [3]. At a temperature of 12°, the oxidation was complete after two minutes. It may be expected that the glycerol side-chain in guaiacylglycerol (I) is split at a similar rate.

In order to obtain some preliminary information about the rate of the nuclear oxidation, the consumption of sodium periodate by guaiacol at 12° was examined. As shown in Fig. 2, about 1.5 moles of periodate per mole of guaiacol were consumed during the first two minutes, this rapid phase being followed by a comparatively slow further oxidation. During the rapid phase the solution acquired a red-brown colour (*cf.* also [9]).

The rate of the initial phase of this nuclear oxidation appears to be of the same order as the rate of cleavage of the side-chain in veratrylglycerol (II). Hence, in the oxidation of guaiacylglycerol, the breakdown of the phenolic nucleus could be expected to interfere to a considerable extent with the forma-

tion of vanillin. In fact, for each mole of methoxyl contained in the syrupy product (I) approximately 2.9 moles of periodate — instead of 2.0 moles required by the equation above — were rapidly consumed (Fig. 2), the solution turning reddish brown. Vanillin could be isolated as 2,4-dinitrophenyl-hydrazone, but the yield (after an oxidation time of ten minutes) was only 0.54 mole (calc. 1.0 mole) per mole of guaiacylglycerol.

In agreement with the equation above, nearly one mole of formaldehyde and one mole of formic acid per methoxyl were detected in the reaction mixtures obtained after 10 minutes' treatment of the syrupy product (I) with excess periodate.

Neither formaldehyde nor formic acid were obtained, however, on periodate oxidation of guaiacol, thus indicating that the formation of these products from guaiacylglycerol is solely due to the cleavage of the glycerol side-chain.

4. *Diazomethane methylation and subsequent acetylation* (Scheme 2). Provided that the syrupy product has structure I, methylation with diazomethane should yield veratrylglycerol (II). A veratrylglycerol, m.p. 109—110°, had been obtained [3] by the action of lithium aluminium hydride upon the triacetate IX, but diazomethane methylation of I, however, yielded a non-crystallizing syrup, which, in accord with the solid veratrylglycerol (II), could not be distilled without decomposition. When the solid veratrylglycerol (II) was treated with diazomethane, it was recovered unchanged, which indicated that, in the methylation of I, no disturbing reactions in the side-chain were to be expected.

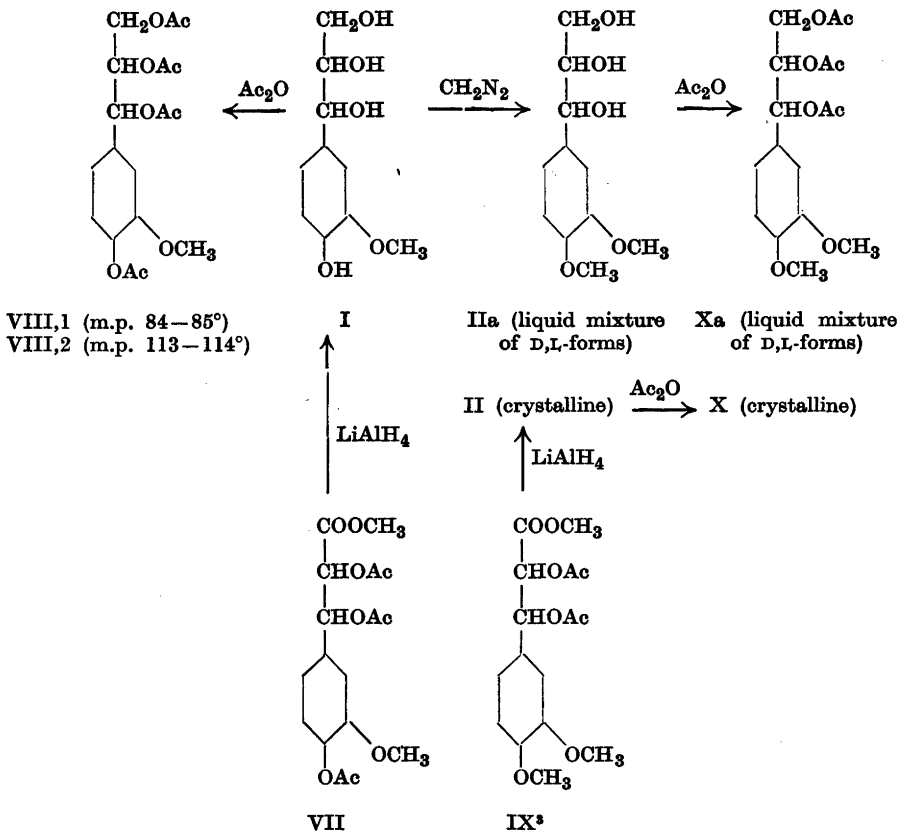
On periodate oxidation, the syrupy methylation product of I consumed 2 moles of periodate and yielded 1 mole each of formaldehyde and veratric aldehyde, based on 2 methoxyl equivalents, which is in harmony with a veratrylglycerol structure (II a).

Treatment of the methylation product (IIa) with acetic anhydride in pyridine yielded a syrup, from which no crystals could be obtained. It could be purified by distillation at 0.05 mm Hg (bath temperature 170°) and then had the analytical composition of the expected veratrylglycerol triacetate (Xa, *cf.* Scheme 2).

When this product was saponified with cold alcoholic potassium hydroxide, the resulting solution, after dilution with water, and reneutralization, consumed 2 moles of periodate per 2 equivalents of methoxyl, which indicates that the glycerol side-chain had been retained during the acetylation and saponification.

The crystalline veratrylglycerol [3], m.p. 109—110° (II), yielded a crystalline triacetate, m.p. 68—69° (X). This substance distilled without decomposition at 0.05 mm Hg (bath temperature 170°), and the oily distillate crystallized

Scheme 2.



readily on treatment with suitable solvents such as ethyl ether. On saponification of the crystalline triacetate X, the crystalline veratrylglycerol II was regenerated.

The similarity of the ultraviolet absorption curves of the oily product Xa and the crystalline veratrylglycerol triacetate (X) (Fig. 3) supports the conception that both products have identical structures.

On the basis of these results and those reported in sections 1, 2, and 3 it can be concluded that the syrupy product (I) is identical with guaiacylglycerol. The non-crystallizability of the methyl ether IIa and its triacetate Xa may be due to the fact that these products are mixtures of the two possible D,L-forms, the presence of which in the guaiacylglycerol product is indicated by the isolation of the two isomeric tetraacetates (VIII, 1 and VIII, 2) (*cf.* p. 572). Which of these belongs to the same steric series as the crystalline veratrylglycerol

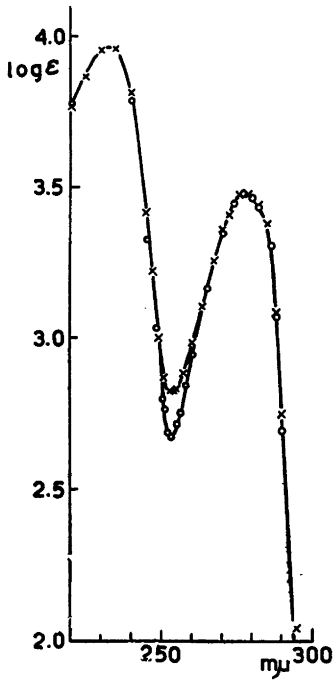


Fig. 3. Ultraviolet absorption of

O—O—O *veratrylglycerol triacetate, crystalline form (X), and*

×—×—× *veratrylglycerol triacetate, liquid mixture of* D,L*-forms (Xa) (in 96 per cent ethanol).*

II[3], previously obtained from IX, and its triacetate X, cannot be decided at the moment.

5. *Sulphonation.* Like veratrylglycerol [7], the syrupy product (I) was converted into a sulphonic acid when heated with a sodium bisulphite solution (pH 3). The barium salt of the sulphonic acid was obtained in a crystalline state, and had the analytical composition expected for the barium salt of a monosulphonic acid. When treated with sodium periodate, it yielded one mole of formaldehyde per mole. (The consumption of periodate exceeded 1 mole IO_4^- per mole of the sulphonic acid, and the reaction mixture turned rapidly red-brown, indicating oxidation of the phenolic nucleus, *cf.* p. 573).

These results establish the structure 1-(3-methoxy-4-hydroxyphenyl)-2,3-dihydroxy-*n*-propane-1-sulphonic acid and constitute additional evidence for the identity of the syrupy starting material with guaiacylglycerol (I).

Experiments on the rate and pH-dependence of the sulphonation as well as on the action of alcoholic hydrochloric acid upon guaiacylglycerol, and some other lignin model reactions of this substance will be reported later.

EXPERIMENTAL

α,β-Dibromo-acetylhydroferulic acid methyl ester (V). Dibromohydroferulic acid methyl ester (IV)[8] (25 g) was dissolved by gentle warming in a mixture of acetic acid (150 ml) and acetic anhydride (150 ml). After cooling 2 ml of conc. sulphuric acid were added. The mixture was set aside at room temperature for 24 hours and then poured into 2 l of ice-water. The resulting oil solidified on standing. Recrystallization from ethylacetate-hexane yielded prismatic plates of m.p. 146—147°. Yield 65 %. (Found: C 38.0, H 3.47, OCH_3 15.1; Calc. for $C_{13}H_{14}O_5Br_2$ (410.1): C 38.1, H 3.44, OCH_3 15.1.)

α-Bromo-β-acetoxy-acetylhydroferulic acid methyl ester (VI). When the dibromide V (1 mole) was heated for five hours at 100° in acetic acid solution with potassium acetate (1 mole) no reaction took place, the unchanged dibromide being recovered on dilution with water. Silver acetate however, reacted readily with the β-bromine atom:

A solution of 5.5 g of dibromide V (13.4 millimoles) in 50 ml of acetic acid was heated on a water-bath for 10 minutes with 2.35 g of silver acetate (13.5 millimoles). The reaction was completed by refluxing the mixture for 3 minutes. The silver bromide (yield almost quantitative) was filtered off and the solvent removed by evaporation in vacuum. The remaining syrup was dissolved in methanol and some colloidal silver bromide removed by filtration through a layer of kieselguhr. The filtrate was concentrated to a volume of 10 ml. On addition of a little water the diacetate VI precipitated. Needles, after recrystallization from 80 per cent methanol and from methanol, m.p. 100—101°; yield 70 %. (Found: C 45.8, H 4.37, Br 19.7, OCH_3 16.1; Calc. for $C_{15}H_{17}O_7Br$ (389.2): C 46.3, H 4.40, Br 20.5, OCH_3 16.0.)

α,β-Diacetoxy-acetylhydroferulic acid methyl ester (VII). — 1. A solution of 69 g α,β-dibromo-acetylhydroferulic acid methyl ester (V) (0.168 mole) in a mixture of 600 ml acetic acid and 500 ml acetic anhydride was refluxed (oil bath) under stirring for 45 minutes with 60 g of silver acetate (0.36 mole). After cooling the silver bromide was filtered off and washed with acetone. The washings were combined with the filtrate, and the solution concentrated in vacuum to about 300 ml. The acetic anhydride was decomposed by the addition of 400 ml of water and the solvent removed under reduced pressure. The remaining oil was dissolved in chloroform, and the chloroform solution was washed with sodium bicarbonate and water, dried (Na_2SO_4), and evaporated in vacuum. A syrup remained which was dissolved in 100 ml of ether. The crystalline material obtained on cooling was recrystallized from ethylacetate-hexane, forming prismatic plates, m.p. 109—110°; yield 70 %. (Found: C 55.7, H 5.60, OCH_3 16.7; Calc. for $C_{17}H_{20}O_9$ (368.3): C 55.4, H 5.47, OCH_3 16.9.)

2. In a similar way the triacetate VII was obtained when the diacetate VI was heated with 1 mole of silver acetate per mole in an acetic acid — acetic anhydride mixture.

α-(3-Methoxy-4-hydroxyphenyl)-glycerol ("Guaiacylglycerol") (I). The centre neck of a three-necked flask was equipped with an extraction tube and a reflux condenser. In the extraction tube was placed a glass-crucible provided with a coarse sintered glass-disk. The crucible contained 4.0 g of α,β-diacetoxy-acetylhydroferulic acid methyl ester (VII). One of the side-necks was provided with a gas-inlet tube, and the other one with an outlet tube which passed to the bottom of the flask and was kept closed during the reduction. The flask contained lithium aluminium hydride (2.2 g) and dry ether (300 ml), and the mixture was heated on a water-bath in a nitrogen atmosphere until the triacetate (VII) had been completely dissolved by the refluxing ether (about 30 minutes).

After a further 30 minutes heating the reaction mixture was cooled and slowly pressed with nitrogen gas through the outlet tube into a flask containing 200 ml of ice-cooled and vigorously stirred 1 *N* sulphuric acid. The aqueous layer was filtered and passed through a column of a cation exchange resin in the H^+-state (Amberlite IR-120). The effluent was immediately neutralized with $BaCO_3$, filtered and concentrated under reduced pressure in an atmosphere of carbon dioxide. Some barium carbonate which precipitated during the evaporation was removed, and the clear solution further concentrated to a volume of about 10 ml. Residual water was removed by repeatedly adding ethanol and benzene and evaporating under reduced pressure. The remaining syrup was purified by dissolving in 100 ml of acetone, filtering off a small amount of insoluble material and evaporating in vacuum.

The product thus obtained was a clear, practically colourless, highly viscous syrup which was free of inorganic material. It was readily soluble in water, alcohols, acetone, acetic acid, ethyl acetate, and dioxan, and sparingly soluble in ethyl ether, chloroform, benzene and petroleum ether.

Guaiacylglycerol tetraacetates (VIII, 1 and 2). Guaiacylglycerol was dissolved in acetic anhydride-pyridine mixture. After 16 hours the mixture was poured into water. The resulting oil was dissolved in ether, and the ether solution was washed with 0.5 *N* sulphuric acid, aqueous bicarbonate, and water, dried (Na_2SO_4), and concentrated. Addition of a little hexane yielded six-edged prismatic plates, recrystallized from ethylacetate-hexane, m.p. 84—85°. (Found: C 56.2, H 5.72, OCH_3 8.20, CH_3CO 46.1; Calc. for $C_{18}H_{22}O_9$ (382.4): C 56.5, H 5.80, OCH_3 8.11, CH_3CO 45.0.)

The ether-hexane mother liquor was concentrated *in vacuo* leaving a yellow oil. This was distilled between 160—170° (bath temperature) (0.01 mm) yielding an almost colourless oil, which crystallized readily on treatment with ether. Regular six-edged plates, recrystallized from ethylacetate-hexane, m.p. 113—114°. (Found: C 56.4, H 5.66, OCH_3 8.03, CH_3CO 42.6; Calc. for $C_{18}H_{22}O_9$ (382.4): C 56.5, H 5.80, OCH_3 8.11, CH_3CO 45.0.)

Oxidation of guaiacylglycerol with periodate. a) *Periodate consumption.* An aqueous solution (100 ml) containing guaiacylglycerol (with 42.2 mg OCH_3 = 1.36 millimoles) and sodium periodate (7.0 millimoles) was kept in a thermostat at + 12°. The consumption of periodate was determined by adding samples of 5 ml of the solution to 10 ml of a solution containing sodium arsenite (0.04 mole per litre), potassium iodide (2.5 per cent), and sodium bicarbonate (1 per cent) and titrating the excess arsenite with 0.05 *N* iodine. The results obtained are presented in Fig. 2.

In a similar way the periodate consumption of veratrylglycerol (II, m.p. 109—110°)[3], guaiacol, and vanillin was determined (*cf.* Fig. 2).

b) *Formation of formaldehyde.* One ml of 0.7 M sodium periodate was added to 10 ml of an aqueous solution of guaiacylglycerol containing 0.136 millimole of methoxyl. After 10 minutes at room temperature excess periodate and the iodate formed were precipitated by the addition of 2 ml of a 20 per cent lead nitrate solution [10]. The precipitate was filtered off and washed with water, and the combined aqueous solutions (about 50 ml) were distilled in an atmosphere of nitrogen, water being added to keep the volume constant.

Dimedone (0.5 g) dissolved in 2 *N* NaOH (2 ml), followed by 2 *N* acetic acid (4 ml), was added to the distillate (200 ml). The mixture was set aside overnight in the refrigerator and the precipitate was collected. Needles, m.p. 183—185°, no depression with an authentic sample of methylene-bis-dimedone. (Calc. for 1 mole HCHO per OCH_3, 39.8 mg; found 34.6 mg = 87 %.)

c) *Formation of formic acid.* Ten ml of an aqueous solution of guaiacylglycerol, containing 1.09 millimole of methoxyl, were mixed with 10 ml of an aqueous solution of 3.27 millimoles of sodium periodate. After 10 minutes at room temperature 0.1 ml of ethylene glycol (to remove the excess periodate) and after further 10 minutes 55 ml of 1 per cent lead chloride were added. The precipitate of lead iodate was filtered off and washed with water. The combined aqueous solutions were evaporated to dryness under reduced pressure (bath temperature 45°). The receiver flask containing 10 ml of 0.1646 *N* potassium hydroxide solution was cooled by running water during the distillation. The residue was then dissolved in 20 ml of distilled water and the solution evaporated under vacuum, this procedure being repeated once. The content of the receiver was titrated with 0.1010 *N* hydrochloric acid. 6.7 millilitres of this solution were required. (Calc. for 1 mole HCOOH per OCH_3, 1.09 millimole formic acid; found 0.97 millimole formic acid = 89 %.) When heated on a water-bath, the neutralized distillate reduced mercuric chloride to calomel.

d) *Formation of vanillin.* One ml of 0.7 *M* $NaIO_4$ was added to 10 ml of an aqueous guaiacylglycerol solution containing 0.136 millimole of methoxyl. After 10 minutes at room temperature 1 ml of 2 *N* H_2SO_4 was added followed by some solid potassium iodide. A concentrated solution of sodium arsenite was then added drop by drop until the iodine colour disappeared. Finally, the solution was extracted six times with benzene, and the combined benzene extracts were shaken with 50 ml of a 0.3 per cent solution of 2,4-dinitrophenylhydrazine in 2 *N* HCl. In order to separate the vanillin-2,4-dinitrophenylhydrazone present in the benzene solution from unreacted dinitrophenylhydrazine and the dinitrophenylhydrazones of benzene-soluble carbonyl compounds which may have been formed by the breakdown of the guaiacyl nucleus, the benzene solution was treated as follows:

After washing with water and drying (Na_2SO_4) the benzene solution was concentrated to a volume of 30 ml and passed through a column (44 × 1.3 cm) of aluminium oxide (Brockmann). From the chromatogram unreacted 2,4-dinitrophenylhydrazine and the unidentified hydrazones mentioned above were eluted with a mixture of benzene and ethanol (99 : 1). The adsorbent was then extracted in a Soxhlet apparatus with ethanol-benzene (1 : 1). The red solid remaining after evaporation of the extract had the m.p. 244—246° (after recrystallization from pyridine-ethanol, m.p. 258—260°), undepressed on admixture with vanillin-2,4-dinitrophenylhydrazone. (Vanillin-2,4-dinitrophenylhydrazone: Calc. for 1 mole of vanillin per mole of methoxyl, 45.1 mg; found 24.6 mg = 54 %.)

Veratrylglycerol [*IIa (liquid mixture of* D,L-*forms)*]. A distilled solution of diazomethane in ether (50 ml) was added to a solution of guaiacylglycerol (0.5 g) in dioxan (10 ml). An amorphous precipitate appeared and was partly redissolved by the addition of methanol (50 ml). After 16 hours the mixture was evaporated in vacuum. Attempts to convert the remaining oil into crystalline material by dissolving in a little chloroform and seeding with veratrylglycerol (II), m.p. 109—110°[3], were unsuccessful. The chloroform was evaporated and residual solvents removed by repeatedly adding water and distilling off under reduced pressure. Finally, the oil was dissolved in water to a total volume of 50 ml (solution A) and the methoxyl content of the solution was determined.

Five ml of solution A, containing 0.37 millimole OCH_3, were treated with excess sodium periodate; IO_4^- *consumption:* Calc. 0.37 millimole; found 0.33 millimole = 90 %.

Twenty ml of solution A, containing 1.47 millimole OCH_3, were oxidized with 0.5 g $NaIO_4$ (2 hrs., room temp.). The *formaldehyde* content of the mixture was determined (*cf.* p. 578). *Methylene-bis-dimedone:* Calc. for 1 mole HCHO per 2 OCH_3, 215 mg;

found 200 mg = 93 %. The methylene-bis-dimedone obtained had m.p. 183—185°, undepressed on admixture with an authentic sample.

Another sample of solution A was oxidized with the calculated amount of periodate, and then precipitated with 2,4-dinitrophenylhydrazine dissolved in 2 *N* HCl. The orange-red precipitate was dissolved in benzene and passed through a column of aluminium oxide (Brockmann). Elution first with benzene and then with 1 % ethanol in benzene yielded the 2,4-dinitrophenyl-hydrazones of formaldehyde, m.p. 162—164°, and of *veratric aldehyde* (84 % of the calculated amount), m.p. 258—260°, no depression with authentic samples of these substances.

Veratrylglycerol triacetate [*Xa (liquid mixture of* D,L*-forms)*]. Diazomethane was distilled from a dioxan solution into the solution of 1 g of guaiacylglycerol in a mixture of 50 ml of dioxan and 25 ml of methanol. After 2 days the solvents were removed under vacuum, and the remaining oil was acetylated with a mixture of 5 ml of pyridine and 5 ml of acetic anhydride. The oily acetate could not be converted into crystalline material. Two subsequent distillations (0.05 mm Hg, bath temp. 170°) yielded an almost colourless syrup. No crystallization occured on treatment with solvents and seeding with solid veratrylglycerol triacetate (X), m.p. 68—69° (see below). (Found: C 57.2, H 6.25, OCH_3 17.7, CH_3CO 35.2; Calc. for $C_{17}H_{22}O_8$ (354.4): C 57.6, H 6.26, OCH_3 17.5, CH_3CO 36.9.)

Veratrylglycerol triacetate [*X (crystalline)*]. Veratrylglycerol (II), m.p. 109—110°[3], was acetylated with acetic anhydride in pyridine solution. The acetate crystallized readily from ether-hexane and when recrystallized from ethylacetate-hexane formed six-edged plates, m.p. 68—69°. (Found: C 57.5, H 6.21, OCH_3 17.6, CH_3CO 36.6; Calc. for $C_{17}H_{22}O_8$ (354.4): C 57.6, H 6.26, OCH_3 17.5, CH_3CO 36.9.)

1-(3-Methoxy-4-hydroxyphenyl)-2,3-dihydroxy-n-propane-1-sulphonic acid, barium salt. A mixture of 30 ml of an aqueous solution of guaiacylglycerol, obtained by lithium aluminium hydride reduction of 4 g of *α,β*-diacetoxy-acetylhydroferulic acid methyl ester (VII) (*cf.* p. 577) and 30 ml of an aqueous $NaHSO_3$-SO_2 solution of pH 3 and a total SO_2 content of 10 %, was heated in a sealed tube for 3 hours at 135°. Na^+ was removed by filtration through a cation exchange resin (Amberlite IR-120), and SO_2 was removed by concentrating the filtrate (300 ml) under reduced pressure. The resulting solution (200 ml) was neutralized with barium carbonate, filtered, and concentrated in vacuum to a volume of about 5 ml and finally filtered through a layer of kieselguhr. Addition of ethanol, followed by ethyl ether, to the clear filtrate, produced an oily precipitate. After several hours the solvent was decanted, and the solid obtained on treating the oil with ethanol was collected and washed with ether. Yield, 2.8 g of crude barium sulphonate.

From a solution of the crude product in 5 ml of water, a mixture of two different types of crystals separated (prismatic plates and fine needles). The prismatic material, which constituted only a small part of the total product was less soluble than the other component and could be partially isolated by fractional crystallization from water. It proved to consist of barium thiosulphate. In order to remove residual thiosulphate from the remaining material, this was dissolved in water and the solution was acidified with sulphuric acid (final concentration about 1 *N* H_2SO_4), which decomposed the thiosulphate yielding $BaSO_4$, SO_2, and S. Sulphur dioxide was distilled off in vacuum, and the remaining solution was neutralized with $BaCO_3$, filtered, and further concentrated in vacuum to a volume of a few millilitres. After a final filtration which removed some residual inorganic material, some acetone was added, and the mixture was set aside in the refrigerator. The uniform, fine needles which separated were collected and washed with acetone

and ether. (Found: OCH_3 9.02, S 9.17, Ba 19.78; Calc. for $(C_{10}H_{13}O_7S)_2Ba$ (691.9): OCH_3 8.97, S 9.27, Ba 19.85.)

Periodate oxidation. An aqueous solution (5 ml) of the barium sulphonate (60 mg) was mixed with 10 ml of 0.1 *M* sodium periodate. After a reaction period of 10 minutes the formaldehyde present in the solution was determined as described above. (Methylene-bis-dimedone: Calc. 50.7 mg; found 43.5 mg = 86 %.) The dimedone compound had m.p. 184—186°, undepressed on admixture of authentic methylene-bis-dimedone.

SUMMARY

α-(3-Methoxy-4-hydroxyphenyl)-glycerol ("guaiacylglycerol") has been prepared by lithium aluminium hydride reduction of α,β-diacetoxy-acetyl-hydroferulic acid methyl ester. It was obtained as a non-crystallizing syrupy mixture of the two possible D,L-forms. Acetylation yielded the two DL-tetraacetyl derivatives in a crystalline state. Methylation with diazomethane gave "veratrylglycerol" which was converted into its triacetate. The latter products were not resolved into the corresponding D,L-forms.

The oxidation of guaiacylglycerol with periodate has been examined.

On heating guaiacylglycerol with aqueous bisulphite solution (pH 3) the hydroxyl group in the position *alpha* to the aromatic nucleus was replaced by SO_3H; a crystalline barium salt of the sulphonic acid was obtained.

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