Aromatic Keto- and Hydroxy-polyethers
as Lignin Models. II *

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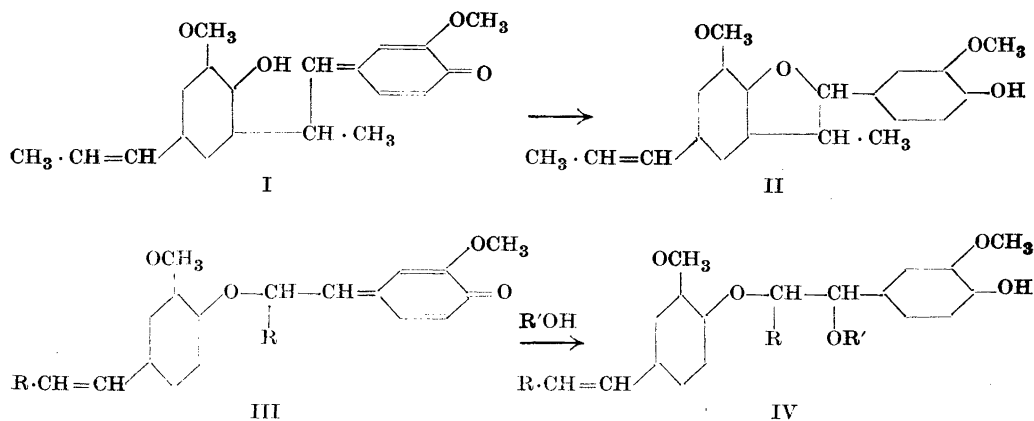
Studies on the analytical composition, physical properties, and degradation of lignins and lignin derivatives conclusively demonstrate the fundamental correctness of the view that lignin is related to phenyl propane which was already advanced by P. Klason more than fifty years ago.

Much interest is now devoted to the mechanism of lignin formation, the nature of the lignin precursors, and the reactive groups of the lignins which are responsible for their facile sulphonation with sulphites and their reactions with several other reagents.

A reaction of great interest in connection with lignin formation is the dehydrogenation of *iso*eugenol with phenol oxidases or ferric chloride to 'dehydrodi-*iso*eugenol'. The investigation of this compound revealed that it is not a diphenyl derivative, as previously supposed, but a coumarane derivative [1]. The coupling takes place between two molecules of *iso*eugenol in such a way that the carbon atom in the ortho position to the hydroxyl group in one molecule is linked to the β-carbon atom in the side chain of another molecule (II), probably via the intermediate quinone I.

Another type of coupling should be theoretically possible, namely, the formation of ethers of structure IV. The introduction of the benzyl alcoholic hydroxyl group involves the addition of the elements of water (R' = H) in the same way as the formation of dehydrodi-*iso*eugenol from the postulated quinonoid intermediate I. Such a reaction would be of very great interest in relation to the chemistry of lignin, and during the last fifteen years several attempts have been made in these laboratories to effect the dehydrogenation of *iso*eugenol and similar substances to compounds of this type. The products,

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* Part I. Preliminary communication. *Acta Chem. Scand.* 2 (1948) 535.

OCH$_3$ OH CH= OCH$_3$ O

CH·CH$_3$

CH$_3$·CH=CH

I

→

OCH$_3$ O CH OCH$_3$ OH

CH·CH$_3$

CH$_3$·CH=CH

II

OCH$_3$ O—CH—CH= OCH$_3$ O

R

R·CH=CH

III

R'OH →

OCH$_3$ O—CH—CH— OCH$_3$ OH

R OR'

R·CH=CH

IV

however, invariably were ill-defined and amorphous, and similar to those obtained by Freudenberg and his collaborators [2].

Since such coupling reactions could easily be imagined to proceed further with the formation of high molecular products containing only very few free phenolic hydroxyl groups, it was suggested in 1933 that lignin may owe its formation in Nature to the dehydrogenation of progenitors of coniferyl type [1]. This theory now appears to be widely accepted [3] and quite recently Freudenberg reported the dehydrogenation of coniferyl alcohol to products which resemble 'Brauns native lignin', a lignin-like material that occurs in most woods [4]. In many respects, however, these products differ from the main portion of lignin.

Elements of type IV contain hydroxyl groups of the benzyl alcoholic type which, according to Holmberg [5], may be responsible for the sulphonation of lignin. In these laboratories Lindgren recently showed that such alcohols are excellent lignin models provided that the nuclei are substituted as in lignin [6].

Pending advance in our continued experiments on the dehydrogenation of C$_6$—C = CH—R compounds, we have decided to synthesize substances of type IV by orthodox methods.

We have chosen to start with acetoguaiacone, but experiments with propioguaiacones are also in progress (B. Lindgren).

A series of compounds of general type V have been prepared.

$$R\left[\begin{array}{c} CH_3O \\ -O- \end{array}-CO\cdot CH_2-\right]_n H$$

n = 2—4   R = CH$_3$ or H

V

6
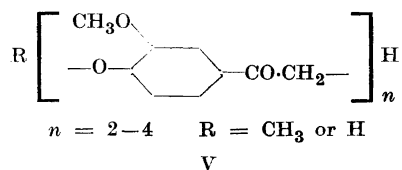
The syntheses were carried out according to the following scheme:

$$CH_3O{-}\langle\ \rangle{-}O{-}\langle\ \rangle{-}CO\cdot CH_2{-}[Br + Na]{-}O{-}\langle\ \rangle{-}CH_3O{-}\langle\ \rangle{-}CO{-}$$
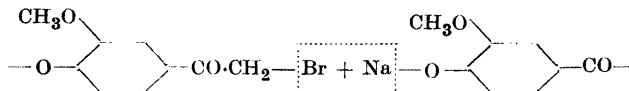
In the synthesis of the members of the 'phenol series' (R = H) the hydroxyl group had to be protected by acetylation or, preferably, benzoylation. The condensations were generally carried out in anhydrous methyl ethyl ketone in the presence of potassium carbonate, but sometimes in absolute alcohol, using the sodium salt of the phenol.

In the latter case, it was advantageous to use an excess of the phenol in order to prevent deacylation and other complications. Good yields of the phenolic ethers (V, R = H) were obtained by deacylation with piperidine in alcohol.

Ultraviolet absorption spectra.
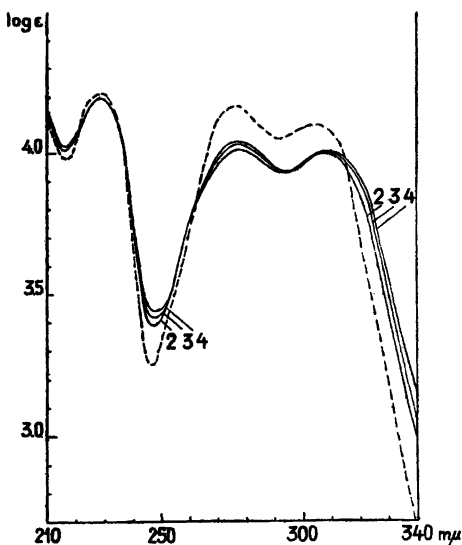(Extinctions per C_6C_2-unit.)

Fig. 1. 2 : V, n = 2, R = H;
         3 : V, n = 3, R = H;
         4 : V, n = 4, R = H;
dashed line: acetoguaiacone;
all in absolute alcohol.

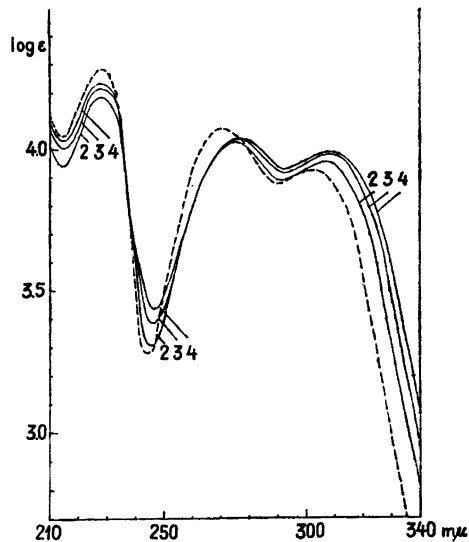Fig. 2. 2 : V, n = 2, R = CH_3;
         3 : V, n = 3, R = CH_3;
         4 : V, n = 4, R = CH_3;
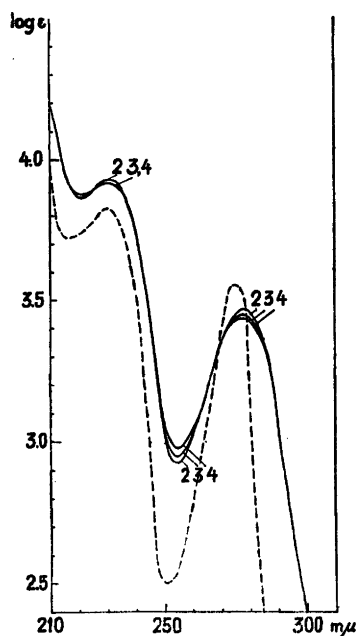dashed line: acetoveratrone;
all in absolute alcohol.

Fig. 3. 2 : VI, n = 2;
     3 : VI, n = 3;
     4 : VI, n = 4;
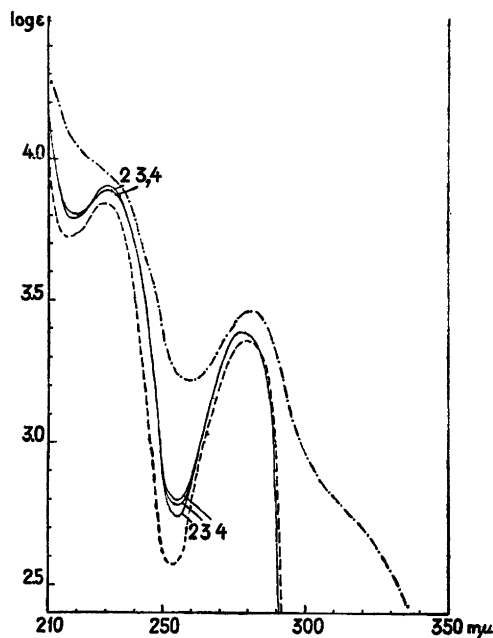dashed line: vanillyl alcohol *;
all in absolute alcohol.

Fig. 4. The sulphonic acids of
     2 : VI, n = 2;
     3 : VI, n = 3;
     4 : VI, n = 4;
— — — — vanillyl alcohol *;
—.—.—.   lignin;
all in water.

The various ketonic ethers (V, R = CH_3) were reduced to the corresponding alcohols (VI).

$$CH_3 \left[-O-\bigcirc-\underset{\underset{OH}{|}}{CH}-CH_2- \right]_n H$$

n = 2—4

VI
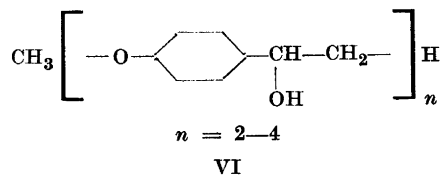
The reduction was accomplished by the Meerwein-Ponndorff method, and the reaction was first tested in the case of 3,4-dimethoxyphenacyl coerulignol ether (VII). This was easily converted into the dihydroderivative VIII.

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* These spectra have kindly been put at our disposal by Dr. B. Lindgren.

CH₃O groups and structures:

$$CH_3O\text{---}\langle\ \rangle\text{---}CO\cdot CH_2\cdot O\text{---}\langle\ \rangle\text{---}CH_2CH_2CH_3 \qquad CH_3O\text{---}\langle\ \rangle\text{---}CH\cdot CH_2O\cdot\text{---}\langle\ \rangle\text{---}CH_2CH_2CH_3$$

VII   VIII
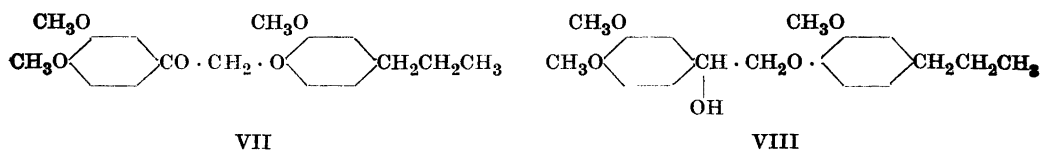
Both compounds are crystalline solids. The reduction of the compounds V ($n = 2$—4 R = CH₃) must lead to a mixture of diastereoisomerides, and the products obtained from these ketones were amorphous but showed no ketonic properties. The compounds V (R = COCH₃ or CO—C₆H₅), as expected, could not be properly reduced by this method. Complications occurred owing to deacylation and formation of products with an abnormally high alkoxyl content.

Spectrochemically, the ketones V (R = H or CH₃) as well as the secondary alcohols VI (R = CH₃) offered no surprises (Fig. 1—4). Only small but regular changes were observed with increasing molecular weight as was to be expected from the results of several similar instances already studied.

All alcohols VI and the alcohol VIII were subjected to sulphite cooks under varying conditions. In all cases the hydroxyl groups were replaced by sulphonic acid groups, and the sulphonic acids from VI were all amorphous and yielded no crystalline derivatives. The barium salt of the sulphonic acid from VIII, possessing only one asymmetric carbon atom, yielded a crystalline salt with S-l-naphthylmethylthiuronium chloride.

The fundamental studies of Hägglund, on the sulphonation of lignin during the sulphite delignification, clearly indicate the presence of two different groups in lignin characterized by different reactivity to sulphites [7].

One group ('A') reacts readily with sulphite at any pH (even in alkaline solution). This yields the low sulphonated, solid, insoluble, lignin sulphonic acids of Hägglund. It is believed that these groups are benzyl alcoholic hydroxyl groups, as assumed by Holmberg, and belong to elements of type IV [8].

In Hägglund's laboratories one of the present authors showed that certain reactive phenols condense easily with the groups A in lignin to form high-molecular insoluble products [9]. This reaction takes place only under acid conditions. It was therefore of interest to investigate the influence of phenols (resorcinol) on the sulphonation of our lignin models (VI), which are all substituted benzyl alcohols.

Table 1 summarises the results of these experiments.

The yields of sulphonic acids formed under various conditions were determined by isolation of the barium salts according to methods described earlier [10]

and also indirectly by determining the sum of undissolved solid organic material and products which could be extracted from the 'waste liquors' with chloroform. At low pH's the insoluble materials just mentioned were hard, resinous condensation products.

Table 1. Sulphonation of lignin models under various conditions.

Substance (1.0 g was always employed)	Time h	Per cent yield of sulphonic acid (The total amount of 'sulphur dioxide' was always 6.0 % and the amount of 'sodium hydroxide' present in the cooking acids as well as the pH' s (at room temperature) are indicated below. Reaction temperature 135°. Amount of cooking acid 65 ml.)				
		1.4 % NaOH pH = 1.1-1.2	2.8 % NaOH pH = 1.7-1.8	4.0 % NaOH pH = 3.5	7.5 % NaOH pH = 6.5	11.0 %NaOH pH = 11.5
VI. $n = 2$	1.0	70	70			
»	3.5	100	90	70	30	
»	19.0					15
VI. $n = 2 +$ 1.0 g resorcinol	3.5	18		50		
VI. $n = 3$	1.0	25	35			
»	3.5	50	80			
VI. $n = 4$	3.5	20	35			
VIII.	1.0		5	10		
»	3.5	10	15			
»	19.0	60				

As seen from this table the rate of sulphonation decreases with increasing chain length. This conforms with the results of Lindgren [6], who found that the 'monomolecular' lignin models, vanillyl and veratryl alcohol, are sulphonated more rapidly than lignin. The decreasing solubility of the higher molecular compounds in sulphite cooking acid reduces the rate of sulphonation. The 'trimolecular' lignin model VI ($n = 3$) is more easily sulphonated at pH 1.8 than at pH 1.1. This may be due to the fact that condensation and sulphonation occur simultaneously, the rates of both reactions depending on the acidity as well as the chain length. The condensation of the 'dimolecular' lignin model VI ($n = 2$) with resorcinol is far greater at pH 1.1 than at pH 3.5. This is in agreement with the assumption that the group 'A' in lignin is of a benzyl alcohol type. Substance VIII reacts much more slowly than the compounds VI ($n = 2$—4). This may be explained by its low solubility in sulphite cooking acid due to the hydrophobic character of the coerulignol part of the molecule.

The sulphonic acids obtained were precipitable as S-1-naphthylmethyl-thiuronium salts but not with the reagents ordinarily employed for the precip-itation of lignin sulphonic acids. This conforms with the known difficulty to precipitate the highly sulphonated low molecular lignin sulphonic acids. Such acids, however, may be precipitated with the above-mentioned reagent.

The group B in lignin which is hydrolyzed and sulphonated in the second step of the sulphite delignification is nonreactive with phenols. It has already been assumed that this group constitutes a cycloacetal group [10]. It is presum-ably similar to dehydrodi-*iso*eugenol, but has been assumed to possess an hydroxyl group instead of the hydrogen atom at carbon atom 2 in the coumar-ane ring. It could be imagined to be formed by dehydrogenation of a glucos-idic derivative of α-hydroxy coniferyl alcohol. Acetal linkages in lignin have already been assumed by Holmberg [11]. Further experiments on the synthesis of suitable model substances of type B are in progress.

The degradation of the various ketones, alcohols and sulphonic acids described in this paper with nitrobenzene and alkali will be the subject of forthcoming communications which will also contain degradation experiments with dehydrodi-*iso*eugenol and compounds similar to V but also containing dehydrodi-*iso*eugenol components.

EXPERIMENTAL

Acetoveratrone

30 g of acetoguaiacone and 60 ml of dimethyl sulphate were dissolved in 300 ml of alcohol. 60 ml of sodium hydroxide (40 g per 100 ml) were slowly added, in order to keep the temperature of the mixture below 50° C. After refluxing for one hour and cooling, the solution was poured into 750 ml of water. The resulting mixture was extracted with ether, the ethereal solution washed with water, dried over sodium sulphate and evapor-ated. A readily crystallizing pale yellow oil was obtained.

Yield 24.9 g (78 %). M. p. 50—51°. (M. p. of the pure product 52—53° [12].)

The product may be further purified by distillation under reduced pressure, but in this case the crude product was used directly for further syntheses.

ω-Bromo-acetoveratrone

The compound was prepared mainly according to Mannich and Hahn [13], but the product was recovered in a more careful manner in order to avoid discoloration and to increase the yield.

20 g of acetoveratrone were dissolved in 100 ml of chloroform. 17.7 g of bromine in 50 ml of chloroform were slowly added at room temperature. At the beginning, a dark red solution was obtained. When still more bromine was added, however, the colour dis-appeared and hydrogen bromide was formed. After all bromine had been added, the solution was more or less reddish. On shaking the latter with bicarbonate solution, the

red colour disappeared. The solution was washed with water and dried over sodium sulphate. The chloroform was evaporated under reduced pressure. In order to avoid excessive discoloration of the product, 200 ml of light petroleum (b. p. 40—60°) were added in several portions during the distillation. On cooling, the resulting light brown oil crystallized. The product was recrystallized from a small amount of methanol. Yield 24 g (84 %). M. p. 80—81°.

Acetoguaiacyl-acetoguaiacone methyl ether[14]
(V, $n = 2$, R = CH_3)

20 g of ω-bromo-acetoveratrone and 10 g of acetoguaiacone were dissolved in 300 ml of absolute alcohol in a flask provided with a reflux condenser and an inlet for nitrogen. The mixture was heated to boiling on the steam bath and nitrogen was passed in, in order to remove all the air from the flask. Then 14.5 g of the sodium salt of acetoguaiacone were added. The reddish yellow mixture was boiled until all solids dissolved and then another five minutes. (About 15 minutes total.) On cooling, small needle shaped crystals separated. The crystals were collected by filtration and the filtrate concentrated to about 75 ml, yielding more crystals on cooling. Yield 24 g (83 %). The product was recrystallized twice from alcohol. M. p. 138—139°.

$C_{19}H_{20}O_6$ Calc.   C 66.3   H 5.86 OCH_3 27.0
              Found   » 66.1   » 5.90   »   27.0

The first batches of this product had a m. p. of 120.5—121°. This substance was shown to be a dimorphous modification of the above-mentioned substance of m. p. 138—139°. By dissolving in hot alcohol and seeding the cooled solution with the substance of m. p. 138—139°, a product crystallized identical with the latter.

The compound (0.5 g) was boiled for three hours with semi-carbazide hydrochloride (0.5 g) and potassium acetate (0.5 g) in alcohol. A white crystalline *semi-carbazone* was obtained. Recrystallization from dilute acetic acid yielded crystals of m. p. 235—236° (decomp.).

$C_{21}H_{26}O_6N_6$ Calc. OCH_3 20.3   Found OCH_3 20.5

ω-Bromo-acetoguaiacyl-acetoguaiacone methyl ether

15 g of acetoguaiacyl-acetoguaiacone methyl ether were dissolved in 100 ml of chloroform. 7.2 g of bromine in 50 ml of chloroform were slowly added. The reaction was started by irradiation with ultraviolet light and gentle warming. After all bromine was added, the slightly red mixture was extracted with bicarbonate solution, washed with water, and dried over sodium sulphate. The chloroform was evaporated under reduced pressure. The resulting oil crystallized on cooling. Yield 12.2 g (66 %). M. p. 133—138°. Repeated recrystallization from ethyl acetate yielded small crystal needles of m. p. 148.5—149.5°.

$C_{19}H_{19}O_6Br$ Calc.   Br 18.9 OCH_3 22.0
              Found   » 18.9   »   22.2

D i-(a c e t o g u a i a c y l)-a c e t o g u a i a c o n e   m e t h y l   e t h e r
(V, $n = 3$, R $= CH_3$)

a) 5 g of ω-bromo-acetoguaiacyl-acetoguaiacone methyl ether and 1.75 g of aceto-guaiacone were dissolved in 150 ml of boiling absolute alcohol in a nitrogen atmosphere. Then 2.37 g of the sodium salt of acetoguaiacone were added, and the mixture was treated as described above. On cooling, a yellowish powder separated. Yield 6 g (80 %). M. p. 140—140.5°. The product was recrystallized twice from dioxane. A white crystalline substance containing dioxane was obtained. This product was dissolved in a small amount of chloroform. To the boiling solution a large amount of alcohol was added. The mixture was boiled in order to evaporate the chloroform and then filtered. On cooling small, colourless crystals separated. M. p. 145—146°.

$C_{28}H_{28}O_9$	Calc.	C	66.1	H	5.56	OCH$_3$	24.4	Mol. wt.	508	
	Found	»	65.8	»	5.57	»	24.6	» »	511	(Rast)

b) 1.5 g of acetoguaiacyl-acetoguaiacone (see p. 1368) and 1.18 g of ω-bromo-aceto-veratrone were dissolved in 50 ml of absolute methyl ethyl ketone. 2 g of anhydrous potassium carbonate were added. After boiling under anhydrous conditions for 45 minutes, the mixture was filtered. On cooling, a yellowish powder (1.0 g) separated from the filtrate. The filter cake was dissolved in dilute sulphuric acid, yielding another 0.8 g of the product. After recrystallization according to a) a colourless product was obtained. M. p. 144—145°. Mixed m. p. with the product of a), 143—145.5°.

A *semi-carbazone* was obtained as described above. M. p. 241—242° (decomp.).

$C_{31}H_{37}O_9N_9$ Calc. OCH$_3$ 18.3   Found OCH$_3$ 18.6

T r i-(a c e t o g u a i a c y l)-a c e t o g u a i a c o n e   m e t h y l   e t h e r
(V, $n = 4$, R $= CH_3$)

2.75 g of acetoguaiacyl-acetoguaiacone, 2.24 g of ω-bromo-acetoguaiacyl-acetoguaia-cone methyl ether and 0.36 g of sodium ethoxide in 120 ml of absolute alcohol were treated as described above. A precipitate was formed even in the boiling solution, and the amount increased on cooling. The yellowish powder (3.9 g, 70 %) was collected by filtration and recrystallized three times from dioxane, yielding a colourless product containing dioxane. On repeated recrystallizations from methyl ethyl ketone a micro-crystalline product of m. p. 145—147° was obtained.

$C_{37}H_{36}O_{12}$	Calc.	C	66.1	H	5.40	OCH$_3$	23.1	Mol. wt.	672	
	Found	»	65.9	»	5.79	»	23.2	» »	702	(Rast)

A crystalline semi-carbazone could not be obtained from this compound.

ω-B r o m o-a c e t y l-a c e t o g u a i a c o n e

10 g of acetyl-acetoguaiacone (prepared according to Finnemore [15]) were dissolved in 75 ml of chloroform. 7.7 g of bromine in 35 ml of chloroform were slowly added. The reaction was started by adding a drop of concentrated hydrochloric acid and irradiation

with ultraviolet light. The chloroform solution was treated as described above. Evaporation of the chloroform yielded a readily crystallizing oil. On recrystallization from alcohol, needle shaped crystals of m. p. $88-88.5°$ were obtained. Yield 8.7 g (67 %).

$C_{11}H_{11}O_4Br$ Calc.   C   46.0   H   3.86 OCH_3 10.8
            Found   »   46.0   »   3.86   »   10.8

Acetoguaiacyl-acetoguaiacone acetate
(V, $n = 2$, R $= COCH_3$)

5 g of ω-bromo-acetyl-acetoguaiacone and 3.3 g of the sodium salt of aceto-guaiacone were refluxed in 200 ml of absolute alcohol for 15 minutes. After cooling, the solution was poured into ether, yielding a white precipitate, consisting partly of sodium bromide. By dissolving in a hot mixture of benzene and petroleum (b. p. $120-140°$) and filtering, the product was separated from the sodium bromide. On cooling, white crystals separated. Recrystallization from alcohol yielded 0.7 g (13 %) of needle shaped crystals. M. p. $126-127°$.

$C_{20}H_{20}O_7$ Calc. OCH_3 16.7   Found OCH_3 16.7

Benzoyl-acetoguaiacone

To 10 g of acetoguaiacone in 20 ml of anhydrous pyridine, 7.0 ml of benzoyl chloride were added in small portions. The temperature of the mixture increased, and finally a crystal slurry was formed. After about half an hour 100 ml of water were added, yielding a white, crystalline product. The product was collected by filtration, dried and dissolved in a small amount of benzene. Petroleum (b. p. $120-140°$) was added until the solution just turned cloudy. Long thin colourless needles of m. p. $108-109°$ [12] slowly separated. Yield 14.5 g (90 %).

ω-Bromo-benzoyl-acetoguaiacone

10 g of benzoyl-acetoguaiacone were brominated as described above. Yield 11.5 g (88 %). Recrystallization from alcohol yielded long, colourless needles of m. p. $105-106°$.

$C_{16}H_{13}O_4Br$ Calc.   Br   22.9   Found   Br   22.7

Acetoguaiacyl-acetoguaiacone benzoate
(V, $n = 2$, R $= C_6H_5CO$)

10 g of ω-bromo-benzoyl-acetoguaiacone and 4.75 g of acetoguaiacone were dissolved in 100 ml of anhydrous methyl ethyl ketone, containing 15 g of anhydrous potassium carbonate, and boiled under anhydrous conditions for 20 minutes. The mixture was poured into water and acidified. The oily layer was separated and the water phase extracted with ether. The oil and the ethereal solution were combined, dried over sodium sulphate and evaporated. On cooling, the resulting oil crystallized. Yield 8.8 g (70 %).

M. p. 110—132°. The product was recrystallized three times from methanol. Colourless crystal needles of m. p. 138—139°.

$C_{25}H_{22}O_7$ Calc.   C   69.1   H   5.11
              Found   »   68.9   »   5.13

The compound was also prepared as described above, in absolute alcohol. A more discoloured product was obtained in a lower yield (55 %).

ω- B r o m o-a c e t o g u a i a c y l-a c e t o g u a i a c o n e   b e n z o a t e

To 5 g of acetoguaiacyl-acetoguaiacone benzoate in 100 ml of chloroform, 1.85 g of bromine in 35 ml of chloroform were slowly added. The reaction was very difficult to start, and only after adding a drop of concentrated hydrochloric acid, irradiation with ultraviolet light and heating to boiling, did the colour of the bromine disappear. The reaction continued comparatively slowly. After being treated in the usual way, the chloroform solution was filtered through a column of aluminium oxide. The resulting colourless solution was evaporated, yielding a slightly yellow oil. On treating with methanol the oil crystallized after cooling in the refrigerator. Yield 4.4 g (73 %).

The compound was very difficult to purify and even after repeated recrystallizations from different solvents the bromine content was found to be somewhat too low. M. p. 137—138°.

$C_{25}H_{21}O_7Br$ Calc.   Br   15.6   Found   Br   15.1

A c e t o g u a i a c y l-a c e t o g u a i a c o n e
(V, $n = 2$, R = H)

a) 0.5 g of acetoguaiacyl-acetoguaiacone acetate were refluxed in a nitrogen atmosphere with 0.2 g of potassium hydroxide in 50 ml of alcohol for ten minutes. The solution was poured into water and extracted with ether. The water phase was acidified and extracted with chloroform. The chloroform solution was washed with water, dried over sodium sulphate and filtered through a column of aluminium oxide. On evaporation there remained a yellowish, readily crystallizing oil. Yield 0.30 g (67 %). Recrystallization from methanol yielded crystal needles of m. p. 141—143°.

b) 5 g of acetoguaiacyl-acetoguaiacone benzoate were hydrolyzed by refluxing with 2 g of piperidine in 100 ml of alcohol for 20 minutes. The solution was poured into water, acidified and extracted with chloroform. The chloroform solution was treated in the above-mentioned way, yielding 5.2 g of an oil. On treatment with ether the oil crystallized, yielding 3.1 g (90 %) of crystals. M. p. 136—139°. (From the ether solution 1.8 g (91 %) of benzoyl-piperidine, m. p. 42—43° were obtained.) On recrystallization, needles of m. p. 140—142° were obtained. Mixed melting point with the product of a) 140—142°.

$C_{18}H_{18}O_6$ Calc.   C   65.5   H   5.50 OCH_3 18.8
              Found   »   65.6   »   5.62   »   18.9

The compound was soluble in alkali and gave a blue green colour with ferric chloride.

0.2 g were dissolved in acetone and an excess of diazomethane in ether was added. Evolution of gas was observed. After standing in the refrigerator for 24 hours the solu-

tion was evaporated, yielding a solid residue (0.2 g). Recrystallization from alcohol yielded thin needles of m. p. 119—120°. Mixed m. p. with acetoguaiacyl-acetoguaiacone methyl ether 119—120°.

(These experiments were carried out with one of the first batches of the product, before the dimorphous modification of m. p. 138—139° had been obtained.)

The *semi-carbazone* of the compound was prepared as described above. M. p. 180—182° (from alcohol).

$C_{20}H_{24}O_6N_6$ Calc.   OCH$_3$ 14.0   Found   OCH$_3$ 13.9

Di-(acetoguaiacyl)-acetoguaiacone benzoate
(V, $n = 3$, R $= C_6H_5CO$)

a) To 1.5 g of acetoguaiacyl-acetoguaiacone and 1.6 g of ω-bromo-benzoyl-acetoguaiacone in 50 ml of anhydrous methyl ethyl ketone, 2 g of anhydrous potassium carbonate were added. The reaction was accomplished as described above. 1.8 g (68 %) of a yellowish product was obtained. The substance was recrystallized twice from ethyl acetate. Thin needles of m. p. 169—171°.

b) 7.75 g of ω-bromo-acetoguaiacyl-acetoguaiacone benzoate and 2.25 g of acetoguaiacone were reacted with 2.85 g of the sodium salt of acetoguaiacone in 250 ml of absolute alcohol in the manner described above. After evaporating the solution to 75 ml, 4.5 g (50 %) of a yellowish powder separated on cooling. On recrystallization according to a), thin needles, m. p. 170.5—171.5°, were obtained. Mixed m. p. with the product, prepared according to a), 168—171°.

$C_{34}H_{30}O_{10}$ Calc.   OCH$_3$ 15.6   Found   OCH$_3$ 15.7

Di-(acetoguaiacyl)-acetoguaiacone
(V, $n = 3$, R $= H$)

2 g of di-(acetoguaiacyl)-acetoguaiacone benzoate were hydrolyzed with 0.6 g of piperidin in 50 ml of alcohol by the procedure described above. 1.0 g (60 %) of an oil was obtained. The oil crystallized on treatment with methanol. The substance was recrystallized from dioxane, followed by recrystallization from methyl ethyl ketone. On further recrystallizations from methanol, thin needles of m. p. 184—186° were obtained.

$C_{27}H_{26}O_9$ Calc.   OCH$_3$ 18.8   Found   OCH$_3$ 18.8

To 0.05 g of the compound in acetone an excess of diazomethane in ether was added. On standing in the refrigerator for 24 hours, colourless crystals of m. p. 144—145° (0.05 g) separated. Mixed m. p. with di-(acetoguaiacyl)-acetoguaiacone methyl ether 144—145°.

The *semi-carbazone* was prepared as before. M. p. 198—199° (from a large amount of alcohol).

$C_{30}H_{35}O_9N_9$ Calc.   OCH$_3$ 14.0   Found   OCH$_3$ 14.0

T r i-(a c e t o g u a i a c y l)-a c e t o g u a i a c o n e   b e n z o a t e
$(V, n = 4, R = C_6H_5CO)$

a) 1.1 g of di-(acetoguaiacyl)-acetoguaiacone, 0.49 g of ω-bromo-benzoyl-acetoguaia-cone, and 0.098 g of sodium ethoxide in 110 ml of absolute alcohol were treated as de-scribed above. On cooling, 0.5 g (45 %) of a yellowish product separated. After boiling with acetone to remove impurities, the product was recrystallized twice from methyl ethyl ketone. Flat crystals were obtained of m. p. 181—182° (decomp.).

b) 1.5 g of acetoguaiacyl-acetoguaiacone, 1.47 g of ω-bromo-acetoguaiacyl-aceto-guaiacone benzoate, and 3 g of anhydrous potassium carbonate in 50 ml of absolute methyl ethyl ketone were treated as described above. 1.8 g (85 %) of a yellowish product were obtained. The product was treated according to a). M. p. 182—183°. Mixed m. p. with the substance of a) 181—183°.

$C_{43}H_{38}O_{13}$ Calc. OCH_3 16.3   Found OCH_3 16.2

T r i-(a c e t o g u a i a c y l)-a c e t o g u a i a c o n e
$(V, n = 4, R = H)$

1.2 g of tri-(acetoguaiacyl)-acetoguaiacone benzoate were hydrolyzed with 0.5 g of piperidine in 100 ml of alcohol as described above. 0.7 g (70 %) of an oil, crystallizing on treatment with methanol, resulted. After three recrystallizations from methyl ethyl ketone, colourless small crystals of m. p. 201—202° (decomp.) were obtained.

$C_{36}H_{34}O_{12}$ Calc. OCH_3 18.8   Found OCH_3 18.9

0.05 g of the compound in methyl ethyl ketone were methylated with diazomethane as described above. After 24 hours in the refrigerator, small crystals of m. p. 145—146° separated. Mixed m. p. with tri-(acetoguaiacyl)-acetoguaiacone methyl ether 145—147°.

The *semi-carbazone* was prepared as described above and recrystallized from a mixture of alcohol and acetic acid. M. p. 212—214° (decomp.).

$C_{40}H_{46}O_{12}N_{12}$ Calc. OCH_3 14.0   Found OCH_3 14.3

3,4-D i m e t h o x y p h e n a c y l   c o e r u l i g n o l   e t h e r   (VII)

5 g of ω-bromo-acetoveratrone, 4.5 g coerulignol, and 1.3 g of sodium ethoxide in 150 ml of absolute alcohol were treated as described above. The mixture was poured into 350 ml of water and extracted with ether. The ethereal extract was washed with 0.2-n sodium hydroxide and water and dried over sodium sulphate. After evaporation, an oil was obtained. The oil could be distilled at a pressure of 1 mm of mercury, yielding 5.0 g (75 %) of an almost colourless oil, crystallizing on treatment with methanol. Re-crystallization from methanol yielded crystals of m. p. 73—74°.

$C_{20}H_{24}O_5$ Calc.   C   69.7   H   7.03
                   Found   »   69.7   »   7.04

REDUCTION OF THE KETO GROUPS[16]

Dihydro-3,4-dimethoxyphenacyl coerulignol ether (VIII)

6.88 g of 3,4-dimethoxyphenacyl coerulignol ether and 4.0 g of aluminium isopropoxide were boiled in 25 ml of anhydrous isopropyl alcohol until no more acetone was formed. The product was hydrolyzed with dilute hydrochloric acid, yielding a yellow oil. The water phase was extracted with ether. The ethereal solution was combined with the oily layer, washed with water, and dried over sodium sulphate. The solution was filtered through a column of aluminium oxide and evaporated, yielding a light yellow crystallizing oil. Yield 5.3 g (75 %). M. p. 57—59°. On repeated recrystallization from ether, flat crystals of m. p. 62—63° were obtained. Mixed m. p. with the unreduced product (m. p. 73—74°) 45—52°. The analyses showed that the substance contained one mole of water of crystallization.

$$C_{20}H_{26}O_5 + H_2O \quad \text{Calc.} \quad C \quad 65.9 \quad H \quad 7.76 \quad OCH_3 \quad 25.5$$
$$\text{Found} \quad » \quad 66.3 \quad » \quad 7.78 \quad » \quad 25.6$$

On fusing the substance *in vacuo* and recrystallization from anhydrous ether, crystals of m. p. 65—66° were obtained.

$$C_{20}H_{26}O_5 \quad \text{Calc.} \quad OCH_3 \quad 26.9 \quad \text{Found} \quad OCH_3 \quad 27.0$$

The compound did not form a precipitate with 2,4-dinitrophenyl-hydrazine.

Tetrahydro-acetoguaiacyl-acetoguaiacone methyl ether (VI, $n = 2$)

6.4 g of acetoguaiacyl-acetoguaiacone methyl ether and 16.0 g of aluminium isopropoxide in 60 ml of absolute isopropyl alcohol were treated as described above, extracting with chloroform instead of ether. On drying *in vacuo*, the resulting oil turned into a yellowish, amorphous powder. Yield 4.5 g (70 %). No precipitate with 2,4-dinitrophenyl-hydrazine.

$$C_{19}H_{24}O_6 \quad \text{Calc.} \quad OCH_3 \quad 26.7 \quad \text{Found} \quad OCH_3 \quad 26.3$$

When the substance was heated in a capillary tube, softening commenced at about 50°. The 'melt' was very viscous but became transparent at about 60°. 'Collaps' took place at about 100°.

Hexahydro-di-(acetoguaiacyl)-acetoguaiacone methyl ether (VI, $n = 3$)

5.6 g of di-(acetoguaiacyl)-acetoguaiacone methyl ether and 12 g of aluminium isopropoxide in 60 ml of absolute isopropyl alcohol were treated as above. An almost white, amorphous powder was obtained. Yield 4.4 g (74 %). No precipitate with 2,4-dinitrophenyl-hydrazine.

$$C_{28}H_{34}O_9 \quad \text{Calc.} \quad OCH_3 \quad 24.1 \quad \text{Found} \quad OCH_3 \quad 24.7$$

Octahydro-tri-(acetoguaiacyl)-acetoguaiacone methyl ether
(VI, $n = 4$)

2.9 g of tri-(acetoguaiacyl)-acetoguaiacone methyl ether and 5 g of aluminium iso-propoxide in 35 ml of absolute isopropyl alcohol were treated as described above. 2.66 g (90 %) of an amorphous powder were obtained. No precipitate with 2,4-dinitrophenyl-hydrazine.

$$C_{37}H_{44}O_{12} \qquad Calc. \ OCH_3 \ 22.8 \qquad Found \ OCH_3 \ 22.8$$

When the substance was heated in a capillary tube, softening commenced at about 70°. The 'melt' was very viscous but became transparent at about 100°. 'Collaps' took place at about 130°.

Sulphite cookings

The ketonic compounds (V) were treated in the following manner:

0.5—1 g of the substance and 100 ml of sulphite cooking acid (5—6 % SO_2 and 1.4 % NaOH) were sealed in a pyrex glass tube. The tube was heated in an oven at 135° for 20 hours.

After cooling, all the tubes contained undissolved residues, consisting of unchanged starting material. Since the recovery of the latter amounted to 88—100 %, no attempts were made to work up the aqueous solutions.

The compounds also were heated with a cooking acid, containing 9—10 % SO_2 and 0.7 % NaOH as described above. The compounds were slightly decomposed, but more than 80 % could be recovered.

The above mentioned alcohols (VI and VIII) were cooked in autoclaves, rotating in an oil bath under conditions specified in table 1.

The 'waste liquors' were treated in the following way:

After removing the excess sulphur dioxide by passing in carbon dioxide or nitrogen, the solution was extracted with chloroform in order to dissolve decomposition products. The cations of the solution were then exchanged for hydrogen ions in a column of amber-lite. SO_2 was removed and an excess of a slurry of barium carbonate in water was added. After standing over night, the mixture was heated to boiling and filtered hot. The filtrate was evaporated to dryness. The residue was dissolved in a small amount of water and filtered. The resulting solution was precipitated with alcohol and ether, yielding the barium salt of the sulphonic acid as a white precipitate of small particle size. The latter was centrifuged off and washed with alcohol and ether. For purification the precipitation was repeated several times.

The barium salts obtained were dissolved in water and precipitated with an aqueous solution of S-1-naphthylmethylthiuronium chloride. The resulting products were isolated and analyzed in only two cases.

Sulphonic acid from VIII.
Barium salt:

$(C_{20}H_{25}O_7S)_2Ba$　　　Calc.　Ba　14.4　　OCH_3　19.5
　　　　　　　　　　　　　Found　〃　14.7　　　〃　　19.3

Naphthylmethylthiuronium salt:
Recrystallized from water. M. p. 148—150°.

$C_{32}H_{38}O_7N_2S_2$ Calc.   S   10.2 OCH_3 14.9
                Found   »   10.3   »   15.1

Sulphonic acid from VI, n = 2.
  Barium salt:

$C_{19}H_{22}O_{10}S_2Ba$ Calc.   Ba   22.5 OCH_3 15.2
                Found   »   22.6   »   15.1

Naphthylmethylthiuronium salt:

$C_{43}H_{48}O_{10}N_4S_4$ Calc.   S   14.1
                Found   »   13.8

Sulphonic acid from VI, n = 3.
  Barium salt:

$(C_{28}H_{31}O_{15}S_3)_2Ba_3$ Calc.   Ba   22.7 OCH_3 13.6
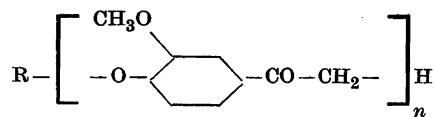   Found   »   22.5   »   13.4

Sulphonic acid from VI, n = 4.
  Barium salt:

$C_{37}H_{40}O_{20}S_4Ba_2$ Calc.   Ba   22.8 OCH_3 12.8
                Found   »   23.0   »   12.8

SUMMARY

A series of ethers of ω-hydroxy-acetoguaiacone of the general formula

$$R-\left[-O-\underset{}{\bigcirc}\!\!\!\!\overset{CH_3O}{}\!\!\!\!-CO-CH_2-\right]_n H$$

have been prepared and reduced to the corresponding secondary alcohols.

The sulphonation of the compounds with sulphite cooking acid has been studied.

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