

OLIGOMERIC PRODUCTS FROM BASIC HYDROLYSIS OF 4-HYDROXYBENZYL PHENYL SULFONES*

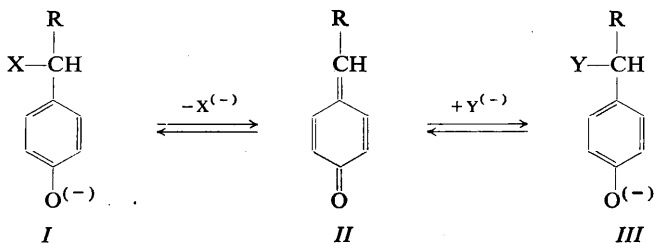
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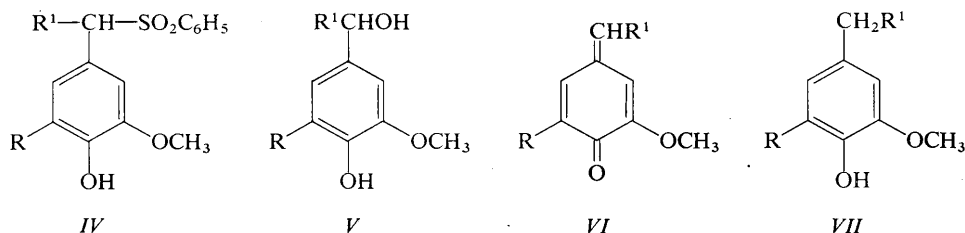
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When subjected to basic hydrolysis in the presence of potassium borohydride, 4-hydroxy-3-methoxybenzyl phenyl sulfone and 4-hydroxy-3-methoxybenzyl alcohol afford oligomeric products derived from 2,4'- or 4,4'-dihydroxydiphenylmethane. Analogous dimers are also formed from 1-(4-hydroxy-3-methoxyphenyl)ethyl phenyl sulfone and from 3,5-dimethoxy-4-hydroxybenzyl phenyl sulfone. 4-Alkylidene-2-methoxy (or 2,6-dimethoxy)-2,5-cyklohexadienone represents the non-isolable intermediate of condensation reactions. The ratio of products in the reaction mixture depends on the molar ratio and structure of reactants.

4-Hydroxybenzyl phenyl sulfones and the structurally related derivatives *I* ($X = \text{Cl}, \text{Br}, \text{OH}, \text{OR}, (^+)\text{N}(\text{CH}_3)_3, \text{SR}, \text{BO}_2, \text{SO}_2\text{R}$) belong to a group of compounds which exhibit an anomalously high alkylating ability in basic media¹⁻⁷. Since their electrophilic reactivity cannot be correlated⁸ with the Hammett σ_p constant of the phenoxide oxygen atom, 4-alkylidene-2,5-cyclohexadienone (*p*-quinone methide) *II* is assumed as the actual reactive particle. The formation rate of the quinone methide from the phenol *I* is mainly determined by the electron properties of the leaving group *X*. The concentration of *II* in the presence of the nucleophile *Y* is given by the equilibrium constants of both reactions. In sufficiently basic aqueous solutions, the concentration of hydroxyl ions is as high as that the recombination reaction can be neglected from the qualitative point of view. Thus, the substituted 4-hydroxybenzyl alcohol *III* ($Y = \text{OH}$) should be the single product.



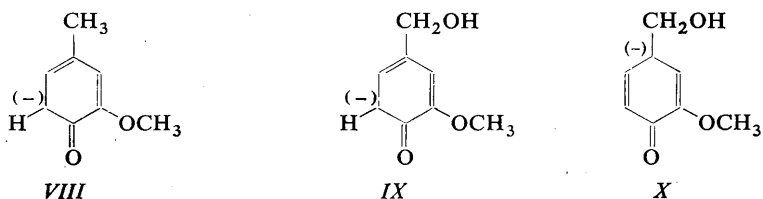
* Part IV in the series Quinone Methides and Fuchsones; Part I-III: This Journal 40, 142, 1768, 2093 (1975).



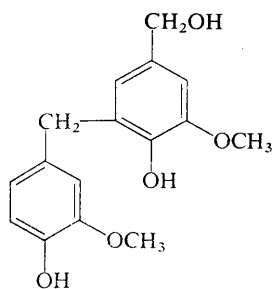
In formulae IV–VII: a, $\text{R} = \text{R}^1 = \text{H}$; b, $\text{R} = \text{H}$, $\text{R}^1 = \text{CH}_3$; c, $\text{R} = \text{OCH}_3$, $\text{R}^1 = \text{H}$.

In the present paper attention has been paid to investigation on products resulting from the basic hydrolysis of substituted 4-hydroxybenzyl phenyl sulfones IV and 4-hydroxybenzyl alcohols V. Substituents R and R^1 of sulfones IV and alcohols V were selected with respect to the potential application of the present results to the delignification of wood^{9,10} and bleaching of cellulose¹¹.

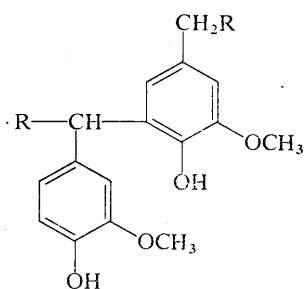
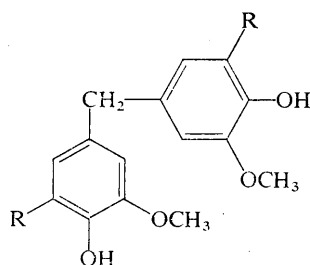
In preliminary hydrolyses of the sulfone IVa with 2M-KOH at 25–40°C, the reaction mixture contained only the unreacted sulfone in addition to the alcohol Va. At 100°C, the phenylsulfonyl group was completely split off, but the main reaction product was a polymer accompanied by a small amount of the alcohol Va and 2-methoxyphenol. As indicated by the presence of 2-methoxyphenol, the original alcohol Va undergoes at elevated temperatures a retroaldol reaction. The liberated formaldehyde is instantaneously involved into polycondensation reactions with the formation of phenol-formaldehyde-type resins. Similarly, the highly reactive intermediate II affords at a sufficiently high concentration a polymer of the benzyl ether type. An attempt was therefore made to suppress the two undesired side reactions by effecting the hydrolysis in the presence of potassium borohydride which is known to reduce both formaldehyde¹² and quinone methides¹³. The thus-modified agent reduced the sulfones at 100°C very fastly. The formation of polymers has not been observed in any case. As shown by a detailed examination of the hydrolytical course, 4-hydroxybenzyl alcohol is the initial reaction product. In preparative runs, the sulfones IVb and IVc were therefore replaced by the corresponding alcohols Vb and Vc.



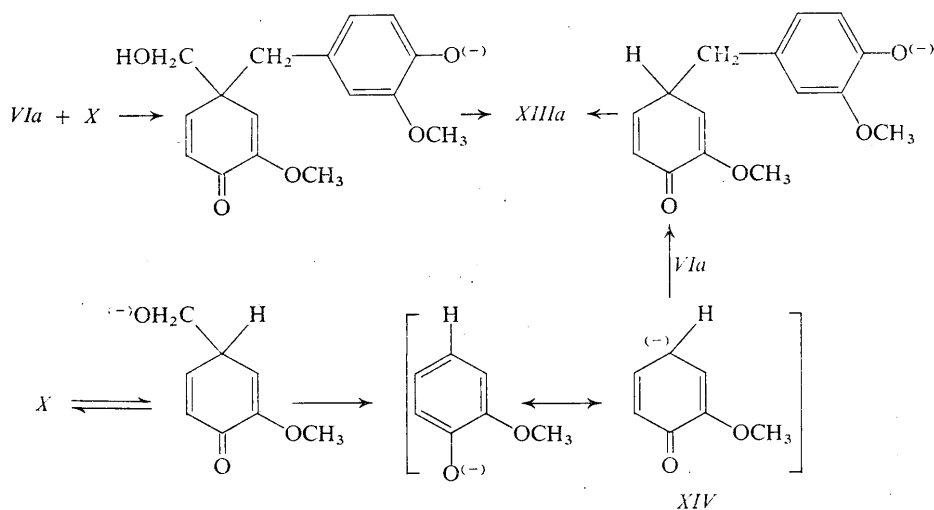
After the hydrolysis of 4-hydroxy-3-methoxybenzyl alcohol (Va), there were isolated seven compounds. At a high concentration of hydride ions ($[\text{KBH}_4]/[\text{Va}] = 20$),



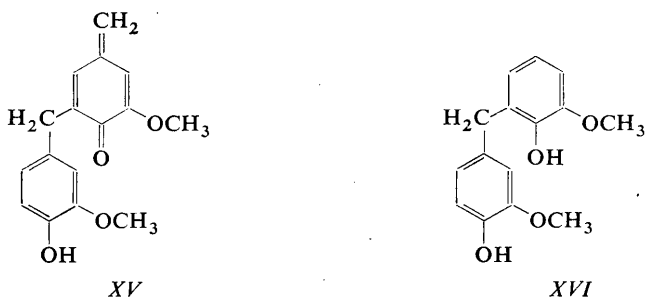
XII

XIa; R = H
XIb; R = CH₃XIIIa; R = H
XIIIb; R = OCH₃

reduction of the intermediary quinone methide *Vla* to 3-methoxy-4-methylphenol (*VIIa*) represents the main reaction. With the use of equimolecular concentrations of both reactants, those reactions predominate in which the canonic structures *VIII*–*X* of the phenoxide anion *VII* and the starting alcohol *Va* assert themselves. The carbanions *VIII* and *IX* are very easily attacked by the electrophilic centre of the quinone methide *Vla*. The intermediary tetrahedral species are aromatised by deprotonation to unsymmetrical diarylmethanes *XIa* and *XIIIa*. The diarylmethane *XIa* may of course also result by reduction of the quinone methide *XV*, formed by dehydration of the dimeric alcohol *XII*. This reaction probably predominates in initial phases of hydrolysis when concentration of 2-methoxy-4-phenol in the reaction mixture is low. The symmetrical diarylmethane *XIII* might be formed by two routes. One of them is

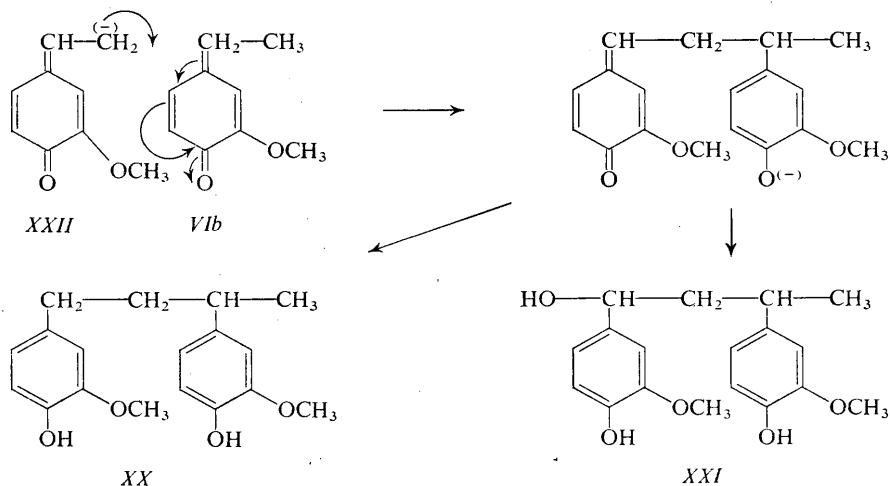


SCHEME 1



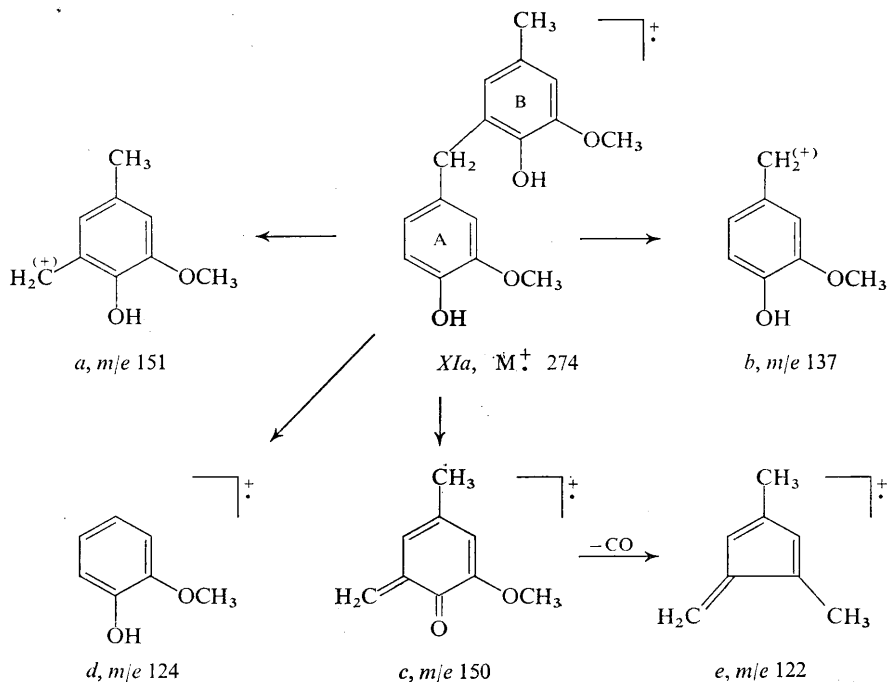
based on addition of the carbanion *X* to the quinone methide *Via* followed by removal of formaldehyde (Scheme 1). The other route requires addition of the mesomeric carbanion *XIV* (liberated from the alcohol *Va* by the retroaldol reaction) to the quinone methide *Via*. The latter reaction is undoubtedly faster than addition of the quinone methide *Via* to the sterically more hindered carbanion *X*; participation of the two mechanisms on the formation of the diarylmethane *XIII* must be therefore controlled by the rate of the retroaldol reaction. Since the diarylmethane *XVI* has never been found in the reaction mixture, the latter step is assumed to be slow and the symmetrical diarylmethane *XIIIa* is probably formed by the former mechanism.

The trimers *XVII* and *XVIII* are probably products of the reaction of the quinone methide *Via* with carbanions derived from dimers *XI* and *XIII*; the tetramer *XIX* is analogously derived from the trimer *XVIII*. The yields of compounds *XVII*–*XIX* are very small.



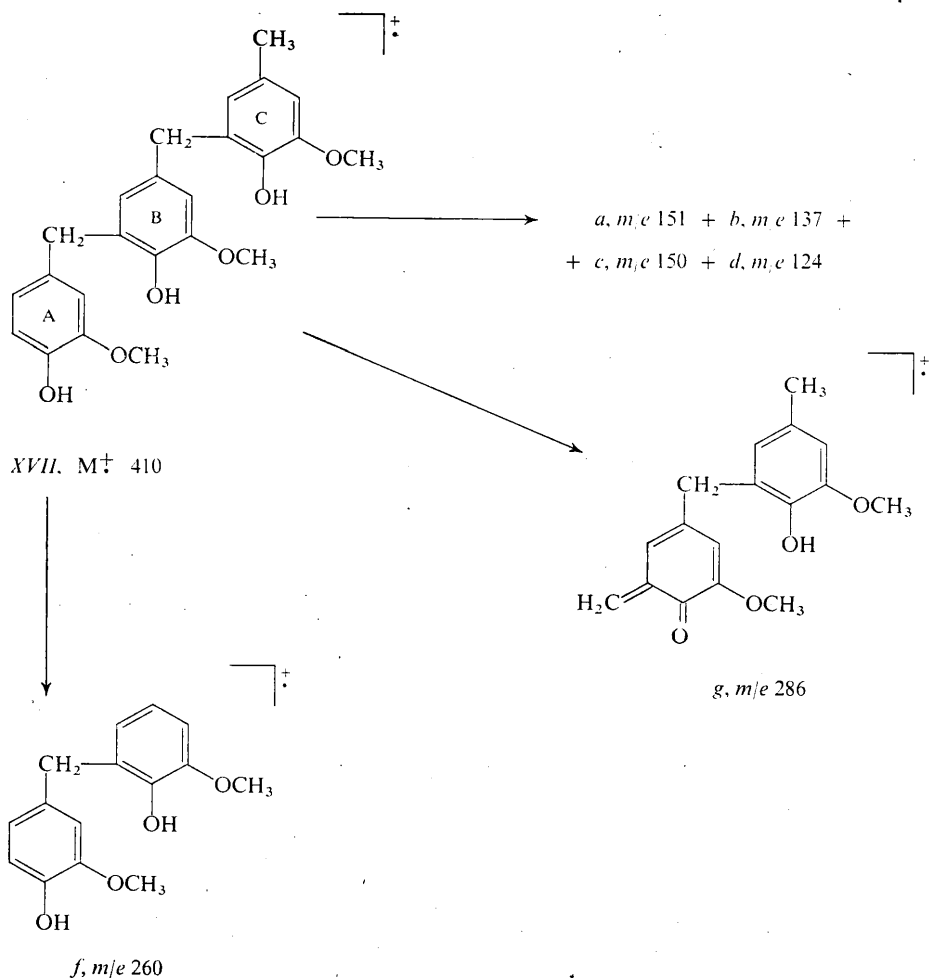
SCHEME 2

In hydrolysis of 4-(1-hydroxyethyl)-2-methoxyphenol (*Vb*), the sterical effect of the methyl group asserts itself to a considerable extent. 2-Methoxy-4-ethylphenol (*VII*) (formed by reduction of the quinone methide *VIb*) as the main product is accompanied by a very small amount of the dimeric product *XII* while the symmetrical 1,1-bis(4-hydroxy-3-methoxyphenyl)ethane (corresponding to the diarylmethane *XIIIa*) is not formed at all. Trace amount of compounds *XX* and *XXI* with the 1,3-diarylbutane structure have also been found. The methyl group of the quinone methide *VIb* is assumed to afford by the action of a base the carbanion *XXII* which attacks the electrophilic centre of the ethylenecyclohexadienone *VIb* (Scheme 2). To the quinonoid intermediate, either a hydroxide or hydride ion is then added. Other mechanisms of the formation of dimers *XX* and *XXI* such as dimerisation of 2-methoxy-4-vinylphenol or addition of this vinylphenol to the quinone methide *VIb* appear less probable since 4-vinylphenols are known to undergo polymerisation¹⁴ under conditions similar to the present ones. Hydrolysis of 4-hydroxy-3,5-dimethoxybenzyl alcohol (*Vc*) furnished the expected products, namely, approximately equal amounts of 2,6-dimethoxy-4-methylphenol (*VIIc*) (reduction product of the quinone methide *VIc*) and the symmetrical diarylmethane *XIIIb*.



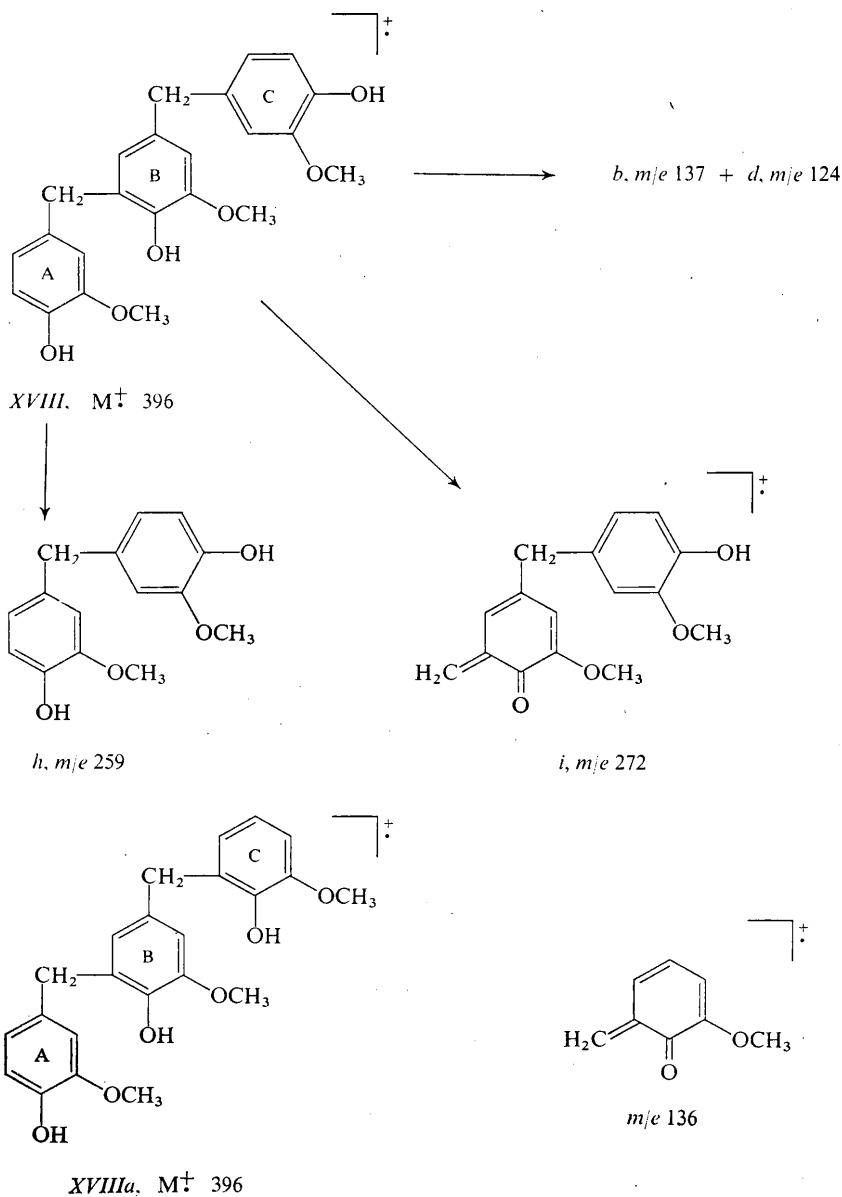
SCHEME 3

Suggested structures of the isolated compounds were confirmed by high resolution mass spectra. All the examined phenols exhibit an intensive molecular peak attributable to the stability of resonance structures of the quinonoid type including nonbonding electrons of oxygen-bearing functional groups. Decomposition of the molecular ion of hydroxyarylmethanes is relatively simple and may be demonstrated on 2,4'-dihydroxy-3,3'-dimethoxy-5-methyldiphenylmethane (*XIa*), the structure of which has been unambiguously established¹⁵. Bond cleavage between the methylene group and ring A or ring B (Scheme 3) affords ions *a* and *b* in almost equal amounts. However, the base peak is formed by the ion *c* of *m/e* 150, the direct precursor of which



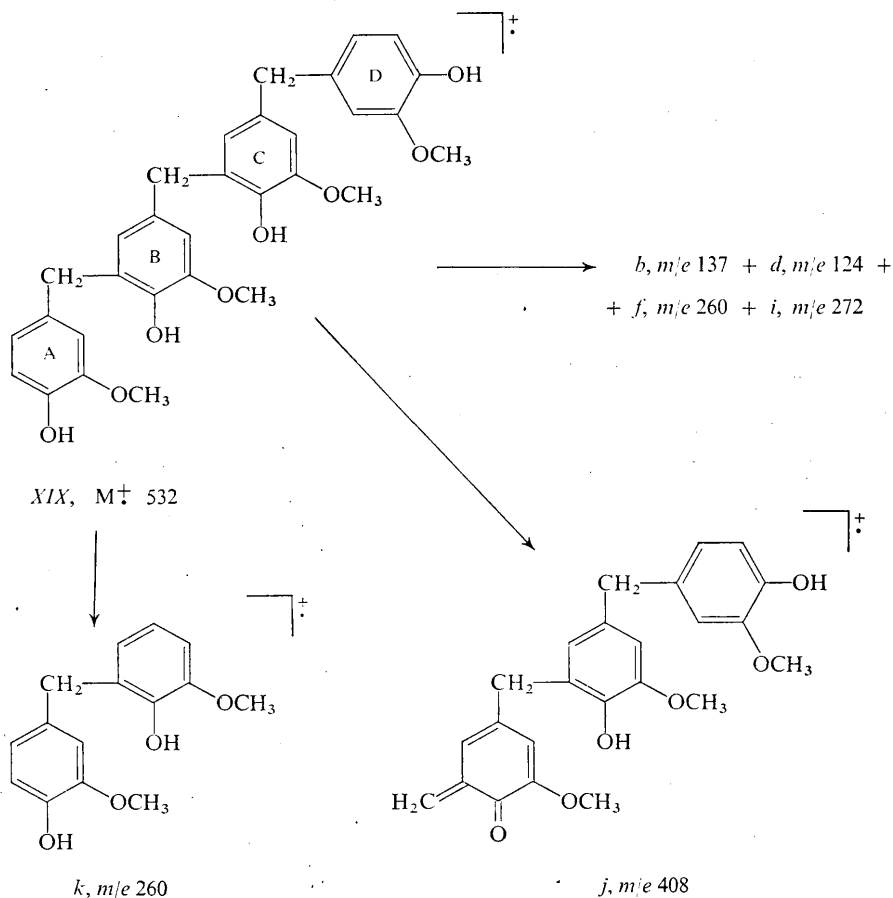
SCHEME 4

is the molecular ion M^+ (metastable peak at the mass of 82.0; calculated, 82.2). Formation mechanism of the fragment *c* and the complementary ion *d* may be inferred from interpretation of the mass spectrum of the diarylmethane *XIa*, the phe-



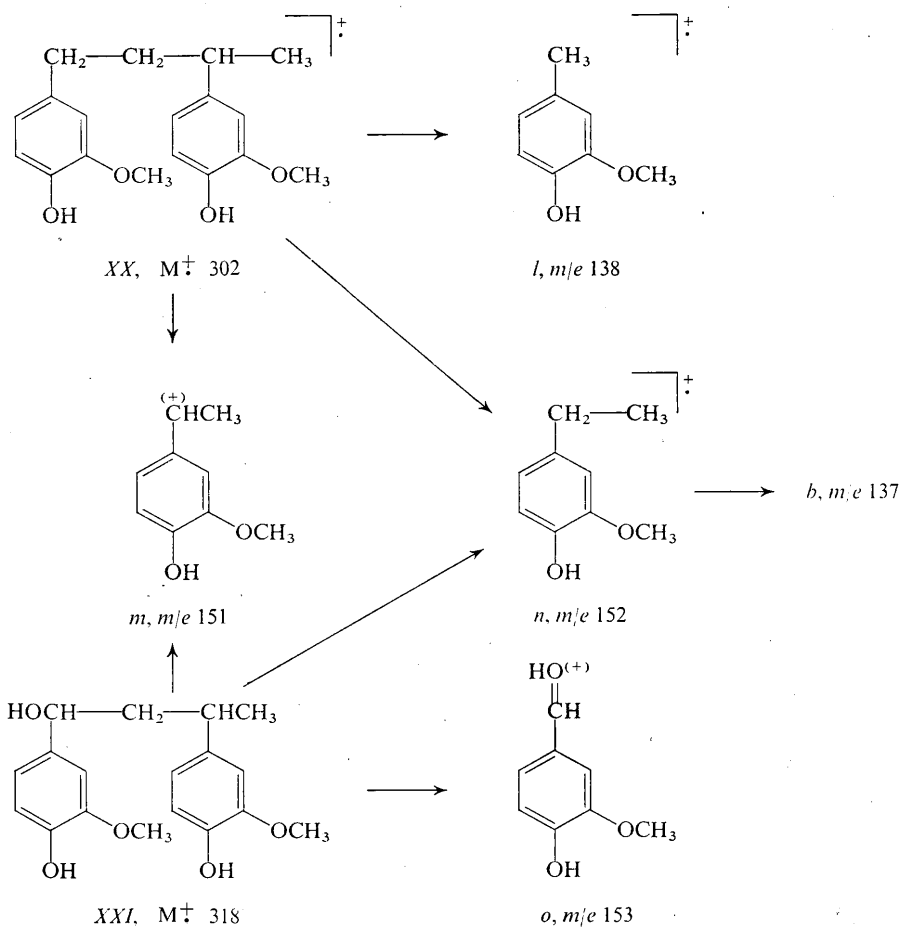
SCHEME 5

nolic protons of which had been replaced by deuterium. The mass of the fragment *d* increased by two units, *i.e.*, during the decomposition of the molecular ion, a cyclic transfer of deuterium occurred from the phenolic group of ring B onto the C₍₁₎ carbon atom of ring A. This fragmentation is typical of all 2-hydroxyarylmethanes (*vide infra*) and constitutes another example of the so called *ortho*-rearrangements (*e.g.*¹⁶). The spectrum of the diarylmethane *XIa* also contains an intensive peak *e*, formed by removal of carbon monoxide from the quinone methide ion *c*. The mass spectrum of the trimer *XVII* displayed fragments *a*, *b*, *c* and *d* (Scheme 4) along with ions *f* of *m/e* 260 and *g* of *m/e* 286. The coexistence of fragments *d* and *g* is attributable to the substitution of ring B by a benzyl group in *ortho*-position to the phenolic hydroxyl group. The same type of substitution in ring C is confirmed by intensive peaks of ions *c* and *f*.



SCHEME 6

The mass spectrum of the trimer XVIII (Scheme 5) is considerably simpler than that one of the trimer XVII and contains in addition to ions *b* and *d* also the heavier fragments *h* and *i*. From combination of these ions, two alternative formulae XVIII and XVIIIa may be inferred (the trimer XVIIIa may be formed by *ortho*-condensation of compound XIIa with 2-methoxyphenol). In addition to ions *b*, *d*, *h*, and *i*, the spectrum of the trimer XVIIIa should however exhibit an ion of m/e 136 corresponding to fragmentation between rings B and C accompanied by an *ortho*-rearrangement. Owing to the absence of the latter ion in the spectrum, the structure XVIIIa may be excluded. The structure of the tetramer XIX is based on combination of fragments *d* and *j*, and *i* and *k* (Scheme 6) and on the absence of the ion of m/e 136.



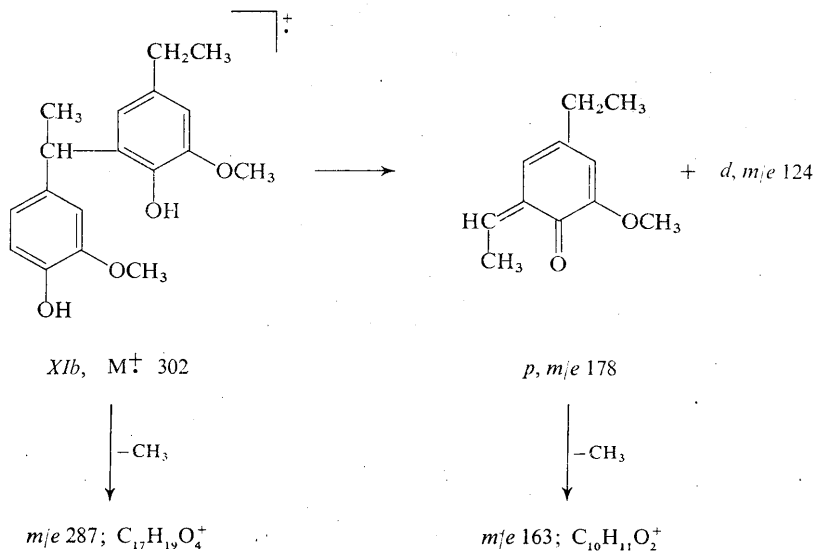
SCHEME 7

Mass spectra of dimers *XX* and *XXI* exhibit as the base peak the ion *m* of m/e 151 (Scheme 7) along with the slightly less intensive peak *n* of m/e 152. These two ions could favour an alternative symmetrical 2,3-diarylbutane structure. Such a structure can be however excluded particularly on the basis of the presence of ion *l* in the spectrum of the dimer *XX* which is formed by β -cleavage¹⁷ from the molecular ion (m^* 63.00; calculated 63.06). Similarly, the oxonium ion *o* with a benzylic hydrogen is conclusive for the proposed structure of the hydroxy compound *XXI*.

An *ortho*-rearrangement of the molecular ion also occurs in the case of compound *XIb*. In accordance with fragmentation of the analogous dimer *XIa*, the base peak (m/e 178) can be ascribed the stable *o*-quinone methide structure *p* (Scheme 8). However, the accompanying ion *d* (m/e 124) exhibits a very low intensity. A significant feature in the spectrum of the dimer *XIb* consists in demethylation of both the molecular ion and the quinonoid ion *p*, as confirmed by the presence of metastable peaks.

EXPERIMENTAL

- Melting points were taken on a heated microscope stage (Kofler block) and are uncorrected. Analytical samples were dried at 0.1 Torr and room temperature for 7 h. The IR spectra were measured in chloroform on a IR-20 spectrophotometer (Carl Zeiss, Jena, German Democratic Republic). Mass spectra were taken on an A.E.I. MS 902 mass spectrophotometer (electron energy, 70 eV; source temperature, 110–230°C; accuracy (high resolution), 2 p.p.m.).



SCHEME 8

4-Hydroxybenzyl Phenyl Sulfones *IVa*—*IVc*

Compounds *IVa*—*IVc* were prepared from the corresponding alcohols and sodium benzenesulfinate in acetic acid according to Jerkeman and Lindberg⁷ in 90—95% yields. Analytical samples were crystallised from ethanol. 4-Hydroxy-3-methoxybenzyl phenyl sulfone (*IVa*), m.p. 133—134°C; for $C_{14}H_{14}O_4S$ (278.3) calculated: 60.41% C, 5.07% H; found: 60.50% C, 5.06% H. 1-(4-Hydroxy-3-methoxyphenyl)ethyl phenyl sulfone (*IVb*), m.p. 123—125°C; for $C_{15}H_{16}O_4S$ (292.4) calculated: 61.62% C, 5.51% H, 10.96% S; found: 61.70% C, 5.43% H, 10.95% S. 4-Hydroxy-3,5-dimethoxybenzyl phenyl sulfone (*IVc*), m.p. 134—135°C; for $C_{15}H_{16}O_5S$ (308.3) calculated: 58.43% C, 5.23% H, 10.40% S; found: 58.50% C, 5.15% H, 10.45% S.

Hydrolysis of 4-Hydroxy-3-methoxybenzyl Phenyl Sulfone (*IVa*)

A mixture of sulfone *IVa* (20 mmol), potassium borohydride (20 mmol), potassium hydroxide (60 mmol), and water (30 ml) was heated under nitrogen at 100°C for 150 min, cooled down, adjusted to pH 4 with ice-cold 2M-HCl, and extracted with five 30 ml portions of chloroform. The extracts were combined, washed with two 30 ml portions of saturated aqueous sodium hydrogen carbonate and two 30 ml portions of water, dried over anhydrous magnesium sulfate, and evaporated under diminished pressure. The components of the residue were isolated either by preparative thin-layer chromatography or gradient elution on a column of silica gel in the solvent system light petroleum-ether. The sulfones *IVb* and *IVc* and alcohols *Va*—*Vc* were hydrolysed under the same conditions. The identity of products from hydrolyses of compounds *IVb* and *Vb*, as well as *IVc* and *Vc* was established qualitatively by thin-layer chromatography; the separation of products from reaction mixtures was then performed with hydrolyses of alcohols *Vb* and *Vc* only.

The following compounds were isolated: 2-Methoxy-4-methylphenol (*VIIa*), m.p. 219—220°C (reported¹⁸, 220—221°C). 4-Ethyl-2-methoxyphenol (*VIIb*), b.p. 107—108°C/9 Torr (reported¹⁹, b.p. 107—109°C/9 Torr). 2,6-Dimethoxy-4-methylphenol (*VIIc*), m.p. 39—40°C (reported²⁰, m.p. 39—40°C). 2-(4-Hydroxy-3-methoxybenzyl)-6-methoxy-4-methylphenol (*XIa*), m.p. 108 to 109°C (reported²¹, m.p. 114—115°C). 2-(4-Hydroxy-3-methoxybenzyl)-4-hydroxymethyl-6-methoxyphenol (*XII*), m.p. 79—81°C; for $C_{16}H_{18}O_5$ (290.3) calculated: 66.20% C, 6.20% H; found: 66.28% C, 6.20% H. 4-(4-Hydroxy-3-methoxybenzyl)-2-methoxyphenol (*XIIIa*), m.p. 108—109°C (reported²¹, m.p. 109—110°C). 4-(4-Hydroxy-3,5-dimethoxybenzyl)-2,6-dimethoxyphenol (*XIIIb*), m.p. 112—113°C (reported²¹, m.p. 112—113°C). 2-[3-(4-Hydroxy-3-methoxybenzyl)-4-hydroxy-5-methoxybenzyl]-6-methoxy-4-methylphenol (*XVII*), m.p. 106—108°C; for $C_{24}H_{26}O_6$ (410.5) calculated: 70.22% C, 6.38% H; found: 70.06% C, 6.50% H. 4-[3-(4-Hydroxy-3-methoxybenzyl)-4-hydroxy-5-methoxybenzyl]-2-methoxyphenol (*XVIII*), m.p. 63—65°C; for $C_{23}H_{24}O_6$ (396.4) calculated: 69.68% C, 6.10% H; found: 69.48% C, 6.30% H. 4-[3-(3-(4-Hydroxy-3-methoxybenzyl)-4-hydroxy-5-methoxybenzyl)-4-hydroxy-5-methoxybenzyl]-2-methoxyphenol (*XIX*), noncrystalline solid; for $C_{31}H_{32}O_8$ (532.6) calculated: 69.91% C, 6.06% H; found: 69.98% C, 5.87% H.

The phenols *XIb*, *XX*, and *XXI* were isolated in amounts below 1 mg and their purity was established by thin-layer chromatography in solvent systems light petroleum-benzene and light petroleum-ether. Their brutto formulae were determined by high-resolution mass spectral measurements.

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