

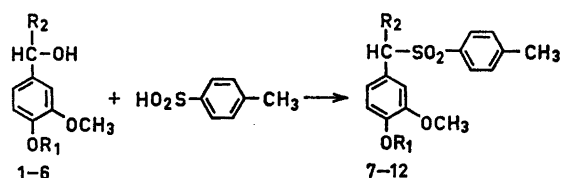
Sulphones of Lignin Models, Synthesis and Reactions in Alkali

PER JERKEMAN and BENGT LINDBERG

Träkemiska avdelningen, Svenska Träforskningsinstitutet, Stockholm, Sweden

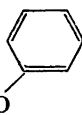
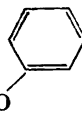
The *p*-tolylsulphones (7-12) of a number of ligninlike benzyl alcohols (1-6) have been prepared. On treatment of these substances with alkali, those containing a methoxyl group in the *para*-position suffered the expected elimination of an aroxyl group in the β -position and a subsequent "retro aldol condensation". For those with a hydroxyl group in the *para*-position elimination of sulphinic acid occurred in favour of the "retro aldol condensation". The benzyl alcohol (3) and its sulphone (9) on treatment with alkali yielded the dimeric 2,5-di(4-hydroxy-3-methoxyphenyl)-1,4-dioxan (18).

In a previous paper,¹ the synthesis of some sulphones from benzyl alcohols, *e.g.* vanillyl alcohol (1) and veratryl alcohol (2), were reported. This investigation has now been extended to the synthesis of sulphones from some more lignin like benzyl alcohols, and to a study of their reactions with alkali.



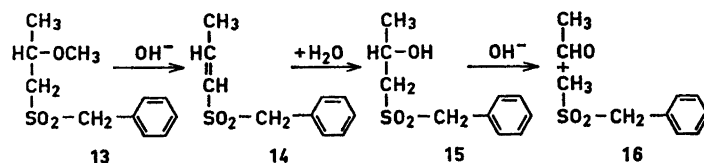
The benzyl alcohols were prepared by conventional methods, as described in the experimental section. The sulphones were prepared by heating equivalent amounts of the benzyl alcohol and toluene-*p*-sulphonic acid in aqueous acetic acid at 100°. The concentration of each component was about 0.05 M. The reaction conditions, yields of the sulphones and their melting points are listed in Table 1. As previously observed the benzyl alcohols possessing a *p*-hydroxy group (3,4) reacted more readily than those with a *p*-methoxy group (5,6). The presence of an aroxyl group at C-2 in the side chain (4,6) reduced the rate of reaction considerably, especially when (as in 6) there was

Table 1. Sulphones from some lignin like benzyl alcohols

Benzyl alcohol	Reaction conditions		Sulphone	M.p.	Yield %
	Reaction medium	Time, h			
1. R ₁ = R ₂ = H	3 M AcOH	3	7	175–176°	91
2. R ₁ = CH ₃ , R ₂ = H	3 M AcOH	3	8	176–177°	61
3. R ₁ = H, R ₂ = CH ₂ OH	3 M AcOH	3	9	148–149°	69
4. R ₁ = H, R ₂ = CH ₂ O 	50% aq. AcOH-EtOH, 4.2:1	6	10	69–72°	95
5. R ₁ = CH ₃ , R ₂ = CH ₂ OH	50% aq. AcOH-EtOH 10:3	16	11	113–115°	82
6. R ₁ = CH ₃ , R ₂ = CH ₂ O 	95% aq. AcOH-EtOH, 2:1	18	12	74–76°	51

no free *p*-hydroxy group. These results are in good agreement with those of earlier studies,² concerning the reactions of the same or similar benzyl alcohols with sulphite.

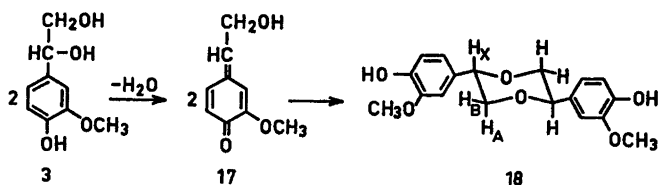
The reactions of sulphones in alkaline solutions have been studied extensively (*cf.* Refs. 3–7). A typical example³ is the reaction of benzyl-2-methoxypropyl sulphone (13) with alkali which eliminates methanol to give benzyl prop-1-enyl sulphone (14). This substance adds water to give benzyl 2-hydroxypropyl sulphone (15), which is then subjected to a reverse aldol condensation type of reaction, yielding acetaldehyde and benzyl methyl sulphone (16).



The same types of reactions could be expected to occur when the sulphones prepared in this study were subjected to similar treatments. (3,4-Dimethoxyphenyl)-methyl *p*-tolylsulphone (8) was recovered unchanged after treatment with 2 M aqueous sodium hydroxide at 100° for 3 h. On treatment of 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-ethyl *p*-tolylsulphone (12) with 2 M aqueous sodium hydroxide at room temperature, guaiacol was eliminated and 1-(3,4-dimethoxyphenyl)-2-hydroxyethyl *p*-tolylsulphone (11) was obtained. Similar treatment of either of the sulphones 11 or 12, but at 100°, yielded the sulphone 8.

The reactions of the sulphones with a free *p*-hydroxy group were more complicated. (4-Hydroxy-3-methoxyphenyl)-methyl *p*-tolylsulphone (7) was fairly stable in 2 M sodium hydroxide at room temperature and could be methylated to 8 in a good yield by treatment with dimethyl sulphate and alkali. In 2 M sodium hydroxide at 100°, however, it was completely degraded. Vanillyl alcohol (1) and di-(4-hydroxy-3-methoxyphenyl)-methane could be isolated from the reaction mixture. The latter is one of the main components obtained on alkaline treatment of vanillyl alcohol, and the first step in the degradation is obviously the elimination of toluene-*p*-sulphinic acid from the sulphone. This acid, however, could not be isolated from the mixture, probably because of its instability under the reaction conditions. By analogy with this result, sulphone 7 could not be isolated after alkaline treatment, at 100°, of either 1-(4-hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)-ethyl *p*-tolylsulphone (10) or 1-(4-hydroxy-3-methoxyphenyl)-2-hydroxy-ethyl *p*-tolylsulphone (9). The presence of guaiacol was, however, observed in the complex reaction product obtained from the former, showing that some β -elimination had taken place.

A substance, m.p. 213–214°, was obtained as the main reaction product when either 1-(4-hydroxy-3-methoxyphenyl)-1,2-dihydroxyethane (3) or its corresponding sulphone (9) were treated with 2 M alkali at 100°. The analyses were in agreement with the formula $[C_8H_7O(OCH_3)]_n$ where *n* has a value of 2 as indicated by molecular weight determination. It gives a diacetate and is most probably a dimer of the methylene quinone (17) formed from (3) by elimination of water.



The NMR spectrum (of the diacetate in deuterio chloroform) was in good agreement with the structure of 2,5-di-(4-hydroxy-3-methoxy-phenyl)-1,4-dioxan. In addition to the three acetyl protons ($\tau = 7.68$) three methoxyl protons ($\tau = 6.11$), and three aromatic protons (τ about 2.96), an ABX spectrum (see formula 18) of three protons ($\tau = 6.23, 5.85$ and 5.28) was obtained. The following coupling constants for the ABX spectrum were observed: $J_{AX} = 10.0$, $J_{BX} = 3.0$ and $J_{AB} = 12.0$ cps.

A *trans*-arrangement of the two guaiacyl groups appears to be most probable and comparison with the NMR spectra of the two 2,5-diphenyl-1,4-dioxans⁸ supports this assumption. The bands due to the hydrogen atoms in the dioxan ring of *trans*-2,5-diphenyl-1,4-dioxan and 2,5-di(4-acetoxy-3-methoxyphenyl)-1,4-dioxan were superimposable. The spectrum of the *cis*-2,5-diphenyl-1,4-dioxan was quite different.

EXPERIMENTAL

Melting points are corrected. Extracts were dried over magnesium sulphate and concentrated under reduced pressure. Thin layer chromatography was performed on silica gel G.⁹

1-(4-Benzoyloxy-3-methoxyphenyl)-acetoxy ethanone. 1-(4-Benzoyloxy-3-methoxyphenyl)-2-bromo ethanone¹⁰ (90 g) and potassium acetate (27 g) were dissolved in anhydrous ethanol (600 ml). Sodium iodide (1.80 g) was added and the solution boiled under reflux for 1.5 h. The mixture was then poured into water (600 ml) and extracted with chloroform (3 × 300 ml). The chloroform layer was washed with water, dried and concentrated to a syrup. Crystallisation from ethanol yielded the title compound (71 g), m.p. 133–135°. (Found: C 68.9; H 6.14; O 25.6. C₁₈H₁₆O₅ requires: C 68.8; H 5.78; O 25.5).

1-(4-Benzoyloxy-3-methoxyphenyl)-2-hydroxy ethanone. 1-(4-Benzoyloxy-3-methoxyphenyl)-2-acetoxy ethanone (7.0 g) was dissolved in 60 % aqueous ethanol (1500 ml) in which barium carbonate (30 g) was suspended. The mixture was boiled under reflux for 15 h, filtered, and the filtrate extracted with chloroform (3 × 300 ml). The chloroform solution was washed with water, dried and concentrated to a syrup (5.4 g). This syrup, which was chromatographically pure yielded the substance on crystallisation from ethanol, m.p. 118–119°. (Found: C 70.6; H 6.05; O 23.6. C₁₆H₁₆O₄ requires: C 70.6; H 5.94; O 23.5).

(4-Hydroxy-3-methoxyphenyl)-ethane-1,2-diol (3) was prepared by catalytic hydrogenation (palladium on charcoal) of a suspension of the previous compound in anhydrous ethanol. It was obtained in almost quantitative yield as a colourless oil, giving only one spot on thin layer chromatography (ethyl acetate). The substance has previously been prepared by Axelrod, Kopin and Mann¹¹ who followed a different route.

1-(4-Hydroxy-3-methoxyphenyl)-2-hydroxyethyl p-tolylsulphone (9). The benzyl alcohol 3 (3.7 g), sodium toluene-*p*-sulphinat tetrahydrate (5.4 g) and sulphuric acid (1.0 g) were dissolved in 3 M aqueous acetic acid (160 ml) and the solution heated on a steam bath for 3 h. Hot water (160 ml) was added and the solution kept at room temperature overnight, during which time the crystalline sulphone precipitated. Further material was obtained by extracting the mother liquor with chloroform, the total yield being 4.5 g. Crystallisation from benzene-ligroin yielded the pure substance, m.p. 148–149°. (Found: S 10.06. C₁₈H₁₈O₅ S requires: S 9.94).

1-(4-Hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)-ethyl p-tolylsulphone (10). 1-(4-Hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)-ethanol (0.40 g), prepared according to Gierer and Norén,¹² and sodium toluene-*p*-sulphinat tetrahydrate (0.56 g) were dissolved in a mixture of 50 % aqueous acetic acid (80 ml) and ethanol (24 ml). Sulphuric acid (0.1 g) was added and the solution heated on a steam-bath for 6 h, neutralised with sodium hydroxide and extracted with chloroform. The chloroform solution was washed with water, dried and concentrated. The resulting syrup (0.56 g) which gave essentially one spot on thin layer chromatography (chloroform) was crystallised from benzene-ligroin, yielding colourless crystals, m.p. 69–72°. (Found: S 7.36. C₂₃H₂₄O₆S requires: S 7.49).

(3,4-Dimethoxyphenyl)-ethane-1,2-diol (5), previously prepared by Freudenberg,¹³ was prepared from 1-(3,4-dimethoxyphenyl)-2-hydroxy ethanone¹⁴ by reduction with sodium tetrahydrido borate in 85 % ethanol. The yield of the product, m.p. 82–83°, was almost quantitative.

1-(3,4-Dimethoxyphenyl)-2-hydroxyethyl p-tolylsulphone (11). The benzylalcohol 5 (2.0 g) and sodium toluene-*p*-sulphinat tetrahydrate (4.0 g) were dissolved in a mixture of 50 % acetic acid (400 ml) and ethanol (120 ml). Sulphuric acid (0.8 g) was added and the mixture heated on a steam-bath for 16 h. It was then diluted with water (500 ml), neutralised with sodium hydroxide and extracted with chloroform. The chloroform solution was washed with water, dried and concentrated to a syrup (2.8 g). This syrup, which was chromatographically pure, was crystallised from ethanol, yielding the substance, m.p. 113–115°. (Found: OCH₃ 18.11; S 9.36. C₁₇H₂₀O₆S requires OCH₃ 18.45; S 9.53).

1-(3,4-Dimethoxyphenyl)-2-(2-methoxyphenoxy)-ethyl p-tolylsulphone (12). 1-(3,4-Dimethoxyphenyl)-2-(2-methoxyphenoxy)-ethanol (6), (1.0 g), prepared according to Gierer and Norén,¹² and sodium toluene-*p*-sulphinat tetrahydrate (1.0 g) were dissolved in a mixture of 95 % acetic acid (50 ml) and ethanol (25 ml). Sulphuric acid (0.2 g) was

added and the mixture was heated on a steam-bath for 18 h, diluted with water (300 ml), neutralised with sodium hydroxide and extracted with chloroform. The chloroform solution was washed with water, dried and concentrated. The resulting syrup (0.74 g) was crystallised from ethanol to yield the pure substance, m.p. 74–76°. (Found: OCH₃, 21.02; S 7.33. C₂₄H₂₆O₆S requires: OCH₃, 21.04; S 7.24).

Alkaline treatment of the sulphones

Sulphones 8, 11, and 12 (30 mg of each) were treated with 2 M aqueous sodium hydroxide (10 ml) at 100° for 3 h. The solutions were then allowed to cool, neutralised with sulphuric acid and extracted with chloroform. The chloroform layer was washed with water, dried and concentrated. Sulphone 8 was recovered unchanged. From the sulphones 11 and 12, crystalline (3,4-dimethoxyphenyl)-methyl *p*-tolyl sulphone (8), m.p. 176–177° was obtained in yields of 24 mg and 12 mg, respectively. The presence of guaiacol in the reaction mixture obtained from the latter was demonstrated by thin layer chromatography (chloroform).

Sulphone 12 (10 mg) was dissolved in a mixture of 2 M aqueous sodium hydroxide (10 ml) and ethanol (4 ml), kept at room temperature for 3 h and then worked up as above. Sulphone 11 (2 mg), m.p. 112–114°, could be isolated, by thin layer chromatography (benzene-methanol 96:4), from the reaction mixture, which also contained several other components.

Sulphone 7, when treated with 2 M sodium hydroxide and the mixture worked up as above, yielded a product from which vanillyl alcohol (6), m.p. 112–114°, could be obtained by crystallisation from benzene. One of the main components in the mother liquors was isolated by thin layer chromatography (chloroform). It was obtained crystalline, m.p. 101–104°, and proved to be identical with an authentic sample of di-(4-hydroxy-3-methoxyphenyl)-methane. When the alkaline treatment was performed at room temperature for 3 h, most of the sulphone was unchanged.

Sulphone 7 (300 mg) was dissolved in a mixture of ethanol (10 ml) and dimethyl sulphate (1.5 ml). 2 M sodium hydroxide (10 ml) was added in portions over a period of 2 h, after which the mixture was kept for 2 h at room temperature and then, after addition of 2 M sodium hydroxide (50 ml) was heated on a steam-bath for 1.5 h. From the mixture the sulphone 8 (128 mg), m.p. 176–177° could be isolated, the greater part of which crystallised when the solution was cooled.

Sulphones 9 and 10, on alkaline treatment at 100° as above, yielded products containing several components, as shown by thin layer chromatography. Guaiacol was detected in the product obtained from sulphone 10. The starting materials could not be detected in the products.

2,5-Di-(4-hydroxy-3-methoxyphenyl)-1,4-dioxan. Sulphone 9 (100 mg) was dissolved in 2 M aqueous sodium hydroxide, kept at 100° for 3 h and the product worked up as above. A substance (11 mg), m.p. 213–214°, was obtained from the resulting syrup by crystallisation from ethanol. (Found: OCH₃, 18.62; C 65.6; H 6.24; O 28.3. C₁₈H₂₀O₆ requires: OCH₃, 18.68; C 65.0; H 6.08; O 28.9). A diacetate, m.p. 220°, was obtained by acetylation with acetic anhydride and pyridine, and crystallisation of the product from ethanol (Found: C 63.0; H 5.80; O 31.3. C₂₂H₂₄O₈ requires: C 63.5; H 5.83; O 30.7).

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