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The Cleavage of β-Mercaptoalkyl-arylethers with Alkali

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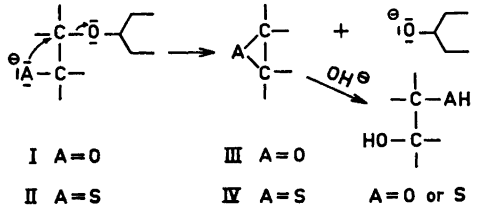
Three guaiacylethers of thioglycerols (VIII, XIII, XVIII) have been prepared and their behaviour towards 2 N sodium hydroxide investigated. Comparison of these with the corresponding guaiacylethers of glycerol revealed that the sulphur-containing compounds were cleaved much more easily. This has been attributed to the more extensive dissociation of the mercapto groups and the stronger nucleophilicity of the mercaptide anions compared with the hydroxyl groups and alcoholate anions, respectively. The possible significance of these findings in the chemistry of sulphate cooking is briefly outlined.

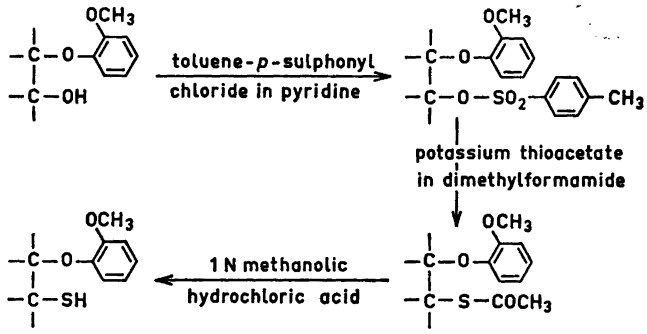
In connection with investigations on the alkaline degradation of lignin it has been recently shown[1,2] that the splitting of β-hydroxylalkyl-arylethers (type I) with alkali proceeds *via* the corresponding epoxides (III).



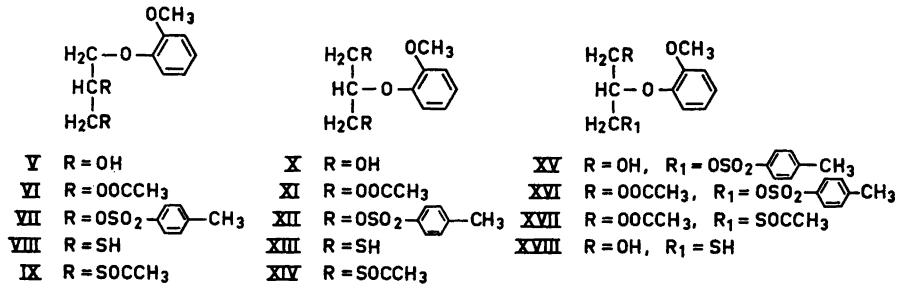
During sulphate cooking mercapto groups may be introduced into the side-chains of lignin,[3] giving rise to the formation of β-mercaptoalkyl-arylether structures (type II). It therefore seemed desirable to study the behaviour of model compounds, representing this structural type (II), towards alkali.

Three alkyl-arylethers, containing at least one neighbouring mercapto group (VIII, XIII, and XVIII) were prepared from the corresponding hydroxy compounds (V and X), *via* the toluene-*p*-sulphonyl esters (VII, XII, and XV) and thioacetates (IX, XIV, and XVII).[4]

For the preparation of compound XVIII, the hydroxyl group in the intermediate toluene-*p*-sulphonyl ester XV was protected by acetylation before the toluene-*p*-sulphonyloxy group was exchanged for the thioacetyl group.



The toluene-*p*-sulphonyl esters and the dithioacetates were all crystalline. Their melting points and analyses are given in the experimental section. The free thiols, however, were obtained as faintly coloured oils. For the study of the alkaline cleavage of the arylether linkages in compounds VIII, XIII, and XVIII it was more convenient to use the corresponding *S*-acetates IX, XIV, and XVII. In separate experiments it was demonstrated that the alkaline



hydrolysis of the *S*-acetyl groups, preceding the alkaline splitting of the arylether linkages, was not the rate-determining step in the splitting of compounds IX, XIV, and XVII.

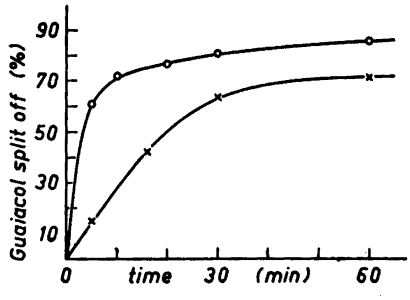


Fig. 1. Treatment of 2,3-di-*S*-acetyl-1-*O*-(*o*-methoxy-phenyl)-2,3-dithioglycerol (IX) with 2 N NaOH at 30° (×) and at 60° (O).

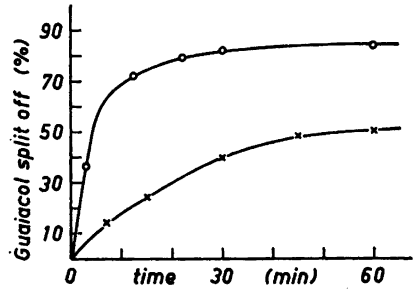


Fig. 2. Treatment of 1,3-di-*S*-acetyl-2-*O*-(*o*-methoxy-phenyl)-1,3-dithioglycerol (XIV) with 2 N NaOH at 60° (×) and at 100° (O)

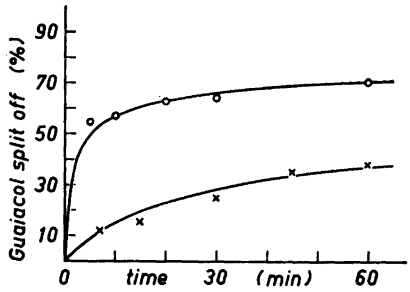


Fig. 3. Treatment of 3-*O*-acetyl-1-*S*-acetyl-2-*O*-(*o*-methoxy-phenyl)-1-monothioglycerol (XVII) with 2 N NaOH at 60° (×) and at 100° (O).

The thioacetates IX, XIV, and XVII were treated with 2 N sodium hydroxide at 30°, 60°, and 100° and the guaiacol split off was determined by gas chromatography.[5] As can be seen from Table 1 and Figs. 1, 2, and 3, the guaiacylether linkage in the thiols VIII, XIII, and XVIII, which result from the thioacetates IX, XIV, and XVII, respectively, was split at these low temperatures to a considerable degree, whereas the guaiacylether linkage in the corresponding hydroxy compounds V and X proved to be stable under the same conditions and also after prolonged reaction times (see Table 1).

The remarkable ease of splitting of the arylether bond in β-mercaptoalkyl-arylethers (type II) is undoubtedly due to a neighbouring group effect of the mercaptide anion resulting in the formation of the corresponding episulphides (IV). Thus, the cleavage of alkyl-arylethers containing a neighbouring mercapto group provides a new example of an intramolecular displacenent leading to fission of a C-O bond. The mechanism involved is apparently analogous to the mechanism of the mild alkaline splitting of α-mercaptoesters. Of the latter type of reaction many examples are known (*cf.* hydrolysis of *O*-acetyl-mercaptoethanol,[6] *trans*-1-acetoxy-2-mercaptocyclohexane,[6] *trans*-1-chloro-2-mercapto-cyclopentane,[7] β-chloro-ethylmercaptan,[8] 1-*O*-acetyl-2,3-dithioglycerol ("BAL-*O*-acetate")[6] and others).

The greater lability of β-mercaptoalkyl-arylethers towards alkali compared with the corresponding β-hydroxy compounds may be explained by the com-

Table 1.

Substance	Reaction temperature (°C)	Reaction time, h	Guaiacol split off (%)
IX	30	1	72
IX	60	1	86
XIV	60	1	51
XIV	100	1	84
XVII	60	1	38
XVII	100	1	70
VI	100	4	0
XI	100	4	0

plete dissociation of the mercapto groups under the conditions used, and by the stronger nucleophilic attack of the resulting mercaptide anions on the neighbouring carbon atom.

Thus, if it is assumed that during sulphate cooking mercapto groups enter the side-chains of lignin in positions adjacent to arylether bonds, the resulting β-mercaptoalkyl-arylether structures (II) can be expected to undergo fission of the ether linkages with participation of the mercapto groups (see also Ref.[9]). This type of splitting reaction, requiring only relatively mild conditions, may possibly explain the strongly enhancing effect of the inorganic sulphide ions present in the sulphate cooking liquor on the alkaline degradation and dissolution of lignin during sulphate cooking.

EXPERIMENTAL

All melting points are corrected. Evaporations were carried out at 40° *in vacuo*.

1-O-(o-Methoxy-phenyl)-2,3-di-O-toluene-p-sulphonyl-glycerol (VII). A solution of 1-*O*-(*o*-methoxy-phenyl)-glycerol (V) (10 g) in pyridine (30 ml) was cooled to −10° and a slight excess of toluene-*p*-sulphonyl chloride (21 g) added. After keeping at −10° for 3 h the mixture was allowed to react at room temperature for a further 24 h. Acidification with 2 N sulphuric acid, extraction of the aqueous emulsion with chloroform and of the chloroform extract successively with dilute sulphuric acid, dilute sodium hydroxide solution and water yielded a colourless solution. After drying and removal of solvent the resulting oil crystallised. Recrystallisation from ethanol afforded prisms (yield 87 %), m.p. 77−78°. (Found: C 58.00; H 5.12; O 24.74; S 12.24. $C_{24}H_{26}O_8S_2$ requires: C 56.92; H 5.13; O 25.28; S 12.66).

2-O-(o-Methoxy-phenyl)-1,3-di-O-toluene-p-sulphonyl-glycerol (XII) was similarly prepared from 2-*O*-(*o*-methoxy-phenyl)-glycerol (X) and obtained as needles (yield 87 %) m.p. 64.5−65.5°. (Found: C 57.15; H 5.29; O 25.27; S 12.58. $C_{24}H_{26}O_8S_2$ requires: C 56.92; H 5.13; O 25.28; S 12.66).

2-O-(o-Methoxy-phenyl)-1-O-toluene-p-sulphonyl-glycerol (XV). A solution of 2-*O*-(*o*-methoxy-phenyl)-glycerol (X) (5 g) in pyridine (15 ml) was cooled to −10° and vigorously stirred. The equivalent amount (4.8 g) of toluene-*p*-sulphonyl chloride was added in small portions over a period of 5 h. After stirring over night at room temperature the reaction mixture was worked up as described for compound VII. Recrystallisation from benzene−light petroleum yielded colourless needles (5.1 g, 57 %), m.p. 86−87°. (Found: C 58.04; H 5.85; O 27.04; S 8.98. $C_{17}H_{20}O_6S$ requires: C 58.25; H 5.68; O 27.25; S 9.10).

Acetylation of XV with acetic anhydride − pyridine yielded *3-O-acetyl-2-O-(o-methoxy-phenyl)-1-O-toluene-p-sulphonyl-glycerol (XVI)*, as prisms, which were recrystallised from chloroform − hexane. Yield 95 %, m.p. 60.5−61.5°. (Found: C 57.80; H 5.55; O 28.35; S 8.06; CH_3CO 10.97. $C_{19}H_{22}O_7S$ requires: C57.88; H 5.58; O 28.41; S 8.11; CH_3CO 10.91).

2,3-Di-S-acetyl-1-O-(o-methoxy-phenyl)-2,3-dithioglycerol (IX). Potassium thioacetate (5 g) was added in small portions to a stirred solution of 1-*O*-(*o*-methoxy-phenyl)-2,3-di-*O*-toluene-*p*-sulphonyl-glycerol (VII) (5.5 g) in dimethylformamide (25 ml) and the stirring continued at 5° for 48 h. The dimethylformamide solution was then poured into water and the mixture extracted 3 times with chloroform. After washing the chloroform solution with water, drying with sodium sulphate and evaporating, the resulting oily residue was distilled, 160−165° (bath temperature), 10^{-3} mm Hg. yielding an almost colourless oil (2.1 g, 60 %). On standing the distillate crystallised slowly, m.p. 30−31°. Attempts to recrystallise this substance from low-boiling solvents were unsuccessful. (Found: C 53.64; H 5.74; O 20.32, S 20.26; CH_3CO 26.52. $C_{14}H_{18}O_4S_2$ requires: C 53.50; H 5.73; O 20.36; S 20.40; CH_3CO 27.38).

1,3-Di-S-acetyl-2-O-(o-methoxy-phenyl)-1,3-dithioglycerol (XIV) was similarly prepared from 2-*O*-(*o*-methoxy-phenyl)-1,3-di-*O*-toluene-*p*-sulphonyl-glycerol (XII), except that the reaction temperature was first maintained at −10° for 4 h, then at +5° over night and finally at 20° for 8 h. Distillation, 145−147°, 10^{-3} mm Hg, gave a colourless oil (yield 75 %), which crystallised, m.p. 31−32°. (Found: C 53.77; H 5.84; O 20.53; S 20.26. $C_{14}H_{18}O_4S_2$ requires: C 53.50; H 5.73; O 20.36; S 20.40).

3-O-Acetyl-1-S-acetyl-2-O-(o-methoxy-phenyl)-1-monothioglycerol (XVII) was obtained similarly by reacting potassium thioacetate with 3-*O*-acetyl-2-*O*-(*o*-methoxy-phenyl)-1-*O*--toluene-*p*-sulphonyl-glycerol (XVI) in dimethylformamide. Distillation, 132—133°, 10^{-2} mm Hg gave a yellowish oil (yield 80 %). (Found: C 56.22; H 5.95; O 26.86; S 10.76; CH_3CO 28.65. $C_{14}H_{18}O_5S$ requires: C 56.38; H 6.03; O 26.83; S 10.75; CH_3CO 28.85).

2-O-(o-Methoxy-phenyl)-1,3-dithioglycerol (XIII). 1,3-Di-*S*-acetyl-2-*O*-(*o*-methoxy-phenyl)-1,3-dithioglycerol (XIV) (0.5 g) was dissolved in 1 N methanolic hydrogen chloride (10 ml) under an atmosphere of nitrogen and kept at room temperature for 24 h. At the end of the reaction time water was added, most of the methanol evaporated and the dithiol extracted with chloroform. After evaporation of the solvent the residue was distilled, 120—130° (bath temperature), 10^{-2} mm Hg, and the resulting oil kept in a refrigerator under an atmosphere of nitrogen. All operations were carried out as much as possible with the exclusion of air. (Found: C 52.32; H 6.10; O 14.11; S 27.78. $C_{10}H_{14}O_2S_2$ requires: C 52.17; H 6.08; O 13.90; S 27.85).

The acidic hydrolysis of 2,3-di-*S*-acetyl-1-*O*-(*o*-methoxy-phenyl)-2,3-dithioglycerol (IX) and of 3-*O*-acetyl-1-*S*-acetyl-2-*O*-(*o*-methoxy-phenyl)-1-monothioglycerol (XVII) were carried out in a similar manner and yielded 1-*O*-(*o*-methoxy-phenyl)-2,3-dithioglycerol (VIII) and 2-*O*-(*o*-methoxy-phenyl)-1-monothioglycerol (XVIII), respectively.

2,3-Di-O-acetyl-1-O-(o-methoxy-phenyl)-glycerol (VI) was obtained as a colourless oil by acetylation of 1-*O*-(*o*-methoxy-phenyl)-glycerol (V) with acetic anhydride—pyridine followed by distillation, 145—147°, 0.1 mm Hg. (Found: C 59.63; H 6.35; O 33.94. $C_{14}H_{18}O_6$ requires: C 59.59; H 6.38; O 34.02).

1,3-Di-O-acetyl-2-O-(o-methoxy-phenyl)-glycerol (XI) was similarly prepared from 2-*O*-(*o*-methoxy-phenyl)-glycerol (X). (Found: C 59.70; H 6.26; O 34.05. $C_{14}H_{18}O_6$ requires: C 59.59; H 6.38; O 34.02).

Treatment of the model compounds with 2 N sodium hydroxide in 50 % ethanol. The treatments of the model compounds with alkali at 60 and 100° were carried out in stainless steel autoclave tubes. To ensure complete solubility throughout all runs the substances (60—100 mg of each) were dissolved in ethanol (5 ml) and to these solutions 4 N aqueous sodium hydroxide (5 ml) was added. The air was replaced by nitrogen and the reaction tubes rotated in a polyglycol bath at the appropriate temperature. After reaction the tubes were cooled, the solutions neutralised by addition of solid carbon dioxide, extracted with chloroform and the extracts dried with sodium sulphate. These extracts were used directly for the gas chromatographic determination [5] of the guaiacol split off.

The treatments at 30° were carried out in test tubes in a water bath with stirring, while nitrogen was allowed to pass over the solutions.

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