

The Cleavage of Aromatic Methylethers by Neutral Sulphite

A Kinetic Investigation

JOSEF GIERER and BOHUMÍR KOUTEK*

Swedish Forest Products Research Laboratory, Department of Wood Chemistry, Stockholm Ö, Sweden

The splitting of aromatic methylether linkages by neutral sulphite was found to be an S_N2 displacement on the methyl carbon atom, the rate depending on the concentrations of the methylether and the sulphite (and hydrosulphite) ions. The energy of activation was found to be 18.6 kcal per mole and the Hammett reaction constant +1.24. This sulphitolytic reaction is compared with other nucleophilic demethylation reactions of technical importance, such as the cleavage of methylether bonds by hydrosulphide and mercaptide ions (sulphate pulping) and the alkaline hydrolysis of methoxyl groups (alkaline pulping).

A method for the gas chromatographic determination of methane sulphononic acid (as methylester) has been developed.

Under the conditions of various pulping and bleaching processes lignin suffers partial demethylation. Thus, during alkaline pulping,¹ bleaching with chlorine² or with hypochlorite³ some of the methylether linkages are cleaved forming methanol. Sulphate pulping gives rise to a mixture of aliphatic cleavage products consisting of methyl mercaptan, dimethylsulphide and small amounts of methanol.⁴

Some years ago a further demethylation reaction was reported to take place when neutral sulphite solutions (pH 7) are allowed to react with lignin model compounds under conditions similar to those of neutral sulphite pulping.⁵ Recently, the extent of this demethylation reaction has been determined from the amount of methanol liberated assuming a hydrolytic splitting of the methylether bond.⁶

However, an investigation of the reaction products, obtained after treatment of dimeric, methoxyl-containing model compounds with neutral sulphite solutions, revealed that methane sulphononic acid, and not methanol, constitutes

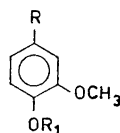
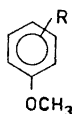
* On leave from the Institute of Chemical Process Fundamentals, Czechoslovakian Academy of Sciences, Prague-Suchbát 2.

the main aliphatic cleavage product.^{7,8} This acid could be isolated from the reaction mixtures and characterised as its *p*-bromo-phenacylester,⁷ whereas methanol was either not detected or found in negligibly small amounts. In a separate experiment it was shown that methanol does not react with neutral sulphite under the conditions used.

Table 1. Cleavage of aromatic methylethers by neutral sulphite (pH 7, 180°, 3 h).

Aromatic methylether	Methane sulphonic acid formed (% of total -OCH ₃ , originally present)	Qualitative composition of the combined chloroform and ether extracts ^a
I	3.1	phenol
II	1.8	<i>m</i> -cresol
III	0.7	<i>p</i> -cresol
IV	10.1	<i>m</i> -nitro-phenol
V	10.3	<i>p</i> -nitro-phenol, <i>p</i> -amino-phenol
VI	3.6	resorcinol
VII	1.1	hydroquinone
VIII	4.2	resorcinol monomethylether
IX	1.8	hydroquinone monomethylether
X	1.7	<i>p</i> -bromo-phenol
XI	10.5	pyrocatechol
XII	7.1	4-methyl-pyrocatechol
XIII	7.0	guaiacol (5 parts), pyrocatechol (1 part)
XIV	6.1	0 (complete sulphonation in the side chain)
XV	8.7	veratrumaldehyde, vanillin, proto-catechualdehyde
XVI	12.8	4-aceto-pyrocatechol, guaiacol (traces)
XVII	18.2	4-aceto-guaiacol, 4-aceto-pyrocatechol
XVIII	5.5	pyrogallol-1-monomethylether, pyrogallol

^a All extracts, except that from compound XIV, contained starting material.



I R = H
 II R = *m*-CH₃
 III R = *p*-CH₃
 IV R = *m*-NO₂
 V R = *p*-NO₂
 VI R = *m*-OH
 VII R = *p*-OH
 VIII R = *m*-OCH₃
 IX R = *p*-OCH₃
 X R = *p*-Br

XI R = R₁ = H
 XII R = CH₃, R₁ = H
 XIII R = H, R₁ = CH₃
 XIV R = CH₂OH, R₁ = H
 XV R = CH₂OH, R₁ = CH₃
 XVI R = COCH₃, R₁ = H
 XVII R = COCH₃, R₁ = CH₃
 XVIII 2,6-dimethoxy-phenol

This demethylation reaction is important since it increases the solubility of lignin and forms leucochromophoric groups of the pyrocatechol type.⁵ Moreover, it may be of practical use as a relatively mild procedure for the cleavage of certain types of arylothers.⁹ Therefore, it was considered of interest to study the scope and the kinetics of the reaction.

The aromatic methylethers I—XVIII were treated with a solution of neutral sulphite (pH 7) at 180° for 3 h (Table 1) or, in the kinetic runs, for varying lengths of time. The extents of reaction were determined by analysing for methane sulphonic acid (as methylester) by GLC. The demethylations of anisole and of guaiacol were also studied by analysing for the phenols liberated and the results of the two gas chromatographic methods are compared in Table 2.

Table 2. Demethylation of anisole and guaiacol by neutral sulphite.

Aromatic methylether	Composition of the chloroform and ether extracts		Methane sulphonic acid (%) in the aqueous solution	Sum of material accounted for (%)
	starting material recovered (%)	phenolic demethylation product (%)		
I	95.0	3.45	2.75	98.8
XI	86.6	10.75	9.43	98.5

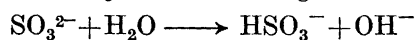
The phenol analyses gave results 20 % and 12 % higher, respectively, than the methane sulphonic acid analyses. These discrepancies may be due to losses of methane sulphonic acid during the working-up procedure or, less likely, to small amounts of methanol not accounted for.

The reaction of anisole was studied in more detail and found to be of second order, its velocity depending upon the concentration of sulphite ion and of anisole:

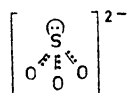
$$v = k \cdot [\text{SO}_3^{2-}] \cdot [\text{anisole}]$$

Using a large molar excess (about 10-fold) of sulphite ion relative to the substrate, the kinetics could be calculated as pseudo-first-order as shown in Fig. 1. The effect of the sulphite concentration on the pseudo-first-order rate constant was determined in a separate series of runs and is shown in Fig. 2. Since the composition of the sulphite solution at a certain pH value and at elevated temperature is not known exactly,¹⁰ the sulphite concentration is given as moles of sulphur per l.

At room temperature and pH 7 sulphite (SO_3^{2-}) and hydrosulphite (HSO_3^-) ions are present in about equal concentrations.^{10,11} When the temperature is raised to about 180°, as used in the present work, a portion of the SO_3^{2-} ions are converted into HSO_3^- ions according to the equation



causing the pH value of the solution to increase to about 7.7.¹¹ However, the OH^- ions formed in this reaction do not successfully compete with the sulphite (and hydrosulphite) ions in the cleaving of the methylether bond, as shown by the formation of methane sulphonic acid, rather than methanol, as main aliphatic reaction product (see above, *cf.* also Ref. 12). The reason for the greater efficiency of the sulphite ion in the cleavage process probably lies in its stronger nucleophilic character due to its polarizability (α -effect).¹³ To account for this characteristic feature of the sulphite ion, structure



has been proposed,¹² providing the sulphur atom with a convenient orbital for bond formation.

From the reaction products formed (methane sulphonic acid and the corresponding phenols) and from the kinetic data illustrated in Figs. 1 and 2,

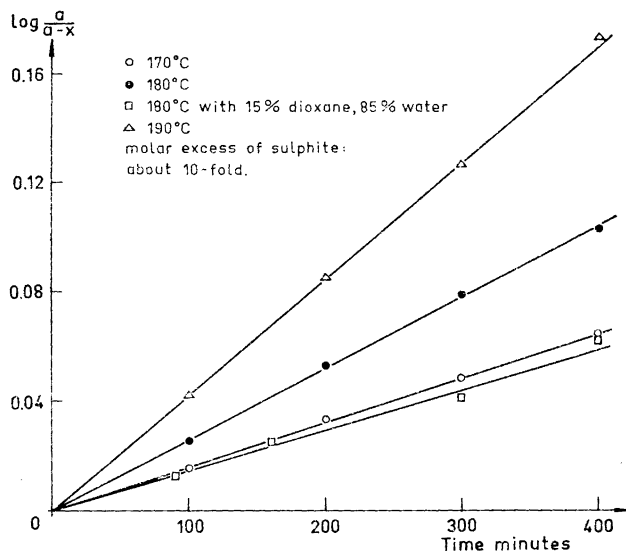
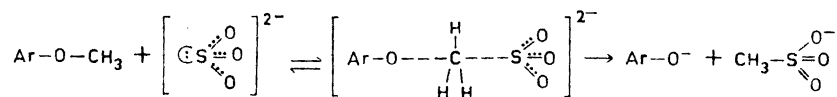




Fig. 1. Pseudo-first order rate plots for the demethylation of anisole.

it can be concluded that the demethylation of anisole and its various derivatives involves an $\text{S}_{\text{N}}2$ displacement on the methyl carbon atom,¹⁴ the SO_3^{2-} (and the HSO_3^-) ions acting as nucleophiles:



Thus, the splitting of aromatic methylether linkages by neutral sulphite constitutes a predominantly sulphitolytic process (*cf.* Ref. 15). Experimental support for this view is provided as follows.

Aliphatic methylethers, such as ethylene glycol monomethylether and ethylene glycol dimethylether, were not split by neutral sulphite to any noticeable degree under the conditions used. After treatment of methyl α -D-glucopyranoside and methyl β -D-glucopyranoside no methane sulphonic acid could be found in the reaction mixtures by means of gas chromatography and only traces were detected using a paper electrophoretic method.¹⁶ From these results it can be concluded that the sulphitolytic cleavage of methylether linkages under the conditions used is limited to the aromatic series, where

mesomeric forms like \ominus  $=\text{O}^{\ominus}-\text{CH}_3$ and  $=\text{O}^{\ominus}-\text{CH}_3$ (*cf.* Ref. 17) can contribute to the resonance hybrid facilitating the formation of the transition state.

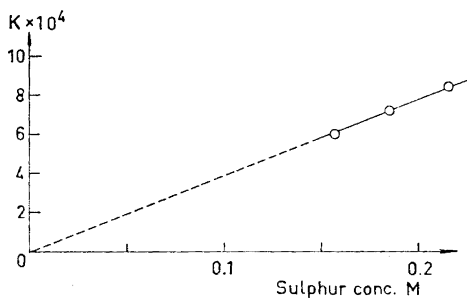


Fig. 2. First-order rate constant of the demethylation of anisole as a function of sulphite concentration.

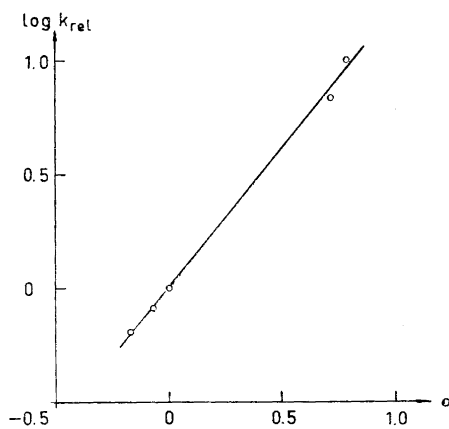


Fig. 3. Straight-line relationship between $\log k_{rel}$ and Hammett's σ values for some substituted anisoles (see Table 3).

As could be predicted, the nucleophilic attack of the sulphite ion on the methyl group is enhanced by the presence of electron-withdrawing substituents (NO_2 , CH_3CO) on the aromatic nucleus (Table 1). For the cleavage of *meta*- and *para*-substituted anisole derivatives Hammett's equation¹⁸ should be valid:

$$\log (k/k_0) = \log k_{rel} = \rho \cdot \sigma$$

Here k and k_0 are the rate constants for the sulphitolytic cleavage of the substituted and unsubstituted anisole, respectively. ρ is a parameter characteristic of the reaction and σ is a constant of the substituent. In Fig. 3 the values of $\log k_{rel}$ for *meta* and *para* methyl- and nitroanisoles are plotted against the corresponding σ values (see Table 3). From the straight-line rela-

Table 3. Relative velocity constants for the demethylation of some methyl-, nitro-, hydroxy-, and methoxy-substituted anisoles by neutral sulphite at 180°.

Substituted anisole	k_{rel}^a in water	k_{rel}^a in dioxane (15 %) and water (85 %)	σ -value of the substituent ^b
II	0.82	0.80	-0.069
III	0.64	0.65	-0.170
IV	6.89	6.60	+0.710
V	10.05	10.18	+0.778
XI	4.08		
VI	2.27		-0.002
VII	0.53		-0.357

^a $k_{rel} = k_{subst. anisole} / k_{anisole}$

^b taken from Jaffé, H. H. *Chem. Revs.* 53 (1953) 191.

tionship obtained, the ρ value for the reaction was calculated to be +1.24. The positive value of this constant is consistent with the postulated nucleophilic character of the cleavage reaction.

To eliminate possible complications due to incomplete solubility, some of the demethylation reactions were also carried out using a mixture of dioxane (15 parts) and water (85 parts) as solvent. The addition of dioxane caused the rate constant of the cleavage of anisole to decrease from $6.01 \times 10^{-4} \text{ min}^{-1}$ to $3.4 \times 10^{-4} \text{ min}^{-1}$. The relative rate constants (k_{rel}) of the methyl- and nitro-substituted anisoles, however, remained almost unaffected (Table 3).

A further support that the sulphitolytic ether cleavage reaction is an S_N2 type displacement on alkyl was furnished by the behaviour of phenetole towards neutral sulphite. In accordance with the stronger positive inductive effect of the ethyl group, as compared with the methyl group, the degree of cleavage (1.2 %) amounted only to about 40 % of the value for anisole (3.1 %, see Table 1).

The behaviours of the hydroxy- and methoxy anisoles (see Table 1) merit special comment. In both series the *ortho*-substituted derivatives (XI and XIII) were demethylated most extensively (10.5 and 7.0 %), the *meta*-substituted derivatives (VI and VIII) were cleaved considerably less (3.6 and 4.2 %) and the *para*-substituted derivatives (VII and IX) were attacked to even a smaller extent (1.1 and 1.8 %) than was unsubstituted anisole (3.1 %). This order of reactivity is in agreement with the positive resonance (+R) and the negative inductive (-I) effects exhibited by these substituents. In the *para*-substituted compounds the strong positive resonance effects causing electron release dominate over the negative inductive effects, whereas in the *meta*-substituted compounds the importance of the two effects is reversed. Finally, in the *ortho*-substituted anisoles, one may expect strong +R and -I effects operating in opposite directions. The relatively large degrees of cleavage observed with the latter compounds can be interpreted as due to a predominance of the -I effects, although proximity effects may also be operative. Since the +R and -I effects of hydroxy and methoxy groups are rather

similar, the extents of cleavage of the hydroxy anisoles do not differ much from those of the corresponding methoxy anisoles. These differences (calculated in percent of total-OCH₃, originally present) should become still smaller, when the sulphitolytic cleavage reaction is allowed to proceed for a longer period of time, the methoxy anisoles becoming increasingly converted into the corresponding hydroxy anisoles. After a 3 h treatment of veratrole (XIII) with neutral sulphite under the conditions given above, the resulting mixture contained guaiacol and pyrocatechol in a ratio of 5:1 (Table 1).

The unexpected behaviours of *p*-bromo-anisole (X) and of vanillyl alcohol (XIV) (Table 1) is due to competing reactions (replacement of bromine by sulphite^{12,20} and nucleophilic substitution at the side chain carbon atom *via* the methylene quinone,²¹ respectively).

The sulphitolytic cleavage of the methylether bonds during neutral sulphite pulping is analogous to the cleavage of the same type of bonds by hydrosulphide and mercaptide ions taking place during the sulphate process and yielding, as main aliphatic cleavage products, methylmercaptan and dimethylsulphide, respectively.⁴ A further analogy exists with the alkaline hydrolysis of methoxy groups during alkaline pulping.¹ It is of interest to compare these demethylation reactions occurring during the various pulping processes in terms of their energies of activation.

The dependance of the sulphitolytic demethylation rate of anisole upon the temperature is shown in Table 4. An Arrhenius plot of the rate constants

Table 4. Effect of temperature on the sulphitolytic demethylation rate of anisole.

Temperature °C	First-order rate constant $k \text{ sec}^{-1}$
170	3.72×10^{-4}
180	6.01×10^{-4}
190	9.78×10^{-4}

obtained in the range 170–190° was almost linear and gave an activation energy of 18.6 kcal per mole. The activation energy for the demethylation of veratrole by aqueous alkali was found to be 34.8 kcal per mole¹ and that for the demethylation of anisole by an ethanolic mercaptan solution 16.4 kcal per mole.²² Although the conditions of these demethylation reactions were not strictly comparable, the order of reactivity of the nucleophiles involved, $\text{RS}^- > \text{SO}_3^{2-} > \text{OH}^-$, is in agreement with the general order of nucleophilic strengths given in the literature.^{12,13}

When anisole was treated with neutral sulphite at 190° for 24 h, the extent of sulphitolytic cleavage of the methylether bond increased to 65 %.⁹ This result indicates that the reaction may be used as a relatively mild preparative method for the cleavage of certain types of aromatic ether linkages.

EXPERIMENTAL

Methane sulphonic acid methylester was prepared by reacting the silver salt with methyl iodide in acetonitrile at room temperature for 24 h (*cf.* Refs. 23 and 8). The crude product was distilled under reduced pressure (12 mm Hg), b.p. 80°, yielding the pure compound (gas chromatography, NMR spectrum).

The anisole and substituted anisoles were commercial products purified by recrystallisation or distillation.

Neutral sulphite solution. NaHSO₃ (0.51 mole) in distilled water (1 l) adjusted to pH 7 with 2 N NaOH. In the kinetic runs and when the method of competing reactions was used, the concentration was suitably varied.

Reaction conditions. The compound (2 g) dissolved or suspended in the cooking liquor (80 ml) was heated in an autoclave of stainless steel at 180° for 3 h or for the period of time required in the kinetic runs.

Working-up procedure. After acidification with SO₂ the reaction mixtures were repeatedly extracted with diethyl ether and with chloroform. The combined and dried (Na₂SO₄) extracts containing the unreacted portions of the starting materials and the phenolic compounds liberated were evaporated and investigated by thin-layer chromatography and/or gas chromatography, in some instances after acetylation of the crude mixtures with acetic anhydride in pyridine. Samples of the original ether and chloroform extracts were found to be free from methanol (gas chromatography).

The aqueous solutions (after extraction with ether and chloroform) were passed through a column of Dowex 50W-X8 cation exchange resin (in the H⁺ form) and after concentration under reduced pressure to about 80 ml neutralised with barium hydroxide at 60°. The precipitates of barium sulphate were filtered off and the filtrates evaporated to dryness. The dried residues were extracted with chloroform to remove small amounts of water-soluble phenols. The conversions of the barium salt of methane sulphonic acid into the methylester were performed as described previously⁸ for other barium sulphonates.

Thin-layer chromatography. The components of the combined ether and chloroform extracts were separated by thin-layer chromatography using silica gel HF and chloroform or a mixture of chloroform and acetone (9:1) as solvent systems. Iodine vapour, in some

Table 5. Summary of the gas chromatographic data.

Type of analysis	Column packing	Temperature °C	Internal standard	Remarks
Determination of methane sulphonic acid as methylester	OV-17	80	anisole	see Tables 1 and 2
Analyses of mixtures of anisole, phenol and substituted phenols (Method of competing reactions)	OV-17	90	—	see Tables 2—4 and Figs. 1—3
Analyses of mixtures of veratrole, guaiacolacetate, pyrocatecholdiacetate, etc.	BDS	158	phenol	see Tables 2—3 and Fig. 3
Test for methanol	Porapak T	167	—	see general part

OV-17, Methylphenyl silicone oil (10 %) on Chromosorb.

BDS, Butane-1,4-diol succinate (5 %) on Chromosorb.

Porapak T, porous polymer beads, Product from Water Associates, Inc.

instances a solution of 2,6-dibromo-quinonemonoimide chloride in ethanol and 0.01 N NaOH or a solution of 3,5-dinitrophenyl hydrazine in 0.2 N HCl served as developers.

Gas chromatography. The gas chromatographic separations were performed by injecting 0.5–2.0 microliter aliquots (Perkin-Elmer instrument, model 800, equipped with a flame ionisation detector). Columns of 6 mm diameter and 2 m length and a nitrogen flow rate of 30 ml/min were used. The column packings, temperatures and internal standards used for the various types of gas chromatographic separations are given in Table 5.

*Method of competing reactions.*²⁴ This method was used to determine the relative rate constants (k_{rel} values, see Table 3). The methylether under test and the reference compound (anisole) (3–10 mmoles of each) were weighed, treated with a small amount (0.9 mmoles) of neutral sulphite in 80 ml of solvent and the resulting mixtures worked up and analysed for the phenols liberated by means of gas chromatography as described above. The relative rate constants (k_{rel}) were calculated from the equation:

$$k_{rel} = \frac{k_1}{k_0} = \frac{p_1}{p_0} \cdot \frac{a_0}{a_1} \cdot \frac{Mp_0}{Mp_1} \cdot \frac{Ma_1}{Ma_0}$$

where p = amount of demethylation product, a = amount of starting material, and M = molecular weight. The indices 0 and 1 refer to the reference compound (anisole) and the methylether being studied, respectively.

Acknowledgement. The authors are indebted to the *Royal Swedish Academy of Engineering Sciences* for financial support.

REFERENCES

1. Sarkanen, K. V., Chirkin, G. and Hrutford, B. F. *Tappi* **46** (1963) 375.
2. Dence, C. and Sarkanen, K. V. *Tappi* **43** (1960) 87.
3. Richtzenhain, H. and Alfredsson, B. *Acta Chem. Scand.* **10** (1956) 719.
4. Enkvist, T., Turunen, J. and Ashorn, T. *Tappi* **45** (1962) 128.
5. Croon, I. and Swan, B. *Svensk Papperstid.* **67** (1964) 177.
6. Hayashi, A. and Namura, Y. *Nippon Mokuzai Gakkaishi* **13** (1967) 24.
7. Gellerstedt, G. and Gierer, J. *Acta Chem. Scand.* **22** (1968) 2510.
8. Gellerstedt, G. and Gierer, J. *Acta Chem. Scand.* **22** (1968) 2029.
9. Gierer, J. and Koutek, B. *Unpublished results.*
10. Ingruber, O. V. *Svensk Papperstid.* **65** (1962) 448.
11. Ingruber, O. V. and Allard, G. A. *Tappi* **50** (1967) 597.
12. Adeniran, M. A., Bevan, C. W. L. and Hirst, J. J. *J. Chem. Soc.* **1963** 5868.
13. Edwards, J. O. and Pearson, R. G. *J. Am. Chem. Soc.* **84** (1962) 16.
14. Gould, E. S. *Mechanism and Structure in Organic Chemistry*, Holt, Rinehart and Winston, New York 1959, p. 251.
15. Rydholm, S. A. and Lagergren, S. *Svensk Papperstid.* **62** (1959) 103.
16. Theander, O. *Personal Communication.*
17. Burwell, Jr., R. L. *Chem. Revs.* **54** (1954) 660.
18. Hammett, L. P. *Physical Organic Chemistry*, McGraw, New York and London 1940.
19. Ref. 14, pp. 207 and 218.
20. Gilbert, E. E. *Sulfonation and Related Reactions*, Wiley, New York-London-Sidney 1965, p. 172.
21. Ivnäs, L. and Lindberg, B. *Acta Chem. Scand.* **15** (1961) 1081.
22. Koutek, B. and Setinek, K. *Collection Czech. Chem. Commun.* **33** (1968) 866.
23. Emmons, W. D. and Ferris, A. F. *J. Am. Chem. Soc.* **75** (1953) 2257.
24. Ingold, C. K. and Shaw, F. R. *J. Chem. Soc.* **1927** 2918.

Received October 4, 1968.