THE ACTION OF HYDROGEN PEROXIDE

ON

PHENOLIC POLYALKYL ETHERS

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for the Degree of Doctor of Philosophy
by
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ABSTRACT

Kenyon and Mason (J. Chem. Soc., 1952, 4664), attempting to prepare the sulphone from p-tolyl trimethoxydiphenylmethyl sulphide by oxidation with peracetic acid, obtained instead the unexpected 2,6-dimethoxy-1,4-benzoquinone.

This apparently anomalous reaction stimulated this research into the behaviour of other aromatic compounds when acted upon by peracetic acid: a number of compounds, the majority being phenolic ethers, have been studied in this respect.

In some cases, no reaction was observed; in others, the compound underwent ring-cleavage and produced a complex mixture of aliphatic residues; in many cases, however, the aromatic ring survived in the quinonoid form, e.g.,

\[
\begin{array}{c}
\text{MeC} \\
\text{CMe}
\end{array}
\quad \xrightarrow{\text{MeC}}
\quad \begin{array}{c}
\text{OMe} \\
\text{MeC}
\end{array}
\]

The likely reaction mechanisms involved in this type of oxidation are discussed.
The work described in this thesis was carried out under the direction of Dr. J. Kenyon, F.R.S., to whom the author wishes to express thanks for his kindly encouragement and help. His thanks are also due to the Head of the Chemistry Department, Dr. F.R. Goss, for his general interest, and to Dr. A.G. Davies, for his most helpful suggestions. He also wishes to express his gratitude to the British Oxygen Company for generously allowing him to carry out much of the experimental work at their Research Centre at Morden.
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1.

INTRODUCTION

Extensive work, carried out during the past fifty years on the chemistry of the organic peroxycarboxylic acids $\text{RCOO}_2\text{H}$, has shown these compounds to be very convenient oxidizing agents since they may be used in solution under mild conditions and frequently give a minimum amount of byproducts. Furthermore, the ready formation of peroxycarboxylic acids from carboxylic acids and hydrogen peroxide enables the reagent to be prepared in situ from readily available materials, and, in the case of peroxycetic acid, the reaction may be carried out in a wide range of solvent media.

Organic Peroxyacids.

The most commonly used of the organic peracids has been peracetic acid. In early work this was used in dilute aqueous solution, prepared by the hydrolysis of benzoyl acetyl peroxide, (Clover and Houghton, *Amer. Chem. J.*, 1904, 32, 43) but later D'Ans and Friederich, (Ber., 1910, 43, 1830) obtained concentrated solutions of the peracid by the interaction of hydrogen peroxide (90%) with acetic acid, acetyl chloride or acetic anhydride. Subsequent techniques have used the acid or anhydride, since the acid chloride may give rise to acetyl peroxide.
An equimolecular solution of acetic acid and hydrogen peroxide (38%) to which sulphuric acid (1%) has been added, reaches equilibrium after 12 - 16 hours at room temperature and then contains 50% of the peracid (D'Ans and Frey, Ber., 1912, 45, 1845). D'Ans and Frey showed that the pure acid could be obtained from this mixture by fractional distillation followed by fractional freezing.

Pure peracetic acid is a colourless liquid, d_4^{15} = 1.226, m.p. 0.1°C, b.p. 105°C (Arbusow, J. Frakt. Chem., 1931, 131, 357). It is violently explosive on heating, but whereas it is rapidly decomposed to acetic acid and oxygen by catalysts (manganese salts and platinum black) and to hydrogen peroxide by alkalis, concentrated solutions are relatively stable at room temperature, 90% solutions being unaltered after over a month (D'Ans and Kneip, Ber., 1915, 48, 1135).

The other homologous aliphatic peroxyacids have been described up to perpalmitic acid (Parker, Ricciuti, Ogg and Swern, J. Amer. Chem. Soc., 1955, 77, 4037; ibid, 5537).

Perorotonic, pertrichloroacetic, permonochloroacetic, and some dibasic saturated acids such as persuccinic and perglutaric have also been reported (Swern, Chem. Rev., 1949, 45). All are prepared by
the action of hydrogen peroxide on the acid, acid chloride or anhydride. They are more stable than peracetic acid but decompose slowly at room temperature and more rapidly - often with violence - on heating.

Aromatic peroxyacids are somewhat more stable than those in the aliphatic series, while retaining their powerful oxidizing properties: monoperphthalic acid (Baeyer and Villiger, Ber., 1901, 34, 762) is a white, crystalline solid which softens at 110°C and is converted into phthalic acid with evolution of oxygen; it is soluble in water (aqueous hydrolysis converts it into hydrogen peroxide and phthalic acid) and shows typical peracid oxidizing properties, (idem, loc. cit.). It is relatively stable - more so than perbenzoic acid (q.v.) - and on keeping loses about 20% of its active oxygen in 30 days at room temperature. Diperterephthalic acid (idem, loc. cit.) and percinnamic acid (Bodendorf, Ber., 1933, 663, 165) have been prepared and are white crystalline solids similar in both their physical and chemical (oxidizing) reactions to the other peroxyaromatic acids.

The best known, and most widely used, of these acids is perbenzoic acid, which was originally prepared (Baeyer and Villiger, Ber., 1900, 33, 858) by treating benzoyl peroxide with sodium ethoxide in ether-alcohol solution, followed by acidification. Later workers
used toluene as solvent (Levy and Lagrange, Bull. soc. chim., 1931, 42, 1765) and improved the yield to 90%.

Much work has been carried out on the preparation of this acid by the controlled oxidation of benzaldehyde by oxygen (Swern, Chemical Reviews, 1949, 45, 12) and has illustrated the sensitivity of this reaction to trace impurities.

Perbenzoic acid is a white crystalline solid, slightly soluble in water and most organic solvents; it has a strong, unpleasant odour, similar to that of hypochlorous acid. In common with the other peracids it liberates iodine rapidly from potassium iodide, decolourises indigo and oxidizes ferrous and manganese salts.

Oxidations by Peroxyacids.

Peroxyacids have been used mainly as preparative or analytical reagents for oxidizing olefins to α-glycols (Prileschajew, Ber., 1909, 42, 4311 et seq.). Perbenzoic acid has been the one most frequently used, although more recently, peracetic acid (Arbuzow and Michailow, J. Prakt. Chem., 1930, 127, 92) and latterly peroxytrifluoroacetic have been used.

The oxidation of organic sulphur compounds (Hinsberg, Ber., 1909, 41, 2335 et seq.), and nitrogen compounds (D'Ans and Kneip, Ber., 1915, 49, 1135 et seq.)
with peracetic acid has been studied in some detail.

In all these oxidations the peroxyacid behaves as an electrophilic reagent which undergoes nucleophilic attack by the compound undergoing oxidation, i.e.,

\[
\begin{align*}
R - C - O - C + Y & \rightarrow R - C - O + H^+ + O_2 - Y \\
\end{align*}
\]

(Oberberger and Cummins, J. Amer. Chem. Soc., 1953, 75, 4250). Reaction is facilitated by electron attraction by the acyl group; thus the peroxyacids are more powerful oxidizing agents than hydrogen peroxide or alkyl hydroperoxides, and peroxyfluoracetic acid is more powerful than peroxyacetic acid.

The specific reaction rates for the reaction between peracids and olefinic compounds have been studied, (Swern, J. Amer. Chem. Soc., 1947, 69, 1692); it was shown that the marked differences between these rates was compatible with the above assumption that the peroxide-oxygen in organic peracids is electrophilic, providing allowance was made for the electron-releasing or attracting effects of groups attached to, or near to, the double bond of the olefin.

The Nuclear Oxidation of Aromatic Compounds.

The study of the nuclear oxidation of aromatic compounds is not, as yet, very extensive. The first
work in this field was that of Henderson and Boyd (J. Chem. Soc., 1910, 97, 1653) who used hydrogen peroxide (30%) - "perhydrol" - in acetic acid solution. Various phenols were submitted to the action of this reagent and, in general, gave mixtures of further hydroxylated phenols and \( \gamma \)-quinones (Table 1). In each case where a nuclear alkyl substituent was present this survived oxidation, the first step in which appeared to involve hydroxylation. The same authors also showed that whereas benzene, toluene and 1:3 diethylbenzene were not attacked by this reagent, naphthalene, anthracene and phenanthrene yielded phthellic acid, anthraquinone and phenanthraquinone respectively.

\[
\begin{array}{c|c|c}
\text{PHENOL} & \text{PRODUCTS} \\
\hline
\begin{array}{c}
\text{OH} \\
\text{CH}_3
\end{array} & \begin{array}{c}
\text{OH} \\
\text{CH}_3
\end{array} + \begin{array}{c}
\text{O} \\
\text{Me}
\end{array} + \begin{array}{c}
\text{CH} \\
\text{OH}
\end{array} \\
\hline
\end{array}
\]

**Table 1.**

Oxidation of Phenols with Hydrogen Peroxide (30\%) and Acetic Acid (Henderson and Boyd).
Table 1 - Continued.

\[
\begin{align*}
\text{CH}_3 & \xrightarrow{\text{Me}} \text{CH}_{3}\text{OH} + \text{MeOH} \\
\text{Me} & \xrightarrow{\text{CH}} \text{MeOH} \\
\text{Me}_3 & \xrightarrow{\text{CH}} \text{Me}_3\text{OH} \\
\text{Me} & \xrightarrow{\text{O}} \text{Me}_3\text{OH} \\
\text{Me} & \xrightarrow{\text{O}} \text{Me}_3\text{OH} \\
\text{Me} & \xrightarrow{\text{O}} \text{Me}_3\text{OH} \\
\text{Me} & \xrightarrow{\text{O}} \text{Me}_3\text{OH} \\
\end{align*}
\]
Böseken and Engelberts (Proc. Acad. Sci. Amsterdam, 1932, 26, 750; ibid, 1931, 34, 1292) continued this work and showed that phenol is converted into cis, cis-muconic acid in very good yield, together with some p-benzoquinone. Catechol also yielded muconic acid, together with fumaric acid, whilst hydroquinone yielded quinhydrone and fumaric acid.

The results of Grundman and Trischmann (Ber., 1936, 69B, 1755) are even more germane to the present investigation: 2,2'-dihydroxydiphenyl yielded two products which were tentatively identified as 2(2-hydroxyphenyl)quinone and 2-(hydroxyphenyl) muconic lactone.

Other workers (Böseken and Emitt, Rec. Trav. Chim., 1933, 58, 125) showed that whereas 1,8-dihydroxy-naphthalene is converted to tars by peracetic acid, its monomethyl ether yields a mixture of 8-methoxy-1-naphthoquinone and a dehydration product of methoxy-3-carboxyaallocinnamic acid.

Elvidge, Linstead and Sims (J. Chem. Soc., 1951, 3385) demonstrated the use of peracetic acid (13%) in aromatic nuclear cleavage; both p-cresol and homocatecho with this reagent yielded 2-methyl cis-trans-muconic acid. Concentration of the mother-liquors of the oxidizing solutions which yielded this product gave an
interesting lactone as byproduct: 3-carboxymethyl-2-methyl-1-butenolide.

Other interesting advances in this field have been made by Friess (Friess, Soloway, Morse and Ingersoll, J. Amer. Chem. Soc., 1952, 74, 1305) who used perbenzoic acid in chloroform solution but obtained results analogous to those in which peracetic acid has been used. In this work, which concerned methoxyphenyl ethers (Table 2), a more quantitative approach was used than previously and some study was made of the kinetics of the reactions.
Table 2.

Nuclear Oxidation of Aromatic Ethers with Perbenzoic Acid (Priess).

<table>
<thead>
<tr>
<th>Ether</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Ether I" /></td>
<td>None isolated.</td>
</tr>
<tr>
<td><img src="image2" alt="Ether II" /></td>
<td>CH$<em>3$COO-$(CH$-CH)</em>{2}$-COCCOCH$_3$ cis, cis- and trans, trans- forms of dimethyl muconate</td>
</tr>
<tr>
<td><img src="image3" alt="Ether III" /></td>
<td><img src="image4" alt="Product III" /></td>
</tr>
<tr>
<td><img src="image5" alt="Ether IV" /></td>
<td><img src="image6" alt="Product IV" /></td>
</tr>
<tr>
<td><img src="image7" alt="Ether V" /></td>
<td><img src="image8" alt="Product V" /> + small yields of oxalic acid derivatives.</td>
</tr>
<tr>
<td><img src="image9" alt="Ether VI" /></td>
<td></td>
</tr>
</tbody>
</table>
The conclusions drawn from these results were, firstly, that the order of increasing reactivity towards peracid was

I < II - IV < V < III < VI (Table 2).

Further, with the exception of the unusual reactivity of resorcinol dimethyl ether (III), it appeared that an increase in the number of electron-supplying methoxy groups on the benzene ring produces a corresponding increase in sensitivity to peracid attack: the peroxyacid therefore, attacks the ring electrophilically of olefins and sulphides. The kinetic studies (on V) showed that two moles of peracid were consumed in the oxidation stage and the following reaction scheme was proposed:

\[
V + \text{ArCO}_2H \quad \text{(slow)} \quad \rightarrow \quad \text{ArCO}_2H
\]

\[
\text{(fast)} \quad + \text{ArCO}_2H
\]

\[
\text{MeC} \quad \text{MeC}
\]

\[
\text{MeC} \quad \text{MeC}
\]

\[
\text{MeC} \quad \text{MeC}
\]

\[
\text{MeC} \quad \text{MeC}
\]
Friess's work also showed that the solvent media used in peracid oxidations affect the course of the reaction. Both anisole and veratrole consumed several moles of peracid, a result at variance with a previous observation by Fernholz (Angew. Chem., 1948, 60A, 62; Ber., 1951, 84, 110) that little or no absorption occurred when benzene was the solvent.

The present investigation was initiated after the observation of an anomalous oxidation of $p$-tolyl trimethoxydiphenylmethyl sulphide by hydrogen peroxide in acetone or acetic acid: instead of the expected sulphone, there was formed 2:6-dimethoxy-1:4-benzoquinone (Kenyon and Mason, J. Chem. Soc., 1952, 4664). The same workers also prepared, by this method, the same quinone from 2:4:6-trimethoxydiphenylmethanol and also from 2:4:6-trimethoxybenzene. It was reported that a careful search for other oxidation products was fruitless.

It became of interest to examine the reaction of peracetic acid with other phenolic ethers for appreciation of the scope of the general method and to clarify the orienting effect of substituent groups. In this study, a number of alkyl- and halogeno-substituted phenolic ethers have been prepared and their nuclear oxidation products isolated and examined.
DISCUSSION.

Experimental Results.

The compounds used in this study of the oxidative effect of peracetic acid were hydroxy-, alkyl-, and halogeno-substituted aryl ethers.

Their reaction with the peracid permitted the classification of these substances into one of three groups: (a), those which remained inert even after prolonged contact with high concentrations of peracid; (b), those which underwent ring cleavage with the production of water-soluble products; and (c), those which yielded a significant proportion of quinone or quinones.

(a) Unreactive Compounds.

Some of the compounds examined (Table 5) were quite inert to peracetic acid even after a month's exposure to relatively high concentrations of the reagent: the fully nuclear brominated methyl ether of pyrogallol, and p-bromo-veratrole, for example, were unchanged - the former after 14 days' solution in peracetic acid (50%) was quantitatively recovered.

(b) Ring Cleavage.

The majority of compounds which did not yield quinones underwent oxidation to water-soluble products (Table 5). The proportion of the material oxidized
and the nature of the products were dependent on the concentration of the peracid: some materials, phenols in particular, were converted into aliphatic hydroxylated oxidation products even by brief treatment with very dilute peracid. The methyl ether of m-cresol, for instance, was completely destroyed in 1 - 2 hours by a 3% solution of the peracid. Variation in the concentration of the oxidizing solution always caused variation in the proportion of the material destroyed but in no case furnished quinones from materials which, under more stringent conditions, had yielded aliphatic products.

The nature of these aliphatic derivatives was not examined in detail except in the case of 4-bromo-1:3-dimethoxybenzene (q.v.). In the former instances, the peracetic acid solution was coloured brown and evaporation or repeated extraction after neutralisation yielded pale yellow, water-soluble oils which could not be brominated, nitrated, benzylated or caused to undergo any of the reactions indicative of aromaticity. Crystallisation could not be initiated even under the most favourable conditions, and attempted distillation, under reduced nitrogen pressure, usually caused extensive decomposition.

The mother-liquor from the oxidation of 4-bromo-1:3-dimethoxybenzene was investigated more
thoroughly. Small amounts of oxalic acid and formaldehyde were shown to be present, although undoubtedly these were but two out of a complex mixture of breakdown-products. It is of interest that Friess, (*J. Amer. Chem. Soc.*, 1952, 74, 1305), investigating the action of perbenzoic acid in chloroform solution upon selected aromatic ethers, showed that veratrole yielded dimethyl muconate - which could be formed by nuclear mono-cleavage:

\[
\begin{align*}
\text{CH}_3 \quad \text{O} \\
\text{C} & \quad \text{H} \\
\text{C} & \quad \text{H}
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3\text{COOC-} & \quad \text{(CH-CH)}_2\text{-COOCH}_3 \\
\text{C} & \quad \text{H} \\
\text{C} & \quad \text{H}
\end{align*}
\]

and that under the same conditions 1:2:3- and 1:3:5-trimethoxybenzenes underwent ring-cleavage to give small yields of two-carbon fragments of oxalic acid and its derivatives.

(c) *Quinone Formation.*

The compounds which furnished quinones never did so in high yield. Oxidation and ether-group elimination reactions occurred which left the carbocyclic ring intact, but undoubtedly many different oxidation steps are involved and would account for the low yields of the quinone.
Two facts, in particular, stand out in the results obtained in this work: only \( \beta \)-quinones were isolated from any of the reactions investigated, and, although some quinones were formed without group elimination, when elimination did occur the displaced groups were generally methoxyl and hydrogen; alkyl and halogeno-groups were retained - unless, of course, ring cleavage occurred. The single exception to this general behaviour was the loss of the halogen when 1-bromo-2:4:5-trimethoxybenzene underwent conversion to 2:5-dimethoxy-1:4-benzoquinone.

**Quinone Formation with Bromine Transfer.**

Two unusual reactions were encountered in the series of compounds which gave quinones. The first, which initiated this study, was the oxidation of 4-bromo-1:2-dimethoxybenzene. After a few days, a solution of this material in acetic acid containing hydrogen peroxide (30%) deposited a mixture of colourless and deep-red crystals. Separation and analysis of these products identified them as follows:

\[
\begin{align*}
\text{Br} & \quad \text{OMe} \quad \rightarrow \\
\text{Br} & \quad \text{CMe} \quad + \\
\text{Br} & \quad \text{CMe} \quad + \\
\end{align*}
\]
With more concentrated peracid, and with sulphuric acid present as a catalyst, only the quinone was obtained, whereas when dilute peracid was used or when an excess of the ether was present, the dibromo-derivative alone could be isolated. Oxidation of the mono-bromo-ether by nitric acid also yielded the dibromo-product (only) together with some water-soluble materials. It was demonstrated that both products of the original reaction were stable to peracid in the concentration used and also that the original monobromo-ether immediately precipitated the dibromo-ether on treatment with free bromine. It would thus appear that when direct oxidation to quinone takes place:

\[
\begin{align*}
\text{Br} & \quad \text{CMe} \\
\text{CMe} & \quad \text{Br} \\
\end{align*}
\rightarrow
\begin{align*}
\text{O} & \quad \text{CMe} \\
\text{CMe} & \quad \text{Br} \\
\end{align*}
\]

some nuclear cleavage and fragmentation concurrently occurs with liberation of free halogen, which immediately reacts with a second molecule of ether and is removed from the solution:

\[
\begin{align*}
\text{Br} \quad \text{CMe} \\
\text{CMe} \quad \text{Br} \quad + \quad \text{Br}_2 \\
\end{align*}
\rightarrow
\begin{align*}
\text{Br} \quad \text{CMe} \\
\text{CMe} \quad \text{Br} \\
\end{align*}
\]
18.

A similar system to this was discovered later with 2,4-dibromo-1,3,5-trimethoxybenzene:

and also with the corresponding dichloro-derivative.

Quinone Formation with Nuclear Coupling.

The second reaction of interest involved the oxidation of resorcinol dimethyl ether. In view of the above result, this was expected to react as follows:

In fact, no reaction occurred at all except with 90% hydrogen peroxide in the presence of sulphuric acid, when 1(4-methoxy-2,5-quinonyl)-4-methoxy-2,5-benzoquinone was formed:

A parallel result was obtained when the dibenzylxoxy-ether of resorcinol was used:
Note: Friess (vide supra) found that with parbenzoic acid the dimethyl ether of resorcinol gave 2-hydroxy-5-methoxy-1,4-benzoquinone:

This nuclear coupling occurs probably, but not necessarily, by a free radical mechanism. Nuclear coupling by a free radical mechanism occurs when an \(-\cdot-OH\) group is capable of giving rise to an \(-\cdot-O\) group ortho- or para- to the position of coupling; this is due to the possibility of the free radical being stabilised by resonance:

\[
\begin{align*}
\text{MeC} & \quad \rightarrow \\
\end{align*}
\]

(Moore and Waters, J. Chem. Soc., 1954, 243; Baltes and Volbert, C.A., 1955, 49, 13330). A free radical reaction might be catalysed by minute traces of metals of univariant valence (Cu**, Fe**) and this might account for the difference between the results herein
described and those of Friess. Additional work is required to ascertain whether coupling is a free radical reaction and further, whether oxidation occurs first and coupling later or conversely. One possible mechanism is:

\[
\begin{align*}
\text{OMe} & \quad \text{HO}^+ \\
\text{OMe} & \quad 2 \text{ moles}
\end{align*}
\]

Three ethers which had proved particularly sensitive to peracetic acid were submitted to the action of tert.-butyl hydroperoxide, tert.-butyl peracetate and tert.-butyl perbenzoate. Neither 1:2:3- and 1:2:4-trimethoxybenzenes nor 4-bromo-1:3-dimethoxybenzene reacted with these peroxy-compounds, which are evidently less active than peracetic acid. These reagents are less reactive towards amines, sulphides and olefins than is hydrogen peroxide but it is, nevertheless, somewhat surprising that no reaction occurred with tert.-butyl peracetate, even in the presence of sulphuric acid. Reaction might occur if conditions were made more drastic, although then the peroxide might preferentially undergo acid-catalysed decomposition.
All the trimethoxy-compounds examined reacted with peroxoacetic acid; the presence of nitro- or halogen substituents in the ring appears to reduce this reactivity. When quinones are formed, the oxygen is found at the position on the ring most susceptible to electrophilic substitution, i.e., at those positions which are most activated by electron-releasing methoxyl- or methyl- groups and deactivated by nitro- or halogen groups.

Thus it seems likely that the reaction is initiated by electrophilic attack by the reagent (compare the electrophilic oxidation of olefins, nitrogen and sulphur compounds cited in the Introduction), i.e.,

\[
\text{O} \quad \text{CH}_3\text{O}-\text{O}^- + \text{H}^+ \\
\text{CH}_3\text{O}-\text{O}^- \\
\text{H} \\
\text{CH}_3\text{O}-\text{O}^- \quad \text{H} \\
\text{CH} \\
\]

leading to substitution of a hydroxyl group at a position eventually occupied by the CO group. This is particularly apparent in the work of Henderson and Boyd (see Introduction) where the intermediate hydroxyl compounds were sometimes isolated. This mechanism is in accord with the conclusions reached by Friess (q.v.).
The reactions which occur subsequently are here discussed with reference to the groups which are displaced, as follows.

The Displaced Groups.

A classification of the compounds which react with peroxyacetic acid may be made on the basis of the nature of the two groups which suffer displacement at the points of quinone formation. These are usually H—OMe; a few are MeO—OMe or H—H. One example appears to be Br—OMe.

H—OMe Displacement.

Hydroxylation may occur p- to a methoxyl group (which is subsequently lost), e.g.,

\[
\begin{align*}
\text{Me} & \quad \text{Me} \\
\downarrow & \quad \downarrow \\
\text{Me} & \quad \text{Me}
\end{align*}
\]

Two possible mechanisms for this subsequent step suggest themselves:

1. C—Me fission

(a)
23.

The H of the hydroxyl group with both electrons being lost to the oxidizing agent.

(b)

\[
\begin{align*}
\text{Me} & \quad \text{Me} \\
\text{H-C} & \quad \text{Me} \\
\text{Me} & \quad \text{Me} \\
\end{align*}
\]

\[
\text{Me} \quad \text{O} \quad \text{CO-Me} \quad \rightarrow \quad \text{Me} \\
\text{Me} \quad \text{Me} \\
\text{H} \\
\]

\[
\begin{align*}
\text{Me} & \quad \text{Me} \\
\text{H} & \quad \text{MeOH} \\
\text{Me-CC-0}^- & \\
\end{align*}
\]

In both (a) and (b) the quinone oxygen originates in the alkoxy group. If the methoxy group were replaced by an optically-active alkoxy group (-OR) and the configuration of the alcohol produced on oxidation would be diagnostic of mechanism (a) or (b): if (a), optical inversion and racemisation of R would be observed; if (b), complete inversion would be expected.

2. The other possible mechanism is that proposed by Friess, in which, essentially, electrophilic CH\(^+\) replaces nucleophilic -OME:

\[
\begin{align*}
\text{HO-C} & \quad (A) \quad \text{OMe} \quad \rightarrow \quad \text{Me} \\
\text{Me} & \quad \text{Me} \\
\text{CH}_2\text{CO}_2\text{H} & \quad \text{Me} \quad \text{OMe} \\
\text{Me} & \quad \text{Me} \\
\text{H-O} & \quad \text{OH} \\
\text{Me} & \quad \text{Me} \\
\text{Me} & \quad \text{Me} \\
\end{align*}
\]

\[
\begin{align*}
\text{MeC}^- & \quad + \quad \text{H}^+ \\
\end{align*}
\]
Here the configuration of the alkoxy group remains unchanged and an optically-active group would retain its configuration. Further, labelling this group with $^{18}O$ would establish the position of bond fission. Priess and his co-workers assume that the initial hydroxylation is a slow (bimolecular) reaction, and that the second stage is rapid. This could be tested by the preparation of "A" and measurement of its rate of oxidation to quinone, with peroxycid.

**H—H Displacement.**

The scheme outlined above allows for this if initial hydroxylation be assumed. The two alternatives are:

![Chemical structures](image-url)
MCO—OMe Displacement.

The mechanism responsible for bringing about this displacement is not clear. Recent work (Davies, Hilton and Patai, Unpublished work) has indicated that some phenols can be readily methylated with methanol and H⁺ and also that they will exchange their oxygen with that in H2¹⁸O, polyhydroxy phenols being more reactive than phenol itself. If the exchange OR ⇌ CH is possible then the displacement reaction may well be:

followed by the reaction outlined above.

Reactions Involving Nuclear Rupture.

The tables show that those compounds which when treated with peroxyacid, tend to undergo nuclear cleavage to water-soluble products, are nearly always those which might be expected to give rise to quinones, i.e., compounds containing the electron-releasing methoxy- or alkyl- groups. Correspondingly, compounds which contain the de-activating nitro- or halogeno- groups do not undergo ring rupture. At first sight, this might indicate that nuclear rupture involves oxidation at a quinone group, =C=O. Although the evidence is scanty, a possible mechanism for this reaction would be the analogue of that which is accepted for the Baeyer-Villiger
oxidation of ketones with peroxides forming esters, (Leffler, Chem. Rev., 1949, 45, 385), i.e.,

\[
\begin{array}{c}
\text{HC} \\
\text{CH} \\
\text{HC} \\
\text{CH} \\
\text{HC} \\
\text{CH} \\
\text{HC} \\
\text{CH} \\
\end{array} \xrightarrow{\text{H}_2\text{CO}_2} \begin{array}{c}
\text{HC} \\
\text{CH} \\
\text{HC} \\
\text{CH} \\
\text{HC} \\
\text{CH} \\
\text{HC} \\
\text{CH} \\
\end{array} \to \begin{array}{c}
\text{HC} \\
\text{CH} \\
\text{HC} \\
\text{CH} \\
\text{HC} \\
\text{CH} \\
\text{HC} \\
\text{CH} \\
\end{array}
\]

\[
\begin{array}{c}
\text{HO} \\
\text{OH} \\
\text{HO} \\
\text{=CH} \\
\end{array} \to \begin{array}{c}
\text{HO} \\
\text{OH} \\
\text{HO} \\
\text{=CH} \\
\end{array}
\]

ETC.

In any case, it has been shown (Karrer and Schneider, Helv. Chim. Acta., 1947, 30, 859) that an oxygen atom can be introduced into an o-quinone molecule by means of perbenzoic acid:

\[
\begin{array}{c}
\text{PhCO}_2\text{H} \\
\end{array} \to \begin{array}{c}
\text{Ph} \\
\text{OC} \\
\end{array}
\]

However, experiment showed that one quinone, at least, (2-bromo-5-methoxybenzoquinone) was stable to peracetic
acid. A more likely mechanism, therefore, is the following - which is known to apply in alkaline media (Fieser, J. Amer. Chem. Soc., 1939, 61, 3216 and Zigehler, ibid, 1940, 62, 2866):

followed by the scheme outlined above.
EXPERIMENTAL SECTION

(a) Oxidations
## INDEX

Experimental Section - (a) Oxidations.

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</tr>
</tbody>
</table>
Oxidation of Phenolic Polyalkyl Ethers with Hydrogen Peroxide in Acetic Acid Solution.

Mono-

\[
\begin{align*}
\text{Me} & \quad \text{Me} \\
\text{Me} & \quad \text{Me} \\
\end{align*}
\]

\[
\begin{align*}
\text{Me} & \quad \text{Me} \\
\text{Me} & \quad \text{Me} \\
\end{align*}
\]

Di-

\[
\begin{align*}
\text{MeO} & \quad \text{Me} \\
\text{MeO} & \quad \text{Me} \\
\end{align*}
\]

\[
\begin{align*}
\text{MeO} & \quad \text{Me} \\
\text{MeO} & \quad \text{Me} \\
\end{align*}
\]

\[
\begin{align*}
\text{MeO} & \quad \text{MeO} \\
\text{MeO} & \quad \text{MeO} \\
\end{align*}
\]

\[
\begin{align*}
\text{MeO} & \quad \text{MeO} \\
\text{MeO} & \quad \text{MeO} \\
\end{align*}
\]

\[
\begin{align*}
\text{MeO} & \quad \text{MeO} \\
\text{MeO} & \quad \text{MeO} \\
\end{align*}
\]

\[
\begin{align*}
\text{MeO} & \quad \text{MeO} \\
\text{MeO} & \quad \text{MeO} \\
\end{align*}
\]

\[
\begin{align*}
\text{MeO} & \quad \text{MeO} \\
\text{MeO} & \quad \text{MeO} \\
\end{align*}
\]
Table 3 (Continued)

\[ \text{Me} \text{Me} \xrightarrow{\text{Me}} \text{Me} \text{Me} \]
\[ \text{OMe} \xrightarrow{\text{OMe}} \text{OMe} \]
\[ \text{R} \xrightarrow{\text{NO}_2} \text{Ph} \cdot \text{CH}_2\text{O}(\text{R}) \]

\[ \text{Me} \text{Me} \]
\[ \text{OMe} \xrightarrow{\text{OMe}} \text{OMe} \]
\[ \text{Me} \text{Me} \]
\[ \text{OMe} \xrightarrow{\text{OMe}} \text{OMe} \]
\[ \text{R} \xrightarrow{\text{NO}_2} \text{Ph} \cdot \text{CH}_2\text{O}(\text{R}) \]

\[ \text{Me} \text{Me} \]
\[ \text{OMe} \xrightarrow{\text{OMe}} \text{OMe} \]
\[ \text{Me} \text{Me} \]
\[ \text{OMe} \xrightarrow{\text{OMe}} \text{OMe} \]
\[ \text{R} \xrightarrow{\text{NO}_2} \text{Ph} \cdot \text{CH}_2\text{O}(\text{R}) \]

\[ \text{Tri} \]
\[ \text{Me} \text{Me} \]
\[ \text{OMe} \xrightarrow{\text{OMe}} \text{OMe} \]
\[ \text{Me} \text{Me} \]
\[ \text{OMe} \xrightarrow{\text{OMe}} \text{OMe} \]
\[ \text{R} \xrightarrow{\text{NO}_2} \text{Ph} \cdot \text{CH}_2\text{O}(\text{R}) \]
Table 3 (Continued)

\[
\begin{align*}
\text{OMe} & \xrightarrow{\text{Br}} \text{MeO} \\
\text{MeO} & \xrightarrow{\text{Br}} \text{Br} \\
\text{MeO} & \xrightarrow{\text{CMe}} \text{CMe} \\
\text{Cl} & \xrightarrow{\text{CMe}} \text{CMe}
\end{align*}
\]
1:3-Dimethyl-5-Methoxybenzene.

A solution of this ether (15g.) in acetic acid (40 mls.) containing hydrogen peroxide (90% : 5 mls.) and sulphuric acid (2 drops) became dark brown but deposited no crystals after several weeks. Dilution with water followed by distillation in a current of steam yielded volatile brownish-yellow crystals; after crystallisation from butanol these yielded 2:6-dimethyl-1:4-benzoquinone, rosettes of golden-yellow rods (1.7g.) m.p. 72°. (Noelting and Forel, Ber., 1885, 18, 2679 report m.p. 72-73°). Oxidizing solutions less concentrated than that cited yielded no quinone.

Reductive Acetylation of 2:6-Dimethylbenzoquinone to 1:4-Diacetoxy-2:6-Dimethylbenzene.

On reductive acetylation of the quinone (1.0g.) by heating with acetic anhydride (3 mls.) and zinc dust (1 g.) in the presence of a few drops of pyridine there was readily obtained 1:4-diacetoxy-2:6-dimethylbenzene (1.1 g.) which separates from light petroleum in thick glassy leaflets, m.p. 92-93°.

Found: C, 65.1; H, 6.2. C₁₂H₁₄O₄ requires C, 64.9; H, 6.4%.

This convenient procedure has been applied in several cases for the characterisation of new quinones; in the sequel it is referred to briefly as "reductive acetylation".
1:2-Dimethoxy-4-Methylbenzene.

To a cooled solution of the ether (6 g.) in 25 ml. acetic acid (25 ml.) was added hydrogen peroxide (30%, 4 ml.) and sulphuric acid (6 drops). After keeping overnight at 8°, the solution deposited orange plates (2.4 g.). These, after crystallisation from butanol, gave 2-methoxy-5-methyl-1:4-benzoquinone, golden-yellow prismatic rods, m.p. 175-176°.

Found: C, 63.5; H, 5.2. Calc. for C₁₅H₁₄O₅: C, 63.2; H, 5.3%.


Reductive Acetylation of 2-Methoxy-5-methyl-1:4-benzoquinone to 1:4-Diacetoxy-2-methoxy-5-methylbenzene.

By the procedure previously described there was obtained in good yield 1:4-diacetoxy-2-methoxy-5-methylbenzene, which separated from ethanol in long prismatic rods, m.p. 129-130°.

Found: C, 60.0; H, 6.1. C₁₈H₁₄O₅ requires C, 60.4; H, 5.9%.

2:3-Dimethoxynaphthalene.

A solution of this ether (m.p. 115°, 6 g.) hydrogen peroxide (30%, 2.5 ml.) and sulphuric acid (6 drops) in acetic acid (60 ml.) after 4 days deposited 2:3-dimethoxy-1:4-naphthaquinone (2.6 g.), clusters of fine, golden-yellow needles, m.p. 116-117°, after crystallisation.
from ligroin.

Found: C, 66.0; H, 4.7. Calc. for C₁₂H₁₀O₄ C, 66.0; H, 4.6%.


**m-Dimethoxybenzene.**

Hydrogen peroxide (90% - 1 ml.) was added during one hour to a solution of m-dimethoxybenzene (2 g.) in acetic acid (30 ml.) at 10° - sulphuric acid (2 drops) was then added. After three days at 5-10° the brown solution deposited yellow rods (0.5 g.), recrystallisation of which from dioxan yielded 1(4-methoxy-2:5-quinonyl)-4-methoxy-2:5-benzoquinone, golden-yellow rods, m.p. 231-232° (decomp.): unchanged after sublimation (at 150°) in a high vacuum.

Found: C, 61.4; H, 3.9. C₁₄H₁₀O₆ requires C, 61.3; H, 3.7%.

In the absence of sulphuric acid no product separated during three months although the solution became dark.

**Reductive Acetylation of 1(4-Methoxy-2:5-quinonyl)-4-methoxy-2:5-benzoquinone to 4:4'-dimethoxy-2:5,2':5'-tetra-acetoxydiphenyl.**

The quinone was heated with acetic anhydride and zinc dust in the presence of a few drops of pyridine: the resultant tetra-acetoxy-derivative separated from
ethanol in irregular rhombs, m.p. 187-187.5°.
Found: C, 59.3; H, 5.1; M.W.333 (Rast). \( \text{C}_{22}\text{H}_{22}\text{O}_{10} \)
requires C, 59.2; H, 5.0%. M.W.446.

Note: Several repetitions of the above experiment, using dioxan as solvent, yielded no quinone. The ether was recovered, after one month, completely unchanged.

\textbf{m-Dibenzyloxybenzene.}

A suspension of the ether (m.p. 75°; 2 g.) in acetic acid (35 mls.) together with hydrogen peroxide (90%; 0.75 mls.) and sulphuric acid (2 drops) gave overnight a dark-red solution which deposited red crystals (0.4 g.). Recrystallisation from acetic acid and subsequently from nitrobenzene yielded (2-benzyloxy-5-quinonyl)-5,2-benzyloxy-1,4-benzoquinone, orange-yellow, short prismatic rods. m.p. 258° (explosively).

Found: C, 72.9; H, 4.3. M.W.410 (Rast). \( \text{C}_{26}\text{H}_{18}\text{O}_{6} \)
requires C, 73.2; H, 4.3%. M.W.428.

\textbf{1:3-Dimethoxy-5-methylbenzene -(Crocinol dimethyl ether).}

A solution of the ether (2 g.) in acetic acid (15 mls.) to which hydrogen peroxide (90%; 1 ml.) and sulphuric acid (2 drops) had been added became deep red after several days and deposited golden-yellow, fern-like plates (0.2 g.). After crystallisation from cyclohexane these yielded yellow plates (or needles from a concentrated solution), m.p. 149-150.5°, of 2-methoxy-6-methyl-4-benzoquinone.
Found: C, 62.9; H, 5.1. Calc. for C₈H₈O₃: C, 63.2; H, 5.3%.

Heinrich and Naehingall, (Ber., 1903, 36, 339) give m.p. 147°.

1,3-Dimethoxy-4-ethylbenzene.

A solution of the ether (2 g.) in acetic acid together with hydrogen peroxide (30% ; 3 mls.) and sulphuric acid (3 drops) deposited golden-yellow, prismatic needles (0.5 g.) after a week. Crystallisation from ethanol yielded 2-ethyl-5-methoxy-1:4-benzoquinone, golden-yellow prismatic needles, m.p. 154-155°. Found: C, 65.2; H, 6.0. C₉H₁₀O₃ requires C, 65.0; H, 6.1%.

Reductive Acetylation.

By reductive acetylation this quinone yielded 2-ethyl-5-methoxy-1:4-diacetoxybenzene, silky, prismatic needles from cyclohexane, m.p. 112-113°. Found: C, 62.3; H, 6.3. C₁₃H₁₆O₅ requires C, 61.9; H, 6.4%.

1,3-Dimethoxynaphthalene.

Hydrogen peroxide (90% - 3 mls.) was added dropwise to a cooled solution of the ether (6 g.) in acetic acid (60 mls.) containing sulphuric acid (6 drops). After 5 days at room temperature the solution deposited orange needles (1.5 g.) which, after recrystallisation from butanol yielded 2-methoxy-1:4-naphthaquinone, golden-yellow needles, m.p. 183-184°. Found: C, 70.6; H, 4.4. Calc. for C₁₁H₈O₃: C, 70.2; H, 4.3%. Fieser (J. Amer. Chem. Soc., 1926, 48, 2352) gives m.p. 183.5°.

Reductive acetylation of the quinone yielded 1:4-diacetoxy-2-methoxynaphthalene, rectangular plates from aqueous methanol or hemispherical pellets from cyclohexane, m.p. 130.5-131.5°. Fieser, (loc. cit.) gives m.p. 129-130°.
39.

**p-Dimethoxybenzene.**

(1) Hydrogen peroxide (90%; 1 ml.) was added from a microburette during 30 minutes to a cooled (5°) solution of p-dimethoxybenzene (2 g.) in glacial acetic acid (20 mls.) containing concentrated sulphuric acid (2 drops). After 2 days at room temperature there had separated yellow rods (0.3 g.), m.p. over 300° (decomp.) which, after recrystallisation from acetic acid, yielded 2:5-dimethoxy-1:4-benzoquinone as deep, golden-yellow, fern-like leaflets, m.p. 300° (decomp.).

(11) A solution of the ether (5 g.) in acetic acid (50 mls.) and hydrogen peroxide (30%; 25 mls.) deposited during 5 days golden-yellow rods (1.5 g.) m.p. 300° (decomp.) of 2:5-dimethoxy-1:4-benzoquinone.

Found: C, 56.9; H, 4.7. Calc. for C₈H₈O₄ C, 57.2; H, 4.8%.

Anslow and Raistrick, (J. Chem. Soc., 1939, 1450) give m.p. 303° whilst Priess et al. (J. Amer. Chem. Soc., 1952, 74, 1305) give m.p. 220° which is therefore likely to be an error.

**Reduction of 2:5-Dimethoxy-1:4-benzoquinone to 1:4-Dihydroxy-2:5-dimethoxybenzene.**

The quinone (0.5 g.) was heated under reflux with a solution of stannous chloride (2 g.) in ethanol (15 mls.) for 2 hours: the product of the reaction separated from
Acetic acid as prismatic rods, m.p. 171-172.5°, of 1:4-dihydroxy-2:5-dimethoxybenzene.

Found: C, 56.2; H, 5.9. Calc. for C₈H₁₀O₄ C, 56.5; H, 5.8%.

Neitzky and Rechberg (Ber., 1891, 23, 1217) give m.p. 166°; Schuler (Arch. Pharm., 1907, 245, 280) gives m.p. 170°.

1:4-Dimethoxy-2:5-dimethylbenzene, (p-XYLOQUINOLDIMETHYL ETHER).

The ether (1.5 g.) in acetic acid (25 mls.) containing hydrogen peroxide (90%; 0.3 mls.) and sulphuric acid (2 drops) was kept for a week and the resulting brown solution then diluted with water. The precipitate (0.9 g.) when crystallised from light petroleum, yielded 2:5-dimethyl-1:4-benzoquinone, bright golden rods; m.p. 125-126° alone and when mixed with an authentic specimen of p-XYLOQUINONE.

1-Methoxy-4-p-nitrobenzylOXYBENZENE.

A solution of the ether (0.75 g.) in acetic acid (25 mls.) containing hydrogen peroxide (90%; 1.5 mls.) and sulphuric acid (3 drops) after 48 hours yielded clusters of yellow needles (0.25 g.). These, after two recrystallisations from acetic acid, gave 2-methoxy-5-p-nitrobenzylOXY-1:4-benzoquinone, clusters of fine, yellow needles, m.p. 253-255° (decomp.).

Found: C, 53.4; H, 4.3; N, 5.0. C₁₄H₁₁O₆N requires C, 53.1; H, 3.8; N, 4.8%.
41.

**1:2:3-Trimethoxybenzene.**

A solution of the ether (1.0 g.) hydrogen peroxide (90%; 1.6 mls.) and sulphuric acid (1 drop) in acetic acid (15 mls.) after 48 hours deposited 2:6-dimethoxy-1:4-benzoquinone (0.15 g.), rosettes of orange-yellow rods, m.p. 252° (decomp.) alone or when mixed with the quinone obtained from the isomeric 1:3:5-trimethoxybenzene.

**1:3:5-Trimethoxybenzene.**

By similar treatment this isomer (1.5 g.) yielded the same 2:6-dimethoxy-1:4-benzoquinone, orange-yellow rods (0.3 g.) m.p. 252° (decomp.) alone or when mixed with the quinone from 1:2:3-trimethoxybenzene.

**1:2:4-Trimethoxybenzene.**

A solution of the ether (2 g.), hydrogen peroxide (90%; 0.8 mls., or 30%, 2.5 mls.) and sulphuric acid (2 drops) in acetic acid (8 mls.) after half an hour deposited orange crystals (0.5 g.); these, by crystallisation from acetic acid, yielded 2:5-dimethoxy-1:4-benzoquinone, orange prismatic rods, m.p. 300°.

Found: C, 57.4; H, 4.8. C₈H₆O₄ requires C, 57.2; H, 4.8%.

By reductive acetylation this quinone yielded 1:4-diaceetoxy-2:5-dimethoxybenzene, glassy rhombs, m.p. 182.5 - 183.5°, alone or when mixed with the specimen obtained by the reductive acetylation of the quinone.
obtained from 1:4-dimethoxybenzene.

Found: C, 56.5; H, 5.6. \( \text{C}_{13} \text{H}_{16} \text{O} \) requires C, 56.7; H, 5.6%.

1:2:4:5-Tetramethoxybenzene.

A solution of the ether (0.5 g.), hydrogen peroxide (90%; 0.3 mls.), and sulphuric acid (1 drop) in acetic acid (3 mls.) after 15 minutes deposited yellow platelets of 2:5-dimethoxy-1:4-benzoquinone which, after crystallisation from acetic acid, had m.p. above 300° (decomp.). This quinone was characterised by its reductive acetylation product, which had m.p. 182.5-183.5° alone and when mixed with a specimen of 1:4-diacetoxy-2:5-dimethoxybenzene (see under 1:2:4-Trimethoxybenzene).

4-Bromo-1:3-dimethoxybenzene.

(1) A solution of 4-bromo-1:3-dimethoxybenzene (5 g.) in acetic acid (60 mls.) and hydrogen peroxide (30%; 40 mls.) after a week at room temperature had deposited a mixture of colourless and bright-red crystals (3 g.; dibromo-compound 2.0 g. + quinone 1.0 g. - see below). This mixture was separated in two ways:

(a) The mixture (0.2 g.) was warmed with sodium hydroxide (3N; 25 mls.) and the residual colourless crystals (0.6 g.) m.p. 141-142°, removed by filtration. By recrystallisation from ethanol they yielded 4:6-dibromo-1:3-dimethoxybenzene, needles, m.p. 142-143°, alone or when mixed with an authentic specimen prepared by the
bromination of dimethoxyresorcinol.

Found: C, 32.7; H, 2.3; Br, 54.0. Calc. for C₈H₆Br₂, C, 32.5; H, 2.7; Br, 54.0%. Beilstein gives m.p. 142°.

(b) The mixture (1.5 g.) was extracted with boiling cyclohexene (30 mls.); the undissolved 2-bromo-5-methoxy-1:4-benzoquinone separated from benzene in rosettes of golden-yellow rods (0.5 g.), m.p. 190-191°.

Found: C, 39.1; H, 2.5; Br, 36.4. C₇H₅OBr requires C, 38.7; H, 2.3; Br, 36.8%.

Reductive Acetylation of 2-bromo-5-methoxy-1:4-benzoquinone.

By the usual procedure there was readily obtained in good yield 2-bromo-1:4-diacetoxy-5-methoxybenzene which separated from ethanol in prismatic rods, m.p. 136-137°.

Found: C, 44.1; H, 4.1; Br, 25.8. C₁₁H₁₁O₂Br requires C, 43.6; H, 3.7; Br, 26.4%.

Examination of the Mother Liquor.

The acetic acid - hydrogen peroxide filtrate from which the 3 g. of mixed crystals had been separated was diluted with four volumes of water, when a yellow emulsion was formed. This emulsion was extracted five times with ether (150 mls.; 4×100 mls.) and the combined extracts dried with sodium sulphate, and the solvent evaporated. (The yellow aqueous solution was evaporated at 30° under reduced pressure but left no residue).
The residue from the ethereal extract was mixed with water which caused the separation of a copious precipitate of bright-yellow crystals (1.2 g.): these were separated by fractional crystallisation from ethanol into 4:6-dibromo-1:3-dimethoxybenzene (0.6 g.) m.p. 140-142°C and 2-bromo-5-methoxybenzoquinone (0.3 g.) m.p. 190-192°C.

The brown aqueous solution was extracted with chloroform and the extract dried and evaporated; the residual pungent, sternutatory oil was dissolved in ether and the solution extracted with sodium hydroxide (3N; 50 mls.). The alkaline extract was acidified (N.HCl) and again extracted with ether; this yielded a light-brown oil of pleasant odour (2.4 g.).

This oil was soluble in water, dilute acid and alkali and could not be distilled without decomposition; it reacted with potassium permanganate with violence; it yielded no bromo- or nitro-derivative nor would it form a crystalline picrate. It was faintly acid to litmus and gave positive reactions for the presence of bromine and formaldehyde (resorcinol test). A portion of the oil (1 g.) was heated on a steam-bath for 6 hours with p-toluidine (2 g.), and the reaction product, after treatment with dilute hydrochloric acid, recrystallised twice from acetic acid. A few milligrams of crystals
were obtained which had m.p. 270-272°, either alone or mixed with oxal-di-p-toluidide.

Thus the original 4-bromo-1:3-dimethoxybenzene (5 g.) yielded 4:6-dibromo-1:3-dimethoxybenzene (2.6 g.), 2-bromo-5-methoxy-1:4-benzoquinone (1.3 g.) and small amounts of oxalic acid, formaldehyde and probably other water-soluble products. Parallel results were obtained in a second experiment.

(ii) A solution of 4-bromo-1:3-dimethoxybenzene (6 g.) in acetic acid (30 mls.) containing hydrogen peroxide (90%; 6 mls.) and sulphuric acid (10 drops) deposited 2-bromo-5-methoxy-1:4-benzoquinone (4 g.) which, after crystallisation from benzene, had m.p. 190-191° alone or when mixed with the specimen from (i)(b).

(iii) A solution of 4-bromo-1:3-dimethoxybenzene (7.5 g.) in acetic acid (30 mls.) and hydrogen peroxide (30%; 60 mls) began to deposit crystals after 85 hours. The crystals were removed after 33 hours and subsequent crops of crystals were removed at intervals and separated into their components by method (i)(a). The results are shown in Table 4.
Table 4

<table>
<thead>
<tr>
<th>Time (hrs)</th>
<th>Total Crystals (g.)</th>
<th>Dibromo-quinone (by diff.) (g.)</th>
<th>% Dibromo-quinone in mixed crystals</th>
</tr>
</thead>
<tbody>
<tr>
<td>93</td>
<td>0.11</td>
<td>0.33</td>
<td>0.05</td>
</tr>
<tr>
<td>111</td>
<td>0.27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>135</td>
<td>0.35</td>
<td>0.35</td>
<td>0.01</td>
</tr>
<tr>
<td>162</td>
<td>0.34</td>
<td>0.43</td>
<td>0.43</td>
</tr>
<tr>
<td>183</td>
<td>0.43</td>
<td>0.35</td>
<td>0.33</td>
</tr>
<tr>
<td>255</td>
<td>0.42</td>
<td>0.19</td>
<td>0.23</td>
</tr>
<tr>
<td>Totals</td>
<td>2.43</td>
<td>1.43</td>
<td>1.05</td>
</tr>
</tbody>
</table>

Bromine Balance.

Initial monobromo-ether contains - 2.50 g. bromine
Final dibromo-compound contains - 0.75 " 
Final quinone contains - 0.40 " 
Remaining in diluted solution\(^{\text{x}}\) 1.35 g. bromine

\(^{\text{x}}\)This deposited only a trace of the dibromo-compound, m.p. 142°.

Hence it would appear that some two-thirds of the original compound is converted into water-soluble compounds and some 50% of the bromine also.

(iv) This experiment was devised to maintain an excess of the 4-bromo-1,3-dimethoxybenzene throughout its course.
A solution of the ether (4.5 g.) in acetic acid (55 mls.) and hydrogen peroxide (30%; 2 mls.) was prepared and additional hydrogen peroxide was added at intervals - 20 mls. was added during 300 hours at irregular intervals. The crystals (1.7 g.) were separated from the dark-brown solution and recrystallised once from ethanol when they had m.p. 142° alone or when mixed with an authentic specimen of 1:3-dibromo-4:6-dimethoxybenzene. No quinone could be isolated during this experiment.

Non-Inter-convertibility of 4:6-Dibromo-1:3-dimethoxybenzene and 2-Bromo-5-methoxy-1:4-benzoquinone.

A solution of acetic acid (60 mls.) and hydrogen peroxide (30%; 40 mls.) was prepared and to two separate 10 ml. portions was added (a) 0.05 g. of the dibromo-derivative and (b) 0.05 g. of the quinone. After keeping several months (a) yielded quantitatively unchanged material, (b) a trace of quinone had dissolved but was otherwise unchanged.

On the other hand, when to the mother-liquor from (b) was added 3 drops of the original 4-bromo-1:3-dimethoxybenzene, colourless needles of the dibromo-1:3-dimethoxybenzene separated after only 40 hours. It would thus appear that the dibromo-ether and the mono-bromo-quinone are not interconvertible under the conditions of the original oxidation procedure.
Action of Nitric Acid on 4-Bromo-1,3-dimethoxybenzene.

Nitric acid (5 ml.) was added to a solution of the ether (3 g.) in glacial acetic acid (10 ml.); an immediate reaction occurred resulting in a green solution from which water precipitated a greenish solid. This separated from ethanol in colourless needles (1.7 g.) and after further crystallisation from the same solvent yielded 4:6-dibromo-1,3-dimethoxybenzene, m.p. 139°, alone or when mixed with an authentic specimen.

4-Chloro-1,3-dimethoxybenzene.

A solution of the ether (2 g.) in acetic acid containing hydrogen peroxide (1.2 ml.; 90%) and sulphuric acid (3 drops) became brown but deposited no crystals during a week. Dilution with water yielded a buff precipitate (0.75 g.), which, after crystallisation from butanol, gave 2-chloro-5-methoxy-1,4-benzoquinone, mustard-yellow, fern-like needles, m.p. 174°.

Found: C, 49.2; H, 3.0; Cl, 20.9. C₇H₅O₃Cl requires C, 43.6; H, 2.9; Cl, 20.6%.

Reductive Acetylation.

This quinone, by the usual procedure, yielded 1:4-diacetoxy-2-chloro-5-methoxybenzene, which, after two crystallisations from methanol, formed rhombs, m.p. 127°.

Found: C, 51.5; H, 4.3; Cl, 13.8. C₁₁H₁₁O₃Cl requires C, 51.1; H, 4.25; Cl, 13.7%. 
x-Bromo-3:5-dimethoxy-1-methylbenzene.

A solution of this ether (0.9 g.) in acetic acid (6.0 mls.) containing hydrogen peroxide (0.75 mls.; 90%) and sulphuric acid (2 drops), after standing overnight deposited yellow needles (0.25 g.); by dilution with water a further quantity (0.3 g.) separated.

Crystallisation from methanol gave x-bromo-3-methyl-5-methoxy-1:4-benzoquinone, golden-yellow needles, m.p. 150-151°.

Found: C, 41.5; H, 3.1; Br, 34.1. \( \text{C}_{10}\text{H}_{7}\text{O_5Br} \) requires C, 41.6; H, 3.1; Br, 34.6%.

Reductive Acetylation.

By the usual procedure, this quinone yielded 2:5-diacetoxy-3-methoxy-x-bromotoluene which separated from ethanol in glassy, hexagonal plates, m.p. 133-134°.

Found: C, 45.7; H, 4.4; Br, 24.9. \( \text{C}_{12}\text{H}_{13}\text{O_5Br} \) requires C, 45.4; H, 4.1; Br, 25.2%.

2:4-Dibromo-1:3:5-trimethoxybenzene.

A solution of this ether (2 g.), hydrogen peroxide (90%; 3 mls.) and sulphuric acid (5 drops) in acetic acid (50 mls.) after a week was transferred to a vacuum desiccator containing soda-lime. The crystalline residue was washed with water, dried and extracted with warm cyclohexane. Evaporation of the combined extracts yielded colourless crystals (0.6 g.) slightly contaminated with the orange quinone; the latter was removed by
extraction with warm sodium hydroxide. Crystallisation of the residue from light petroleum yielded 1:3:5-tribromo-2:4:6-trimethoxybenzene (0.4 g.), silky rods, m.p. 140-141° alone or when mixed with an authentic specimen. The insoluble residue (from the cyclohexane extraction), recrystallised from ligroin (b.p. 100-120°), yielded 2:6-dibromo-3:5-dimethoxy-1:4-benzoquinone, bright reddish-orange plates - or prismatic rods from a concentrated solution - (0.4 g.), m.p. 176-177°.

Hoffmann (Ber., 1873, 11, 332) and Will (ibid, 1838, 21, 609) give m.p. 175°.

Found: C, 29.5; H, 1.3; Br, 49.0. Calc. for C_6H_4Br_2 C, 29.8; H, 2.1; Br, 49.0%.

1-Bromo-2:4:5-trimethoxybenzene.

A solution of the ether (2.5 g.) hydrogen peroxide (30%; 1.2 mls.) and sulphuric acid (2 drops) in acetic acid (15 mls.) after several hours deposited crystals (0.4 g.) which, after crystallisation from nitrobenzene, yielded 2:5-dimethoxy-1:4-benzoquinone, golden blades, m.p. over 200°.

Found: C, 57.3; H, 4.7. Calc. for C_6H_4O_4 C, 57.2; H, 4.8%.

It was further characterised as its reduction-acetylation product, m.p. 183-184° alone or when mixed with the analogous product obtained from the unbrominated 1:2:4-trimethoxybenzene.
The filtrate, from which the 2:5-dimethoxy-1:4-
benzoquinone had been removed, deposited 2-bromo-5-methoxy-
1:4-benzoquinone on dilution with water; this, after
recrystallisation from butanol, weighed 0.4 g. and had
m.p. 183-191° alone or when mixed with a specimen obtained
from 2:4-dimethoxy-1-bromobenzene.

2-Bromo-1:3:5-trimethoxybenzene.

A solution of the ether (2.5 g.) hydrogen peroxide
(90%; 0.9 mls.) and sulphuric acid (3 drops) in acetic
acid (25 mls.) after four days deposited yellow needles
(0.5 g.) which, after recrystallisation from propanol,
yielded 3-bromo-2:6-dimethoxy-1:4-benzoquinone, long,
yellow needles, m.p. 143-149°. Levene (J. Amer. Chem.
Soc., 1928, 48, 797) gives m.p. 143°.
Found: C, 39.2; H, 2.3; Br, 22.1. Calc. for C₁₇H₁₄Br
C, 39.9; H, 2.9; Br, 22.3%.

2:4-Dichloro-1:3:5-trimethoxybenzene.

A solution of the ether (2 g.), hydrogen peroxide
(90%; 2 mls.) and sulphuric acid (5 drops) in acetic
acid (25 mls.) after a week deposited a mixture of colour-
less and golden-yellow crystals (1.5 g.). Extraction
of the mixture with boiling light petroleum (b.p. 40-60°)
left behind the yellow crystals: these, after crystallisa-
tion from ligroin yielded 2:6-dichloro-3:5-dimethoxy-1:4-
benzoquinone, golden-yellow rods, m.p. 149-150°.
Found: C, 41.0; H, 2.7; Cl, 29.1. Calc. for C₁₇H₁₄Cl₂
C, 40.5; H, 2.6; Cl, 29.9%

Graebe and Hess (Annalen, 1903, 340, 240) give m.p. 151-158°.

The light petroleum extracts were washed with warm sodium hydroxide and then with water; after drying and concentration the solution deposited colourless crystals (0.9 g.). These, after recrystallisation from light petroleum yielded 1:3:5-trichloro-2:4:6-trimethoxybenzene, long needles, m.p. 112° alone or when mixed with an authentic specimen.
EXPERIMENTAL SECTION

(b) Unsuccessful Oxidations

The following Table (Table 5) enumerates the ethers from which significant amounts of quinone could not be isolated after prolonged treatment with hydrogen peroxide in glacial acetic acid together with a small amount of sulphuric acid.

In most cases the oxidizing medium turned brownish but on the addition of water the ether was recovered almost quantitatively, and with unchanged melting point. In the few cases where a depression of the melting point by a few degrees was observed a single recrystallisation was sufficient to raise it to the original value.

The reaction occasionally was vigorous. In some such cases the quinone could then be isolated by using dilute hydrogen peroxide, or by adding the hydrogen peroxide slowly to the cooled reaction mixture. More usually, however, oxidation to water-soluble products occurred up to the limit when conditions were so mild that no reaction took place.
### Table 5

**Ethers from which Quinones were not obtained**

<table>
<thead>
<tr>
<th>No.</th>
<th>Ether</th>
<th>Wt.</th>
<th>HOC.&lt;sub&gt;5&lt;/sub&gt;</th>
<th>H&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;</th>
<th>H&lt;sub&gt;2&lt;/sub&gt;SO&lt;sub&gt;4&lt;/sub&gt;</th>
<th>Period</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>g.</td>
<td>ml.</td>
<td>ml.</td>
<td>%</td>
<td>drops</td>
<td>days</td>
</tr>
<tr>
<td>1</td>
<td>methoxybenzene</td>
<td>1.0</td>
<td>14.0</td>
<td>8.0</td>
<td>30</td>
<td>2</td>
<td>60</td>
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<tr>
<td></td>
<td>methoxybenzene</td>
<td>1.0</td>
<td>14.0</td>
<td>2.0</td>
<td>90</td>
<td>2</td>
<td>3-hrs. Water-sol.</td>
</tr>
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<td>2</td>
<td>1:2-dimethoxybenzene</td>
<td>2.0</td>
<td>15.0</td>
<td>0.5</td>
<td>90</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>1:2-dimethoxybenzene</td>
<td>2.0</td>
<td>5.0</td>
<td>0.5</td>
<td>90</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>1-hydroxy-4-methoxybenzene</td>
<td>1.5</td>
<td>15.0</td>
<td>1.0</td>
<td>90</td>
<td>1</td>
<td>2-3 hrs. Water-sol.</td>
</tr>
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<td>1.0</td>
<td>60.0</td>
<td>20.0</td>
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<td>0.3</td>
<td>90</td>
<td>1</td>
<td>3-hrs. Water-sol.</td>
</tr>
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<td>0.5</td>
<td>60.0</td>
<td>20.0</td>
<td>90</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10% recovery</td>
</tr>
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<td>1.0</td>
<td>90</td>
<td>1</td>
<td>12</td>
</tr>
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<td>12.0</td>
<td>2.0</td>
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<td>1</td>
<td>5</td>
</tr>
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<td>31</td>
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<td>10.0</td>
<td>1.2</td>
<td>90</td>
<td>1</td>
<td>14</td>
</tr>
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<td>5.0</td>
<td>1.5</td>
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<td>30</td>
</tr>
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<td>65.0</td>
<td>25.0</td>
<td>30</td>
<td>0</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>1-bromo-4-methoxy-2-methylbenzene</td>
<td>3.0</td>
<td>15.0</td>
<td>2.0</td>
<td>90</td>
<td>1</td>
<td>50</td>
</tr>
<tr>
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<td>4-bromo-1-methoxy-2-nitrobenzene</td>
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<td>40.0</td>
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<td>21</td>
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<td>1.5</td>
<td>1.0</td>
<td>90</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>11</td>
<td>1-chloro-4-methoxy-2-methylbenzene</td>
<td>3.0</td>
<td>30.0</td>
<td>2.0</td>
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<td>2</td>
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</tr>
<tr>
<td>12</td>
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<td>10.0</td>
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<td>90</td>
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<td>40</td>
</tr>
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<td>60</td>
</tr>
<tr>
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<td>1.0</td>
<td>90</td>
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</tr>
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<td>HClAc.</td>
<td>H₂O₂</td>
<td>H₂SO₄</td>
<td>Period</td>
<td>Observation</td>
</tr>
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<td>-----------------------------</td>
<td>-----</td>
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<td>25</td>
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<td></td>
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<td>ml.</td>
<td>%</td>
<td>drops</td>
<td>Unchanged</td>
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<td>30</td>
<td>2</td>
<td>20</td>
</tr>
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<td>10.0</td>
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<td>90</td>
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<td>65</td>
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<td>75.0</td>
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<td>5.0</td>
<td>75.0</td>
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<td>ml.</td>
<td>ml.</td>
<td>%</td>
<td>drops</td>
<td>92% recovery</td>
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<td>%</td>
<td>drops</td>
<td>Unchanged</td>
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<td>65</td>
</tr>
<tr>
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<td>diphenyl ether</td>
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<td>ml.</td>
<td>%</td>
<td>drops</td>
<td>90% recovery</td>
</tr>
<tr>
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<td>15.0</td>
<td>2.0</td>
<td>90</td>
<td>3</td>
<td>31</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>ml.</td>
<td>ml.</td>
<td>%</td>
<td>drops</td>
<td>Unchanged</td>
</tr>
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<td>34</td>
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<td>ml.</td>
<td>%</td>
<td>drops</td>
<td>Unchanged</td>
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<td>2.0</td>
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<td>Unchanged</td>
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<td>30</td>
<td>2</td>
<td>2 hrs.</td>
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<td>11</td>
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<td>150</td>
<td>10.0</td>
<td>30</td>
<td>2</td>
<td>Water-sol.</td>
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<tr>
<td>30</td>
<td>5-methoxy-1:3-</td>
<td>15.0</td>
<td>40</td>
<td>5.0</td>
<td>90</td>
<td>2</td>
<td>10</td>
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<td></td>
<td>dimethylbenzene</td>
<td></td>
<td>ml.</td>
<td>ml.</td>
<td>%</td>
<td>drops</td>
<td>Unchanged</td>
</tr>
<tr>
<td>31</td>
<td>x-bromo-5-methoxy-</td>
<td>1.0</td>
<td>20</td>
<td>1.0</td>
<td>90</td>
<td>2</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>1:3-dimethylbenzene</td>
<td>1.0</td>
<td>15</td>
<td>1.0</td>
<td>90</td>
<td>2</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>Trace tri-Br</td>
<td></td>
<td>ml.</td>
<td>ml.</td>
<td>%</td>
<td>drops</td>
<td>90% recovery</td>
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<td>32</td>
<td>1:4-dimethoxy-</td>
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<td>10</td>
<td>1.0</td>
<td>90</td>
<td>1</td>
<td>14</td>
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<td>naphthalene</td>
<td></td>
<td>ml.</td>
<td>ml.</td>
<td>%</td>
<td>drops</td>
<td>Unchanged</td>
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<tr>
<td>33</td>
<td>1-methoxy-3-</td>
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<td>25</td>
<td>1.0</td>
<td>90</td>
<td>2</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>phenoxybenzene</td>
<td></td>
<td>ml.</td>
<td>ml.</td>
<td>%</td>
<td>drops</td>
<td>Unchanged</td>
</tr>
</tbody>
</table>
Notes on Table 5.

1. In the cases of methoxybenzene, 2-bromo-1:4-dimethoxybenzene and 1:5-dimethoxynaphthalene a number of intermediate concentrations of oxidizing solution, between those cited, were tried. In every case a mixture of water-soluble material and unchanged ether was obtained, the amount of the latter decreasing with increasing hydrogen peroxide concentration.

2. Oxidation of 1:2-dimethoxybenzene and methoxybenzene was also attempted in dioxan solution in place of acetic acid. The results were very similar to those cited for acetic acid.

3. "Unchanged" implies a recovery of over 98% of the ether. "Water-sol." implies that the solution, after reaction for the stipulated period, could be diluted with ten times its own volume of water without clouding or giving a precipitate.
Attempted Oxidations Using Tert.-Butyl Peroxides.

The following oxidations were attempted using tert.-butyl peracetate, perbenzoate and hydroperoxide. In each case unchanged ether was recovered quantitatively. The solvent used was glacial acetic acid (10 mls.) with the exception of the last experiment in which dioxan (10 mls.) was used.

Table 6

Attempted Oxidations Using Tert.-Butyl Peroxides

<table>
<thead>
<tr>
<th>Ether (1 g.)</th>
<th>Peroxide (1 g.)</th>
<th>$\text{H}_2\text{SO}_4$ (drops)</th>
<th>Period (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:2:4-trimethoxybenzene</td>
<td>t-butyl hydroperoxide</td>
<td>None 1.0</td>
<td>12</td>
</tr>
<tr>
<td>1:2:3-trimethoxybenzene</td>
<td>t-butyl hydroperoxide</td>
<td>None 1.0</td>
<td>14</td>
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<tr>
<td>1:2:3-trimethoxybenzene</td>
<td>t-butyl peracetate</td>
<td>None 1.0</td>
<td>8</td>
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<tr>
<td>4-bromo-1:3-dimethoxybenzene</td>
<td>t-butyl hydroperoxide</td>
<td>None 1.0</td>
<td>12</td>
</tr>
<tr>
<td>4-bromo-1:3-dimethoxybenzene</td>
<td>t-butyl peracetate</td>
<td>None 1.0</td>
<td>9</td>
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<tr>
<td>4-bromo-1:3-dimethoxybenzene</td>
<td>t-butyl hydroperoxide</td>
<td>None 21</td>
<td></td>
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</tbody>
</table>
(1) Masters' Degrees (excluding M.S. and M.D.S.), Ph.D., D.Mus.

For all examinations for Masters' Degrees (except the M.S. and M.D.S.) pro rata fees are payable as set out below, but the total fees payable for any number of candidates up to four examined together is limited to £50 per examination with a further £10 for every candidate in excess of four examined at the same time, unless the Senate have laid down by Regulation a set form of examination which involves a greater expense.

**Setting Papers**

For each paper set (fee divisible between the Examiners taking part) .......................... £ 6 0 0

[M.Sc. History and Philosophy of Science—Part I: A fixed fee of £30 is divisible between the External Examiners for their work in setting papers]

Mathematics (including Mathematical Statistics) ............................................................ £ 8 0 0

For transcribing the whole or the major part of a paper into an Oriental script for reproduction by photography ............................................................... £ 1 1 0

For modification of a paper for Overseas ........................................................................ £ 1 0 0

Papers in connection with Practical Overseas Examinations: see Practical Examinations below.

**Marking Scripts**

For each of two markings or readings, for each script (£25 per 100) ....................... £ 5 0

At the D.Mus. Examination payment for three markings is allowed.

**Oral Examinations (and Practical Tests at M.A.)***

Master’s Degree Examinations:

Per candidate (maximum fee £7 10s. 0d. per day) .................................................. £ 2 1 0 0

If more than one Internal Examiner acts in addition to the External Examiner, £2 10s. 0d. per candidate is divisible among the Internal Examiners.

Ph.D. Degree Examinations:

To each of two Examiners and to a third if called upon by the Principal, or to each of three Examiners appointed from more than one Faculty, per candidate (maximum fee £7 10s. 0d. per day) .................................................. £ 2 1 0 0

If three Examiners are appointed from the same Faculty to act in the first instance, the following fees will be payable:

Internal Examinations.—A fee of £5 per candidate shared equally between three teachers, or a fee of £2 10s. 0d. per candidate to the Examiner external to the University and a fee of £2 10s. 0d. per candidate shared equally between two teachers.

External Examinations.—A fee of £2 10s. 0d. per candidate to each Examiner, provided that the appointment of the three Examiners has been specifically approved by the External Council after consideration of a special report of the appropriate Board of Studies.

**Practical Examinations (and Oral Examinations at D.Mus.)**

For each practical paper set (fee divisible between the Examiners taking part) ........ £ 6 0 0

For attendance (including marking of candidates' work):—

Whole day ........................................... £ 6 0 0

Half-day ............................................ £ 3 1 0 0

If oral examinations for the Intermediate Examination in Music, B.Mus. and D.Mus. Examinations are held consecutively on the same day, payment will be made for the whole time for which Examiners are present, and not for separate periods for each examination.

If an External or Staff Examiner resides outside the University radius of 30 miles his attendance, if required for a single examination period only on any day, is to be reckoned as attendance for a day.

* For M.Sc. Degree in Geophysics see under *M.Sc. Geophysics.*
If three Examiners read a Thesis or Dissertation in the first instance, the fee for two Examiners is divisible between them.

### Ph.D. Degree Examinations:

For examination of a thesis, to each of two Examiners and to a third if called upon by the Principal, or to each of three Examiners appointed from more than one Faculty:

- £6 0 0

If Examiner is candidate's Supervisor:

- £5 0 0

If three Examiners are appointed from the same Faculty to act in the first instance, the following fees will be payable:

**Internal Examinations.**—A fee of £4 to each of three teachers, including the Supervisor, or a fee of £6 to the Examiner external to the University and half the prescribed fee to each of two teachers (£2 10s. 0d. to the Supervisor and £3 to the other teacher).

**External Examinations.**—A fee of £6 to each Examiner, provided that the appointment of the three Examiners has been specifically approved by the External Council after consideration of a special report of the appropriate Board of Studies.

No fee shall be payable to a Teacher of the University for reading and reporting on a Thesis or Dissertation submitted in the joint names of the candidate and himself.

For re-reading a thesis or dissertation submitted for a Ph.D. Examination and re-submitted for a Master’s Examination or for re-reading a thesis or dissertation re-presented in connection with further tests in oral, written or practical examinations, the fees payable are half the fees prescribed for the first reading.

For re-reading a thesis or dissertation submitted in a revised form, the fees payable are as for the first reading.

| **Problem (at Mathematics)** (fee divisible between the Examiners taking part) | 8 0 0 |
| **Musical Exercise (D.Mus.)** (fee divisible between the Examiners taking part) | 12 0 0 |
| **M.Sc.-Geophysics, to cover reading the dissertation, examination of course-work and attendance at oral examination, per candidate, to each of two Examiners** | 2 10 0 |
| **Special ad hoc Qualifying Examination**—fee per candidate (fee divisible between the Examiners taking part) | 5 5 0 |

**Chairmen’s Fees**

- **LL.M.** | £6 0 0
- **M.Th.** | £6 0 0
- **M.Sc. History and Philosophy of Science** | £10 0 0
- **External M.A. and M.Sc. Mathematics** | £15 0 0
- **M.A. English: December examination** | £5 0 0
- **May examination** | £8 0 0

**Meetings**

To each External or Staff Examiner, for attendance at each Meeting if summoned by the University:

- £2 10 0

Maximum fee £7 10s. 0d. per day

No fee if held concurrently with a Practical Examination

**Minimum Fee to ad loc.**—Staff or External Examiner

- £6 0 0

* For M.Sc. Degree in Geophysics see under M.Sc. Geophysics.

(2) **D.D., D.Lit., LL.D., D.Sc., D.Sc.(Eng.), D.Sc.(Econ.)**

To each Examiner who acts, inclusive fee, per candidate

- £12 12 0

**Travelling Expenses**

For each occasion on which an Examiner is required by the University to travel a distance of more than 30 miles from his usual residence for Practical Examinations, Oral Examinations, or Examiners’ Meetings, he may claim for journeys actually performed first-class return railway fare, together with the following allowances:

- For necessary absence from home not involving a night:
  - For a period of 5-10 consecutive hours, 5s. 6d.
  - For a period of more than 10 consecutive hours, 12s. 0d.
  - For a necessary period of absence up to 24 hours involving a night away from home, £1 17s. 6d.

- For journeys to or from Berwick or Carlisle or stations in Scotland or Northern Ireland, an allowance of £1 per journey, in addition to the subsistence allowance of £1 17s. 6d.

J. HOOD PHILLIPS

Secretary to the Senate

February 1957
(d) Preparatory Section

Preparation of Ethers
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Preparation Section - Preparation of Ethers.

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<th>Page No.</th>
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</tr>
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<td>59</td>
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<tr>
<td>1:3-Dibenzylbenzene</td>
<td>60</td>
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<td>1-Hydroxy-4-Methoxybenzene</td>
<td>60</td>
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<td>2-Methoxy-1:3-Dimethylbenzene</td>
<td>61</td>
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<tr>
<td>1:3-Dimethoxy-4-Ethylbenzene</td>
<td>62</td>
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<td>2:4-Dichloro-1:3:5-Trimethoxybenzene</td>
<td>71</td>
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1:3-Dimethoxybenzene (Resorcinol Dimethyl Ether)

Resorcinol (20.4 g.) in aqueous sodium hydroxide solution (163 mls. of 10%) was mixed with dimethyl sulphate (46.6 g.; 35 mls.) and vigorously shaken for 15 minutes, during which the violet solution became yellow-brown and warm and the lower layer of the dimethyl sulphate was replaced by an upper oily layer.

The upper layer was separated after one hour and the lower layer extracted with ether (2 x 50 mls.). The ethereal extract was combined with the oil, washed with sodium hydroxide solution (50 mls. of 10%) and water (2 x 50 mls.), and dried with sodium sulphate.

Removal of the ether yielded a light-brown, pleasant-smelling oil (19.1 g.; 75%). Fractionation of the oil at 15 m.m. gave a colourless oil, b.p. 115°/760 m.m., m.p. -48°.

Heilbron reports b.p. 216.5 - 217.7°, m.p. -52°.

1:2-Dimethoxybenzene (Veratrole).

The same quantities and technique were used as quoted for 1:3-dimethoxybenzene.

The yield was 65%, and the distilled oil, b.p. 205°, crystallised, after several days, giving long needles, m.p. 20.5°.
Beilstein reports b.p. 206 - 207°, m.p. 19 - 20°
or 22.5°.

1:3-Dibenzylxyloxybenzene.

Resorcinol (22 g.), potassium hydroxide (11.5 g.)
and benzyl chloride (55 g.) were heated under reflux in
ethanol (175 ml.) for 3 hours. Water was added to
dissolve the precipitated potassium chloride and the
product was extracted with ether. The ethereal extract
was washed with potassium hydroxide solution (3X with
10%), and with water and dried over calcium chloride.

After evaporating the ether, the product was
crystallised from methanol, yielding pink platelets
(20.5 g.) m.p. 75°. Heilbron gives m.p. 76°.

1:4-Dimethoxybenzene (Quinol dimethyl ether) and
1-Hydroxy-4-methoxybenzene (Quinol monomethyl ether).


Quinol (110 g.) in aqueous sodium hydroxide solution
(100 g. in 700 ml. of water), contained in a hydrogen-
filled flask, was cooled to 12° and vigorously shaken
after the addition of neutral dimethyl sulphate (120 ml.).
The mixture became warm and after five minutes was cooled
and the dimethyl ether filtered off, (33 g.) m.p. 58°.
Beilstein, 6, 843, gives m.p. 56°.
The filtrate was acidified with hydrochloric acid and the mixture cooled to 8° for one hour, when the monomethyl ether was extracted with ether and washed with ice-water. Removal of the ether gave the monomethyl ether (30 g. - m.p. 41-46°), as colourless leaflets which were recrystallised from water, m.p. 51-52°. Heilbron reports m.p. 53°.

1:3-Dimethoxy-5-methylbenzene (Orcinol dimethyl ether).

(Ludwinowsky and Tambor, Ber., 1906, 39, 4039).

Orcinol (50 g.) in potassium hydroxide solution (43 g. in 125 mls. of water) was mixed with dimethyl sulphate (75 mls.) and vigorously shaken. Considerable heat was developed and an oil separated; the mixture was heated for half-an-hour on a steam-bath. The cooled mixture was extracted with ether, the ethereal layer was washed with sodium hydroxide solution (5N) and with water, and dried. The 1:3-dimethoxy-5-methylbenzene distilled at 228-230° (30 g.) as a colourless oil. Ludwinowsky and Tambor give b.p. 244°.

2-Methoxy-1:3-dimethylbenzene (Dimethyl anisole).

1:3-Dimethoxy-4-ethylbenzene.

The phenol was prepared by the method of Skraup and Bohm, (Ber., 1926, 59, 1012); it was then methylated with dimethyl sulphate. The ether was obtained as a liquid, b.p. 235°/760 m.m., or 116°/10 m.m.

Skraup and Bohm, (ibid), report b.p. 113°/13 m.m.

1-Methoxy-3-phenoxybenzene (m-methoxydiphenylether) and 1-Methoxy-4-phenoxybenzene (p-methoxydiphenylether).


A mixture of m-methoxyphenol (15.5 g.), bromobenzene (15.5 g.), potassium hydroxide (6.2 g.) and copper bronze (0.1 g.), was heated under reflux for 2½ hours in an oil-bath at 240°.

The product was isolated by steam-distillation, the excess of bromobenzene being collected first. A benzene extract of the steam-distillate was washed with sodium hydroxide solution (2N) and water, and then dried with sodium sulphate. Distillation yielded an oil (19 g.) b.p. 175°/20 m.m., 287°/760 m.m. Heilbron gives b.p. 303°/760 m.m. and Lea and Robinson, loc.cit. b.p. 175°/20 m.m.

The above preparation was repeated using p-methoxyphenol instead of the m-derivative, and yielded 1-methoxy-4-phenoxybenzene (15 g.), as a colourless oil b.p. 188°/32 m.m., which crystallised at -10° but melted at room temperature. Lea and Robinson loc.cit. report
b.p. 163-165°/14 m.m.

1:4-Dimethoxy-2:5-dimethylbenzene (p-Xyloquinol dimethyl ether).

A solution of p-xyloquinone (13.1 g.) and stannous chloride (4 g.) in ethanol (55 mls. of 96%) was heated under reflux for 30 minutes. The product was poured into a mixture of crushed ice and hydrochloric acid; the crystals (14 g.) which separated were recrystallised from water, giving 1:4-dihydroxy-2:5-dimethylbenzene, colourless leaflets, m.p. 216-217°. Heilbron reports m.p. 217°.

Methylation was effected in the usual way with dimethyl sulphate and the crude product was crystallised from ethanol, yielding colourless needles of 1:4-dimethoxy-2:5-dimethylbenzene, m.p. 95°. Heilbron reports m.p. 90°.

1:3-Dimethoxy-2-p-nitrobenzyloxybenzene.

2:6-Dimethoxyphenol (7.5 g.; m.p. 55°), p-nitrobenzyl bromide (11.5 g.) and sodium hydrogen carbonate (5.5 g.) were heated under reflux in ethanolic solution (containing sufficient water to attain complete solution) for one hour. The cooled solution was diluted with water and the precipitate filtered off and recrystallised from methanol (100 mls.), yielding yellow rhombs (12.5 g.) m.p. 81-82°. Three further recrystallisations from methanol gave 1:3-dimethoxy-2-p-nitrobenzyloxybenzene, m.p. 82-83°, as light-yellow rhombs. Found: N, 4.75. C₁₅H₁₅O₅N requires N, 4.84%.
1,3-Dimethyl-5-methoxybenzene (3,5-Xylen-1-ol methyl ether).

3,5-Xylen-1-ol (ex. B.D.H.) was methylated in the usual way with dimethyl sulphate. After washing the ethereal extract with alkali and then with water it was distilled and gave 1,3-dimethyl-5-methoxybenzene as a colourless oil, b.p. 198-200°. Heilbron reports b.p. 193°.

4,4'-Dimethoxydiphenylether.

(Ullmann, Annalen, 1905, 332, 38).

A mixture of 4-methoxyphenol (15 g.), 4-bromoanisole (16 g.), potassium hydroxide (6.2 g.) and copper bronze (0.1 g.) was heated under reflux for 2½ hours at 180° (oil-bath). The excess of 4-bromoanisole was removed by steam-distillation and the residue cooled in ice. The non-volatile solid was extracted with ethanol for two hours in a Soxhlet apparatus and gave 4,4'-dimethoxydiphenylether (8 g.), m.p. 101-102°. Heilbron reports 101-102°.

1-Methoxy-4-p-nitrobenzylolxybenzene (p-nitrobenzylolxyanisole).

A solution of 4-methoxyphenol (2.5 g.), p-nitrobenzyl bromide (4.5 g.) and sodium hydrogen carbonate (2.5 g.) in ethanol (50 mls. of 96%) and water (13 mls.) was heated under reflux for 1½ hours. After filtration and cooling, the solution deposited long, light-yellow rods of 1-methoxy-4-p-nitrobenzylolxybenzene (3.4 g.) which, after recrystallisation from ethanol, had m.p. 90.5-91.5°.

Found: C, 64.3; H, 5.0; N, 6.12. C₁₄H₁₃O₄N requires C, 64.9; H, 5.02; N, 6.2%. 

64.
1:2-Dimethoxy-4-methylbenzene.


4-Methyl catechol (25 g.) and dimethyl sulphate (55 g.; 42 mls.), were dissolved in methanol and cooled to -5°. Potassium hydroxide (32 g.), in water (70 mls.), was added and the mixture shaken for 30 minutes at -5°. It was then slowly warmed and finally heated for half an hour on a steam-bath. After cooling, the two layers were separated. The lower aqueous layer was extracted with ether and the extract combined with the upper layer. This ethereal solution was washed with sodium hydroxide solution and with water, dried with sodium sulphate and distilled; it yielded 1:2-dimethoxy-4-methylbenzene (24 g.) as a colourless oil, b.p. 219-220° (Perkin and Weizman, loc. cit., report b.p. 216°).

1-Bromo-4-methoxy-2-methylbenzene.

A solution of p-cresyl methyl ether (75 g.) and N-bromosuccinimide (45 g.) in carbon tetrachloride (150 mls.) was heated on a steam-bath for 12 hours. The precipitated succinimide was filtered off and washed with carbon tetrachloride, the washings being added to the filtrate. The extracts were washed three times with 2N-sodium hydroxide solution, and once with water, and finally dried over sodium sulphate. Distillation yielded a main fraction, b.p. 75-84°/5 m.m.

Redistillation gave 1-bromo-4-methoxy-2-methylbenzene (33 g.).
b.p. 84-85°/1 m.m., 232-235°/760 m.m.


**x-Bromo-3:5-dimethoxy-1-methylbenzene.**

A solution of orcinol dimethyl ether (25 g.) and N-bromosuccinimide (10 g.) in carbon tetrachloride (150 mls.) was heated for 10 hours on a boiling water-bath. The liberated succinimide was filtered off and washed with carbon tetrachloride. The combined washings and filtrate were extracted three times with 2N-sodium hydroxide solution, once with water and dried with sodium sulphate. Distillation yielded a main fraction (16 g.) b.p. 112-120°/21 m.m., which was recrystallised twice from methanol and yielded **x-bromo-3:5-dimethoxy-1-methylbenzene** as colourless, fern-like needles, m.p. 49-50°. Found: C, 46.5; H, 4.7; Br, 34.2. C\(_9\)H\(_{11}\)O\(_2\)Br requires C, 46.8; H, 4.8; Br, 34.6%.

**2-Bromo-1:4-dimethoxybenzene.**

(Buu-Hoi, Annalen, 1944, 556, 1).

A solution of **2-dimethoxybenzene** (60 g.) and N-bromosuccinimide (36 g.) in carbon tetrachloride (125 mls.) was heated for 12 hours on a steam-bath. The liberated succinimide was filtered off and washed with carbon tetrachloride. The combined extract and filtrate was washed three times with 2N-sodium hydroxide solution and once with water. After drying the solution with sodium sulphate, the product was distilled and gave two main fractions, (1) b.p. 76-110°/3 m.m., and (11) b.p. 111-113°/3 m.m.
Fraction (11) was redistilled and gave 2-bromo-1,4-dimethoxybenzene as an oil (20 g.) b.p. 111-112°/3 m.m., 249°/750 m.m.

Buu-Hoï (loc.cit.) reports b.p. 252-258° and Beilstein, 6, 852, reports b.p. 262-263°.

4-Chloro-1,3-dimethoxybenzene.

A solution of 4-chloro-1,3-dihydroxybenzene (14.15 g.; ex. B.D.H.) in sodium hydroxide (80 mls. of 10%) was shaken with dimethyl sulphate (25.2 g.; 19 mls.) for 30 minutes. The resultant oil was extracted with ether and the ethereal extract washed with sodium hydroxide solution (2 x 30 mls. of 10%) and water. The extract was dried and distilled, under reduced pressure, and gave 4-chloro-1,3-dimethoxybenzene as a colourless oil, b.p. 233°/760 m.m.

Found: C, 61.2; H, 5.7; Cl, 22.2. C₇H₅O₂Cl requires C, 61.3; H, 5.7; Cl, 22.7%.

4-Bromo-1,3-dimethoxybenzene, (Bromo-dimethoxyresorcinol).

Method (a).

4-Bromo-1,3-dimethoxybenzene was prepared via the following series of reactions which call for no special comment. The resorcylic acid was prepared by the method given in "Organic Syntheses", Collective Volume II - Blatt.
Method (b).

The bromo-ether was prepared from the ether by direct bromination, using N-bromosuccinimide, (cf. preparation of 2-bromo-1:4-dimethoxybenzene), by the method of Buu-Hoi (Annalen, 1944, 556, 7, Chem. Abs. 1948, 40, 4669). The product from either reaction is a colourless liquid, b.p. 140-142\(^\circ\)/20 m.m., which slowly crystallizes into long needles melting at about room temperature. Buu-Hoi, (ibid., loc. cit.) describes 4-bromo-1:3-dimethoxybenzene as crystals or liquid, b.p. 159/159\(^\circ\)/20 m.m.

1:2:3-Trimethoxybenzene. (Pyrogallol trimethyl ether).

A mixture of pyrogallol (25.2 g.), dimethyl sulphate (65 mls.), and sodium hydroxide (250 mls. of 10\% solution) under an atmosphere of nitrogen was vigorously shaken for 30 minutes while being cooled in cold water. The dark mixture was filtered and yielded yellowish needles, which were recrystallized from ethanol, giving rhombic crystals (14 g.) m.p. 46-47\(^\circ\). Beilstein reports m.p. 47\(^\circ\).
1:2:4-Trimethoxybenzene.

1:2:4-Trimethoxybenzene (25 g., ex Battersea Polytechnic) in methanol (75 mls.) together with dimethyl sulphate (35 mls.) was heated to reflux and aqueous potassium hydroxide (55 g. in 125 mls. of water) slowly added during two hours. The solution was cooled, the oily layer removed and washed with 2N-sodium hydroxide solution and then distilled under reduced pressure. The product was a colourless oil, b.p. 243°/760 m.m. Beilstein reports b.p. 247°.

1-Bromo-2:3:5-trimethoxybenzene.

This compound was prepared by the bromination of 1:2:4-trimethoxybenzene according to the method of Fabinyi and Szeki (Ber., 1910, 43, 2873). The product, recrystallised from ethanol, consisted of long, colourless needles, m.p. 53.5-54°. Eelbron gives m.p. 54.5°.

2-Bromo-1:3:5-trimethoxybenzene.

A solution of 1:3:5-trimethoxybenzene (8.4 g.) in acetic acid (40 mls.) was cooled to 5° and treated with a solution of bromine (8 g.) in acetic acid (10 mls.) also at 5°. After 30 minutes the reaction mixture was filtered and the product recrystallised from ethanol, yielding 2-bromo-1:3:5-trimethoxybenzene, colourless platelets, m.p. 96°. Beilstein (6, 1104) reports m.p. 99°.
2:4-Dibromo-1:3:5-trimethoxybenzene.

The monobromoderivative (vide supra) (1.6 g.) in acetic acid (10 mls.) was cooled to 5°, and bromine (2.5 g.) in acetic acid (15 mls.; also at 5°) added slowly. After 30 minutes, the crystals were removed and recrystallised twice from ethanol, yielding 2:4-dibromo-1:3:5-trimethoxybenzene as colourless needles, m.p. 132°. Beilstein (6, 1104) reports m.p. 132-133°.

1:2:4:5-Tetramethoxybenzene.

2:5-Dimethoxybenzoquinone, prepared by oxidation of 1:4-dimethoxybenzene (q.v.) was reduced with stannous chloride (see under the preparation of 1:4-dimethoxy-2:5-dimethylbenzene) to 1:4-dihydroxy-2:5-dimethoxybenzene, which was then methylated with dimethyl sulphate. Recrystallisation from ethanol gave 1:2:4:5-tetramethoxybenzene, fine colourless needles, m.p. 102°. Heilbron reports m.p. 103°.

1:3- and 2:3-Dimethoxynaphthalenes.

These ethers were prepared by the method of Perkin and Weizman (J. Chem. Soc., 1905, 82, 1619) (cf. the preparation of 1:2-dimethoxy-1:4-dimethoxy-1-methylbenzene) by the methylation of naphthoresorcinol and 2:3-dihydroxynaphthalene respectively.

1:3-Dimethoxynaphthalene: colourless crystals, m.p. 107°.

Found: C, 76.4; H, 6.33. C_{12}H_{12}O_{2} requires C, 76.6; H, 6.4%.
2:3-Dimethoxynaphthalene: Colourless needles from ligroin, m.p. 115°. Heilbron reports m.p. 116.5°.

2:4-Dichloro-1:3:5-trimethoxybenzene.

Floroglucinol trimethyl ether (3.4 g.) in acetic acid (50 mls.) was treated with the chlorine evolved from potassium permanganate (6.3 g.) and excess of hydrochloric acid. The yellowish crystalline product was washed with sodium hydroxide solution (5N) and water and recrystallised from n-butanol.

2:4-Dichloro-1:3:5-trimethoxybenzene (6 g.) was obtained as glistening, colourless plates, m.p. 155°.

Found: C, 45.4; H, 4.1; Cl, 29.7. \( \text{C}_2\text{H}_10\text{O}_3\text{Cl}_2 \) requires C, 45.6; H, 4.2; Cl, 29.0%. 