SC

ELECTROCHEMICAL METHOXYLATION OF ORGANIC COMPOUNDS

by

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1963

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To Dr. Bernard Belleau, I wish to express my deepest respect for teaching me "to dream" independently and thereby showing me the excitement in research.

To my wife, Hannah, for her constant encouragement and sincere understanding, I express my love.

Thanks are also due to Mr. Guy Chaton for drawings and photographs, to Mr. Egon Kristof for glassblowing and the sketch of the equipment, to Mrs. Pat Revelle for typing this thesis, and to the National Cancer Institute of Canada and the National Research Council for generous grants in support of this research.

"I was busy writing on my text-book but could make no progress -- my mind was on other things. I turned my chair to the fire and sank into a doze. Again the atoms were before my eyes. Little groups kept modestly in the background. My mind's eye, trained by the observation of similar forms, could now distinguish more complex structures of various kinds. Long chains here and there more firmly joined; all winding and turning with a snake-like motion. Suddenly one of the serpents caught its own tail and the ring thus formed whirled exasperatingly before my eyes. I woke as by lightning, and spent the rest of the night working out the logical consequences of the hypothesis. If we learn to dream we shall perhaps discover truth. But let us beware of publishing our dreams until they have been tested by the waking consciousness."

Friedrich August Kekulé, 1829 - 1896

(A History of Chemistry, F.J. Moore,
McGraw-Hill Book Company, New York,
page 213, 1918)

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INTRODUCTION

The observation by M. Faraday (1) in 1834 that a hydrocarbon was formed on electrolysis of an aqueous sodium acetate solution may be regarded as the cornerstone of organic electrochemistry. H. Kolbe (2) in 1849 elaborated on this reaction which eventually became one of the most widely studied organic electrochemical processes.

Since the time of M. Faraday and H. Kolbe, the field of organic electrochemistry has not witnessed the spectacular developments that nowadays characterise most branches of chemistry including inorganic electrochemistry. The reasons for this may lie in the special technical problems that are encountered in organic applications of electrochemistry. Inorganic electrochemical reactions are usually straightforward and free of complications; this does not usually apply, however, to organic electrochemical processes mostly because the choice of suitable solvents is rather limited and the courses adopted by such reactions are normally multiple.

The increasing availability in recent years of a variety of stable organic solvents of high dielectric constant and the growing interest in organic electrode processes (e.g. fuel cell research) may provide the stimulus needed to eventually bring organic electrochemistry on a par with inorganic electrochemistry.

PART A

I. The Kolbe Reaction

The electrolysis of an aqueous solution of an alkali-metal carboxylate was found by H. Kolbe (2) to yield a symmetrical hydrocarbon and carbon dioxide:

$$2RCO_2^- \xrightarrow{-2e} R-R + 2CO_2$$

Later A. Wurts (3) obtained symmetrical and unsymmetrical hydrocarbons by electrolysis of mixtures of two fatty acid salts. A. Crum-Brown and O. J. Walker (4) electrolysed half esters of aliphatic dicarboxylic acids and in this way made available a new and valuable synthesis of diesters.

$$2RO_2C(CH_2)_nCO_2^- \xrightarrow{-2e} RO_2C(CH_2)_{2n}CO_2R + 2CO_2$$

A side reaction frequently encountered in aqueous media and referred to as the Hofer-Moest reaction (5,6) consists in the formation of alcohols. This reaction is favoured by the use of alkaline solutions and by the addition of salts such as perchlorates, sulfates, and bicarbonates. For example, it has been shown (5) that under suitable conditions electrolysis of acetic acid can afford methanol in high yield. Furthermore the reaction can produce alcohols by introduction of the hydroxyl group in the α,β or even γ position to the eliminated carboxyl group (7,8,9) of long-chain fatty acids.

The Kolbe electrolysis is most conveniently carried out by dissolving the carboxylic acid(s) in methanol containing a sufficient quantity of alkali (usually added as sodium methoxide) to neutralise only about 2% of the acid(s). The solution is then electrolysed using smooth platinum electrodes until it becomes slightly alkaline. When carried out in aqueous solution the reaction is found to be more sensitive to such conditions as electrode composition, temperature, concentration, and current density.

There are several limitations in the use of the Kolbe reaction. These have been reviewed in detail by B.C.L. Weedon (10). It has been observed that saturated dibasic acids (from malonic to sebacic acid) can give olefins and alcohols, containing two carbon atoms less than the starting material as well as saturated and unsaturated acids through the loss of only one carbon atom (11). Cycloalkanes have never been isolated from the electrolysis of dibasic acids (12). In the case of unsaturated acids it was found that αβ- and βγ-unsaturated acids (13) as well as aromatic acids (14) do not undergo the Kolbe reaction to any appreciable extent. Only the corresponding decarboxylated products are usually found. R.P. Linstead <u>et al</u> (15) have also reported that N-acylglycines and N-acyl-DL-α-alanines afford N-alkoxymethylamides respectively in high yield when the electrolysis is carried out in alcoholic solution.

$$XNHCHRCO_2H + R'OH \longrightarrow XNHCHROR' + CO_2$$

(X is acyl, R is H or CH_3, R' is alkyl)

Of interest also is the observation that under essentially the same conditions phenylacetic acid will yield dibenzyl (16), whereas diphenylacetic acid (17) and triphenylacetic acid (16) give rise to methyl diphenylmethyl ether and methyl triphenylmethyl ether respectively in a Hofer-Moest type reaction.

$$C_6H_5CH_2CO_2H \longrightarrow C_6H_5CH_2CH_2C_6H_5 \text{ (50\% yield)}$$

$$(C_6H_5)_2CHCO_2H \longrightarrow (C_6H_5)_2CHOCH_3 \text{ (35\% yield)}$$

$$(C_6H_5)_3CCO_2H \longrightarrow (C_6H_5)_3COCH_3 \text{ (60\% yield)}$$

It was found that the nature of the substituent in the α-position to the carboxyl group has a pronounced influence on the course of the reaction. Thus progressive branching by alkyl substituents in the α-position promotes the formation of olefins, esters, and alcohols at the expense of the normal Kolbe products.

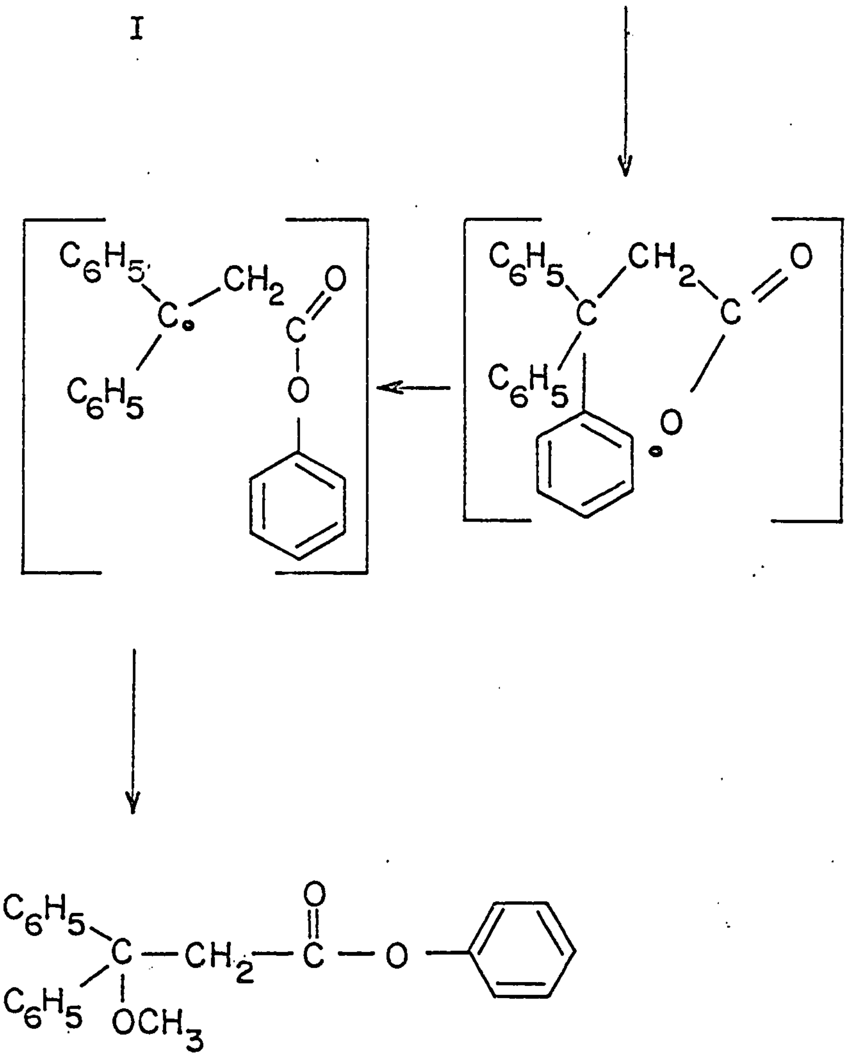
H. Breederveld and E.C. Kooyman (18) attempted to generate the triphenylethyl radical by electrolysis of a methanolic solution of 3,3,3-triphenylpropionic acid (I) but instead obtained a 55% yield of phenyl diphenylmethoxypropionate (II). This result is probably due to intramolecular addition by the acyloxy radical as the primary step.

L.F. Fieser et al obtained a 9% yield of trinitro-m-xylene (IV) on electrolysis of a solution of sodium acetate in glacial acetic acid containing trinitrotoluene (III). This reaction is probably the result of direct attack on the benzene ring by methyl radicals. Under similar conditions, however, R.P. Linstead et al (16) obtained 25% of α-naphthol together with small amounts of the β-isomer, after hydrolysis of the product obtained when the Kolbe reaction was attempted in the presence of naphthalene. This work provided some evidence for the presence of acetoxy radicals as intermediates.

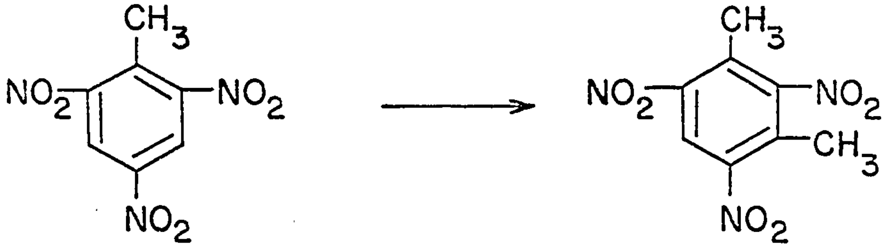
Recently, E.J. Corey et al (20) have generated carbonium ions by a modification of the Kolbe reaction carried out at high voltages. Electrolysis of exo- or endo-norbornane-2-carboxylic acid (V and VI respectively) in methanol (50 volts at 10° using platinum electrodes and added triethylamine) produced exo-norbornyl methyl ether (VII) in 35 - 40% yield. No endo methyl ether was detected and the methyl ether (VII)

$$(C_6H_5)_3\,CCH_2\,CO_2H \longrightarrow (C_6H_5)_3\,CCH_2\,CO_2\cdot$$

I



II



III

IV

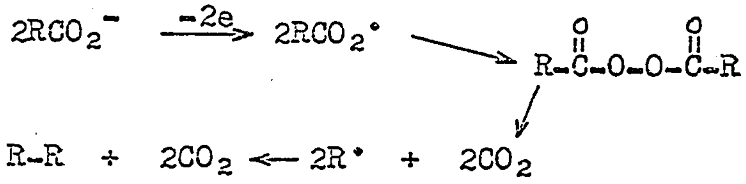
prepared from the optically active acid (V) was found to be racemic. These workers also obtained cycloheptanone (IX) in 53% yield from the electrolysis of 1-hydroxycyclohexylacetic acid (VIII) in acetonitrile (175 volts, 10°) and have successfully applied this very promising ring expansion reaction to several cycloalkyl derivatives.

II The Mechanism Of The Kolbe Reaction

H. Kolbe (2) originally considered the reaction mechanism to involve the oxidation of the carbonyl group of the carboxylic acid by oxygen which is generated by the electrolysis of water.

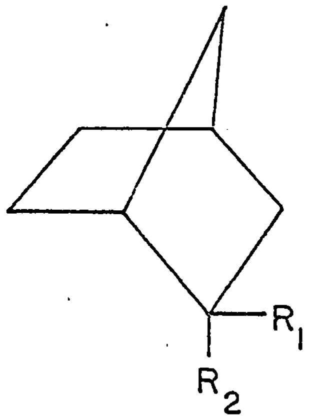
$$2CH_3CO_2H + \tfrac{1}{2}O_2 \longrightarrow C_2H_6 + 2CO_2 + H_2O$$

Alternatively, C. Schall (21) and F. Fichter (22) proposed that diacy peroxides may be intermediates in this reaction.

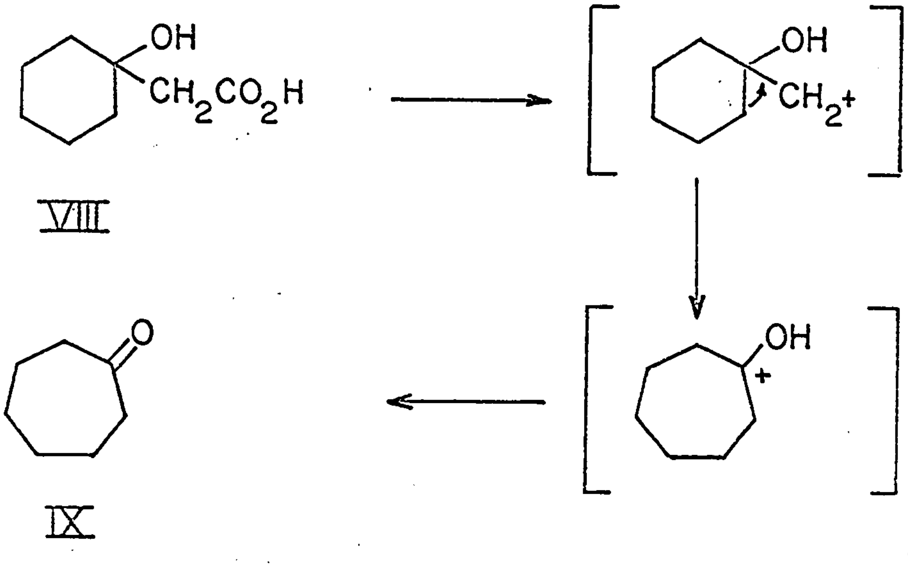


$$2RCO_2^- \xrightarrow{-2e} 2RCO_2^\cdot \longrightarrow R-\overset{O}{\overset{\|}{C}}-O-O-\overset{O}{\overset{\|}{C}}-R$$
$$R-R + 2CO_2 \longleftarrow 2R^\cdot + 2CO_2$$

S. Glasstone and A. Hickling (23) modified this theory somewhat by expressing the view that hydrogen peroxide is



V R_1 is CO_2H , R_2 is H
VI R_1 is H , R_2 is CO_2H
VII R_1 is OCH_3 , R_2 is H



first formed at the anode in aqueous acetate solutions from discharged hydroxyl ions. The hydrogen peroxide would then react with acetate ions to yield ethane and carbon dioxide.

$$2OH^- \xrightarrow{-2e} H_2O_2$$

$$H_2O_2 + 2CH_3CO_2^- \longrightarrow C_2H_6 + 2CO_2 + 2OH^-$$

The formation of acetoxyl radicals was thought to involve an intermediate step such as the following:

$$H_2O_2 + 2CH_3CO_2^- \longrightarrow 2CH_3CO_2^{\cdot} + 2OH^-$$

The possibility of a further reaction leading to a diacyl peroxide was also considered.

All of the above hypotheses however, are unacceptable for several reasons. The Kolbe reaction proceeds efficiently in non-aqueous media where no direct oxygen evolution can occur. Furthermore, no conclusive evidence for peroxide intermediates has ever been produced.

A most satisfactory general theory of the reaction mechanism consists in the free radical mechanism proposed by A. Crum-Brown and O.J. Walker (4) and subsequently modified by K. Clusius _et al_ (24,25). In this theory, the carboxylate ion is first oxidized on the anode to the carboxylate radical which would then decarboxylate to yield the corresponding alkyl radical.

$$RCO_2^- \xrightarrow{-e} RCO_2\cdot \longrightarrow R\cdot + CO_2$$

Subsequent coupling of the radicals would then generate the Kolbe product (or other side products). More recently B.E. Conway and M. Dziecíuch (26) (see also the work of T. Dickinson and W.F.K. Wynne-Jones (27)) have made a kinetic study of the Kolbe reaction using formic and trifluoroacetic acids. Their basic observations led them to propose the following steps to account for the behaviour of trifluoroacetate:

$$CF_3CO_2^- \xrightarrow{-e} CF_3CO_2\cdot\,(M)$$

$$CF_3CO_2\cdot(M) \longrightarrow CF_3\cdot(M) + CO_2$$

$$2CF_3\cdot \longrightarrow C_2F_6$$

(where (M) indicates a site on the metal surface to which the adsorbed species would be bound).

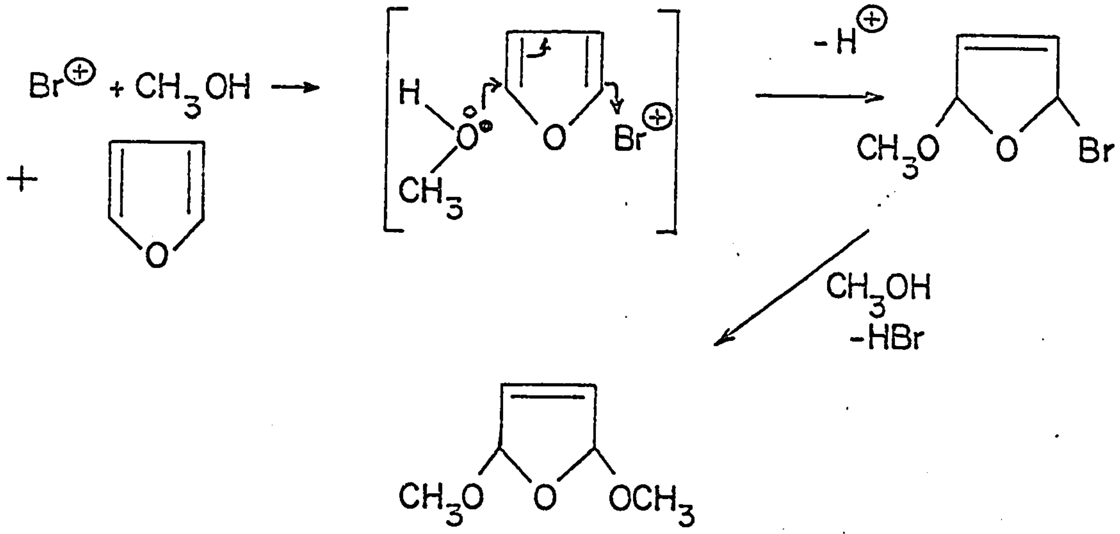
III Electrochemical Methoxylation of Furans

Treatment of furan with a methanolic solution of chlorine or bromine is known to give 2,5-dimethoxy-2,5-dihydrofuran (X) in good yield (28). A possible mechanism for this reaction is given below.

$$NH_4Br \longrightarrow NH_4^{\oplus} + Br^{\ominus}$$

$$2NH_4^{\oplus} + 2e \longrightarrow 2NH_3 + H_2 \qquad \text{(Cathodic reaction)}$$

$$2Br^{\ominus} \longrightarrow Br_2 + 2e \qquad \text{(Anodic reaction)}$$



yield 73%

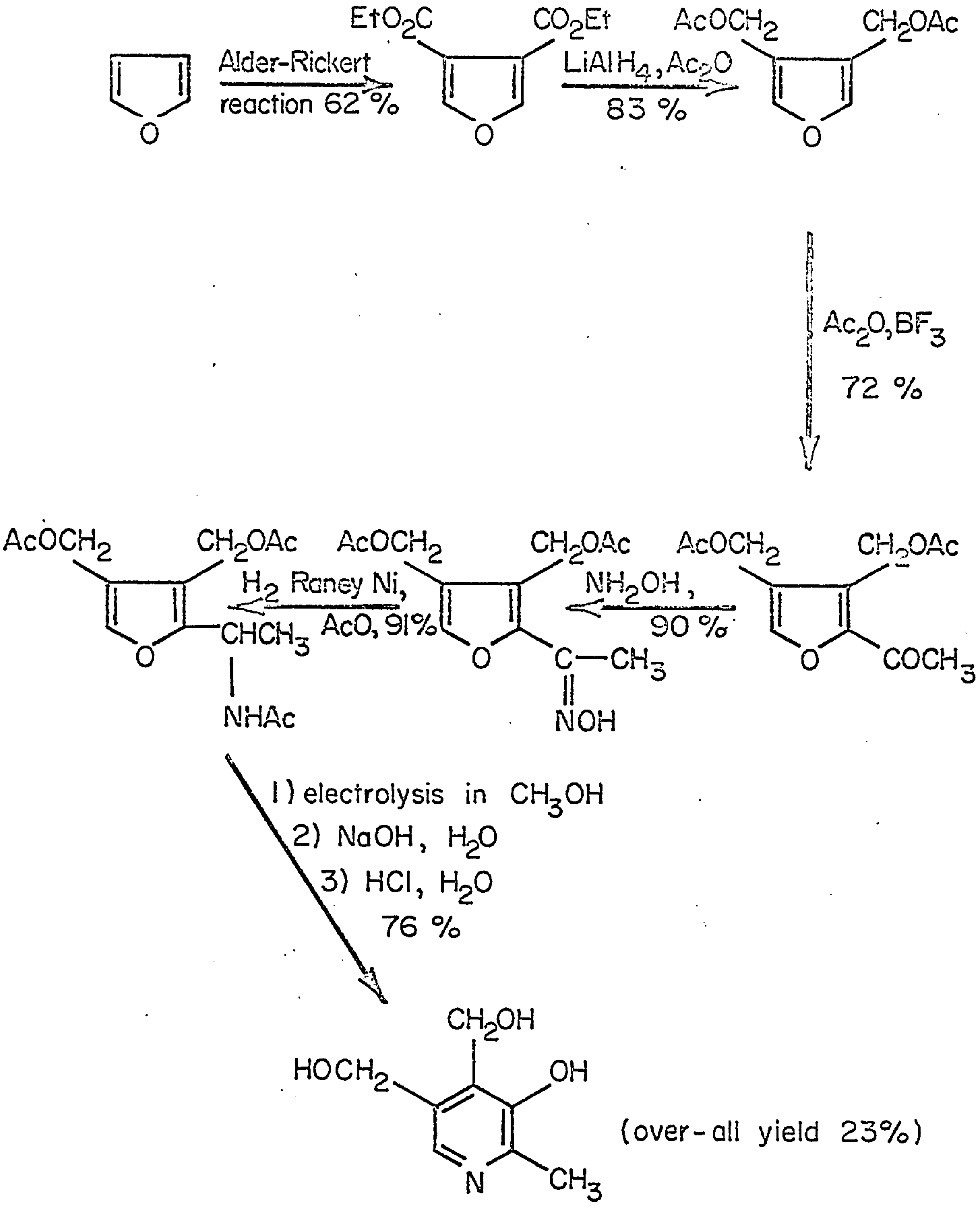
(Current efficiency 86%)

X

An electrochemical method for the preparation of this diacetal (X) was developed by N. Clauson-Kaas et al (28). They reported that electrolysis of a methanolic solution of furan in the presence of a catalytic amount of ammonium bromide at -14° using a nickel cathode and a platinum anode leads to the formation of the diacetal (X) in excellent yield. Although no mechanism has been proposed for such electrochemical methoxylation reactions, M.J. Allen (30) has suggested that the bromine liberated from the ammonium bromide at the anode would react with the methanol solvent and the furan substrate to give the desired compound presumably by an ionic mechanism as shown on page 11. The hydrogen bromide thus formed would then react with the liberated ammonia at the cathode and in this way regenerate the ammonium bromide catalyst. However an ionic mechanism fails to account for the observation that the diacetal (X) is also formed in comparable yield when furan is electrolyzed in the presence of other electrolytes such as sodium hydroxide, sodium formate and sulfuric acid (30, 31, 32).

Electrochemical methoxylation reactions have been extended to the synthesis of a variety of substituted methoxylated dihydrofurans. This subject as well as an account of the uses of these acetals as intermediates in several important syntheses have been reviewed by N. Elming (33).

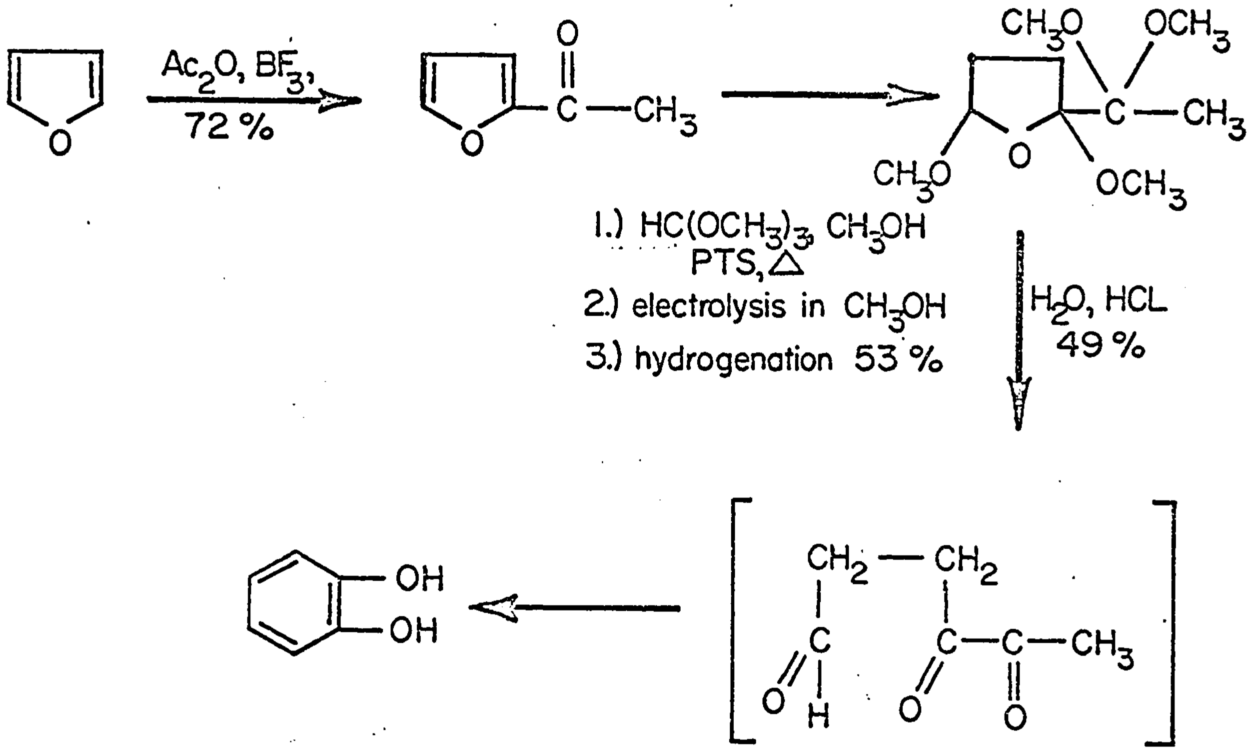
One important application consists in the synthesis of pyridoxine (XI) (34) from furan:



(over-all yield 23%)

XI

The preparation of substituted phenols (33) from furans is another useful synthesis and is described in the following:



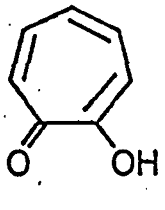
These selected examples serve to illustrate the great importance of electrochemical methoxylation processes in organic synthesis.

PART B

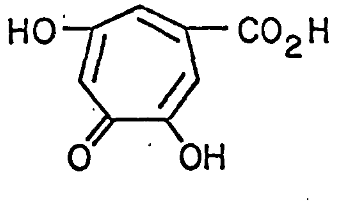
The Synthesis of Tropolones

In 1942 J.H. Birkinshaw et al (35) isolated stipitatic acid from a penicillin mould. Stipitatic acid was found to have the empirical formula $C_8H_6O_5$, and in 1945 M.J.S. Dewar (36) suggested the structure (XIII) on the basis of its chemical properties. Since that time many other tropolones, including tropolone itself (XII), have been synthesized or isolated from natural sources, and have proved to be of fundamental interest in the fields of organic chemistry and biochemistry. To cite only a few examples, the thujaplicins (XIV) found in the western red cedar possess antibiotic properties. Colchicine (XV) is found in the autumn crocus and has the interesting property of arresting cell division at the metaphase in plants and in animals. The total synthesis of colchicine has recently been achieved by A. Eschenmoser et al (37) and by E.E. Van Tamelen et al (38) in 1959.

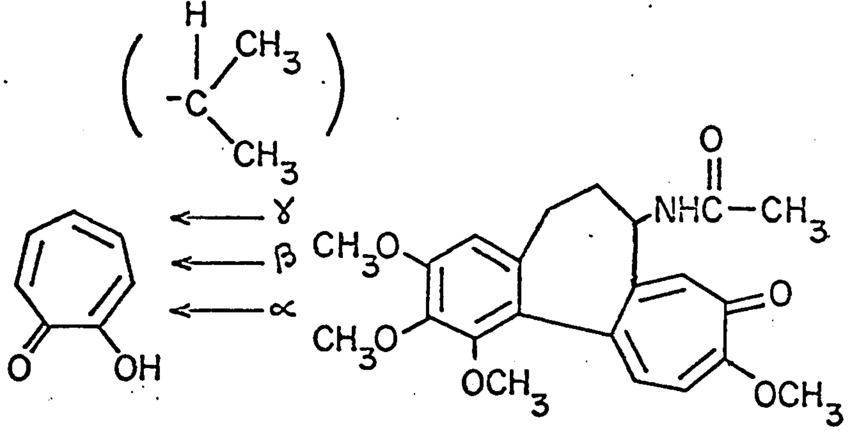
It is also of interest to note that B. Belleau and J. Burba (39) have found that 4-methyltropolone is a potent competitive inhibitor of catechol methyltransferase which is the enzyme responsible for the disposition of the catecholamine hormones. Thus the study of tropolones from the



XII



XIII



XIV

XV

medicinal and biochemical standpoints should be a promising field of investigation.

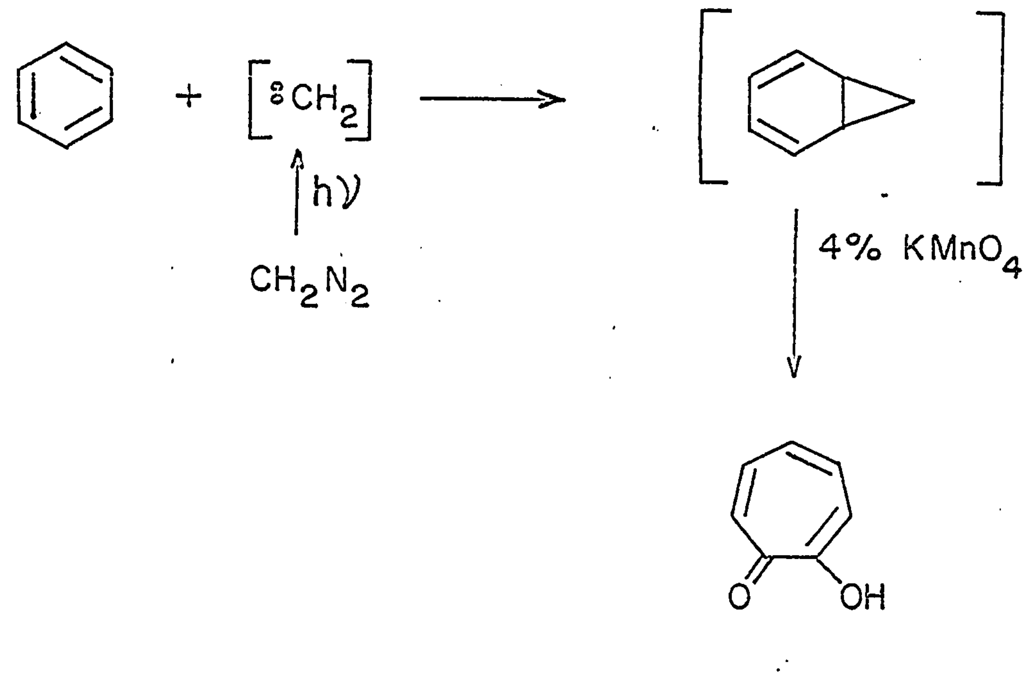
Such investigations are seriously limited, however, by the scarcity of suitably substituted tropolones. In addition, existing synthetic methods of preparation have been characterised until recently, by long and inefficient syntheses which bring the production costs to prohibitive levels. A few of the most important of these syntheses of tropolones will be briefly described below.

(a) Ring Expansion Using Diazomethane

In 1950 W. von E. Doering and L.H. Knox (40) generated carbene by photolysis of a solution of diazomethane in benzene. Treatment of the resultant solution with 4% aqueous potassium permanganate led to a 1% yield of tropolone (XII) isolated as the copper complex.

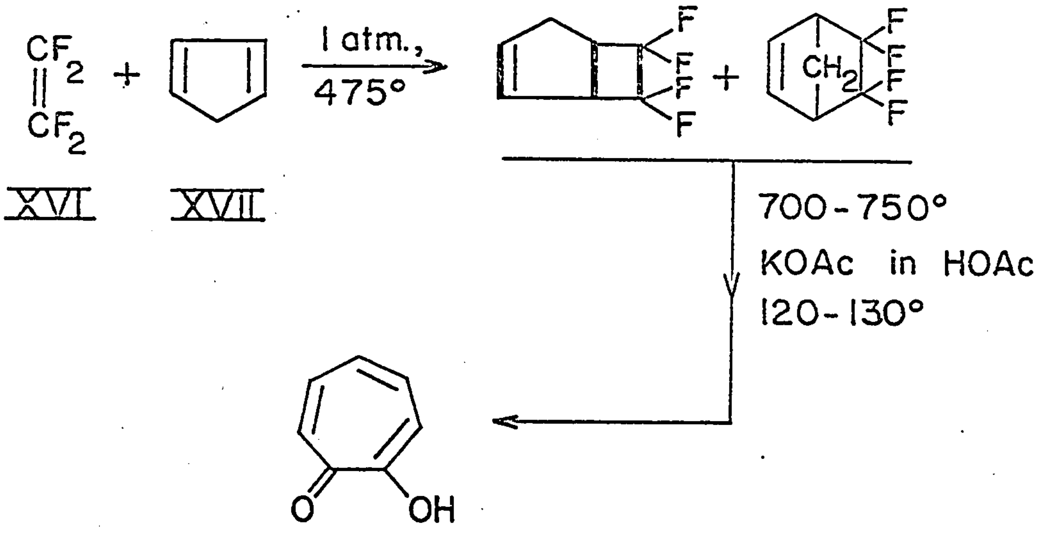
(b) From Tetrafluoroethylene (XVI) And Cyclopentadiene (XVII)

J.J. Drysdale et al (41) have developed a practical synthesis of tropolone (XII) by condensation of tetrafluoroethylene (XVI) and cyclopentadiene (XVII) at 475°. Pyrolysis of the mixture of addition products at 700-750° and subsequent



$:CH_2$
$h\nu$
CH_2N_2
4% $KMnO_4$
O
OH

XII



CF_2
CF_2
XVI
XVII
1 atm., 475°
F
F
F
F
CH_2
F
F
F
F
700-750°
KOAc in HOAc
120-130°
O
OH

XII

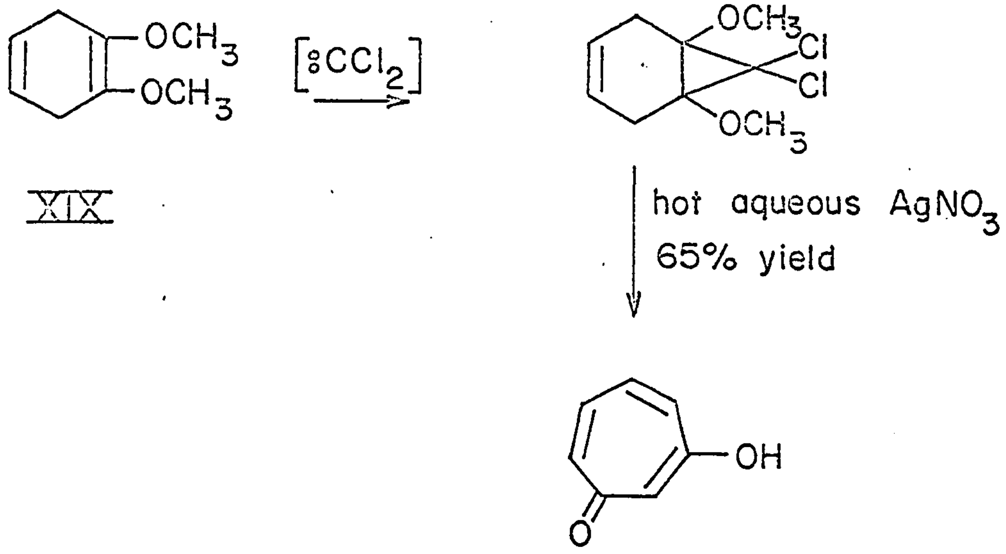
hydrolysis by potassium acetate in aqueous acetic acid at 120-130° afforded (XII) in 20% yield.

(c) From The Dihalocarbene Derivatives Of 1,2-Dimethoxy-1,4-Cyclohexadiene (XIX) And 1-Methoxy-1,4-Cyclohexadiene (XXI)

By a modification of a reaction first described by W.E. Parham *et al* (42), A.J. Birch and J.M.H. Graves (43) claim that they were able to obtain a 65% yield of 3-hydroxytropone (XX) from 1,2-dimethoxy-1,4-cyclohexadiene (XIX) and a 75% yield of tropone (XXII) from 1-methoxy-1,4-cyclohexadiene (XXI). It is well known that tropone and its substituted derivatives may be converted to tropolones in various yields (44,45).

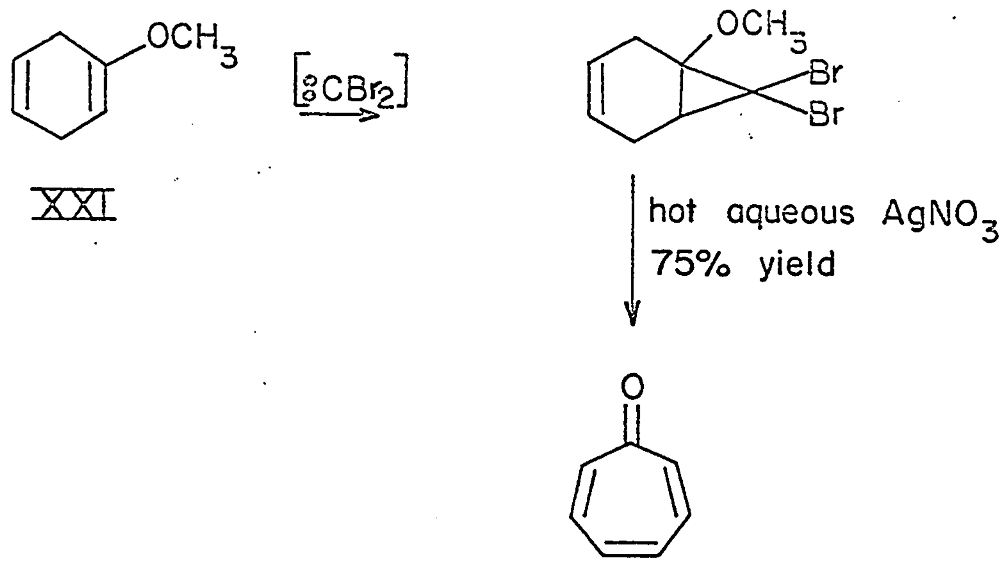
(d) The Solvolysis of 1,4-Dihydrobenzyl Tosylates

In 1963 O.L. Chapman and P. Fitton (46) described an interesting synthesis of tropolone (XII) from 2,3-dimethoxybenzoic acid (XXIII). The acid (XXIII) was converted by a Birch reduction to 2,3-dimethoxy-1,4-dihydrobenzoic acid (XXIV). Reduction of (XXIV) with lithium aluminum hydride gave 2,3-dimethoxy-1,4-dihydrobenzyl alcohol (XXV). The p-toluenesulfonate (XXVI) of this alcohol (XXV) was then prepared and solvolysed in refluxing collidine to give a mixture of 1,2-dimethoxycycloheptatrienes (XXVII). This mixture on oxidation with



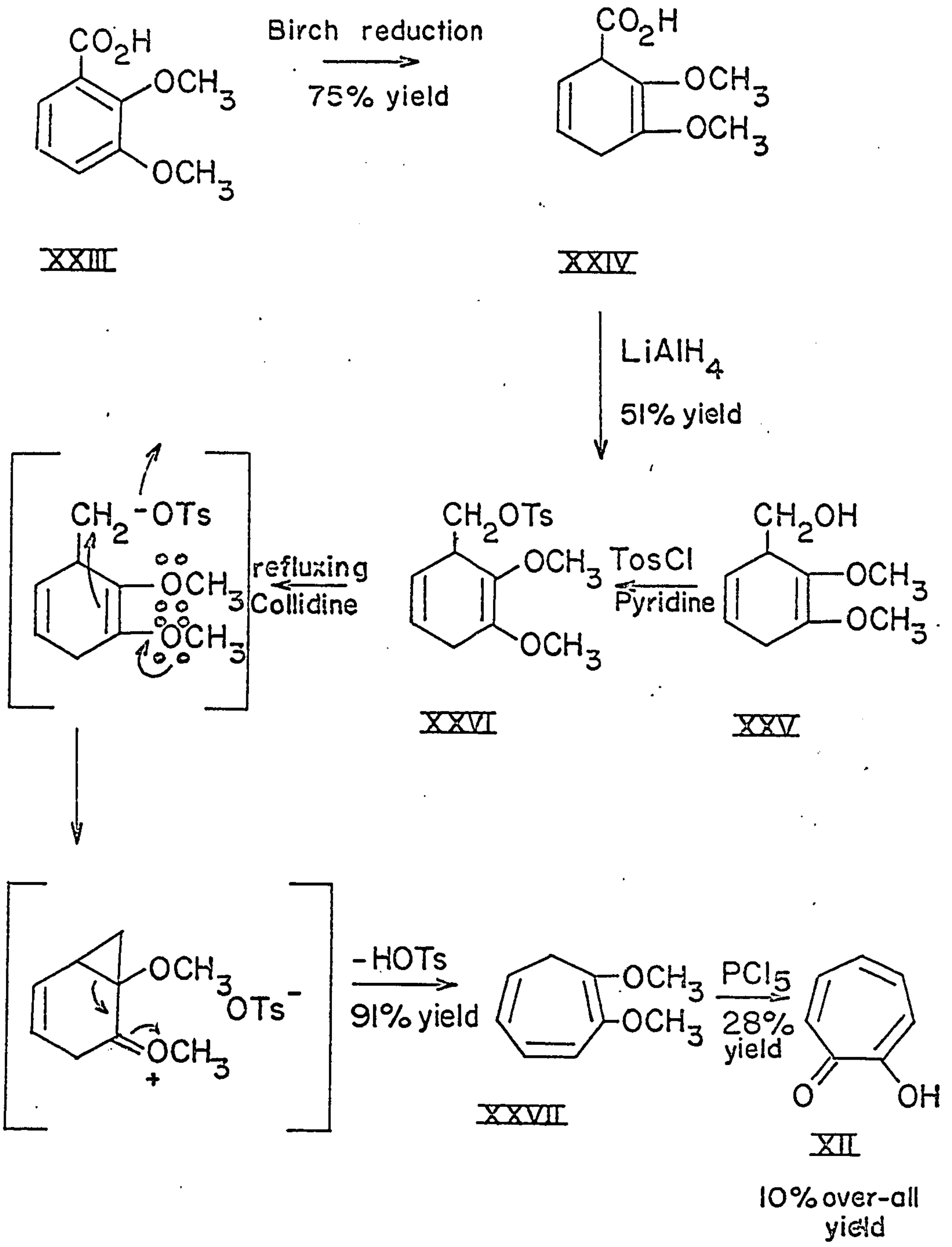
XIX

XX



XXI

XXII


CO_2H
OCH_3
OCH_3
Birch reduction
75% yield
XXIII
XXIV
$LiAlH_4$
51% yield
CH_2OH
CH_2OTs
TosCl
Pyridine
XXV
XXVI
refluxing
Collidine
CH_2-OTs
-HOTs
91% yield
OTs^-
XXVII
PCl_5
28% yield
O
OH
XII
10% over-all yield

phosphorus pentachloride gave tropolone (XII).

From the discussion of Part A of this introduction, it can be easily seen that electrochemical methoxylation reactions could provide appropriate starting materials for an independent and practical synthesis of tropolones. Thus addition of a carbon moiety at an intermediate stage in a sequence similar to the electrochemical preparation of pyrocatechol from furan (equation on page 14) should give substituted tropolones on hydrolysis. The aim of the work that will be described in the next section was to discover the potentialities of electrochemical methoxylation and to work out a synthesis of tropolones.

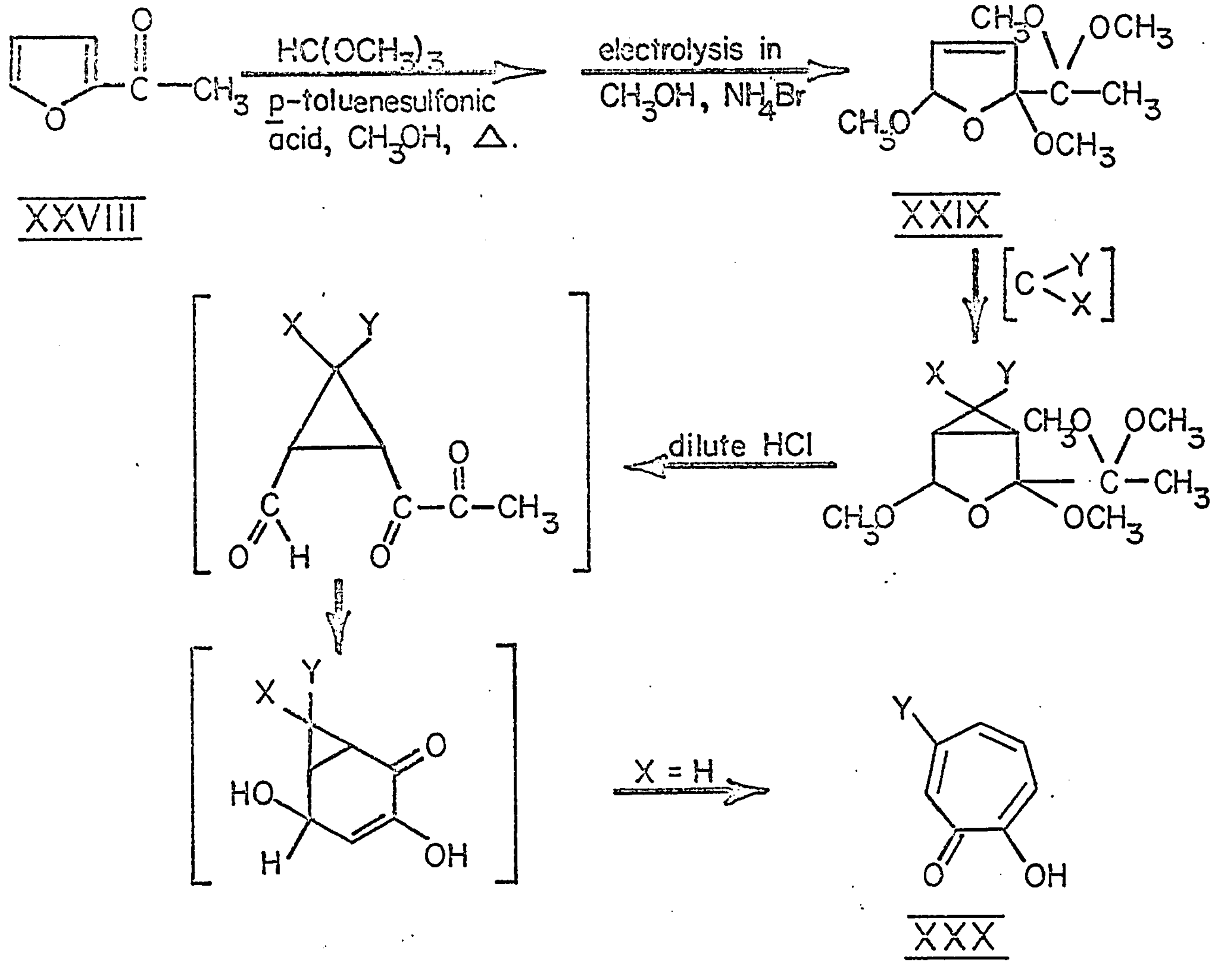
RESULTS AND DISCUSSION

It was pointed out in the introduction to this thesis that electrochemical methoxylation of appropriate starting materials could provide the proper oxidation level for the synthesis of substituted tropolones. During the course of these investigations it was discovered that electrochemical methoxylation of a variety of unsaturated compounds occurs readily, affording unusual compounds which are inaccessible by classical routes.

In the following discussion the attempted synthesis of substituted tropolones from furans will be dealt with first, followed by a description of a number of investigations into the general field of electrochemical methoxylation of organic compounds.

I Attempted Preparation of Substituted Tropolones From Furans

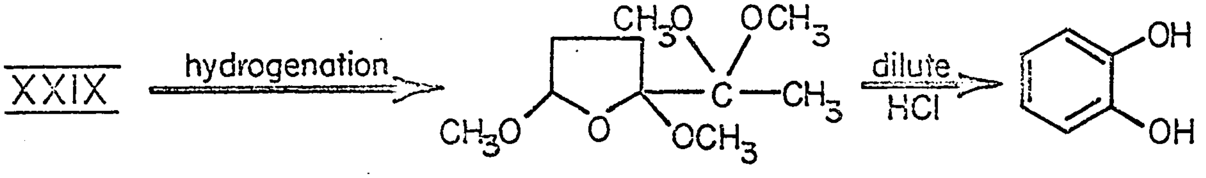
An expedient but theoretical route to substituted tropolones is depicted below. The preparation of 2,5-dimethoxy-2-(α,α-dimethoxyethyl)-dihydrofuran (XXIX) was carried out by the method of N. Clauson-Kaas et al (47) from 2-acetylfuran (XXVIII). It was hoped that a cyclopropane ring could be introduced into the ketal (XXIX) through the addition of a suitable carbene or carbon moiety onto the double bond. Subsequent hydrolysis ought to produce a tropolone derivative as shown (XXX). This scheme was derived by analogy with the known



XXVIII

XXIX

XXX



XXXI

formation of pyrocatechol by acid hydrolysis of the reduced ketal (XXXI). It is also known that bicyclic cyclopropane derivativew readily undergo ring enlargement reactions (discussed in the Introduction). Accordingly, attempts to cause addition to the ketal (XXIX) of a substituted carbon generated from the reagent of H.E. Simmons and R.D. Smith (48), from the thermal decomposition of diazoacetic ester (49), from trichloroacetic ester and strong base (50), or from the iodomethylzinc iodide reagent of G. Wittig and K. Schwarzenbach (51), were all abortive, the starting material (XXIX) being recovered in each case in yields greater than 90%.

An explanation for the unreactive nature of the carbon-carbon double bond in the ketal (XXIX) toward all these otherwise effective cyclopropane ring generators, lies most probably in the strong deactivating influence of the allylic methoxy groups. Electron withdrawal by the oxygens ought to make the double bond much less vulnerable to electrophilic* attack by carbenoid species. Additional examples of this deactivating effect of allylic methoxy groups will be described later.

An alternative scheme for the synthesis of tropolones was therefore envisaged and involves the intermediacy of a

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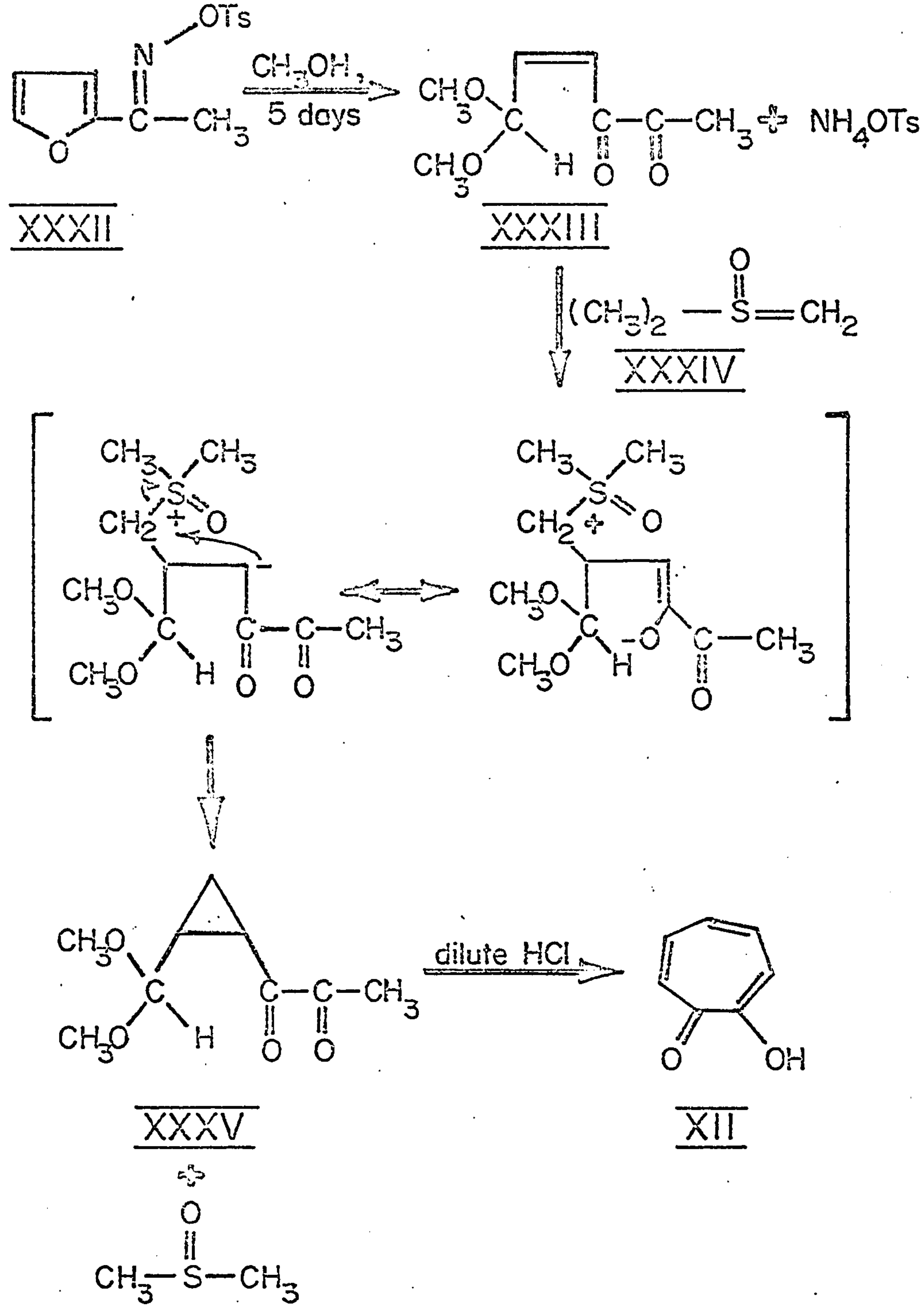
* Epoxidation by peracids of 2,5-dimethoxy-2,5-dihydrofuran (X) is also ineffective (52). The cyclopropane-forming reagents behave like other electrophilic reagents in their reactivity to double bonds (53,54,55).

more reactive species than the ketal (XXIX). This approach centers around the key intermediate hexen-2-dione-4,5-dimethoxyacetal-1 (XXXIII), an interesting substance thought to have been prepared by L. Vargha et al (56) by treatment of 2-acetylfuran oxime p-toluenesulfonate (XXXII) with methanol. Theoretically, reaction of this dione (XXXIII) with Corey's reagent (dimethylsulfoxonium methylide (XXXIV)) (57) should yield the cyclopropane derivative (XXXV). This, after hydrolysis with mineral acid ought to give tropolone (XII).

Repetition of Vargha's work produced a compound whose empirical analysis agreed with the proposed structure (XXXIII) but which possessed spectroscopic properties in total disagreement with Vargha's formulation. Thus, when the reaction was carried out in methanol, a yellowish oil was obtained whose IR spectrum showed the presence of a single strong carbonyl absorption at 1720 cm^{-1}; also the UV spectrum showed only a very weak absorption at 300 $m\mu$., $\varepsilon=550$ (in ethanol). Both these spectra are consistent only with an unconjugated ketone structure. Although the NMR spectrum exhibited the expected ratio for the areas under the methoxy hydrogen region to all other types of hydrogens in Vargha's structure, it failed to support the latter formulation in that one can distinguish four different kinds of methoxy groups. This observation cannot be reconciled with the dione structure (XXXIII) in which only two equivalent methoxy groups are present.


XXXII
CH3OH, 5 days
XXXIII
+ NH4OTs
(CH3)2 — S=CH2
XXXIV
XXXV
+
CH3—S—CH3
dilute HCl
XII

In spite of these inconsistencies it should be noted that L. Vargha <u>et al</u> (56) have produced chemical evidence (but without any spectroscopic data) which was interpreted as establishing the α-diketone structure (XXXIII). Vargha's evidence can be summarized as follows (for the ethoxylated analogue):

(i) the product has the yellow colour characteristic of α-diketones (e.g. biacetyl).

(ii) the elemental analysis and molecular weight determination are in agreement with the proposed structure (XXXIII).

(iii) since the oil does not react with maleic anhydride, it no longer possesses the furan ring.

(iv) one molecular equivalent of hydrogen is consumed on reduction over palladium catalyst, thus establishing the presence of one double bond.

(v) treatment with ozone followed by boiling for 2 hours and then with phenylhydrazine in acetic acid gives glyoxal bisphenylhydrazone.

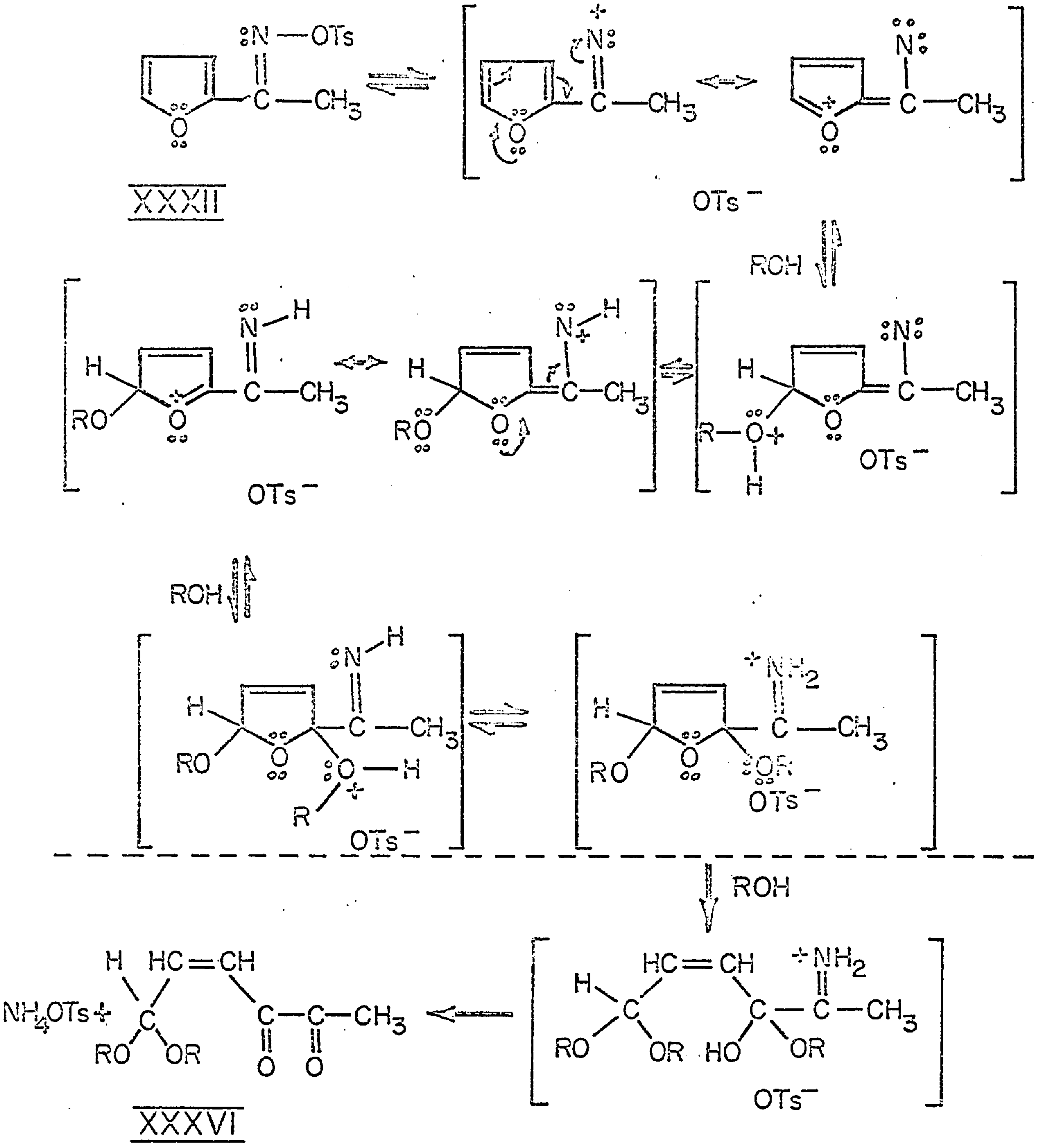
(vi) treatment with hydrogen peroxide in boiling acetic acid affords maleic acid.

(vii) oxidation with alkaline potassium permanganate followed by treatment with sulfuric acid gives acetic acid.

(viii) the yellow oil was claimed to decompose explosively on distillation above 130°, a property which did not awaken the author's suspicions.

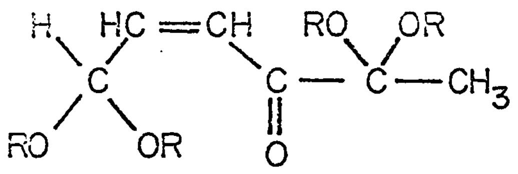
Furthermore, these workers (56) claimed that the presence of water is not necessary for the formation of the dione (XXXIII), a result which A.P. Dunlop and F.N. Peters (58) find surprising. The latter authors proposed the mechanism below to account for the conversion of the oxime tosylate (XXXII) to the dione (XXXVI). This scheme requires the participation of a stiochiometric quantity of water which leads these authors (58) to reason that the product formed under anhydrous conditions should be the ketal (XXXVII) or (XXXVIII) rather than the diketone (XXXVI).

In our hands, the reaction of the oxime ester (XXXII) in pure methanol under strictly anhydrous conditions, gave rise to a mixture of compounds, the NMR spectrum of which showed a peak at 8.76 τ (for a methyl group attached to a saturated carbon) and a band at 7.78 τ (which is characteristic of a methyl ketone). These results, taken in conjunction with others described below, offered conclusive

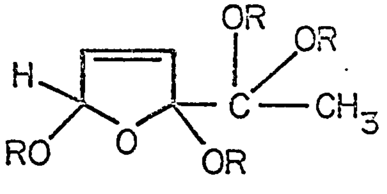


XXXII

XXXVI



XXXVII



XXXVIII

evidence that the product isolated by L. Vargha et al (56) was in fact 2,5-dimethoxy-2-acetyl-dihydrofuran (XXXIX). The other component which is formed under anhydrous conditions is most probably 2,5-dimethoxy-2-(α,α-dimethoxyethyl)-dihydrofuran (XXIX) in agreement with the prediction of A.P. Dunlop and F.N. Peters (58).

A close examination of the several proofs given by L. Vargha et al (56) for their diketone structure (XXXIII) reveals that the chemical evidence presented is also consistent with our revised structure (XXXIX). Firstly, the product in question is a yellow oil (like many other organic substances) probably because of the presence of impurities absorbing in the visible region. Furthermore, it is not sufficient to state that since an adduct with maleic anhydride and the product is not formed, the furan ring is no longer present; the evidence is negative and a number of substituted furans (including 2-acetylfuran) are known not to partake in the Diels-Alder reaction. One molecular equivalent of hydrogen should also be consumed by (XXXIX) upon catalytic hydrogenation. Ozonization of the dihydrofuran (XXXIX) followed by boiling for two hours in aqueous solution and treatment with phenylhydrazine in acetic acid should also give glyoxal bisphenylhydrazone (XI). In the same way the dihydrofuran (XXXIX) should also afford some acetic acid upon treatment with potassium permanganate in basic solution by the procedure described (56). Vigorous treatment of (XXXIX) with a boiling solution of hydrogen peroxide in acetic acid would similarly be expected to give maleic acid (XLI). In contrast with Vargha's observations, the yellow oily product was not found to be explosive. The observed instability was probably due to contamination of the product by the oxime tosylate (XXXII) which was found to decompose violently when heated to 75°. Thermal decomposition of the tosylate was also carried out in ethylene glycol dimethyl ether solution, but only suspended carbonaceous material was formed.*

Direct chemical evidence for the dihydrofuran structure (XXXIX) was obtained by electrolysis of a methanolic solution of 2-acetylfuran (XXVIII) in the presence of a small amount of concentrated sulfuric acid. The resulting product was a yellow oil which gave IR and NMR spectra identical to those of the yellow oil obtained according to L. Vargha <u>et al</u> (56). Furthermore, comparison of the IR and NMR spectra of the corresponding electrolysis product from 2-(α-hydroxyethyl)-furan (XLIII) with the compound obtained by sodium borohydride reduction of Vargha's ketone showed that they are also identical.

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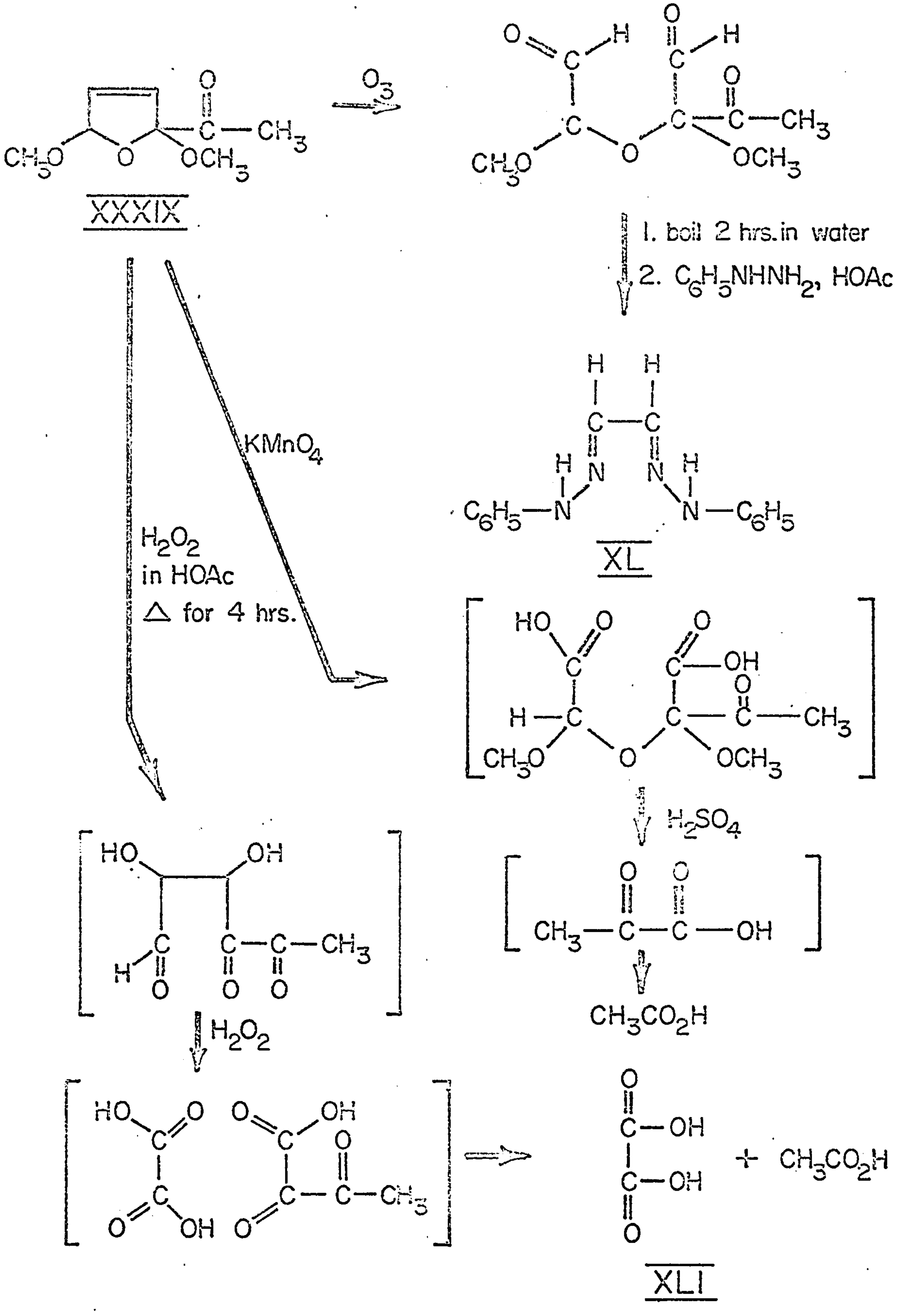
* It may be that the ready decomposition of this oxime ester occurs via the formation of a reactive nitrene intermediate (XLII).

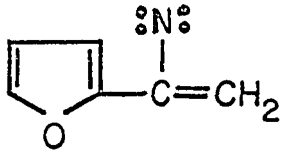


XXXIX

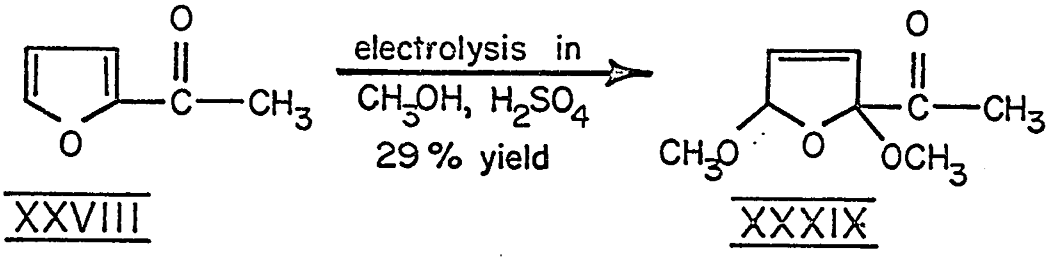
XL

XLI

O_3
1. boil 2 hrs. in water
2. $C_6H_5NHNH_2$, HOAc
$KMnO_4$
H_2O_2 in HOAc △ for 4 hrs.
H_2SO_4
CH_3CO_2H
H_2O_2
+ CH_3CO_2H

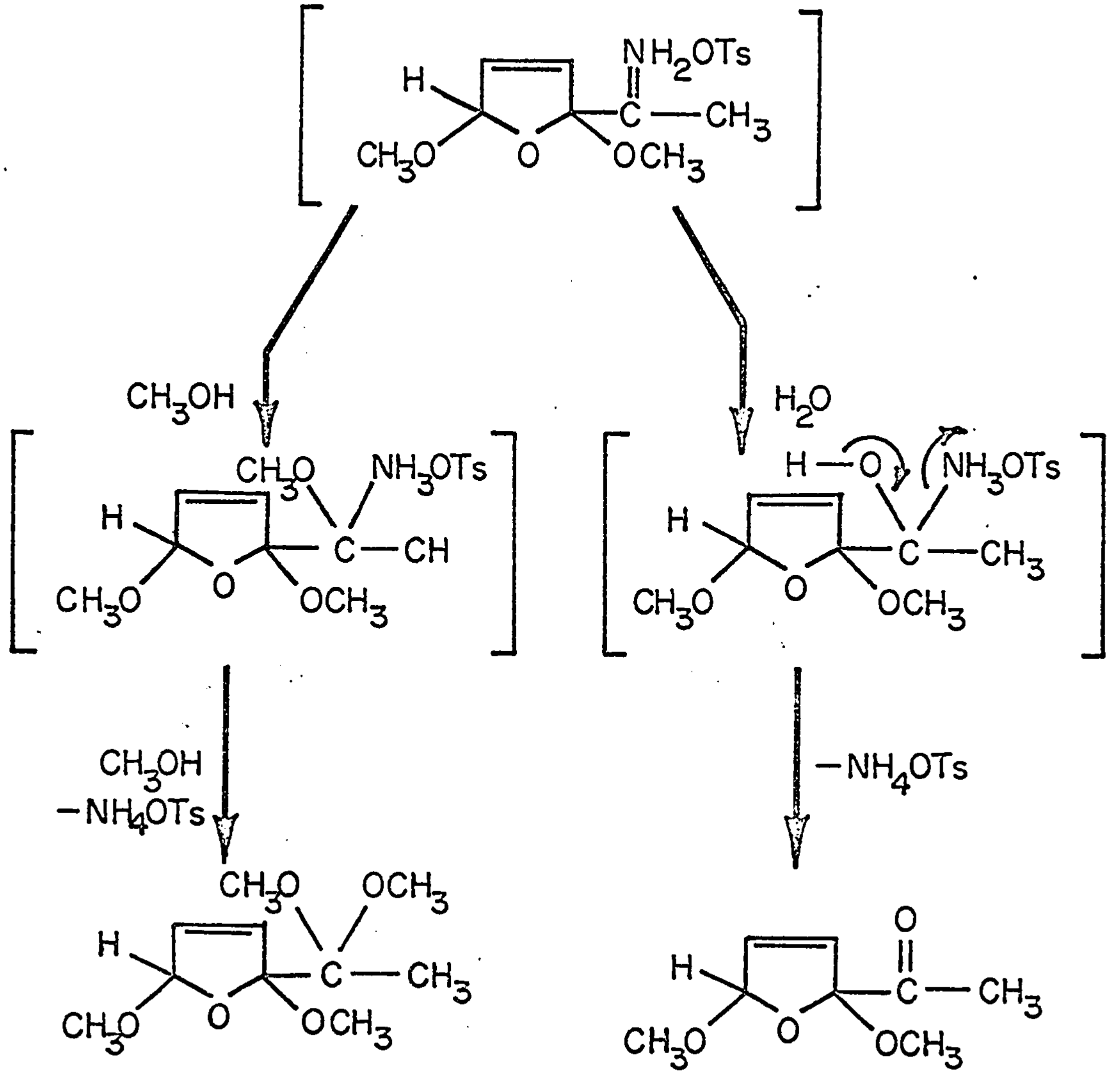


XLII



electrolysis in
CH_3OH, H_2SO_4
29 % yield
XXVIII
XXXIX
$NaBH_4$
$NaBH_4$
electrolysis in
CH_3OH, KOH
38 % yield
XLIII
XLIV

A probable mechanism for the formation of the dihydrofuran (XXXIX) can be derived using in part the rationalizations shown on page 30 but with the following modifications:



XXIX

XXXIX

II Electrochemical Methoxylation of Unsaturated Organic Compounds

The furans are known to possess aromatic character to a considerable degree, yet they are readily methoxylated electrochemically with consequent cancellation of the resonance energy.

It was already noted (page 12) that the proposed ionic mechanism for the methoxylation of furans does not agree with the observation that electrolytes other than ammonium bromide can be used in this reaction. Indeed, it would appear that the sole purpose of the various electrolytes is to allow for the flow of current; it is doubtful that the bromine atoms that are generated electrochemically when ammonium bromide is the electrolyte play an important role in the overall methoxylation reaction of furans.

The successful methoxylation of furans could proceed at least equally well through attack by methoxy radicals. This expectation agrees with the well known observation that formaldehyde is a normal product of the electrolysis of methanol, a reaction which undoubtedly proceeds by way of methoxy radicals. If such radicals are formed, then they should induce polymerization of suitable dienes such as isoprene. In fact, this was confirmed experimentally.

There are several proposals in the literature relating to the formation of methoxy radicals (59,60) by anodic oxidation. For example, T.O. Pavela (60) proposed the following theory of radical formation in aqueous solution using as a basis the kinetics of electrode behaviour coupled with actual isolation of key products:

(a) $CH_3OH \text{ (bulk)} \longrightarrow CH_3OH \text{ (adsorbed)}$

(b) $CH_3OH \text{ (adsorbed)} \xrightarrow{-e} CH_3O\cdot + H^+$

(c) $CH_3O\cdot \xrightarrow{-e} HCHO + H^+$

(d) $HCHO + OH^- \longrightarrow CH_2(OH)O^- + H^+$
$CH_2(OH)_2 \text{ (or } \xrightarrow{-e} CH_2(OH)O\cdot)$

(e) $CH_2(OH)O\cdot \xrightarrow{-e} HCO_2H + H^+$

(f) $OH^- + H^+ \longrightarrow H_2O$

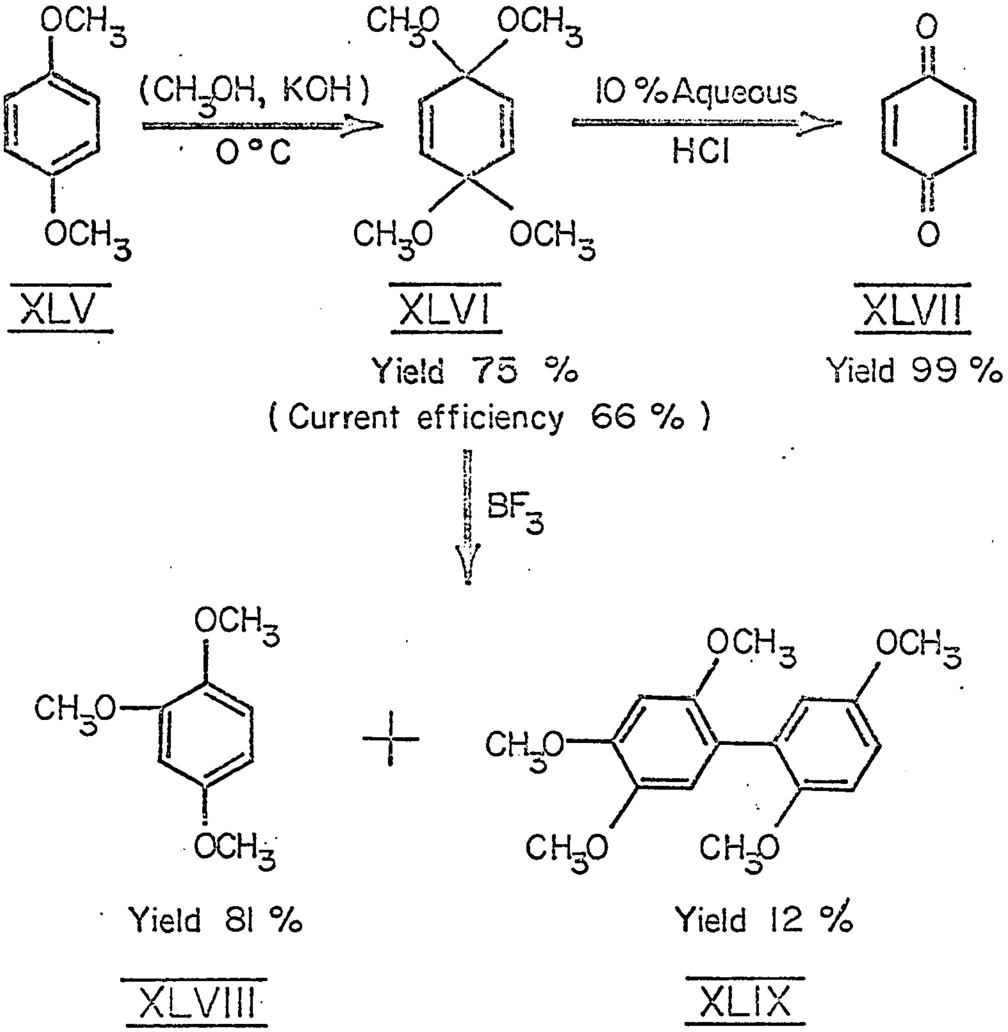
In non-hydroxylic media (e.g. pure methanol) where reactions (d), (e), and (f) are non-existent, formaldehyde should be the end product of the electrochemical oxidation of methanol. More definitive evidence for the existence and nature of methoxy radicals generated in this manner is needed however. This may perhaps be provided to some extent by electron paramagnetic resonance studies and precise kinetic observations using anhydrous methanol solutions.

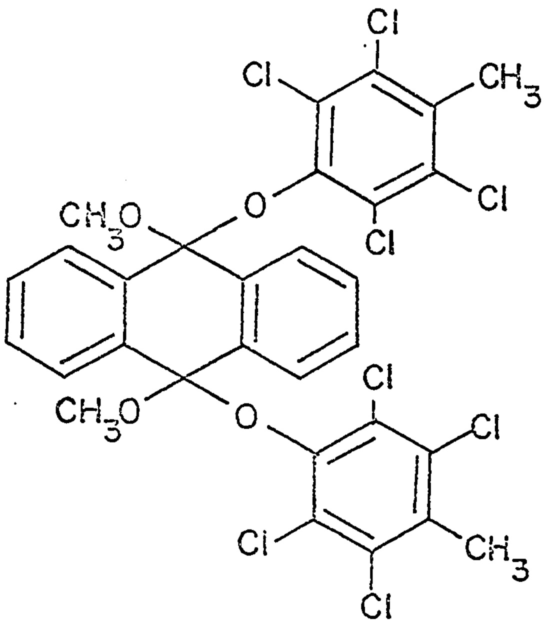
(A) Electrochemical Methoxylation of 1,4-Dimethoxybenzene (XLV), Anisole (LI), and 9,10-Dimethoxyanthracene (LIII)

The electrochemical methoxylation of 1,4-dimethoxybenzene (XLV) proceeded smoothly to give a 75% yield (66% current efficiency) of 3,3,6,6-tetramethoxy-1,4-cyclohexadiene (XLVI). The structure proof for this crystalline solid, m.p. 42.0 - 42.5°, involved quantitative hydrolysis in dilute hydrochloric acid solution to p-benzoquinone (XLVII). The NMR spectrum showed, as expected, two peaks at 6.75τ, corresponding to the methoxy groups and at 4.03τ, corresponding to the four olefinic hydrogens. An 88% yield of (XLVI) could be obtained if a large excess of current was passed through the solution.

It is of interest to note that this stable quinone diketal (XLVI) is a member of a hitherto inaccessible class of compounds. For example, attempted ketal formation by classical routes (61) with p-benzoquinone leads, as is well known, to 2,5-dialkoxy-p-benzoquinone rather than diketals. However, an anthraquinone diketal (L) has been suggested (62) as an intermediate in the free radical reaction of anthrahydraquinone dimethyl ether with tetrachloro-p-cresol.

Aromatization of the quinone diketal (XLVI) as catalyzed by boron trifluoride in dry benzene afforded 1,2,4-trimethoxybenzene (XLVIII) and a pentamethoxybiphenyl, tentatively assigned the structure (XLIX). Examination of Table I reveals that this reaction is highly sensitive to the concentration of the quinone diketal (XLVI). An increase


OCH3
(CH3OH, KOH)
0 °C
CH3O
OCH3
10 % Aqueous
HCl
O
XLV
XLVI
Yield 75 %
(Current efficiency 66 %)
XLVII
Yield 99 %
BF3
CH3O
Yield 81 %
XLVIII
Yield 12 %
XLIX



L

in concentration of (XLVI) or prior addition of 1,2,4-trimethoxybenzene (XLVIII) favours the formation of the biphenyl (XLIX).

Table I. Concentration Dependence of the Aromatization of (XLVI)

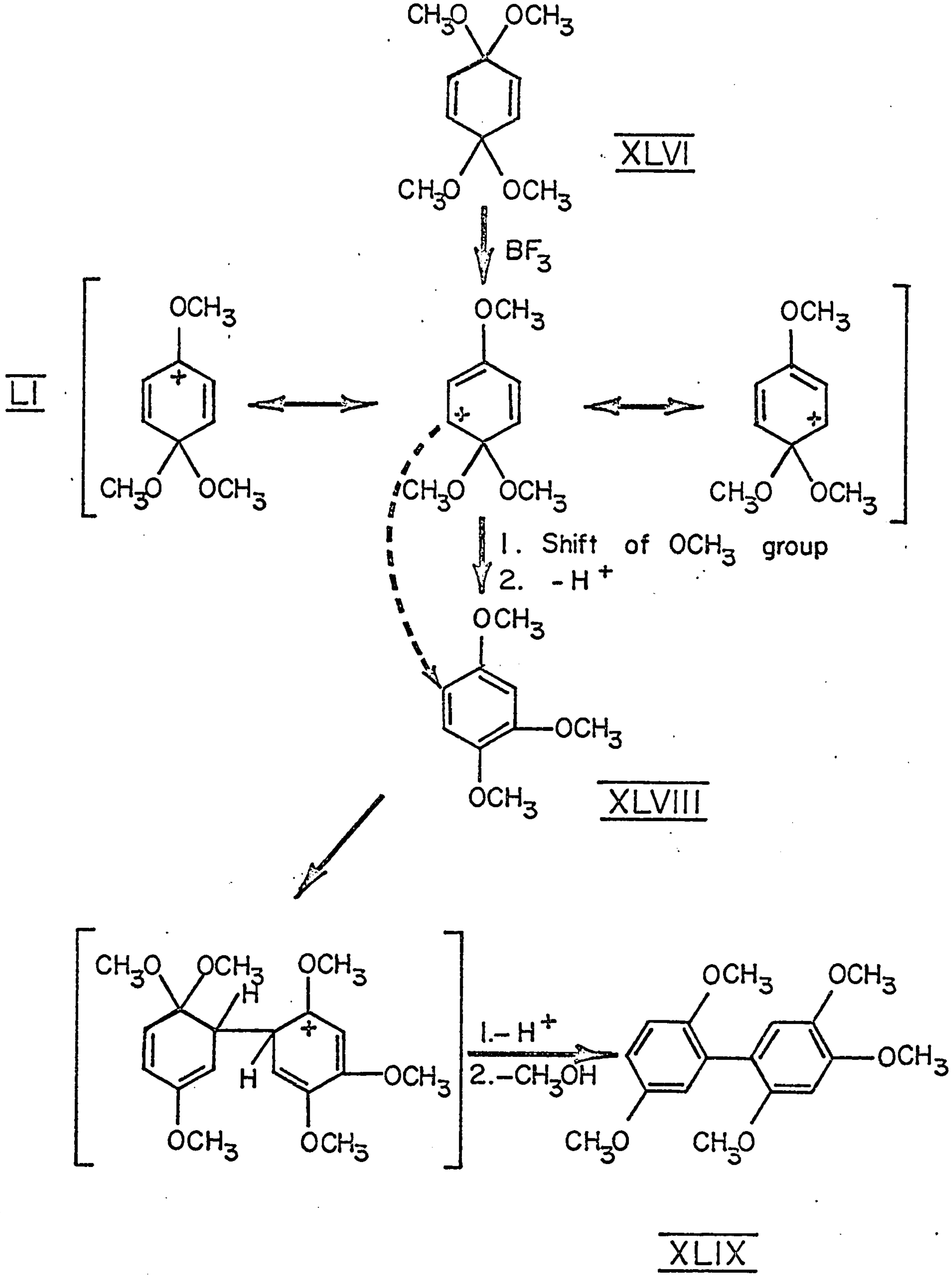
	Reaction Conditions	Yield of 1,2,4-trimethoxybenzene (XLVIII)	Yield of the biphenyl (XLIX)
I	0.5 M (XLVI) in benzene	81%	12%
II	1.0 M (XLVI) in benzene	36%	19%
III	1.4 M (XLVI) in benzene plus trimethoxybenzene	32%	60%

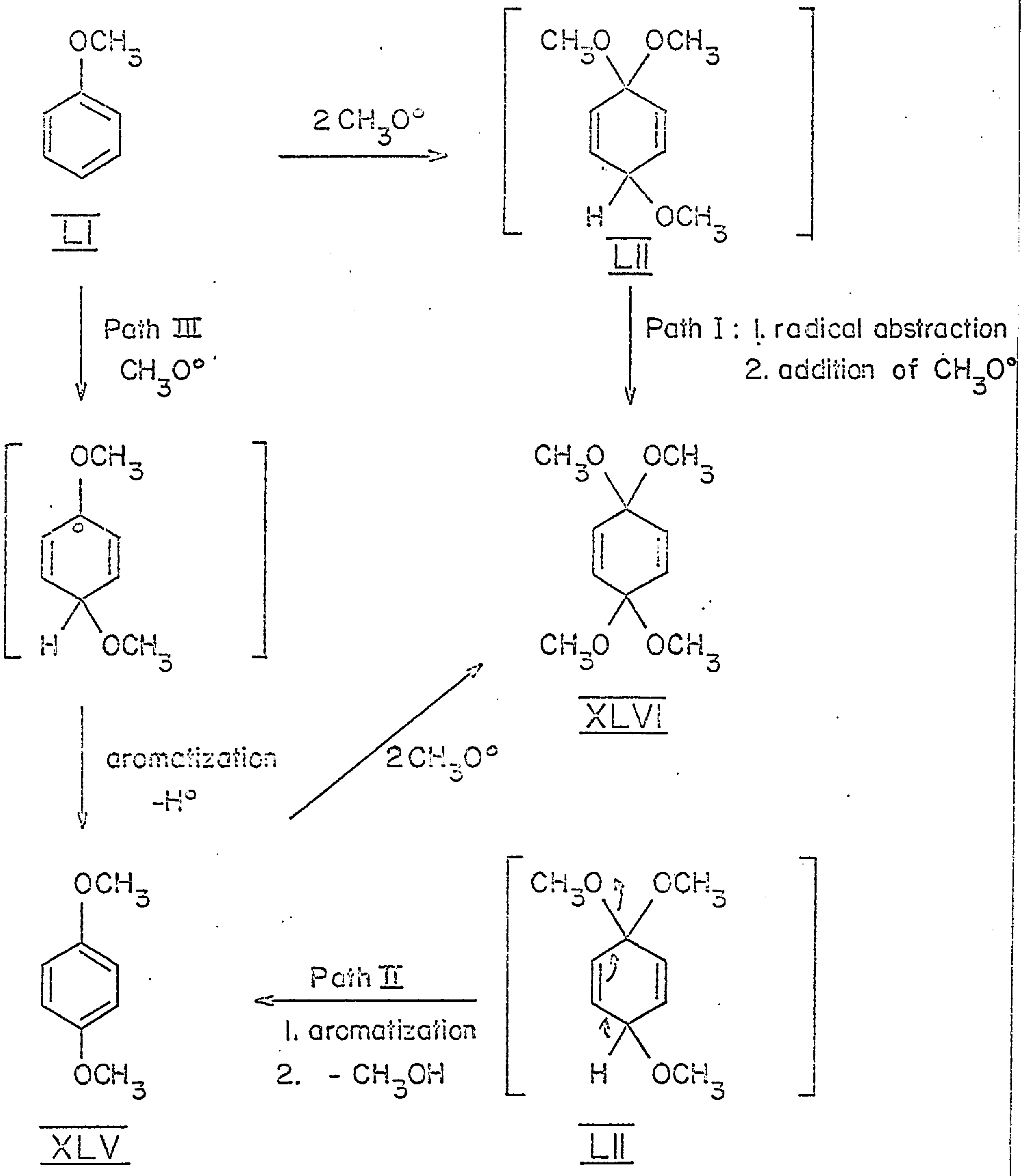
The mechanism of the boron trifluoride catalyzed aromatization of the quinone diketal (XLVI) probably involves the formation of a resonance stabilized cation intermediate (LI). The observations of Table I are in agreement with the suggestion that this cation (LI) can either rearrange with elimination of a proton to give 1,2,4-trimethoxybenzene (XLVIII) or it can attack the already formed (XLVIII) (or (XLVIII) which has been added to the solution) to yield the pentamethoxybiphenyl (XLIX).

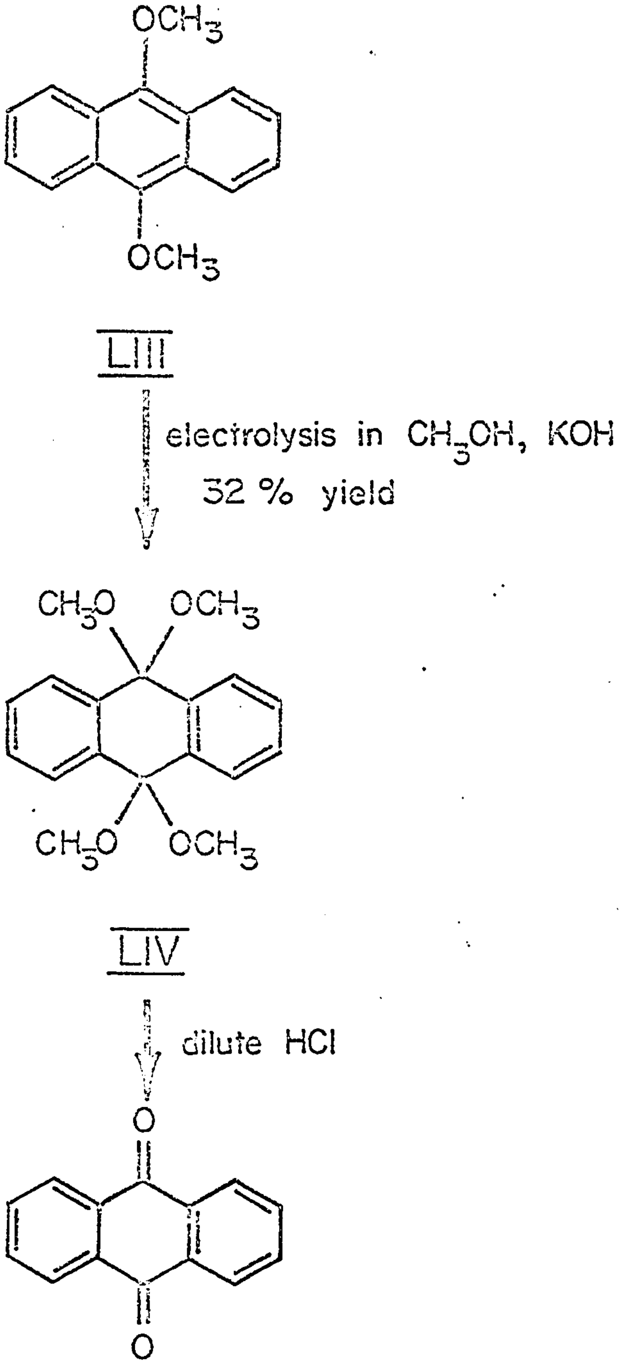
An examination of the literature failed to disclose any examples of 1,2- rearrangements of alkoxy groups. That the methoxy group does undergo rearrangement in this case is probably due to the relatively large driving force for aromatization in (LI).

Electrochemical methoxylation of anisole (LI) also occurred but only after passage of a large excess of current. In this way, a 17% yield of the quinone diketal (XLVI) was obtained along with a considerable amount of an unidentified high boiling oil. Neither 3,6,6-trimethoxy-1,4-cyclohexadiene (LII) nor 1,4-dimethoxybenzene (XLV) could be isolated from the reaction mixture, thus making it difficult to deduce the mechanisms involved. At least three mechanisms need be considered as outlined on page 44. This problem will be discussed below in connection with similar reactions carried out with 1,3- and 1,2-dimethoxybenzene.

Methoxylation of 9,10-dimethoxyanthracene (LIII) gave the corresponding quinone diketal (LIV) in 32% yield. (This relatively low yield may be due to the insolubility of the starting material (LIII) in methanol solution). Hydrolysis of (LIV) with dilute mineral acid afforded a quantitative yield of 9,10-anthracenequinone (LV).


XLVI
BF_3
LI
1. Shift of OCH_3 group
2. $-H^+$
XLVIII
1.$-H^+$
2.$-CH_3OH$
XLIX


LI
2 CH3O°
LII
Path III
CH3O°
Path I : 1. radical abstraction
2. addition of CH3O°
XLVI
aromatization
-H°
2 CH3O°
Path II
1. aromatization
2. - CH3OH
XLV
LII


OCH3
OCH3
electrolysis in CH3OH, KOH
32 % yield
CH3O
OCH3
CH3O
OCH3
dilute HCl
O
O

LIII

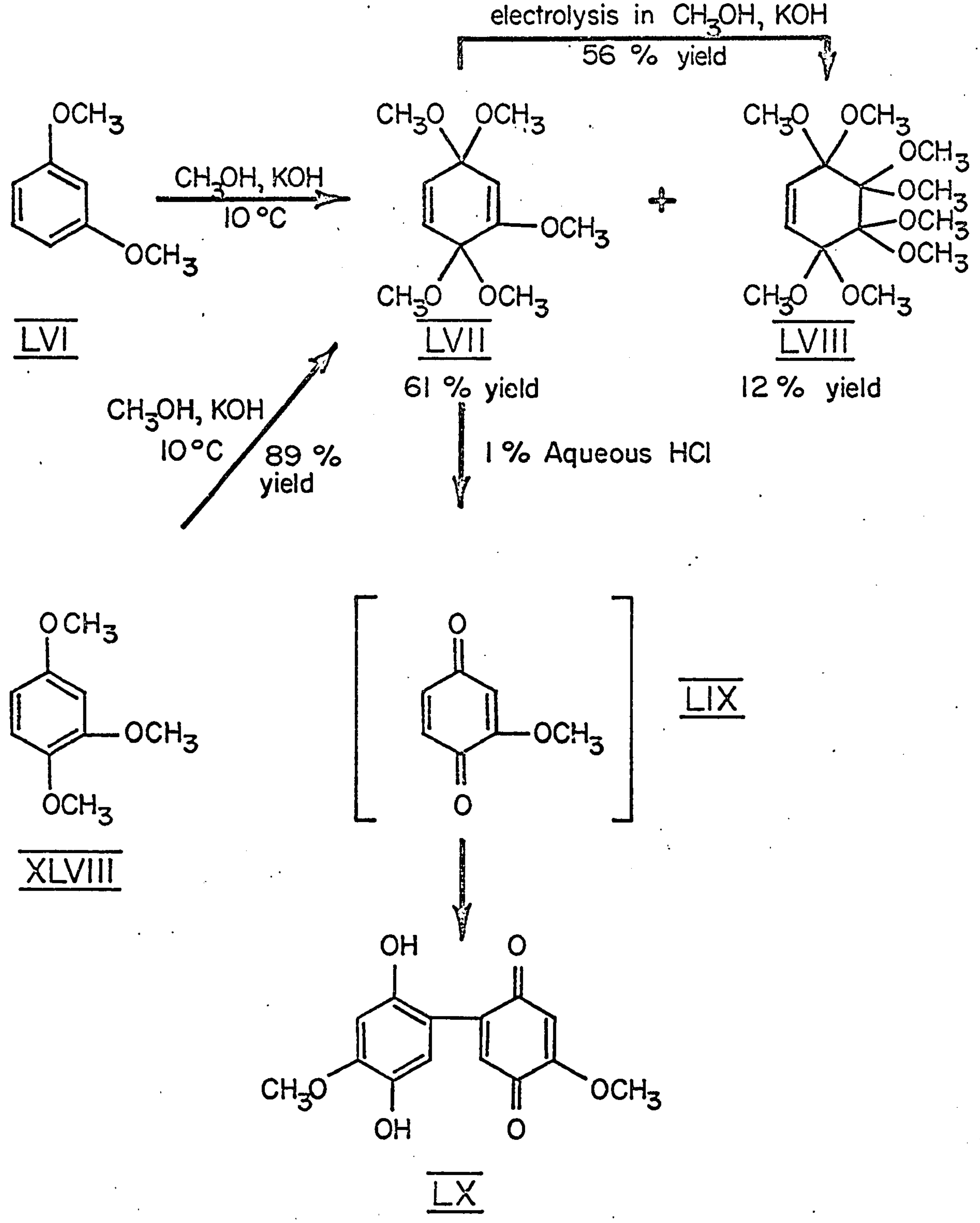
LIV

LV

(B) Electrochemical Methoxylation of 1,3-Dimethoxybenzene (LVI) and 1,2,4-Trimethoxybenzene (XLVIII)

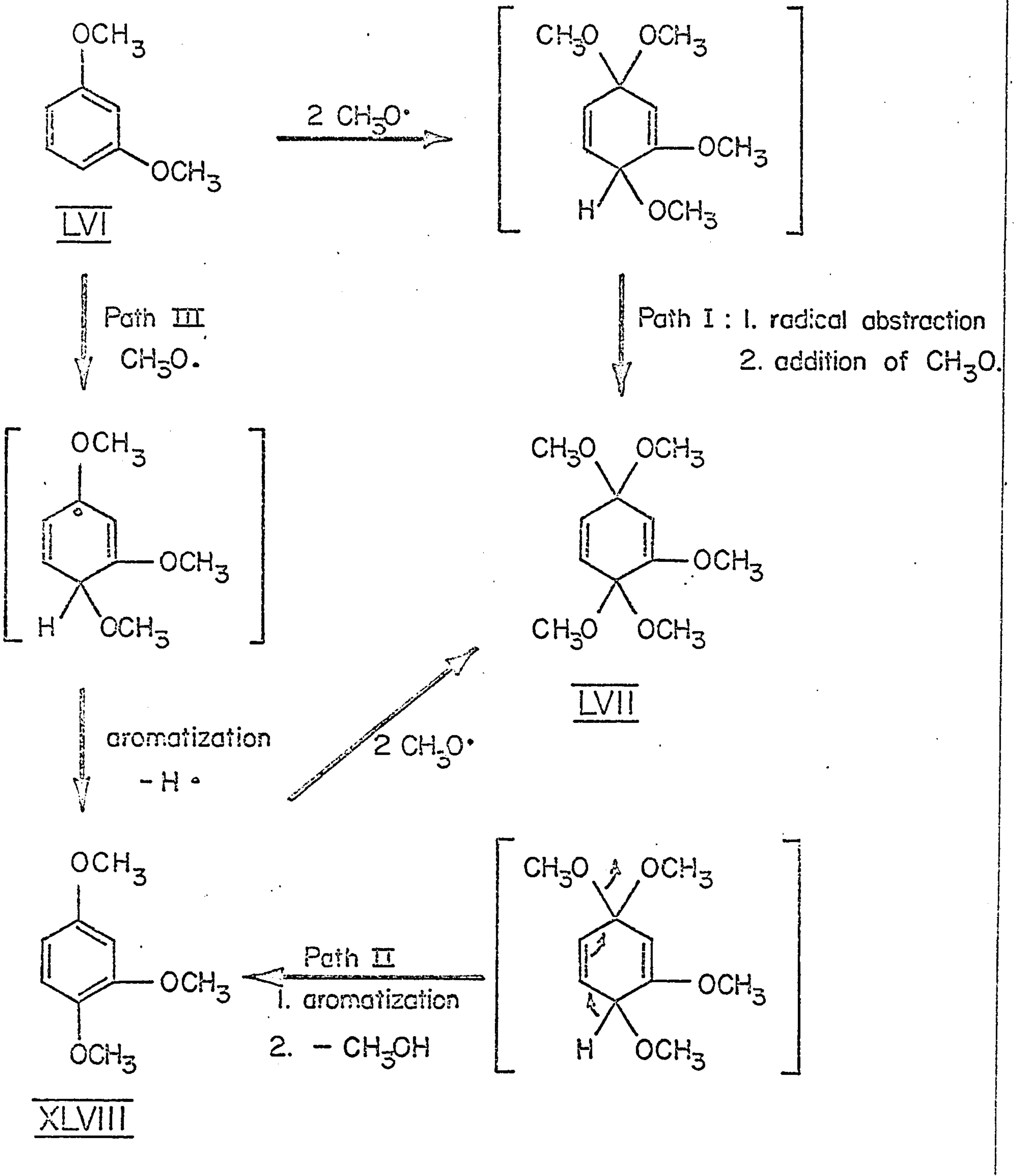
Continuing our explorations in the dimethoxybenzene series, the electrolysis of 1,3-dimethoxybenzene (LVI) was next examined. Two products were readily obtained in this case. They were identified as 2,3,3,6,6-pentamethoxy-1,4-cyclohexadiene (LVII), a colourless oil formed in 61% yield and a higher boiling colourless oil obtained in 12% yield and tentatively assigned the structure 3,3,4,4,5,5,6,6-octamethoxycyclohexene (LVIII). In addition a trace of 1,2,4-trimethoxybenzene (XLVIII) was identified by VPC analysis. The IR spectrum of the diene (LVII) showed two olefinic absorptions at 1680 and 1650 cm.$^{-1}$ while the NMR spectrum exhibited a characteristically complex olefinic region that analyzed well for an ABX system (63) with $J_{AB} = 10.0$, $J_{AX} = 2.23$, and $J_{BX} = 0.18$ c.p.s. These coupling constants are in agreement with known values for analogous systems (64). Upon hydrolysis of the methoxy-*p*-quinone diketal with dilute hydrochloric acid, the quinhydrone (LX) was obtained in 95% yield. This deep blue solid (LX) proved identical with a sample prepared according to the procedure of I.S. Ioffe and A.F. Sukhina (65) using methoxy-*p*-benzoquinone (LIX) as starting material.

Conclusive evidence for the structure of (LVII) was provided by electrochemical methoxylation of 1,2,4-trimethoxybenzene (XLVIII) which gave in 88% yield, the methoxy-*p*-benzoquinone diketal (LVII).


electrolysis in CH$_3$OH, KOH
56 % yield
CH$_3$OH, KOH
10 °C
LVI
LVII
61 % yield
LVIII
12 % yield
CH$_3$OH, KOH
10 °C
89 % yield
1 % Aqueous HCl
XLVIII
LIX
LX

The proposed structure for the octamethoxycyclohexene (LVIII) rests upon spectroscopic properties: weak olefinic absorption in the IR at 1650 cm.$^{-1}$; strong NMR absorption centered at $6.75\,\tau$ (for ketal methoxy hydrogens) and very weak absorption in the 5.0 to $2.0\,\tau$ region (olefinic hydrogen region). Attempted acid hydrolysis of (LVIII) led only to a tarry material which was not examined further. Electrochemical methoxylation of the diketal (LVII) using a large excess of current afforded a 56% yield of the same octamethoxycyclohexene (LVIII) thus establishing that the diketal (LVII) is a precursor of (LVIII).

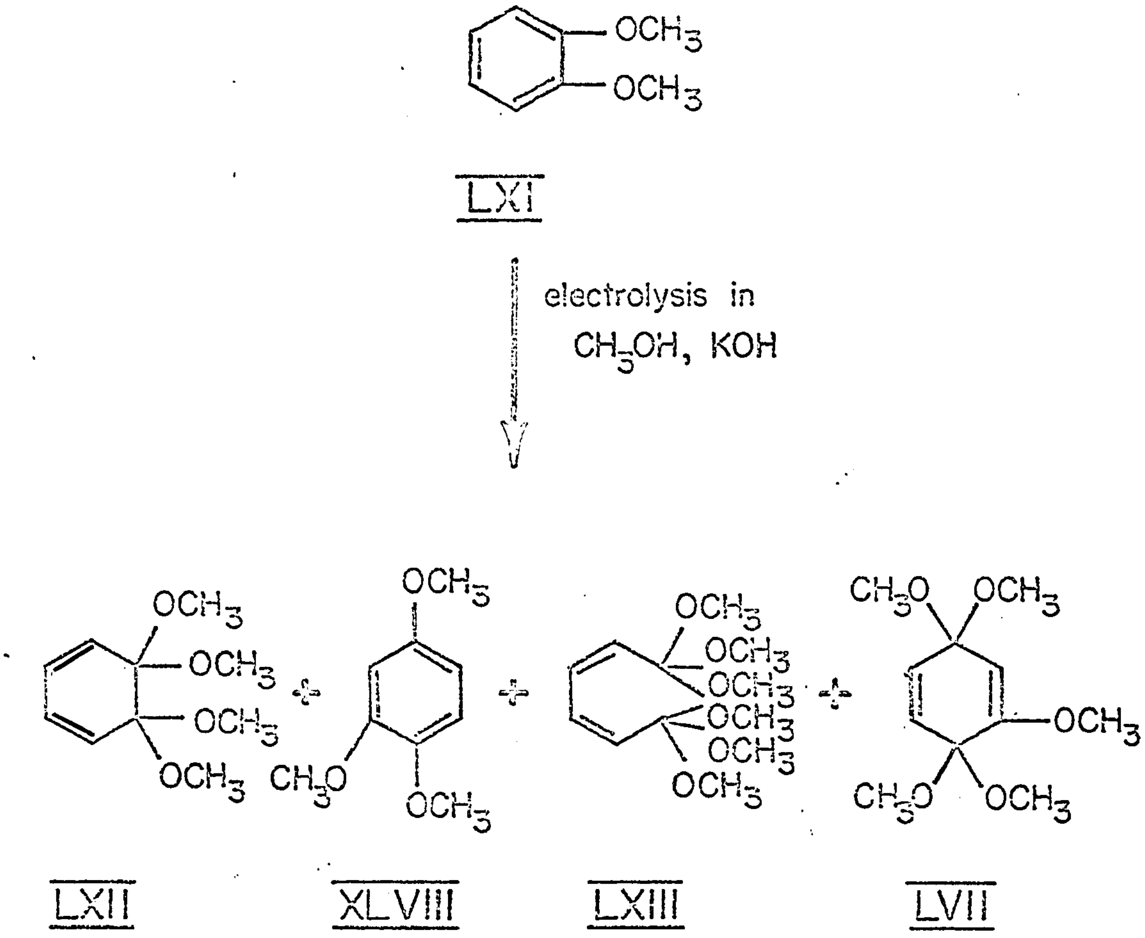
The mechanism of the electrochemical methoxylation of 1,3-dimethoxybenzene (LVI) to the diketal (LVII) ought to be analogous to the conversion of anisole (LI) to the *p*-benzoquinone diketal (XLVI). From the identification of a trace of 1,2,4-trimethoxybenzene (XLVIII) by VPC analysis, Path I may be readily eliminated. Further insight into the mechanism of these novel reactions was gained through the use of isotopically labelled resorcinol dimethyl ether (LVI). After electrochemical methoxylation of methyl-C^{14}-1,3-dimethoxybenzene, the resulting methoxy-*p*-benzoquinone diketal (LVII) had the same specific radioactivity as the starting material. Since Path II involves the loss to the solvent of one-quarter of the label in the final product (LVII) this reaction pathway is also unlikely. However, no loss of label occurs through Path III and this route is therefore the most probable of the three proposed.


OCH3
OCH3
LVI
2 CH3O·
CH3O
OCH3
OCH3
H
OCH3
Path III
CH3O·
Path I : 1. radical abstraction
2. addition of CH3O.
OCH3
OCH3
H
OCH3
CH3O
OCH3
OCH3
CH3O
OCH3
LVII
aromatization
- H ·
2 CH3O·
OCH3
OCH3
OCH3
XLVIII
Path II
1. aromatization
2. – CH3OH
CH3O
OCH3
OCH3
H
OCH3

(C) Electrochemical Methoxylation of 1,2-Dimethoxybenzene (LXI) and 1,4-Benzodioxane (LXVIII)

The electrochemical methoxylation of 1,2-dimethoxybenzene (LXI) gave a mixture of products which could be separated into four major constituents by fractional distillation: a 12% yield of 5,5,6,6-tetramethoxy-1,3-cyclohexadiene (LXII); a 15% yield of 1,2,4-trimethoxybenzene (XLVIII); a 1.5% yield of hexamethyl-cis,cis-orthomuconate (LXIII); a 9% yield of 2,3,3,6,6-pentamethoxy-1,4-cyclohexadiene (LVII). The remainder of the electrolysis mixture consisted of non-volatile tarry material, which was not further examined.

The o-benzoquinone diketal (LXII) showed only two peaks in the NMR spectrum at 6.72 τ (methoxy hydrogens) and 4.27 τ (olefinic hydrogens). On expansion of the low field region, a complex splitting pattern appeared. No detailed analysis of this region was attempted because of the poor resolution but the complex pattern observed is at least in accord with expectations for an A_2B_2 system (64). The UV spectrum was unusual in that two maxima were observed (in ethanol): one at 235 mμ (ε=3100) and another one at 265 mμ (ε=2500). It is conceivable that the short wave-length peak could mark the appearance of a $\pi \rightarrow \pi^*$ transition of lower energy than normal for a single double bond; oxygen-oxygen interactions in (LXII) can be effectively relieved if one carbon-carbon double bond is free to twist. This effect should tend to stabilize the $\pi \rightarrow \pi^*$ transition.



LXI

LXII 12 % yield

XLVIII 15 % yield

LXIII 1.5 % yield

LVII 9 % yield

The 265 mμ peak is however quite characteristic of a cisoid homoannular diene (1,3-cyclohexadiene absorbs at λmax. 256 mμ, ε = 8000 in hexane (66)). Treatment of the ethanolic solution of the o-benzoquinone diketal (LXII) with a drop of 5% aqueous hydrochloric acid, completely altered the UV spectrum to give two new peaks at 227 mμ, ε=7600 and 288 mμ, ε=3100 (o-benzoquinone exhibits a maximum in diethyl ether at 390 mμ, ε= 16,000 (67)).

Reductive hydrolysis of the o-benzoquinone diketal (LXII) using zinc dust and hydrochloric acid gave an oil which was shown to contain pyrocatechol (25% yield) and two other unidentified components by VPC analysis. Treatment of (LXII) with dilute hydrochloric acid afforded a reddish-brown coloured tarry material as would be expected if o-benzoquinone is generated.

There are very few examples known of compounds in which there are four alkoxy groups situated on adjacent carbon atoms. Glyoxal-bis-diethylacetal (LXIV) (68,69,70) and 2-(4-methyl-1,3-dioxolan-2-yl)-2-phenyl-4-methyl-1,3-dioxolane (LXV)* are examples that have been described in the literature. The o-benzoquinone diketal (LXII) represents a unique structure in the sense that the four methoxy groups must be situated in such a manner that they

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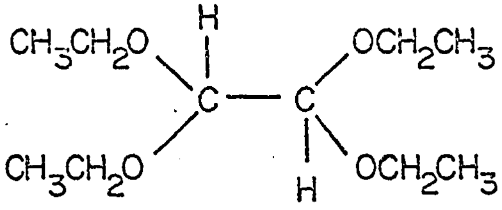
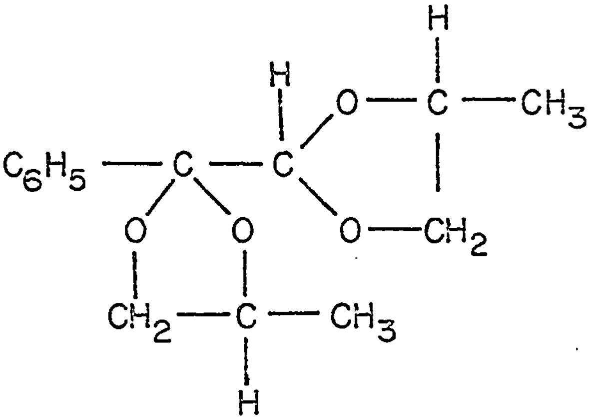
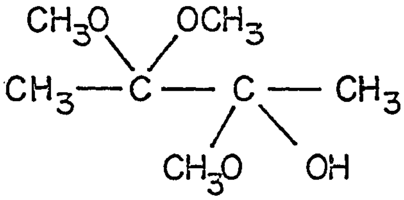
* There is some uncertainty that (LXV) is the correct structure.



LXIV



LXV

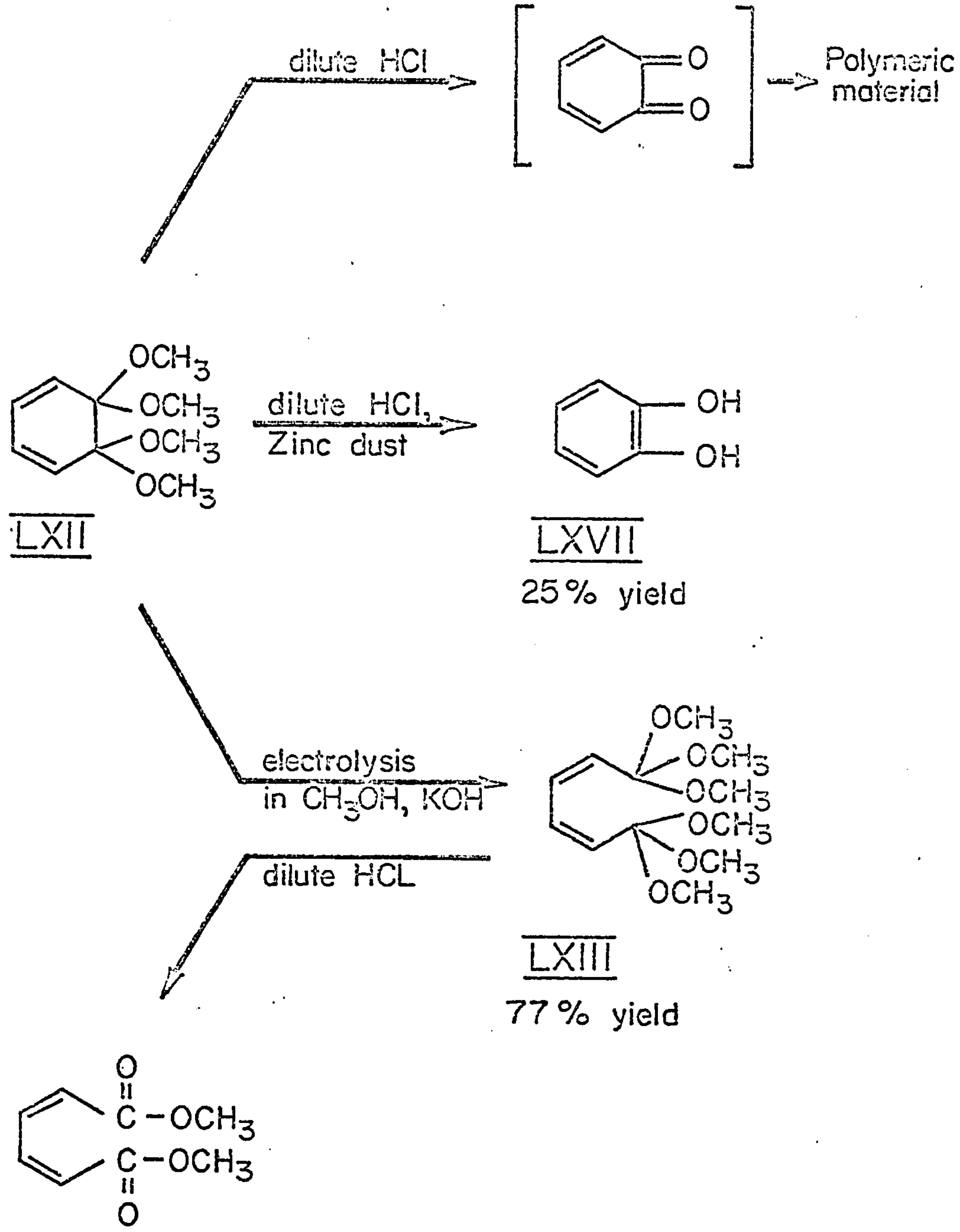


LXVI

are almost facing each other. Furthermore, the scarcity of diketals of this type is readily appreciated when it is observed that aliphatic α-diketones such as biacetyl afford only monoketals when submitted to classical methods for the synthesis of ketals. Diketal formation is prevented presumably by prohibitive steric repulsions that would be present in the monoketal hemiketal intermediate (LXVI).

The presence of 1,2,4-trimethoxybenzene (XLVIII) as a contaminant in several fractions of the electrochemical reaction mixture was confirmed by actual isolation of this compound. Where isolation in a pure form by distillation proved difficult because of co-distillation with methoxy-p-benzoquinone diketal (LVII), the mixture was analyzed both by VPC and by refractive indices using a standard curve (see Figure I).

One of the most interesting products resulting from the electrochemical methoxylation of 1,2-dimethoxybenzene (LXI), however, is hexamethyl cis, cis-orthomuconate (LXIII). This diorthoester (LXIII) is a colourless crystalline solid (m.p. 97.5 - 99.5°) with a UV spectrum exhibiting a characteristic diene absorption at 234 mμ, $\varepsilon = 10,200$ (ethanol). Addition of a drop of dilute hydrochloric acid to the alcoholic solution altered the UV spectrum to give a peak at 261 mμ, $\varepsilon = 17,600$ (reported (70) for cis, cis-dimethyl muconate (LXIX), in ethanol, λmax. 259 mμ, $\varepsilon = 26,400$).



LXII

LXVII

25 % yield

LXIII

77 % yield

LXIX

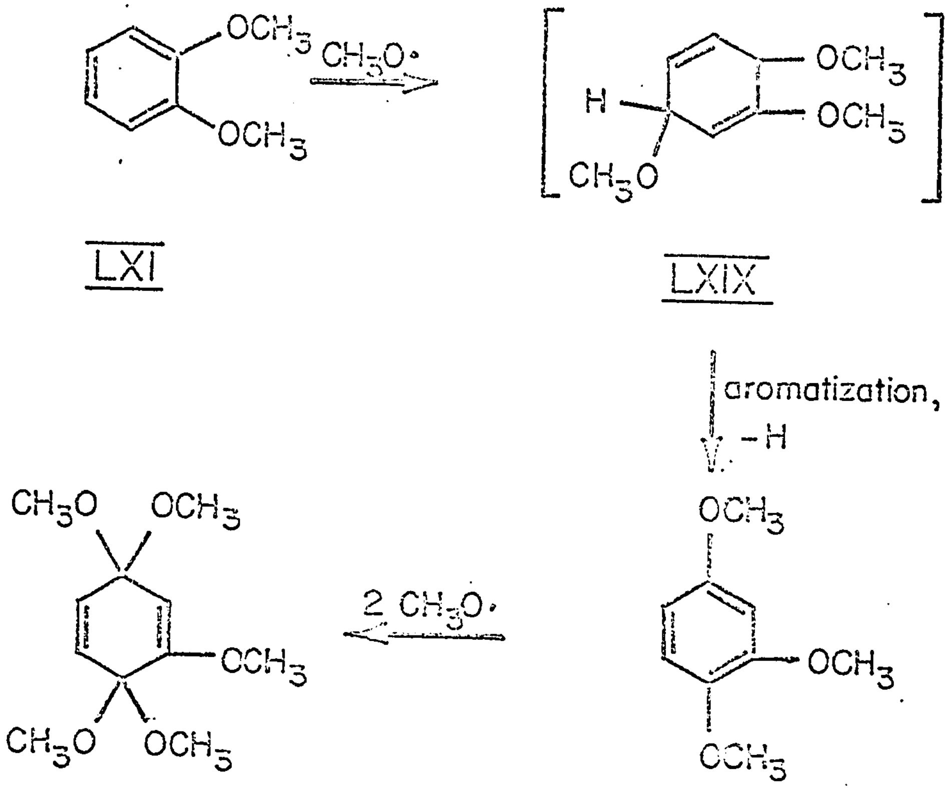
84 % yield

The NMR spectrum of (LXIII) on analysis gave $J_{AB} = 11.2$, $J_{AB'} = -1.5$, $J_{AA'} = 11.0$, and $J_{BB'} = \pm 1.2$ c.p.s. These coupling constants were in close agreement with those obtained for cis, cis-dimethyl muconate, a result which is not surprising since the geometry of both of these dienes should be identical.

The diorthoester (LXIII) was rapidly hydrolyzed in cold dilute hydrochloric acid solution affording an 84% yield of cis, cis-dimethyl muconate (LXVIII), while catalytic hydrogenation of (LXIII) proceeded with the quantitative uptake of two molecular equivalents of hydrogen.

The precursor of the diorthoester (LXIII) was conclusively shown to be the o-benzoquinone diketal (LXII) which could be methoxylated electrochemically to give a 77% yield of the diorthoester (LXIII).

Several conclusions may be drawn from the results of the electrochemical methoxylation of 1,2-dimethoxybenzene (LXI). Since a known precursor (1,2,4-trimethoxybenzene (XLVIII)) of methoxy-p-benzoquinone diketal (LVII) was actually isolated from the methoxylation mixture, the mechanism of formation of (LVII) may best be explained in the manner depicted by Path III on page 49, which pertains to the electrochemical methoxylation of 1,3-dimethoxybenzene (LVI) (or Path III of page 44 for the electrochemical methoxylation of anisole (LI)). Thus the mechanism could involve the formation of the radical intermediate (LXIX) which would in turn undergo methoxylation to give the methoxy-p-benzoquinone diketal (LVII) as follows:



LXI

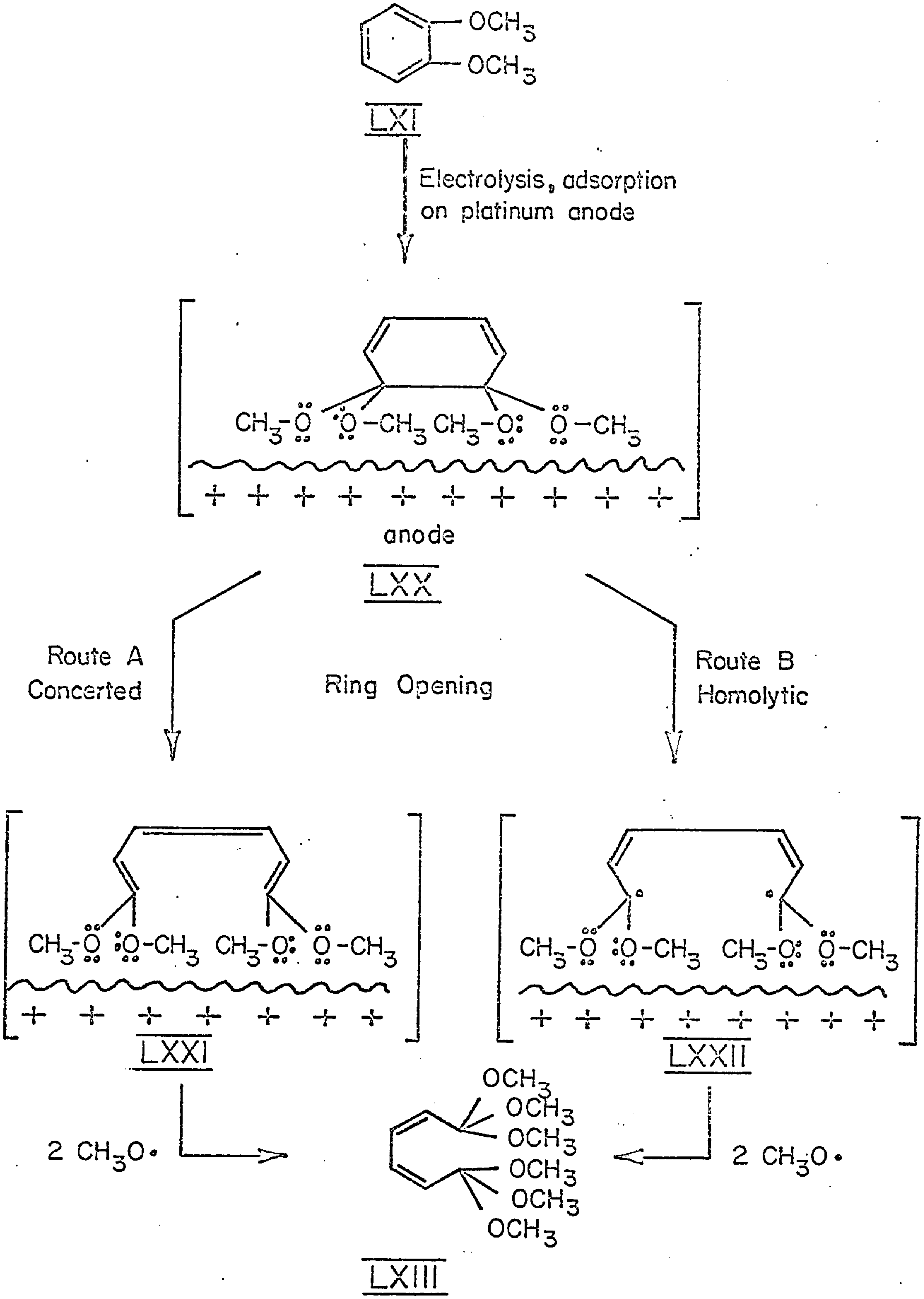
LXIX

LVII

XLVIII

On the basis of the above results, it is reasonable to assume that Path III may also represent the most probable mechanism accounting for the electrochemical methoxylation of anisole (LI) as well as 1,3-dimethoxybenzene (LVI).

It is interesting also to speculate on the mechanism involved in the formation of the diorthoester (LXIII). Since the product obtained in this unusual reaction is the thermodynamically least stable isomer of the three possible geometric forms (i.e. <u>trans</u>, <u>trans</u>-, <u>cis</u>, <u>trans</u>-, and <u>cis</u>, <u>cis</u>- isomers) and since the direct precursor of this cleavage product was shown to be the <u>o</u>-benzoquinone diketal (LXII), it is tempting to imagine that the mechanism may be represented either by Route A or B shown below. Both schemes require the adsorption of the <u>o</u>-benzoquinone diketal (LXII) on the anode surface, a condition which can serve to explain the stereochemical outcome of the cleavage process. The two mechanisms shown differ in that the adsorbed diketal (LXX) would in one case (Route A) undergo concerted ring opening followed by 1,6- addition of adsorbed methoxy radicals to the intermediate triene (LXXI) to give (LXIII). Alternatively, the adsorbed diketal (LXX) could suffer homolytic ring opening (Route B) to give an intermediate diradical which would be stabilized by adsorption on the electrode thus preventing electron delocalization through resonance. Subsequent attack by methoxy radicals would finally yield


OCH3
OCH3
LXI
Electrolysis, adsorption on platinum anode
CH3-O O-CH3 CH3-O O-CH3
anode
LXX
Route A
Concerted
Ring Opening
Route B
Homolytic
LXXI
LXXII
2 CH3O•
2 CH3O•
OCH3
LXIII

the observed product (LXIII). The ring opening step in either mechanism is no doubt facilitated and possibly conditioned by a considerable weakening of the carbon-carbon bond due to the large repulsive forces acting between the four adjacent oxygen atoms. There is little doubt that this latter effect would create considerable ring strain (see the UV spectrum) which can be partially relieved only through appreciable distortions of the bond angles. It would seem that relief of this strain can provide the driving force for ring fission.

Effective interaction of the o-benzoquinone diketal (LXII) with the anode is probably made possible to a large degree by the participation of the unshared electrons of the four methoxy groups and to a lesser extent by the electrons of the diene system. This hypothesis is substantiated by the observation that both benzene and p-xylene which have no ethereal oxygens are essentially inert towards electrochemical methoxylation.

In view of the interesting results obtained in the electrochemical methoxylation of 1,2-dimethoxybenzene (LXI), it was reasoned that the electrochemical methoxylation of benzodioxane (LXXIII) could perhaps lead to observations that might be more easily interpretable from the mechanistic standpoint. Interestingly, the electrochemical methoxylation of benzodioxane (LXXIII) afforded in 31% yield a colourless solid, m.p. 88.5 - 89.5° accompanied by a high boiling liquid which was not examined further. The solid proved to be 9,10-dihydro-9,10-dimethoxybenzodioxane (LXXIV).

The UV spectrum of this cyclic o-quinone diketal (LXXIV) was almost identical to that of the o-benzoquinone diketal (LXXII): it exhibited peaks at 225 mμ, $\varepsilon = 2900$, and 265 mμ, $\varepsilon = 2800$ (ethanol). Addition of a drop of dilute hydrochloric acid to the ethanol solution altered the UV spectrum which now showed peaks at 225 and 289 mμ. The NMR spectrum showed a symmetrical but complex splitting pattern between 6.71 and 5.91 δ (the ethylenedioxy hydrogen region). The pattern could be analyzed as an A_2B_2 spectrum with $J_{AB} = 9.3$, $J_{AB'} = 1.7$, $J_{AA'} = 14.9$, and $J_{BB'} = 1.6$ c.p.s., which can only arise if the two rings are locked in the rigid non-invertible trans-fused manner*. A cis-fused ring system would show only one resonance line for the ethylenedioxy hydrogens because of rapid conformational inversion causing the hydrogens to become equivalent.

Reductive hydrolysis of this bicyclic o-quinone diketal (LXXIV) led to a 76% yield of pyrocatechol (LXVII) whereas treatment with dilute hydrochloric acid gave dark coloured polymeric material resulting from polymerization of o-benzoquinone.

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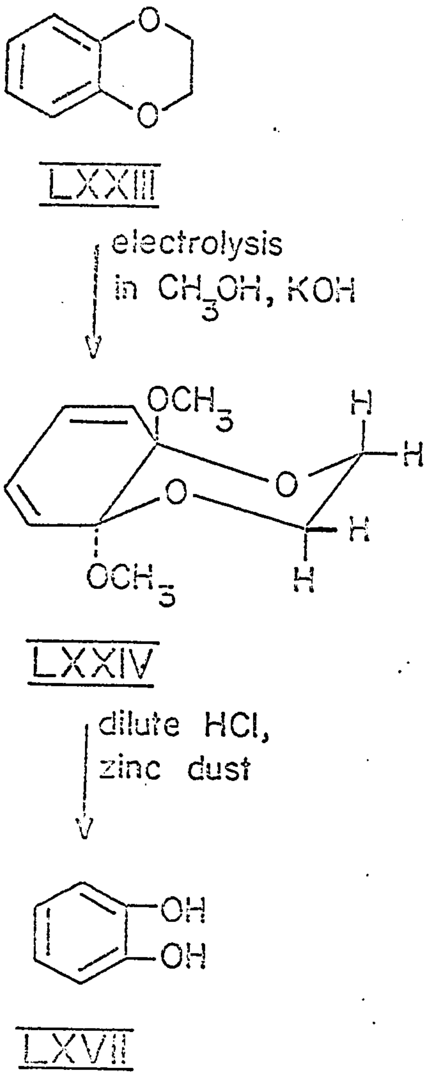
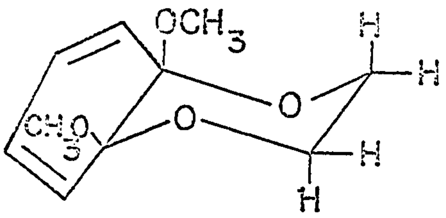
* J. Musher and R.E. Richards (71) using NMR spectroscopy have demonstrated that trans-decalin is a rigid molecule whereas cis-decalin has two interconvertible conformations.


LXXIII
electrolysis
in CH_3OH, KOH
OCH_3
H
H
H
H
OCH_3
LXXIV
dilute HCl,
zinc dust
OH
OH
LXVII


OCH_3
CH_3O
H
H
H
H

LXXV

Due to the limited time available, it has not been possible to ascertain whether the corresponding cis-fused isomer (LXXV) is produced in the electrochemical methoxylation of benzodioxane (LXXIII), thus making it premature to discuss the stereochemistry of these methoxylation reactions. It is nevertheless conceivable that the introduction of the methoxy groups proceeds with some degree of stereoselectivity*.

(D) Miscellaneous Electrochemical Methoxylation Reactions

A number of exploratory experiments were carried out in order to gain an insight into several facets of electrochemical methoxylation reactions. Many of these investigations are forcibly incomplete but in a good many instances they are informative and provide a basis for further research.

(i) Electrochemical Methoxylation of 1,3-Cyclohexadiene (LXXVI) and 1,4-Cyclohexadiene (LXXIX)

The electrochemical methoxylation of 1,3-cyclohexadiene (LXXVI) afforded a mixture of dimethoxycyclohexenes in 4% yield; it is probable that the structure of these isomers corresponds to 3,6- and 3,4-dimethoxycyclohexene ((LXXVII) and (LXXVIII)).

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* For examples of stereospecific free radical additions to olefins see the recent review of B.A. Bohm and P.I. Abell (72).

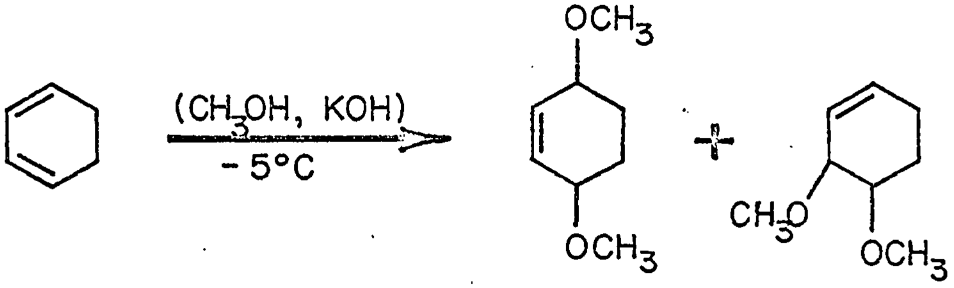
The IR spectrum of this mixture showed characteristic olefinic absorption at 3050 and 1650 cm.$^{-1}$ while the NMR spectrum, although complex, was in accord with the expected structures. A VPC analysis exhibited three peaks, two of which overlapped considerably.

It can be seen on the basis of structures (LXXVII) and (LXXVIII) that there are two possible geometric isomers for each case. In theory, a total of four peaks should have been observed in the VPC analysis if resolution is optimal. Failure to detect a fourth component is probably attributable to instrumental inadequacies.

Catalytic hydrogenation of this mixture led to an uptake of one molecular equivalent of hydrogen as expected.

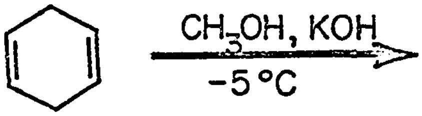
Repetition of the electrolysis using a large excess of current produced the same mixture of (LXXVII) and (LXXVIII) in 11% yield and provided a new component in 9% yield which is believed to have the structure of a trimethoxycyclohexene. The IR and NMR spectra of this new material are consistent with this assignment. Tentative structures for this trimethoxycyclohexene are (LXXX) or (LXXXI), both of which correspond to having replaced an allylic hydrogen of (LXXVII) or (LXXVIII) by a methoxy radical.

Attempted methoxylation of 1,4-cyclohexadiene (LXXIX) afforded no detectable reaction product, the starting material being recovered in 90% yield (the 10% loss is attributable to volatilization during the course of the reaction).



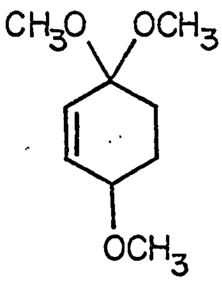
LXXVI LXXVII LXXVIII

Yield 15 %
(Current efficiency 11 %)

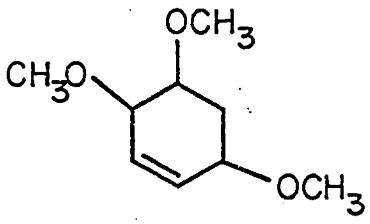


No detectable product
(91 % of starting material recovered)

LXXIX



LXXX



LXXXI

(ii) Electrochemical Methoxylation of Naphthalene

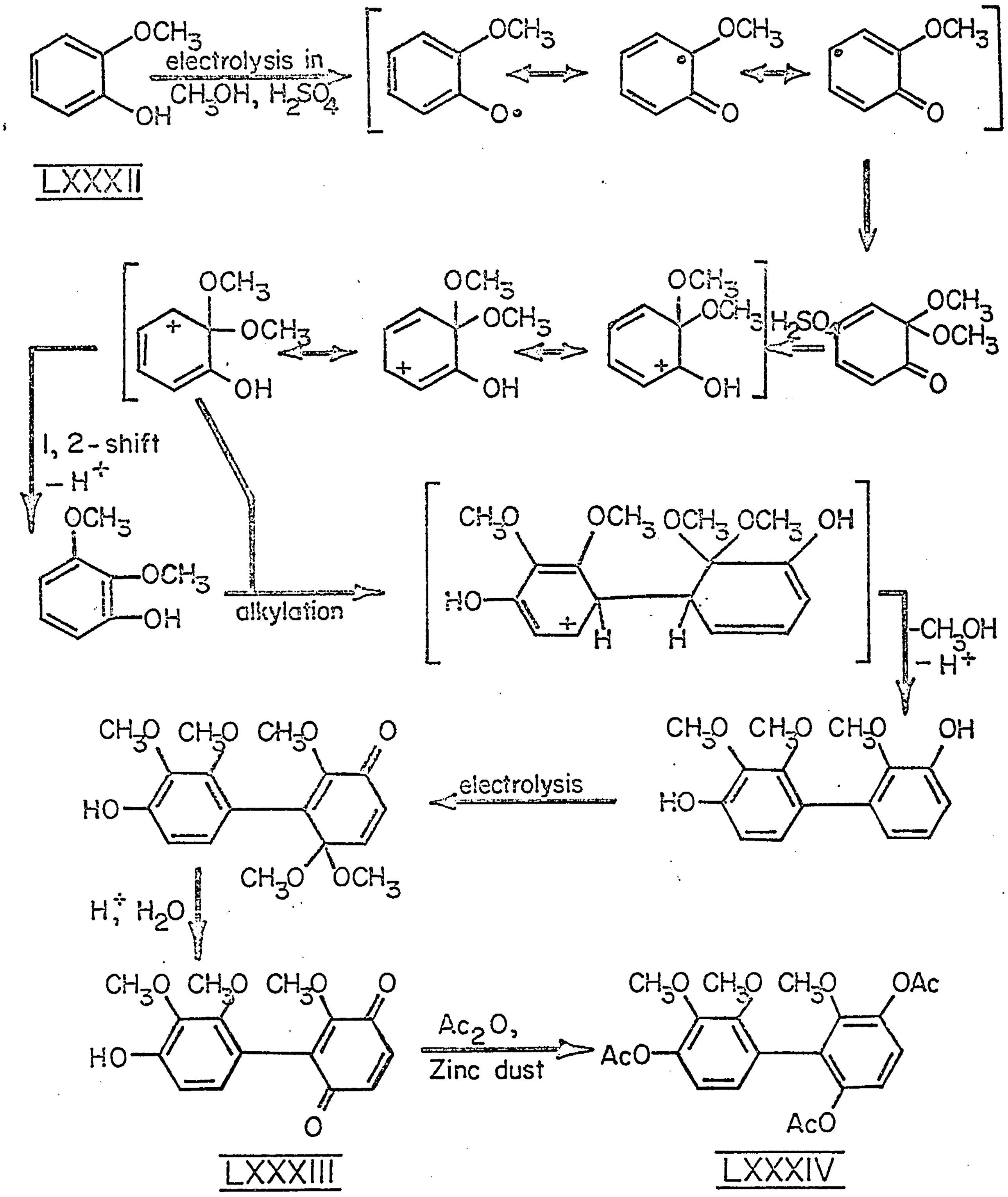
Evidence was obtained that naphthalene undergoes electrochemical methoxylation to some extent. Upon treatment of the electrolysis products with water, a deep blue oil is produced. The colour was readily discharged by shaking the oil with 85% phosphoric acid or by heating, but it appeared to be quite stable at room temperature. No further examination of this intriguing blue compound was made.

(iii) Electrochemical Methoxylation of Gualacol (LXXXII)

When gualacol (LXXXII) was electrolyzed in a basic methanolic solution an uncharacterizable tarry material was produced. However, using concentrated sulfuric acid as the electrolyte, a red crystalline solid was obtained in 46% yield. This compound which will be referred to as the "Gualacol Red Solid" had m.p. 201.5 - 203.0° and was assigned the tentative structure (LXXXIII).

The IR spectrum of the "Gualacol Red Solid" showed hydroxyl absorption at 3580 $cm.^{-1}$ and carbonyl absorption at 1675 $cm.^{-1}$ The NMR spectrum did not disagree with the proposed structure (LXXXIII).

The "Gualacol Red Solid" (LXXXIII) on treatment with acetic anhydride and zinc dust gave a 54% yield of a colourless solid believed to be a triacetoxy,trimethoxybiphenyl (LXXXIV). The IR spectrum of this derivative showed acetate



LXXXII

LXXXIII

LXXXIV

carbonyl absorption at 1760 cm.$^{-1}$; the NMR spectrum exhibited three sharp peaks for acetoxy hydrogens at 7.62 to 7.87 τ and three sharp peaks for methoxy hydrogens at 6.12 to 6.26 τ.

The mechanism of formation of the "Guaiacol Red Solid" (page 67) may involve a cationic intermediate which would undergo alkylation in a manner similar to that described for the boron trifluoride aromatization of the p-benzoquinone diketal(XLVI). The red colour of the product (LXXXIII) must be associated with the presence of a quinonoid grouping; hydrogen bonding of the phenolic hydrogen with the carbonyl groups of the quinone is also very likely to occur.

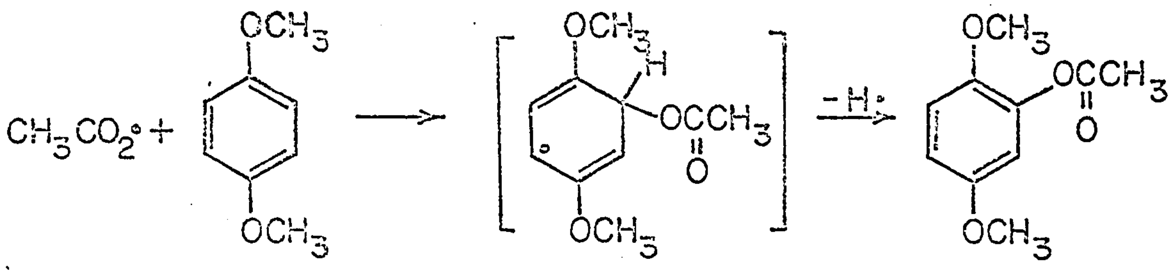
No further attempt was made to substantiate the structure of these interesting compounds.

(iv) Electrochemical Acetoxylation of 1,4-Dimethoxybenzene (XLV)

An attempt was made to apply the conditions of the Kolbe reaction in the absence of water (using potassium acetate and glacial acetic acid) but in the presence of a potential acceptor of acetoxy or methyl radicals. For this purpose 1,4-dimethoxybenzene (XLV) was used in the hope that either acetoxy radicals or methyl radicals would add in a manner similar to that already observed in the case of methoxy radicals. It was at least gratifying to observe that a 62% yield of 1,4-dimethoxy-2-acetoxybenzene (LXXXV) resulted under these conditions.

(a) $CH_3CO_2^- \xrightarrow{-e} CH_3CO_2\cdot$

(b)

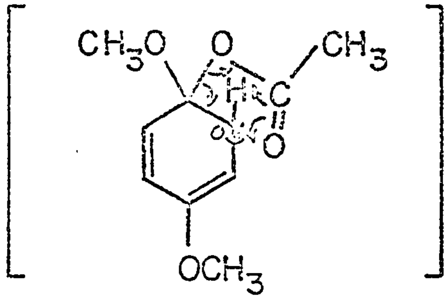


XLV

LXXXV

(c) $CH_3CO_2\cdot \longrightarrow CO_2 + CH_3\cdot$

(d) $2\ CH_3\cdot \longrightarrow C_2H_6$



LXXXVI

This result clearly supports the view that acetoxy radicals are important intermediates in the Kolbe reaction.

At first glance, there seems to be a fundamental difference in the behaviour of acetoxy and methoxy radicals towards 1,4-dimethoxybenzene. Whereas the latter lead readily to destruction of the aromatic resonance state to give ketals, the former lead directly to a substitution product in which the aromatic character of the starting material is preserved. However, the mechanism of interaction between aromatic ethers and either acetoxy or methoxy radicals may nevertheless be closely related, a possibility which can be obscured by the fact that an initial adduct such as (LXXXVI) could readily undergo spontaneous rearrangement* to the observed product (LXXXV). Since this is not likely to occur when methoxy radicals are involved, the diverging nature of the end products respectively involved does not necessarily reflect differences in the fundamental electrode process.

A major difference between methoxy and acetoxy radicals lies in that the former are probably more reactive than the latter which can benefit from resonance stabilization. It follows that the intermediates which would result from attack

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* Recently C.L. Wilson and T. Hayashi (73) have found that the Kolbe reaction carried out in the presence of anisole gave o-acetoxyanisole as the major product. This evidence clearly supports such an intermediate as (LXXXVI) in the acetoxylation of 1,4-dimethoxybenzene.

by methoxy radicals should be more reactive and possibly more likely to allow the overall reaction to follow a different course.

It would be of considerable interest in this regard to examine the course of the reaction (addition or substitution) upon electrolysis of other materials such as thiocyanate, thiols, or amines in the presence of 1,4-dimethoxybenzene (XLV) (in suitable inert solvents).

III Reactivity of Various Organic Compounds Toward Electrochemical Methoxylation

Examination of Table II shows in a general manner the effect that the presence of ether groups in various starting materials has on susceptibility to attack by methoxy radicals. Thus, electrochemical methoxylations proceed most efficiently in all those cases which include an activating function such as the oxygen atom of furan and the methoxy substituents of aromatic systems. From the evidence accumulated thus far, it seems certain that the activating groups have at least a two-fold purpose: the ethereal oxygens are necessary to stabilize the radical intermediates or transition states resulting from attack by methoxy radicals. This stabilizing influence of ethereal oxygen on free radicals has been recognized by others (74,75) but is as yet poorly understood. The second purpose, and we believe this to be the most important

Table II Yields and Current Efficiencies in Some Electrochemical Methoxylation Reactions

	Compounds Electrolyzed	Yield of Major Product	Current Efficiency for Major Product
a	furan	73%	86%
b	1,4-dimethoxybenzene	75%	66%
c	1,3-dimethoxybenzene	75%	13.5%
d	1,2,4-trimethoxybenzene	90%	40%
e	5,5,6,6-tetramethoxy-1,3-cyclohexadiene	77%	4.5%
f	1,3-cyclohexadiene	4%	3%
g	benzene, p-xylene, or 1,4-cyclohexadiene	nil	nil

one, is to facilitate the organic molecule in becoming adsorbed onto the electrode surface through interaction with the unshared electrons of the ethereal oxygens.

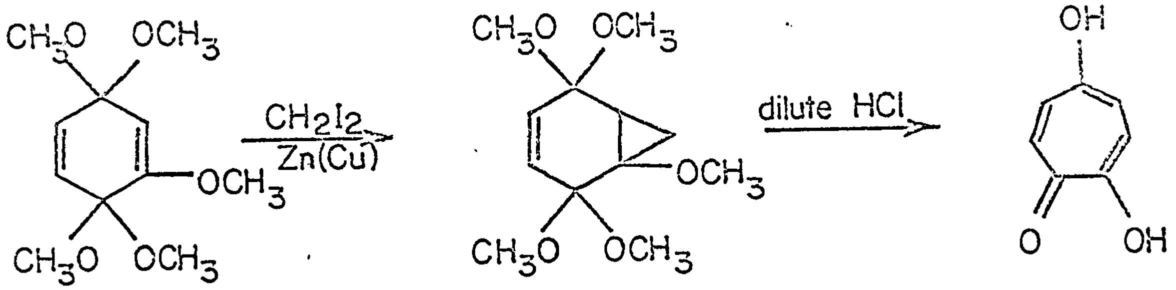
In agreement with these requirements, 1,3-cyclohexadiene is attacked with difficulty and the specificity of the attack is low (giving a mixture of (LXXVII) and (LXXVIII)). Furthermore, benzene, p-xylene, and 1,4-cyclohexadiene do not add methoxy radicals at all because of the absence of substituent groups necessary for adsorption onto the anode. On the other hand, the aromatic ethers are all quite reactive towards methoxylation and the specificity of the attack can be quite high in some cases.

It should also be noted that allylically disposed methoxy groups considerably deactivate the carbon-carbon double bond (see page 25 for the case of substituted furans). Thus in the p-benzoquinone diketal (XLVI), the double bonds are inert towards further methoxylation, whereas in the methoxy-p-benzoquinone diketal (LVII), while the 4,5- double bond is clearly unreactive, the 1,2- double bond is activated by a vinyl methoxy group and can undergo further reaction.

Another example of the effect of allylically placed methoxy groups is encountered in the electrochemical methoxylation of the o-benzoquinone diketal (LXII). Here, the diene system should be much less reactive than in 1,3-cyclohexadiene (LXXVI). This was experimentally verified when methoxylation was found to produce carbon-carbon bond fission rather than attack on the diene system.

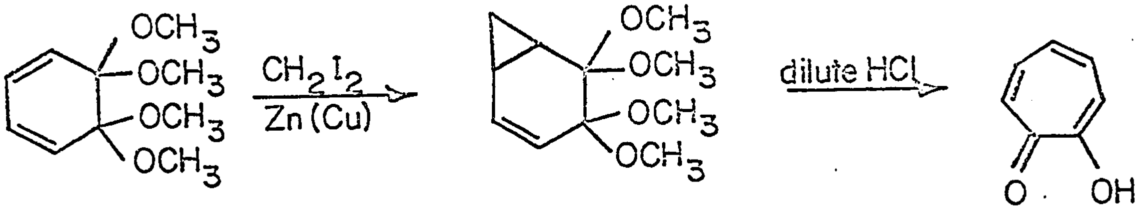
IV Some Proposals for the Synthesis of Substituted Tropolones

There are several possibilities that are apparent for a rational synthesis of substituted tropolones using some of the quinone diketals prepared as described above. For



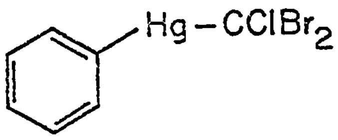
LVII

LXXXVII



LXII

XII



LXXXVIII

example, methoxy-*p*-benzoquinone diketal (LVII) could conceivably be converted to 4-hydroxy tropolone (LXXXVII) while the *o*-benzoquinone diketal (LXII) could lead to tropolone (XII) itself through the application of methods already discussed earlier. Should the cyclopropane forming reagents (page 25) prove insufficiently reactive, the recently described (76) and more efficacious reagent, phenyl chlorodibromomethylmercury (LXXXVIII) could be advantageously applied. The dibromocyclopropane derivative which should be formed could then be reductively dehalogenated (77).

CONCLUSION

The electrochemical methoxylation reactions described in this work have significantly extended the relatively unexplored realm of organic electrochemistry. Moreover, it has been shown that unusual products, inaccessible by any other route, can be prepared in high yields, thus providing novel starting materials for the field of organic synthesis. As an example, one of these compounds has led to a new synthesis of substituted biphenyls. It is felt that this thesis has unveiled some of the unsuspected richness of organic electrochemistry, a field which certainly will be most rewarding to those delving into it in the future.

EXPERIMENTAL

General

Methanol was purified under dry nitrogen by the method of H. Lund and J. Bjerrum (78). Capillary melting points and refractive indices were corrected using reliable standards. Molecular weight (MW) determinations (Rast) were carried out using d-camphor, m.p. 174 - 178° (Eastman Reagent Grade).

Infra-red (IR) spectra were obtained with a Perkin-Elmer Infracord instrument, nuclear magnetic resonance (NMR) spectra with a Varian Model V-4302 NMR spectrometer operating at 60 Mc.sec.$^{-1}$, and ultraviolet (UV) spectra with a Beckman DK-2 spectrophotometer. Only the most characteristic bands are reported for IR spectra; whereas NMR spectra are reproduced in full in Appendix B. The designation "identical" for comparison of IR spectra should be interpreted to mean identical with regard to band positions, without implying that band intensities are completely matched. Vapour phase chromatography (VPC) was carried out with a Perkin-Elmer Vapour Fractometer, Model 154. The electrolysis cell consisted of two platinum gause anodes with a total geometrical surface area of 160 cm.^{2}, and a nickel cathode with a geometrical surface area of 240 cm.^{2} The anodes were arranged concentrically about the cathode as described in the diagram of the cell given in Appendix A. The cell was provided with a thermometer, a cold finger for internal cooling, and two cell containers (300 ml. and 1000 ml.) each of which was designed for magnetic stirring. The source of direct current was a 6 - 12 volt battery charger (Canadian Tire Corporation, Model T 1225), connected to a variable transformer (Variac), which in turn was connected to an alternating current supply. The current was kept approximately constant during the electrolysis by manually adjusting the Variac. Current efficiency whenever calculated was based on the yield of purified product unless otherwise noted.

General Electrolysis Methods

Method A

To a magnetically stirred solution of 2 g. potassium hydroxide pellets (Eastman Reagent Grade) dissolved in 250 ml. of dry methanol contained in the 300 ml. cell was added 0.1 mole of the material to be electrolyzed. The solution was cooled to the desired temperature using tap water (10 - 20°) or an ethylene glycol-water mixture pumped from a 10 gallon constant temperature bath (-20 to 0°). After the passage of the required amount of current, the cell contents were transferred to a 1000 ml. round bottom flask and the methanol was removed on a rotary evaporator at 30 - 40°/20 - 30 mm. To the residue was added 250 ml. of ether and the mixture was extracted with 3 x 50 ml. portions of water. The ether layer was dried over anhydrous magnesium sulfate, filtered, and evaporated. The residue was subsequently worked up as described separately for each individual case.

Method B

Method A was followed up to the point of addition of 250 ml. of ether. However, instead of washing out salts with water, the salts were precipitated by adding dry ether, followed by filtration on a Buchner funnel. The ether filtrate was then evaporated and the residue worked up as described below.

EXPERIMENTAL . PART I

1 Attempts to Prepare Cyclopropane Derivatives of 2,5-Dimethoxy-2-(α,α-Dimethoxyethyl)-Dihydrofuran (XXIX)*

The following methods for cyclopropane ring formation on DDD (addition of a carbene moiety to the double bond of DDD (XXIX)) were attempted:

(i) using the H.E. Simmons and R.D Smith (48) reagent from

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* This compound, which will be designated DDD, was prepared by electrolysis of 2-acetylfuran dimethyl ketal essentially according to N. Clauson-Kaas et al (47) by electrolytic methoxylation. The NMR spectrum of (XXIX) is given in Appendix B.

methylene iodide and zinc-copper couple.

(ii) using the addition of carbethoxy carbene generated from diazoacetic ester (see for example H.M. Walborsky and F.M. Hornyak (49)).

(iii) using dichlorocarbene generated from trichloroacetic ester by the method of W.E. Parham and E.E. Schweizer (50).

(iv) using the iodomethylzinc iodide reagent of G. Wittig and K. Schwarzenbach (51).

In all of the above reactions, no cyclopropane derivative could be isolated and the yield of DDD recovered was in each instance greater than 90%.

2. Attempted Preparation of Hexen-2-Dione-4,5-Dimethoxyacetal-1 (XXXIII)

(i) Under Anhydrous Conditions

The procedure of L. Vargha et al (56) was followed for the preparation of p-toluenesulfonyl 2-acetofuranoxime (XXXII) from 2-acetylfuran (XXVIII). This oxime ester, (8.0 g., 0.028 mole) was treated in 50 ml. of dry methanol again using the method outlined by these authors (56). The solution was stirred at room temperature for 5 days in the dark and under an atmosphere of dry nitrogen. However, no precipitate formed as was claimed by these workers (56).

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* The 2-acetylfuran (XXVIII) was prepared by the acylation of furan in acetic anhydride using boron trifluoride etherate as catalyst (see for comparison, J.V. Heid and R. Levine (79)).

After 6 days, 0.50 g. (0.028 mole) of water was then added. Within 6 hr., a solid was deposited from the solution and after an additional 3 day period, the solid was collected and dried in air. It consisted of 4.6 g. (0.024 mole; 86% yield) of ammonium p-toluenesulfonate. The IR spectrum (nujol mull) of this salt was identical to that of an authentic sample of ammonium p-toluenesulfonate (prepared by dissolving p-toluenesulfonic acid in concentrated aqueous ammonium hydroxide solution and evaporating the resulting solution to dryness).

The filtrate from the above reaction was evaporated and the residue was distilled in vacuo to give 3.7 g. of a pale yellow oil, b.p. 65°/0.1mm. The UV spectrum showed $\lambda_{\max.}^{EtOH}$ 300 mμ, $\varepsilon = 100$. There was no absorption in the range 900 - 340 mμ. The IR spectrum (thin film) had a characteristic peak at 1720 (s) $cm.^{-1}$ and a series of strong broad bands extending from 1200 to 950 $cm.^{-1}$ The NMR spectrum (Appendix B) could be interpreted to represent a mixture of 55% of 2,5-dimethoxy-2-acetyldihydrofuran (XXXIX) which is described in the next section and 45% of DDD (XXIX).

Several other attempts were made to analyze this mixture by gas chromatography using either the Pye Argon apparatus or the Perkin-Elmer Fractometer equipped with columns packed with apiezon, diisobutylphthalate, versamide or silicon oil on fire-brick in a 200 cm. column. A temperature range of 50 - 180° was used. In all these cases interpretation of the results was complicated by thermal decomposition of the injected materials. Methanol could be identified as a pyrolysis product.

(ii) Under Wet Conditions. The Preparation of 2,5-Dimethoxy-2-Acetyldihydrofuran (XXXIX)

A solution of 7 g. (0.025 mole) of the oxime ester (XXXII) in 35 ml. of 95% methanol was stirred for 5 days. Then 50 ml. of dry ether was added and 4.3 g. (0.023 mole; 92% yield) of ammonium p-toluenesulfonate was filtered off. The filtrate was concentrated in vacuo at 30° and the residual oil dissolved in ether and extracted with 3 x 15 ml. of water; the extract was dried over anhydrous magnesium sulfate, filtered, and the solvent was evaporated to leave 3.2 g. of an oil. Distillation of this oil afforded 2.7 g. (0.016 mole; 64% yield) of a middle fraction which was identified as 2,5-dimethoxy-2-acetyldihydrofuran (XXXIX), b.p. 60°/0.8 mm., n_D^{23} 1.4453.

Anal. Calcd. for $C_8H_{12}O_4$: C, 55.80%; H, 7.02%.

Found: C, 55.75%; H, 6.84%.

This liquid was not found to be explosive even upon heating to 150° in contrast to Vargha's claim (56). The UV spectrum gave a peak with λ_{max}^{EtOH} 300 mμ, $\varepsilon = 550$. There was no absorption band in the region 900 - 340 mμ. The IR spectrum (thin film) when compared with that of a pure authentic sample of 2,5-dimethoxy-2-acetyldihydrofuran (see Section 3) was found to be identical with the latter's: characteristic bands at 1720(s), 1625(w), 1190(s), 1140(s), 1100(s), 1080(s), 1030(s), 1010(s), 974(s), 820(m), 802(m), 735(m) cm.$^{-1}$ were observed. The NMR spectrum (Appendix B) exhibited relative areas of methyl to methoxyl to all other hydrogens of 1:2:1 (calculated 1:2:1).

3. Electrochemical Preparation of 2,5-Dimethoxy-2-Acetyldihydrofuran (XXXIX)

Using electrolysis Method A, a solution of 11 g. (0.10 mole) of 2-acetylfuran (XXVIII) containing 0.4 g. of concentrated sulfuric acid in 150 ml. of methanol was electrolyzed at -10°(0.6 amp. at 11 - 12 volt for 16 hr.). A solution of 1 g. of sodium acetate in 5 ml. of water was then added and the methanol was evaporated off. After removal of the inorganic salts, 13.3 g. of a crude product was obtained. This was distilled three times, each time a middle fraction being removed, to give a purified fraction of 5 g. (0.029 mole; 29% yield; 16% current efficiency) of the ketone (XXXIX), b.p. 98 - 100°/23 mm., n_D^{27} 1.4400. The IR (thin film) and NMR spectra were identical to those of the ketone prepared as in Section 2(ii).

4. Preparation of 2,5-Dimethoxy-2(α-Hydroxyethyl)-Dihydrofuran (XLIV)

(i) Electrochemical Methoxylation of 2-(α-Hydroxyethyl)-Furan (XLIII)

A solution of 6.0 g. (0.16 mole) of sodium borohydride in 25 ml. of water was added dropwise over a period of one hr. to a magnetically stirred solution of 46 g. (0.42 mole) of 2-acetylfuran (XXVIII) in 50 ml. of methanol at 25°. Stirring was continued for one hr. and then glacial acetic acid was added carefully until gas evolution ceased. The solution was evaporated in vacuo and 100 ml. of water added to the residue. This solution was extracted with 3 x 50 ml. chloroform and the combined extracts dried over anhydrous magnesium sulfate, filtered, and evaporated in vacuo to leave 39.0 g. (0.35 mole; 83% yield) of the furanol (XLIII), n_D^{27} 1.4740 (reported (80), n_D^{25} 1.4735). It was not purified further.

The furanol (XLIII) (14.0 g., 0.12 mole) in 150 ml. of methanol containing 1 g. of potassium hydroxide was electrolyzed at -8° using Method A at 1.9 amp. and 7 to 12 volt for 4.5 hr. Purification of the reaction mixture yielded 8.4 g. (0.046 mole; 38% yield; 29% current efficiency) of (XLIV), b.p. 82 - 90°/8 mm., n_D^{27} 1.4557 (reported (81), b.p. 104 - 107°/10 - 11 mm., n_D^{25} 1.4540).

(ii) Reduction of the Vargha Ketone

A solution of 7.0 g. (0.025 mole) of the oxime tosylate (XXXII) in 35 ml. of 95% methanol was stirred for 5 days at room temperature, after which time 100 ml. of dry ether was added to precipitate ammonium p-toluenesulfonate which was then filtered off. The filtrate was evaporated and the residual oil dissolved in 50 ml. of methanol was treated, while stirring, with 0.4 g. (0.01 mole) of sodium borohydride added portionwise over a period of 5 min. The solution was stirred for an additional hr., then it was evaporated under reduced pressure at 35°, and 25 ml. of saturated aqueous sodium chloride solution added to the residue. The mixture was extracted with 3 x 50 ml. of ether, dried over anhydrous magnesium sulfate, and evaporated to leave 3.0 g. of an oil which on distillation afforded a middle fraction consisting of 2.7 g. (0.015 mole; 60% yield) of 2,5-dimethoxy-2(α-hydroxyethyl)-dihydrofuran (XLIV), b.p. 87 - 92°/8mm., n_D^{27} 1.4535. The IR and NMR spectra of this material and that of the dihydrofuranol (XLIV) prepared as described in Section 4(i) were identical.

5. Decomposition of p-Toluenesulfonyl 2-Acetofuran Oxime (XXXII)

In a dry 2.5 x 15 cm. test-tube was placed 2.5 g. of the oxime tosylate (XXXII). The open test-tube was heated at 75° in an oil bath behind a shield of safety glass.

Within a few minutes an explosive decomposition occurred with evolution of black smoke. Examination of the test-tube, which had cracked in several places showed that much carbonisation had occurred.

The thermal decomposition of the oxime tosylate (XXXII) was repeated using 2 g. of material dissolved in 50 ml. of ethylene glycol dimethyl ether (pre-purified by distillation under a dry nitrogen atmosphere from lithium aluminum hydride). The solution was heated gently under reflux and within 15 min. it had turned black and contained much carbonaceous material in suspension. No further examination was made of this unpromising reaction mixture.

EXPERIMENTAL . PART II

1. 3,3,6,6-Tetramethoxy-1,4-Cyclohexadiene (XLVI) From 1,4-Dimethoxybenzene (XLV)

(i) Small Scale Preparation

Method B was used in the electrolysis of 13.8 g. (0.100 mole) of 1,4-dimethoxybenzene (XLV) at 0°(2.0 amp., 3.6 - 3.8 volt, 3 hr.). Evaporation left 16 g. of an oily solid which after crystallization from 50 ml. petroleum ether (40 - 60) afforded 15 g. (0.075 mole; 75% yield; 66% current efficiency) of 3,3,6,6-tetramethoxy-1,4-cyclohexadiene (XLVI) as large colourless crystals, m.p. 40 - 41°. Sublimation of this solid at 35°/0.1 mm. raised the m.p.

to 42.0 - 42.5°. The compound was readily soluble in water.

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 59.98%; H, 8.05%; MW, 200.

Found: C, 60.18%; H, 7.89%; MW, 217.

The IR spectrum (nujol mull) had characteristic peaks at 1645(w)*, 1110(s), 1070(s), 1020(s), 975(s), 960(s) cm^{-1}. The NMR spectrum (Appendix B) showed only two peaks at 6.75 τ for methoxy and 4.03 τ for olefinic hydrogens. The areas under the two peaks were in the ratio of 3:1 (calculated 3:1).

(ii) Large Scale Preparation

Repetition of the above electrolysis was carried out on a larger scale using 69.0 g. (0.500 mole) of 1,4-dimethoxybenzene (XLV) in 200 ml. methanol containing 2 g. potassium hydroxide. The 1,4-dimethoxybenzene was added in 5 - 10 g. portions over a period of 2 hr. The temperature of the solution was maintained at 25 - 40°, the current at 5.0 amp. and the voltage between 7 to 8 volt for 24 hr. The residue, on application of Method B, smelled strongly of formaldehyde and afforded 88 g. (0.44 mole; 88% yield; 19% current efficiency) of the quinone diketal (XLVI) after crystallization from 200 ml. of petroleum ether (40 - 60) (m.p. 39 - 41°).

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* Relative peak intensities for IR spectra are designated as follows: weak, (w); medium (m); strong (s).

2. Reactions of 3,3,6,6-Tetramethoxy-1,4-Cyclohexadiene (XLVI)

(i) Acid Hydrolysis to p-Benzoquinone (XLVII)

To 1.00 g. (0.00500 mole) of the quinone diketal (XLVI) dissolved in 15 ml. of water was added 5 ml. of 10% hydrochloric acid. After 5 min. the yellow solid was filtered and sublimed at 60°/0.01 mm. to give 0.535 g. (0.00495 mole; 99% yield) of p-benzoquinone (XLVII), m.p. 113 - 114°(sealed capillary tube). A mixed m.p. of this solid with an authentic sample of p-benzoquinone was not depressed and the IR spectra of the two samples (nujol mull) were identical.

(ii) Reaction Catalyzed by Boron Trifluoride in Dilute Benzene Solution

To a solution of 5.0 g. (0.025 mole) of the quinone diketal (XLVI) in 50 ml. of benzene (dried over calcium hydride) was added one drop of boron trifluoride etherate. An exothermic reaction commenced immediately accompanied by a progressive colour change from red to dark brown. After leaving the reaction mixture 24 hr. at room temperature the benzene was evaporated, 25 ml. of water was added and the mixture extracted with 3 x 50 ml. portions of ether. The combined ether extracts were dried over anhydrous magnesium sulfate, filtered, and the ether evaporated in vacuo. To the residue was added 50 ml. of petroleum ether

(40 - 60), and after leaving the mixture for 24 hr., 1.0 g. of a sticky solid had deposited and was collected. This solid was recrystallized from 15 ml. of ethanol-water (1:1) after decolourization with Darco to give 0.46 g. (0.0015 mole; 12% yield) of the pentamethoxybiphenyl (XLIX), m.p. 108 - 112°. Sublimation of this solid at 100°/0.1 mm. raised the m.p. to 112.0 - 113.5°.

Anal. Calcd. for $C_{17}H_{20}O_5$: C, 67.09%; H, 6.62%; MW, 304.

Found: C, 66.34%; H, 6.35%; MW, 347.

The IR spectrum (chloroform) showed characteristic absorption at 3050(m), 2980(m), 2880(w), 1615(m), 1590(m), 1520(s), 1050(s), 1035(s) $cm.^{-1}$ The NMR spectrum (Appendix B) showed relative areas of methoxy to olefinic hydrogens of 3:1 (calculated 3:1).

Evaporation of the petroleum ether mother liquor solution left an oil which on distillation at 115 - 120°/10 mm. yielded 3.4 g. (0.0202 mole; 81% yield) of 1,2,4-trimethoxybenzene (XLVIII), n_D^{27} 1.5273. The NMR and IR spectra of this liquid were identical with an authentic sample of 1,2,4-trimethoxybenzene.

(iii) Reaction Catalyzed by Boron Trifluoride in a Concentrated Benzene Solution

The reaction described above in Section 2(ii) was repeated using 5.0 g. (0.025 mole) of quinone diketal (XLVI) but only 25 ml. of benzene. After working-up the reaction mixture, 1.4 g. (0.003 mole; 19% yield) of the pentamethoxybiphenyl (XLIX) and 1.5 g. (0.009 mole; 36% yield) of 1,2,4-trimethoxybenzene (XLVIII) were obtained.

(iv) Reaction Catalyzed by Boron Trifluoride in 1,2,4-Trimethoxybenzene (XLVIII) as the Solvent

The reaction described above in Section 2(ii) was repeated using 10.0 g. (0.050 mole) of quinone diketal (XLVI) in a solution of 6.0 g. (0.036 mole) of 1,2,4-trimethoxybenzene (XLVIII) and 20 ml. of benzene. Purification of the reaction mixture yielded 4.5 g. (0.015 mole; 60% yield) of the pentamethoxybiphenyl (XLIX) and 8.7 g. (0.052 mole; 32% yield) of 1,2,4-trimethoxybenzene (XLVIII).

3. 3,3,6,6-Tetramethoxy-1,4-Cyclohexadiene (XLVI) from Anisole (LI)

Method A was used in the electrolysis of 21.6 g. (0.200 mole) of anisole (LI) at -10°. After 3.5 hr. using 3.0 amp. and 6.5 - 7.0 volt, distillation of the residue yielded no detectable reaction product, 95% of the starting material being recovered.

The reaction was repeated with 21.6 g. (0.200 mole) of anisole (LI) electrolyzed at 18° for 68 hr. using 5.0 amp. and 8.6 to 10.3 volt. Distillation of the crude electrolysis product (26 g.) gave 6.9 g. (0.0345 mole; 17% yield) of the quinone diketal (XLVI), b.p. 95 - 100°/1.25 mm., n_D^{27} 1.46368 which crystallized overnight, m.p. 41 - 42°. The mixed m.p. with a sample of quinone diketal (XLVI) prepared from the electrolysis of 1,4-dimethoxybenzene (XLV) was not depressed and their IR spectra (nujol mulls) were identical. The residue of the distillation consisted of a non-volatile tarry oil.

4. 2,3,3,6,6-Pentamethoxy-1,4-Cyclohexadiene (LVII)

(i) From 1,3-Dimethoxybenzene (LVI)

Method B was applied to 13.8 g. (0.100 mole) of 1,3-dimethoxybenzene (LVI) at 0° using 4.5 amp. at 7.5 - 7.9 volt for 10 hr. The crude material (21.7 g.) was separated into 3 fractions by distillation: 1.5 g. of a fore-run, b.p. 95 - 120°/2.0 mm.; 14.0 g. (0.061 mole; 61% yield) of 2,3,3,6,6-pentamethoxy-1,4-cyclohexadiene (LVII), b.p. 115 - 120°/1.5 mm., n_D^{27} 1.4767; a residue of 5.6 g. which partially crystallized.

The centre fraction was redistilled and a heart-cut with b.p. 118°/1.5 mm. was collected for analysis.

Anal. Calcd. for $C_{11}H_{18}O_5$: C, 57.38%; H, 7.88%; MW, 230.

Found: C, 56.84%; H, 7.89%; MW, 256.

The IR spectrum (thin film) shows characteristic peaks at 2980(m), 2850(w), 1680(w), 1650(m), 1085(s) cm.$^{-1}$ The NMR spectrum (Appendix B) exhibited relative areas of methoxy to olefinic hydrogens of 5:1 (calculated 5:1).

From the distillation residue, a heart-cut was collected of 3.7 g. (0.012 mole; 12% yield), b.p. 140 - 150°/2.5 mm., n_D^{27} 1.4597, and is tentatively assigned the structure 3,3,4,4,5,5,6,6-octamethoxycyclohexene (LVIII).

Anal. Calcd.
for $C_{14}H_{26}O_8$: C, 52.16%; H, 8.13%; OCH_3, 77.02%; MW, 322.

Found: C, 52.50%; H, 7.87%; OCH_3, 64.40%; MW, 331.

Duplicate: C, 52.22%; H, 7.69%.

The IR spectrum (thin film) had characteristic absorptions at 1650(w), 1190(m), 1150(s), 1080(s) cm.$^{-1}$ The NMR spectrum of this material consisted of a broad absorption band centered at 6.75 τ (methoxy hydrogens) with only very weak absorption in the 5.0 to 2.0 τ region (olefinic hydrogens). Acid hydrolysis (10% hydrochloric acid) of this material (2.0 g. in 25 ml. of acid) deposited a tarry substance which was not examined further.

The fore-run of 1.5 g. when subjected to VPC analysis (using a 90 cm. column packed with 0.2% apiezon on glass beads and maintained at 120° and 10 lb.in.$^{-2}$ argon pressure) exhibited two peaks which were found to consist of about 10% of 1,2,4-trimethoxybenzene (XLVIII) and 90% of the diketal (LVII) with retention times of 1.9 and 3.9 min. respectively. No evidence for the presence of a peak corresponding to 1,3-dimethoxybenzene (LVI) was found (a sample of 1,3-dimethoxybenzene injected into the machine under the above conditions had a retention time of 0.5 min.).

(ii) From 1,2,4-Trimethoxybenzene (XLVIII)

A solution of 9.2 g. (0.050 mole) of 1,2,4-trimethoxybenzene* (XLVIII) and 2 g. potassium hydroxide in 250 ml. methanol was electrolysed at 10° using 4.0 amp. at 6.0 - 6.6 volt for 2.5 hr. Using Method B, 16.0 g. of crude material was isolated, having a strong odour of formaldehyde. The crude material was distilled to give the following fractions: a fore-run of 1.1 g., b.p. up to 110°/0.6 mm., followed by 10.4 g. (0.045 mole; 90% yield; 40% current efficiency) of 2,3,3,6,6-pentamethoxy-1,4-cyclohexadiene (LVII), n_D^{27} 1.4731 (identical as ascertained by NMR and IR analysis with a sample prepared as described in Section 4(i)). A tarry resi-

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* Prepared by the method of T.R. Govindachari et al (82).

due weighing 0.9 g. was discarded.

5. Electrochemical Methoxylation of 2,3,3,6,6-Pentamethoxy-1,4-Cyclohexadiene (LVII)

Method B was employed in the electrolysis of 23.0 g. (0.100 mole) of the methoxy-p-benzoquinone diketal (LVII) at 20° using 4.0 amp. at 9.5 - 11.2 volt for 42 hr. The crude material thus obtained weighed 30 g. and smelled strongly of formaldehyde. Distillation of this oil gave the following fractions: 4.2 g. of an oil, b.p. 70 - 95°/0.25 mm.; 18.1 g. (0.056 mole; 56% yield) of the polymethoxylated oil (LVIII), b.p. 110 - 120°/0.6 mm., n_D^{27} 1.4544; a tarry residue. The middle fraction was identified by NMR and IR analysis as the same oil already obtained from the electrolysis of 1,3-dimethoxybenzene (LVI).

6. The Mechanism of Electrochemical Methoxylation of 1,3-Dimethoxybenzene (LVI) as Studied with Carbon-14

(a) Preparation of Methyl-C^{14}-1,3-Dimethoxybenzene

The directions for the preparation of diazomethane were essentially those of Th.J. De Boer (83). A solution of 130 ml. of diethyl ether containing 21.5 g. (0.10 mole) of N-methyl-N-nitroso-p-toluenesulfonamide (Aldrich,"Diazald") and 0.0055 g. (0.000030 mole) of N-C-14-methyl-N-nitroso-p-toluenesulfonamide (New England Nuclear Corp., "Diazal-C^{14}")

having a specific radioactivity of 0.10 millicuries, was added dropwise by means of a dropping funnel to a solution of 5 g. of potassium hydroxide in 25 ml. of ethanol (95%) and 8 ml. of water in a 100 ml. distilling flask. This flask, which was fitted with a condenser set downward for distillation was heated at 65° on a water bath. The condenser was connected to two 250 ml. receiving flasks in series which were cooled to 0°. The second of these contained a solution of 3.3 g. (0.030 mole) of resorcinol (Eastman Reagent Grade) in 30 ml. of ether.

After all the diazomethane had co-distilled with ether into the first receiver, the cooling bath was replaced by a water-bath maintained at 50° and the diazomethane collected in the second receiver (cooled to 0°). The latter flask was disconnected from the apparatus and was fitted with a one-hole rubber stopper in which was inserted a glass-tube (30 cm. in length) drawn off into a fine capillary. At the end of one week, during which time the resorcinol solution was kept in the dark at 25°, a drop of boron trifluoride etherate was added along with 11 g. of pure 1,3-dimethoxybenzene (Eastman Reagent Grade). The ether solvent was removed by evaporation at 35°/20 - 30 mm. and the residue was distilled to give a heart-cut of 13.5 g. of liquid, b.p. 94 - 101°/ 13 mm. This fraction was allowed to stand over 3 g. potassium hydroxide pellets for 6 hr., after which time it was filtered and redistilled to give 12.7 g. (0.092 mole) of the pure radioactive 1,3-dimethoxybenzene. The IR spectrum (thin film) of this material was identical to that of an authentic sample of 1,3-dimethoxybenzene. The radioactivity measured by the scintillation technique of the 1,3-dimethoxybenzene in toluene solution (84) was found to be 5.59×10^8 counts $min.^{-1}$ $mole^{-1}$ (Nuclear Chicago Liquid Scintillation Counter).

(b) Electrochemical Methoxylation of Methyl-C^{14}-1,3-Dimethoxybenzene

Electrolysis following Method B was applied to 10.5 g. (0.076 mole) of the radioactive 1,3-dimethoxybenzene at 25° using 4.0 amp. at 5.8 - 5.9 volt for 5.5 hr. Distillation of the residue at 92 - 94°/0.2 mm. gave 13.1 g. (0.057 mole; 75% yield; 13.5% current efficiency) of 2,3,3,6,6-pentamethoxy-1,4-cyclohexadiene (LVII), n_D^{27} 1.4775. The residue (2.5 g.) of the distillation was identified (IR spectrum) as the already known polymethoxy oil (LVIII). The pentamethoxy compound (LVII) was redistilled to give a heart-cut, b.p. 103°/0.4 mm., n_D^{27} 1.4765. The radioactivity of this fraction (measured under the same conditions as for the sample of starting material) was found to be 5.54×10^8 counts $min.^{-1}$ $mole.^{-1}$

7. Hydrolysis of 2,3,3,6,6-Pentamethoxy-1,4-Cyclohexadiene (LVII)

A sample of 5.0 g. (0.022 mole) of the methoxy-p-quinone diketal (LVII) was dissolved in 100 ml. of water and 5 ml. of 5% aqueous hydrochloric acid was added. A deep yellow colour developed immediately, followed by a progressive deepening to a reddish brown. After 48 hr., the mixture was filtered and the blue precipitate collected and washed thoroughly with 100 ml. water and then with some ethanol; it was dried in air to yield 5.8 g. (0.021 mole; 95% yield) of the intramolecular quinhydrone (LX), m.p. 230 - 232°. A small amount of this solid was sublimed at 180°/0.01 mm. to give blue crystals, m.p. 235°. A mixed m.p. of this solid with an authentic sample of the quinhydrone (LX) (prepared according to I.S. Ioffe and A.F. Sukhina (65) by treatment of methoxy-p-benzoquinone* (LIX) in dilute hydrochloric acid solution) was not depressed; the IR spectra (nujol mulls) were superimposable.

Anal. Calcd. for $C_{14}H_{12}O_6$: C, 60.87%; H, 4.38%.

Found: C, 60.75%; H, 4.28%.

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* Vanillin was converted to methoxyhydroquinone by the method of C. de Corral (85) followed by oxidation to methoxy-p-benzoquinone (LIX) according to E. Adler and R. Magnusson (86).

8. Electrochemical Methoxylation of 1,2-Dimethoxybenzene (LXI)

Electrolysis of a solution of 69 g. (0.50 mole) of 1,2-dimethoxybenzene (LXI) in the presence of 5 g. of potassium hydroxide in 750 ml. of methanol was carried out at 10° in the 1000 ml. cell. Method B was applied (4.0 amp. with 7.3 - 8.6 volt for 22.5 hr.). The crude residue weighed 102 g. (methoxy determination of crude product: 51.65%). This mixture was fractionally distilled using a Todd Column apparatus (glass helices). The results of this distillation are given in Table III.

Examination after distillation of the traps inserted in the vacuum line revealed that 14 g. (0.44 mole) of methanol, b.p. 66°/755 mm., n_D^{27} 1.3293 had been eliminated during the process. The IR spectrum (thin film) was identical to that of a pure sample of methanol.

(i) 5,5,6,6-Tetramethoxy-1,3-Cyclohexadiene (LXII)

Fractions 2 and 3 (Table III) were combined and refractionated using the Todd Column to give 12.0 g. (0.060 mole; 12% yield) of 5,5,6,6-tetramethoxy-1,3-cyclohexadiene (LXII), n_D^{27} 1.4763.

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 59.98%; H, 8.05%.

Found: C, 59.77%; H, 7.85%.

Table III Distillation of the Electrolysis Products of 1,2-Dimethoxybenzene (LXI)

Fraction	Boiling Point at 2.5 mm.	n_D^{27}	Weight g.
1	up to 63	-	0.5
2	81 - 84	1.4775	14.3
3	84 - 87	1.4795	2.0
4	93	1.4903	5.0
5	93 - 98	1.5100	1.3
6	98	1.5121	11.7
7	98 - 111	-	0.6
8	111	1.4873	2.5
9	111 - 114	1.5033	3.3
10	114 - 118	-	21.5
		Total:	62.7 g.
11	Tarry residue		

The UV spectrum exhibited two peaks with λ^{EtOH}_{max} 235 mμ., $\varepsilon = 3100$ and λ^{EtOH}_{max} 265 mμ., $\varepsilon = 2500$. A drop of 5% aqueous hydrochloric acid completely altered the UV spectrum to give two peaks at λ^{EtOH}_{max} 227 mμ., $\varepsilon = 7600$ and λ^{EtOH}_{max} 288 mμ., $\varepsilon = 3100$. The IR spectrum (thin film) exhibited the following characteristic peaks: 1650(w), 1600(m), 1150(s), 1110(s), 1065(s), 1050(s), 1015(m), 935(s) cm^{-1}. The NMR spectrum (Appendix B) showed peaks for methoxy and olefinic hydrogen absorption, the areas under which were in the ratio of 3:1 (calculated 3:1).

The o-quinone diketal (LXII) (0.69 g., 0.0035 mole) was treated with 1.0 g. of zinc dust in 25 ml. of 1% aqueous hydrochloric acid with shaking until the mixture was colourless. The mixture was filtered and the filtrate extracted with 5 x 10 ml. of chloroform. The combined chloroform extracts were dried over anhydrous magnesium sulfate, filtered, and the solvent evaporated off in vacuo, leaving a small amount of a yellowish oil. Examination of this oil by VPC (apiezon on glass beads at 120° and 4 lbs. $in.^{-2}$ argon pressure) showed three peaks with retention times and relative areas as follows: 5.2 min., 25%; 7.3 min., 10%; 13.4 min., 65%. Pyrocatechol under the same conditions gave a peak with a retention time of 5.2 min.

(ii) 1,2,4-Trimethoxybenzene (XLVIII)

Fractions 5 and 6 (Table III) were combined and redistilled. A heart-cut, b.p. 105°/2.0 mm., n_D^{27} 1.5258 was collected, affording 7.3 g. (0.044 mole; 9% yield) of 1,2,4-trimethoxybenzene (XLVIII). This material was identical (IR and NMR spectra) with an authentic sample of 1,2,4-trimethoxybenzene prepared by the method of T.R. Govindachari et al (82).

(iii) Hexamethyl *cis*, *cis*-Orthomuconate (LXIII) and *cis*, *cis*-Dimethyl Muconate (LXVIII)

Fraction 10, which had partially crystallized on standing, was filtered and the sticky solid (3.0 g.) thus obtained was twice recrystallized from 10 ml. of 95% ethanol to give 2 g. (0.0076 mole; 1.5% yield) of hexamethyl *cis*, *cis*-orthomuconate* (LXIII), m.p. 97.5 - 99.5°.

Anal. Calcd. for $C_{12}H_{22}O_6$: C, 54.95%; H, 8.45%; MW, 262.

Found: C, 55.59%; H, 8.43%; MW, 192.

Duplicate Analysis: C, 54.88%; H, 8.56%.

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* On repetition of the electrolysis of 1,2-dimethoxybenzene (LXI) under the same conditions, the crude residue obtained by application of Method B (90 g.) was left in the refrigerator. Crystallization occurred after two days, and after one week, the crystals (7.0 g.) were filtered off and recrystallized from 20 ml. of methanol to give 5.9 g. (0.0225 mole; 4.5% yield) of the diorthoester (LXIII), m.p. 97 - 99°. The remainder of the crude reaction mixture was not worked up further.

The UV spectrum of this solid showed λ_{max}^{EtOH} 234 mμ., $\varepsilon = 10{,}200$. A drop of a 1% hydrochloric acid solution added to an ethanol solution of the product (LXIII) shifted the UV absorption peak to 261 mμ., $\varepsilon = 17{,}600$. The IR spectrum (chloroform) showed the following major bands: 3040(s), 2960(s), 2360(m), 1600(m), 1460(m), 1435(m), 1360(s), 1240(s), 1140(s), 1095(s), 1030(s), 985(s) $cm.^{-1}$ The NMR spectrum (Appendix B) showed relative areas of methoxy to olefinic hydrogens of 4.5:1 (calculated 4.5:1) with $J_{AB} = 11.2$, $J_{AB'} = -1.5$, $J_{AA'} = 11.0$, and $J_{BB'} = \pm 1.2$ c.p.s. These coupling constants are almost identical to those for *cis*, *cis*-dimethy$\overset{\leftrightarrow}{\text{l}}$muconate (87). A solution of 0.0630 g. (0.000240 mole) of the diorthoester (LXIII) in 20 ml. of methanol containing 0.038 g. of 10% of palladium on charcoal (Matheson, Coleman and Bell) was hydrogenated at atmospheric pressure. The uptake of hydrogen gas (8 hr.) corrected to S.T.P. was found to be 11 ml. (0.00049 mole) corresponding to 102% of the theoretical amount for 2 carbon-carbon double bonds in the product (LXIII).

Hydrolysis of the diorthoester (LXIII) was carried out by dissolving 1.0 g. (0.038 mole) of the solid in a solution of 30 ml. of methanol, 10 ml. of water, and 1 ml. of 10% aqueous hydrochloric acid. After allowing the mixture to stand for 0.5 hr. at 25°, the methanolic solution was concentrated in vacuo and the residual solid filtered and dried in air to give 0.55 g. (0.032 mole; 84% yield of *cis*, *cis*-

dimethyl muconate (LXVIII), m.p. 71 - 73°. Sublimation of this material raised the m.p. to 73.5 - 74.0°. A mixed m.p. of this solid with an authentic sample of *cis*, *cis*-dimethyl muconate prepared by the method of R.P. Linstead (70a) was not depressed, and the NMR spectra (Appendix B) of the two samples were identical. The IR spectra (nujol mulls) of the two samples were identical.

Anal. Calcd. for $C_8H_{10}O_4$: C, 56.46%; H, 5.92%.

Found: C, 56.06%; H, 5.83%.

(iv) 2,3,3,6,6-Pentamethoxy-1,4-Cyclohexadiene (LVII)

The filtrate from fraction 10 (Table III) of Section 7(ii) on redistillation was separated into four fractions: fraction 10A, 6.6 g., b.p. 99 - 101°/0.6 mm., n_D^{27} 1.5020; fraction 10B, 7.3 g., b.p. 105 - 110°/0.6 mm., n_D^{27} 1.4816; fraction 10C, 1.4 g., b.p. 110 - 112°/0.6 mm., n_D^{27} 1.4806; a non-volatile residue.

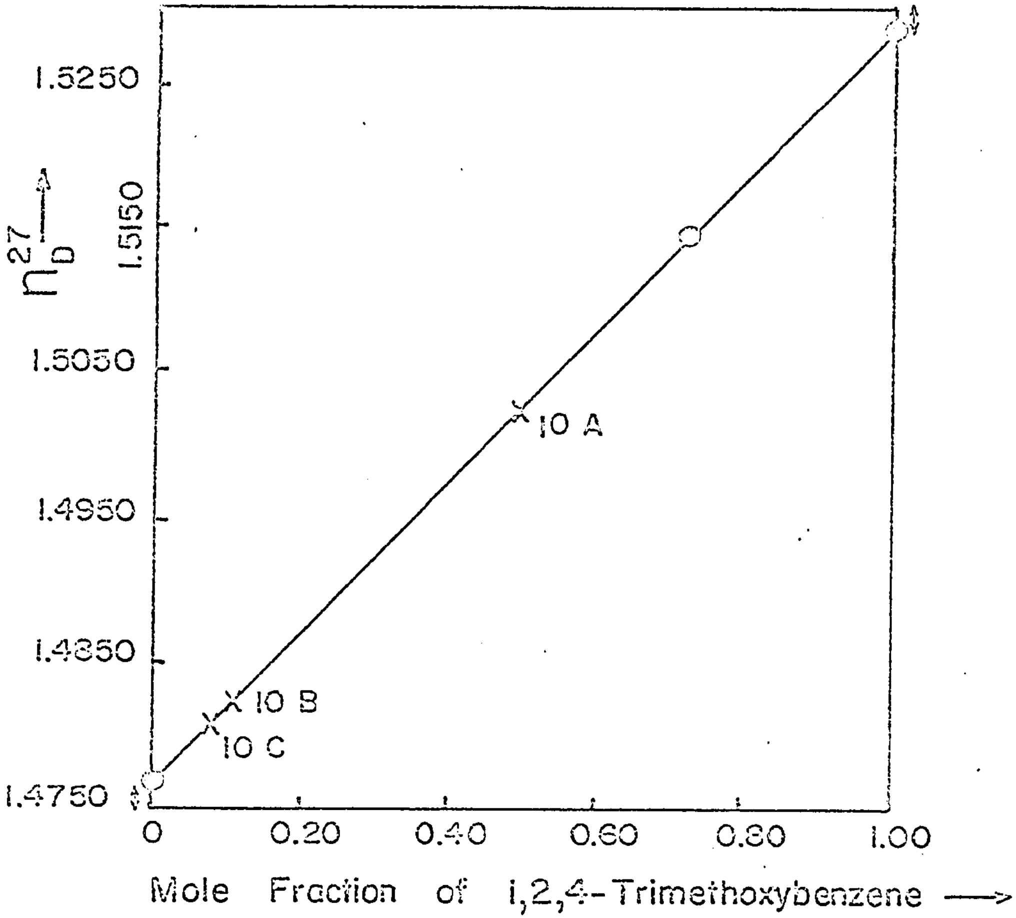
A few drops of fraction 10B were added to 25 ml. of 1% aqueous hydrochloric acid and the solution was allowed to stand for 24 hr. A blue solid was filtered off and dried in air; it had m.p. 230°. A mixed m.p. of this material with an authentic sample of the intramolecular quinhydrone (LX) was not depressed; the IR spectra (nujol) were also identical.

Fractions 10A, 10B, and 10C when subjected to VPC analysis (Perkin-Elmer Fractometer using a 90 cm. column packed with 0.2% apiezon on glass beads and operated at 121° and 10 lb. in.$^{-2}$ argon pressure) were found to consist of 1,2,4-trimethoxybenzene (XLVIII) (retention time 1.9 min.) and the methoxy-p-benzoquinone diketal (LVII) (retention time 3.5 min.). On the basis of this knowledge a standard curve (Figure I) relating refractive index to the content (as the mole fraction) of 1,2,4-trimethoxybenzene (XLVIII) in the sample was constructed. By interpolation (see Figure I) the yield of 1,2,4-trimethoxybenzene (XLVIII) was found to be 5.2 g. (0.031 mole; 6% yield). In the same way the yield of 2,3,3,6,6-pentamethoxy-1,4-cyclohexadiene (LVII) was found to be 10.1 g. (0.044 mole; 9% yield).

9. Electrochemical Methoxylation of 5,5,6,6-Tetramethoxy-1,3-Cyclohexadiene (LXII)

Method B was applied in the electrochemical methoxylation of 5.2 g. (0.026 mole) of the o-benzoquinone diketal (LXII) at 20° for 6 hr. using 4.0 amp. at 4.9 to 7.4 volt. The crude gummy solid thus obtained was crystallised from 25 ml. of 95% ethanol to yield 5.3 g. (0.020 mole; 77% yield; 4.5% current efficiency) of hexamethyl cis, cis-orthomuconate (LXIII), m.p. 96 - 98°. A mixed m.p. of this solid with a sample prepared as in Section 8(iii) was not depressed and

Figure I. Refractive Indices of Solutions of 1,2,4-Trimethoxybenzene and 2,3,3,6,6-Pentamethoxy-1,4-Cyclohexadiene.



the IR spectra (chloroform solution) of the two samples were identical.

10. Electrochemical Methoxylation of Benzene and p-Xylene

Reagent grade benzene and p-xylene (Eastman) were each electrolysed (0.1 mole scale) using Method A. Even after a large excess of current had been passed (about ten times the theoretical amount of current) no methoxylated material could be identified after distillation, only starting material being recovered. In the case of benzene, however, a minute amount (0.05 g.) of a solid was deposited on the anode. This solid was insoluble in methanol, benzene, chloroform, and dimethylformamide. It was not examined further.

11. Electrochemical Methoxylation of 9,10-Dimethoxyanthracene (LIII)

Using Method A, 11.9 g. (0.050 mole) of 9,10-dimethoxyanthracene (LIII), (prepared by the method of V. Meyer (88) from anthraquinone) was electrolysed at 20° with 4.0 amp. at 6.4 - 6.7 volt for 3.75 hr. At no time during the reaction was the reaction mixture homogeneous. Instead of adding ether to the residue after evaporation of the methanol, 250 ml. of water was added and the resulting yellow solid was filtered off and dried in air (crude weight 12.6 g., m.p. 130 - 145°). This was crystallized from 50 ml. of benzene containing 1 g. Darco. A mixture of yellow plates and large colourless cubes separated from the solution. This mixture of crystals was mechanically separated to give 6 g. of cubic crystals, m.p. 145 - 155° and 5.3 g. of the plates, m.p. 157 - 174°. The cubic crystals were recrystallised from 20 ml. of benzene to give 4.8 g. (0.016 mole; 32% yield; 6% current efficiency) of the anthraquinone diketal (LIV), m.p. 159.5 - 161.0°.

Anal. Calcd. for $C_{18}H_{20}O_4$: C, 71.98%; H, 6.71%; OCH_3, 41.30%.
Found: C, 72.19%; H, 6.80%; OCH_3, 39.30%.

The IR spectrum (nujol mull) showed characteristic peaks at 1600(w), 1260(s), 1075(s), 1005(s), 930(s), 775(s), 755(m) cm.$^{-1}$ The NMR spectrum (Appendix B) showed relative areas of methoxy to olefinic hydrogens of 1.5:1 (calculated 1.5:1). The anthraquinone diketal (LIV) (0.194 g., 0.000645 mole) was dissolved in 5 ml. of hot 95% ethanol followed by the addition of two drops of 5% aqueous hydrochloric acid which caused instantaneous separation of pale yellow anthraquinone (LV) which was collected and dried in air; it weighed 0.130 g. (0.000625 mole; 97% yield), m.p. 284°. A mixed m.p. with an authentic sample of anthraquinone was not depressed, and the IR spectra (nujol mulls) of the two solids were identical.

Recrystallization of the yellow plates, m.p. 157 - 174°, from 20 ml. of 95% ethanol (after treatment with 0.5 g. of

Darco) gave 5.0 g. (0.021 mole; 42% yield) of recovered 9,10-dimethoxyanthracene (LIII), m.p. 202°. The mixed m.p. with an authentic sample of 9,10-dimethoxyanthracene was not depressed.

12. Preparation and Electrochemical Methoxylation of Benzodioxane (LXXIII) to 9,10-Dihydro-9,10-Dimethoxybenzodioxane (LXXIV)

Benzodioxane (LXXIII) was prepared* by gently boiling a mixture of 330 g. (3.0 mole) of pyrocatechol in 900 g. (4.8 mole) of 1,2-dibromoethane (in a 2 liter round bottom flask, fitted with a wide bore condenser). To this mixture was added 400 g. of potassium carbonate in small portions over a period of 6 hr. After an additional 6 hr. the heating was stopped and 500 ml. of water was added to the flask and the contents steam distilled until 3 liters of liquid had been collected. The organic layer of the steam distillate was separated and the aqueous layer extracted with 5 x 200 ml. of chloroform. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and evaporated to leave an oil which on distillation afforded 192 g. (1.4 mole; 47% yield) of benzodioxane (LXXIII), b.p. 102 - 106°/20 mm., n_D^{27} 1.5470 (reported (88), b.p. 103 - 105°/17 mm.). The NMR spectrum of (LXXIII) is given in Appendix B.

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* Compare this procedure with that of I.A. Dobrowsky (89).

A solution of 13.6 g. (0.100 mole) of benzodioxane (LXXIII) in methanol was electrolysed at 20° following Method B at 3.0 amp. and 7.5 to 8 volt for 5 hr. The crude electrolysis product (16 g.) had an IR spectrum which exhibited three characteristic bands at 1680(w), 1645(w) and 1580(w) cm.$^{-1}$ This crude material was twice distilled, a middle-fraction being collected each time, to give 6.1 g. (0.031 mole; 31% yield; 11% current efficiency) of 9,10-dihydro-9,10-dimethoxybenzodioxane (LXIV), b.p. 102 - 106°/ 1.5 mm., n_D^{26} 1.4990. The remainder of the reaction product consisted of an oil with b.p. 110 - 145°/ 1.5 mm. and was not examined further.

This o-quinone diketal (LXXIV) crystallized after standing for 1 day and was collected; m.p. 50 - 80°. Recrystallisation from water and then sublimation gave large colourless crystals, m.p. 88.5 - 89.5°.

Anal. Calcd. for $C_{10}H_{14}O_4$: C, 60.59%; H, 7.12%; OCH_3, 31.31%.

Found: C, 60.37%; H, 6.89%; OCH_3, 30.72%.

The UV spectrum exhibited two absorptions at λ_{max}^{EtOH} 225 mμ., $\varepsilon = 2900$ and λ_{max}^{EtOH} 265 mμ., $\varepsilon = 2800$. Upon addition of 1 drop of 5% aqueous hydrochloric acid to the ethanol solution, the UV spectrum was completely altered and now exhibited peaks at λ_{max}^{EtOH} 225 mμ., $\varepsilon = 2800$ and λ_{max}^{EtOH} 289 mμ., $\varepsilon = 5700$. The IR spectrum of (LXXIV) (chloroform) had the following characteristic peaks: 3050(m), 2960(m), 2880(w), 1580(w), 1395(m), 1190(m), 1160(s), 1120(m), 1100(s), 1060(s), 1040(s), 1030(s), 925(s), 885(m), 876(m) cm.$^{-1}$ The NMR spectrum (Appendix B) exhibited relative areas of methoxy to ethylenedioxy to olefinic hydrogens of 1.5:1:1 (calculated 1.5:1:1).

13. Hydrolysis of 9,10-Dihydro-9,10-Dimethoxybenzodioxane (LXIV) to Pyrocatechol (LXVII)

To a solution of 1.0 g. of the o-quinone diketal (LXIV) in 10 ml. of water was added 1 drop of 5% hydrochloric acid. The solution immediately turned deep red, changing rapidly to brown and soon deposited a tarry material.

The reaction was repeated using 0.250 g. (0.00125 mole) of the o-quinone diketal (LXIV) in 10 ml. of water. To this was added 1 g. of zinc dust and then 5 ml. of 5% hydrochloric acid. The mixture was shaken by hand for 5 min. to keep the zinc suspended and then filtered, and the zinc metal was washed with 15 ml. of water. The filtrate was extracted with 5 x 10 ml. of ether and the combined ether layers were dried over anhydrous magnesium sulfate, filtered, and the filtrate evaporated to give an oil which slowly solidified on standing. This solid was then sublimed at 70°/0.01 mm. to afford 0.100 g. (0.0944 mole; 75.5% yield) of pyrocatechol (LXVII), m.p. 104°. A mixed m.p. with an authentic sample of pyrocatechol was not depressed and the IR spectra (nujol mulls) were identical.

14. Coulombic Yield Determination in the Electrolysis of 1,4-Dimethoxybenzene (XLV)

A cell was set up consisting of two weighed copper electrodes (0.1 x 6 x 8 cm.^{3}) in a 500 ml. beaker containing 300 ml. of a copper sulfate solution (1 liter of aqueous solution contained 150 g. of copper sulfate pentahydrate, 50 g. of sulfuric acid and 50 g. of 95% ethanol). This copper coulometer was placed in series with the 300 ml. electrolysis cell which contained 13.8 g. (0.100 mole) of 1,4-dimethoxybenzene (XLV) in methanolic potassium hydroxide (see Section 1(i)). The electrolysis of the hydroquinone dimethyl ether (XLV) was carried out at 20° at 2.0 amp. and 3.0 - 3.1 volt for 1.90 hr. At the end of this time, the copper electrodes were rinsed carefully with water, then with 95% ethanol, and were dried in an oven at 100° and then weighed. The loss of metal from the anode was 4.709 g. (0.0741 g. atom) of copper, whereas the gain for the cathode was 4.708 g. (0.0741 g. atom) of copper.

The methanolic solution, on removal of salts using Method B, left 17.5 g. of organic material. The NMR spectrum showed peaks characteristic of the presence of the p-benzoquinone diketal (XLVI) and starting material (XLV); the areas under the peaks for the ketal methoxy hydrogens and aromatic methoxy hydrogens were in the ratio of 1.56:1.00, thus corresponding to a mixture of 43.8% of (XLVI) and 56.2%

of (XLV). Therefore the current efficiency of the electrochemical methoxylation of (XLV) is 59.3%.

EXPERIMENTAL . PART III

This section will describe a number of exploratory experiments in the field of organic electrochemistry. Most of these experiments have not been studied exhaustively due to lack of time; it is felt however that they can provide a useful basis for further work in this largely unexplored field. At least definitive evidence will be given as to whether a reaction has occurred or not on the electrode surface.

1. Electrochemical Methoxylation of 1,3-Cyclohexadiene (LXXVI)

(i) Applying About Twice the Theoretical Amount of Current

A solution of 20 g. (0.25 mole) of 1,3-cyclohexadiene* (LXXVI) in 150 ml. of methanol containing 2 g. of potassium hydroxide was electrolysed at -5° using Method A at 2.0 amp. and 6 to 7 volt for 9.5 hr. The residue (5.3 g.) was thrice distilled, each time with removal of a heart-cut which was redistilled; in this way, 2.0 g. (0.014 mole; 4% yield; 3%

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* 1,3- and 1,4-cyclohexadiene were purchased from the Farchem Chemical Co.

current efficiency) of a mixture of dimethoxycyclohexenes, ((LXXVII) and (LXXVIII)), b.p. 93 - 96°/55 mm., n_D^{30} 1.4547 was obtained.

Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57%; H, 9.93%; OCH_3, 43.64%.

Found: C, 66.57%; H, 9.63%; OCH_3, 38.73%.

VPC analysis of this oil (Perkin-Elmer Fractometer, using diisobutyl phthalate on firebrick in a 200 cm. column at 120° and 4 lb.in.$^{-2}$ argon pressure) showed three peaks with retention times and relative areas as follows: 45.6 min., 29%; 49.2 min., 33%; 52.0 min., 38%.

Hydrogenation at atmospheric pressure of 0.125 g. (0.000880 mole) of this mixture in 10 ml. of methanol using 0.0170 g. of 10% palladium on charcoal (Matheson, Coleman and Bell) led to an uptake of 19.5 ml. (0.000871 mole; 99% uptake for one carbon-carbon double bond per molecule) of hydrogen (corrected to S.T.P.).

The IR spectrum (thin film) showed the following peaks: 3050(w), 1650(w), 1185(m), 1095(s), 1015(m), 940(m), 735(m) cm.$^{-1}$ The NMR spectrum (Appendix B) exhibited relative areas of olefinic to all other hydrogens of 1:4 (calculated 1:4).

<u>(ii) With a Large Excess of Current</u>

A solution of 20 g. (0.25 mole) of 1,3-cyclohexadiene (LXXVI) in 250 ml. of methanol was electrolyzed at -15° at

4.0 amp. and 10 - 12 volt for 15 hr. The crude material (29 g.) isolated after application of Method B was distilled using a 10 cm. Vigreaux column to give five fractions: #1, 7.3 g., b.p. 68 - 85°/7 mm., n_D^{27} 1.4538; #2, 4.0 g., b.p. 85°/7 mm., n_D^{27} 1.4546; #3, 5.0 g., b.p. 106 - 130°/7mm., n_D^{27} 1.4596; #4, 1.8 g., b.p. 130 - 160°/7 mm., n_D^{27} 1.4843; #5, a tarry residue. Fractions #1 and #2 were combined and redistilled to give two new fractions: 3.8 g. (0.027 mole; 11% yield) of the dimethoxycyclohexene mixture, b.p. 68 - 75°/12 mm., n_D^{27} 1.4550; 3.9 g. (0.023 mole; 9% yield) of a trimethoxycyclohexene (tentative formulas: (LXXX) or (LXXXI)), b.p. 85 - 91°/12 mm., n_D^{27} 1.4563.

Anal. Calcd. for $C_9H_{16}O_3$: C, 62.76%; H, 9.36%.

Found: C, 62.50%; H, 9.23%.

The IR spectrum (liquid film) showed the following bands: 3050(w), 1650(w), 1185(m), 1110(s), 1050(s), 945(m), 920(m), 755(m) $cm.^{-1}$ The NMR spectrum (Appendix B) showed relative areas of olefinic to all other hydrogens of 1:7 (calculated 1:7).

2. Electrochemical Methoxylation of 1,4-Cyclohexadiene (LXXIX) and Isoprene

After passage of one theoretical equivalent of current (enough for the addition of two methoxyl groups) through a methanolic solution of 8.0 g. (0.10 mole) of 1,4-cyclohexadiene (LXXIX), the reaction mixture was carefully distilled using a Todd Column (glass helices) to give 90% of recovered 1,4-cyclohexadiene. Only a trace of a higher boiling residue was obtained.

The electrolysis of isoprene was attempted under similar conditions but had to be interrupted when the current dropped from 4 amp. to 0 amp. (12 volt) over a period of 3 hr. Examination of the anode showed that a rubbery coating had formed. This was insoluble in water and only very slightly soluble in chloroform.

3. Electrochemical Methoxylation of Guaiacol (LXXXII)

(i) Using Basic Conditions

A solution of 12.4 g. (0.100 mole) of guaiacol (LXXXII) in 200 ml. of methanol was electrolysed at 10^{0} in the presence of 2 g. of potassium hydroxide. Application of Method B in the work-up (3.0 amp. and 11 - 12 volt for 3 hr.) left a tarry black solid (15 g.) which was insoluble in ether. This product was not examined further.

(ii) Using Acidic Conditions. Preparation of the "Guaiacol Red Solid" (LXXXIII)

A solution of 24.8 g. (0.200 mole) of guaiacol (LXXXII) in 250 ml. of methanol containing 4.0 g. of concentrated sulfuric acid was electrolyzed at -3° at 1.5 amp. and 3 to 4.5 volt for 25 hr. The electrolysis solution acquired a gradually deepening red colour and a reddish solid separated out after about 10 hr. The methanolic mixture was then poured into 1 liter of water and the red solid was filtered off and dried in air to give 20 g. of crude product, m.p. 175 - 190°. This was recrystallized from 100 ml. of chloroform and then twice sublimed at 175°/0.01 mm. to afford 12.5 g. (0.046 mole; 46% yield) of the "Guaiacol Red Solid" (tentative structure (LXXXIII)), m.p. 201.5 - 203.0°.

Anal. Calcd. for $C_{15}H_{14}O_5$: C, 65.69%; H, 5.15%; MW, 274.

Found: C, 63.97%; H, 5.03%; MW, 309.

The IR spectrum (chloroform) had the following peaks: 3580(m), 3100(w), 2950(m), 2490(w), 1675(m), 1610(s), 1590(s), 1510(s), 1090(s), 1040(s) $cm.^{-1}$ The NMR spectrum (Appendix B) showed relative areas of methoxy to all other hydrogens of 1.3:1 (calculated 1.8:1).

To a solution of 0.7 g. (0.0025 mole) of the "Guaiacol Red Solid" in 2.5 ml. of pure acetic anhydride was added 0.5 g. of zinc dust and 0.1 g. of powdered anhydrous sodium acetate. The mixture was warmed gently until the red colour was discharged, whereupon the mixture was boiled for 5 min. Glacial acetic acid (2 ml.) was added, the mixture was boiled for an additional 10 min., then filtered, and the solids washed with

5 ml. of hot glacial acetic acid. Enough water was then added to the filtrate to produce a definite cloudiness, and after cooling a colourless solid precipitated out which was collected and dried in air. The solid (0.8 g.) was recrystallised from 10 ml. of 95% ethanol to give 0.6 g. (0.0014 mole; 54% yield) of a triacetoxytrimethoxybiphenyl (tentative structure (LXXXIV)), m.p. 144.0 - 145.0°.

Anal. Calcd. for $C_{21}H_{22}O_9$: C, 60.28%; H, 5.30%.

Found: C, 60.35%; H, 5.36%.

The IR spectrum (nujol mull) showed the following peaks: 1760(s), 1615(m), 1590(m), 1515(m), 1305(m), 1280(m), 1215(s), 1190(s), 1175(s), 1110(s), 1040(s) $cm.^{-1}$ The NMR spectrum (Appendix B) had relative areas of acetoxy to methoxy to aromatic hydrogens of 3:3:1 (calculated 3:3:1).

No attempts were made to substantiate the proposed structures.

4. Electrochemical Methoxylation of Naphthalene

A solution of 25.6 g. (0.200 mole) of naphthalene in 250 ml. of methanol containing 2 g. of potassium hydroxide was electrolyzed at 20° at 4.0 amp. and 7 - 8 volt for 6 hr. The resultant deep brown mixture was poured into a liter of water. A deep blue oil slowly collected on the surface of the liquid and after 6 hr. this oil was extracted with

10 x 100 ml. of hexane. The combined hexane extracts were dried over anhydrous magnesium sulfate, filtered, and the filtrate evaporated to give 15.9 g. of a deep blue oil. The blue colour of this liquid was not discharged even after 2 weeks of standing at room temperature, but when a little was shaken in hexane solution with 85% phosphoric acid the blue colour of the solution quickly turned to a pale brown. Upon distillation in vacuo, the blue colour was also discharged and a middle fraction weighing 6.8 g. and consisting of a colourless liquid, b.p. 150 - 160°/15 mm., n_D^{27} 1.5671 was collected. This fraction was redistilled to give a heart-cut of b.p. 111°/1.0 mm., n_D^{27} 1.5620.

Anal. Found: C, 74.51%; H, 7.13%.

The IR spectrum (thin film) showed the following peaks: 3080(w), 2960(m), 2840(m), 1630(w), 1595(m), 1515(w), 1460(s), 1385(s), 1270(s), 1235(s), 1190(m), 1100(s), 1070(s), 794(m), 766(s), 722(m) $cm.^{-1}$ The NMR spectrum showed relative areas of methoxy to olefinic hydrogens of 1.4:1.

The structure of these compounds remain to be determined.

EXPERIMENTAL . PART IV

Electrochemical Methoxylation of 1,4-Dimethoxybenzene (XLV) Using the Conditions of the Kolbe Reaction

A solution of 27.6 g. (0.200 mole) of 1,4-dimethoxybenzene (XLV) in 250 ml. of reagent grade glacial acetic acid containing 20.0 g. of anhydrous potassium acetate was electrolyzed at 12° at 1.5 amp. and 8 - 10 volt for 7.5 hr. The acetic acid was evaporated off at reduced pressure and to the cooled oily residue was added 300 ml. of anhydrous ether. A precipitate formed which was filtered off and washed with 100 ml. of dry ether. Evaporation of the filtrate left a gummy solid which was crystallized from 70 ml. of petroleum ether (40 - 60) - chloroform (1:1) to give 24 g. (0.12 mole; 62% yield; 62% current efficiency) of 1,4-dimethoxy-2-acetoxybenzene (LXXIV), m.p. 60 - 63°. Sublimation raised the m.p. to 66.0 - 66.5° (reported (90), m.p. 68°).

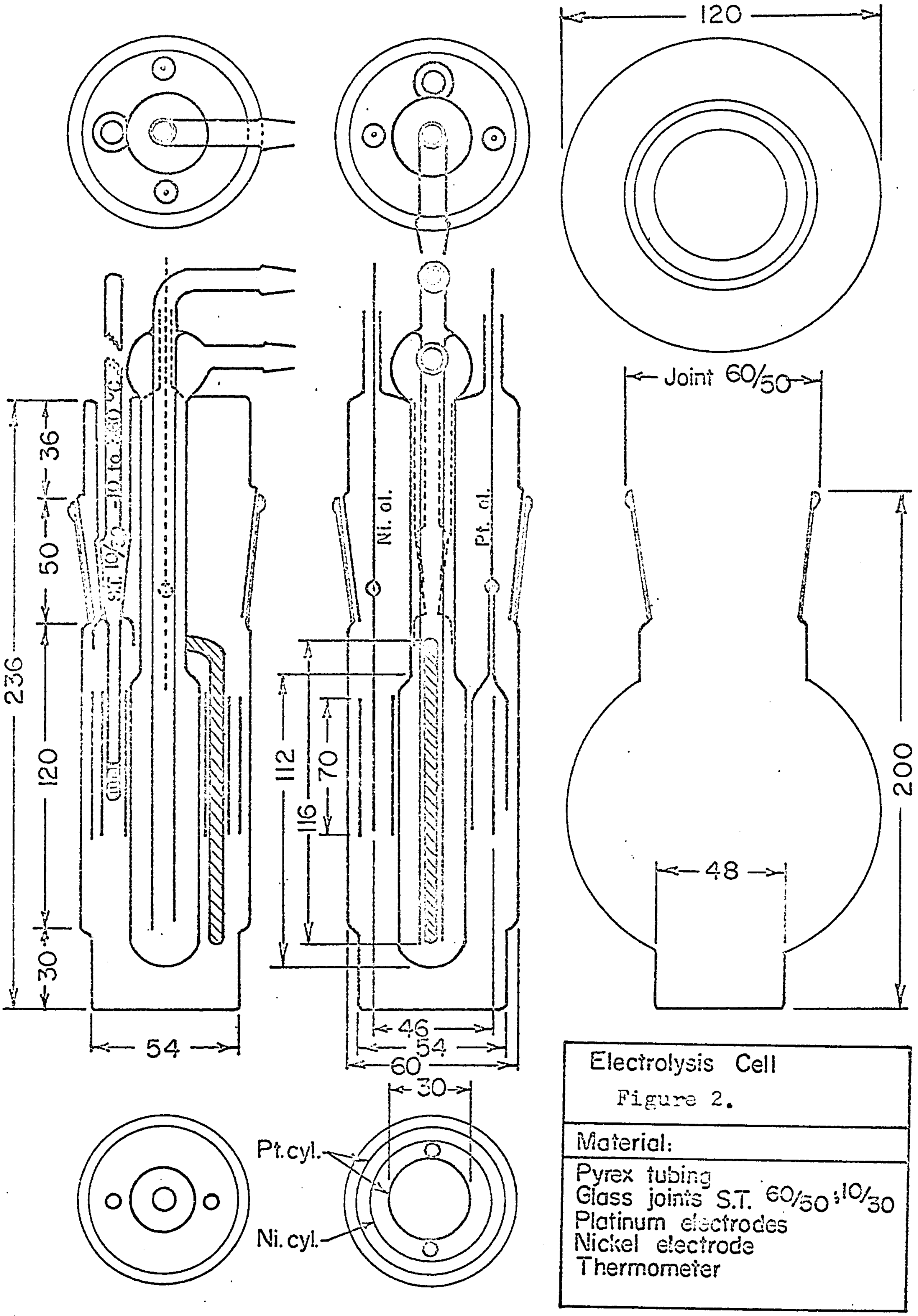
Anal. Calcd. for $C_{10}H_{12}O_4$: C, 61.21%; H, 6.17%.

Found: C, 60.94%; H, 6.06%.

The IR spectrum (nujol mull) had the following peaks: 1750(s), 1610(w), 1580(w), 1500(s), 1200(s), 1170(s), 1145(s), 1105(s), 1030(s), 1010(s) $cm.^{-1}$ The NMR spectrum (Appendix B) exhibited relative areas of acetoxy to methoxy to aromatic hydrogens of 1:2:1 (calculated 1:2:1).

APPENDIX A

THE ELECTROLYSIS APPARATUS
DIAGRAM AND PHOTOGRAPHS



Electrolysis Cell

Figure 2.

Material:

Pyrex tubing
Glass joints S.T. 60/50 ; 10/30
Platinum electrodes
Nickel electrode
Thermometer

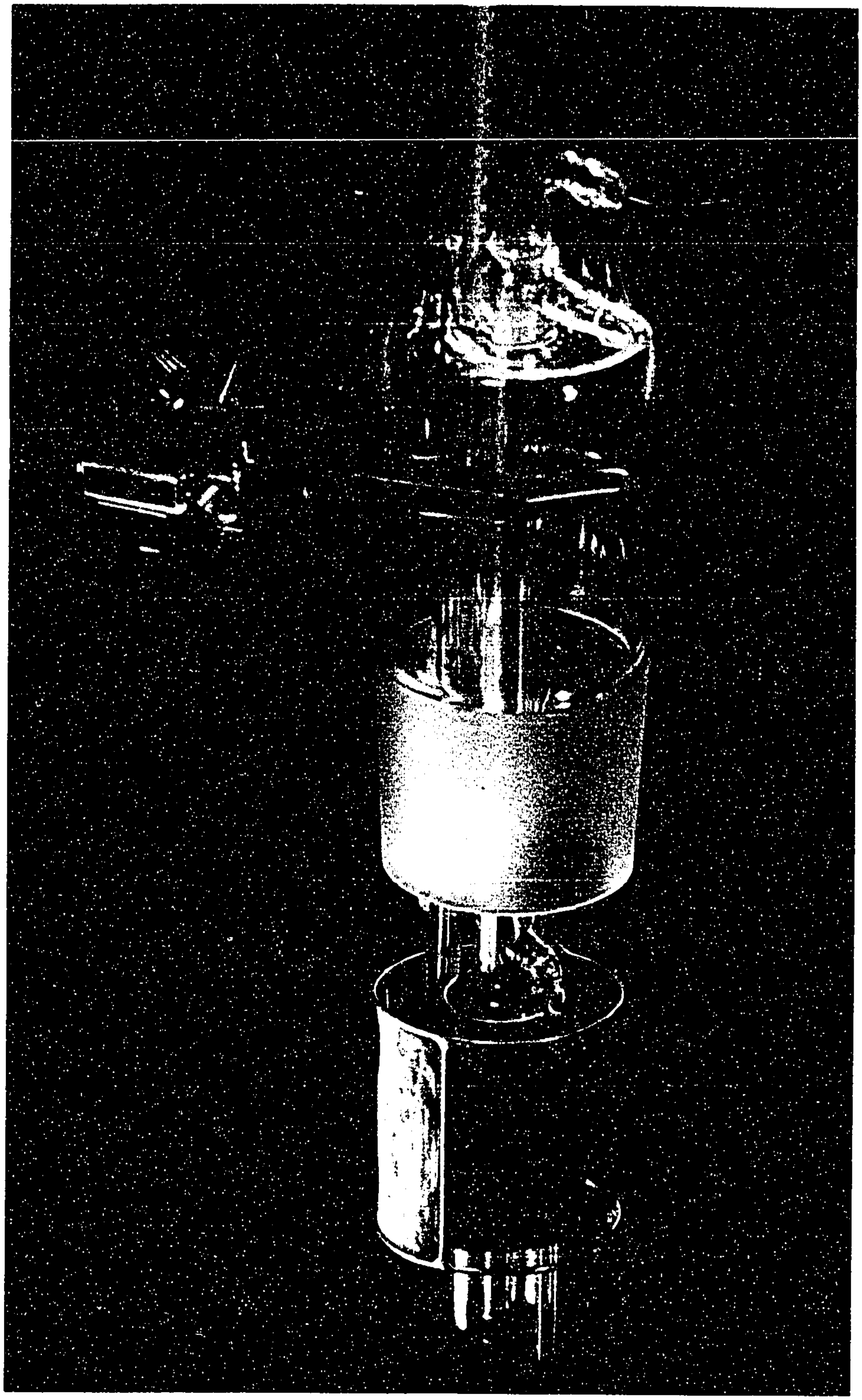


Figure 3. Photograph of Cell. Side View.

Figure 4. Photograph of Cell. Bottom View.

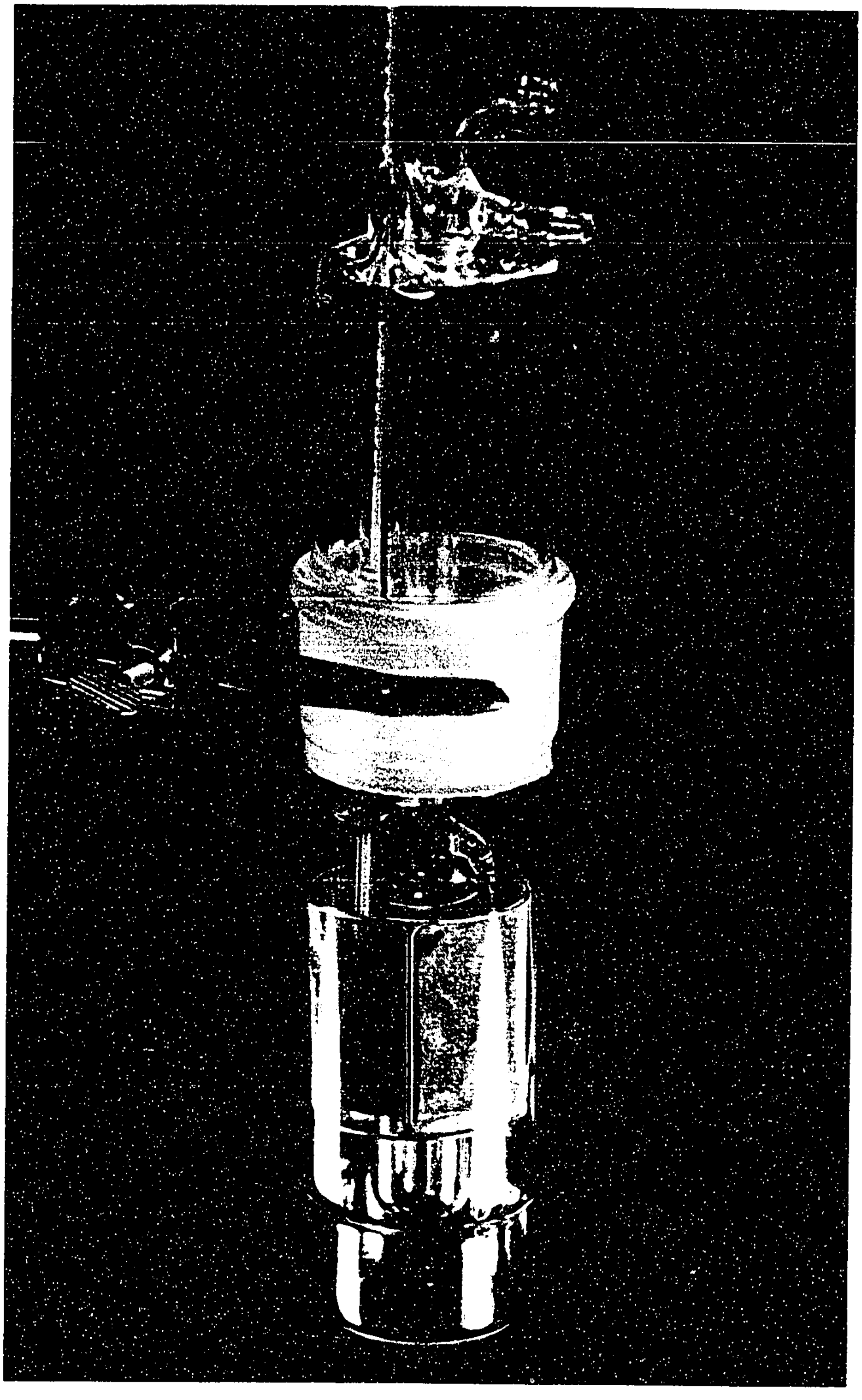


Figure 5. Photograph of Cell. Side View, With 300 ml. Container.

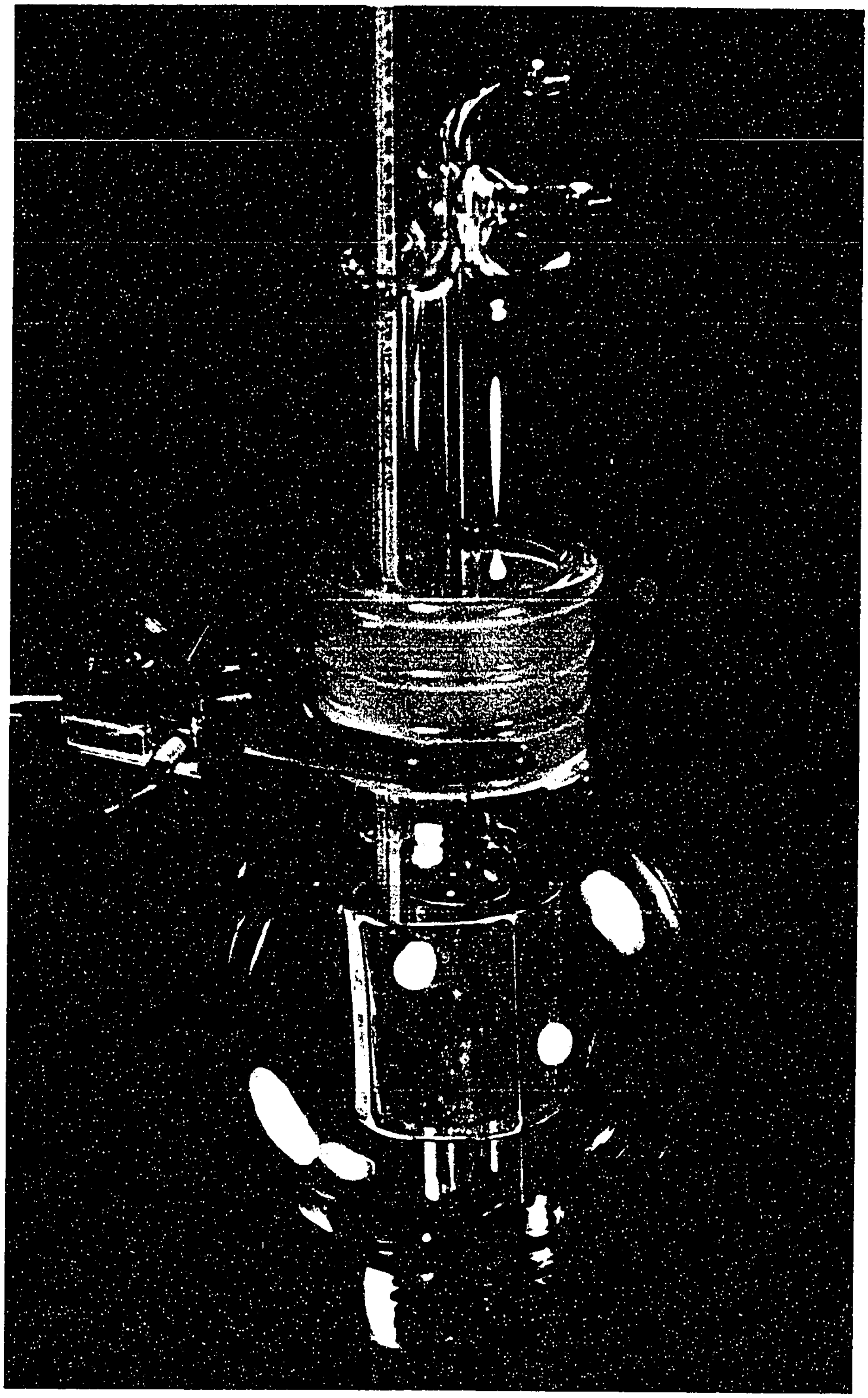


Figure 6. Photograph of Cell. Side View With 1000 ml. Container.

APPENDIX B

NMR SPECTRA

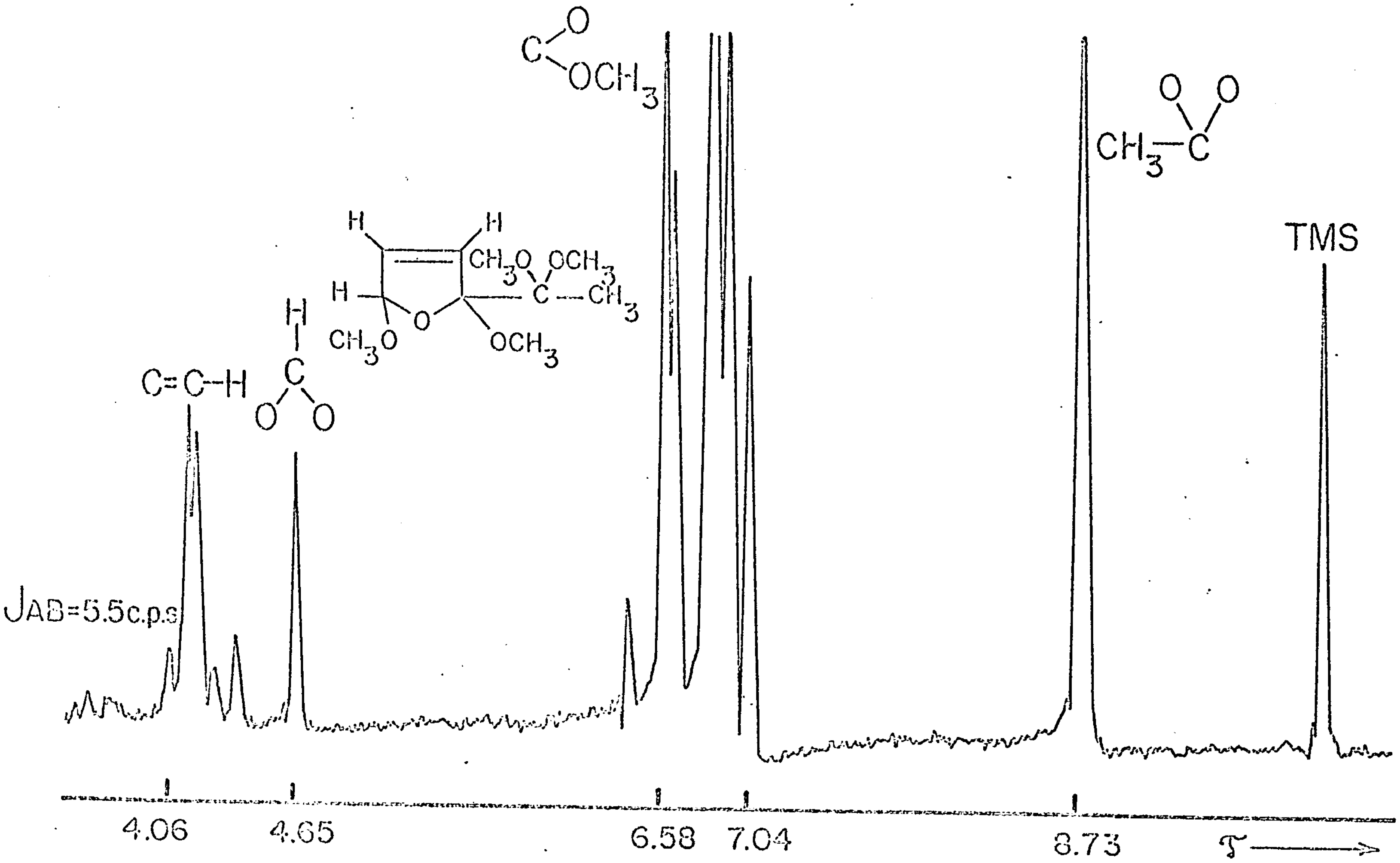


Figure 7. The NMR spectrum of 2,5-dimethoxy-2-(α,α-dimethoxyethyl)-dihydrofuran (XXIX) measured in CCl_4.

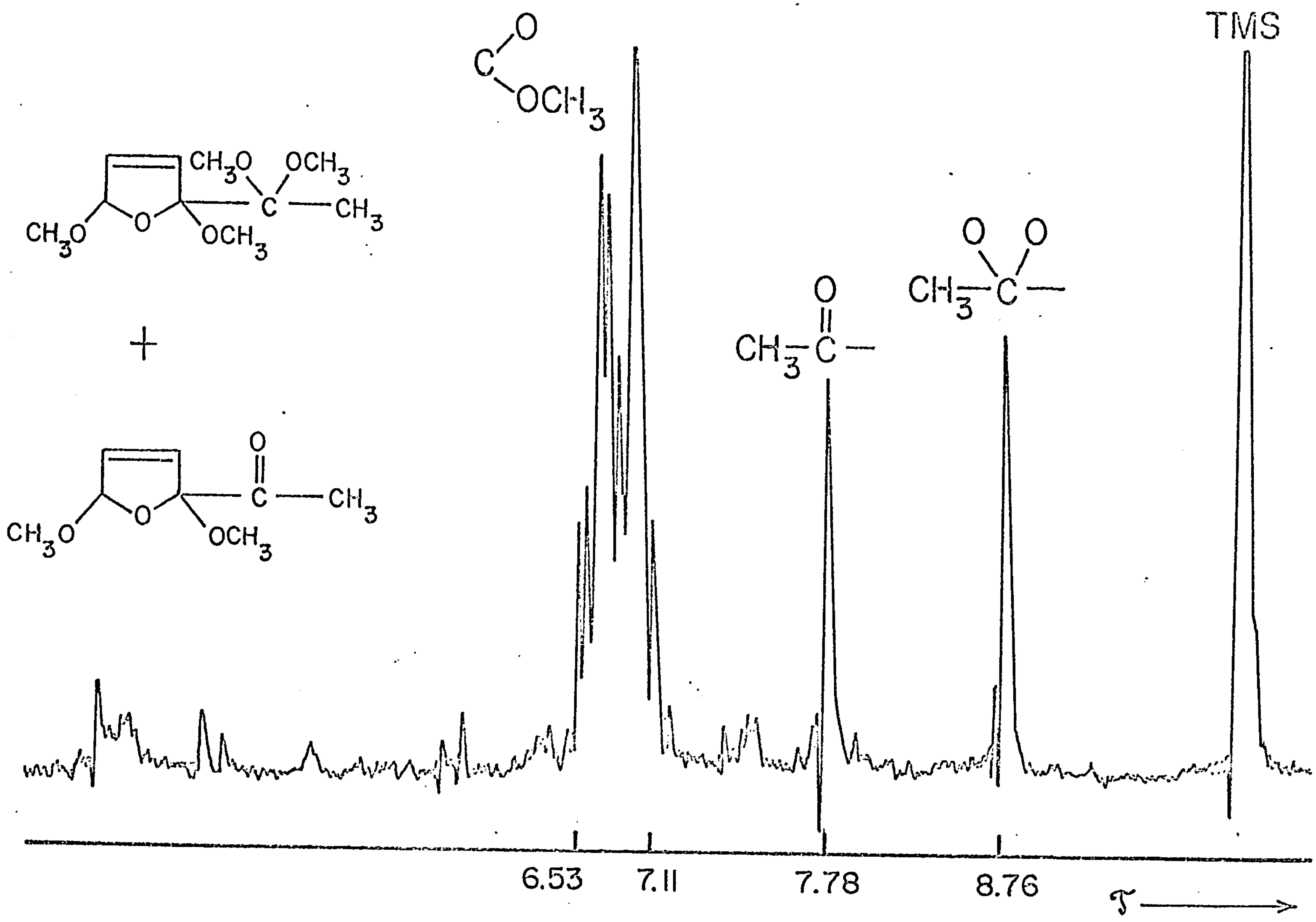


Figure 8. The NMR spectrum of the mixture of (XXIX) and (XXXIX) measured in CCl_4.

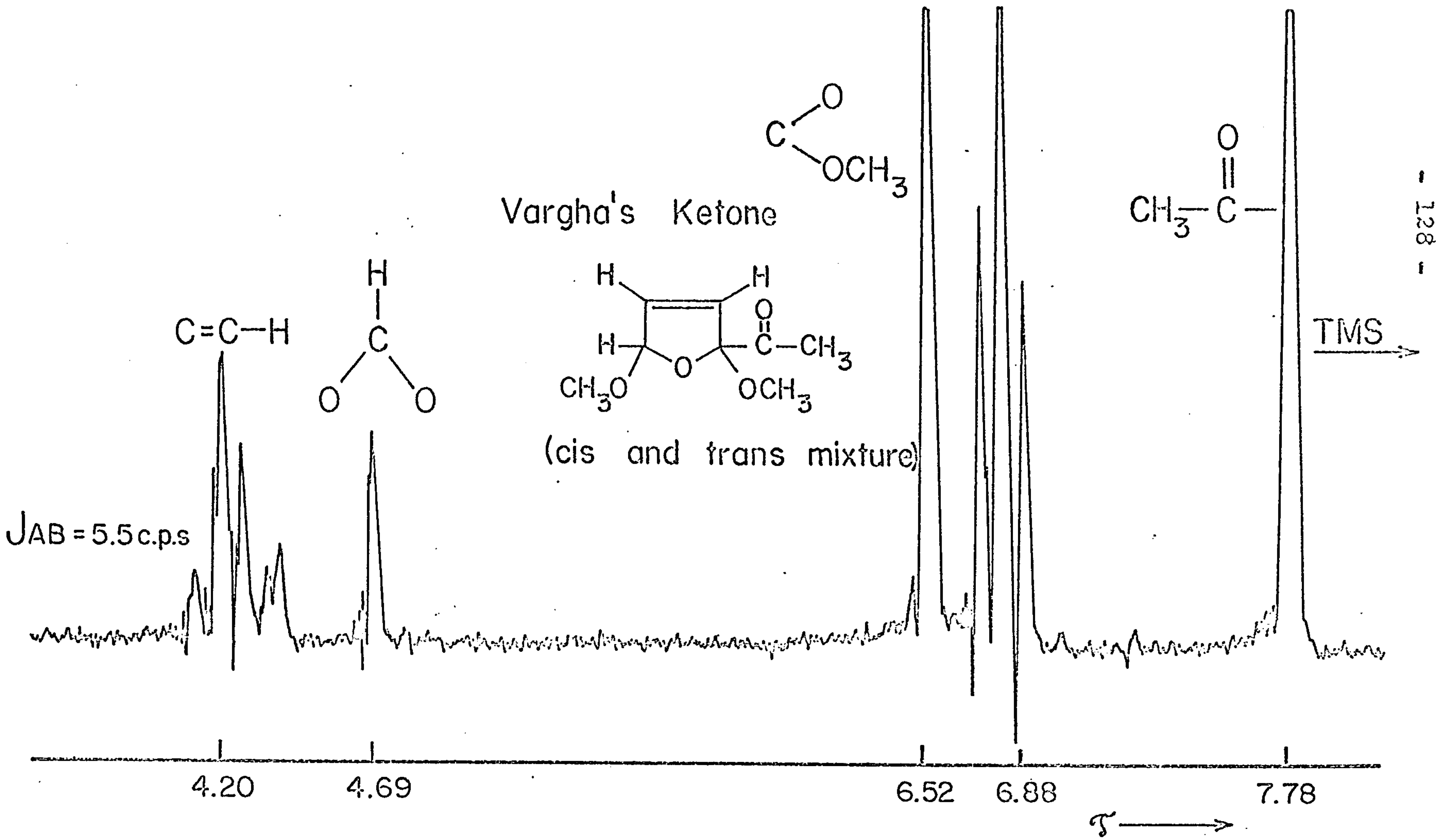


Figure 9. The NMR spectrum of 2,5-dimethoxy-2-acetyldihydrofuran (XXXIX) measured in CCl_4.

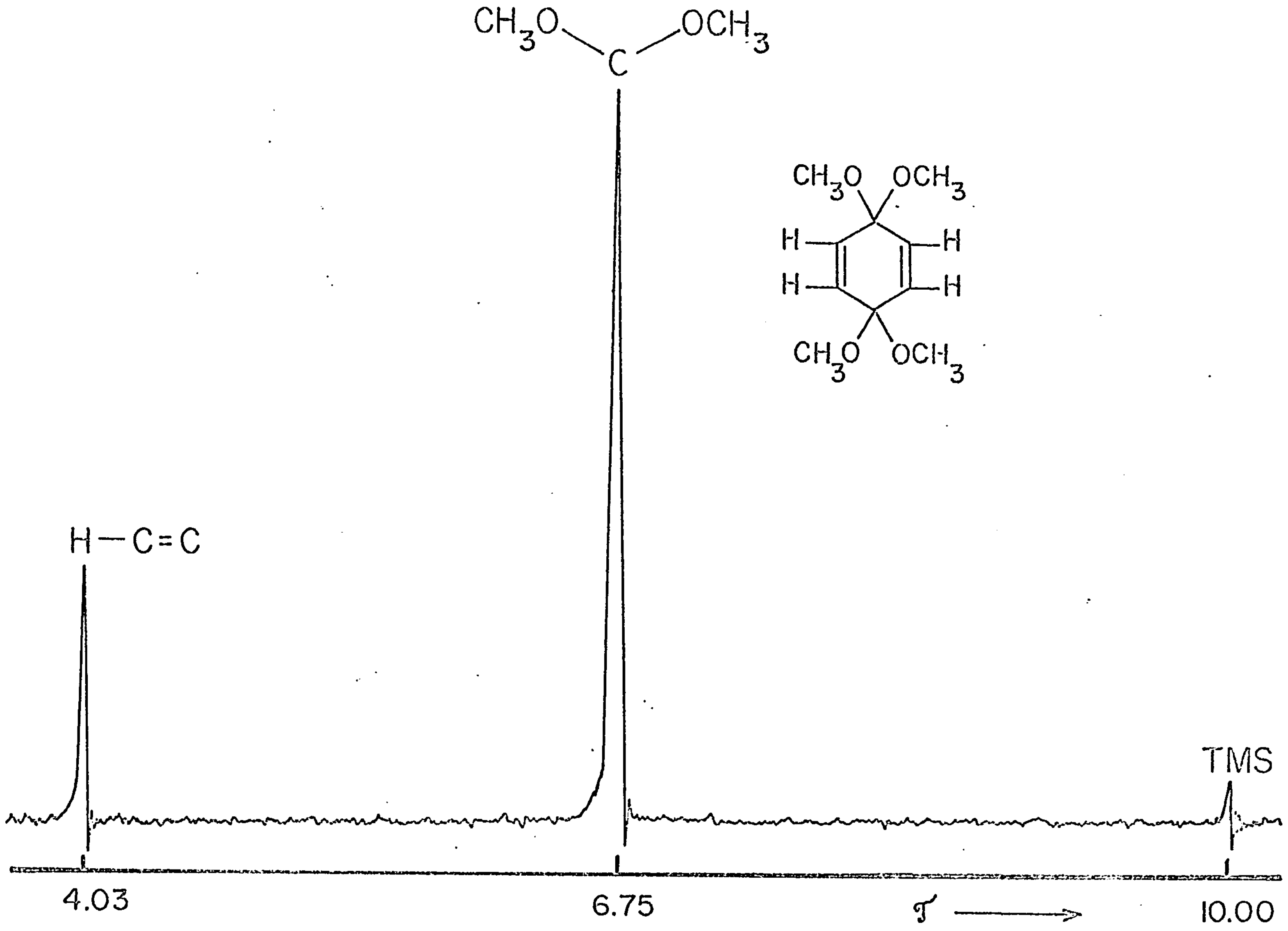


Figure 10. The NMR spectrum of 3,3,6,6-tetramethoxy-1,4-cyclohexadiene (XLVI) measured in CCl_4.

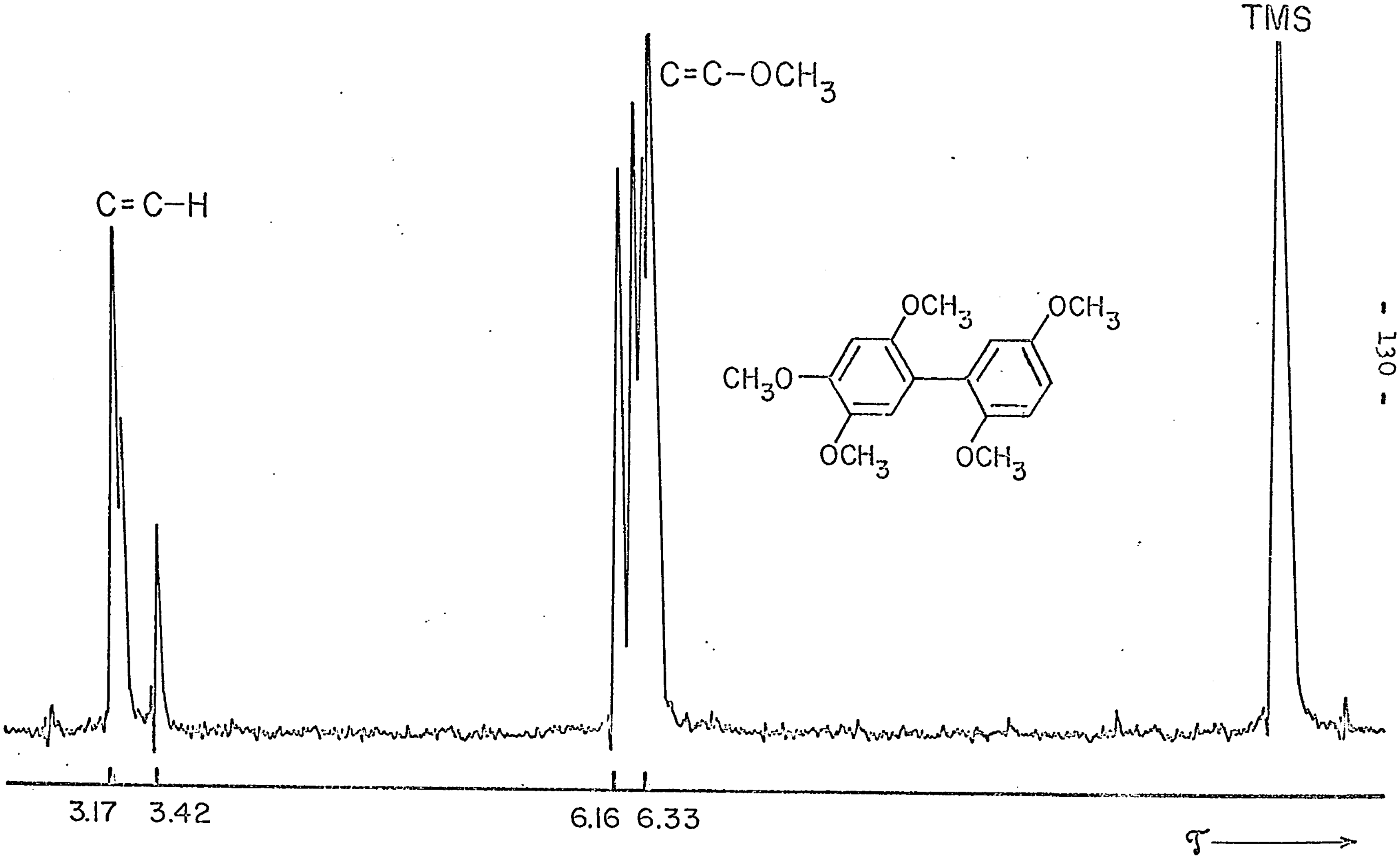


Figure 11. The NMR spectrum of the pentamethoxybiphenyl (XLIX) measured in CCl_4.

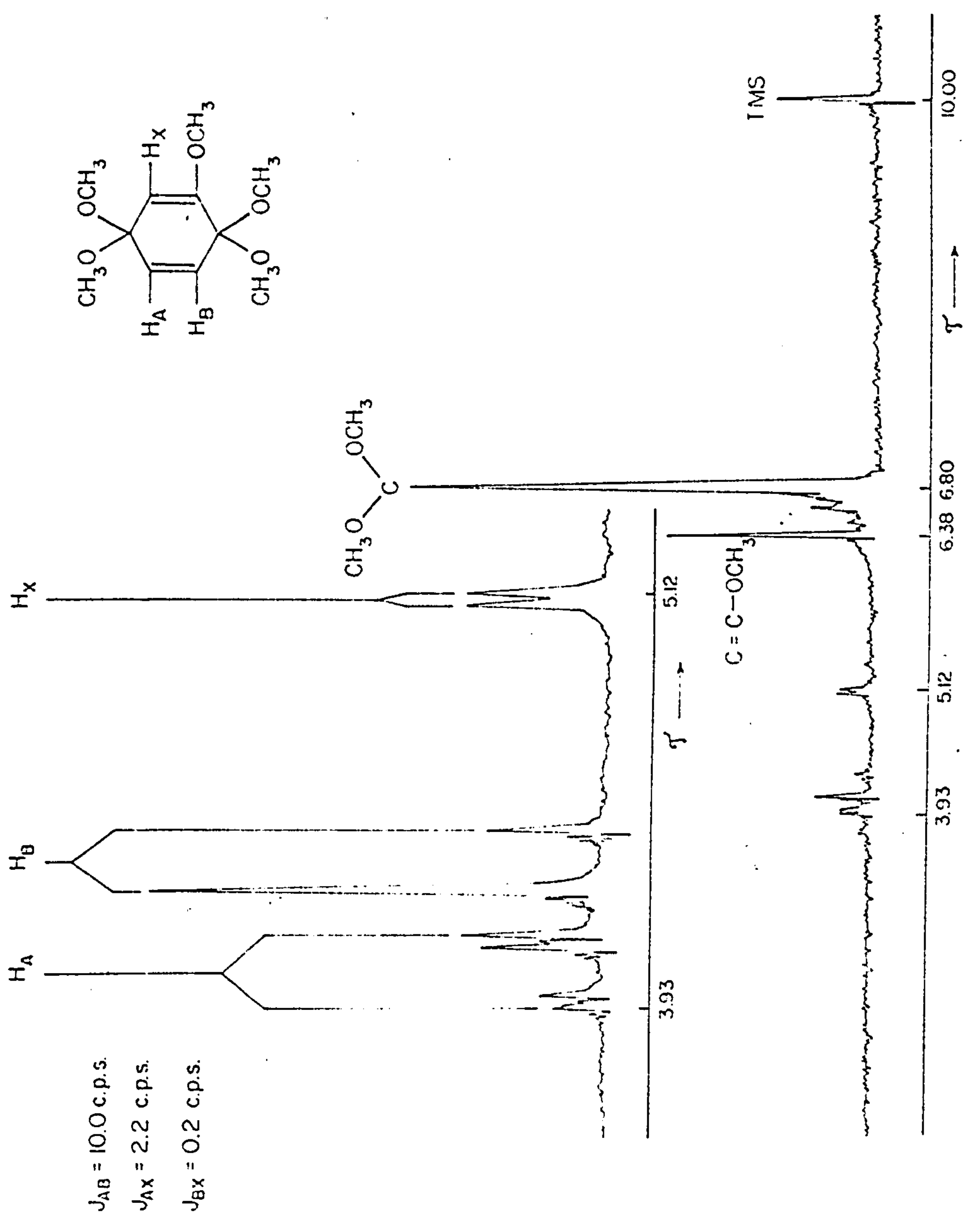


Figure 12. The NMR spectrum of 2,3,3,6,6-pentamethoxy-1,4-cyclohexadiene (LVIII) measured in CCl_4.

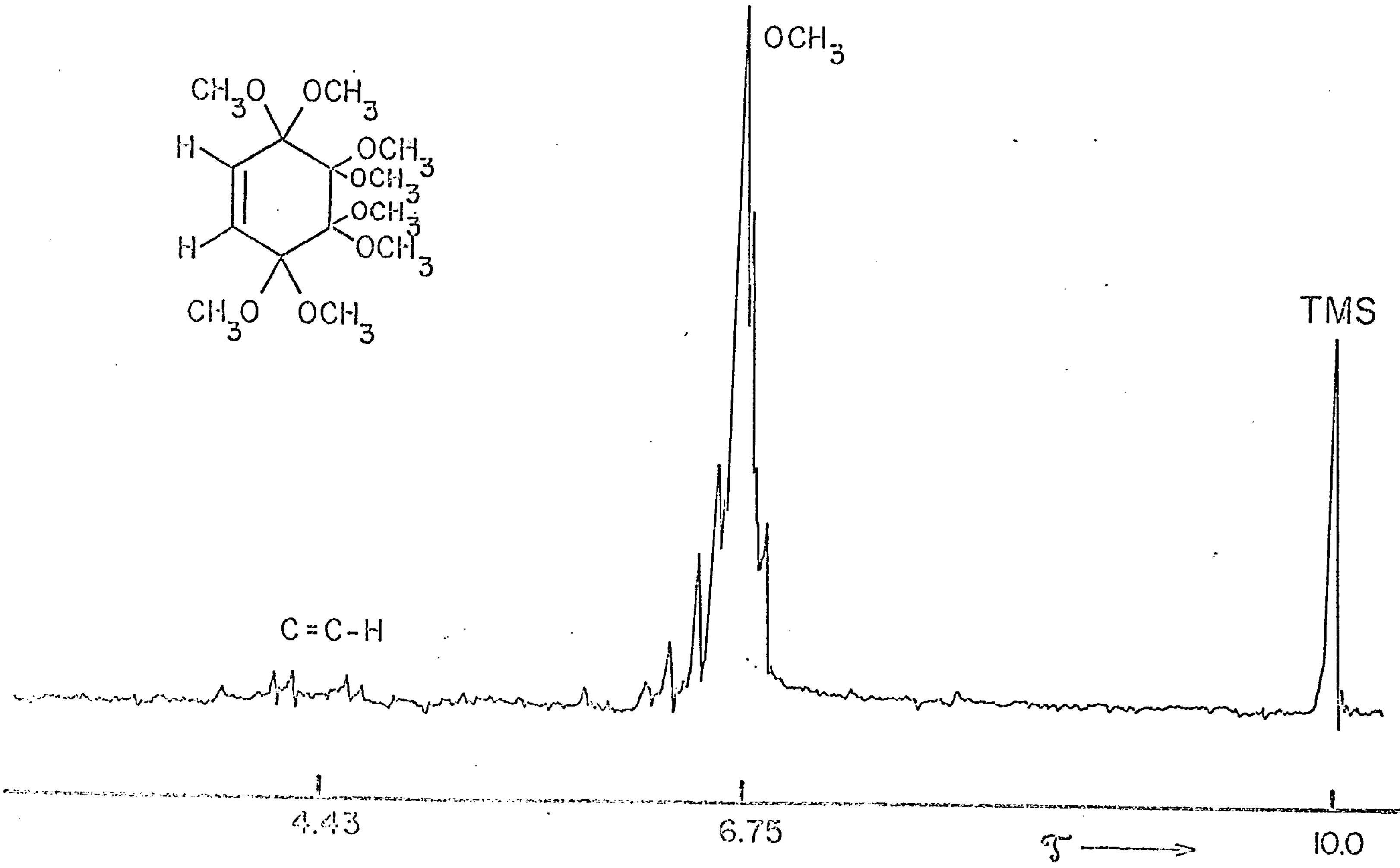


Figure 13. The NMR spectrum of 3,3,4,4,5,5,6,6-octamethoxycyclohexene measured in CCl_4.

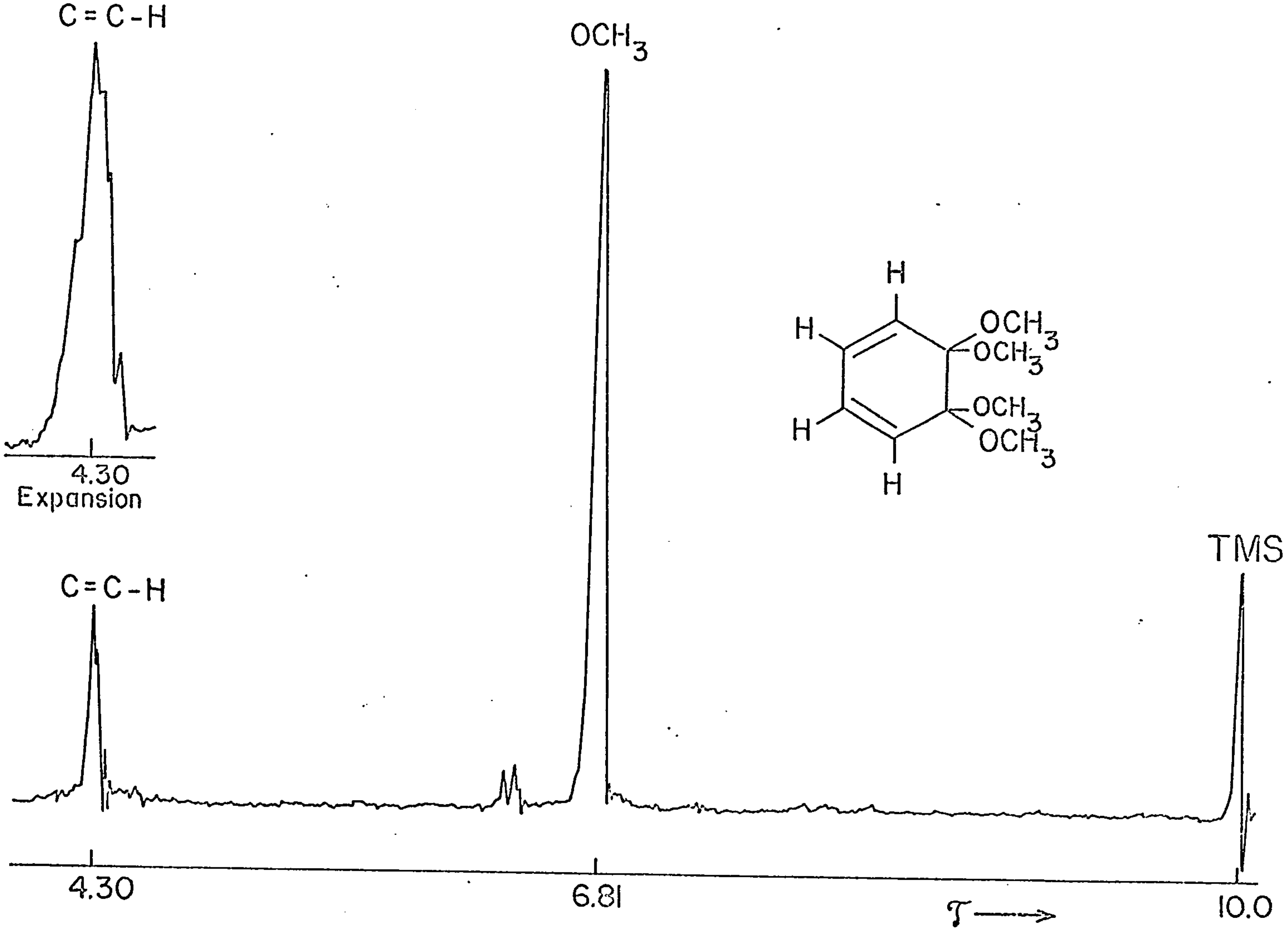


Figure 14. The NMR spectrum of 5,5,6,6-tetramethoxy-1,3-cyclohexadiene (LXII) measured in CCl_4.

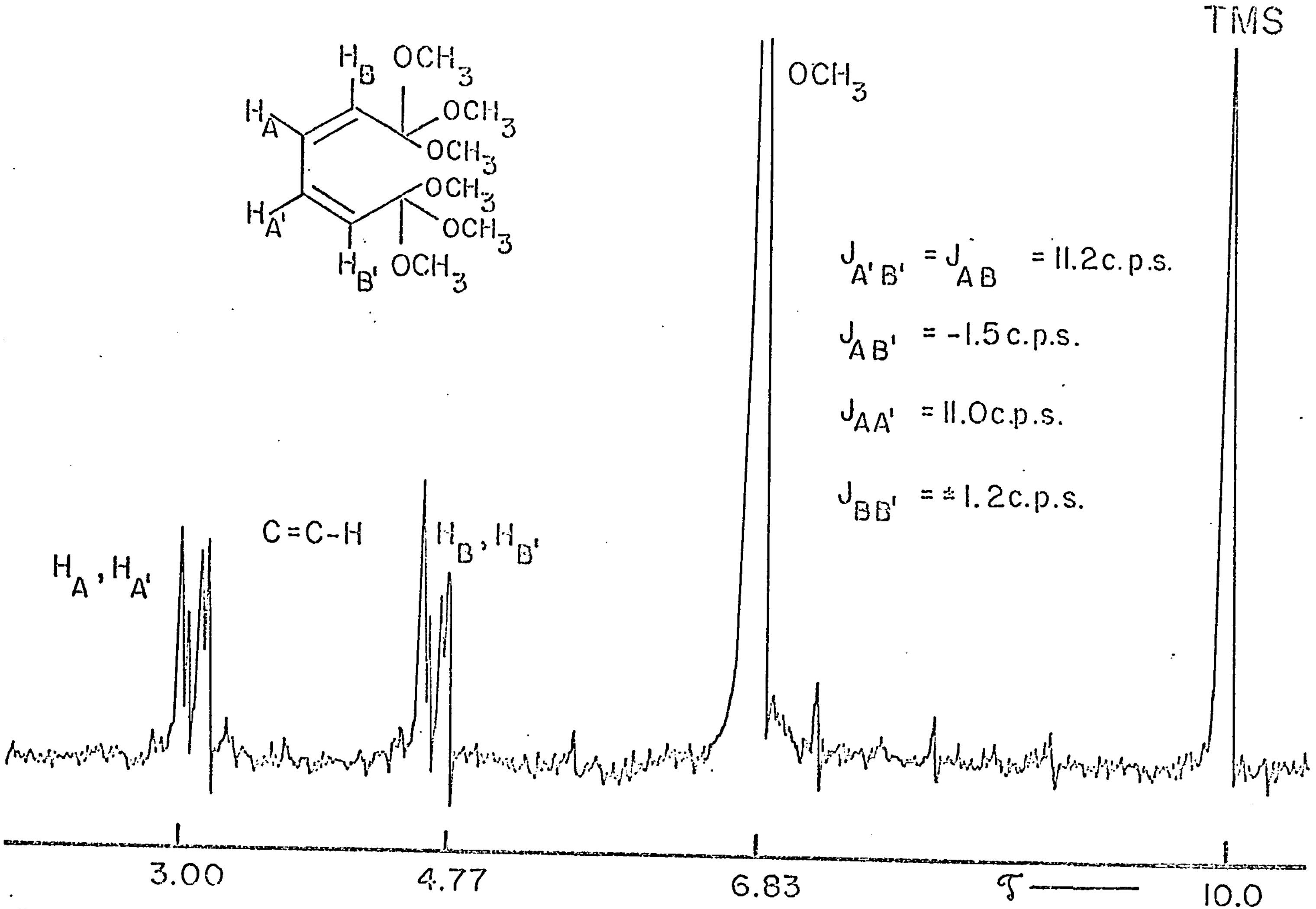


Figure 15. The NMR spectrum of hexamethyl *cis, cis*-orthomuconate measured in CCl_4.

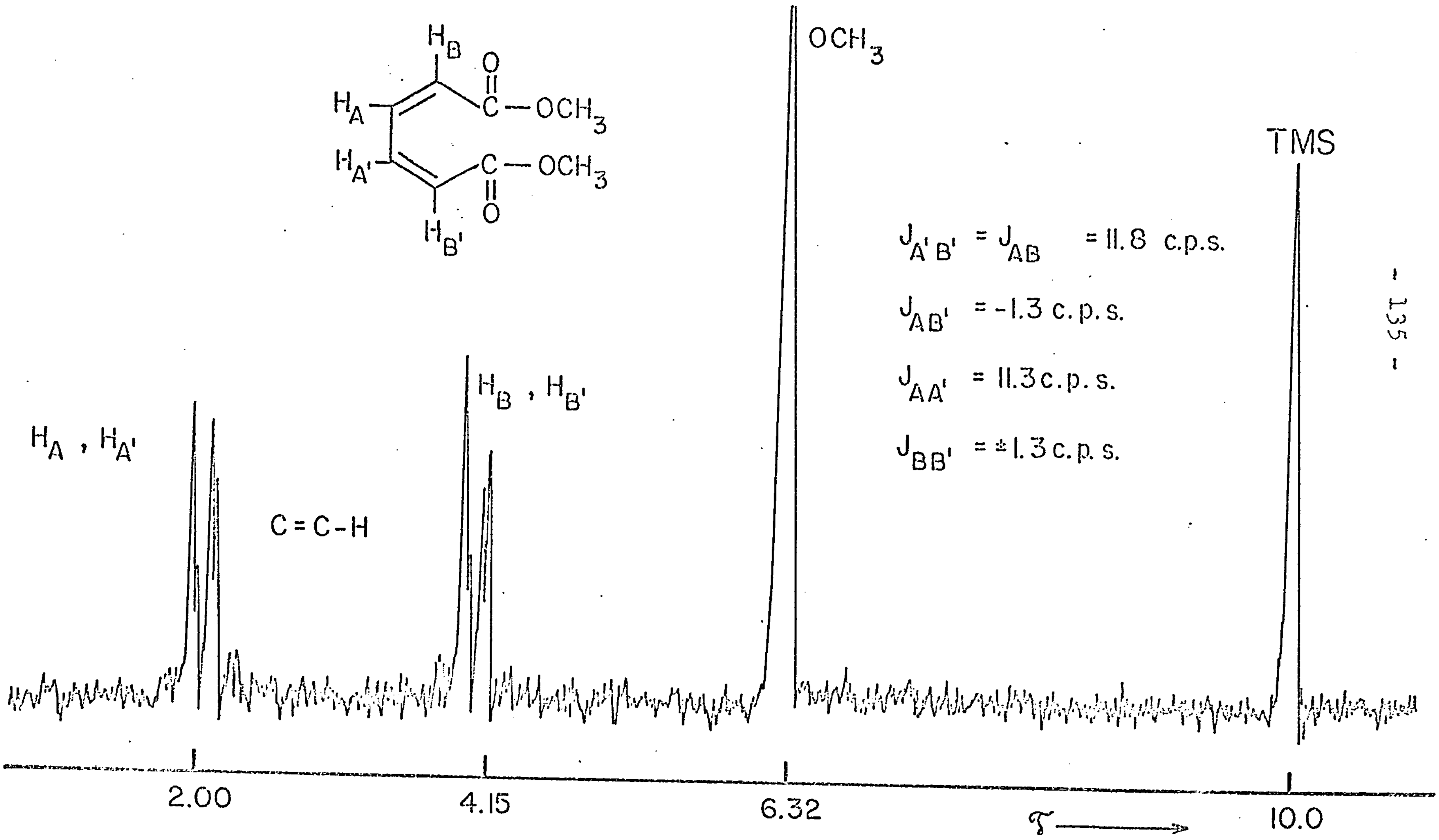


Figure 16. The NMR spectrum of cis, cis-dimethyl muconate measured in CCl_4.

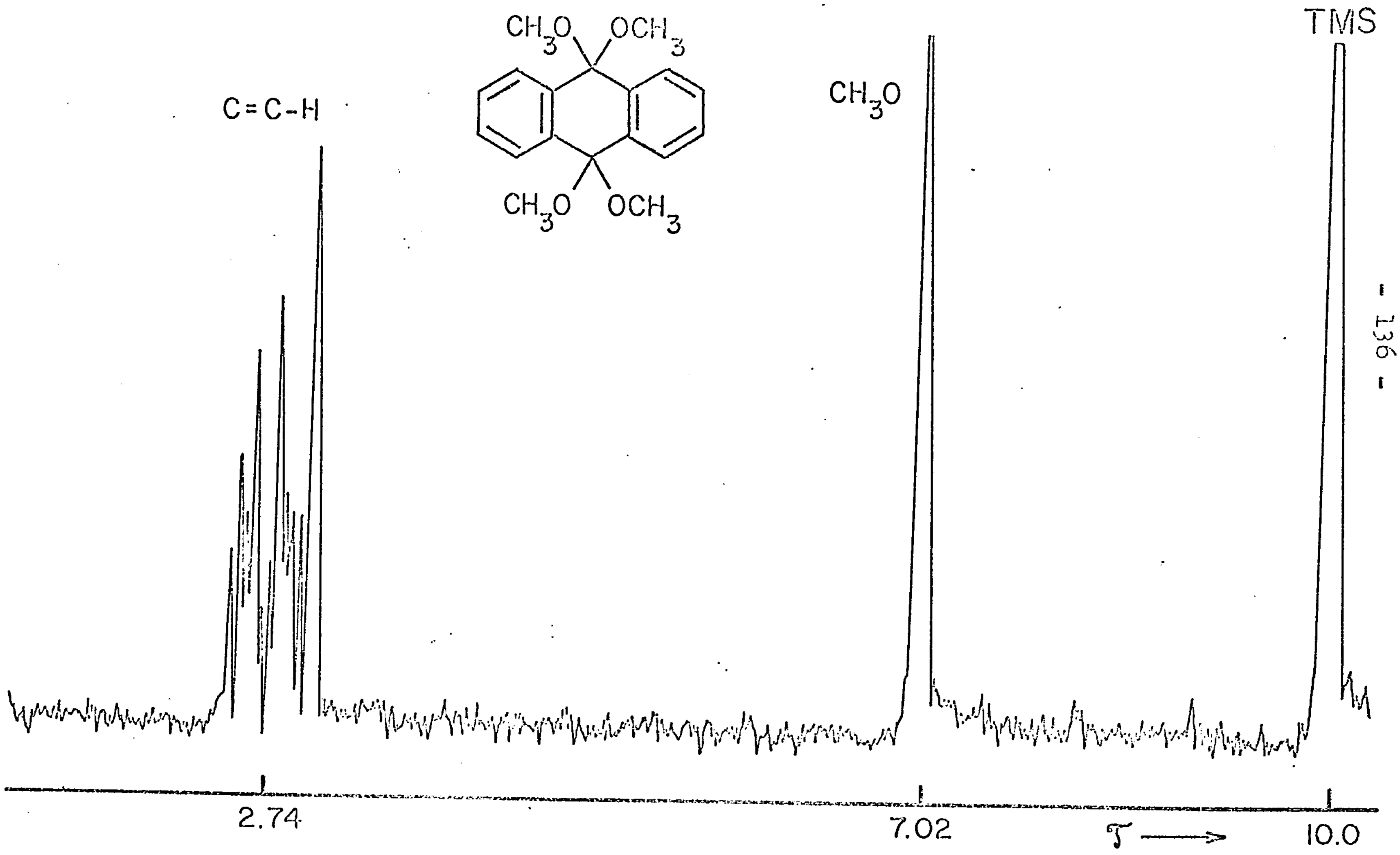


Figure 17. The NMR spectrum of 9,10-dihydro-9,9,10,10-tetramethoxyanthracene measured in $DCCl_3$.

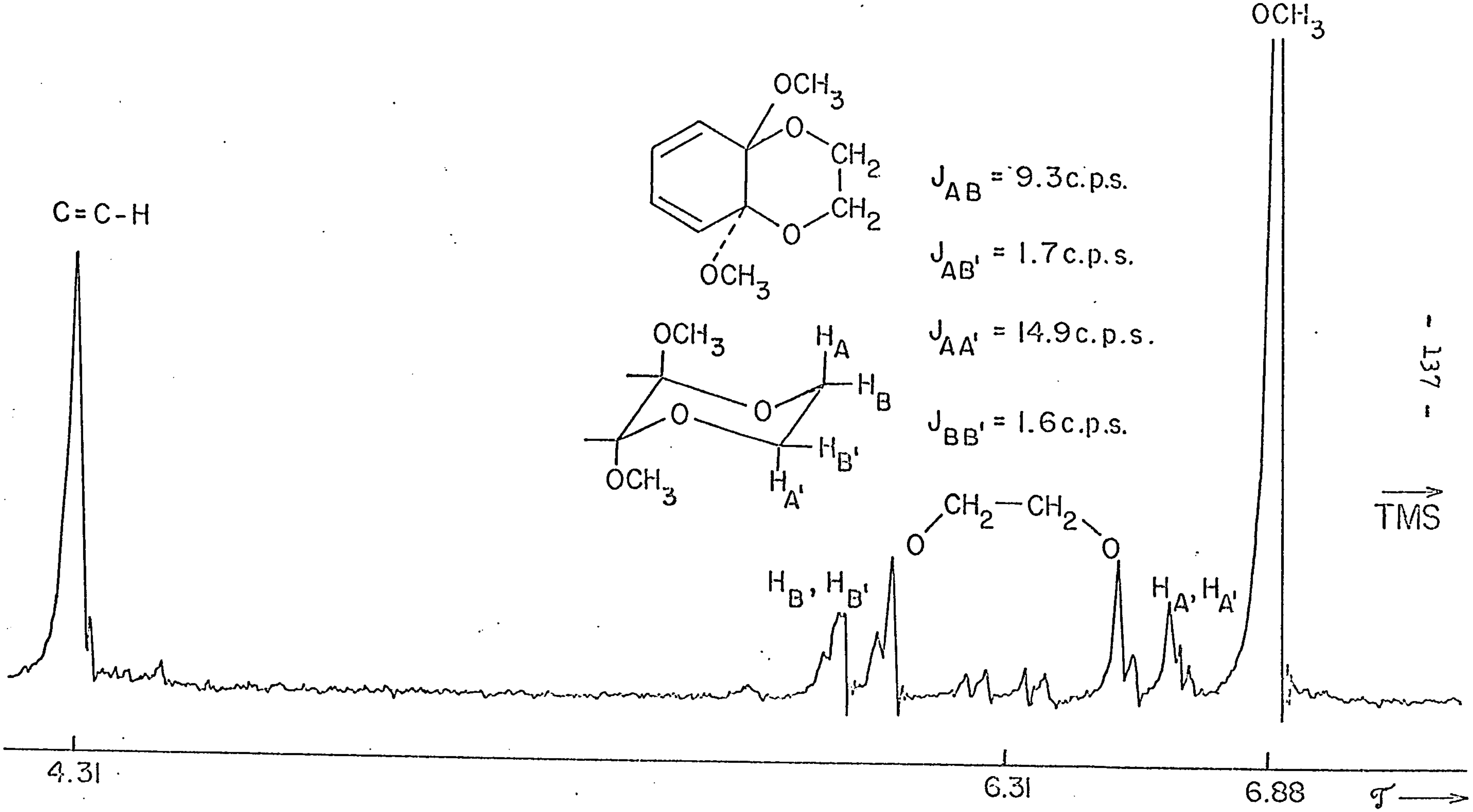


Figure 18. The NMR spectrum of 9,10-dihydro-9,10-dimethoxybenzodioxane (LXXIV) measured in CCl_4.

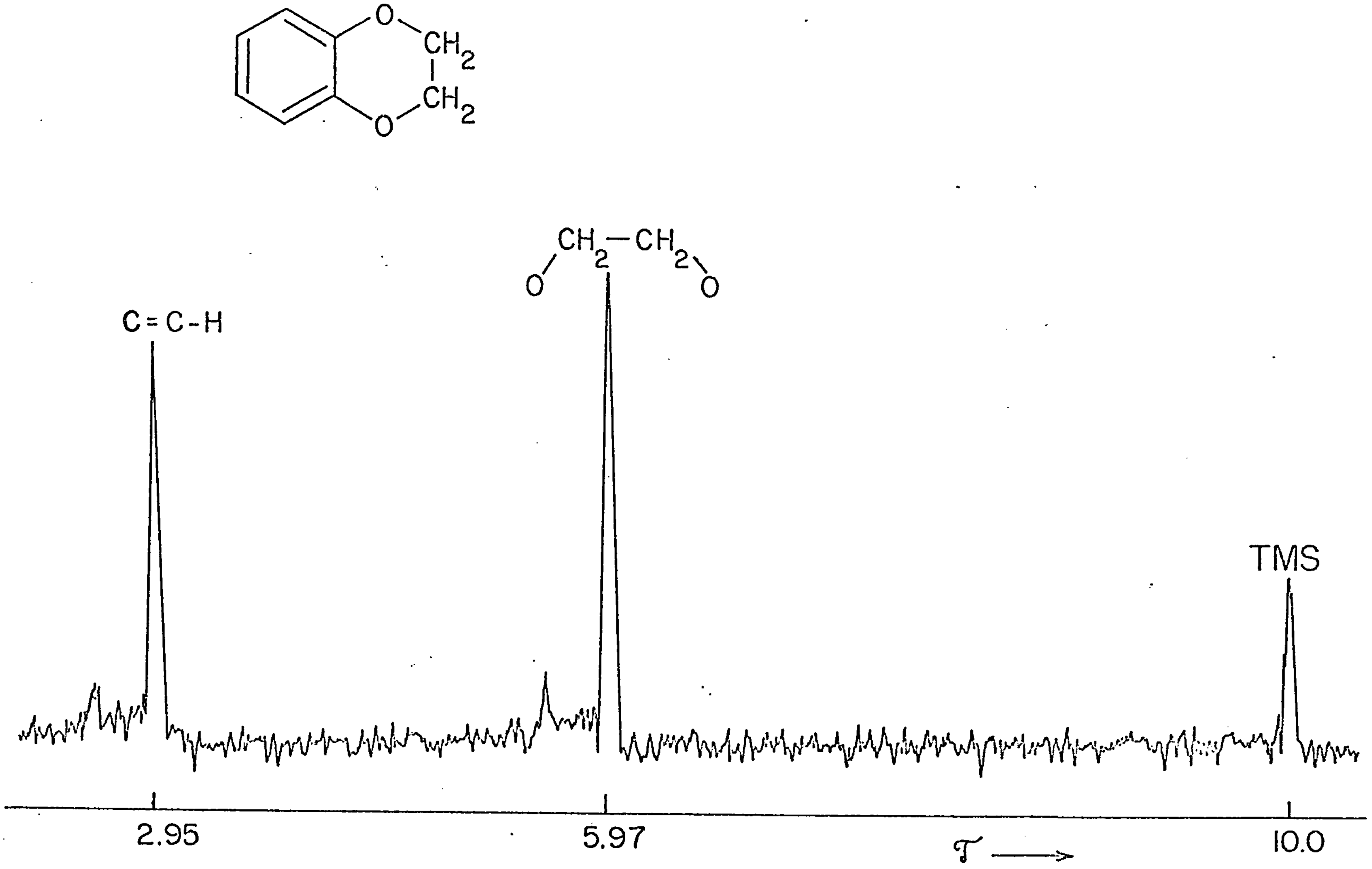


Figure 19. The NMR spectrum of benzodioxane (LXXIII) measured in CCl_4.

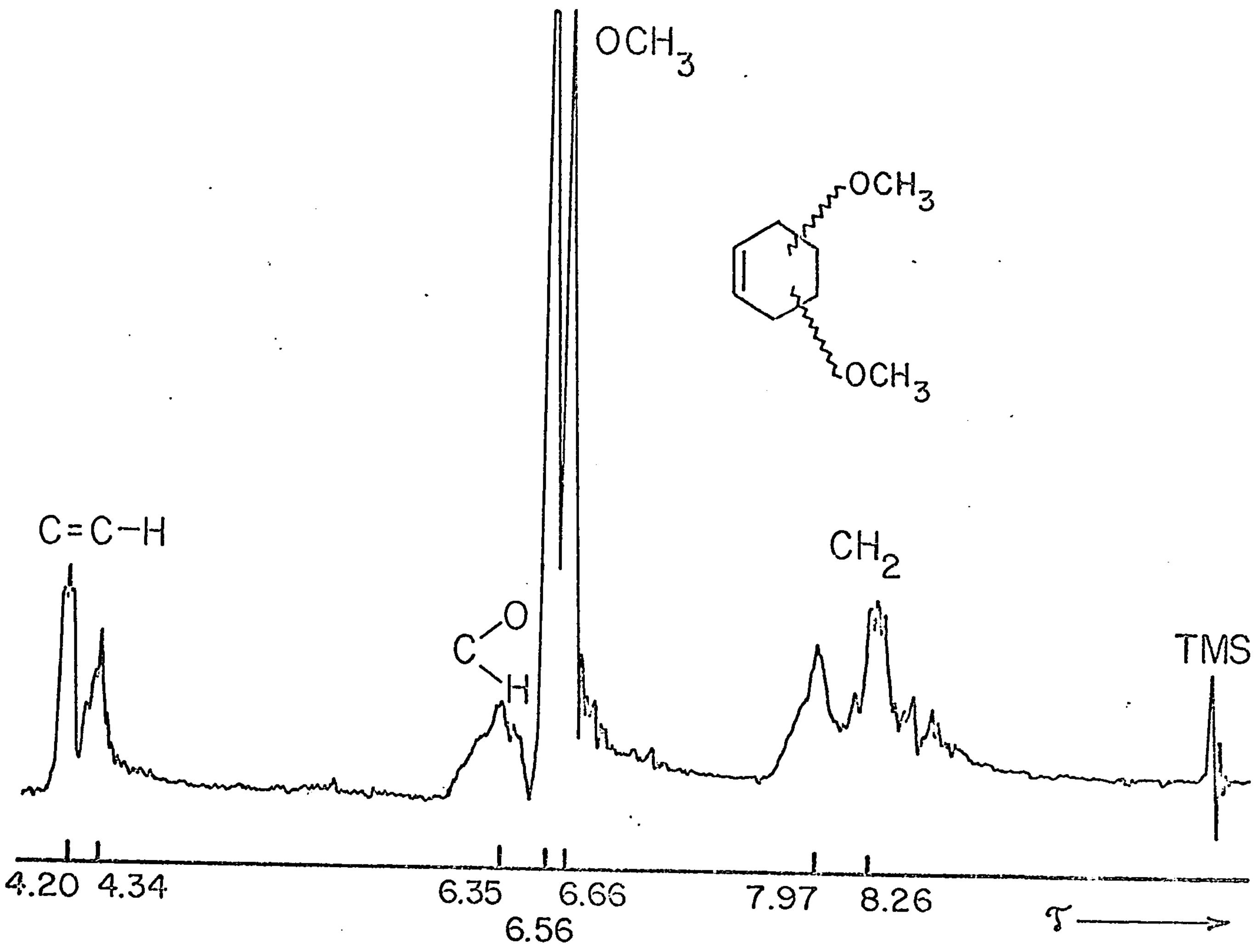


Figure 20. The NMR spectrum of the mixture of dimethoxycyclohexenes (LXXVII) and (LXXVIII) measured in CCl_4.

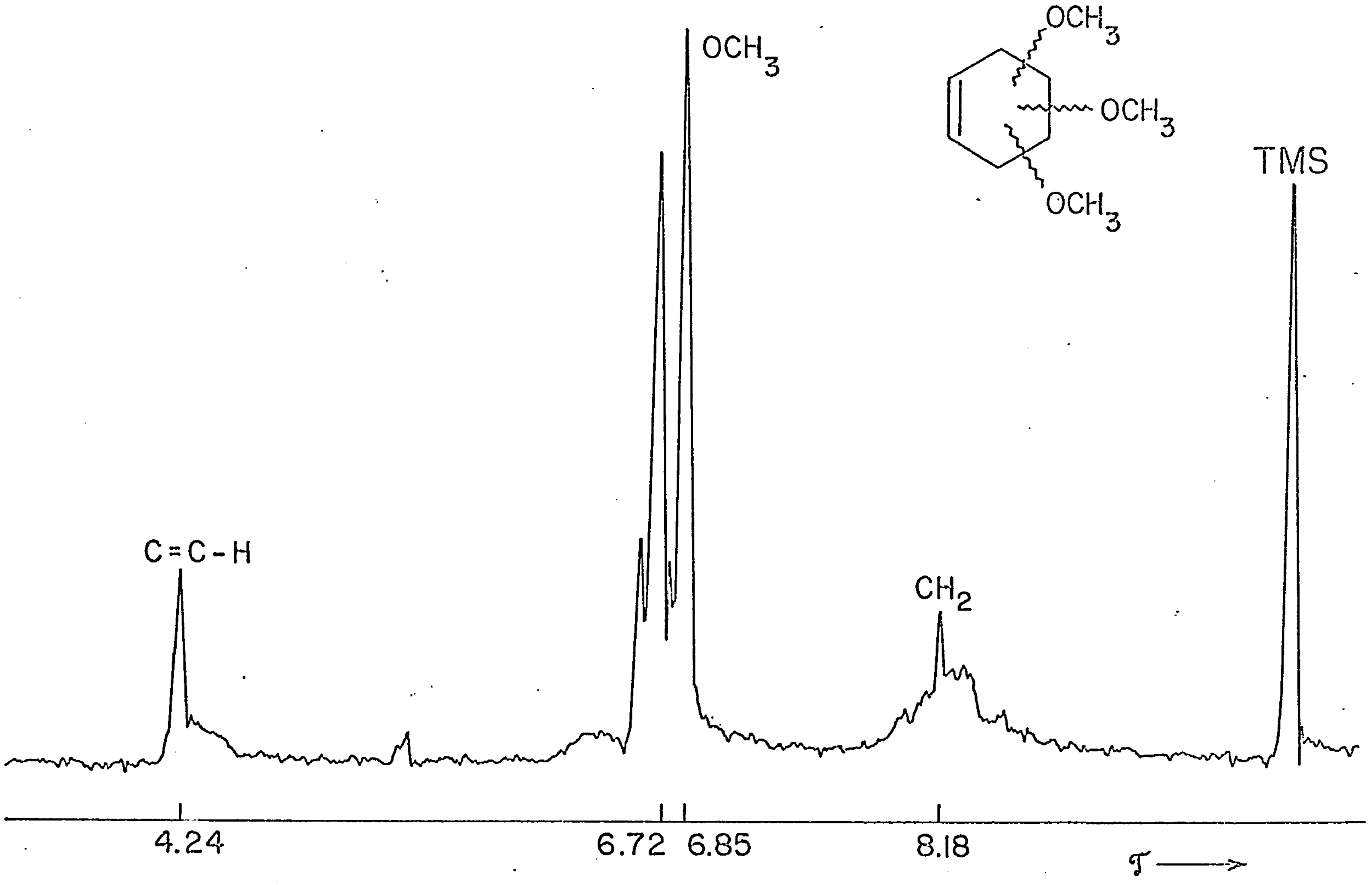


Figure 21. The NMR spectrum of the trimethoxycyclohexene (LXXX) or (LXXVIII) measured in CCl_4.

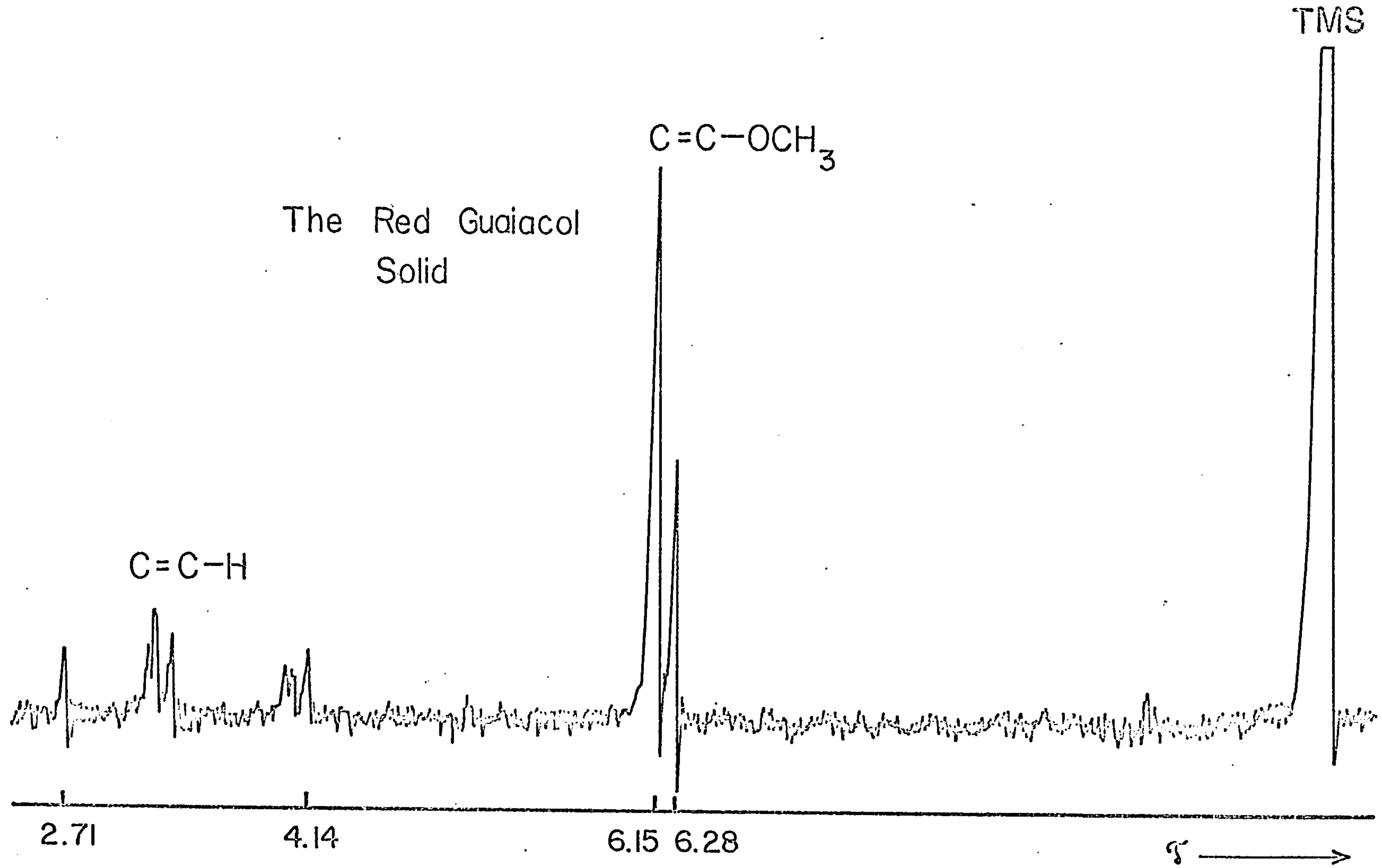


Figure 22. The NMR spectrum of "The Red Guaiacol Solid" (LX) measured in $DCCl_3$.

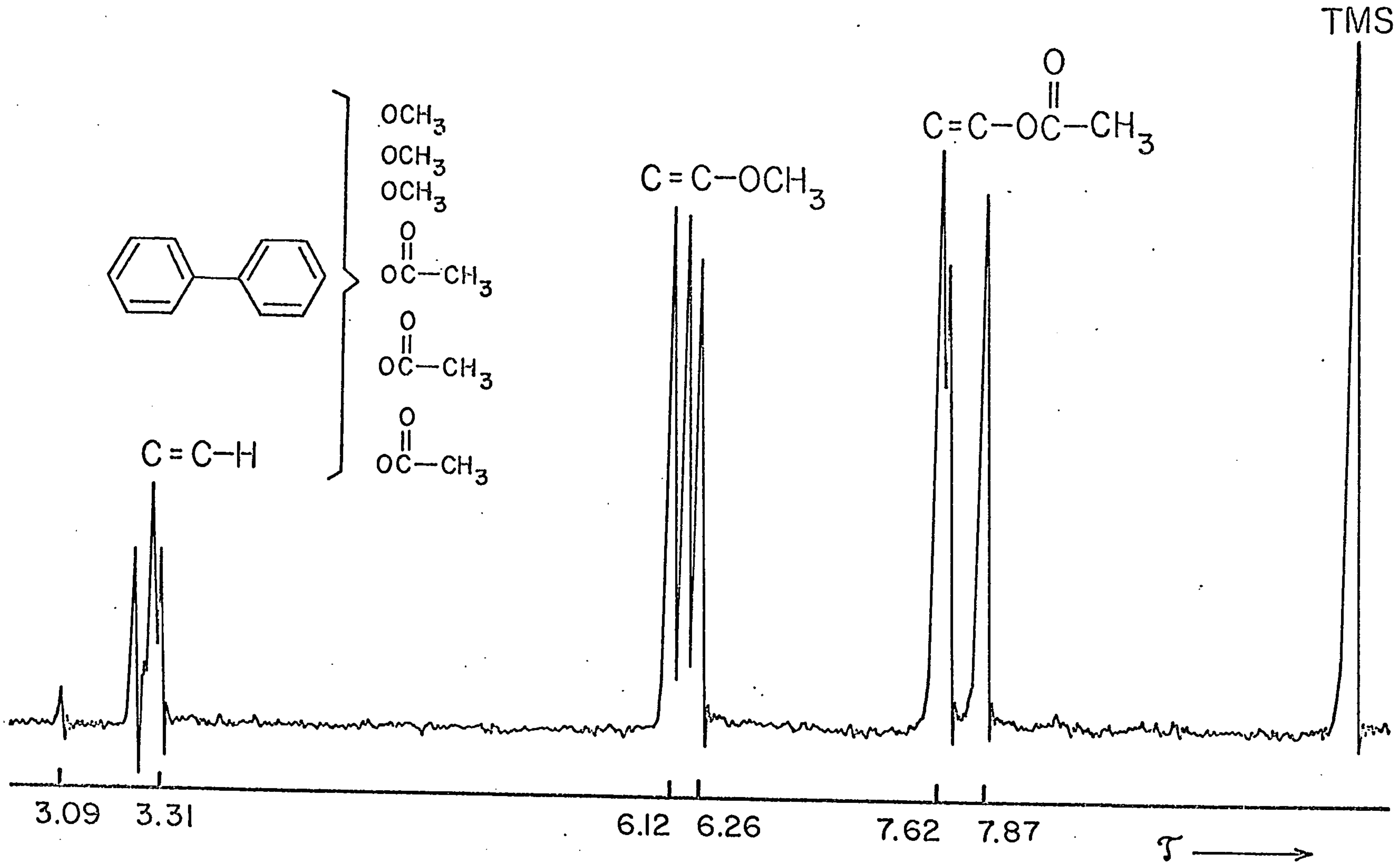


Figure 23. The NMR spectrum of the triacetoxytrimethoxybiphenyl (LXXXIV) measured in $DCCl_3$.

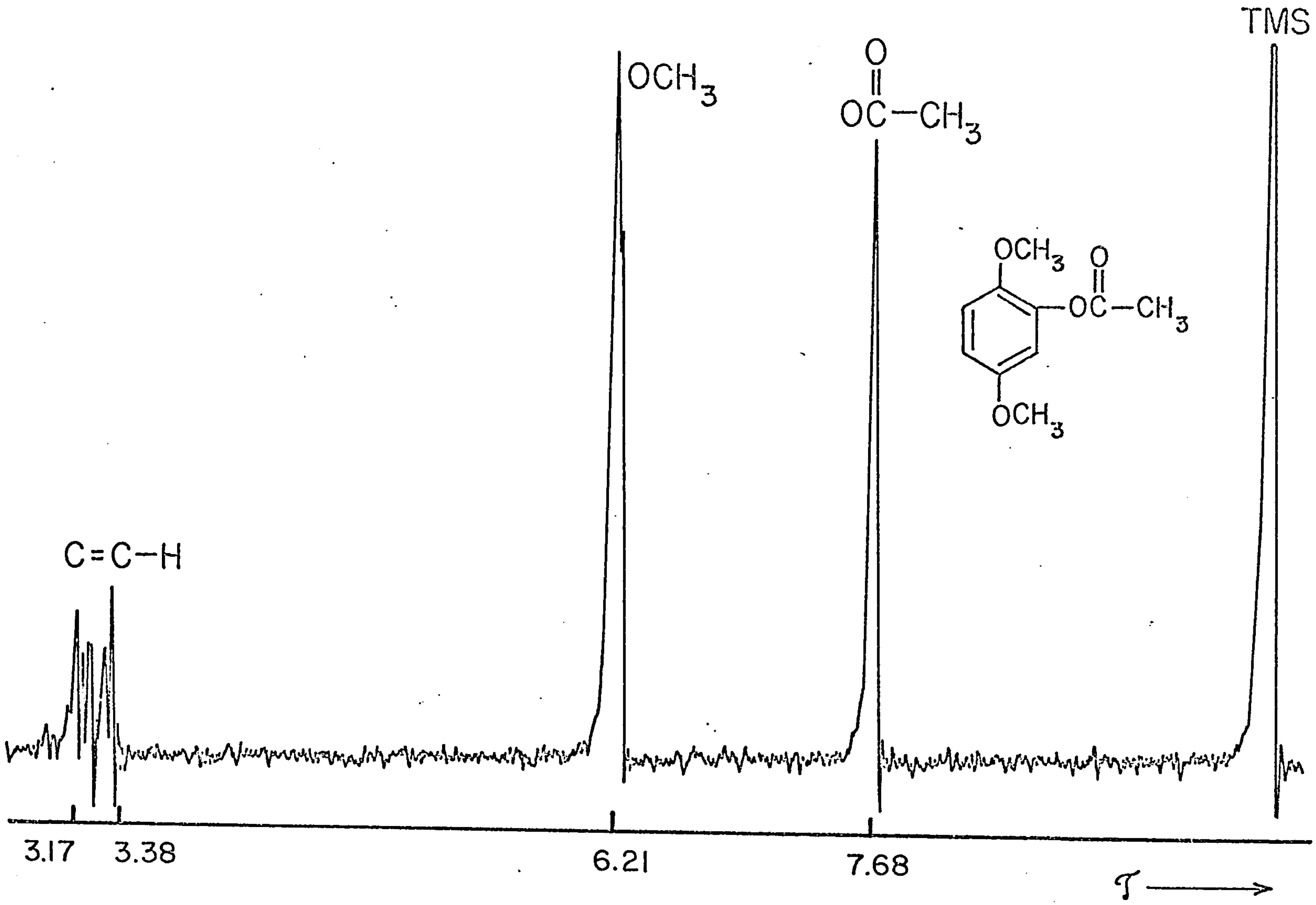


Figure 24. The NMR spectrum of 1,4-dimethoxy-2-acetoxybenzene (LXXXV) measured in $DCCl_3$.

CLAIMS TO ORIGINAL RESEARCH

1. An error in the literature has been corrected. Treatment of 2-acetylfuranoxime p-toluenesulfonate in methanol has been found to give 2,5-dimethoxy-2-acetyldihydrofuran instead of hexe -2-dione-4,5-dimethoxyacetal-1 as claimed.

2. The following compounds have been successfully methoxylated electrochemically to give new and highly unusual compounds: 1,4-, 1,3-, and 1,2-dimethoxybenzene; anisole; 9,10-dimethoxyanthracene; 1,2,4-trimethoxybenzene; 1,4-benzodioxane; 2,3,3,6,6-pentamethoxy-1,4-cyclohexadiene; 5,5,6,6-tetramethoxy-1,3-cyclohexadiene; 1,3-cyclohexadiene; naphthalene; guaiacol.

3. Several structural requirements for successful electrochemical methoxylation have been elucidated.

4. In the case of 1,4-dimethoxybenzene, the electrochemical methoxylation product has been shown to undergo an aromatization reaction, the mechanism of which has been clarified.

5. Two products have been shown to result from the methoxylation of 1,3-dimethoxybenzene: 2,3,3,6,6-pentamethoxy-1,4-cyclohexadiene, the mechanism of formation of which

has been elucidated by a carbon-14 study; an octamethoxycyclohexene (tentative structure).

6. Several products have been shown to result from the methoxylation of 1,2-dimethoxybenzene including 5,5,6,6-tetramethoxy-1,3-cyclohexadiene and hexamethyl cis, cis-orthomuconate. Electrochemical methoxylation of the former has been found to afford the latter in high yield. Two mechanisms have been proposed on the basis of the observed stereochemistry to incorporate the view that adsorption on the anode surface plays an important role in these reactions.

7. The electrochemical methoxylation of benzodioxane has been shown to yield the trans-fused o-quinone diketal.

8. The mechanism of formation of p-benzoquinone diketals from anisole, 1,3-, and 1,2-dimethoxybenzene has been shown to most probably involve a radical abstraction mechanism.

9. The Kolbe reaction carried out in the presence of 1,4-dimethoxybenzene has been shown to yield the substitution product, 2-acetoxy-1,4-dimethoxybenzene.

10. Electrochemical methoxylation of guaiacol has been shown to yield a methoxylated biphenyl with no ketal properties.

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