CHAPTER I

CHLOROMETHYLATION OF SOME PHENOLIC COMPOUNDS

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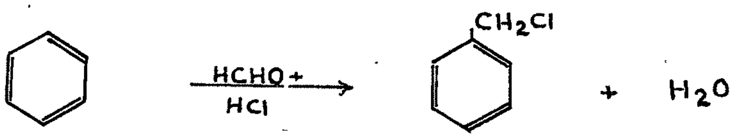
Chloromethylation of some Phenolic compounds

Theoretical

Introduction of a - CH_2Cl group by the replacement of a hydrogen atom (generally of an aromatic compound) in a single operation is known as chloromethylation. This is achieved by interaction with formaldehyde and hydrogen chloride sometimes in the presence of a catalyst such as zinc chloride.



A survey of the chloromethylation of aromatic compounds upto 1941 has been made by Fuson and McKeever[1].

Chloromethylation is an excellent tool in the synthetic work as the chloromethyl group undergoes substitution reactions with various reagents, for example, the chlorine of the chloromethyl group can be replaced by a hydroxy, cyano, methoxy, acetoxy or other groups by treating it with appropriate reagents. Further, on Sommelet reaction the chloromethyl group can be replaced by the formyl group. On oxidation the chloromethyl derivative is readily converted into the corresponding acid and on reduction it gives rise to the methyl derivative.

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1. Fuson and McKeever., Organic reactions Vol. I., John Wiley and Sons, New York., 1942, P.63.

Applications of the reaction : Chloromethylation is generally applicable to aromatic hydrocarbons ; though the application to the aliphatic compounds is not uncommon. Aromatic hydrocarbons such as benzene, naphthalene, anthracene, phenanthrene, diphenyl and many of their derivatives have been successfully chloromethylated. Substituents such as hydroxyl, alkyl and alkoxy accelerate the reaction and the reaction proceeds even in the absence of a catalyst to form the mono or dichloromethyl derivative in good yield. The reactivity increases rapidly with electropositive substituents. Highly alkylated homologues react rapidly in the absence of a catalyst. Thus mesitylene can be chloromethylated without any catalyst and the mono as well as the bis-chloromethyl derivatives obtained[2]. Monoalkyl benzene derivatives give a higher percentage of the para-isomer than the ortho isomer. A second chloromethyl group usually can be introduced sometimes with excellent yields. m-Xylene on chloromethylation gives the bis-chloromethyl derivative in more than 75% yield[3]. An electro negative group in the benzene ring deactivates the molecule. Thus p-nitro toluene and o-nitro toluene[4] have been found

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2. Nauta and Dienske., Rec.Trav.Chim., 55, 1000 (1936) ; C.A. 31, 1776 (1937).
3. Braun and Nelles., Ber., 67, 1094 (1933).
4. Stephen, Short and Gladding., J.Chem.Soc., 117, 510 (1920)

to give chloromethyl derivatives in low yields. Similarly, the presence of a halogen atom in the nucleus retards the reaction, but, by using drastic methods the yield can be increased. Nazarov and Semenovskii[5] in their studies on chloromethylation found that halobenzenes give good yields when the reaction is carried out using drastic conditions. While more highly halogenated derivatives generally fail to undergo chloromethylation, the presence of alkyl groups in the nucleus counteract the influence of these substituents and sometimes give high yields of chloromethyl derivatives as in bromomesitylene[6].

Nitro group in the aromatic ring has a retarding influence on the rate of the reaction. Stephen et al[4] found that nitrobenzene and o- and p-nitrotoluenes give chloromethyl derivatives but in low yeild. Substances like o- and p-chloronitrobenzene and m-dinitrobenzene fail to react[4]. Here also the presence of alkyl, hydroxy or alkoxy group in the nucleus counteracts the influence of these substituents. Masao et al[7] has chloromethylated 2-ethoxy and 3-ethoxy nitrobenzene and obtained the monochloromethyl derivatives.

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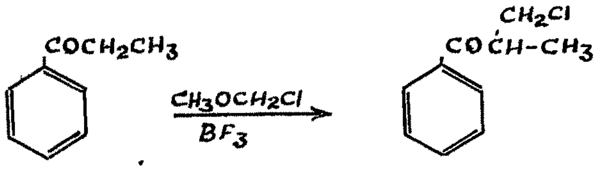
5. Nazarov and Semenovskii., Izvest.Akad.Nauk.S.S.R., Otdel.Khim.Nauk., 1957, 212 ; C.A. 51, 10400 (1957).
6. Vavon et al., Bull.Soc.Cheim., 6, 1025 (1939).
7. Masao Wakae, You Fukui and Konishi., Osaka Furitsu Kogyo Shoreikan Hokoku., 21, 38 (1959) ; C.A. 54, 10921 (1960).

2-Nitro-4-chlorotoluene gave the 6-chloromethyl derivative[8].

Ketones are generally unreactive. Fuson and McKeever[9] found that benzophenone cannot be chloromethylated. Similarly chloromethylation of anthraquinone was also not successful[4]. Here also the presence of groups such as alkyl, hydroxy, alkoxy etc. in the nucleus counteracts this influence[9]. In aromatic ketones such as acetophenone the chloromethyl group can enter either the side chain or the nucleus[10,11]. Thus β-chloromethyl ethylphenyl ketone(II) was obtained on chloromethylation of ethyl phenyl ketone(I) with CH_3OCH_2Cl in the presence of BF_3 as catalyst[10].



I

II

However in the case of o-hydroxyphenyl ethyl ketone[12], 2-methyl-4-methoxy acetophenone[13] and o- and p-hydroxy acetophenones[14,15] the chloromethyl group entered only the nucleus.

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[8] Saul R.Buc., U.S.Patent., 2758137 (1956) ; C.A., 51, 2858 (1957).

[9] Fuson and McKeever., J.Amer.Chem.Soc., 62, 784 (1940).

[10] Tilichenko and Popova., Zhur.Obshchei Khim., 23, 118 (1953) ; C.A., 48, 637 (1954).

[11] Chaikovskaya., Izvest.Vysshikh Ucheb.Zavedenii.Khim.i Khim.Tekhnol., 2, 895 (1959) ; C.A., 54, 12046 (1960).

Aromatic amines react vigorously but it has not been possible to isolate their simple chloromethyl derivatives[16].

Hydroxy groups in the nucleus greatly promote the rate of reaction and the reaction proceeds vigorously giving polymeric products. Simple phenol[17] on chloromethylation gave a dichloromethyl dioxan derivative. A suitable device for getting around the difficulty of the formation of resinous products is to convert the phenols into esters by treatment with ethyl carbonate[18]. The activating influence of the hydroxy groups may be sufficiently moderated by deactivating groups such as nitro,carboxy or acetyl to make a smooth reaction possible. While o-chlorophenol[19] (III) gives the 4-chloromethyl derivative (IV), p-chlorophenol[20] (V) gives the dioxan derivative (VI).

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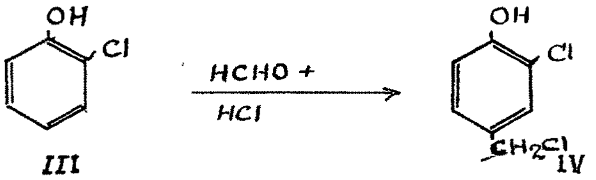
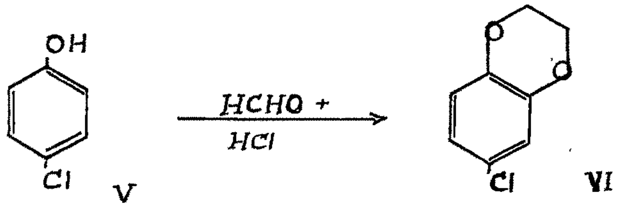
12. Paolo Da Re and Lucia Verlicchi., Ann.Chim(Rome), 46, 910 (1956) ; C.A., 51, 6618(1957).
13. Jacques Delobella., Marcel Fetizon and Gills Moreau., Compt.rend., 251, 1136 (1960) ; C.A., 55, 4445 (1961).
14. Roberto,Trave.Gazz.Chim it al., 80, 502 (1950) ; C.A., 45, 7047(1951).
15. Idem. Ibid., 81, 773 (1951) ; C.A., 46, 8048(1952).
16. Wagner., J.Am.Chem.Soc., 55, 724 (1933).
17. Fr.Pat. 695602 (1930) ; Brit.Pat. 347887 (1931).
18. Sommelet et.al. Compt.rend., 197, 256 (1933); 198, 2256 (1934).
19. Buchler, Brown, Holbert, Fulmer and Parker., J.Org.Chem. 6, 902 (1941).





Nitrophenols[21] and Cresols[22] and hydroxy benzoic acids[23] give good results and in all the cases the chloromethyl group goes to the ortho or para position with respect to the hydroxyl group. Polyhydric phenols have not been successfully chloromethylated so far. Attempts to chloromethylate resorcinol and hydroquinone met with failure.

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[20] Buchler, Bass, Darling and Lubs., J.Am.Chem.Soc., 62, 890 (1940).

[21] Buchler, Kirchner and Diebel., Org.Synth., 20, 59 (1940).

[22] I.G.Farbenindustrie. Fr.Pat., 695602 (1930).

[23] F.Bayer and Company., Ger.Pat., 113723 (1900).

Phenol ethers react smoothly. Phenol ethers containing other groups such as aldehyde, acetyl, nitro etc. also react in a satisfactory manner. Thus m-nitroanisol[24], o-ethoxynitrobenzene[25] and p-alkoxy acetophenone[26] give chloromethyl derivatives in good yields.

Mudzhoyan and Aroyan[27] studied the effects of the alkoxy groups in chloromethylation. They chloromethylated anisole, phenetole, isopropyloxy benzene and butyloxybenzene and they found that the yield decreases according to the bulk of the group. While they could isolate the dichloromethyl derivative of anisole in 90% yield,the butyloxy benzene gave only 48% dichloromethyl derivative. Study of Profft and Drux[26] on chloromethylation of alkoxy benzenes also confirm the same conclusion. While they could get the monochloromethyl derivative of the phenetole in 71% yield the amyloxy benzene gave only 59% monochloromethyl derivative.

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[24] Masao Wakae and Kenzokonishi., Yuki Gosei Kagaku Kyokaishi., 17, 697 (1959) ; C.A., 54, 2220 (1960).

[25] Masao Wakae, You Kukui and Konishi., Osaka Furitsu Kogyo-Shoreikan Hokoku., 21, 38 (1959) ; C.A., 54, 10921 (1960).

[26] Profft and Drux., J.Prakt.Chem., (4) 4, 236 (1957) ; C.A., 51, 12037 (1957).

[27] Mndzhoyan and Aroyan., Izvest.Akad. Nauk Armyan.S.S.R., Scr.Khim.Nauk., 10, 203 (1957) ; C.A., 52, 7194 (1958).

Aromatic compounds with more than one ether group react vigorously as expected. Several alkoxy derivatives of hydroquinone[28] were chloromethylated and the mono as well as the dichloromethyl derivatives were isolated. However, the dimethyl ethers of resorcinol and catechol did not give pure products on chloromethylation. Negative groups in the polyalkoxy benzenes retard the reaction considerably giving rise to chloromethyl derivatives in a **satisfactory** manner. For example, 2-bromo-4,5-dimethoxy benzylchloride was obtained from 3,4-dimethoxy bromobenzene[29].

Very little work has been done on the chloromethylation of biphenyl derivatives. Simple biphenyl[30] has been chloromethylated, and the mono and dichloromethyl derivatives have been obtained. But no work has been reported on free hydroxybiphenyl derivatives. Quelet and Matarrasso[31] successfully chloromethylated 3,3'-dimethoxy-biphenyl and 3,3',4,4'-tetramethoxybiphenyl and obtained the 6,6'-dichloromethyl derivatives in 80-90 % yield. They found that if the chloromethylation was carried out in acetic acid no pure product was obtained but when dioxan was used,

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[28] Melnikov and Prilutskaya., Vilniaus Univ. Mokslo Darbai., 7, 205 (1957) ; C.A., 54, 10929 (1960).

[29] Raymond Quelet., Bull.Soc.Chim.France., No. 10.C. 46-8 (1953).

[30] Braun, Irmish and Nelles., Ber., 66, 1471 (1933).

[31] Raymond Quelet and Elizabeth Matarrasso., Compt.rend. 242, 918 (1956) ; C.A., 50, 15476 (1956).

the dichloromethyl derivative was formed in good yield. No other chloromethylation of an alkoxybiphenyl derivative appears to have been reported so far.

<u>Mechanism</u> : The previous reports[32,33] on the relative rate measurements for the chloromethylation of aromatic hydrocarbons showed that the reaction appeared to involve an electrophillic attack on the aromatic nucleus. It seems to mean that the attacking species in the rate determing step is either $\overset{+}{C}H_2Cl$ or $\overset{+}{C}H_2OH$. But there is no evidence to decide which is the more probable one. Packer and Vaughan[34] suggested a mechanism similar to that of Friedel-Crafts acylation reaction when a catalyst such as zinc chloride is used. But they have suggested another mechanism in the absence of a catalyst and when chloromethyl ether or dichloromethyl ether is used in place of formaldehyde. Under these conditions the first step may be ionisation of the protonated ether to give the strongly electrophillic chloromethyl cation which would then substitute in the benzene molecule ; or if such ionisation does not occur, attack may be by the polarised protonated chloro ether, the carbon atom of the methylene group having a partial positive charge as a

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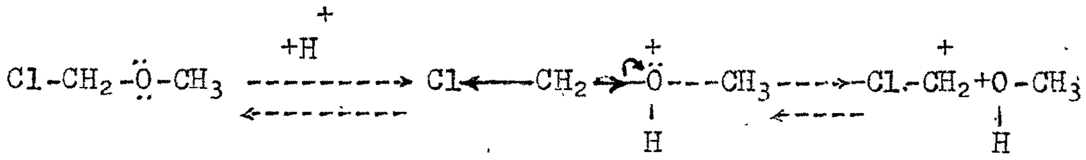
[32] Vavon, Bolle and Calin., Bull.Soc.Chim.France., (5) <u>6</u>, 1025 (1939).

[33] Szmant and Dudek., J.Am.Chem.Soc., <u>71</u>, 3763 (1949).

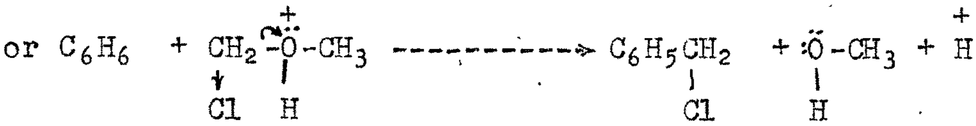
[34] Organic Chemistry By Packer and Vaughan (Oxford Press) P. 535-36.

result of the inductive effects of the chlorine and of the positive oxygen atoms.



$$Cl-CH_2-\ddot{O}-CH_3 \overset{+H^+}{\rightleftharpoons} Cl\longleftarrow CH_2 \rightarrow \underset{H}{\overset{+}{\ddot{O}}}---CH_3 \rightleftharpoons Cl-CH_2+\underset{H}{\overset{+}{O}}-CH_3$$

$$C_6H_6 + \overset{+}{C}H_2Cl \longrightarrow C_6H_5-CH_2Cl + \overset{+}{H}$$



$$\text{or } C_6H_6 + \underset{Cl}{CH_2}-\underset{H}{\overset{+}{\ddot{O}}}-CH_3 \longrightarrow C_6H_5\underset{Cl}{CH_2} + :\underset{H}{\ddot{O}}-CH_3 + \overset{+}{H}$$

Yoshiro Ogata and Masaya Okano[35] studied the rate of the chloromethylation of mesitylene in acetic acid containing 10 volumesof water at 60° by estimating the consumed formaldehyde iodometrically and the consumed chloride ion. It was confirmed that mesityl carbinol and mesityl methyl chloride are in mobile equilibrium under the experimental conditions. Their results are consistent with a mechanism which involves a rate determining attack of protonated formaldehyde on mesitylene followed by the rapid reversible formation of the chloromethyl compound. In short they gave the mechanism as follows.

$$CH_2O + \overset{+}{H} \rightleftharpoons \overset{+}{C}H_2OH \text{ (mobile)}$$

$$Ar\ H + \overset{+}{C}H_2OH \longrightarrow Ar\ CH_2OH + \overset{+}{H} \text{ (slow)}$$

$$Ar\ CH_2OH + HCl \rightleftharpoons Ar\ CH_2Cl + H_2O \text{ (mobile)}$$

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35. Ogata and Oksno., J.Am.Chem.Soc., 78, 5423 (1956).

The postulated mechanism explains the effect of the substituents on the rate ; i.e. an electron releasing group in an aromatic nucleus facilitates the electrophillic attack by $\overset{+}{C}H_2OH$ while with an electron withdrawing group the reverse is true. The formation of diaryl methane or methylene bridged resin as by products is also explicable in terms of this scheme. According to them the attack of $\overset{+}{C}H_2Cl$ is improbable.

The role of catalysts, solvents and temperature in chloromethylation : A variety of procedures have been utilised for chloromethylation. The formaldehyde may be added as formalin (40 %) or it may be generated in the reaction mixture by depolymerisation of paraformaldehyde. Paraformaldehyde is preferred as it can be weighed accurately and is most suitable whenever anhydrous conditions are to be maintained. Instead of formaldehyde, other aldehydes such as paraldehyde[36] and chloroacetaldehyde[37] can be used depending upon the kind of group which is to be introduced.

A catalyst may or may not be required. Catalysts which have been reported to be very useful are zinc chloride and acetic acid. The latter also acts as a solvent. Blanc[38] introduced the chloromethyl group into aromatic hydrocarbons

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[36] Sommelet and Marszak., Fr.Patent., 787655 (1935) ; C.A., 30, 1185 (1936).

[37] Quelet and Allard., Bull.Soc.Chim., (5) 7, 215 (1949).

[38] Blanc., Bull.Soc.Chim., 33, 312 (1923).

by means of a mixture of formalin or paraformaldehyde and hydrochloric acid in the presence of zinc chloride. Darzens and Levy[39] in their synthesis of derivatives of naphthalene employed paraformaldehyde and hydrochloric acid in acetic acid solution. Many other catalysts such as sulphuric acid, phosphoric acid and aluminium chloride are also used, though these catalysts tend to favour the formation of diarylmethane derivatives. Fieser and Seligman[40] found that the yield of the chloromethyl product was increased three fold when a little anhydrous aluminium chloride was used with fused zinc chloride in the chloromethylation of p-bromotoluene. Sommelet[41] used stannic chloride with success with compounds which normally resist chloromethylation. In the chloromethylation of 5-nitrosalicylaldehyde it is found that unless a large amount of anhydrous aluminium chloride is used as a catalyst no chloromethylation takes place[42].

For liquids no diluent is required. Sometimes excess of the liquid compound itself acts as the solvent. For solids which do not dissolve in hydrochloric acid a solvent is used. Acetic acid, carbon disulphide, ethylene dichloride and dioxan are used as solvents. In the chloromethylation of

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[39] Darzens and Levy., Compt.rend., 202, 313 (1923).

[40] Feiser and Seligman., J.Chem.Soc., 57, 942 (1937).

[41] Sommelet., Compt.rend., 157, 1443 (1913).

[42] Taylor and Davis., J.Org.Chem., 28, 1713 (1963).

3,3'-dimethoxy biphenyl and 3,3',4,4'-tetramethoxybiphenyl only dioxan gives the 6,6'-dichloromethyl derivative while acetic acid gave an unchlorinated product[31].

Rate of reaction also depends upon the temperature of reaction. A variety of reaction temperatures are used depending upon the type of compound to be chloromethylated. Highly reactive compounds react at room temperature or even at 0°C while temperatures of 60-70° are much favoured for less reactive compounds. Sometimes reactions are carried out at 140° and under pressure.

Chloromethylation may be accomplished by the use of chloromethyl ether (CH_3OCH_2Cl) or dichloromethyl ether ($CH_2Cl\text{-}O\text{-}CH_2Cl$). The reaction often proceeds smoothly in the absence of a catalyst. Stannic chloride may be used as catalyst with less reactive compounds. Carbon disulphide or other indifferent solvents may be used as diluents. The chloromethyl ether is preferably used in excess and the reaction proceeds without hydrochloric acid and without any catalyst.

Large number of aromatic hydroxy compounds and their alkyl ethers have been chloromethylated ; but not much work appears to have been done on the chloromethylation of aromatic polyhydroxy compounds. This may be due to the extreme reactive nature of these compounds giving rise to polymeric products instead of the expected chloromethyl products. It is known, however, that a negative group in the nucleus retards the reaction and affords the expected products. Therefore it was thought of interest to study the chloromethylation of some aromatic polyhydroxy compounds and their alkyl ethers with or without negative substituent in the nucleus. The present work deals with the chloromethylation of resacetophenone, methyl β-resorcylate, 4-nitro resorcinol, 2-nitro resorcinol, 4,4'-dihydroxy biphenyl and 2,2'-dimethoxy biphenyl and their alkyl ethers with different molecular proportions of paraformaldehyde under different conditions.

Chloromethylation of resacetophenone and its dimethylether : Resacetophenone on chloromethylation with one or more moles of paraformaldehyde in either acetic acid or dioxan at room temperature did not give a pure product. However, its dimethylether (VII) on chloromethylation with 1.2 moles of paraformaldehyde in dioxan at room temperature afforded a monochloromethyl derivative which on oxidation with alkaline potassium permanganate afforded the known 4,6-dimethoxy isophthalic acid[43] (IX). It was identical with the acid obtained by oxidising the known methyl 2,4-dimethoxy-5-acetyl benzoate[44] (X) with alkaline potassium permanganate. 2,4-Dimethoxy-5-chloromethyl acetophenone (VIII) structure has therefore been assigned to the chloromethyl derivative. On heating with glacial acetic acid in the presence of fused sodium acetate the chloromethyl derivative (VIII) gave 2,4-dimethoxy-5-acetoxymethyl acetophenone (XI) and when heated with hexamine in chloroform it gave 2,4-dimethoxy-5-formyl acetophenone (XII) which was characterised by the formation of the di-2,4-dinitrophenylhydrazone derivative.

Along with the chloromethyl derivative a chlorine free compound was also isolated, to which the 5,5'-methylene bis(2,4-dimethoxy acetophenone)(XIII) structure is

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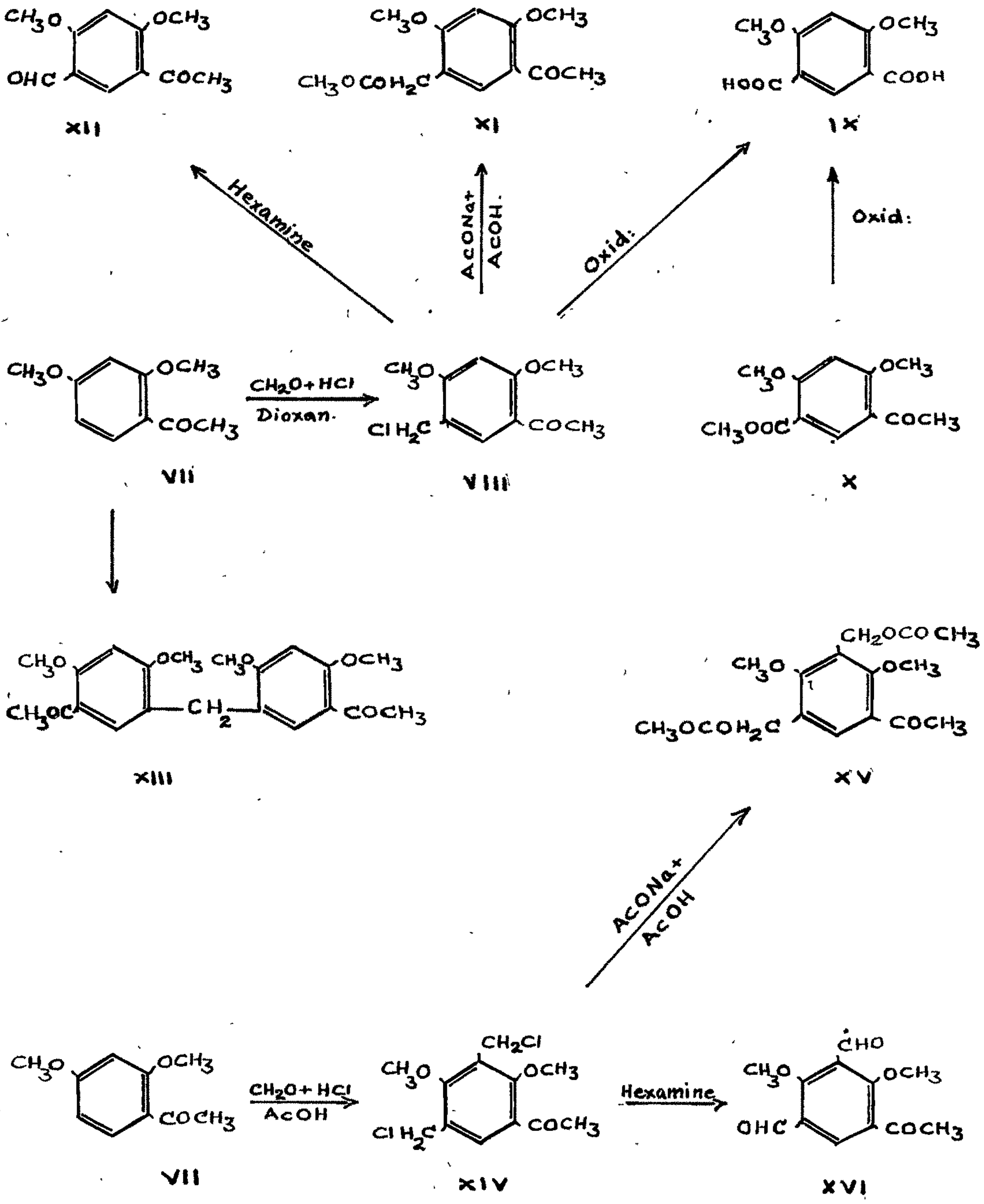
[43] Eijkman et al., Chem.Weekblad, 2, 59, 79 (1905).

[44] Trivedi and Sethna., J.Ind.Chem.Soc., 28, 245 (1951).


CH3O
OCH3
OHC
COCH3
XII
CH3O
OCH3
CH3OCOH2C
COCH3
XI
CH3O
OCH3
HOOC
COOH
IX
Hexamine
AcONa+
AcOH.
Oxid:
Oxid:
CH3O
OCH3
COCH3
VII
CH2O+HCl
Dioxan.
CH3O
OCH3
ClH2C
COCH3
VIII
CH3O
OCH3
CH3OOC
COCH3
X
CH3O
OCH3
CH3O
OCH3
CH3OC
CH2
COCH3
XIII
CH2OCOCH3
CH3O
OCH3
CH3OCOH2C
COCH3
XV
AcONa+
AcOH
CH3O
OCH3
COCH3
VII
CH2O+HCl
AcOH
CH2Cl
CH3O
OCH3
ClH2C
COCH3
XIV
Hexamine
CHO
CH3O
OCH3
OHC
COCH3
XVI

tentatively assigned on the basis of the analysis and the formation of a di-2,4-dinitrophenylhydrazone derivative.

2,4-Dimethoxy acetophenone (VII) on chloromethylation with excess of paraformaldehyde in glacial acetic acid at room temperature gave a dichloro methyl derivative in 71 % yield to which the 2,4-dimethoxy-3,5-dichloromethyl acetophenone (XIV) structure has been assigned which on treatment with glacial acetic acid and fused sodium acetate gave the 2,4-dimethoxy-3,5-di-acetoxymethyl acetophenone (XV). On Sommelet reaction the above dichloromethyl derivative gave a product to which the 3,5-diformyl structure (XVI) has been tentatively assigned. It gave only a di-2,4-dinitrophenylhydrazone derivative. Probably the formyl group in between the two methoxy groups does not react because of steric hindrance.

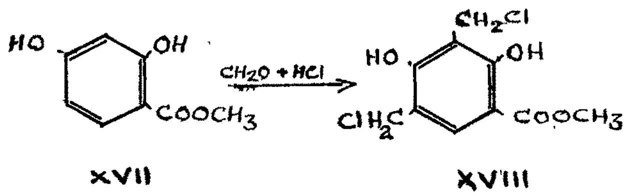
Chloromethylation of β-resorcylic acid; methyl β-resorcylate and methyl-2,4-dimethoxy benzoate : B-Resorcylic acid on chloromethylation with one mole or excess of paraformaldehyde and hydrogen chloride gas in glacial acetic acid or dioxan at room temperature gave a substance from which no pure chloromethyl derivative could be isolated. Methyl-B-resorcylate (XVII) on chloromethylation with one mole of paraformaldehyde did not give any pure product but with excess of paraformaldehyde in dioxan, below 20°, it gave a dichloromethyl derivative to which methyl 2,4-dihydroxy-3,5-dichloromethylbenzoate (XVIII) structure has been assigned as there is no other possibility.

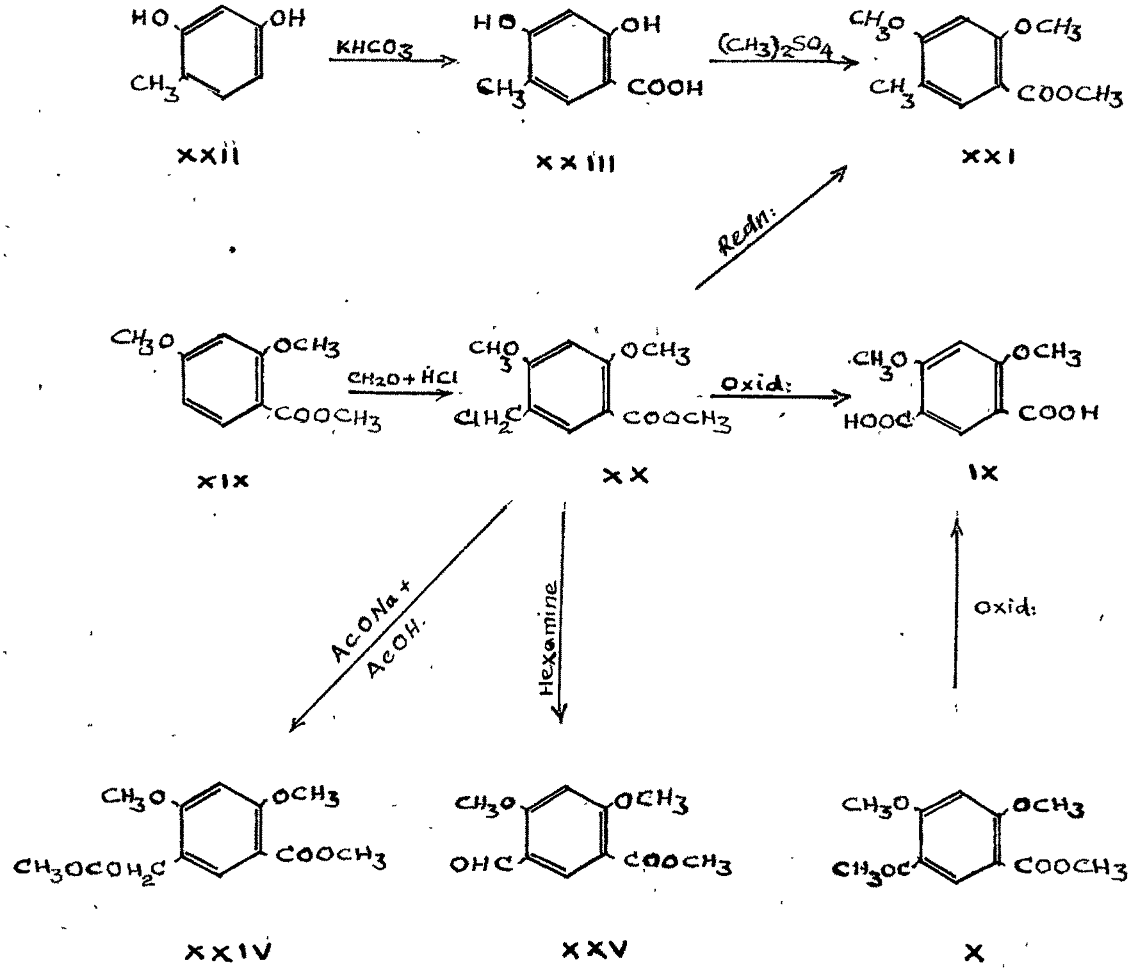
Methyl-2,4-dimethoxy benzoate (XIX) on

chloromethylation with one mole or excess of paraformaldehyde in glacial acetic acid at 70-80° gave a monochloromethyl derivative which on oxidation with alkaline potassium permanganate gave a dicarboxylic acid (IX) which was identical with the one obtained on oxidation of methyl 2,4-dimethoxy-5-acetyl benzoate[44] (X) with alkaline potassium permanganate. Methyl-2,4-dimethoxy-5-chloromethyl benzoate (XX) structure has therefore been assigned to the product.

Methyl-2,4-dimethoxy-5-chloromethyl benzoate (XX) on reduction with zinc and hydrochloric acid in dioxan gave a product which was found to be identical on direct comparison with the product obtained when 4-methyl resorcinol (XXII) was carboxylated with potassium bicarbonate and the resulting acid (XXIII) was methylated and esterified with dimethyl sulphate and anhydrous potassium carbonate in acetone. The reduction product is therefore methyl-2,4-dimethoxy-5-methyl benzoate (XXI).

The acetoxymethyl derivative (XXIV) of the above chloromethyl derivative was prepared by heating the chloromethyl derivative with glacial acetic acid and fused sodium acetate. When the chloromethyl derivative (XX) was refluxed with hexamethylene tetramine in chloroform and the complex hydrolysed with dilute acetic acid, the 5-formyl derivative (XXV) was obtained which was characterised by the formation of its 2,4-dinitrophenyl hydrazone derivative.


XVII
CH2O + HCl
XVIII


XXII
KHCO3
XXIII
(CH3)2SO4
XXI
Redn:
XIX
CH2O + HCl
XX
Oxid:
IX
AcONa + AcOH.
Hexamine
Oxid:
XXIV
XXV
X

Chloromethylation of 4-nitroresorcinol and its dimethyl ether : Chloromethylation of 4-nitroresorcinol with one mole or excess of paraformaldehyde and hydrogen chloride gas in dioxan or acetic acid at room temperature did not give a pure product. Its dimethyl ether (XXVI), however, gave a monochloromethyl derivative in 89 % yield with one mole or excess of paraformaldehyde and hydrogen chloride gas in glacial acetic acid at room temperature. The chloromethyl derivative on oxidation with alkaline potassium permanganate afforded 2,4-dimethoxy-5-nitrobenzoic acid (XXX) as seen by direct comparison with the acid prepared by the nitration of β-resorcyclic acid (XXXII) and simultaneous methylation and esterification of the nitro derivative[45] (XXXIII) to the methyl 2,4-dimethoxy-5-nitrobenzoate (XXXI) and subsequent hydrolysis of the ester. 2,4-Dimethoxy-5-chloromethyl nitrobenzene (XXVII) structure has therefore been assigned to the chloromethyl derivative.

The above chloromethyl derivative (XXVII) on reduction with tin and hydrochloric acid afforded 2,4-dimethoxy-5-methylaniline (XXXVIII). It was found to be identical with the product obtained on nitration of 2,4-dimethoxytoluene (XXXIX) in glacial acetic acid below 5°, and the reduction of the mononitro derivative (XL) obtained.

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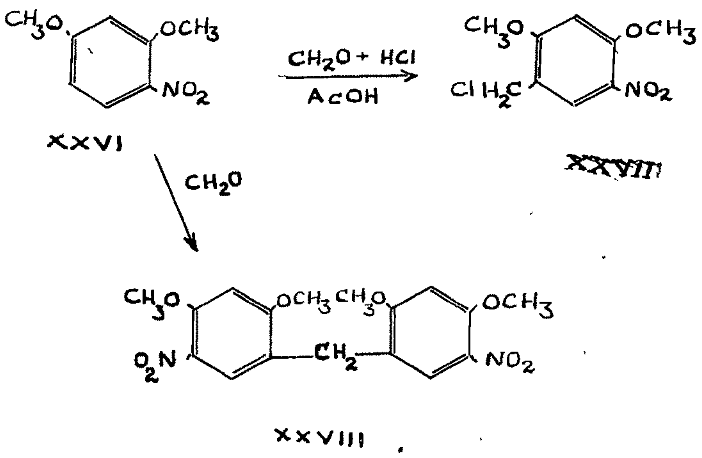
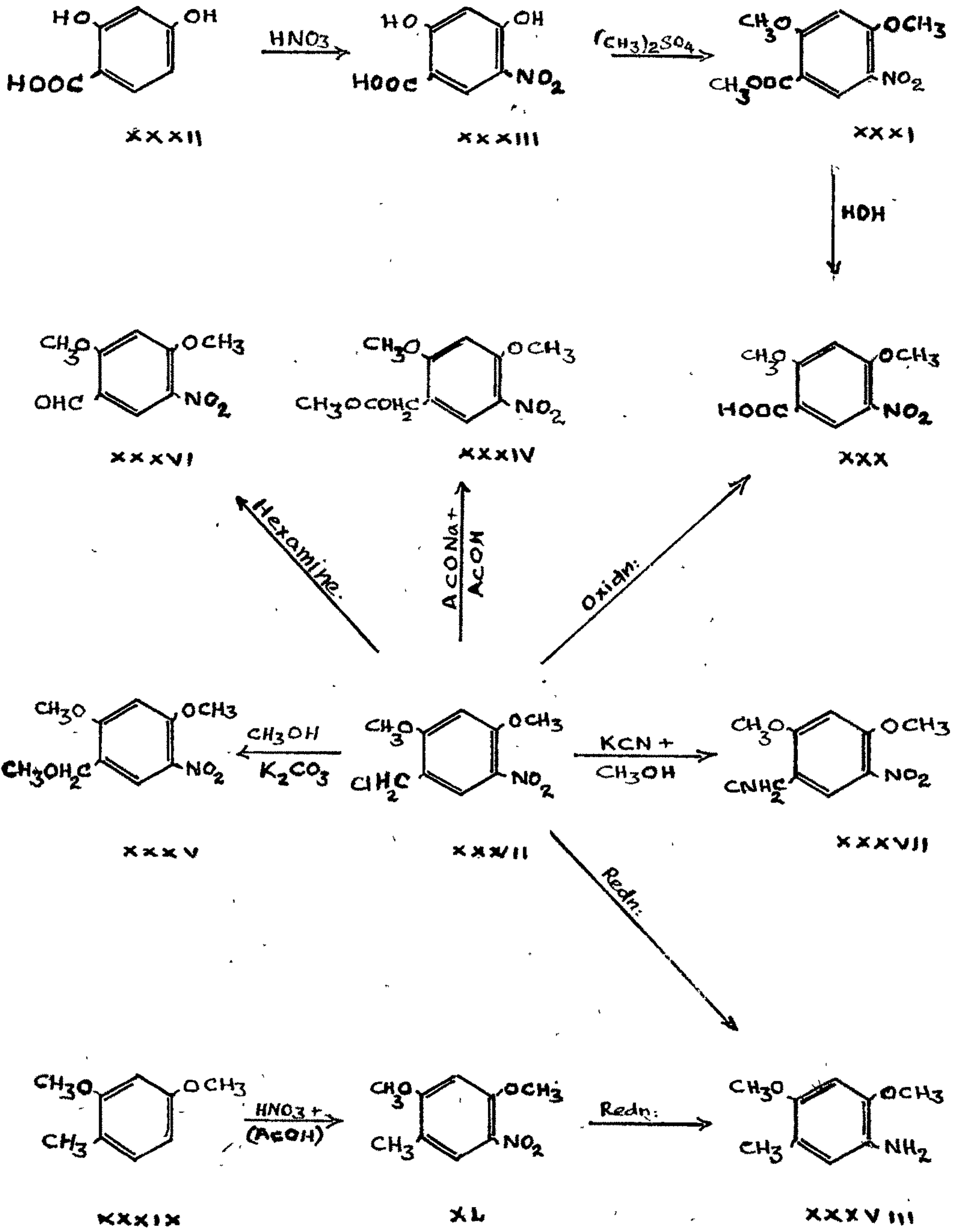
45. Parekh and Shah., J.Univ.Bombay., IIA, Part 5, 101 (1943).

Along with the chloromethyl derivative a chlorine free compound was also isolated. Its analysis indicated that it might be methylene bis(2,4-dimethoxy nitrobenzene) (XXVIII).

The chloromethyl derivative with glacial acetic acid and fused sodium acetate gave 2,4-dimethoxy-5-acetoxy-methyl nitrobenzene(XXXIV). Methoxy methyl derivative(XXXVI) was prepared by refluxing the chloromethyl derivative with absolute methanol and anhydrous potassium carbonate. The cyanomethyl derivative (XXXVII) was prepared by refluxing the chloromethyl derivative with potassium cyanide and methyl alcohol. The chloromethyl derivative on Sommelet reaction gave 2,4-dimethoxy-5-formyl nitrobenzene (XXXIVI). This was characterised by the formation of a 2,4-dinitrophenylhydrazone.

Further chloromethylation of 2,4-dimethoxy-5-chloromethyl nitrobenzene with excess of paraformaldehyde at higher temperature did not succeed.




HO
OH
HOOC
XXXII
HNO3
HO
OH
HOOC
NO2
XXXIII
(CH3)2SO4
CH3O
OCH3
CH3OOC
NO2
XXXI
HOH
CH3O
OCH3
OHC
NO2
XXXVI
CH3O
OCH3
CH3OCOH2C
NO2
XXXIV
CH3O
OCH3
HOOC
NO2
XXX
Hexamine.
AcONa+
AcOH
Oxidn:
CH3O
OCH3
CH3OH2C
NO2
XXXV
CH3OH
K2CO3
CH3O
OCH3
ClH2C
NO2
XXXII
KCN +
CH3OH
CH3O
OCH3
CNH2C
NO2
XXXVII
Redn:
CH3O
OCH3
CH3
XXXIX
HNO3 +
(AcOH)
CH3O
OCH3
CH3
NO2
XL
Redn:
CH3O
OCH3
CH3
NH2
XXXVIII

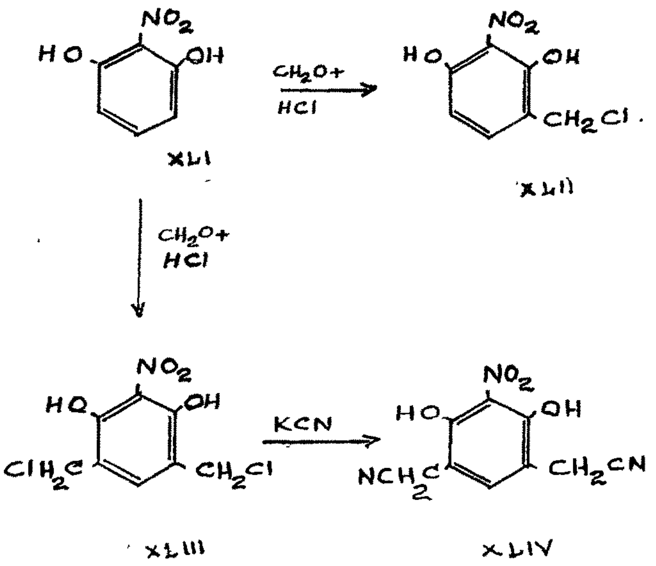
Chloromethylation of 2-nitroresorcinol and its dimethyl ether : When 2-nitroresorcinol (XLI) was chloromethylated with one mole of paraformaldehyde in minimum quantity of glacial acetic acid at room temperature a monochloro methyl derivative was obtained which could only be the 2,6-dihydroxy-3-chloromethylnitrobenzene(XLII). Sommelet reaction on this chloromethyl derivative gave only an unworkable mass.

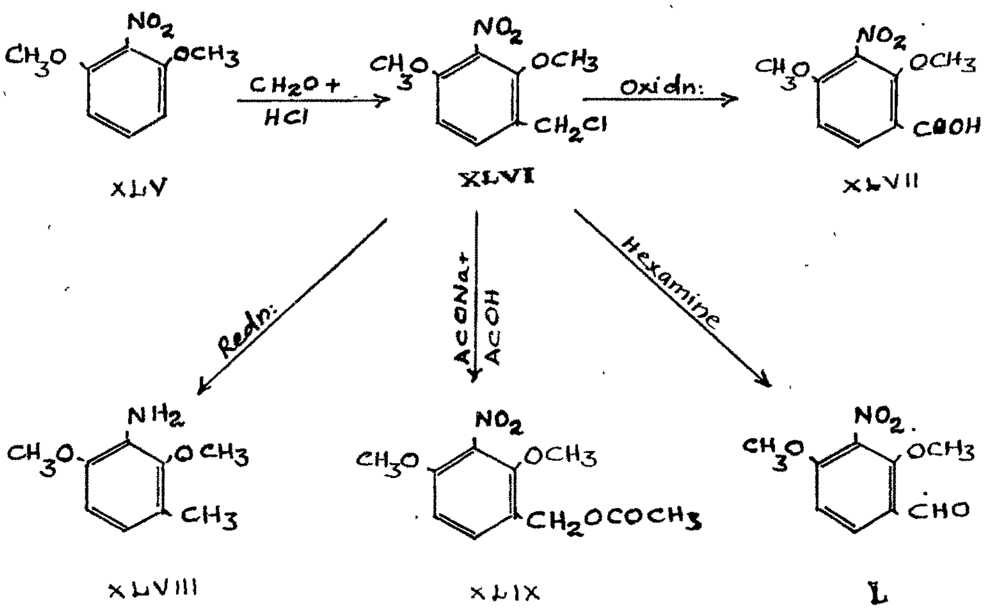
With excess of paraformaldehyde in minimum quantity of glacial acetic acid at room temperature 2-nitroresorcinol (XLI) gave a dichloromethyl derivative to which 2,6-dihydroxy-3,5-dichloromethyl nitrobenzene structure(XLIII) has been assigned since there is no other possibility. The dichloromethyl derivative on treatment with aqueous potassium cyanide gave a dicyanomethyl derivative (XLIV).

Sommelet reaction on the above dichloromethyl derivative (XLIII) gave only a polymeric product. Attempts to reduce the chloromethyl derivative also did not succeed.

2,6-Dimethoxy nitrobenzene (XLV) on chloromethylation in dioxan gave the original product. However, it gave a monochloromethyl derivative on chloromethylation with excess of paraformaldehyde in glacial acetic acid at 60-70° to which 2,6-dimethoxy-3-chloromethyl nitrobenzene (XLVI) structure has been assigned.

The acetoxymethyl derivative (XLIX) of the chloromethyl product (XLVI) was prepared in the usual way. When the chloromethyl derivative (XLVI) was oxidised with alkaline potassium permanganate it afforded 2,4-dimethoxy-


XLI
CH2O+
HCl
XLII
CH2O+
HCl
XLIII
KCN
XLIV

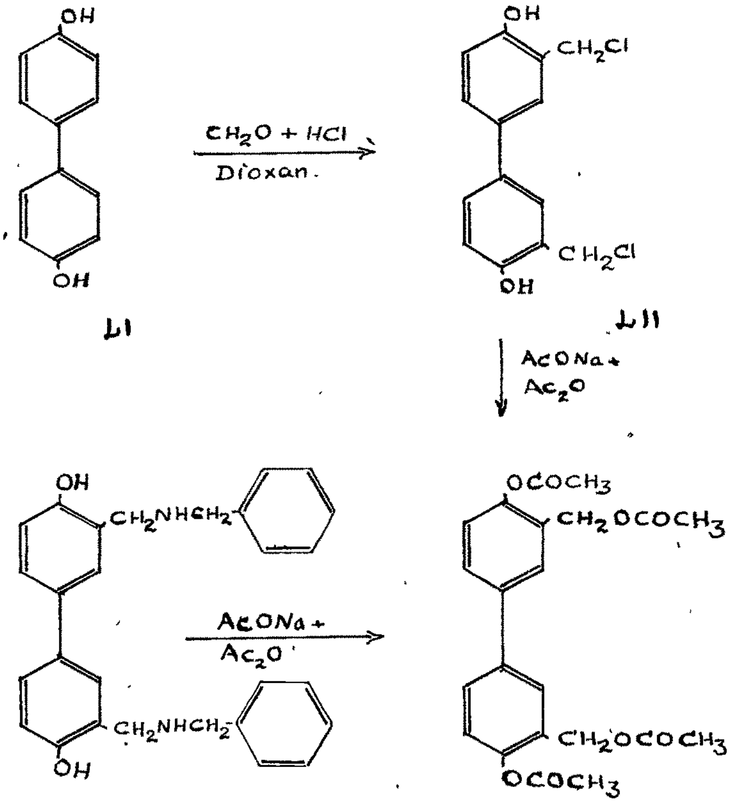

XLV
CH2O +
HCl
XLVI
Oxidn:
XLVII
Redn:
AcONa+
AcOH
Hexamine
XLVIII
XLIX
L

3-nitrobenzoic acid (XLVII) and on reduction with tin and hydrochloric acid it gave 2,6-dimethoxy-3-methyl aniline (XLVIII). Sommelet reaction on (XLVI) afforded the 2,6-dimethoxy-3-formyl nitrobenzene (L) which was characterised by the formation of the 2,4-dinitrophenyl hydrazone.

Further chloromethylation of the 3-chloromethyl derivative did not succeed.

Chloromethylation of 4,4'-dihydroxy biphenyl and its dimethyl ether : 4,4'-Dihydroxy biphenyl (LI) on chloromethylation with two or more moles of paraformaldehyde in minimum quantity of dioxan at room temperature gave a dichloromethyl derivative to which 4,4'-dihydroxy-3,3'-dichloromethyl biphenyl(LII) structure has been assigned,, since on treatment with sodium acetate and acetic anhydride it gave 4,4'-diacetoxy-3,3'-diacetoxymethyl biphenyl(LIIa) which was obtained from 4,4'-dihydroxy-3,3'-di-benzylaminomethyl biphenyl LIIb on treatment with sodium acetate and acetic anhydride (p.159). Reduction of the above dichloromethyl derivative did not succeed. Sommelet reaction on (LI) gave an unworkable mass.

4,4'-Dimethoxy biphenyl (LIII) on chloromethylation with excess of paraformaldehyde in 90 % acetic acid at 80-90° gave a dichloromethyl derivative in almost quantitative yield. The above dichloromethyl derivative on oxidation with potassium permanganate in glacial acetic acid gave a dicarboxylic acid which was identified as 4,4'-dimethoxy biphenyl-3,3'-dicarboxylic acid(LV).

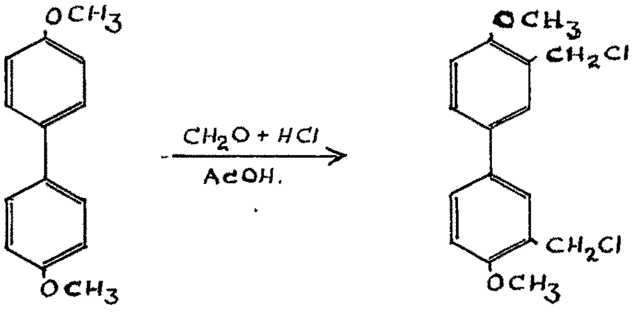


LI

LII

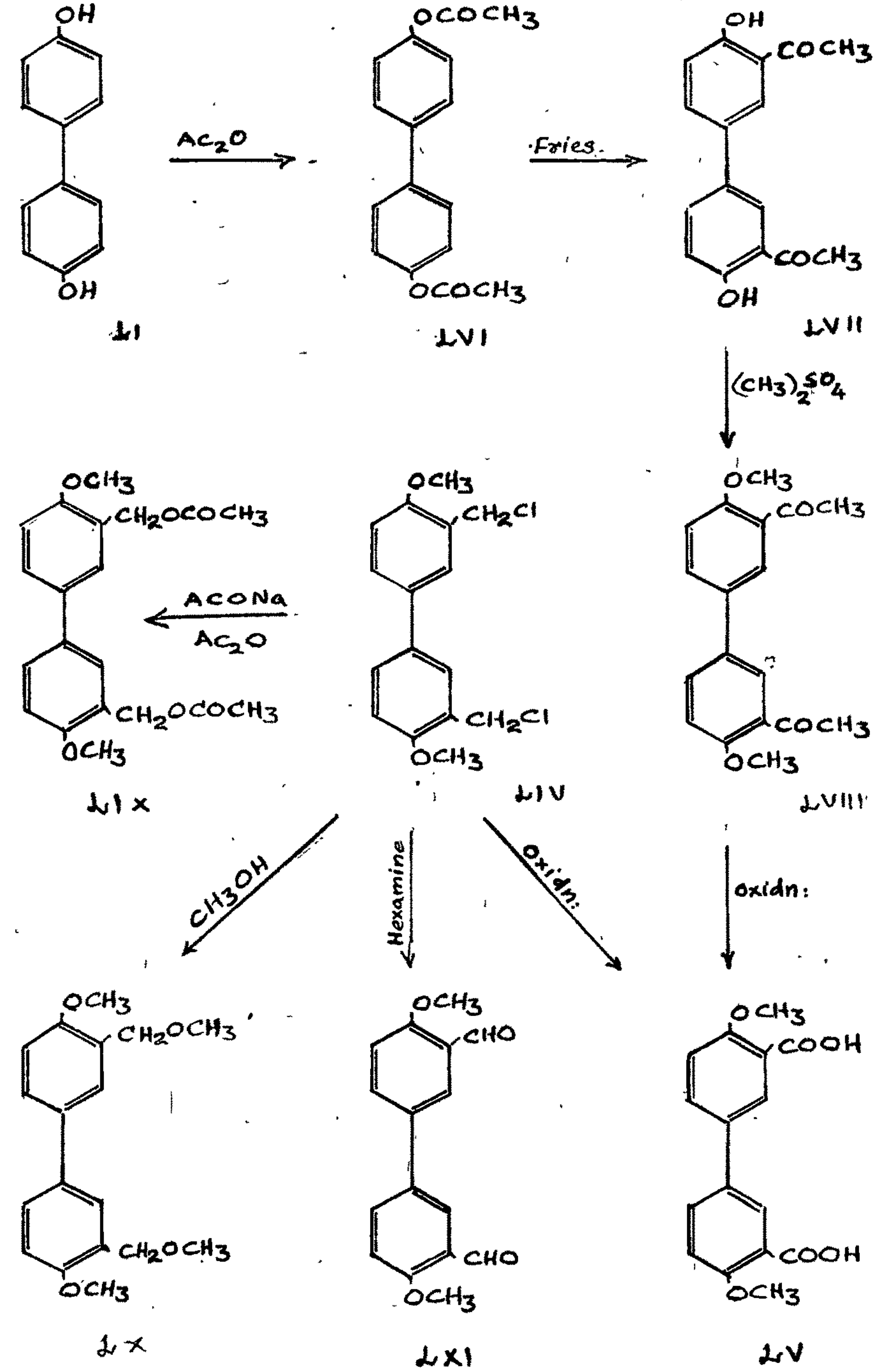
LIIb

LIIa



LIII

LIV


OH
OH
LI
Ac_2O
$OCOCH_3$
$OCOCH_3$
LVI
Fries.
OH
$COCH_3$
$COCH_3$
OH
LVII
$(CH_3)_2SO_4$
OCH_3
CH_2OCOCH_3
CH_2OCOCH_3
OCH_3
LIX
AcONa
Ac_2O
OCH_3
CH_2Cl
CH_2Cl
OCH_3
LIV
OCH_3
$COCH_3$
$COCH_3$
OCH_3
LVIII
CH_3OH
Hexamine
Oxidn.
oxidn.
OCH_3
CH_2OCH_3
CH_2OCH_3
OCH_3
LX
OCH_3
CHO
CHO
OCH_3
LXI
OCH_3
COOH
COOH
OCH_3
LV

It was identical with the acid prepared as follows: 4,4'-Dihydroxy biphenyl (LI) was converted into the diacetoxy derivative (LVI) with acetic anhydride and this was then subjected to Fries migration when 4,4'-dihydroxy-3,3'-diacetyl biphenyl[46] (LVII) was obtained which was methylated with dimethylsulphate to 4,4'-dimethoxy-3,3'-diacetylbiphenyl (LVIII) and oxidised with alkaline potassium permanganate to the acid (LV). Mixed m.p. with the oxidation product of the dichloromethyl derivative was not depressed. Therefore 4,4'-dimethoxy-3,3'-dichloromethyl biphenyl (LIV) structure has been assigned to the product. Its acetoxymethyl (LIX) and methoxymethyl (LX) derivatives were prepared in the usual way. Sommelet reaction on the chloromethyl derivative (LIV) gave the 4,4'-dimethoxy-3,3'-diformyl biphenyl (LXI) which was characterised by the formation of the di-2,4-dinitrophenyl hydrazone derivative.

<u>Chloromethylation of 2,2'-dihydroxy biphenyl and its dimethyl ether</u> : Chloromethylation of 2,2'-dihydroxy biphenyl in acetic acid or dioxan at room temperature gave only a pasty mass from which no pure product could be isolated. However, 2,2'-dimethoxy biphenyl (LXII) on chloromethylation with excess of paraformaldehyde in dioxan at room temperature gave a dichloromethyl derivative which on oxidation with alkaline potassium permanganate gave an acid identical with 2,2'-dimethoxy biphenyl-5,5'-dicarboxylic acid[47] (LXIV) which was prepared for comparison

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[46] Boon-Long., J.Pharm.Assoc.Siam., 1, No.4, 5 (1948) ; C.A., 43, 5017 (1949).

[47] Gilman et al., J.Am.Chem.Soc., 62, 1963 (1940).

as follows :

p-Hydroxybenzoic acid (LXV) was iodinated with iodine and iodic acid to get the 3-iodo-4-hydroxybenzoic acid (LXVI). This on methylation with dimethyl sulphate gave methyl-3-iodo-4-methoxy benzoate[48] (LXVII). The above ester (LXVII) on Ullmann reaction gave dimethyl-2,2'-dimethoxy biphenyl-5,5'-dicarboxylate (LXVIII) which on hydrolysis gave the acid (LXIV). Gilman[47] who obtained the same acid by another method recorded the same m.p. 2,2'-dimethoxy-5,5'-dichloromethyl biphenyl (LXIII) structure has therefore been assigned to the dichloromethyl derivative.

The diacetoxymethyl (LXIX) and diformyl (LXX) derivatives were prepared in the usual way. The latter was characterised by the formation of its di-2,4-dinitrophenyl hydrazone derivative.

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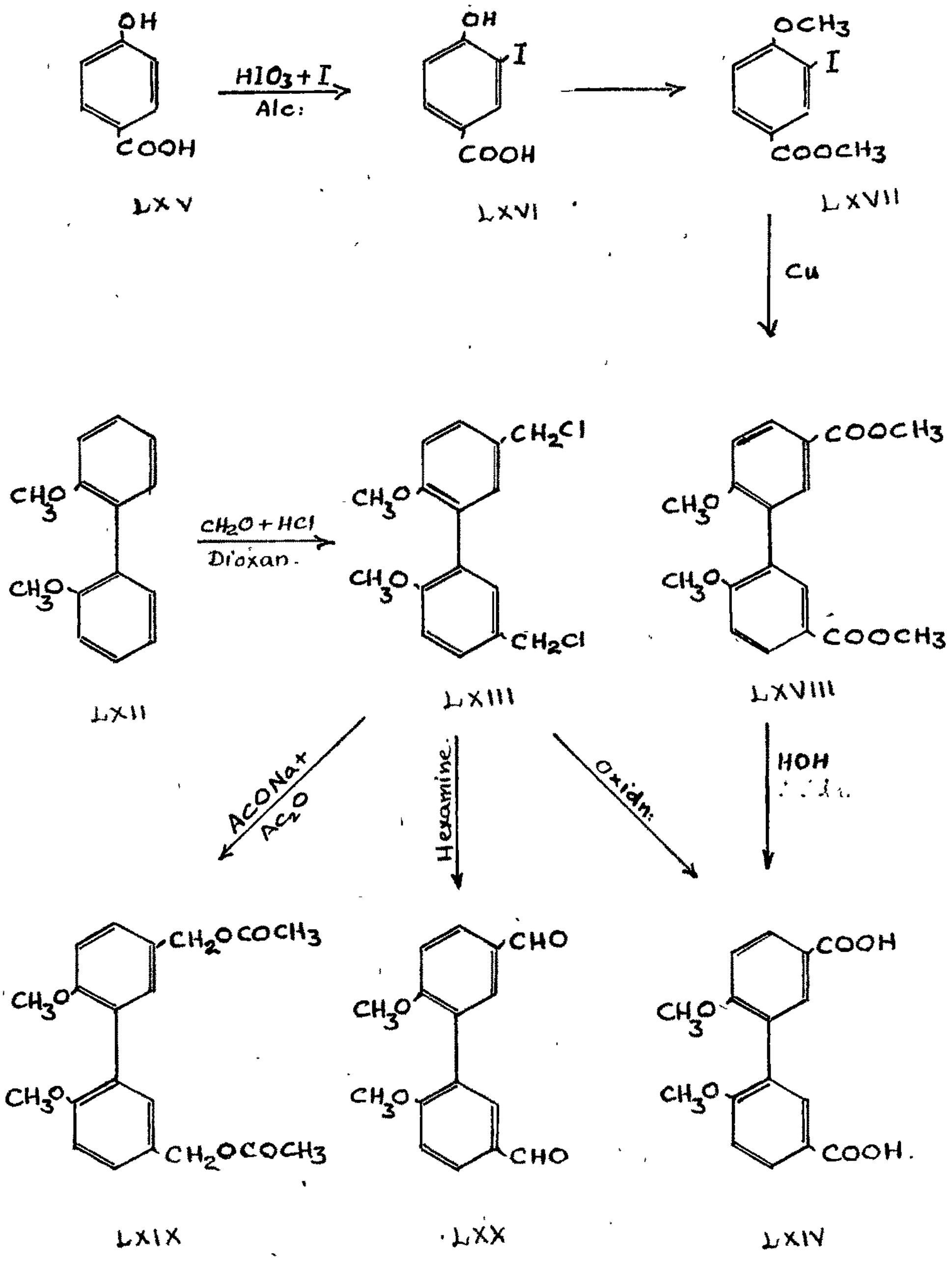
48. Nicolau., C.A., 50, 16858 (1956).


LXV
HIO3 + I
Alc:
LXVI
LXVII
Cu
LXII
CH2O + HCl
Dioxan.
LXIII
LXVIII
AcONa+
Ac2O
Hexamine.
Oxidn.
HOH
LXIX
LXX
LXIV

EXPERIMENTAL

Chloromethylation of 2,4-dimethoxy acetophenone.

2,4-Dimethoxy-5-chloromethyl acetophenone: Paraformaldehyde (1.5 g. ; 0.04 mole) was taken in dioxan (10 c.c.) and dry hydrogen chloride gas was passed to saturation. 2,4-Dimethoxy acetophenone (7.2 g. ; 0.04 mole) was then added and hydrogen chloride gas passed for further ten minutes. The mixture became slightly brownish. It was then diluted with petroleum ether (b.p. 40-60). An oily layer separated. The upper layer was removed by decantation. The product obtained on removal of the solvent was taken in benzene. Petroleum ether was then added when tarry matter separated which was removed by filtration. The clear solution on keeping in a refrigerator gave colourless needles, m.p. 130°. Yield 71 %. Along with the chloromethyl compound some polymeric product was also formed.

Analysis : 4.214 mg. of the substance gave 8.882 mg. of carbon dioxide and 2.072 mg. of water ; 8.346 mg. of the same substance gave 5.344 mg. of silver chloride.

Found : C=57.5 % ; H=5.5 % ; Cl=15.8 %.

$C_{11}H_{13}ClO_3$ requires : C=57.7 % ; H=5.7 % ; Cl=15.5 %.

5,5'-Methylene bis-(2,4-dimethoxyacetophenone): When the mixture after chloromethylation was poured into water a chlorine free product melting at 189-90° was obtained. It was crystallised from benzene.

Analysis : 4.134 mg. of the substance gave 10.208 mg. of carbon dioxide and 2.338 mg. of water.

Found : C=67.4 % ; H=6.3 %.

$C_{21}H_{24}O_6$ requires : C=67.7 % ; H=6.4 %.

2,4-Dinitrophenylhydrazone of the above bis-compound was prepared by heating a mixture of the bis-compound in alcohol and 2,4-dinitrophenylhydrazine hydrochloride in alcohol over a water bath for 30 minutes. The hydrazone was recrystallised from nitrobenzene, m.p.282°.

Analysis : 5.146 mg. of the substance gave 0.693 c.c. of nitrogen at 34°C and 751 mm. pressure.

Found : N=14.8 %.

$C_{33}H_{32}N_8O_{12}$ requires : N=15.3 %.

2,4-Dimethoxy-5-acetoxymethyl acetophenone: 2,4-Dimethoxy-5-chloromethyl acetophenone (1 g.) was heated with glacial acetic acid (5 c.c.) and fused sodium acetate (1 g.) for 2 hours on a steam bath. The reaction mixture was poured into water and the precipitate obtained crystallised from benzene-petroleum ether mixture,m.p.117°.

Analysis : 4.570 mg. of the substance gave 10.428 mg. of carbon dioxide and 2.646 mg. of water.

Found : C=62.3 % ; H=6.5 %.

$C_{13}H_{16}O_5$ requires : C=61.9 % ; H=6.3 %.

2,4-Dimethoxy-5-formyl acetophenone : The above chloromethyl derivative (1 g.) and hexamethylene tetramine (5 g.) were refluxed in chloroform on a steam bath for 2 hr. The product which separated was refluxed in acetic acid (20 % ; 50 c.c.)on a steam bath for 4 hr. On cooling, the colourless formyl derivative separated which was crystallised from benzene, m.p. 167°.

Analysis : 5.366 mg. of the substance gave 12.550 mg. of carbon dioxide and 2.928 mg. of water.

Found : C=63.8 % ; H=6.1 %.

$C_{11}H_{12}O_4$ requires : C=63.5 % ; H=5.8 %.

The di-2,4-dinitrophenyl hydrazone : Prepared as usual and crystallised from nitrobenzene gave m.p. 275-77°.

Analysis : 5.078 mg. of the substance gave 0.936 c.c. of nitrogen at 751 mm. pressure and 33°C.

Found : N=18.8 %.

$C_{23}H_{20}O_{10}N_8$ requires : N=19.4 %.

4,6-Dimethoxy isophthalic acid : 2,4-Dimethoxy-5-chloromethyl acetophenone (1 g.) was suspended in sodium hydroxide (10 % ; 25 c.c.) and potassium permanganate (3 g.) was added. The reaction mixture was heated on a steam bath for 8 hrs. The mixture was filtered and the excess of potassium permanganate was destroyed with sodium bisulphite and the filtrate was acidified. The precipitated acid was crystallised from glacial acetic acid, m.p. 266°

Analysis : 4.738 mg. of the substance gave 9.266 mg. of carbon dioxide and 2.002 mg. of water.

Found : C=53.4 % ; H=4.7 %.

$C_{10}H_{10}O_6$ requires : C=53.1 % ; H=4.4 %.

The same acid was also prepared by refluxing a mixture of 2,4-dimethoxy-5-acetyl benzoate (1 g.) potassium permanganate (3 g.) and sodium hydroxide solution (10 % ; 20 c.c.) over a wire-gauze for 4 hrs. The acid obtained on working up as usual was crystallised from glacial acetic acid. M.p. and mixed m.p. with the acid obtained on oxidation of 2,4-dimethoxy-5-chloromethyl acetophenone was 266°

2,4-Dimethoxy-3,5-dichloromethyl acetophenone : Dry hydrogen chloride was passed through paraformaldehyde (3 g. ; 0.01 mole) in glacial acetic acid (10 c.c.) at room temperature till saturation. The above mixture was added to 2,4-dimethoxy acetophenone (1.8 g. ; 0.01 mole) with stirring. 2,4-Dimethoxy acetophenone dissolved in the above mixture and the solution became intense red. On keeping overnight the dichloromethyl derivative separated out in long stout needles. It was filtered, washed with a little carbon tetrachloride and crystallised from benzene-petroleum ether mixture, m.p. 110°. Yield 71 %. The filtrate on pouring in water gave a chlorine free compound. It has not been investigated further.

Analysis : 4.132 mg. of the substance gave 7.874 mg. of carbon dioxide and 1.966 mg. of water. 12.106 mg. of the same substance gave 12.610 mg. of silver chloride.

Found : C=52.0 % ; H=5.3 % ; Cl=25.8 %.

$C_{12}H_{14}O_3Cl_2$ requires : C=52.0 % ; H=5.5 % ; Cl=25.6 %.

2,4-Dimethoxy-3,5-diacetoxymethyl acetophenone : The dichloromethyl derivative (1 g.) was mixed with glacial acetic acid(10 c.c.) and fused sodium acetate(2 g.) and heated on a steam bath for 4 hrs. The product obtained on pouring the reaction mixture in water was crystallised from benzene, m.p. 219°.

Analysis : 4.144 mg. of the substance gave 9.296 mg. of carbon dioxide and 1.896 mg. of water.

Found : C=61.2 % ; H=5.1 %.

$C_{12}H_{12}O_5$ requires : C=61.0 % ; H=5.1 %.

The di-2,4-dinitrophenyl hydrazone : Prepared in the usual way and crystallised from nitrobenzene. The analysis indicated that only two carbonyl groups react with the 2,4-dinitrophenyl hydrazene.

Analysis : 5.192 mg. of the substance gave 0.883 ml. of nitrogen at 757 mm. pressure at 30°.

Found : N=19.1 %.

$C_{24}H_{20}O_{11}N_8$ requires : N=18.8 %. (for 2 carbonyl groups)

$C_{30}H_{24}O_{14}N_{12}$ requires : N=21.7 %. (for 3 carbonyl groups)

Attempted chloromethylation of resacetophenone : Paraformaldehyde (3 g. ; 0.01 mole) was taken in glacial acetic acid (20 c.c.) and dry hydrogen chloride was passed to saturation. Resacetophenone (5 g. ; 0.033 moles) was then added and hydrogen chloride was passed for further 10 minutes. The mixture was kept for 2 days. A white solid separated which on treatment with benzene gave a product melting at 160-62° with decomposition. But analysis did not agree with any particular formula. When the mixture after chloromethylation was poured into water a chlorine free solid separated from which no pure product could be isolated. The experiment was repeated with dioxan as solvent but no pure product could be isolated.

Chloromethylation of methyl-β-resorcylate :

Methyl-2,4-dihydroxy-3,5-dichloromethyl benzoate :- A mixture of paraformaldehyde (3 g. ; 0.1 Mole) and dioxan (30 c.c.) was saturated with dry hydrogen chloride gas at 20°. To this mixture methyl-β-resorcylate (6.72 g. ; 0.04 mole) was added and the reaction mixture kept overnight. The solvent was evaporated at room temperature and the residue was treated with benzene- petroleum ether mixture. The product insoluble in the solvent was rejected. The benzene-petroleum ether extract on cooling gave white crystals of methyl-2,4-dihydroxy-3,5-dichloromethyl benzoate, m.p. 122°. Yield 41 %. Large amount of gummy mass was also formed from which the isolation of chloromethyl derivative was very difficult.

In an alternative procedure the mixture after the reaction was diluted with petroleum ether (40-60°) and the clear dioxan-petroleum ether mixture after filtration was evaporated at room temperature and the 3,5-dichloromethyl derivative obtained.

When glacial acetic acid was used as solvent in the reaction only a pasty mass was formed.

Analysis : 4.886 mg. of the substance gave 8.086 mg. of carbon dioxide and 1.742 mg. of water. 12.662 mg. of the same substance gave 13.436 mg. of silver chloride.

Found : C=45.2 % ; H=4.0 % ; Cl=26.3 %.

$C_{10}H_{10}O_4Cl_2$ requires : C=45.3 % ; H=3.8 % ; Cl=26.8 %.

Chloromethylation of methyl-2,4-dimethoxybenzoate :

Methyl-2,4-dimethoxy-5-chloromethylbenzoate :- Hydrogen chloride gas was passed through a mixture of paraformaldehyde (3 g. ; 0.1 mole) and glacial acetic acid (20 c.c.) till saturation. Methyl-2,4-dimethoxybenzoate (8 g. ; 0.04 mole) was added and the mixture kept at 60-70° over a water bath for 2 hr. while a slow stream of hydrogen chloride was passing through the mixture. The mixture was cooled and mixed with chloroform (50 c.c.) and then with water. The separated chloroform layer was washed thoroughly with water and a little sodium bicarbonate solution. It was then dried over calcium chloride. The product obtained on removal of chloroform on crystallisation from benzene- petreleum ether gave long white needles, m.p. 124°. Yield 89 %.

Analysis : 4.100 mg. of the substance gave 8.112 mg. of carbon dioxide and 1.906 mg. of water. 11.026 mg. of the substance gave 6.350 mg. of silver chloride.

Found : C=54.0 % ; H=5.2 % ; Cl=14.3 %.

$C_{11}H_{13}O_4Cl$ requires : C=53.9 % ; H=5.3 % ; Cl=14.5 %.

4,6-Dimethoxy isophthalic acid :- A mixture of methyl-2,4-dimethoxy-5-chloromethylbenzoate (1 g.) potassium permanganate (3 g.) and sodium hydroxide solution (10 % ; 20 c.c.) was refluxed on a wire gauze for 2 hr. The acid obtained on working up as before crystallised from acetic acid. Mixed m.p. with 4,6-dimethoxy isophthalic acid described before was not depressed, m.p. 266°.

Methyl-2,4-dimethoxy-5-methylbenzoate :- Methyl-2,4-dimethoxy-5-chloromethylbenzoate (1 g.) was taken in dioxan (20 c.c.) and zinc dust (3 g.) and concentrated hydrochloric acid were added. The reaction mixture was heated over a steam bath for 4 hrs. The mixture was cooled, filtered and the filtrate was diluted with water. The separated product was crystallised from benzene, m.p.151°.

Analysis : 4.012 mg. of the substance gave 9.232 mg. of carbon dioxide and 2.224 mg. of water.

Found : C=62.8 % ; H=6.2 %.

$C_{11}H_{14}O_4$ requires : C=62.9 % ; H=6.7 %.

The same product was also prepared by refluxing a mixture of 2,4-dihydroxy-5-methyl benzoic acid (1 g.) dimethyl sulphate (3 c.c.), anhydrous potassium carbonate (10 g.) and acetone (50 c.c.) on a steam bath for 6 hrs. and working up as usual.

Methyl-2,4-dimethoxy-5-acetoxymethylbenzoate :- A mixture of methyl-2,4-dimethoxy-5-chloromethylbenzoate (1 g.) glacial acetic acid (5 c.c.) and fused sodium acetate (2 g.) was heated over a steam bath for 4 hrs. The mixture was poured into water and worked up as usual, m.p. 122°, Crystallised from benzene.

Analysis : 4.952 mg. of the substance gave 10.654 mg. of carbon dioxide and 2.690 mg. of water.

Found : C=58.7 % ; H=6.1 %.

$C_{13}H_{16}O_6$ requires : C=58.2 % ; H=5.9 %.

Methyl-2,4-dimethoxy-5-formylbenzoate :- Methyl-2,4-dimethoxy-5-chloromethylbenzoate (1 g.) was refluxed in chloroform (20 c.c.) with hexamethylene tetramine on a steam bath for 2 hrs. The product obtained on working up as usual crystallised from benzene, m.p. 167°

Analysis : 4.974 mg. of the substance gave 10.830 mg. of carbon dioxide and 2.380 mg. of water.

Found : C=59.4 % ; H=5.4 %.

$C_{11}H_{12}O_5$ requires : C=58.9 % ; H=5.4 %.

The 2,4-dinitrophenyl hydrazone prepared as usual gave m.p. 255-57°.

Analysis : 5.490 mg. of the substance gave 0.683 ml. of nitrogen at 34° and 751 mm. pressure.

Found : N=13.7 %.

$C_{17}H_{16}O_8N_4$ requires : N=13.9 %.

Attempted chloromethylation of β-resorcylic acid- Dry hydrogen chloride was passed through a mixture of paraformaldehyde (3 g. ; 0.1 mole) and dioxan (30 c.c.) at room temperature till the mixture got saturated with hydrogen chloride. To the above mixture β-resorcylic acid (6.16 g. ; 0.04 mole) was added with stirring. The mixture was kept overnight. No pure compound could be isolated from the reaction mixture.

2,4-Dimethoxy-5-chloromethyl nitrobenzene :- Paraformaldehyde (3 g. ; 0.1 mole) in glacial acetic acid (15 c.c.) was saturated with hydrogen chloride. 2,4-Dimethoxy nitrobenzene (6 g. ; 0.4 mole) was added with stirring when a clear solution was obtained. On keeping overnight long shining needles separated. These were recrystallised from carbon tetrachloride. M.P.116°. The filtrate, after separating the product from the reaction mixture, on pouring into water gave another crop of impure chloromethyl derivative. The over all yield was 88 %.

Analysis : 4.636 mg. of the substance gave 7.886 mg. of carbon dioxide and 1.742 mg. of water. 7.918 mg. of the same substance gave 0.430 ml. of nitrogen at 29° and 749 mm. pressure. 11.930 mg. of the same substance gave 7.356 mg. of silver chloride.

	Found	: C=46.4 % ; H=4.2 % ; N=6.1 % ; Cl=15.2 %.
$C_9H_{10}O_4NCl$	requires	: C=46.6 % ; H=4.3 % ; N=6.1 % ; Cl=15.3 %.

Methylene bis(5-nitro-2,4-dimethoxybenzene) :- The filtrate after treating with water was extracted with ether which gave a chlorine free compound which crystallised from benzene in bright yellow needles, m.p. 164°.

Analysis : 4.486 mg. of the substance gave 8.922 mg. of carbon dioxide and 2.018 mg. of water. 7.128 mg. of the same substance gave 0.476 ml. of nitrogen at 31° and 750 mm. pressure.

	Found	: C=54.2 % ; H=5.0 % ; N=7.4 %.
$C_{17}H_{18}N_2O_8$	requires	: C=53.9 % ; H=4.7 % ; N=7.4 %.

5-Nitro-2,4-dimethoxy benzoic acid :- A mixture of 2,4-dimethoxy-5-chloromethyl nitrobenzene (1 g.), potassium permanganate (3 g.) and sodium hydroxide (10 % ; 30 c.c.)

was heated over a steam bath for 4 hrs. The acid obtained on working up as before was recrystallised from acetic acid, m.p. 210°. The same acid was prepared for comparison by a different method as follows :

2,4-Dihydroxy-5-nitro benzoic acid was refluxed with dimethyl sulphate and anhydrous potassium carbonate in dry acetone over a water bath for 8 hrs. The mixture was poured into water and the precipitate of methyl-2,4-dimethoxy-5-nitro benzoate was collected. The above crude ester was then boiled with 10 % sodium hydroxide for 4 hrs. and the clear solution was acidified with hydrochloric acid and the precipitate of 2,4-dimethoxy-5-nitrobenzoic acid was collected. It was crystallised from acetic acid. Mixed m.p. of the above acid with the oxidation product of 2,4-dimethoxy-5-chloromethyl nitrobenzene was not depressed.

<u>5-Methyl-2,4-dimethoxyaniline</u> :- 2,4-Dimethoxy-5-chloromethyl nitrobenzene was heated with tin and hydrochoric acid on a steam bath for 2 hrs. The resulting clear solution was made alkaline with sodium hydroxide and then extracted with ether. The product obtained on removal of ether was crystallised from benzene-light petroleum ether mixture. M.P. 91°

<u>Analysis</u> : 4.328 mg. of the substance gave 10.274 mg. of carbon dioxide and 2.948 mg. of water. 6.892 mg. of the same substance gave 0.518 ml. of nitrogen at 33° and 751 mm. pressure.

Found : C=64.7 % ; H=7.6 % ; N=8.3 %.

$C_9H_{13}O_2N$ requires : C=64.7 % ; H=7.7 % ; N=8.4 %.

2,4-Dimethoxy-5-methyl aniline was also obtained when the dimethyl ether of 4-methyl resorcinol in glacial acetic acid was nitrated with con.nitric acid in the cold and the resulting 5-methyl-2,4-dimethoxy nitrobenzene was reduced with zinc and hydrochloric acid as before. Mixed m.p. with the former was not depressed.

2,4-Dimethoxy-5-acetoxymethyl nitrobenzene :- 2,4-Dimethoxy-5-chloromethyl nitrobenzene (1 g.) was heated with glacial acetic acid (5 c.c.) and fused sodium acetate (1 g.) over a steam bath for 2 hrs., The product obtained on working up as before crystallised from dil.acetic acid or benzene-petroleum ether mixture colourless needles, m.p. 113°.

Analysis : 4.090 mg. of the substance gave 7.712 mg. of carbon dioxide and 1.860 mg. of water. 7.364 mg. of the same substance gave 0.359 ml. of nitrogen at 31° and 750 mm. pressure.

Found : C=51.4 % ; H=5.1 % ; N=5.4 %.

$C_{11}H_{13}O_6N$ requires : C=51.7 % ; H=5.1 % ; N=5.5 %.

2,4-Dimethoxy-5-methoxymethyl nitrobenzene :- 5-Chloromethyl-2,4-dimethoxy nitrobenzene (1 g.) was mixed with absolute methyl alcohol(5 c.c.) and anhydrous potassium carbonate (2 g.) and heated over a steam bath for 2 hrs. The product obtained on working up as before crystallised from benzene-petroleum ether mixture, m.p.112°.

Analysis : 4.496 mg. of the substance gave 8.706 mg. of carbon dioxide and 2.244 mg. of water. 8.724 mg. of the same substance gave 0.474 ml. of nitrogen at 33° and 751 mm. pressure.

Found : C=52.8 % ; H=5.6 % ; N=6.0 %.

$C_{10}H_{13}O_5N$ requires : C=52.8 % ; H=5.7 % ; N=6.2 %.

2,4-Dimethoxy-5-cyanomethyl nitrobenzene :- 2,4-Dimethoxy-5-chloromethyl nitrobenzene (1 g.) was dissolved in absolute methyl alcohol (5 c.c.) and potassium cyanide (2 g.) was added. The reaction mixture was refluxed on a steam bath for 4 hrs. The mixture was poured into water and the precipitated cyanomethyl derivative was collected and crystallised from acetic acid, m.p. 152°.

Analysis : 4.128 mg. of the substance gave 8.134 mg. of carbon dioxide and 1.602 mg. of water. 8.966 mg. of the same substance gave 1.008 ml. of nitrogen at 29° and 750 mm. pressure.

Found : C=53.8 % ; H=4.3 % ; N=12.5 %.

$C_{10}H_{10}O_4N_3$ requires : C=54.1 % ; H=4.5 % ; N=12.6 %.

2,4-Dimethoxy-5-formyl nitrobenzene :- 2,4-Dimethoxy-5-chloromethyl nitrobenzene (1 g.) was dissolved in chloroform (25 c.c.) and refluxed with hexamine(5 g.) on a steam bath for 2 hrs. The product obtained on working up as usual was crystallised from acetic acid in white needles, m.p. 193°.

Analysis : 5.096 mg. of the substance gave 9.550 mg. of carbon dioxide and 1.820 mg. of water. 10.144 mg. of the same substance gave 0.623 ml. of nitrogen at 30° and 744 mm. pressure.

Found : C=51.1 % ; H=3.9 % ; N=6.7 %.

$C_9H_9O_5N$ requires : C=51.2 % ; H=4.2 % ; N=6.6 %.

The 2,4-dinitrophenyl hydrazone of the above formyl derivative was prepared as usual. Crystallised from nitrobenzene. M.P. > 300°.

Analysis : 6.642 mg. of the substance gave 1.079 ml. of nitrogen at 31° and 754 mm. pressure.

Found : N = 17.6 %.

$C_{15}H_{13}O_8N_5$ requires : N = 17.9 %.

Attempted chloromethylation of 4-nitroresorcinol :- To the hydrogen chloride saturated mixture of paraformaldehyde (3 g. ; 0.1 mole) and dioxan (20 c.c.) 4-nitroresorcinol (2.46 g. ; 0.02 mole) was added and kept overnight. On evaporation of the solvent at room temperature only an unworkable mass was obtained.

Chloromethylation of 2-nitroresorcinol : 2,6-Dihydroxy-3-chloromethyl nitrobenzene :- Paraformaldehyde (0.9 g. ; 0.03 mole) in acetic acid (5 c.c.) was saturated with hydrogen chloride at room temperature and 2-nitroresorcinol (5 g. ; 0.03 mole) was added with stirring. The clear red solution obtained was kept overnight and the chloromethyl derivative which separated in stout red needles was crystallised from benzene, m.p. 120°. Yield 68 %.

Analysis : 5.012 mg. of the substance gave 7.610 mg. of carbon dioxide and 1.142 mg. of water. 10.356 mg. of the same substance gave 0.623 ml. of nitrogen at 30° and 745 mm. pressure. 10.674 mg. of the substance gave 7.620 mg. of silver chloride.

Found : C=41.4 % ; H=2.5 % ; N=6.6 % ; Cl=17.7 %.

$C_7H_6O_4NCl$ requires : C=41.3 % ; H=2.9 % ; N=6.9 % ; Cl=17.4 %.

2,6-Dihydroxy-3,5-dichloromethyl nitrobenzene - To paraformaldehyde (3 g. ; 0.1 mole) in glacial acetic acid (10 c.c.) saturated with hydrogen chloride 2-nitroresorcinol (8 g. ; 0.05 mole) was added with stirring. The clear red solution obtained was kept overnight. The chloromethyl product separated out in stout red needles. It was recrystallised from benzene, m.p. 144°. Yield 74 %.

Analysis : 4.666 mg. of the substance gave 6.536 mg. of carbon dioxide and 1.218 mg. of water. 12.834 mg. of the same substance gave 14.530 mg. of silver chloride. 7.438 mg. of the substance gave 0.371 ml. of nitrogen at 28° and 749 mm. pressure.

Found : C=38.2 % ; H=2.9 % ; N=5.6 % ; Cl=28.0 %.
$C_8H_7O_4NCl_2$ requires : C=38.1 % ; H=2.8 % ; N=5.6 % ; Cl=28.2 %.

2,6-Dihydroxy-3,5-dicyanomethyl nitrobenzene :- 2,6-Dihydroxy-3,5-dichloromethyl nitrobenzene (1 g.) was dissolved in methyl alcohol and potassium cyanide (2 g.) was added. The mixture was heated over a steam bath for 2 hrs. It was poured into water, and acidified with hydrochloric acid. The precipitated dicyanomethyl derivative was collected and crystallised from acetic acid in brown crystals, m.p. 182°.

Analysis : 5.188 mg. of the substance gave 9.820 mg. of carbon dioxide and 1.368 mg. of water. 5.062 mg. of the same substance gave 0.832 ml. of nitrogen at 29° and 749 mm. pressure.

Found : C=51.7 % ; H=3.0 % ; N=18.3 %.
$C_{12}H_{11}O_4N_3$ requires : C=51.5 % ; H=3.0 % ; N=18.0 %.

Chloromethylation of 2,6-dimethoxy nitrobenzene : 2,6-Dimethoxy-3-chloromethyl nitrobenzene: - Paraformaldehyde (3 g. ; 0.1 mole) 2,6-dimethoxynitrobenzene (4 g. ; 0.02 mole) were taken in glacial acetic acid (20 c.c.) and hydrogen chloride gas was passed till saturation at 80-90°. After keeping at room temperature overnight the reaction mixture was poured into water. The chloromethyl derivative which separated was crystallised from benzene as a light yellow powder, m.p. 51°. Yield 88 %.

Analysis : 4.204 mg. of the substance gave 7.202 mg. of carbon dioxide and 1.548 mg. of water. 14.322 mg. of the same substance gave 8.782 mg. of silver chloride. 10.770 mg. of the substance gave 0.613 ml. of nitrogen at 33° and 747 mm. pressure.

Found : C=46.8 % ; H=4.1 % ; N=6.4 % ; Cl=15.2 %.

$C_9H_{10}O_4NCl$ requires : C=46.6 % ; H=4.3 % ; N=6.0 % ; Cl=15.3 %.

2,4-Dimethoxy-3-nitro benzoic acid :- A mixture of 2,6-dimethoxy-3-chloromethyl nitrobenzene (1 g.), potassium permanganate (3 g.) and sodium hydroxide (10 % ; 20 c.c.) was heated on a steam bath for 6 hrs. The acid obtained on working up as usual was crystallised from acetic acid,m.p.215°.

Analysis : 4.652 mg. of the substance gave 8.124 mg. of carbon dioxide and 1.570 mg. of water. 8.520 mg. of the same substance gave 0.495 ml. of nitrogen at 33° and 750 mm. pressure.

Found : C=47.7 % ; H=3.8 % ; N=6.4 %.

$C_9H_9O_6N$ requires : C=47.6 % ; H=3.9 % ; N=6.2 %.

2,6-Dimethoxy-3-methylaniline :- 2,6-Dimethoxy-3-chloromethyl nitrobenzene was reduced with tin and hydrochloric acid. The clear solution after reduction was made alkaline and extracted with ether. On Evaporation of the solvent and crystallising from benzene-petroleum ether mixture gave colourless crystals, m.p. 46°.

Analysis : 4.318 mg. of the substance gave 10.160 mg. of carbon dioxide and 2.894 mg. of water. 6.640 mg. of the same substance gave 0.505 ml. of nitrogen at 33° and 751 mm. pressure.

	Found	: C=64.2 % ; H=7.5 % ; N=8.4 %.
$C_9H_{13}O_2N$	requires	: C=64.7 % ; H=7.8 % ; N=8.4 %.

2,6-Dimethoxy-3-acetoxy methyl nitrobenzene :- Acetoxymethyl derivative of the chloromethyl derivative was prepared by heating a mixture of the chloromethyl derivative with glacial acetic acid and fused sodium acetate for 4 hrs. over a steam bath. It was poured into water and worked up as usual.

Analysis : 4.628 mg. of the substance gave 9.772 mg. of carbon dioxide and 2.018 mg. of water. 8.916 mg. of the same substance gave 0.456 ml. of nitrogen at 31° and 757 mm. pressure.

	Found	: C=51.8 % ; H=4.9 % ; N=5.7 %.
$C_{11}H_{13}O_6N$	requires	: C=51.8 % ; H=5.1 % ; N=5.5 %.

2,6-Dimethoxy-3-formyl nitrobenzene :- 2,6-Dimethoxy-3-chloromethyl nitrobenzene (1 g.) was refluxed with hexamine in chloroform and the separated complex was decomposed with dilute acetic acid and worked up as usual. It was crystallised from benzene in white needles, m.p. 102°.

<u>Analysis</u> : 5.386 mg. of the substance gave 10.108 mg. of carbon dioxide and 2.252 mg. of water. 9.596 mg. of the same substance gave 0.534 ml. of nitrogen at 30° and 744 mm. pressure.

Found : C=51.2 % ; H=4.7 % ; N=6.1 %.

$C_9H_9O_5N$ requires : C=51.2 % ; H=4.3 % ; N=6.6 %.

<u>The 2,4-dinitrophenyl hydrazone</u> of the above formyl derivative was prepared as usual, m.p. 277-78°.

<u>Analysis</u> : 4.424 mg. of the substance gave 0.713 ml. of nitrogen at 32° and 754 mm. pressure.

Found : N = 17.9 %.

$C_{15}H_{13}O_8N_5$ requires : N = 17.9 %.

<u>Chloromethylation of 4,4'-dihydroxy biphenyl : 4,4'-Dihydroxy-3,3'-dichloromethyl biphenyl</u> :- Paraformaldehyde (3 g. ; 0.1 mole) was suspended in dioxan (15 c.c.) and dry hydrogen chloride gas was passed through the mixture till the paraformaldehyde dissolved completely. 4,4'-Dihydroxy biphenyl(7.5 g.) was then added. More hydrogen chloride gas was passed through the mixture till the biphenyl dissolved. The mixture was kept overnight. The separated chloromethyl derivative was filtered washed with a little carbon tetrachloride and crystallised from benzene petroleum ether mixture, m.p. 179°. Yield 40 %.

Analysis : 4.444 mg. of the substance gave 9.646 mg. of carbon dioxide and 1.788 mg. of water. 10.492 mg. of the same substance gave 10.780 mg. of silver chloride.

Found : C=59.2 % ; H=4.5 % ; Cl=25.4 %.
$C_{14}H_{12}O_2Cl_2$ requires : C=59.4 % ; H=4.2 % ; Cl=25.1 %.

4,4'-Diacetoxy-3,3'-diacetoxymethyl biphenyl :- 1 g. of 4,4'-dihydroxy-3,3'-dichloromethyl biphenyl was mixed with 3 g. of fused sodium acetate and 8 c.c. of acetic anhydride and heated over a steam bath for 6 hrs. It was cooled, and poured into water. The precipitated product was crystallised from acetic acid in white needles, m.p. 148°.

Analysis : 4.396 mg. of the substance gave 10.310 mg. of carbon dioxide and 4.396 mg. of water.

Found : C=64.0 % ; H=5.5 %.
$C_{22}H_{22}O_8$ requires : C=63.8 % ; H=5.3 %.

Chloromethylation of 4,4'-dimethoxy biphenyl : 4,4'-Dimethoxy-3,3'-dichloromethyl biphenyl :- Through a mixture of paraformaldehyde (6 g. ; 0.2 mole) 4,4-dimethoxy biphenyl (8.5 g. ; 0.04 mole) and acetic acid (90 % ; 25 c.c.) was heated over a steam bath and hydrogen chloride was passed for 2 hrs. On cooling The mixture was then poured into water and the precipitated dichloromethyl derivative was crystallised from benzene petroleum ether mixture in light yellow needles, m.p. 145°. Yield 72 %.

Analysis : 4.926 mg. of the substance gave 11.140 mg. of carbon dioxide and 2.318 mg. of water. 14.212 mg. of the substance gave 13.020 mg. of silver chloride.

Found : C=61.7 % ; H=5.3 % ; Cl=22.7 %.
$C_{16}H_{16}O_2Cl_2$ requires : C=61.7 % ; H=5.1 % ; Cl=22.8 %.

4,4'-Dimethoxy biphenyl-3,3'-dicarboxylic acid :- 4,4'-Dimethoxy-3,3'-dichloromethyl biphenyl (1 g.) was refluxed with potassium permanganate (3 g.) and sodium hydroxide (10 % ; 20 c.c.). The product obtained on working up as usual was crystallised from acetic acid, m.p. 236°.

Analysis : 4.770 mg. of the substance gave 11.102 mg. of carbon dioxide and 1.948 mg. of water.

Found : C= 63.5 % ; H= 4.6 %.
$C_{16}H_{14}O_6$ requires : C= 63.6 % ; H= 4.6 %.

The same dicarboxylic acid was also prepared as follows: for comparison, according to
4,4'-Dihydroxy-3,3'-diacetyl biphenyl was methylated with dimethyl sulphate in the usual way and the resulting 4,4'-dimethoxy-3,3'-diacetyl biphenyl was mixed with alkaline potassium permanganate and refluxed for 6 hrs and worked up as usual. It was crystallised from acetic acid. Mixed m.p. with the former was 236°.

4,4'-Dimethoxy-3,3'-diacetoxymethyl biphenyl :- 4,4'-Dimethoxy-3,3'-dichloromethyl biphenyl was refluxed with glacial acetic acid and fused sodium acetate for 2 hrs.

It was poured into water and worked up as usual. It was crystallised from acetic acid, m.p. 154°.

Analysis :

4.696 mg. of the substance gave 11.502 mg. of carbon dioxide and 2.548 mg. of water.

Found : C= 66.8 % ; H= 6.1 %.
$C_{20}H_{22}O_6$ requires : C= 67.0 % ; H= 6.1 %.

4,4'-Dimethoxy-3,3'-dimethoxymethyl biphenyl :- It was prepared from 4,4'-dimethoxy-3,3'-dichloromethyl biphenyl by refluxing with methyl alcohol and anhydrous potassium carbonate on a steam bath for 4 hrs. and was crystallised from benzene-petroleum ether mixture, m.p. 81°.

Analysis : 4.588 mg. of the substance gave 11.946 mg. of carbon dioxide and 2.996 mg. of water.

Found : C= 71.1 % ; H= 7.3 %.
$C_{18}H_{22}O_4$ requires : C= 71.5 % ; H= 7.3 %.

4,4'-Dimethoxy-3,3'-diformyl biphenyl :- The above 3,3'-dichloromethyl derivative (1 g.) was dissolved in chloroform (20 c.c.) and hexamine (5 g.) was added. The mixture was refluxed on a steam bath for 2 hrs. The separated complex was hydrolysed with 50 % acetic acid by refluxing for 4 hrs. The diformyl derivative crystallised from acetic acid in long light needles, m.p. 213°.

Analysis : 4.600 mg. of the substance gave 11.910 mg. of carbon dioxide and 2.068 mg. of water.

Found : C= 70.7 % ; H= 5.0 %.
$C_{16}H_{14}O_4$ requires : C= 71.1 % ; H= 5.2 %.

The di-2,4-dinitrophenyl hydrazone of the above diformyl derivative was prepared in the usual way and recrystallised from nitrobenzene, m.p. > 300°.

Analysis : 5.736 mg. of the substance gave 0.891 ml. of nitrogen at 34° and 751 mm. pressure.

Found : N = 17.1 %.

$C_{28}H_{24}O_{10}N_8$ requires : N = 17.7 %.

Chloromethylation of 2,2'-dihydroxy biphenyl :- Through a mixture of paraformaldehyde (3 g. ; 0.1 mole) 2,2'-dihydroxy biphenyl (8.5 g. ; 0.04 mole) and dioxan (20 c.c.) dry hydrogen chloride gas was passed for 1 hr. From the pasty product obtained on the evaporation of the solvent at room temperature, no pure product could be isolated. The same experiment was repeated with acetic acid instead of dioxan as the solvent but with no better results.

Chloromethylation of 2,2'-dimethoxy biphenyl : 2,2'-Dimethoxy-5,5'-dichloromethyl biphenyl :- Paraformaldehyde (3 g. ; 0.1 mole) in dioxan (20 c.c.) was saturated at room temperature with hydrogen chloride gas. 2,2'-Dimethoxy biphenyl(9 g. ; 0.04 mole) was added and the hydrogen chloride passed for 30 minutes more. The solvent was then evaporated at room temperature and the residue was repeatedly crystallised from benzene-petroleum ether mixture. White crystals, m.p. 101°. Yield 66 %.

Analysis : 4.550 mg. of the substance gave 10.220 mg. of carbon dioxide and 2.066 mg. of water. 10.460 mg. of the same substance gave 9.528 mg. of silver chloride.

Found : C=61.3 % ; H=5.1 % ; Cl=22.5 %.

$C_{16}H_{16}O_2Cl_2$ requires : C=61.7 % ; H=5.1 % ; Cl=22.8 %.

2,2'-Dimethoxy biphenyl-5,5'-dicarboxylic acid :- 2,2'-Dimethoxy-5,5'-dichloromethyl biphenyl (1 g.)was mixed with potassium permanganate (3 g.) and the sodium hydroxide (10 % ; 20 c.c.) and refluxed on a sand bath for 8 hrs. The product obtained on working up as usual crystallised from acetic acid,m.p. 335-40°. Gilman et al. (J.Am.Chem. Soc.,62,1963(1940)) has reported the same m.p.

Analysis : (After heating under cacuum at 120°) 4.434 mg. of the substance gave 10.306 mg. of carbon dioxide and 1.736 mg. of water.

Found : C=63.4 % ; H=4.4 %.

$C_{16}H_{14}O_6$ requires : C=63.6 % ; H=4.6 %.

The same dicarboxylic acid was prepared for comparison by the method given below.

Dimethyl-2,2'-dimethoxy biphenyl-5,5'-dicarboxylate:- Methyl-3-iodo-4-methoxy benzoate (1 g.) was mixed with copper bronze (1 g.) and heated at 180-200° in an oil bath for 1 hr. The mixture was extracted with hot benzene. The product obtained after removal of the solvent was crystallised from benzene, m.p. 170-72°.

Analysis : 4.182 mg. of the substance gave 9.994 mg. of carbon dioxide and 1.992 mg. of water.

Found : C = 65.2 % ; H = 5.3 %.

$C_{18}H_{18}O_6$ requires : C = 65.5 % ; H = 5.5 %.

2,2'-Dimethoxybiphenyl-5,5'-dicarboxylic acid : - The above ester (0.3 g.) was heated with alcoholic sodium hydroxide on a steam bath for 1 hr. and then acidified. The acid was crystallised from acetic acid, m.p. 335-40°. Mixed m.p. with the acid obtained above was not depressed.

2,2'-Dimethoxy-5,5'-diacetoxymethyl biphenyl:- 2,2'-Dimethoxy-5,5'-dichloromethyl biphenyl (1 g.) was heated with glacial acetic acid (5 c.c.) and fused sodium acetate (2 g.) for 4 hrs. The mixture was poured into water and worked up as usual, m.p. 70°.

Analysis : 4.238 mg. of the substance gave 10.470 mg. of carbon dioxide and 2.388 mg. of water.

Found : C= 67.4 % ; H= 6.3 %.

$C_{20}H_{22}O_6$ requires : C= 67.0 % ; H= 6.1 %.

2,2'-Dimethoxy-5,5'-diformyl biphenyl:- 2,2'-Dimethoxy-5,5'-dichloromethyl biphenyl(1 g.) was dissolved in chloroform (25 c.c.) and heated with hexamine (5 g.) on a steam bath for 2 hrs. The separated complex was hydrolysed with 50 % acetic acid. The product obtained was crystallised from alcohol, m.p. 134°. ÷

÷ Gattermann (Ann. 357, 382 (1907) ~~has~~ prepared the same compound by a different method and reported m.p. 130°.

Analysis : 4.666 mg. of the substance gave 12.190 mg. of carbon dioxide and 2.180 mg. of water.

Found : C= 71.3 % ; H= 5.2 %.

$C_{16}H_{14}O_4$ requires : C= 71.1 % ; H= 5.2 %.

The 2,4-dinitro phenyl hydrazone :- Prepared as usual was crystallised from nitrobenzene, m.p. > 300°.

Analysis : 5.440 mg. of the substance gave 0.832 ml. of nitrogen at 30° and 754 mm. pressure.

Found : N= 17.5 %.

$C_{28}H_{24}O_{10}N_8$ requires : N= 17.7 %.