STUDIES ON CHLORINATION OF SOME XYLENOLS & TAR ACIDS FROM LOW TEMPERATURE TAR

Thesis

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SAJID HUSAIN,
M. Sc., (Alig.)

REGIONAL RESEARCH LABORATORY,
HYDERABAD.

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DECLARATION OF THE CANDIDATE

The work recorded in this thesis is original and has not been submitted for any other degree of this or other University.

(SAJID HUSAIN)

Regional Research Laboratory
HYDERABAD-9

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CHAPTER V. Relationship between Chemical Structure and Bactericidal Activity of Chlorinated Xylenols

PREFACE

PREFACE

Chloroxylenols, like 4-chloro-3,5-xylenol (PCMX) and 2,4-dichloro-3,5-xylenol (DCMX) are well-known active ingredients used in the manufacture of antiseptic and disinfectant formulations. The source of primary xylenols for the manufacture of these agents is usually the tars obtained in the coal carbonisation industry. The Regional Research Laboratory, Hyderabad, where the present work has been carried out is operating an experimental prototype low temperature carbonisation (l.t.c.) plant (25 tonne/day) of the Lurgi Spuelgas type with the following broad ends in view:

(a) to help establishment of l.t.c. industry in the country to meet the basic demand of smokeless fuel from otherwise low grade coals;

(b) to carry out experiments in by-product recovery, processing and utilisation since the economics of larger plants is closely linked with utilisation of various by-products of coke production.

The present work is a part of the overall programme of utilisation of the tar acid fractions from the l.t.c. tars. L.t.c. of Singareni coals (high ash, low grade, non-caking, meta-lignitious coals) yields tars which contain about 30% of tar acids, of which about 2.5% consist of cresols and about 3% of xylenols. One obvious outlet for utilisation of tar acid fractions is the isolation of pure xylenols and their conversion into useful, known and new chloro-compounds of high disinfectant activity. Chlorination of xylenol-rich fractions of tar acids by industrially feasible methods, can also yield commercially useful products. A study of available literature brought out the fact that chlorination of xylenols has not been adequately reported except its mention in patent literature. As a prelude to industrial utilisation of xylenols or xylenol-rich fractions of the tar acids, a systematic study of chlorination of xylenols is necessary and this was undertaken as the major objective for the present work. The investigation was expected to fulfil the following objectives:

(a) to arrive at industrially feasible methods of preparation of some chloro-xylenols;

(b) to know the behaviour of xylenols to various chlorinating agents;

(c) to study and compare the spectral data (UV, IR & NMR) of the chloroxylenols. It may be mentioned that this aspect is not at all covered in the available literature though, chloroxylenols have been known for quite some time.

(d) To establish analytical chromatographic separation techniques of the various products;

(e) to test the bactericidal activity of the chloroxylenols and of chlorinated tar acid fractions rich in xylenols, and attempt to find out structural relationships to disinfectant activity.

For this study, four commercially available xylenols viz. 2,5-, 2,3-, 3,5- and 3,4-xylenols and definite cuts of the tar acid fractions obtained in the l.t.c. plant mentioned earlier, formed the raw materials. The following three chlorinating agents were chosen:

(a) gaseous chlorine - it is a cheap and industrially available chlorinating agent;

(b) sulphuryl chloride - it is a widely used and industrially available chlorinating agent,

(c) ter-butylhypochlorite - it is described as principally an *ortho*-chlorinating agent in contrast to gaseous chlorine and sulphuryl chloride.

For convenience, presentation and discussion of the results have been divided into several chapters.

The first chapter begins with a discussion on chlorinating agents in use for benzenoid compounds, use of catalysts or carriers and mode of action of these agents. This is followed by a summary of orientation effects of the various substituents in an aromatic ring on the course of chlorination. Also included, is a critical review giving the present state of knowledge on chlorophenols as a class. The chapter is concluded by a statement in detail of the problem chosen for the dissertation.

The second chapter presents the results obtained in chlorination of the four xylenols with three different chlorinating agents. The progress of reactions was followed by the TLC technique and the products characterised by chemical and physical methods. Convenient preparative routes are described to obtain 4-chloro-2,5-xylenol and 4-chloro-2,3-xylenol in good yields. 4,6-Dichloro-2,3-xylenol has been obtained now for the first time and its structure verified by UV, IR and NMR. The behaviour of 3,4-xylenol towards these chlorinating agents stimulated considerable interest. Here, besides the expected chloroxylenols, non-phenolic oxidation products are also formed. The latter have been separated chromatographically and identified by chemical and spectral means. A theoretical explanation involving chlorinium ion (Cl^+) as the reactive entity is advanced to explain these results.

One of the most useful and widely employed modern tools in research is chromatography in its various forms, particularly paper, column, thin-layer and gas-liquid. However, except a few reports on paper chromatography of some chlorocresols, chromatography has not so far been applied to study of chlorocresols and chloroxylenols. Considerable attention was paid to application of chromatographic procedures to study these compounds and the results are presented in the third chapter. Particular mention may be made of the development of a quantitative TLC procedure and standardisation of conditions designed to achieve the best results. For paper chromatography, formamide-impregnated papers, xylene-saturated with formamide as solvent system and the descending technique were found to give a good combination. Spots were well-defined. R_f values were sensitive to experimental conditions and rigid adherence to experimental conditions was found necessary to obtain reproducible results. Plotting R_M values against number of carbon or chlorine atoms indicated that the partition phenomenon was responsible for chromatographic separation with polar solvent systems. With non-polar solvents, influence of adsorption phenomenon becomes noticeable in these separations.

The fourth chapter contains spectroscopic data of the chlorocresols and chloroxylenols. Ultraviolet, IR and NMR spectral data are presented and discussed. In the UV-study, an attempt has been made to correlate structure of these chlorophenols in terms of bathochromic or hypsochromic effects in the absorption bands. From a study of the infrared spectra of different chloroxylenols, it has been possible to assign characteristic CH deformation and C-Cl stretching absorption bands in the 650-900 cm^{-1} region. This may be of use in their identification. The hydroxyl absorption bands in the 3615-3530 cm^{-1} region reveal differences in the types of free and intramolecular bonds in the various compounds examined. These differences may be utilised in fixing the position of chlorine in the aromatic nucleus. The NMR spectra of most of the chlorocresols and chloroxylenols have been obtained and spectral absorption assignments made; convincing proof of structure of the compounds is provided.

The last chapter discusses the results obtained for the bactericidal activity of chloroxylenols against S-typhi, both as active ingredients and as formulations. It depicts the broad correlation between chemical structures and bactericidal values and brings out the potentiality of the hitherto unknown 4,6-dichloro-2,3-xylenols as an active bactericidal agent of commerce.

The results obtained with chlorinated tar acid mixtures indicate that these possess sufficient bactericidal activity. Since these would be cheaper to produce than DCMX, the products would have great economic potentiality.

CHAPTER I

CHLORINATION OF AROMATIC COMPOUNDS

Chlorination essentially consists in the introduction of one or more chlorine atoms in a molecule of an organic compound. This may take place either by addition or substitution reaction or by replacement of any functional group present in the molecule. In general, chlorination is an exothermic reaction. The heat of reaction (ΔH) in substitutive chlorination is of the order of -23000 to -27000 cals. regardless of the nature of the compound[1].

Preparative methods of chlorination, generally fall into three main classes. In the first class, molecules of halogens or any other neutral species themselves act as electrophilic reagents. These reagents are most useful for chlorination in the aromatic nuclei which are already activated by electron donating substituents. These activating substituents direct the entering group (chlorine) almost exclusively to the <u>ortho</u>- and <u>para</u>-positions, the former predominating[2]. The second class deals with chlorination of aromatic compounds of reactivity similar to or less than that of benzene; here, the molecular species of halogens reacts rather slowly and usually, it is convenient to employ a "carrier" or a catalyst. The third class comprises methods which involve positively charged chlorinating species. It has been recently elaborated[3] that a positive chlorine can be supplied under non-oxidizing conditions (e.g. in concentrated H_2SO_4, with silver sulphate to remove any hydrogen halide liberated). The conditions are conducive to heterolytic reaction and facilitate the chlorination of otherwise quite unreactive compounds.

Chlorinating agents

Molecular chlorine is one of the most commonly used neutral chlorinating agent, especially as a solution in a reasonably polar organic solvent. In this form it rapidly attacks aromatic compounds which are more reactive than toluene. Such compounds, usually contain ortho-para-directing substituents and the product is a mixture of ortho- and para-chloro-isomers. From a preparative angle, these reactions are useful in special structural situations where only one isomer is possible, or alternatively, when the required component can readily be separated from the reaction mixture. Acetic acid is one of the most convenient and commonly used solvent, e.g. in the preparation of 3-chloro-2,6-dimethylacetanilide[4]. Orton and Bradfield[5] have discussed the kinetics of chlorination with molecular chlorine in solutions which are nearly anhydrous. Here, chlorine is the effective electrophilic reagent. The rate of chlorination of phenolic ethers and of anilides in 99 per cent acetic acid has been shown by these authors to be governed by:

$$-d(Cl_2)/dt = K_2(ArH)(Cl_2)$$

The second-order rate-coefficient K_2 has been shown to be little affected by the addition of hydrogen chloride. Robertson et al.[6] studied the effect of electrolytes like perchloric acid, sulphuric acid, hydrogen chloride, sodium acetate, etc., on the rates of chlorination of naphthalene and of meta-xylene in anhydrous acetic acid and found that all of them accelerate the reaction to a small extent. The extent of catalysis is reasonably closely related to the degree of ionization of these electrolytes. Their results perfectly agree with the view that the molecular chlorine is formed as the intermediate. The little catalytic effect of the electrolytes or increase in the rate of reaction on addition of water to the solvent, probably results from the fact that the transition state for the reaction involves polarization of molecules of both chlorine as well as of aromatic compound. The transition state is, therefore, more polar than the starting materials, and the reaction is facilitated by an increase in the ionizing power of the environment[3,6,7]. Kinetics of chlorination by molecular chlorine in other solvents (e.g. nitrobenzene, chloroform) has been studied by Roberts and Soper[8] shown to be in the following form: $-d(Cl_2)/dt = K(ArH)(Cl_2)$. No further details of the reaction have been established.

Catalysts which promote nuclear substitution in the benzene ring are generally used when the substances have lesser reactivity than toluene. These catalysts include ferric chloride, aluminium chloride, chlorides of other metals[9-11], iodine[12] and pyridine etc. The mode of their action differs considerably in details and is not known with certainty, except that they polarise the interhalogen bond at some intermediate stage of the reaction. Use of such catalysts minimises homolytic processes, which, otherwise, often supervene when the reaction mixture is irradiated or the aromatic compound simply contains an alkyl group. The preparation of meta-chlorobenzoyl chloride from benzoyl chloride[13] illustrates the action of $FeCl_3$ in the chlorination. Here, the substitution takes place in the meta-position due to the deactivating influence exercised by the acid chloride group and the other two isomers are only obtained in small quantities. In the chlorination of naphthalene, the catalytic activity of antimony, iron, aluminium chlorides and alumina[14] have been reported in the decreasing order. Iodine in combination with iron[15] has been used as a powerful catalyst for the rapid chlorination of nitrobenzene, *ortho*- and *para*-nitrotoluenes and *para*-chloronitrobenzene. Chlorination can be carried out at lower temperatures with this catalyst and the reaction is so fast that external cooling is necessary. Mixtures of sulphur, antimony trichloride and lead have been mentioned as catalysts for the chlorination of benzene and naphthalene[16]. It has also been pointed out that heat and light cause the chlorine molecule to become dissociated into chlorine atoms[17]. Active carbon[18] has been used in chlorination as a catalyst but its action can also be interpreted as the effect of the increased surface area[19].

A *positive chlorine* has been shown to be the reactive entity in several chlorination reactions, e.g. the electrophilic chlorinating agent is positive in the case of hypochlorous acid in presence of aqueous mineral acid[20]. Under these or analogous conditions, the positive entity is available *in situ* and plays a special preparative role. Relatively unreactive compounds can be chlorinated in this way and the chlorination of *p*-nitrotoluene to yield 2-chloro-4-nitrotoluene[21] can be cited as an example. Through a study of kinetics of chlorination of sodium toluene-ω-sulphonate[20], benzene and toluene[22] with hypochlorous acid in aqueous solution, it has been suggested that the reaction proceeds through one of the following mechanisms:

(a) where hypochlorous acidium ion is the active chlorinating agent.

$$\mathrm{ClOH} + \mathrm{H}^+ \rightleftharpoons \mathrm{ClOH}_2^+$$

$$\mathrm{ClOH}_2^+ + \mathrm{ArH} \longrightarrow \text{products}$$

(b) where the hypochlorous acidium ion is further in equilibrium with chlorinium ion (Cl^+) and the latter is the reactive entity

$$\mathrm{ClOH}_2^+ \rightleftharpoons \mathrm{Cl}^+ + \mathrm{H}_2\mathrm{O}$$

$$\mathrm{Cl}^+ + \mathrm{ArH} \longrightarrow \text{products}$$

Work with more reactive substances e.g., anisole[23] has led to the conclusion that under the same conditions, the rate of such chlorinations is limited by the rate of fission of the hypochlorous acid or the hypochlorous acidium ion into the chlorinium ion.

$$\mathrm{ClOH} \longrightarrow \mathrm{Cl}^+ + \mathrm{OH}^- ; \quad \mathrm{ClOH}_2^+ \longrightarrow \mathrm{Cl}^+ + \mathrm{H}_2\mathrm{O}$$

Evidence in favour of Cl^+ acting as an intermediate in these chlorinations was given by Swain & Ketley[24] by measuring the rate of reaction in $\mathrm{D}_2\mathrm{O}$. However, thermodynamic calculations[25] have come in the way of universal acceptance of the hypothesis that Cl^+ is the effective intermediate in these reactions. These calculations do not favour the formation of Cl^+. It may also be pointed out that the analogies drawn while assigning the energy and entropy of solvation of these ions may not be based on very sound comparisons.

N-chloroamides or anilides have been used as source of chlorine. Orton & coworkers[5,26] have made use of this elegant method of chlorination.

Though the reaction $R_2NCl + HCl \rightleftharpoons R_2NH + Cl_2$ is a reversible one, the forward reaction is usually rapid and the equilibrium lies so far to the right that this process can be considered to be practically irreversible. The amount of hydrochloric acid controls the amount of chlorine; the former is kept constant by regeneration in the actual chlorination of the aromatic compound. Thus, employing a catalytic amount of HCl, the standing concentration of both chlorine and acid can be kept to a minimum. This method has a special preparative value when highly reactive and readily oxidisable organic compounds are to be chlorinated, such as, aromatic amines, phenols and their derivatives, etc. Since aromatic chlorinating agents falling in this group can replace, not only the aromatic hydrogen but also the hydrogen of OH, NH_2 or NHR groups, the corresponding classes of positively charged species also exist, e.g.,

$$ClO^+HR,\ ClN^+H_2R,\ Cl^+NHR_2,\ ClN^+R_3$$

these can, in principle, act as electrophilic chlorinating agents. Hence, chlorine or hypochlorous acid in presence of hydroxylic solvent or an amine can lead to the existence of the following type of equilibrium:

$$ClOH + HOAc \rightleftharpoons ClOAc + H_2O$$

$$ClOAc + H^+ \rightleftharpoons ClOHAc^+$$

This complicates interpretation of chlorination process in mixture of acetic acid and water and there is evidence to show that the above mentioned equilibria are important in the system[27,28]. The fact that pyridine and other tertiary amines act as powerful catalysts for chlorination suggests that the ions of the type $PYCl^+$ formed by the equilibria shown in the following equation may be the effective chlorinating agent:

$$Py + Cl_2 \rightleftharpoons PyCl^+ + Cl^-$$

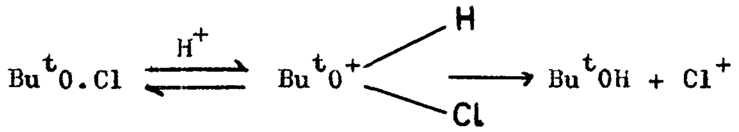
Brown and Sopper's[29] work on the reaction of diethylchloramine with phenol has shown that the reactants in this case are the ions.

$$R_2NHCl \;+\; OAr^- \longrightarrow \text{Chlorinated product}$$

N-chlorosuccinamide[30] has also been used in chlorination of reactive aromatic compounds though orientation in these chlorinations is not the same as that found with other chlorinating agents.

Sulphuryl chloride either alone or in presence of a catalyst, like aluminium chloride[31,32] has been used as a chlorinating agent for aromatic hydrocarbons, phenols and its derivatives, aliphatic hydrocarbon etc. Brown[33] has discussed the versatility and potentialities of sulphuryl chloride in organic synthesis. The simplicity of the reaction, high yields and ease of control have made this reagent an important industrial raw material.

ter-Butylhypochlorite and other esters of hypochlorous acid have also been employed as chlorinating agents for many organic compounds, the nature of the species responsible for chlorination depending on the reactivity as well as the conditions of chlorination. For example, chlorination of methylene group in allylic systems[34], and of methyl group in toluene and substituted toluenes[35] by *ter*-butylhypochlorite has been shown to involve an attack by chlorine atoms. Olefines react with this reagent in acidic or neutral aqueous solution to form chlorohydrins[36,37] and in alcoholic solution to form chlorohydrin ethers. These reactions are analogous to two-stage ionic addition of molecular chlorine in these solvents[38]. The reaction of *ter*-butylhypochlorite with benzenoid compounds, however, neither involves atomic nor molecular chlorine. *Ortho*- and *para*-chlorotoluenes are obtained in the ratio of 3:2 on chlorination of toluene with molecular chlorine[39] whereas the former[40] alone is obtained in 93% yield in the reaction of toluene with *ter*-butylhypochlorite. Likewise, anisole and phenol[41] give *ortho*-chloroderivative with *ter*-butylhypochlorite in yields of 87% and 94%, respectively, as compared to the respective yields of 21%[42] and 50%[43] obtained in their reaction with molecular chlorine. In these reactions, chlorinium ion is the reactive species, the formation of which has been recently explained by Norman et al.[44] in hydroxylic solvents.



Homolytic processes involving halogen atoms have not proved very useful for substitution reactions in aromatic systems. Instead, addition reaction is often the preferred course. In such chlorinations of aromatic compounds having alkyl side-chains, side-chain chlorination products are often formed, unless light is rigorously excluded. Under certain conditions, either in presence of peroxides or when the reaction is carried out at elevated temperatures, the side chain chlorination is the predominant or even the exclusive process.

Chlorination of aromatic compounds can be envisaged under alkaline conditions; however, the available reagents for such processes are limited. Hypochlorous acid has acidic dissociation constant in the region of 10^{-8} to 10^{-9}, and can exist in reasonable concentrations as the free molecular species under alkaline conditions. However, it has been shown to be unreactive with anisole[45]. It nevertheless, haloganates phenoxide ions and tertiary amines[46].

STRUCTURAL EFFECTS OF CHLORINATION

Chlorination of benzene derivatives is explained satisfactorily by qualitative electronic theory. Furthermore, chlorination studies have provided a sensitive method for investigating and clarifying the nature of electronic movements which occur during these electrophilic substitutions. The data in literature are scattered and restricted in most cases to reaction under preparative conditions. Some of the more significant comparisons available for mono-substituted benzenes are given in Table I.

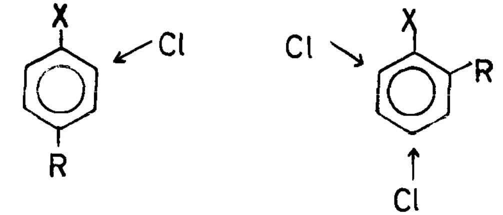
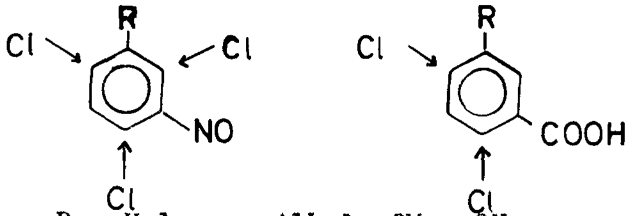
Available data regarding the orientation in the chlorination of disubstituted benzenes are collected in Table II. The general pattern of orientation is similar to that found in nitration and fits well with qualitative electronic theory of organic chemistry. A qualitative observation has also been recorded that when ortho-, para-directing groups are meta- to each other, electrophilic substitution often occurs between them[2]. To support this observation, the example of chlorination of meta-hydroxybenzaldehyde[64] and of meta-nitrophenol can

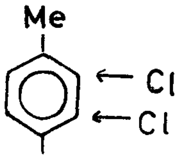
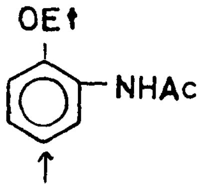
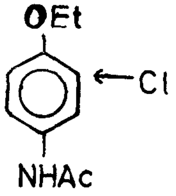
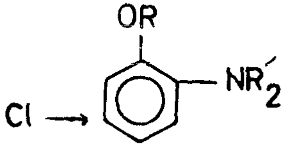
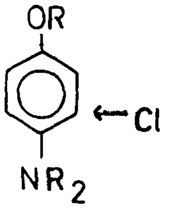
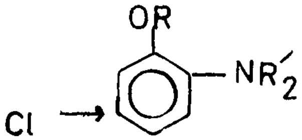
Table I - Isomers distribution in chlorination of mono-substituted benzenes with molecular chlorine

Compound	Directing substituent	isomers, per cent			References
		ortho-	meta-	para-	
Phenol	OH	50	-	50	47
Acetanilide	$NHCOCH_3$	30	-	70	5
Anisole	OCH_3	21	-	79	48, 42
Diphenyl	C_6H_5	ca. 30	-	ca. 50	49, 50, 51
Toluene	CH_3	59.8	0.48	39.7	52, 53
ter-Butylbenzene	$(CH_3)_3 \cdot C$	(74.7) 21.8	(2.2) 2.1	(23.1) 76.1	52, 53
Fluorobenzene	F	-	-	ca. 90	54
Chlorobenzene	Cl	39	6	55	47, 54, 55
Bromobenzene	Br.	42	6	52	47, 54, 55
Benzoic acid	COOH	-	ca. 100	-	55, 56
Nitrobenzene	NO_2	1	95	4	55, 57, 58

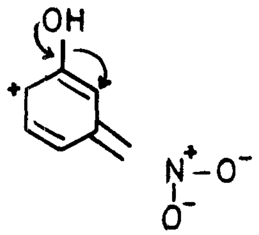
1. Chlorination of bromobenzene is catalysed by metallic halides
2. Values in ( ) are for chlorinium ion (Cl^+)
3. In most cases in which the absence of isomer is indicated, component is not sought exclusively.

Table II - <u>Influence of directing groups of disubstituted benzenes in chlorination</u>

Group	Aromatic compound	Reference	Remarks
(1)	(2)	(3)	(4)
A	 X = NH_2, NMe_2, NHAc, $NH.SO_2Ac$, OH, OMe, OPh R = Ph, Alkyl, Halogen, or <u>meta</u>-directing groups	58, 59	Illustrates dominance of NH_2 and OH and derived groups over less powerfully <u>ortho</u>-, <u>para</u>-directing substituents
B	 R = Halogen, Alkyl, OMe, OH, NHAc, NH_2, NMe_2.	58, 61	Illustrates that an <u>ortho</u>-, <u>para</u>- directing substituent usually takes control over <u>meta</u>-directing substituents

(1)	(2)	(3)	(4)
C	 	60	Illustrates that methyl and chlorine are similar in directing power
D	 	62	Illustrates apparent dominance in directing power of OEt over NHAc contrast nitration
E	  R = Me, Et, etc; R^1= H, Me, Et.	62, 63	Illustrates the dominance of NH_2 and related groups over OMe, OEt etc

be cited. It has been suggested that the mesomeric effect of the electron withdrawing group favours structures as given below:

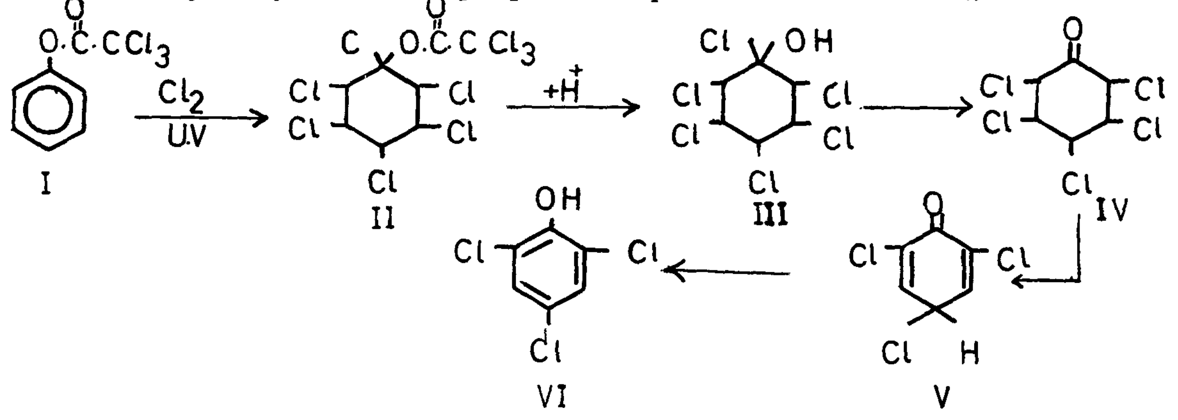


This type of orientation is seldom exclusive and by no means always dominant as is apparent in the cited examples in Table II.

CHLORINATION OF PHENOLS AND CRESOLS

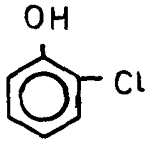
Chlorination of phenol and all the three cresols is known for a long time. Properties and methods of preparation of all possible isomeric chlorophenols and chlorocresols are well documented by Huntress[65]. This literature is not discussed in detail here. Direct substitutive chlorination of phenol and cresols with electrophilic reagents like molecular chlorine, sulphuryl chloride etc., generally introduces chlorine at positions where electron densities are increased due to hydroxy substituents i.e. ortho- and para-positions. Thus, ortho-chloro, 2,4-dichloro and 2,4-6-trichlorophenols etc., have been prepared by direct chlorination methods[66 to 70]. Extent of chlorination and yields of compounds are generally dependent on the nature of chlorinating agents, experimental conditions, solvents etc. The reaction of molecular chlorine with phenol with or without a solvent, gives monochloro-, and 2,4-dichlorophenol. Further chlorination leads to

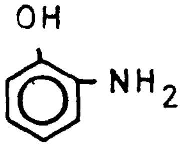
2,4,6-trichlorophenol. Imamura[71] worked out conditions of stepwise chlorination of phenol with chlorine gas employing ferric chloride, iron, aluminium chloride, antimony chloride and antimony as catalysts for preparation of mono-, di-, tri, tetra- and penta-chlorophenols. *Para*-chlorophenol is obtained by chlorination of phenol with sulphuryl chloride[72] using stoichiometric quanity of the latter, whereas chlorination of phenol with *ter*-butylhypochlorite[73] in hydroxylic solvent has been reported to yield *ortho*-chlorophenol as major component. Recently, Campbell et al.[74] have studied the effect of solvent on mechanism of chlorination of *ortho*-cresol. The ratio of 4-chloro-*o*-cresol : 6-chloro-*o*-cresol produced has been correlated with the phenomenon of steric hindrance. Anomalous high yields of 4,6-dichloro-*o*-cresol in polar solvents at low temperatures, have been explained in terms of hydrogen bonding involving the aromatic π-electron of *ortho*-cresol. Rosen et al.[75] carried out a study of addition-chlorination of phenol. Normally, a benzene derivative like phenol undergoes substitution chlorination only, due to presence of strong electron-releasing group, like hydroxyl. These authors modified this property of the hydroxy group by attaching electron-withdrawing group to the oxygen atom and thus readily explained addition-chlorination to give 1, 2, 3, 4, 5, 6-hexachloro-cyclohexyl trichloroacetate (II). The structure of (II) was established as it gave 2,4,6-trichlorophenols (VI) on acid hydrolysis. The proposed sequence of reactions are indicated below:

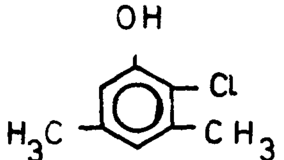


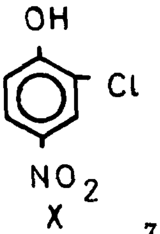
CHLORINATION OF XYLENOLS

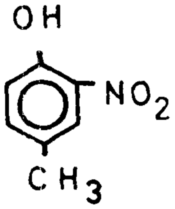
Chlorination of xylenols has not been so far exhaustively studied. It might be due to the fact that indirect preparative methods have to be applied for synthesis of specific chloroxylenols. Lesser and Gad[76] chlorinated 3,5-xylenol with sulphuryl chloride in chloroform and reported the formation of 2-chloro-3,5-xylenol in addition to 4-chloro-3,5-xylenol. They also commented that sulphuryl chloride is not a para-chlorinating agent[77] only. When chlorination was carried out further they obtained a dichloro-isomer. They surmised that phenols with negative substituent ortho- to hydroxyl and with the para-position blocked, do not get chlorinated with sulphuryl-chloride. According to them, the following phenols did not respond to chlorination by this reagent:

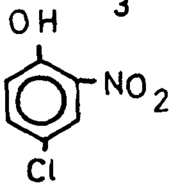

VII


VIII

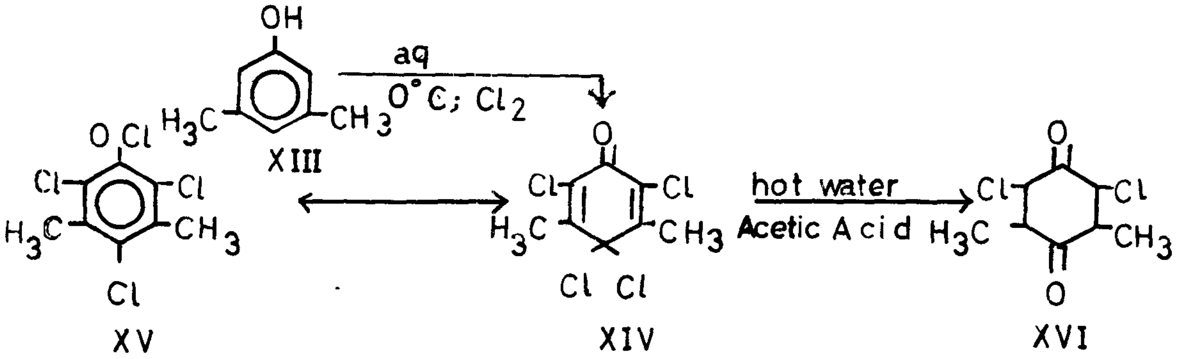

IX


X

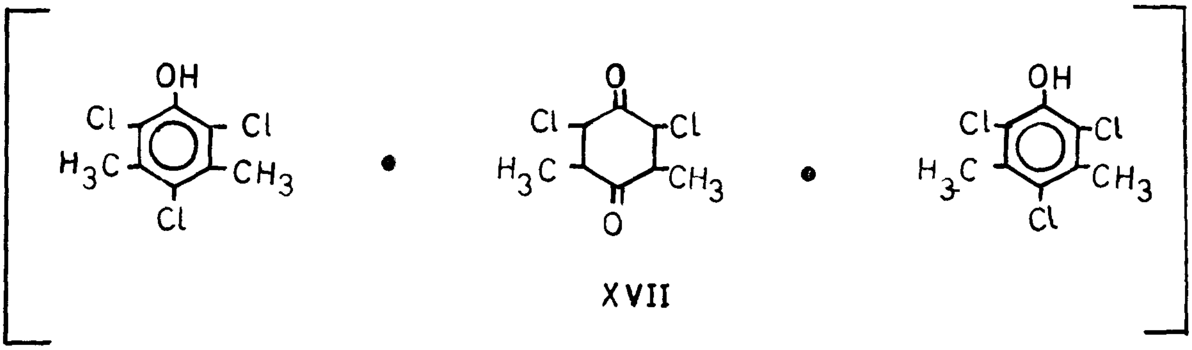

XI


XII

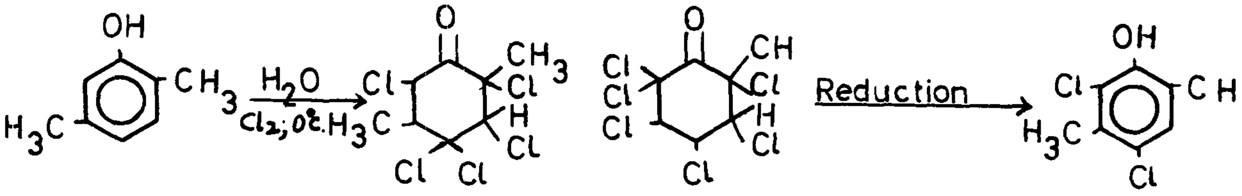
Later Jones[78] obtained 2,4-dichloro-3,5-xylenol (DCMX) from 4-chloro-3,5-xylenol (PCMX) by chlorination with N-chloroacetamide applying the Orton and Kings[26] method and reported its melting point as 83°C., later corrected by Gamell[79] as 94-95°C. The wrong reporting of melting point by Jones[98] has created a confusion in the literature, and has led Huntress[65] to classify the dichloro-isomer obtained by Lesser and Gad[76] to be 2,6-dichloro-3,5-xylenol. On the basis of Gamell's work, it can be taken that 2,6-dichloro-3,5-xylenol is not known. Lockemann and Kuzmann[80] chlorinated 2,3-, 3,4-, 3,5- and 2,5-xylenols with sulphuryl chloride in acetic acid. Their results were corrected by Heicken[81], who also published the bactericidal action of chloroxylenols. Interesting results have been published by Mueller & Linde[82] on the action of gaseous chlorine on 2,5- and 3,5-xylenols. Action of chlorine on 3,5-xylenol (XIII) in aqueous dispersion at 0° C. yielded 2,4,4,6-tetrachloro-3,5-dimethylcyclohexa-2,5-dien-1-one (XIV)



along with a small quantity of hypochlorite of 2,4,6-trichloro-3,5-xylenol (XV), which according to authors is the tautomeric form of (XIV). At higher temperatures in presence of acetic acid, the product was 2,6-dichloro-3,5-dimethyl-p-benzoquinone (XVI). In addition, a molecular compound (XVII) of the following structure containing 2-molecules of 2,4,6-trichloro-3,5-xylenol and one molecule of 2,6-dichloro-3,5-dimethyl-p-benzoquinone was also isolated.



Chlorination of 2,5-xylenol under similar conditions, instead of yielding the expected tri- or tetrachloro-derivatives, gave pentachloro-compound, 2,3,4,5,6-pentachloro-2,5-dimethyl-5-cyclohexane-1-one (XIX) and an oil. On longer standing, the oily by-product gave a pentachloro-compound; this on reduction, yielded 4,6-dichloro-2,5-xylenol (XXI) and the pentachloro-compound was assigned a structure 2,3,4,5,6-pentachloro-2,5-dimethyl-cyclohexane-4-one-1 (XX). They

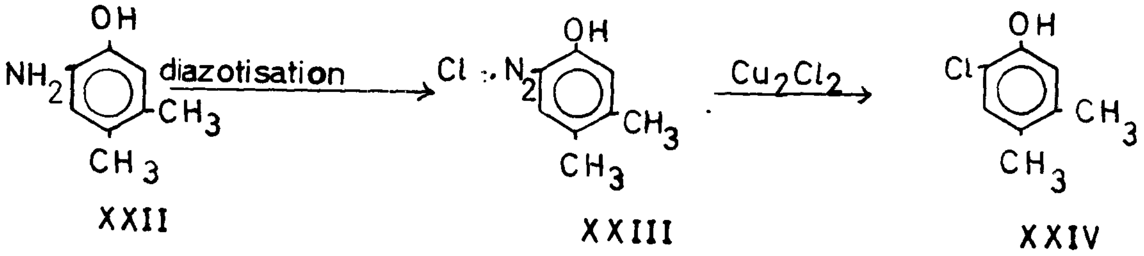


XVIII XIX XX XXI

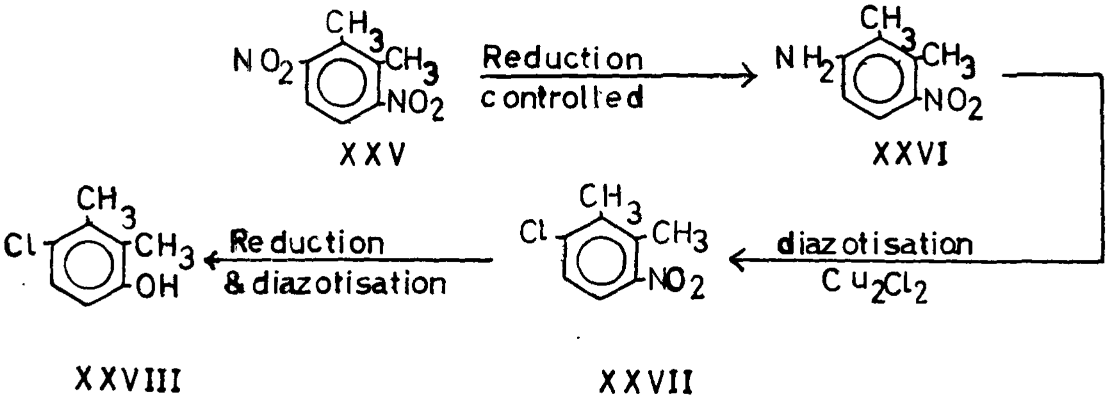
concluded that in general, in phenols where *ortho-* and *para*-positions are free, as in phenol, *meta*-cresol and 3,5-xylenol, prolonged chlorination in aqueous acidic medium leads to 90 to 100% quinone formation. This can lead one to conclude that only the *para*-dichlorocyclohexadien-one compound is formed as a major intermediate. In xylenols where *ortho-*, and *para*-positions are partially or fully occupied, the chlorinated quinones are found in lower yields because the intermediate *ortho*-chloro compound is not hydrolysable to give a quinone (cf. 2,5-xylenol).

Indirect methods have been frequently employed to prepare mono-, di-, and trichloro-xylenols[83 to 88] and these are exemplified below:

(a) from the corresponding amino-dimethylphenol via diazotisation and reaction with cuprous chloride[86]



(b) from dinitroxylene[86]

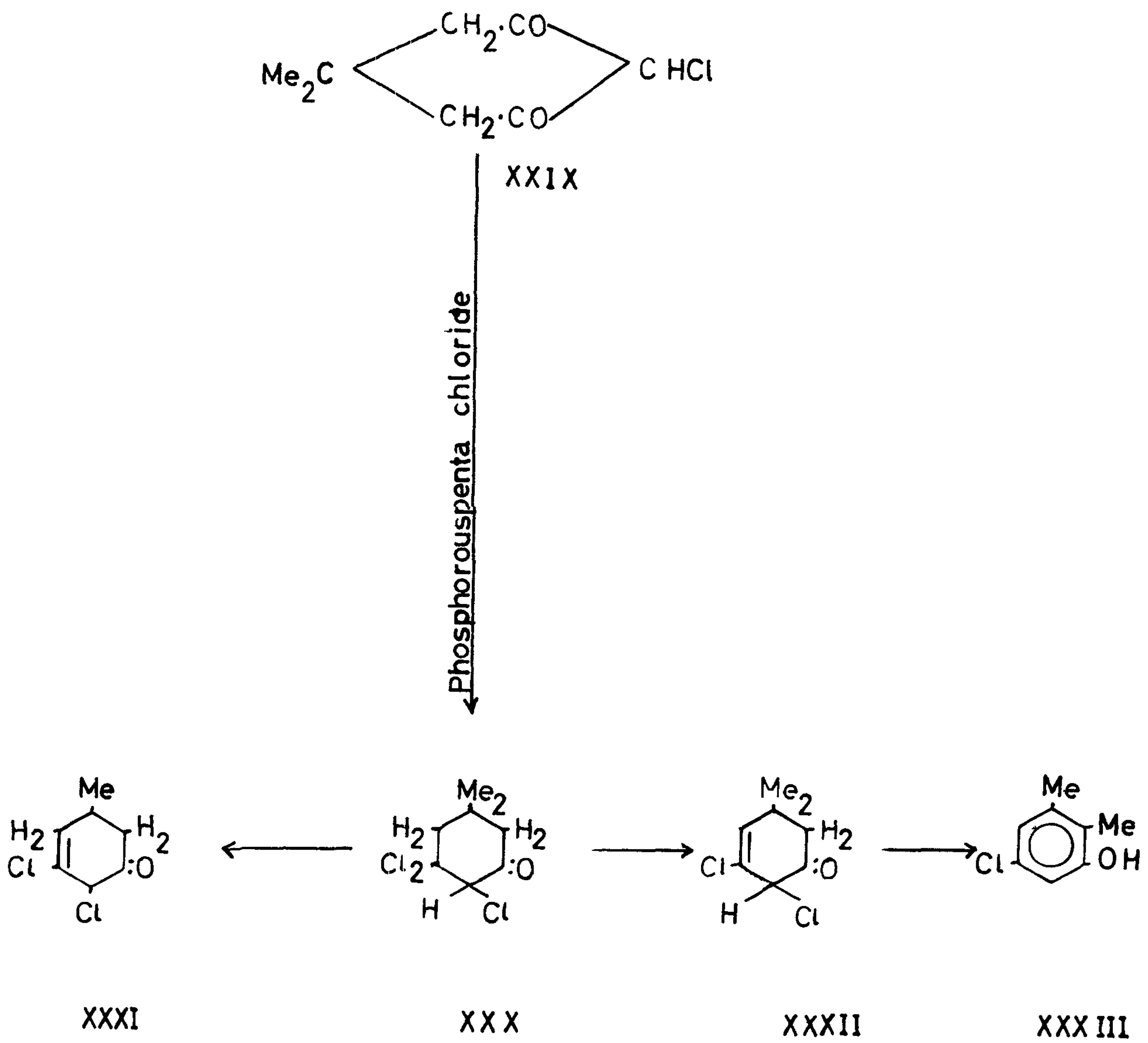


(c) replacement of sulphonic group by chlorination[89]

It has been found that when a current of chlorine gas is introduced in an aqueous solution of sulfonic acid, the sulphonic group is detached with the simultaneous production of the corresponding chloro-derivative.

(d) conversion of hydroaromatic to aromatic compounds[87]

Chloro-dimethyldihydroresorcinol (XXIX) on reacting with phosphorus pentachloride gives a chloroxylenol (XXXIII). The mechanism of formation of chloroxylenol is shown below:



STATEMENT OF PROBLEM - STUDIES ON CHLORINATED XYLENOLS

It would be apparent from the preceding review that chlorination of xylenols has not been adequately investigated. In particular the direct chlorination of xylenols has not received much attention and published work in this direction has been limited and scattered. Hence, a systematic study of chlorination of xylenols was undertaken as the major objective. Chlorination of four available xylenols viz., 2,5-, 2,3-, 3,5- and 3,4-xylenols was carried out with (a) gaseous chlorine, (b) sulphuryl chloride, and (c) ter-butylhypochlorite. Search for suitable methods for identification of the products of chlorination, especially when present in mixtures, led to a study and development of paper-chromatographic separation of chlorophenols, chlorocresols and chloroxylenols. These results have yielded interesting theoretical correlations based on Martin's equation[90]. The paper-chromatographic technique, however, was found time-consuming and not suitable for studying the progress of the various chlorination procedures. A better method was found in the application of thin-layer chromatography (TLC). Since, hardly any data were available on the TLC of chlorophenols as a class, a systematic investigation of the separation of chlorophenols, chlorocresols and chloroxylenols by the TLC procedure was also included as an important aspect in this study. The work also led to development of a quick method for quantitative estimation of chloroxylenols. So far as the author is aware, quantitative TLC technique has not hitherto been applied to this class of compounds.

Apart from the TLC method, other available physical tools which are normally employed in understanding chemical structures and reactions namely UV, IR, and NMR spectroscopy, have also been utilised wherever necessary. Interesting correlations arrived at from these spectral data are discussed at appropriate places in this thesis. The behaviour of the chlorophenols in gas-liquid chromatography (GLC) was also examined but the results were not very encouraging or particularly useful in respect of these compounds. Hence only a preliminary account of the GLC work is included.

Since, chlorinated xylenols, especially 2,4-dichloro-3,5-xylenol (DCMX) is a commercial product of high disinfectant activity, a relative evaluation of disinfectant activity of various other chloroxylenols and its relation to structural features was considered interesting. The results obtained in this study prompted, further, only from a commercial angle, chlorination of mixtures of tar acids (predominant in xylenols and their evaluation for Riedel-Walker Coefficient (RWC) has also been included. For this purpose, tar acid fractions, obtained as definite cuts in the fractionation of phenolic by-products of the low-temperature carbonisation plant (l.t.c.) working at the Regional Research Laboratory, Hyderabad, (25 tonne/day) were available.

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CHAPTER II

CHLORINATION OF SOME XYLENOLS

The following four available xylenols were chlorinated with (a) gaseous chlorine (b) sulphuryl chloride and (c) _ter_-butylhypochlorite:

2,5-xylenol,
2,3-xylenol,
3,5-xylenol, and
3,4-xylenol

Gaseous chlorine was chosen as an example of a molecular chlorinating reagent. It is cheap and has industrial potentialities.

Sulphuryl chloride is known to be a predominantly _para_-chlorinating reagent and was employed to get _para_-chloro-compounds which are reported to have higher RWC[1].

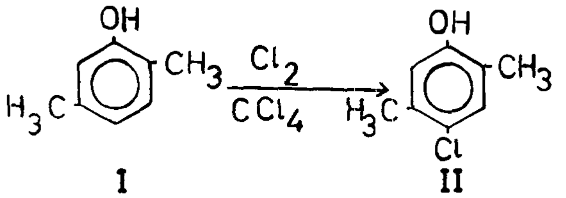
ter-Butylhypochlorite is an _ortho_-chlorinating reagent of considerable promise. Freshly prepared reagent has been described to yield only chlorinium ion (Cl^+) as the chlorinating species[2].

In every case, besides studying the progress of chlorination with TLC, attempts were made to crystallise and separate the products of chlorination. The experimental details are described separately. The salient results obtained with each xylenol are described in this chapter and these are followed by discussion and correlation of some of these.

A. 2,5-XYLENOL

(a) Reaction with gaseous chlorine

When 2,5-xylenol (I; R_f = 0.25) dissolved in carbon tetrachloride was reacted with gaseous chlorine at $20 \pm 2^{\circ}$C., and the progress of reaction studied by TLC, it was noted that monochlorination started almost immediately. A sample of the product taken after half-an-hour reaction, showed the presence of 4-chloro-2,5-xylenol (II; R_f = 0.31), besides large quantity of the unreacted 2,5-xylenol. After this period, dichlorination product, 4,6-dichloro-2,5-xylenol (III; R_f= 0.76) was also detectable on the chromatogram (1-hr. sample; see Fig. 1). Then chlorination proceeded further with increased formation of the dichloro-derivative, and a decrease in the amount of the starting xylenol; the monochloro-derivative was persistent throughout till all the starting phenol was fully reacted. Finally, 4,6-dichloro-2,5-xylenol was the only product (Fig. 1). This took about 5½ hours.



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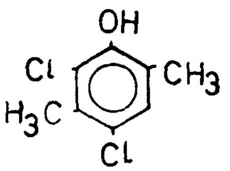
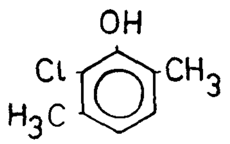


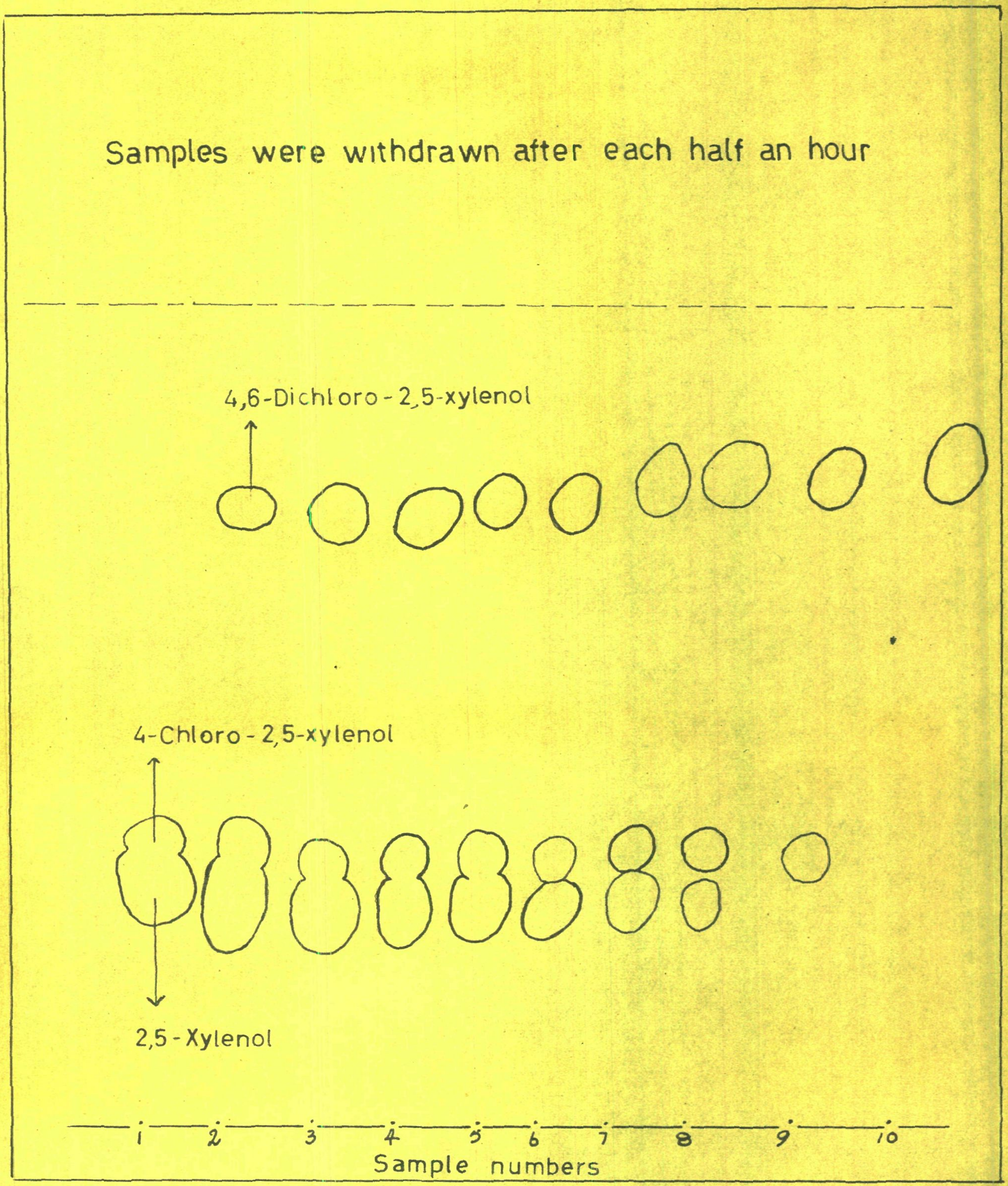
III



IV

Both, 4-chloro-2,5-xylenol (m.p. 74° C.) and 4,6-dichloro-2,5-xylenol (m.p. 84°C.) are already described in the literature[3,4]. The latter, further, gave a para-toluenesulphonate (m.p. 116.5°C.) and an aryloxyacetic acid (m.p. 195°C.).

The UV-spectrum of the dichloro-compound (Fig. 2) shows maximum absorptions at two wavelengths, viz. (i) 281 mμ; ϵ = 2208, and



TLC STUDY OF REACTION OF 2,5-XYLENOL WITH GASEOUS CHLORINE

FIG. 1

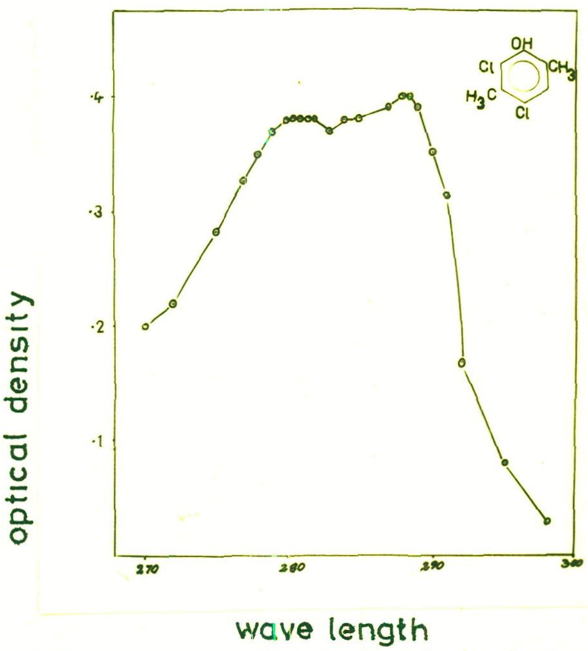


Fig. 2 UV spectrum of 4,6-dichloro-2,5-xylenol

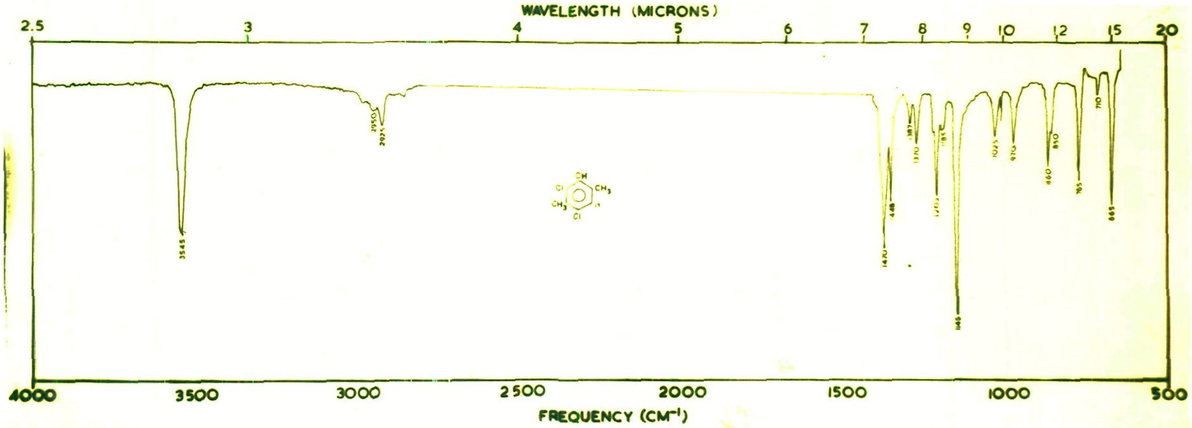


Fig. 3 IR spectrum of 4,6-dichloro-2,5-xylenol

(ii) 288 mμ; ε = 2327

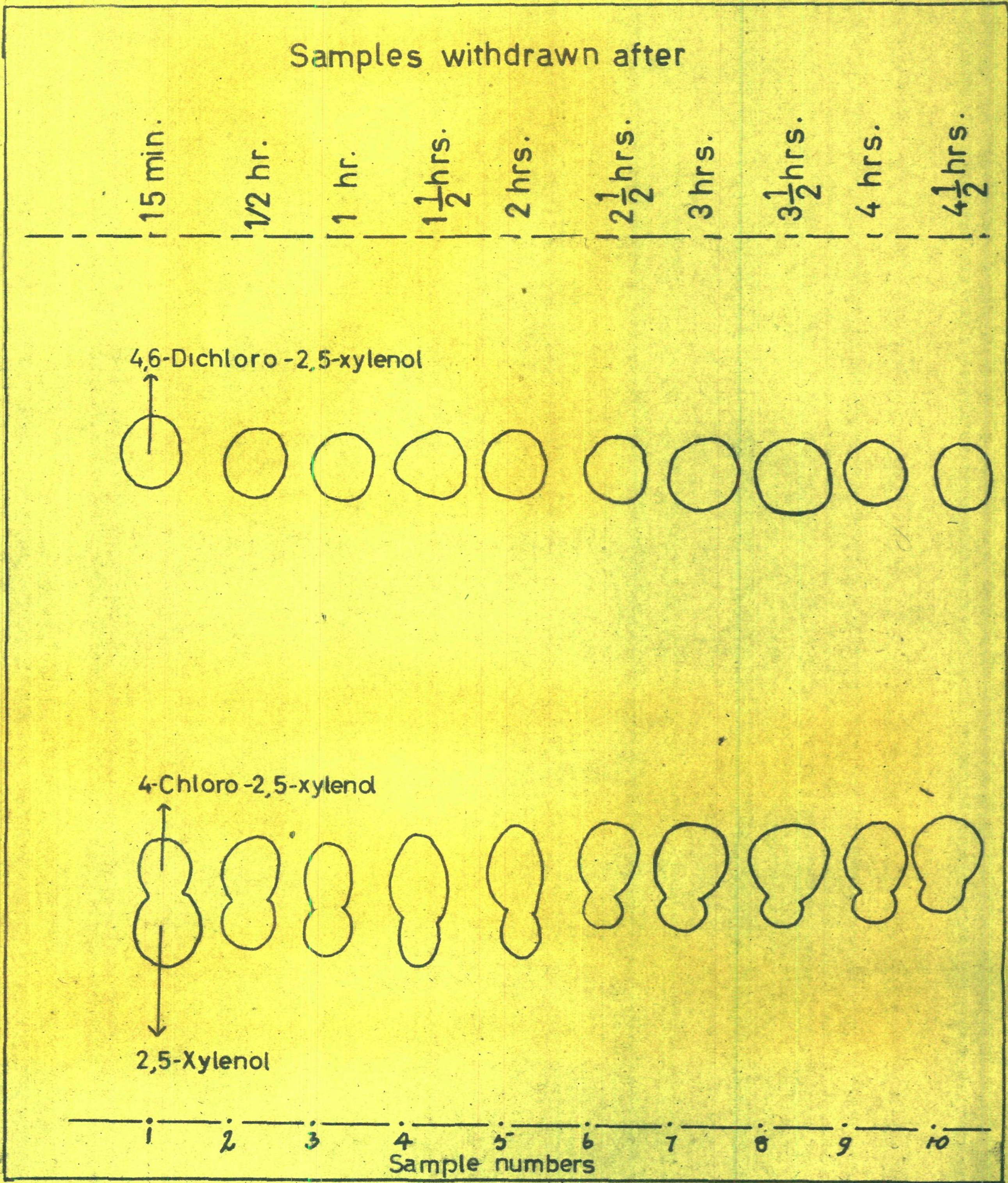
Its IR-spectrum (Fig. 3) indicates OH absorption at 3545 cm^{-1}, C-Cl stretching-vibration at 765 cm^{-1} and 665 cm^{-1} and the CH deformation-vibration at 860 cm^{-1}.

(b) Reaction with sulfuryl chloride

The course of chlorination of 2:5-xylenol with varying quantities of sulfuryl chloride in chloroform (one-, two- and three-molar ratios) at 0-2°C., are shown in Figs. 4, 5 and 6.

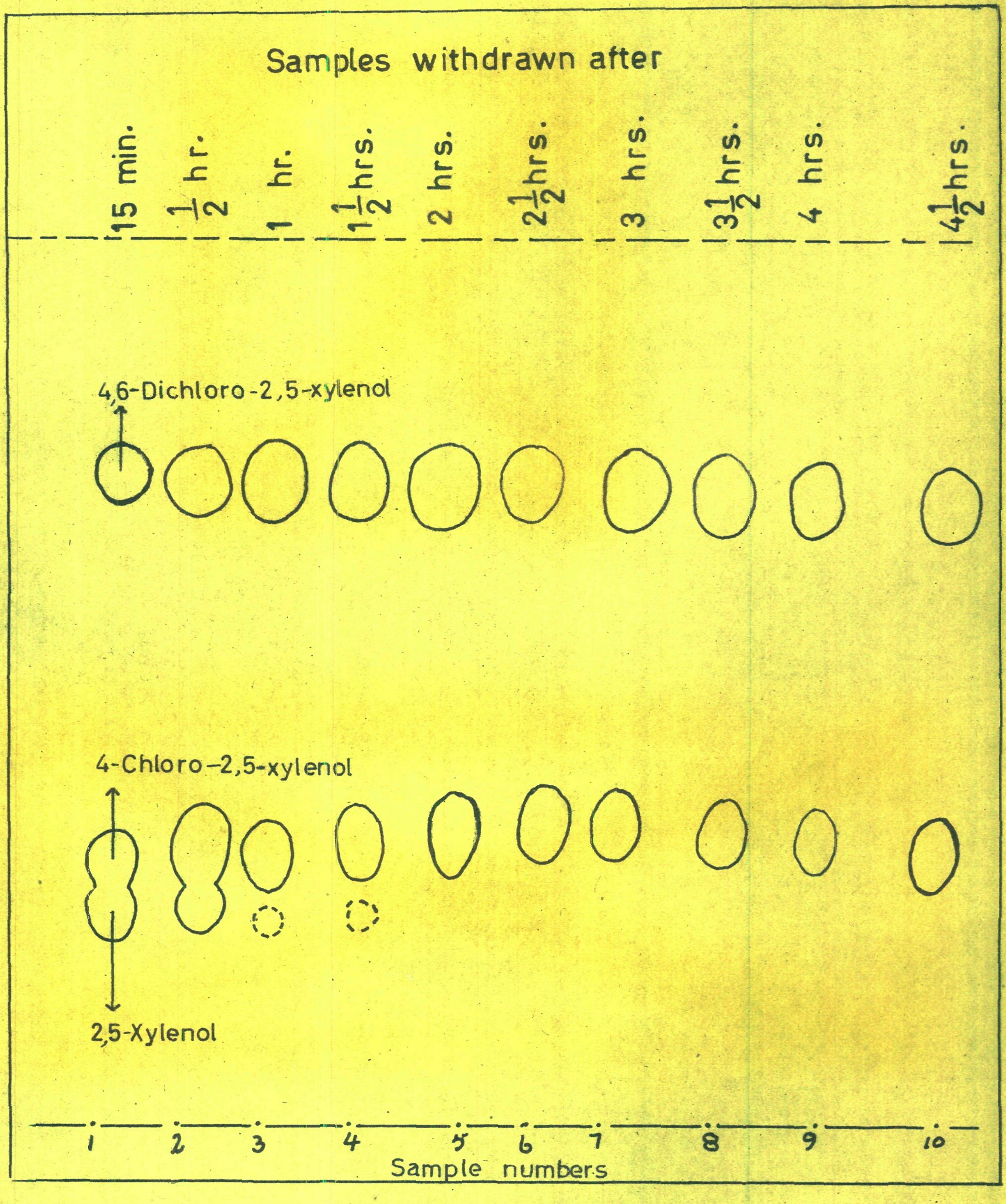
Sulphuryl chloride is a stronger chlorinating agent than gaseous chlorine and the dichloro-derivative, 4,6-dichloro-2,5-xylenol (III) makes its appearance within a very short time even with one molar reaction. However, the mono- and dichloro-derivatives are always present as a mixture in the reaction mass. The monochloro-derivative i.e. 4-chloro-isomer (II) could be isolated in 51% yield by fractional crystallisation (from pet. ether, 60-80°C.) of the two-molar reaction product. The yield of product is improved, if dry ether is used as a reaction medium and even with one-molar proportion of sulphuryl chloride, it could be isolated in about 75% yield. The product was further characterised as the _para_-toluenesulphonate, m.p. 80°C., and aryloxyacetic acid, m.p. 118°C. When three-molar quantity of the reagent was used, the dichloro-derivative (III) was the only detectable product, even just after half an hour reaction time.

The UV and IR-spectra of the monochloro derivative (II) are given in Figs. 7 and 8, respectively. Its λ -maxima values are



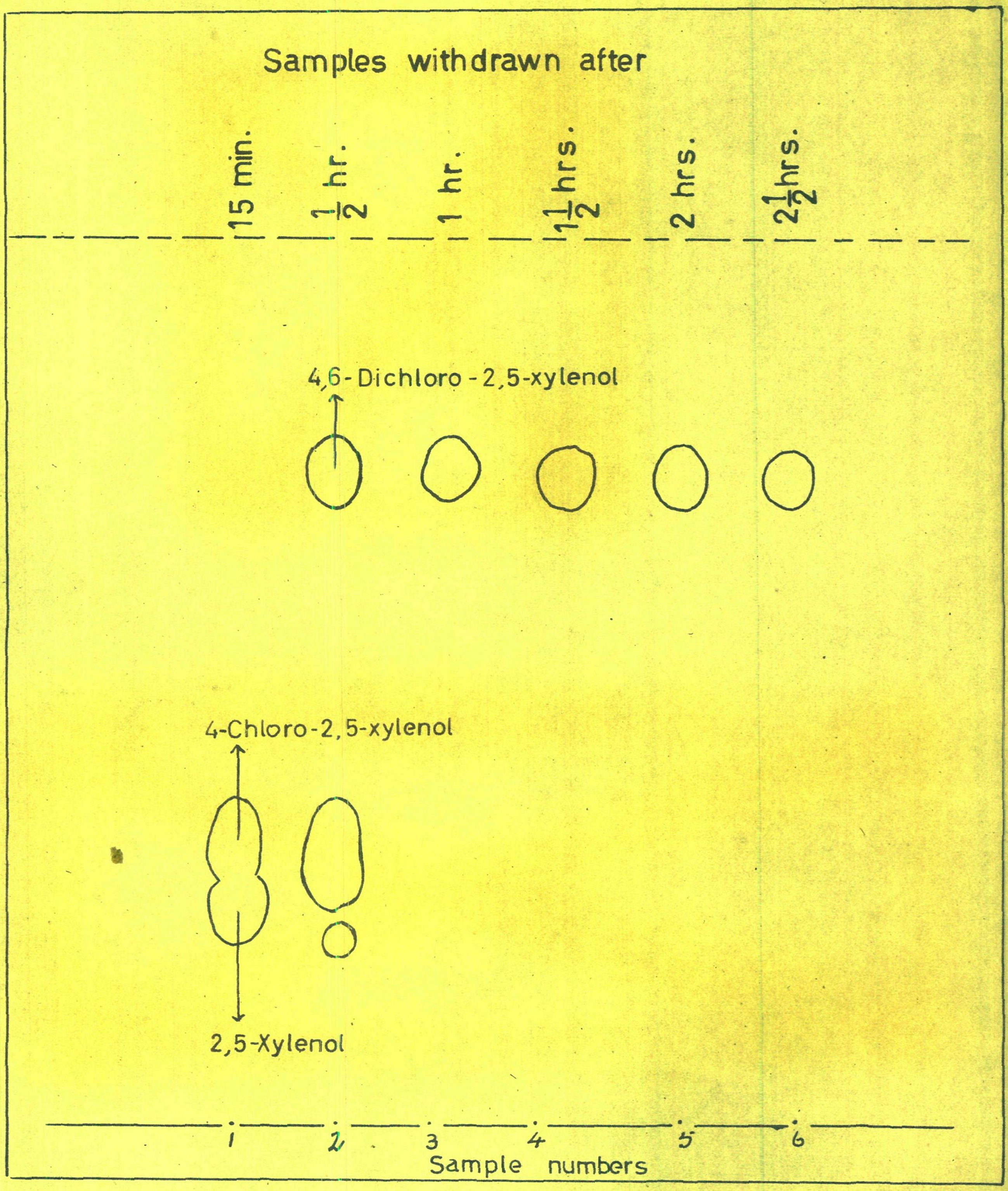
TLC STUDY OF CHLORINATION OF 2,5-XYLENOL WITH ONE MOLAR RATIO OF SULPHURYL CHLORIDE

FIG. 4



TLC STUDY OF CHLORINATION OF 2,5-XYLENOL WITH TWO MOLAR RATIO OF SULPHURYL CHLORIDE

FIG. 5



TLC STUDY OF CHLORINATION OF 2,5-XYLENOL WITH THREE MOLAR RATIO OF SULPHURYL CHLORIDE

FIG. 6

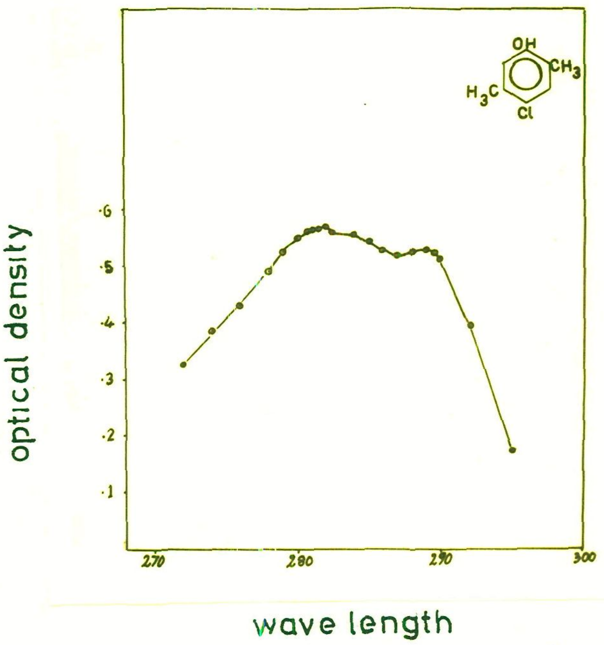


Fig. 7 UV spectrum of 4-chloro-2,5-xylenol

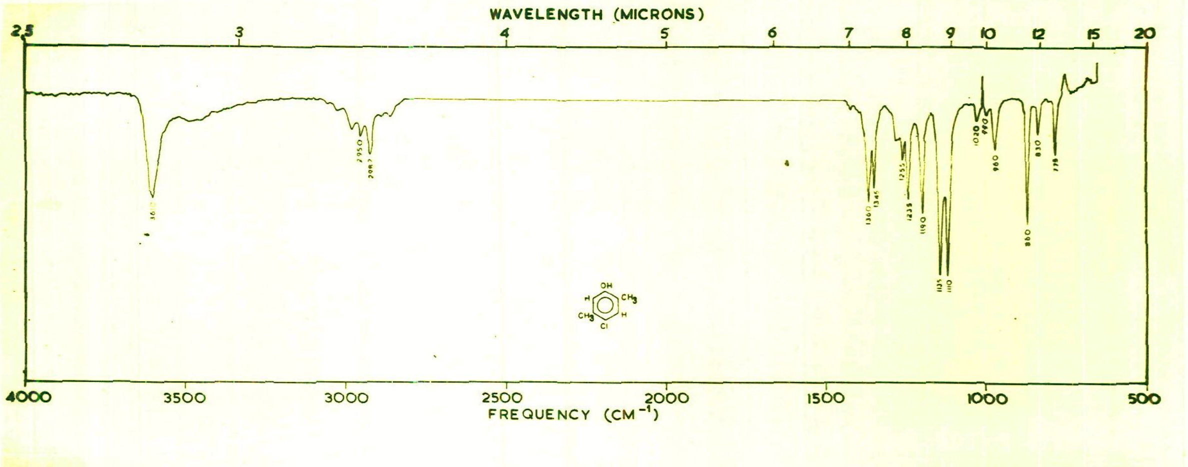


Fig. 8 IR spectrum of 4-chloro-2,5-xylenol

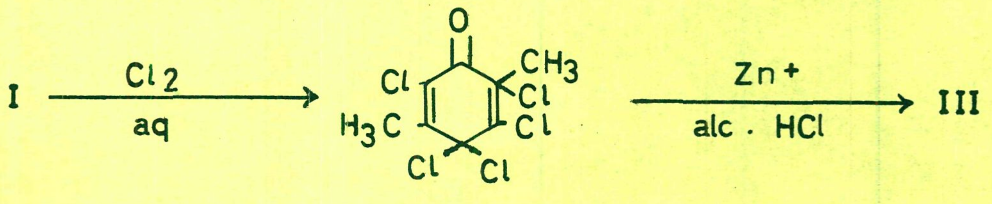
(i) 282 mμ; ϵ = 4440, and (ii) 289 mμ; ϵ = 4112. It gives OH absorption at 3610 cm^{-1}; its characteristic C-Cl stretching-vibration is at 775 cm^{-1} and a strong band of CH deformation at 860 cm^{-1}. The CH deformation-absorption is very characteristic and could be used as a criterion for identification of 4-chloro-2,5-xylenol.

(c) Reaction with ter-butylhypochlorite

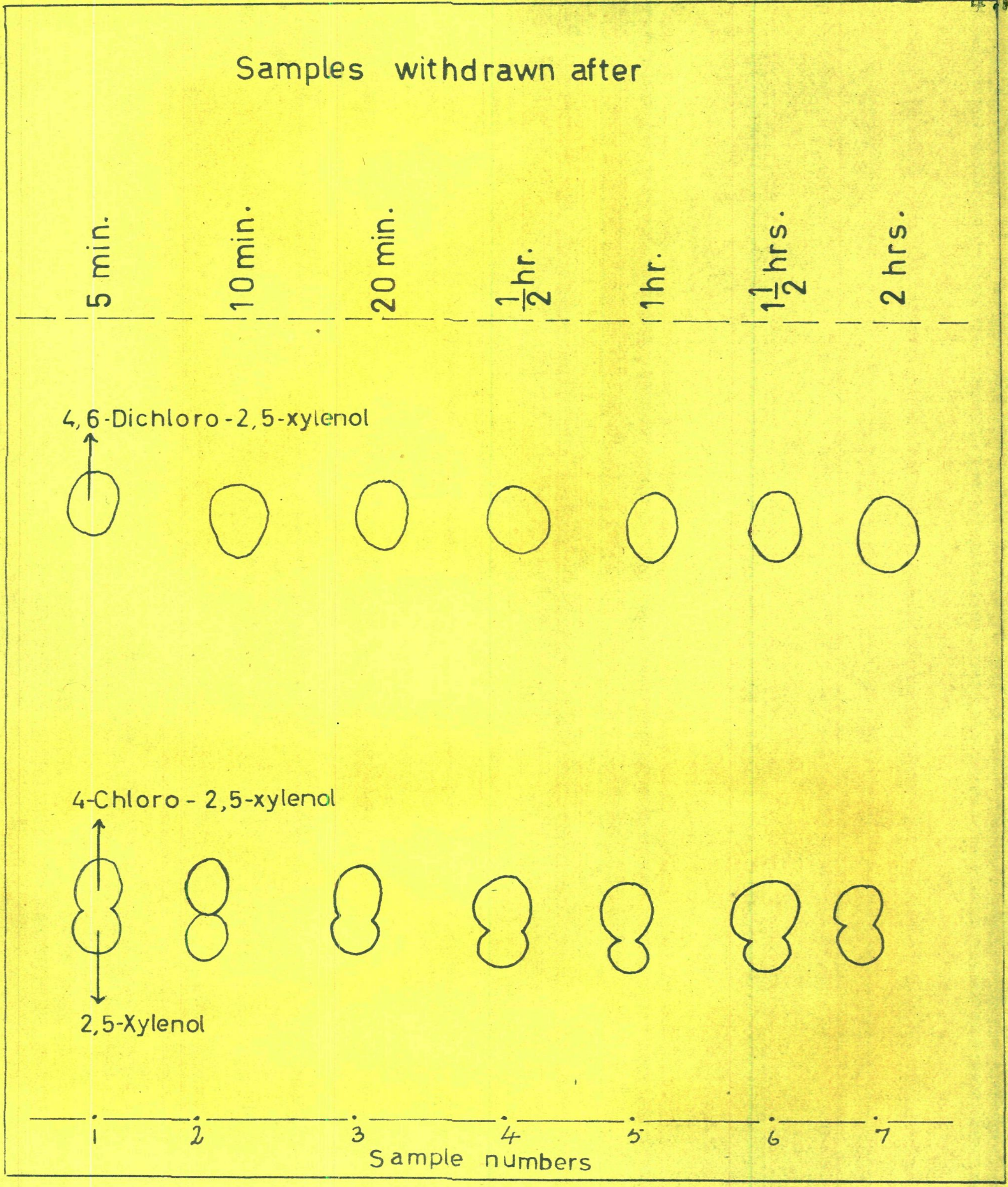
Studies on the chlorination of 2:5-xylenol with ter-butylhypochlorite, the known ortho-chlorinating agent, indicated that 4-chloro-2,5-xylenol (II) was formed as the first product of chlorination, as seen from the TLC diagram (Fig. 9). It is noteworthy that the 6-chloro-isomer (IV; ortho-isomer) was not at all detectable.

Use of one or two-molar quantities of this reagent gave a mixture of 4-chloro-2,5-xylenol and 4-6-dichloro-2,5-xylenol. However, with three-molar quantity, the dichloro-derivative was formed almost instantaneously, as the exclusive phenolic product (Figs. 10 and 11).

It may be stressed that the 4,6-dichloro-2,5-xylenol (III) can be directly prepared by any one of these methods. The best yield (71%) is obtained in the reaction with three-molar quantity of sulphuryl chloride. Mueller et al.[4] had obtained the dichloro-derivative indirectly through the reduction of 2,3,4,4,6-pentachloro-2,5-dimethylcyclohexadien-1-one (V) with zinc and alcoholic hydrogen chloride.

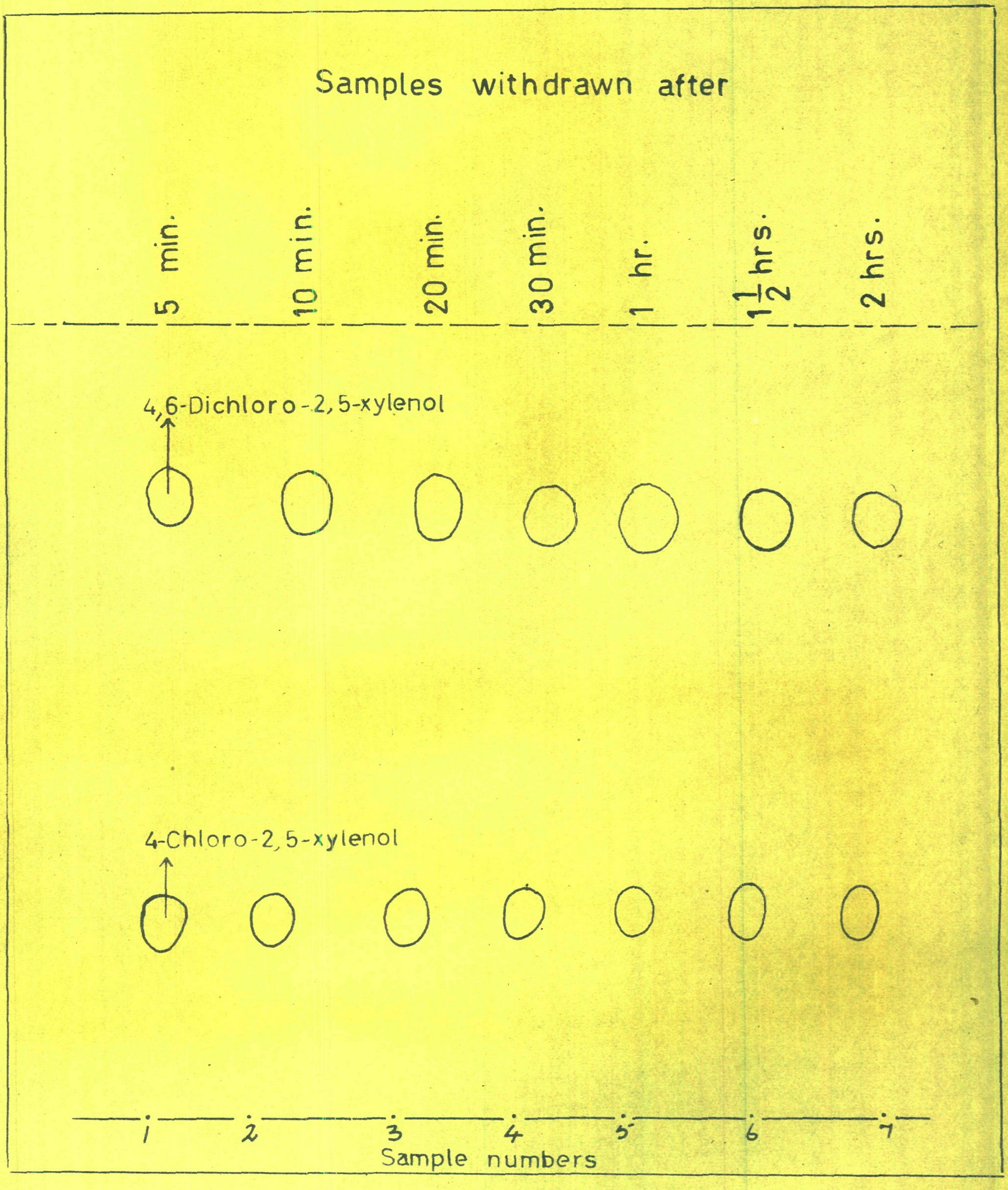


V



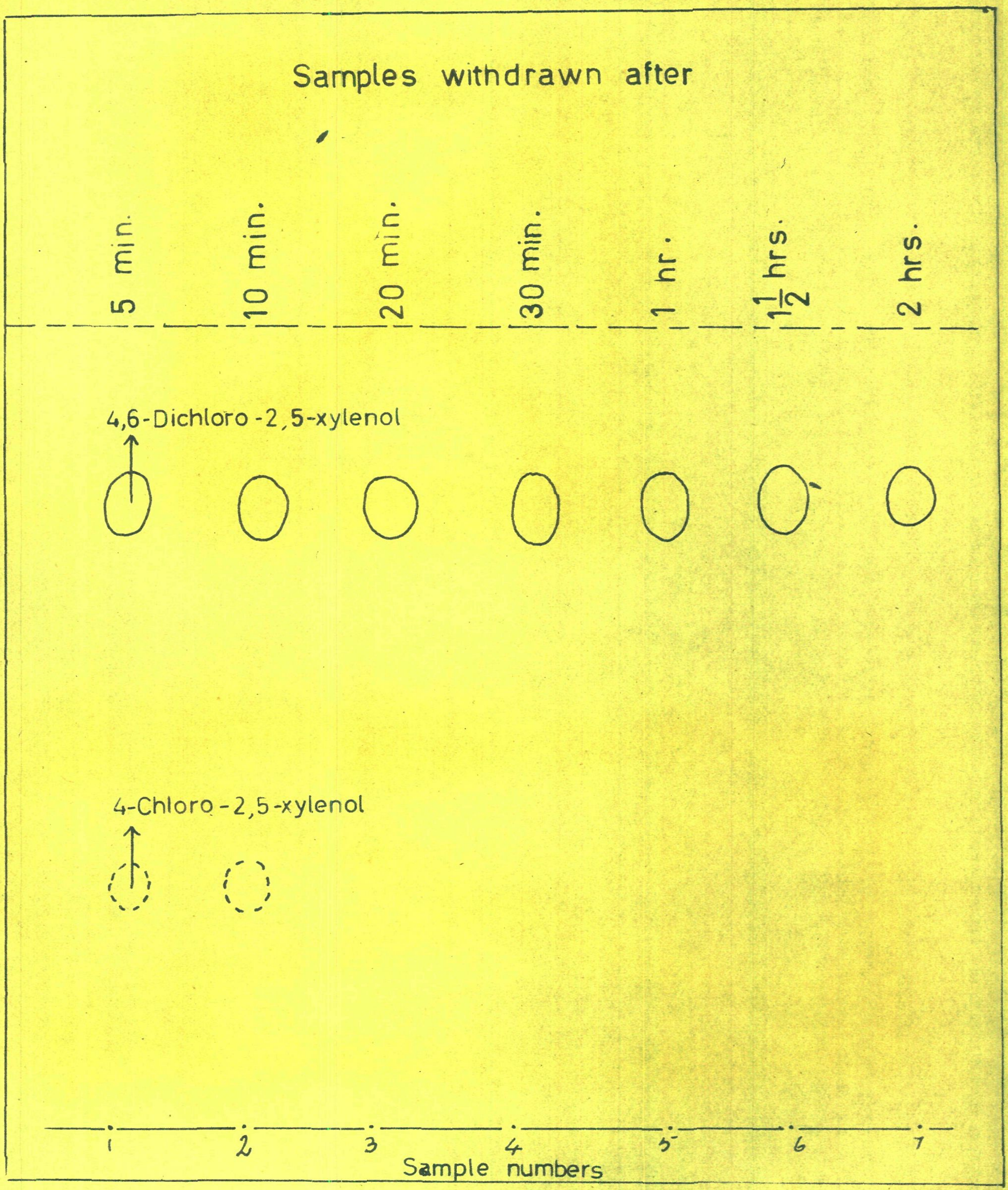
TLC STUDY OF CHLORINATION OF 2,5-XYLENOL WITH ONE MOLAR RATIO OF $(CH_3)_3$ C.O.Cl

FIG. 9



TLC STUDY OF CHLORINATION OF 2,5-XYLENOL WITH TWO MOLAR RATIO OF $(CH_3)_3$ C.O.Cl

FIG. 10



TLC STUDY OF CHLORINATION OF 2,5-XYLENOL WITH THREE MOLAR RATIO OF $(CH_3)_3C\cdot O\cdot Cl$

FIG. 11

A good preparative method for 4-chloro-2,5-xylenol has been found to be by chlorination of 2,5-xylenol with equimolar quantity of sulphuryl chloride in dry ether. Gad et al.[5] and Heikens[3] have already described this compound. They obtained it by the reaction of the same reagents in chloroform or acetic acid. However, no further details were given.

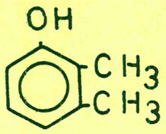
The non-formation of the 6-chloro-2,5-xylenol with all these chlorinating agents (even with $(CH_3)_3$ C.O. Cl) is noteworthy. It may also be observed that, in general the chlorination followed the normal orientation rules.

B. 2,3-XYLENOL

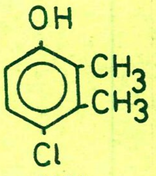
(a) Reaction with gaseous chlorine

The pattern of chlorination of 2,3-xylenol (VI) with gaseous chlorine is similar to that obtained with 2,5-xylenol, as is clear from the TLC diagram (Fig. 12).

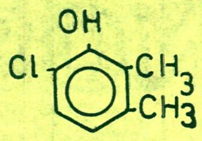
The 4,6-dichloro-2,3-xylenol (IX; $R_f = 0.79$) is the end product, after one hour of chlorination. The reaction proceeds through the formation of 4-chloro-2,3-xylenol (VII; $R_f = 0.31$) which is detectable in the reaction mixture throughout, till about 5-5½ hours, though in decreasing amounts. In this case also, the 6-chloro-2,3-xylenol (VIII; *ortho*-isomer) is not formed.



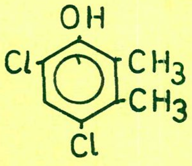
VI



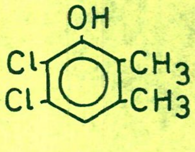
VII



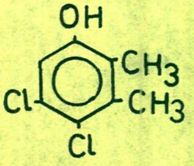
VIII



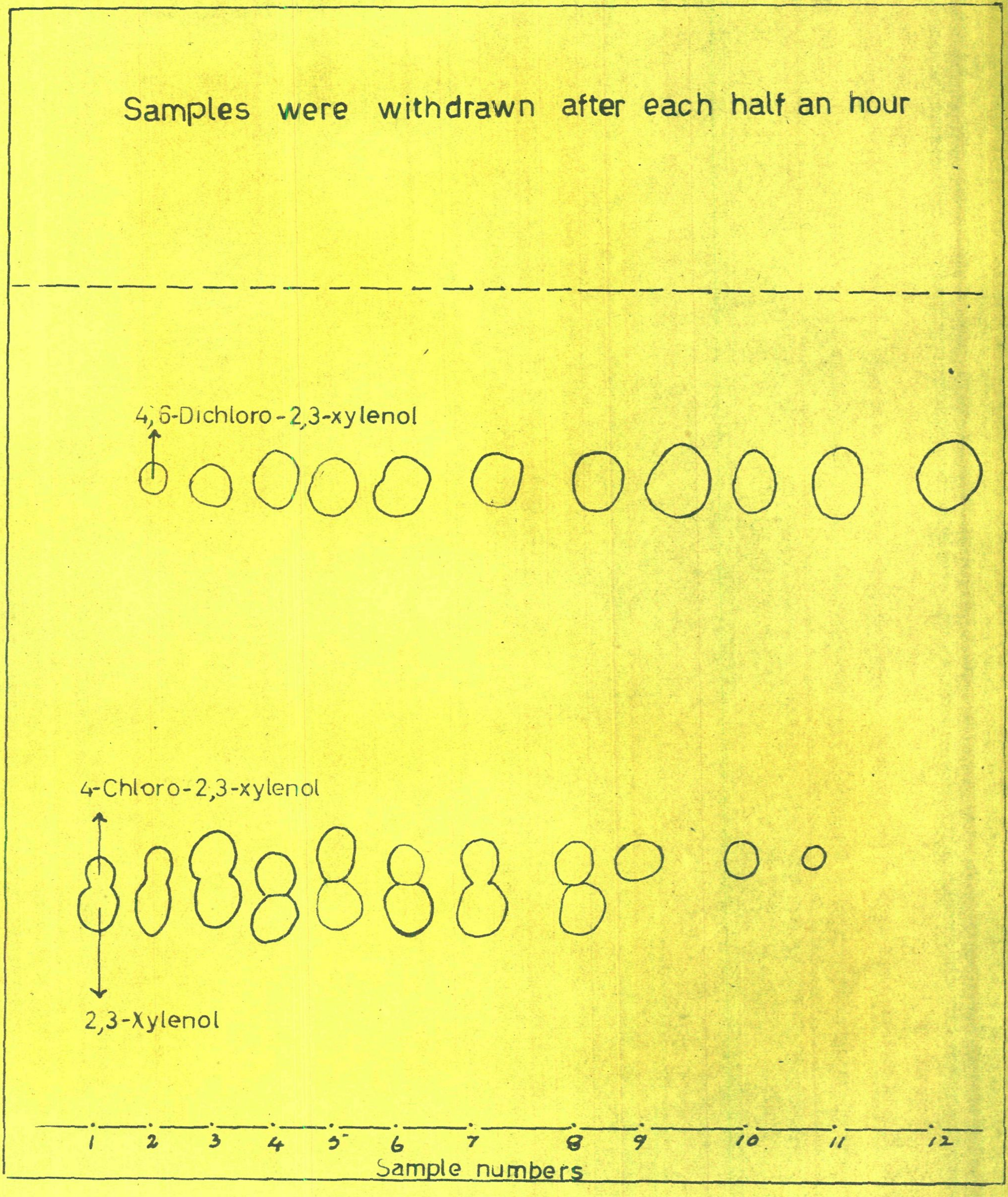
IX



X



XI



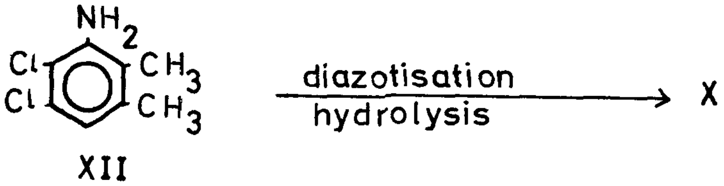
TLC STUDY OF REACTION OF 2,3-XYLENOL WITH GASEOUS CHLORINE

FIG. 12

The dichloro-derivative, m.p. 56-57°C., formed in this chlorination, has been assigned the 4,6-dichloro-structure out of the possible three structures (4,6-, 5,6-, and 4,5-; IX, X and XI) for the following reasons:

(a) chlorine first enters the 4-position, since the monochloro-compound has been identified as the 4-chloro-isomer (VII) (verified through mixed m.p. with the authentic sample and further characterised by UV and IR spectra);

(b) the 5,6-dichloro derivative (X) is already known (m.p. 90°C.) and was prepared by Hinkel et al.[6] through its unambiguous synthesis from 2,3-dimethyl-5,6-dichloroaniline (XII) via diazotisation and hydrolysis;



(c) the 4,5-dichloro-derivative (XI) is an unlikely product, keeping the normal rules of orientation in view;

(d) the results of UV-spectrum of the dichloro-compound (Fig. 14) also favour the 4,6-dichloro structure. The λ— max. for 4-chloro-2,3-xylenol is at 279.4 mμ (Fig. 13) and that of the dichloro-derivative at 281 mμ,

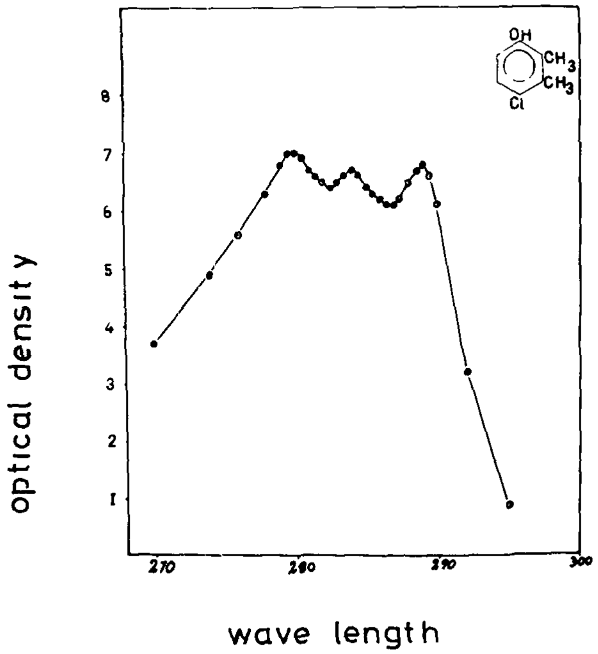


Fig. 13 UV spectrum of 4-chloro-2,3-xylenol

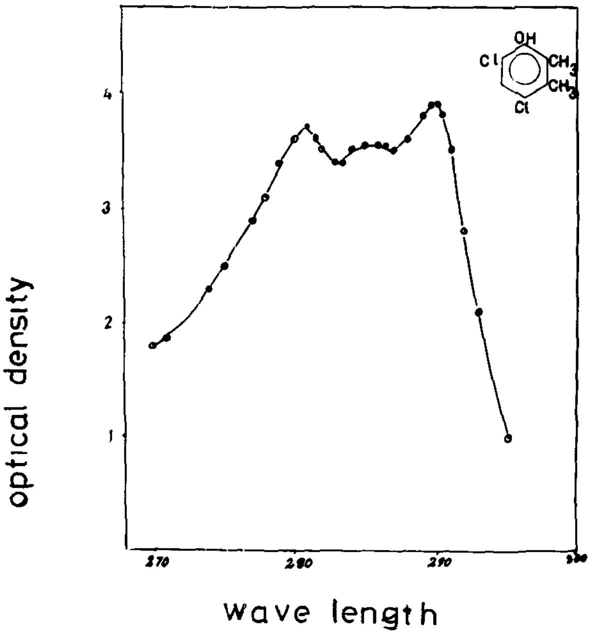


Fig. 14 UV spectrum of 4,6-dichloro-2,3-xylenol

the observed shift in the B-band being only 2.5 mμ. This indicates that the chlorine group is nearer to OH (steric factor). If the chlorine group was in the 5-position, the shift should have been much more (of the order of about 7 mμ) as shown by Dearden[7];

(e) the position of IR-absorption bands (Figs. 15 and 16) of OH also confirm the above stipulation. The OH-absorption peak for the isolated dichloro-compound is at 3545 cm^{-1} (Fig. 16), showing a shift to a lower wave number (due to intramolecular bonding). The shift would have been much less if the second chlorine group was at 5-position.

4,6-Dichloro-2,3-xylenol was converted to the following derivatives:

(i) *para*-toluenesulphonate, m.p. 95-96.5°C., and (ii) aryloxyacetic acid, m.p. 182°C.

(b) reaction with sulfuryl chloride

When 2:3-xylenol was treated with one-molar quantity of sulfuryl chloride, the chlorination mixture consisted of unreacted xylenol, 4-chloro-2,3-xylenol and some 4,6-dichloro-2,3-xylenol as can be seen from the TLC diagram (Fig. 17).

The formation of dichloro-derivative was observed within 15 minutes of the start of the reaction, though, the mono-isomer could be isolated in good yield (63%) even after 4 hours' reaction which was also characterised as its (i) *para*-toluenesulphonate, m.p. 84-84.5°C., and (ii) aryloxyacetic acid, m.p. 117°C.

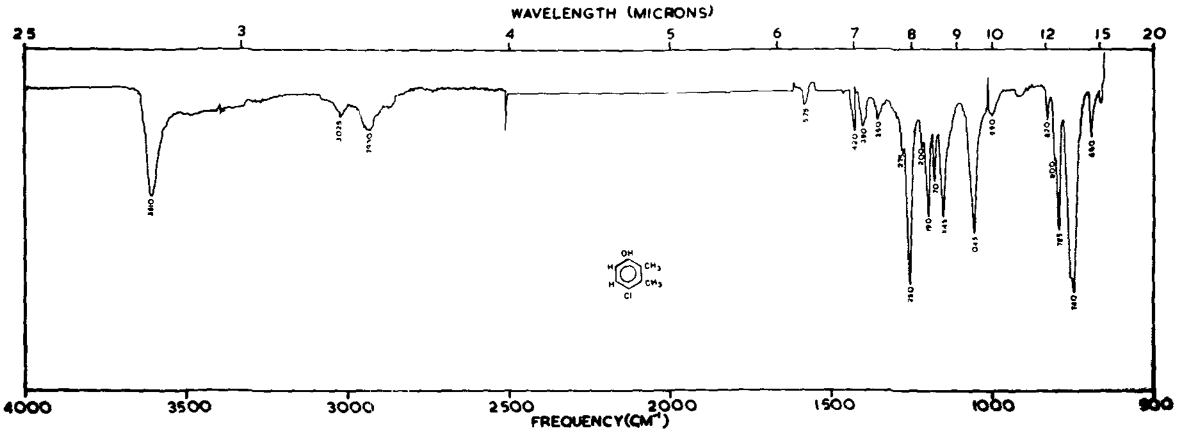


Fig. 15 IR spectrum of 4-chloro-2,3-xylenol

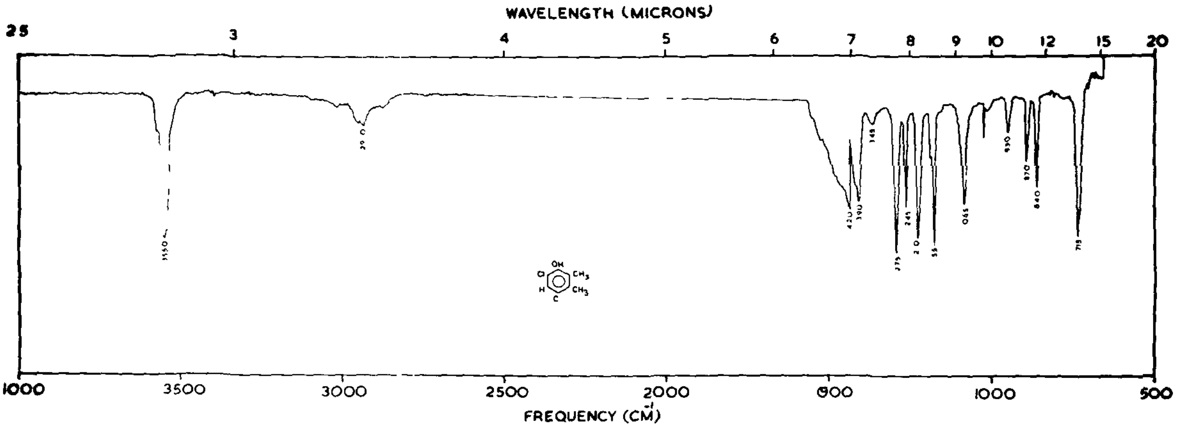
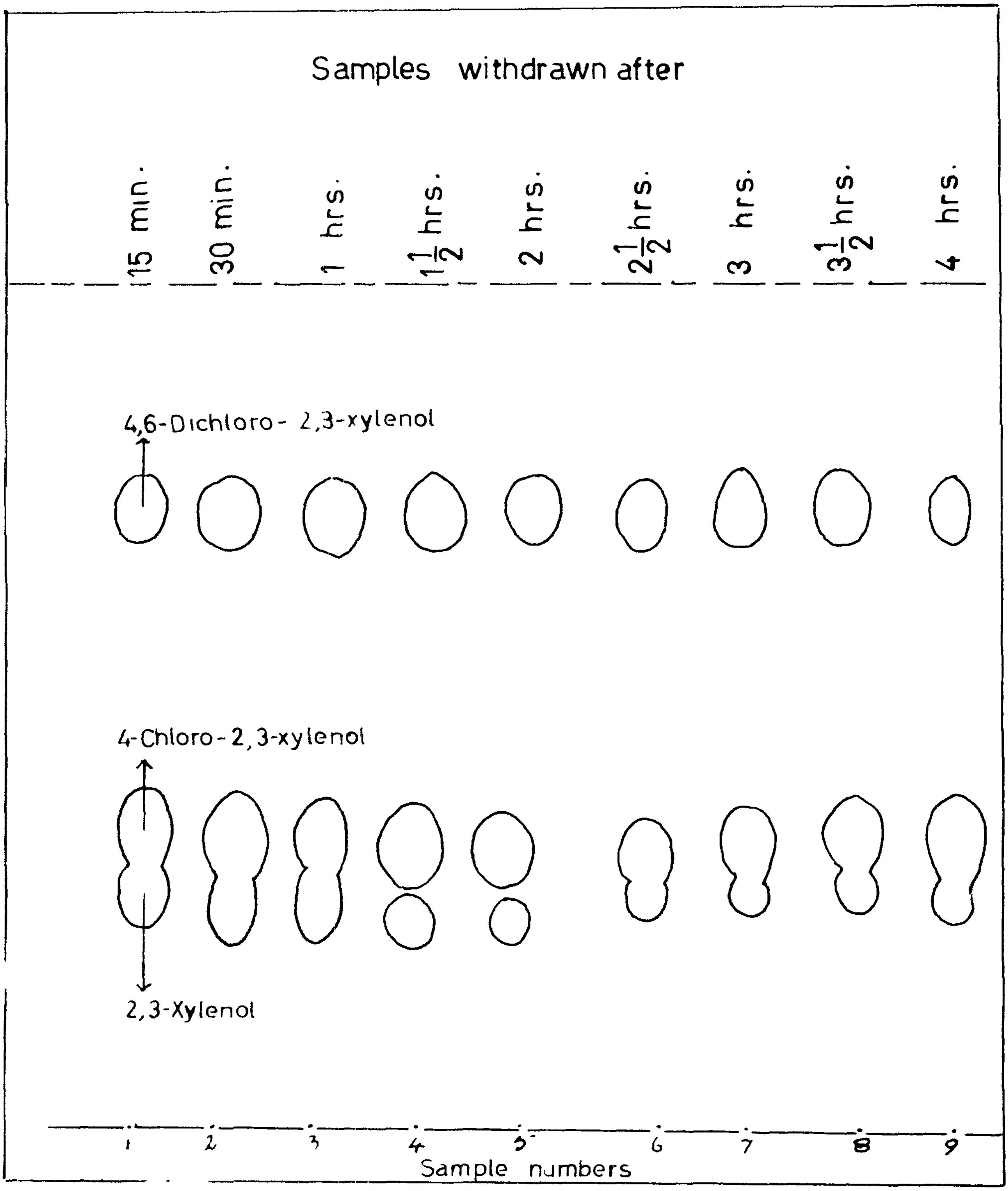


Fig. 16 IR spectrum of 4,6-dichloro-2,3-xylenol



TLC STUDY OF CHLORINATION OF 2,3-XYLENOL WITH ONE MOLAR RATIO OF SULPHURYL CHLORIDE

FIG. 17

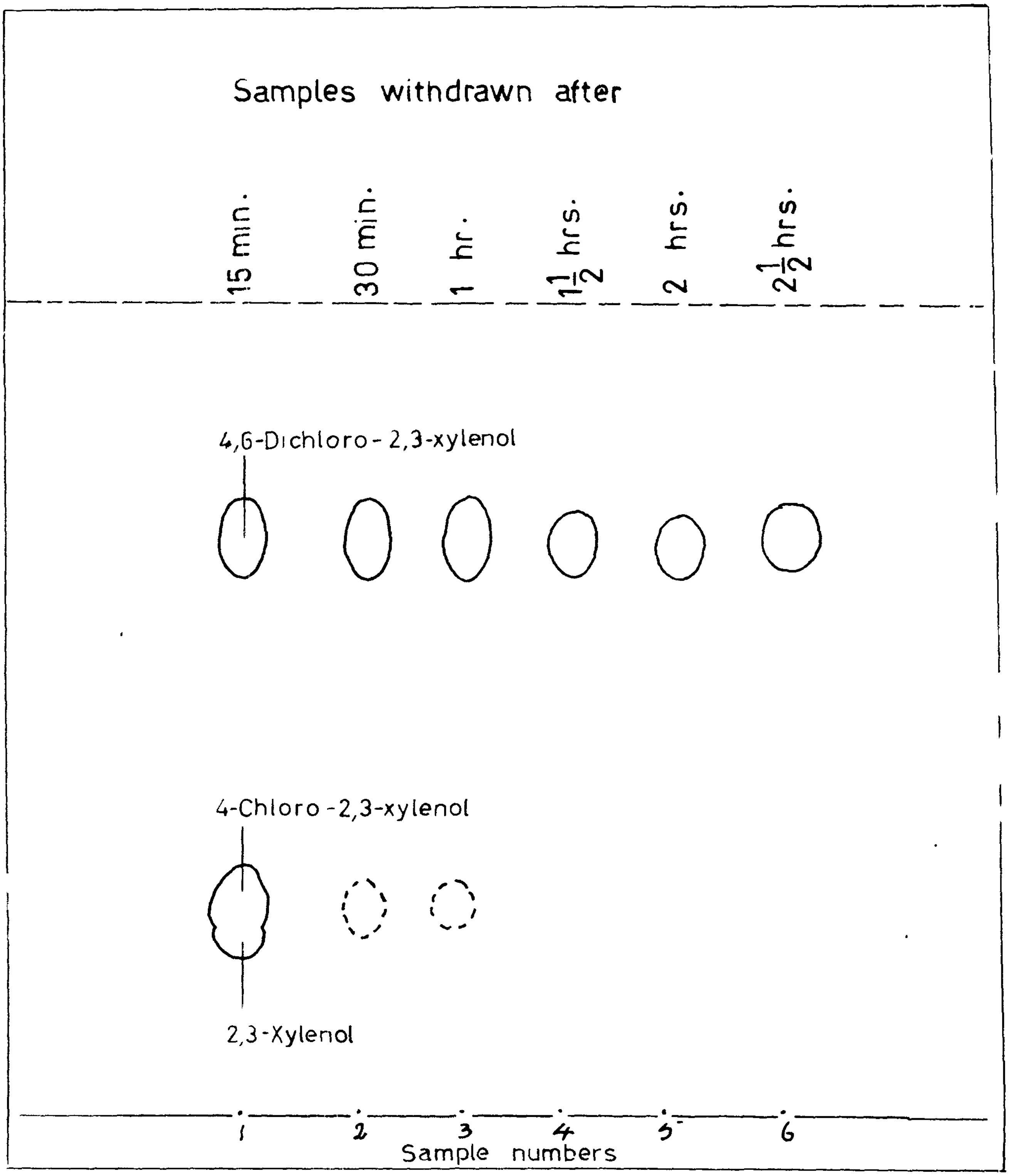
The same reaction, with two- or three-molar proportions of sulphuryl chloride led to the rapid formation of 4,6-dichloro-2,3-xylenol as was observed from the chromatograms (Figs. 18 and 19) and was isolated in 80-90% yield from these reaction mixtures.

(c) Reaction with ter-butylhypochlorite

From the chromatograms given in Figs. 20, 21 and 22, and obtained to study the chlorination of 2,3-xylenol with *ter*- butylhypochlorite, it could be seen that the pattern is similar to that obtained with 2,5-xylenol. Using three-molar proportion of *ter*-butylhypochlorite, 4,6-dichloro-compound was formed instantaneously and was the exclusive product of the reaction. It could be isolated in 76% yield.

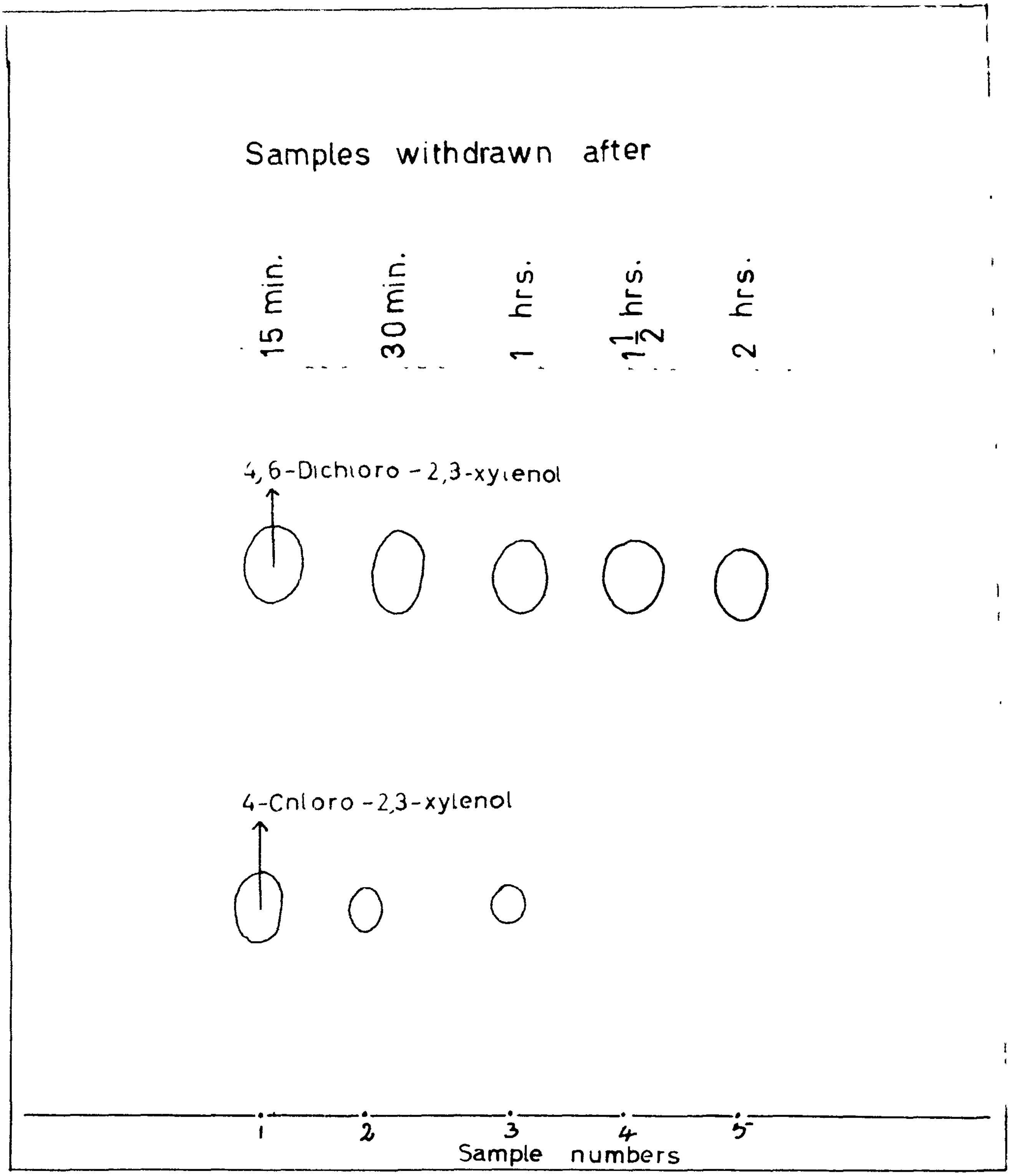
With lower proportions of this reagent, the mono-isomer (4-chloro-2,3-xylenol) was present in the reaction mixture in varying quantities, depending upon the quantity of the reagent. When equimolecular quantity of the reagent was used, even the starting xylenol was detectable on the chromatogram (even after 2½ hours rection). 4,6-Dichloro-2,3-xylenol was isolated in only about 24% yield from this reaction mixture using silica-gel column chromatography. However, 4-chloro-derivative could not be isolated in a pure state.

This study has brought out that the hitherto unknown 4,6-dichloro-2,3-xylenol (IX) can be prepared in good yield employing any one of the reagents described above. Further, the 4-chloro-2,3-xylenol could also be prepared by the direct chlorination method, using equimolecular quantity of sulphuryl chloride in acetic acid. It may be mentioned



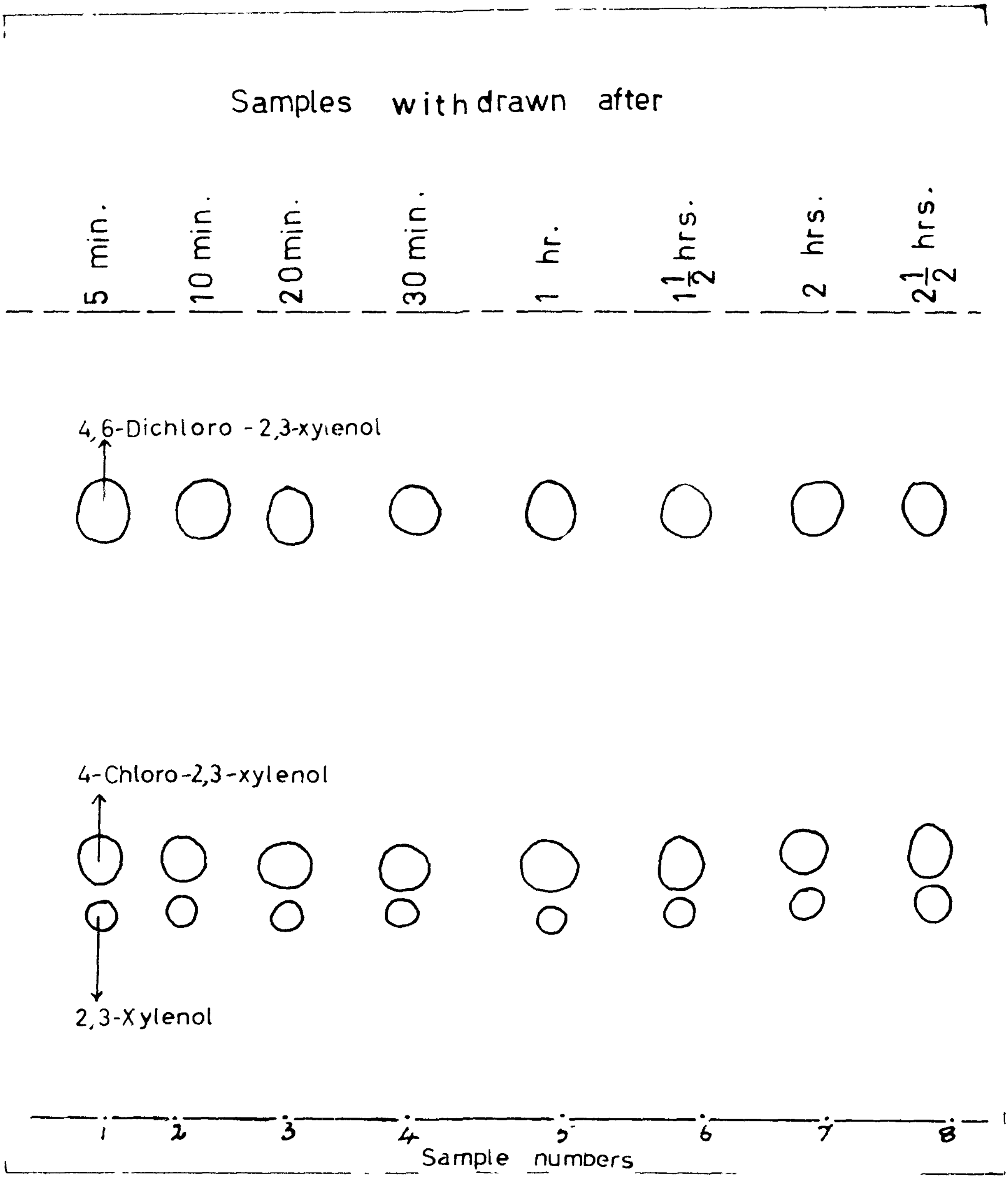
TLC STUDY OF CHLORINATION OF 2,3-XYLENOL WITH TWO MOLAR RATIO OF SULPHURYL CHLORIDE

FIG. 18



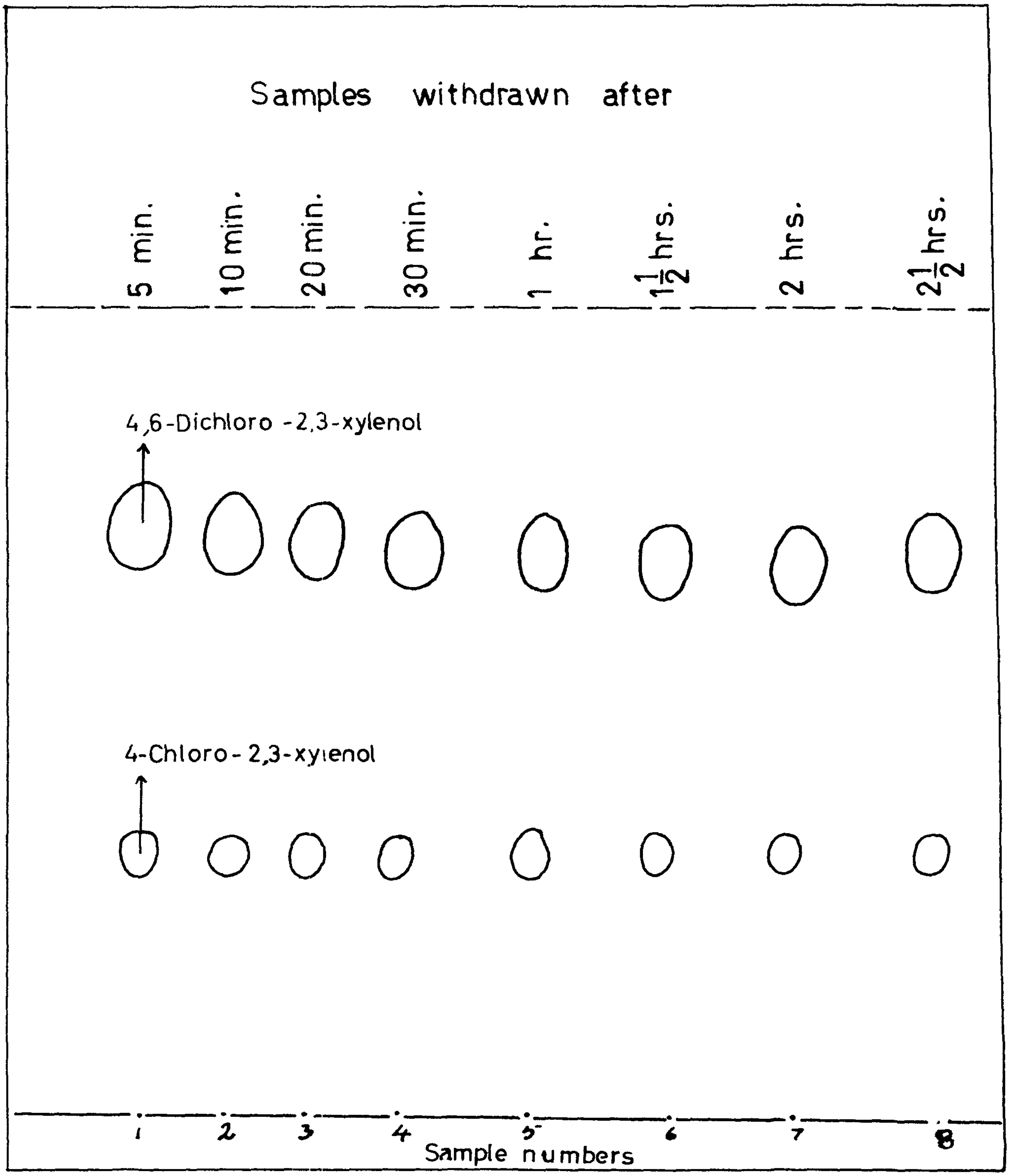
TLC STUDY OF CHLORINATION OF 2,3-XYLENOL WITH THREE MOLAR RATIO OF SULFHURYL CHLORIDE

FIG. 19



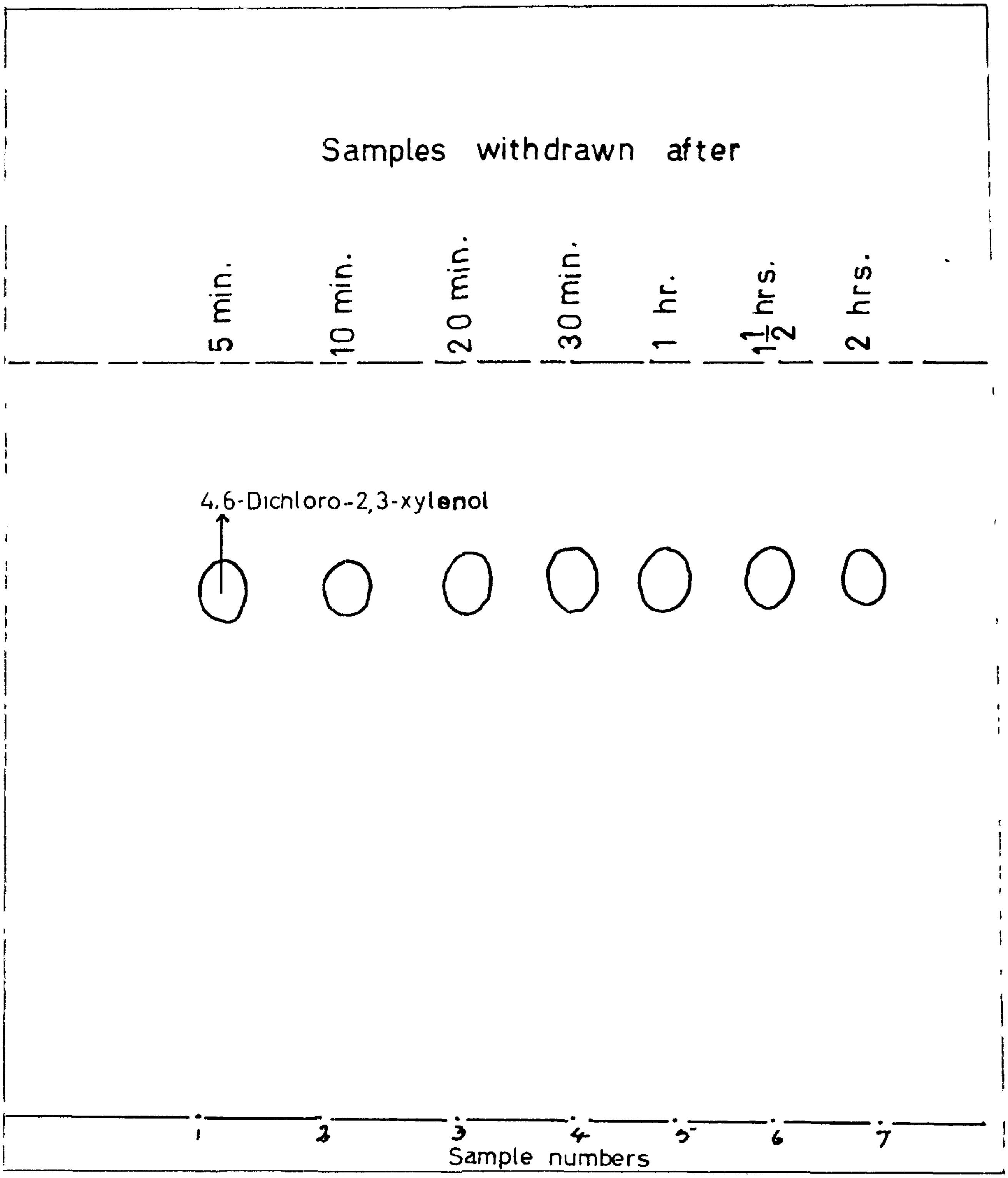
TLC STUDY OF CHLORINATION OF 2,3-XYLENOL WITH ONE MOLAR RATIO OF $(CH_3)_3C.O.Cl$

FIG 20



TLC STUDY OF CHLORINATION OF 2,3-XYLENOL WITH TWO MOLAR RATIO OF $(CH_3)_3C{\cdot}O{\cdot}Cl$

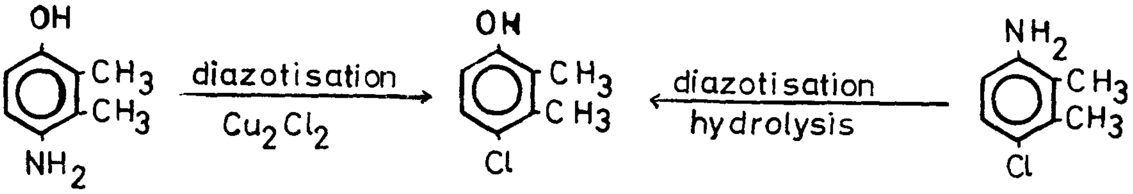
FIG. 21



TLC STUDY OF CHLORINATION OF 2,3-XYLENOL WITH THREE MOLAR RATIO OF $(CH_3)_3C.O.Cl$

FIG. 22

that it has been described in literature to have been obtained indirectly, as follows[8]:



XII VII XIII

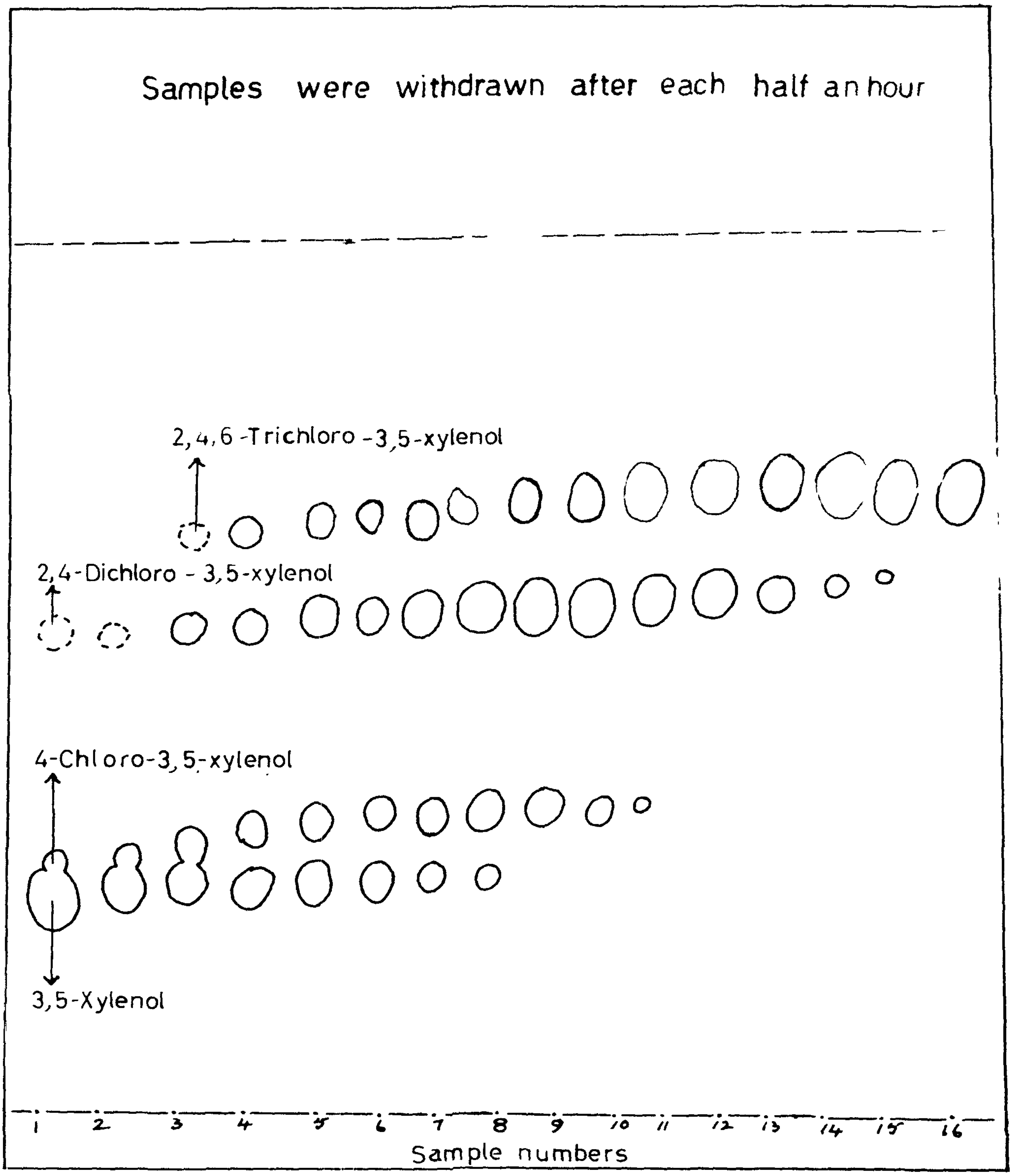
It is noteworthy that, here again, the 6-chloro-derivative was not detected in any chlorination.

C. 3,5-XYLENOL

(a) Reaction with gaseous chlorine

Exhaustive treatment of 3,5-xylenol ($R_f = 0.22$) with gaseous chlorine in carbon tetrachloride was carried out and the TLC chromatograms taken at regular intervals. These chromatograms showing the progress of the reaction are given in Fig. 23.

It could be seen, that the reaction though slow, led to a mixture of 4-chloro-3,5-xylenol ($R_f = 0.28$), 2,4-dichloro-3,5-xylenol (DCMX) ($R_f = 0.53$) and 2,4,6-trichloro-3,5-xylenol (TCMX) ($R_f = 0.62$). Traces of the starting phenol were noticeable even after four hours and it took about eight hours to give a single product, i.e., 2,4,6-trichloro-3,5-xylenol. It was isolated in 87% yield and characterised as its para-toluenesulfonate, m.p. 158°C. and aryloxyacetic acid, m.p. 75°C.



TLC STUDY OF REACTION OF 3,5-XYLENOL WITH GASEOUS CHLORINE

FIG. 23

The UV-spectrum of the 2,4,6-trichloro-3,5-xylenol (Fig. 24) showed maximum absorptions at (a) 282 mμ; ϵ = 2749, and (b) 291 mμ; ϵ = 3371. IR-spectrum of the compound is reproduced in Fig. 25, and shows OH-absorption at 3530 cm^{-1} along with the characteristic C-Cl stretching-vibration at 715 cm^{-1}.

(b) Reaction with sulphuryl chloride

Using sulphuryl chloride as the chlorinating agent in one-, two- and three-molar proportions and chloroform as a solvent, it was found that the reaction proceeds through 4-chloro-3,5-xylenol, followed by the formation of 2,4-dichloro-3,5-xylenol and finally leading to 2,4,6-trichloro-3,5-xylenol (see Figs. 26, 27 and 28).

It may be mentioned that contrary to the observation of earlier workers[6], 2-chloro-3,5-xylenol was found to be singularly absent at every stage of chlorination. The earlier workers (loc cit) had reported its presence in the product of chlorination of crude coal tar fractions, containing mainly 3,5-xylenol with these reagents. Similarly, 2,6-dichloro-3,5-xylenol has not been detected and one could presume that the 4-position is the most reactive. This is expected from the electronic theory.

With three-molar quantities of sulphuryl chloride, 2,4,6-trichloro-3,5-xylenol was the exclusive product isolated in 94% yield. Using two moles of sulphuryl chloride, 2,4-dichloro-3,5-xylenol could be isolated in 53% yield and characterised as its para-toluenesulfonate, m.p. 114°C., and aryloxyacetic acid, m.p. 140°C.

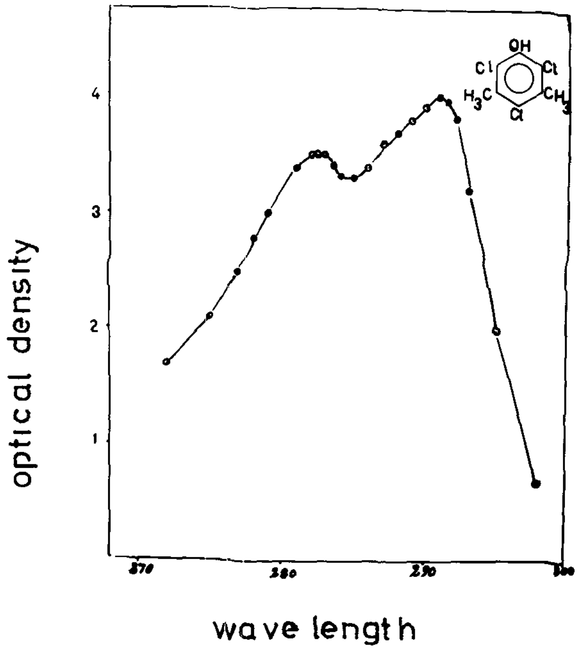


Fig. 24 UV spectrum of 2,4,6-trichloro-3,5-xylenol

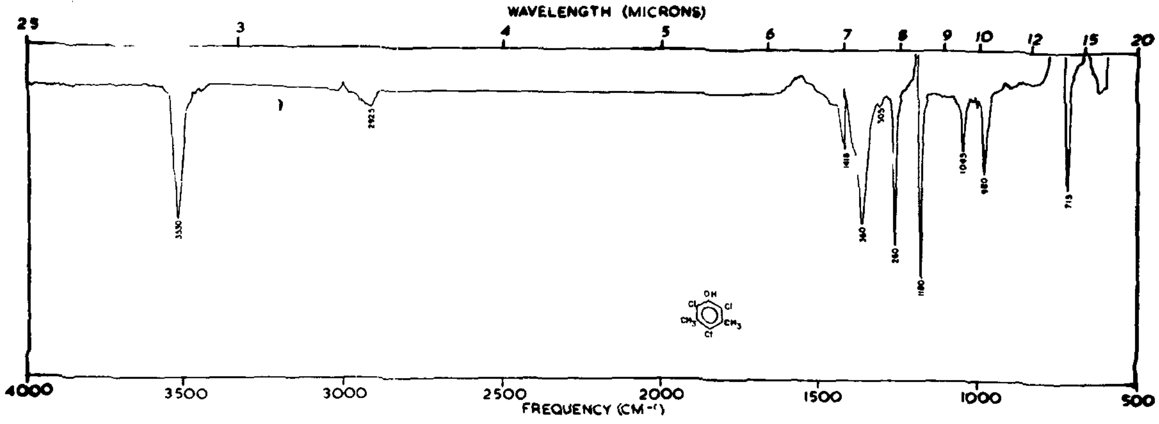
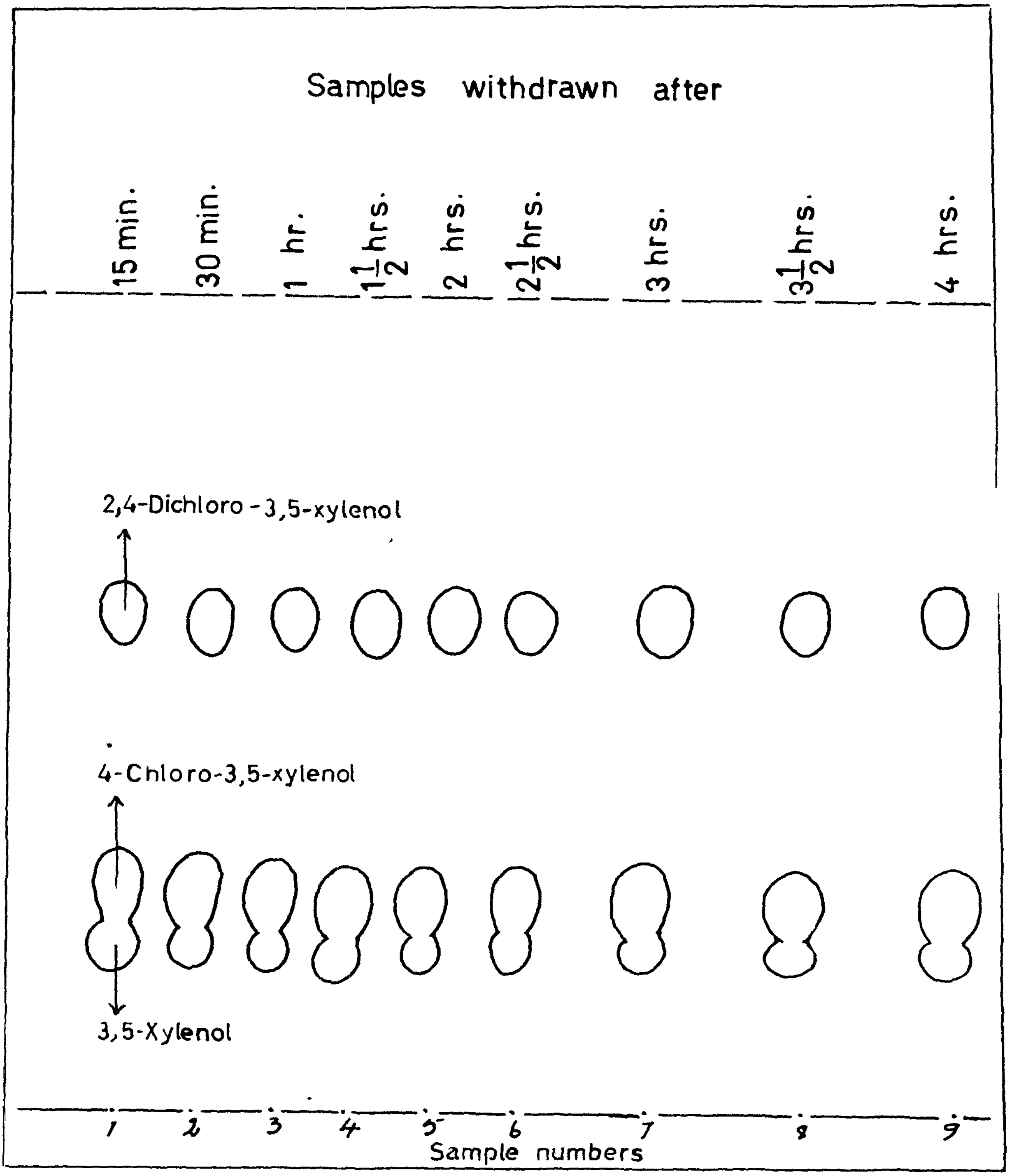
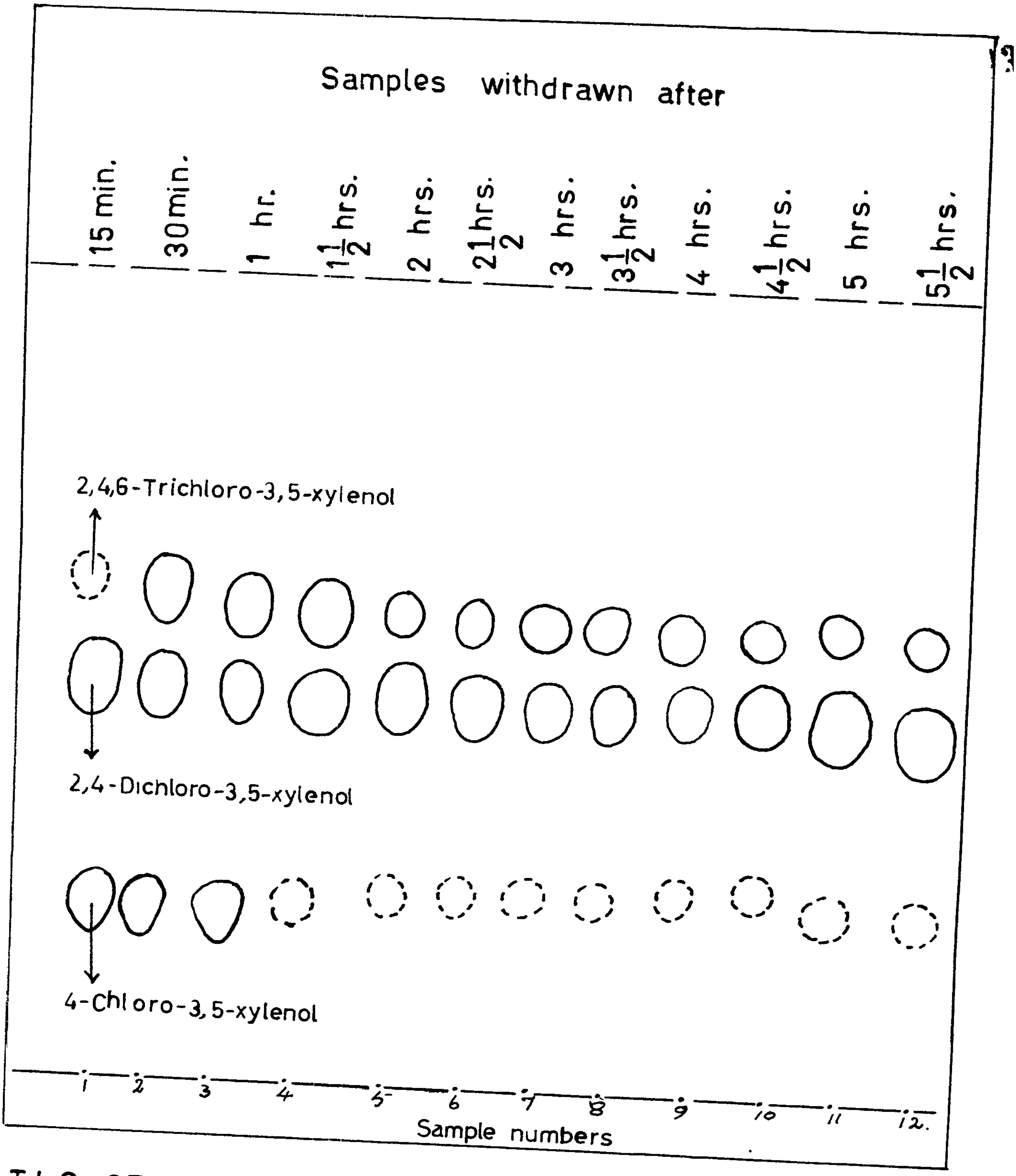


Fig. 25 IR spectrum of 2,4,6-trichloro-3,5-xylenol



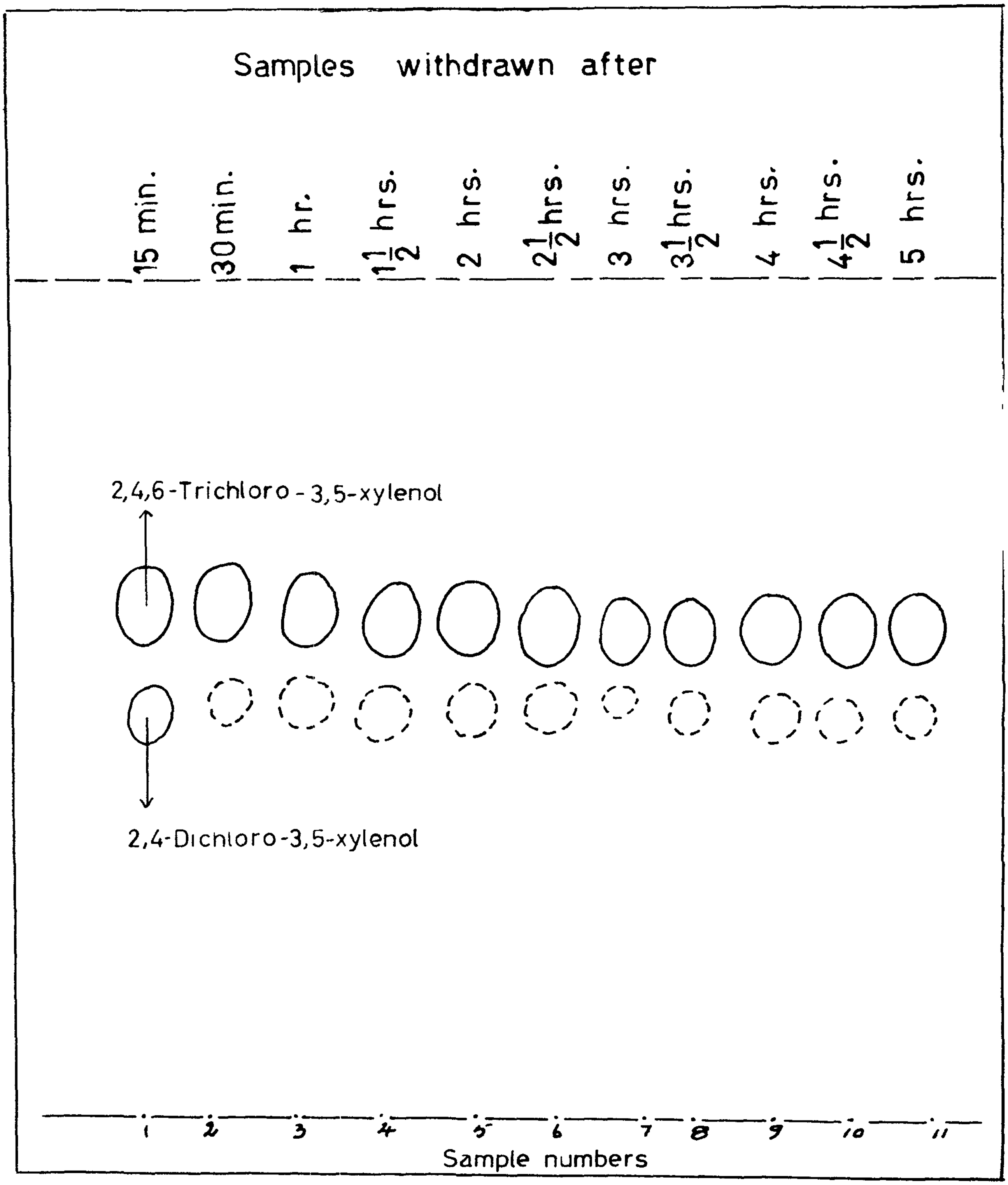
TLC STUDY OF CHLORINATION OF 3,5-XYLENOL WITH ONE MOLAR RATIO OF SULPHURYL CHLORIDE

FIG. 26



TLC STUDY OF CHLORINATION OF 3,5-XYLENOL WITH TWO MOLAR RATIO OF SULPHURYL CHLORIDE

FIG. 27



TLC STUDY OF CHLORINATION OF 3,5-XYLENOL WITH THREE MOLAR RATIO OF SULPHURYL CHLORIDE

FIG. 28

The UV-spectrum of 2,4-dichloro-3,5-xylenol (Fig. 29) shows λ-max. at (a) 281 mμ; ϵ = 4601 (b) 286 mμ; ϵ = 2460 and (c) 290 mμ; ϵ = 2610. Its IR-spectrum is reproduced in Fig. 30 and shows the OH-absorption at 3540 cm^{-1} and characteristic C-Cl stretching-vibration at 690 cm^{-1}.

4-Chloro-3,5-xylenol, however, could only be isolated in good yield (82.5%) from the reaction mixture, where one-molar proportion of sulphuryl chloride was used. It was characterised as (i) para-toluenesulfonate, m.p. 103.5°C., and (ii) aryloxyacetic acid, m.p. 143°C. Its UV and IR-spectra are reproduced in Figs. 31 and 32, respectively. Its λ.max. are at 279 mμ; ϵ = 2096 and 287 mμ; ϵ = 2077. The OH-absorption peak is at 3600 cm^{-1}, CH deformation band at 840 cm^{-1} and C-Cl stretching-vibration at 745 cm^{-1}.

(c) Reaction with ter-butylhypochlorite

The TLC-diagram of the progress of reaction with ter-butyl-hypochlorite on 3,5-xylenol in three different molar proportions (one-, two- and three-) are given in Figs. 33, 34 and 35. It would be seen that the results are analogous to those obtained with sulphuryl chloride and the reagent does not behave as an ortho-chlorinating reagent.

From preparative angle, the results were not very satisfactory for 4-chloro-and 2,4-dichloro-compounds. The former could not be isolated in a pure form; the latter could be isolated in 12% yield from the reaction mixture of one-molar proportion of the reactants, employing column chromatography on silica-gel. The reaction product of

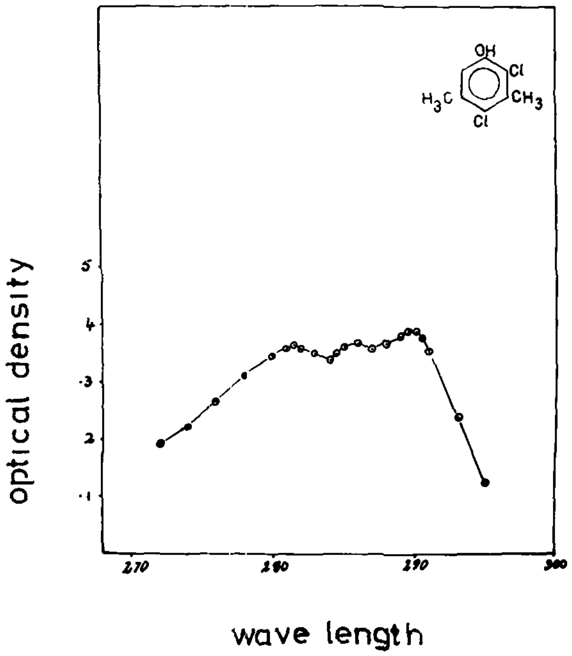


Fig. 29 UV spectrum of 2,4-dichloro-3,5-xylenol

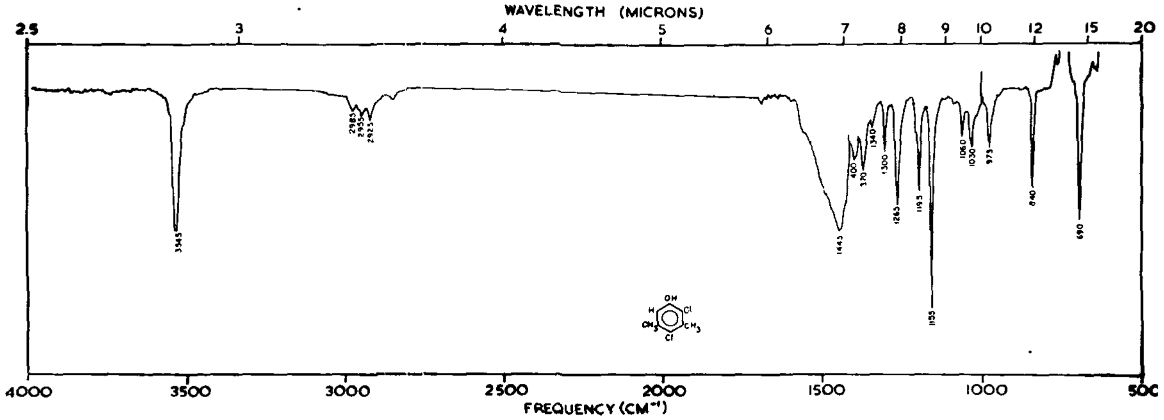


Fig. 30 IR spectrum of 2,4-dichloro-3,5-xylenol

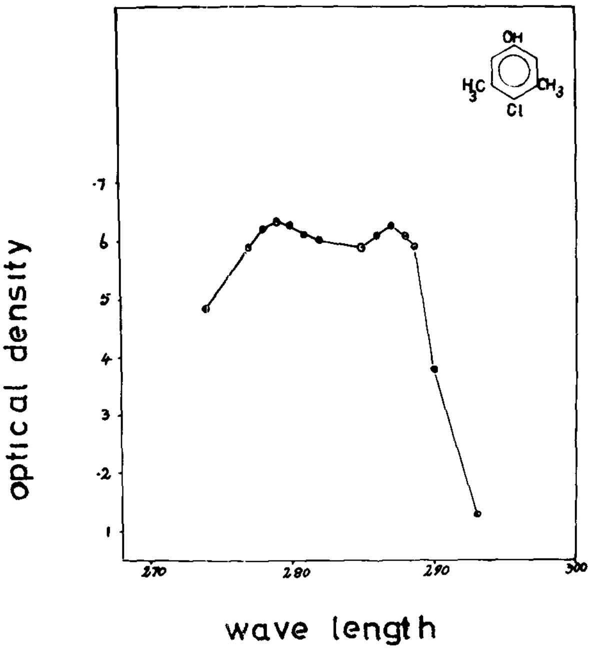


Fig. 31 UV spectrum of 4-chloro-3,5-xylenol

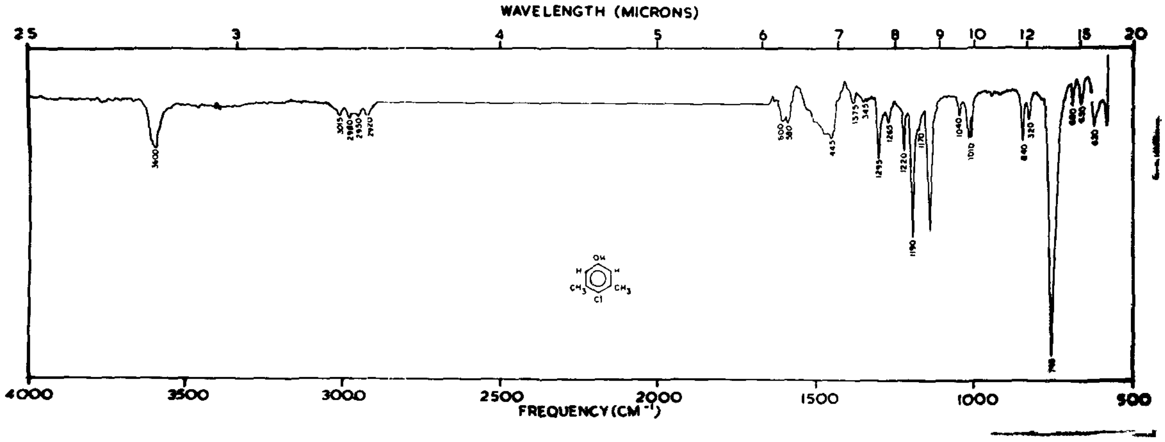
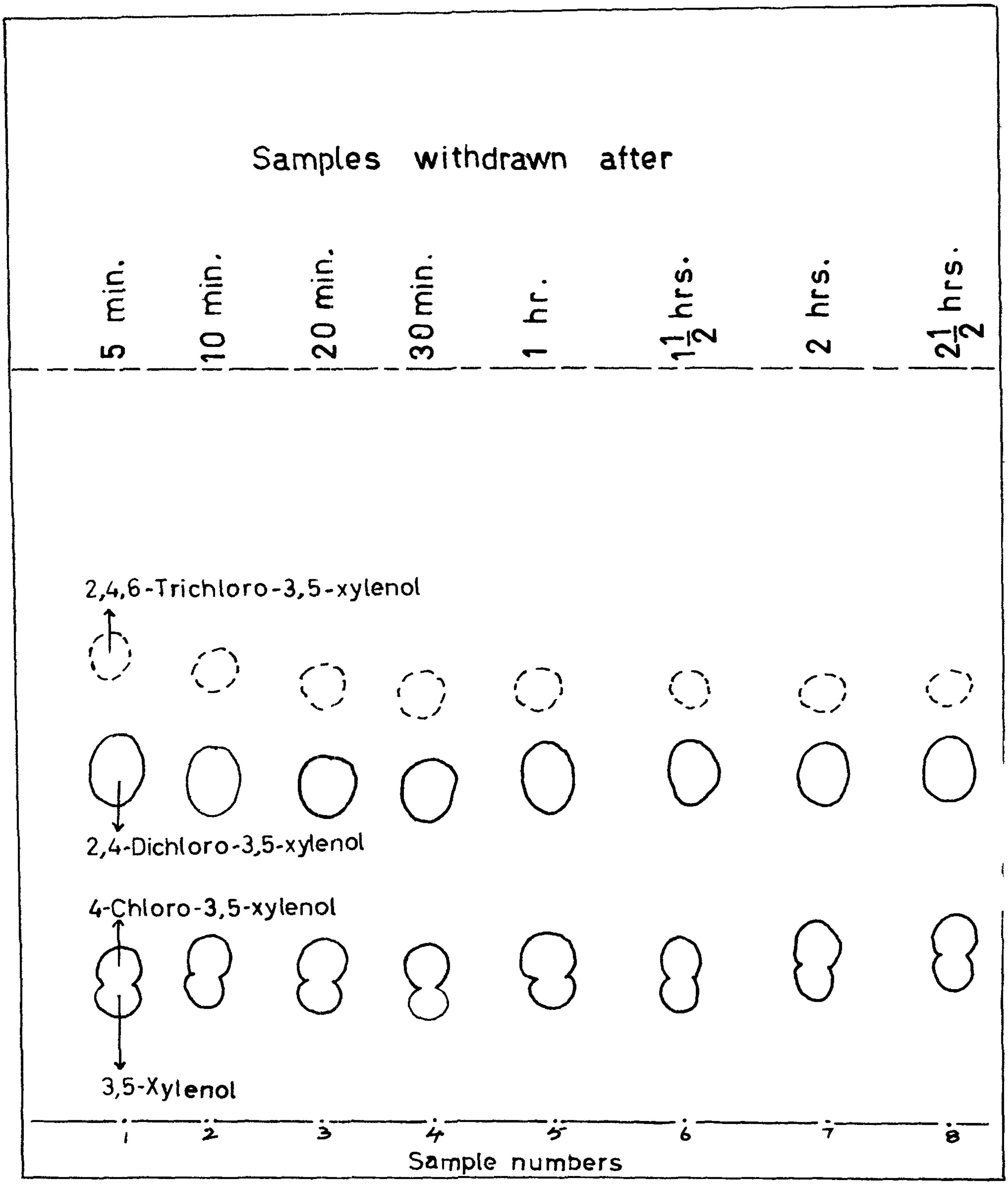
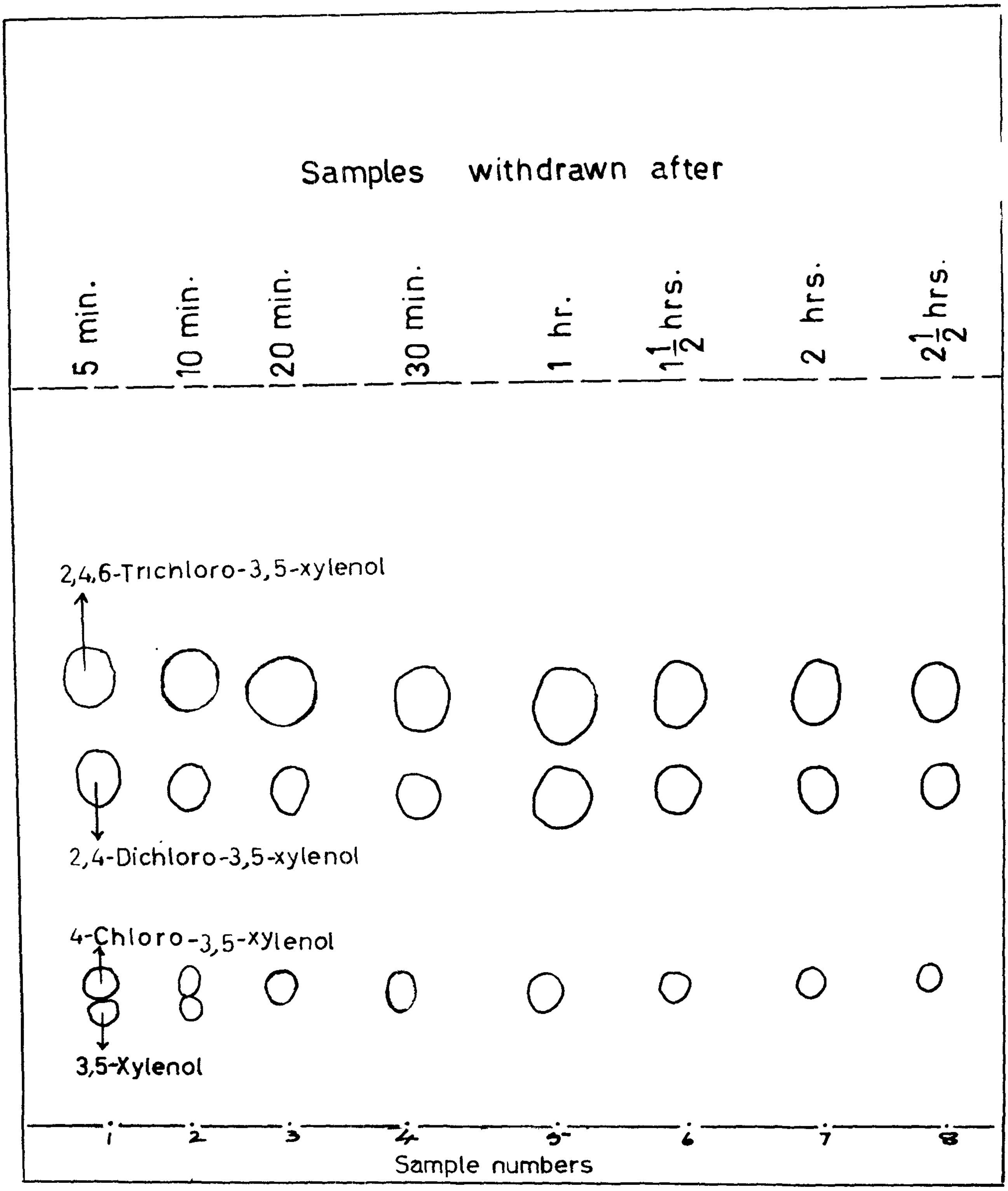


Fig. 32 IR spectrum of 4-chloro-3,5-xylenol



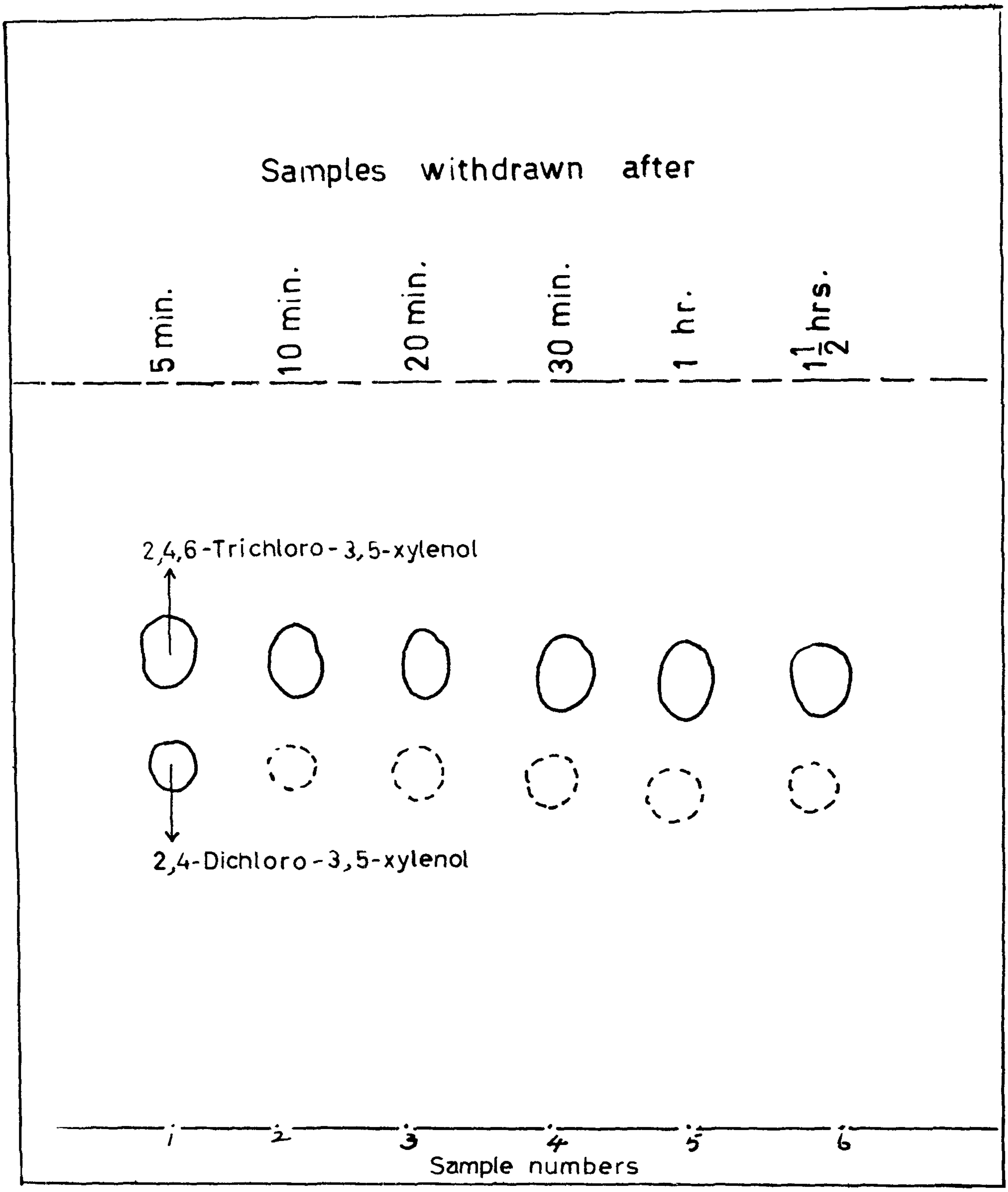
TLC STUDY OF CHLORINATION OF 3,5-XYLENOL WITH ONE MOLAR RATIO OF $(CH_3)_3C{\cdot}O{\cdot}Cl$

FIG. 33



TLC STUDY OF CHLORINATION OF 3,5-XYLENOL WITH TWO MOLAR RATIO OF $(CH_3)_3C{\cdot}O{\cdot}Cl$

FIG. 34



TLC STUDY OF CHLORINATION OF 3,5-XYLENOL WITH THREE MOLAR RATIO OF $(CH_3)_3C{\cdot}O{\cdot}Cl$

FIG. 35

2-molar quantities behaved similarly. However, it yielded the following compounds in pure form by preparative TLC.

(i) 4-chloro-3,5-xylenol (11.9%); (ii) 2,4-dichloro-3,5-xylenol (17.5%); and (iii) 2,4,6-trichloroxylenol (20.3%) (losses 50.3%).

In the preparative TLC special attempt was made to look for compounds other than the above, especially the ortho-chloro-compounds but they were not noticeable.

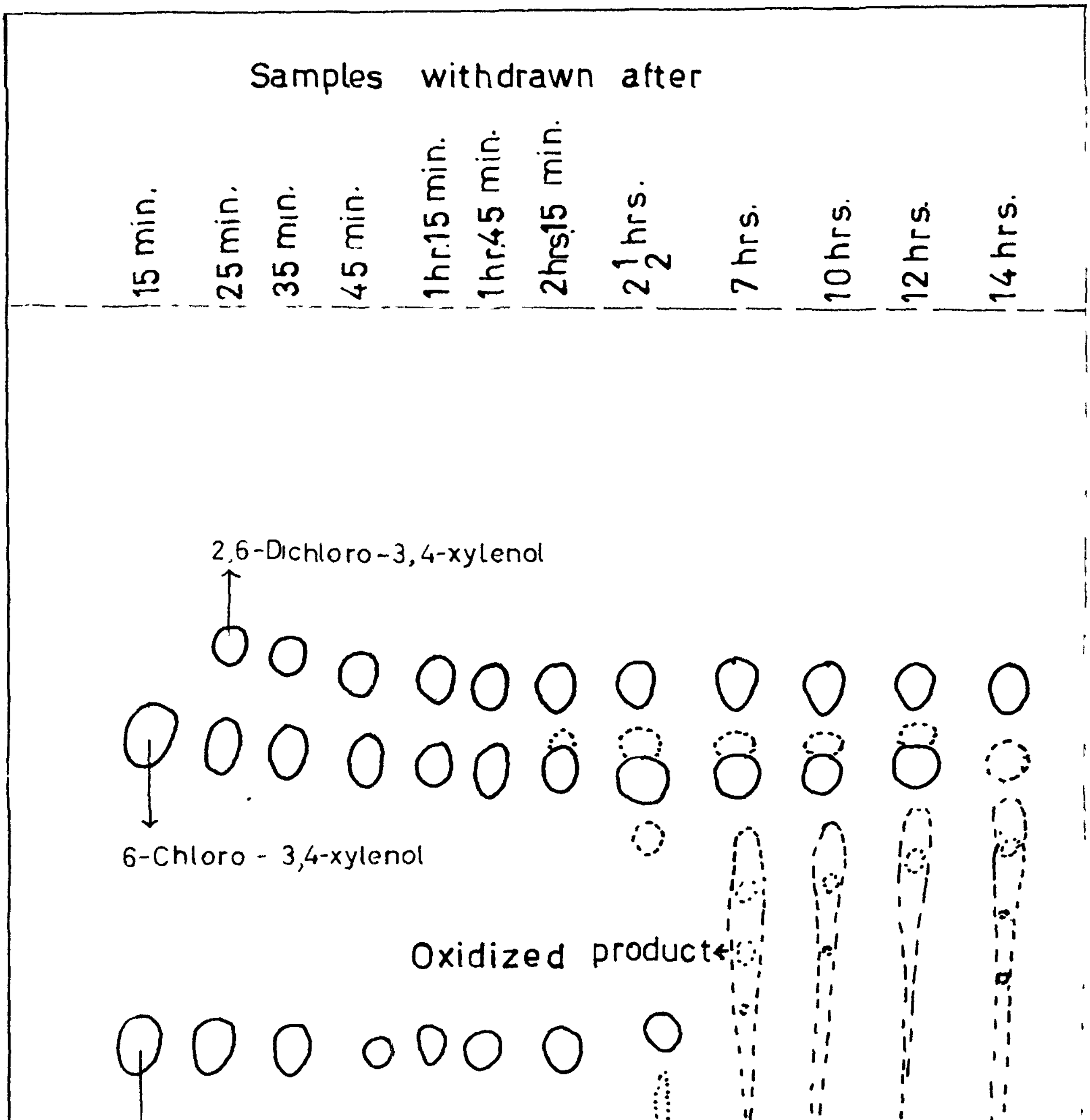
Using three mole-proportions of the reagent, 2,4,6-trichloro-3,5-xylenol was the only product and was isolated in 45% yield, in a pure form.

It would be concluded that 4-chloro-3,5-xylenol (using 1 molar-proportion of sulphuryl chloride), 2,4-dichloro-3,5-xylenol (using 2 molar-proportion of sulfuryl chloride) and 2,4,6-trichloro-3,5-xylenol (by any method) can be prepared in good yields.

D. 3,4-XYLENOL

(a) Reaction with gaseous chlorine

The chlorination of 3,4-xylenol with gaseous chlorine in carbon tetrachloride gives 6-chloro-3,4-xylenol ($R_f = 0.44$) within 15 minutes as indicated on the TLC plate (Fig. 36). 2,6-Dichloro-3,4-xylenol ($R_f = 0.58$) was noticeable after 25 minutes. Prolonged chlorination did not qualitatively change the composition of the reaction mixture which consisted of 6-chloro- and 2,6-dichloro-3,4-xylenols besides



TLC STUDY OF REACTION OF 3,4-XYLENOL WITH GASEOUS CHLORINE

FIG. 36

small quantities of other unidentified substances.

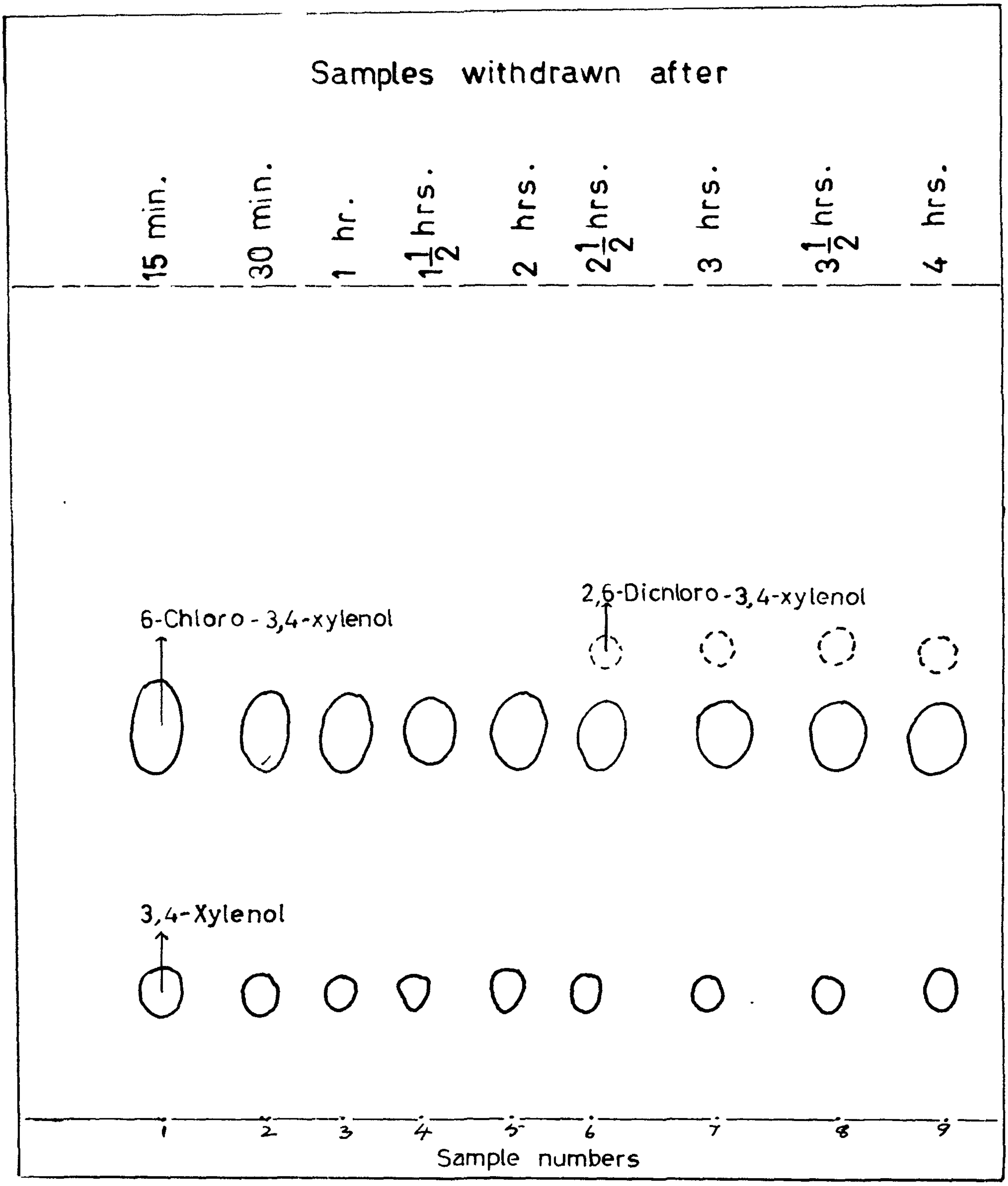
No single product could be isolated and attempts to crystallise the products resulted in polymerisation. Probably, this is caused by the side-reaction oxidation products. A quantitative picture of the reaction mixture (obtained through quantitative TLC) upto about 2¼ hour reaction time is indicated by values given in Table I.

Table I - Isomer-distribution in progressive chlorination of 3,4-xylenol with gaseous chlorine

S.No.	Time of chlorination, minutes	3,4-Xylenol per cent	6-Chloro-3,4-xylenol per cent	2,6-Dichloro-3,4-xylenol per cent
1	5	100	-	-
2	15	88.3	11.7	-
3	25	67.0	25.3	7.7
4	35	65.0	26.8	8.2
5	45	60.0	27.1	10.9
6	75	58.7	17.4	23.9
7	105	54.5	15.9	29.6
8	135	23.4	12.8	63.8

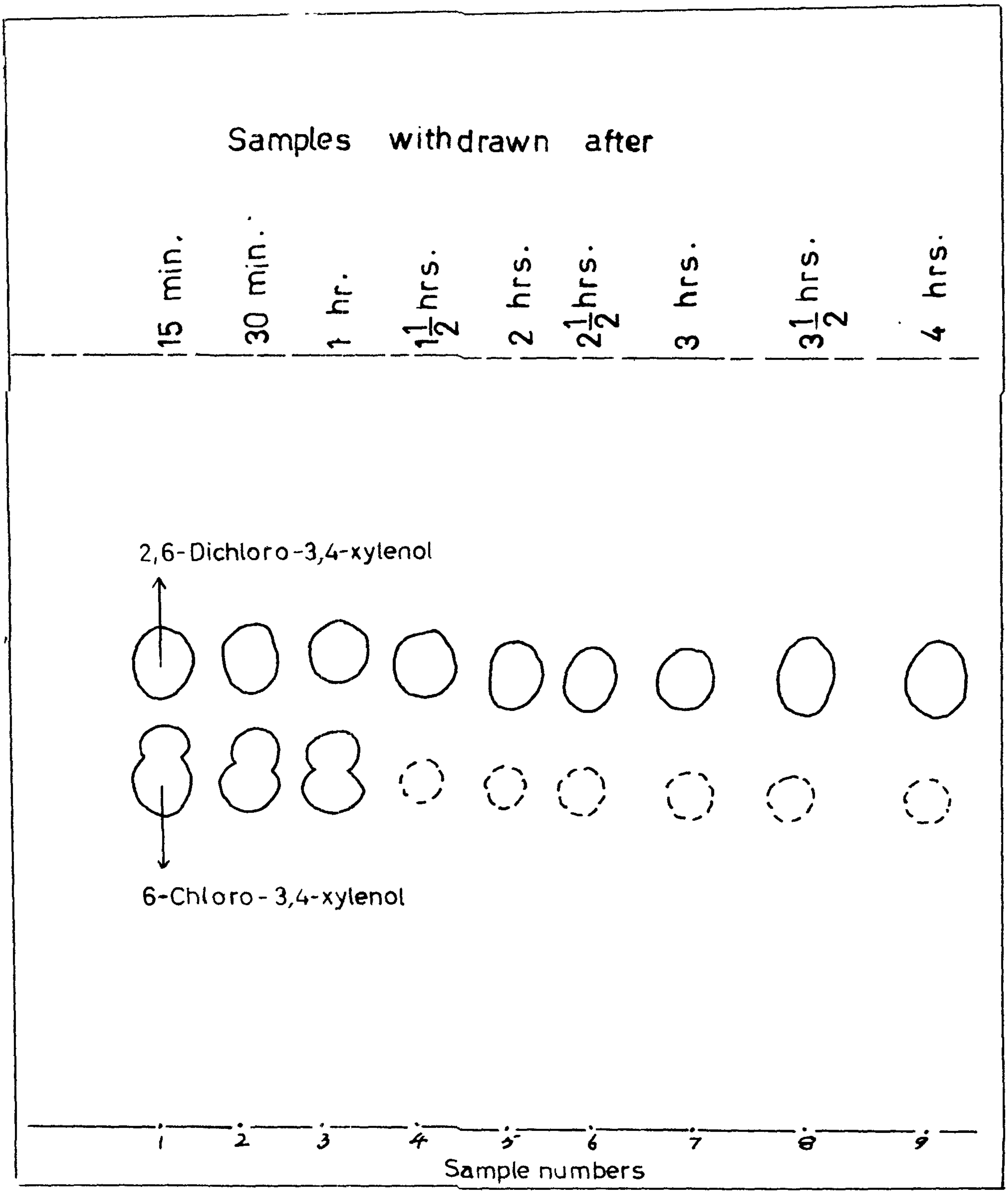
(b) Reaction with sulphuryl chloride

3,4-Xylenol was chlorinated with 1-molar-, 2-molar- and 3-molar proportions of sulphuryl chloride as in the previously discussed xylenols. The TLC chromatograms of each of these reactions are reproduced in Figs. 37, 38 and 39 indicating the progress of the reaction.



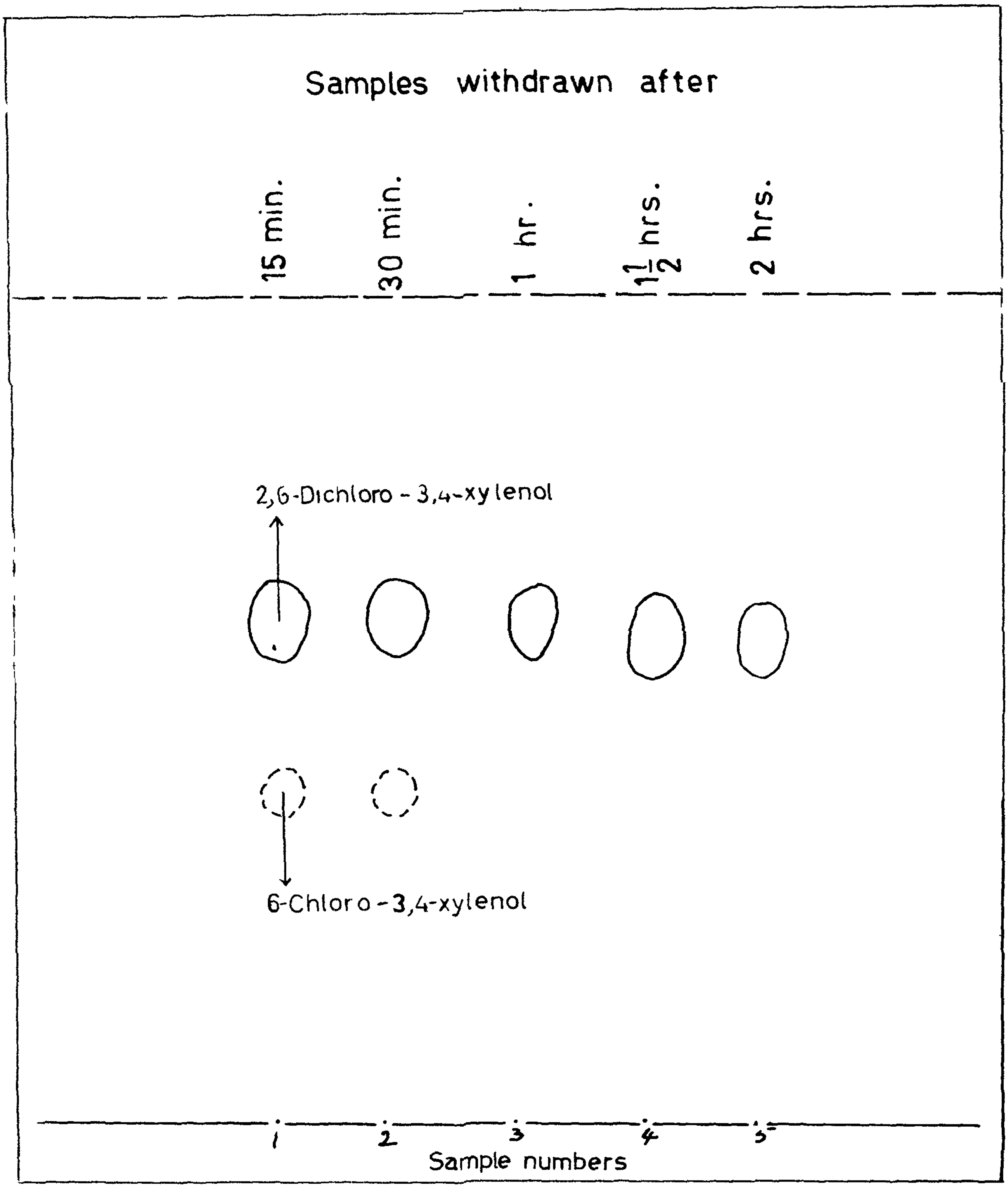
TLC STUDY OF CHLORINATION OF 3,4-XYLNOL WITH ONE MOLAR RATIO OF SULPHURYLCHLORIDE

FIG. 37



TLC STUDY OF CHLORINATION OF 3,4-XYLENOL WITH TWO MOLAR RATIO OF SULPHURYL CHLORIDE

FIG. 38



TLC STUDY OF CHLORINATION OF 3,4-XYLENOL WITH THREE MOLAR RATIO OF SULPHURYL CHLORIDE

FIG. 39

From these chromatographic studies, it became apparent that using one molar-proportion of sulphuryl chloride, the reaction was not complete and the starting phenol (R_f = 0.21) was noticeable even after three hours of reaction (with Folin Denis reagent). The two products (both phenolic in nature) had R_f 0.44 and 0.58 and have been identified as 6-chloro- and 2,6-dichloro-3,4-xylenol, respectively. Use of 2-molar proportion of sulphuryl chloride did not make any qualitative change, except that no starting material was noticeable in the reaction mixture after three hours. The ratios of 6-chloro- and 2,6-dichloro-3,4-xylenol, as determined by quantitative TLC are given in Table II.

Table II - Isomer distribution in chlorinated product of 3,4-xylenol with one- and two- molar quantity of sulphurylchloride and ter-butylhypochlorite

Reagent	Product	Percentage
Sulphuryl chloride (one molar)	3,4-xylenol	27.19
	6-chloro-3,4-xylenol	60.75
	2,6-dichloro-3,4-xylenol	12.08
Sulphuryl chloride (two molar)	6-chloro-3,4-xylenol	7.68
	2,6-dichloro-3,4-xylenol	92.32
ter-butylhypochlorite (one molar)	some impurities	7.98
	3,4-xylenol	38.76
	6-chloro-3,4-xylenol	38.76
	2,6-dichloro-3,4-xylenol	14.50
ter-butylhypochlorite (two molar)	3,4-xylenol	17.49
	6-chloro-3,4-xylenol	47.92
	2,6-dichloro-3,4-xylenol	39.59

In the three-molar reaction, only one phenolic compound (R_f = 0.58), corresponding to 2,6-dichloro-3,4-xylenol was identified on the TLC plate. However, a non-phenolic constituent (R_f = 0.44) identified by sulphuric acid charring method was also present in the reaction mixture. It was later shown to be 4,6-dichloro-3,4-dimethylcyclohexadien-1-one (for discussion see p.92). Attempts to crystallise the phenolic constituents, led to polymerisation of the reaction product. However, it was possible to separate the phenolic constituent present in the 3-molar reaction mixture by steam distillation, yielding 2,6-dichloro-3,4-xylenol in 38.7%. The non-phenolic components could not be isolated.

2,6-Dichloro-3,4-xylenol gave <u>para</u>-toluenesulphonate, m.p. 90°C., and aryloxyacetic acid, m.p. 156-157°C. Ultraviolet spectrum reproduced in Fig. 40 gave, λ- max. (i) 281.5 mμ; ϵ = 2421 and (ii) 290 mμ; ϵ = 2731. In the infrared spectrum (Fig. 41), the characteristic OH-absorption can be seen at 3540 cm^{-1} and C-Cl stretching-vibration at 782 cm^{-1} and CH deformation band at 850 cm^{-1}.

(c) Reaction with ter-butylhypochlorite

Chlorination of 3,4-xylenol with <u>ter</u>-butylhypochlorite gave very interesting and revealing results. Reaction with 1-molar and 2-molar proportions of <u>ter</u>-butylhypochlorite in 90% acetic acid, gave the normal products, i.e. 6-chloro- and 2,6-dichloro-3,4-xylenol as identified on TLC plates (Figs. 42 and 43). The quantitative data are already given in Table II. However, except for identification of

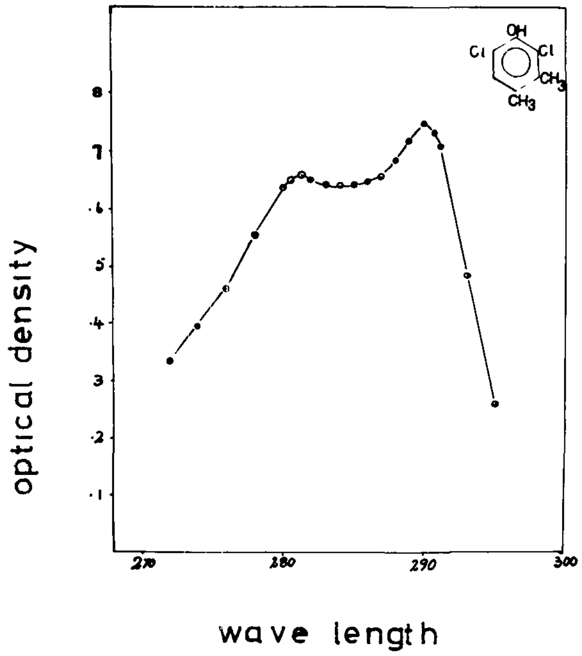


Fig. 40 UV spectrum of 2,6-dichloro-3,4-xylenol

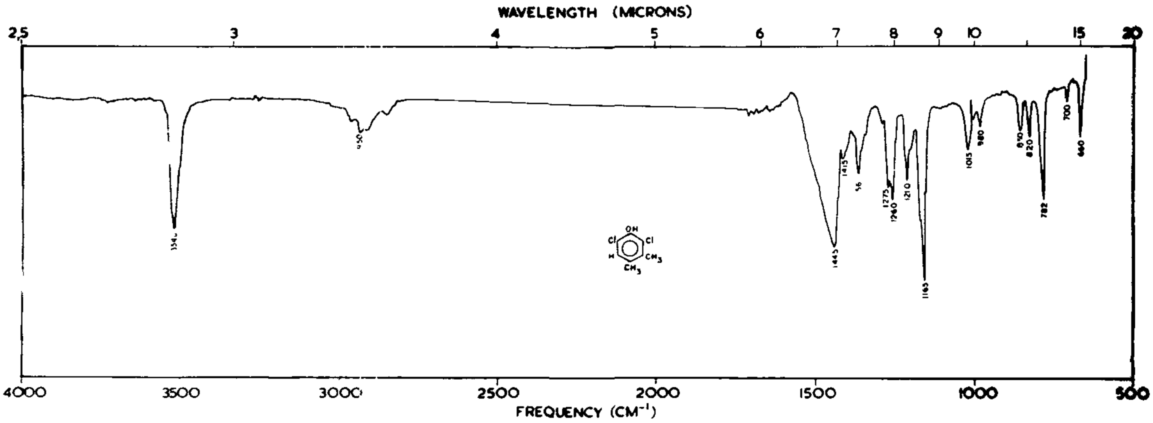
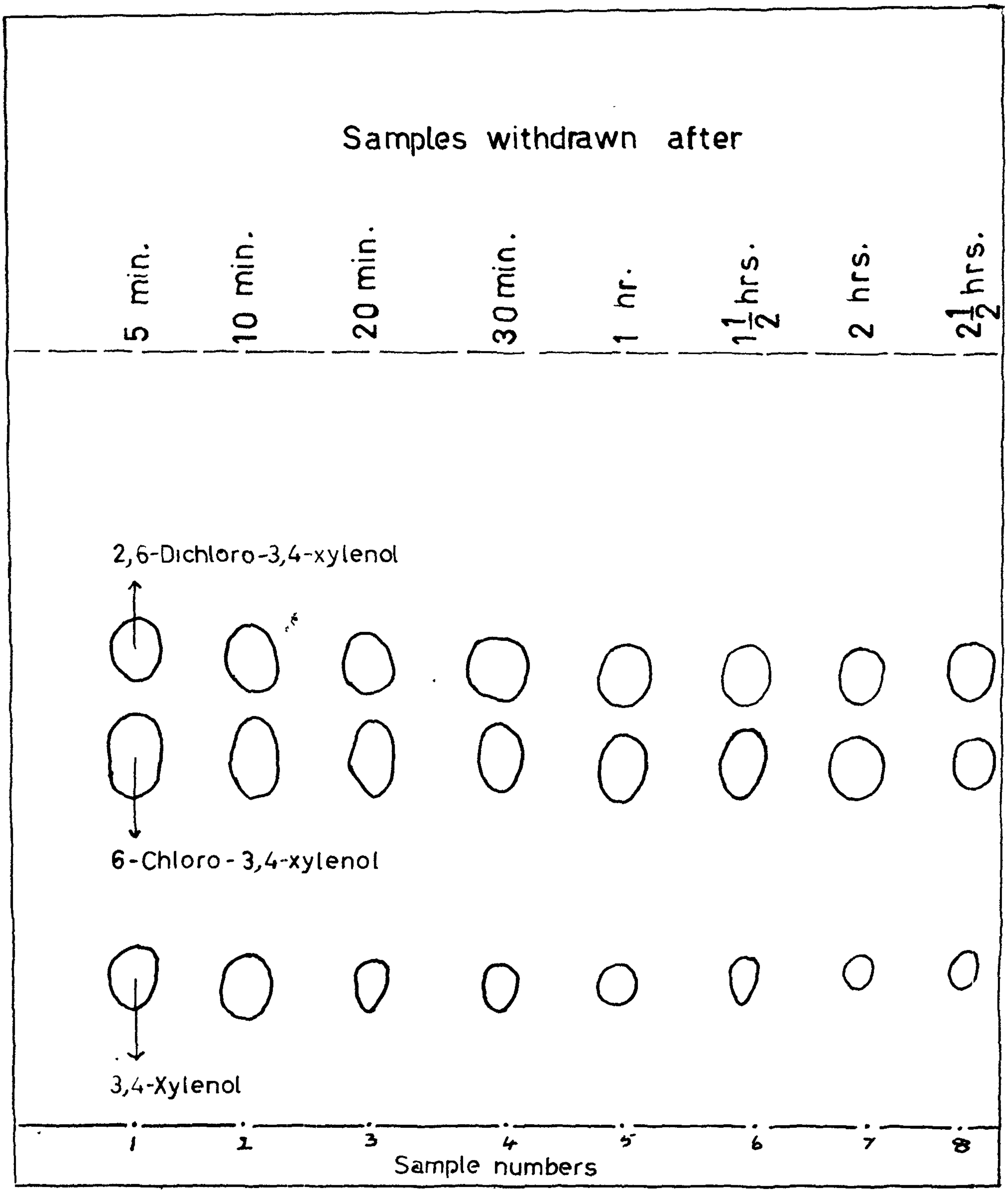
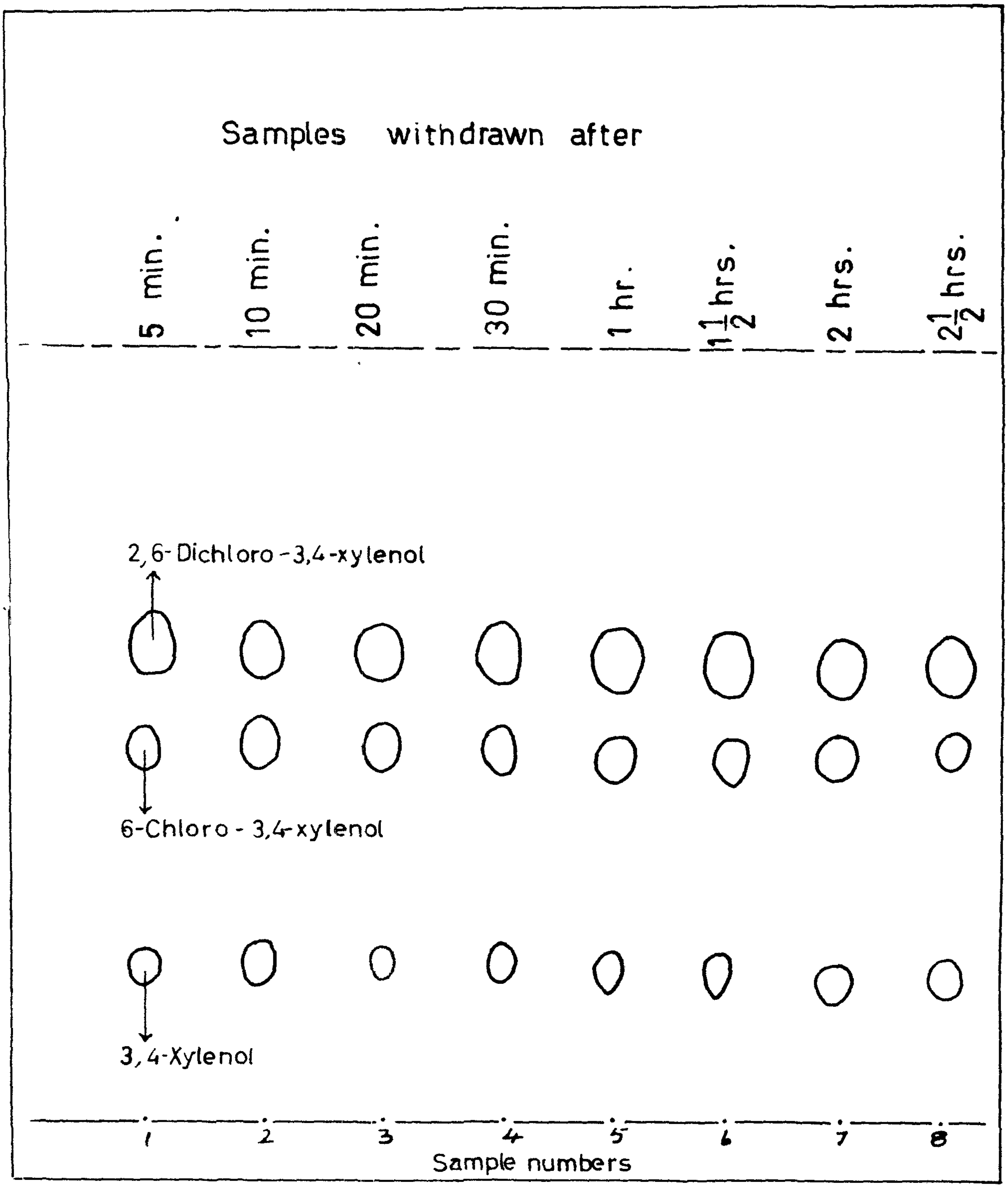


Fig. 41 IR spectrum of 2,6-dichloro-3,4-xylenol



TLC STUDY OF CHLORINATION OF 3,4-XYLENOL WITH ONE MOLAR RATIO OF $(CH_3)_3C{\cdot}O{\cdot}Cl$

FIG. 42



TLC STUDY OF CHLORINATION OF 3,4-XYLENOL WITH TWO MOLAR RATIO OF $(CH_3)_3C.O.Cl$

FIG. 43

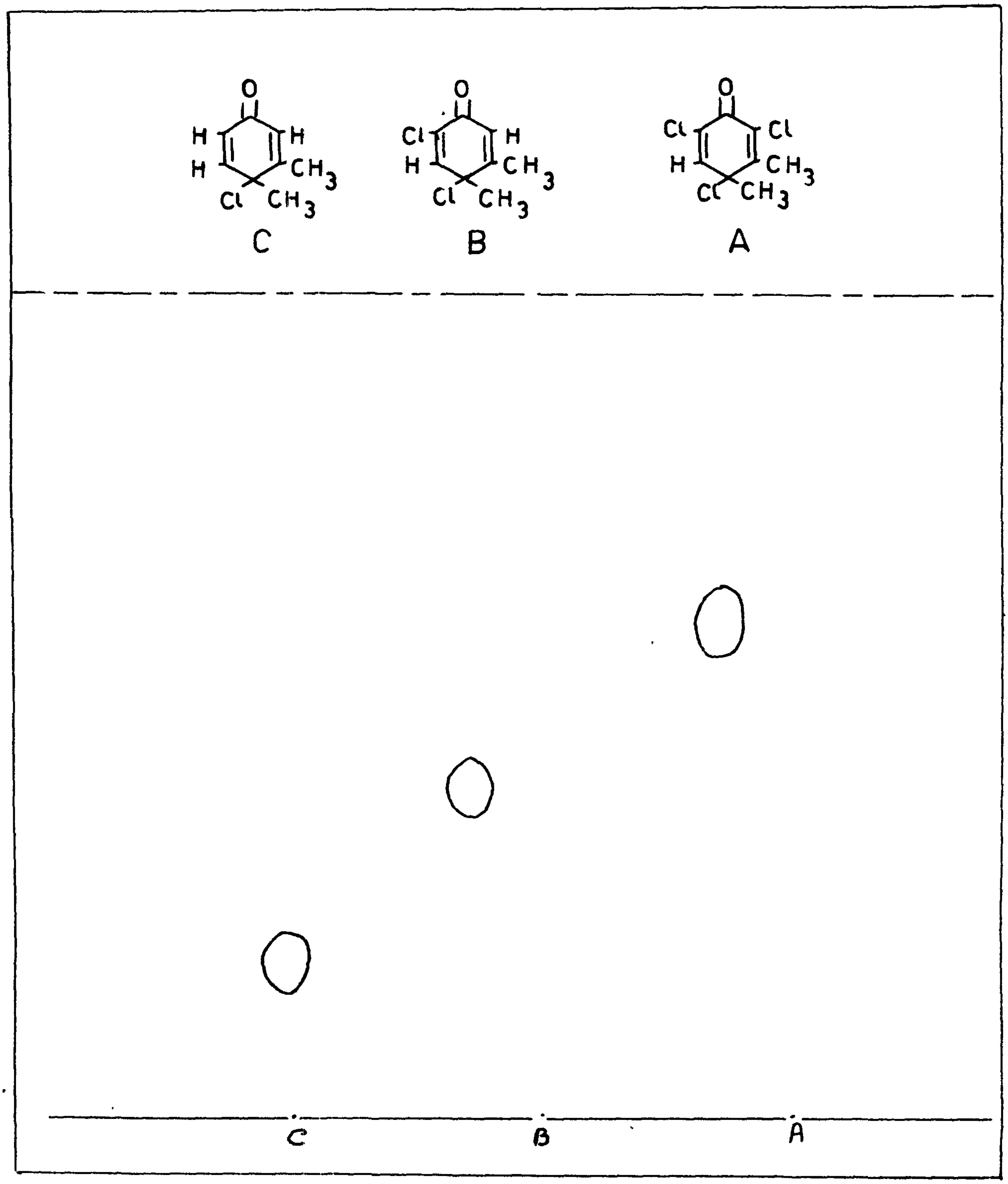
products on TLC plate, these could not be isolated through crystallisation due to polymerisation.

Use of 3-molar-proportion of ter-butylhypochlorite, gave entirely different products. Within a very short time of reaction, no phenolic constituent was identifiable in the reaction mixture. Instead, as seen in Fig. 44, three non-phenolic constituents A, B and C (R_f = 0.21, 0.44 and 0.58) surprisingly tallying with R_f-values of phenolic constituents were noted on the TLC-plate by sulphuric acid charring method. It was possible to separate these three components by careful silica-gel column chromatography using chloroform as solvent and some of the data are given below:

	A	B	C
Nature	non-phenolic	non-phenolic	non-phenolic
State	solid	liquid	solid
Melting point	85.5°C.	-	not determined
Chlorine content, %	47.75	37.15	22.76
Column chromatography, yield, %	41.00	29.00	20.00
Quantitative TLC, yield, %	41.66 (R_f = 0.58)	33.34 (R_f= 0.44)	25.00 (R_f = 0.21)

Identification of non-phenolic products (compounds A, B and C)

The infrared spectra of A, B and C (Figs. 45, 46 and 47) indicated the absence of OH-peak. Instead, strong carbonyl-peaks at 1680 cm^{-1}, 1675 cm^{-1} and 1665 cm^{-1}, respectively were noticeable in the spectra for compound A, B and C. The NMR-spectrum was obtained



TLC PLATE SHOWING SEPARATION OF COMPOUNDS 'A', 'B' & 'C'

FIG. 44

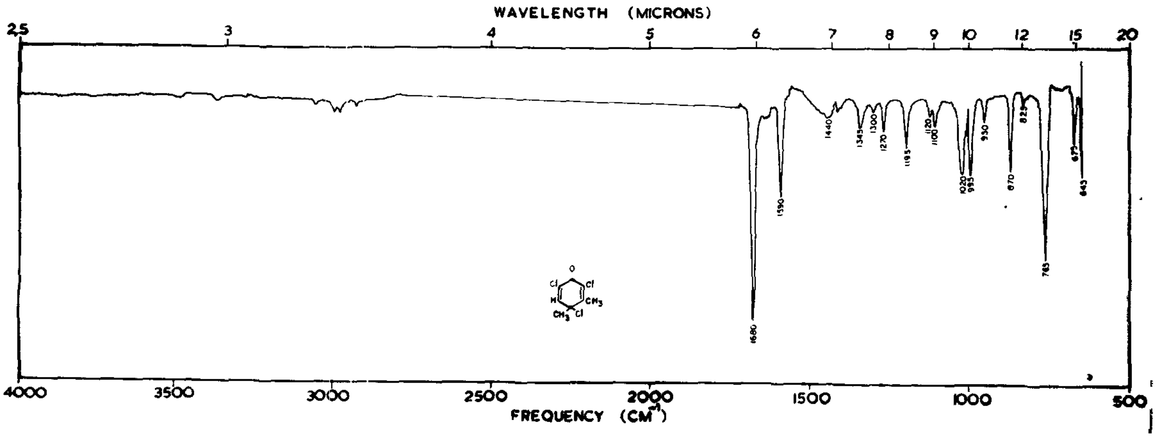


Fig. 45 IR spectrum of compound A

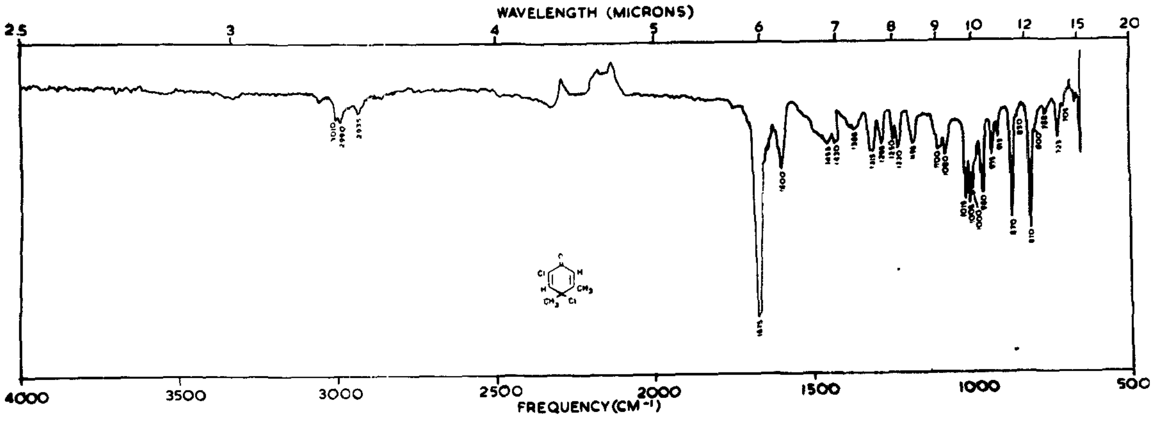


Fig. 46 IR spectrum of compound B

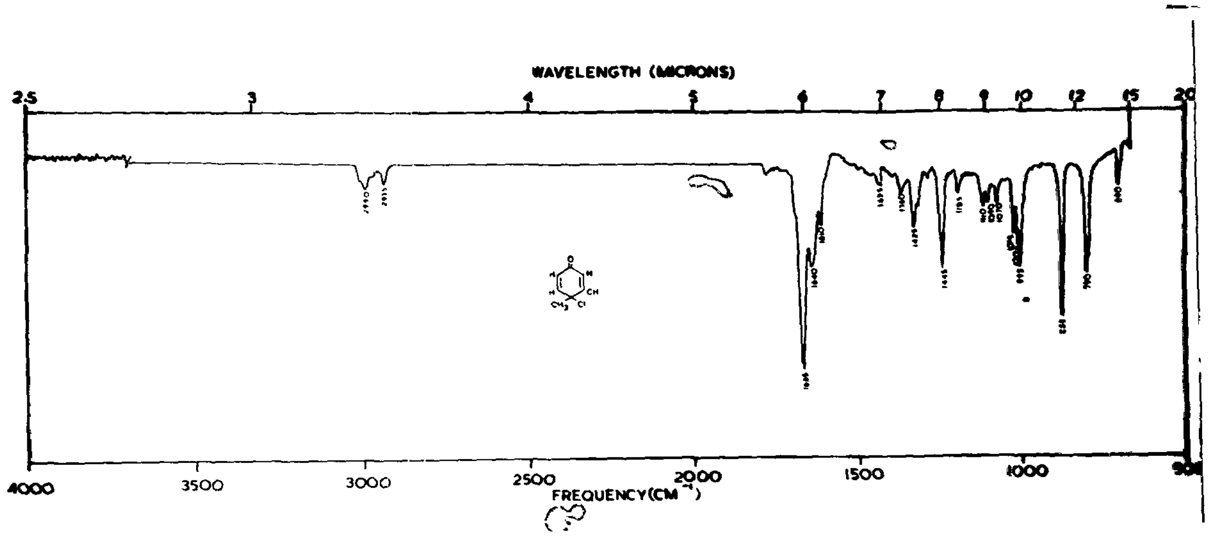


Fig. 47 I.R. spectrum of compound C

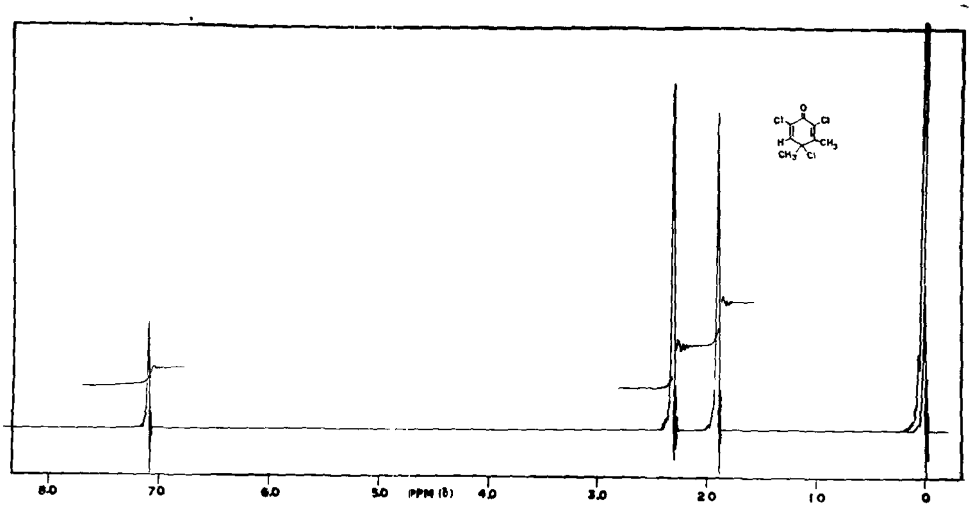
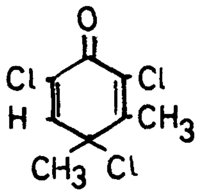


Fig. 48 N.M.R. spectrum of compound A

for A only, and it is reproduced in Fig. 48, indicating two methyl groups and one free proton.

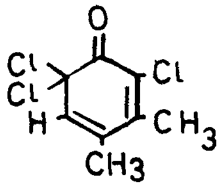
All the three compounds liberated iodine from methanolic potassium iodide solution. Further, A on reduction with zinc and hydrochloric acid, gave a phenolic compound, identified as 2,6-dichloro-3,4-xylenol (R_f mixed m.p. and IR-spectral data). Similarly, B and C on reduction gave 6-chloro-3,4-xylenol and 3,4-xylenol, respectively.

Consistent with the above observations and the chlorine percentages, the following alternative structures are possible for A, B and C.

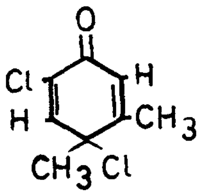


XIV

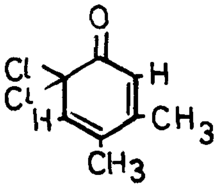
Compound A



XV

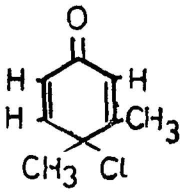


XVI



XVII

Compound B



XVIII

Compound C

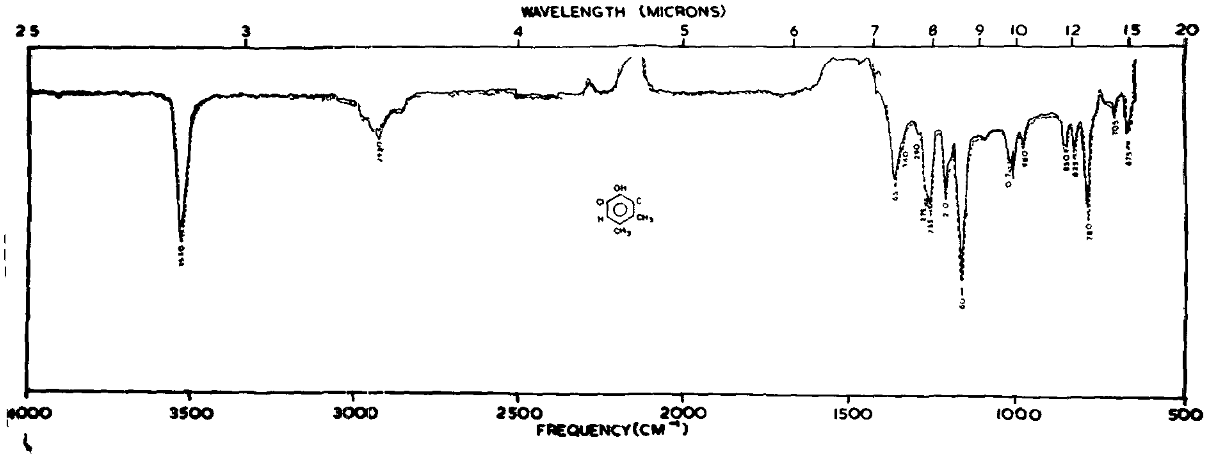


Fig. 49 IR spectrum of reduced product of compound A and authentic sample of 2,6-dichloro-3,4-xylenol

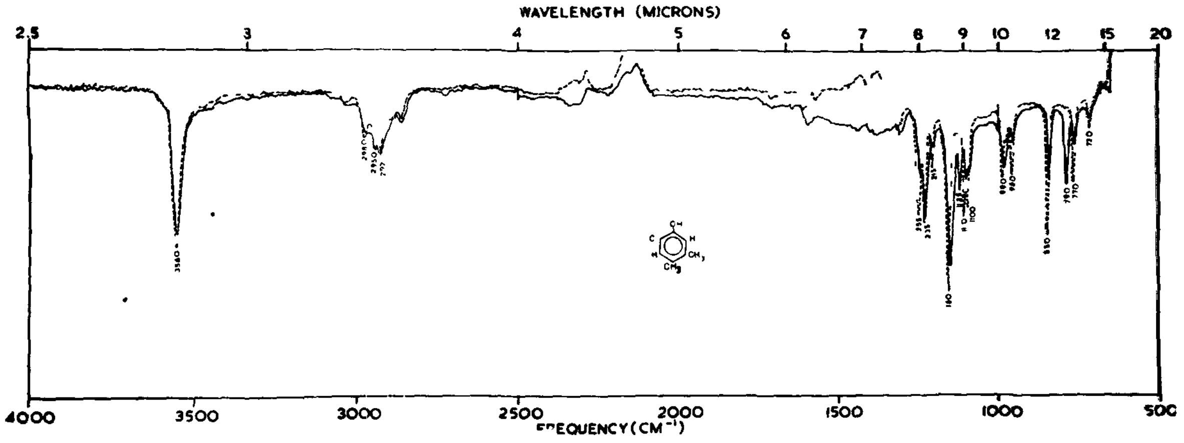


Fig. 50 IR spectrum of reduced product of compound B and authentic sample of 6-chloro-3,4-xylenol

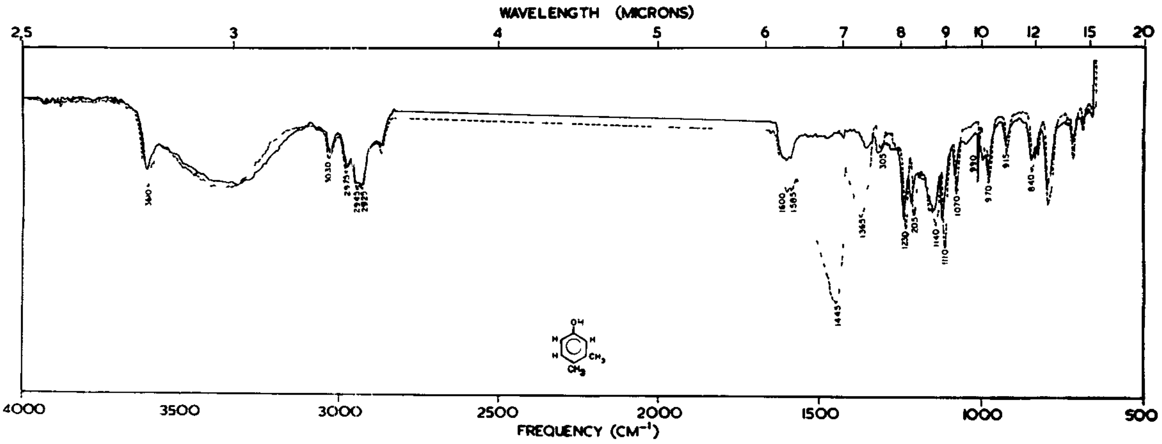


Fig. 51 IR spectrum of reduced product of compound C and authentic sample of 3,4-xylenol

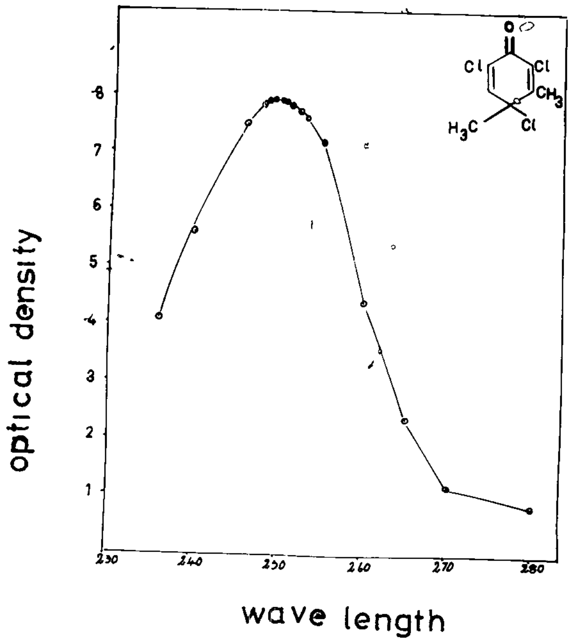


Fig. 52 UV spectrum of compound A

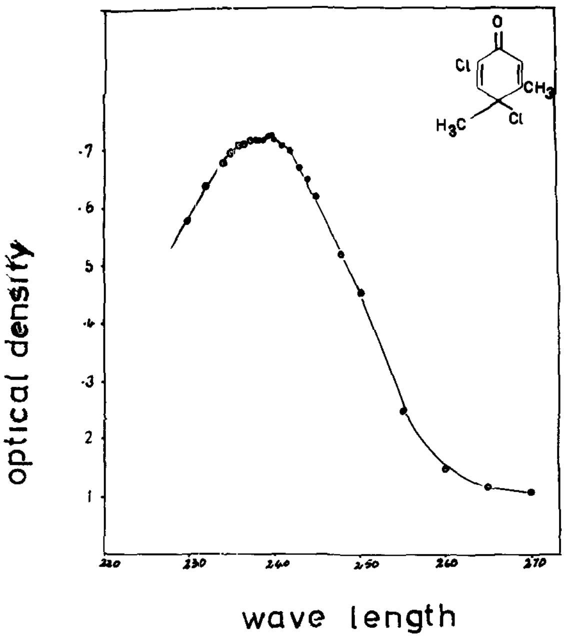


Fig. 53 UV spectrum of compound B

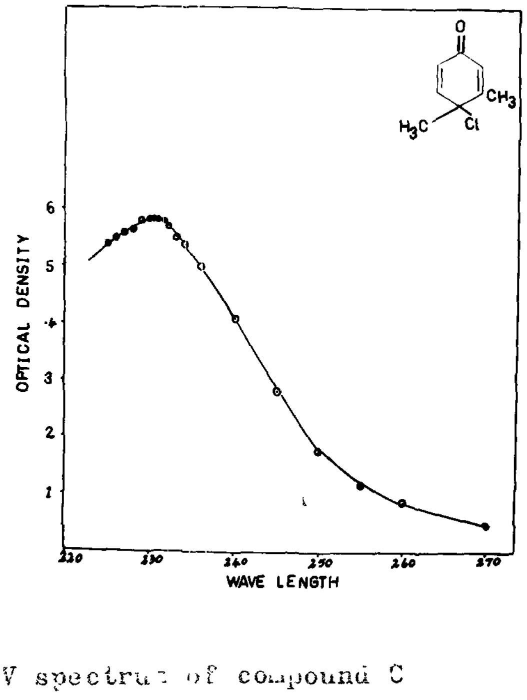
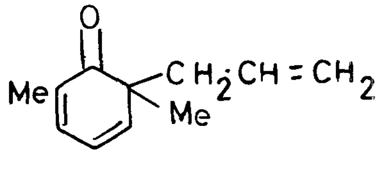
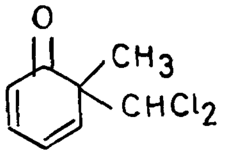


Fig. 54 UV spectrum of compound C

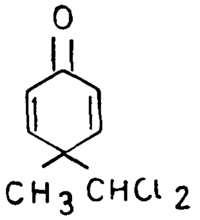
The IR spectra of the reduced product of A, B and C are given in Figs. 49, 50 and 51. The UV spectra for A, B and C are given in Figs. 52, 53 and 54. It would be apparent that λ-max. for all the three compounds, lie within 232–250 mμ. If analogies could be drawn from the <u>ortho</u>-quinoid structures (XIX and XX) which have λ -max. at 303 and 299 mu respectively and from the <u>para</u>-quinoid structure (XXI) having λ-max. at 232, <u>para</u>-quinoid structures for A, B and C should be preferred. It may further be stated that Wynberg[9], has generalised the UV-absorption data for these two types of structures and have used them as aid in the rapid identification of the two isomeric structures. The structure (XXI) is cross-conjugated and shows maximum absorption at 232 mμ, with only 2 to 3 mμ bathochromic shifts caused by an additional alkyl-group. The linearly conjugated systems of the type (XIX and XX) on the other hand, show maximum absorption between 299–348 mμ. Thus, the structures assigned are- for A, 2,4,6-trichloro-3,4-dimethyl-cyclohexadien-1-one (XIV), for B, 4,6-dichloro-3,4-dimethylcyclohexadien-1-one (XVI), and for C, 4-chloro-3,4-dimethylcyclohexadien-1-one (XVIII).



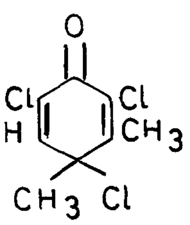
XIX



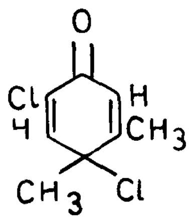
XX



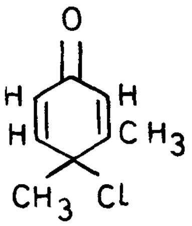
XXI



XIV



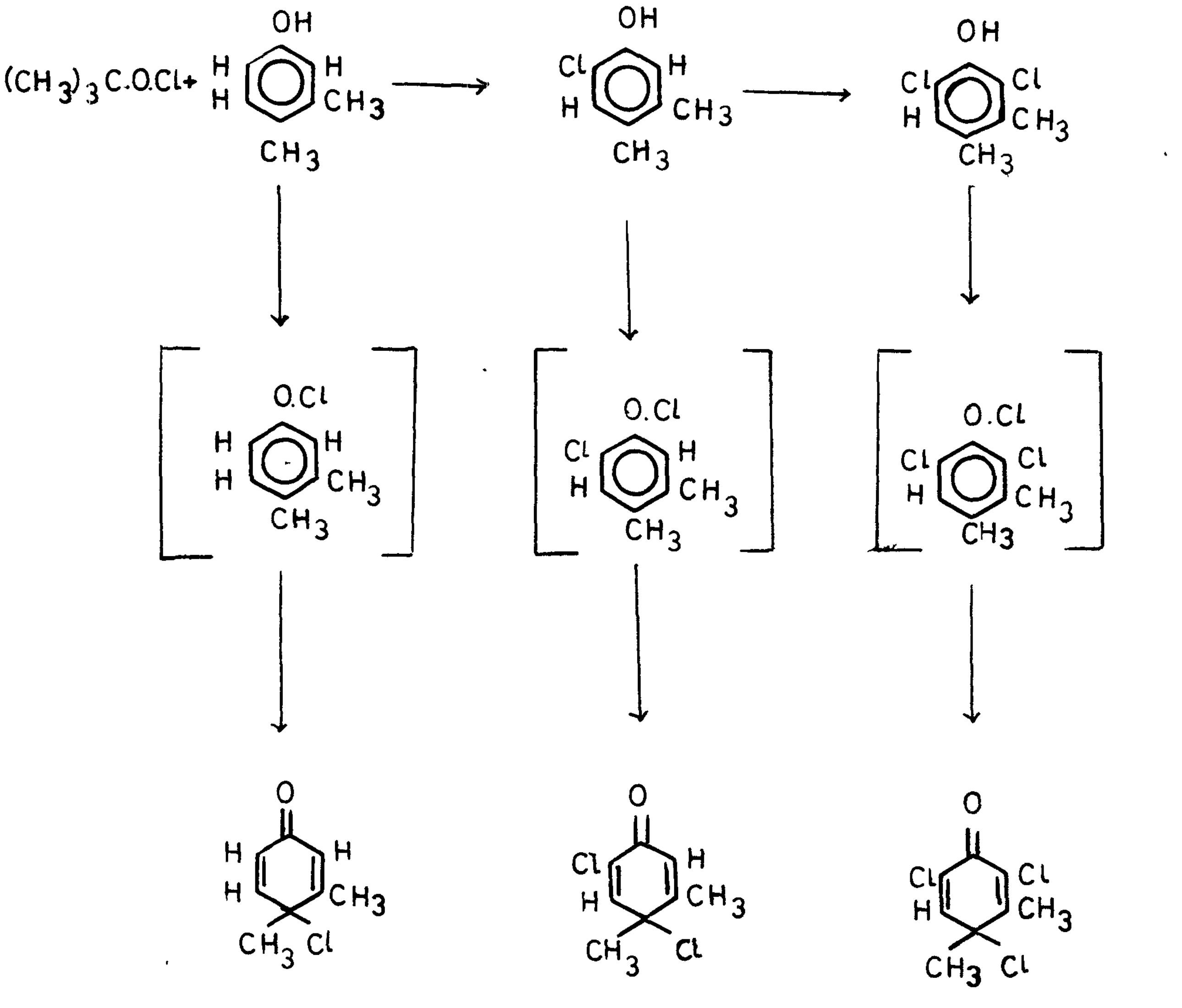
XVI



XVIII

Referring to the compound (R_f = 0.44) obtained through sulphuryl chloride reaction (p.79) it tallies with compound B.

Since with 1-molar and 2-molar proportion of ter-butylhypochlorite, the major products are the 6-chloro-, and 2,6-dichloro-3,4-xylenols; one can safely assume that chlorination with 3-molar proportion of ter-butylhypochlorite also proceeds through these compounds; a possible route of formation for A, B and C is indicated schematically in the following scheme:

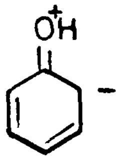


C B A

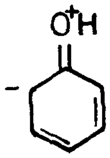
Analogy for the formation of the intermediate hypochlorite has been drawn from Mueller and Linde's[4] work who have also reported formation of a hypochlorite in gaseous chlorination of 2,5- and 3,5-xylenol in aqueous acetic acid. It may be recalled that attempts to crystallise the product of chlorination of 3,4-xylenol led to polymerization. These polymeric products were dark red in colour and may be of the type mentioned by Mueller and Linde (loc cit). It is also very likely that some quinoid compounds are also formed in the chlorination of 3,4-xylenol with gaseous chlorine as well as with sulphuryl chloride.

GENERAL DISCUSSION

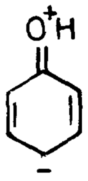
(i) As already mentioned, chlorination of the four xylenols with gaseous chlorine in a solvent, proceeded according to normal rules of orientation applicable to electrophilic attack by chlorine. In this reaction, wherever para-position was free i.e. in cases of chlorination of 2,5-, 2,3- and 3,5-xylenols, the mono para-chloro compounds were always noticed first, followed by dichlorinated products. The second chlorine entered at one of the ortho-positions. Chlorine entered in both the ortho-positions in the case of 3,5-xylenol leading to 2,4,6-trichloro-3,5-xylenol. The mono-ortho-chlorination took place only in the case of 3,4-xylenol, where the para-position was blocked. Here, the final product was 2,6-dichloro-3,4-xylenol, i.e. chlorine entered in both the ortho-positions. From this, it could be concluded that the para-position is more reactive and the structure (c) shown below, contributes maximum to the transition state in the case of xylenols:



(a)



(b)



(c)

Thus it explains the absence of mono-*ortho*-chloro compounds in these chlorinations. The stoppage of chlorination at the dichlorinated stage in the case of 2,5-, 2,3- and 3,4- xylenols could be attributed, either to strong *ortho*- and *para*-directing influence of hydroxyl or to mesomeric effect of chlorine group or to both.

(ii) Sulphuryl chloride reacted almost similarly as gaseous chlorine. It yielded different proportions of mono-, or di-chlorinated xylenols, depending upon the molar concentration of the reagent. Here also, mono- *ortho*-chloroproducts were conspicuous by their absence.

(iii) *ter*-Butylhypochlorite as mentioned earlier, was selected as a reagent to obtain *ortho*-chlorinated products, since most of the available literature[10] pointed out to the specificity of this reagent as an *ortho*-chlorinating agent, especially for phenols. Contrary to the reported work mentioned during the course of discussion elsewhere, it may be pointed out that the results obtained in this work using *ter*-butylhypochlorite are different from the expected.

Some of the results obtained by earlier workers[10] on the reaction of phenols with hypochlorite, especially *ter*-butylhypochlorite, are reproduced in Table III. From these results, it could be seen that

Table III - Reaction of Phenols with ter-Butylhypochlorite[10]

Phenol	Solvent	Products	Yield %	References
Phenol	C_2H_5OH	o-&p-Chlorophenol		11
	"	o-Chlorophenol	94	2
	"	2,4-Dichlorophenol	87	2
	"	2,4,6-trichlorophenol	82	2
	"	Tetrachloroquinone	83	2
	$CHCl_3$	o-Chlorophenol	46-52	2
		p-Chlorophenol	36-42	2
	CCl_4	o-Chlorophenol	57	2
		p-Chlorophenol	29	2
Thymol	CCl_4	4-Chloro-3-methyl-6-isopropylphenol	48	2
Catechol	CCl_4	Chlorocatechol	78	2
Resorcinol	CCl_4	Chlororesorcinol	72	2
Hydroquinone	C_2H_5OH	Quinhydrone	77	11
o-Cresol	CCl_4	6-Chloro-o-cresol	31	12
		4,6-Dichloro-o-cresol	18	12
p-Cresol	CCl_4	6-Chloro-p-cresol	69	12
m-Cresol	CCl_4	6-Chloro-m-cresol	44	12
		4-Chloro-m-cresol	48	12
o-Chlorophenol	CCl_4	2,6-Dichlorophenol	73	12
p-Chlorophenol	CCl_4	2,4-Dichlorophenol	60	12

except for thymol, in all other cases, the products contained chlorine *ortho-* to hydroxyl group. Norman and Harvey's[13] findings obtained with anisole, chlorobenzene and phenol brought out the fact that the results reported by earlier workers were not fully correct and that a mixture of ortho- and para-monochlorinated products are obtained. The ratio of ortho- and para-isomers depends upon whether an acidic or non-acidic medium is used. Some of their results are reproduced in Tables IV, V and VI.

Table IV - Chlorination of Anisole with ter-Butylhypochlorite[13]

Solvent	Isomer, per cent	
	ortho-	para-
Carbon tetrachloride	23.0	77.0
Dioxan	20.0	80.0
Acetonitrile	20.5	79.5
ter-Butanol	20.1	79.9
Acetic acid	33.5	66.5
Acetic acid & sulphuric acid	35.5	64.5

Table V - Chlorination of Chlorobenzene[13]

Conditions	Orientation		
	ortho-	meta-	para-
ter-Butylhypochlorite in acetic acid	44.9	1.1	54.0
ter-Butylhypochlorite in acetic acid-sulphuric acid	44.1	1.4	54.5
Chlorinium ion in carbon tetrachloride-water	39.7	1.6	58.7

Table VI - Chlorination of Phenol[13]

Conditions	Orientation	
	ortho-	para-
ter-Butylhypochlorite in carbon tetrachloride	51.0	49.0
ter-Butylhypochlorite in sulphuric acid	50.8	49.2
Chlorine gas in carbon tetrachloride	72.0	26.0
Chlorine gas in molten phenol	39.5	60.5
Chlorinium ion in water	51.4	48.6

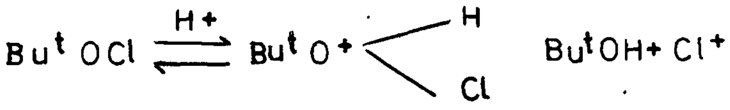
For convenience, the products obtained in the course of present work on reaction of *ter*-butylhypochlorite in acetic acid are given in Table VII.

Table VII - Products of Reaction of Xylenols with ter-Butylhypochlorite

Starting Xylenol	ter-Butylhypochlorite		
	one-molar-	two-molar-	three-molar-
2,5-	4-Chloro-, 4,6-Dichloro-,	4-Chloro-, 4,6-Dichloro-,	4-Chloro-, 4,6-Dichloro-,
2,3	4-Chloro-, 4,6-Dichloro-,	4-Chloro-, 4,6-Dichloro	4-Chloro-, 4,6-Dichloro-,
3,5	4-Chloro-, 2,4-Dichloro-, 2,4,6-Trichloro-,	4-Chloro-, 2,4-Dichloro-, 2,4,6-Trichloro-,	4-Chloro-, 2,4-Dichloro-, 2,4,6-Trichloro-,
3,4	6-Chloro-, 2,6-Dichloro-,	6-Chloro-, 2,6-Dichloro-,	Compounds A, B and C

From the data given in Table VII it is clear that in no case where the para-position was free, the ortho-position was first attacked and no ortho-mono-chloroproduct was even detected.

The nature of species responsible for chlorination with ter-butylhypochlorite is known to be different in various reactions. Chlorine atoms have been shown to be involved in its reaction on allylic system[14] and methyl group of toluene and substituted toluenes[15]. Its reactions with olefins in aqueous solution in presence of acids and in alcoholic solutions have been reported[16] to be two-stage ionic addition of molecular chlorine. In the reaction with benzenoid compounds, however, neither atomic nor molecular chlorine is involved. Free radical intermediates have also been suggested[17] to be involved in the chlorination with ter-butylhypochlorite; though it is improbable since the direct replacement of hydrogen atoms attached to aromatic nuclei by halogen atoms takes place under extremely vigorous conditions. Norman[13] also concluded that in the reactions carried out at least in presence of acids, the species involved is the chlorinium ion (Cl^+), which is formed as shown below:

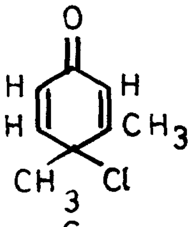


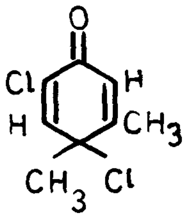
$$\mathrm{Bu^{t}OCl} \overset{H^{+}}{\rightleftharpoons} \mathrm{Bu^{t}O^{+}} {<} \begin{matrix}\mathrm{H}\\ \mathrm{Cl}\end{matrix} \qquad \mathrm{Bu^{t}OH + Cl^{+}}$$

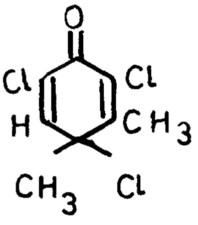
And based on this conclusion, it appears plausible to assume that the chlorinium ion (Cl^+) is the chlorinating species involved in the reaction of ter-butylhypochlorite with xylenols.

(iv) Oxidation by means of *ter*-butylhypochlorite is known; but the mechanism by which it takes place is not well understood. It has been assumed that in most cases of oxidation of hydroxyl compounds the primary intermediate is the corresponding hypochlorite[18-22], which rearranges to the quinonoid structure though ionic oxidation mechanism has also been postulated by some workers[20]. Other investigators have shown that the mechanism of decomposition in specific cases is through free radical formation[23]. It is also possible that both the mechanisms may operate together. Schmid[24] has shown this to be the case in the oxidation of various alcohols in the presence of pyridine.

However, in the present investigation, it can be seen that when 3,4-xylenol was chlorinated with 3-molar proportions of *ter*-butylhypochlorite, it yielded chlorocompounds with the following structures:


C


B


A

Based on a theoretical stand point and on the analogy to the work of Mueller and Linde (loc cit), the mechanism and the route of the formation of *para*-quinonoid structure as explained earlier appears plausible. Since the phenolic compound 2,4-dichloro-3,4-xylenol is isolated in 2-molar proportion of *ter*-butylhypochlorite it appears reasonable to postulate that the hypochlorite formation does not precede substitutive chlorination.

(v) The work led to preparative methods for following chloroxylenols by the indicated procedure in Table VIII.

Table VIII - Yields and Preparative Methods of Chloroxylenols

Xylenol	Gaseous Chlorine yield;%	Sulphuryl chloride yield; %			ter-Butylhypochloride yield; %		
		one-molar-	two-molar-	three-molar-	one-molar-	two-molar-	three-molar-
4-Chloro-2,5 -xylenol	-	(a) 74.5 (b) 47.0	-	-	-	-	-
4,6-Dichloro-2,5-xylenol	64	-	51	71.4	31.8	60.2	49.5
4-Chloro-2,3-xylenol	-	62.5	-	-	-	-	-
4,6-Dichloro-2,3-xylenol	54	-	79.7	89.4	24.6	67	76
4-Chloro-3,5-xylenol	-	82.5	-	-	-	11.9	-
2,4-Dichloro-3,5-xylenol	-	-	53	-	11.9	17.5	-
2,4,6-Trichloro-3,5-xylenol	87	-	-	94	-	20.3	44.5
2,6-Dichloro-3,4-xylenol	-	-	38.7	-	-	-	-

(vi) 4,6-Dichloro-2,3-xylenol has not been described by other workers and is reported for the first time. So far 4-6-dichloro-2,5-xylenol and 2,6-dichloro-3,4-xylenol have been reported to be obtained by indirect methods. In the present work, direct methods for preparation of these are established for their preparation.

For convenience of presentation, the general discussion on chromatography and spectroscophy are being given separately.

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CHAPTER III

CHROMATOGRAPHIC STUDIES ON CHLOROPHENOLS

It has been already mentioned in the earlier chapter that the technique of chromatography-paper, thin-layer, and gas-liquid chromatography were studied with a view to establish suitable methods of separation and identification of the various products of chlorination of phenols. For convenience, the results obtained by these techniques are described and discussed in this chapter. It is recalled that some of these results have also been included at appropriate places, elsewhere in this dissertation.

PAPER CHROMATOGRAPHY OF CHLOROPHENOLS

Paper chromatography of phenols has been extensively studied by other workers and it has also been a subject matter for several reviews[1,2]. Paper chromatography of chlorophenols however is not so much studied. Only workers in this field have been Weiss et al.[3], Siegel[4], Azouz et al.[5], Bray et al.[6], Choguill et al.[7] and Grebenovsky[8]. Except for Siegel[4] and Grebenovsky[8], others chromatographed only a few chlorophenols at a time, either as free chlorophenols or as their azodyes. They mentioned difficulties like tailing of the spots or the complications due to volatality of the lower chlorophenols. Grebenovsky (loc cit) eliminated the influence of volatality of lower chlorophenols by using formamide-impregnated papers and conducting the development in between two glass plates. He also applied the same technique to the separation of chlorophenols. His results are summarised in Table I. No paper chromatography study on chloroxylenols has been so far reported.

Table I - R_f and R_M values of different phenols and chlorophenols[8]

No.	Compound	R_f	R_M
1	Phenol	0.21	+ 0.57
2	4-Chlorophenol	0.37	+ 0.23
3	2-Chlorophenol	0.58	- 0.14
4	2,4-Dichlorophenol	0.71	- 0.39
5	2,6-Dichlorophenol	0.80	- 0.60
6	2,5-Dichlorophenol	0.71	- 0.39
7	2,4,6-Trichlorophenol	0.89	- 0.91
8	*para*-Cresol	0.39	+ 0.19
9	2-Chloro-*p*-cresol	0.75	- 0.48
10	2,4-Dichloro-*p*-cresol	0.90	- 0.96
11	*ortho*-Cresol	0.49	+ 0.02
12	4-Chloro-*o*-cresol	0.67	- 0.31
13	6-Chloro-*o*-cresol	0.88	- 0.87
14	4,6-Dichloro-*o*-cresol	0.94	- 1.19
15	*meta*-Cresol	0.39	+ 0.19
16	4-Chloro-*m*-cresol	0.57	- 0.12
17	6-Chloro-*m*-cresol	0.77	- 0.52
18	4,6-Dichloro-*m*-cresol	0.94	- 1.20
19	2,4,6-Trichloro-*m*-cresol	0.96	- 1.38

In the present study, it was found unnecessary to carry out development of the chromatograms in between two glass plates and satisfactory results were obtained with impregnated paper alone. Formamide-impregnated papers (Whatman No. 1) and descending technique were tried using the solvent-systems mentioned in Table II.

Table II - Solvent-systems studied for Paper Chromatography

Type	Solvent-systems	Remarks
A	Xylene, saturated with formamide	A, B and C gave good separation
B	Petroleum ether, saturated with formic acid	
C	Benzene : acetic acid : water (2:2:1, v/v; organic layer)	
D	Acetic acid : water (1:19, v/v)	D to J did not give encouraging results. E did not give compact spots after development. F to I had poor resolving power.
E	Methylethylketone : water : diethylamine (9211:77:2, v/v)	
F	Methylethylketone : acetone : water : formic acid (40:2:6: 1, v/v)	
G	Methylisobutylketone : formic acid (100:48, v/v; organic layer)	
H	Ethylacetate : acetic acid : water (2:1:2, v/v; organic layer)	
I	n-Butanol : NH_4OH (4:1, v/v)	
J	n-Hexane : isopropylether (9:1, v/v)	

Out of these solvent-systems, A, B and C gave good preliminary results and hence these alone were used for detailed studies. The results are tabulated in Tables III and IV. It would be seen that

Table III - R_f and R_M values of chlorinated- phenols, cresols and xylenols

Temperature 20±2°C.; time of run *ca.* 2.5 hr; solvent system A.

No.	Compounds	R_f	R_M	Mixtures of phenols (No. in column 1)
1	2	3	4	5
1	Phenol	0.24	+0.50	1-5
2	2-Chlorophenol	0.63	-0.23	
3	4-Chlorophenol	0.36	+0.25	
4	2,4-Dichlorophenol	0.69	-0.35	
5	2,4,6-Trichlorophenol	0.85	-0.75	
6	*ortho*-Cresol	0.50	0	6-9
7	6-Chloro-*o*-cresol	0.89	-0.91	
8	4-Chloro-*o*-cresol	0.66	-0.29	
9	4,6-Dichloro-*o*-cresol	0.91	-1.00	
10	*meta*-Cresol	0.34	+0.29	10-14
11	6-Chloro-*m*-cresol	0.73	-0.43	
12	4-Chloro-*m*-cresol	0.55	-0.09	
13	4,6-Dichloro-*m*-cresol	0.84	-0.72	
14	2,4,6-Trichloro-*m*-cresol	0.90	-0.95	
15	2,3-Xylenol	0.62	-0.21	15-16
16	4-Chloro-2,3-xylenol	0.73	-0.43	

1	2	3	4	5
17	2,5-Xylenol	0.60	-0.18	17-18
18	4-Chloro-2,5-xylenol	0.76	-0.50	
19	3,4-Xylenol	0.44	+0.10	19.21
20	6-Chloro-3,4-xylenol	0.79	-0.58	
21	2,6-Dichloro-3,4-xylenol	0.92	-1.07	
22	3,5-Xylenol	0.59	-0.16	22-24
23	4-Chloro-3,5-xylenol	0.72	-0.41	
24	2,4-Dichloro-3,5-xylenol	0.91	-1.00	
25	5-Ethyl-3-methylphenol	0.70	-0.37	25-27
26	4-Chloro-5-ethyl-3-methylphenol	0.81	-0.63	
27	2,4-Dichloro-5-ethyl-3-methylphenol	0.92	-1.07	

Table IV - R_f and R_M values of chlorinated- cresols and xylenols

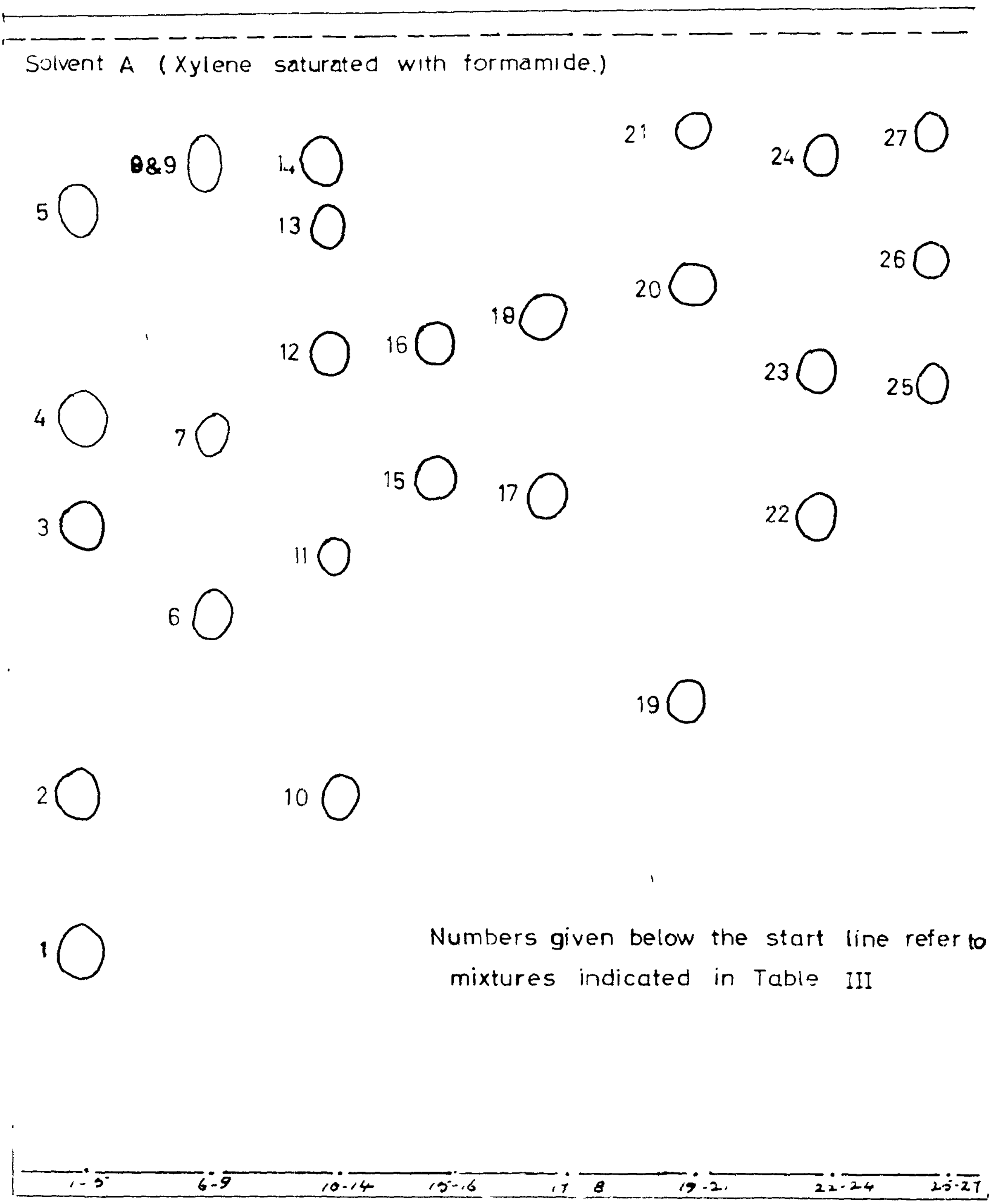
Temperature 20±2°C; Time of run ca. 2.5 hrs.; solvent systems B and C

No.	Compounds	Solvent B		Solvent C		Mixtures of phenols (No. in column 1)
		R_f	R_M	R_f	R_M	
1	2	3	4	5	6	7
6	ortho-Cresol	0.08	+1.06	0.50	0	6-9
7	6-Chloro-o-cresol	0.88	-0.87	0.92	-1.07	
8	4-Chloro-o-cresol	0.19	+0.63	0.66	-0.29	
9	4,6-Dichloro-o-cresol	0.86	-0.79	0.93	-1.12	
10	meta-Cresol	0.05	+1.28	0.42	+0.14	10-14
11	6-Chloro-m-cresol	0.70	-0.37	0.76	-0.50	
12	4-Chloro-m-cresol	0.10	+0.95	0.59	-0.16	
13	4,6-Dichloro-m-cresol	0.62	-0.21	0.84	-0.72	
14	2,4,6-Trichloro-m-cresol	0.73	-0.43	0.94	-1.19	
15	2,3-Xylenol	0.20	+0.60	0.67	-0.31	15-16
16	4-Chloro-2,3-xylenol	0.26	+0.45	0.79	-0.58	
17	2,5-Xylenol	0.25	+0.48	0.76	-0.50	17-18
18	4-Chloro-2,5-xylenol	0.34	+0.29	0.86	-0.80	

1	2	3	4	5	6	7
19	3,4-Xylenol	0.08	+1.06	0.56	-0.11	19.21
20	6-Chloro-3,4-xylenol	0.64	-0.25	0.85	-0.75	
21	2,6-Dichloro-3,4-xylenol	0.79	-0.58	0.94	-1.19	
22	3,5-Xylenol	0.11	+0.90	0.63	-0.23	22-24
23	4-Chloro-3,5-xylenol	0.25	+0.55	0.76	-0.50	
24	2,4-Dichloro-3,5-xylenol	0.36	+0.25	0.92	-1.07	
25	5-Ethyl-3-methylphenol	0.30	+0.37	0.76	-0.50	25-27
26	4-Chloro-5-ethyl-3-methylphenol	0.34	+0.29	0.89	-0.91	
27	2,4-Dichloro-5-ethyl-3-methylphenol	0.36	+0.25	0.93	-1.12	

along with R_f values, calculated R_M values, using the formula $R_M = \log(1/R_f - 1)$, are also given. The separations of synthetic mixtures of chlorinated phenols are illustrated in Figs. 1, 2 and 3.

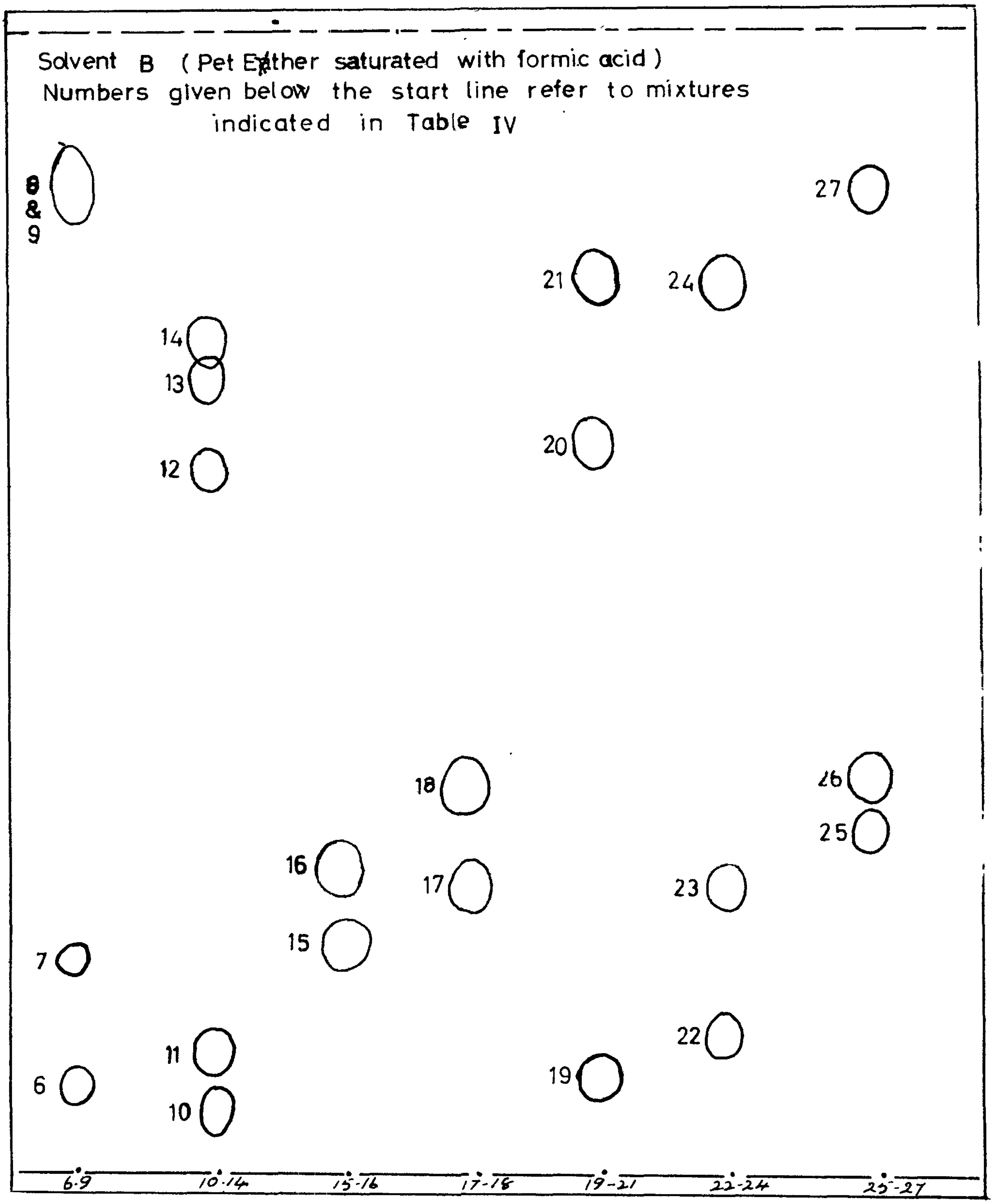
From these data it would be apparent that it was possible to obtain good separation for all the chlorophenols studied as mixtures. Their spots were also free of tailing. However, 6-chloro-*o*-cresol could not be separated from 4,6-dichloro-*o*-cresol in these experiments. R_f values of chlorophenols exhibited in solvents A and C


Solvent A (Xylene saturated with formamide.)

Numbers given below the start line refer to mixtures indicated in Table III

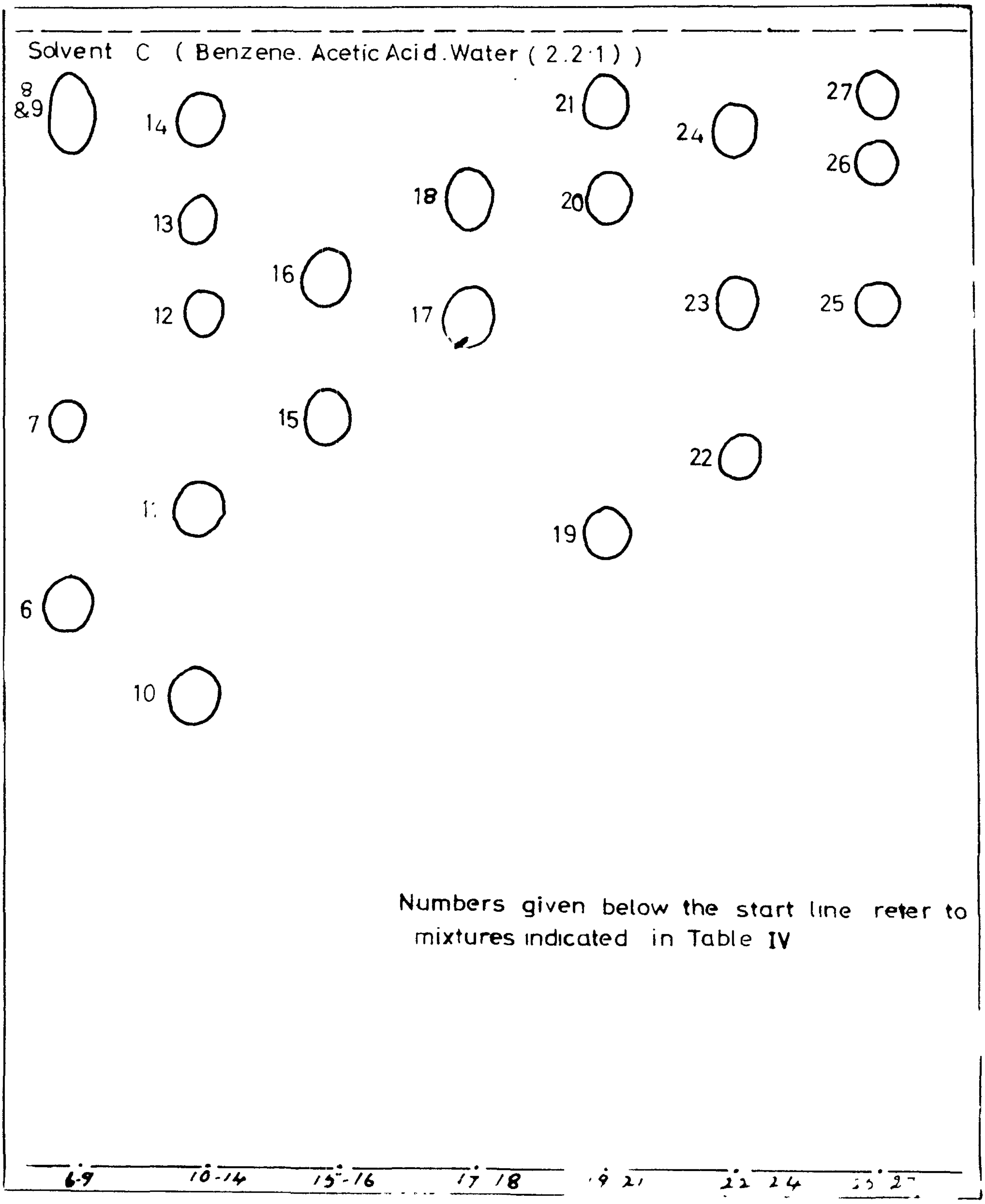
PAPER CHROMATOGRAM OF SOME SYNTHETIC MIXTURES OF CHLOROPHENOLS CHLOROCRESOLS & CHLOROXYLENOLS

FIG.1



PAPER CHROMATOGRAM OF SOME SYNTHETIC MIXTURES OF CHLORCRESOLS & CHLOROXYLENOLS

FIG. 2



PAPER CHROMATOGRAM OF SOME SYNTHETIC MIXTURES OF CHLOROCRESOLS & CHLOROXYLENOLS

FIG. 3

were almost the same. It may be noted that the R_f values increased generally, with increasing substitution in the nucleus except that 6-chloro-o-cresol and 6-chloro-m-cresol showed comparatively high R_f values as compared to corresponding dichlorophenols in solvent B. Further, R_f values for ortho-substituted compounds were higher than for the corresponding meta-isomers, a result, perhaps of the ortho-effect[10]. This is clear from the values for ortho- and meta-substituted compounds given below:

ortho-Compound	R_f	meta-Compound	R_f
ortho-Cresol	0.50	meta-Cresol	0.34
6-Chloro-o-cresol	0.73	4-Chloro-m-cresol	0.55
6-Chloro-3,4-xylenol	0.79	3,4-Xylenol	0.44

This effect is more pronounced in the 2,6-disubstituted products as seen in the R_f values for some phenols compared below. 4-Chloro-o-cresol 0.66; 6-chloro-o-cresol 0.89; 6-chloro-3,4-xylenol 0.79; 2,6-dichloro-3,4-xylenol 0.92. However, in all the solvents studied, the relative order of separation of these compounds was the same.

The R_f values of all the chlorophenols were found to be very sensitive to experimental conditions, particularly to the amount of formamide on paper. Reproducible values were obtained only when the same conditions were applied. With decreasing amount of formamide, higher R_f values were noticed.

The R_M values given in Tables III and IV are calculated from the corresponding R_f values using the equation[12] $R_M = \log (1/R_f - 1)$, have been used to find out the kind of molecular interaction involved in the chromatographic separation of chlorophenols with a view to study the structural effects and to test the validity of Martins equation[13]. It in its simplest form, the latter can be written as $R_{M_B}/R_{M_A} = \Delta \mu x/RT$; where, A and B are the two components, B differing from A by a group x (e.g. CH_2). That is, if R_M is plotted against the number of similar groups in a homologous series, a straight line should result. While no attempt is made to give the derivation of the Martins equation, it is stressed that it is valid only if ideal partition phenomenon occurs during chromatographic separation. The validity of this relationship which has also been used to predict the structural effects of various groups in the separation, has been tested by various workers, viz. Bate-Smith, Bremner[14], Serchi[15], Pardee[16], etc. It was, however, questioned by Howe[17]; but later, the exhaustive work of Green and his co-workers[18] have put the equation on a very sound footing.

The relationship between R_M values and the number of chlorine groups in chlorinated-phenols, meta-cresols, 3,4-xylenols and 5-ethyl-3-methylphenols obtained with solvent-system A are shown in Figs. 4, 5, 6 and 7. Similarly, its relationship with the number of carbon atoms in phenols and substituted-ortho-cresols using solvent A are depicted in Figs. 8 and 9, respectively. Again, the two curves in Fig. 10 show the relationship between R_M and the number of chlorine groups in chlorinated-m-cresols in two different solvents, viz. B and C.

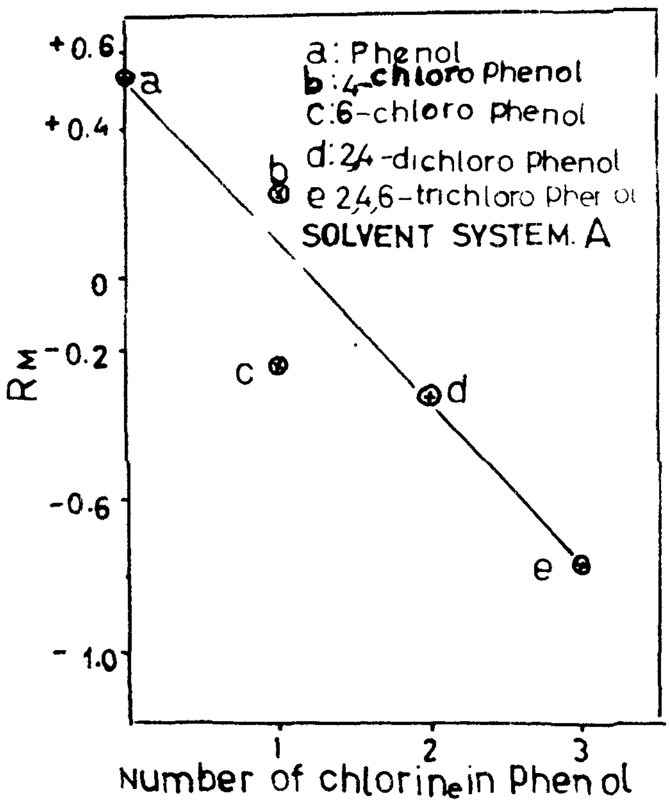


Fig. 4

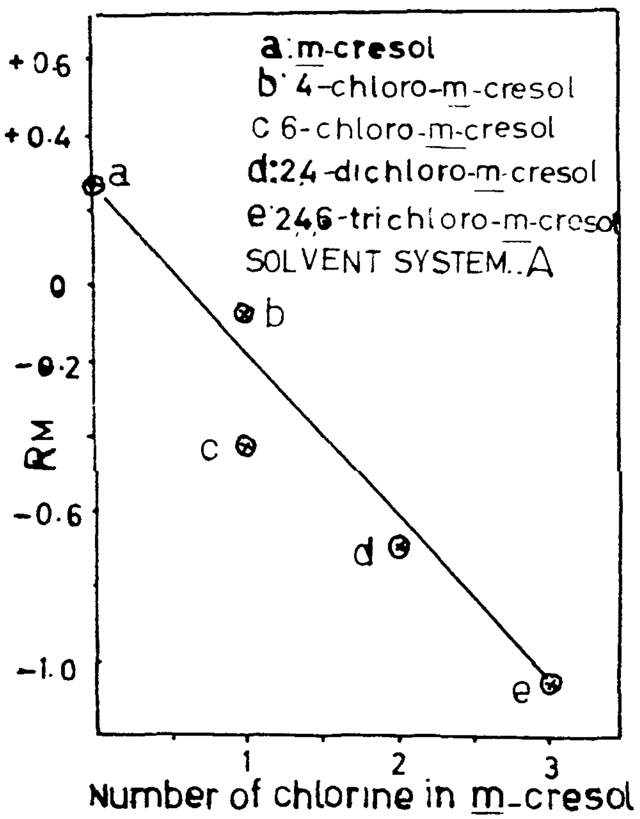


Fig. 5

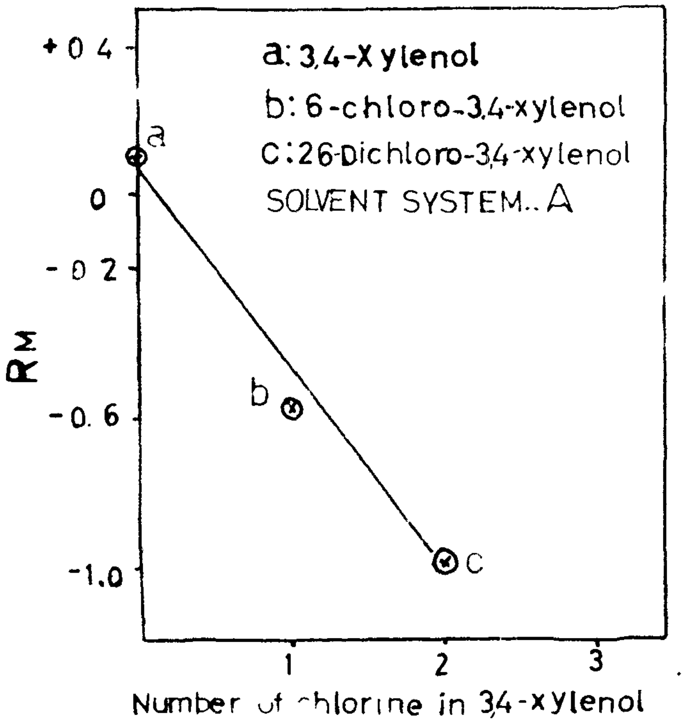


Fig. 6

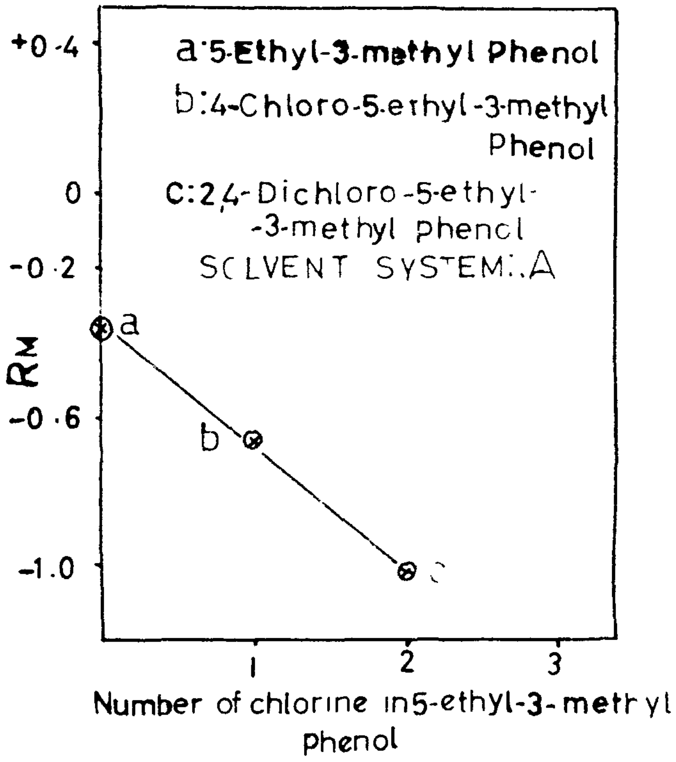


Fig. 7

RELATIONSHIP BETWEEN RM VALUES AND CHLORINE ATOMS

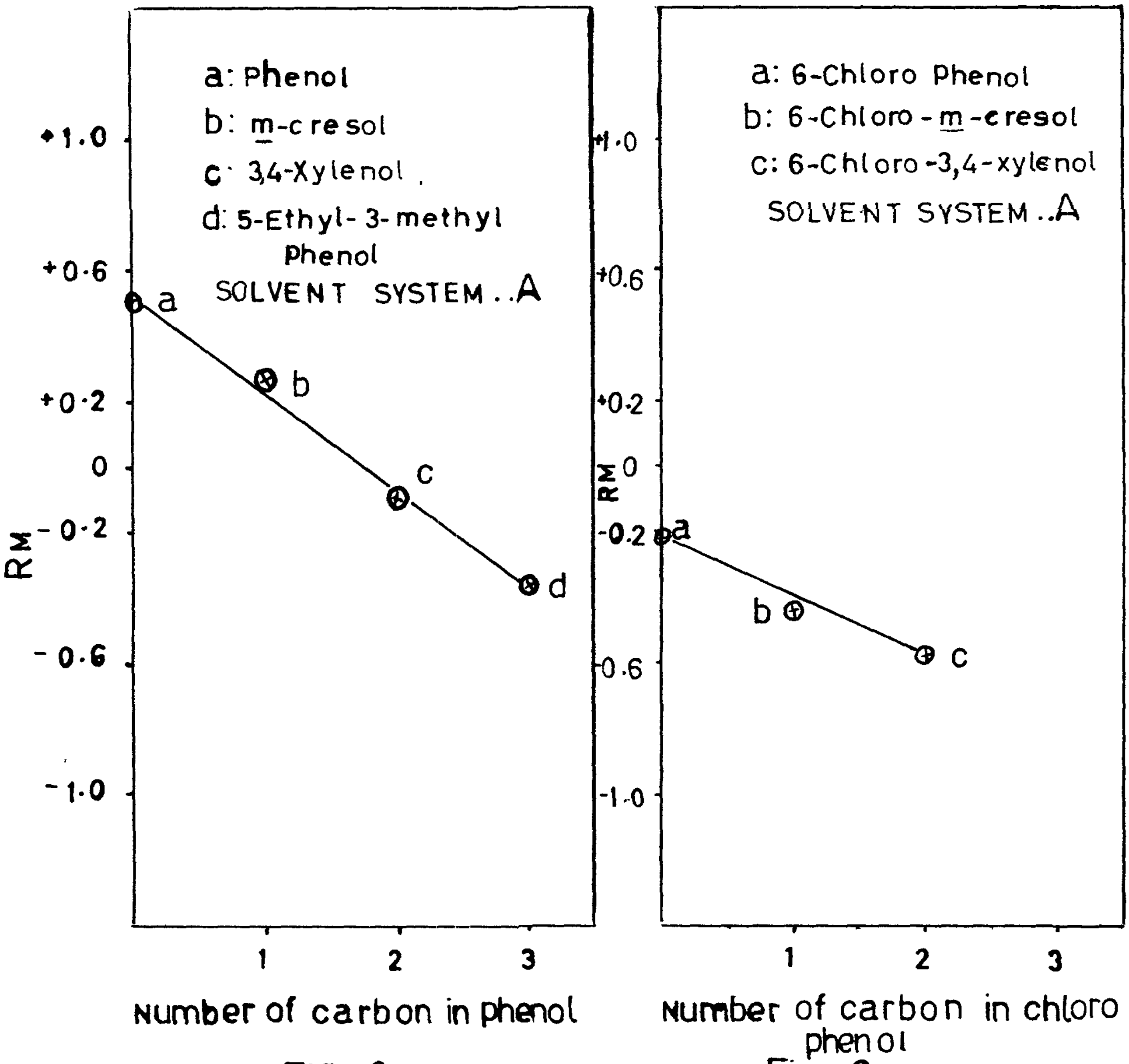


Fig. 8 Fig. 9

RELATIONSHIP BETWEEN RM VALUES AND CARBON ATOMS

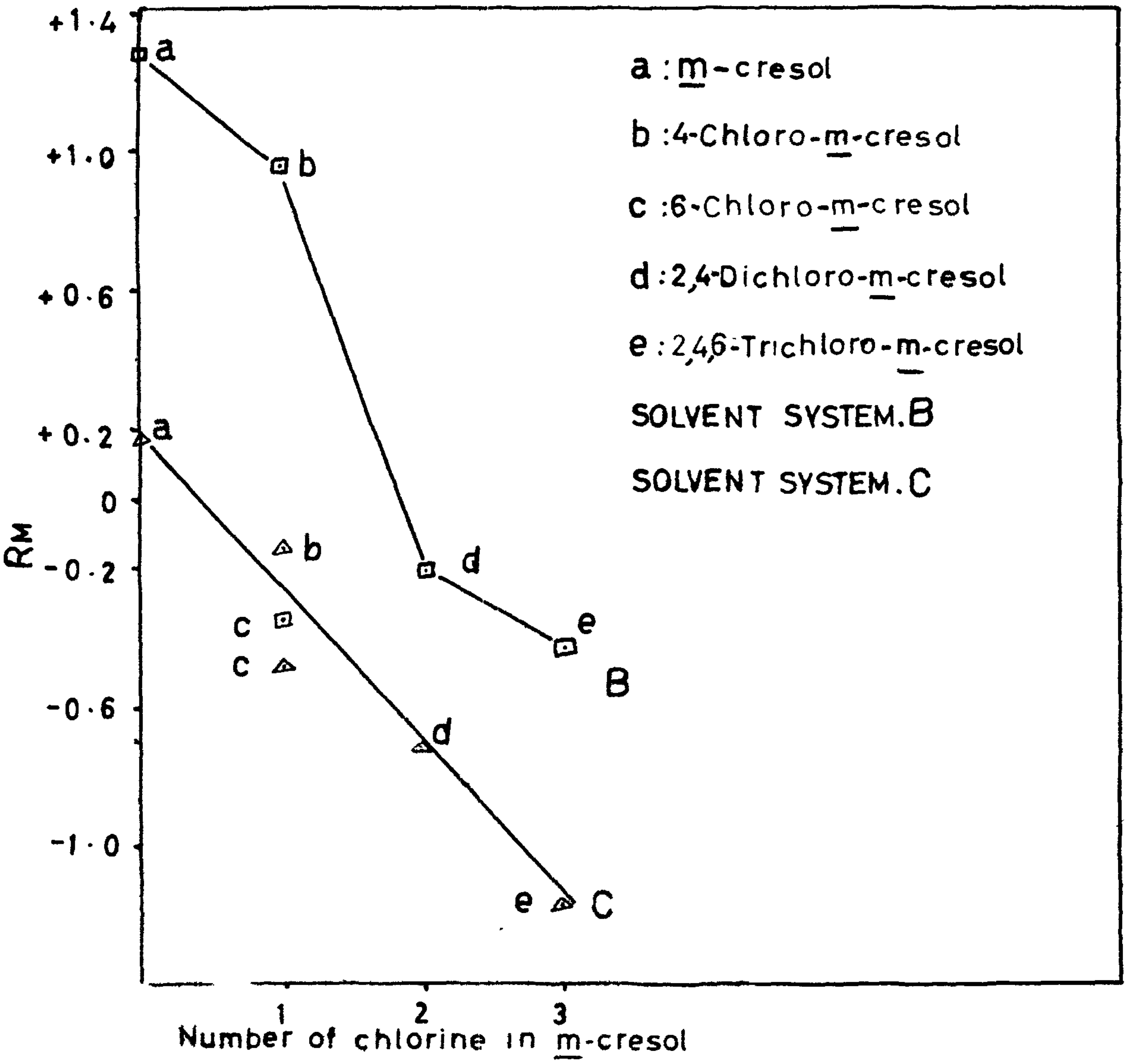


Fig.10

RELATIONSHIP BETWEEN RM VALUES AND CHLORINE ATOMS

From Figs. 4 to 9, it can be seen that

(a) increase of chlorine or carbon number in different phenols changes the R_M values in a set order so that a linearity is observed. It can be concluded that partition phenomenon alone is playing a dominant role in the separation of these phenolic compounds.

(b) from Figs. 4 and 5, it is further noticed that <u>ortho</u>-chlorophenol and 6-chloro-<u>m</u>-cresol deviate from the straight line. This, the author believes, is due to <u>ortho</u>-effect. It may be stated that Green et al.[14] had, to the contrary, indicated the absence of <u>ortho</u>-effect in <u>ortho</u>-chlorophenol in the chromatographic separation of <u>ortho</u>-, <u>meta</u>- and <u>para</u>-chlorophenols. Perhaps, their results are not strictly analogous since they had different experimental conditions.

(c) it is apparent from Fig. 10, that the partition phenomenon is dominant in the separation of chlorinated-<u>m</u>-cresols with solvent C; whereas other factors, especially adsorption plays important role in the separation with solvent B, since the linearity is disturbed. This agrees with the observation of Green et al.[19] that with hexane as the solvent, R_f values might be especially sensitive to the amount of moisture on the paper, or alternatively, adsorption might play a part when a part of the mobile phase is completely non-polar (as is the case with solvent B). The author is inclined to agree that the latter is influencing the separation with the solvent B.

Some of these results have already been published by the author[11].

THIN LAYER CHROMATOGRAPHY (TLC) OF CHLOROPHENOLS

The most extensive and comprehensive contributions to the development of TLC were made by Kirchner, Miller and their coworkers[20,21]. Actually, the method remained in obscurity until 1956 when Stahl[22,23] described the equipment and procedure for the preparation of chromatographic plates. Its simplicity, quickness and efficiency as compared to paper chromatography has led to its widespread use for analytical and preparative separations.

In the present investigations, the TLC was extensively employed for separation and identification of chlorinated products obtained from phenol, cresols and xylenols. It was also used as a tool to study the progress of chlorination; these results are already presented in the second chapter. Considerable time was spent to standardise conditions of separations of chlorophenols as well as to find out suitable solvent systems as prior to this work, there has been no report on the application of this technique to chlorophenols. Peifer's[24] technique of microplate TLC was generally used wherever quick results were required. Considerable time was also devoted to development of quantitative TLC of chlorophenols and results within 2% error have been achieved.

The following solvent systems were tried:

A = xylene saturated with formamide,

B = petroleum ether (80–100°C.) saturated with formic acid, and

C = benzene : acetic acid : water (2:2:1 v/v; organic layer).

The results along with R_f and R_M values of chlorophenols, are given in Tables V and VI and illustrated in Figs. 11, 12 and 13

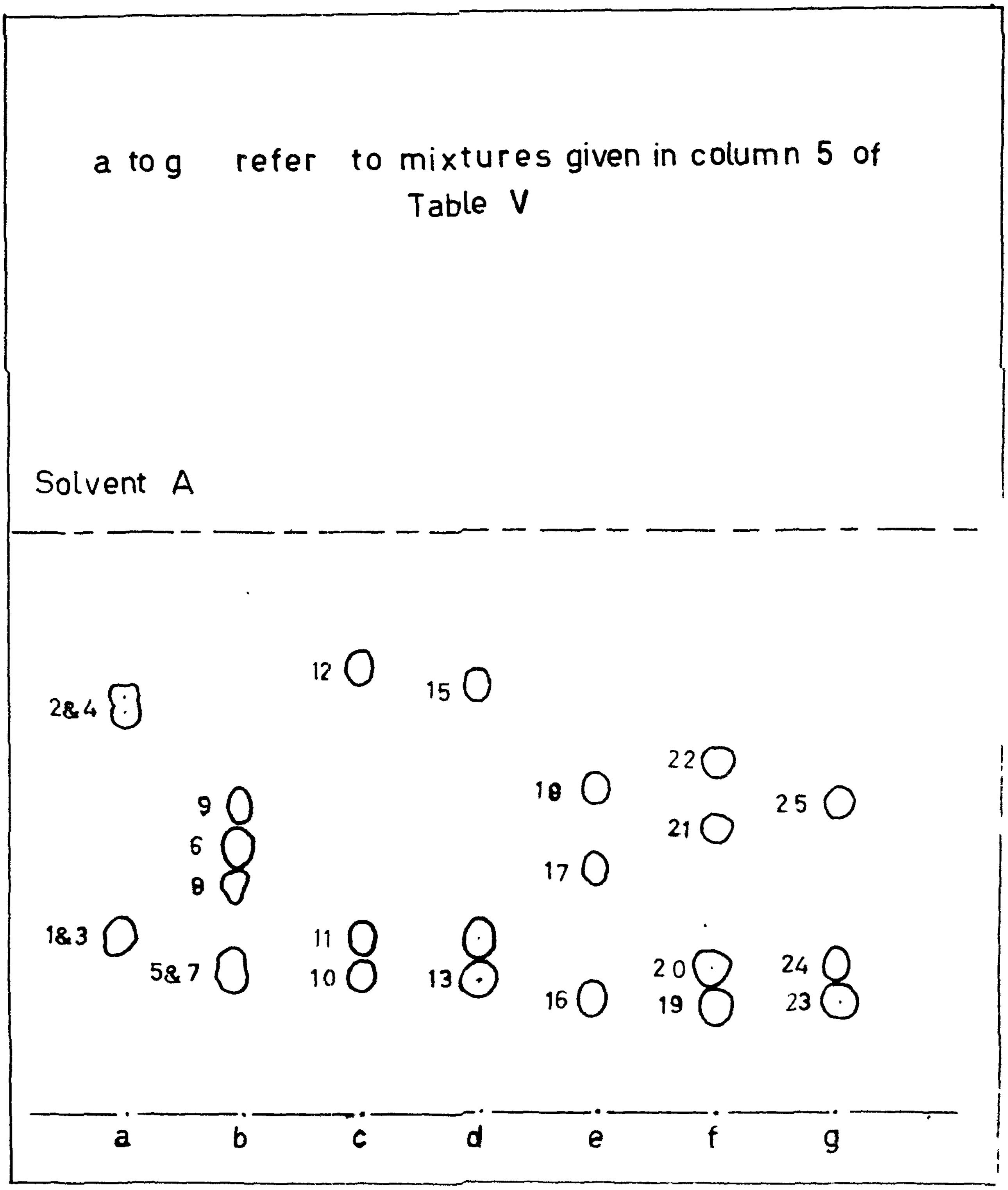
Table V - R_f and R_M values of chlorocresols and chloroxylenols

Temperature 25±3°C; time of run 40-60 min.; solvent A

No.	Compounds	R_f	R_M	Mixtures of phenols
1	2	3	4	5
1	ortho-Cresol	0.32	+0.33	
2	6-Chloro-o-cresol	0.72	-0.41	
3	4-Chloro-o-cresol	0.31	+0.35	1-4[a]
4	4,6-Dichloro-o-cresol	0.74	-0.45	
5	meta-Cresol	0.26	+0.45	
6	6-Chloro-m-cresol	0.47	+0.05	
7	4-Chloro-m-cresol	0.25	+0.48	5-9[b]
8	4,6-Dichloro-m-cresol	0.40	+0.18	
9	2,4,6-Trichloro-m-cresol	0.56	-0.12	
10	2,3-Xylenol	0.26	+0.45	
11	4-Chloro-2,3-xylenol	0.31	+0.35	10-12[c]
12	4,6-Dichloro-2,3-xylenol	0.79	-0.58	

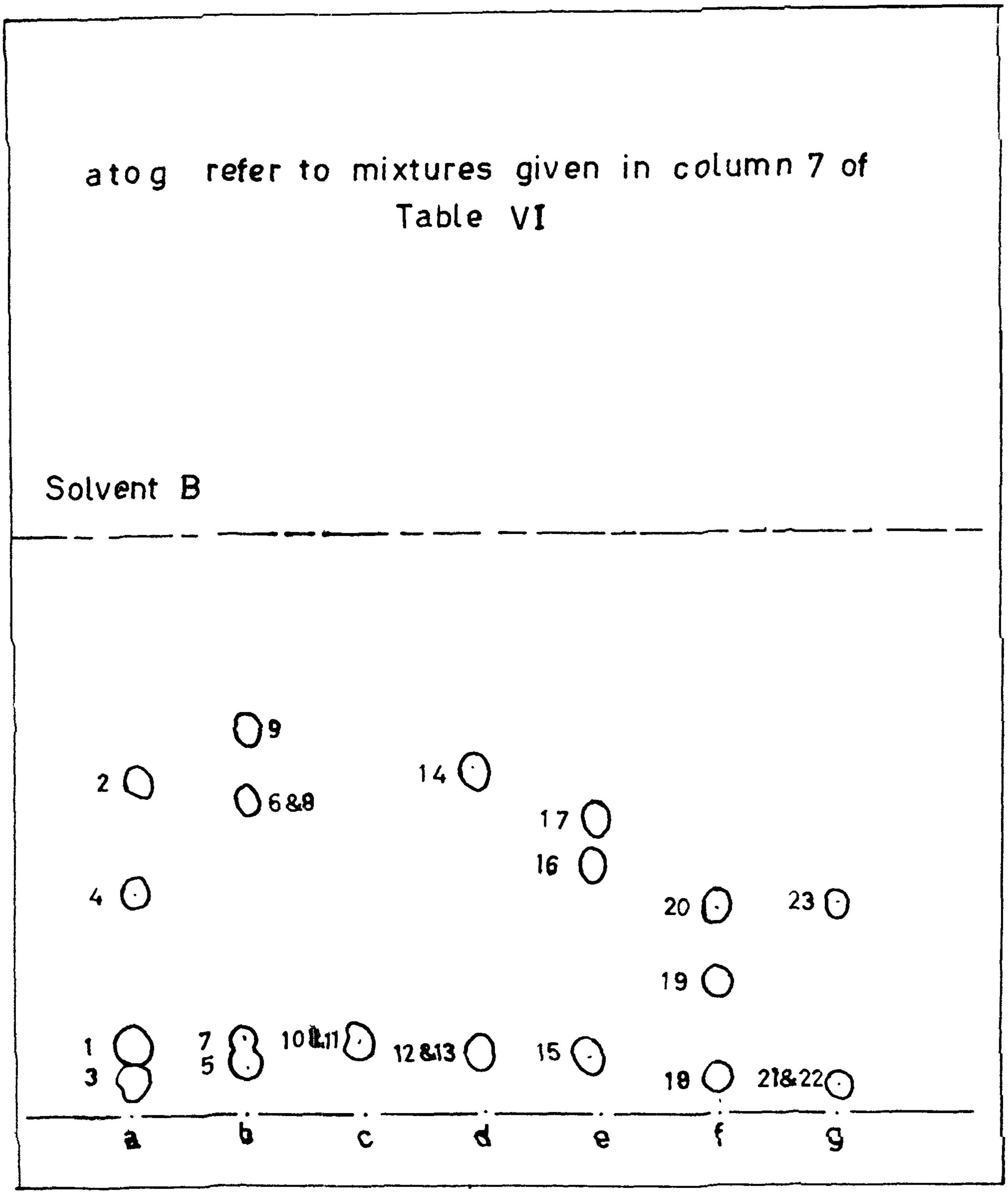
1	2	3	4	5
13	2,5-Xylenol	0.25	+0.48	13-15[d]
14	4-Chloro-2,5-xylenol	0.31	+0.35	
15	4,6-Dichloro-2,5-xylenol	0.76	-0.50	
16	3,4-Xylenol	0.21	+0.58	16-18[e]
17	6-Chloro-3,4-xylenol	0.44	+0.10	
18	2,6-Dichloro-3,4-xylenol	0.58	-0.14	
19	3,5-Xylenol	0.22	+0.55	19-22[f]
20	4-Chloro-3,5-xylenol	0.28	+0.41	
21	2,4-Dichloro-3,5-xylenol	0.53	-0.05	
22	2,4,6-Trichloro-3,5-xylenol	0.62	-0.21	
23	5-Ethyl-3-methylphenol	0.22	+0.55	23-25[g]
24	4-Chloro-5-ethyl-3-ethylphenol	0.27	+0.43	
25	2,4-Dichloro-5-ethyl-3-methylphenol	0.56	-0.12	

Note: The superscripts a to g against entries in column 5 refer to code employed in Fig. 11.



a to g refer to mixtures given in column 5 of Table V

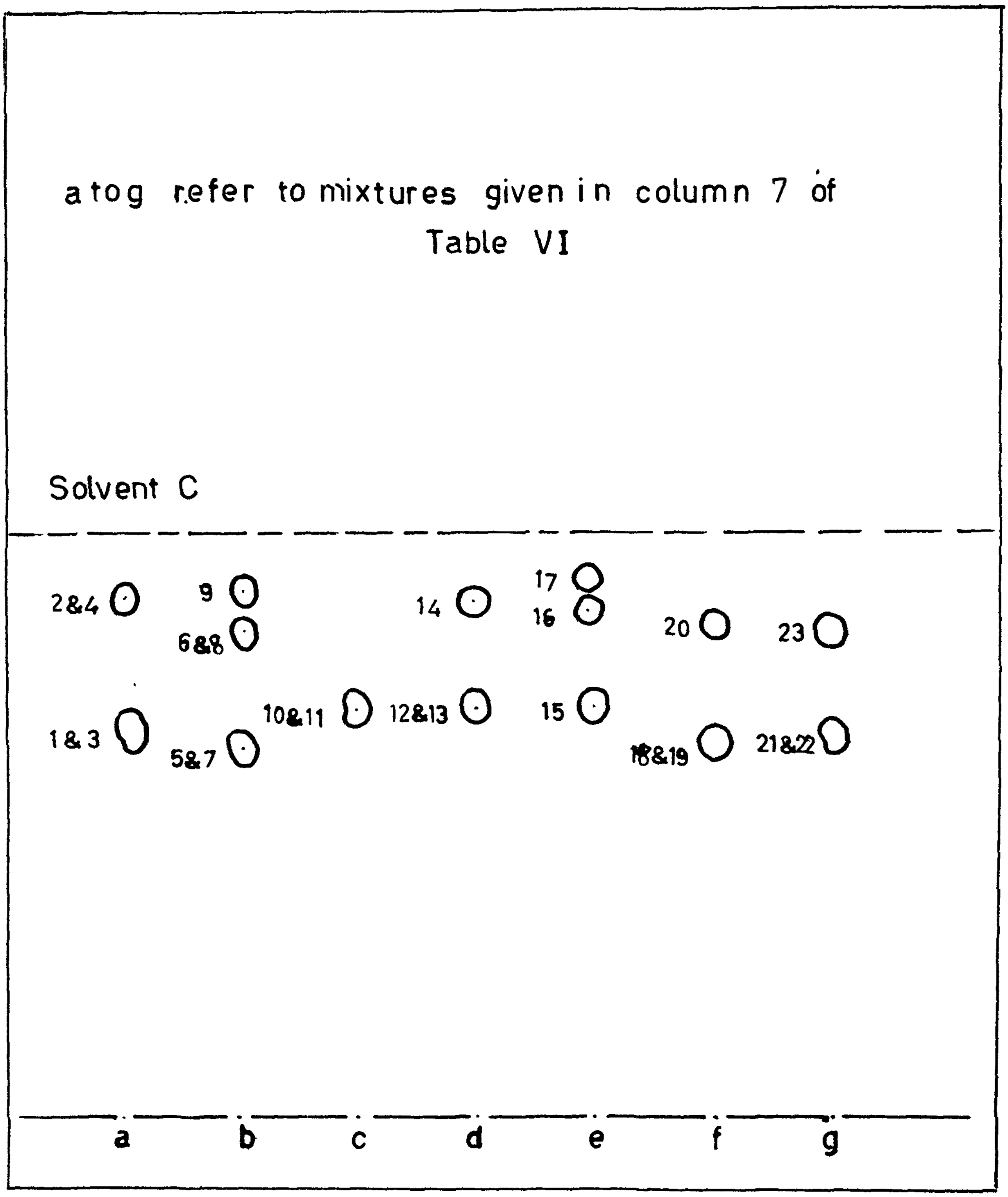
TLC OF SOME MIXTURES OF CHLOROCRESOLS AND CHLOROXYLENOLS
FIG.11



a to g refer to mixtures given in column 7 of Table VI

TLC OF SOME MIXTURES OF CHLOROCRESOLS AND CHLOROXYLENOLS

FIG.12



T L C OF SOME MIXTURES OF CHLOROCRESOLS AND CHLOROXYLENOLS

FIG. 13

Table VI - R_f and R_M values of chlorocresols and chloroxylenols in solvent B and C

Temperature 25±3°C; Time of run for both solvent systems = 40-60 min.

No.	Compound	Solvent B		Solvent C		Mixtures of phenols
		R_f	R_M	R_f	R_M	
1	2	3	4	5	6	7
1	*ortho*-Cresol	0.11	+0.90	0.67	-0.31	1-4[a]
2	6-Chloro-*o*-cresol	0.58	-0.14	0.89	-0.91	
3	4-Chloro-*o*-cresol	0.06	+1.19	0.65	-0.27	
4	4,6-Dichloro-*o*-cresol	0.39	+0.19	0.89	-0.91	
5	*meta*-Cresol	0.09	+1.00	0.63	-0.23	5-9[b]
6	6-Chloro-*m*-cresol	0.55	-0.09	0.89	-0.91	
7	4-Chloro-*m*-cresol	0.12	+0.87	0.63	-0.23	
8	2,6-Dichloro-*m*-cresol	0.55	-0.09	0.83	-0.63	
9	2,4,6-Trichloro-*m*-cresol	0.66	-0.29	0.89	-0.91	
10	2,3-Xylenol	0.12	+0.87	0.71	-0.39	10-11[c]
11	4-Chloro-2,3-xylenol	0.12	+0.87	0.71	-0.39	
12	2,5-Xylenol	0.10	+0.95	0.71	-0.39	12-14[d]
13	4-Chloro-2,5-xylenol	0.10	+0.95	0.71	-0.39	
14	4,6-Dichloro-2,5-xylenol	0.59	-0.16	0.89	-0.91	
15	3,4-Xylenol	0.09	+1.00	0.71	-0.39	15-17[e]
16	6-Chloro-3,4-xylenol	0.43	+0.12	0.88	-0.87	
17	2,6-Dichloro-3,4-xylenol	0.49	+0.01	0.91	-1.00	

1	2	3	4	5	6	7
18	3,5-Xylenol	0.05	+1.28	0.65	-0.27	18-20[f]
19	4-Chloro-3,5-xylenol	0.22	+0.55	0.65	-0.27	
20	2,4-Dichloro-3,5-xylenol	0.35	+0.27	0.85	-0.75	
21	5-Ethyl-3-methylphenol	0.04	+1.38	0.66	-0.29	21-23[g]
22	4-Chloro-5-ethyl-3-methylphenol	0.04	+1.38	0.66	-0.29	
23	2,4-Dichloro-5-ethyl-3-methylphenol	0.35	+0.27	0.84	-0.72	

Note: The superscripts a to g against entries in column 7 refer to code employed in Figs. 12 and 13.

From these data, it is evident (a) that xylene saturated with formamide gave better results for the separation of chlorocresols and chloroxylenols. However, pairs like *ortho*-cresol and 4-chloro-*o*-cresol, *meta*-cresol and 4-chloro-*m*-cresol, 6-chloro-*o*-cresol and 4,6-dichloro-*o*-cresol gave overlapping spots in all the three solvent systems.

(b) that R_f values for *ortho*-substituted phenols were higher than the corresponding *meta*-substituted phenols; 2,6-disubstitution increased them further as indicated below:

ortho-Compounds	R_f	*meta*-Compounds	R_f
ortho-Cresol	0.32	*meta*-Cresol	0.26
6-Chloro-*o*-cresol	0.72	4-Chloro-*m*-cresol	0.25

6-Chloro-3,4-xylenol	0.44	3,4-Xylenol	0.21
6-Chloro-<u>o</u>-cresol	0.72	4,6-dichloro-<u>o</u>-cresol	0.74
6-Chloro-3,4-xylenol	0.44	2,6-Dichloro-3,4-xylenol	0.58

This increase can be caused by various factors. One of these could be the close proximity of the <u>ortho</u>-substituent (s). Due to group interaction, the molar volume and/or the cohesion energy of a molecule gets affected, thus influencing the stability of the transition state. Such factors affecting R_f values have been discussed by Dikstein[25].

(c) that all chlorophenols with chloro in the 4-position have higher R_f values than the corresponding phenols, except that pairs like 4-chloro-<u>m</u>-cresol and its parent phenol i.e. <u>meta</u>-cresol, 4-chloro-2,3-xylenol and 2,3-xylenol, and 4-chloro-2,5-xylenol and 2,5-xylenol had the same R_f values in solvent B and C. These exceptions are probably due to solvent effect[26].

These observations could be used to indicate the type of bonding that is taking place between chlorophenols and the adsorbent (silica gel). The introduction of chlorine groups increases the acidity of phenols and should lead to stronger bonding between the hydrogen of hydroxyl and oxygen attached to Si of the adsorbent ($\text{Ar-O-H} \leftarrow \text{O-Si}$). This should result in lowering of R_f values. However, an increase in R_f value is experimentally observed and it can safely be assumed that the above bonding is not predominant. Other possible bondings are, either of type $\text{Ar-}\underset{\underset{\text{H}}{|}}{\text{O}} \rightarrow \text{H-O.Si}$, or of the type where coordination between oxygen of the aromatic ring to Si exists. Either of these two could be the deciding type. An interaction between the halogen group(s) and the adsorbent need not be considered. Further, the relationship between R_M values and the number of chlorine or carbon groups is not linear; this strongly indicates the existence of adsorption phenomena.

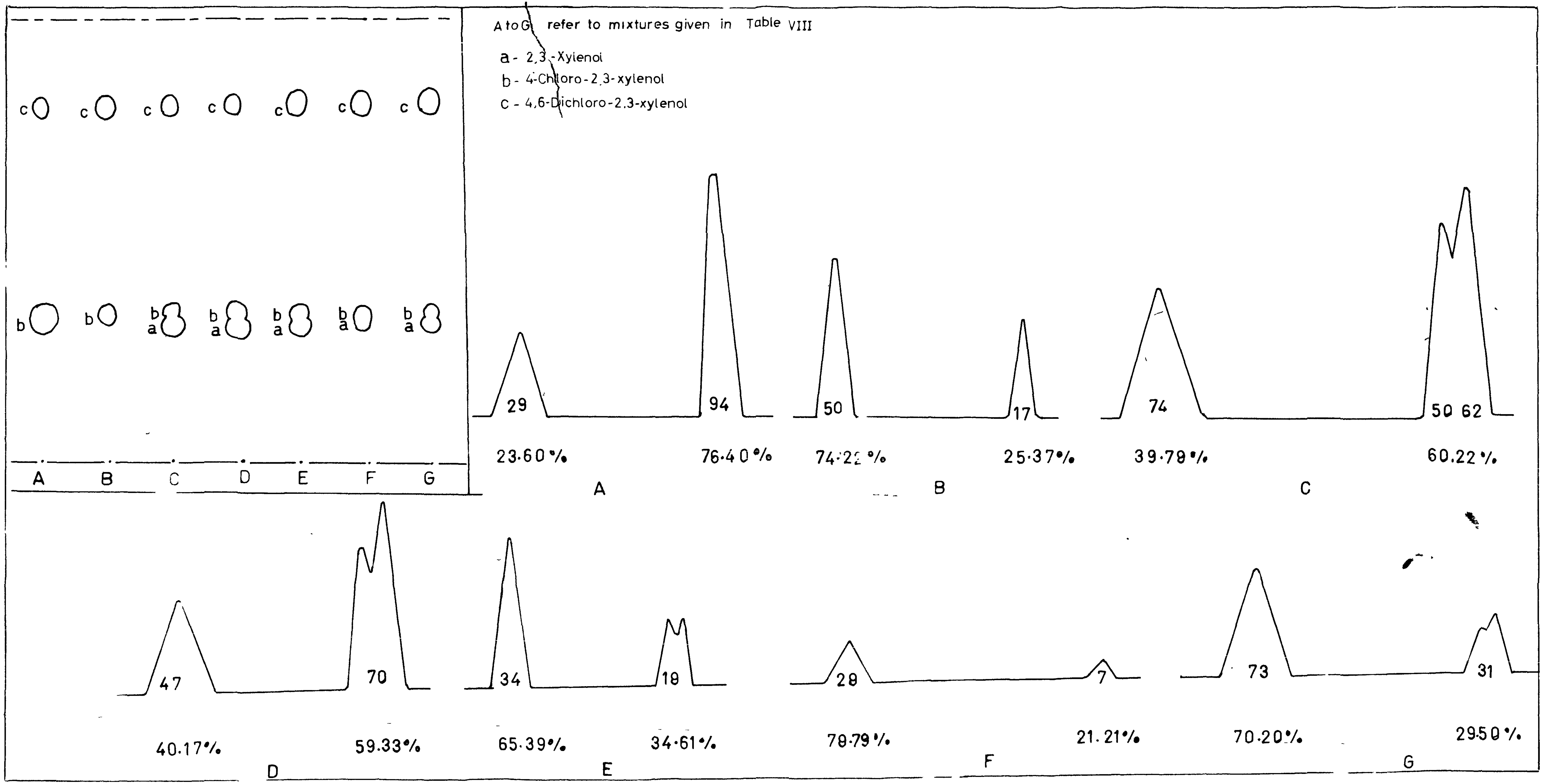
QUANTITATIVE THIN LAYER CHROMATOGRAPHY

The quantitative TLC technique was developed both on big plates (20 cm x 2.1 cm) and on microslides (7 x 2.4 cm). Scanning of the developed spots was done on Joyce Chromoscan densitometer[27]. Optimum quantity for spotting was first determined using different amounts of a mixture of 4-chloro-3,5-xylenol and 2,4,6-trichloro-3,5-xylenol. These results are given in Table VII.

Table VII - Sensitivity of the quantitative TLC method

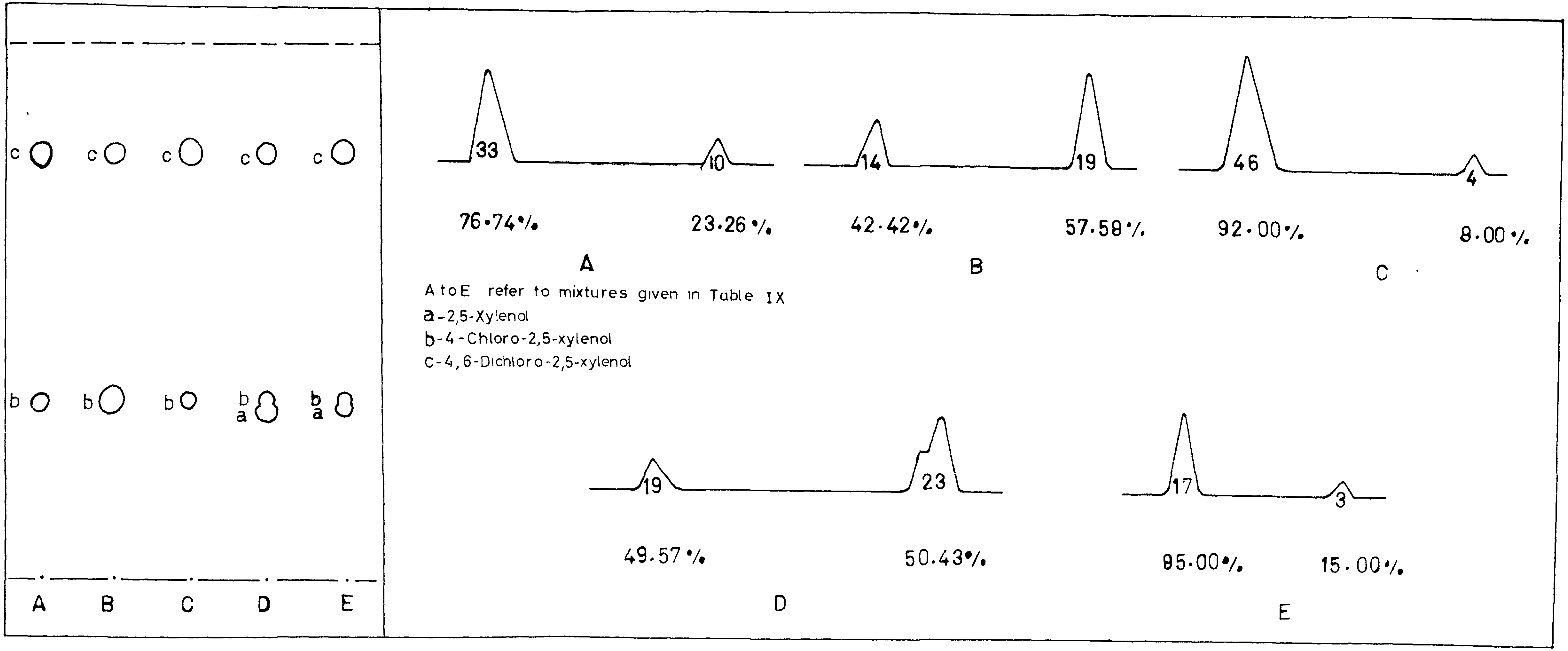
Mixture used : 4-chloro-3,5-xylenol (a) and 2,4,6-trichloro-3,5-xylenol (b)

Quantity of mixture spotted µg	Actual %	Found %	Error %
253.2	(a) 27.97 (b) 72.03	(a) 44.19 (b) 55.81	16.22
126.6	(a) 27.97 (b) 72.03	(a) 36.11 (b) 63.89	8.14
84.4	(a) 27.97 (b) 72.03	(a) 29.63 (b) 70.37	1.66
50.6	(a) 27.97 (b) 72.03	(a) 28.57 (b) 71.43	0.60
36.1	(a) 27.97 (b) 72.03	(a) 29.02 (b) 70.98	1.03



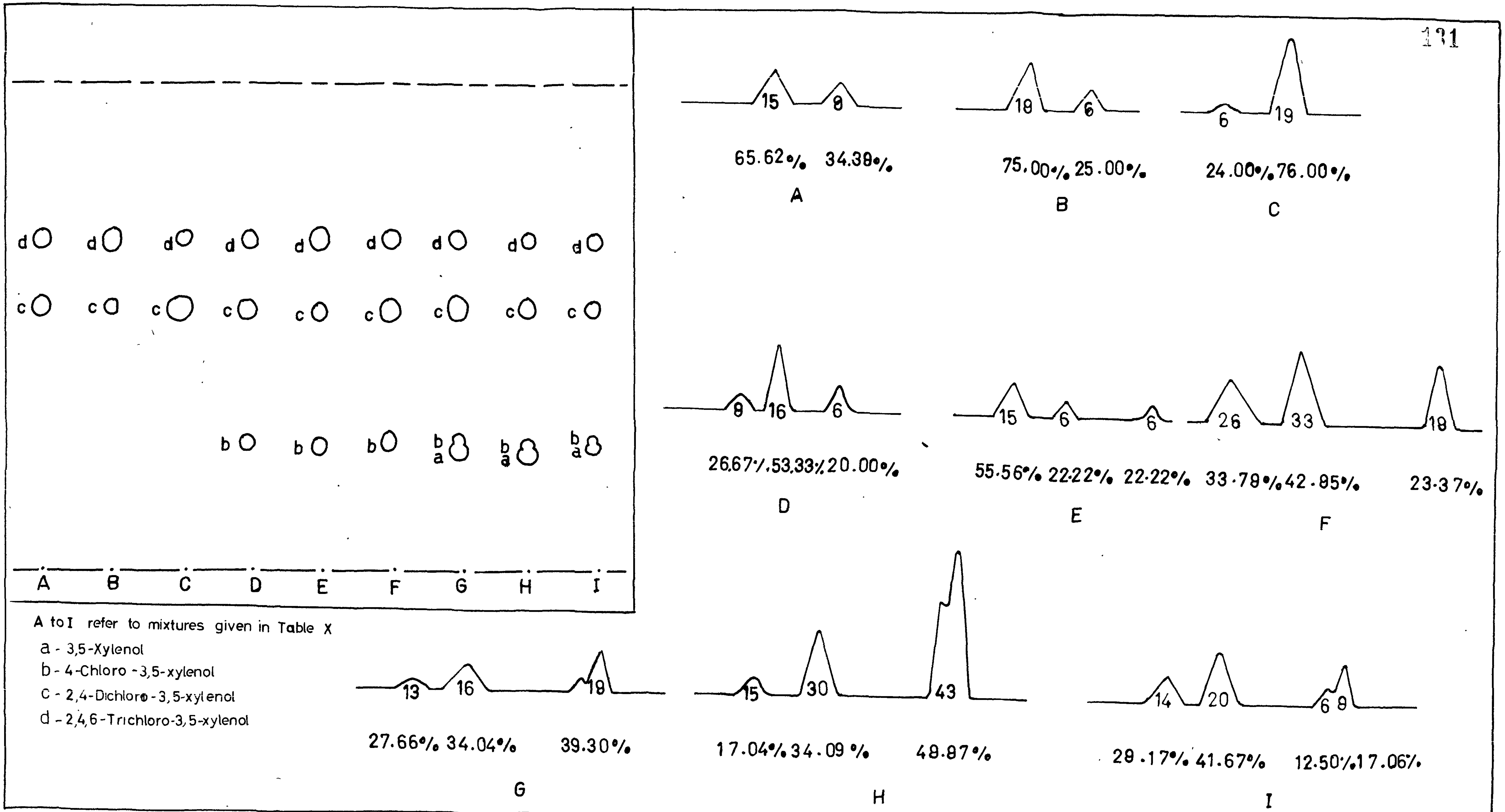
TLC DIAGRAM AND CHROMOSCAN DATA ON SOME MIXTURES OF CHLORODERIVATIVES OF 2,3-XYLENOLS

FIG. 14



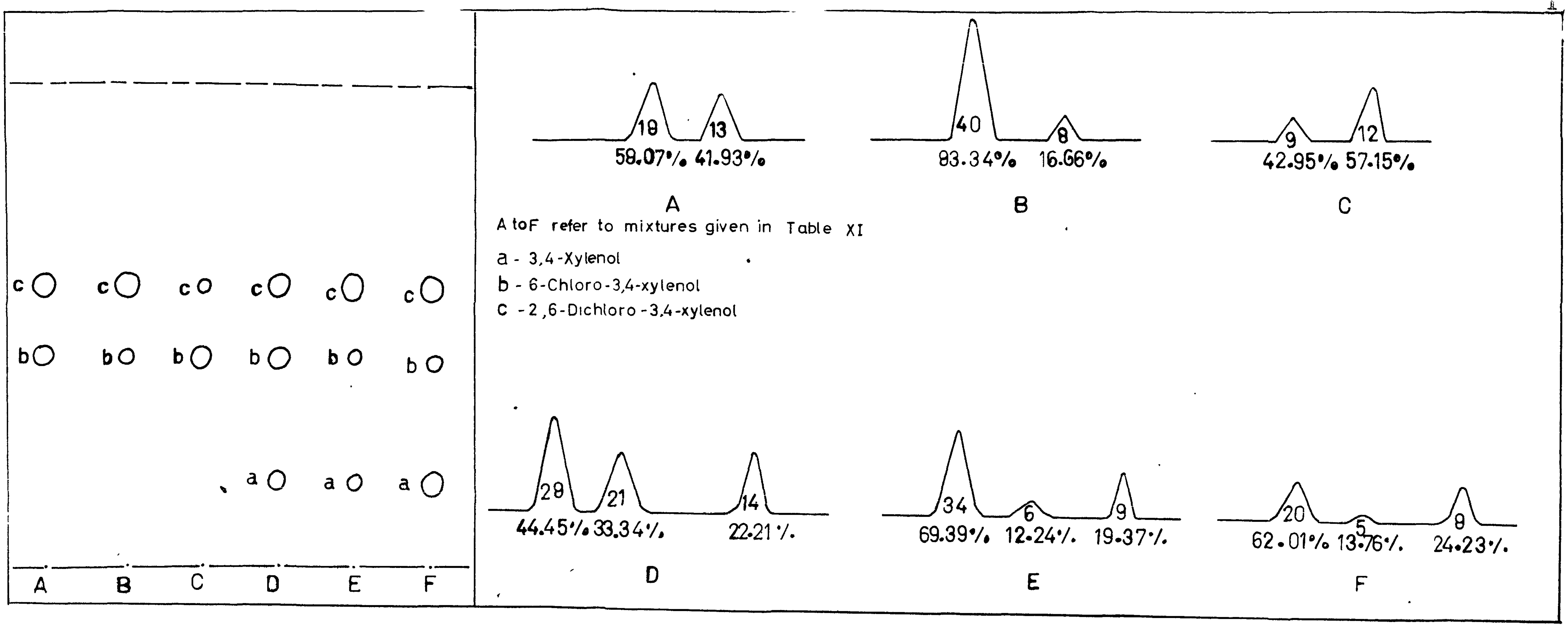
TLC DIAGRAM AND CHROMOSCAN DATA ON SOME MIXTURES OF CHLORODERIVATIVES OF 2,5-XYLENOLS

FIG.15



TLC DIAGRAM AND CHROMOSCAN DATA ON SOME MIXTURES OF CHLORODERIVATIVES OF 3,5-XYLENOLS

FIG.16



TLC DIAGRAM AND CHROMOSCAN DATA ON SOME MIXTURES OF CHLORODERIVATIVES OF 3,4-XYLENOLS

FIG.17

Though reasonable accuracy was obtained with 84.4 µg of the mixture, for detailed studies, 50 µg was uniformly used. Higher concentration gave larger spots (> 1 cm) and scanning was difficult due to limited slit width. Different mixtures of xylenols and chloroxylenols were estimated. The results on 20 x 2.1 cm plates are shown in Tables VIII, IX, X and XI and Figs. 14, 15, 16 and 17.

Table VIII - Quantitative TLC of 2,3-xylenol and its chloroderivatives

Mixture	Components	Composition,% Taken	Composition,% Found	Error, %
1	2	3	4	5
A	4-Chloro-2,3-xylenol	73.89	76.40	2.51
	4,6-Dichloro-2,3-xylenol	26.11	23.60	
B	4-Chloro-2,3-xylenol	22.93	25.37	2.44
	4,6-Dichloro-2,3-xylenol	77.02	74.63	
C	2,3-Xylenol	24.13	60.22	1.35
	4-Chloro-2,3-xylenol	34.74		
	4,6-Dichloro-2,3-xylenol	41.13	39.78	

1	2	3	4	5
D	2,3-Xylenol	28.45	59.83	1.08
	4-Chloro-2,3-xylenol	30.30		
	4,6-Dichloro-2,3-xylenol	41.25	40.17	
E	2,3-Xylenol	9.30	34.61	2.01
	4-Chloro-2,3-xylenol	23.30		
	4,6-Dichloro-2,3-xylenol	67.40	65.39	
F	2,3-Xylenol	10.56	21.21	0.24
	4-Chloro-2,3-xylenol	10.41		
	4,6-Dichloro-2,3-xylenol	79.03	78.79	
G	2,3-Xylenol	11.88	29.80	1.72
	4-Chloro-2,3-xylenol	16.20		
	4,6-Dichloro-2,3-xylenol	71.92	70.20	

Table IX - Quantitative TLC of 2,5-xylenol and its chloro-derivatives

Mixture	Components	Composition, %		Error, %
		Taken	Found	
1	2	3	4	5
A	4-Chloro-2,5-xylenol	23.95	23.24	0.69
	4,6-Dichloro-2,5-xylenol	76.05	76.74	
B	4-Chloro-2,5-xylenol	59.55	57.58	1.97
	4,6-Dichloro-2,5-xylenol	40.45	42.42	
C	4-Chloro-2,5-xylenol	5.74	8.00	2.26
	4,6-Dichloro-2,5-xylenol	94.26	92.00	
D	2,5-Xylenol	28.81	50.43	1.27
	4-Chloro-2,5-xylenol	22.89		
	4,6-Dichloro-2,5-xylenol	48.30	49.57	
E	2,5-Xylenol	7.97	15.00	1.36
	4-Chloro-2,5-xylenol	8.39		
	4,6-Dichloro-2,5-xylenol	83.64	85.00	

1	2	3	4	5
F	4-Chloro-3,5-xylenol	20.83	23.37	2.54
	2,4-Dichloro-3,5-xylenol	42.62	42.85	0.23
	2,4,6-Trichloro-3,5-xylenol	36.55	33.78	2.79
G	3,5-Xylenol	24.47	48.80	2.02
	4-Chloro-3,5-xylenol	24.82		
	2,4-Dichloro-3,5-xylenol	32.07	84.09	1.60
	2,4,6-Trichloro-3,5-xylenol	18.64	17.04	2.59
H	3,5-Xylenol	22.17	38.30	2.59
	4-Chloro-3,5-xylenol	13.54		
	2,4-Dichloro-3,5-xylenol	32.43	34.04	1.61
	2,4,6-Trichloro-3,5-xylenol	31.86	27.66	4.21
	3,5-Xylenol	15.85	16.66	0.81
	4-Chloro-3,5-xylenol	12.62	12.50	0.12
	2,4-Dichloro-3,5-xylenol	37.36	41.67	4.31
	2,4,6-Trichloro-3,5-xylenol	34.17	29.17	5.00

Table X - Quantitative TLC of 3,5-xylenol and its chloro-derivatives

Mixture	Components	Composition, %		Error, %
		Taken	Found	
1	2	3	4	5
A	2,4-Dichloro-3,5-xylenol	31.16	34.38	3.22
	2,4,6-Trichloro-3,5-xylenol	68.84	65.62	
B	2,4-Dichloro-3,5-xylenol	23.87	25.00	1.13
	2,4,6-Trichloro-3,5-xylenol	76.13	75.00	
C	2,4-Dichloro-3,5-xylenol	77.00	76.00	1.00
	2,4,6-Trichloro-3,5-xylenol	23.00	24.00	
D	4-Chloro-3,5-xylenol	20.46	20.00	3.06
	2,4-Dichloro-3,5-xylenol	53.19	53.33	0.14
	2,4,6-Trichloro-3,5-xylenol	34.75	26.67	1.92
E	4-Chloro-3,5-xylenol	20.92	22.23	1.30
	2,4-Dichloro-3,5-xylenol	20.08	22.22	2.14
	2,4,6-Trichloro-3,5-xylenol	59.00	55.56	3.44

Table XI - Quantitative TLC of 3,4-xylenol and its chloro-derivatives

Mixture	Components	Composition, %		Error, %
		Taken	Found	
A	6-Chloro-3,4-xylenol	43.16	41.93	1.23
	2,6-Dichloro-3,4-xylenol	36.84	58.07	3.54
B	6-Chloro-3,4-xylenol	13.12	16.66	3.54
	2,6-Dichloro-3,4-xylenol	86.88	83.34	
C	6-Chloro-3,4-xylenol	60.37	57.15	3.22
	2,6-Dichloro-3,4-xylenol	39.63	42.85	
D	3,4-Xylenol	21.76	22.21	0.45
	6-Chloro-3,4-xylenol	31.86	33.34	1.48
	2,6-Dichloro-3,4-xylenol	46.38	44.45	1.93
E	3,4-Xylenol	15.80	18.37	2.57
	6-Chloro-3,4-xylenol	10.28	12.24	1.96
	2,6-Dichloro-3,4-xylenol	73.92	69.39	4.53
F	3,4-Xylenol	26.33	24.23	2.10
	6-Chloro-3,4-xylenol	13.39	13.76	0.37
	2,6-Dichloro-3,4-xylenol	60.28	62.01	1.71

From these it is evident that this technique can be employed for quantitative estimations of xylenols and their chloroderivatives in mixtures within 2 per cent error. Results obtained on microslides were as good as those with larger plates (see Table XII).

Table XII - A typical comparison between results of quantitative TLC study on plates of different sizes

Mixture	Components	Composition taken %	Composition, found, % on 20x2.1 cm plates	Composition, found, % 7x2.4 cm plates	Error, %
A	4-Chloro-3,5-xylenol	27.97	29.63	29.41	0.22
	2,4,6-Dichloro-3,5-xylenol	72.03	70.37	70.59	0.22
B	4-Chloro-3,5-xylenol	68.82	68.42	68.75	0.33
	2,4,6-Dichloro-3,5-xylenol	31.18	31.58	31.25	0.33
C	4,Chloro-2,3-xylenol	-	61.53	61.30	0.23
	4,6-Dichloro-2,3-xylenol	-	38.47	38.70	0.23

Note: The composition of mixture C was not known as it was not a synthetic mixture but a product obtained by the chlorination of 2,3-xylenol with sulphuryl chloride.

Since scanning of a microslide takes only about 2 minutes and the entire operation about ten minutes, the method can well serve as a control while chlorinating unknown mixture of phenols.

GAS LIQUID CHROMATOGRAPHY (GLC) OF CHLOROCRESOLS AND CHLOROXYLENOLS

There are only a few reports in literature on the GLC of chlorophenols. Fitzgerald[28] and Norman et al.[29] could not separate chlorophenols on GLC and recommended their GLC after their conversion to methyl ethers. Recently Barry et al.[30] and Barkely et al.[31] have analysed a few chlorophenols in the free form.

In the present study, chlorophenols were analysed using Reoplex 100 at 209±2°C., silicone vacuum grease (Dow Corning) at 202±2°C., and silicone elastomer-30 (SE-30) at 173° C. and 159°C. as stationary liquid phases deposited on celite or firebrick powder. Data of relative retention times (relative to 6-chloro-*o*-cresol) are given in Table XIII.

Table XIII - Relative retention times of chlorocresols and chloroxylenols

Stationary liquid phases: (I) Reoplex 100 (30% w/w on celite)
(II) Silicone high vacuum grease (30% w/w on celite)

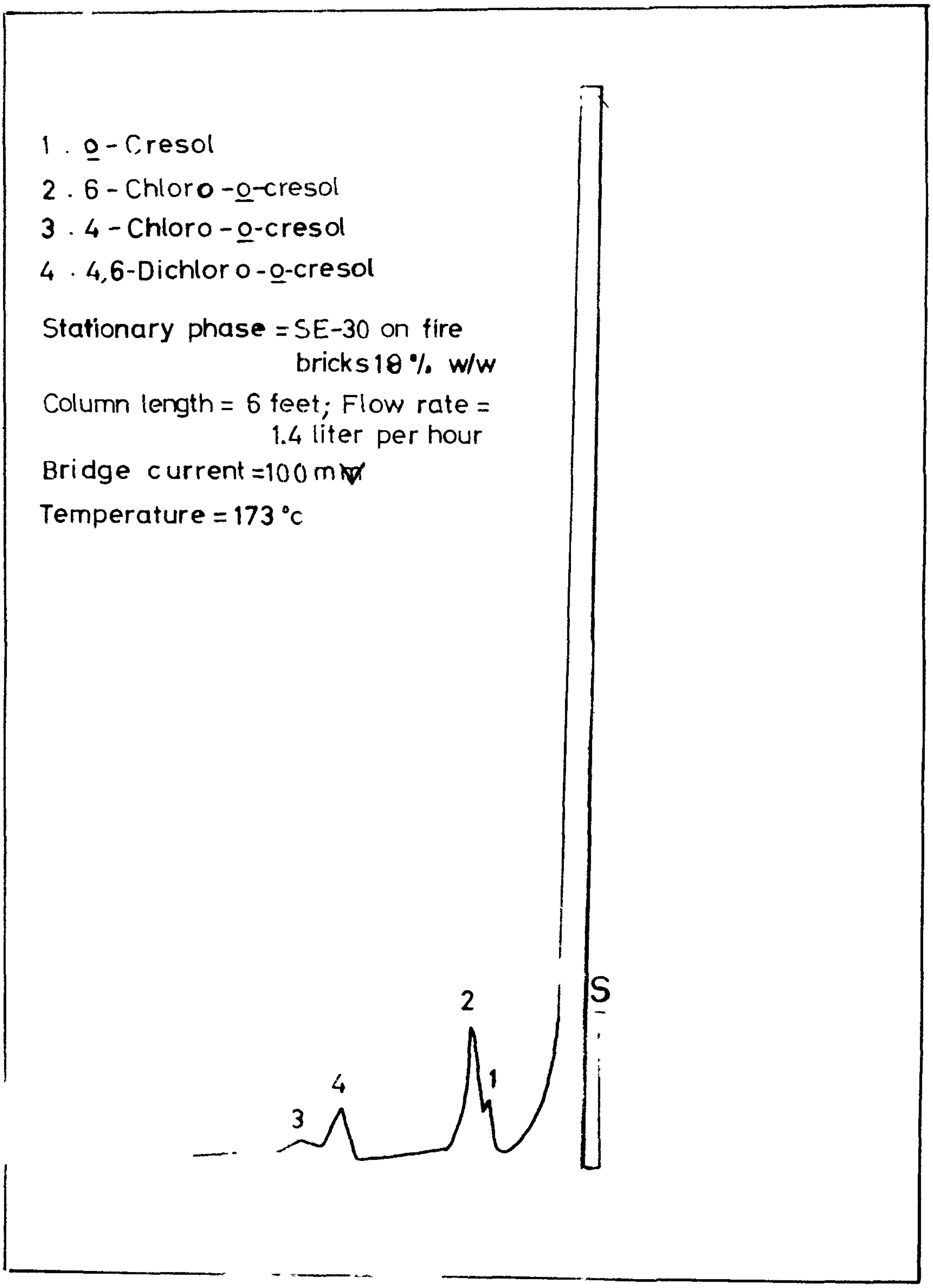
Carrier gas : nitrogen, Column length : 9 ft.

Name	Relative retention time (relative to 6-chloro-*o*-cresol) I 208±2°C.	II 201±2°C.
1	2	3
6-Chloro-*o*-cresol	1.00	1.00
4-Chloro-*o*-cresol	1.18	1.87

1	2	3
4-Chloro-3,5-xylenol	1.43	2.62
6-Chloro-*m*-cresol	1.21	1.00
4-Chloro-*m*-cresol	1.31	2.00
4,6-Dichloro-*o*-cresol	2.15	1.75
4,6-Dichloro-*m*-cresol	2.81	2.00
2,4,6-Trichloro-*m*-cresol	-	4.00
6-Chloro-3,4-xylenol	2.06	1.75
4-Chloro-2,5-xylenol	2.56	2.50
4-Chloro-2,6-xylenol	3.90	-
2,4-Dichloro-3,5-xylenol	3.56	-
2,4-Dichloro-3-ethyl-5-methylphenol	3.75	-
2,4-Dichloro-5-ethyl-3-methylphenol	5.00	-
2,6-Dichloro-3,4-xylenol	4.62	-
4-Chloro-3-ethyl-5-methylphenol	7.06	-

A few synthetic mixtures of chlorocresols were tried on SE-30 and the preliminary results so obtained are reproduced in Figs. 18, 19 and 20. Detailed work using this technique was given up as it would be apparent from Fig. 20, that there was poor detector response, which might be due to poor volatality of the compounds at the operating temperatures. Though these data are of elementary nature, the following salient observations are recorded:

(a) chloro-derivatives of *meta*-cresols have a higher retention time compared to the corresponding chloroderivative

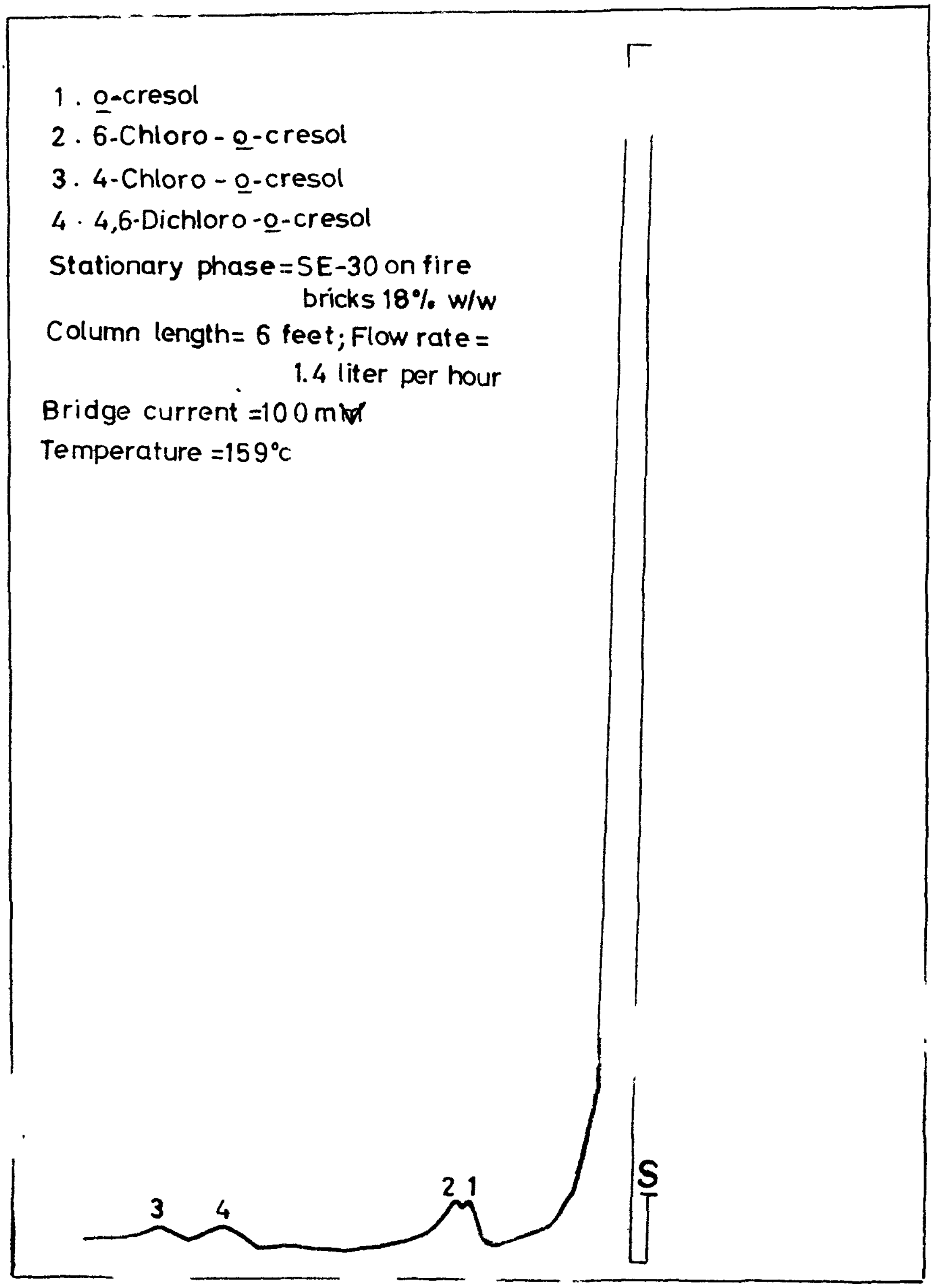


1 . o - Cresol
2 . 6 - Chloro -o-cresol
3 . 4 - Chloro - o-cresol
4 . 4,6-Dichloro-o-cresol

Stationary phase = SE-30 on fire bricks 10 % w/w
Column length = 6 feet; Flow rate = 1.4 liter per hour
Bridge current = 100 mV
Temperature = 173 °c

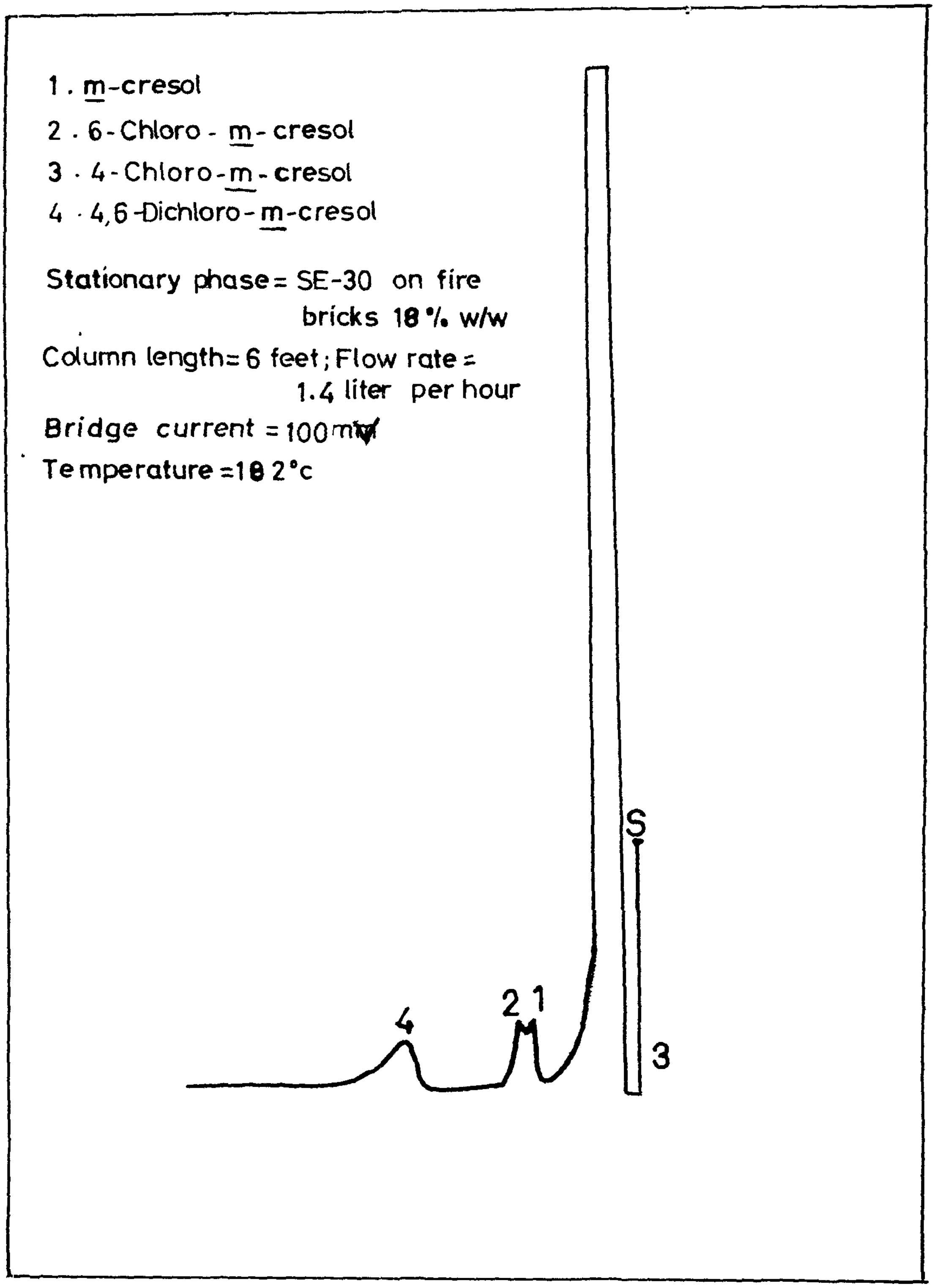
GLC SEPARATION OF O- CRESOLS AND ITs CHLORODERIVATIVES

FIG 18



GLC SEPARATION OF O-CRESOLS AND ITs CHLORODERIVATIVES

FIG.19



GLC SEPARATION OF m-CRESOLS AND ITs CHLORODERIVATIVES

FIG.20

of ortho-cresols;

(b) para-chlorocresols, in general, have a higher retention time than the ortho-isomers, at least on Reoplex 100;

(c) as the number of chlorine groups increases, the retention time also increases. However, exception is 4-chloro-3-ethyl-5-methylphenol (7.06) as compared to 2,4-dichloro-3-ethyl-5-methylphenol (3.95);

(d) in general, better separations are given by stationary phase I when compared with II;

(e) on the stationary phase II, 6-chloro-3,4-xylenol emerges earlier than 4- chloro-3,5-xylenol; the reverse is true on I.

(f) fig. 20 shows that 4-chloro-m-cresol did not emerge even at 182°C. on SE-30, showing the poor detector response.

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CHAPTER IV

SPECTROSCOPIC STUDIES ON CHLOROCRESOLS AND CHLOROXYLENOLS

In the previous chapter, qualitative and quantitative chromatographic methods for separation of chlorophenols are presented. These methods were very helpful in determining the progress of chlorination reactions and also the purity of the compounds; but these do not throw much light on the structure of these chlorophenols because of inherent limitations. By mere examination of R_f value of a compound, exact nature of the isomer cannot be established and to achieve it, methods other than chromatography need to be exploited.

Modern methods of spectroscopy in different regions of the electromagnetic spectrum have provided the chemist with powerful tools for analysis and investigation of structures. These methods include electronic (ultraviolet and visible) infra red, Raman, microwave, mass and nuclear magnetic resonance (NMR) spectroscopy. The choice of the method of spectroscopy for a specific problem depends, among other factors, upon the structure and properties of the specimen and the nature of information sought. Thus, a detailed structural information on certain type of molecules may be obtained from microwave, NMR or mass spectroscopy. Infra red spectroscopy is a good tool for structural investigation. because of the ideal wave length region ($4000\ cm^{-1}$-$660\ cm^{-1}$) it covers in the electromagnetic spectrum. The infra red spectrum of a molecule has both group character and considerable structural character. Ultra violet spectroscopy, on the other hand, does not give much information on the detailed structural features of molecules, but throws light on the group character. However, by studying the electronic spectra of a large number of different types of molecules, it has been possible to correlate the spectra with structure.

Identification of organic compounds by their absorption spectra has become a routine procedure for the past several years. It is common practice now, to record either the IR or UV spectra while proposing a structure for a new compound or while reporting its physical properties. The NMR spectrum provides much more information concerning structural environment and offers quite convincing proof of structure for an organic compound. Electronic absorption spectroscopy is used as confirmatory evidence for the identity of a previously known compound, just as any other physical property, for example, melting point, refractive index etc. Examples are abundant where a particular structure of a compound was arrived at from several possibilities on the basis of its ultra violet or visible spectrum. The light intensity of many of the absorption bands in the near ultra violet and visible regions not only permit the identification with minute quantities of material, but also serve as an aid in the control of purification of substances.

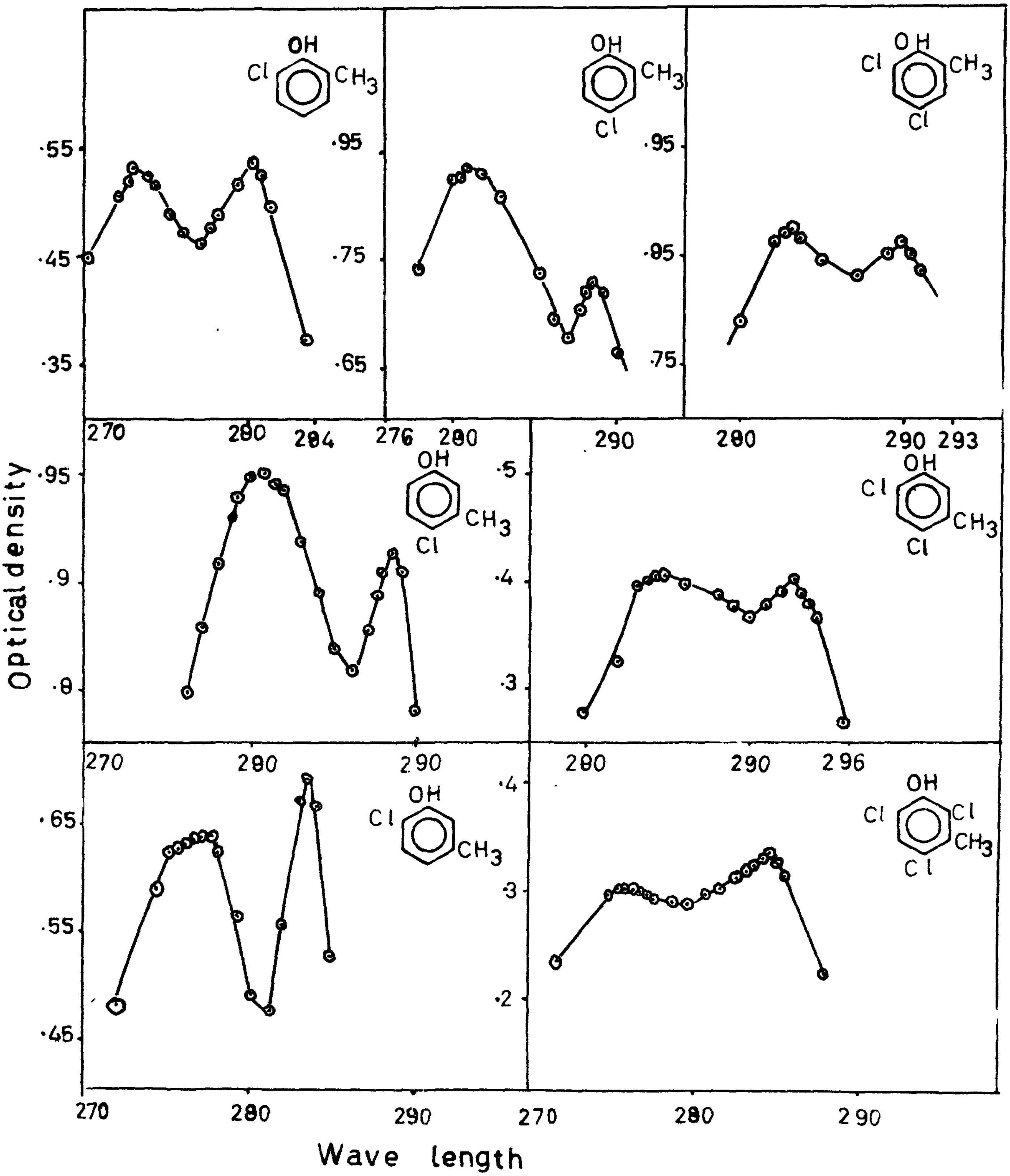
In this chapter the results of (a) UV (b) IR and (c) NMR spectra of chlorophenols are systematically presented. In interpreting the UV data, an attempt has been made to correlate the structure of these chlorophenols which are modified by chlorine substitution, in terms of bathochromic or hypsochromic shifts or hypsochromic and hyperchromic effects observed in the absorption bands. The IR and NMR spectra of these chlorophenols are discussed to confirm the identity and structure of these chlorocompounds.

ULTRAVIOLET ABSORPTION DATA OF CHLOROCRESOLS AND CHLOROXYLENOLS

The UV spectra of a number of phenols have previously been investigated by many workers[1-5]. Chlorocresols and chloroxylenols generally exhibit two absorption bands between 270 and 300 mμ. The band at longer wave length is referred to as the C-band, and the band at shorter wave length, the B-band. This assignment corresponds to the B- and C-bands of benzene and aniline, which has been explained by Dearden et al.[5]

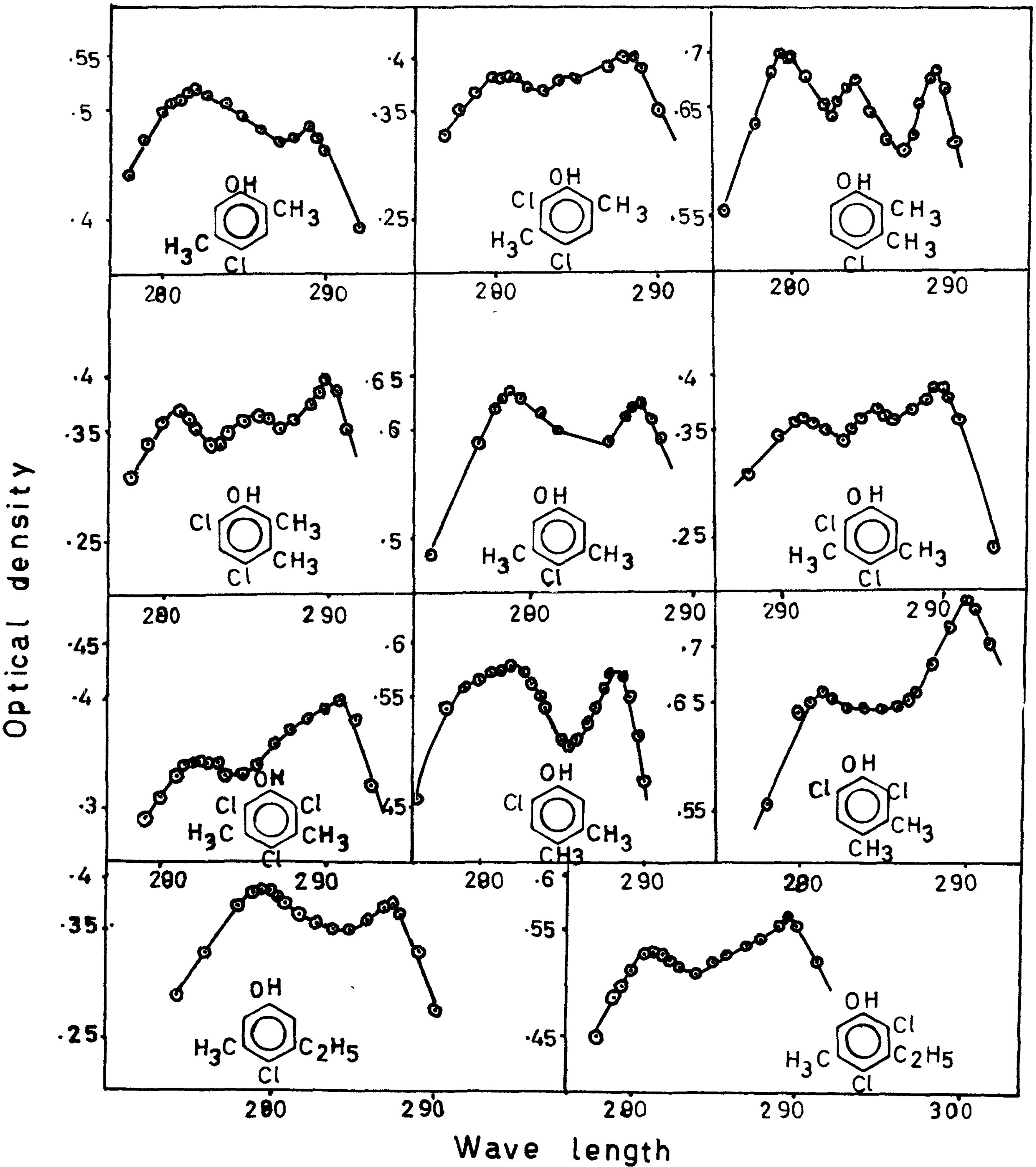
The spectra of chlorinated cresols and chlorinated xylenols are listed in Tables I and II and reproduced in Figs. 1 and 2.

The B-band in phenol is shown to be displaced to a longer wave length on *para*-substitution. If the *para*-substituent is electron withdrawing, this displacement is greater and is qualitatively related to the electron-withdrawing effect of the substituent. In such cases, the usual high intensity band corresponding to an extended conjugated system is obtained. The wave length displacements with respect to phenols in cyclohexane are parallel to the displacement in the aniline series[6]. As already shown by Dearden et al.[5], the



UV SPECTRA OF CHLOROCRESOLS

FIG. 1



UV SPECTRA OF CHLOROXYLENOLS

FIG.2

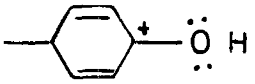
Table I - Absorption maxima and extinction coefficients of chlorocresols

Compound	B-band		C-band	
	λ-max (mμ)	ϵ	λ-max (mμ)	ϵ
6-Chloro-o-cresol	273	1840	278	1995
4-Chloro-o-cresol	281	1643	288.5	1425
4,6-Dichloro-o-cresol	282.5	2283	290	2287
6-Chloro-m-cresol	277.5	2058	283.5	2238
4-Chloro-m-cresol	281	2120	288.5	1898
4,6-Dichloro-m-cresol	284.5	3144	292.5	3112
2,4,6-Trichloro-m-cresol	286	2739	295	2991

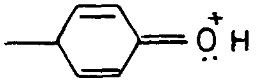
Table II - Absorption maxima and extinction coefficients of chloroxylenols

Compound	B-band		C-band	
	λ-max (mμ)	ε	λ-max (mμ)	ε
4-Chloro-2,5-xylenol	282	4440	289	4112
4,6-Dichloro-2,5-xylenol	281	2208	288	2327
4-Chloro-2,3-xylenol	279.5	2334	(a) 284 (b) 289	2228 2280
4,6-Dichloro-2,3-xylenol	281	2041	285	2175
4-Chloro-3,5-xylenol	279	2096	287	2077
2,4-Dichloro-3,5-xylenol	281.5	2460	(a) 286 (b) 290	2460 2610
2,4,6-Trichloro-3,5-xylenol	282	2749	291	3371
6-Chloro-3,4-xylenol	282	3238	288	3238
2,6-Dichloro-3,4-xylenol	281.5	2421	290	2731
4-Chloro-5-methyl-3-ethylphenol	279.5	2360	286.5	2310
2,4-Dichloro-5-methyl-3-ethylphenol	281.5	2267	289.5	2410

difference can be rationalised by assuming that the B-band in phenol involves transition which should be associated to an appreciable extent with locally excited states of type I. In support of this hypothesis, the following may be cited: (i.) the B-band of phenol at 210 mμ in cyclohexane is displaced by about 7 mμ from the corresponding band in benzene, a wave length displacement similar to that associated with short-range interaction of the hydroxyl groups,



I



II

(ii) if phenol is assumed to absorb at longer wave length, because the hypothetical structure of type II contributes more appreciably to the electron excited state, the above mentioned relationship between wave length displacement in *para*-substituted phenols becomes more nearly quantitative[5]. The bathochromic wave length displacement obtained for *meta*-substituted phenols compared with the spectrum of phenols where the *meta*-substituent is electron-withdrawing can be explained since electron withdrawing substituent has been assumed to facilitate resonance[6] forms of type II and this can account for the anomalous bathochromic wave length shift.

In the case of *para*-substituted cresols and xylenols, the expected bathochromic wave length shift has been obtained in B- and C-bands. However, changes in the intensities of different bands in different chlorocompounds are specific to their molecular structure. Cresols and xylenols with the exception of *para*-cresol, exhibit absorption maxima at two different wave lengths. Their chloro-derivative, also behave similarly. Cresols and chlorocresols for example, have absorption maxima at 273 and 279 mμ and 280 and 290 mμ, respectively, with the exception of 6-chloro-o-cresol which gives absorption maxima at 273 and 278 mμ (Tables I and II). Among monochlorocresols, an isomer with the chlorine atom in the vicinity of hydroxyl group absorbs at a lower wave length. Similarly, there is no appreciable wave length displacement in B-bands of 3,4-xylenol, 6-chloro-3,4-xylenol and 2,6-dichloro-3,4-xylenol (Table II) and also the intensity of B-band of 2,6-dichloro-3,4-xylenol is lesser as compared to 6-chloro-3,4-xylenol confirming the steric interaction in the molecule.

With increase in number of chlorine atoms in the molecule, the absorption maxima shifts to longer wave lengths (Tables I and II).

In the case of chloroxylenols the maximum absorption is exhibited at 280 and 290 mμ. The xylenols have also shown bathochromic shift on chlorination. However, in the case of 4-chloro-2,3-xylenol and 2,4-dichloro-3,5-xylenol the presence of additional absorption band at about 285 mμ is also indicated. Introduction of a second chlorine atom in xylenol only slightly affects the absorption maxima. A similar conclusion can be drawn from the UV of the chlorinated 5-methyl-3-ethylphenol (Table II).

On the other hand, the differences in the ϵ values are often appreciable enough to permit the detection and analysis of individual compounds. Thus, 6-chloro-o-cresol has a much higher molar extinction coefficient than 4-chloro-o-cresol (Table I). Similarly, the value of the second band of 6-chloro-m-cresol is much higher than that of the 6-chloro-m-cresol. Also, the dichloro derivative in both o- and m-cresol show much higher ϵ values. In the case of xylenol, the monochloroderivatives are having higher ϵ values than dichloroderivatives (except 3,5-xylenol). Ultraviolet spectroscopy could nevertheless be of great use as a complementary technique in the identification of the individual compounds.

The spectra have been determined in various dilutions and are found to obey Beer's Law. This may be of advantage in quantitative estimation of various isomers.

INFRARED ABSORPTION DATA ON CHLOROXYLENOLS

The infrared spectra of some isomeric xylenols and their chloroderivatives which have been synthesised in the present investigation have been examined. From the bands observed in the region 650-900 cm^{-1}, it has been possible to assign the characteristic CH deformation frequency band and C-Cl stretching vibration band for different compounds which may be helpful for their identification. The absorption for hydroxyl groups in the region of 3615-3530 cm^{-1} reveals differences in the types of free and intramolecular bonds in the different compounds. These may be utilised in fixing the position of chlorine in the aromatic nucleus.

Figures already included in chapter II, show the spectra between 650-4000 cm^{-1} of some isomeric xylenols and their chloroderivatives. Tables III to VI give the frequencies of the different bands observed in

Table III - Infrared spectral data of 2,5-xylenol and its chloroderivatives

2,5-Xylenol		4-Chloro-2,5-xylenol		4,6-Dichloro-2,5-xylenol	
Wave No. cm^{-1}	Intensity	Wave No. cm^{-1}	Intensity	Wave No. cm^{-1}	Intensity
3605	s	3610	s	3545	s
3030	vw	2950	vw	2950	vw
2950					
2920	w	2922	w	2925	vw
1620	m				
1570	m				
1420	w				
1375	m	1360	m	1470	s
				1448	m
1345	w	1345	mw	1387	vw
1280	sh			1370	w
1260	sh	1255	w	1205	m
1245	s	1235	m		
1200	s	1190	s	1185	sh
1150	m	1135	s	1145	vs
1125	m	1110	s		
1090	m				
1020	vw	1020	w	1025	m
975	m	990	vw	970	m
915	w	960	s	860	ms
850	vw	830	w	850	sh
830	vw	775	m	765	s
790	vs			710	w
740	vw			665	s
710	w				

Note: s = strong; m = medium; w = weak; v = very; sh = shoulder

Table IV - Infrared spectral data of 2,3-xylenol and its chloro-derivatives

2,3-Xylenol		4-Chloro-2,3-xylenol		4,6-Dichloro-2,3-xylenol	
Wave No. cm^{-1}	Intensity	Wave No. cm^{-1}	Intensity	Wave No. cm^{-1}	Intensity
3615	s	3610	s	3550	s
3040	w	3025	vw		
2928	vw	2930	vw	2930	vw
2845	w				
2860	w				
1605	sh				
1580	m	1575	w		
1450	w	1420	w	1420	m
1350	w	1390	w	1390	m
		1350	vw		
1280	w	1275	vw	1345	vw
1245	vs	1250	vs	1275	ms
1185	m	1200	vw	1245	s
1155	w	1190	s	1210	s
		1170	m		
1135	m	1145	s	1145	s
1075	ms				
1045	s	1045	s	1065	s
970	vw	990	vw	930	w
891	w	820	w	870	m
805	vw	800	sh		
755	vs	785	s	840	m
695	s	740	s	715	s
		680	m		

Note: s = strong; m = medium; w = weak; v = very; sh = shoulder

Table V - Infrared spectral data of 3,5-xylenol and its chloro-derivatives

3,5-Xylenol		4-Chloro-3,5-xylenol		2,4-Dichloro-3,5-xylenol		2,4,6-Trichloro-3,5-xylenol	
Wave No. cm^{-1}	Intensity	Wave No. cm^{-1}	Intensity	Wave No. cm^{-1}	Intensity	Wave No. cm^{-1}	Intensity
3600	ms	3600	ms	3545	s	3530	s
3570	broad						
3030	w	3015	vw	2985	vw	2925	vw
2930	m	2980	vw	2955	vw		
		2950	vw	2925	vw		
2860	w	2920	vw				
1610	s	1600	w				
1585	s	1580	w				
1445	vs	1445	w	1445	s		
1410	vw	1375	w	1400	w	1418	m
1340	vw	1345	w	1370	m	1360	s
1280	s	1295	m	1340	vw		
1260	s	1265	w	1300	m	1305	vw
1160	m	1190	s	1265	ms	1260	s
		1170	vw				
1140	m	1135	s	1195	ms	1180	s
				1155	vs		
1125	vs	1040	w	1060	w	1045	m
1010	m	1010	w	1030	w	980	m
930	m	840	m	975	w	715	ms
850	w	820	w	840	s		
820	s	745	vs	690	s		
670	s	680	w				
		650	w				

Note: s = strong; m = medium; w = weak; v = very; sh = shoulder

Table VI - Infrared spectral data of 3,4-xylenol and its chloro-derivatives

3,4-Xylenol		6-Chloro-3,4-xylenol		2,6-Dichloro-3,4-xylenol	
Wave No. cm^{-1}	Intensity	Wave No. cm^{-1}	Intensity	Wave No. cm^{-1}	Intensity
3605	s	3555	s	3540	s
3020	vw	2975	w		
2970	vw	2945	w	2950	w
		2925	w		
2860	vw	2860	w		
1590	m	1620	vw		
1445	m	1450	m	1445	s
1350	w	1420	vw	1415	vw
		1355	w	1365	m
1265	s	1280	ms	1275	m
1240	s	1265	ms	1260	
1165	s	1235	m	1210	m
1130	s	1180	vs	1165	s
1095	m				
1010	m	1130	s		
		1115	s	1015	m
990	m	1005	w	980	w
935	w	990	vw		
		970	m		
850	vw	855	s	850	w
830	vw			820	mw
800	m	795	vw	782	s
790	m				
720	w	770	ms	700	w
690	vw	720	m	660	m

Note: s = strong; m = medium; w = weak; v = very; sh = shoulder

different compounds. Each of the spectra is complex, yet a few correlations are obvious. All the compounds show one or more intensive bands in the region 690-860 cm^{-1} and these are of particular interest. It has previously been found[7] that substituted benzenes have more or less characteristic frequencies in this region according to the number and position of the substituents and these are in great measure independent of nature of the substituents. The normal vibration of benzene in which the group of six carbon atoms moves in a rigid plane perpendicularly to the plane containing the six hydrogen atoms, has a frequency of 671 cm^{-1}. Previous results[8] have shown that when the substituent is attached to the ring, this type of vibration which is essentially a deformation of the remaining CH bonds, is displaced to 740-760 cm^{-1}. In substituted benzenes, the corresponding vibration has a frequency which depends on the relative position of the substituents, with <u>ortho</u>-derivatives, it usually lies at 740-760 cm^{-1}, with <u>meta</u>-compound at 770-790 cm^{-1} and with <u>para</u>-compound at 810-830 cm^{-1}. With tri- and tetra-substituted benzenes, the corresponding deformation of the residual CH bonds also appears to have fairly definite frequencies. Whiffen et al.[8] have also utilised the CH deformation frequencies for the identification of cresols and xylenols in cresylic acid mixture. The CH deformation frequencies, obtained by Whiffen et al.[8] and in the present investigation are given below; these are quite comparable.

Compound	Observed cm^{-1}	Reported[8] cm^{-1}
2,5-Xylenol	790	-
2,3-Xylenol	755	770
3,5-Xylenol	820	830
3,4-Xylenol	800	800

The chloro-xylenols examined in the present investigation have one or two ring hydrogen atoms. According to Bellamy[8] these types of compounds show absorption frequency in the region 860-800 cm^{-1} for the out of plane CH vibration. Therefore, bands obtained in this region for the different chloroxylenols have been assigned to CH deformation and are given in Table VII. These can be utilised in identifying these compounds.

Work on simple molecules containing a single chlorine, indicates that C-Cl absorption occurs in the region 750-700 cm^{-1}. The frequency corresponding to the more stable trans-configuration, and in alkyl chlorides in solution it is accompanied by a second absorption band due to the gauche-isomer,[10,11] which is found near 650 cm^{-1}. However, with substitution, the range is extended to 800 cm^{-1} and also a medium intensity band usually shows up at 1510-1410 cm^{-1} representing the first overtone. In the present study, the C-Cl stretching bands obtained for the different chloroxylenols fall in the region between 665-782 cm^{-1} given in Table VII. These are quite strong and can be used for the identification of the particular compounds. In all the cases, only one band is assigned for C-Cl stretching vibration except in 4,6-dichloro-2,5-xylenol where two bands are observed in this region. Both the bands are assigned for C-Cl. Out of them, the lower band might be due to trans-configuration of the molecule[11] . The absorption range[12,13] for the OH valance-stretching of an unbonded hydroxyl group is usually between 3650-3590 cm^{-1}. Kuhn[14] has carried out accurate measurement of the free OH frequencies for a range of thirty five alcohols and phenols. In all cases, the

Table VII - Characteristic bands of xylenols and its chloro derivatives

Compounds	OH		C-Cl		CH-deformation	
	Wave No. cm^{-1}	Intensity	Wave No. cm^{-1}	Intensity	Wave No. cm^{-1}	Intensity
2,3-Xylenol	3615	s	-	-	755	m
4-Chloro-2,3-xylenol	3610	s	740	vs	785	s
4,6-Dichloro-2,3-xylenol	3550	s	715	vs	840	m
2,5-Xylenol	3605	s	-	-	790	vs
4-Chloro-2,5-xylenol	3610	s	775	m	860	s
4,6-Dichloro-2,5-xylenol	3545	s	(a) 765 (b) 665	ms s	860	ms
3,5-Xylenol	3600	m	-	-	820	s
4-Chloro-3,5-xylenol	3600	m	745	vs	840	m
2,4-Dichloro-3,5-xylenol	3540	s	690	s	640	s
2,4,6-Trichloro-3,5-xylenol	3530	s	715	s	-	-
3,4-Xylenol	3605	s	-	-	800	m
6-Chloro-3,4-xylenol	3555	s	770	s	855	s
2,6-Dichloro-3,4-xylenol	3540	s	782	s	850	m

Note: s = strong; m = medium; w = weak; v = very absorption occurred between 3644 and 3605 cm^{-1}. The influence of the aromatic ring in lowering the free OH frequency slightly, is confirmed by the work of Ingraham et al.[15], who found this band at 3616-3588 cm^{-1} in twenty substituted phenols and at 3615-3592 cm^{-1} in fourteen substituted catechols. Single bridge complexes are found only in special cases in which steric effects prevent full polymeric association. A common case of such steric effect is that of an ortho-substituted phenol which has been studied by many workers[16-18]. The hydrogen bond is weak and absorption occurs in the region of 3570-3450 cm^{-1}.

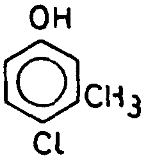
It can be seen from the Table VII that isomeric xylenols and para-chloroxylenols give OH absorption band in the region 3600-3615 cm^{-1} indicating the free OH. Chlorophenols having chlorine at ortho-position(s) show a lowering of 65-70 cm^{-1} in the OH band, which is due to intramolecular hydrogen bonding. By the examination of the OH band of the chloroxylenol, the ortho-substitution of chlorine can be confirmed.

In all the chloroxylenols, the bands between 2000-1600 cm^{-1} and which are used for characterization of benzene ring substitution[19] are very weak or absent. This might be due to the solvent effect. It is impossible to assign the bands between 1500-1000 cm^{-1} to particular normal modes although this region will include vibration of the groups C-O-C, C-O-H, CH_2 and CH_3, as well as of the skeleton of the aromatic rings. It is however, apparent that in these cases, the exact position of a particular band depends upon the environment of the group within the molecule.

NUCLEAR MAGNETIC RESONANCE (NMR) ABSORPTION DATA OF CHLOROCRESOLS AND XYLENOLS

The availability of a complete series of isomeric chlorocresols and xylenols in the present investigation prompted an examination of their NMR spectra. There is no doubt that NMR data provide convincing proof for structure and authenticity of a compound. The NMR spectra for isomeric chlorocresols and chloroxylenols have not been reported earlier in literature. These were obtained through the kind courtesy of Riker Laboratories, Northridge, U.S.A. Following is a presentation of the NMR spectra of each compound together with details of assignments. For a quicker comparative study of all these compounds, their absorption data are summarised in a Table VIII.

(i) 4-Chloro-m-cresol



The NMR spectrum (Fig. 3) is in full conformity with the given structure. The sharp singlet at 2.25* integrating for 3 protons represents the C_3-methyl group. The phenolic hydroxyl group peak occurs at 6.00 and disappears on exchange with D_2O. Protons C_5 and C_6 show the expected *ortho*-splitting as doublets. By integration, the

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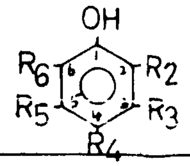
[*] All values are in δ units (parts per million) relative to internal tetramethylsilane standard. The spectra were recorded in a varian A-60 spectrometer.



COMPOUNDS	8″	7″	6″	5″	4″	3″	2″	1″
(cresols) $R_3 = CH_3$; $R_4 = Cl$		7.2 ⟷ 6.6 (aromatic)	6.0 (b) (OH)				2.3 (s) (methyl)	
$R_3 = CH_3$; $R_6 = Cl$		7.2 ⟷ 6.6 (aromatic)		5.32 (b) (OH)			2.25 (s) (methyl)	
$R_2 = CH_3$; $R_4 = Cl$		7.2 ⟷ 6.6 (aromatic)		4.83 (OH)			2.25 (s) (methyl)	
$R_2 = CH_3$; $R_6 = Cl$		7.2 ⟷ 6.6 (aromatic)		5.65 (s) (OH)			2.2 (s) (methyl)	
$R_2 = CH_3$; $R_4 = R_6 = Cl$		7.2 ⟷ 7.0 (aromatic)		5.5 (b) (OH)			2.25 (methyl)	
$R_3 = CH_3$; $R_4 = R_6 = Cl$		7.26 ⟷ 6.86 (S) (aromatic)		5.5 (b) (OH)			2.35 (methyl)	
$R_3 = CH_3$; $R_2 = R_4 = R_6 = Cl$		7.26 (S) (aromatic)		5.66 (OH)			2.43 (methyl)	
(xylenol) $R_2 = R_3 = CH_3$		6.9 ⟷ 6.3 (aromatic)		4.8 (S) (OH)			2.23 || 2.1 (methyl)	
$R_2 = R_3 = CH_3$; $R_4 = Cl$		7.2 ⟷ 6.6 (aromatic)			4.3 (s) (OH)		2.31 | | 2.18 (methyl)	
$R_3 = R_5 = CH_3$; $R_4 = Cl$			6.55		4.7 (s)		2.3 (S) (methyl)	
$R_2 = R_5 = CH_3$; $R_4 = Cl$		7.05 ⟷ 6.6 (S) (aromatic)			4.58 (b) (OH)		2.26 | | 2.16 (s) (methyl)	
$R_2 = R_3 = CH_3$; $R_4 = R_6 = Cl$		7.18 (aromatic)		5.41 (s) (OH)			2.26 ‖ 2.21 (s) (methyl)	

(S) sharp ; (b) broad.

TABLE VIII - NMR SPECTRAL DATA OF CHLOROCRESOLS AND CHLOROXYLENOLS.

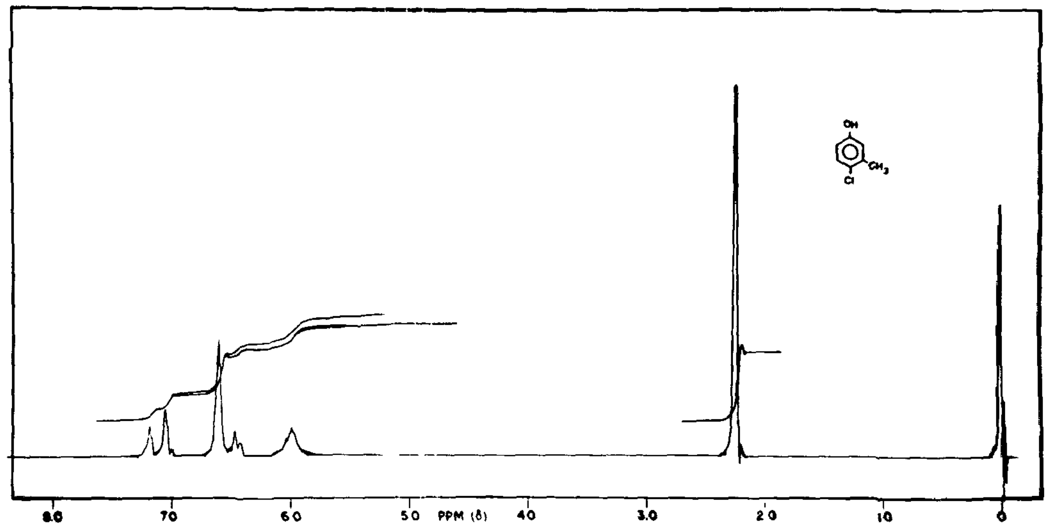


Fig. 3 NMR spectrum of 4-chloro-*m*-cresol

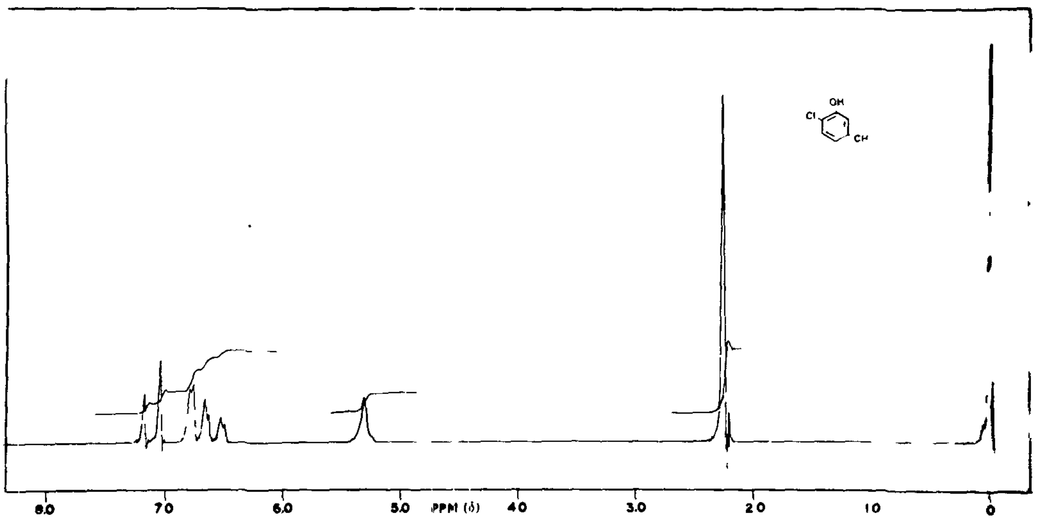
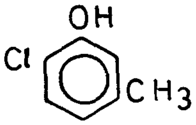


Fig. 4 NMR spectrum of 6-chloro-*m*-cresol

doubtlet centered at 6.5 represents the C_2 and C_6 protons. On the short limb of the C_6 proton doublet, one can notice also the <u>meta</u>-coupling due to C_2 and C_6 protons. The clean doublet centered at 7.1 is due to the C_5 proton, the slight downfield shift explainable by the proximity to the electronegative chlorine atom.

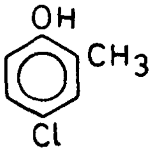
$$J_{26} = 3\text{ cps} \qquad J_{56} = 7{\cdot}5\text{ cps}$$

(ii) <u>6-Chloro-m-cresol</u>



The methyl group on C_3 gives rise to the sharp single peak at 2.25 (Fig. 4). The peak at 5.32 is in the proper region for the phenolic hydroxyl group. Of the three aromatic protons, that at carbon 5 is clearly seen as a doublet in the downfield region and centered at 7.16. The coupling constant (J) with the C_4 proton is 7.5 cps. The C_2- and the C_4-protons are then represented by the peaks between 6.5 and 6.8 in which the <u>ortho</u>- and <u>meta</u>-couplings can also be seen. These peak assignments are confirmed by the integrals.

(iii) <u>4-Chloro-o-cresol</u>



In the spectrum (Fig. 5), the C_2-methyl group comes up as a sharp singlet at 2.2. The phenolic hydroxyl, neighboured by the methyl group gives a sharp singlet at 4.83, exchanged out completely upon

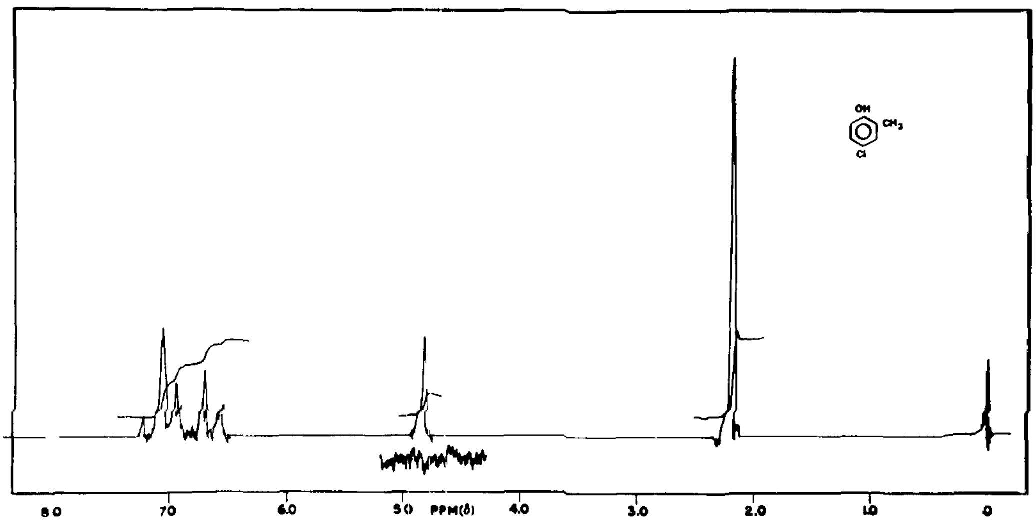


Fig. 5 NMR spectrum of 4-chloro-o-cresol

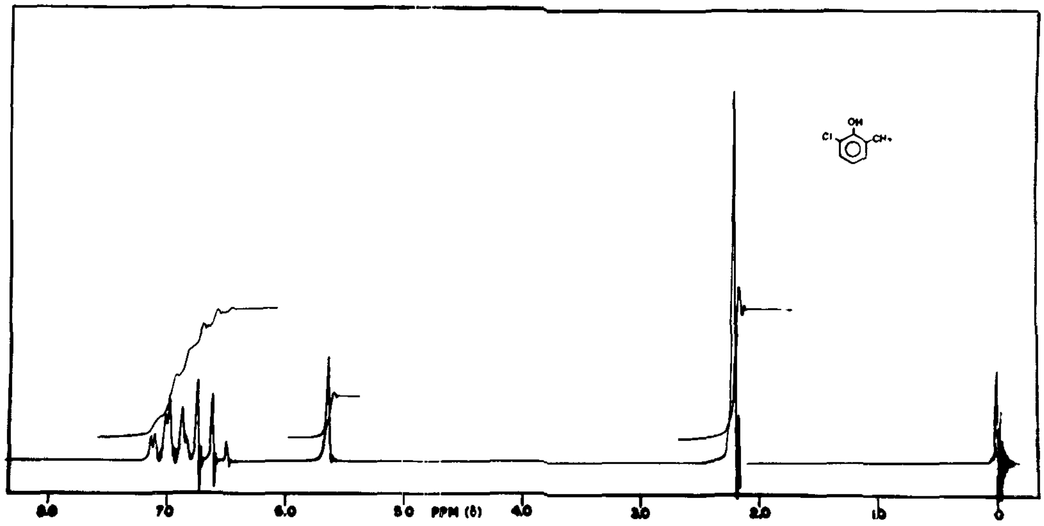
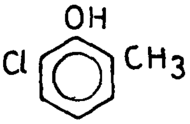


Fig. 6 NMR spectrum of 6-chloro-o-cresol

addition of D_2O. Of the aromatic protons, the C_3- and C_5-protons are represented by the doublet centered at 7.00, in which the meta-coupling (C_3-C_5) is also clearly seen, the doublet itself arising from the C_5-C_6 coupling. The single C_5 proton is represented by the doublet centered at 6.63 (J = 8cps). The integration is satisfactory.

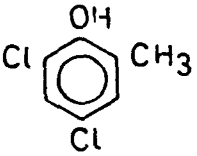
(iv) 6-Chloro-o-cresol



The following assignments agree with the given structure (Fig. 6).

The singlet at 2.21 represents the methyl group. The phenolic hydroxyl is a singlet at 5.65. The most downfield doublet (J = 7.5 cps) centered at 7.03 showing additional meta-couplings (J = 2.5 cps) represents the C_5 proton which is neighboured by the chlorine atom. The next upfield doublet at 6.8 in which one limb hides the meta-coupling (with C_5) represents the C_3-proton. The clean doublet showing no other coupling is therefore due to the C_4-proton which ortho-couples with both the C_3- and C_5-proton. The integrals are entirely in conformity.

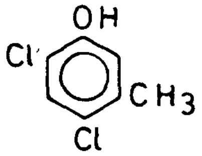
(v) 4,6-Dichloro-o-cresol



In the spectrum (Fig. 7) of this compound, the singlet at 2.25

represents the methyl group; the peak at 5.5 confirms the phenolic hydroxyl. There are only two aromatic protons, i.e. the C_3- and C_5. Out of these, the C_5 would be expected to show up more downfield in view of its location between two chlorine atoms. Further, these two protons would be expected to show meta-coupling if the structure is correct. These expectations are confirmed in the spectrum, the peak at 7.15 and 7.0 being assignable to the C_5- and C_3-proton respectively, and the meta-couplings are seen in both the cases. The integration is satisfactory.

(vi) 4,6-Dichloro-m-cresol



The NMR spectrum (Fig. 8) readily confirms the given structure. The singlet at 2.25 arises from the methyl group and the broad singlet with a chemical shift of 5.5 represents the phenolic hydroxyl. In the downfield regions, there are only two singlets free of any other identifications of coupling and this at once suggests the presence of two separate protons not neighboured by any other proton. Since no meta-coupling is seen, these two protons should have only a para-relationship, the para-coupling being negligible ($<$ 1 cps). Out of the two peaks, the downfield one represents the C_5-proton and the up-field peak, the C_3. These peaks and assignments confirm the structure 4,6-dichloro-m-cresol and the integrals are in order.

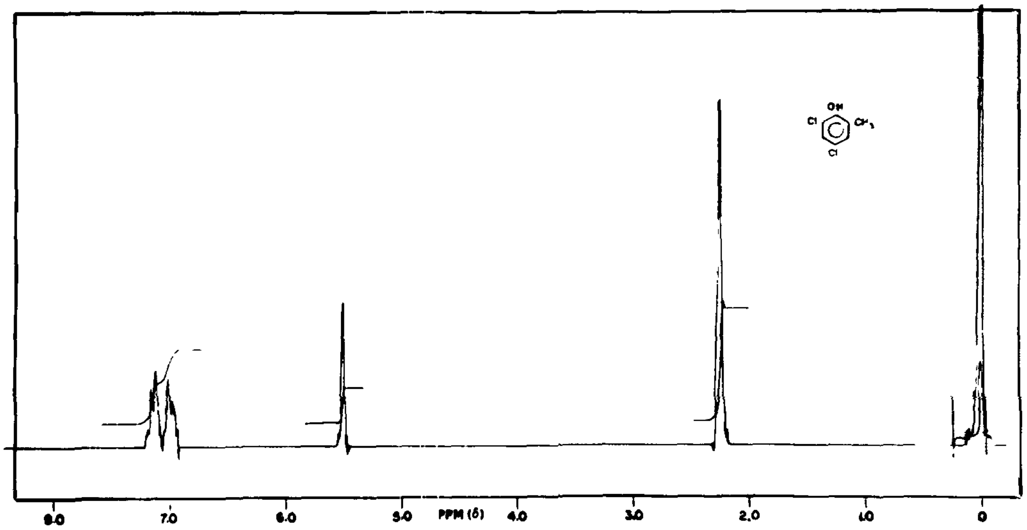


Fig. 7 NMR spectrum of 4,6-dichloro-*o*-cresol

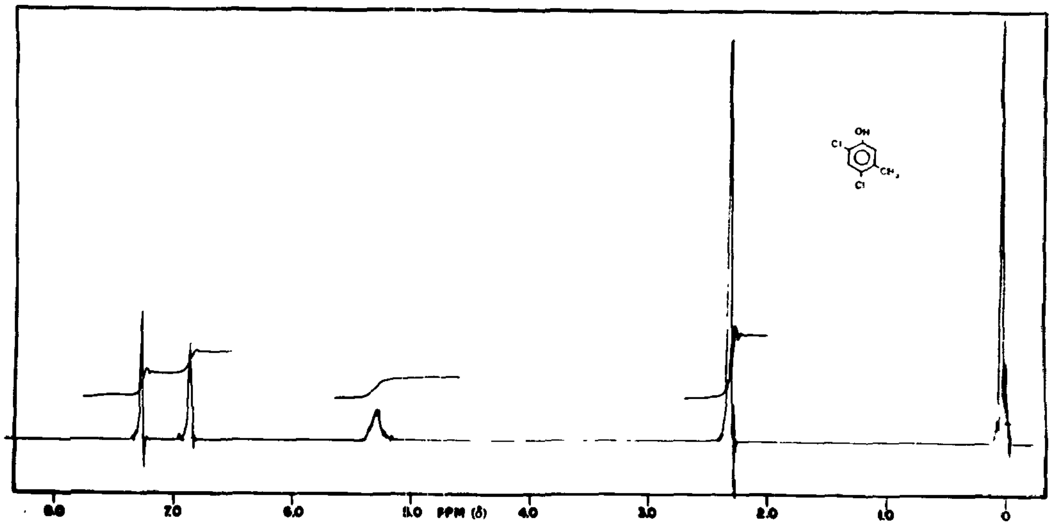
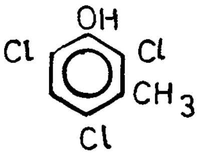


Fig. 8 NMR spectrum of 4,6-dichloro-*m*-cresol

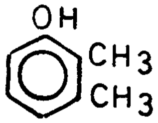
(vii) 2,4,6-Trichloro-m-cresol



Assignments of the peaks in the NMR spectrum (Fig. 9) have been made as follows:

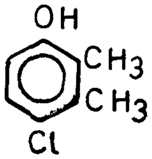
The singlet at 2.41 represents the methyl group while the phenolic hydroxyl produces the broad absorption centered at 5.66. The singlet at 7.26 arises from the only aromatic proton neighboured by the chlorine atoms. The integration is in conformity.

(viii) 2,3-Xylenol.



The NMR spectrum (Fig. 10) agrees with the above structure. The two singlets at 2.1 and 2.33, each integrating for 3 protons are in the proper region for the two methyl groups, C_2-methyl and C_3-methyl, respectively. The singlet at 4.8 equals to one proton, arises from the hydroxyl. The multiplet in the aromatic region represents the 3 aromatic protons C_4H, C_5-H, and C_6-H in which the *ortho*-couplings are clearly seen.

(ix) 4-Chloro-2,3-xylenol



The two singlets in the upfield region (Fig. 11) at once confirm the two methyl groups in the structure. It is reasonable to assign the

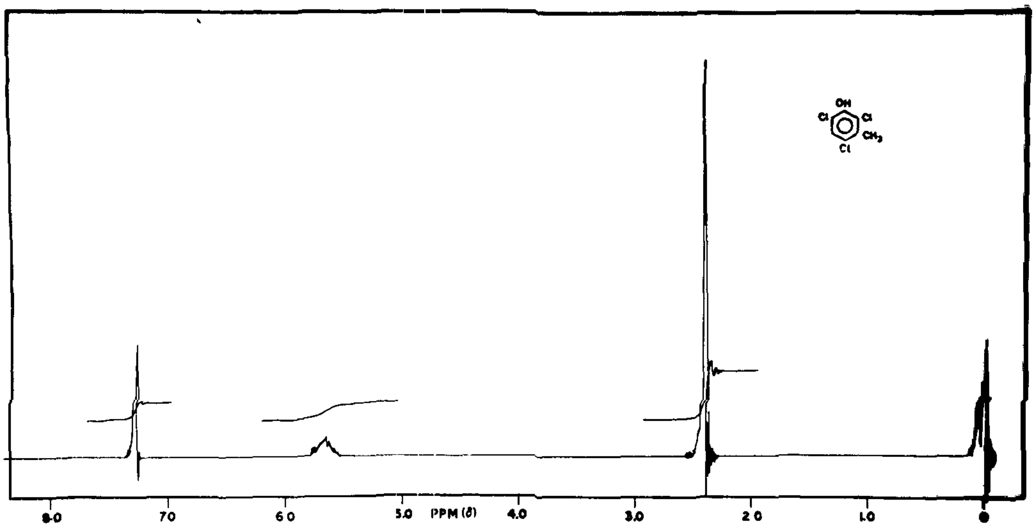


Fig. 9 NMR spectrum of 2,4,6-trichloro-_m_-cresol

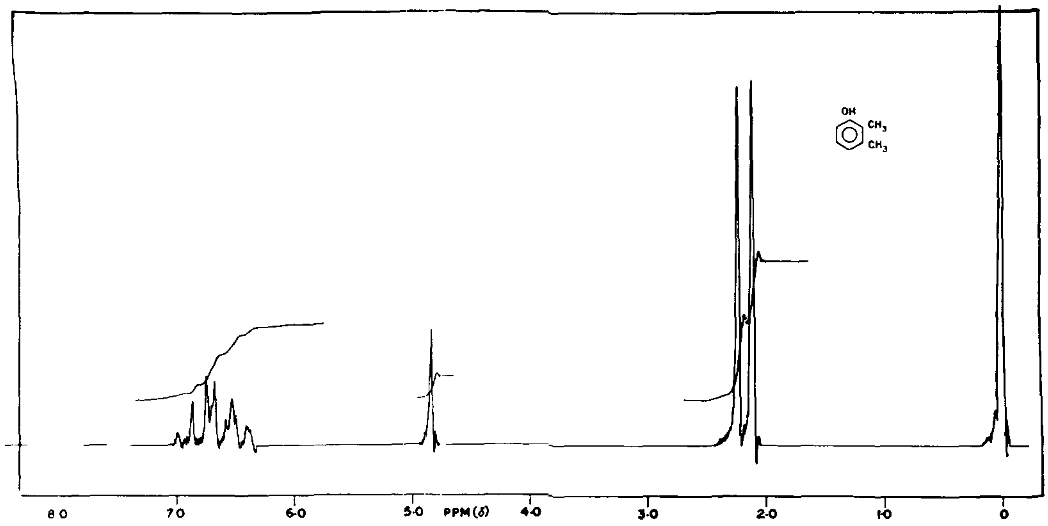
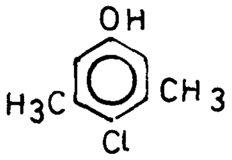


Fig. 10 NMR spectrum of 2,3-xylenol

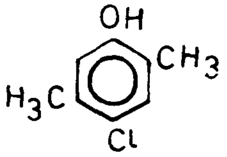
peak at 2.18 to the methyl group (on C_2) adjacent to the hydroxyl and the singlet at 2.31 to the methyl group (on C_3) neighboured by the chlorine atom. The phenolic hydroxyl, as in most of the previous cases, is a singlet at 4.63. There are only two aromatic protons, <u>ortho</u> to each other and this is perfectly borne out by the two doublets downfield ($J \doteq 8$ cps). The doublet centered at 6.54 may be assigned to the C_6-proton and the doublet centered at 7.07 to the C_5-proton. The integration confirms the assignments.

(x) <u>4-Chloro-3,5-xylenol</u>



The spectrum in Fig. 12 and the integrals are quite in conformity with the given structure. The two methyl groups being equivalent, give rise to a singlet at 2.3. Similarly, the two equivalent aromatic protons (C_2-H and C_6-H) are represented by the sharp singlet at 6.55. The phenolic hydroxyl is confirmed by the peak at 4.7.

(xi) <u>4-Chloro-2,5-xylenol</u>



Spectral (Fig. 13) peak assignments have been made as follows: The singlets at 2.16 and 2.26 represent the C_2-methyl and C_5-methyl, respectively. The broad singlet at 4.58 arises from the phenolic

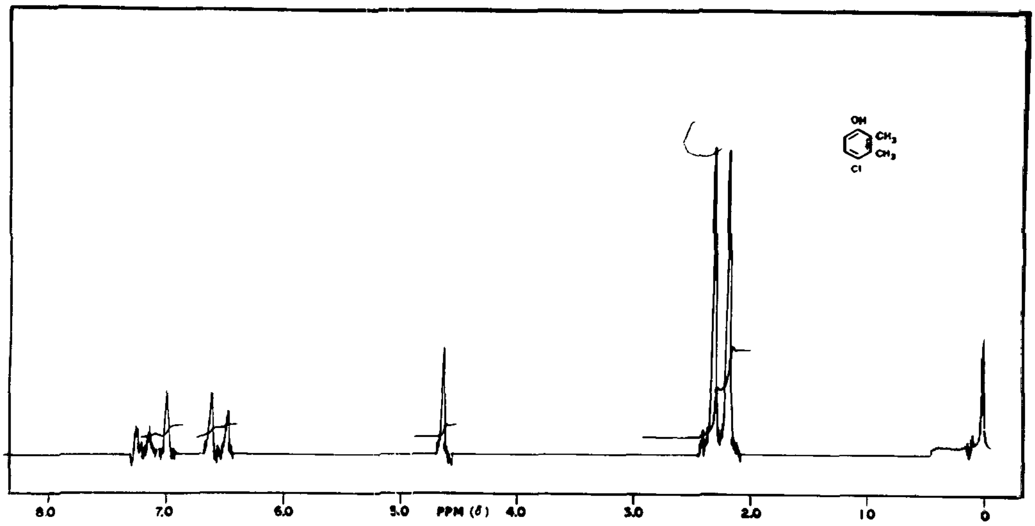


Fig. 11 NMR spectrum of 4-chloro-2,3-xylenol

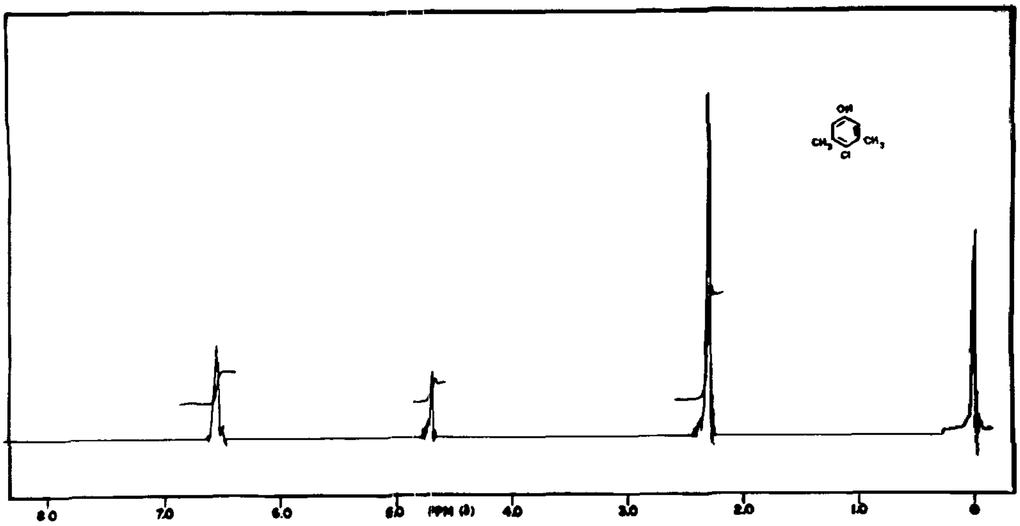
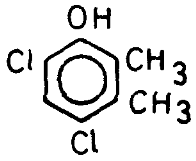


Fig. 12 NMR spectrum of 4-chloro-3,5-xylenol

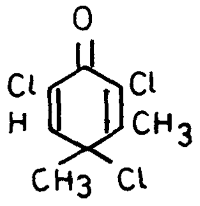
hydroxyl group. The two aromatic protons at carbon atoms C_3 and C_6 are confirmed by the sharp singlets at 7.05 and 6.61, respectively. The absence of any meta or ortho-couplings further support the position of the substituents.

(xii) 4,6-Dichloro-2,3-xylenol



In the spectrum (Fig. 14), the two sharp singlets at 2.21 and 2.26 confirm the presence of the two methyl groups, assigned to C_2 and C_3 respectively. The phenolic hydroxyl group shows up as a sharp singlet at 5.41. The only aromatic proton situated between the two electronegative chlorine atoms gives rise to the sharp singlet at 7.18. The integration is entirely in conformity.

(xiii) 2,4,6-Trichloro-3,4-dimethylcyclohexadien-1-one



This product resulted from the chlorination of 3,4-xylenol with ter-butylhypochlorite as discussed earlier in chapter II.

The NMR spectrum (Fig. 15) has been used in arriving at the above structure. The spectrum was conspicuous by the absence of any absorption due to the phenolic hydroxyl. This immediately raised the possibility of a different reaction course resulting in the replacement

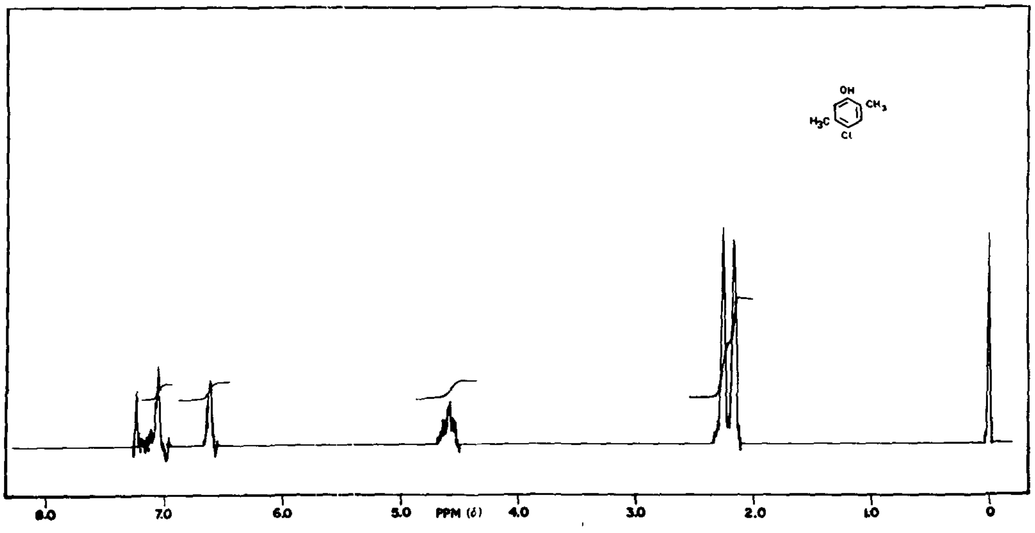


Fig. 13 NMR spectrum of 4-chloro-2,5-xylenol

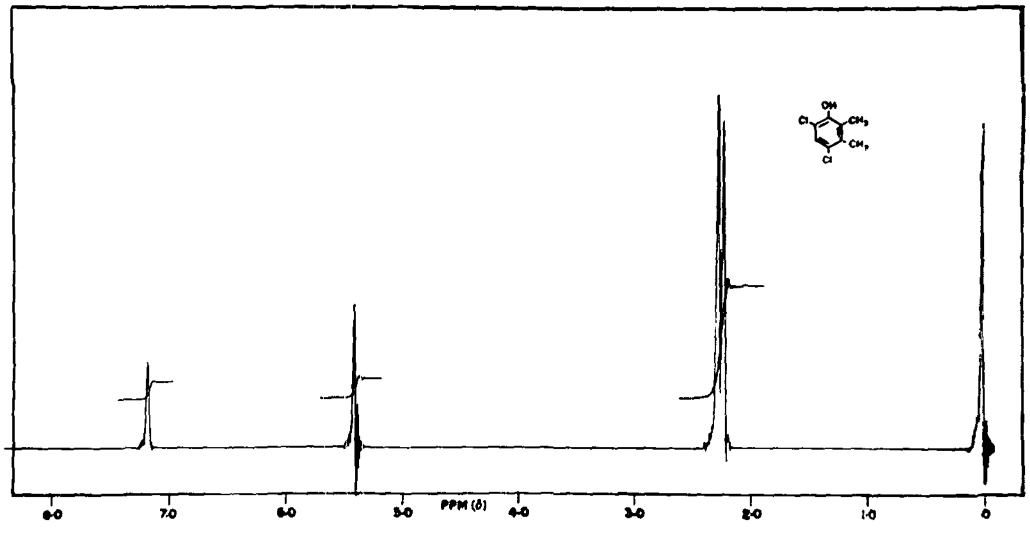


Fig. 14 NMR spectrum of 4,6-dichloro-2,3-xylenol

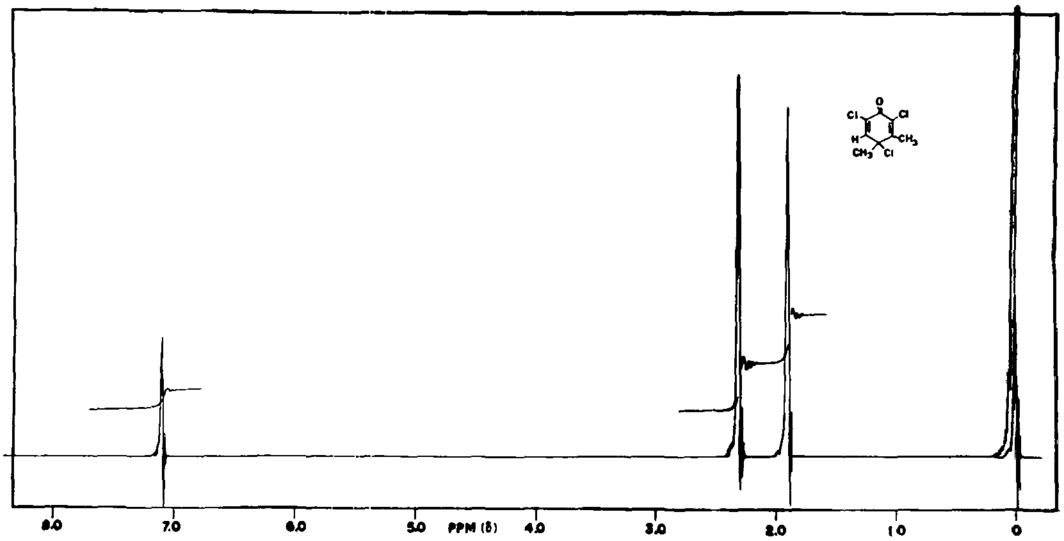
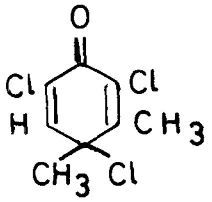


Fig. 15 NMR spectrum of 2,4,6-trichloro-3,4-dimethylcyclohexadien-1-one

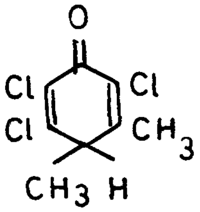
of the hydroxyl by some other group or oxidation[20]. The presence of two singlets in the upfield region, however, indicated that the two methyl groups of the starting material were unaffected. The downfield region had only one peak which, by integration, corresponded to one proton.

Chemical tests taken in conjunction with infrared and ultraviolet data pointed to the following structure.

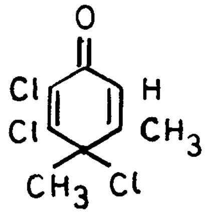


The present NMR spectrum supports this. The two singlets arise from the two methyl groups. The peak at 1.90 and 2.31 are tentatively assigned to the C_3 and C_4-methyl, respectively. It is reasonable to expect a slight downfield shift of the methyl group attached to the same carbon as the chlorine atom. The signal at 7.1 would then be in the proper region for the proton on C_5.

Further, the spectrum does not allow alternative structures such as I and II.



I



II

Structure such as I, in which the C_4 carries a methyl and a hydrogen, would certainly give rise to a doublet for the methyl and a quartet for the splitting proton, with J of the order of 6-7 cps. Absence of any such data in the spectrum rules out structure I. Similarly, for structure II, a splitting of the C_3-methyl group by the C_2 proton would be expected, though of a small order ($J = 2-3$ cps) of magnitude compared to I.

A perusal of the foregoing NMR spectral absorption data of the various chlorocresols and chloroxylenols shows that the chemical shift of the phenolic hydroxyl is influenced considerably by the proximity of the electronegative chlorine atoms. In all cases of cresols, where the chlorine is in _ortho_-relationship to the OH group, the latter absorption arises at about 5.5-5.6. Introduction of an additional chlorine atom (compounds V, VI) or even two chlorine atoms (compound VII), does not affect the OH absorption any further. The only deviation from this general pattern is exhibited by 4-chloro-_m_-cresol where the OH absorption arises at 6.0. A CH_3 group in _ortho_-position, where there is no chlorine in the vicinity, causes a marked shift in the OH absorption to the extent of about 0.5.

The absorption of the aromatic protons occurs in the region 6.6-7.3 and differences in the substitution pattern are discernible in these cases. As discussed earlier, the aromatic absorption pattern has helped to provide convincing proof of structures of these compounds from the intensity and multiplicity of the peaks.

Introduction of an additional methyl group in certain positions, causes an upfield shift in the OH absorption, noticeable in the xylenols.

The OH absorption now arises around 4.6-4.7 and is consistent with shielding effect of the methyl group. In the case of cresols and xylenols, however, chemical shift of the CH_3 groups does not appear to be markedly altered by the differences in the substitution patterns. The CH_3-absorption shows up in the region 2.2-2.4.

In view of the fact that NMR spectra of the isomeric chloroxylenols have not so far been recorded and published in literature, the foregoing description of their spectral patterns and assignments may be of value in their identification and structural elucidation. The spectra do not reveal the presence of any impurities and use of chloroform as solvent in all these cases enables a comparison of chemical shift data obviating any differences due to solvent effect.

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CHAPTER V

RELATIONSHIP BETWEEN CHEMICAL STRUCTURE AND THE BACTERICIDAL ACTIVITY OF CHLORINATED XYLENOLS

The introduction of a halogen in a molecule of a phenol always enhances its bactericidal activity, the extent depending upon the degree and the nature of halogen. As early as 1906, it was observed[1] that polychloro- and polybromoderivatives of phenol and of beta-naphthol possessed considerable activity against corynebacterium diphtheriae and pyogenes var. aureus, though their effectiveness was reduced in presence of organic matter.

Relationship of chemical structure of phenols to germicidal activity has been extensively discussed by Suter[2]. However, these discussions are not wholly conclusive as the findings are based on only a partial series of compounds. Namely, there are three mono-, six di-, six tri-, three tetra- and one penta chlorophenol in the series of chlorinated phenols. Suter has cited the data on only the three mono-chlorophenols, one dichloro- and two trichlorophenols. Wolf and Westveer[3] showed that the germicidal activity in chlorophenols increases through mono-, di- and trichloro series but decrease in the tetra and penta series. Klarmann et al.[4] have discussed the relationship between chemical structure and germicidal action of aliphatic and aromatic substituted derivatives of para- and ortho-chlorophenols. Heicken[5] studied the activity of mono-chloroderivative of xylenols and showed that 4-chloro-2,3-xylenol, 4-chloro-2,5-xylenol and 4-chloro-3,5-xylenol are 50-70 times more active than phenol (against E. coli); 6-chloro-3,4-xylenol, 4-chloro-2,6-xylenol and 6-chloro-2,4-

xylenol are only 15 to 20 times more effective. In these studies phenol coefficient (R.W.C.) was used as the criterion of germicidal activity. It may be stressed that methods for the determination of R.W.C. have many limitations and the results depend upon many factors, like technique of solubilisation of the active ingredient, test organism, temperature, pH[6] and concentration of the final solution etc. Some of these influences have been clearly brought out in Table I.

Table I - Germicidal activity of alkylphenols[7]

Compound	Phenol coefficient (R.W.C.) against					
	S. typhi		S. aureus		Myco-tuberculosis	Monilia albicans
	1^{**}	2^{*}	3^{*}	4^{***}	5^{*}	6^{*}
Phenol	1.0	1.0	1.0	1.0	1.0	1.0
4-Methylphenol	2.0	2.3	2.3	-	2.0	2.0
4-Ethylphenol	7.5	6.3	6.3	10.0	6.7	7.8
4-n-Propylphenol	20.0	18.3	16.3	14.0	17.8	17.8
4-n-Butylphenol	70.0	46.7	43.7	21.0	44.4	44.4
4-n-Arylphenol	104.0	53.3	125.0	20.0	133.0	156.0
4-n-Hexylphenol	90.0	33.3	313.0	-	389.0	333.0
4-n-Heptylphenol	20.0	16.7	62.5	21.0	617.0	556.0

*Coefficient measured at 37°C (Gates et al.; 1934)

**R.W. value at 18°C (Coulthard et al.; 1930)

***Coefficient measured at 37°C (Niederl et al.; 1937)

The influences of temperature (column 1 and 2), procedure of testing (column 3 and 4) and use of different test organisms (column 2, 3, 5 and 6) are evident. The effect of increased chain length on their germicidal activity with different test organisms is also seen in Table I.

Further, limitation of this method, can also be seen in the work of Withell who employing varying concentration exponents of the different phenols, obtained values of 4.55 for phenol (ct. 1) and 8.3 for 4-chloro-m-cresol. However under similar conditions of testing a phenol coefficient assessment is suitable for a preliminary evaluation, but as pointed out by Suter[2],'if too much reliance is placed on such a value it only beclouds the issue of true activity'. Further these data are mostly of a theoretical interest in that they illustrate the relationship between the chemical structure of the phenol derivatives and their antibacterial potential under a particular testing conditions.

PRESENT STUDIES ON XYLENOLS AND THEIR CHLORODERIVATIVES

The four xylenols (2,5-, 2,3-, 3,5- and 3,4-xylenol) and their chloroderivatives obtained in the present investigation were tested for their R.W.C. and the results are given in Table II. It would be seen that the method is not of general applicability in this series due to inherent lack of solubility; yet, the following broad conclusions can be derived from these results.

Table II - R.W.C. results of xylenols and their chloroderivatives

Compounds	R.W.C.	Remarks
2,5-Xylenol	7	
4-Chloro-2,5-xylenol	27	
4,6-Dichloro-2,5-xylenol	1	Part of the sample powder remained undissolved
2,3-Xylenol	6	
4-Chloro-2,3-xylenol	26	
4,6-Dichloro-2,3-xylenol	51	
3,5-Xylenol	5	
4-Chloro-3,5-xylenol	27	
4,6-Dichloro-3,5-xylenol	71	
2,4,6-Trichloro-3,5-xylenol	1	Part of the sample powder remained undissolved
3,4-Xylenol	6	
6-Chloro-3,4-xylenol	16	
2,6-Dichloro-3,4-xylenol	15	

(a) The introduction of two methyl groups in a phenol molecule increases the R.W. C. 5-7 times.

(b) para-Chloroxylenols are more reactive than the corresponding ortho-chloroxylenols. This may be due to effect of interaction between the visinal hydroxyl and chlorine.

(c) The bactericidal activity in chloroxylenols increases through mono- and di-series but thereafter falls, with a further increase in the degree of chlorination.

(d) 4,6-Dichloro-2,3-xylenol a compound described for the first time has potentiality of an active bactericidal agent of commerce when compared with DCMX.

Since the above method was found not to be of general applicability, chloroxylenols were also tested after incorporating these in a standard formulation. The results are given in Table III. These results are more reliable and may represent a true picture of bactericidal activity.

Table III - R.W.C. of xylenols and chloroxylenols in Dettol type formulation

Xylenols		Monochloro-xylenols		Dichloro-xylenols		Trichloro-xylenols	
Compound	R.W.C	Compound	R.W.C.	Compound	R.W.C.	Compound	R.W.C.
2,5-Xylenol	1.5	4-Chloro-2,5-xylenol	5	4,6-Dichloro-2,5-xylenol	4	-	-
2,3-Xylenol	1	4-Chloro-2,3-xylenol	5	4,6-Dichloro-2,3-xylenol	7.5-8	-	-
3,5-Xylenol	2.5	4-Chloro-3,5-xylenol	4	2,4-Dichloro-3,5-xylenol	4	2,4,6-Trichloro-3,5-xylenol	1-2
3,4-Xylenol	1-1.5	6-Chloro-3,4-xylenol	2	2,6-Dichloro-3,4-xylenol	2.5	-	-

Further, general conclusions mentioned earlier could also be drawn from these results. The action of 4,6-dichloro-2,3-xylenol becomes more pronounced, about 1½ times of DCMX.

STUDIES ON CHLORINATION OF l.t.c. TAR ACIDS AND THEIR R.W.C.

From an industrial point of view, it was considered worthwhile to chlorinate xylenols-rich fractions of l.t.c. tar acids and determine their R.W.C. with a view to find their commercial utilisation. The cuts of l.t.c.* tar acids used in this study along with their composition (as determined by GLC and paper-chromatography) are shown in Table IV.

Table IV - Physical properties and composition of l.t.c. tar acid fractions

Crude	Boiling range °C	Refractive index	Sp.gr.	Composition
Fraction A	204-214	1.516	1.01	m/p-cresol o-ethylphenol 2,5-xylenol 2,4-xylenol 2,3-xylenol 3,5-xylenol and 8% neutral oil
Fraction B	214-228	1.514	1.001	m/p-cresol o-ethylphenol 2,5-xylenol 2,4-xylenol 2,3-xylenol 3,5-xylenol 3,4-xylenol and 9% neutral oil

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* The tar acids were isolated from the l.t.c. tar obtained in 25 tonne/day Lurgi Spuel gas prototype plant installed at R.R.L. Hyderabad

The method of chlorination used here were the same as employed with pure xylenols. The chlorinated mixtures obtained by chlorination with gaseous chlorine and sulphuryl chloride were tested for R.W.C. both in the concentrated form as well as an active ingredient in a standard formulation. The results are given in Table V.

Table V - R.W.C. of l.t.c. tar acids fractions and their chlorinated products

Fraction A - R.W.C.=7; Fraction B - R.W.C. = 15

Details of sample	Chlorinated fraction A R.W.C.		Chlorinated fraction B R.W.C.
	(i)	(ii)*	(i)
Gaseous chlorination			
I - Stage (22% chlorine)	12	4	27
II - Stage (37% chlorine)	52	4	33
III-Stage (47% chlorine)	60	5-6	1
Chlorination with (SO_2Cl_2)			
1-Molar	21	3	43.1
2-Molar	25	4	32.1
3-Molar	25	4	13.7

* Used as active ingredients in Dettol type formulations in a concentration of 4.25%

The data given in Table V is of preliminary nature and points to the following:

Fraction A can yield an active product either chlorinating with gaseous chlorine or with sulphuryl chloride which can be used commercially. This product may be favourably comparable to DCMX, now used in commercial practice.

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EXPERIMENTAL

EXPERIMENTAL

A. Chlorination of Xylenols

(a) by Gaseous Chlorine (General Procedure)

In a 4-neck flask, fitted with a motorised stirrer, a thermometer, a reflux condenser and a gas inlet tube, xylenol (10 g, 0.85 mole) was dissolved in carbon tetrachloride (100 ml) and the solution cooled to 20±2°C. Chlorine gas from a cylinder (bubbled through concentrated sulphuric acid) was introduced at a slow rate. The chlorination was continued for 6-8 hrs. Every 30 minutes, a micro-sample of the reaction solution was withdrawn and spotted on a TLC plate of silica gel and developed using xylene saturated with formamide. Chlorination was stopped at a stage when only one spot was visible on the chromatogram. The solvent was then distilled off and the residue redissolved in ether. After washing the ethereal solution with 0.5% sodium bicarbonate solution (50 ml), it was dried over anhydrous sodium sulphate. The product recovered after ether removal, was purified by repeated recrystallisation from petroleum ether (60-80°C.). The products were characterised by mixed m.p. determination (wherever necessary) and as *para*-toluenesulphonates and aryloxyacetic acids. The data for individual xylenols are given in Table I.

Table I - Chlorination of xylenols with gaseous chlorine in carbon tetrachloride at 20±2°C.

A - 2,5-xylenol; B - 2,3-xylenol; C - 3,5-xylenol; D - 3,4-xylenol

PTS - *para*-toluenesulphonate; AOA - aryloxyacetic acid

Starting xylenol	Time of reaction, hrs.	Final product (derivatives)	m.p. °C	Yield %	Chlorine,% Found	Chlorine,% Calcd.	Remarks
A	5½	4,6-Dichloro-A	83.5	64	36.82	37.17	x,a
		(PTS - A)	115-116	-	20.50	20.57	
		(AOA - A)	195	-	28.65	28.51	
B	6	4,6-Dichloro-B	56.57	54	36.93	37.17	x,b
		(PTS - B)	95-96	-	20.88	20.57	
		(AOA - B)	182	-	28.40	28.51	
C	8	2,4,6-Trichloro-C	175	87	46.95	47.22	x,c
		(PTS - C)	158	-	28.01	28.06	
D	14	No single product	-	-	-	-	y,d

Note:
(a) For progress of chlorination, see Fig. 1, Chapter II
(b) Ditto, see Fig. 12, Chapter II
(c) Ditto, see Fig. 23, Chapter II
(d) Ditto, see Fig. 36, Chapter II
(x) Chloroproducts were recrystallised from petroleum ether (60-80°C.)
(y) The product polymerised during crystallisation

(b) by Sulphuryl chloride (General Procedure)

A solution of xylenol (10 g; 0.85 mole) in chloroform (100 ml) was taken in a round bottom flask fitted with an efficient stirrer, reflux condenser, a dropping funnel and a thermometer. The contents were cooled in an ice bath (1-5°C.) and sulphuryl chloride (11.2 g; 7.5 ml; 0.85 mole) was added dropwise. After the addition was complete, stirring was continued for another 2-4 hours. Chloroform was then distilled off under reduced pressure. The reaction product after redissolution in ether, was washed with 0.5% sodium bicarbonate solution and dried over anhydrous sodium sulphate. The solvent again distilled off. The residual product was purified by fractional crystallisation from petroleum ether (60-80°C.). As described above, course of the reaction was followed by TLC. If necessary, the product was purified with column chromatography.

The above procedure was also adopted in experiments with two or three molar proportion of sulphuryl chloride. In some cases, chlorination was studied in dry ether as solvent. The relevant data are presented in Tables II, III and IV.

Table II - Reaction of xylenols with sulphuryl chloride (one-molar-proportion) in chloroform

A - 2,5-xylenol; B - 2,3-xylenol; C - 3,5-xylenol; D - 3,4-xylenol

PTS - *para*-toluenesulphonate; AOA - aryloxyacetic acid

Starting xylenol	Time of reaction, hrs.	Chloroproduct isolated (derivatives)	m.p. °C	Yield %	Chlorine,%		Remarks
					Found	Calcd.	
A	4½	4-Chloro-A	74	74.5* 47	22.15	22.65	x,a
		(PTS - A)	81	-	11.3	11.46	
		(AOA - A)	118	-	16.45	16.55	
B	4½	4-Chloro-B	83	62.5	22.35	22.65	x,b
		(PTS - B)	84.5	-	12.2	11.46	
		(AOA - B)	117	-	16.68	16.55	
C	4½	4-Chloro-C	114.5	82.5	22.15	22.65	y,c
		(PTS - C)	103.5	-	12.2	11.46	
		(AOA - C)	143	-	16.68	16.55	
D	4½	Product polymerised on keeping	-	-	-	-	z,d

Note: (a) For progress of chlorination, see Fig. 4, Chapter II
(b) Ditto , see Fig. 17, Chapter II
(c) Ditto , see Fig. 26, Chapter II
(d) Ditto , see Fig. 37, Chapter II
(x) Chloroproducts were recrystallised from petroleum ether (60-80°C.)
(y) Chlorocompound was isolated through column chromatography
(z) For quantitative TLC of the product after 2¼ hr reaction time see Table II, Chapter II

*Dry ether was used as solvent

Table III - Reaction of xylenols with sulphuryl chloride (two-molar-proportion) in chloroform

A - 2,5-xylenol; B - 2,3-xylenol; C - 3,5-xylenol; D - 3,4-xylenol

PTS - *para*-toluenesulphonate; AOA - aryloxyacetic acid

Starting xylenol	Time of reaction, hrs.	Chloroproduct isolated (derivatives)	m.p. °C	Yield %	Chlorine,%		Remarks
					Found	Calcd.	
A	4	4,6-Dichloro-A	83.5	51	36.93	37.17	x,a
		(PTS - A)	115-116	-	20.45	20.57	
		(AOA - A)	195	-	28.60	28.51	
B	2	4,6-Dichloro-B	56-57	79.7	36.95	37.17	x,b
		(PTS - B)	95-96	-	20.80	20.57	
		(AOA - B)	182	-	28.20	28.51	
C	4	2,4-Dichloro-C	94.5	53	36.42	37.17	x,c
		(PTS - C)	114	-	20.40	20.57	
		(AOA - C)	139-140	-	28.30	28.51	
D	4	Polymeric product on keeping	-	-	-	-	d,y

Note:
(a) For progress of chlorination, see Fig. 5, Chapter II
(b) Ditto, see Fig. 18, Chapter II
(c) Ditto, see Fig. 27, Chapter II
(d) Ditto, see Fig. 38, Chapter II
(x) Chloroproducts were recrystallised from petroleum ether (60-80°C)
(y) For quantitative TLC of the reaction products, see Table II, Chapter II

Table IV - Reaction of xylenols with sulphuryl chloride (three-molar-proportion) in chloroform

A - 2,5-xylenol; B - 2,3-xylenol; C -3,5-xylenol; D - 3,4-xylenol

PTS - *para*-toluenesulphonate; AOA - aryloxyacetic acid

Starting xylenol	Time of reaction, hrs.	Chloroproduct isolated (derivatives)	m.p. °C	Yield %	Chlorine,% Found	Chlorine,% Calcd.	Remarks
A	1	4,6-Dichloro-A	83.5	71.4	39.92	37.17	x,a
		(PTS - A)	115-116	-	20.40	20.57	
		(AOA - A)	195	-	28.35	28.51	
B	1½	4,6-Dichloro-B	56-57	89.4	36.78	37.17	x,b
		(PTS - B)	95-96	-	20.85	20.57	
		(AOA - B)	182	-	28.50	28.51	
C	4	2,4,6-Trichloro-C	175	94	47.1	47.22	x,c
		(PTS - C)	158	-	28.04	28.06	
		(AOA - C)	75	-	37.45	37.56	
D	2	2,6-Dichloro-D	56	38.7	36.95	37.17	y,d
		(PTS - D)	89-90	-	20.3	20.57	
		(AOA - D)	156-157	-	28.15	28.51	

Note: (a) For progress of chlorination, see Fig. 6, Chapter II
(b) Ditto, see Fig. 19, Chapter II
(c) Ditto, see Fig. 28, Chapter II
(d) Ditto, see Fig. 39, Chapter II
(x) Chloroproducts were recrystallised from petroleum ether (60-80°C)
(y) The chloroproduct was isolated by steam distillation; non-volatile product polymerised.

(c) by ter-Butylhypochlorite (General Procedure)

(i) Preparation of ter-butylhypochlorite

Freshly distilled *ter*-butylalcohol (80 ml) was added in *one lot to cold aqueous solution of caustic soda (82 g. in 300-400 ml)* and the reaction mixture shaken vigorously. Distilled water was then added to the reaction mass till it became homogeneous. Chlorine gas was then bubbled into this solution at about 10-15 bubbles per second under constant stirring for 3-4 hours. Afterwards, the upper layer was separated and dried over anhydrous calcium chloride and distilled. The fraction boiling between 76-80°C., was collected, stored in a refrigerator. It was again redistilled just before use.

(ii) Xylenol (10 g; 0.85 mole) solution in acetic acid (90%; 50 ml) was cooled to 0±2°C., and freshly distilled *ter*-butylhypochlorite (11 ml; 0.85 mole) added to it gradually under stirring. Stirring was further continued for 1-3 hours. The content were then poured over crushed ice and the separated solid was filtered, washed, dried and purified by fractional crystallization from petroleum ether or by column chromatography on silica gel with xylene saturated formamide as a mobile phase. *para*-Toluene sulphonate and aryloxyacetic acid derivatives were prepared for characterisation. In the case of 3,4-xylenol, no solid separated on dilution of acid and the product polymerised on keeping. The quantitative TLC data is already given in Table II, Chapter II. The data for one-molar reaction for individual xylenols are given in Table V.

Table V - Reaction of xylenols with ter-butylhypochlorite (one-molar-proportion) in 90% acetic acid

A - 2,5-xylenol; B - 2,3-xylenol; C - 3,5-xylenol; D - 3,4-xylenol

Starting xylenol	Time of reaction hrs.	Chloroproduct isolated	m.p. °C	Yield %	Chlorine,%		Remarks
					Found	Calcd.	
A	2	4,6-Dichloro-A	83.5	31.8	36.94	37.17	x,a
B	2	4,6-Dichloro-B	56-57	24.0	37.01	37.17	z,b
C	4	2,4-Dichloro-C	94-95	11.9	36.82	37.17	z,c
D	4	Polymeric product on keeping	-	-	-	-	y,d

Note: (a) For progress of chlorination, see Fig. 9, Chapter II

(b) Ditto , see Fig. 20, Chapter II

(c) Ditto , see Fig. 33, Chapter II

(d) Ditto , see Fig. 42, Chapter II

(x) Chloroproduct recrystallised from petroleum ether (60-80°C)

(y) For quantitative TLC of reaction mixture, see Table II, Chapter II

(z) Chloroproduct was separated by column chromatography

Similarly, xylenols were reacted with 2-molar and 3-molar proportions of the reagent and the data are given in Table VI and VII for 2,5-, 2,3- and 3,5-xylenols. The behaviour of the reaction mass and the product in the case of 3-molar reaction with 3,4-xylenol was different and hence it is dealt separately below.

(iii) Chlorination of 3,4-xylenol with 3-molar quantity of the reagent

In this case, as already shown in Fig. 44, Chapter II the phenolic products were not present. After the reaction, the reaction mass was poured over ice and the organic product extracted with ether. The ethereal extract was separated washed with water and sodium bicarbonate solution and dried over anhydrous sodium sulphate. The residue obtained after solvent removal, was separated into three compounds (A, B and C) by column chromatography on silica gel using chloroform. These compounds were identified as:

A - 2,4,6-Trichloro-3,4-dimethylcyclohexadien-1-one
B - 4,6-Dichloro-3,4-dimethylcyclohexadien-1-one
C - 4-Chloro-3,4-dimethylcyclohexadien-1-one

B. General method for preparing aryloxyacetic acids of chloroxylenols

About (1 g) of the chloroxylenol was dissolved in 3.5 ml. of 33% caustic soda solution and 2.5 ml. of 50% aqueous chloroacetic acid solution was added to it. The reaction mass was heated on a water bath for one hour. After cooling, it was diluted with 10 ml. of water, acidified to congo red with dilute hydrochloric acid and

Table VI - Reaction of xylenols with ter-butylhypochlorite (two-molar-proportion) in 90% acetic acid

A - 2,5-xylenol; B - 2,3-xylenol; C - 3,5-xylenol; D - 3,4-xylenol

Starting xylenol	Time of reaction hrs.	Chloroproduct isolated	m.p. °C	Yield %	Chlorine,%		Remarks
					Found	Calcd.	
A	2	4,6-Dichloro-A	83.5	60.2	36.46	37.17	w,a
B	2	4,6-Dichloro-B	56-57	67	36.93	37.17	x,b
C	4	4-Chloro-C	114	11.9	22.45	22.65	y,c
		2,4-Dichloro-C	94-95	17.4	36.94	37.17	
		2,4,6-Trichloro-C	175	20.58	47.20	47.22	
D	4	Polymeric product on keeping	-	-	-	-	z,d

Note:
(a) For progress of chlorination, see Fig. 10, Chapter II
(b) Ditto , see Fig. 21, Chapter II
(c) Ditto , see Fig. 34, Chapter II
(d) Ditto , see Fig. 43, Chapter II
(w) Chloroproduct was separated by column chromatography
(x) Chloroproduct was recrystallised from petroleum ether (60-80°C)
(y) Chloroproducts were isolated by preparative TLC
(z) For quantitative TLC of the reaction products, see Table II, Chapter II

Table VII - Reaction of xylenols with ter-butylhypochlorite (three-molar-proportion) in 90% acetic acid

A - 2,5-xylenol; B - 2,3-xylenol; C - 3,5-xylenol; D - 3,4-xylenol

Starting xylenol	Time of reaction hrs.	Chloroproduct isolated	m.p. °C	Yield %	Chlorine,% Found	Chlorine,% Calcd.	Remarks
A	2	4,6-Dichloro-A	83.5	49.4	37.2	37.17	x,a
B	2	4,6-Dichloro-B	56-57	76	36.84	37.17	x,b
C	2	2,4,6-Trichloro-C	175	44.5	47.10	47.22	x,c
D	3	-	-	-	-	-	z

Note:

(a) Progress of chlorination, see Fig. 11, Chapter II

(b) Ditto, see Fig. 22, Chapter II

(c) Ditto, see Fig. 35, Chapter II

(x) Chloroproduct was recrystallised from petroleum ether (60-80°C)

(z) Dealt separately

extracted with 30 ml. of ether. The extract was washed with 10 ml. of water. Then it was treated with 25 ml. of 5% sodium carbonate solution. The sodium carbonate extract was acidified with dilute HCl to congo red. The aryloxyacetic acid so separated was filtered. It was purified by crystallisation from ethanol.

C. General method for the preparation of para-toluene sulphonate of chloroxylenols

The chloroxylenol (ca. 1 g) was taken in pyridine (2.5 ml.) and about 2 g of *para*-toluene sulphonyl chloride was added. The contents were heated on a water bath for 15 minutes and then poured into 25 ml. of cold water and scratched till the oil solidified. The solid was filtered, washed with cold dilute hydrochloric acid (to remove any pyridine) followed with a washing of dilute caustic soda (to remove unreacted phenol) and then with cold water. The dried solid was recrystallised with methanol.

D. Column chromatography

A glass column, about 80 mm long and 25 mm in diameter, packed with 30 g of silica gel G (Merck; 0.08 mm) was used. Xylene saturated with formamide served as the mobile phase and about 1 g of the substance dissolved in xylene was generally used for the separation.

E. Paper chromatography

Phenols and chlorophenols (obtained from commercial sources or synthesised) were used. Whatman No. 1 filter paper (16 x 19 in.)

impregnated with methanol-formamide solution (100 : 30 v/v) and dried at room temperature for 30-40 minutes was employed. Solution of each compound (0.5 - 1%) in acetone was spotted with a fine glass capillary (10-20 μu). Development was carried out in a glass tank at 30±2°C., using descending technique. Phosphotungstomolybdic acid (Folin-Denis reagent) was sprayed on the developed chromatogram. After exposure to ammonia, blue spots resulted.

F. Qualitative thin layer chromatography of chlorophenols

Using a thin layer applicator (Desaga, Heidelberg), glass plates (20 x 20 cm) were coated as usual with a well stirred suspension of silica gel G (E. Merck, Darmstadt; 30 g in 60 ml. water) to give a layer, approximately 270 μ in thickness. The compounds were dissolved in acetone and about 10 μg were spotted with a glass capillary, 2-3 cm from one edge of the plate. This was then placed under the chamber for development. After 40-60 minutes development (solvent front covers about 15 cm), the plates were sprayed with Folin-Denis reagent and exposed to ammonia. The compounds were seen as blue spots on a white background.

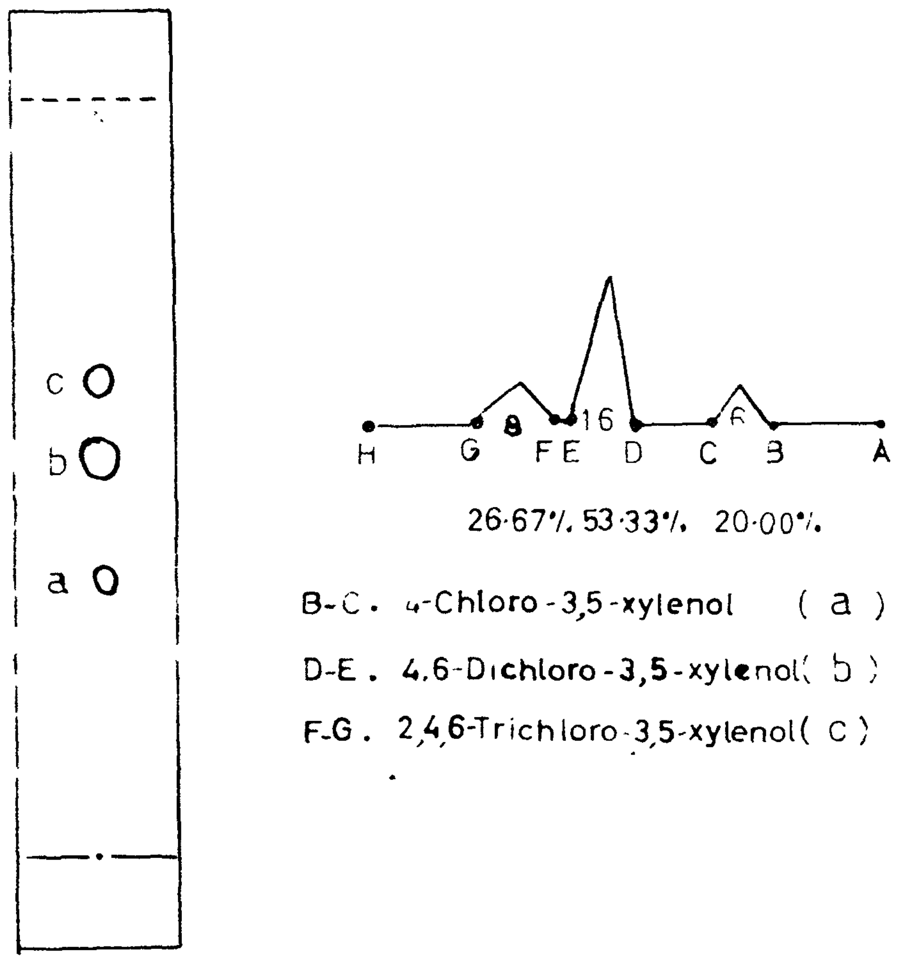
G. Quantitative TLC of chlorophenols

The development was carried out on plates (20 x 2.1 cm) or microslides (7.2 x 2.4 cm). The bigger plates were prepared as already described. The microslides were prepared by dipping them in a well-stirred suspension of silica gel G (30 g) in a mixture of 80 ml. of chloroform and 20 ml. of methanol. Known volumes of various dilutions of solutions of compounds in acetic acid were applied with an Agla micrometer syringe on TLC plates and the optimum dilution range determined. The sample was then spotted (ca. 50 μg) with a glass capillary or a micro syringe. The chromatogram was developed in a xylene saturated with formamide (solvent A), a sufficient quantity of Folin-Denis reagent was sprayed and the plate exposed to ammonia vapours. The compounds appeared as blue spots on a white background.

An automatic Joyce Chromoscan Densitometer was used to measure the relative optical densities of the spots. For scanning, the developed plate (Fig. I) was held in the densitometer and the base line adjusted for stability and maximum peak recording. The plate was then scanned with a slit opening of 1 x 10 mm when peaks were obtained for each coloured spots (Fig. I). After this initial scanning, the process was repeated at the corners of the bases of the peaks (points B to C, D to E and F to G in Fig. I) to obtain integrated numbers for the peak area. The relative percentage of each compound was then calculated.

H. Gas liquid chromatography (GLC)

The GLC unit used in this study was Griffin and George's MK II model provided with a thermal conductivity cell as the detector. The unit was slightly modified by providing an electrical flash heater at the point of injection of the samples.



TLC DIAGRAM AND CORRESPONDING PEAKS OBTAINED BY CHROMOSCAN

FIG.1

The following stationary liquid phases were used on celite 545 (+ 120 mesh) or fire brick (+ 60 mesh):

(i) Polyol propylene sebacate (Reoplex 100)
(ii) Dow-Corning High Vacuum silicone grease
(iii) Silicone Elastomer-30

I. Ultraviolet spectra

The UV absorptions were determined by standard method using a Beckman model D.U. spectrophotometer. For each compound at least two independent sets of observations were made. The chlorinated cresols were mostly from commercial sources, further purified by distillation or recrystallisation. The chloroxylenols used for UV studies were synthesised in the course of the present investigation and made chromatographically pure. The solvent (cyclohexane) was of spectroscopic grade.

J. Infrared spectra

A Perkin and Elmer model 221 spectrophotometer (recording type) was used to determine the IR spectra. Solutions were made as 6% w/v in carbondisulphide.

K. Nuclear magnetic resonance spectra

The NMR spectra were recorded in a varian A-60 spectrometer. Calibrations were made by the standard side band procedure. Chemical shifts with respect to tetramethylsilane were accurate within ± 0.01 p.p.m. The concentration of the compound in chloroform was normally 10% w/v. These spectra were determined through the kind courtesy of Messrs Riker Laboratories, Northridge, U.S.A.

L. Preparation, identification, chlorination and R.W.C. determination of xylenols rich l.t.c. tar acid mixtures

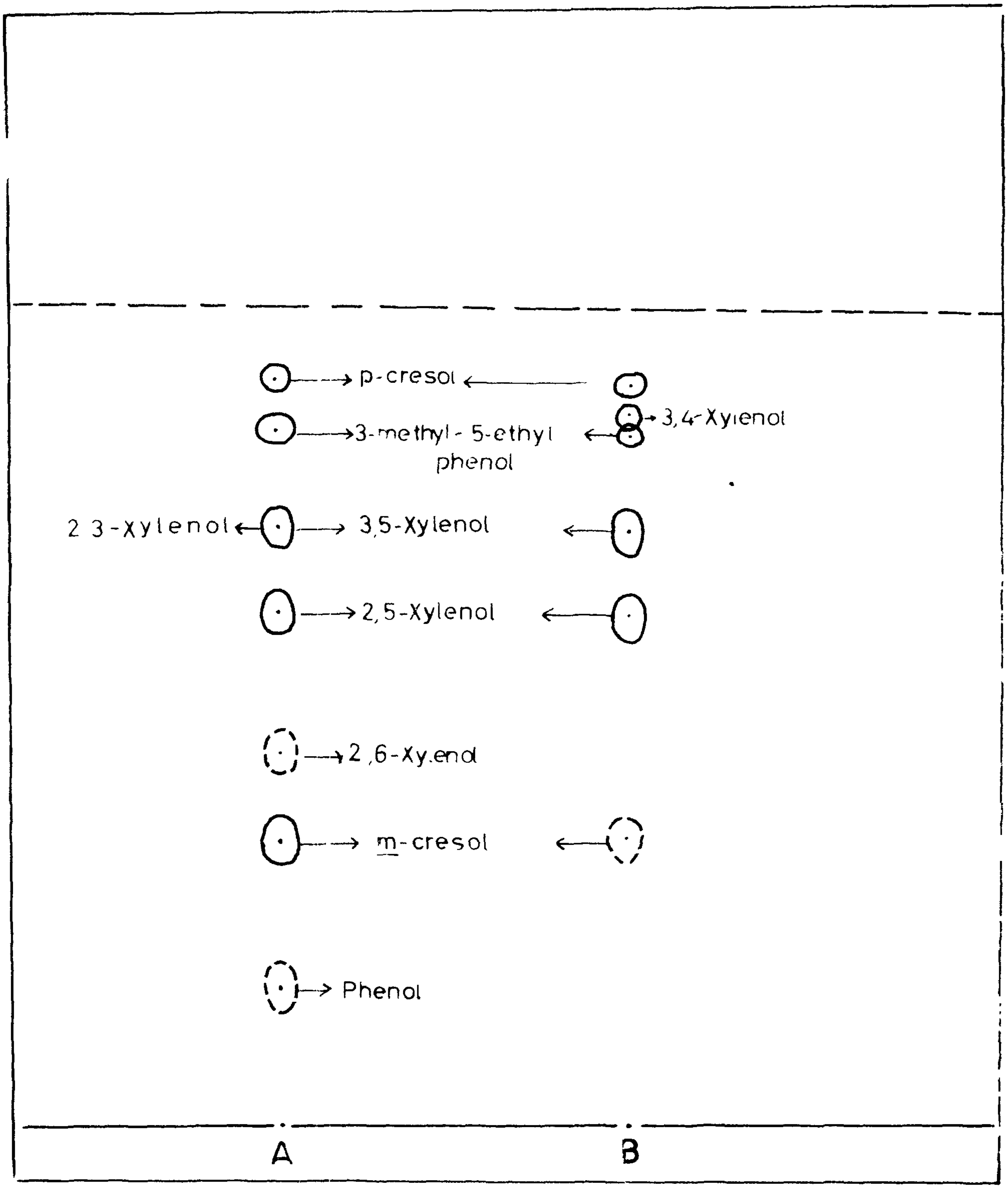
Crude tar acids (boiling range 200-230°C) were extracted from the light tar obtained from l.t.c. of coal. It was distilled under vacuum at 75±2 mm and two fractions A and B were collected for further work. The physical properties of these are already given in Table IV, Chapter V. The tar acids fractions (A and B) were analysed by paper and GLC. Paper chromatography (Fig. 2) of these tar acids was done on filter paper No. 1 (impregnated with 4% sodium carbonate) using ethylmethyl ketone saturated with water as solvent. Time of run to cover the distance of 45 cm was 19 hours. The components identified in tar acid fraction with this technique are as follows:

Fraction A = Phenol (traces), m/p-cresol, 2,6-xylenol, 2,5-xylenol, 3,5-xylenol, 3-methyl-5-ethylphenol and 2,3-xylenol

Fraction B = m-Cresol, 2,5-xylenol, 3,5-xylenol, 2,3-xylenol, 3-methyl-5-ethylphenol and 3,4-xylenol

Figs. 3 and 4 give the GLC of these fractions, components identified and conditions for operation.

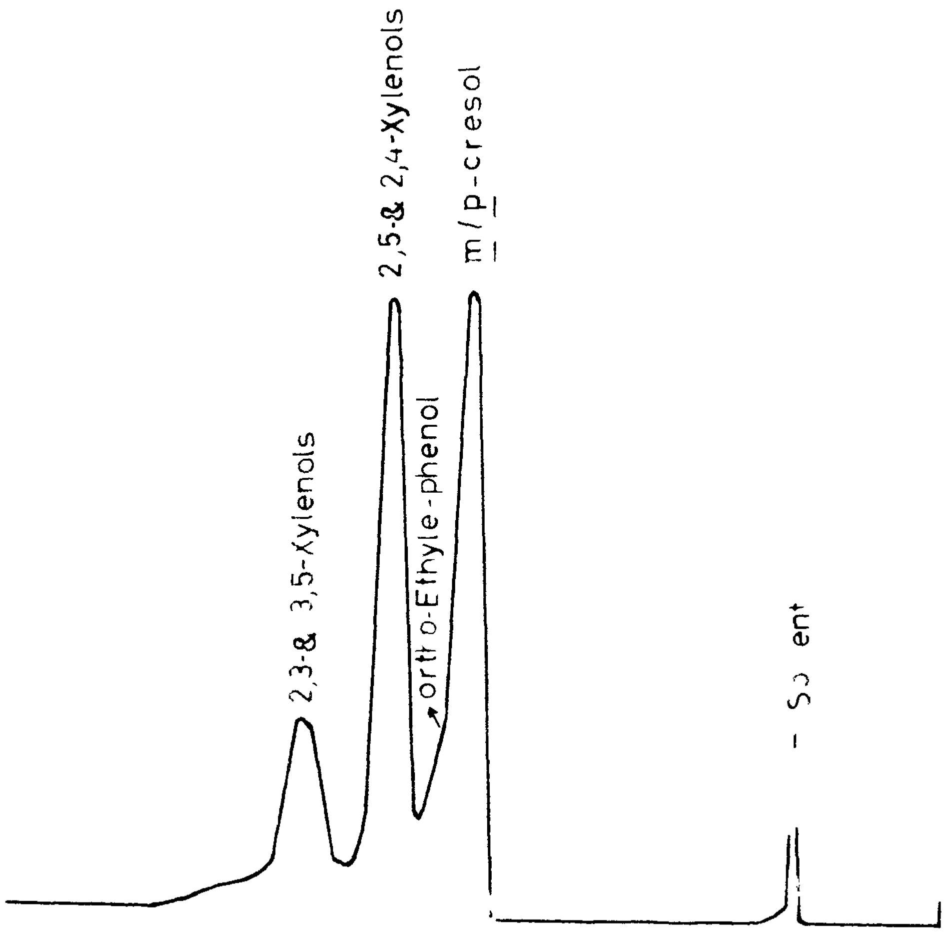
These fractions were chlorinated with gaseous chlorine and with sulphuryl chloride as described earlier for pure xylenols.



PAPER CHROMATOGRAM OF TAR ACID FRACTIONS A& B

FIG. 2

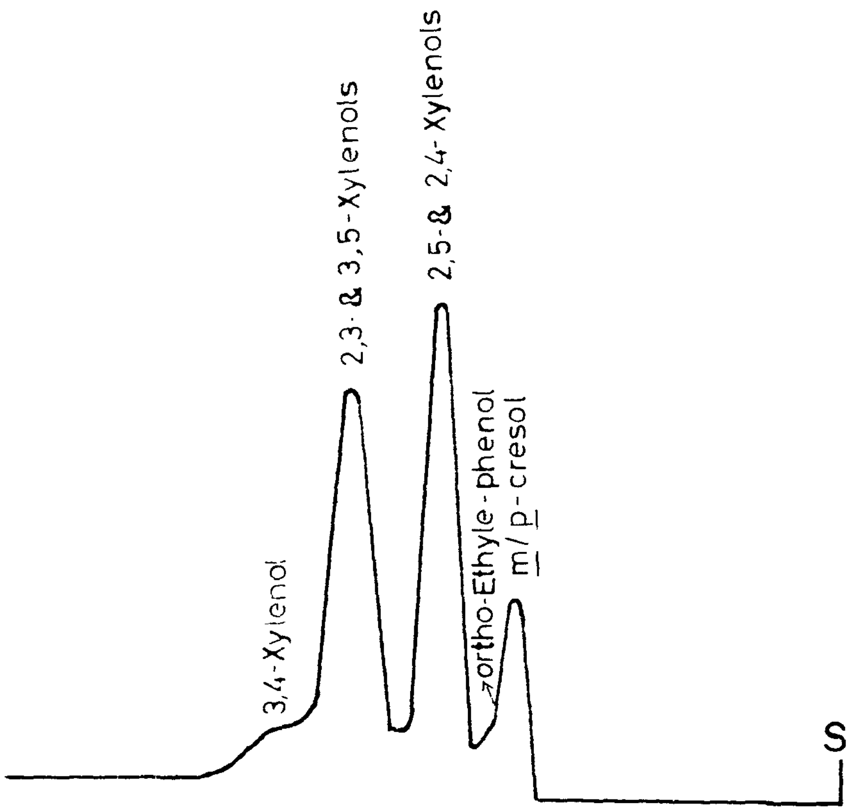
Stationary phase = SE - 30; 6 feet column +
Reoplex 100 ; 6 feet column on fire bricks (+60 mesh)
Flow rate = 1.2 litre per hour
Bridge current = 100 mV
Temparature = 180°c



GLC SEPARATION OF TAR ACID FRACTION A

FIG. 3

stationary phase=SE- 30 ; 6 feet column +
Reoplex 100 ; 6 feet column on fire bricks(+60mesh)
Flow rate=1.2 litre per hour
Bridge current -100 mA
Temparature =180° c



GLC SEPARATION OF TAR ACID FRACTION B

FIG. 4

The tar acids fractions and their chlorinated cuts were tested for R.W.C. These were also tested for R.W.C. in a standard (Dettol type) formulation. The R.W.C. determination was done according to ISI specification method (IS : 1061-1964) against <u>S. typhi</u>.

Solubilisation of chlorinated tar acids (active ingredient) was done in 5% castor oil soap.

Dettol type of formulation using chlorinated tar acid was prepared using the following proportions:

Chlorinated tar acids	4.25 g w/v
-Terpenol	9 cc v/v
Alcohol	13 cc v/v

Remaining castor oil soap and water to make 100 cc.

SUMMARY

SUMMARY

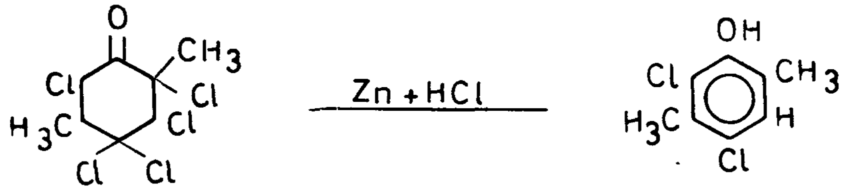
Chapter I

The first chapter begins with a discussion on the available chlorinating agents in use for benzenoid compounds, use of catalysts or carriers and mode of action of the various agents. This is followed by a summary of the orientation effects of various substituents in the aromatic ring in the course of chlorination. Also included, is a critical review giving the present state of knowledge on chlorophenols, as a class. The chapter is concluded by a statement in detail of the problem chosen for this dissertation.

Chapter II

The second chapter deals with the results obtained in the chlorination of xylenols and these are discussed under each xylenol. The progress of chlorination has been followed using the TLC technique. The products have been characterized by m.p. determination, derivatives and spectral studies.

Gaseous chlorine reacts with 2,5-xylenol, first attacking at the 4-position and followed by its entry at 6-position also. Thus the products of chlorination are the 4-chloro-2,5-xylenol and 4,6-dichloro-2,5-xylenol. Sulphuryl chloride and <u>ter</u>-butylhypochlorite also react similarly. It is noteworthy that with none of these xylenols, the 6-chloro-mono-isomer is detectable. From a preparative angle, 4,6-dichloro-2,5-xylenol (II) can be prepared in good yields with anyone of these reagents used in the right proportion. This compound has been described in literature to have been obtained by Mueller et al. by the reduction of 2,3,4,4,6-pentachloro-2,5-dimethyl- 5-cyclohexen-1-one

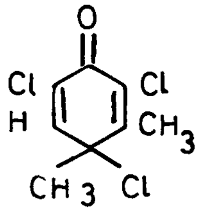


I II

The 4-chloro-2,5-xylenol can be separated in about 50% yield from the reaction product of one-molar proportion of sulphuryl chloride.

Chlorination of 2,3- and 3,5-xylenols carried out under similar conditions yielded, first the mono-chloro-<u>para</u>-derivative, leading to dichloro-derivatives, the second chlorine entering the <u>ortho</u>-position. Here again, it was striking that the mono-chloro-<u>ortho</u>-isomer was not formed at all. 4,6-Dichloro-2,3-xylenol has been prepared for the first time during this work. Its structure has been established comparing its data with the known, 5-6-dichloro-2,3-xylenol as well as with the help of UV, IR and NMR spectra. Further, 4-chloro-2,3-xylenol has been prepared for the first time by a direct method. Hitherto, it is described to be obtained from 4-amino-2,3-dimethylphenol or from 4-chloro-2,3-dimethylaniline through diazotisation reactions. In the case of 3,5-xylenol, the chlorination proceeds to trichloro-stage and the final product, 2,4,6-trichloro-3,5-xylenol has been isolated in very good yields.

The chlorinating agents behaved somewhat differently with 3,4-xylenol and besides the chloroxylenols, oxidation products are also formed. These oxidation products become the exclusive products with the 3-molar proportion of ter-butylhypochlorite. These non-phenolic oxidation products in this case, have been separated by column chromatography and their structures established through chemical and spectral data. These are as follows and reported for the first time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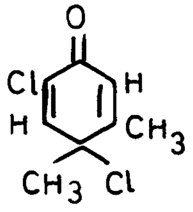
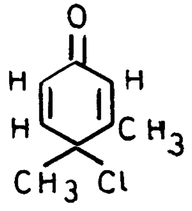
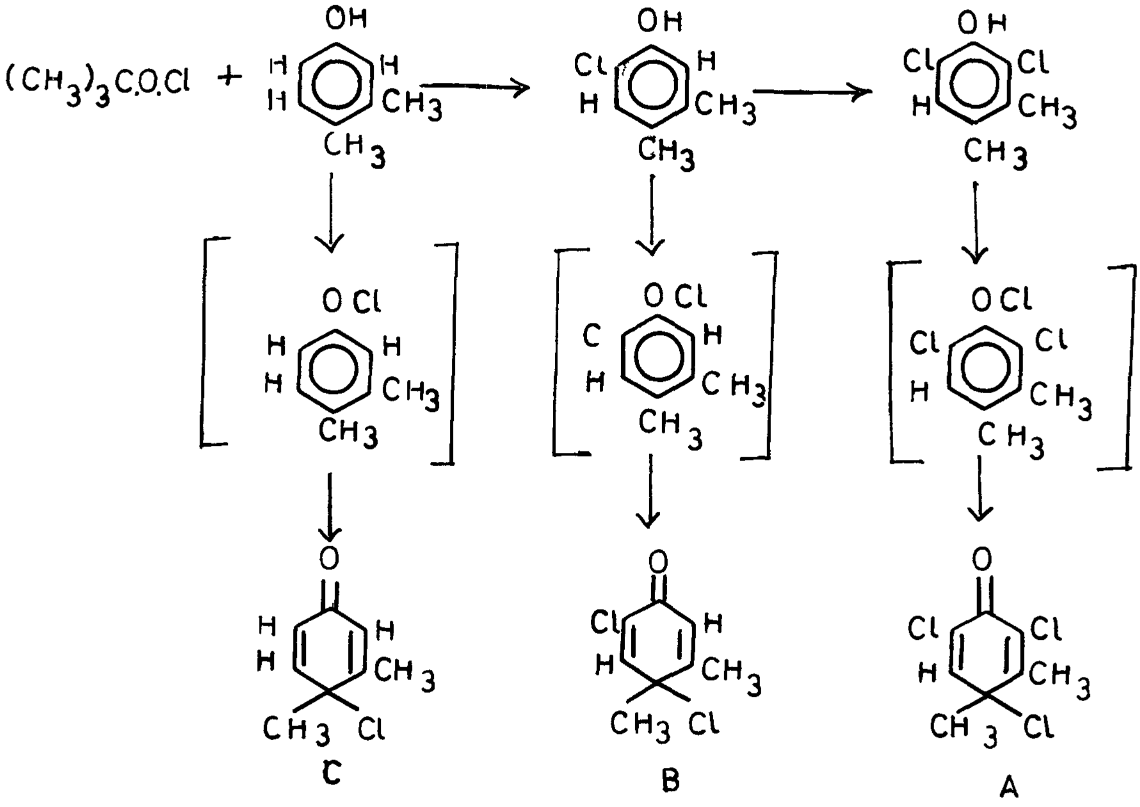

II


III

A possible course of reaction leading to formation of these is discussed and is also indicated below



From a theoretical stand point, it has been attempted to explain the non-formation of mono-ortho-chloro-isomers, when the para-position is free. Finally, ter-butylhypochlorite as a chlorinating agent in phenols in general and xylenols in particular has been discussed and it is surmised that here, the chlorinium ion (Cl^+) is the reaction entity.

Chapter III

The third chapter records the data obtained during the present work on the paper, thin-layer and gas-liquid chromatographic studies on chlorophenols in general and chloroxylenols in particular. It is observed that except for some information available the paper chromatography of chlorocresols, almost all the information recorded here is being reported for the first time. Studies made to find a good solvent system for the paper chromatography of chlorocresols and chloroxylenols, established that formamide impregnated papers, xylene saturated with formamide as solvent system and the descending techniques were good combination for this study. The spots were well defined and earlier reported use of paper in-between two glass plates (technique by Grebenovsky) is not absolutely essential. The R_f-values have been found to be very sensitive to experimental conditions and to obtain reproduceable results, the conditions of experimentation had strictly adhered to. The calculation of R_M values and their plotting against number of carbon atoms or chlorine groups has indicated that with polar solvent system the partition phenomenon was responsible for chromatographic separation; with non-polar solvent, the adsorption phenomenon's role becomes noticeable. The TLC technique has been developed for application to chlorophenols as a class. Conditions have been standardised for its application both on regular size and microplates. Quantitative TLC technique has been developed and extensively applied during the course of this work. The results are discussed and correlation established. Since, the GLC technique did not give good results due to poor detector response, only preliminary data has been presented and salient observations made are recorded.

Chapter IV

The fourth chapter contains spectroscopic data of chlorocresols and chloroxylenols UV, IR and NMR data are presented and discussed. In the UV an attempt has been made to correlate the structure of these chlorophenols in terms of bathochromic or hypsochromic effects in the absorption bands. From a study of the infrared spectra of the various chloroxylenols it has been possible to assign characteristic CH deformation and C-Cl stretching absorption bands in the 650-900 cm^{-1} region and this may be of use for their identification. The hydroxyl absorption bands in the 3615-3530 cm^{-1} region reveal differences in the types of free and intramolecular bonds in the different compounds examined. These differences may be utilised in fixing the chlorine position in the aromatic nucleus. The NMR spectra of most of the chlorocresols and chloroxylenols have been obtained and spectral absorption assignments have been made, and convincing proof of structure of the compounds provided.

Chapter V

The last chapter discusses the results obtained in the testing of bactericidal activity of chloroxylenols against S-typhi both as active ingredient and as formulation. It depicts the broad correlations between chemical structure and bactericidal value and brings out the potentiality of the hitherto unknown 4,6-dichloro-2,3-xylenol as an active bactericidal agent of commerce.

The results obtained with chlorinated mixtures of tar acid indicate that they themselves possess sufficient bactericidal activity and since they would be cheaper to produce than DCMX, have good economic potentiality.

REPRINTS

Reprinted from Low Temperature Carbonization of Non-Caking Coals & Lignites and Briquetting of Coal fines: Symposium Vol. II (Pages 198—202)

Chlorination of Coal Tar Acids : Part I

SAJID HUSAIN, D. P. AGRAWAL, M. G. KRISHNA & S. H. ZAHEER

Regional Research Laboratory
Hyderabad

The low temperature tar contains about 30 per cent tar acids, consisting mainly of cresols, xylenols and high boiling tar acids of high bactericidal value. The literature on the use of xylenols and high boiling tar acids with and without chlorination is reviewed.

The results of chlorinating a xylenol-cut tar acid fraction obtained from a Lurgi-Spuelgas low temperature carbonization pilot plant working at the Regional Research Laboratory, Hyderabad, are presented.

The low temperature (l.t.) tar produced from the 25 ton/day Lurgi-Spuelgas low temperature carbonization (l.t.c.) pilot plant operating at the laboratory, contains about 30 per cent tar acids, consisting mainly of cresols, xylenols and high boiling tar acids (HBTA) of high bactericidal value[1]. Alkali-soluble tar acids boiling from 230° to 355°C. and above are broadly termed HBTA and form a complex mixture of several tar acids mostly homologues of monohydric phenols. Of these, trimethyl phenol, 3-methyl-5-ethyl phenol, hydroxy hydrindenes, diphenols and naphthols among the monohydric and catechols, resorcinols and hydroquinones among dihydrics have been reported as major constituents in 230-300°C. fraction[2].

The uses of phenols and cresols are well established in industries like plastics, dyes and intermediates, antiseptics, pharmaceuticals, etc. The xylenols and HBTA are used to a limited extent and mostly in the preparation of disinfectants and antiseptics. In recent years modified tar acids, mostly chlorinated products, have assumed greater industrial importance. The use of pentachloro phenol[3] (PCP) for wood preservation, parachloro meta cresol[4] (PCMC), parachloro meta xylenols[5] (PCMX) and dichloro meta xylenols[6-8] (DCMX) as preservatives in cosmetics, soaps, pharmaceuticals and other industries is well known.

The literature on chlorination of tar acids is limited and mostly covered by patents. The present paper gives a review of the literature and describes the results of chlorinating a xylenol-cut of tar acids obtained from l.t. tar.

Chlorination, in general, is an exothermic reaction and the heat of reaction in substitutive chlorination is reported to be in the range of —23000 to —27000 cals. regardless of the nature of the organic molecule[9]. The position of chlorine in the molecule, i.e. in nucleus or in the side chain depends upon several factors like unsaturation in molecules, temperature and pressure of chlorination, catalyst, etc. The kinetics of chlorination have been summarized by Groggins[10] into six major items. The unsaturated bond in the side chains generally gets chlorinated first. Nuclear substitution occurs[11] in the presence of halogen carriers such as iron, aluminium or iodine, usually at relatively low temperatures with the exclusion of light. The direct chlorination of phenol, normally at temperatures below 100°C. often in the presence of solvents such as carbon tetrachloride, sometimes in the presence of halogen carriers such as iron, aluminium chloride, leads primarily to substitution in ortho and para positions and later in meta position[12]. The rate of chlorination is favourably affected by the concentration of the molecules in the associating solvent[13].

The apparatus for chlorination[14] is usually of glass though quartz apparatus has been suggested, specially when ultraviolet light is used for catalizing the reaction. Henri[15] used an apparatus mainly of iron and lined with an insoluble halide such as calcium fluoride or silver chloride, at a temperature of 500 to 600°C. An apparatus for speeding the chlorination reaction by improved mixing has been reported by Kipper[16]. Application of the technique of the measurement of oxidation-reduction potential to control acid catalyst in the hydrochlorination has also been mentioned[17]. The principal chlorinating agent is gaseous chlorine alone (with light or heat as promoter) or in the presence of a catalyst. Other agents, such as hydrogen chloride, sulphuryl chloride, phosgene, hypochlorites, and thionyl chloride are used for the substitution of hydrogen, addition to the unsaturated linkages, and replacement of functional groups, such as hydroxyl groups in alcohols[9].

A Russian worker[18] discussed the mechanism of chlorination of organic and inorganic compounds by free chlorine and its derivatives in the presence of some inorganic chlorides as catalyst with or without the addition of carbon. The order of activity of the catalyst during chlorination of naphthalene is reported[19] as Sb > Fe (powder) > $AlCl_3$. Though the selection of a catalyst depends upon the nature of the reaction and the end-product required, the commonly used catalysts are Fe[20], Te[21] and its compounds, activated charcoal and chlorides of Te, Fe, Sn, Bi, Sb, Al[22] and P. Iodine in combination with iron has been reported to be a very powerful catalyst for organic compounds[23]. A mixture of sulphur, antimony chloride and lead has been successfully used as catalyst for the nuclear chlorination of benzene[24]. Bondy[25] suggested sulphuryl chloride as catalyst for chlorination of tar acids from l. t. tar.

Of all the isomeric forms of alkyl phenols and cresols, straight chain primary products are most active. A given number of carbon atoms in a single alkyl chain contributes[26] more activity than when distributed between two or more chains. The position[27] of alkyl groups with respect to hydroxyl group has little significance, e.g. ortho-, meta- or para-cresol, all have a Rideal Walker coefficient of 2·2. The germicidal activity increases against all organisms as alkyl chain is lengthened until the n-amyl compound is reached and thereafter further increase of the chain length results in decrease in activity against *salmonella typhi*. The effect on the gram positive organisms is uncertain[28]. The dihydrics of l.t. tar generally have[29] low antibacterial activity except hydroquinone (R. W. about 12). Suter[30] has stated, "The effect of halogen substitution, in general, increases with increasing atomic weight of the halogen" and "this increase is less for the ortho position than for the para, perhaps owing to interaction between the hydroxyl groups and the halogen atoms. Little evidence is available for meta compounds".

Chemically, the chlorophenols behave very much like phenols. The main differences[12] are the higher acidity as indicated by the ionization constant and the increase of bactericidal value as obtained from the phenol coefficient. Sixteen of the nineteen possible chlorophenols have been examined in an investigation into the relationship between chemical structure and germicidal activity[31]. From this it emerged that activity increased progressively to the trichloro derivatives, but decreased in the tetra- and penta-chloro series. The only reason advanced for the decrease was the limited solubilities of the compounds and higher *p*H values required for the solution.

EXPERIMENTAL

Materials. 1. Tar acid (boiling range 125 to 140°C. at 5 to 5·5 in. Hg, mainly a xylenol-cut fraction) was obtained by alkali extraction of l.t. tar oil followed by fractionation in a 80 lb. per batch capacity stainless steel unit. 2. Chlorine from commercial gas cylinders supplied by Messrs Mettur Chemicals Ltd., Mettur.

Procedure. Chlorine was passed through 500 g. of the tar acid fraction contained in a one litre, 4-necked glass flask, at a fairly constant rate at room temperature (30±1°C.) without any catalyst. Chlorine was passed through a sulphuric acid bubbler, a manometer and finally into the reaction flask. Excess chlorine along with the hydrogen chloride gas produced in the reaction was allowed to escape through a bubbler. In industrial practice excess chlorine after removal of the hydrogen chloride gas by absorption is compressed and reused. A stirrer was used continuously throughout the experiment and the gain in weight due to absorption of chlorine was recorded every two hours.

Five samples containing different per cent of chlorine were collected during the experiment. The samples were thoroughly washed with water to remove free HCl and Cl_2 and dried using ether as solvent. All these samples were studied for specific gravity, refractive index and colour of their emulsions.

RESULTS AND DISCUSSION

There was practically no further increase in weight after passing chlorine for 28 hr. If the increase in weight is assumed to be due to absorption of chlorine alone, the final product contained 59·47 per cent by weight of chlorine. The analyses of the different samples are given in Table 1.

Chlorinated samples 2, 3 and 4 were dark in colour, particularly No. 3, which had a dark magneta colour. The colour improved considerably with increase in chlorine content, the final sample No. 6 having only light orange colour. Towards the end of the reaction the quantity of excess chlorine increased and may have exerted bleaching action resulting in the light colour of the product. The emulsions from all the six samples gained colour after keeping for 24 hr. Maximum colour was again observed for sample No. 3 followed by 2. Raw tar acid fraction gave minimum colour to the emulsion.

Sample with 44 per cent by wt of chlorine deposited needle-shaped crystals. The crystals were washed, and recrystallized. The melting point of the crystals had a wide range of 70° to 92°C , the major portion melting between 88° and 92°C., and indicated mixed chlorinated tar acid products.

TABLE 1—ANALYSES OF THE CHLORINATED TAR ACIDS

No.	DETAILS OF SAMPLE	Cl_2 CONTENT (calculated) % by wt	SP. GR. 30°C	REFRACTIVE INDEX 30°C
1.	Tar acids fraction	..	1 003	1 529
2.	Chlorinated tar acid	10 07	1 047	*
3.	do	20 07	1 147	*
4.	do	44 73	1 396	*
5.	do	55 24	1 494	1 5653
6.	do	59 47	1 521	1·5583

*—Could not be determined due to dark colour of the product

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Infrared & Ultraviolet Spectra of Chlorinated Tar Acids

SAJID HUSAIN & R VAIDYESWARAN
Regional Research Laboratory, Hyderabad 9

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Ultraviolet and infrared spectra of some chlorinated tar acids are reported and their possible use in the identification of these compounds is suggested.

A NUMBER of methods for the analysis of isomeric cresols and xylenols have been reported in literature[1-6]. Both ultraviolet[7] and infrared[8,9] methods have earlier been employed for the identification of chlorinated *o*-cresols. In the present communication ultraviolet and infrared spectra of some pure chlorinated phenols and their utility in identification and estimation of the individual compounds are reported.

4-Chloro-3-methylphenol, 4-chloro-3,5-dimethylphenol and 2,4-dichloro-3,5-dimethylphenol were obtained from Robert Haldane & Co. Ltd, Paisley. 6-Chloro-2-methylphenol, 4-chloro-2-methylphenol, 6-chloro-3-methylphenol, 4,6-dichloro-2-methylphenol, 4,6-dichloro-3-methylphenol, 2,4,6-trichloro-3-methylphenol, 6-chloro-3,4-dimethylphenol and 2,6-dichloro-3,4-dimethylphenol were obtained from Coalite & Chemical Products Ltd, Bolsover, and 4-chloro-2,3-dimethylphenol, 4-chloro-2,6-dimethylphenol, 4-chloro-5-methyl-3-ethylphenol and 2,4-dichloro-5-methyl-3-ethylphenol were supplied by Aldrich Chemical Co Inc., Wisconsin. These compounds were chromatographically pure.

Ultraviolet spectra were determined in spectral grade cyclohexane using a Beckman model DU spectrophotometer while infrared spectra were recorded as nujol mull on a Perkin-Elmer 221 spectrophotometer having sodium chloride optics.

Ultraviolet spectra — The absorption maxima and the molar extinction coefficient of the individual compounds are given in Table 1.

Cresols and xylenols[10], with the exception of *p*-cresol, exhibit absorption maxima at two different wavelengths. Their chloro derivatives also behave similarly. Cresols and chlorocresols, for example, have their absorption maxima at 273 and 279 mμ and 280 and 290 mμ respectively, with the exception of 6-chloro-2-methylphenol, which gives absorption maxima at 273 and 278 mμ (Table 1). In monochlorocresols, an isomer with the chlorine atom in the vicinity of the hydroxyl group absorbs at a lower wavelength. Also, with an increase in the number of chlorine atoms in the molecule, the absorption maxima shift to a longer wavelength (Table 1).

In the case of chloroxylenols the maximum absorption is exhibited at 280 and 290 mμ. The xylenols have also shown bathochromic shift on chlorination. However, in the case of 4-chloro-2,3-dimethylphenol and 2,4-dichloro-3,5-dimethylphenol the presence of an additional absorption band at about 285 mμ is also indicated. Introduction of a second chlorine atom in xylenols only slightly affects the absorption maxima. Similar conclusions can be drawn from the ultraviolet spectra of the chlorinated 5-methyl 3-ethylphenol (Table 1).

TABLE 1 — INFRARED AND ULTRAVIOLET SPECTRA OF CHLORINATED TAR ACIDS

Substituted phenol	Ultraviolet spectral data		Infrared spectral data	
	λ_{max} mμ	ε	New bands due to introduction of chlorine μ	Key bands μ
4 Chloro 2 methyl	281	1643	12.3	12.3
	288.5	1425	12.43 (m)	12.4
6 Chloro 2 methyl	273	1840	8.82 (s)	8.82
	278	1995	12.17 (w)	
4 Chloro 3 methyl	280.5	2120	8.82 (w)	12.35
	281			
	288.5	1898	10.55 (m)	
			12.35 (s)	
6 Chloro 3 methyl	277.5	2058	8.83 (w)	12.6
	283.5	2238	12.6 (m)	
4 6 Dichloro 2 methyl	282.5	2283	11.5 (m)	13.7
	290	2287	13.7 (s)	
			14.0 (s)	
4 6 Dichloro 3 methyl	284	3144	11.5 (s)	11.5
•	284.5			
	292.5	3112	13.7 (m)	
			14.45 (s)	
2 4 6 Trichloro 3 methyl	286	2739	8.85 (vw)	14.75
	295	2991	14.0 (w)	
			14.75 (s)	
4 Chloro 2 3 dimethyl	279.5	2334	12.0 (w)	12.45
	284	2228	12.45 (s)	
	289	2280		
4 Chloro 2 5 dimethyl	282	4440	12.65 (s)	12.65
	289	4112		
4 Chloro 2 6 dimethyl	279.5	1716	11.3 (w)	11.57
	287.5	1657	11.57 (s)	13.9
			11.7 (s)	
			13.9 (s)	
6 Chloro 3 4 dimethyl	282	3238	12.7 (m)	12.7
	288	3238		
4 Chloro 3 5 dimethyl	279	2096	9.4 (m)	14.3
	287	2077	14.3 (s)	
2 6 Dichloro 3 4 dimethyl	281.5	2421	13.95 (w)	14.7
	290	2731	14.7 (s)	
2 4 Dichloro 3 5 dimethyl	281.5	2460	9.3 (w)	14.15
	286	2460	9.55 (w)	
	290	2610	10.05 (w)	
			14.15 (s)	
4 Chloro 5 methyl 3 ethyl	279.5	2360	11.65 (s)	11.65
	286.5	2310	13.9 (w)	
2 4 Dichloro 5 methyl 3 ethyl	281.5	2267	12.5 (s)	12.5
	289.5	2410		

s, strong; m, medium; w, weak; and vw, very weak

Since the absorption maxima in almost all the chlorinated phenols lie in a short region, their use in the identification of compounds should be limited. On the other hand the differences in the ε values are often appreciable enough to permit the detection and analysis of individual compounds. Thus, 6-chloro-2-methylphenol has a much higher molar extinction coefficient than 4-chloro-2-methylphenol (Table 1). Similarly, ε value of the second band of 6-chloro-3-methylphenol is much higher than that of the 4-chloro-3-methylphenol. Also, the dichloro derivatives in both *o*- and *m*-cresols show much higher ε values. In the case of chloroxylenols, however, further data are required to draw general conclusions. Ultraviolet spectroscopy could nevertheless be of great use as a complementary technique in the identification of the individual compounds.

These spectra have been determined in various dilutions and are found to follow Beer's law. This may be of advantage in quantitative estimation of various isomers.

Infrared spectra — The infrared spectra of all the chlorinated phenols were compared with those of the respective parent phenol. The new bands observed in each case as also the characteristic bands of the particular compounds are recorded in Table 1. The additional bands due to C-Cl stretching vibrations are generally observed from 8.5 to 9.5 and 11.5 to 15.0 μ. A definite strong band could be assigned to individual compounds which can be used for its identification and estimation.

Our thanks are due to Messrs Robert Haldane & Co, Paisley, UK and Coalite & Chemical Products Ltd, Bolsover, UK for free samples of the compounds. Thanks are also due to Shri V. Kumar of the Osmania University for help in recording the infrared spectra and Dr G. S. Sidhu, Director for his keen interest.

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Separation of chlorinated cresols and chlorinated xylenols by paper chromatography

This work arose out of studies on the chlorination of tar acids from low temperature tars Paper chromatography has been applied to the separation and identification of isomeric cresols[1], xylenols[2], chlorophenols[3] and chlorocresols[4] Successful separation of chlorocresols and chloroxylenols in mixtures is now reported

Materials

Whatman No 1 (16 × 9 in) filter was impregnated with methanol–formamide solution (30 100, v/v) and dried at room temperature for 15–30 min Solutions (0 5–1 %) of each compound in acetone were spotted with a fine glass capillary (10–20 µg) Three solvent systems were used

(A) Petroleum ether (80–100°) saturated with formic acid

(B) Xylene saturated with formamide

(C) The organic layer from a mixture of benzene–acetic acid–water (2 2 1 v/v)

The chlorocresols and chloroxylenols used for separation were chromatographically pure and obtained from Coalite and Chemical Products Ltd , Bolsover and Aldrich Chemical Company Inc , Wisconsin

Detection of the spots Phosphotungstomolybdic acid (Folin Denis reagent) was sprayed on the developed chromatogram When exposed to ammonia, blue spots resulted

TABLE I

R_F VALUES OF DIFFERENT CHLORINATED CRESOLS AND CHLORINATED XYLENOLS

Temperature of chromatography, 20 ± 2° Time of run for all solvent systems, *ca* 2 5 h

No	*Compounds*	*R_F values (× 100) in various solvent systems*			*Mixtures of phenols (indicated as their No in column 1)*
		A	*B*	*C*	
1	*o* Cresol	8	50	50	
2	6-Chloro *o* cresol	88	89	92	
3	4 Chloro-*o* cresol	19	66	66	1–4
4	4,6-Dichloro *o* cresol	86	91	93	
5	*m*-Cresol	5	34	42	
6	6 Chloro *m* cresol	70	73	76	
7	4-Chloro *m*-cresol	10	55	59	
8	4,6 Dichloro *m* cresol	62	84	84	5–9
9	2,4 6-Trichloro-*m* cresol	73	90	94	
10	2 3-Dimethylphenol	20	62	67	
11	4-Chloro 2,3-dimethylphenol	26	73	79	10 and 11
12	2,5-Dimethylphenol	25	60	76	
13	4-Chloro-2,5-dimethylphenol	34	76	86	12 and 13
14	3,4-Dimethylphenol	8	44	56	
15	6 Chloro 3,4-dimethylphenol	64	79	85	14–16
16	2,6-Dichloro-3,4-dimethylphenol	79	92	94	
17	3,5-Dimethylphenol	11	59	63	17–19
18	4-Chloro-3,5-dimethylphenol	25	72	76	
19	2,4-Dichloro-3,5-dimethylphenol	78	91	92	
20	5-Ethyl-3 methylphenol	30	70	76	
21	4 Chloro 5-ethyl-3-methylphenol	34	81	89	20–22
22	2 4 Dichloro 5-ethyl-3-methylphenol	86	92	93	

Results and discussion

Table I lists the R_F values of the chlorocresols and chloroxylenols. The spots were free of tailing. 6-Chloro-*o*-cresol could not be separated from 4,6-dichloro-*o*-cresol with any of the solvent systems tried. Low R_F values were exhibited in solvent system A which has the lowest polarity R_F values in solvents B and C were about the same. Generally the R_F values increased with increasing substitution in the nucleus; 6-chloro-*o*-cresol and 6-chloro-*m*-cresol showed comparatively high R_F values in solvent A The R_F values for *o*-substituted compounds are higher than for the corresponding *m*-isomer, a result perhaps of the *ortho* effect[5] Thus the $R_F \times 100$ values in solvent B were: *m*-cresol 34, *o*-cresol 50, 4-chloro-*m*-cresol 55, 6-chloro-*o*-cresol 73, 3,4-dimethylphenol 44, 6-chloro-3,4-dimethylphenol 79 The effect is more pronounced in the 2,6-disubstituted products as seen in the $R_F \times 100$ values for 4-chloro-*o*-cresol 66, 6-chloro-*o*-cresol 89, 6-chloro 3,4-dimethylphenol 79, and 2,6-dichloro-3,4-dimethylphenol 92. In these disubstituted products the relative order was generally maintained in all the three solvent systems.

Regional Research Laboratory, Hyderabad (India) SAJID HUSAIN

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Separation of chlorinated cresols and chlorinated xylenols by thin-layer chromatography

The separation of tar acids by thin-layer chromatography (TLC) has been described recently[1-3]. This paper describes the separation of chlorocresols and chloroxylenols by TLC and its usefulness in following the progress of chlorination of these tar acids. The paper chromatographic separation of these compounds has been reported earlier[4].

Materials and methods

The chlorocresols and chloroxylenols used for the separations were obtained from commercial sources[5].

Using a thin-layer applicator (Desaga, Heidelberg), glass plates (20 × 20 cm) were coated as usual with a well stirred suspension of silica gel G (E. Merck, Darmstadt; 30 g in 60 ml water) to give a layer approximately 270 μ in thickness. The plates were dried at 105–110° for 30 min and preserved in a desiccator. The compounds were dissolved in acetone and about 10 μg was applied with a glass capillary on starting points 2–3 cm from the edge of the plate. The plate was then placed inside the chamber for development. Three solvent systems, A, B and C, were used:

(A) Petroleum ether (80–100°) saturated with formic acid.
(B) Xylene saturated with formamide.
(C) The organic layer from a mixture of benzene–acetic acid–water (2:2:1, v/v)

About 40–60 min were taken for the solvent front to cover a distance of 15 cm The plates were then sprayed with phosphotungstomolybdic acid (Folin-Denis reagent) and exposed to ammonia, which revealed the compounds as blue spots on a white background.

Results and discussion

Table I lists the R_F values of the chlorocresols and chloroxylenols in the three solvent systems, and gives the composition of the mixtures spotted. Fig. 1 shows the separation of these mixtures of chlorocresols and chloroxylenols using solvent B, which gave the best separations. Resolution of *p*-chlorocresols from parent cresols and of 6-chloro-2-methylphenol from 4,6-dichloro-2-methylphenol could not be achieved with any of the solvent systems tried.

Generally the R_F values increased with increasing substitution in the nucleus, an exception being 4,6-dichloro-3-methylphenol in solvent system B. The R_F values for *o*-substituted compounds were higher than for the corresponding *m*-isomer, probably due to the *ortho* effect[6]. Thus $R_F \times 100$ values in solvent B were: *m*-cresol = 26, *o*-cresol = 32, 4-chloro-3-methylphenol = 25, 6-chloro-2-methylphenol = 72, 3,4-dimethylphenol = 21, and 6-chloro-3,4-dimethylphenol = 44. The effect was more pronounced in the 2,6-disubstituted products, as seen in the $R_F \times 100$ values for: 4-chloro-2-methylphenol = 31, 6-chloro-2-methylphenol = 72, 6-chloro-3,4-dimethylphenol = 44, and 2,6-dichloro-3,4-dimethyl-phenol = 58. In disubstituted products this relative order was followed in all the solvent systems.

The technique was tried in following the progress of chlorination of 2,5-dimethylphenol in carbon tetrachloride with gaseous chlorine at 20 ± 2°. Samples withdrawn every 30 min were spotted. Fig. 2 reveals that 4-chloro-2,5-dimethylphenol is the

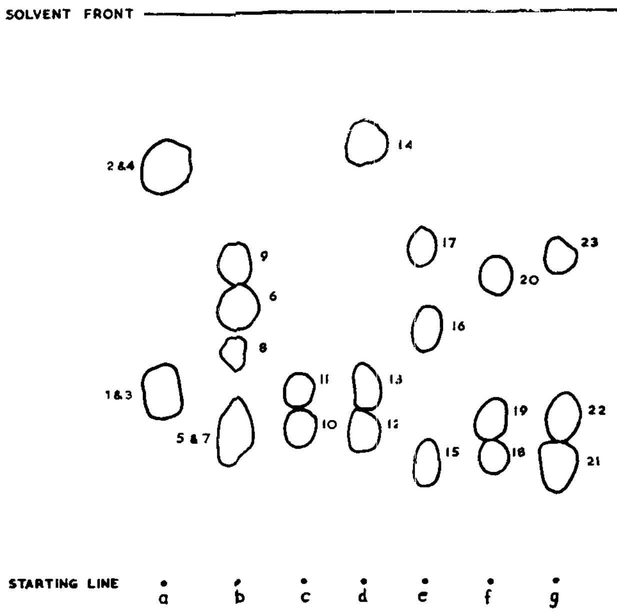

Fig. 1. Separation of chlorocresol and chloroxylenol mixtures. For the constituents of the mixtures a–g see Table I.

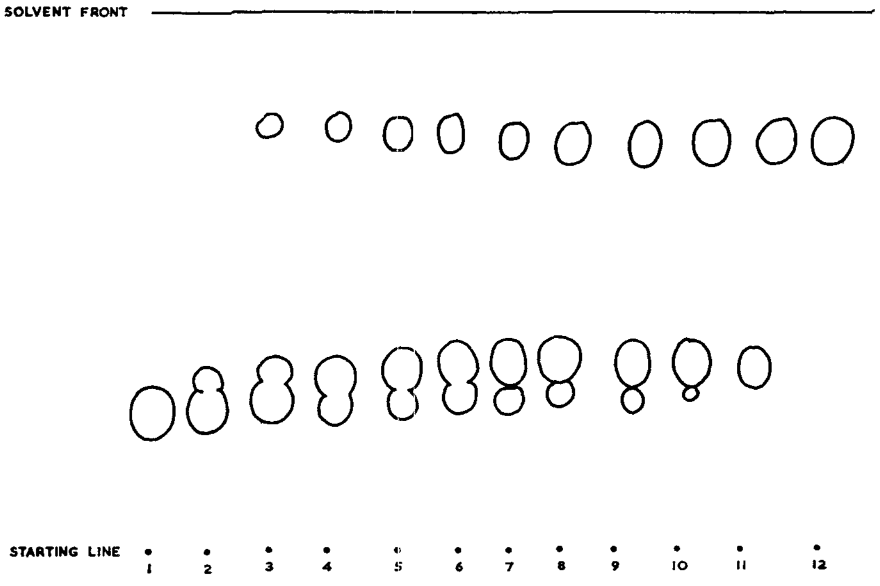

Fig. 2. Separation of chlorinated 2,5-xylenol samples withdrawn every 30 min

TABLE I

R_F VALUES OF DIFFERENT CHLORINATED CRESOLS AND CHLORINATED XYLENOLS

Temperature of chromatography: 25 ± 3°.
Time of run for all solvent systems: 40–60 min.

Sl. No.	*Compounds*	*R_F values × 100 in various solvent systems*			*Phenol mixtures*	
		A	*B*	*C*	*Sl Nos.*	*Code in Fig. 1*
1	2-Methylphenol	11	32	67	1 to 4	a
2	6-Chloro-2-methylphenol	58	72	89		
3	4-Chloro-2-methylphenol	06	31	65		
4	4,6-Dichloro-2-methylphenol	39	74	89		
5	3-Methylphenol	09	26	63	5 to 9	b
6	6-Chloro-3-methylphenol	55	47	89		
7	4-Chloro-3-methylphenol	12	25	63		
8	4,6-Dichloro-3-methylphenol	55	40	83		
9	2,4,6-Trichloro-3-methylphenol	66	56	89		
10	2,3-Dimethylphenol	12	26	71	10 and 11	c
11	4-Chloro-2,3-dimethylphenol	12	31	71		
12	2,5-Dimethylphenol	10	25	71	12 to 14	d
13	4-Chloro-2,5-dimethylphenol	10	31	71		
14	4,6-Dichloro-2,5-dimethylphenol	59	76	89		
15	3,4-Dimethylphenol	09	21	71	15 to 17	e
16	6-Chloro-3,4-dimethylphenol	43	44	88		
17	2,6-Dichloro-3,4-dimethylphenol	49	58	91		
18	3,5-Dimethylphenol	05	22	65	18 to 20	f
19	4-Chloro-3,5-dimethylphenol	22	28	65		
20	2,4-Dichloro-3,5-dimethylphenol	35	53	85		
21	5-Ethyl-3-methylphenol	04	22	66	21 to 23	g
22	4-Chloro-5-ethyl-3-methylphenol	04	27	66		
23	2,4-Dichloro-5-ethyl-3-methylphenol	35	56	84		

primary product of reaction. The dichloro (4,6) product appears only after one hour of chlorination. After 5 h, 2,5-dimethylphenol was totally converted to the mono- and dichloro-derivative. Half an hour later the monochloro-2,5-dimethylphenol was completely eliminated and only the dichloro-derivative was present.

Conclusions

In this study on the separation of chlorocresols and chloroxylenols by thin-layer chromatography xylene saturated with formamide appeared to be the best solvent system Resolution of *p*-chlorocresols from the parent cresols and of 6-chloro-2-methylphenol from 4,6-dichloro-2-methylphenol could not be achieved

The application of TLC technique as an analytical tool in following the extent of chlorination is suggested

Regional Research Laboratory, Hyderabad (India) SAJID HUSAIN

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