I

SOME ASPECTS OF THE CHEMISTRY OF SULPHUR DYES AND OTHER SULPHUR COMPOUNDS

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C O N T E N T S

P A R T - 1

CONSTITUTION OF CIBANONE ORANGE R

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INTRODUCTION

The sulphurized vat dyes constitute a small but important group of dyes occupying an intermediate position between the vat dyes and the sulphur dyes. They are distinguished from the former by their inferior fastness properties and the fact that addition of sodium sulphide is advantageous at times in preparing vats with alkaline hydrosulphite, and from the latter by their greater fastness, insolubility or sparing solubility in sodium sulphide and by their being dyed from an alkaline hydrosulphite vat. The sulphurized vat dyes have a more definite constitution than the sulphide dyes. The great technical value of sulphur dyes is due to their low cost and high order of fastness, except to chlorine, which is improved in case of sulphurized vat dyes.

The sulphur and sulphurized vat dyes are generally prepared by heating organic intermediates with sulphur, sodium sulphide or polysulphide - the procedure is called 'thionation'. Most organic compounds are capable of forming these dyes by thionation (sulphurisation) under appropriate conditions, but a limited number of well defined intermediates are used for the preparation of technically useful dyes.

Condition of thionation

The conditions of a thionation process have to be carefully specified and controlled, since the same intermediate can give dyes having a variety of shades in accordance with the relative proportions of sodium sulphide and sulphur, solvent, if any, temperature, use of pressure and addition of metallic salts. Other treatments like oxidation brings further alteration in shade. In general with more vigorous conditions of sulphurization dyes having deeper shades are produced, because the size of the molecule increases continuously due to the further addition of sulphur atoms and the formation of sulphur containing ring systems. In general manufacturing processes, intermediates of high purity and standard set of operating procedures are employed to obtain a uniform product of reproducible quality. Sodium polysulphide is the main thionating agent prepared by heating sodium sulphide and sulphur, but sulphur alone is also used for some dyes. Manufacturing methods fall into two distinct classes: (1) dry heating or baking (200-350^{o}); and (2) heating the reactants in solution. Addition of certain metal salts have been suggested in order to modify the shades or to assist the reaction in other ways. The temperature of thionation is a vital factor which controls the yield and shade of the final product.

In spite of the standard thionation process used for preparing homogeneous dyes with specific dyeing properties, the nature of the thionation process shows that a sulphur dye is likely to be a mixture of compounds varying in molecular size, sulphur content and other properties.

It has been mentioned earlier that sulphurised vat dyes occupy an intermediate position between vat dyes and the sulphur dyes and that they are dyes of complex, but more definite constitution than the sulphide dyes. The probable structure of a few sulphurised vat dyes have been elucidated.

Sulphurised vat dyes are classified as follows:

(a) Sulphurised indophenol derivatives prepared by thionation of indophenols with sodium polysulphide in alcoholic solvent. This series include important dyes of the 'Hydron Blue' series.

(b) Sulphurised anthracene and anthraquinone derivatives are prepared by baking processes in which the intermediates are heated with excess (4-5 times by weight of elemental sulphur.

(c) Dyes prepared by thionation of arylaminobenzoquinones.

The chemistry of sulphur and sulphurised vat dyes has been fully discussed by Venkataraman.[1] Only the work on sulphurised vat dyes derived from 2-methyl anthraquinone

and its derivatives is briefly referred to now because of its bearing on the present work.

Cibanone Orange R (CI 1169) and Cibanone Yellow R (CI 1170) (CIBA, Mayer and Schaarsmidt, 1908)[2] are sulphurised vat dyes obtained by thionation of 2-methylanthraquinone or its halogen derivatives in which chlorine or bromine substitutes in the 1- or 3-position or in the methyl group. The intermediates cited in the patents are: 2-methylanthraquinone, 1-chloro-2-methylanthraquinone, 2-chloromethylanthraquinone, 2-dichloromethylanthraquinone, 1-chloro-2-chloromethylanthraquinone, 1-chloro-2-dichloromethylanthraquinone, 3-chloro-2-methylanthraquinone, 3-chloro-2-chloromethylanthraquinone and 3-chloro-2-dichloromethylanthraquinone. Mixtures containing 2-chloromethyl- and 2-dichloromethylanthraquinones obtained by the chlorination of a mixture containing 1-chloro- and 3-chloro-2-methylanthraquinone have also been mentioned.

The thionation procedure consists in heating any one of the above mentioned intermediates (or sometimes a mixture formed during chlorination) with a large excess (4-5 times by weight) of sulphur at temperatures of the order of 222-330° for 3-4 hours, cooling and extracting the mixture with aqueous sodium sulphide or carbondisulphide which removes unreacted sulphur and a solvent like pyridine which removes unreacted intermediate and then dissolving the residue in concentrated sulphuric acid (heating is mentioned in some cases), precipitating the dye, washing it free from acid and finally treating

the product with alkaline sodium hypochlorite at 80-85° to get the dyessuitable for marketing. The temperature of thionation is higher (300°-330°) in case of Cibanone Orange R and lower in case of Cibanone Yellow R (220-300°) and hence it is probable that both the dyes are related to each other in their chemical constitution and the former is probably derived from the latter by further thionation. The thionation process, as in the case of sulphur dyes, probably leads to a mixture of products.

Cibanone Yellow R and Orange R dye bright attractive shades with excellent fastness to chlorine, the light fastness grade[2] is only 4 for Yellow R, but 6-7 for Orange R. Both these dyes have been withdrawn from the commercial range of Cibanone colours because of their tendering action on cellulose when the dyed material is exposed to light. Cibanone Yellow R is the most active tenderer and ranks first in the actinic degradation of cotton, the next tenderer being Cibanone Orange R. A dye like Caledon Jade Green having excellent fastness to light fades rapidly on exposure to light when dyed in admixture with either of these dyes.

The constitution of Cibanone Yellow R and Cibanone Orange R was first examined by Fierz-David and Geering.[5] The commercial dyes were extracted with hot water to remove inorganic salts and then extracted with alcohol, when 2-methylanthraquinone was isolated from the extracts of both of the dyes. Fierz-David and Geering[5] concluded that Cibanone Orange R is related to

Cibanone Yellow R in the same way as Primuline is related to dehydrothiotoluidine. Cibanone Yellow R was assigned to structure (I), but a specific structure for Cibanone Orange R was not formulated. However, the analytical values obtained by Fierz-David suggest the empirical formula, $C_{15}H_6O_2S$, for Cibanone Orange R. Without citing any evidence or reference, Moren and Stonehill,[5] have assigned structure (I) to Cibanone Orange R and given its absorption spectrum in ethanol.

Schaarschmidt and Lewyoff[7] analysed Cibanone Orange R crystallised from nitrobenzene and found that the dye (m.p. 500°) contained one atom of sulphur per mole of 2-methylanthraquinone. From a study of oxidation reduction potentials, Atherton and Turner[8] showed that Cibanone Orange R contained two pairs of carbonyl groups and had molecular weight 513. This is very improbable knowing that the compound contains only C, H, O and S. The latter was determined by catalytic reduction of the commercial dye, reoxidation of the leuco compound and determination of the hydrogen peroxide formed.

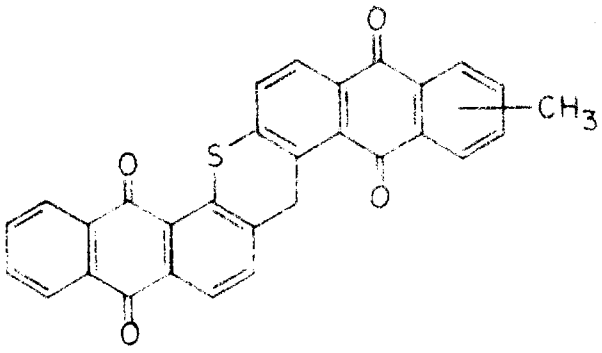
THe constitution of both the dyes was re-examined by Shah et al.[9,9a] and Chandavarkar.[9a,10] The elemental analysis of Cibanone Orange R after purification according to Fierz-David extraction with acetylene tetrachloride and two crystallisation from nitrobenzene was in agreement with the empirical formula, $C_{15}H_6O_2S$. The acetylene tetrachloride extract gave 10% of Cibanone Yellow R when chromatographed on alumina, so that neither Fierz-David and Geering nor Atherton and Turner were

dealing with a homogeneous dye. Clar reduction[9,11] of Cibanone Orange R or β,β'-dianthraquinonyl-ethylene (Anthraflavone) gave 2-methylanthracene, and oxidation of either dye with nitric acid in acetic acid,[10] gave anthraquinone-2-carboxylic acid. Structure (I) was, therefore, considered improbable since it should have led to 1-methylanthracene and anthraquinone-1-carboxylic acid, together with the 2-substituted products. Cibanone Orange R would appear to contain an anthraflavone skeleton. The structure (II) and (III) was therefore proposed.

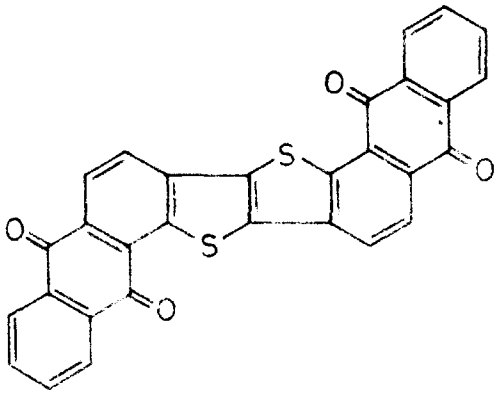
Bhavsar[11] reinvestigated the constitution of Cibanone Orange R, first by confirming the empirical formula to be $C_{15}H_6O_2S$, given by earlier workers. The emperical formula indicated one methylanthraquinone residue per atom of sulphur. The dye therefore could be represented by either of the three possible thiophthene structures(II) (angular), (III) (linear) and (IV) (partly linear and partly angular). Bhavsar prepared compounds (II) and (III) by thionation of 1-bromo-2-bromo methyl anthraquinone and 3-bromo-2-bromomethyl anthraquinone respectively, and compared the products with purified Cibanone Orange R. The constitution of the products (II) and (III) followed from the analogous formation of dibenzthiophthens (VI) by thionation of O-chloro or O-bromobenzyl bromide.[12] By comparing colour, crystalline nature, colour of the sulphuric acid solution, absorption spectrum in sulphuric acid, colour of the vat, and the shades obtained on cotton of twice crystallised Cibanone

Orange R with compound (II) and (II), she assigned structure (III) to the main tinctorial constituent of Cibanone Orange R. She tried to synthesise (III) by condensation of dibenzthiophthene(VI) with phthallic anhydride in an aluminium chloride-sodium chloride melt, but the product was found to be a mixture of several possible isomers. An unsuccessful attempt was made by her to synthesise (II) and (III) by the action of phosphorous pentoxide and tetralin on dicarboxy-dianthraquinonyl disulphides. Attempts to elucidate the constitution of Cibanone Orange R by Raney nickel desulphurization and alkali fusion proved inconclusive.

Recently Manjrekar[13] has obtained the tinctorial constituent of the dye in a purer form by preparing the tetramethyl ether of the dye and chromatographing the crude tetramethyl ether through a short column of silica gel. The parent dye was generated by precipitating the tetramethyl ether from sulphuric acid. The dye so obtained was crystallised from nitrobenzene in orange needles. Based on the elemental analysis and its molecular weight obtained from the mass spectrum, the molecular formula of the dye has been revised to $C_{30}H_{16}O_4S_2$. This is in agreement with the mass spectral molecular weight of the tetramethyl ether (564), tetraacetylated product (676). The parent dye which he regenerated from the tetramethyl ether of the dye also showed the molecular ion at m/e 504. He has recorded the NMR spectrum of tetramethyl ether of the dye in tetramethyl urea and pyridine, and has assigned a symmetrical structure (III) for the dye, which he suggested to be the dimer of anthraquinone-2-thioaldehyde.



(I)



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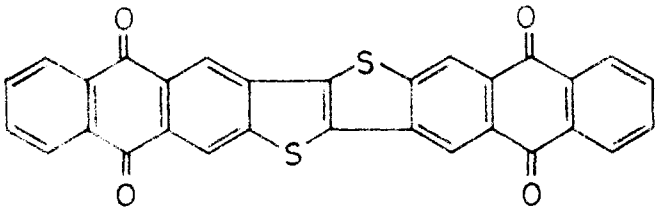

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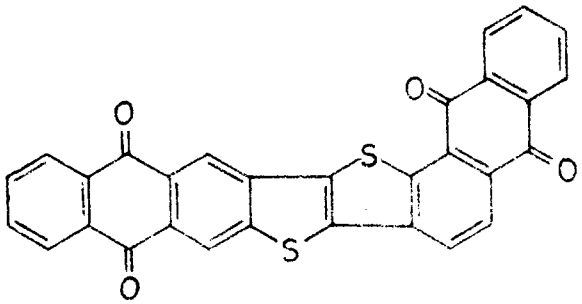

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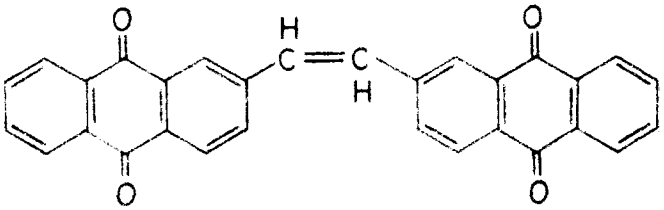

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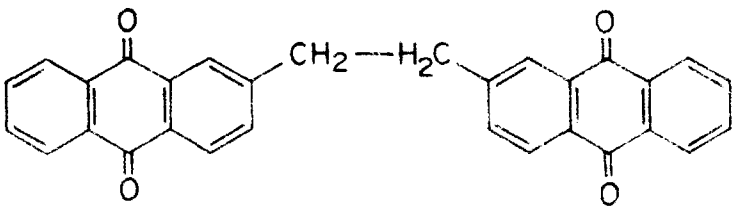
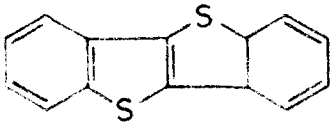


(VA)

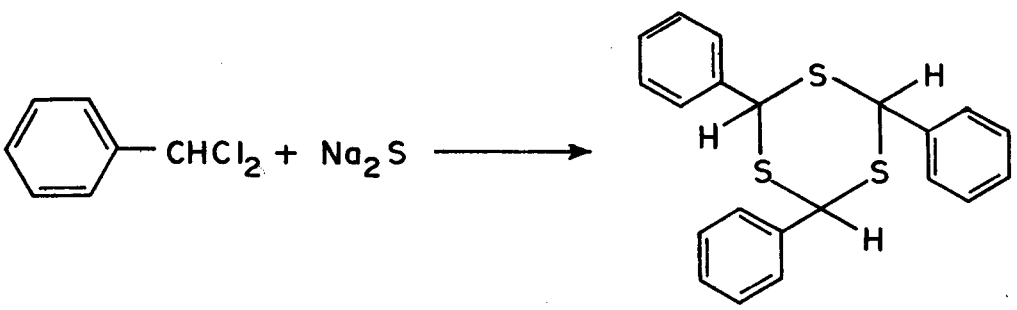


(VI)

PRESENT WORK

In continuation of earlier work, particularly keeping in mind the structure (VII) suggested by Manjrekar,[13] the constitution of Cibanone Orange R has been reinvestigated in the present work. The structure (VII) has been assumed by Manjrekar to be the dimer of anthraquinone-2-thioaldehyde, giving rise to a 1,3-dithiacyclobutane ring system in its molecule. However, no thioaldehyde is known to dimerise to give 1,3-dithiacyclobutane ring. The 9-thioaldehyde of phenanthrene invariably trimerizes to give 1,3,5-trithiane skeleton.[14] The trimerization of all thioaldehydes yet has not found a exception. The idea that anthraquinone-2-thioaldehyde dimerizes because of its bulk cannot be substantiated because of the trimerization of an equally bulkier unit of anthracene-9-thioaldehyde.

In the present study an attempt has been made to synthesise anthraquinone-2-thioaldehyde from ω-dibromo-2-methylanthraquinone and then dimerizing it, following the procedure of converting benzaldichloride to the trimer (VIII), by the action of sodium sulphide.[13]



(VIII)

In the attempts to do so, ω-dibromo-2-methylanthraquinone was prepared under the modified Ullman's condition[37] which necessitated a different molar proportion of bromine and 2-methylanthraquinone in nitrobenzene. ω-Dibromo-2-methylanthraquinone, thus prepared, was refluxed with an equimolar amount of anhydrous sodium sulphide (Na_2S) in solvents like anhydrous acetone, ethanol, dioxane, 2-methoxy ethanol and diglyme, led to a product identical with Cibanone Orange R (elemental analysis and superimposable infrared spectrum). The sample thus obtained by the above method showed the molecular ion ($M^{\cdot+}$) at m/e 504. The yield of the product in the above set of reactions was varying from 9-16% and the rest was a mixture of anthraquinone-2-aldehyde and 2-dibromomethylanthraquinone. Traces of moisture in the reaction mixture did not affect the yield of Cibanone Orange R but anthraquinone-2-aldehyde was obtained depending upon the extent of hydrolysis. For example, when the reaction was carried out in once distilled acetone, Cibanone Orange R was obtained in only 9% yield and anthraquinone-2-aldehyde in 79% yield, but the yield of Cibanone Orange R hardly increased when anhydrous acetone was taken, but anthraquinone-2-aldehyde was obtained in 7% yield.

The product in all these reactions was found to be identical with the commercial Cibanone Orange R and the assumption that anthraquinone-2-thioaldehyde as an intermediate in the reaction between 2-dibromomethylanthraquinone and sodium

sulphide cannot be ruled out with an analogy of the reaction between benzaldichloride and sodium sulphide. Therefore, the dimer of anthraquinone-2-thioaldehyde as to be the possible structure of Cibanone Orange R cannot be neglected, but to assume structure (VII) to Cibanone Orange R is doubtful, because the colour of the product representing structure (VII) should not be deeper than the colour of 2-methylanthraquinone.

In an another attempt to synthesise compound VII, 2-mercaptomethylanthraquinone was oxidised with elemental sulphur in equimolar ratio at 340-350°. Similarly, bis-anthraquinonyl-2-methyl monosulphide (1 mole) was reated with sulphur (2 atoms) at 340-350°. The product resulted from these two reactions, on crystallisation from o-dichlorobenzene, was identical with Cibanone Orange R. Thus their elemental analysis corresponded with the molecular formula, $C_{30}H_{16}O_4S_2$ and showed their $M^{+\cdot}$ at 504. Their IR spectra are also superposable with that of Cibanone Orange R spectrum. Their vats when applied on the cellulose fibre gave an orange shade, comparable to that of commercial Cibanone Orange R.

The probable synthetic routes in all these reactions, i.e. 2-dibromomethylanthraquinone with sodium sulphide, the sulphur fusion reaction of 2-mercaptomethylanthraquinone and of bis-anthraquinonyl-2-methylmonosulphide are same, involving a transient intermediate of anthraquinone-2-thioaldehyde, as shown in Chart 1.

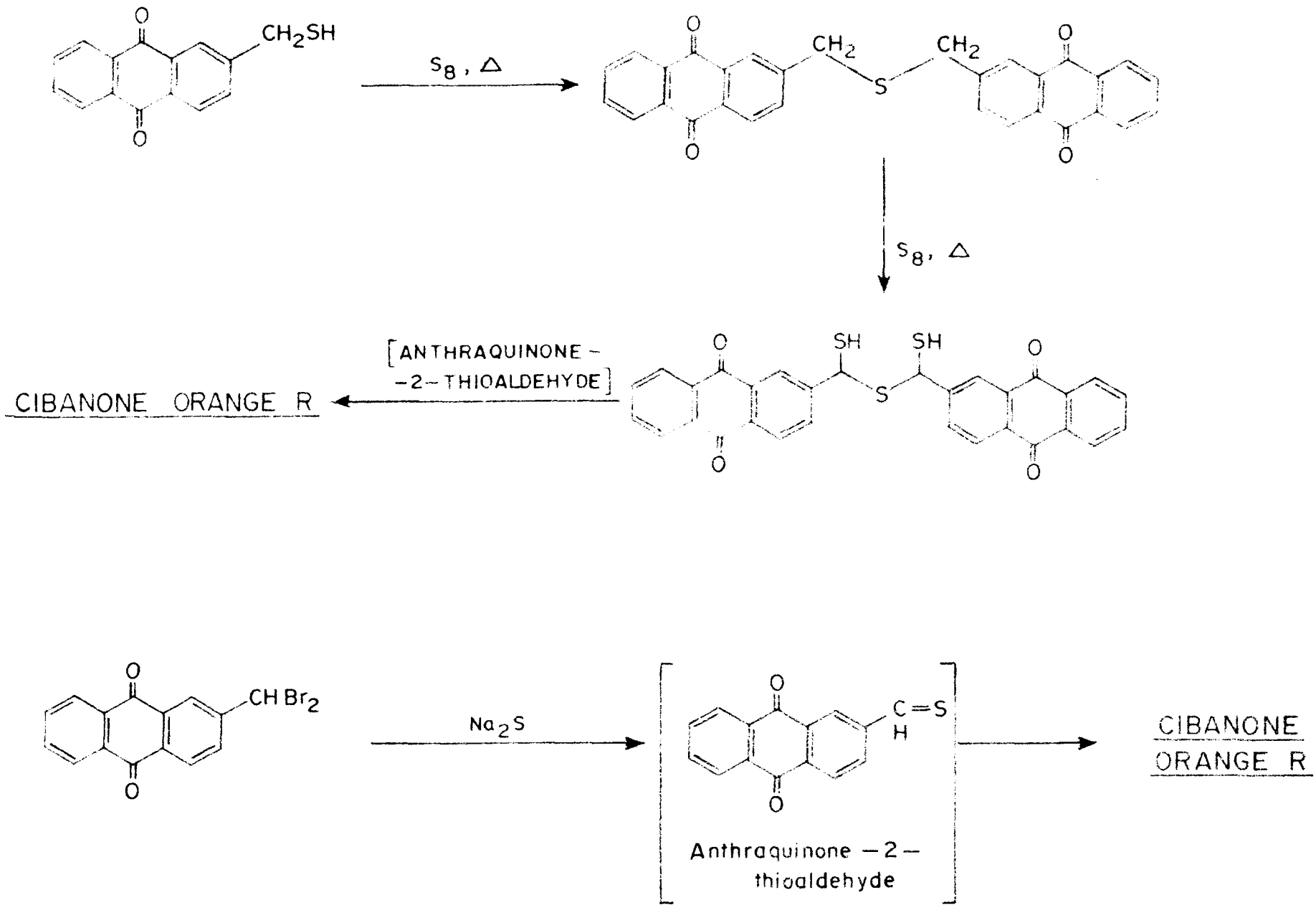
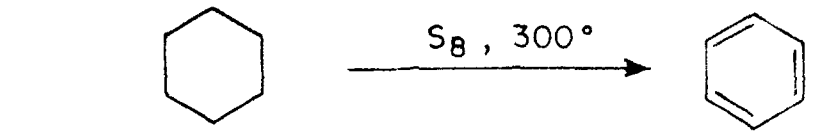
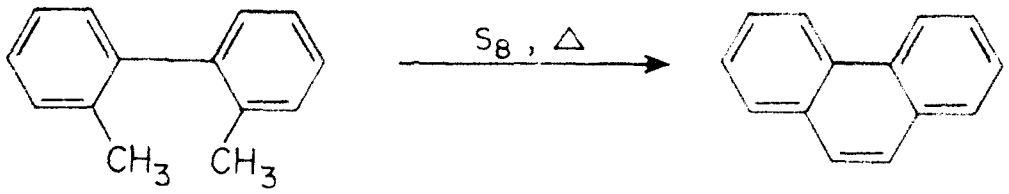

CH2SH
S8, Δ
CH2
CH2
S
S8, Δ
SH
SH
S
[ANTHRAQUINONE – –2–THIOALDEHYDE]
CIBANONE ORANGE R
CHBr2
Na2S
C=S
H
Anthraquinone –2– thioaldehyde
CIBANONE ORANGE R

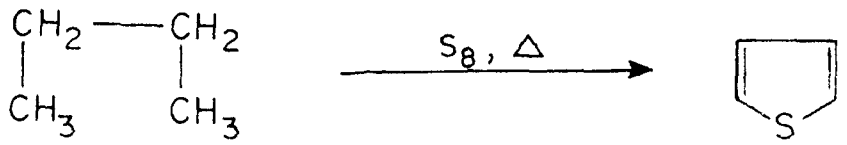
CHART – I

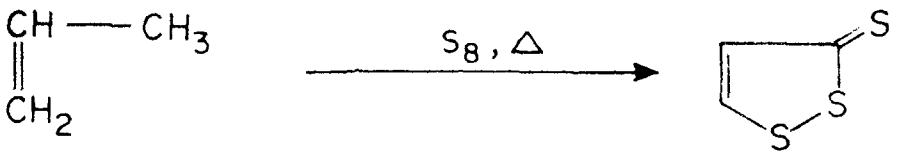
Cibanone Orange R was also synthesised by the sulphur fusion reaction of anthraflavone (V) or dihydroanthraflavone (VA) at 340-350°. Perhaps in the reaction of anthraflavone and sulphur, the sulphur incorporation takes place at the double bond giving rise to anthraquinone-2-thioaldehyde, which further reacts to give Cibanone Orange R and the reaction of dihydroanthraflavone and sulphur follows the same course after the formers conversion to anthraflavone.

Sulphur abstracts hydrogen from organic compounds at 200-300° or above to produce fragments which ultimately give stable products by aromatization, ring formation, or dimerization. Sulphur may become incorporated in the product. The oxidation of the organic substrate is balanced by the reduction of sulphur to hydrogen sulphide (Chart II). The mechanism of these dehydrogenation reactions by sulphur remains speculative. Whether radical species are involved is of particular interest since it arises in all the sulphur reactions. It is known that thiyl and polysulphenyl radicals abstract hydrogen from carbon atoms in facile reactions[15] and these dehydrogenation reactions occur at temperatures where sulphenyl radicals are definitely present in liquid sulphur.[16] The classic analogy of the reaction of peroxide and toluene suggests that the dimerization like (5) involve the coupling of radicals, but the conclusive evidence for radicals has been established in the gas phase dehydrogenation of aliphatic hydrocarbons by sulphur at 320-50°, and the products are unrearranged terminal olefins, typical of radical cracking processes.[17]


S8 , 300°


CH3
CH3
S8 , △


CH2
CH2
CH3
CH3
S8 , △
S


CH
CH3
CH2
S8 , △
S
S
S

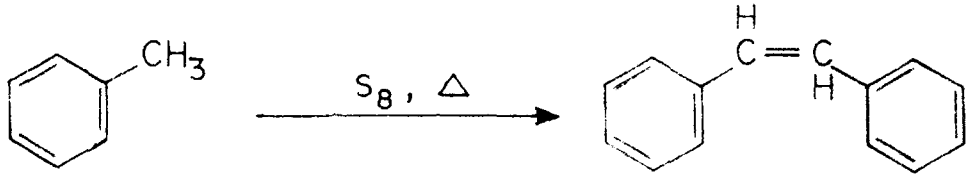

CH3
S8 , △
H
C
C
H

CHART – II

Table 1 shows that dehydrogenations by sulphur are catalyzed by many polar substances. This is most likely because of their ability to open sulphur rings and should not be taken as proof of the ionic nature of the hydrogen abstraction reactions involved.

T A B L E 1

Reaction between S_8 and --	Product	°C	Catalyst	Ref.
Cyclohexanol	Phenol	150	Silicates	18
tetralin	Naphthalene	200	Organic sulphides and polysulphides	19
Tetralin	Naphthalene	200	Amines	20
Dicyclohexyl	Diphenyl	-	Sulphur compounds	22
Tetralin	Naphthalene	140	Na_2S	21
Cumene	4-Phenyl-trithione	150	Guanadines	23
Diphenylmethane	Thiobenzo-phenone	180	Aniline	24
"	"	180	Sulphides and polysulphides	25
Styrene	Diphenyl-thiophene	-	2-Mercapto-benzothiazole	26

The occurrence of dimeric products is consistent with radical reactions, but the absence of dimers does not preclude a radical mechanism. p-Toluic acid dimerizes when heated with sulphur to produce 4,4'-stilbene dicarboxylic acid.[27] In aqueous solution these same reactants produce terephthalic acid.[28] In the latter case, the dimer would not be expected to be stable, even if formed, since ethyl benzene is oxidised to benzoic acid.

When an intimate mixture of 2-methylanthraquinone(1 mole) and elemental sulphur (5 atom) is fused at 350-60° till hydrogen sulphide evolution stops, the only product isolated was Cibanone Orange R, which was crystallised from o-dichlorobenzene. However, when the same reaction was carried out decreasing the 2-methyl anthraquinone and sulphur ratio at a temperature of 300-310°, three other products could be isolated. They were identified as dihydroanthraflavone (VA), anthraflavone (V) and Cibanone Yellow R. The isolation of anthraflavone and dihydroanthraflavone in the sulphur fusion reaction of 2-methylanthraquinone clearly hints at the radical nature of the reaction with an analogy of the sulphur fusion reaction of toluene[28] and p-toluic acid. That the Cibanone Orange R is the final oxidation product in the hydrogen abstraction reaction of 2-methylanthraquinone and sulphur is evident from the fact that Cibanone Orange R remains unaffected on heating a mixture of Cibanone Orange R with excess of sulphur at 360-370°. The chain of hydrogen abstraction reaction proceeds initially by a carbon-carbon single bond

formation, evident from the isolation of dihydroanthraflavone and then carbon-carbon double bond formation by the abstraction of two hydrogens by an atom of sulphur giving rise to anthraflavone. The next step of the fusion reaction is followed by the incorporation of sulphur atom giving anthraquinone-2-thioaldehyde which further reacts to give rise to Cibanone Orange R. Alternatively, a sulphur atom introduction can take place to anthraflavone giving rise to Cibanone Yellow R (described in the next section).

When 2-methylanthraquinone (1 mole) was fused with sulphur (1.2 atom) at 250-70° in a metal bath till hydrogen sulphide evolution stops, only one compound, crystallised from toluene, m.p. 331-33°, was obtained in 80% yield. This was identified as dihydroanthraflavone (M^{+} 442). 2-Methylanthraquinone could be recovered from this reaction only in 10% yield. However, when the fusion reaction was carried out at 300-310° with the same molar proportion of the reactants, dihydroanthraflavone could be obtained in over 50% yield, and anthraflavone (M^{+} 440) was isolated in 23%, the 2-methylanthraquinone could be recovered in 14% yield. Further, when an intimate mixture of 2-methylanthraquinone (1 mole) and sulphur (2.3 atom) was fused at 300-310°, till the evolution of hydrogen sulphide stopped, anthraflavone could be isolated from the reaction mixture in 67% yield, dihydroanthraflavone in 7% yield, and 2-methylanthraquinone, however, could be recovered in 4% yield.

When dihydroanthraflavone (0.1 mole) was thoroughly mixed with sulphur powder (0.13 atom) and fused at 300-310° till hydrogen sulphide evolution stopped, anthraflavone could be isolated from the reaction mixture in 79% yield. Surprisingly no reaction was found to occur (detected by the absence of hydrogen sulphide evolution) below 280°. Cibanone Orange R could be obtained by fusing an intimate mixture of anthraflavone (0.1 mole) and sulphur powder (0.24 atom) at 350-360° in only 32% yield, because of the formation of charred material in the reaction. The reaction between anthraflavone and sulphur to give Cibanone Orange R never took place below 310°. The absence of the reaction was also indicated by the absence of hydrogen sulphide gas evolution.

This becomes quite obvious that the formation of Cibanone Orange R from 2-methylanthraquinone and sulphur fusion does not involve single step. 2-Methylanthraquinone goes through different stages of hydrogen abstraction by the sulphur atom and then finally sulphur incorporation takes place. The stages of this thionation reaction is temperature dependent. For instance, for the dihydroanthraflavone (dimerization stage) and anthraflavone stages the temperature of the reaction should be respectively 270-285° and 300-315°, and for the last stage of the thionation reaction, the temperature is around 350-360°.

Desulphurization of Cibanone Orange R in 15% aqueous sodium hydroxide with Raney nickel (W-4), taken 3 times in excess, gave a sulphur free product which was dissolved in chloroform and

on chromatographing this solution, a major homogeneous ffaction was obtained, by eluting with 10% acetone benzene mixture. A solid crystallised out from benzene, m.p. 248-250°. Elementary analysis suggested it to be decahydroanthraflavone. Anthraflavone under similar conditions with 15% sodium hydroxide and Raney nickel (3-times in excess) gave a product identical with the one obtained in the desulphurization reaction of the dye. The occurrence of decahydroanthraflavone by the desulphurisation of Cibanone Orange R leads to the conclusion that the dye is a sulphurized derivative of anthraflavone.

When Cibanone Orange R was oxidised with nitric acid in glacial acetic acid, only anthraquinone-2-carboxylic acid was obtained in a quantitative yield. No anthraquinone-1-carboxylic acid was obtained. On a similar treatment of nitric acid in glacial acetic acid, anthraflavone gave only anthraquinone-2-carboxylic acid. The occurrence of only anthraquinone-2-carboxylic acid in the oxidation product of Cibanone Orange R provides evidence for the linkage of two anthraquinonyl residues with two sulphurs through the carbon attached at 2-position of the anthraquinone ring.

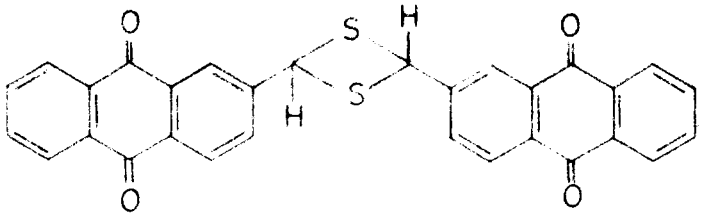
When the purified dye was fused with a mixture of zinc chloride, sodium chloride and zinc dust and gradually heated to 430-440° (clar reduction)[10] and kept at this temperature for 15 minutes - a yellowish red solid sublimed above 340° which gave on resublimation at 320-330°/6 mm., lustrous, colourless flakes, m.p. 200-202°, identified as 2-methylanthracene. Clar reduction

on anthraflavone also gave 2-methylanthracene. So a fission of carbon-sulphur bond in the former carbon-carbon bond in the latter have taken place in this reaction which further substantiates evidence for β,β'-benzalic carbon linkage of the two anthraquinonyl moieties in Cibanone Orange R.

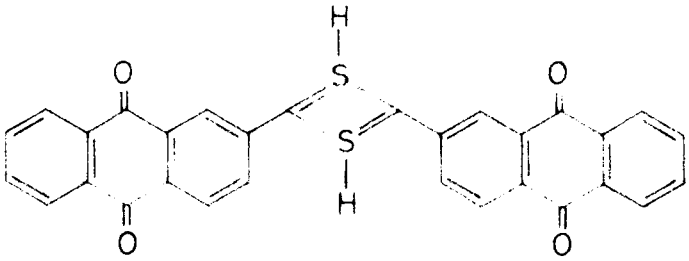
All the above experiments could not rule out the possibility of structure (VII) for Cibanone Orange R, and have not led to any definite structure for this compound, particularly in view of its deeper colour. To explain the colour of Cibanone Orange R, three possible structures (IX), (X) and (XI) were considered in preference to structure (VII). Narasimhan et al.[29] have calculated the resonance energies (β) for these three structures (IX), (X) and (XI) assuming that all of them are planar, an assumption which appears reasonable, and treating these systems in d-orbital framework for sulphur and have obtained the following resonance energies:

	R:E(β)
Structure (IX)	14.46
Structure (X)	14.87
Structure (XI)	13.98

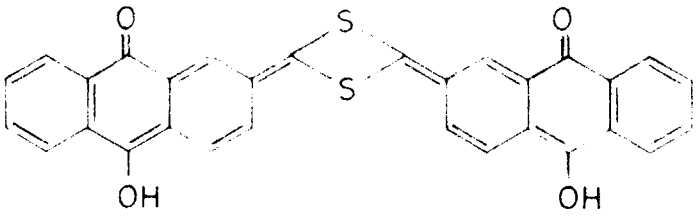
The resonance energies of (IX), (X) and (XI) cannot be directly compared with (VII). Even if one assumes that the 1,3-dithiacyclobutane ring is planar, the two anthraquinone units in (VII) will not be in one plane and hence extended conjugation will not be possible. Obviously the resonance energy of (VII) will be less than that of (IX), (X) and (XI).



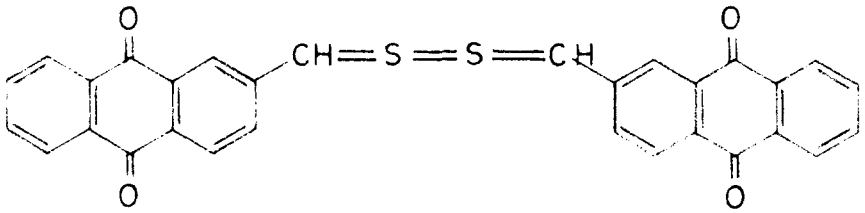
(VII)



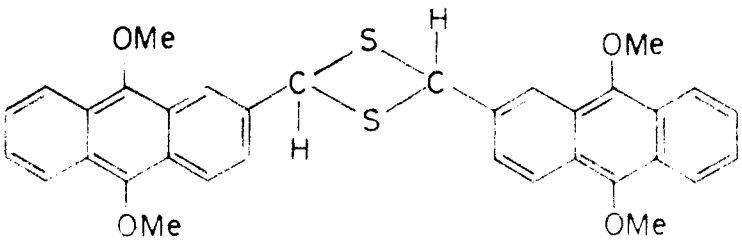
(IX)



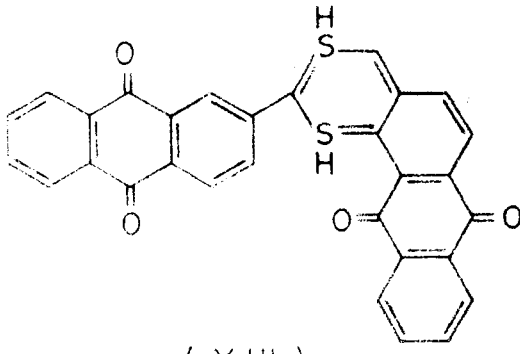
(X)



(XI)



(XII)



(XIII)

Structure (XI) can be ruled out in view of the behaviour of Cibanone Orange R as a vat dye and its stability to fission at S=S bond and desulphurization by a variety of reagents, such as mercuric chloride and mercuric oxide, sodium amalgan and hydrazine and potassium hydroxide in boiling diethylene-glycol. The idea that the two hydrogens possibly exist as in the tautomeric structure (X) has been excluded by the absence of any bathochromic shift in the absorption spectrum on the addition of sodium ethoxide in dimethyl formamide solution of the dye and by the absence of eny hydroxyl group absorption in infrared spectrum and the resistance to the desulphurization by the dye. To differentiate between the two structures (VII) and (IX) for Cibanone Orange R, the chemistry of such similar compounds has been compared. On a careful survey of the literature[30-34] it was observed that a hydrogen when flanked by two sulphur atoms at 1,3-position is prone to be abstracted by a good base and can generate a stable carbanion. The carbanion thus formed can undergo an electrophilic substitution reaction easily. In order to elucidate the acidity of the benzalic protons of triphenyl-s-trithiane, a close analogue of structure (VII), a dioxane solution of s-trithiane was refluxed with a 20% solution of sodium deuteroxide in deuterium oxide for 48 hr. and it was observed that the protons in the hetero-cyclic ring could be completely exchanged with deuterium ions, confirmed by mass spectrometry and NMR. Obviously it was

thought if benzalic hydrogens flanked by two sulphur atoms (1,3-position) at all exist in Cibanone Orange R, then under a proper condition, it would generate a carbanion and would therefore undergo a deuterium exchange. But when a dioxane solution of the red active methylation product of Cibanone Orange R (XII) was refluxed in 40% sodium deuteroxide solution in deutorium oxide for a period of 72 hr. the compound was recovered completely undeuterated (checked by mass spectral molecular weight) and therefore (VII) to be possible structure of Cibanone Orange R was excluded.

Therefore, the alternative structure left to be considered as to be the probable structure for Cibanone Orange R is (IX). Structure (IX), a derivative of 1,3-dithiacyclobutadiene explains the absence of benzalic hydrogens in Cibanone Orange R. The dp^3 hybridized sulphurs have been assumed to be present in structure (IX) instead of a regular p-orbital configuration in bivalent sulphurs to explain the ter- or tetra- covalent nature of sulphur in 1,3-dithia-cyclobutadiene ring system. In dp^3 configuration, sulphur expands its octet to decet and this becomes possible for the sulphur atom because of the availability of empty d-orbitals. The conception of a ter- or tetra- covalent sulphur attached to a hydrogen atom is itself new and has not been reported in the literature. Tetracovalent sulphur attached with fluorine, chlorine, bromine and perchlorate has been reported[35] by several groups of workers,[36] but none attached to hydrogen.

When Cibanone Orange R was refluxed in aniline for 19 hr., a crystalline brown solid separated out on cooling, which was filtered and washed with benzene to remove the traces of aniline. The brown crystalline solid analysed for an adduct of Cibanone Orange R with two molecules of aniline. The NMR spectrum could not be recorded because of its poor solubility in solvents like arsenic trichloride, trifluoro acetic anhydride, dimethyl sulphoxide, etc. However, the infrared spectrum showed an "ammonium band" at 2625 cm^{-1}. Anthraflavone, 2-methylanthraquinone, 2-mercaptomethylanthraquinone, bis-anthraquinonyl-2-methyl monosulphide on refluxion in aniline for 24 hr. remain unaffected. That Cibanone Orange R - aniline complex is a loose adduct of the dye and aniline is evident from the breaking of the complex at 140-45°/6 mm into aniline and Cibanone Orange R.

When the reductive methylation product of Cibanone Orange R (0.01 mole) was refluxed in anhydrous condition with triphenylmethyl perchlorate (0.035 mole) in dry chloroform for 14 hr., a product was obtained, whose infrared absorption (nujol mull) showed a strong perchlorate ion absorption from 1150 to 1090 cm^{-1} and at 935 cm^{-1}. The residue obtained after evaporation of the filtrate wascrystallised from pet.ether, m.p. 89-90° (M^{+} 244), undepressed on m.m.p. with an authentic sample of triphenylmethane. The triphenylmethane obtained was equivalent to the abstraction of two hydrides from the dye molecule by the trityl cation. Similarly, the parent dye also

on refluxion in triphenyl methyl perchlorate in o-dichlorobenzene gave the perchlorate salt and triphenyl methane. The repetition of triphenyl methyl perchlorate reaction on anthraflavone, 2-methylanthraquinone, 2-mercaptomethylanthraquinone and bis-anthraquinonyl-2-methyl monosulphide in dry chloroform gave no perchlorate salt and the starting material was recovered.

The occurrence of anilinium salt, perchlorate of Cibanone Orange R, and triphenylmethane in above reactions, perhaps adequately show that both the sulphurs in the dye molecule are ter- or tetracovalent in nature.

The di-perchlorate salt of the dye could be hydrolysed by refluxing in water to the corresponding dihydroxy derivative confirmed by hydroxyl group stretching in infrared spectrum (nujol mull) at 3640 cm^{-1} and elemental analysis.

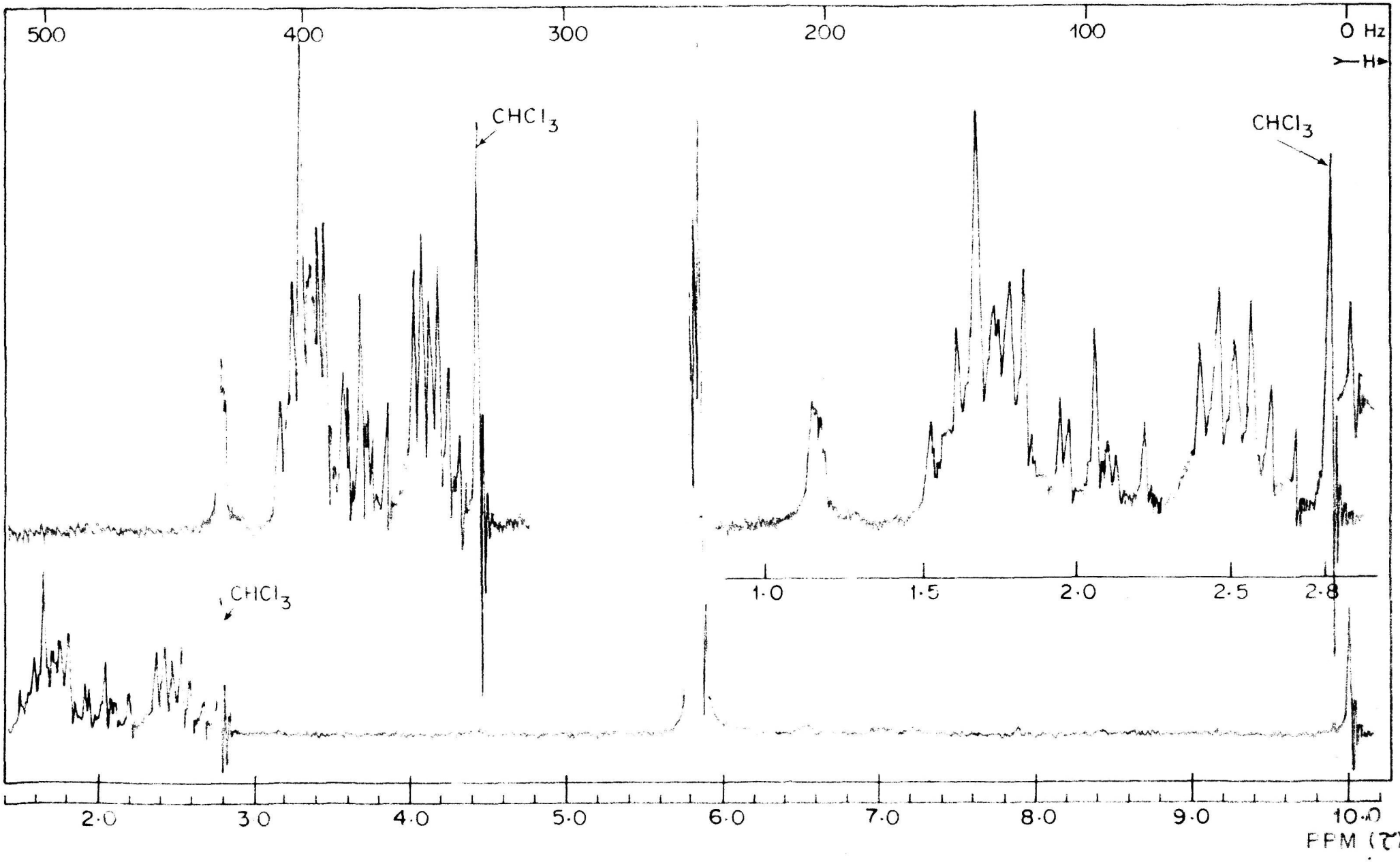
The perchlorate salt when hydrogenated over platinum oxide in glacial acetic acid gave back the parent dye - Cibanone Orange R.

Although structure (IX) is considered most appropriate with all the evidence so far obtained, no attempt has been made to analyse the NMR spectrum of Cibanone Orange R because of its insolubility in most of the solvents that can be employed for this purpose. Similar problems have been encountered in case of many anthraquinonoid vat dyes also. However, it has been found that the reductive methylation products (methyl ethers of the leuco compounds) of quinones are much more soluble in

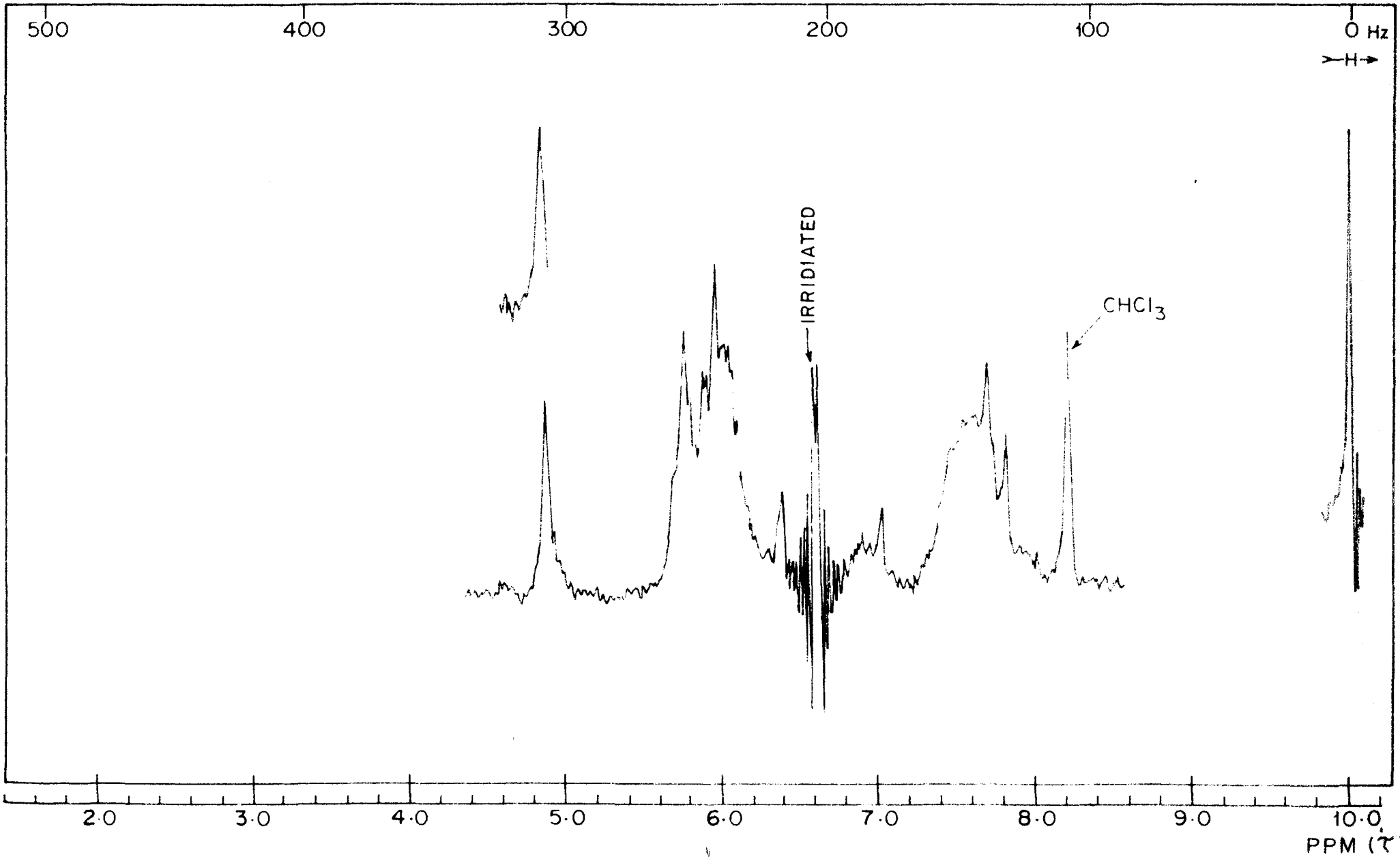
solvents such as $CDCl_3$ and tetramethylurea. By this technique it was shown that bromination of 16,17-dimethoxyviolanthrone gives the 3,12-dibromo derivative.[37]

The NMR spectrum of the reductive methylation product of Cibanone Orange R in $CDCl_3$ (5% solution) recorded on a T-60 spectrometer showed the presence of three singlets at 5.81, 5.82 and 5.83 (chemical shifts on the τ scale) in the ratio 2:1:1, and can be assigned to 4-methoxyl groups. There are no aliphatic protons in the spectrum. In the aromatic region, it shows the presence of 14 hydrogens. The lowest signal is a doublet (J=1.5 Hz) at 1.4 representing a single proton showing *meta* coupling. The other aromatic protons are seen in much more complex pattern in the region between 1.5 to 2.7. However, this complex region can be carefully analysed into three groups; the protons in the region 1.5 to 1.8 representing seven hydrogens, between 1.9 and 2.3 indicating the presence of two hydrogens and in the rest of the region a complex multiplet showing the presence of four hydrogens.

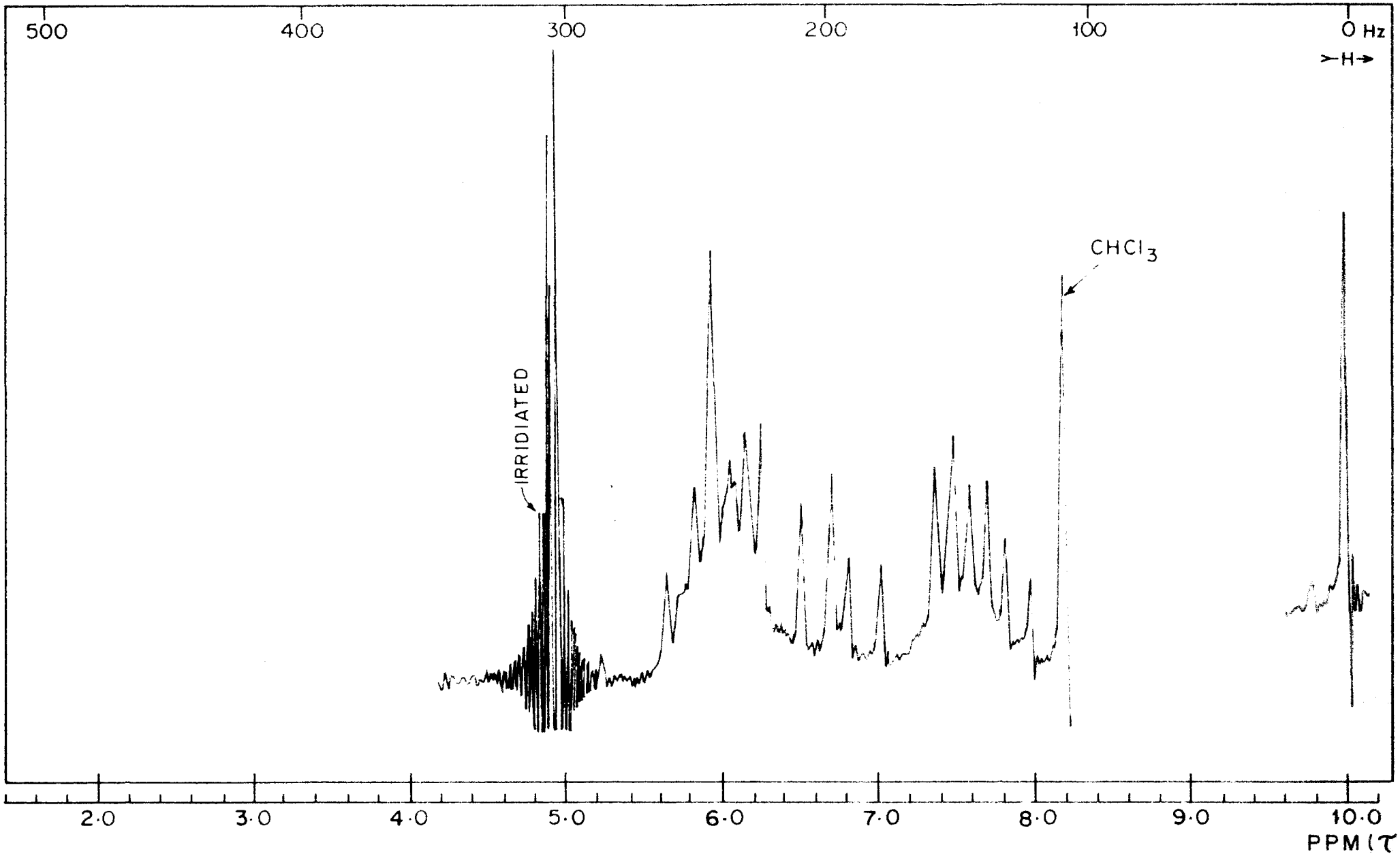
The two protons in the middle region is better resolved and one of them is a quartet ($J_{BX} \simeq$ 1.5, J_{AB}= 9.5 Hz) centered at 2.05 and the other is a doublet (J=9.5 Hz) centered at 2.1. Double irradiation experiments have shown that the quartet and the *meta* coupled doublet at 1.4 are coupling to each other. Thus when the signal at 1.4 was irradiated, the quartet collapsed to a doublet (J = 9.5 Hz). Similarly when the



NMR SPECTRUM OF TETRAMETHYL ETHER OF CIBANONE ORANGE R IN DEUTEROCHLOROFORM



NMR SPECTRUM OF TETRAMETHYL ETHER OF CIBANONE ORANGE R IN DEUTEROCHLOROFORM
(AROMATIC REGION DECOUPLING)



NMR SPECTRUM OF TETRAMETHYL ETHER OF CIBANONE ORANGE R IN DEUTEROCHLOROFORM

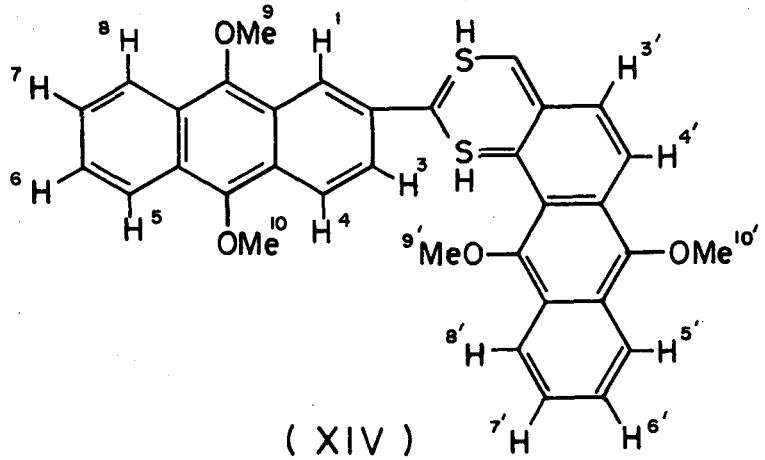
(AROMATIC REGION DECOUPLING)

quartet was irradiated the signal at 1.4 has appeared as a sharp singlet. From this it is clear that the signals at 1.4 and 2.05 together with a α-proton of a β-substituted anthraquinone unit constitute the ABX pattern. The corresponding α-proton might have burried together with other similar protons in the region 1.5 - 1.8. The doublet centered at 2.1 must be a β-proton of an another anthraquinonoid unit substituted at 1,2-positions.

The appearance of the methoxyl groups as 2:1:1 ratio and also the unsymmetrical manner the aromatic protons have appeared indicates that the two anthraquinone units in Cibanone Orange R may not be symmetrically substituted. If this is so, structure (IX) is not tenable to account for the chemical shifts in its NMR spectrum. The only alternative to accommodate all the physical and chemical data, so far obtained on this product, is to represent Cibanone Orange R by structure (XIII). Further, the NMR spectrum of the reductive methylation product can well be analysed by structure (XIV) (Table III). The appearance of the methoxyl in the ratio 2:1:1 is understandable from their environment. The lowest doublet at 1.4 can be assigned to the proton at position 1. The quartet at 2.05 and the doublet at 2.1 can be assigned to the protons at 3 and 3'-position respectively. Further, the appearance of 1,3- and 3'-H in the downfield compared with similar protons in 9,10-dimethoxyanthracene (see Table II) is probably due to the anisotropic effect of the 1,3-dithio-

TABLE III

NMR spectrum of the reductive methylation product of Cibanone Orange R (solvent: $CDCl_3$)



(XIV)

Chemical shift (τ)	Multiplicity	No. of H	Assignment
1.4	d (J=1.5 Hz)	1	1-H
1.5-1.8	m	6	4-,5-,8-,4'-,5'-,8'-H.
1.67	s	1	H- of the 1,3-dithio-pyrilium ring
2.05	q (J=9.5; 1.5 Hz)	1	3-H
2.1	d (J=9.5 Hz)	1	3'-H
2.3-2.7	m	4	6-,7-, and 6'-,7'-H
5.81	s	3	9'-OMe
5.83	s	3	10'-OMe
5.85	s	6	9-,10-OMe

s= singlet; d= doublet; q= quartet; m= multiplet.

pyrilium unit on these protons. The sharp singlet at 1·67 overlapping with the multiplet can be assigned to the lone proton of the 1,3-dithiopyrilium heterocyclic ring. The only drawback in the NMR spectrum is the absence of signals corresponding to the hydrides attached to the two sulphur atoms.

The mass spectrum of Cibanone Orange R shows relatively few peaks. The base peak is the molecular ion at m/e 504, indicating the stability of the molecule. This factor is in agreement with structure (XIII) for Cibanone Orange R compared with all other structures considered so far. There are minor peaks in the spectrum corresponding to the loss of H_2S (m/e 470); SH (m/e 471); loss of one sulphur (m/e 472) and two sulphur atoms (m/e 440) in the relative abundance of 37%, 13%, 14% and 0.8% respectively. There are also peaks corresponding to the loss of hydrogen radicals from the molecular ion. The peak at m/e 252 corresponding to the doubly charged ion, and such ions are common in many polynuclear compounds.

The reductive methylation and reductive acetylation products of Cibanone Orange R show the corresponding molecular ions at m/e 564 and m/e 676 respectively. The molecular ion (564) in the reductive methylation product losses four methyl radicals giving rise to the fragments at m/e 549, 534, 519 and 504, and is a common feature in the mass spectra of methyl

ether of leucoanthraquinone derivatives. The rest of the fragments from 504 (M^{+}) are as in Cibanone Orange R spectrum. The peak at m/e 282 corresponds to the doubly charged molecular ion.

TABLE II

Compounds	Solvents	∝-protons	β-protons	Methoxyl CH_3
Anthraquinone	DMSO	1.78(m)	2.03(m)	-
9,10-Dimethoxy-anthracene	$CDCl_3$	1.68(m)	2.52(m)	5.88(s)-2-OCH_3
9,10,9',10'-tetramethyl ether of anthraflavone	$AsCl_3$	1.75(m)	2.44(m)	6.17(s)-2-OCH_3 5.9(s)-2-OCH_3
9,10,9',10'-tetramethyl ether of Cibanone Yellow R	$AsCl_3$	1.60(m)	2.29(m)	5.83(s)-2-OCH_3 5.74(s)-2-OCH_3

EXPERIMENTAL

1. Preparation of anhydrous sodium sulphide

Anhydrous sodium sulphide was prepared following the procedure given by Vogel (A. Vogel, Text Book of Quantitative Inorganic Analysis, Longman, Green and Co., London, 1957) except the fusion being carried out under reduced pressure.

2. Preparation of 2-dibromomethylanthraquinone (Modification of Ullman's method)[37]

Bromine (14.2 ml, 0.25 mole) in nitrogenzene (13 ml) was added during 14 hr. to a mechanically stirred solution of 2-methylanthraquinone (22.2 g., 0.1 mole) in nitrobenzene (20 ml) kept at 145-50°. Bromine was absorbed slowly and hydrobromic acid was evolved. The solution was stirred at 145-50° for further 2 hr., cooled and the solid separated out was extracted with hot ethanol. The dark yellow residue (36 g), m.p. 204-208°, was found to contain mainly (95%) one product on silica gel TLC (benzene-acetone, 8:2). The residue was washed several times with hot ethanol till almost colourless ethanolic extract was filtered. The residue was crystallised from toluene, m.p. 217-218° (lit.[37] m.p. 218°).

3. Synthesis of Cibanone Orange R from 2-dibromomethylanthraquinone and anhydrous sodium sulphide

(a) An intimate mixture of 2-dibromomethylanthraquinone and anhydrous sodium sulphide (2.6 g, and 0.69 respectively in 1:1 molar ratio) was heated over a metal bath at 350-60° for 8 hr., cooled and ground to a fine powder. The ground powder

was then extracted, soxletting with solvents like water (to remove inorganic impurities like sodium bromide and sulphide), toluene (to remove unreacted 2-dibromomethylanthraquinone) and carbondisulphide (to remove traces of sulphur formed in the reaction). Thus the partially purified greyish black mass gave a yellow orange product (0.2 g; 12% yield) on crystallisation from o-dichlorobenzene. The yellow orange product did not melt till 360° (Found: C, 71.1; H, 2.9; S, 12.4. $C_{30}H_{16}O_4S_2$ requires C, 71.42; H, 3.1; S, 12.69%). The compound showed the molecular ion ($M^{+\cdot}$) at m/e 504 and gave a superimposable IR spectrum with the authentic Cibanone Orange R.

(b) A mixture of 2-dibromomethylanthraquinone and anhydrous sodium sulphide (2.1 g and 0.6 g respectively in 1:1.1 molar proportion) was suspended in dry methanol (20 ml) and was refluxed for 9 1/2 hr. The crude product thus obtained on evaporating ethanol gave the characteristic violet pink colouration with concentrated sulphuric acid. The product was purified by soxletting with water, acetone, toluene and carbondisulphide and the insoluble product was crystallised from o-dichlorobenzene in orange yellow needles (0.14 g) which gave a superimposable IR spectrum with the authentic Cibanone Orange R. On evaporation of acetone and toluene extracts, a solid was isolated (1.8 g). This solid was purified through the phenylhydrazone, obtained by treating a solution of the product in acetic acid (7 ml) with phenyl

hydrazine (1.5 ml) and filtered. The residue (0.15 g) was characterised as 2-dibromomethylanthraquinone by m.p. and m.m.p. The hydrazone crystallised out as reddish violet needles (2.7 g) m.p. 239-40° (lit.[37] m.p. for phenyl hydrazone of 2-aldehyde anthraquinone 242°). The phenyl hydrazone was warmed with acetic acid (10 ml), formaldehyde (8 ml) and sulphuric acid(1 ml) and the mixture was refluxed for 10 minutes. The solution gave, on cooling, pale yellow plates, m.p. 188-89°, undepressed when mixed with anthraquinone-2-aldehyde prepared according to Ullman.[37]

(c) A mixture of 2-dibromomethylanthraquinone and anhydrous sodium sulphide (1 g and 0.3 g respectively in 1:1:1 molar proportion) was refluxed in dry acetone (25 ml) under anhydrous condition for 7 hr. After the reaction period, acetone was evaporated and the product was purified following the procedure described in (3a) and (3b). The product thus obtained in 7% yield was identified as Cibanone Orange R by a superimposable IR with the authentic sample. Anthraquinone-2-aldehyde and 2-dibromomethylanthraquinone were isolated from the crude product following the procedure described in (3b) in 85% and 4% yields respectively.

(d) A mixture of 2-dibromomethylanthraquinone and anhydrous sodium sulphide (2 g. and 0.6 g respectively in 1:1:1 molar proportion) was refluxed in anhydrous 2-methoxy ethanol (24 ml) for 24 hr. After the reaction period, 2-methoxy

ethanol was distilled off under reduced pressure and the residue thus obtained was purified following the procedure adopted in the (3a) and (3b). The partially purified product thus obtained was reductive methylated by treating 5% of NaOH suspension of the product with sodium dithionite (3 g), and dimethylsulphate (4 ml). The crude product was chromatographed over a neutral alumina column (2 1/2 ft. long and 2 cm. dia.) using benzene for development and elution. The fast moving yellow fluorescent band was collected and concentrated. The product crystallized out (0.17 g) in fine needles, m.p. 202-205°, which gave a superimposable IR spectrum with the authentic 9,10,9',10'-tetramethyl ether of leuco Cibanone Orange R (Found: C, 72.5; H, 4.8; S, 11.0. $C_{34}H_{28}O_4S_2$ requires C, 72.4; H, 5.0; S, 11.3%). The methylated product gave a molecular ion at m/e 564.

Anthraquinone-2-aldehyde and 2-dibromomethylanthraquinone were isolated from the acetone and toluene extracts in 78% and 7% yield respectively.

In a similar reaction condition as of (3d), but using dry dioxane as the solvent, the yield of Cibanone Orange R could be hardly improved (42%). The method of the purification of the crude reaction product was followed of (3d).

4. Preparation of 2-bromomethylanthraquinone

Bromine (6.4 ml, 0.105 mole) in nitrobenzene (12 ml) was added during 13 hr. to a mechanically stirred solution of 2-methylanthraquinone (22.2 g., 0.1 mole) in nitrobenzene (20 ml), kept at 145-50° on a oil bath. Bromine was absorbed slowly and hydrobromic acid was evolved. The solution was stirred at 140-50° for 1 1/2 hr more, cooled and the solid separated out. It was extracted with hot alcohol till almost colourless ethanolic extract was filtered. The pale yellow residue (29.2 g) was found to contain 95% 2-bromomethyl-anthraquinone and 5% 2-dibromomethylanthraquinone from the amount of pyridinium salt formed when a small part (0.2 g) of the mixture was treated with pyridine. Repeated crystallisation of this mixture from glacial acetic acid gave 85% of 2-bromo-methylanthraquinone in pure form, m.p. 200-202° (lit.[38] m.p. 202°).

5. Preparation of 2-norcaptomethylanthraquinone

Sodium hydrogen sulphide was prepared following either of these procedures: (a) A solution of crystalline sodium sulphide (20 g) in water (200 ml) was saturated with hydrogen sulphide for 6 hr. in an salt-ice bath (-5°), filtered, and the clean solution of sodium hydrogen sulphide stored in the deep freeze. (b) Alternatively, sodium hydrogen sulphide[39] can be generated by adding sodium bicarbonate (1 mole) to a 14% aqueous ethanolic solution of crystalline sodium sulphide, maintaining the temperature below 5°.

The solution of sodium hydrogen sulphide thus obtained was added to a solution of 2-bromomethylanthraquinone (4 g) in 2-methoxy ethanol (600 ml) at room temperature. The colour of the solution darkened and almost after an hour, a pale yellow solid precipitated out, which was then filtered and crystallised from glacial acetic acid in thin needles. This was found to be the sodium salt of thiol. This sodium thiolate of 2-methyl-anthraquinone did not liberate the corresponding thiol by glacial acetic acid. The thiol could be easily regenerated by suspending the compound for half an hour in 8N hydrochloric acid; filtered and crystallised from glacial acetic acid, m.p. 230-33°, yield 51% (Found: S, 12.3. $C_{15}H_{10}O_2S$ requires S, 12.6%). Weak -SH absorption (nujol mull) at 2650 cm^{-1} carbonyl absorption (nujol mull) 1675 cm^{-1}.

6. Oxidation of 2-mercaptomethylanthraquinone to the disulphides:- 2,2'-dianthraquinonyl dimethyl disulphide

(a) The mercapto compound (1 g) was dissolved in glacial acetic acid (50 ml) and hydrogen peroxide (25 ml., 96 vols.) was added. The mixture was warmed on water bath for 1 hr. and on cooling gave the disulphide in a crystalline form (0.82 g), m.p. 198-200° (Found: S, 12.1. $C_{30}H_{20}O_4S_2$ requires S, 12.62%).

(b) Crystalline sodium sulphide (1 g) was fused with sulphur (0.1 g). The solid sodium disulphide (Na_2S_2) thus obtained was dissolved in alcohol (100 ml). This solution was next added to a hot solution of 2-bromomethylanthraquinone (2 g) in alcohol (120 ml). The product that separated on

boiling for 25 min. was collected by filtering the mixture while hot and crystallised from glacial acetic acid in clusters of long white needles (0.73 g), m.p. 198-99°; the disulphide prepared in the previous experiment remained undepressed on m.mp..

7. Preparation of 2,2'-dianthraquinonyl dimethyl sulphide

(a) Crystalline sodium sulphide (2 g) was added to a solution of 2-bromomethylanthraquinone (4 g) in hot ethyl alcohol (300 ml) and the brown solution obtained was heated under reflux for 30 min. The sulphide (1.6 g) which separated was crystallised from acetic acid in pale yellow needles (Found: C, 75.7; H, 4.1; S, 6.5. $C_{30}H_{18}O_4S$ requires C, 75.9; H, 3.8; S, 6.75%).

(b) When 2-bromomethylanthraquinone (2 g), crystalline sodium sulphide (6 g), and ethyl alcohol (200 ml) were boiled together for 4 days, a greenish yellow solid (1.2 g) was obtained. This solid on crystallisation from O-dichlorobenzene gave short yellow needles, m.p. 419-21°, m.m.p. with anthraflavone remained undepressed.

8. Synthesis of Cibanone Orange R by condensing sulphur with 2,2'-dimethylanthraquinonyl sulphide.

An intimate mixture of 2,2'-dimethylanthraquinonyl sulphide (0.2 g) and sulphur (0.07 g; 1:3 molar proportion) was heated at 350-60° on a metal bath till hydrogen sulphide evolution ceases (3 hr). The melt was cooled, powdered, and purified following the procedure described in experiment 3,

and finally crystallised from o-dichlorobenzene (0.035 g), which gave a superimposable IR with the authentic Cibanone Orange R. (Found: C, 71.1; H, 2.8; S, 12.3. $C_{30}H_{16}O_4S_2$ requires C, 71.4; H, 3.1; S, 12.69%). No other products could be isolated from the tarry material.

9. Synthesis of Cibanone Orange R by condensing sulphur with 2-mercaptomethylanthraquinone

An intimate mixture of 2-mercaptomethylanthraquinone and sulphur (1 g. and 0.39 g respectively in 1:3 molar proportion) was heated slowly on a metal bath till no hydrogen sulphide evolution was observed. The mixture melted at 210° and the evolution of H_2S started. The reaction temperature was maintained at 345-60° for 2 1/2 hr. and by that time H_2S evolution could no more be detected. The melt was cooled, powdered and treated with 5% aqueous sodium hydroxide (40 ml) and sodium dithionite (4 g). After stirring for 15 min. a further quantity of 5% aqueous sodium hydroxide (15 ml) and sodium dithionite (2 g) were added with shakings for 15 min. The vat solution coloured orange brown and was filtered quickly to remove any unvattable impurity. The filtrate was again vatted to get a clean solution with the addition of alkali and sodium dithionite. The clean vat thus obtained was oxidised by air. The solid was filtered, dried, and extracted by the soxletting process with o-dichlorobenzene (150 ml) for 5 hr. On concentrating the o-dichlorobenzene extract, an orange red solid was separated (0.085 g). Its IR spectrum was superposable with

the authentic Cibanone Orange R. No other products could be isolated from the black tarry mass.

10. Preparation of anthraquinone-2-aldehyde

(a) To a solution of 2-bromomethylanthraquinone (3.0 g; 0.01 mole) in hot acetic acid (50 ml), hexamine (2.24 g, 0.02 mole) was added and the solution was refluxed for 3 hr. Water (2 ml) and concentrated hydrochloric acid (2 ml) were then added and the refluxing continued for 1/2 hr. more. The pale yellow product (1.9 g), obtained on dilution was purified through the phenylhydrazone, which was obtained by treating a solution of the product in acetic acid (25 ml) with phenylhydrazine (2 ml). The hydrazone crystallised out in reddish violet needles (1.4 g), m.p. 239-240° (lit. m.p.[37] 242°). The phenyl hydrazone thus obtained was refluxed with acetic acid (5 ml), formaldehyde (5 ml) and sulphuric acid (0.5 ml) for 10 minutes. The solution gave on cooling, pale yellow plates of anthraquinone-2-aldehyde (0.7 g), m.p. 188-89° undepressed when mixed with anthraquinone-2-aldehyde prepared according to Ullman's procedure.[37]

(b) 2-Bromomethylanthraquinone (3.0 g; 0.01 mole) was dissolved in dimethylsulphoxide (20 ml) and refluxed for 1 1/2 hr., cooled and diluted with water. A solid precipitated out (2 g), which was crystallised from benzene-acetone mixture (1.6 g), m.p. 188-90° undepressed when mixed with anthraquinone-2-aldehyde.

11. Clar reduction of Cibanone Orange R

The dye (0.5 g), fused zinc chloride (1.8 g), sodium chloride (0.4 g), and zinc dust (1.5 g) were mixed and gradually heated to 430-440° and maintained the temperature for 15 min. The yellowish red solid (0.065 g) sublimed above 330°. The product was resublimed at 280-90°/4 mm. to give lustrous colourless flakes, m.p. 200-202°, identified as 2-methyl-anthracene (m.p. 205-207°).

12. Synthesis of anthraflavone from bis-2-methylanthraquinonyl sulphide

Bis-2-methylanthraquinonyl sulphide (0.6 g) was heated at 250-60° for 2 hr. when hydrogen sulphide was evolved. The solid mass was powdered (0.45 g) and recrystallised from nitrobenzene (100 ml) (0.31 g), m.p. 429-31° (lit.[37] m.p. 432°).

13. Oxidation of Cibanone Orange R

Finely precipitated Cibanone Orange R (by dissolving in sulphuric acid and diluting with water) (0.5 g) was suspended in acetic acid (60 ml) and fuming nitric acid (sp.gr. 1.4 g) was added (20 ml), heated on water bath for one hour and refluxed for 18 hr. more, when the dye went in solution. The acetic acid filtrate was concentrated to 30 ml. and diluted with cold water (100 ml). A yellow precipitate was obtained, which was taken in ammonia, filtered, and reprecipitated with hydrochloric acid (0.2 g). It was crystallised from dilute

acetic acid in colourless needles, m.p. 275-77°, undepressed with anthraquinone-2-carboxylic acid.

14. Condensation of sulphur with anthraflavone

An intimate mixture of anthraflavone (0.1 g) and sulphur (180 mg, the reactants are 1:5 molar proportion) was heated at 350-60° for 2 1/2 hr., hydrogen sulphide gas being evolved during the reaction period. The crude product (0.17 g) was isolated on cooling and was partially purified by soxhlet extracting as in experiment (3). This partially purified product was finally crystallised (25 mg) from o-dichlorobenzene in orange colour compound which gave characteristic pink colouration with concentrated sulphuric acid, and gave superimposable IR with the authentic Cibanone Orange R.

When the above reactants were tried, exactly in the same molar ratio, to react at a lower temperature (310-315°), the reaction was found to be very sluggish, and at the end of heating for 4 hr., starting materials were recovered over 75% yield.

15. Condensation of sulphur with dihydroanthraflavone

Dihydroanthraflavone (0.1 g) and sulphur (0.36 g), (reactants are in 1:10 molar proportion) were mixed together and heated at 370-80° for 3 hr. The crude black product was powdered and purified following the procedure shown in section (3), and crystallised from o-dichlorobenzene in

orange coloured compound which gave a superimposable IR with the authentic Cibanone Orange R.

When the same reactants in the same molar proportion were heated at a lower temperature (300-310°) for 3 1/2 hr. the hydrogen sulphide evolution ceased. The yellow product (28 mg) obtained after removal of sulphur by soxhlet extraction with carbon di sulphide did not melt till 360°. This was reductively methylated (m.p. 201-2°), and the product was prepared following the procedure described in (3d), and found to be similar with 9,10,9',10'-tetramethyl ether of leuco-anthraflavone on TLC (solvent benzene) (M^+ 500).

16. Preparation of dihydroanthraflavone by dehydrogenation using sulphur

An intimate mixture of 2-methylanthraquinone (1 g) and sulphur (80 mg,, the reactants are taken in 1:1·2 molar proportion) was mixed with diphenyl (10 g) and refluxed for 2 hr. in a metal bath during which hydrogen sulphide gas evolved profusely. The light brown residue (0.83 g) obtained after purification was crystallised from o-dichlorobenzene in pale yellow needles, m.p. 330-332° (lit.[37] 331-33°), undepressed with the authentic sample. 2-Methylanthraquinone could be recovered from the reaction in 10% yield.

17. Thionation of 2-methylanthraquinone with sulphur

A mixture of 2-methylanthraquinone (4 g) and sulphur (8 g) was heated at 310-320° for 3 hr. The thionation melt

was powdered and the unreacted sulphur was removed with carbon di sulphide (200 ml). The black residue (4.8 g) was continuously soxhletted for a period of 24 hr. with glacial acetic acid (70 ml) and filtered hot. The acetic acid Filtrate on cooling gave an amorphous substance (1.1 g), m.p. 329-31° (M^+ 442); m.m.p. with authentic dihydroanthraflavone remained undepressed.

Acetic acid mother liquor on prolonged cooling gave a Crop of amorphous substances (0.42 g), which showed the absence of sulphur, and was crystallised from o-dichlorobenzene. The product did not melt till 360°. The reductive methylated product of this compound showed the molecular ion at m/e 500, m.p. 207-210°, remained undepressed on m.m.p. with the authentic sample.

The glacial acetic insoluble residue was washed with acetone and dried. The reductive methylation of this compound gave a solid, which showed mainly a mixture of two compounds on TLC (~~solvent~~ benzene). They were separated by column chromatography using neutral alumina as adsorbant, developed and eluted by benzene. Two fluorescent compounds were isolated. The fast moving fluorescent compound (0.27 g) had m.p. 202-205° (M^+ 564), m.m.p. with the 9,10,9',10'-tetramethyl ether of leuco-Cibanone Orange R. The slower moving fluorescent compound, m.p. 282° (Found: S, 5.68%), the 9,10,9',10'-tetramethyl ether of leuco Cibanone Yellow R requires S, 5.82%) undepressed on m.m.p. with the authentic tetramethyl ether of Cibanone Yellow R.

18. Reaction between aniline and Cibanone Orange R

Cibanone Orange R (0.08 g) was taken in aniline (20 ml) and refluxed for 18 hr. The reaction mixture was cooled and filtered. The residue was washed with hexane and with aqueous 1N hydrochloric acid to remove the traces of aniline. The residue (0.11 g) was sparingly soluble in chloroform and shows single spot on silica gel TLC (benzene). It forms a clean dark red vat at room temperature with 5% sodium hydroxide and sodium dithionate (Found: C, 72.9; H, 4.2; S, 9.1; N, 4.23. $C_{42}H_{30}O_4S_2$ requires C, 73.0; H, 4.3; S, 9.2; N, 4.0%).

19. Reaction between aniline and methylated Cibanone Orange R

Reductive methylated Cibanone Orange R (0.04 g) was taken in aniline (10 ml) and refluxed for 14 hr. After the reaction mixture was cooled, methanol (50 ml) was added to it slowly - a brown red compound precipitated - filtered and dried. On silica gel TLC it showed the presence of starting material which was removed by crystallising from benzene. Its IR showed the carbonyl stretching frequency at 1675 cm^{-1} as in the condensation product of the parent dye and aniline indicating that during the reaction demethylation has occurred and an ammonium band at 2625 cm^{-1}.

20. Deuteration of reductive methylated Cibanone Orange R

Reductive methylated Cibanone Orange R (0.08 g) was dissolved in dry and distilled dioxane (5 ml). To this solution, dry and freshly cut sodium (2 g) dissolved in

deuterium oxide (5 ml, isotopic purity 99.4 atom %D) was added and refluxed for 60 hr. The solvent was distilled off at low pressure. Excess of deuterium oxide was added to the residue. And the residue was extracted by dry chloroform (3 x 10 ml). The chloroform extract was dried over anhydrous magnesium sulphate and distilled on a water bath till 2-3 ml of the solution was left. The solid separated was collected and dried. Molecular ion of this compound was shown at m/e 564 corresponding to undeuterated compound.

21. Reaction between triphenylmethyl perchlorate and reductive methylated Cibanone Orange R

(a) Preparation of triphenylmethyl perchlorate:

To a well cooled and stirred solution of triphenyl carbinol (4 g) in acetic anhydride (50 ml), perchloric acid (70%, 4 ml) was added dropwise. The stirring of the mixture was continued for an hour, then the precipitate was filtered off and washed well with dry ether. Triphenylmethyl perchlorate (4.4 g) was obtained in a yellowish red prisms(m.p. 142-43°).

(b) Reaction between methylated Cibanone Orange R and triphenylmethyl perchlorate

Reductive methylated Cibanone Orange R (0.5 g) was taken in dry chloroform (10 ml), slightly warmed on the water bath for obtaining a homogeneous solution, filtered through a cotton plug and transferred in a R:B: flask. Similarly triphenylmethyl perchlorate (300 mg, reactants being taken in 1:2 molar ratio respectively) was taken in

dry chloroform (10 ml), slightly warmed and a homogeneous solution was obtained which is filtered through cotton plug and added to methylated Cibanone Orange R solution in chloroform. This solution was refluxed for 14 hr. To the reaction mixture pet.ether (30 ml) was added to precipitate the reaction product. The residue was collected, washed with dry ether (4 x 10 ml). The ether and pet.ether filtrates on silica gel TLC showed the presence of the same product and therefore mixed together and concentrated. The residue was washed with benzene (5 x 10 ml), chloroform (5 x 10 ml) and dried. Its IR showed a very strong perchlorate ion absorption from 1150 to 1090 cm^{-1} and at 935 cm^{-1}.

The residue (0.4 g) obtained after evaporation of the solvent showed single spot on silica gel TLC (benzene-acetone 9:1) melts at 89-90°, undepressed with authentic ǂ triphenylmethane, m.p. 92-94°.

22. Reaction between 9,10-dimethoxyanthracene and triphenyl methyl perchlorate

9,10-Dimethoxy anthracene (0.2 g) and triphenyl methyl perchlorate (0.1 g) freshly prepared and dried were taken in dry benzene and refluxed for 4 hr. After working up the product was characterised as anthraquinone (m.p. and IR).

23. Reaction between triphenyl methyl perchlorate and Cibanone Orange R

Purified dye (0.1 g), obtained by demethylation of the reductive methylated Cibanone Orange R and triphenyl methyl

perchlorate (0.185 g; reactants being taken in 1:2 molar proportion respectively) in dry and distilled O-dichlorobenzene and refluxed for 24 hr. The dark solution was cooled; some solid precipitated, filtered and washed with dry chloroform to remove any unreacted triphenyl methyl perchlorate. The solid was crystallised from O-dichlorobenzene (0.08 g). In the IR spectrum (nujol), the perchlorate band was seen at 1150 cm^{-1} to 1090 cm^{-1} and at 935 cm^{-1}.

From the filtrate the solvent was removed under reduced pressure and the solid obtained (0.06 g) was crystallised from pet.ether-benzene in fine plates, m.p. 89-91°, and therefore identified as triphenyl methane.

24. Hydrolysis of the perchlorate salt of Cibanone Orange R

The perchlorate salt of the dye (0.1 g) was suspended in water and refluxed for 4 hr. The residue was collected, washed several times with water and finally with acetone (5 x 15 ml).

Its IR spectrum (nujol) showed a free hydroxyl stretching absorption band at 3640 cm^{-1} indicating the displacement of perchlorate by hydroxyl group. (Found: C, 66.7; H, 3.2; S, 11.7. $C_{30}H_{18}O_6S_2$ requires C, 66.9; H, 3.3; S, 11.9%).

25. Hydrogenation of the perchlorate salt of Cibanone Orange R

The perchlorate salt of the dye (0.18 g) in glacial acetic acid (20 ml) was hydrogenated using Adam's catalyst. After the absorption of two moles of hydrogen, the solution

was filtered, concentrated and the solid thus obtained was crystallised from o-dichlorobenzene and the product (53 mg) thus obtained gave a superimposable infrared spectrum with the authentic Cibanone Orange R. (Round: C, 71.3; H, 2.3; S, 12.6. $C_{30}H_{16}O_4S_2$ requires C, 71.42; H, 3.1; S, 12.7%).

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P A R T - II

CONSTITUTION OF CIBANONE YELLOW R

Cibanone Yellow R (Mayer and Schaarschmidt, 1908)[1] is a sulfurised vat dye which dyes bright orange yellow shades from a red brown alkaline hydrosulphite vat. It is insoluble in aqueous sodium sulphide. This dye is prepared by the thionation of a variety of intermediates derived from 2-methyl anthraquinone. The intermediates cited in patent literature are: 2-methylanthraquinone, 2-chloromethylanthraquinone, 3-chloro-2-methylanthraquinone, 3-chloro-2-chloromethyl-anthraquinone and 3-chloro-2-dichloromethylanthraquinone. The method of preparation consists in heating any one of the above intermediates or a mixture of them in a definite proportions with a large excess of sulphur at temperatures of the order of 300-330^{o} for 1-2 hr., cooling and extracting the mixture with a solvent to remove unreacted sulphur, dissolving the residue in sulphuric acid, reprecipitating the dye by treatment with aqueous sodium hypochlorite. The thionation process, as in the case of sulphur dyes, leads to a mixture of products.

The dye dyes an attractive yellow shade on cotton with excellent fastness to washing and chlorine,[3] but fastness to light[4] is poor. The dye was withdrawn from the commercial range of Cibanone colours on account of its tendering action on cellulose when the dyeings are exposed to light. In fact it is the dye of choice for investigators studying the actinic degradation of cellulose.[3]

It also hastens the fading of a relatively innocuous dye like Caledon Jade Green when the two are dyed in admixture. The constitution of Cibanone Yellow R was first examined by Fierz-David et al.[4], Shah et al.[5,5a] and Chandavarkar[5a,6] and later on by Bhavsar.[10]

Work done by Fierz-David.[4] The commercial dye was extracted with alcohol after removing inorganic salts by means of hot water and from the alcoholic extract of 2-methylanthraquinone was isolated. Based on elemental analysis and its molecular weight by Rost method, they suggested the molecular formula, $C_{30}H_{16}O_4S$ to the purified dye. The oxidation with chromic acid in sulphuric acid or glacial acetic acid gave anthraquinone-2-carboxylic acid, but the dye was stable to hydrogen peroxide. From these results the dye was considered to be a bis-anthraquinone thiopyran (diphthaloylthioxanthene) (I) or (II) with a methyl substituent.

The linear compound (II) was synthesised by the condensation of thioxanthene with phthalic anhydride in presence of aluminium chloride, followed by cyclisation of the diketo acid. The synthetic product did not analyse correctly for (II) but its constitution was based on the observation of Scholl and Seer[7] that o-phenylenedisulphide (thianthrene) gave a linear compound (II, S in place of CH_2)

by phthalic anhydride condensation and subsequent cyclisation. The product (II) dyed much weaker shades than Cibanone Yellow R and gave a dark solution in sulphuric acid, whereas the dye gave a blue solution in sulphuric acid. Fierz-David[4] therefore suggested the angular structure (I) for the dye.

Work done by Shah et al.[5] The constitution (I) was considered improbable by Shah et al.[5] because of the following.

(a) The sulphur content obtained by Fierz-David is not in agreement with the required value.

(b) Generally the diaryl sulphides will be oxidised to sulphones with chromic acid in glacial acetic acid[8] and will not undergo fission. However, oxidation accompanied with desulfurisation in case of (I) should give a mixture of anthraquinone-2-carboxylic acid and anthraquinone-1-carboxylic acid, whereas only the former acid was isolated.

(c) The colouration in sulphuric acid as observed by Fierz-David is blue for the dye (I) and dark green for the synthetic product (II). However, purified Cibanone Yellow R gives a purple solution in sulphuric acid similar to 2,2'-dianthraquinonyl ethylene (III) (anthraflavone).

Shah has further showed that the purified dye assumed to be homogeneous by Fierz-David was a mixture of several substances, when a solution of the purified yellow R in acetylene tetrachloride was chromatographed on alumina,

three small bands developed on the column. The major part of the dye, eluted as an unadsorbed portion, was recovered by concentration of the percolate, when yellow needles, m.p. 368-70°, were obtained. The latter were considered to be homogeneous and regarded as essential tinctorial constituent of Cibanone Yellow R. Further concentration of the mother liquor gave anthraflavone. The dye purified by chromatography analysed for C, 76.1; H, 3.6; S, 4.4. $C_{45}H_{26}O_7S$ requires C, 76.1; H, 3.7; S, 4.5%, indicating three methyl anthraquinone residues to one atom of sulphur.

Taking into consideration the elemental analysis of the dye and its formation from 2-chloro methylanthraquinone, it was suggested that the dye has the constitution (IV).

An alternative structure (V) derived from anthraflavone, was also suggested in view of the following: (1) the conversion of bis-2-anthraquinonyl methyl sulphide (AQ CH_2SCH_2AQ) to anthraflavone at 250°; (2) the occurrence of anthraflavone in the commercial dye; (3) the possibility of an addition reaction between anthraflavone and 2-mercaptomethylanthraquinone.

The fact that the dye is a derivative of 2-methylanthraquinone was proved by Clar reduction,[5,9] which gave only 2-methylanthracene. 2-Methylanthraquinone and anthraflavone also gave 2-methylanthracene on a similar reduction.

To distinguish between the three structures, (I), (IV) and (V) Shah studied Raney nickel reduction of the dye. Removal of sulphur from (I) should give 1,2-dianthraquinonyl methane or its hydrogenated derivatives, and (V) should give 2,2'-dianthraquinonyl ethane (dihydroanthraflavone) together with 2-methylanthraquinone or their hydrogenated derivatives. However, anthraflavone was found to be stable under identical conditions of reduction. On Raney nickel reduction of the dye, Shah obtained several products which after exhaustive purification by chromatography and crystallisation, gave low melting products, having a molecular weight of about 250°, indicating that they are probably derivatives of 2-methylanthraquinone. The experiments are summarised below.

(a)	Dye	Raney nickel Morpholine	Yellow needles, m.p. 170-72° Found: C, 81.3; H, 7.3. MW 250.
(b)	Dye	Raney nickel 1.5% aq.NaOH	Colourless needles, shrinks 232°, m.p. 235-40°(minor product) Yellow needles, m.p.225-227° (Found: C, 74.6; H, 6.5%; MW 250.

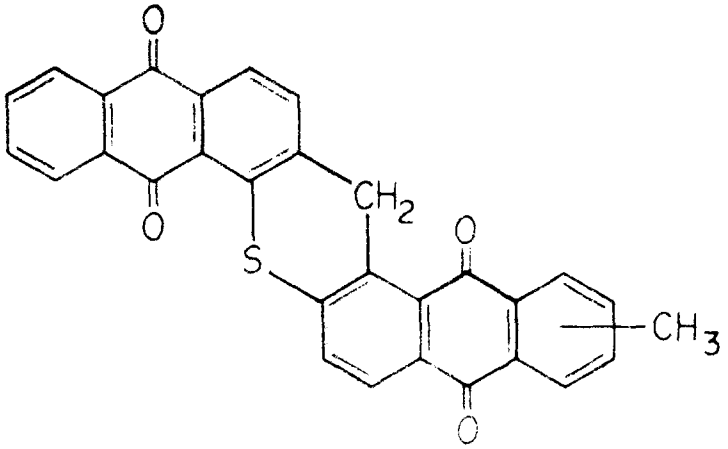
Attempts to synthesise the compound (IV) and other analogous model structures starting from the relevant sulphides such as bis-2-anthraquinonylmethyl sulphide and halogeno derivatives such as 2-chloromethylanthraquinone through the complex sulphonium chlorides [ ].$(AQCH_2)_3SCl$ were unsuccessful .

Work done by Chandavarkar[6] (Constitution of Calco Yellow 5G). As the sample of Cibanone Yellow R was exhausted, Chandavarkar examined Calco Yellow 5G marketed by the Calco Division of the American Cyanamid Co., which is referred to by Fox[8] as equivalent Cibanone Yellow R.

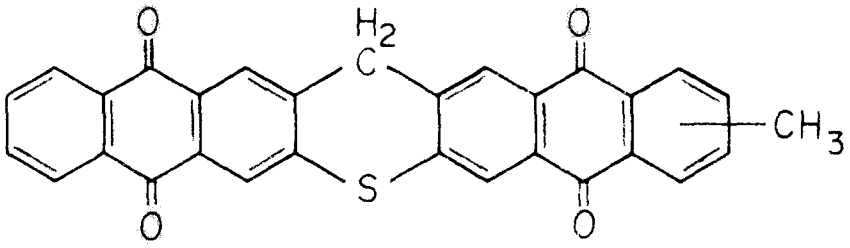
The following data proved the identity of Cibanone Yellow R and Calco Yellow 5G: (1) the two dyes when purified by Fierz-David's exhaustive extraction method had identical dyeing properties, and (2) were equally active as photochemical tenderers; (3) both gave 2-methylanthraquinone from the ethanolic extracts and both contained anthraflavone; (4) Clar reduction of Calco Yellow 5G gave 2-methylanthracene, (5) nitric acid oxidation gave anthraquinone-2-carboxylic acid, (6) elemental analysis of both the dyes, after purification by Fierz-David's method and four crystallisations from nitrobenzene was similar; (7) both the dyes gave similar purple colored solutions and identical absorption spectra in sulphuric acid; (8) a reddish colouration was given by both the dyes in butanol and 50% caustic soda.

Attempts to synthesise structures (IV) (V) and (VI) were unsuccessful.

It was observed by the author that when a solution of purified Calco Yellow 5G in acetylene tetrachloride was run through a column of alumina, a major fraction of the dye was obtained as orange yellow needles, m.p. 382-84° from the



(I)



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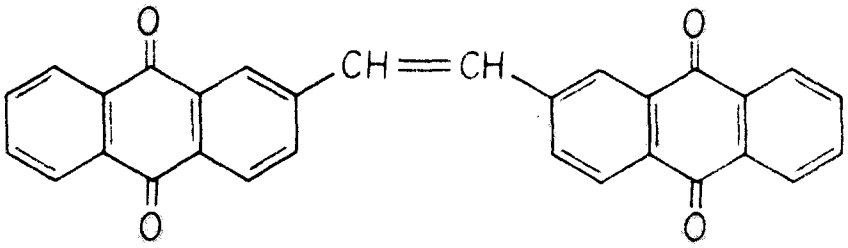
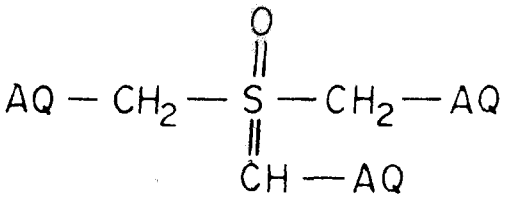
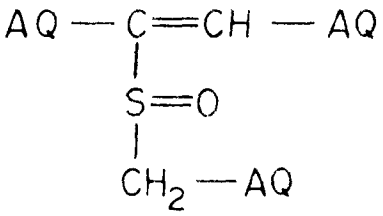


(III)



(IV)



(V)

AQ = 2 – Anthraquinonyl

percolate. The product analysed for C, 75.8; H, 3.5; S, 6.5%. This indicates that Calco Yellow 5G contains two 2-methylanthraquinone residues per atom of sulphur. Chandavarkar therefore suggested a monothiopheno structure (VII) for the dye, which also brings out the analogy of Calco Yellow 5G and anthraflavone (behaviour in Clar reduction, oxidation etc.) and accounts for its synthesis from the intermediates like 2-methylanthraquinone and its derivatives.

The structure (VII) was considered more probably by Chandavarkar because Calco Yellow 5G on further thionation at 10 mm pressure gave a dye similar to Cibanone Orange R constituted as (VIII) by him.

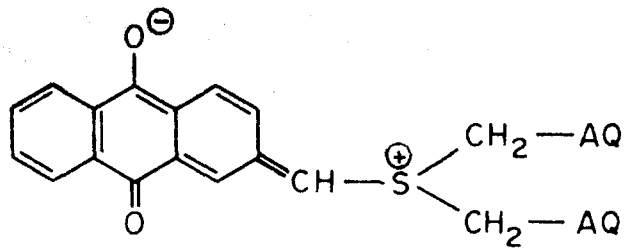
The formation of thiophene ring systems similar to those present in the above two structures (VII) and (VIII) have been sugge sted by Horton[17] in case of thionation of toluene and 2-methylnaphthalene.

Raney nickel reductions studied by Shah[5] wherein he isolated low molecular weight degradation products lost much of their significance, when it was realised that fission of ethylene link joining two anthraquinone residues in anthraflavone occurred in Raney nickel reduction. On the other hand Raney nickel reduction of bis-2-anthraquinonyl methyl sulphide gave anthraflavone, thus indicating a carbon-carbon bond formation.

Work done by Bhavsar.[10] Cibanone Yellow R and Calco Yellow 5G after purification according to Fierz-David's exhaustive extraction method and two or three crystallisations from nitrobenzene, analysed for one sulphur atom for two molecules of 2-methylanthraquinone and gave identical absorption spectra in sulphuric acid. They were therefore considered to be iden i cal and were regarded as ei+her of the two possible monothiopheno derivatives: linear compound (VII) or the angular compound (VIII).

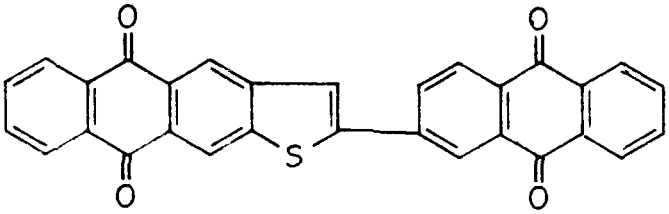
The reduction of the Cibanone Yellow R with aluminium cyclohexoxide gave two anthracene derivatives which were identified as 2,2'-dianthryl ethylene (X) and a sulphur containing product (XI) or (XII) respectively.

In order to elucidate the mode of linkage of sulphur atom in Calco Yellow 5G, Raney nickel reduction of 2-methylanthraquinone, anthraflavone, bis-2-anthraquinonylmethyl sulphone ($AQCH_2SO_2CH_2AQ$) and Calco Yellow 5G was studied. Bis-2-anthraquinonylmethyl sulphone, after 6 hr. shaking, gave 2-methylanthraquinone as the major product and traces of alkali soluble product, which was anthraquinone-2-carboxylic acid. A similar reduction of anthraflavone gave hydrogenated dihydroanthraflavone derivatives, which on dehydrogenation gave dihydroanthraflavone. Calco Yellow 5G was recovered almost unchanged after 6 hrs. of

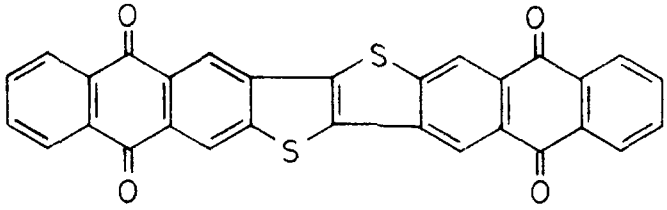


AQ = 2 – Anthraquinonyl ;

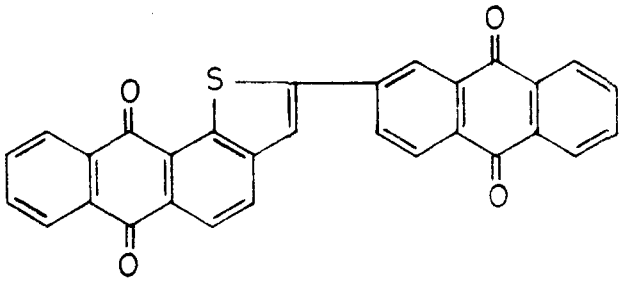
(VI)



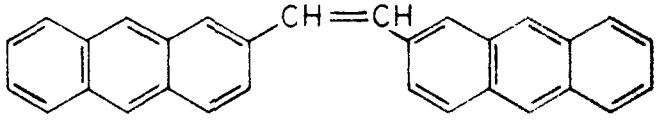
(VII)



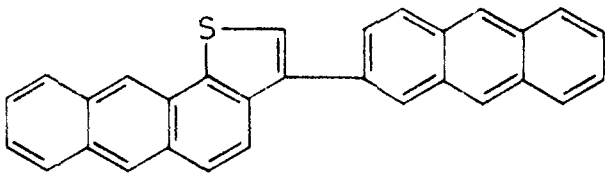
(VIII)



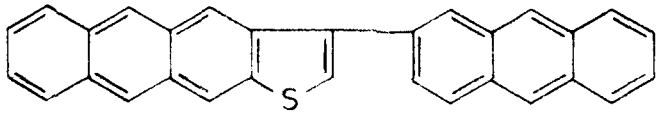
(IX)



(X)



(XI)



(XII)

treatment (5 parts of Raney nickel, 5% NAOH and shaking the mixture under hydrogen atmosphere at 45-46 lbs. per sq.inch at room temperature in a Parr hydrogenator) as above and no 2-methylanthraquinone or its derivative was isolated.

PRESENT WORK

In the present study the constitution of Cibanone Yellow R has been reinvestigated, hoping that its structure may throw some light on the constitution of Cibanone Orange R.

The two commercial products, Cibanone Yellow R and Calico Yellow 5G, have been purified according to Fierz-David's exhaustive method and their identify has been established from their IR spectra which are superposable. The NMR spectrum of this dye could not be obtained because of its poor solubility in a variety of solvents, such as dimethyl sulphoxide, dimethylacetamide, tetramethylurea, and arsenic trichloride.

The reductive methylation product of the dye was prepared by treating its alkaline vat with excess of dimethyl sulphate at room temperature. The crude product thus obtained showed to be a mixture of two compounds on silica gel TLC plate developed with benzene. Their separation on silica gel column was not successful owing to their oxidation. However, the two compounds can best be separated on a neutral alumina column using benzene for development and elution. The two products thus obtained were further purified by repeated crystallisation from a mixture of pet.ether-benzene. The faster moving fluorescent yellow compound (A), m.p. 282°, decomposes when heated above its m.p. (286-87°). The non-fluorescent yellow, slow moving, compound (B) melts at

322-24°, and shows in its IR spectrum, unlike the former, a carbonyl absorption at 1670 cm^{-1} indicating that one of the anthraquinone rings might have not undergone reductive methylation. This assumption has been proved to be correct from their mass spectral molecular weights of these two products (Compound A, M^{+} 530 and Compound B, M^{+} 500), which showed a difference of 30 mass units. Unlike compound (A) compound (B) gives a clear dark red vat when treated with an alkaline solution of sodium dithionite. Compound (B) can be converted to compound (A) by subjecting (B) by further reductive methylation. From this it is obvious that compound (A) is the tetramethyl ether of the leuco product of Cibanone Yellow R while in (B) only one anthraquinone moiety might have reduced to give a dimethyl derivative. However, it was unsuccessful to get exclusively (A) in one step by subjecting Cibanone Yellow R to reductive methylation.

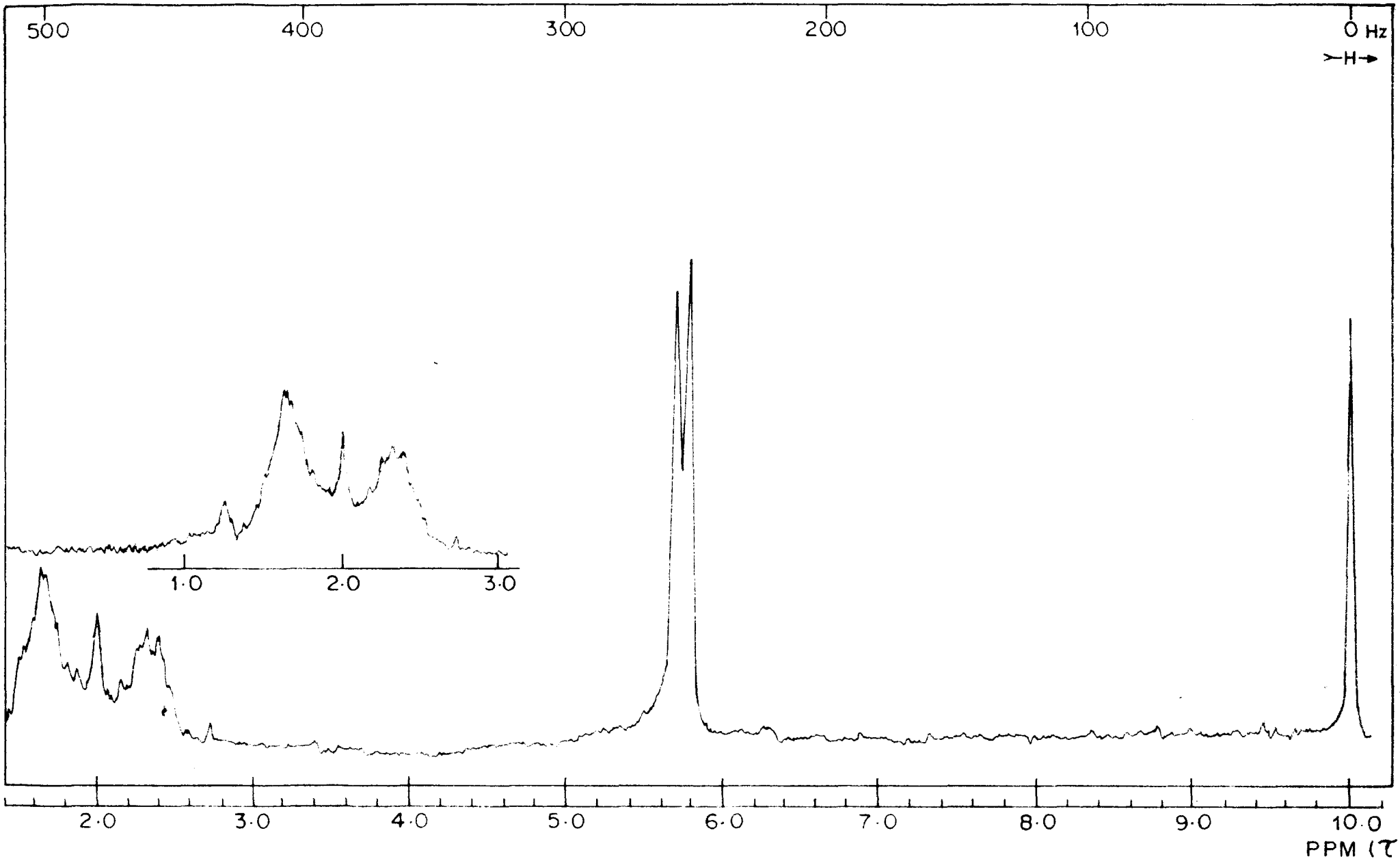
The NMR spectrum of the tetramethyl ether of the leuco Cibanone Yellow R (compound A; Fig. 1) in arsenic trichloride shows two singlets of equal intensity at 5.74 and 5.82 (chemical shifts τ-scale) which can be assigned to two sets of methoxyl groups. There are no aliphatic protons in the spectrum. In the aromatic region, there are fourteen protons in relation to four methoxyl groups, and are seen in the region 1.7 to 2.4. This region can be divided into three groups of signals centered at 2.39, 2.0 and 1.7 representing

6, 2 and 6 hydrogens reppectively. The region is so complex, it is very difficult to conclude the exact nature of these protons.

The NMR spectrum of Compound B (dimethyl ether of the dihydrocibanone yellow R) in DMSO shows a six proton singlet at 5.84 and can be assigned to the two OMe groups. The aromatic protons are seen as a complex spectrum and account for 14 hydrogens in relation to two methoxyl groups.

The mass spectrum of the tetramethyl ether of the leuco Cibanone Yellow R showed the molecular ion at m/e 530 with relative abundance of 6%. The base peak is at m/e 470 and resulted by the successive loss of four methyl radicals respectively at m/e 515 (9%), 500(53%), 485(96%) and 470(100%). All these peaks show the corresponding doubly charged ions. The radical ion at m/e 498(4%) arises due to the expulsion of sulphur radical from the molecular ion.

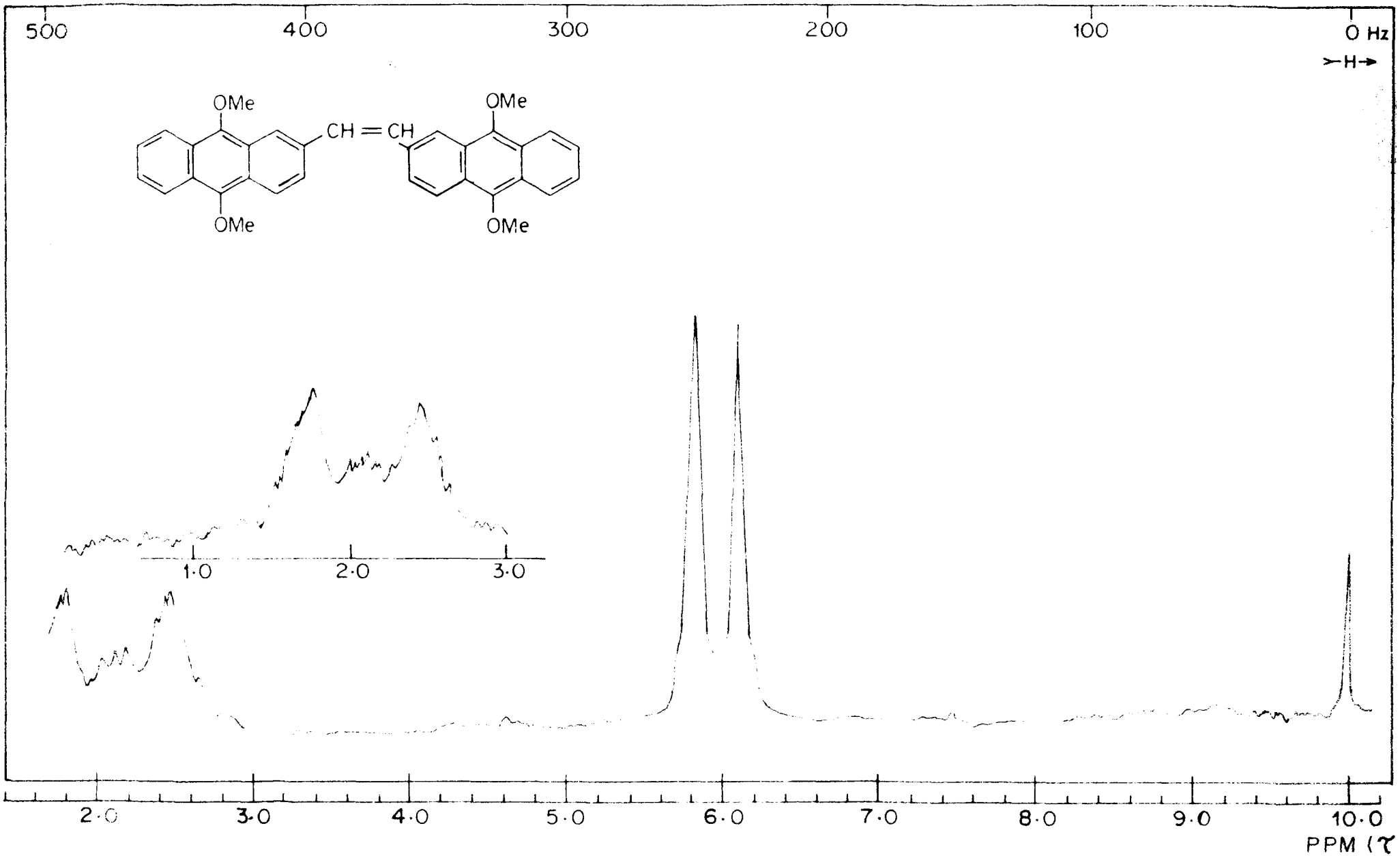
Compound (B) (dimethyl ether of the dihydrocibanone yellow R) shows a strong molecular ion at m/e 500 (94%) in its mass spectrum. The base peak is at m/e 470 corresponding to the molecular weight of Cibanone Yellow R. There are peaks in the mass spectrum corresponding to the loss of sulphur and SH• radicals from the molecular ion.



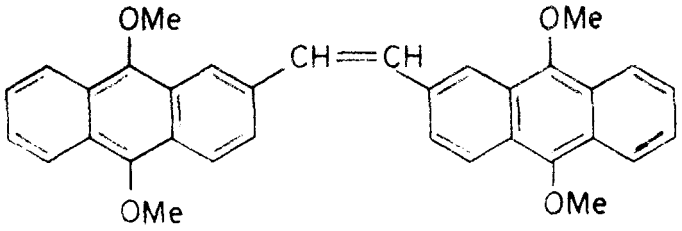
NMR SPECTRUM OF TETRAMETHYL ETHER OF CIBANONE YELLOW R IN ARSENIC TRICHLORIDE

Cibanone Yellow R when subjected to reduction with alkaline sodium dithionite at room temperature and the resultant vat solution was reoxidised after 76 hr by air oxidation, the product isolated was found to be identical with anthraflavone (III). It was further found that the dye reacts with neutral sodium dithionite solution giving off hydrogen sulphide gas at room temperature. Under the conditions of the preparation of the reductive methylation of Cibanone Yellow R in which the dye is vatted with alkaline sodium dithionite (10 min.) and immediately the vat was shaken with excess of dimethyl sulphate resulting in the separation of the reductive methylation products from the solution, it was found that the decomposition of the dye was insignificant and the main product was found to be a mixture of compounds (A) and (B). However, if the dye is vatted and left for 48 hr. and further methylating the vat, the resultant product was found to be a mixture of three compounds, two being (A) and (B) and the third has been identified as the reductive methylation product of anthraflavone (XIII). The dye is also unstable and gives off H_2S gas when subjected to boiling glacial acetic acid, 10% hydrochloric acid and 40% hydrobromic acid.

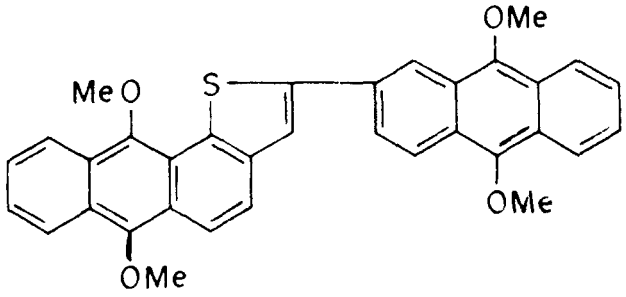
The NMR spectrum of the reductive methylation product of anthraflavone (solvent arsenic trichloride, Fig. II) shows two singlets at 5.82 and 6.19 each representing two methoxyls, as in compound (A). All the other protons have appeared in a complex region 1.8 to 2.5.



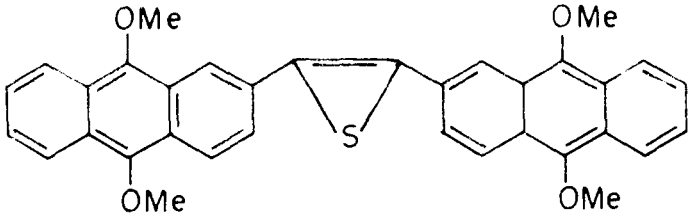
NMR SPECTRUM OF TETRAMETHYL ETHER OF ANTHRAFLARONE IN ARSENIC TRICHLORIDE



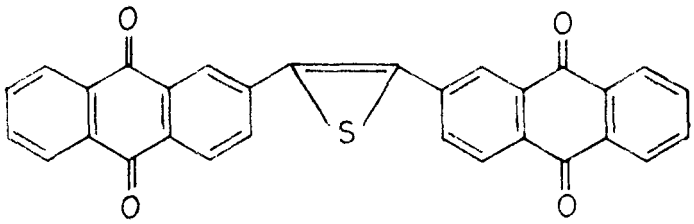
(XIII)



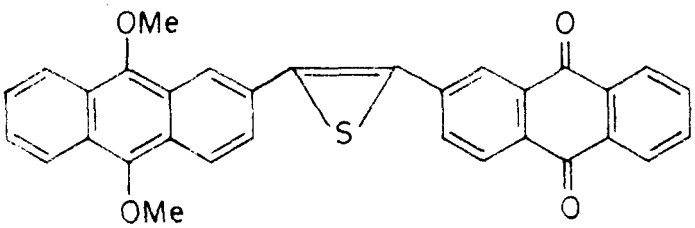
(XIV)



(XV)

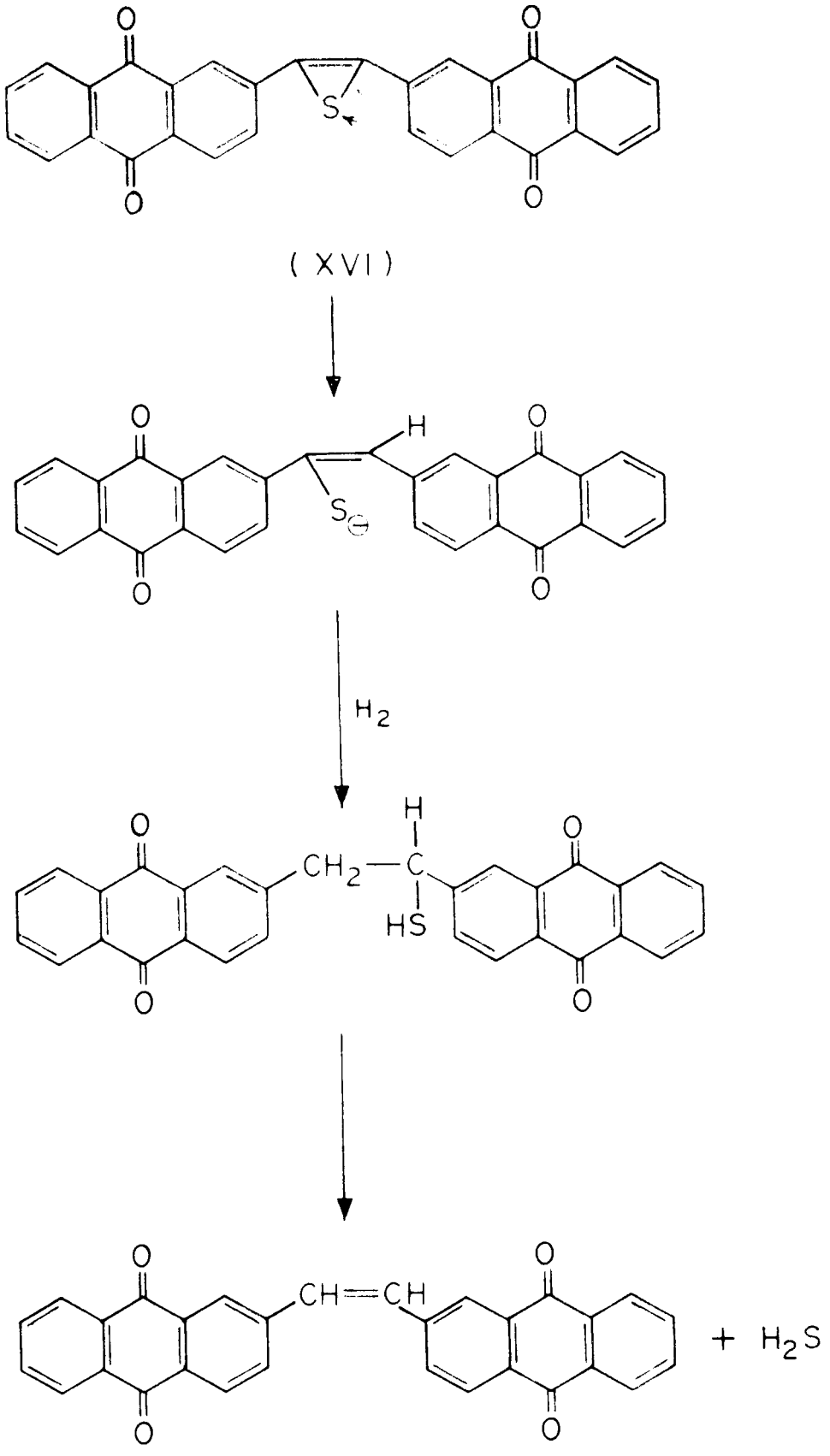


(XVI)



(XVII)

It is very difficult to reconcile all the above facts with the structure (XIV), which is the tetramethyl ether of (IX), proposed earlier by Bhavsar, particularly its behaviour towards sodium dithionite reduction and the appearance of the -OMe groups in its NMR spectra as two sets of singlets. If Cibanone Yellow R has structure (IX), one normally expects -OMe groups as 1:1:2 ratio in the NMR spectrum of its reductive methylation product. An alternative structure such as (XV) for compound (A) a tetramethyl ether of (XVI) may perhaps better explain the data so far obtained on Cibanone Yellow R. Compound (B) is ascribed to the structure (XVII). However, there are many other facts which will not fit with structure (XV) or (XVI) for this dye. It is very difficult to understand the conversion of Cibanone Yellow R to Cibanone Orange R by thionation with sulphur at 350-60°, if Cibanone Yellow R has a thiirene skeleton sandwitched by two anthraquinone units. It is emphasised here that structure (XV) or (XVI) has been proposed as an alternative to (IX) or (XIV) to better explain some of the data obtained so far. Thus the desulphrisation under very mild conditions can be explained as depicted by Chart I. However, such desulphurisation from structure (IX) may also take place as indicated by Chart II. Preferably reductive dimethylation of Cibanone Yellow R cannot be satisfactorily explained by a symmetrical structure as of (XVI). This perhaps can be better explained by a structure like (IX):



(XVI)

(III)

CHART – I

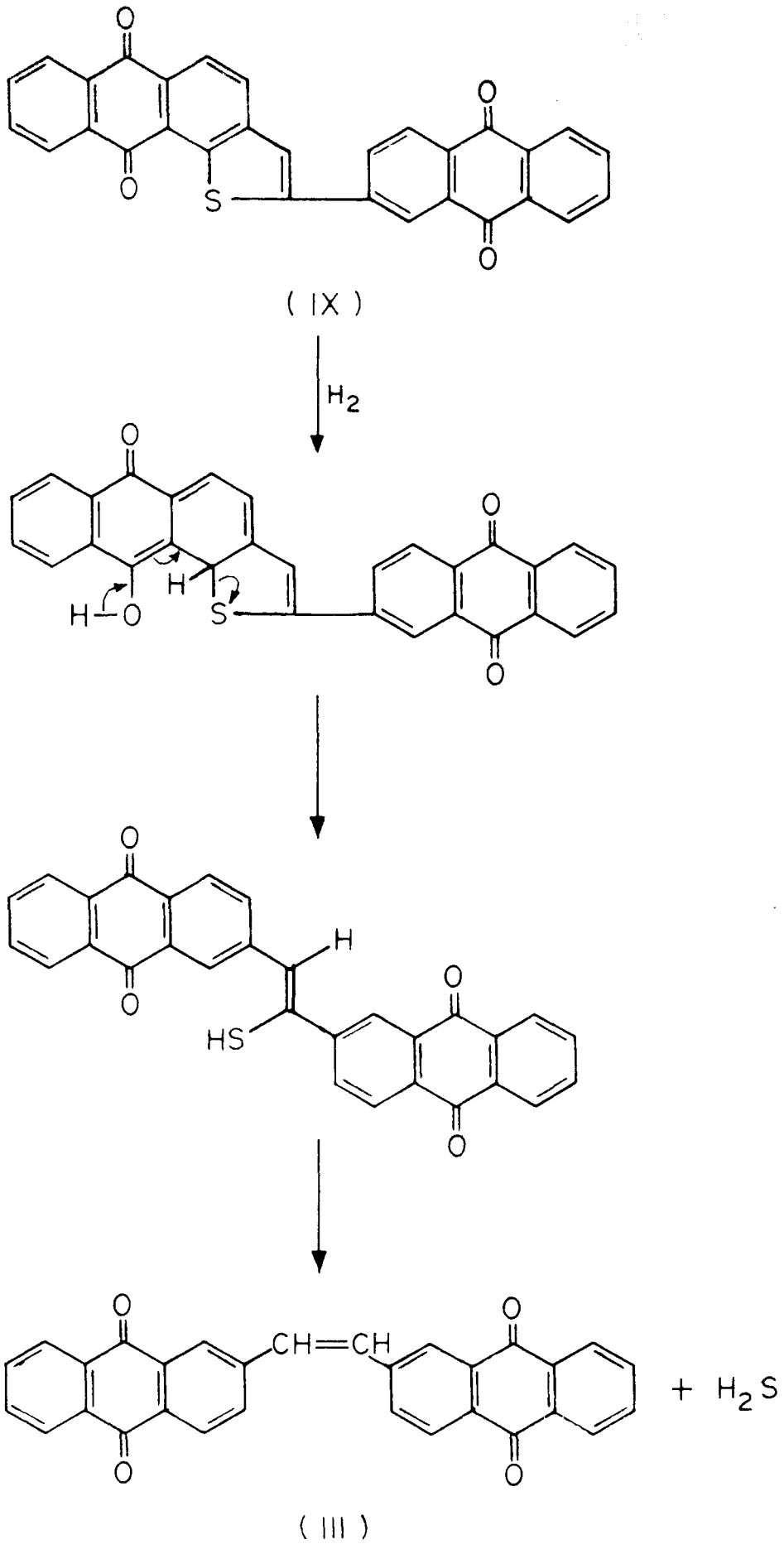
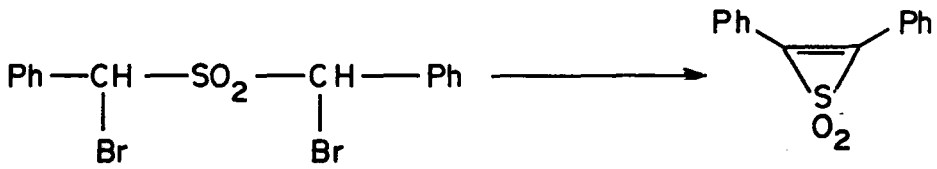


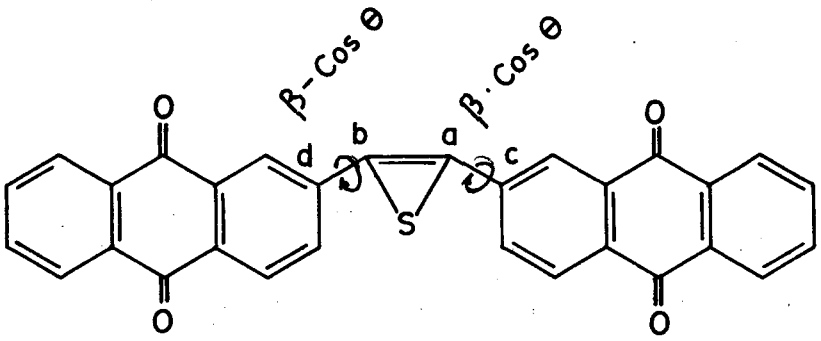
CHART – II

If Cibanone Yellow R is represented by structure (XVI), one has to assume a thiirene or thiacyclopropene skeleton on which very little is known. It has been reported that thiacyclopropene (H-C=C-H, with S bridging the double bond) was obtained as the primary product of reaction between acetylene and atomic sulphur[11] and there is no compound known with such system in which the two hydrogens are replaced by two aryl groups. The only analogy in this regard is 2,3-diphenyl vinylene sulphone (XIX) obtained by the alkaline hydrolysis of (XVIII).[12]



(XVIII) (XIX)

Narasimhan[13] has carried out at our request Huckel molecular orbital (HMO) calculations to explore the probable stability of the molecule (XVI) in terms of the delocalization energy. Zahradnik[14] was the first to carry out the HMO calculation with p- and d-orbital model for sulphur. In the present study delocalization energy of Cibanone Yellow R has been calculated taking care of the nonplanarity of the molecule due to rotation around carbon-carbon bonds as depicted below.



(XVI)

HMO calculation has been made with p-orbital model for sulphur using normal parameters.[14,15]

Since the molecule may not be planar due to rotation around C-C bonds in the structure (XVI), calculations have been carried out taking this into account.

$\beta \cos \theta = \beta_{ac} = \beta_{bd}$	Delocalization energy (in β_{CC} units)	Extra delocalisation* energy (in β_{CE} unit)
1.0 (planar)	12.818	1.302
0.9	12.632	1.116
0.8	12.464	0.948
0.7	12.312	0.796
0.6	12.178	0.662
0.5 (corresponding to $\theta = 60^{\circ}$)	12.060	0.544

* Obtained as DE (Cibanone) - 2DE (Anithraquinone) - DE (Thiirene); DE(Thiirene) was found to be zero (Zahradnik obtained same result with both p and d models for S).

Although DE(Thiirene) is zero, it supports extended conjugation (see extra DE values in the table). In the HMO framework, Cibanone Yellow R is predicted to be stable in spite of zero DE for thiirene. However, the situation may be

different if there is considerable deviation from planarity of the 2-anthraquinone and thiirene units.

Although the thiirene molecule has zero delocelization energy, with substitution of the two anthraquinone units the total molecule i.e. Cibanone Yellow R has non-zero delocalization energy difference. Here by delocalization energy difference we mean the delocalization energy of the molecule minus the delocalization energy of the constituent units, viz. two anthraquinone and thiirene units. The amount of delocalization energy (DE) as well as DE differrance depends on the planarity or deviation from planarity of the anthraquinone units with respect to the thiirene ring. From a consideration of the bonding in the thiirene ring (especially with S bonding to the two C atoms in the thiirene ring) the two anthraquinone units can be inferred to be not in the same plane as the three membered ring. The extent of deviation from planarity is not known and calculations performed by varying this angle show that even if the angle of deviation is 60^{o} the DE value is 12.060 β units and DE difference is 0.564 β units. Therefore from π-electron energy considerations this molecule (Cibanone Yellow R) may be stable. It must be emphasised here that besides π-electron energy considerations there are other important factors such as -energy,steric effects and strain that should not be overlooked.

Reaction of 2-methylnaphthalene with sulphur

In view of the work carried out so far on the thionation of 2-methylanthraquinone, it was felt desirable to look into the products that will be obtained by thionating β-methylnaphthalene (XXVII). Earlier Friedmann[16] thionated β-methylnaphthalene (XXVII) with sulphur under pressure and obtained two uncharacterised sulphur containing products which analysed for $C_{22}H_{14}S$ (C) and $C_{22}H_{12}S_2$ (D) besides 1,2-di-β-naphthylethane (XXVIII) and 1,2-di-β-naphthylene (XXIX). Friedman assigned the structure of (C) as (XX). Horton[17] however suggested the structures (XXI) and (XXII) for compounds (C) and (D) respectively.

Murthy et al.[18] pointed out that in view of the synthesis of 2-phenylthionaphthene and thionaphtheno-(3,2-b)-thionaphthene by thionation of toluene and o-chlorobenzyl chloride, the structures of compounds (C) and (D) can be possibly constituted as (XXIII) and (XXIV) respectively. The structure of (XXIII) for compound (C) was proved by unambiguous synthesis by Murthy et al.

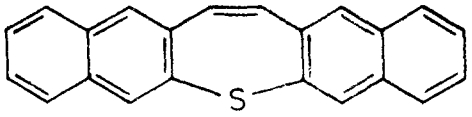
However, when the same thionation reaction of β-methylnaphthalene was carried out at atmospheric pressure only two sulphur containing products in 25 and 36% yield were obtained and analysed for $C_{22}H_{12}S_2$ (E) and $C_{22}H_{14}S_2$ (F) respectively. Based on mass spectral and elemental analysis

the structures (XXIV) and (XXV) are suggested for compounds (E) and (F).

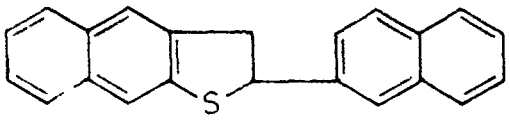
The structure of (XXV) for compound (F) has been confirmed by the conversion of (F) to (E) by thionating one mole of (F) with three atoms of sulphur at 350-70°. The structure of (XXIV) has been confirmed by desulphurisation with W-4 Raney nickel to give 1,2-di-β-naphthyl ethane.

The mechanism of the reaction possibly follows a common intermediate (XXVI) (Chart III) in the reaction conditions of both under pressure and an open tube and the aromatisation of the dihydro thiophene ring takes place giving rise to (XXIII) in the closed tube by dehydrogenation with sulphur. But in the normal atmospheric pressure the nucleppphilic ring closure by sulphur becomes dominant followed by dehydrogenation by sulphur. By quenching the reaction of β-methylnaphthalene and sulphur under pressure in the middle of the reaction no trace of (XXV) could be isolated. The reason for reaction course favouring an aromatisation under pressure is not understood.

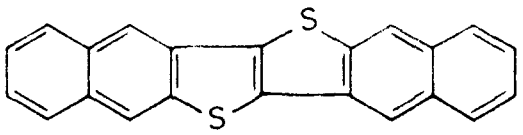
In a controlled experiment, when the thionation with β-methylnaphthalene was carried out at 220-40° in the open tube the yield of (XXV) could be improved to 76% and (XXIV) could be obtained hardly in 4% yield. In another thionation experiment with (XXV) and sulphur (one mole for



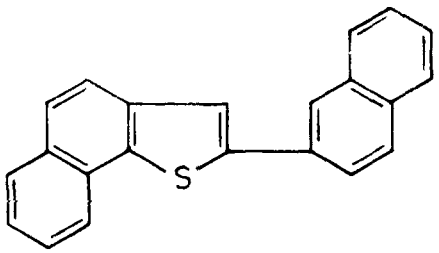
(XX)



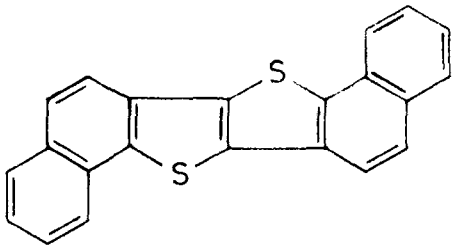
(XXI)



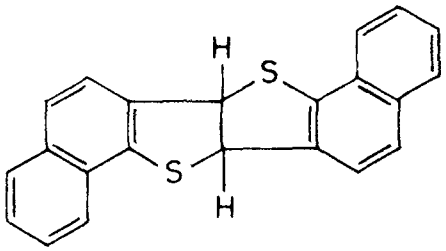
(XXII)



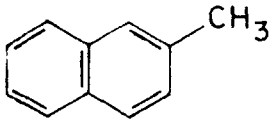
(XXIII)



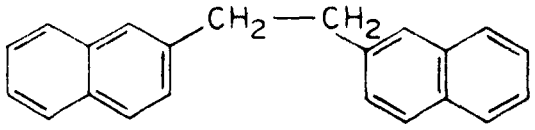
(XXIV)



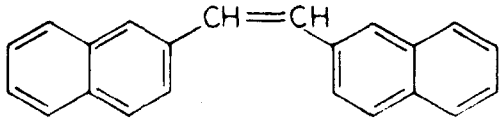
(XXV)



(XXVII)



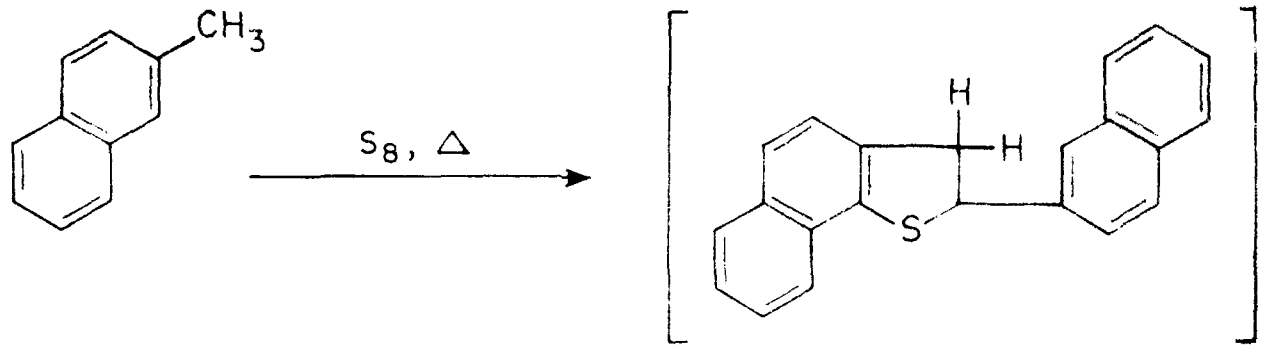
(XXVIII)



(XXIX)

3 atom of sulphur) it was observed that the rate of conversion from (XXV) to (XXIV) was not appreciable till the reaction temperature went above 300° as measured by the rate of hydrogen sulphide evolution. When the thionation reaction of β-methylnaphthalene and sulphur were carried out below 200° for an hour in the open tube and below 160° in the closed tube a mixture of 1,2-di-β-naphthyl ethane and 1,2-di-β-naphthylethylene (XXIX) have been obtained. They were separated by fractional crystallisation and identified by m.p. and m.m.p. 1,2-Di-β-naphthylethane could be easily converted by sulphur (1 mole and 2 atom respectively) to 1,2-di-β-naphthylethylene below 200° in the open tube and 170° in the closed tube with an extra amount of elemental sulphur (3 atom). Compound (XXIX) could be converted to (XXV) in 55% yield at around 240° in the open tube and to (XXIII) in 50% yield in the closed tube (heating carried out at 210°) by thionating (XXIX) with sulphur (1 mole and 2 atom respectively).

From the above experiments it is understood that the reaction of β-methylnaphthalene with sulphur is sequential involving the formation of a carbon-carbon bond initially by dehydrogenation, followed by double bond formation and introduction of sulphur giving rise initially an intermediate like (XXVI); and on this product pressure of the reaction may have pronounced effect on the orientation of the products.

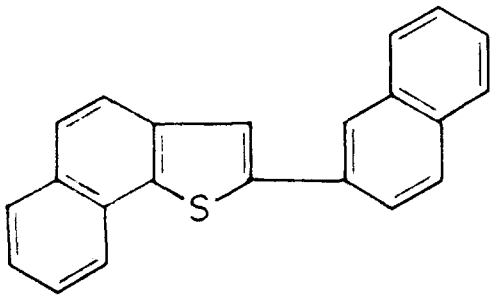


(XXVII)

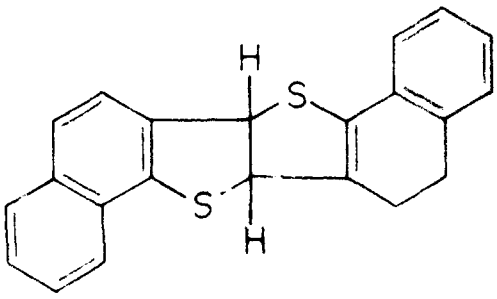
(XXVI)

Closed tube
~△ 270°

Open tube
~△ 300°



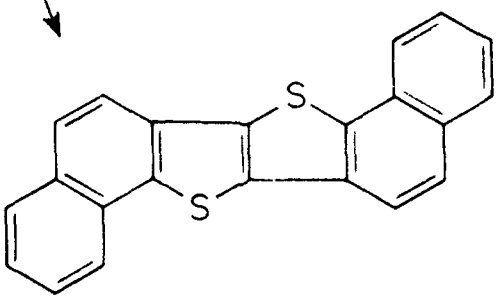
(XXIII)



(XXV)

Closed tube
△ 300°

Open tube
△ 320 - 30°



(XXIV)

CHART — III

EXPERIMENTAL

1. Purification of Cibanone Yellow R

Commercial Cibanone Yellow R (10 g) was purified by the exhaustive extraction method of Fierz-David[4] (extractions with hot water, with cold carbon disulphide, hot chloroform and methanol in a soxhlet). The purified dye (6 g) was dissolved in o-dichlorobenzene (60 ml) (norit treatment), filtered hot and the filtrate was concentrated to 25 ml. The dye obtained partly as yellow needles and partly as yellow transparent round particles, was recrystallised from o-dichlorobenzene (50 ml) in partly crystalline and partly non-crystalline form as reported previously, m.p. 370-74° (Found: C, 76.8; H, 3.6; S, 5.4. $C_{30}H_{14}O_4S$ requires C, 76.6; H, 3.0; S, 6.8%).

The dye gave a purple solution in sulphuric acid and a yellow shade on cotton from a red brown vat.

2. Reductive methylation of Cibanone Yellow R

The alkaline vat of the dye (2 g) was prepared by suspending the dye in aqueous sodium hydroxide solution(5%, 40 ml.) at room temperature and treating with sodium dithionate (3 g) under shaking (10 moles). Dimethyl sulphate (8 ml) was then added gradually with shaking and the temperature of the reactant solution was not allowed to increase. The shaking was continued for half an hour when a yellow precipitate separated (excess alkali and sodium dithionate were

tested). The residue (1.7 g) was filtered, washed with water and dried. The solid on TLC (benzene) showed a mixture of two compounds, one fast moving fluorescent and the second non-fluorescent. The two compounds were separated through column chromatography over neutral alumina (2'x1") using benzene for development and elution. The two fractions thus obtained after repeated crystallisation from pet.ether-benzene mixture were obtained in chromatographically homogeneous form. The fluorescent yellow compound, m.p. 282°; M^+ 530 (Found: C, 76.8; H, 4.8; S, 6.12. $C_{34}H_{26}O_4S$ requires C, 77.0; H, 5.0; S, 6.03%). The non-fluorescent slow moving compound, m.p. 322-24°, M^+ 500 (Found: C, 76.3; H, 4.2; S, 6.6. $C_{32}H_{20}O_4S$ requires C, 76.8; H, 4.0; S, 6.4 %).

3. Demethylation of the reductive methylation product

9,10,9',10'-Tetramethyl ether of the leuco Cibanone Yellow R (0.2 g) was dissolved in 40% hydrobromic acid (2 ml) at room temperature under stirring and left for 15 min. The clear solution was poured on ice. The orange precipitate (0.16 g) after filtration and washing, when monitored on a TLC (benzene-acetone 8:1) found to be a mixture of products, and their separation was unsuccessful by chromatography.

4. Action of neutral sodium dithionate on Cibanone Yellow R

Cibanone Yellow R (1 g) was suspended in water (5 ml) and to this sodium dithionate (2 g) was added in portion at

room temperature. Huge evolution of hydrogensulphide was detected. More of dithionate (1 g) was added till the evolution of hydrogen sulphide stopped (76 hr). Filtered and washed with water. The wet cake was reductively methylated following the procedure described in experiment 2. The solid thus obtained (0.7 g) was crystallised from benzene, m.p. 207-210° (M^{+} 500) undepressed on m.m.p. with an authentic sample of tetramethyl ether of anthraflavone.

5. Oxidation of Cibanone Yellow R with chromic acid in acetic acid

A solution of chromium trioxide (10 g) in 50% acetic acid (20 ml) was added to a boiling mixture of dye (2 g) in glacial acetic acid (20 ml) during 3 hr. The mixture was refluxed for 3 hr. more and diluted with hot water (40 ml), when some white solid separated out. It was reheated to boil and cooled. The product which separated out was washed with dilute acetic acid and extracted with liquor ammonia thrice. The ammonia insoluble portion (0.3 g) was found to be the unaffected dye.

The ammoniacal extracts gave on acidification a pale yellow crystalline solid (1.1 g), m.p. 285-88°, undepressed when mixed with anthraquinone-2-carboxylic acid (m.p.290-92°). The melting point showed a depression of 40° when mixed with anthraquinone-1-carboxylic acid (m.p. 293-94°).

6. Clar reduction of Cibanone Yellow R

Purified Cibanone Yellow R (0.5 g), fused zinc chloride (2.5 g), sodium chloride (0.5 g) and zinc dust (2 g) were powdered together and gradually heated to 430-440° and kept at this temperature for 10 min. A cream coloured solid (0.1 g) sublimed above 320°. The product was resublimed at 280-290°/4 mm when lustrous, colourless flakes were obtained. On crystallisation from benzene, it gave colourless plates, m.p. 204-206° alone or mixed with an authentic specimen of 2-methylanthracene, m.p. 205-07°.

7. Thionation of β-methylnaphthalene

A mixture of β-methylnaphthalene (2.84 g; 0.02 mole) and sulphur (1.28 g., 0.04 g. atom) was heated in a open tube at 300°, whereby a homogeneous melt was formed. The temperature was raised gradually to 300°. During the reaction, hydrogen sulphide profusely evolved. The reaction mixture was cooled and powdered. This was extracted repeatedly with boiling benzene in soxhlet. The benzene extract was refluxed several times with saturated aqueous solution of sodium sulphide. After decolourising with norit (3 g), the benzene solution was concentrated and cooled, a solid (0.9 g) crystallised out, did not melt till 360° (Found: C, 77.1; H, 4.0; S, 18.3. M^{+} 342. $C_{22}H_{14}S_2$ (XXV) requires C, 77.2; H, 4.1; S, 18.7%).

The residue left after the benzene extraction was extracted by O-dichlorobenzene in a soxhlet. Concentration of the o-dichlorobenzene extract gave compound (V) (1.3 g) in shining golden yellow flakes, m.p. 350°. (Found: C, 77.4; H, 3.8; S, 18.3. M^{+} 340. $C_{22}H_{12}S_2$ requires C, 77.6; H, 3.5; S, 18.8%. M^{+} 340).

8. Conversion of (XXV) to (XXIV)

A mixture of compound (VI) (0.34 g; 0.001 mole) and sulphur (0.0015 9 atom) was heated in a open tube at 350-70° for 12 hr. The reaction was worked up following the procedure described in experiment 1 by extracting first with boiling benzene from a soxhlet and then extracted with o-dichlorobenzene. Concentration of o-dichlorobenzene extract gave 5,6,6'-dinaphtho-1,4-(s)-thiophthene (V) which sublimed at 350-60°/3 mm. (0.128 g).

9. Desulphurisation of compound (XXIV)

A mixture of compound (V) (0.3 g) and W-4 Raney nickel (6 g) was refluxed in absolute ethanol (230 ml) for 8 hr. Removal of the nickel and alcohol gave a product (0.1 g) which was crystallised from ethanol in flakes, m.p. 183°, undepressed when mixed with authentic 1,2-di-β-naphthylethane (Found: C, 93.4; H, 6.5. $C_{22}H_{18}$ requires C, 93.6; H, 6.7%).

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P A R T - III

SOME ASPECTS OF THE CHEMISTRY OF TRIARYL-s-TRITHIANES

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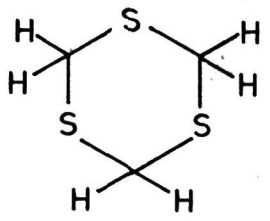
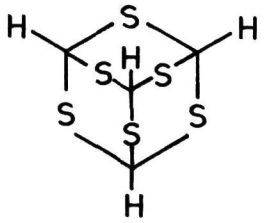
INTRODUCTION

The s-trithianes are the reaction products of aldehydes and ketones with hydrogen sulphide; many examples are known. The latter category also includes an interesting series of compounds related to adamantane in structure.



s-trithiane



Hexathiaadamantane

This class of compounds is indexed in Chemical Abstracts as s-trithiane. It could be called, alternatively, 1,3,5-trithiane or 1,3,5-trithiocyclohexane. In the past, several other names have been used like trimethylene-1,3,5-trisulphide, trithioformaldehyde, trimeric thioformaldehyde, and thialdehyde. s-Trithianes are now named based on aldehyde or ketone from which they are derived. s-Trithianes prepared from aldehydes other than formaldehyde or from unsymmetrical ketones can exist in two isomeric forms. A general agreement exist in the literature to call the more soluble, lower melting, less stable isomer the α-form, and the less soluble, higher melting, stable isomer the β- form. This subject was reviewed in 1946 by Campaigne.[1]

The history of the preparation of triaryl-s-trithianes closely parallels that of the trialkyl compounds. There were

several early reports on ill defined reaction products of benzaldehyde with ammonium sulphide or hydrogen sulphide,[2] benzyl chloride with potassium hydrosulphide.[3,4] Klinger[5] reacted an alcoholic solution of benzaldehyde with hydrogen sulphide and the resulting amorphous solid, m.p. 83-85°, yielded a crystalline solid, m.p. 225-26° on treatment with small amount of acetyl or benzoyl chloride. The crystalline solid melted at 225-26° was the β-isomer of 2,4,6-triphenyl-s-trithiane. This same product could be obtained by treating the amorphous solid with iodine or ethyl iodide[6] or with alcoholic hydrogen chloride.[7,8] Baumann and Fromm[9] are responsible for the method which is now used generally to prepare s-trithianes. The method consists of passing hydrogen sulphide into an alcoholic solution of benzaldehyde containing hydrogen chloride or zinc chloride. Following this procedure they could isolate the α-isomer from a mixture of the two. The β-isomer is the stabler of the two, since the α- isomer can be isomerised to the β-isomer by hydrochloric acid and zinc chloride and also by a variety of acidic materials. High acidity and high temperature favour the formation of the β-isomer which is believed to be a cis-trans form. If the acidity is lowered so as to obtain more of the α- form, which is considered to be cis isomer, linear polymerization takes place. The α- and β- isomers are usually separated by

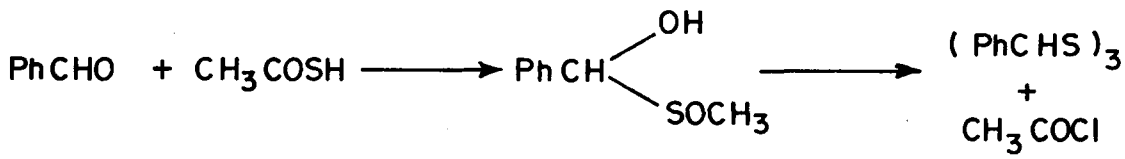
crystallisation from suitable solvents. Tetraphosphorous decasulphide converts aromatic aldehydes and ketones[10,11] to the corresponding trithioaldehydes or trithioketones respectively. The authors have carried out the reactions either by refluxing the reactants in solvents like carbon disulphide and xylene or without solvent at 160-70°. When a mixture of tetraphosphorous decasulphide and benzaldehyde was refluxed in xylene, a 15% yield of stilbene has also been recorded by Bottcher et al.[10] By adding ammonium sulphide to an alcoholic solution of benzaldehyde, Laurent[2] in 1841 obtained a linear polymer thiobenzaldehyde. The same compound was prepared by Rochleder[12] using potassium pentasulphide.

Of the two cyclic trithiobenzaldehydes, the β- form was first isolated[5,8] melting at 228°. Further experiments led to the isolation of the α- form, melting at 167°.[9,13] The two isomers have been well studied and attempts have been made to find the reaction conditions in which either of them can be prepared in high yield. They are separated by crystallisation. The α-isomer is 55 times as soluble in chloroform and 435 times as soluble in benzene at 25° as the β- isomer. If the reaction is carried out in a higher pH, gummy linear polymers of thiobenzaldehyde result. In alkaline solution benzyl mercaptan and dithiobenzoic acid are by-products. These products can be anticipated from

the cannizzaro reaction of the nascent thiobenzaldehyde.[15] A great deal of study has been made of the preparation of ∝- and β- isomers of a number of substituted trithiobenzaldehydes.[16,17,18]

Several early investigators tried to prepare trithiobenzaldehyde by reacting benzal chloride with a metal sulphide,[3,4,19] and landed into thiobenzaldehyde polymers. This method has been used recently to prepare tri thiobenzaldehyde.[15] When an excess of potassium or sodium sulphide was used benzyl disulphide and dithiobenzoic acid were isolated indicating that thiobenzaldehyde had been formed but had undergone the Cannizzaro reaction.[8]

Bohme, Rochr and Schlephack[20] prepared β-s-triphenyltrithiane by treatment of ∝-hydroxybenzyl acetyl sulphide with phosphorous oxychloride.



Other synthesis of triaryl-s-trithianes are relatively unimportant. Barbaglia etal.[21] isolated a small quantity of ∝- 2,4,6-triphenyl-s-trithiane by heating benzaldehyde with sulphur at 180°, the major products were stilbene and benzoic acid. Cairns et al.[22] isolated a mixture of ∝- and β- 2,4,6-triphenyl-s-trithiane in very low yield by heating benzaldehyde under pressure with

hydrogen sulphide at 50°. When thioacetic ester was reacted with benzaldehyde in the presence of water and a trace of piperidine, a polymer of thiobenzaldehyde was isolated. Treatment of this with acetyl or benzoyl chloride at 5° in the presence of a trace of piperidine gave a quantitative yield of β- isomer of the s-trithiane. The reaction could be carried out in one step by treating a mixture of thioacetic ester and benzaldehyde in alcohol with hydrogen chloride.[23]

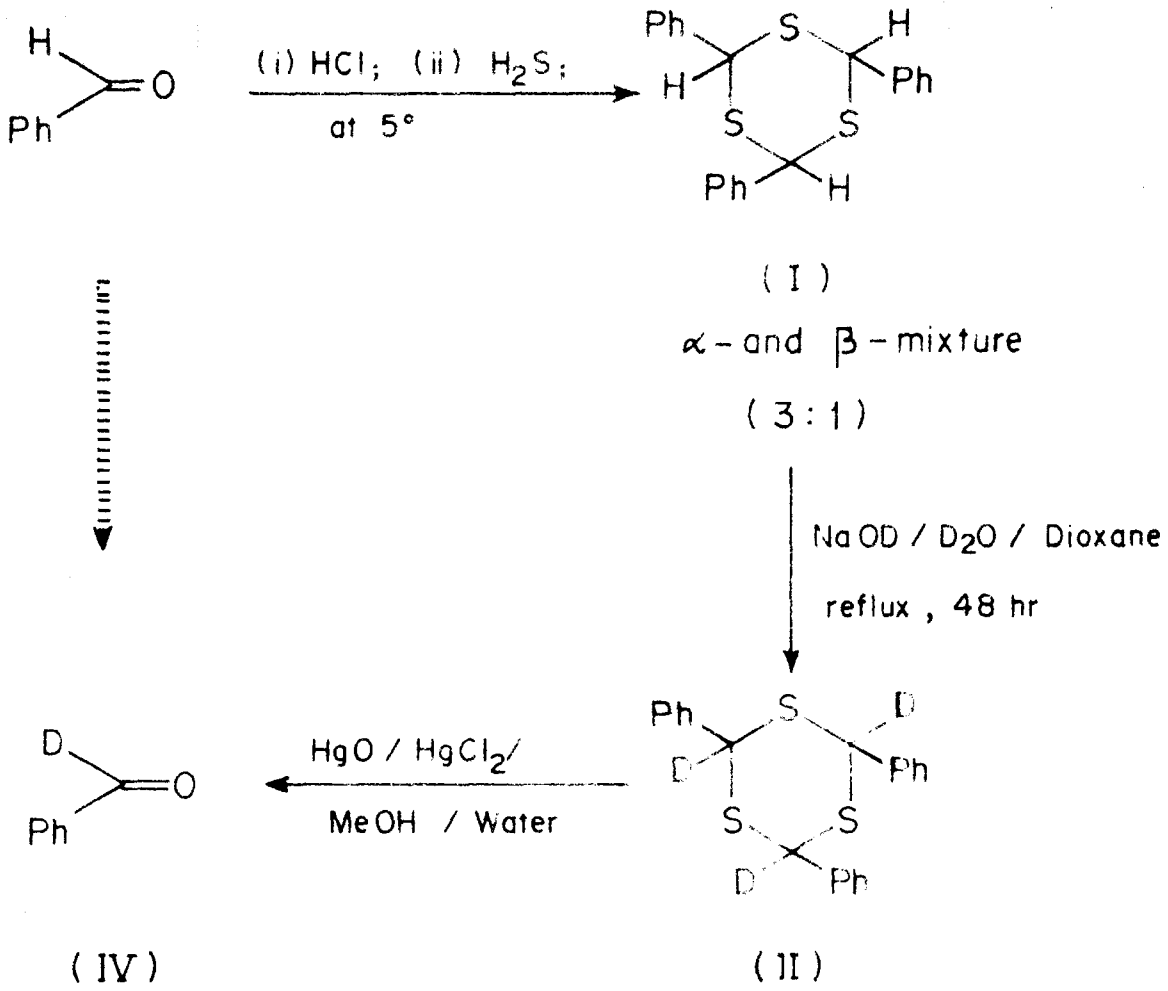
PRESENT WORK

1. Synthesis of α-d-aromatic aldehydes from 2,4,6-triaryl-s-trithianes.

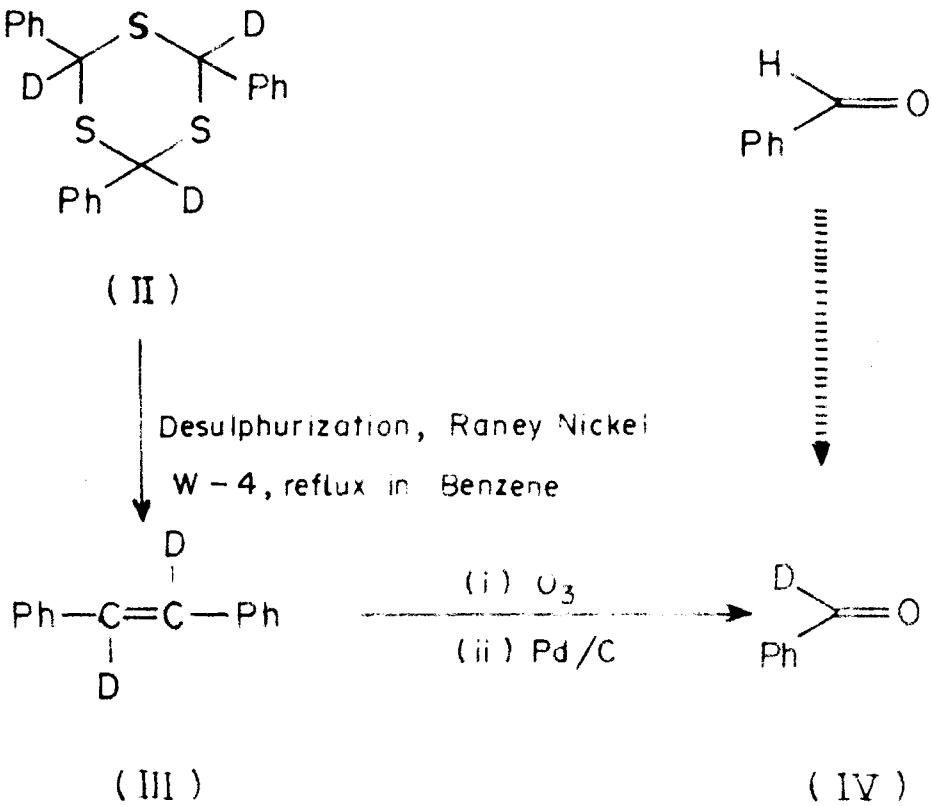
At an earlier stage on the constitution of Cibanone Orange R, it was considered that the dye might be a dimer of anthraquinone-2-thioaldehyde having 1,3-dithiane skeleton (see Cibanone Orange R). In this connection the properties of 2,4,6-triphenyl-s-trithiane (I; the trimer obtained quantitatively when benzaldehyde is treated with H_2S and HCl)[24] were examined, and it was found that it is a very useful intermediate as the carbanion. Thus the three protons of the heterocyclic ring can be completely exchanged by deuterium ions by refluxing a dioxane solution with a 20% solution of NaOD in D_2O, as shown by the disappearance of the proton

signals in the NMR spectrum and the shift of $M^{+\cdot}$ by three mass units in the mass spectrum. Hydrolysis of the tri-deuterated triaryltrithiane (II) by $HgCl_2$ and HgO in boiling aqueous methanol[25] gave α-d-benzaldehyde (Scheme 1). Similarly the p-chloro-, p-methoxy- and 3,4-methylenedioxy-derivatives of α-d-benzaldehyde were obtained in 80-85% yield. They were prepared earlier by different and much less convenient methods.[26-28]

In recent years, there has been considerable interest in chemical and biochemical studies of reaction mechanism using aldehydes labelled with deuterium at C-1,[29] and therefore methods for their preparation are of wide interest. Benzaldehyde-1-d- was prepared earlier by the following methods: (1) Rosenmund reduction of benzoyl chloride with deuterium gas,[30] (2) lithium aluminium deuteride reduction of methyl benzoate to benzyl alcohol-α,α-d_2 and the Sommelet reaction on the corresponding chloride[31] (3) reduction of benzil with lithium aluminium deuteride and lead tetraacetate oxidation of the diol;[26,32] (4) reaction of benzoyl chloride, potassium cyanide and quinoline, followed by hydrolysis of 1-benzoyl-2-cyano-1,2-dihydroquinoline with deuterium chloride, bromide or sulphate in deuterium oxide;[27] (5) treatment of N-t-butylbenzamide with lithium aluminium deuteride and acid hydrolysis;[28] (6) refluxing a mixture of deuterated phenylglyoxylic acid with N-ethylmorpholine;[33]



SCHEME - I



SCHEME - II

(7) reduction of benzonitrile with stannous chloride and deuterium chloride;[34] (8) conversion of benzaldehyde to 2-phenyl-1,3-dithiane, lithiation at C-2, treatment with D_2O and hydrolysis with mercuric chloride and mercuric oxide;[35] (9) from benzaldehyde *via* α-morpholinobenzyl cyanide by deuteration and acid hydrolysis;[36] and (10) cleavage of benzil by cyanide ion in the presence of D_2O;[37] (11) Benzyl triphenyl phosphonium chloride was deuterated at α-position and hydrolysis of N-benzyl aniline-α-*d* formed on reaction with nitroso benzene.[38] (12) hydrolysis of *bis*-iminium cations in deuterium oxide followed by acidification.[39] Beside these methods six less general routes[40-45] to α-*d*-aromatic aldehydes are known.

The triaryltrithianes[17] were obtained starting from benzaldehyde, *p*-chlorobenzaldehyde, anisaldehyde and piperonal in over 90% yield. A mixture of the *cis*- and *trans*-isomers was obtained in each case, the former being the major product. In the NMR spectrum of triphenyltrithiane (I) in DMSO the three hydrogens of the trithiane ring appeared as three singlets at 3.88, 4.18 and 4.41 (chemical shifts on the τ-scale); the first two which are in the ratio of 2:1 can be assigned to the trans-isomer. From the NMR data it is evident that the *cis*- and *trans*- isomers were in a ratio of 1:3. No attempt was made to separate the isomers, because the mixture was suitable for the subsequent reactions.

This method of obtaining the α-d-aromatic aldehydes is more attractive than any one known to this date. Further, the conversion of the aromatic aldehyde to the corresponding trithiane, deuteration at all the three centeres of the heterocyclic ring and subsequent hydrolysis of the trideutero derivative to the corresponding aldehydes are very smooth and quantitative.

2. Synthesis of α,α'-d_2-stilbenes from 2,4,6-triaryl-1,3,5-trithianes

It has been known for a long time that a dry distillation of trithiabenzaldehyde gives stilbene, a part of which is converted to triphenylthiophene by sulphur given off during the distillation.[4,15,46-50] A number of trimeric aromatic thials have been converted to stilbenes by heating. As early as 1877 Klinger[6] reported that heating β-2,4,6-triphenyl-s-trithiane above its melting point with copper gives a good yield of stilbenes. The most commonly used metal is copper or some form of activated copper, but iron, zinc and nickel have also been found effective.[51] The reaction has been applied to a variety of substituted phenyl compound to prepare symmetrical stilbenes by many workers.[51-56] Richtzenhain *et al.*[56] showed that iron could be used in place of copper. Clinc and co-workers[57] refluxed triphenyl-s-trithiane with Raney nickel in xylene and obtained an 18% yield of the expected trans-stilbene.

Hauptman et al.[58] discovered that better yields of olefin were obtained when they used dehydrogenated Raney nickel. The yields in all these reactions in general are low and variable excepting some halogen substituted compounds.[51] Recently Latif et al.[59] have claimed 73-83% yield of trans-stilbene by refluxing trithiane with Raney nickel free of water in dry solvents.

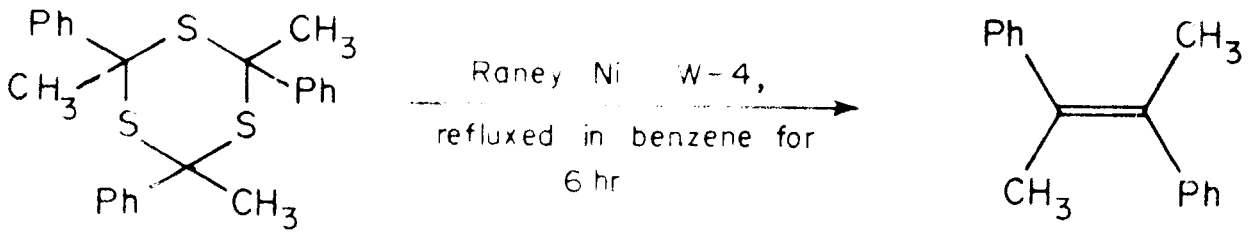
In the present study, when a mixture of s-triphehenyl trithiane and Raney nickel (W-4)[60] in benzene was refluxed, only trans stilbene was obtained almost in quantitative yields. However, it was observed that the desulfurization does not go smmoth when solvents such as ethanol, methanol or acetone have been employed.

In connection with a mass spectral study it was of interest to prepare trans-α,α'-d_2-stilbenes. A survey of the literature revealed that such compounds have not been obtained so far in pure form. Several papers deal with low incorporation of deuterium at α,α'-position of the stilbene molecule for kinetic study.[61,62] The methods so far available for the synthesis of α,α'-d_2-stilbenes are not very convenient. Trans- deuterated stilbenes were prepared by catalytic deuteration of diphenyl acetylene.[61] Cis-α,α'-d_2-stilbene has been made by treatment of diphenylacetylene in tetrahydrofuran with metallic lithium at -78° in high

vacuum and then treating with deuterated methane.[62] In another method,[63] which starts from benzyl-α-α'-$\underline{d}_2$-triphenyl phosphonuim bromide, the percentage incorporation of deuterium was uncertain. Mono deutero stilbene was made by treatment of stilbene oxide with lithium aluminium deuteide to give the corresponding 1,2-diphenyl ethanol-α-$\underline{d}$, followed by base induced elimination of benzoic acid from benzoates.[64] α,α'-Dideuterostilbenes (III) have now been synthesised in over 80% yield starting from 2,4,6-trideutero-triaryl-$\underline{s}$-trithianes, (II). The conversions are good when desulphurisation was carried out with W-4 Raney nickel,[66] in boiling benzene. Adopting this method, the trideutero derivatives of $\underline{p}$-methoxy-, p-chloro- and $\underline{p}$-hydroxytriphenyl-$\underline{s}$-trithianes, were converted to the corresponding α,α'-$\underline{d}_2$-stilbenes. All the stilbenes thus obtained are $\underline{trans}$-isomers as expected.

Further, all the di-deuterated stilbenes were converted to the corresponding α-$\underline{d}$-aromatic aldehydes (IV) in over 80% yield by ozonolysis of an ethylacetate solution at room temperature, followed by the decomposition of the ozonoid by catalytic hydrogenation using palladium charcoal, (Scheme II).

Stilbenes are long known as synthetic sex hormones and this led Cline $\underline{et\ al.}$[57] to investigate the conversion of trithioacetophenone (V) to α,α'-dimethylstilbene (VI). Copper powder did not react, either when fused with the dry


Ph
S
CH3
CH3
Ph
S
S
Ph
CH3
Raney Ni W-4,
refluxed in benzene for
6 hr
Ph
CH3
CH3
Ph

(V)

(trans)
(VI)

compound or when refluxed in boiling xylene, but an 18% yield of (VI) was obtained when excess Raney nickel was refluxed with trithioacetophenone in boiling xylene. Desulfurization using excess of W-4 Raney nickel[60] in boiling benzene, was found to be more convenient and very good conversion of trithioacetophenone (V) to α,α'-dimethylstilbene.

Mozingo et al.[65] have postulated two courses by which Raney nickel might react with organic sulphur compounds to split out sulphur. In the first one, a Wurtz type reaction might occur, in which the two organic radicals would combine and in second the hydrogen present in the nickel might replace the sulphur. The conversion of triphenyl trithianes to the stilbenes belong to the first category.

A mercaptal of benzaldehyde is converted to stilbene.[58] Sodium desulphurizes benzophenone mercaptal to tetraphenyl ethylene[66] easily, whereas a mercaptal of chlostanone or a mercaptal of propionic alddhyde, acetaldehyde are converted to chlolastane, propane or ethane. Similarly butyraldehyde mercaptal gives rise to butane. A Wurtz type reaction is possibly favoured when the stability of the resultant radical is favoured by the delocalization of the radical in the electronic structure of the radical fragment and also by the polarity of the solvent in the reaction medium. Obviously, a nonpolar low boiling solvent and a low hydrogen content of the Raney nickel as in W-4 would favour such radical reactions.

3. Synthesis through carbanions from 2,4,6-triaryl-s-trithianes

From the deuteration experiments, it is clear that carbanions can be generated from triaryl-s-trithianes by the action of a base. A perusal of the literature indicates that such observations have also been made earlier in a variety of compounds having thioacetal groupling. Further, these anions undergo alkylation or acetylation with a wide variety of reagents. It was first in 1959 that Arens et al.[67] have shown that mercaptals of type (VII) can be converted into carbanions (VIII) using alkali metal amides in liquid ammonia. However, they are of not much synthetic applicability because the yields of the alkylated compounds are relatively low, using an excess of primary halide and does not add onto ketones. Shortly after that Oae et al.[68] have shown that aerolein diethyl mercaptal (IX) was isomerised by potassium-t-butoxide to the ketone mercaptal (X).

The stability of the carbanion was explained by the 3d-orbital overlap between a sulphur atom and the adjacent carbanion and the inductive effect of the two mercapto groups were put forth as explanations. Truce et al.[69] have recently studied the metalation of benzaldehyde diphenylmercaptal with various bases and they could successfully alkylate on the carbon flanked by two sulphur atoms. These reports[67-69] that a mercaptal with a strong base gives an anion has opened up some interesting areas of sulphur chemistry.The requirement

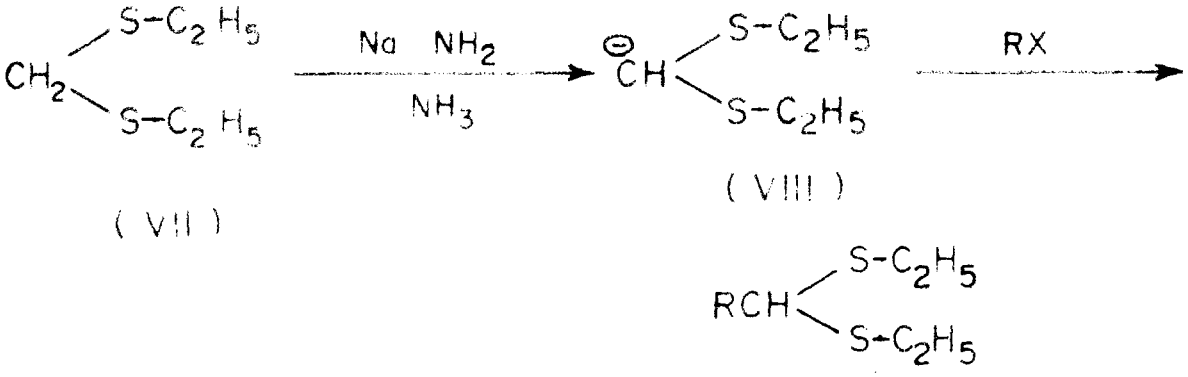
of coplanarity in order for the resonance to occur is less severe if d-orbitals are involved. Resonance may occur using d-hybrid orbitals in compounds that are not planar.[70-79] Thus Doering and Hoffman[80] found that the bicyclo-(2,2,1)-heptane-1-sulphonium ion (XI) exchanges hydrogen for deuterium. Orbital overlap has been postulated to occur even though the sulphur is at a bridgehead. Doering and Levy[81] have shown that the tricyclic trisulphone (XII) is a strong acid with a pK of 3.3 and the acidic hydrogen is the one at the bridgehead.

This tricyclic trisulphone (XII) is almost as acidic as the acyclic analogue, tris-(ethyl sulphonyl)-methane (XIII).

Cyclopropyl phenyl sulphone (XIV)[82] has an acid dissociation constant 1.4 to 1.8 fold larger than that for isopropyl phenyl sulphone (XV). Here again the sulphone group stabilizes the carbanion at the bridgehead.

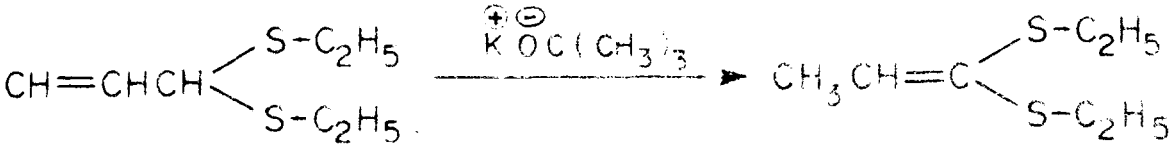
Corey and Seebach[83] have demonstrated that carbanions generated from 1,3-dithians by the action of n-butyl lithium are much more superior in their reactivity and can be alkylated or acylated by a variety of reagents.[84] They in turn can be converted to the carbonyl compounds by a number of reagents.

In the present work, it has been shown that by refluxing a dioxan solution of triphenyl-s-trithianes with sodium hydroxide in D_2O, all the three hydrogens of the



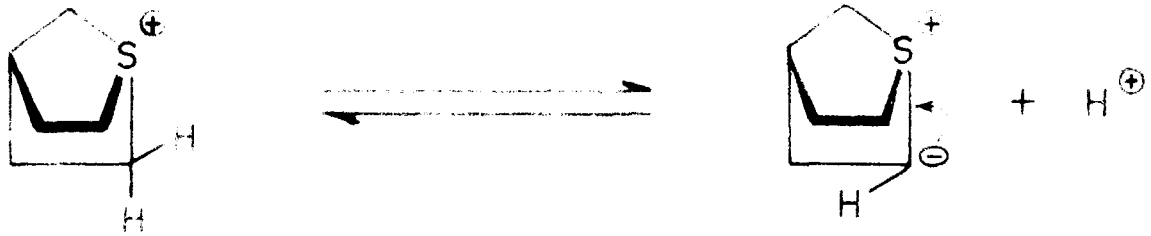
(VII)

(VIII)

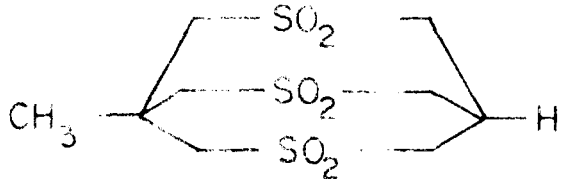


(IX)

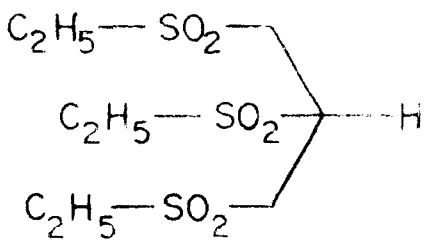
(X)



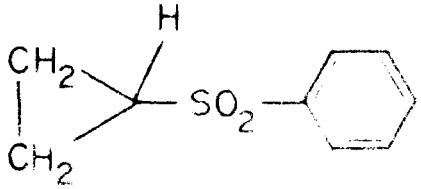
(XI)



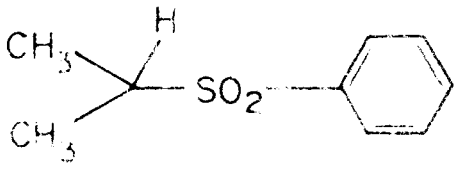
(XII)



(XIII)



(XIV)



(XV)

heterocyclic ring have been exchanged with deuterium thereby showing the possibility of generating the carbanion for reactivity at all the three centers. As the preparation of trithianes from carbonyl compounds is much simpler and inexpensive than building a dithiane system, it was felt worthwhile to study alkylation of trithianes using a strong base. A perusal of the literature indicated that a number of 2-alkyl or acyl derivatives have been claimed in a patent by Corey[116] from 1,3,5-trithianes through lithium, sodium, or potassium salt of 1,3,5-trithianes by reacting with butyl lithium, sodamide, sodium hydride or pot tertiary butoxide in tetrahydrofuran or liquid ammonia.

When trithioformaldehyde was submitted for deuteration under identical condition as that of triphenyl-s-trithiane, the product was recovered. From this it is clear that only in triphenyl-s-trithiane the protons of the heterocyclic ring can be easily removed by a mild base. It has been demonstrated in the present work that anions can be generated at all the three positions of the triphenyl-s-trithianes. Thus when triphenyl-s-trithian was reacted with sodium hydride in dimethyl sulphoxide at room temperature and then alkylated with excess of methyl iodide, 2,4,6-trimethyl-2,4,6-triphenyl-s-trithianes (V) was isolated. This product (V) on hydrolysis yielded three moles of acetophenone. However, attempts to benzylate with benzyl chloride under

similar conditions, followed by hydrolysis gave a mixture of products, one of these being desoxybenzoin. Similarly, acylation using ethyl chloroformate has also met with failure.

4. Two more general methods of synthesis of triaryl-s-trithianes from aromatic aldehydes

Method 1.

While this work was under progress, Oae et al.[85] have reported the conversion of carbonyl compounds into the corresponding thiocarbonyl derivatives by treatment with O,O-diethyldithiophosphoric acid. They reported the formation of the corresponding dimers when cyclohexanone and benzaldehyde were treated with large excess of O,O-diethyl dithiophosphoric acid in benzene. This was the first report of the formation of a thiobenzaldehyde dimer. They had not, however, given any physical or spectral properties of this dimer to substantiate their claims.

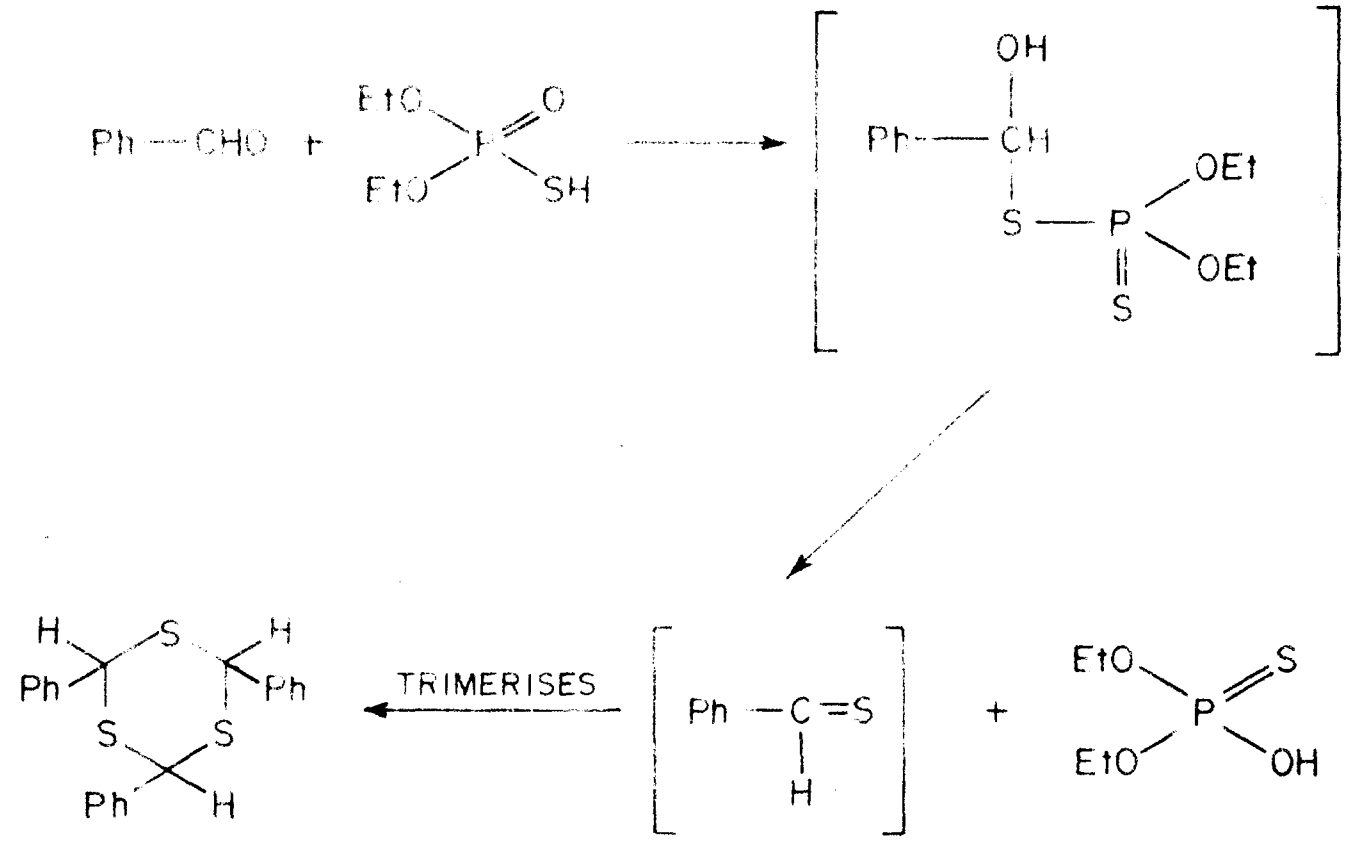
When the reaction was repeated using benzaldehyde and treating with O,O-diethyl dithiophosphoric acid at room temperature for 16 hr. and subsequently refluxing for an hour, the product that was obtained was characterised as 2,4,6-triphenyl-s-trithiane as its β-isomer (from mass spectrum and NMR). This method has been applied successfully to the preparation of a number of substituted triaryl-

s-trithianes. No attempt has been made to isolate the intermediate products and the reaction course has been envisaged as shown in Scheme III.

Method II.

It has been reported by several workers that the acidification of a mixture of formaldehyde and sodium thiosulphate gives rise to symmetrical trithioformaldehyde.[86-93] In the same manner symmetrical trithioacetaldehyde was obtained by reacting paraldehyde[91] with acids such as concentrated hydrochloric, hydrofluoric, hydrobromic, nitric and sulphonic acids, but phosphoric, trichloroacetic and other weak organic acids do not give rise to the reaction. Vanino and Schinner[92] have postulated the mechanism shown in Scheme IV and was substantiated by Schmidt for the existance of the intermediate (XVI).

Vanino and Schinner further found that the above reaction could also be carried out with tetra- and pentathionates, whereas dithionate does not react to give sym-trithioformaldehyde as there is no divalent sulphur. The authors[93] could not detect any trace of sulphur dioxide or hydrogen sulphide and ruled out the possibility of oxymethylenethiosulfate as intermediate in the reaction. The reaction between an aromatic aldehyde and sodium thiosulphate in presence of mineral acids has not been investigated. When sodium thiosulphate and benzaldehyde in 2:1



SCHEME III

$$CH_2O + Na_2S_2O_3 + 2HCl \longrightarrow \left[HO-CH_2-S-SO_3H\right] + NaCl$$

(XVI)

$$3\left[HO-CH_2-S-SO_3H\right] \longrightarrow (CH_2S)_3 + 3H_2SO_4$$

SCHEME IV

molar proportion were reacted with excess of concentrated hydrochloric acid (pH 2 to 2.5) by refluxing for a period of 2 hr, 2,4,6-triphenyl-1,3,5-trithiane was obtained in quantitative yield. The triaryl-s-trithianes thus synthesised adopting the above method, are of p-methoxy, p-hydroxy and p-chloro benzaldehydes. The trithianes obtained are exclusively β-isomers and no α-isomer has been isolated.

5. Conversion of 2,4,6-triaryl-s-trithianes to the corresponding carbonyl compounds

The basis of the hydrolytic cleavage of s-trithiane lies in the initial demarcaptalation experiments of aldose mercaptals.[94,95] Aldose mercaptals are hydrolysed by boiling with dilute acids.[94,95] This is due to large excess of water and to the volatility of mercaptan. The elimination of the mercaptan in this way is slow. Silver nitrate, mercuric chloride and cadmium chloride remove the mercaptan as insoluble mercaptides.[94] The reaction of mercuric chloride with the mercaptan liberates hydrochloric acid and the formation of insoluble mercaptide is favoured by maintaining a low acidity. This is normally achieved by mercuric oxide,[96-99] by cadmium or by cadmium carbonate.[100-109]

Following Grobb's[110] observation Djerassi et al.[110] have decomposed cholestan-3-hemithioketal with mercuric

chloride and one equivalent of sodium hydroxide in ethanol to cholestan-3-one in 91% yield. Corey and Mitra[111] have shown the feasibility of base catalysed mercuric chloride desulfurization using silver oxide to 1,3-dithiane systems to the corresponding carbonyl compounds in high yields.

Besides the normally employed mercuric chloride and mercuric oxide method of converting a thioacetal grouping to the corresponding carbonyl compounds, a few more general methods[84] have also been employed. An oxidative hydrolysis of a thioacetal group in 1,3-dithianes and 1,3,5-trithianes can be achieved by N-bromosuccinimide in aqueous acetone. This reaction can be performed under neutral condition by removing the hydrobromic acid from the reaction by the presence of silver perchlorate, silver nitrate or 2,6-dimethyl pyridine. Similarly N-chlorosuccinimide has also been employed. Another method of oxidative hydrolysis is by subjecting the dithiane or trithiane in acetic acid containing small quantities of hydrochloric acid with a solution of bromine in acetic acid.

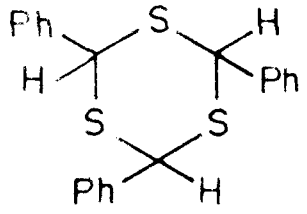
As it is of general interest to find out some better reagents for the hydrolytic cleavage of trithianes to the corresponding carbonyl compounds, some other reagents have been tried. Thus silver oxide in aqueous methanol is found to be convenient in achieving this objective.

When triphenyl-s-trithiane was refluxed in 10% aqueous methanol with silver oxide for a period of 4 hr. and working up as usual gave benzaldehyde in very good yield. All the other substituted triaryl-s-trithianes prepared during the course of the work were also converted smoothly to the corresponding aromatic aldehydes by this reaction. The course of the reaction is shown in Scheme V.

Silver cation being electron deficient can be coordinated by the lone pair available from sulphur and can form the complex. . This can undergo a fission followed by a nucleophilic attack by the hydroxide ions and subsequently aroma giving rise to aromatic aldehyde. After completion of this work, it was found that Gravel et al.[112] have adopted this method for removal of thioacetal group in a number of steroid derivatives.

In addition to the silver oxide method it was found that iodine in dimethyl sulphoxide effects the convérsion of s-trithianes and thioacetals by a novel oxidative desulphurisation into the corresponding aldehydes or ketones in very good yields.

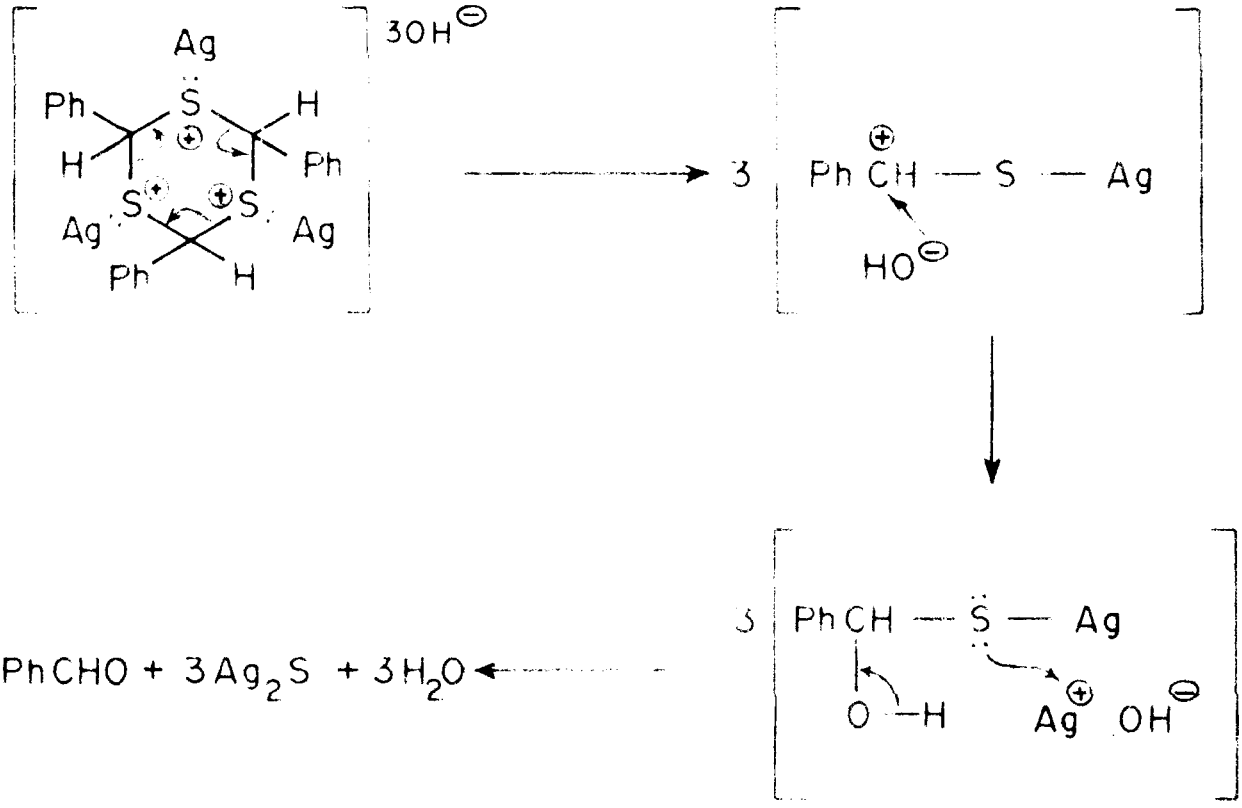
In a typical experiment, a mixture of 2,4,6-triphenyl-s-trithiane (3.66 g., 0.01 mole) and iodine (3.81 g., 0.03 atom) was dissolved in dimethyl sulphoxide (20 ml) and the solution was heated on a steam bath for ana hour. During the course of the reaction a volatile



+ $3HgCl_2$ + $3H_2O$ ⟶

$3PhCHO + 3HgS + 6HCl$

(I)



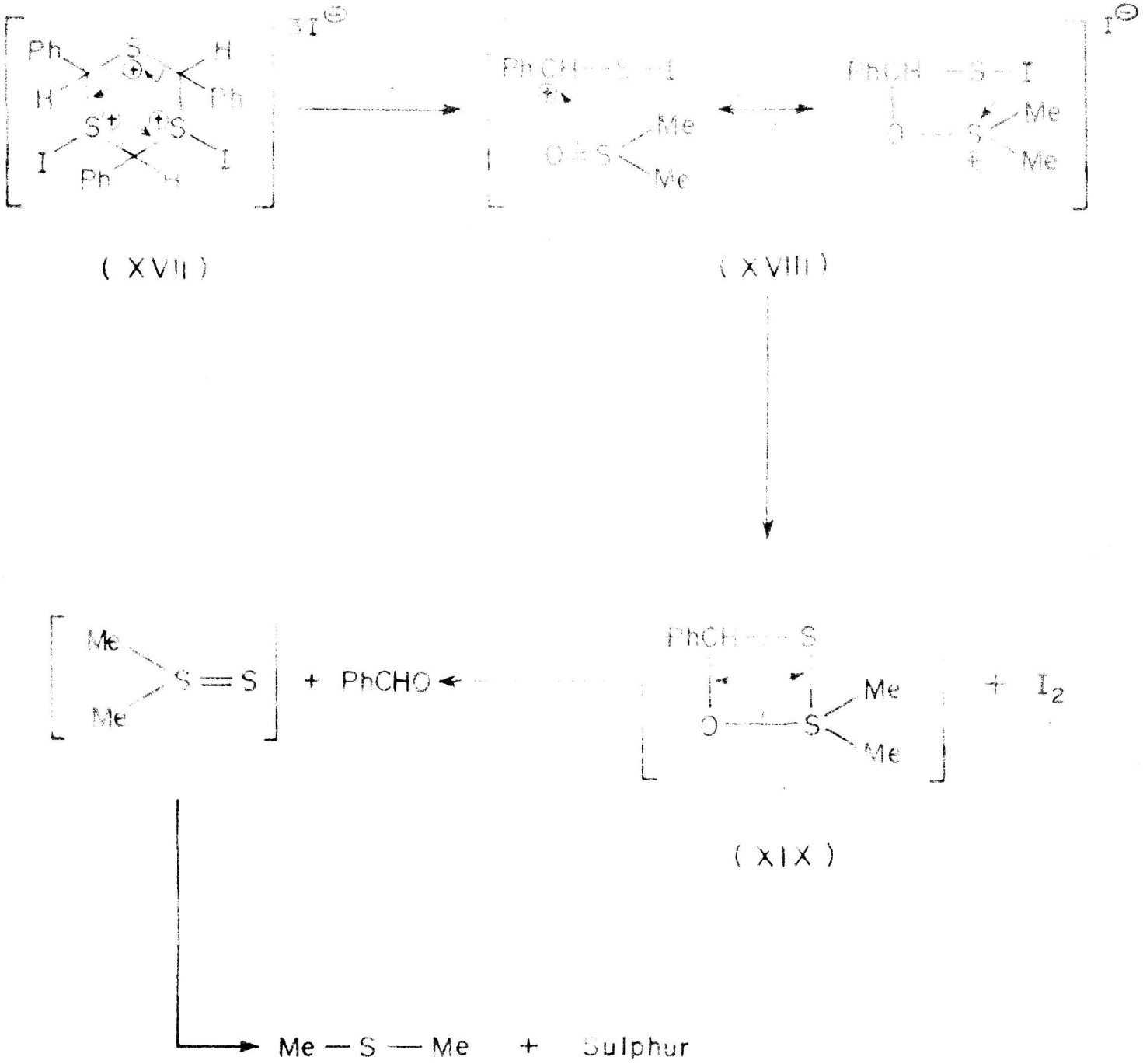
$3PhCHO + 3Ag_2S + 3H_2O$ ⟵

SCHEME - V

fraction, distilling at 35-38°, was collected and characterised as dimethyl sulphide (1.4 g., methyl signals at 7.92 τ compared to dimethyl sulphoxide methyl signals centered as a doublet at 7.5 τ). The solution was cooled, diluted with cold water (100 ml) and the free iodine was destroyed by adding a solution of sodium thiosulphate (4 g) in water (15 ml). A pale yellow solid was precipitated out of the solution (0.8 g., m.p. 121-22°) and identified as elemental sulphur. The aqueous solution was extracted with pet.ether. Removal of the solvent gave an oil (3 g., 94%), characterised as benzaldehyde (b.p.; 2,4-DNP).

Adopting the same procedure, a few s-trithianes and thioacetal derivatives of ketones have been hydrolysed to give the corresponding aldehydes or ketones in good yields, (see Table 1).

The reaction on s-trithianes probably involve the formation of a sulphonium complex with iodine (XVII), followed by the rupture of the ring and the nucleophilic addition of dimethyl sulphoxide to form (XVIII),which breaks down through (XIX) to the aldehyde, dimethyl sulphide and sulphur. (Scheme VI). Iodine is needed only in catalytic amounts, /Alternatively the attack by dimethyl sulphoxide may be followed by ring rupture.


Ph
H
S
H
Ph
I
S
S
I
Ph
H
3I⊖
PhCH—S—I
Me
O=S
Me
PhCH—S—I
O
S
Me
Me
I⊖
(XVII)
(XVIII)
Me
Me
S═S
+ PhCHO
PhCH—S
O
I
S
Me
Me
+ I2
(XIX)
Me — S — Me + Sulphur

SCHEME - VI

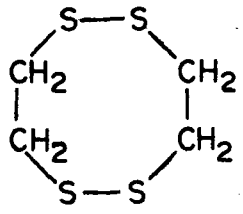
T A B L E - 1

s-Trithianes	Yield* of parent aldehyde or ketone (%)
1. Trithioformaldehyde $(CH_2S)_3$	63+
2. 2,4,6-tris(phenyl)-	94
3. 2,4,6-tris(p-methoxyphenyl)-	79
4. 2,4,6-tris(3,4-methylenedioxyphenyl)-	83
5. 2,4,6-tris(p-chlorophenyl)-	76
6. 2,4,6-tris(methyl-phenyl)-	87
Thioacetal derivative of ketones	
7. Cholestan-3-one	76
8. 4,6-Cholesten-3-one	81
9. Cyclohexanone	84

* Conversions are quantitative, losses are due to working up procedure and purification. All products have been characterised by the melting point or boiling point.

+ Yield based on 2,4-DNP.

The conversion of thioacetal derivative of cholestan-3-one, 4,6-cholesten-3-one and cyclohexanone to the corresponding parent ketones has been achieved, using this reagent, in high yield. The products in the removal of 1,3-dithiopentane ring during the desulphurisation reaction is dimethyl sulphide and a polymer of 1,3-dithio ethane, m.p. 129-31^{o} which could be obtained in quantitative amount by the reaction of ethane dithiol with dimethyl sulphoxide alone on a steam bath. Its infrared spectrum shows the absence of -SH function in the molecule. The molecular weight determination (Rast method) showed its molecular weight to be around 600, indicating that the polymer could be of six or seven units of $\{S\text{-}CH_2\text{-}CH_2\text{-}S\}$ and should be a cyclic polymer. Fasbender[113] obtained a compound (XX) by the oxidation of ethanedithiol with bromine



(XX)

in chloroform for which he suggested the structure (XX) on the basis of elemental analysis alone. This compound was prepared by the same route and compared with the product obtained by heating ethane dithiol with dimethyl sulphoxide on a steam bath, and found that they are identical.

Another method of cleavage of triphenyl-s-trithiane ring system to generate the corresponding aldehyde is by reacting triaryl-s-trithiane with pyridine-N-oxide and iodine. Thus when a mixture of triphenyl trithiane (0.01 mole), iodine (0.03 atom) and pyridine-N-oxide (0.04 mole) in cellosolve was heated to reflux for 8 hr. and then poured on crushed ice and then worked up as in dimethyl sulphoxide-iodine reaction, an oil was obtained which was identified as benzaldehyde in 40% yield. Pyridine has been isolated as an end product. The yield could not be improved by prplonged refluxing the reaction mixture. This is another case of oxidative desulphurisation as in case of dimethyl sulphoxide and iodine reaction with trithiane.

Following the same procedure a number of substituted triaryl-s-trithianes like p-chlorophenyl, p-methoxy phenyl, and 3,4-methylenedioxyphenyl have been oxidatively desulphurized to the corresponding aldehydes.

The mechanism of the pyridine-N-oxide-iodine reaction perhaps keeps a close analogy with dimethyl sulphoxide-iodine reaction with s-trithiane.

Hydrazine, with or without alkali, has been found to desulphurize cyclic and acyclic ethylene thioketals[114] to the corresponding ketone, and it was of interest to explore the action of hydrazine on the triaryl trithianes

in alkaline and neutral conditions. While a mixture of triphenyl-s-trithiane (1 part of weight) in thirteen parts volume of diglyme with four parts by volume of 80% hydrazine and two parts by weight of sodium hydroxide was refluxed for a period of 2 hr., and poured in water. The product thus obtained was identified as benzalazine. The alkali was found to be necessary in all the cases in this reaction, unlike the desulphurisation of thioketals.[114] The sulphur was reduced completely to sulphide, which remained in solution, as there was evolution of hydrogen sulphide gas on acidification. While this reaction was repeated with parent trithiane (i.e. trithioformaldehyde) under similar conditions, the starting material was recovered. The mechanism of the azine formation perhaps involves the thioaldehyde monomer intermediate in some stage of the reaction, otherwise the conception of a nucleophilic attack by the hydrazine on the electron deficient carbon resulting in the formation of an azine is difficult. As triaryl-s-trithiane is stable both in refluxing alkaline-dioxane solution and in 80% hydrazine hydrate in diglyme solution and this observations leads one to assume that possibly an intermediate such as NH_2-$\dot{N}H^{-}Na^{+}$ must be involved in the reaction instead of the hydrazine molecule as such.

EXPERIMENTAL

1. Triphenyltrithiane

Dry hydrogen chloride was passed into a solution of benzaldehyde (5 g) in absolute ethanol (25 ml) cooled to -5^{o} to -10^{o} till the pH reached 2.0 to 2. Dry hydrogen sulphide was then passed through a second entry tube, maintaining the temperature at -10^{o}. The pH of the solution was maintained constant by bubbling dry hydrogen chloride. The colour of the solution turned dark red, and after passing hydrogen sulphide for 45 min. a white precipitate separated, which was collected and washed with dry ethanol till free from acid. Triphenyltrithiane (I; 5.1 g), m.p. 154-55^{o}, was found to be a mixture of *cis*- and *trans*-forms, as shown by the NMR spectrum. The mixture was used for the next step.

An analytical sample was crystallised from benzene in needles, m.p. 328-39^{o}, M^{+} 366 (lit.[24] m.p. for β form of triphenyl-*s*-trithiane 228^{o}).

Following the above general procedure the preparation of triaryl-*s*-trithianes indicated in Table 2 were prepared over 90% yield.

T A B L E - 2

s-Trithianes	Reaction product: α-/β-mixture m.p.(°C)	lit.[24] β-form m.p.(°C)	lit.[24] α-form m.p.(°C)
1. 2,4,6-Tris(phenyl)-	154-55	228-29	164-66
2. 2,4,6-tris(p-methoxyphenyl)-	171-73	183	127
3. 2,4,6-tris(3,4-methylene-dioxyphenyl)-*	211-15	236	183
4. 2,4,6-tris(p-chlorophenyl)-	164-68	189-92	137-38
5. 2,4,6-tris(p-hydroxyphenyl)-*	212-14	215	-
6. 2,4,6-tris(o-hydroxyphenyl)-	207-09	210	-
7. 2,4,6-tris(3-hydroxy,4-methoxyphenyl)-*	235-36	237	-

* Because of the partial insolubility of the corresponding aldehydes in ethanol at 0°, it was preferred to prepare the compounds using 2-methoxy ethanol as a solvent.

2. Deuteration of triphenyltrithiane

A mixture of the trithiane (5.1 g) dissolved in dry dioxane (20 mk) and a solution of sodium (7 g) in deuterium oxide (15 ml) was refluxed for 48 hr. The solution was cooled and diluted with deuterium oxide (5 ml). The white precipitate was collected, washed with deuterium oxide (5 ml), and dried (5.1 g). The operation was repeated for a further 48 hr. The complete exchange of the trithiane hydrogens with deuterium was confirmed by NMR and mass spectra.

The following trideuterated triaryl-s-trithianes were prepared repeating the same reaction condition.

1. 2,4,6-d_3-tris(p-methoxyphenyl)-s-trithiane
2. 2,4,6-d_3-tris(p-chlorophenyl)-s-trithiane
3. 2,4,6-d_3-tris(3,4-methylenedioxyphenyl)-s-trithiane.

None of the above deuterated compounds has been reported in the literature.

3. α-d-Benzaldehyde (Method A)

d_3-Triphenyltrithiane (3.66 g., 0.01 mole) in 90% aqueous methanol (40 ml) was refluxed with freshly prepared mercuric oxide (2.94 g., 0.03 mole) for 2 min. and a solution of mercuric chloride (8.16 g., 0.03 mole) for 2 min., and a solution of mercuric chloride (8.16 g., 0.03 mole) in the

same solvent mixture (15 ml) was added. Immediately a voluminous white precipitate appeared. The mixture was refluxed for 4 hr. in an atmosphere of nitrogen, cooled and filtered and the pH was brought to 5-6. The clear filtrate was distilled under nitrogen to remove methanol and water. The fraction then distilling between 175-79° (2.8 g., 84%) was characterised as α-d-benzaldehyde by the absence of the formyl signal in the NMR spectrum. The aldehyde was stored as the bisulphite compound and regenerated as required.

4. α,α'-d_2-stilbene

To a solution of triphenyltrideuterotrithiane (II; 5.1 g) in dry benzene (30 ml), freshly prepared Raney nickel (W-4) (8 g) was added, and the mixture refluxed for 5 hr.. The hot benzene solution was filtered, and the residue washed several times with hot benzene (5 x 15 ml). The combined filtrate was concentrated to small volume and the dideutero-stilbene was collected (4.35 g). The product was pure enough for the next step, but it can be crystallised from petroleum ether (40-60°) to give essentially trans-stilbene-d_2, m.p. 122-23° (m.p. of trans-stilbene is 124°). The m.ps of the dichloro-, dimethoxy- and bis-methylenedioxy-α,α'-d_2-stilbenes are 153-54°, 214 and 102-103 respectively, nearly identical with the m.ps of the corresponding stilbenes.

5. α,d-Benzaldehyde (Method B)

Through a solution of stilbene-d_2 (4.35 g) in dry ethyl acetate (50 ml) at 0° ozone was bubbled until TLC on silica gel showed the absence of the stilbene. The solution was concentrated to 5 ml. under reduced pressure at room temperature, and the ozonide was reduced with hydrogen in presence of palladium-charcoal. The mixture was filtered and the catalyst washed with ethyl acetate. Removal of solvent by distillation gave an oil (3.8 g), b.p. 177-78°.

The m.ps of the p-chloro- and 3,4-methylenedioxy- and the b.p. of the p-methoxy-α-d-benzaldehydes are 45-46°, 36-37° and 245-246° respectively, nearly identical with the reported m.ps and b.p. of the corresponding benzaldehydes. The m.p. and b.p. of p-chloro and p-methoxy-α-d-benzaldehydes correspond to the lit.[26-28] m.p. and b.p. respectively. This is the first report of 3,4-methylenedioxy-α-d-benzaldehyde.

6. Preparation of α,α'-dimethylstilbene

2,4,6-Trimethyl-triphenyl-s-trithiane (403 mg., 0.001 mole) in dry benzene (20 ml) and to this Raney nickel (W-4, 1 g., 4 times the calculated quantity) was added and the suspension was refluxed for a period of 4 hr. The hot solution was filtered. Hydrogen sulphide evolved when the nickel residue was treated with hydrochloric acid, indicating the presence of

nickel sulphide. Benzene was evaporated from clear benzene solution to dryness, the compound showed homogeneous on silica gel TLC (0.28 g.). This solid was crystallised from pet.ether in colourless plates, m.p. 105-07° (lit.[57] 107°).

7. 2,4,6-Trimethyl-triphenyl-s-trithiane (V)

To a solution of triphenyltrithiane (3.66 g., 0.01 g. mole) in dry dimethylsulphoxide (13 ml), sodium hydride (0.88 g. 0.04 mole) was added under dry nitrogen at 70-75°. When effervescence ceased after two hours, methyl iodide (2.68 ml, 0.04 mole) was added to this deep brown colour solution. The deep brown colour discharged. The solution was kept on stirring for a further period of an hour and poured on crushed ice. A gummy material separated out from which a solid (1.17 g., m.p. 120-21°) was obtained, and was further purify on a column chromatography over silica gel. (Found: C, 69.9; H, 5.3; S, 23.2. $C_{24}H_{24}S_3$ requires C, 70.5; H, 5.8; S, 23.5%). PMR: τ-$CDCl_3$; CH_3 7.4 (s), Phenyl 2.63 (broad singlet).

8. Synthesis of triaryl-s-trithiane from O,O-diethyl dithiophosphoric acid

A mixture of benzaldehyde (2.12 g., 0.02 mole) and O,O-diethyldithiophosphoric acid (3.72 g., 0.02 mole) was allowed to stand at room temperature (32°) for a period of 16 hr. Gradually it turned into a white solid, which was dissolved in benzene (25 ml) and refluxed for an hour.

Benzene was distilled off from the reaction mixture and brought the volume to almost one fourth, and from this solution a white solid crystallised out (2 g), m.p. 226-28° on TLC silica gel (benzene-pet.ether 7:3), the R_f value is same as of β-2,4,6-triphenyl-s-trithiane. The mixed melting point with the β-triphenyl-s-trithiane was remained undepressed. (M^+ 366). The corresponding β-p-chloro-β-p-methoxy- and β-3,4-methylenedioxy derivatives of triaryl-3-trithianes are synthesised following the same procedure.

9. Synthesis of β-triphenyltrithiane using sodium thiosulphate and hydrochloric acid

A mixture of benzaldehyde (5.3 g., 0.05 mole) sodium thiosulphate (24.8 g., 0.1 mole) and concentrated hydrochloric acid (50 ml) was kept at room temperature for a period of 24 hr. Then two portions of hydrochloric acid (2 x 25 ml) was added with a lapse of 8 hr. The reaction was worked up after 72 hr. by diluting the full reaction mixture with water (200 ml) and the insoluble solid was collected (6.2 g), m.p. 225-227°. This was identified as β-2,4,6-triphenyl-s-trithiane (mixed melting point remained undepressed). The corresponding β-p-methoxy-β-p-chloro-β-3,4-methylenedioxy- derivatives of triaryl-s-trithianes have been synthesised following the same procedure. During the reaction no hydrogen sulphide or sulphur dioxide was detected.

10. Synthesis of β-triaryltrithianes using sodium sulphide and hydrochloric acid

To a finely ground powder of fused sodium sulphide (9.6 g., 0.1 mole) benzaldehyde (5.3 g., 0.05 mole) was added at room temperature and a slurry was made. To this concentrated hydrochloric acid (40%) (30 ml) was added and the pH of the solution was maintained at around 2. This reaction mixture was suspended for a period of 24 hr. A solid separated, m.p. 225-27°, identified as β-2,4,6-triphenyl-s-trithiane. The same procedure was repeated for the preparation of the β-p-chloro, β-p-methoxy, β-3,4-methykene dioxy derivagives of triaryl-s-trithianes without anyam difficulty.

11. Hydrolysis of s-trithiane using silver oxide

A suspension of 2,4,6-triphenyl-s-trithiane (I, 3.66 g., 0.01 mole) in aqueous methanol (50 ml; 1:10 v/v) with silver oxixe (9.09 g., 0.04 mole) was refluxed for 3 hr. The reactionm mixture was filtered, the solid mass was washed with methanol and the filtrate was fractionally distilled. The fraction distilled between 175-79° was collected and characterised as benzaldehyde (yield 80%).

Adopting the same procedure, we have hydrolysed tris-(p-methoxyphenyl)-s-trithiane and trimethyl-triphenyl-s-trithiane to yield anisaldehyde (85%) and acetophenone (75%) respectively.

12. Oxidative desulphurisation of s-trithianes and thioacetals

A mixture of 2,4,6-triphenyl-s-trithiane (3.66 g., 0.01 mole) and iodine (3.81 g., 0.03 atom) was dissolved in dimethyl sulphodide (20 ml) and the solution was heated on a steam bath for an hour. During the course of the reaction a volatile fraction, distilling at 35-38°, was collected and characterised as dimethyl sulphide (1.4 g). The solution was cooled, diluted with cold wate (100 ml) and the free iodine was destroyed by adding, a solution of sddium thiosulphate (4 g) in water (15 ml). A pale yellow solid was precipitated out of the solution (0.8 g., m.p. 121-22°) and identified as elemental sulphur. The aqueous solution was extracted with pet.ether. Removal of the solvent gave an oil (3 g; 94%), characterised as benzaldehyde (b.p. 2,4-DNP).

Adopting the same procedure following s-trithianes and thioacetal derivatives of ketones have been hydrolysed to give the corresponding aldehydes or ketones in good yields, trithioformaldehyde $(CH_2S)_3$; 2,4,6-tris(phenyl)-; 2,4,6-tris-(p-methoxyphenyl)-; 2,4,6-tris(3,4-methylenedioxyphenyl)-; 2,4,6-tris(p-chlorophenyl)-; 2,4,6-tris(methyl-phenyl)-.

13. Desulphurization of triaryl-trithianes using hydrazine hydrate/alkali

A mixture of triphenyl-s-trithiane (3.66 g., 1 part by weight), hydrazine hydrate (80%, 4 parts by volume), sodium

hydroxide (2 parts by weight)in diglyme (13 parts by volume) was refluxed for a period of 2 hr. and poured on water. An oil separated out which gradually solidified. The crude solid was homogeneous on TLC, m.p. 90-93° (3 g) and identified as benzalazine (lit.[115] m.p. 93°).

14. Oxidative desulphurization of triaryl-s-trithianes using pyridine-N-oxide and iodine

A mix ture of triphehyl-s-trithiane (3.66 g., 0.01 mole), iodine (3.87 g., 0.03 mole), pyridine-N-oxide(3.8 g., 0.04 mole) in 2-methoxyethanol (30 ml) was refluxed for 8 hr., and the dark coloured solution was poured in water. Excess of iodine was destroyed by an aqueous solution of sodium thiosulphate (4 g) in water (15 ml). The colourless solution on extraction by pet.ether and evaporation of the solvent gave a liquid (1.3 g), which was distilled at 176-79° and was identified as benzaldehyde, [illegible](b.p. ; 2,4-DNP). The aqueous filtrate after pet.ether extraction was extracted with ether (5 x 20 ml). The evaporation of the etheral extract gave a liquid, b.p. 115° (1.7 g) identified as pyridine.

The oxidation of p-chlorophenyl-, p-methoxyphenyl, and 3,4-methylenedioxyphenyl-s-trithianes to the corresponding aldehydes have been carried out following the above procedure. The yield varied from 35-50%.

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P A R T - IV

ELECTRON-IMPACT FRAGMENTATION OF TRIARYL-s-TRITHIANES: A NOVEL SKELETAL REARRANGEMENT INVOLVING SULPHUR-SULPHUR BOND FORMATION.

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INTRODUCTION

The application of mass spectrometry has greatly simplified the elucidation of the structures of organic molecules. The migration of groups other than hydrogen upon electron impact has only been recognised in last ten years. Such processes of migration of groups and thereby bringing about a rearrangement of constituent atoms in the fragment molecule ion are termed as "skeletal rearrangement processes". This is partially important from a mechanistic view point and cannot be predicted a priori with any degree of certainity.

Skeletal rearrangement processes generally fall into two main categories, although in certain cases it is difficult to differentiate between the two. They are (1) the type ABC $\longrightarrow$ AC + B, where A and C are originally joined through B. This process may occur from either an odd or an even electron species; (2) the second type when reorganisation of the molecular ion produces a spectrum which bears little relation to that expected from a molecular ion structure based on that of the intact molecule.

Skeletal rearrangement ions are rare in the mass spectra of cyclic sulphides. Loss of sulphur, $S_2H^{\cdot}$, H_2S, $SH^{\cdot}$, S_2 with carbon-carbon bond formation is common, however, this sort of bond formation is the simplest and common in

sulphur compounds, occurs in the spectra of sulphides[1-7] and disulphides.[8,9] Loss of sulphur, HS• and H_2S are noted. The rearrangements are only pronounced when the alkyl groups are either methyl or contain unsaturation in case of dialkyl sulphides[3] and disulphides[8]. The $M^{+\bullet}$ - SH• process is dominant in the spectra of arylthioureas[3,7] and this rearrangement has been studied by deuterium labelling for the case of thioanisole.

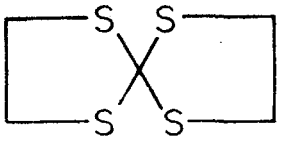
The mass spectra of thioacetals and thioketals are of interest to organic chemists and they have been examined to investigate the ability of this grouping (1,3-disulphide) to direct specific fragmentation in complex natural products. In general, molecular ions are stronger and other fragment ions are scarce compared to the corresponding ethylene ketals. Fragmentation mode of 5α-androstan-3,11-dione-3-ethylene thioketal[10] is best exemplified by these features. The proposed hydrogen shifts have been confirmed by examining the spectra of the 6,6-$\underline{d}_2$- and 2,2,4 4,9,12-$\underline{d}_6$- derivatives of 5α-androstan-3,11-dione-3-ethylene thioketal. The diethyl thioacetals of the acetylated carbohydrates show no molecular ion peak unlike the corresponding ethylene thioacetals derivatives,[11] although many fragment ions are of low intensity. Analysis of the electron impact induced fragmentations of a number of <u>bis</u>-ethylene and -trimethylene-thioacetals of malondialdehyde have been reported.[12] The

mass spectra of a series of spiro compound (I to III) has been reported[13] and they show easily recognizable parent ions.

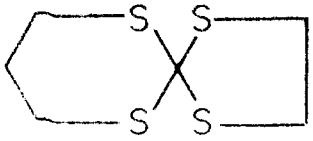
The $M^{+\cdot} - S_2H^{\cdot}$ ion is pronounced in the mass spectrum of propylene dithioacetal (IV) and the process is appropriately substantiated by a metastable peak. The rearrangement decreases when there are substituents attached to the phenyl ring (e.g. -OMe, $-NR_2$ or $-NO_2$) and this process is completely absent in ethylene dithioacetal (V). Deuterium labelling studies[14] show that the loss originate with some scrampling of methylene hydrogens. The mechanism of such $S_2H^{\cdot}$ loss has been assumed to be a multi stage and not a skeletal rearrangement. The loss of sulphur, $H_2S, HS_2^{\cdot}$, $SH^{\cdot}$, S_2 from the cyclic sulphides cannot be called a skeletal rearrangement by definitation, because of the retention of the cyclic nature of the compound. This sort of losses can be compared with the loss of CO from quinones which is also bond forming, but not a fine skeletal rearrangement process.[15,16]

PRESENT WORK

There has been no report to this date on the mass spectral fragmentation of s-trithianes, except a casual remark on the fragmentation behaviour of 1,3,5-trithiacyclohexane (VI), which loses a $\ddot{C}H_2$ group from the molecular ion besides a prominent loss of $S_2H^{\cdot}$ from the



(I)



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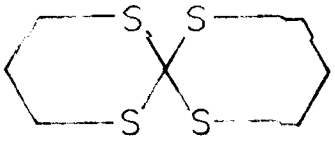

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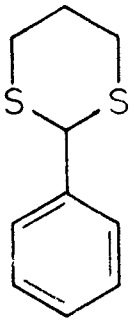

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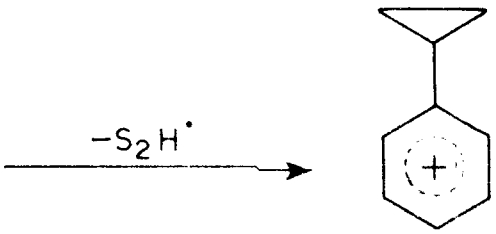
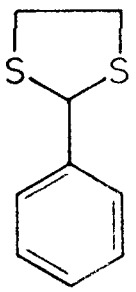


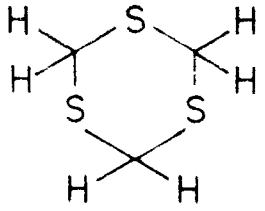


(V)

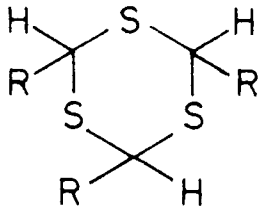
molecular ion. The abnormal loss of even electron species such as carbene is very rare.

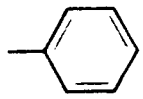
The mass spectra of triaryl-s-trithianes (VII) to (XIII) have been recorded on a CEC-21-110B double focussing mass spectrometer operating at 70 eV using a direct inlet system. The inlet temperature is always much less than the m.ps of the corresponding compounds. The main fragmentation mode of the first five compounds have been shown in Charts I to V and the peaks have been indicated in Figures 1 to 4. All the indicated processes have been confirmed by deuterium labelling experiments. Further, the fragmentation modes are substantiated by appropriate metastable peaks, depicted by asterisks.

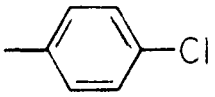
A number of interesting new type of fragmentation pattern has been observed occurring in the title compounds and there is a wide deviation from other sulphur heterocyclic compounds.[18] Thus the mass spectrum of triphenyl-s-trithiane (VII) shows relatively low intensity molecular ion (3.4%). The major fragmentation involves a direct cleavage and cleavage with some interesting rearrangements which are summarised in Chart I. Unlike in many sulphur heterocyclic compounds,[17,18] this compound does not eliminate $S^{\cdot}$, S_2, SH$^{\cdot}$ or $S_2H^{\cdot}$ from the molecular ion. The prominent ions in the mass spectrum of this compound are at m/e 180 (52.3%) and at m/e 186 (45.2%) corresponding to stilbene and $PhCHS_3$

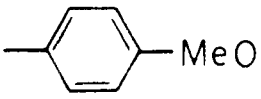


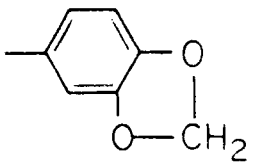
(VI)

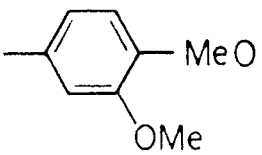


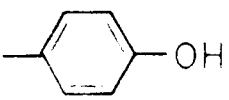
VII ; R = 

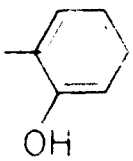
VIII ; R = 

X ; R = 

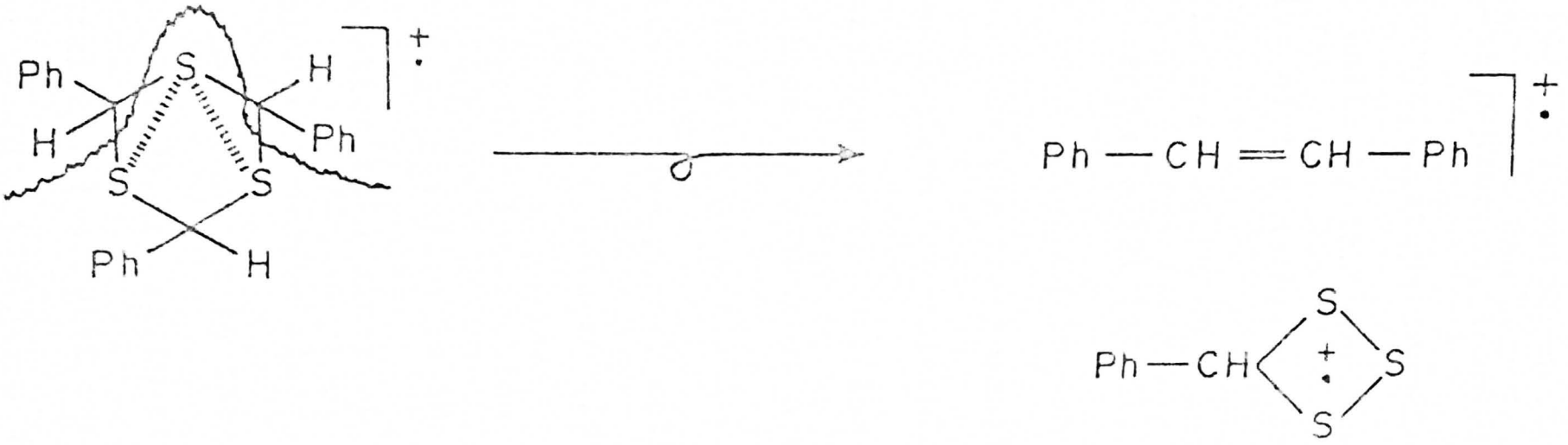
X ; R = 

XI ; R = 

XII ; R = 

XIII ; R = 

radical ions. The composition of these radical ions have been established by deuterium labelling and exact mass measurements. Thus the trideutero derivative of (VII) shows the corresponding peaks at m/e 182 ($PhCD\neq^{+\cdot}$ and m/e 187 ($PhCDS_3^{+\cdot}$) respectively. Further the peak at m/e 180, accounting for the stilbene radical ion exhibited the loss of a methyl radical[19] to give the peak at m/e 165. It is of interest to recall at this stage the formation of stilbene from triphenyl-s-trithianes on heating above its melting point, alone or with copper powder.[20] Several symmetrically substituted stilbenes were prepared from triaryl-s-trithianes by desulphurisation using freshly prepared copper powder,[21,22] copper-bronze[23] or Raney nickel.[24,25] From this it is likely that pyrolytic and electron impact fragmentation of these compounds are similar. Such findings have also been reported recently in the case of s-thiones of benzothiazole, benzoimidazole and benzoxazole[26] and also in the case of 2H-naphtha[1,8-cad]-isothioazole-1,1-dioxide.[27] The mass spectral and pyrolytic fragmentation in these compounds is by the elimination of small and neutral species such as $S^{\cdot}$ and S_2. However, there is no such loss in case of triphenyl-s-trithiane, but the sulphur atom attaches itself to the other two sulphur atoms in the same molecular ion eliminating a stilbene unit as depicted below.


Ph
H
S
H
Ph
S
S
Ph
H
+·
Ph — CH = CH — Ph
+·
Ph — CH
S
S
S
+·
m/e 186

So far no such S-S bond formation has been detected. It is difficult to decide whether this process is of one-step or a multi-step process, involving a series of bond breaking and bond formation steps invoking a number of rearrangements. It is most unlikely that onestep process is operative, irrespective of the mechanism of elimination.

The species $PhCHS_3^{+\bullet}$ and $PhC{\equiv}S^+$ fragments at m/e 122 (71.4%) and m/e 121 (100%), although no metastable peaks have been detected to substantiate these processes. The main process for the formation of thiobenzaldehyde radical ion is from the molecular ion. Further breakdown of thiobenzaldehyde radical ion occurs as happens in case of benzaldehyde by a loss of a H$^\bullet$ to give more stable thiobenzoyl cation at m/e 121 (100%), which can lose carbon monosulphide to give phenyl cation. The latter process can also occur from the thiobenzaldehyde to give C_6H_6 radical ion.

The other interesting features in the mass spectrum of triphenyl-s-trithiane is the loss of a monomer resulting in the formation of a dimer of thiobenzaldehyde (m/e 244; 7.1%). Thiobenzaldehyde always exists only as its trimer and no monomer or dimer is known to have been isolated to this date. The dimer, as in other sulphur heterocycles, loses neutral small species such as S$^\bullet$ and S_2 giving rise to peaks at m/e 212 (25.2%) and m/e 180 respectively. The former peak appears to have formed also by the loss of

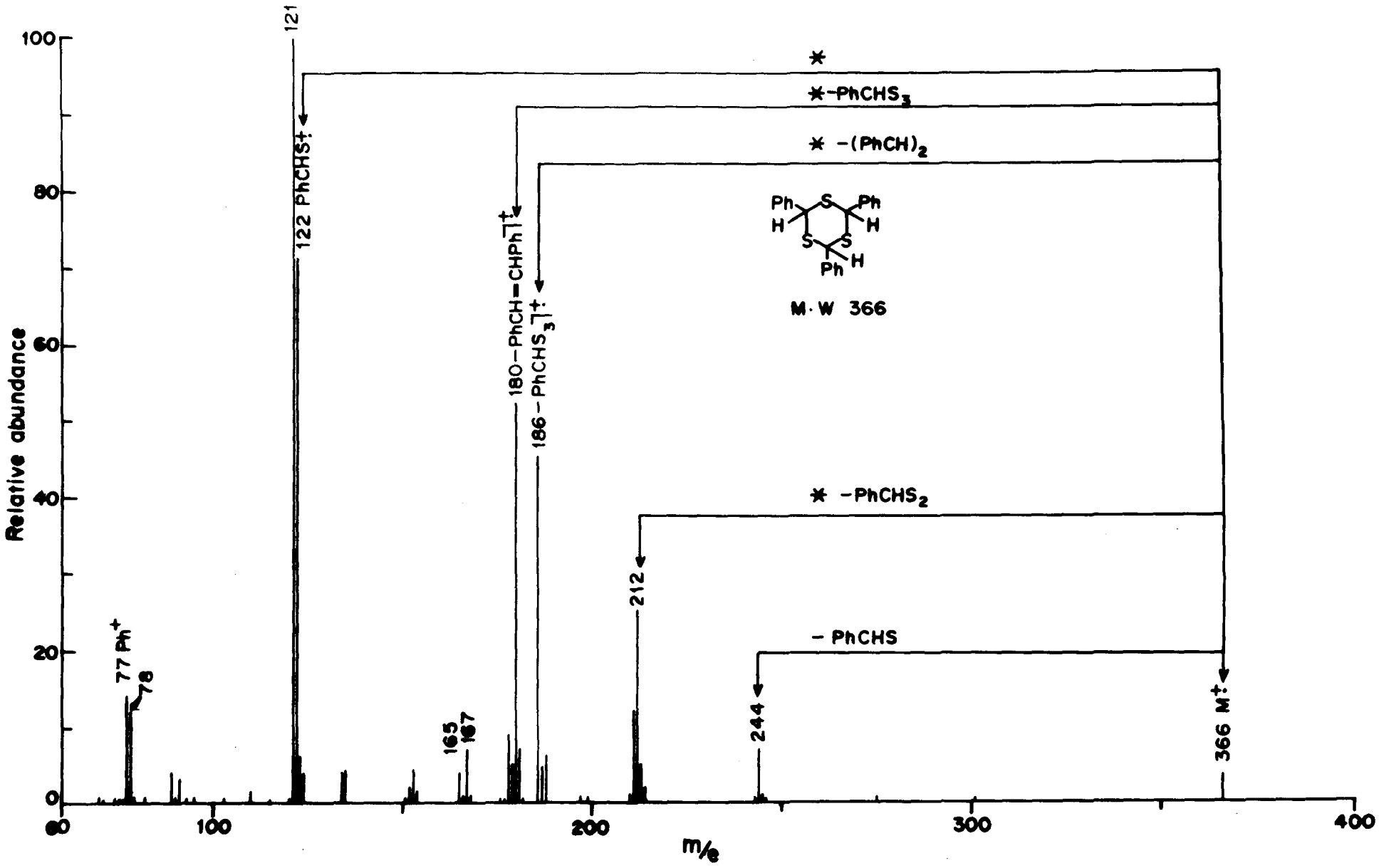
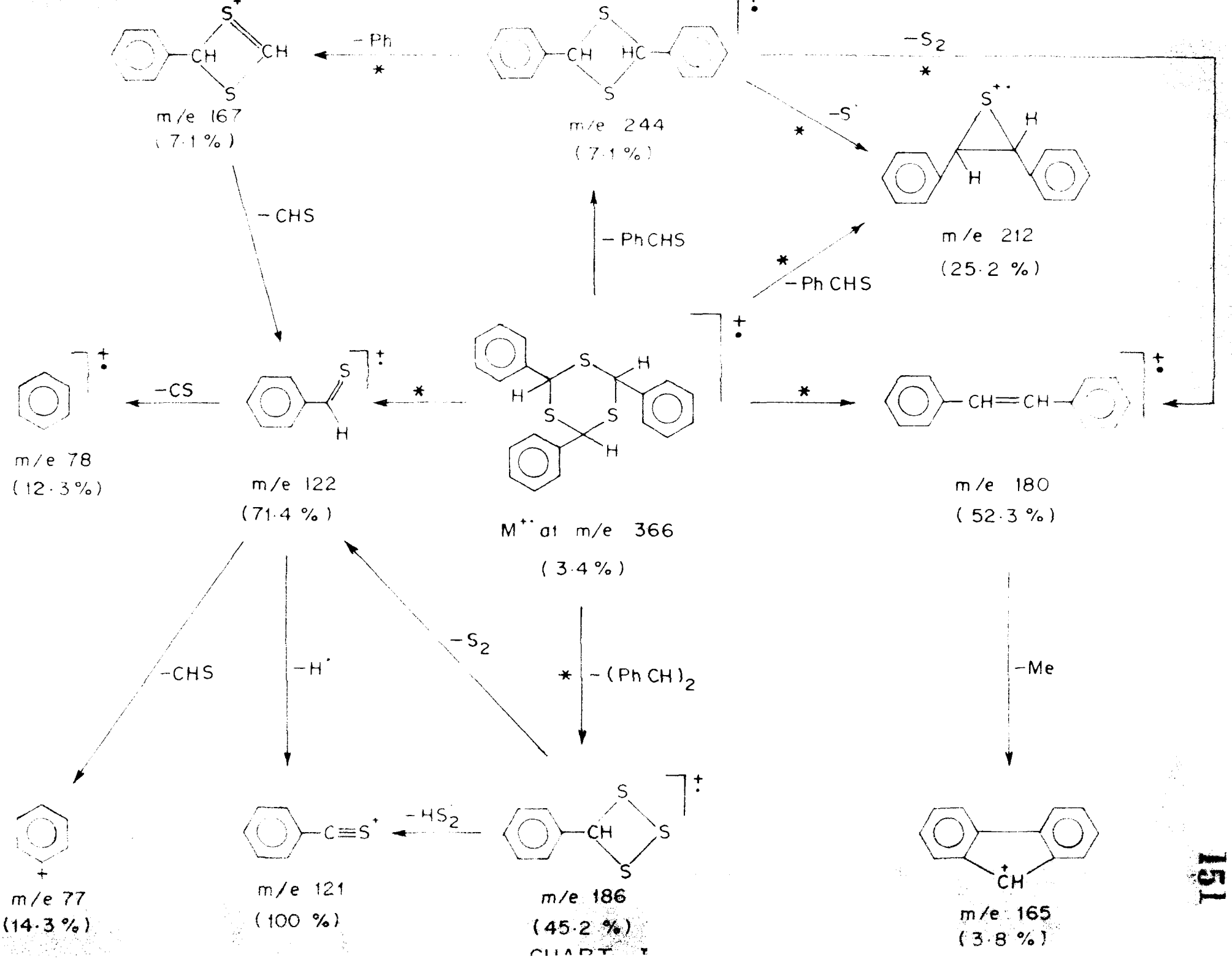

Relative abundance
m/e
100
80
60
40
20
0
60
100
200
300
400
121
122 PhCHS+·
180-PhCH=CHPh]+
186-PhCHS3]+·
77 Ph+
78
165
167
212
244
366 M+·
* -PhCHS3
* -(PhCH)2
* -PhCHS2
- PhCHS
M·W 366

Fig. 1


m/e 167
(7·1 %)
−Ph
m/e 244
(7·1 %)
−S2
−S·
m/e 212
(25·2 %)
−CHS
−PhCHS
−PhCHS
m/e 78
(12·3 %)
−CS
m/e 122
(71·4 %)
M+· at m/e 366
(3·4 %)
m/e 180
(52·3 %)
−CHS
−H·
−S2
*−(PhCH)2
−Me
m/e 77
(14·3 %)
m/e 121
(100 %)
−HS2
m/e 186
(45·2 %)
m/e 165
(3·8 %)

$PhCHS_2$ species. As in many heterocyclic compounds the dimer radical ion loses a phenyl radical giving a relatively more stable sulphonium ion at m/e 167, although its relative intensity is same as that of dimer.

Having outlined the fragmentation of the triphenyl-s-trithiane, it is important to record our finding on the fragmentation pattern occurring in some of the substituted (electron withdrawing and electron donating) derivatives. Thus in the case of 2,4,6-tris-(p-chlorophenyl)-s-trithiane (VIII), (Chart II) the molecular ion is less abundant (0.4%) and the base peak represents the monomer of p-chlorothiobenzaldehyde. The molecular ion, unlike the unsubstituted derivatives, shows the loss of H_2S giving an insignificant peak at m/e 434 (0.1%). Other major modes of fragmentation is same as that of the phenyl compound (VII) except the peaks corresponding to stilbene and $PhCHS_3$ radical ions are of less abundance.

The mass spectrum of 2,4,6-tris-p-methoxyphenyl-s-trithiane (IX), (Chart III) unlike the other two compounds, did not show any detectable molecular ion. However, there are prominent peaks corresponding to the loss of $SH^{\bullet}$ and SH_2 from the molecular ion at m/e 423 (2%) and at 422 (23.5%) respectively. The base peak corresponds to the radical ion of 4,4'-dimethoxystilbene which is expected to be more stable due to resonance stability. The peak representing

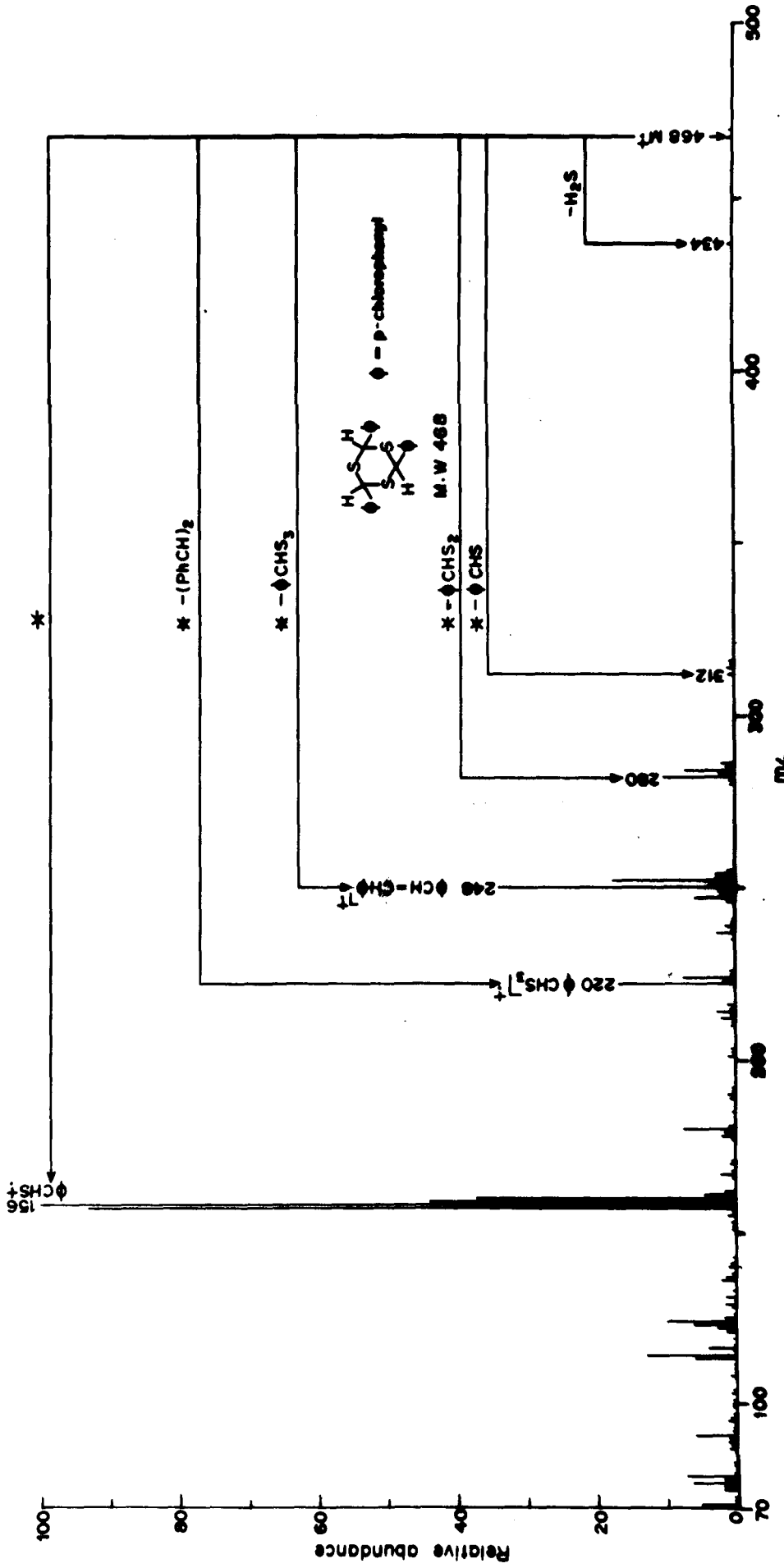

Relative abundance
100
80
60
40
20
0
m/e
500
400
300
200
100
50
468 M⁺
-H₂S
434
312
280
248 ϕCH=CHϕ T⁺
220 ϕCHS₂T⁺
156 ϕCHS⁺
* -(PhCH)₂
* -ϕCHS₃
* -ϕCHS₂
* -ϕCHS
M.W 468
ϕ = p-chlorophenyl

Fig. 2

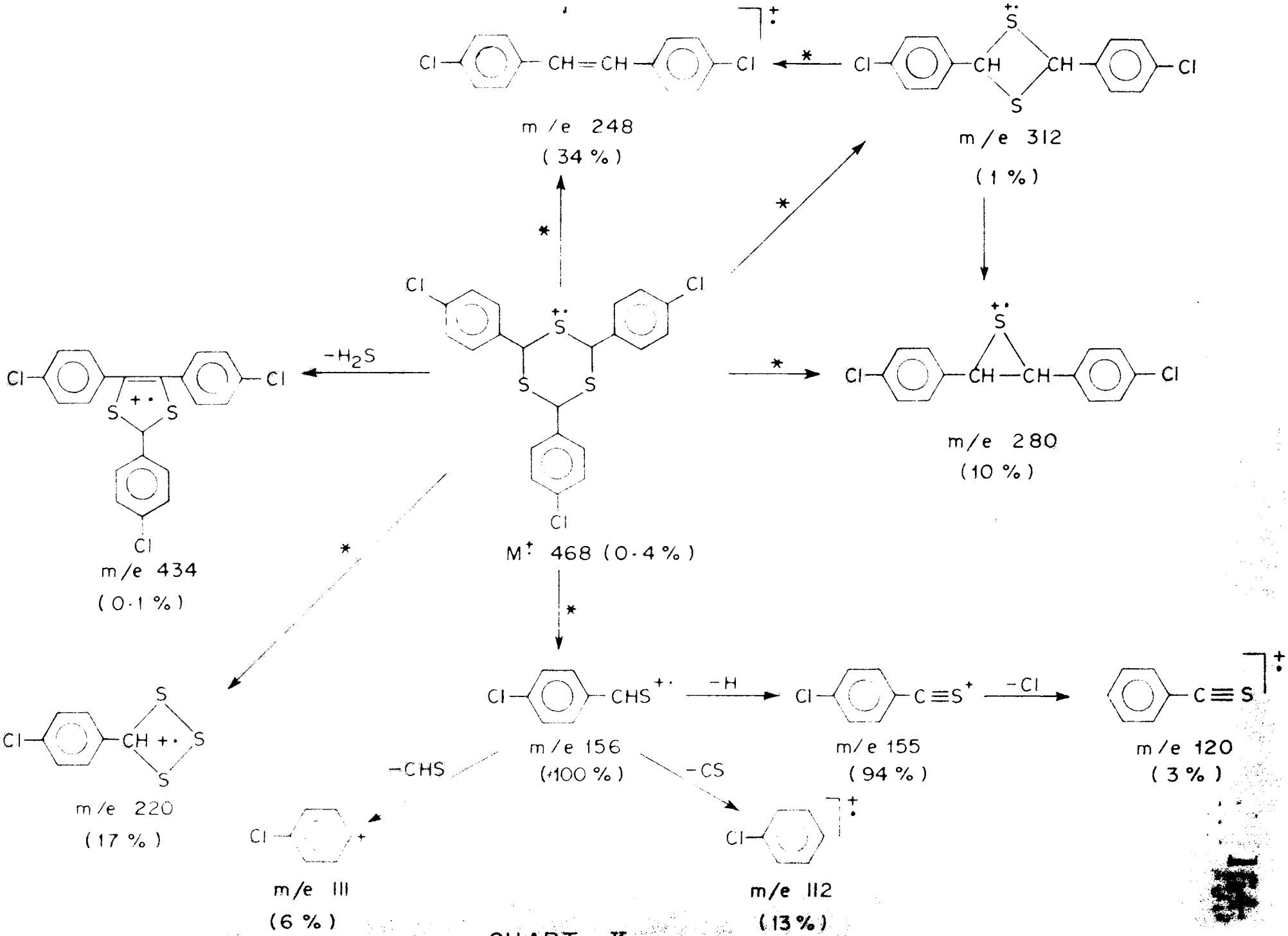
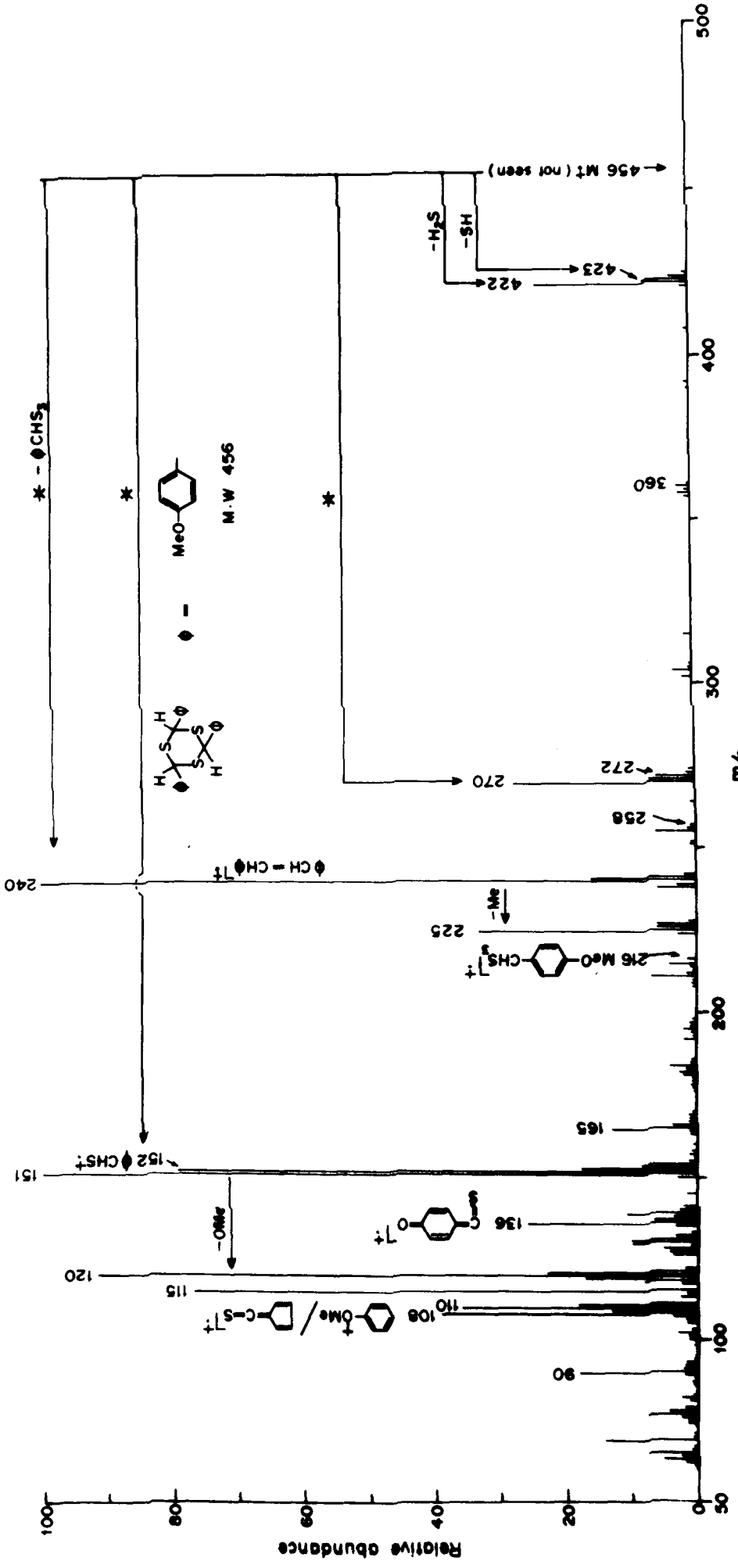

m/e 248
(34 %)
m/e 312
(1 %)
m/e 280
(10 %)
M+ 468 (0·4 %)
m/e 434
(0·1 %)
m/e 220
(17 %)
m/e 156
(100 %)
m/e 155
(94 %)
m/e 120
(3 %)
m/e 111
(6 %)
m/e 112
(13 %)
-H2S
-H
-Cl
-CHS
-CS

CHART – II


Relative abundance
m/e
456 M⁺ (not seen)
423
422
-H₂S
-SH
360
272
270
258
240
225
-Me
216 MeO-CHS₂⁺
165
152 CHS⁺
151
136
-OMe
120
115
110
108
90
M.W 456
MeO
-CHS
CH=CH⁺

Fig·3

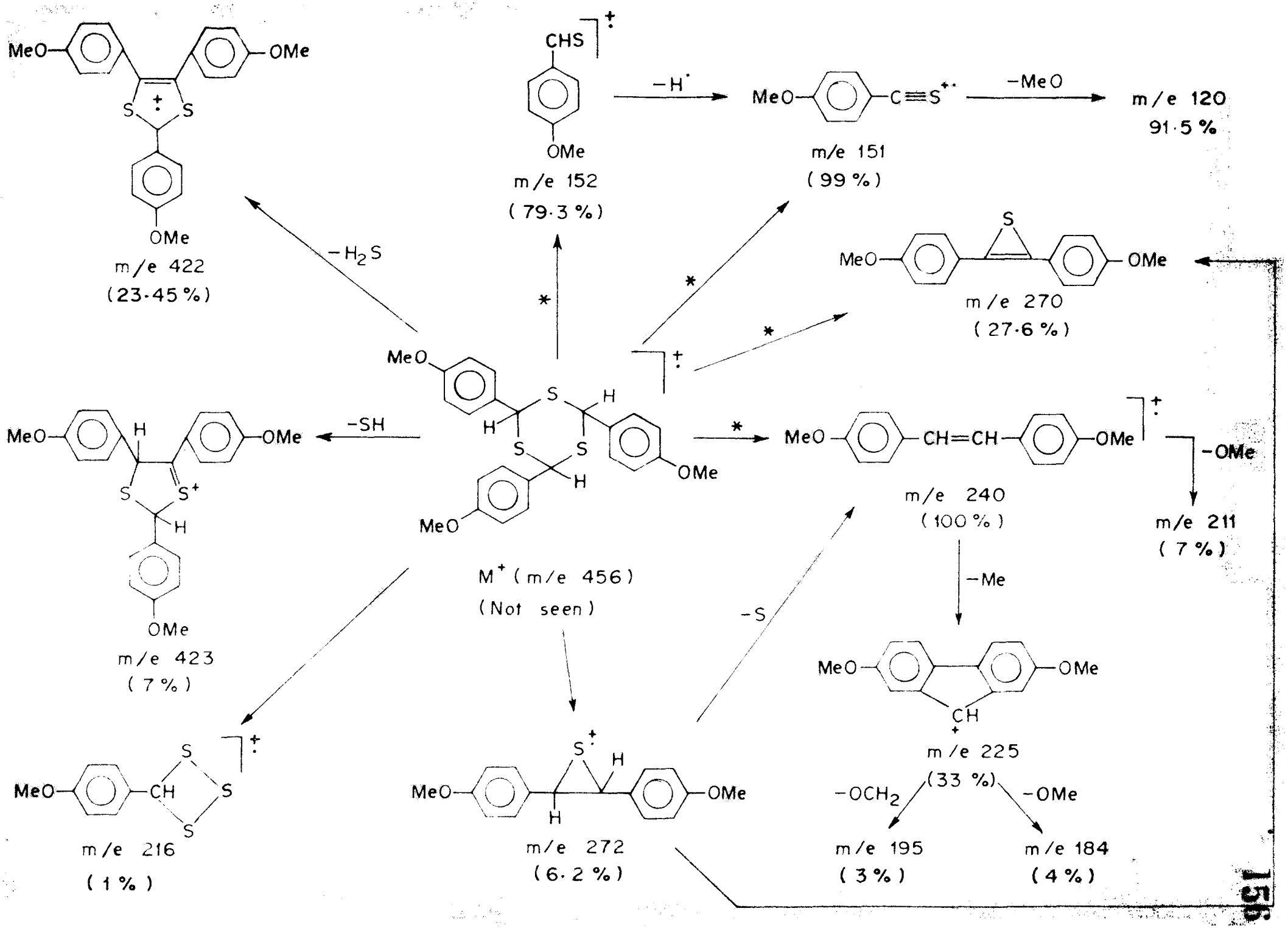

MeO
OMe
m/e 422
(23·45 %)
−H2S
CHS
OMe
m/e 152
(79·3 %)
−H·
MeO
C≡S
m/e 151
(99 %)
−MeO
m/e 120
91·5 %
MeO
OMe
m/e 270
(27·6 %)
M+ (m/e 456)
(Not seen)
−SH
m/e 423
(7 %)
MeO
CH=CH
OMe
m/e 240
(100 %)
−OMe
m/e 211
(7 %)
−Me
−S
m/e 216
(1 %)
m/e 272
(6·2 %)
m/e 225
(33 %)
−OCH2
−OMe
m/e 195
(3 %)
m/e 184
(4 %)

CHART – III

p-MeO-C_6H_4 $CHS_3^{+\cdot}$ is of 1% abundance and this fragment either may not be stable and readily fragmenting further or may be lost as neutral species. The other interesting fragmentation is the loss of p-MeO-C_6H_4-$CH(SH)_2$ from the molecular ion to give a peak at m/e 270 (27.6%), which was not seen in the previous compounds. Although a metastable transition supports its formation from the molecular ion, but it can as well come from the fragment at m/e 422. There are fragmentations at various stages corresponding to the loss of $Me^{\cdot}$, $MeO^{\cdot}$ and OCH_2, which are characteristic for aromatic methoxyl compounds.

We have also studied a number of other methoxy or hydroxy substituted compounds (X to XIII) and found that none of them shows their molecular ions. 2,4,6-Tris(3,4-methylene-dioxy-phenyl)-s-trithiane(X) (Chart IV) behaves analogues to trianisyl derivative (IX) and it is also the case with the trithiane derivedfrom veratraldehyde (XI) (Chart V). There are some deviations in the mass spectral behaviour of the hydroxy derivatives, compared with their methyl ether. Unlike the behaviour of triarisyl-s-trithiane (IX), the tris(p-hydroxyphenyl)-s-trithiane (XII), shows the last peak (base peak) in its spectrum at m/e 138, corresponding to the monomer radical ion. Further fragmentation is as expected in the case of p-hydroxy-thiobenzaldehyde. But the tris-(2-hydroxyphenyl)-s-trithiane (XIII) shows peaks at m/e 274 ($M^{+\cdot}$-p-OH-C_6H_4-$CHSH_2$, compared

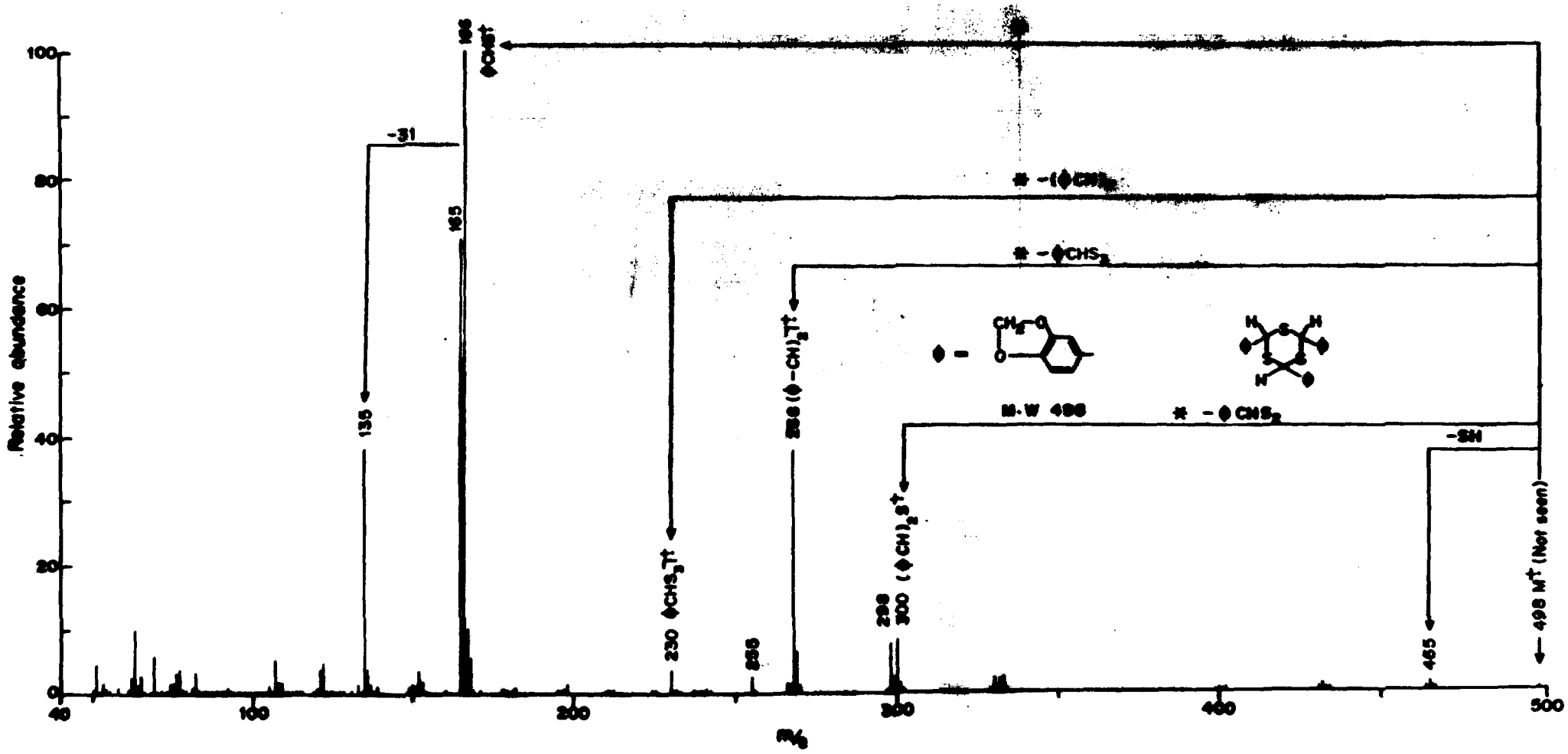

Relative abundance
100
80
60
40
20
0
40
100
200
300
400
500
m/e
-31
135
165
198 ◆CH₂S⁺
230 ◆CH₂S₂T⁺
255
286 (◆-CH₂)T⁺
298
300 (◆CH₂)₂S⁺
465
498 M⁺ (Not seen)
-SH
* -(◆CH₂)₂S₂
* -◆CH₂S₂
◆ -
M.W 498
* -◆CH₂S₂

Fig.4

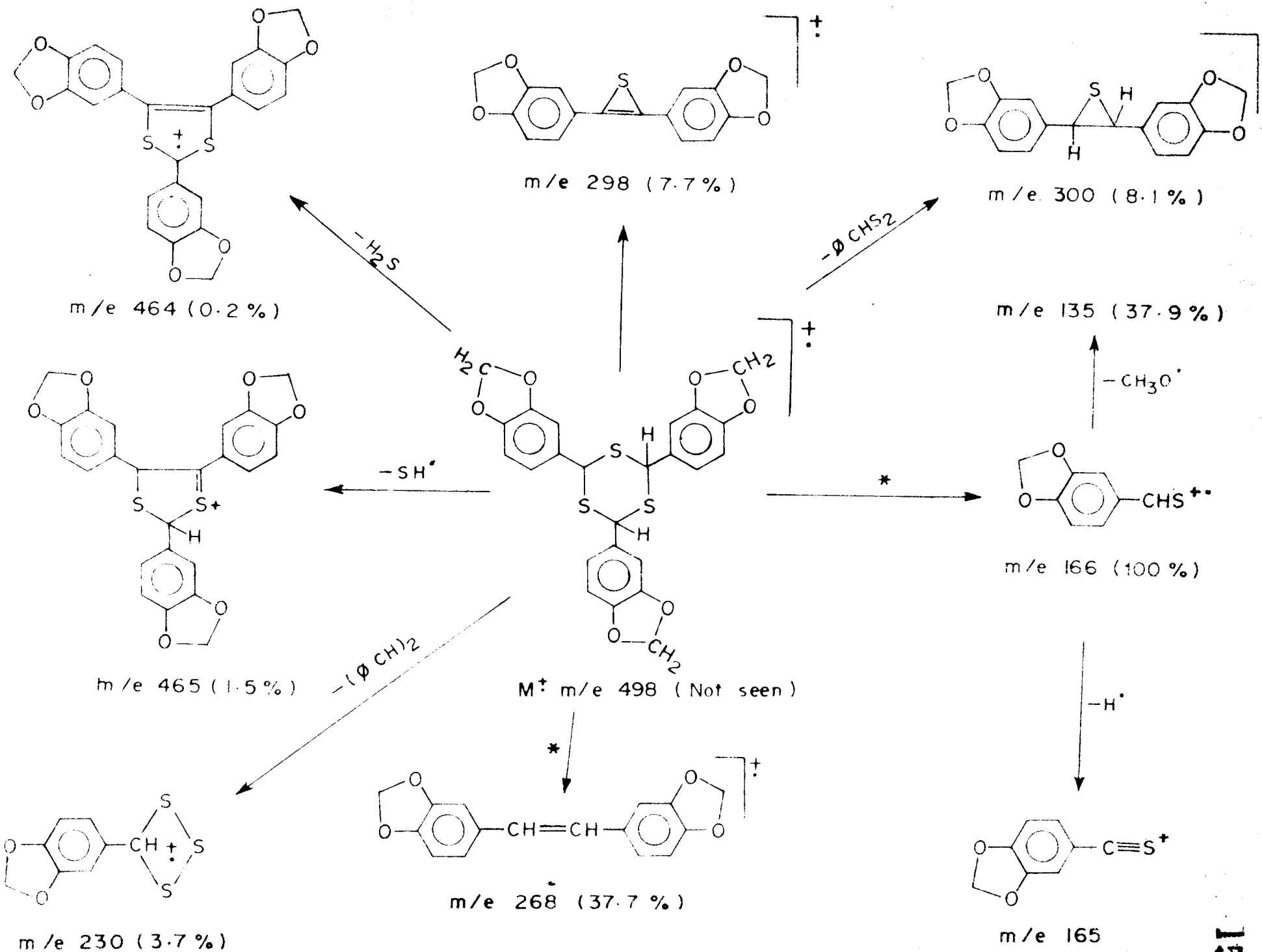

m/e 464 (0·2 %)
m/e 298 (7·7 %)
m/e 300 (8·1 %)
m/e 135 (37·9 %)
m/e 166 (100 %)
m/e 165
m/e 465 (1·5 %)
M+ m/e 498 (Not seen)
m/e 268 (37·7 %)
m/e 230 (3·7 %)
-H2S
-ØCHS2
-CH3O·
-SH·
*
-H·
-(ØCH)2

CHART – IV.

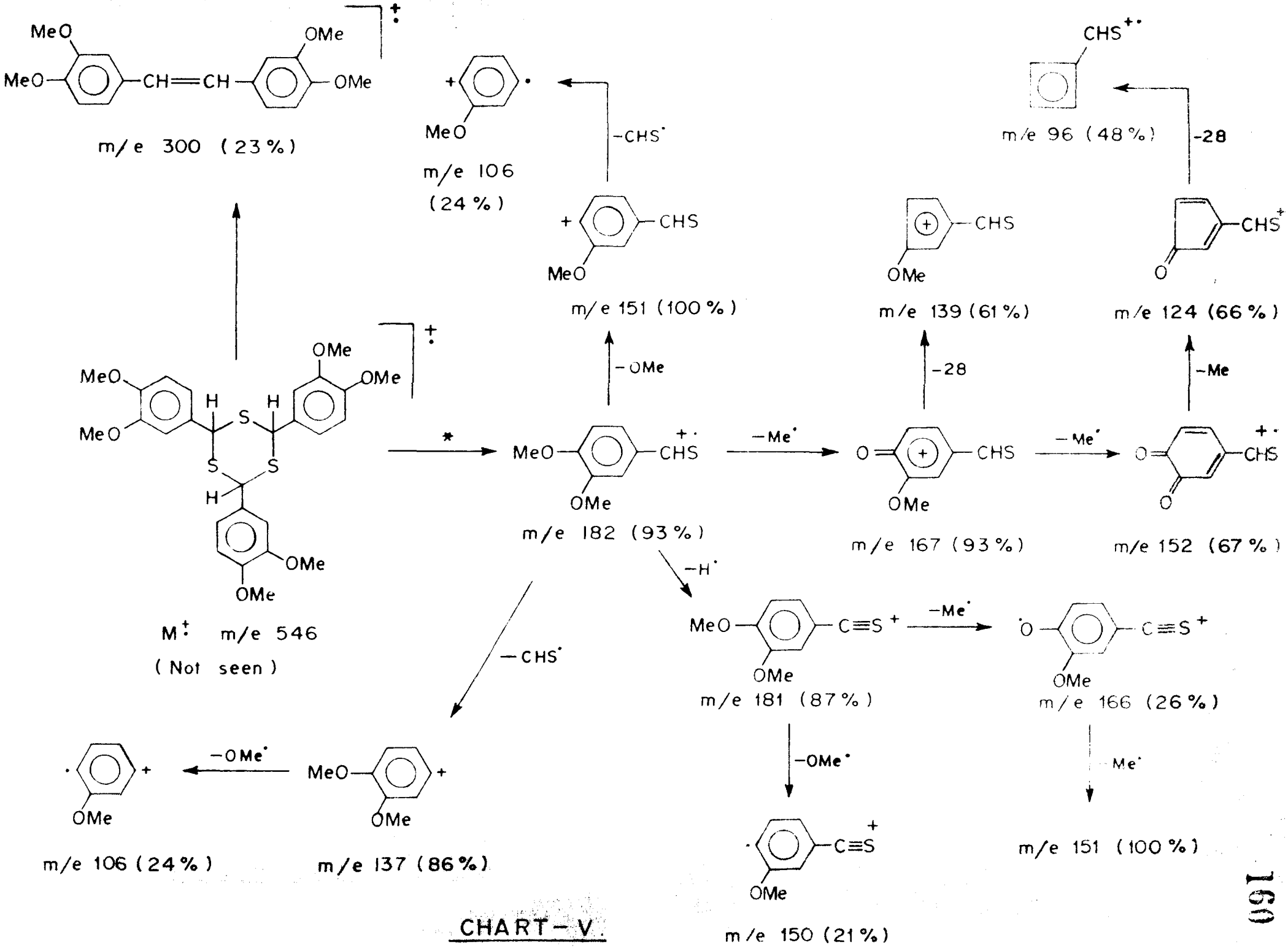

m/e 300 (23%)
m/e 106 (24%)
m/e 151 (100%)
m/e 96 (48%)
-28
m/e 139 (61%)
m/e 124 (66%)
-Me
M+· m/e 546
(Not seen)
m/e 182 (93%)
-Me·
m/e 167 (93%)
m/e 152 (67%)
-H·
-CHS·
m/e 181 (87%)
m/e 166 (26%)
-OMe·
Me·
m/e 106 (24%)
m/e 137 (86%)
m/e 150 (21%)
m/e 151 (100%)

CHART - V

the spectrum of IX) and at m/e 212 (corresponding to 2,2'-dihydroxystilbene radical ion) besides the base peak at m/e 137 representing 2-hydroxythiobenzoyl cation.

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P A R T - V

SYNTHESIS OF SUBSTITUTED THIOUREAS and SCHIFF BASES FROM PHENYLISOTHIOCYANATE IN DIMETHYL SULPHOXIDE:

***

INTRODUCTION

Isothiocyanates, of the general formula R-NCS, are considered as esters of isothiocyanic acid, H-NCS. They are isomeric with thiocyanates, R-SCN, and are derived from the latter by rearrangement. The normal esters, R-SCN, are extremely rare. A survey has been made of naturally occurring isothiocyanates,[1] a number of which are found in volatile oils from plants. The chief constituent of mustard oil is allylisothiocyanate.[2] Mostly isothiocyanates are present as glucosides in nature.

Recent works[3,4] have confirmed the interpretation of dipolemoments and Raman spectra measurement[5] on several isothiocyanates that the isothiocyanate group is linear and represented by structure:

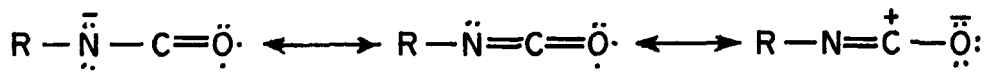
$$R-\overset{+}{N}\equiv C-\overset{-}{S}$$

It has also been established[3,4] that free isothiocyanic acid exists as a resonance hybrid of the following (I to III) canonical structures and the structure (III) contributes least in the resonance. On the other hand, an

$$H-\overset{+}{N}\equiv C-\overset{-}{S} \longleftrightarrow H-N=C=S \longleftrightarrow H-\overset{-}{N}-C\equiv\overset{+}{S}$$

I II III

isocyanate is a resonance hybrid represented by the structure (IV to VI). The molecular orbital theory



IV V VI

indicates that the electron density is least on the carbon atom and greatest on the oxygen atom and nitrogen atom being intermediate carry a net negative charge.[6] If this be the case the electron distribution on isothiocyanates and isocyanates molecules respectively is completely opposite, and this becomes obvious while comparing the reactivity of these two classes of compounds. Isothiocyanates undergo the same type reactions as do isocyanates, but the scale of reactivity is of much of lower order.

Isothiocyanates undergo following typical reactions.

1. Reactions of isothiocyanates with compounds containing labile hydrogen

Isothiocyanates react at the nitrogen-hydrogen, oxygen-hydrogen, and sulphur-hydrogen bond, but probably the most important reactions of isothiocyanates are those with compounds containing a nitrogen-hydrogen bond.

Ammonia or amines both primary and secondary react with isothiocyanates to give substituted thioureas[7,8](1.1).

Substituted thiosemicarbazides or hydrazine dithioamides are similarly formed from hydrozine and phenyl isothiocyanate (1.2).

Hydroxythioureas[9,10] are formed from hydroxylamine and this may dimerize to form oxadiazoles[11] (1.3).

Isothiocyanates react with the sulphonamides of primary amines in aqueous alkali solution to form sulphothioureas[12] (1.4).

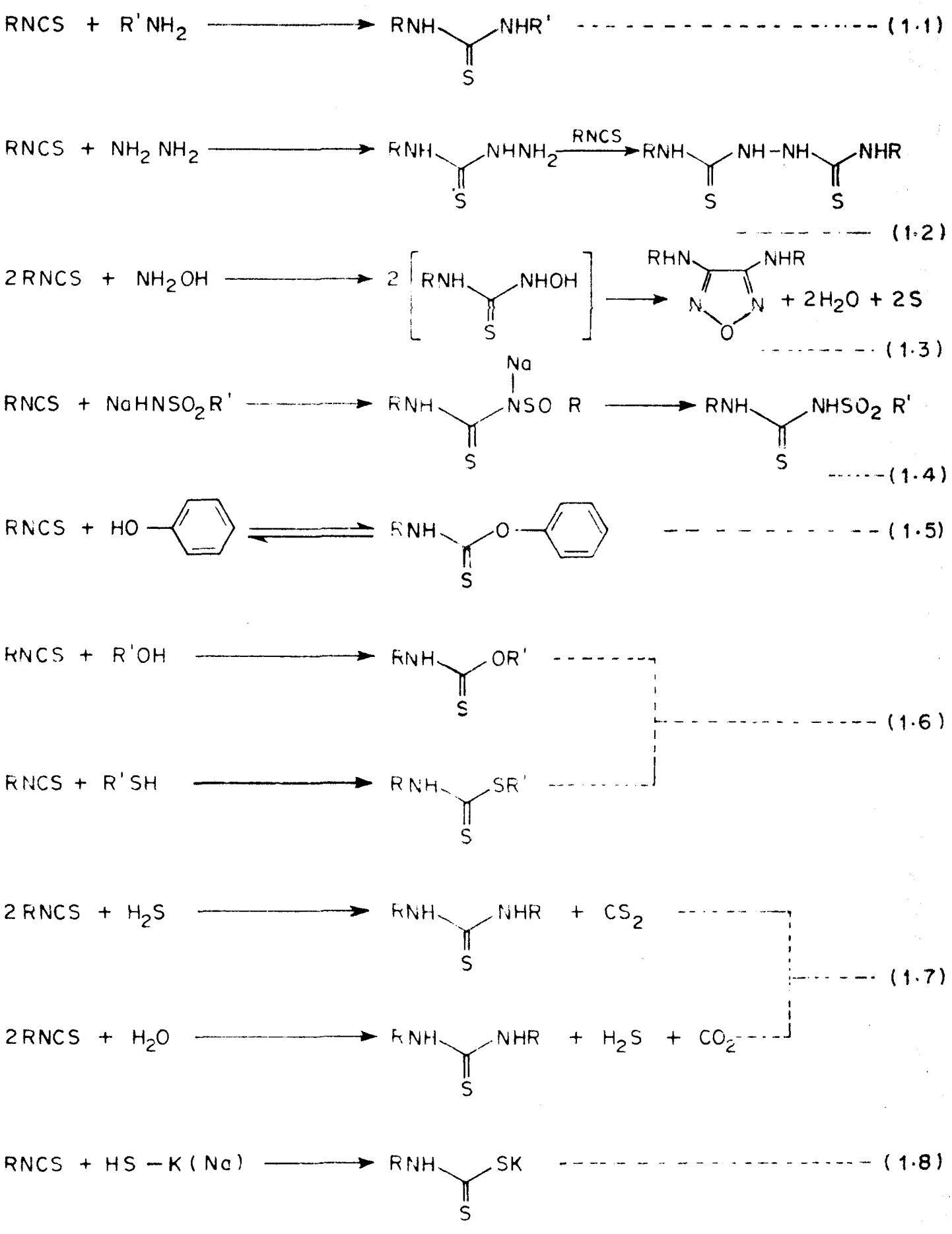
Phenols react sluggishly with isothiocyanates and give a poor yield of monothioureathane[13] (1.5).

Alcohols and mercaptans react with isothiocyanates to give a poor yield of mono- and dithiourethanes respectively. The yield is increased if the corresponding alkoxide or mercaptide is employed[14] (1.6).

Water and hydrogen sulphide react with isothiocyanates under the presence of acidic or basic catalyst or under pressure at elevated temperature to yield symmetrical disubstituted thioureas[15,16] (1.7).

Salts of dithiocarbamic acid is formed when potassium or sodium hydrosulphide reacts with isothiocyanates[17,18] (1.8).

Carboxylic acids or thiocarboxylic acids react with isothiocyanates to yield amides and carbonyl sulphide or


RNCS + R'NH2
RNH NHR'
S
(1·1)
RNCS + NH2 NH2
RNH NHNH2
RNCS
RNH NH-NH NHR
S S S
(1·2)
2RNCS + NH2OH
2 RNH NHOH
S
RHN NHR
N N
O
+ 2H2O + 2S
(1·3)
RNCS + NaHNSO2R'
Na
RNH NSO R
S
RNH NHSO2 R'
S
(1·4)
RNCS + HO
RNH O
S
(1·5)
RNCS + R'OH
RNH OR'
S
RNCS + R'SH
RNH SR'
S
(1·6)
2RNCS + H2S
RNH NHR + CS2
S
2RNCS + H2O
RNH NHR + H2S + CO2
S
(1·7)
RNCS + HS-K(Na)
RNH SK
S
(1·8)

carbon disulphide respectively via the mixed anhydrides,[19,20] (1.9).

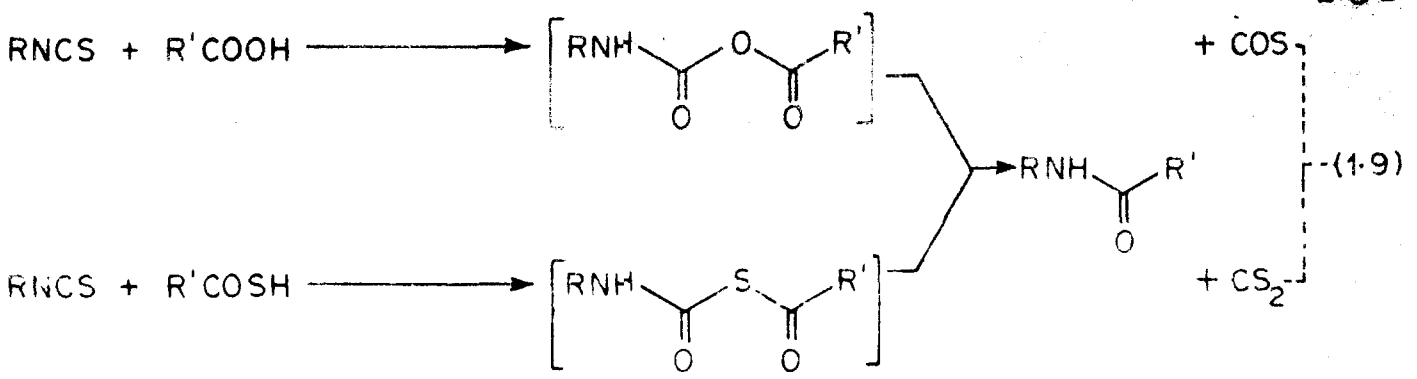
2. Reactions of isothiocyanates at the carbon-hydrogen bond

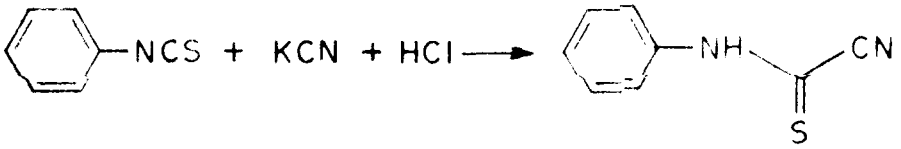
Reactions under this heading mainly include the electrophilic substitution reactions by the highly electron deficient carbon of the isothiocyanate group. Hydrogen cyanide in dilute ethanol yields cyanothioamides.[21] (2.1). Aryl substituted thioamides are formed under Friedel-Crafts condition by the reaction of isothiocyanate on aromatic hydrocarbons,[22] aryl ethers[23] and phenols[24] (2.2). Substituted thioamides are also formed from the alkali metal salts of acetylenes[25,26] (2.3) and from compounds containing active methylene groups[27,28] (2.4).

3. Other reactions

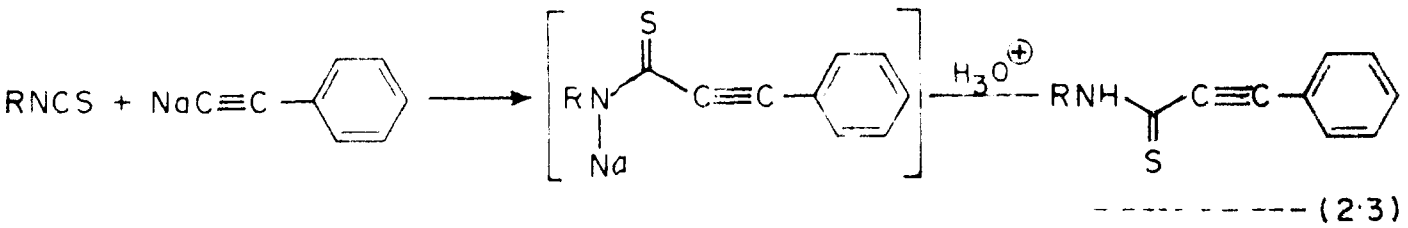
Amines are formed from isothiocyanates under reducing conditions by lithium aluminium hydride[29] and by Raney nickel.[30] Phenylisothiocyanate react with thioglycollic[31] acid and sodium azide[32] to give substituted thiazole[31] and tetrazole ring systems respectively. A commercially important reaction of phenylisothiocyanate is its reaction with sulphur to yield 2-thiobenzthiazoline[33,34] which is vulcanizing accelerator in rubber industry (3.1).

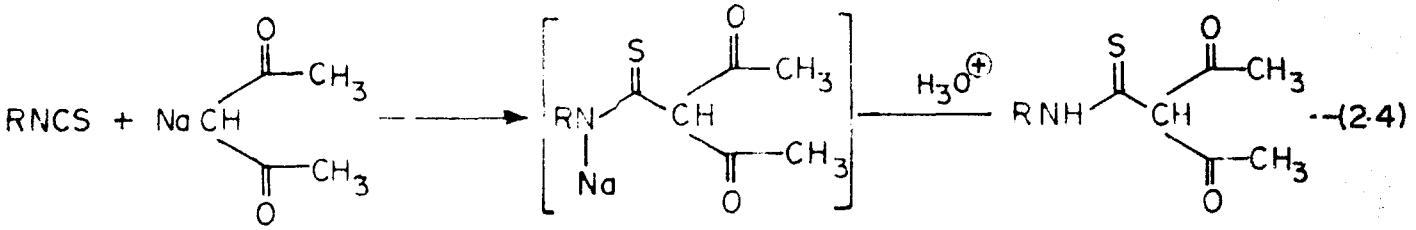
Chlorine reacts vigorously with arylisothiocyanate in inert solvents.[35] Chlorination of phenyl isothiocyanate yields the lachrymatric phenyl isocyanide dichloride. Mercuric oxide abstracts sulphur from iso-


RNCS + R'COOH
RNCS + R'COSH
+ COS
+ CS2
(1·9)

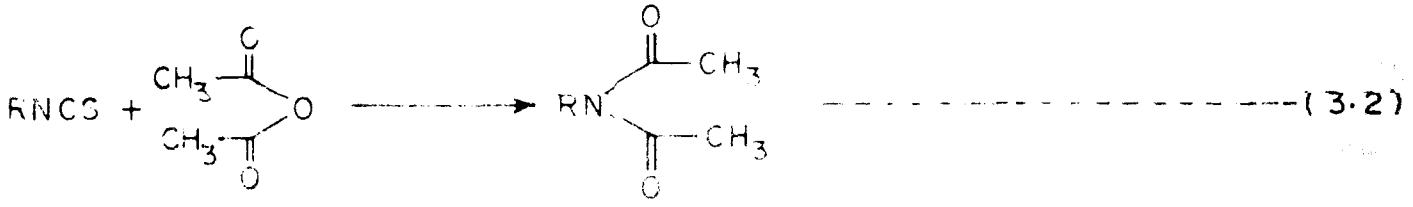

NCS + KCN + HCl
(2·1)


RNCS +
(2·2)


RNCS + NaC≡C
(2·3)


RNCS + Na CH
(2·4)


NCS + S8
SH
(3·1)


RNCS +
(3·2)

thiocyanates to form isocyanates.[36] Grignard reagents yield thioamides with isothiocyanates after hydrolysis of the complexes first formed.[37] Acid anhydrous gives rise to imides with elemination of carbonyl sulphide[20] (3.2).

PRESENT WORK

Symmetrical N,N'-disubstituted thioureas have been prepared by several methods.[38] The principal methods involve:

(I) The reaction of carbondisulphide and primary amine[39] (1.1).

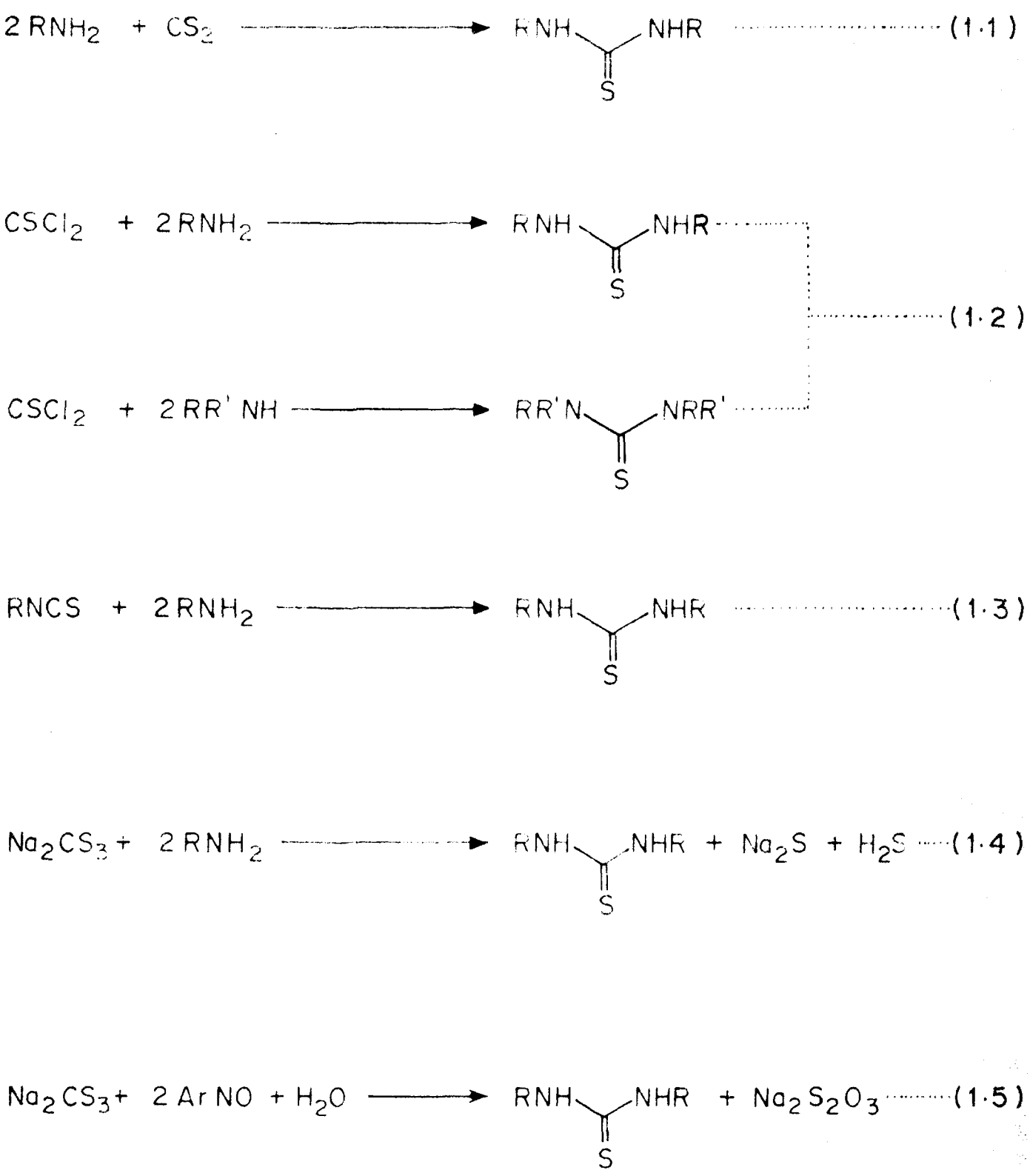
(II) The reaction of primary or secondary amine with thiophosgene[40] (1.2).

(III) The reaction of organic isothiocyanates and a primary amine[41] (1.3).

(IV) The heating of a salt of trithiocarbonic acid with primary amine[42] (1.4).

(V) By the reaction of arylnitroso compound with an aqueous solution of the salt of trithiocarbonic acid[43] (1.5).

(VI) They also can be made from isothiocyanates with water in the presence of acid or base catalyst or under pressure at elevated temperature.[44] Normally "isothiocyanates are so stable towards water that they may be purified by steam distillation."[45]


2 RNH2 + CS2
RNH NHR
S
(1·1)
CSCl2 + 2 RNH2
RNH NHR
S
CSCl2 + 2 RR' NH
RR'N NRR'
S
(1·2)
RNCS + 2 RNH2
RNH NHR
S
(1·3)
Na2CS3 + 2 RNH2
RNH NHR + Na2S + H2S
S
(1·4)
Na2CS3 + 2 Ar NO + H2O
RNH NHR + Na2S2O3
S
(1·5)

In the present work, a self condensation of phenylisothiocyanate in anhydrous dimethylsulphoxide has been reported. This is the first report of the reaction of an organic isothiocyanate with dimethylsulphoxide to give 1,3-disubstituted thiourea. Thus when a mixture of phenylisothiocyanate (0.01 mole) and anhydrous dimethylsulphoxide (0.03 mole) was heated on the steam bath, N,N'-diphenylthiourea was obtained in quantitative yield. The authenticity of the reaction product as to be N,N'-diphenylthiourea has been verified by elemental analysis, NMR in $CDCl_3$, mass spectrometry and by m.m.p. with N,N'-diphenylthiourea prepared by the reaction of phenylisothiocyanate and aniline. However, the yield of the thiourea decreased (30%) when equimolar amounts of isothiocyanate and anhydrous dimethylsulphoxide were treated under identical conditions. Carbonyl sulphide was evolved during the reaction and was identified in the form of its xanthates by passing through an alcoholic potassium hydroxide solution.[46]

From the above reaction, it appears that dimethylsulphoxide participates in the reaction through its oxygen atom giving rise to the thiourea and carbonyl sulphide and the two protons incorporated into the thiourea are evidently from dimethylsulphoxide. This transfer of protons in the neutral condition of the reaction has been substantiated

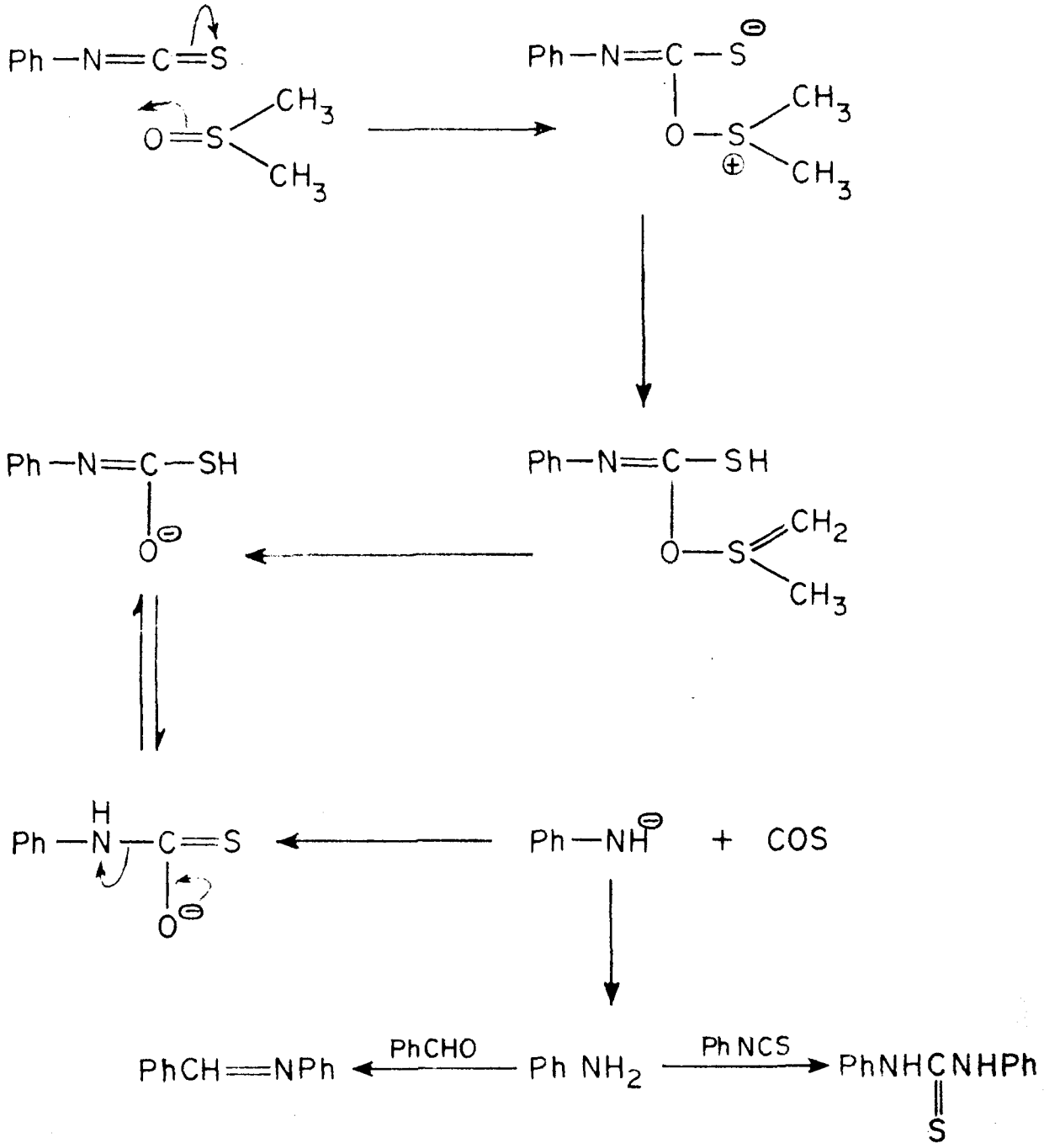
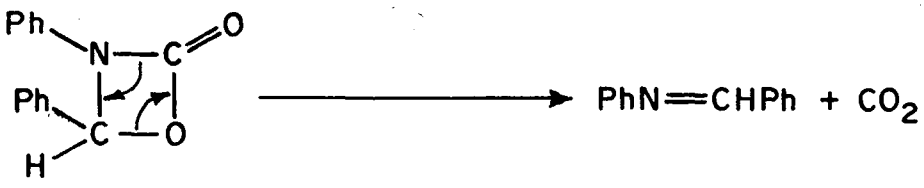

Ph—N=C=S
O=S
CH3
CH3
Ph—N=C—S
O—S
CH3
CH3
Ph—N=C—SH
O
Ph—N=C—SH
O—S
CH2
CH3
Ph—N—C=S
H
O
Ph—NH
+ COS
PhCH=NPh
PhCHO
Ph NH2
PhNCS
PhNHCNHPh
S

CHART — I

by replacing dimethyl sulphoxide with DMSO-$\underline{d}_6$ (isotopic purity > 98 atom % D) and the resultant product was characterised as N,N'-$\underline{d}_2$-diphenylthiourea (mass spectrum). The reaction may be proceeding as indicated in Chart I, by the necleophilic attack of oxygen of dimethyl sulphoxide on the carbon of isothiocyanate group with the formation of aniline and carbonyl sulphide. Aniline in turn reacts with excess of phenyl isothiocyanate giving diphenyl-thiourea. Thus, if aniline is one of the intermediates through which N,N'-diphenylthiourea is formed in the reaction of dimethylsulphoxide and phenylisothiocyanate, then aniline can be trapped during the reaction in the form of a derivative. With this idea in mind, when a mixture of phenylisothiocyanate (0.01 mole) and benzaldehyde (0.01 mole) in dimethylsulphoxide (0.03 mole) was heated on a steam bath for 18 hr., N-benzylidene aniline (65%) and N,N'-diphenyl-thiourea (30%) were obtained. This is the first report of the reaction of phenylisothiocyanate with benzaldehyde on dimethylsulphoxide to give a Schiff base. Schiff base can be produced by reaction of an aldehyde with isocyanate,[47] N-sulphinylamine,[48] sulphurdiimide,[49] and carbodiimide.[50] Isocyanates react with aldehydes due to overall nucleophilic character of nitrogen in the molecule through the transitional complex shown below, N-benzylidene aniline and



carbon dioxide are generated by the decomposition of this complex. Unlike isocyanates, isothiocyanates will not react with the aldehydes due to less nucleophilic character of nitrogen in the latter compared with the former, which in turn reduces the electrophilicity of the carbon in the isothiocyanate group.

Adopting this method, a number of Schiff bases and symmetrically disubstituted thioureas have been prepared with or without benzaldehyde in the reaction medium (see Table).

Phenylisothiocyanate is known to react with benzoic acid[19] to produce amides in high yields when a mixture of phenylisothiocyanate (0.01 mole), benzoic acid (0.01 mole) and dimethyl sulphoxide (0.03 mole) was heated on steam bath for 18 hr., benzanilide was obtained in quantitative amount. The fact that no N,N'-diphenylthiourea has been isolated in this reaction shows a much stronger nucleophilic character of benzoate anion compared to the nucleophilicity of dimethylsulphoxide oxygen.

EXPERIMENTAL

Expt. 1

Phenylisothiocyanate (1.2 ml; 1.35 g., 0.01 mole) and anhydrous dimethyl sulphoxide (freshly distilled and dried; 2.37 ml, 2.57 g., 0.033 moles) were mixed to a solution in an anhydrous condition and heated on a steam bath for 18 hr. The solid separated on cooling was filtered, washed with pet.ether (60-80°). It showed a homogeneous compound on TLC (silica gel) (1.05 g., 95%). Crystallised from benzene-pet.ether mixture (50% v/v) in white shining plates m.p. 153-54°, M^+ 228. PMR showed in $CDCl_3$ two peaks -respectively at 1.8τ and at 2.7τ with an integration ratio of one and five protons respectively. The signal at 1.8 τ disappeared on shaking the deuterochloroform solution with a drop of deuterium oxide. Infrared spectrum showed an -NH stretching absorption at frequency 3140 cm^{-1}. (Found: C,68.6; H, 5.36; S, 13.9; N, 12.07. $C_{13}H_{12}N_2S$ requires C, 68.4; H, 5.26; N, 12.27; S, 14.0%). An authentic sample of N,N'-diphenylthiourea, m.p. 154° gave no depression on m.m.p. with the sample obtained in the above reaction.

Expt. II. General procedure:

A mixture of organic isothiocyanates (0.01 mole) and anhydrous dimethylsulphoxide (0.03 mole) was heated on a

steam bath for a period of 18 hr. The contents of this reaction mixture were cooled and poured over crushed ice (30-50 g). The solid that separated was collected, washed with cold water and dried. It was crystallised from appropriate solvents as indicated in the table.

Expt. III

Phenylisothiocyanate (1.35 g., 0.01 mole) and anhydrous dimethyl sulphoxide (1.17 g., 0.015 mole) were treated as in the Expt. I, and heated on the steam bath for 18 hr., a white solid, which is same as the product of Expt. I, was isolated (0.35 g., 30%).

Expt. IV

The reaction mixture containing the reactants of Expt. I with same amounts, but kept at room temperature (25^{o}) for 44 hr. The conversion to N,N'-diphenylthiourea was about 40% and rest was unconverted phenylisothiocyanate.

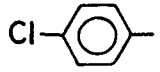
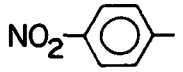
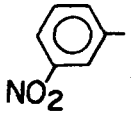
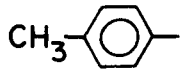
Expt. V

When phenylisothiocyanate (1.35 g) was taken in excess of dimethylformamide (7 ml) and kept on boiling water bath for 24 hr., uncoverted phenylisothiocyanate was isolated.

Expt. VI

A mixture of phenylisothiocyanate (1.35 g., 0.01 mole), anhydrous dimethyl sulphoxide (2.34 g., 0.03 mole)

T A B L E

	R-N=C=S (ISOTHIOCYANATES)	Reaction of RNCS in DMSO alone			Reaction of RNCS in DMSO with benzaldehyde			
		RNH-C(=S)-NHR Yield %*	m. p. (°C)	lit.[51] m.p. (°C)	RN=CHPh (anils)+ Yield %	m.p. (°C)	lit.[52] m.p. (°C)	RNH-C(=S)-NHR Yield %
	R=							
1		93[a]	152	152-3	65	46-8	48	30
2		78[a]	167	167	55	62	62	38
3		92[b]	176	176	62	119	120	29
4		89[b]	162	164	51	73	73	22
5		82[a]	174-5	174-5	43	c	c	47
6	Methyl	87+	52	52	-	-	-	73

* Conversions are quantitative and yield denotes actual isolation.

\+ Crystallised from pet.ether (60-80°).

a Crystallised from benzene

b Crystallised from benzene-alcohol mixture

c b.p. 318°; lit.[14] b.p. 318°.

and benzoic acid (1.22 g., 0.01 mole) was kept on boiling water bath for 21 hr. and cooled. On cooling a solid separated out which is sparingly soluble in benzene. Filtered, washed several times with benzene (1.82 g., m.p. 163.4°). The product showed homogeneous spot on TLC (silica gel, benzene-acetone 9:1). This on mixing with the authentic sample of benzanilide (m.p. 164-5°) gave no depression in melting point.

Expt. VII

A mixture of phenylisothiocyanate (1.35 g., 0.01 mole), dimethylsulphoxide (2.57 g., 0.033 mole) and benzaldehyde (1.06 g., 1 ml, 0.01 mole) was warmed on a steam bath for 18 hr. The resultant brown solution was extracted with pet.ether (15 ml. x 5). Pet.ether extractswere mixed together and washed with 10% aqueous sodium bicarbonate solution (20 ml. x 3) to remove any benzoic acid and then the extract was dried over anhydrous sodium sulphate. Filtered and the solvent was distilled over - an oil was found as the residue (1.58 g., 63%). This oil was distilled at 298-301°). The distilled oil solidied on cooling and melted at 47-48°. This sample on m.m.p. with an authentic sample of N-benzylideneaniline was undepressed.

The solution left after pet.ether extraction was poured in crushed ice, N,N'-diphenyl thiourea separated out as white solid, filtered and dried (0.30 g., 40%). This was crystallised from benzene-pet.ether mixture and melted at 153-54°. On m.m.p. with authentic sample gave no depression.

Expt. VIII. General Procedure:

A mixture of organic isothiocyanate (0.01 mole), benzaldehyde (0.01 mole) and anhydrous dimethyl sulphoxide (0.03 mole) was heated on steam bath for 18 hr. The reaction mixture was cooled and extracted with hexane (20 ml. x 3). The residual liquor was poured over crushed ice and the solid was collected and characterised as thioureas by m.p. and spectral properties. On removal of solvent from the hexane extract, N-benzylidine anilines were obtained and purified by crystallisation or by distillation.

Expt. IX

A mixture of phenylisothiocyanate (1.2 ml., 0.01 mole) and dimethyl sulphoxide (1.1 ml., 0.015 mole) in dry benzene (30 ml) was refluxed for 24 hr., and no trace of N,N'-diphenylthiourea was found in the reaction product. Phenylisothiocyanate was recovered.

Expt. X

A mixture of phenylisothiocyanate (1.2 ml., 0.01 mole) and dimethyl sulphoxide (1.1 ml., 0.015 mole) in dry chloroform (30 ml.) was refluxed for 24 hr., and worked up as usual. The product (0.17 g.) was characterised as N,N'-diphenylthiourea.

Expt. XI

A mixture of phenylisothiocyanate (0.3 ml., 0.0025 mole) and DMSO-$\underline{d}_6$ (0.55 ml., 0.0075 mole, isotopic purity > 98 atom % D) was heated on a steam bath for a period of 18 hr. The mixture was cooled and the solid separated out was collected, and characterised as N,N'-$\underline{d}_2$-diphenylthiourea, m.p. 151-52° (M^+ 230).

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P A R T - VI

ISOMERIZATION OF THE ALDOXIMES TO THE AMIDES UNDER SUBSTANTIALLY NEUTRAL CONDITIONS.

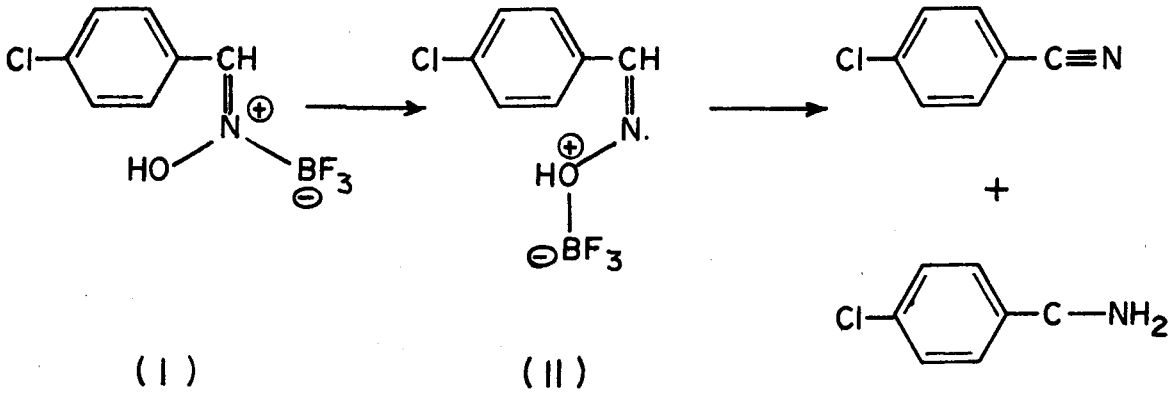
INTRODUCTION

A few limited observations can be cited of the older literature[1-3] on reactions involving the conversion of an aldoxime to an amide via a Beckmann rearrangement. However, in general, the usual conditions of Beckmann rearrangement results in partial or complete dehydration of aldoximes to give the corresponding nitriles, and as a result special or indirect methods have been employed where rearrangement is desired. N-alkyl ethers[4,5] and acetyl derivatives[6] have been used in such studies.

Horning et al.[7] effected Beckmann rearrangement of ketoximes by using polyphosphoric acid and the same author has used[8] polyphosphoric acid as a catalyst for bringing about the conversion of aldoximes to amides to show that the Beckmann rearrangement is a general reaction of both ketoximes and aldoximes. The assignment of configuration to aldoximes has been based upon indirect evidence. Hantsch[9] first recognised the possibility of isomerism of aldoximes and since then it has become a standard practice to treat the acetyl[6] or benzoyl derivatives[10,11] of aldoximes with alkali in order to determine the structure of the oxime. The nitrile is generated from the acetylated anti-oxime, while the syn- compound does not react or regenerates the original oxime. Horning et al.[8] first provided a means of

studying aldoxime structures in a direct way by the rearrangement of an aldoxime to an amide by polyphosphoric acid and thereby isomerizing benzaldoxine to benzamide in 25-40% yield, depending on syn- or anti-oxime was used.

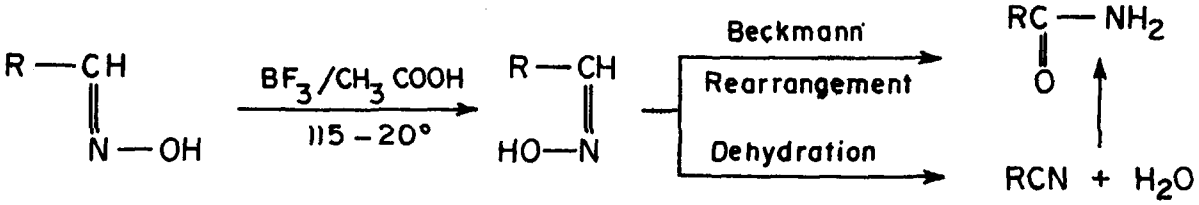
Syn-p-chlorobenzaldoxime was converted by boron trifluoride at room temperatures to the solid N-coordination complex of the anti-aldoxime (I) which was stable even at 135°.[12] The relatively stable complex (I) had undergone dehydration to p-chlorobenzonitrile (37%) or Beckmann rearrangement to p-chlorobenzamide (27%) at 150°



(I) (II)

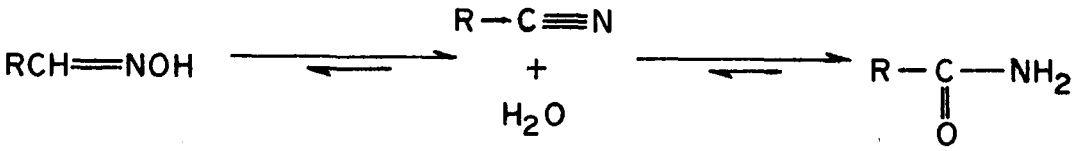
or at 115-120° in acetic acid solution. The Beckmann rearrangement of the boron trifluoride N-complex of the ketoxime also required high temperatures.[13] The products were considered to be formed from (I) through (II) by dehydration and the Beckmann 1,2-shift of hydrogen respectively. The possibility that the amide arose

through the controlled hydration of the nitrile could not be ruled out. The reaction of syn- or anti-p-chlorobenzaldoxime with commercial boron trifluoride-acetic acid complex, consisting of one molecule of boron trifluoride and two of acetic acid, at 115-20° yield exclusively p-chlorobenzamide in 95-99% yield, whereas, the thermal decomposition of the solid complex (I) produced three products. p-Chlorobenzonitrile (37%), p-chlorobenzamide (27%) and p-chloroformamilide (6%). The authors postulated a Beckmann 1,2-shift of hydrogen can account the formation of the amide from the anti-aldoxime. The amide may also



arise from the syn-aldoxime in the same manner after preliminary isomerization to the anti-isomer. The authors, however, did not exclude the idea that the amide might also be formed through trans-dehydration of anti-aldoxime, followed by addition of the by-product water to the resulting nitrile and thus on stopping the reaction before completion, some of the nitrile (5%) was isolated along with the amide (17%) from the reaction mixture of p-chlorobenzaldoxime and

boron trifluoride acetic acid complex. In an another communication,[14] these authors have reported that various nitriles were converted to the corresponding amides by heating the nitrile at 115-20° for ten minutes with the same anhydrous boron trifluoride-acetic acid complex. These observations cast a clean doubt whether at all any Beckmann rearrangement is involved in Hanser *et al*'s work[12] with *p*-chlorobenzaldoxime. The authors argued "A blank experiment indicated that the yield of the nitrile from the aldoxime should have been approximately equal to that of the amide if the dehydration course of reaction occurred exclusively". The fact that less nitrile than amide was isolated might be ascribed to the relative reaction rates.



The isomerization of an aldoxime to an amide catalysed by a metal salt has been first observed by Comstock who found that benzamide resulted when benzaldoxime and cuprous chloride were heated in benzene or toluene.[2] Comstock's isomerisation was not general and the aldehyde often was the principle product.

Reactions, involving such an isomerization, have not attracted the attention it should have "from both the standpoint of their theoretical interest and their promise for synthesis and characterisation."[15] An unambiguous evidence of the Beckmann rearrangement of the aldoximes have not been reported until Paul[16,17] reported the conversion of the aldoximes to the amides while studying the hydrogenation of the former with Raney nickel as catalyst. He was able to show using several aldoximes that the stereo-isomer ordinarily available could be isomerized effectively to a single amide with Raney nickel as catalyst. He further showed that the ketoximes did not react. A nickel-boron-catalyst[18] also could bring about a similar isomerization. Reduced copper at 200° produce amides in low yields in hydrogenation experiments of certain aldoximes and keto-ximes,[19,20] but since ketoximes react, the isomerisation probably differs from that of Paul. Caldwell and Jones[21] have successfully converted some oily unsaturated oximes to solid amides following Paul's condition by heating the oximes with Raney nickel at about 100°. Bryson and Dryer[22] have provided evidence for Paul's suggestion that the reaction proceeds via an aldoxime-nickel complex, the rearrangement of which is promoted by traces of iron or aluminium.

Field *et al.*[15] reinvestigated Paul's reaction of isomerization of the aldoxime to the amide and evaluated

several substances as the effective catalyst for this isomerisation. Table (I) below illustrates this:

T A B L E I

Potential catalysts for isomerisations of benzaldoxime to benzamide.

Potential catalyst	$0^{o}C$ of heating for 1 hr.	Yield (%)
Nickel acetate (tetrahydrate)	185-90	75
Nickel carbonate	184-89	72
Raney nickel	180-85	60
Cupric oxide	120-25	60
Cupric carbonate(basic)	106-111	56
Nickel metal (powder)	205-210	53
Nickelous oxide	210-215	24
Cobaltic oxide	205-210	23

The other substances tried gave only highly coloured oils which did not crystallise include ferric chloride, ferric oxide, cobaltous carbonate, anhydrous cobaltous chloride, cupric chloride, silver oxide, yellow mercuric oxide and iron powder.

Nickel acetate (tetrahydrate) was discovered to be more promising amohg the compounds tried. Field et al.[15] have successfully used this catalyst in a homogeneous liquid system using xylene to convert a series of oximes to the amides under a substantially neutral condition.

PRESENT WORK

In an attempt to dehydrate aldoximes to the corresponding nitriles with silica gel (chromatographic grade prepared by the Fine Chemicals Division of this Laboratory), benzaldoxime was adsorbed on silica gel in 1:5 portions (w/w) and heated at 100-10° in an oven for a period of 60 hr., the product on working up was found to be benzamide (73%) and no traces of benzonitrile was detected. From this it is clear that benzaldoxime isomerised to benzamide under substantially neutral conditions. Earlier various catalysts have been tried to isomerise benzaldoxime to benzamide and found that nickel acetate was most suitable (see Introduction). In an effort to make this method more general, the reaction has been carried out in xylene, which was found to be a more suitable solvent for such isomerisation using nickel catalyst.[15] Thus benzaldoxime (5 g) was refluxed in dry xylene (25 ml) with activated silica gel of thin layer chromatographic grade (activated at 130-40°; 10% of the weight of the oxime) till the solution showed the absence of aldoxime on TLC plates (65 hr). The product was found to be benzamide isolated in 90% yield.

Adopting the above method, various oximes have been isomerised to the corresponding amides and found that in all cases the yields are very high and the method is much

better than all the methods known so far for its simplicity and high conversions. The list of aldoximes that have been isomerised by this method are given in Table 2. The reaction occurred most satisfactorily even in compounds having an o-hydroxyl group which normally interfere in the earlier methods of isomerisation such as nickel acetate method by forming an intermediary nickel coordinated compound. Thus salicylaldoxime was converted to salicylamide in over 83% yield. Boron trifluoride in acetic acid produced salicylamide in 47% yield.[24] Similarly a conjugated double bond with the oxime, as in the case of cinnamaldehyde oxime did not interefere in the smooth conversion. Further, electron donating or electron withdrawing substituents on the aldoximes have not effected the yields and in all cases the conversions are much better when silica gel was employed as catalyst compared with nickel acetate.

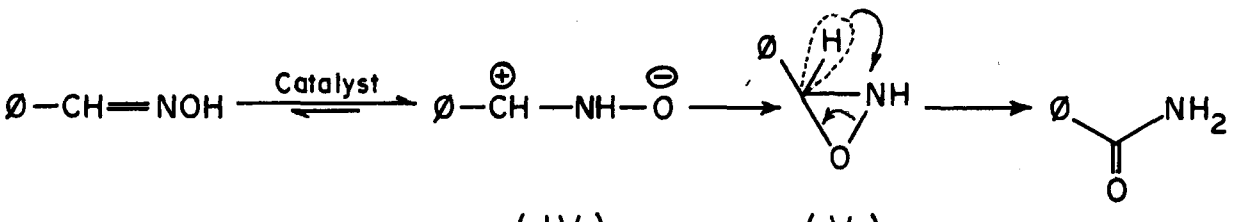
When silica gel was replaced by neutral alumina of chromatographic grade, the isomerisation did occur, although the yields are somewhat lower for the same amount of the catalyst used in the silica gel experiment. Thus when benzaldoxime was submitted for isomerisation using neutral alumina (10% of the weight of aldoxime) in xylene for 80 hr. the conversion is around 40-50%.

The mechanism of this isomerisation is not clearly understood. The possibility of nitrile being an intermediate,

as in most of the acid catalysed isomerisation, is completely ruled out because at no stage the presence of nitrile could be detected. Further, this reaction is only for converting aldoximes to the corresponding amides and not applicable for the conversion of ketoximes. Thus acetophenone oxime, when submitted to the isomerisation reactions for the same length of period, it was recovered quantitatively. Similarly, acetaldoxime gave exclusively acetamide and no traces of N-methylformamide could be detected.

The exact role of silica gel in bringing about this isomerisation is not clear. Silica gel activated at 130-40° does not contain more than 1% of moisture and is known to have bonded with the hydroxyl group of the silica gel, which is a polymer of silicic acid. The chemistry of silica gel has been well reviewed by Mitchell.[25]

Field et al. have suggested a nickel-oxime complex which brings the isomerisation directly. However, the mechanism of isomerisation may or may not be same with silica gel. One possibility is of intramolecular cyclisation through a transitional intermediate (V), which might have arised from a tautomer (IV) which possibly becomes dominant by the presence of the catalyst.



(IV) (V)

EXPERIMENTAL

1. Isomerization of oximes with silica gel in xylene
General Procedure:

A mixture of the aldoxime (I to VIII) (0.02 mole). TLC grade silica gel (pH of the silica gel aqueous suspension is 6.5 to 7) activated before the reaction at 130-40° (0.24 g., 10% of the oxime weight, w/w) in anhydrous xylene (25 ml) was heated at the reflux temperature for a period of 52 to 73 hr. The solution was filtered hot and part of the solvent was distilled from the filtrate. On cooling the contents, crude amide was separated out, and was crystallised from an appropriate solvent.

2. Attempt to identify the intermediate nitrile

A mixture of benzaldoxime (4.8 g., 0.04 mole), TLC grade activated silica gel (0.48 g) in anhydrous xylene was heated at reflux for 20 hr. and solution was filtered while hot and part of the solvent (85%) was distilled off. This concentrated reaction mixture was spotted on silica gel TLC with the authentic benzonitrile; the chromatogram of the reaction mixture was found to contain no benzonitrile, but showed to be a mixture of benzaldoxime and benzamide.

3. Isomerisation of the benzaldoximes with neutral alumina in xylene

A mixture of the benzaldoxime (2.42 g., 0.02 mole), neutral alumina (Brockman activity I, 0.48 g., 20%) of the

oxime weight, w/w) in anhydrous xylene (25 ml) was heated to reflux for a period of 80 hr. The solution was filtered hot and part of the solvent was distilled from the filtrate. On cooling the contents, crude benzamide (m.p. 126-28°; 0.98 g; 40%) was separated out and was crystallised from benzene in flakes, m.p. 128-29°. On removal of the solvent from the *mother liquor a thick oil (1.1 g) was isolated which was* found to be unconverted benzaldoxime on comparison with the authentic sample of benzaldoxime.

TABLE 2

Aldoxime	m.p.(°C) of oxime	Yield* %	amide mp(°C)	amide lit.[26] m.p.(°C)	Time (hr)
I. Benzaldehyde	28-31	92	128[a]	128	69
II. p-Chlorobenzaldehyde	110	91	178-79[b]	179	59
III. p-Hydroxybenzaldehyde	74-75	84	162[b]	162	61
IV: p-Methoxybenzaldehyde	131-3	81	162-3[a]	163	52
V. Piperonal	105-7	93	169[a]	169	64
VI. Cinnamaldehyde	138	79	146-7[b]	147	66
VII. Salicylaldehyde	60-61	83	139-40[b]	140	73
VIII. Acetaldehyde	47	89	81-2[a]	83	57

a Crystallised from benzene

b Crystallised from benzene-alcohol mixture

* Conversions are quantitative, the yield denoted here is the actual amount isolated.

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S U M M A R Y

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Part I: Constitution of Cibanone Orange R

Two dyes, Cibanone Orange R (C.I. 1169) and Cibanone Yellow R (C.I. 1170), obtained by the thionation of 2-methylanthraquinone are obsolete, although they are continued to be of interest as powerful catalysts for the photochemical degradation of cellulose. Manjrekar has suggested structure (I) to Cibanone Orange R as a dimer of anthraquinone-2-thioaldehyde which has been revised to structure (II) in the present work in view of its chemical and spectral data.

When ω-dibromo-2-methylanthraquinone was refluxed with anhydrous sodium sulphide in solvents like acetone, ethanol, dioxane, 2-methoxyethanol and diglyme gave a product identical with Cibanone Orange R in addition to anthraquinone-2-aldehyde. This dye can also be obtained by thionating 2-mercaptomethylanthraquinone and bis-methyl-anthraquinonyl sulphide. Although these experiments may suggest that Cibanone Orange R can well be represented by structure (I), it is difficult to reconcile such a structure in view of its deeper colour. Further, Cibanone Orange R failed to deuterate on refluxing with 40% sodium deuteroxide, indicating the absence of benzalic hydrogen flanked by sulphur atoms and therefore the structure (I) was excluded.

An alternative structure (III) was considered to explain its colour and other properties. The concept of a tetracovalent sulphur attached to a hydride formulated in structure (III) is new and no such example has been found in the literature. However, this view has been substantiated by reacting Cibanone Orange R with triphenylmethyl perchlorate in benzene, resulting in the formation of a diperchlorate salt of the dye and triphenylmethane. The dye also forms a dianilinium salt when refluxed with excess of aniline.

A careful NMR analysis of the reductive methylation product of Cibanone Orange R indicates that the two anthraquinonyl moieties are not symmetrically substituted. On the basis of a detailed analysis of the aromatic region, in addition to the chemical evidences, Cibanone Orange R can be better represented by structure (II).

Part II: Constitution of Cibanone Yellow R

Bhavsar suggested structure (IV) for Cibanone Yellow R, which is also obtained by thionation of 2-methylanthraquinone. Its constitution has been reinvestigated hoping that its structure may throw some light on Cibanone Orange R.

The reductive methylation of Cibanone Yellow R gave two products: a dimethyl ether and a tetramethyl ether of the leuco dye. The dye is unstable to neutral sodium dithionite, boiling 10% hydrochloric acid or 40% hydrobromic acid, giving hydrogen sulphide gas and anthraflavone. Its unstability with these reagents is very difficult to reconcile with the suggested structure (IV) for Cibanone Yellow R. The NMR spectra of the reductive methylation product suggest that the two anthraquinonyl moieties may be symmetrically substituted rather than the structure (IV). An alternate structure (V) has been considered for Cibanone Yellow R to explain its instability to neutral sodium dithionite and to dilute acids. However, the conversion of Cibanone Yellow R to Orange R cannot be explained by either of the structures (IV) or (V), and further evidence is therefore required to obtain to arrive at the correct structure of the dye.

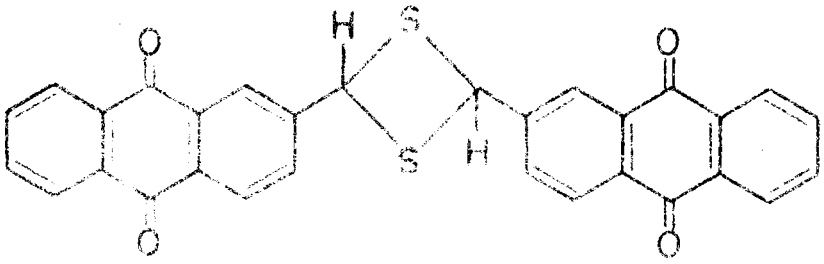
Part III: Some aspects of the chemistry of triaryl-s-trithianes

In connection with the work on the constitution of Cibanone Orange R, the properties of 2,4,6-triphenyl-s-trithiane (VI), the trimer obtained quantitatively when benzaldehyde is treated with H_2S and HCl, were examined, and it was found that it is a very useful intermediate as

the carbanion. Thus the three protons of the heterocyclic ring can be completely exchanged by deuterium ions by refluxing a dioxane solution with a 20% solution of NaOD in D_2O, as shown by the disappearance of the proton signals in the NMR spectrum and the shift of $M^{+\cdot}$ by three mass units in the mass spectrum. Hydrolysis of the trideuterated triaryltrithiane (VII) by $HgCl_2$ and HgO in boiling aqueous methanol gave α-d-benzaldehyde. Similarly the p-chloro-, p-methoxy- and 3,4-methylenedioxy-derivatives of α-d-benzaldehyde were obtained in 80-85% yield. They were prepared earlier by different and much less convenient methods.

The synthesis of α,α'-dideuterostilbenes starting from trideuterated-2,4,6-triaryl-s-trithianes (VII) has been achieved in about 80% yield by desulphurisation with W-4 Raney nickel in boiling benzene. The stilbenes prepared in the present work are the trans isomers as expected. This method is very simple and most convenient compared with all the reported methods.

The successful deuteration at all the three positions of the heterocyclic ring of the triaryl-s-trithiane (VI), suggests the possibility of generating the carbanions for reacting the alkyl or acyl halides at all the three centres. As the preparation of trithianes from carbonyl compounds is much simpler and inexpensive than



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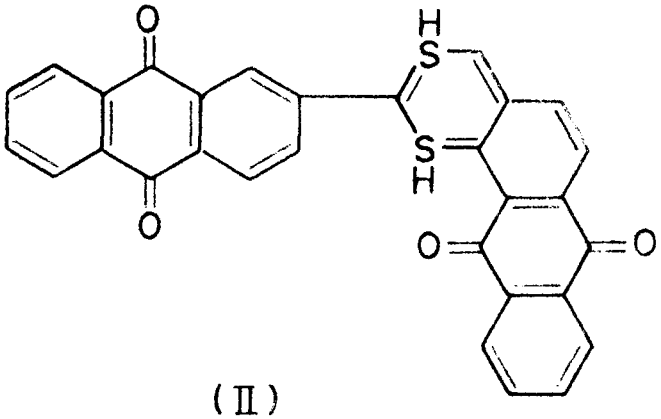

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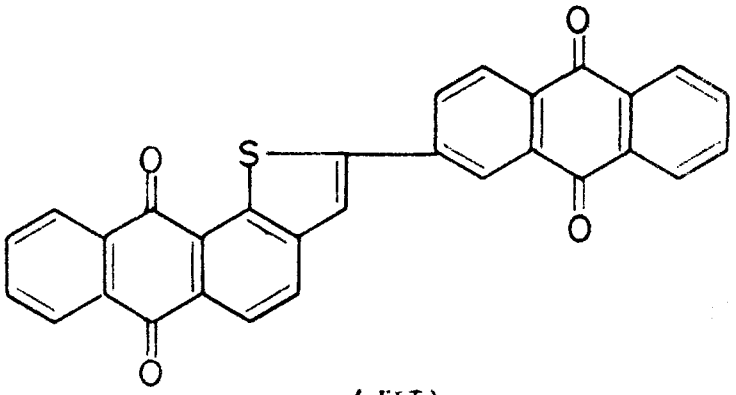

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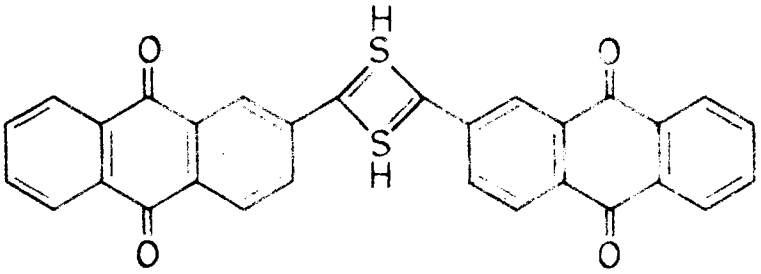
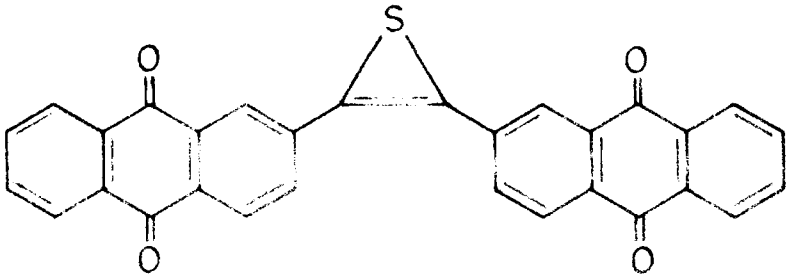
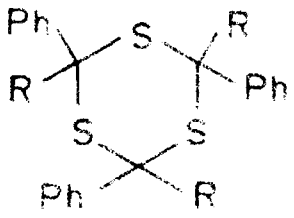


(III)



(V)



VI ; R = H

VII ; R = D

building a 1,3-dithiane system, it was felt worthwhile to study the alkylation of triaryl-s-trithianes. Thus when triphenyl-s-trithiane was reacted with sodium hydride in dimethyl sulphoxide at room temperature and alkylated with excess of methyl iodide, 2,4,6-trimethyl-triphenyl-s-trithiane was obtained, which on hydrolysis yielded three moles of acetophenone. However, the benzylation and the acylation with the ethyl chloroformate were unsuccessful.

Oae et al. have reported the formation of thiobenzaldehyde dimer treating benzaldehyde with excess of O,O-diethyldithiophosphoric acid in benzene. This reaction was repeated and the product thus isolated was characterised as 2,4,6-triphenyl-s-trithiane as its β-isomer. Consequently, a number of triaryl-s-trithianes have been prepared starting from aromatic aldehydes and treating them with O,O-diethyldithiophosphoric acid at room temperature.

Triaryl-s-trithianes have also been prepared by reacting sodium thiosulphate and aromatic aldehydes in 2:1 molar proportion by refluxing with excess of concentrated hydrochloric acid.

Triaryl-s-trithianes can be converted to the corresponding carbonyl compounds by a number of methods; mercuric chloride-mercuric oxide method being common. In

the present work silver oxide in aqueous methanol is found to be convenient in achieving this object.

In the course of this work it has been found that iodine in dimethyl sulphoxide effects the conversion of s-trithianes and thioacetals by a novel oxidative desulphurization into the corresponding aldehydes or ketones in very good yields. The reaction of s-trithiane probably involves the formation of a sulphonium complex with iodine, rupture of the carbon-sulphur bond and the nucleophilic addition of dimethyl sulphoxide gives an intermediate which breaks down to an aldehyde, dimethyl sulphide and sulphur. Iodine is only a catalyst in this reaction.

Another less convenient method of oxidative desulphurization of triaryl-s-trithiane system to the corresponding aldehyde is reported in the present work by reacting s-trithiane with pyridine-N-oxide and iodine.

Part IV: Electron-impact fragmentation of triaryl-s-trithianes: A novel skeletal rearrangement involving sulphur-sulphur bond formation.

The mass spectral fragmentation of seven substituted 2,4,6-triaryl-s-trithianes have been studied and the fragmentation modes have been confirmed by deuterium labelling. Triphenyl-s-trithiane shows some interesting features in its mode of cleavage and does not eliminate S$^{\cdot}$, S_2, SH$^{\cdot}$, H_2S

or $S_2H^{\bullet}$ from its molecular ion. The prominent radical ions in the mass spectrum are at m/e 180 (52.3%) and m/e 186(45.2%) corresponding to stilbene and $PhCHS_3$. Their compositions have been established by deuterium labelling and by accurate mass measurements. The formation of stilbene indicates a relationship between pyrolytic and electron impact studies. The origin of $PhCHS_3^{+\bullet}$ suggests that one of the sulphur atoms attaches itself to the other two sulphur atoms in the molecular ion, eliminating a stilbene radical ion. The other important fragmentation corresponds to the monomer radical ion (thiobenzaldehyde) and the thiobenzoyl cation.

Among the other substituted triaryl-s-trithianes with substituents such as chloro, methoxy, methylenedioxy and hydroxy groups on the phenyl ring, only the tris-(p-chlorophenyl)-s-trithiane shows an insignificant molecular ion. Unlike the triphenyl derivative, the chloro, methoxy and methylenedioxy derivatives show the loss of $HS^{\bullet}$ and/or H_2S from the molecular ion. The spectrum of tris-(p-hydroxyphenyl)-s-trithiane corresponds to the spectrum of p-hydroxy-thiobenzaldehyde.

PART V: Synthesis of substituted thioureas and Schiff bases from phenylisothiocyanate in dimethyl sulphoxide

Symmetrical N,N'-disubstituted thioureas have been prepared earlier by adopting different procedures. In the

present work they have been obtained by reacting organic isothiocyanates with anhydrous dimethyl sulphoxide. Carbonyl sulphide was evolved during the reaction and was identified in the form of its xanthate. From this ~~xxxxxxxxx~~ it appears that dimethylsulphoxide participates in the reaction through its oxygen atom, giving rise to the thioureas and carbonyl sulphide and the two protons incorporated into the thiourea are evidently from dimethyl sulphoxide. This transfer of protons has been substantiated by replacing DMSO with DMSO-$\underline{d}_6$ (isotopic purity $>$ 98 atom %D) and the resultant product was characterised as N,N'-$\underline{d}_2$-diphenylthiourea (mass spectrum). The possible mechanism has been discussed.

When a mixture of phenylisothiocyanate (0.01 mole) and benzaldehyde (0.01 mole) in DMSO (0.02 mole) was heated on steam bath for 18 hr. N-benzylidene aniline (65%) and N,N'-diphenylthiourea (30%) were obtained. This is the first report of the reaction of phenylisothiocyanate with benzaldehyde in DMSO to give a Schiff base.

Adopting this method, a number of Schiff bases and symmetrically disubstituted thioureas have been prepared with or without benzaldehyde in the reaction medium.

Part VI: Isomerization of the aldoximes to the amides under substantially neutral conditions.

Aldoximes are known to isomerize to the corresponding amides by the action of several acidic reagents. The isomerisation has also been achieved by several metal salts and among them nickel acetate was found to be most suitable.

In the present work aldoximes have been isomerised to the corresponding amides, using silica gel as a catalyst. This method is found to be much better than all the methods for its simplicity and high conversions. Unlike acid catalysed isomerisation, the nitrile is not an intermediate in this isomerization.

Isomerisation is also affected by replacing silica gel with neutral alumina but the yields are poor.

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1. A convenient method of preparation of aromatic α-deutero-aldehydes and α,α'-dideuterostilbenes, Ind.J.Chem. (~~in press~~) 11, 374 (1974)
2. A novel oxidative desulphurisation of s-trithianes and thioacetals with iodine in dimethyl sulphoxide, Tetrahedron Letters 3735 (1973).
3. Reaction of benzaldehyde with O,O-diethyl dithiophosphoric acid and hydrolysis of s-trithianes with silver oxide, Ind.J.Chem. (in press).
4. Synthesis of substituted thioureas and Schiff bases from phenylisothiocyanate in dimethyl sulphoxide, Synthesis (in press).
5. Electron-impact fragmentation of triaryl-s-trithianes: A novel skeletal rearrangement involving sulphur-sulphur bond formation, Org. Mass Spectrometry (~~communicated~~).
6. The isomerization of the aldoximes to the amides under substantially neutral conditions, Tetrahedron (communicated).
7. Reaction of 2-methylnaphthalene and sulphur, Ind.J.Chem. (communicated).