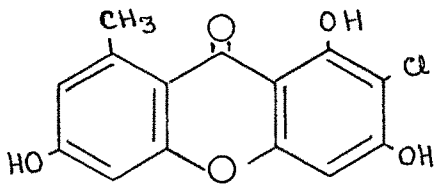
CHAPTER II

IODINATION OF SOME HYDROXYXANTHONES

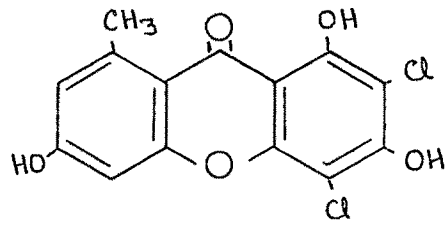
THEORETICAL

IODINATION OF SOME HYDROXYXANTHONES

Recently chloroxanthones such as 2-chloronorlichexanthone[1] (I), 2,4-dichloronorlichexanthone[1] (II), Arthothelin[2] (III) and Thiophanic acid[3] have been isolated from lichens. Halogenoxanthones have been found to have diverse uses. Monopotassium salts of (III) and (IV) act as plant growth regulators. Some of the bromoxanthones have been found to possess urinary antiseptic activity and 3-bromoxanthone and 2,7-dibromoxanthone are used in insecticidal preparations, as already discussed in Chapter I. Chloroxanthones have also been found suitable as catalysts for cross-linking the polymers[4] and as light stabilisers for polymers[5]. Wolcott[6] has reported the use of the 4-iodoxanthone as an organic termite repellent.



(I)



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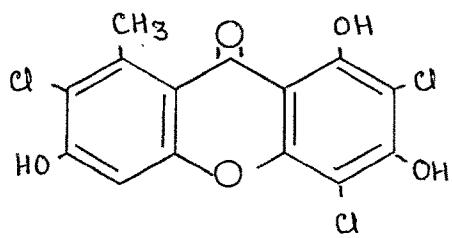

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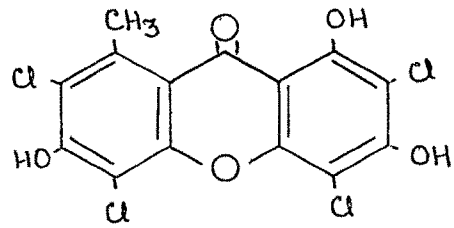


(IV)

It has been seen while discussing halogenation of xanthones that no work has been done on the iodination of xanthones hence the present work has been undertaken and it is a part of the extensive work done in our laboratories on substitution in various oxygen heterocycles. Even though no direct iodination of xanthones is reported, a few iodoxanthones have been synthesised by indirect methods. Brewster and Strain[7] have synthesised 2-iodoxanthone by cyclising 2-(4-iodophenoxy)-benzoic acid. Mann and Turnbull[8] have also prepared 2-iodoxanthone from 2-aminoxanthone through diazotisation and Sandmeyer reaction. Sirkar and Dutt[9] have reported the preparation of 3-iodoxanthone from 3-aminoxanthone and that of 2-iodo-7-nitroxanthone from 2-amino-7-nitroxanthone, through the same series of reactions. 2,7-Diiodoxanthone has been prepared by Bertrand[10] from 2,7-dinitroxanthone.

The present work deals with the iodination of some mono- and di-hydroxyxanthones. The objectives have been mainly to study the pattern of substitution and to utilise the iodo derivatives obtained for further synthetical work such as the synthesis of bixanthonyls and cyanoxanthones.

The iodination of hydroxyxanthones has been studied with two different iodinating agents (i) iodine and iodic acid and (ii) ammonia and iodine. The iodination with these reagents is assumed to take place according to the following equations,

(i) with iodine and iodic acid :

$$5RH + 2I_2 + HIO_3 \longrightarrow 5RI + 3H_2O$$

(ii) with ammonia and iodine :

$$3I_2 + NH_3 \longrightarrow NI_3 + 3HI$$

$$3RH + NI_3 \longrightarrow 3RI + NH_3$$

Iodination with iodine and iodic acid is found to be quite smooth and better yields are obtained by this method. Moreover, the method can be used successfully for progressive iodination, for example, 3,6-dihydroxyxanthone can be iodinated to get the mono-, di-, tri- and tetraiodo derivatives with iodine and iodic acid; while ammonia and iodine affords only the di- or tetraiodo derivative. Iodination of 2-hydroxyxanthone, 3-hydroxyxanthone, 3-hydroxy--6-methoxyxanthone and 3,6-dihydroxyxanthone has now been studied systematically and the structures of the iodo compounds obtained have been established either by an independent synthesis or from the NMR spectral data or wherever possible by both.

ROSENMUND-von- BRAUN REACTION

Aryl nitriles can be prepared by many methods. A survey of all the earlier methods has been made by Mowry[11] in 1948. Merz[12] discovered the classical synthesis of benzonitrile by fusion of the alkali-metal salts of benzene sulphonic acid with potassium cyanide. Further study of this reaction revealed that a good yield of β-naphthonitrile was obtained from sodium β-naphthalene sulphonate by treatment with excess of sodium cyanide. Witt[13] showed that the less toxic potassium ferrocyanide gave somewhat better results. Many variations have been tried to improve the yield of aryl nitriles.

The use of sand in the reaction mixture is also recommended to increase the yield of the nitrile by moderating the exothermic reaction. The introduction of small quantity of iron-filings to aid distribution of heat also improved the yields[14]. Merz and Weith[15] obtained α-naphthonitrile from α-bromonaphthalene by heating with potassium ferrocyanide.

Rosenmund[16] found that the replacement of aryl halogen atom by the cyano group can also be accomplished by the action of anhydrous cuprous cyanide. The use of cuprous cyanide dissolved in cyclic aromatic amines was introduced[17] in 1913. Later, Diesbech et al.[18] reported the conversion of dibromo derivatives to dinitrile derivatives by using dry cuprous cyanide in dry pyridine or quinoline. Newmann[19] also used cuprous cyanide in pyridine to convert α-bromonaphthalene to α-naphthonitrile.

It was observed by von Braun that the bromo derivatives of high boiling aromatic hydrocarbons are smoothly converted into nitriles in a very high yield by treatment with slight excess of cuprous cyanide at 260° without using any solvent or promoter. This method now called Rosenmund-von Braun synthesis has been studied in detail by Koelsch[20], who found that the reaction is autocatalytic and addition of small amount of the nitrile from the previous run shortens the reaction time as it acts as a catalyst. Koelsch and Whitney[21] studied the reaction in detail and also showed that cupric salt has a marked promoting effect. They have also shown that the basic compound such as pyridine,

quinoline or cyclohexylamine have marked accelerating effect like copper sulphate and the nitrile, Braun[22] pointed out that solvents like pyridine, quinoline or phenylacetonitrile or diluents such as nitrobenzene, dichlorobenzene or naphthalene are desirable for large scale runs as it assists in the dissipation of heat of reaction. Later, Friedman and Shechter[23] have shown that the reaction of aryl bromides and sufficiently active aryl chlorides with cuprous cyanide proceeded rapidly and efficiently in refluxing dimethyl formamide. The reactions are exothermic and catalysts are usually unnecessary. They have also developed more effective procedures for decomposing the complexes of the nitrile and cuprous halide formed. Newmann and Boden[24] have suggested the use of N-methyl-2-pyrolidone as a satisfactory solvent for the reaction of aryl halide and cuprous cyanide. Cuprous cyanide is soluble in N-methyl-2-pyrolidone at temperatures above 90°, and reactions in such a homogeneous mixture occur relatively rapidly. They have converted 4-bromo-5,6-benzophenanthrene, in which the bromine occupied the most crowded position possible, into 4-cyano-5,6-benzophenanthrene in 71 % yield.

No one has, so far, applied Rosenmund-von Braun reaction to halogenoxanthones. Only 1-cyanoxanthone has been synthesised by Goldberg and Wragg[25] by indirect route and it has been hydrolysed successfully to get xanthone-1-carboxylic acid.

In the case of iodoxanthones, Friedman and Schechter method has been found to be very convenient. The

reaction proceeds smoothly with mono- and diiodo derivatives, however, with higher iodo derivatives deiodination takes place. For example, 3,6-dimethoxy-2,4,5,7-tetraiodoxanthone gave only 3,6-dimethoxy-4,5-dicyanoxanthone, as a result of deiodination of the two atoms at position 2- and 7-. Eventhough the conversion of the iodoxanthones to the corresponding cyano derivatives proceeded well the attempts to hydrolyse the latter to the xanthone carboxylic acids have not been successful.

Iodination of 2-hydroxyxanthone

2-Hydroxyxanthone (V) on iodination with ammonia and iodine with either one, two or three molecular proportions of iodine gave only a monoiodoxanthone. Iodination affected with iodine and iodic acid also with one, two and three molecular proportions of iodine in alcohol gave the same product. Iodination with excess of iodinating agents did not give any higher iodo derivative. This monoiodo derivative has been assigned 2-hydroxy-1-iodoxanthone structure (VI) on the basis of the NMR spectral data (Fig. 1). The NMR showed only one doublet in the low field region at δ 8.2, which can easily be assigned to H-8. 2-Hydroxy-3-iodoxanthone would have given an additional one-proton singlet due to H-1, in the same low field region. 2-Hydroxy-1-iodoxanthone gave the methylether (VII) with dimethyl sulphate. The structure of this monoiodoxanthone has also been confirmed by an independent synthesis. 2-Hydroxy-1-formylxanthone (VIII), prepared according to Davies et al.[26], was converted

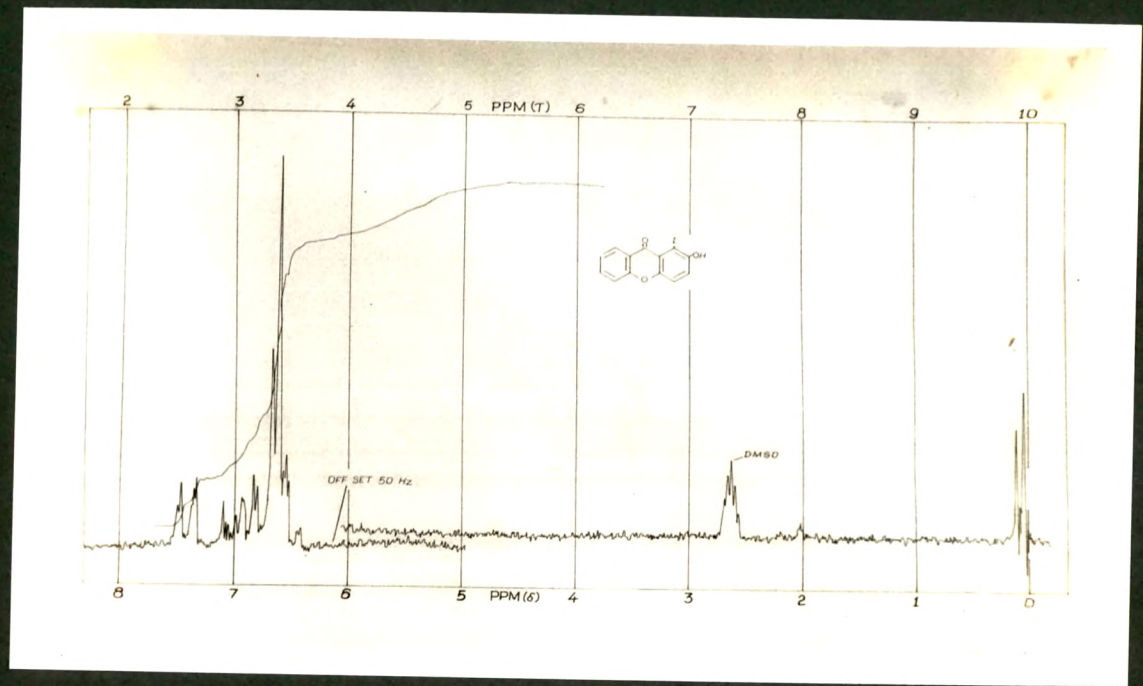
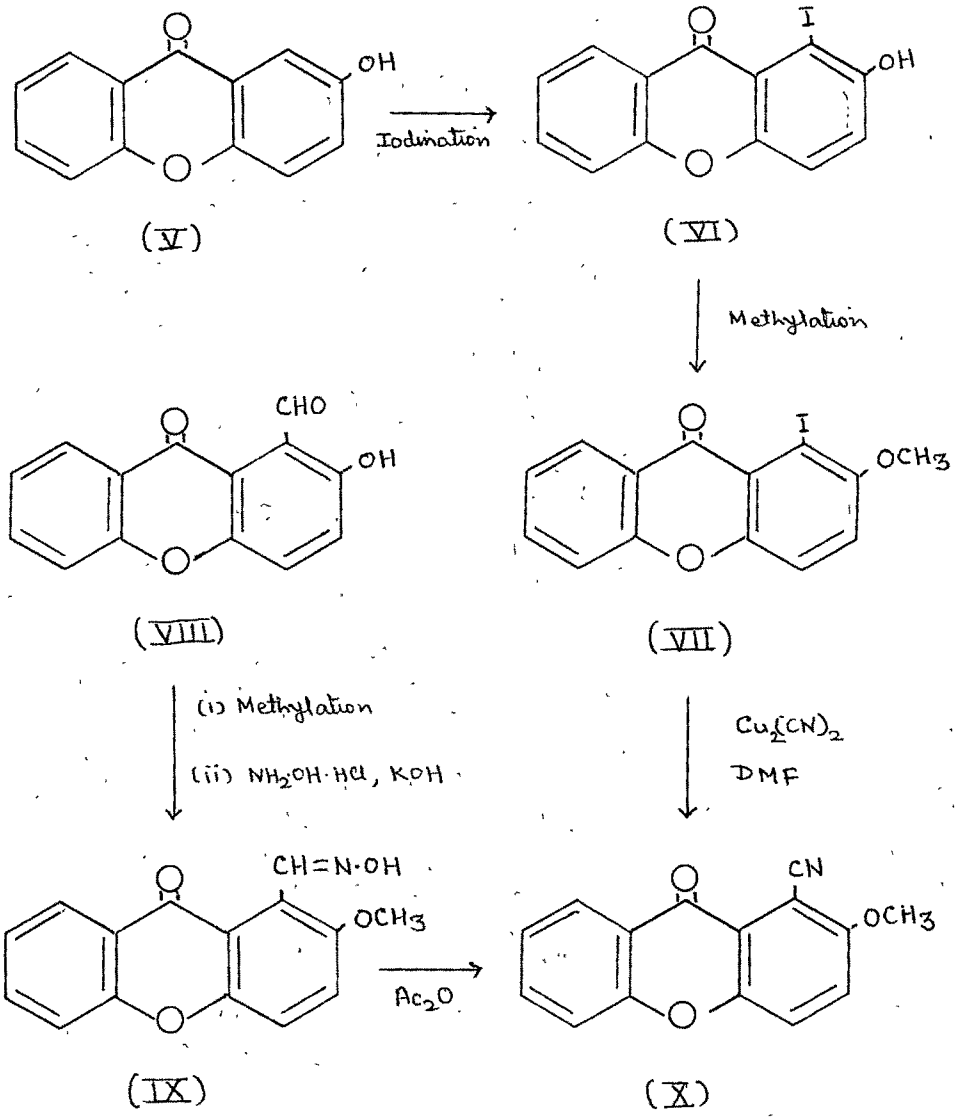


Fig. 1 : NMR spectrum of 2-hydroxy-1-iodoxanthone (VI) in DMSO (60 MHz).

into its methoxy oxime (IX). This oxime on refluxing with acetic anhydride gave the same methoxycyanoxanthone (X) as was obtained from the methoxyiodoxanthone as described later.



2-Methoxy-1-iodoxanthone was converted into 2-methoxy-1-cyanoxanthone by refluxing the former in dimethyl formamide with cuprous cyanide. This method gave a better yield than the baking method.

Attempt to demethylate 2-methoxy-1-cyanoxanthone with aluminium chloride in benzene did not give any pure product.

Attempts to hydrolyse 2-methoxy-1-cyanoxanthone either to the carboxylic acid or to the amide with pyridine and 2N sodium hydroxide solution, even after refluxing for 24 hr. did not succeed and 2-methoxy-1-cyanoxanthone was recovered back. Alcoholic potash also did not work. Hydrolysis with water, sulphuric acid and acetic acid mixture in equal proportion for 16 hr. on a sand bath led to the elimination of the cyano group and also to demethylation.

Iodination of 3-hydroxyxanthone

3-Hydroxyxanthone (XI) on iodination with ammonia and iodine with one, two or three moles and excess of iodine and with iodine and iodic acid in alcohol with one mole gave a monoiodo derivative, to which 3-hydroxy-4-iodo-xanthone structure (XII) has been assigned on the basis of the NMR data (Fig. 2). The two doublets in the low field region at δ 8.0 and δ 8.08 confirm that the iodine is in the 4- position and not in the 2- position. With the iodine in the 2-position, the compound would have given a singlet and a doublet, instead of the two doublets, in the same low field region for the two peri protons. An up field doublet at about δ 6.96 due to H-2 is also discernible. In the case of 3-hydroxy-2-iodoxanthone it would have been due to H-4, but it should have been a singlet.

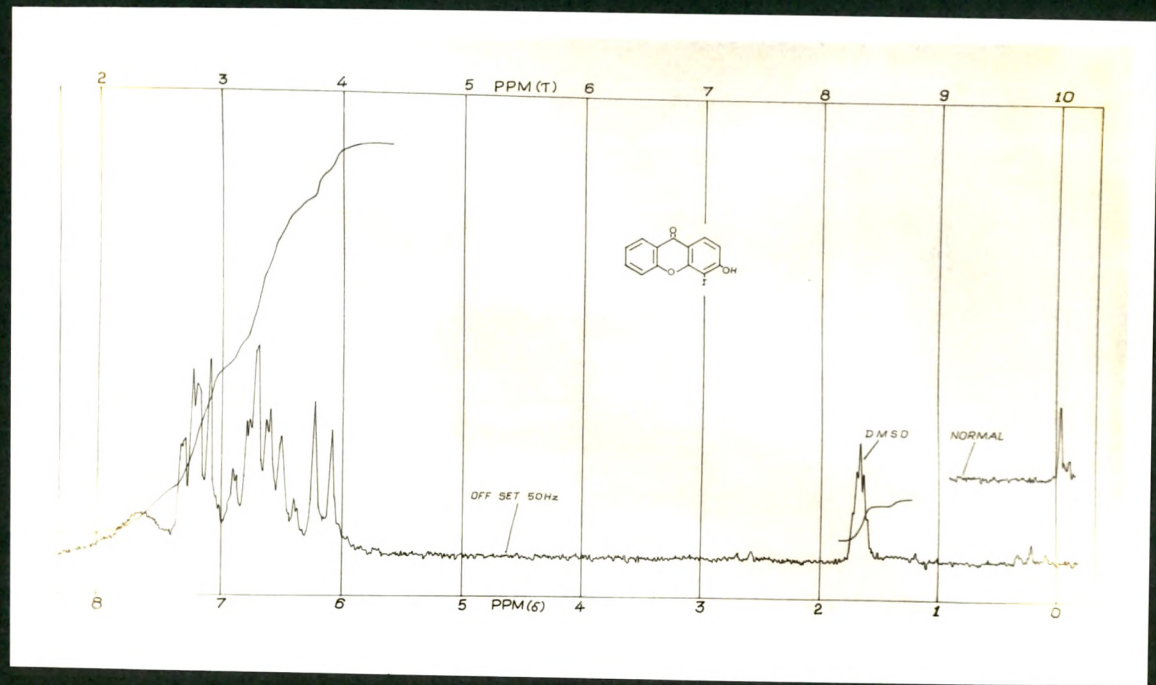
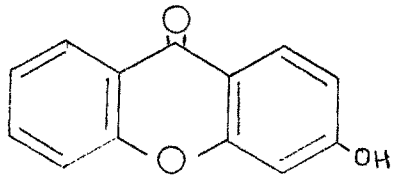


Fig. 2 : NMR spectrum of 3-hydroxy-4-iodoxanthone (XII) in DMSO (60 MHz).

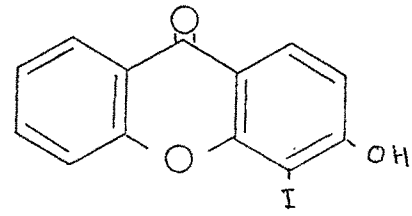
Acetylation of this monoiodoxanthone gave 3-acetoxy-4-iodoxanthone and methylation gave 3-methoxy--4-iodoxanthone (XIII). The 4-iodo structure was further confirmed by the synthesis of 3-methoxy-4-iodoxanthone, from 3-hydroxy-4-nitroxanthone (XV), which was synthesised by an unambiguous route. 2-Nitroresorcinol and salicylic acid in the presence of phosphorus oxychloride and zinc chloride gave 2,2',4-trihydroxy-3-nitrobenzophenone (XIV), which was cyclised in water under pressure to 3-hydroxy-4-nitroxanthone (XV). This xanthone was methylated to get 3-methoxy-4-nitroxanthone (XVI), which was reduced by sodium dithionite in alcohol to 3-methoxy-4-aminoxanthone (XVII). This was diazotised and treated with potassium iodide, whereupon it gave 3-methoxy-4-iodoxanthone (XIII). The m.p. and the mixed m.p. of this and the methoxy derivative of directly iodinated product were not depressed.

Goldberg and Wragg[25] have reported the preparation of 3,6-dimethoxyxanthone from 3,6-dichloroxanthone, by treating the latter with sodium methoxide in dioxan, in the presence of copper bronze. Attempt was therefore made to convert 3-methoxy-4-iodoxanthone into 3,4-dimethoxyxanthone by this method, but it did not work and 3-methoxy-4-iodoxanthone was obtained back.

Banerjee et al.[27] have converted iodophenols into hydroxyphenols by treating the iodophenols with 4N sodium hydroxide solution in the presence of hydrated copper sulphate as a catalyst. But when 3-hydroxy-4-iodo-

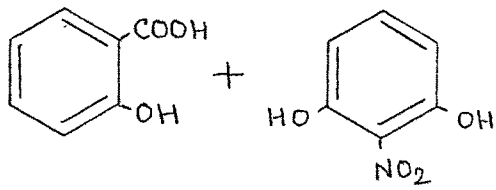


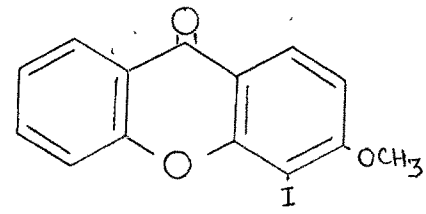
(XI)



(XII)

Methylation

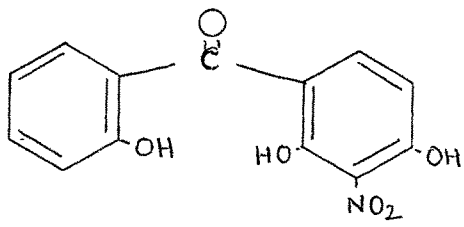




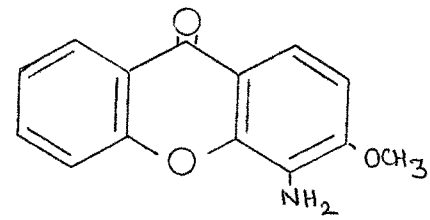
(XIII)

$POCl_3$
$ZnCl_2$

① Diazotisation
(ii) KI

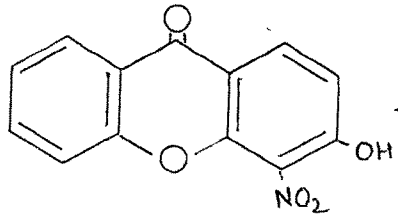


(XIV)

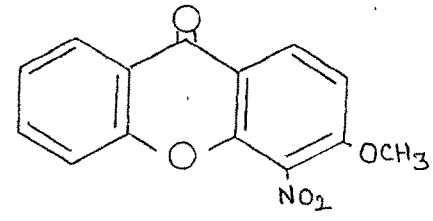


(XVII)

Sodium dithionite



(XV)

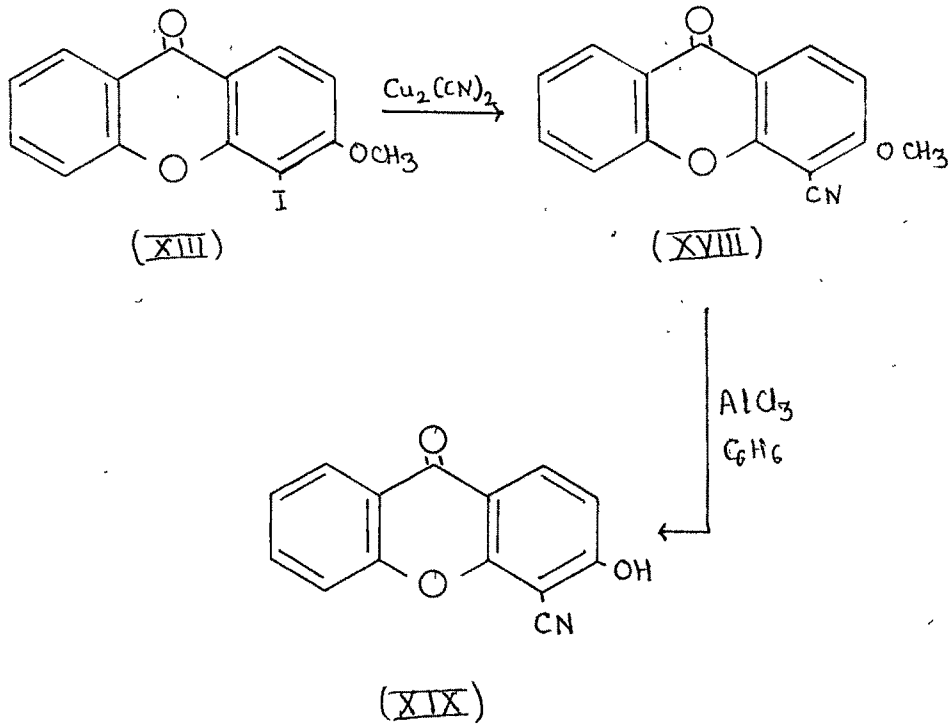


(XVI)

xanthone was treated similarly, it did not react.

3-Methoxy-4-iodoxanthone when treated with cuprous cyanide in dimethyl formamide, gave 3-methoxy-4-cyanoxanthone (XVIII) in good yield.

3-Methoxy-4-cyanoxanthone on demethylation with aluminium chloride in benzene gave 3-hydroxy-4-cyano-xanthone (XIX).



Attempts to hydrolyse 3-methoxy-4-cyanoxanthone have not been successful. On refluxing with either 10 % sodium hydroxide solution or pyridine-sodium hydroxide or alcoholic potassium hydroxide 3-methoxy-4-cyanoxanthone was only demethylated. Prolonged heating also had no effect. With potassium hydroxide in glycol or in 2-methoxyethanol

as solvent also only demethylation took place. Attempt to hydrolyse the cyano group according to Goldberg and Wragg[25] by heating 3-methoxy-4-cyanoxanthone in dioxan with 6N sodium hydroxide solution for 80 hr. on a water bath also failed, the original compound being recovered unchanged. In one attempt the methoxycyanoxanthone was dissolved in acetic acid, and then refluxed for 20 hr. on a wire-gauze by adding same amount of conc. hydrochloric acid, keeping the solution saturated with hydrogen chloride , by passing the gas after every 4 hr. Here also the methoxycyanoxanthone remained unchanged.

Hydrolysis by 60 %, 70% and 80 % sulphuric acid at 80-90° on a steam bath or at 120±40° in an oil bath also did not work. Low temperature and low concentration of sulphuric acid gave original 3-methoxy-4-cyanoxanthone, while higher temperature and high concentrations of sulphuric acid gave a sulphonated water soluble product and/or 3-hydroxyxanthone. High concentration of the acid and low temperature such as 90-100°, for a short interval of time gave 3-hydroxy-4-cyanoxanthone.

Berger et al.[28] have reported the use of polyphosphoric acid for hydrolysis of the cyano group. They have treated the difficultly hydrolysable cyano compounds with 100 % polyphosphoric acid for 1 to 4 hr. at about 150±60° and have converted them into carboxylic acids. Hydrolysis of 3-methoxy-4-cyanoxanthone by 100 % polyphosphoric acid or by orthophosphoric acid alone at 150°

for 6 hr. resulted in a mixture of 3-methoxy- and 3-hydroxyxanthone. For shorter period of heating, the original 3-methoxy-4-cyanoxanthone was recovered back. Prolonged heating (8 to 12 hr.) at about 70° temperature had also no effect.

3-Hydroxy-4-cyanoxanthone also under similar conditions of hydrolysis did not give the required acid. 3-Hydroxyxanthone-4-carboxylic acid could however be prepared by oxidising 3-hydroxy-4-formylxanthone[29] with silver oxide and sodium hydroxide[30].

3-Hydroxyxanthone on treatment with three moles and excess of iodine and iodic acid in alcohol gave a diiodo derivative. As no synthetic proof could be given, NMR spectrum (Fig. 3) for this compound was taken in dimethyl sulphoxide. The NMR shows a doublet at δ 8.1 due to the peri proton H-8 and a singlet at δ 8.4 due to the other peri proton H-1, which confirms the positions of the two iodine atoms to be at C-2 and C-4. The disappearance of the doublet at δ 6.96 due to H-2 in the NMR of 3-hydroxy-4-iodoxanthone (Fig. 2) is also a proof showing that H-2 has been replaced by an iodine atom. Thus the compound has been assigned 3-hydroxy-2,4-diiodoxanthone structure (XX). On methylation and acetylation by usual methods it gave the methoxy and the acetoxy derivatives.

3-Methoxy-2,4-diiodoxanthone on treatment with cuprous cyanide in dimethyl formamide gave 3-methoxy-

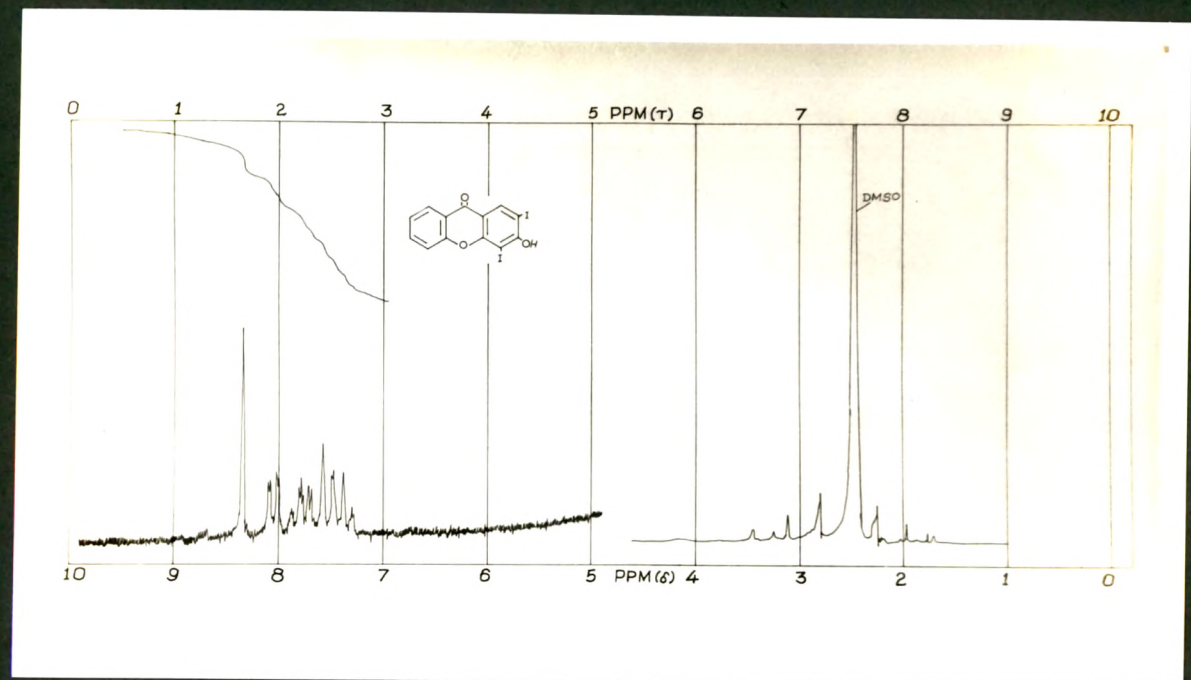
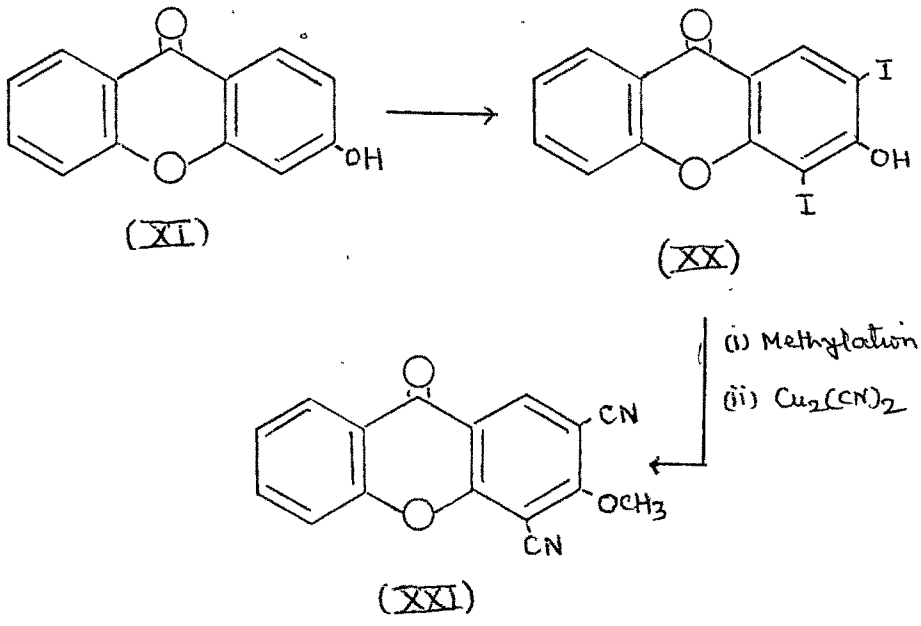


Fig. 3 : NMR spectrum of 3-hydroxy-2,4-diiodoxanthone (XX) in DMSO (90 MHz).

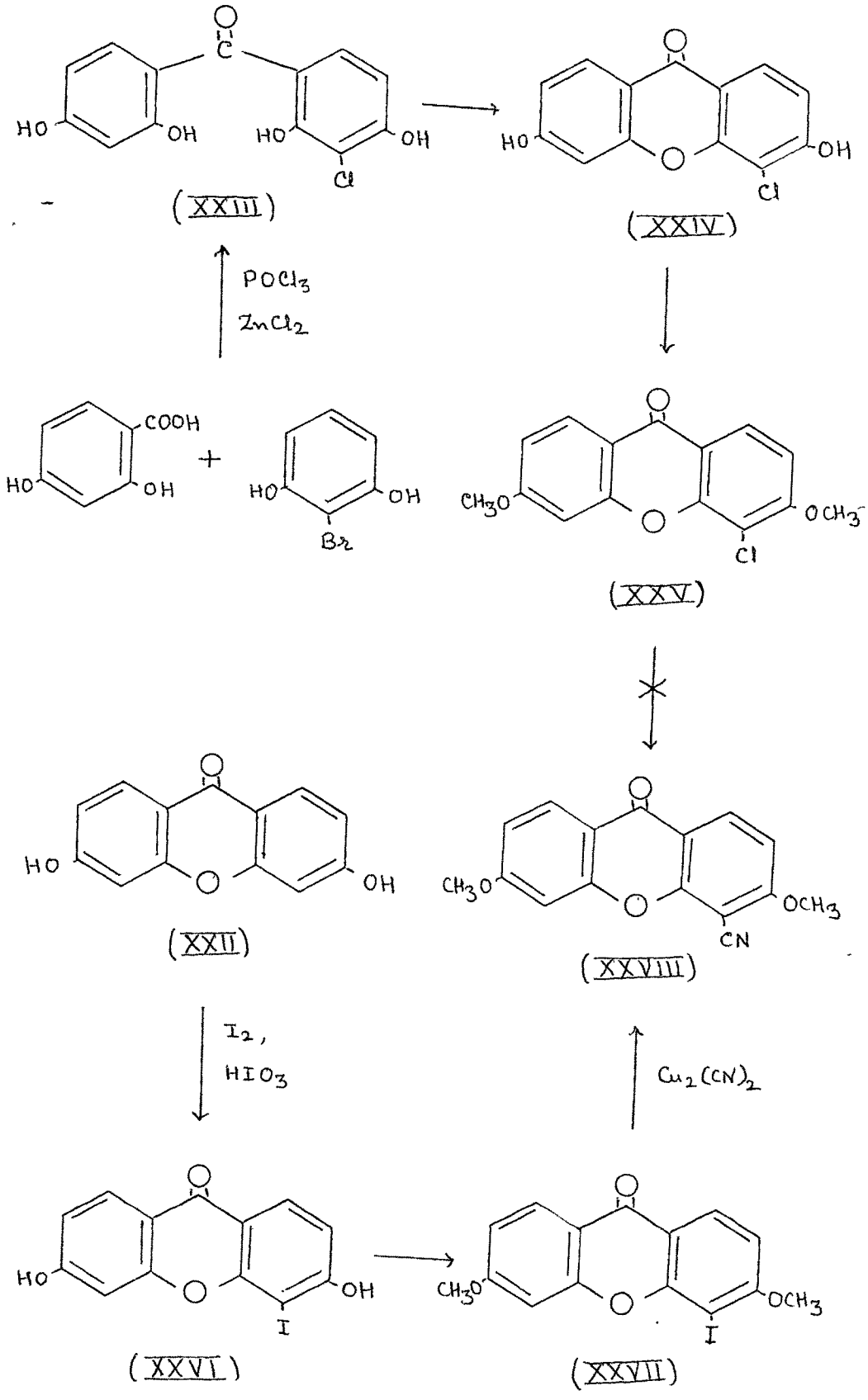


(XI) (XX) (XXI)

-2,4-dicyanoxanthone (XXI).

Iodination of 3,6-dihydroxyxanthone

3,6-Dihydroxyxanthone (XXII) gave a monoiodo derivative with iodine and iodic acid in one mole proportion in alcohol. An attempt was made to prove its structure as follows : The synthesis of 3,6-dihydroxy-4-bromoxanthone was tried first. When β-resorcylic acid and 2-bromoresorcinol were condensed in the presence of zinc chloride and phosphorus oxychloride, it gave a benzophenone (XXIII), which showed the presence of a halogen. The benzophenone derivative on repeated crystallisation could not be purified and so was subjected to cyclisation under pressure. The hydroxy-xanthone (XXIV) and its methoxy derivative (XXV) both were analysed qualitatively. They were found to contain chlorine


HO
OH
HO
OH
Cl
(XXIII)
HO
OH
Cl
(XXIV)
POCl3
ZnCl2
COOH
HO
OH
+
HO
OH
Br2
CH3O
OCH3
Cl
(XXV)
HO
OH
(XXII)
CH3O
OCH3
CN
(XXVIII)
I2,
HIO3
Cu2(CN)2
HO
OH
I
(XXVI)
CH3O
OCH3
I
(XXVII)

instead of bromine. Moreover, the elemental analysis for carbon and hydrogen also tallied with the monochloroxanthone. Thus, instead of getting 3,6-dihydroxy-4-bromoxanthone, 3,6-dihydroxy-4-chloroxanthone was obtained, the bromine atom being replaced by the chlorine atom. Further, the methoxy-chloroxanthone could not be converted either into the monocyanoxanthone by Rosenmund-von Braun reaction or into the bixanthonyl by Ullmann reaction. In both the cases the chloroxanthone was recovered unchanged. If this could have been converted into either the cyano derivative or the bixanthonyl derivative, it would have been possible to compare it with the cyano and the bixanthonyl obtained from the monoiodo derivative. The chloro derivatives are, of course, known to either not undergo or undergo with difficulty the Rosenmund-von Braun or the Ullmann reaction.

As synthetic proof could not be obtained, the structure was settled on the basis of the NMR spectrum (Fig. 4) of the monoiodoxanthone in dimethyl sulphoxide. The NMR showed a two-proton doublet (J = 9Hz) centred at δ 7.81, which could be assigned to the two peri protons H-1 and H-8 in 3,6-dihydroxy-4-iodoxanthone (XXVI) only. 3,6-Dihydroxy-2-iodoxanthone would have given one-proton singlet and a one-proton doublet in the low field region for H-1 and H-8 respectively. This 3,6-dihydroxy-4-iodo-xanthone on methylation and acetylation by usual method gave the dimethyl ether (XXVII) and the diacetoxy derivatives. The same monoiodoxanthone could not be obtained by ammonia and iodine method, which, however, gave a diiodoxanthone.

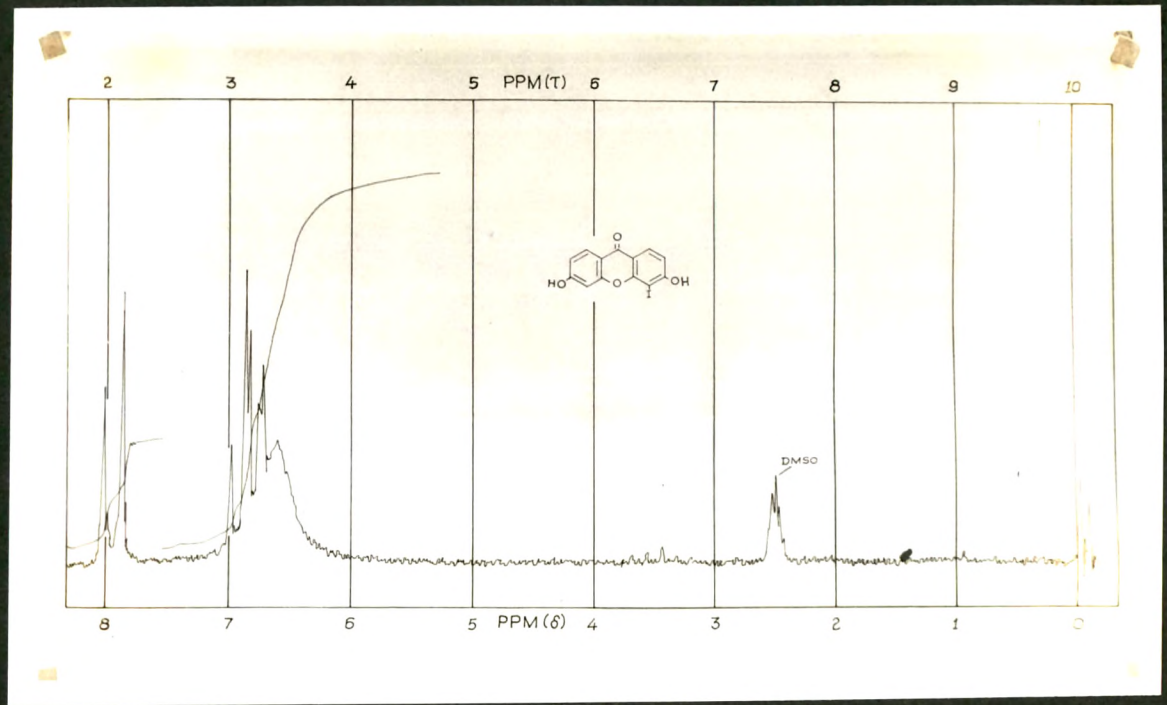


Fig. 4 : NMR spectrum of 3,6-dihydroxy-4-iodoxanthone (XXVI) in DMSO (60 MHz).

When 3,6-dimethoxy-4-iodoxanthone (XXVII) was treated with cuprous cyanide in dimethyl formamide as usual, it gave 3,6-dimethoxy-4-cyanoxanthone (XXVIII).

When the methoxycyanoxanthone was subjected to hydrolysis by alcoholic potassium hydroxide, no acid could be obtained. But it gave a mixture of demethylated cyanoxanthones, which on methylation gave 3,6-dimethoxy-4-cyanoxanthone back. IR spectrum of the mixture in hexachlorobutadiene showed a broad band at 3460 $cm.^{-1}$, characteristic of hydroxyl group and a sharp band at 2240 $cm.^{-1}$, indicating the presence of a cyano group. Xanthone carbonyl stretching was observed at 1620 $cm.^{-1}$ No peak appeared in the region from 1800 $cm.^{-1}$ to 1620 $cm.^{-1}$, which is again a proof that the mixture contains no carboxylic acid.

Potassium hydroxide fusion of 3,6-dimethoxy-4-cyanoxanthone at 200° gave a brownish product, probably a mixture of the mono- and the dihydroxy compounds, as it was soluble in alkali and on methylation it gave 3,6-dimethoxy-4-cyanoxanthone back. Fusion carried out at 300-10° gave a highly water soluble, pasty product, which could not be worked up to get any pure product.

3,6-Dihydroxyxanthone gave a diiodo derivative with iodic acid and iodine in two mole proportions and with ammonia and iodine in the proportion of one and two moles. In order to prove the structure, it was decided to synthesise 3,6-dihydroxy-2,7-dibromoxanthone prepared earlier by Kurdukar and Subba Rao[31] and to convert it into the dicyanoxanthone so that it could be compared with the dicyanoxanthone

from the 3,6-dimethoxy-diiodoxanthone. They have prepared the dibromoxanthone by brominating first 2,2',4,4'-tetrahydroxybenzophenone (XXXI) and cyclising the dibromo derivative (XXXII) obtained under pressure. They have also prepared 2,2',4,4'-tetrahydroxy-3,3',5,5'-tetrabromobenzophenone (XXXIII). Bromination of 2,2',4,4'-tetrahydroxybenzophenone however always gave the tetrabromobenzophenone. Attempt to brominate the tetrahydroxybenzophenone at 0° also resulted in 2,2',4,4'-tetrahydroxy-3,3',5,5'-tetrabromobenzophenone (XXXIII) and not the required and reported 2,2',4,4'-tetrahydroxy-5,5'-dibromobenzophenone (XXXII). The structure was finally assigned on the basis of the NMR data.

There are three possibilities for the diiodoxanthone viz. (i) 3,6-dihydroxy-4,5-diiodoxanthone, (ii) 3,6-dihydroxy-2,7-diiodoxanthone or (iii) 3,6-dihydroxy-2,5-diiodoxanthone. The NMR spectrum of the compound in dimethyl sulphoxide (Fig. 5) showed two doublets only, one two-proton doublet at δ 7.95 characteristic of the peri protons and another two-proton doublet at δ 7.0, up field due to the hydroxyl groups in the ortho position. The spectrum confirms the symmetrical structure (i) 3,6-dihydroxy-4,5-diiodoxanthone (XXIX). The down field two-proton doublet can be assigned to H-1 and H-8, while the other up field two-proton doublet can be assigned to H-2 and H-7. Because the protons H-1 and H-8 as well as H-2 and H-7 have identical environment, the doublets due to these overlap each other. The symmetrical structure (ii) would have given

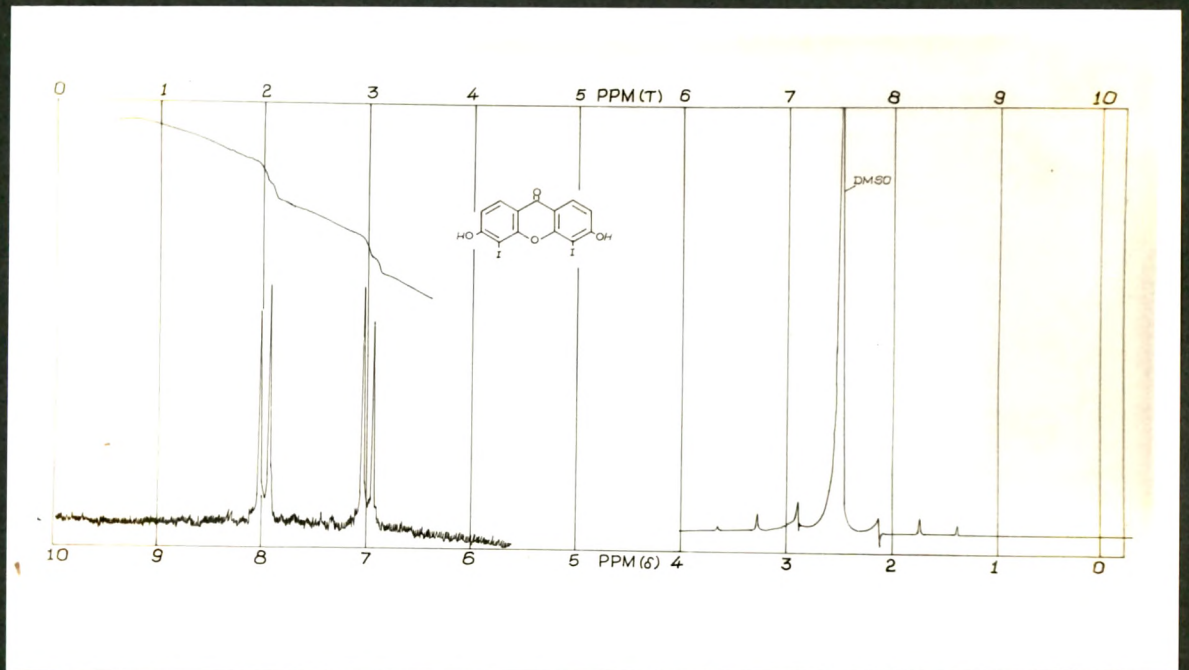
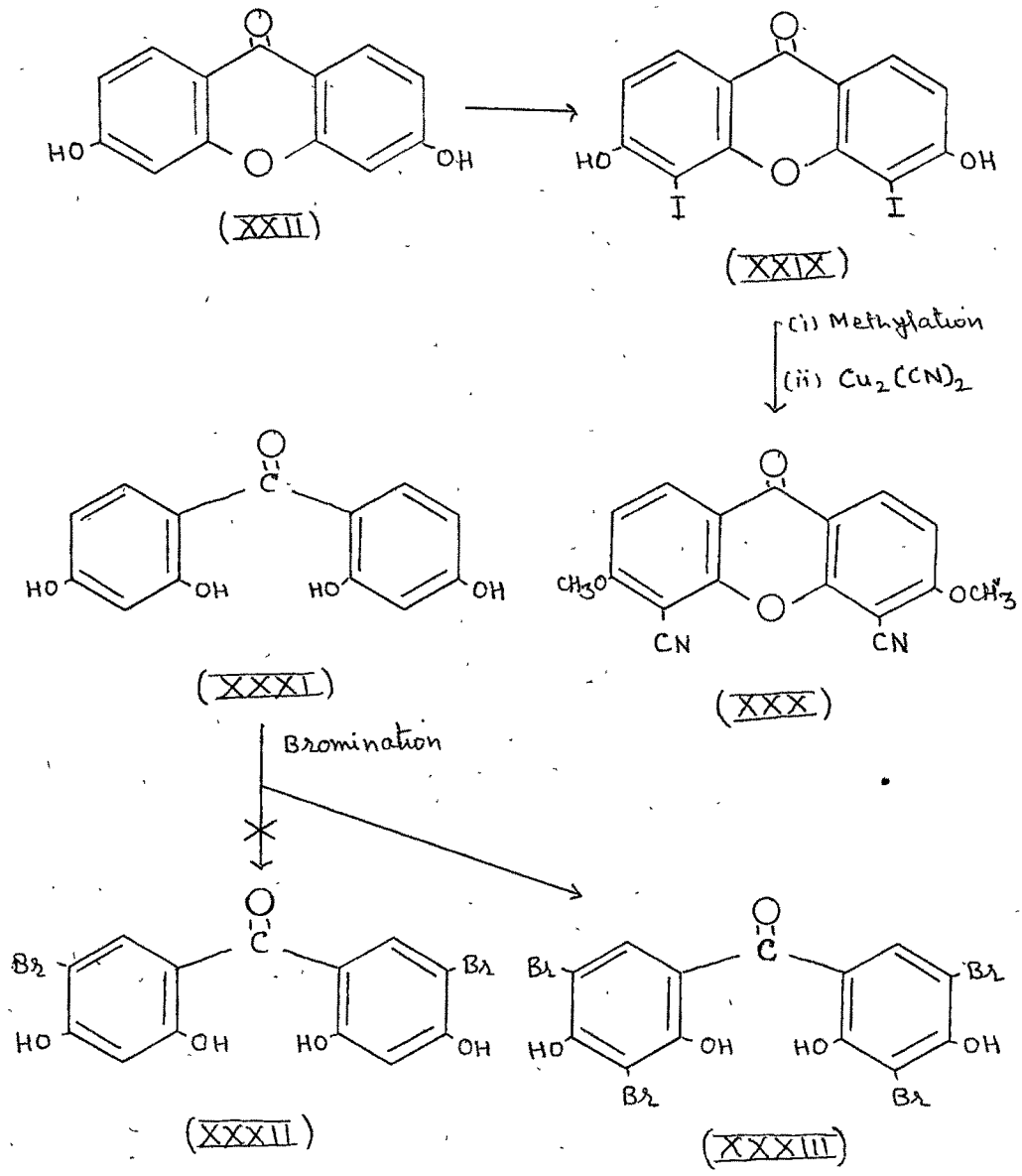


Fig. 5 : NMR spectrum of 3,6-dihydroxy-4,5-diiodoxanthone (XXIX) in DMSO (90 MHz).



two two-proton singlets, while the unsymmetrical structure (iii) would have given a doublet and a singlet due to H-8 and H-1 in the peri proton region and similarly a doublet and a singlet due to H-7 and H-4 in the up field region around δ 7.0. Both the doublets in the case of 3,6-dihydroxy-4,5-diiodoxanthone have the ortho coupling constant J of value 9Hz. This diiodo compound on methylation gave

3,6-dimethoxy-4,5-diiodoxanthone and on acetylation gave 3,6-diacetoxy-4,5-diiodoxanthone.

3,6-Dimethoxy-4,5-diiodoxanthone gave 3,6-dimethoxy-4,5-dicyanoxanthone (XXX) with cuprous cyanide in dimethyl formamide in good yield.

As the dicyanoxanthone was almost insoluble in benzene the demethylation was carried out by baking with aluminium chloride at 150-60°. This gave a brown compound, which on crystallisation from aqueous alcohol separated as a brown powder. The powdery compound on analysis showed only 5.163 % nitrogen as against 10.07 % required for 3,6-dihydroxy-4,5-dicyanoxanthone.

Fusion of 3,6-dimethoxy-4,5-dicyanoxanthone with potassium hydroxide at 250° resulted in an alkali soluble black product, which was also a mixture of demethylated products, as methylation gave the methoxycyanoxanthone back.

Hydrolysis with alcoholic potash gave no bicarb-soluble product, instead an alkali-soluble product was obtained. This was also a mixture of partially and completely demethylated xanthones. The IR of this in hexachlorobutadiene showed bands for hydroxyl group at 3400 $cm.^{-1}$, for cyano group at 2240 $cm.^{-1}$ and for carbonyl group at 1620 $cm.^{-1}$, but no band for carboxylic group was observed.

Raistrick et al.[32] and Asahina and Shibata[33] have reported the cleavage of xanthone to the corresponding diphenyl ether by the action of sodamide in xylene. When 3,6-dimethoxy-4,5-dicyanoxanthone was refluxed in xylene

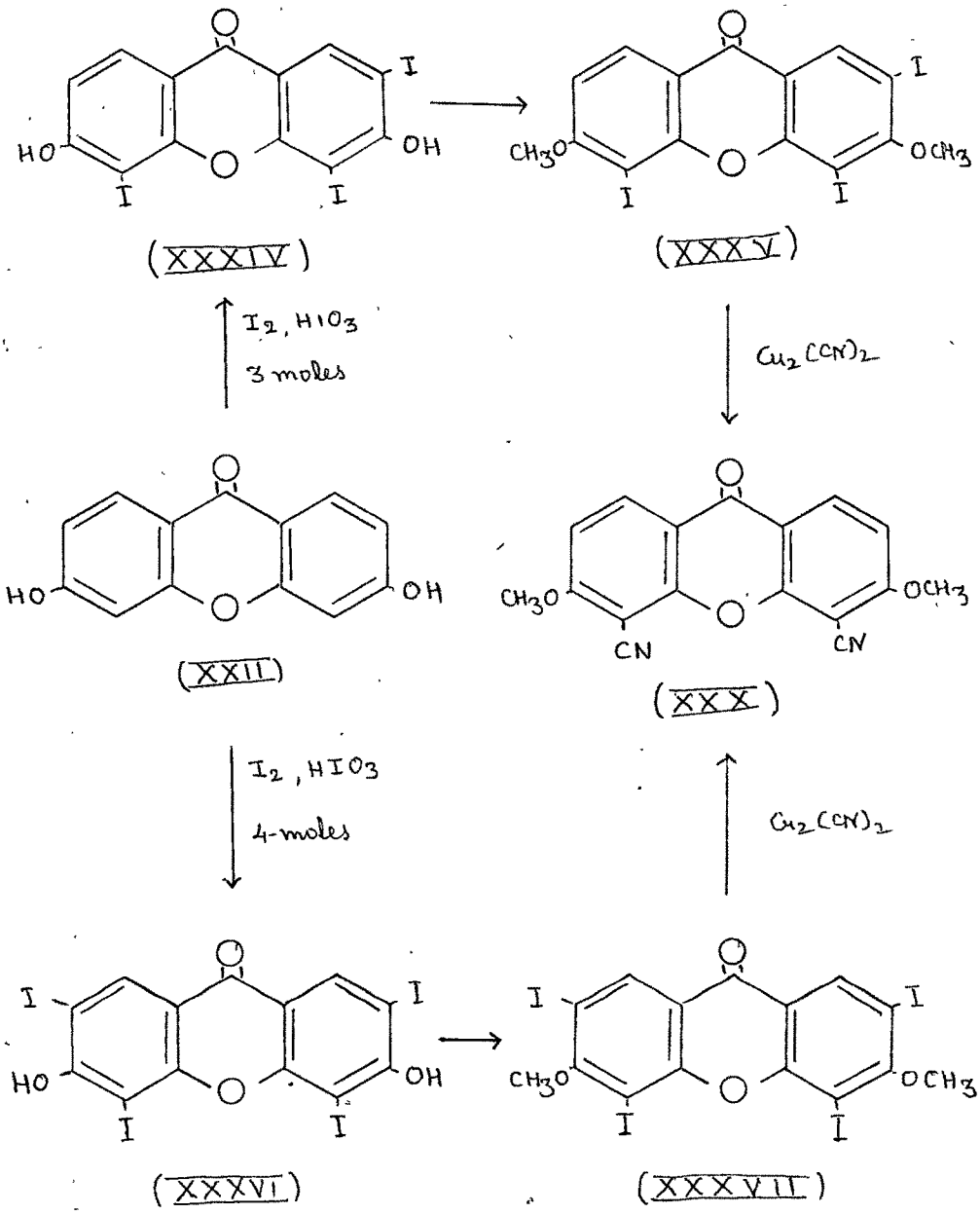
with sodamide for 3 hr. a compound which crystallised in acetic acid and had a sharp m.p. of 315° was obtained. But its IR showed all the characteristics of a cyanoxanthone skeleton i.e. bands for cyano group at 2220 $cm.^{-1}$, for carbonyl group at 1655 $cm.^{-1}$ and for ether group at 1225 $cm.^{-1}$ and 1205 cm^{-1}. The IR spectrum was taken in KBr and in hexachlorobutadiene. The elemental analysis tallied neither with the mono- nor the dicyanoxanthone nor with the mono- and dicyanodiphenyl ether. Due to the insolubility of this compound in either chloroform or dimethyl sulphoxide, the NMR spectrum could not be taken and the final conclusion could not be drawn.

3,6-Dihydroxyxanthone gave a triiodo derivative on reaction with iodine and iodic acid in alcohol in a slight excess over three moles. As the diiodoxanthone is 4,5-diiodo-derivative, the third iodine atom must be entering the 2-position. Therefore, the product has been assigned 3,6-dihydroxy-2,4,5-triiodoxanthone structure (XXXIV). This triiodoxanthone could not be prepared by the ammonia and iodine method, which gave either the di- or the tetraiodo-xanthone. Methylation and acetylation by usual reagents gave the corresponding dimethoxy and diacetoxy derivatives.

When 3,6-dimethoxy-2,4,5-triiodoxanthone (XXXV) was subjected to Rosenmund-von Braun reaction, however, it gave a dicyanoxanthone, identical with 3,6-dimethoxy-4,5-dicyanoxanthone.

Iodination of 3,6-dihydroxyxanthone with 4 moles or more of iodinating agents resulted in the formation of

tetraiodoxanthone. Both the iodinating agents were tried and were found to give the same tetraiodoxanthone. As there are four ortho positions free in the 3,6-dihydroxy-xanthone, 3,6-dihydroxy-2,4,5,7-tetraiodoxanthone structure (XXXVI) has been assigned to it. It decomposes either on exposure to air or when refluxed in a solvent like acetic



acid. Methylation and acetylation gave the corresponding dimethoxy (XXXVII) and diacetoxy-tetraiodoxanthones, which are found to be more stable than the dihydroxy derivative.

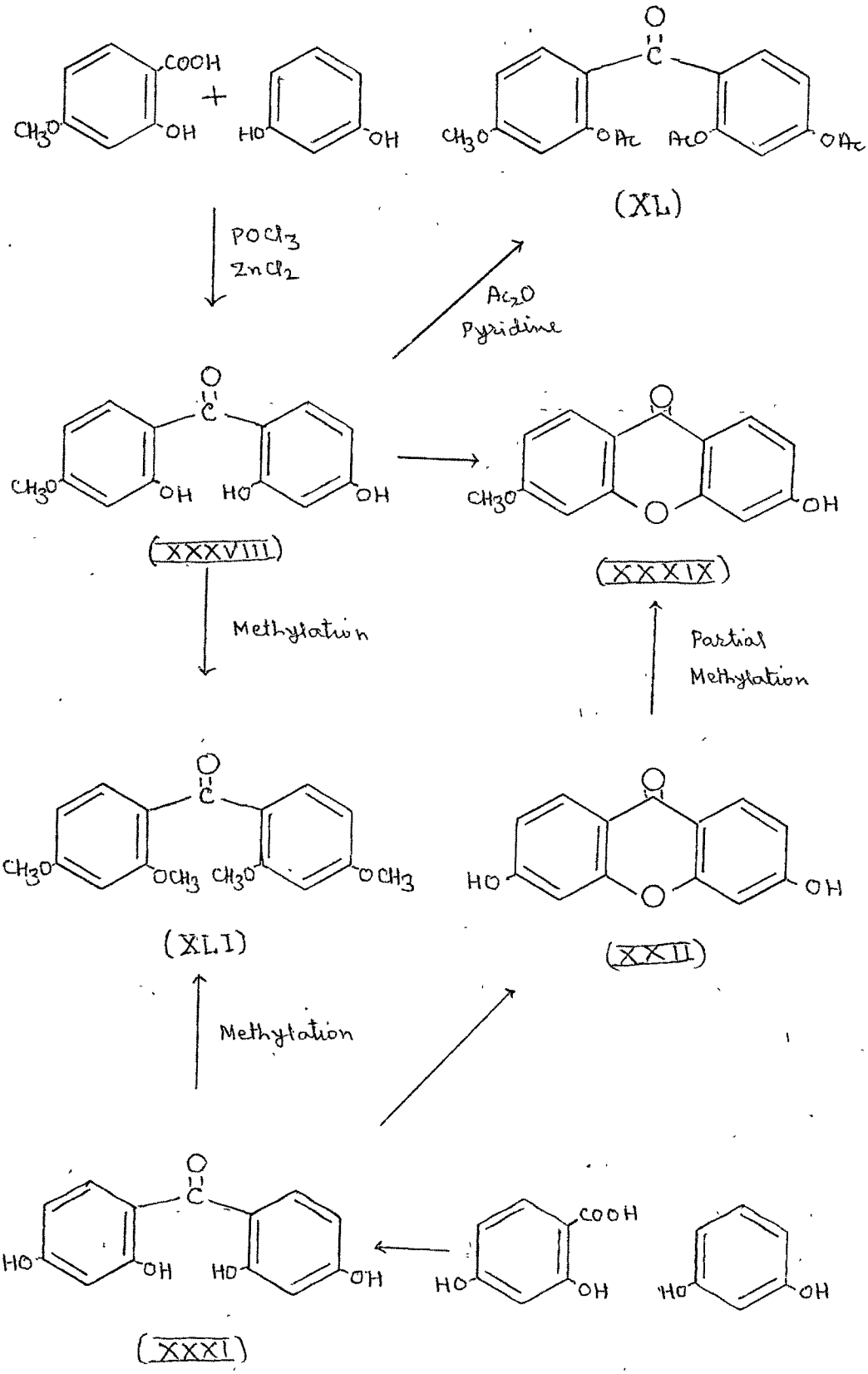
3,6-Dimethoxy-2,4,5,7-tetraiodoxanthone (XXXVII), when subjected to Rosenmund-von Braun reaction gave 3,6-dimethoxy-4,5-dicyanoxanthone instead of the expected tetracyanoxanthone.

Iodination of 3-hydroxy-6-methoxyxanthone

3-Hydroxy-6-methoxyxanthone required was prepared as follows :

3,6-Dihydroxyxanthone was methylated with 1·2 mole of dimethyl sulphate and sodium hydroxide when the 3,6-dimethoxyxanthone separated as an insoluble material, while 3-hydroxy-6-methoxyxanthone was obtained from the alkali solution. The same xanthone was synthesised from 4-methoxy-2-hydroxybenzoic acid and resorcinol by condensing them in the presence of zinc chloride and phosphorus oxychloride. The resulting 2,2',4-trihydroxy-4'-methoxybenzophenone (XXXVIII) was cyclised under pressure in an autoclave to get 3-hydroxy-6-methoxyxanthone. Methylation of this benzophenone gave the same tetramethoxybenzophenone (XLI) as obtained by Grover et al.[34] by methylation of 2,2',4,4'-tetrahydroxybenzophenone. The acetoxy derivative (XL) 2,2',4-triacetoxy-4'-methoxybenzophenone was also prepared.

Iodination of 3-hydroxy-6-methoxyxanthone (XXXIX) with iodine and iodic acid (1 mole) and ammonia and iodine


COOH
OH
CH_3O
HO
OH
$POCl_3$
$ZnCl_2$
Ac_2O
Pyridine
OAc
AcO
OAc
(XL)
(XXXVIII)
(XXXIX)
Methylation
Partial
Methylation
(XLI)
(XXII)
Methylation
(XXXI)

(1,2,3 moles and excess) gave a monoiodo derivative. This monoiodo derivative on methylation gave a dimethoxy-monoiodoxanthone, which was found on direct comparison to be identical with 3,6-dimethoxy-4-iodoxanthone, the structure of which has been proved by NMR spectrum. Acetylation of this gave 3-acetoxy-4-iodo-6-methoxyxanthone.

Iodination of 3-hydroxy-6-methoxyxanthone with three moles and excess of iodine and iodic acid in alcohol gave a diiodo derivative. Methylation of this gave a dimethoxy-diiodoxanthone, which was different from 3,6-dimethoxy-4,5-diiodoxanthone, structure of which is already established. Again iodination of 3,6-dimethoxyxanthone carried out under similar conditions did not give any iodo derivative, but gave the original compound back, which also suggests that the iodination does not take place in the benzene ring in which the methoxy group is present. So, both the iodine atoms in the 3-hydroxy-6-methoxyxanthone must have occupied the two free positions which are ortho to the hydroxyl group. This indicates that 3-hydroxy-2,4-diiodo-6-methoxyxanthone (XLIII) is the possible structure for this diiodoxanthone. The confirmation came from the NMR spectrum of this compound in dimethyl sulphoxide (Fig. 6). The NMR spectrum clearly shows a one-proton singlet at δ 8.36 which can be assigned to H-1, a one-proton doublet (J = 9Hz) at δ 8.1 which can be assigned to the H-8. The proton H-5 and H-7 appeared quite up field at nearly δ 7.0 as a multiplet. The methyl protons of 6-methoxy group appeared at δ 4.0 as three-proton singlet.

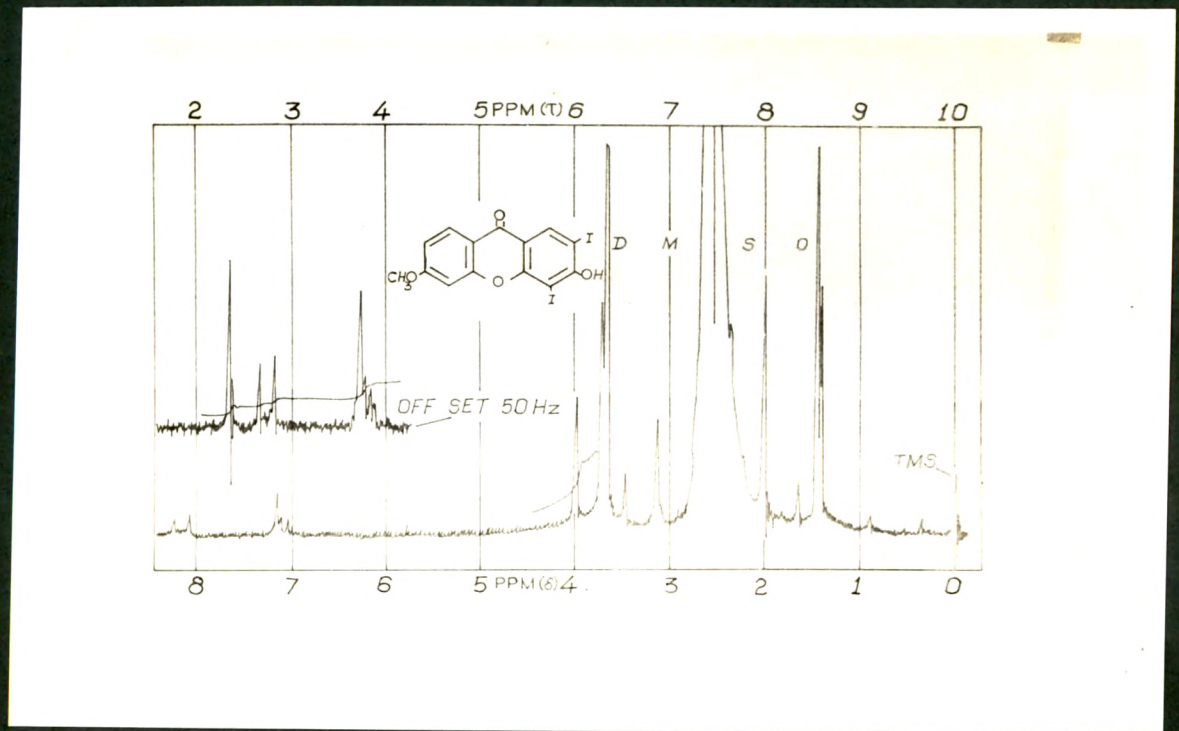
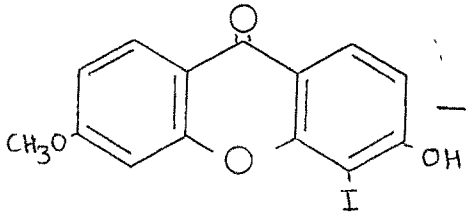
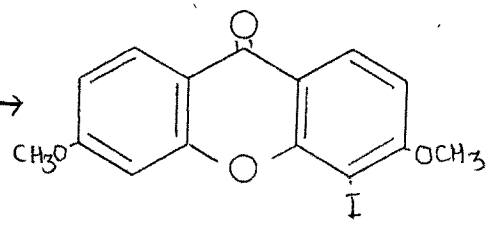


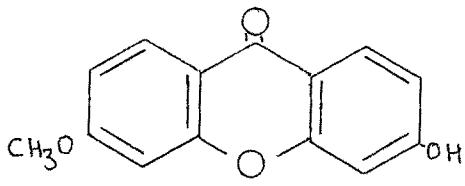
Fig. 6 : NMR spectrum of 3-hydroxy-2,4-diiodo-6-methoxy-xanthone (XLIII) in DMSO (60 MHz).



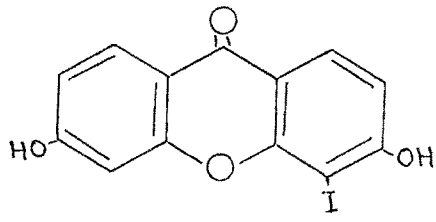
(XLII)



(XXVII)



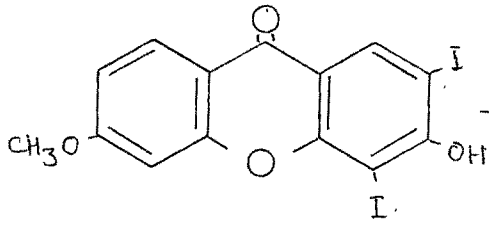
(XXXIX)



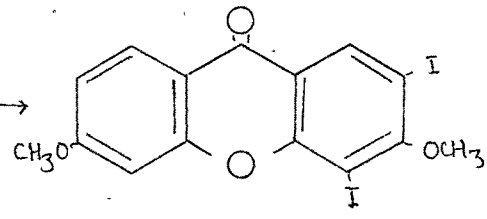
(XXIII)

I_2, HIO_3

3 moles

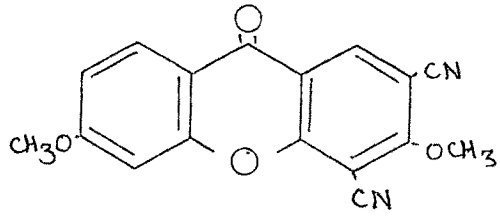


(XLIII)



(XLIV)

$Cu_2(CN)_2$

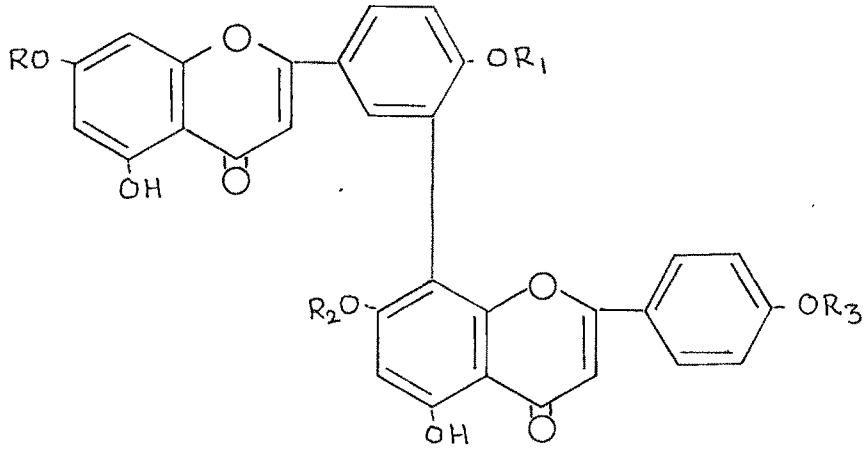


(XLV)

3,6-Dimethoxy-2,4-diiodoxanthone (XLIV) on Rosenmund-von Braun reaction gave 3,6-dimethoxy-2,4-dicyanoxanthone (XLV).

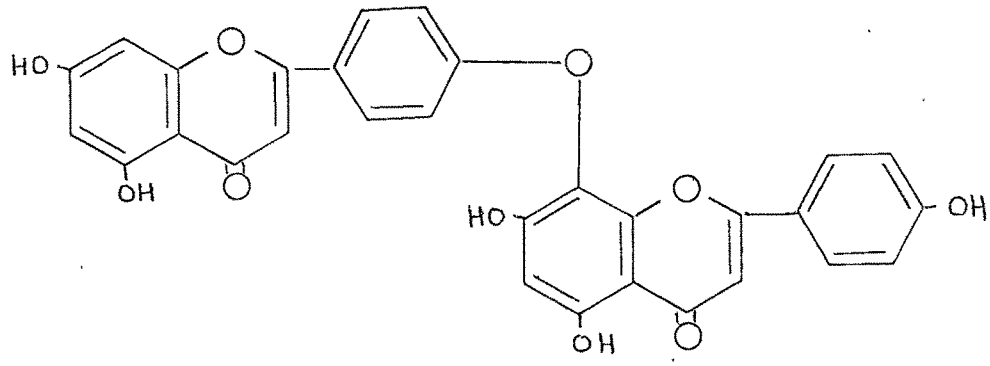
SYNTHESIS OF BIXANTHONYLS

A number of biflavonyls such as Sotetsuflavone[35] (XLVI), Kayaflavone[36] (XLVII) and Ginketin[37,38] (XLVIII) and biflavonyl ether such as Hinokiflavone[39] (XLIX) are known



		R	R_1	R_2	R_3
Sotetsuflavone	(XLVI)	H	H	H	H
Kayaflavone	(XLVII)	H	CH_3	CH_3	CH_3
Ginketin	(XLVIII)	CH_3	CH_3	H	H

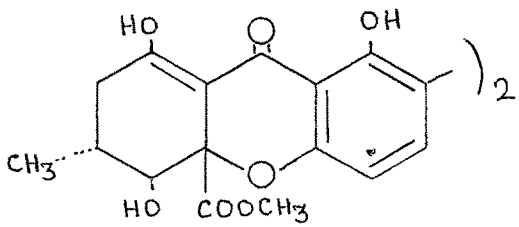
to occur in nature. Some of the biflavonyls have been synthesised in this laboratory[40,41] and some by Chen and



Hinokiflavone (XLIX)

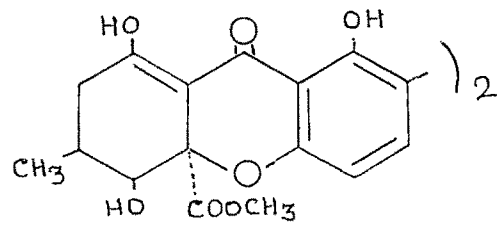
his coworkers[42,43,44].

The literature survey showed that there are no bixanthonyls known to occur in nature and none has been prepared synthetically. Bixanthyls, as they are described in the literature, are however found to occur in nature. Bixanthyls such as Secalonic acid-A (L), Secalonic acid-B (LI) Secalonic acid-C (LII), Secalonic acid-D[45] (LIII),



(a)

Secalonic acid-A (L)



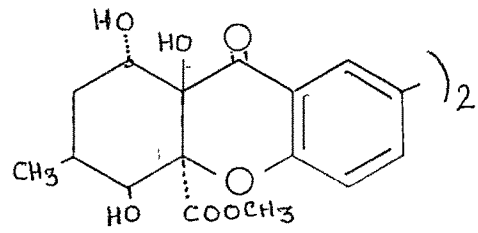
(b)

Secalonic acid-B (LI)

(a) - (b)

Secalonic acid-C

(LII)



(d)

Ergochrome-DD

(LIV)

(a) - (a)

Enantiomer

Secalonic acid-D

(LIII)

(a) - (d)

Ergochrome-AD

(LV)

(b) - (d)

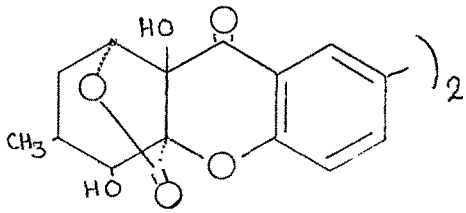
Ergochrome-BD

(LVI)

(c) - (d)

Ergochrome-CD

(LVII)



(c)

Ergoflavin

(LVIII)

(a) - (c)

Ergochrysin-A

(LIX)

(b) - (c)

Ergochrysin-B

(LX)

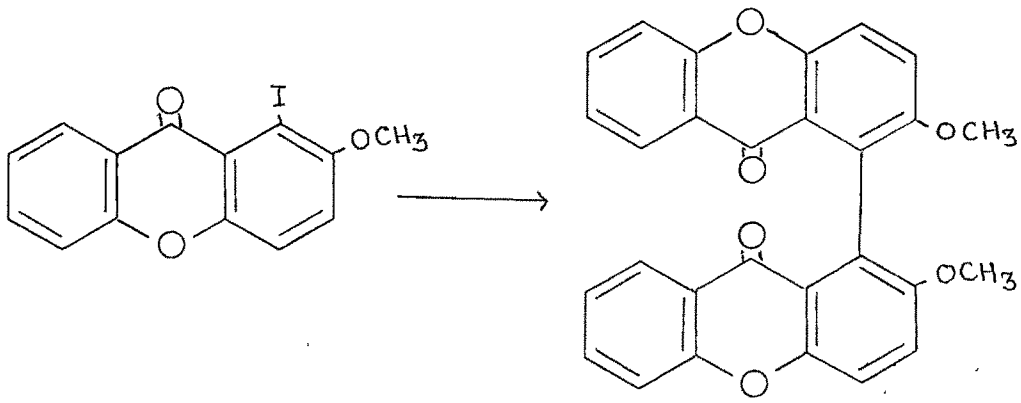
Ergochrome-DD (LIV), Ergochrome-AD (LV), Ergochrome-BD (LVI), Ergochrome-CD[46] (LVII), Ergoflavin[47] (LVIII), Ergochrysin-A[45] (LIX) and Ergochrysin-B[47] (LX) have been reported in the literature so far.

In the present work bixanthonyls have been prepared by the Ullmann reaction on the monoiodomethoxy-xanthones such as 2-methoxy-1-iodoxanthone, 3-methoxy-4-

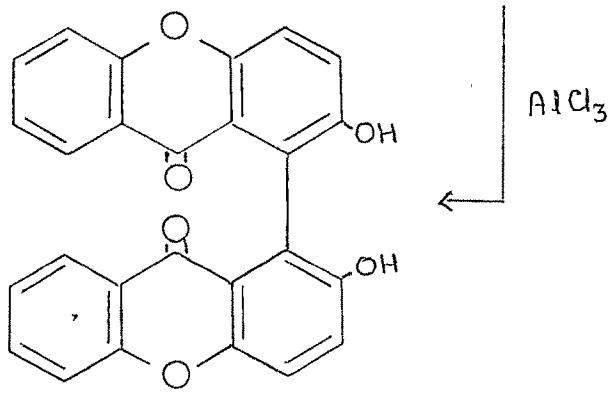
-iodoxanthone and 3,6-dimethoxy-4-iodoxanthone.

Synthesis of 2,2'-dihydroxy-1,1'-bixanthonyl

2-Methoxy-1-iodoxanthone was mixed with activated copper-bronze and heated at about 250-60°, when it gave an iodine free product to which 2,2'-dimethoxy-1,1'-bixanthonyl (LXI) structure has been assigned. The same bixanthonyl can be prepared by refluxing the iodoxanthone in dimethyl formamide with activated copper-bronze. Demethylation of this xanthone gave 2,2'-dihydroxy-1,1'-bixanthonyl (LXII).



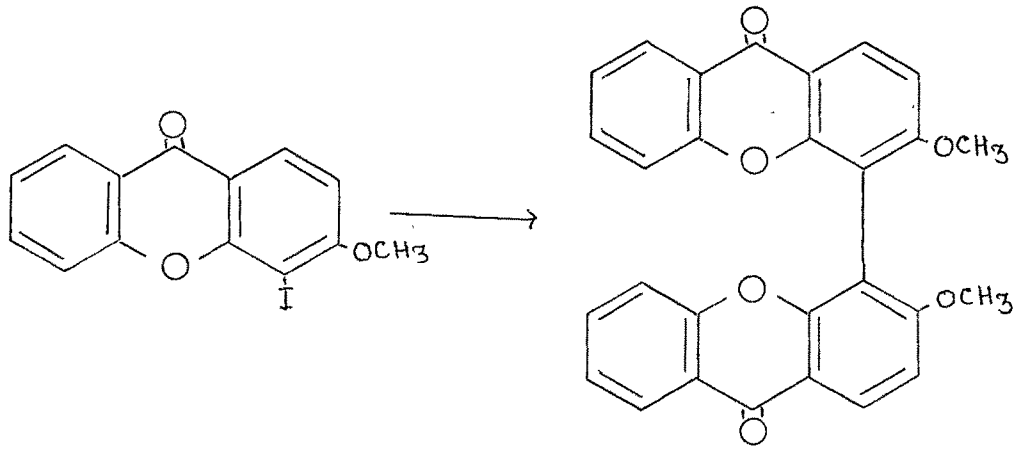
(LXI)



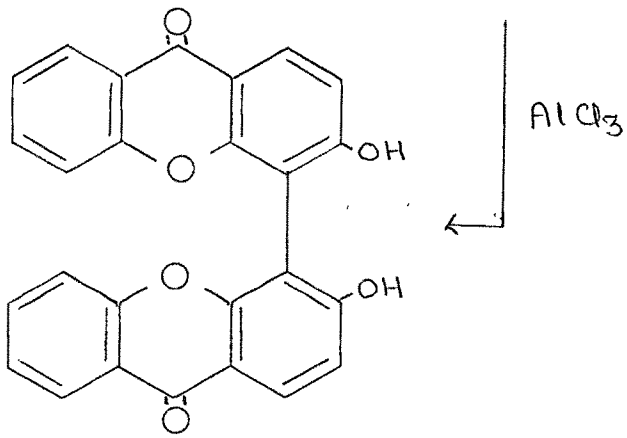
(LXII)

Synthesis of 3,3'-dihydroxy-4,4'-bixanthonyl

Baking of 3-methoxy-4-iodoxanthone with copper bronze at 250° resulted in an iodine free compound, to which 3,3'-dimethoxy-4,4'-bixanthonyl structure (LXIII) has been assigned. Mass spectrum of this compound showed molecular ion peak at 450 m/e corresponding to its molecular weight. Demethylation of the above compound with aluminium chloride gave 3,3'-dihydroxy-4,4'-bixanthonyl (LXIV).



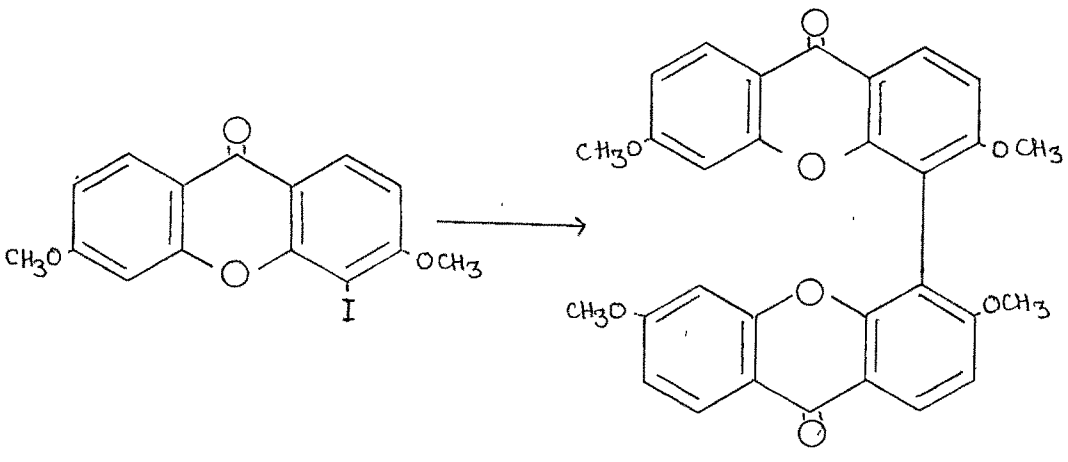
(LXIII)



(LXIV)

Synthesis of 3,3',6,6'-tetramethoxy-4,4'-bixanthonyl

3,6-Dimethoxy-4-iodoxanthone was baked with copper bronze at 260-80° for 20 min. and the mass then extracted in dimethyl formamide. A mixture of three compounds was obtained from this extract. The mixture was purified by TLC using silica gel, with chloroform as a solvent. The upper band, which showed a dark blue fluorescence in UV light was deiodinated 3,6-dimethoxyxanthone, the middle band which showed light blue fluorescence, was the compound with highest



(LXV)

m.p. 305-06° and the last band was of the original 3,6-dimethoxy-4-iodoxanthone. The middle band was taken in chloroform and run again similarly on TLC and then taken up in chloroform. After removing chloroform the product crystallised from acetic acid to which 3,3',6,6'-tetramethoxy-4,4'-bixanthonyl structure (LXV) has been assigned.

EXPERIMENTAL

Iodination of 2-hydroxyxanthone : 2-Hydroxy-1-iodoxanthone :

2-Hydroxyxanthone (1.06 g.) was dissolved in warm ethyl alcohol (20 ml.) and iodine (0.51 g.) in ethyl alcohol (18 ml.) added to it. To this stirred solution iodic acid (0.18 g.) dissolved in minimum quantity of water was added and the reaction mixture was stirred for further 2 hr. The separated product together with the product obtained after dilution of the reaction mixture, crystallised from acetic acid as brown needles (1.1 g.), m.p. 208-10°. IR in nujol : 1630 $cm.^{-1}$ (>CO).

No diiodo derivative could be obtained even with a large excess of iodine and iodic acid. With twice the amount of iodine (1.0 g.) and iodic acid (0.36 g.) the same 2-hydroxy-1-iodoxanthone was obtained in better yield (1.3 g.).

The same monoiodo derivative was obtained on iodination of powdered 2-hydroxyxanthone (0.53 g.) in aqueous ammonia (20 % ; 150 ml.) and adding solution of iodine (0.64 g.) and potassium iodide (1.4 g.) dropwise to the stirred ammoniacal solution during half an hour. Finally, it was acidified with cold dilute sulphuric acid, treated with a pinch of sodium sulphite and filtered. The product crystallised from acetic acid. No higher derivative was obtained with more amount of iodine even with this method.

Analysis : Found : C, 45.88; H, 2.34; I, 37.57 %

$C_{13}H_7O_3I$ requires : C, 46.15; H, 2.07; I, 37.57 %.

The methyl ether :

The above iodoxanthone (0.5 g.) in acetone (25 ml.) was refluxed on a steam bath with dimethyl sulphate (1 ml.) in the presence of anhydrous potassium carbonate (2.0 g.) for 2 hr. The product obtained on removal of acetone was washed with dilute sodium hydroxide solution and crystallised from acetic acid as brown needles (0.5 g.), m.p. 183-84°.

Analysis : Found : C, 47.55 ; H, 2.24 ; I, 35.60 %

$C_{14}H_9O_3I$ requires: C, 47.73 ; H, 2.06 ; I, 36.07 %.

2-Methoxy-1-cyanoxanthone :

2-Methoxy-1-iodoxanthone (0.7 g.) dissolved in dimethyl formamide (8 ml.) was refluxed with cuprous cyanide (0.2 g.) for 4 hr. on a sand bath. This was filtered hot and diluted, when a yellow product separated which was treated with ammonia solution till it did not give blue colour and then crystallised from acetic acid. M.p. 266-68°. Yield 0.45 g. IR in nujol : 2220 $cm.^{-1}$ (-CN); 1650 $cm.^{-1}$ (>CO).

Analysis : Found : C, 71.39 ; H, 3.48 ; N, 5.38 %

$C_{15}H_9O_3N$ requires : C, 71.71 ; H, 3.61 ; N, 5.57 %.

2-Methoxy-1-iodoxanthone (0.5 g.) on baking with cuprous cyanide (0.2 g.) at 250° gave on extraction with dimethyl formamide the cyanoxanthone in poor yield (0.18 g.).

Preparation of 2-methoxy-1-cyanoxanthone from 2-methoxy-1-formylxanthone :

2-Methoxy-1-formylxanthone (0.5 g.), prepared according to Davies et al.[26] was refluxed with hydroxylamine hydrochloride (0.25g.) in alcohol in the presence of potassium hydroxide (0.2 g.) for 2 hr. The yellow product obtained crystallised from aqueous alcohol. M.p. 226-28°. Yield 0.4 g. Analysis : Found : C, 67.87 ; H, 3.85 ; N, 5.01 %
$C_{15}H_{11}O_4N$ requires : C, 68.25 ; H, 4.08 ; N, 5.22 %.

The above oxime (0.4 g.) was refluxed in acetic anhydride (5 ml.) for 15 min. and then poured into ice cold water and left overnight. Next day the product obtained was crystallised from acetic acid. M.p. 266-68°. Yield 0.25g. The m.p. and mixed m.p. of the cyanoxanthone described earlier was not depressed.

Attempted demethylation of 2-methoxy-1-cyanoxanthone :

2-Methoxy-1-cyanoxanthone (0.5 g.) was refluxed with aluminium chloride (1.0 g.) in sodium dried benzene (30 ml.) for 4 hr. and the solvent was removed when a product soluble in alkali was obtained. It was repeatedly crystallised from acetic acid, but it showed a range in melting from 240-50°. It did not show any colour with alcoholic ferric chloride.

Attempted hydrolysis of 2-methoxy-1-cyanoxanthone :

2-Methoxy-1-cyanoxanthone (0.5 g.) when refluxed for 24 hr. in alcohol (5 ml.) with 2N sodium hydroxide

solution (20 ml.) gave the original cyanoxanthone back.

Similarly, the cyanoxanthone (0.5 g.) on refluxing in 5 % potassium hydroxide solution in alcohol on a water bath for 2 hr. remained unchanged.

Hydrolysis of 2-methoxy-1-cyanoxanthone (0.5 g.) with a mixture of equal proportion of water, sulphuric acid and acetic acid (20 ml.) by refluxing for 16 hr. gave no sodium bicarbonate soluble product, instead 2-hydroxyxanthone was obtained.

Iodination of 3-hydroxyxanthone : 3-Hydroxy-4-iodoxanthone :

3-Hydroxyxanthone (1.06 g.) was dissolved in warm ethyl alcohol (25 ml.) and iodine (0.51 g.) solution in ethyl alcohol (18 ml.) added to it. The solution was stirred and iodic acid (0.2 g.) dissolved in minimum quantity of water was added gradually and the stirring continued for further 2 hr. The separated product and the product obtained after dilution with water crystallised from aqueous alcohol in yellow needles (1.2 g.), m.p. 246-47°. IR in nujol : 1640 $cm.^{-1}$ (>CO).

Analysis : Found : C, 46.34 ; H, 2.43 ; I, 37.22 %

$C_{13}H_7O_3I$ requires : C, 46.15 ; H, 2.07 ; I, 37.57 %.

The same monoiodoxanthone was obtained when powdered 3-hydroxyxanthone (0.5 g.) was dissolved in aqueous ammonia (20 % ; 150 ml.) and then treated with iodine (0.64 g.) and potassium iodide (1.4 g.) solution in water (30 ml.) and after acidification with cold dilute sulphuric acid the

product was crystallised from aqueous alcohol. Yield 1.1 g.

No higher iodo derivative was obtained by this method by increasing the amount of iodine.

The methyl ether :

3-Hydroxy-4-iodoxanthone (0.5 g.) was refluxed with dimethyl sulphate (1 ml.) in acetone (30 ml.) in the presence of anhydrous potassium carbonate (1.0 g.) for 2 hr. and the reaction mixture was worked up. The methyl ether crystallised from alcohol as white needles (0.5 g.), m.p. 189°.

Analysis : Found : C, 47.55 ; H, 2.48 ; I, 35.92 %

$C_{14}H_9O_3I$ requires : C, 47.73 ; H, 2.06 ; I, 36.07 %.

The acetoxy ester :

3-Hydroxy-4-iodoxanthone (0.5 g.) in pyridine (8 ml.) and acetic anhydride(1 ml.) was heated on a steam bath for 2 hr. and then poured in cold dilute hydrochloric acid. The product obtained was crystallised from alcohol. M.p. 199°. Yield 0.5 g.

Analysis : Found : C, 47.22 ; H, 2.66 ; I, 32.96 %

$C_{15}H_9O_4I$ requires : C, 47.38 ; H, 2.37 ; I, 33.16 %.

Synthesis of 3-methoxy-4-iodoxanthone : 2,2',4-Trihydroxy--3-nitrobenzophenone :

A mixture of 2-nitroresorcinol (5.0 g.) and salicylic acid (4.0 g.) together with anhydrous zinc chloride (12.0 g.) and phosphorus oxychloride (28 ml.) was kept in a water bath at 60-65° for 3 hr. On pouring the reaction

mixture on crushed ice a gummy mass was separated which was washed with dilute hydrochloric acid and then with water and taken in 10 % sodium hydroxide solution. This was boiled for half an hour and acidified after cooling. The separated gummy mass crystallised from water (1 litre). This was recrystallised and then taken in chloroform and passed through a silica gel column. The product obtained on removal of the solvent crystallised from aqueous methanol. M.p. 118-20°. Yield 0.8 g. The benzophenone was analysed after drying overnight at 100° under vacuum.

Analysis : Found : C, 57.18 ; H, 3.09 ; N, 4.70 %

$C_{13}H_9O_6N$ requires : C, 56.73 ; H, 3.27 ; N, 5.09 %.

3-Hydroxy-4-nitroxanthone :

The above benzophenone (0.5 g.) was dissolved in aqueous alcohol (30 % ; 20 ml.) and the solution was heated in a sealed Carius tube at 220° for 3 hr. The cyclised product was again crystallised from aqueous alcohol as yellow needles (0.3 g.), m.p. 218-20°. This showed brownish red colour with alcoholic ferric chloride solution. This crystallised with one molecule of water as can be seen from its analysis, before and after drying at 110° in vacuum.

Analysis : Found : C, 56.70 ; H, 3.53 %
(before drying)

$C_{13}H_7O_5N.H_2O$ requires : C, 56.72 ; H, 3.27 %.

Analysis : Found : C, 60.75 ; H, 2.67 ; N, 5.17 %
(after drying)

$C_{13}H_7O_5N$ requires: C, 60.70 ; H, 2.73 ; N, 5.45 %.

3-Methoxy-4-nitroxanthone :

Methylation of the above xanthone (0.5 g.) with dimethyl sulphate in acetone solution in the presence of potassium carbonate gave a product which crystallised from acetic acid as white needles (0.5 g.), m.p. 250-52°.

Analysis : Found : C, 62.43 ; H, 3.77 ; N, 5.59 %.

$C_{14}H_9O_5N$ requires : C, 61.99 ; H, 3.32 ; N, 5.17 %.

3-Methoxy-4-aminoxanthone :

3-Methoxy-4-nitroxanthone (0.3 g.) was dissolved in alcohol (90 ml.) and dithionite (0.5 g.) was added . The reaction mixture was refluxed. To this refluxing solution hot water (15 ml.) was added and the heating continued for half an hour. Most of the alcohol was then removed under vacuum and the solution poured into ice cold water. The separated product was taken in hydrochloric acid (50 % ; 20 ml.) and the solution was filtered and then neutralised with alkali. The separated product crystallised from aqueous alcohol as light yellow needles (0.2 g.), m.p. 175-76°.

Analysis : Found : C, 69.85 ; H, 4.73 ; N, 5.51 %

$C_{14}H_{11}O_3N$ requires : C, 69.75 ; H, 4.56 ; N, 5.80 %.

3-Methoxy-4-iodoxanthone :

3-Methoxy-4-aminoxanthone (0.2 g.) was dissolved in dilute sulphuric acid (30 % ; 18 ml.) by warming and the solution was then cooled to 0°, when some sulphate precipitated. This mixture was stirred and sodium nitrite

solution (0.3 g. in 3 ml.) was added with constant stirring and left for half an hour at 0-5°. To the reaction mixture urea (0.4 g.) was added to destroy the excess of nitrous acid and potassium iodide (0.5 g.) in water (5 ml.) was added slowly. The solution was stirred well for about an hour and then kept in water bath at 60° for one more hour. The excess of iodine was removed by adding sodium sulphite. The separated product crystallised from alcohol as white needles (0.22 g.). The m.p. and mixed m.p. of this with 3-methoxy-4-iodoxanthone from directly iodinated product was not depressed.

Attempted preparation of 3,4-dimethoxyxanthone :

3-Methoxy-4-iodoxanthone (0.5 g.) was refluxed for 60 hr. with a solution of sodium methoxide from methanol (30 ml.) and sodium (0.5 g.) in dioxan (50 ml.). The solvent was removed, dilute hydrochloric acid was added and the product was washed with water and crystallised from alcohol, when the original xanthone was obtained.

Attempted preparation of 3,4-dihydroxyxanthone :

3-Hydroxy-4-iodoxanthone (0.5 g.) was refluxed with 4N sodium hydroxide solution (20 ml.) containing hydrated copper sulphate (0.1 g.) for 4 hr. and the solution was cooled and acidified, when the original xanthone was obtained back.

3-Methoxy-4-cyanoxanthone :

3-Methoxy-4-iodoxanthone (0.7 g.) and cuprous cyanide (0.2 g.) were refluxed in dimethyl formamide (8 ml.)

for 4 hr. The solution was filtered hot and diluted with water. The separated solid was treated further with ammonia to make it free from cuprous cyanide, till it did not give a blue colour. The product was crystallised from acetic acid in white needles (0.5 g.), m.p. 272-73°. IR in KBr : 2230 $cm.^{-1}$ (-CN) ; 1660 $cm.^{-1}$ (>CO).

Analysis : Found : C, 71.93 ; H, 3.45 ; N, 5.35 %

$C_{15}H_9O_3N$ requires : C, 71.71 ; H, 3.61 ; N, 5.57 %.

3-Hydroxy-4-cyanoxanthone :

3-Methoxy-4-cyanoxanthone (0.5 g.) in benzene (50 ml.) was refluxed with aluminium chloride (1.0 g.) for 2 hr. On working up the reaction mixture as usual an alkali soluble product was obtained which crystallised from aqueous acetic acid in white needles (0.3 g.), m.p. 310°. The product crystallised with one water molecule. IR in nujol : 3450 $cm.^{-1}$ (-OH); 2222 $cm.^{-1}$ (-CN) ; 1630 $cm.^{-1}$ (>CO).

Analysis : Found : C, 66.31 ; H, 3.17 %

(before drying)

$C_{14}H_7O_3N.H_2O$ requires : C, 65.88 ; H, 3.52 %.

Analysis : Found : C, 71.40 ; H, 3.06 ; N, 6.08 %

(after drying)

$C_{14}H_7O_3N$ requires : C, 70.88 ; H, 2.91 ; N, 5.82 %.

Attempted hydrolysis of 3-methoxy-4-cyanoxanthone :

When 3-methoxy-4-cyanoxanthone (0.2 g.) in alcohol (5 ml.) was refluxed with 10 % sodium hydroxide solution (20 ml.) for 6 hr. and the solution was acidified 3-hydroxy-4-cyanoxanthone was obtained in white needles

(0.13 g.), m.p. 310°. The mixed m.p. of this with the product obtained by demethylation was not depressed.

Similarly, alcoholic potassium hydroxide (5 % ; 20 ml.) solution containing xanthone (0.2 g.)on refluxing on a water bath for 8 hr., removing the solvent, diluting the reaction mixture with water and finally acidifying , gave the same demethylated xanthone with m.p. 310°.

Use of pyridine, glycerol or 2-methoxyethanol as a solvent resulted also in demethylation only.

In order to hydrolyse 3-methoxy-4-cyanoxanthone according to Goldberg and Wragg[25], the xanthone (0.4 g.) was taken in dioxan (20 ml.) and 6N sodium hydroxide solution (30 ml.) was added and the mixture was heated on a water bath for 80 hr. The solvent was removed and water added . The original xanthone separated. Nothing was obtained from the filtrate after acidification.

3-Methoxy-4-cyanoxanthone (0.5 g.) was dissolved in acetic acid (15 ml.) and refluxed after adding conc. hydrochloric acid (15 ml.) for 20 hr., passing hydrochloric acid gas every 4 hr. The original xanthone was obtained back.

3-Methoxy-4-cyanoxanthone (0.8 g.) in sulphuric acid (60 % v/v ; 20 ml.) was kept on a steam bath at 90° for 2 hr. and then diluted with water. The separated product was the original xanthone. Similar results were obtained with (70 %) sulphuric acid. With 80 % sulphuric acid, an alkali soluble demethylated product (0.3 g.) was also

obtained. But when the temperature employed was 120-40° (an oil bath) 60 % and 70 % sulphuric acid gave demethylated xanthone (0.4 g.) and the original xanthone (0.2 g.) while 80 % sulphuric acid gave on pouring in ice-water, the alkali soluble demethylated xanthone (0.3 g.), and rest the water soluble product, which was repeatedly extracted in chloroform (5 x 10 ml.). The chloroform extract washed with water (10 ml.). The product obtained after removing chloroform could not be crystallised but the crude product was found to contain sulphur.

Hydrolysis of 3-methoxy-4-cyanoxanthone with polyphosphoric acid according to Berger et al.[28] was carried out as follows :

3-Methoxy-4-cyanoxanthone (1.0 g.) taken in 100 % polyphosphoric acid (6.0 g. phosphorus pentoxide in 14 ml. 85 % phosphoric acid) and heated in an oil-bath at 150° for 6 hr. Then the reaction mixture was poured on ice and left overnight. The separated solid was washed with water and taken in 2N alkali (20 ml.) when most of it dissolved and was filtered off. The insoluble product crystallised from aqueous alcohol (0.3 g.), m.p. 126-28°. This was found to be the 3-methoxyxanthone (m.p. 129°). The alkaline extract was acidified and the solid obtained crystallised from aqueous alcohol gave m.p. 243°. This was identical with 3-hydroxyxanthone.

Heating at this temperature for short period (30 min.) gave purely 3-methoxy-4-cyanoxanthone, while

heating for 8 hr. gave only 3-hydroxyxanthone. Thus no acid was obtained, instead the cyano group was knocked out.

Similarly, 3-hydroxy-4-cyanoxanthone was subjected to alkaline hydrolysis as described earlier in the case of the methoxyxanthone, when no acid was obtained. In all cases the original xanthone was recovered back.

3-Hydroxyxanthone-4-carboxylic acid :

3-Hydroxy-4-formylxanthone[29] was oxidised[30] with silver oxide as follows :

To silver nitrate (0.4 g.) in water (5 ml.) sodium hydroxide solution (0.1 g. in 8 ml.) was added slowly with stirring. The silver oxide formed was collected and washed with water. It was transferred to a 250 ml. conical flask containing 10 ml. of water and sodium hydroxide pellets (0.5 g.) added to it. The solution was stirred keeping the temperature at 60°. To this solution, the paste prepared from powdered 3-hydroxy-4-formylxanthone (0.48 g.) and sodium hydroxide solution (2N ; 2 ml.) was added. Slowly the silver mirror appeared . The solution was stirred for 4 hr. at 60° and left overnight. Next day it was filtered and the filtrate the acidified with hydrochloric acid (1:1). The solid obtained was purified by extraction with bicarbonate solution and crystallised from aqueous acetic acid, after extracting with chloroform (2 x 15 ml.) from acidified bicarbonate solution. It crystallised as white needles (0.18 g.), m.p. 222°. The product showed pink

colouration with alcoholic ferric chloride. The acid crystallised with one molecule of water. IR. in nujol : 3450 $cm.^{-1}$ (-OH) ; 1670 $cm.^{-1}$ (-COOH) ; 1630 $cm.^{-1}$ (>CO).

Analysis : Found : C, 61.85 ; H, 3.48 %
(before drying)

$C_{14}H_8O_5.H_2O$ requires : C, 61.31 ; H, 3.61 %.

Analysis : Found : C, 65.37 ; H, 2.83 %.
(after drying at 110° under vacuum)

$C_{14}H_8O_5$ requires : C, 65.63 ; H, 3.15 %.

3-Hydroxy-2,4-diiodoxanthone :

To 3-hydroxyxanthone (1.06 g.) in alcohol (30 ml.), iodine (1.53 g.) was added followed by warm alcohol (40 ml.) with stirring. To this solution iodic acid (0.54 g.) dissolved in minimum quantity of water was added and the stirring continued for 2 hr. The pink needles separated were crystallised from alcohol twice when yellow tiny needles (1.2 g.), m.p. 242-43° were obtained. The mixed m.p. of this with 3-hydroxy-4-iodoxanthone was depressed by about 30°.

IR in nujol : 1640 $cm.^{-1}$ (>CO).;

Analysis : Found : C, 33.44 ; H, 1.40 ; I, 54.92 %

$C_{13}H_6O_3I_2$ requires : C, 33.62 ; H, 1.29 ; I, 54.74 %.

The methyl ether :

A mixture of 3-hydroxy-2,4-diiodoxanthone (0.5 g.) and dimethyl sulphate (1 ml.) in acetone (40 ml.) was refluxed with anhydrous potassium carbonate (1.0 g.) on a steam bath for 2 hr. The methyl ether obtained on working

up as before crystallised from acetic acid. M.p. 175-76°. Yield 0.4 g.

Analysis : Found : C, 35.53 ; H, 1.81 ; I, 52.76 %

$C_{14}H_8O_3I_2$ requires : C, 35.14 ; H, 1.67 ; I, 53.13 %.

The acetoxy ester :

3-Hydroxy-2,4-diiodoxanthone (0.5 g.) in warm pyridine (5 ml.) when heated with acetic anhydride (1 ml.) on a steam bath for 2 hr. and the reaction mixture poured into ice cold hydrochloric acid (1:1) gave a product which crystallised from acetic acid as shining needles (0.4 g.), m.p. 252-53°.

Analysis : Found : C, 35.77 ; H, 1.53 ; I, 50.19 %

$C_{15}H_8O_4I_2$ requires : C, 35.75 ; H, 1.58 ; I, 50.19 %.

3-Methoxy-2,4-dicyanoxanthone :

A mixture of 3-methoxy-2,4-diiodoxanthone (0.7 g.) and cuprous cyanide (0.38 g.) was refluxed in dimethyl formamide (10 ml.) for 4 hr. The solution was filtered hot and diluted with water. The separated product was filtered and treated repeatedly with ammonia till it did not give a blue colour. The product crystallised from acetic acid in white needles (0.3 g.), m.p. 280°. IR in nujol : 2222 $cm.^{-1}$ (-CN) ; 1670 $cm.^{-1}$ (>CO).

Analysis : Found : C, 70.05 ; H, 3.28 ; N, 9.86 %

$C_{16}H_8O_3N_2$ requires : C, 69.56 ; H, 2.92 ; N,10.14 %.

Iodination of 3,6-dihydroxyxanthone : 3,6-Dihydroxy-4-iodoxanthone :

3,6-Dihydroxyxanthone (1.14 g.) was dissolved in

alcohol (75 ml.) by warming, iodine (0.51 g.) added to it, followed by more alcohol (15 ml.) and the solution was stirred till the iodine dissolved. Iodic acid (0.18 g.) dissolved in minimum quantity of water was then added with stirring. After about 2 hr. the solution was diluted and the separated product crystallised from alcohol in light pink needles (0.58 g.), m.p. 340° (decomp.). IR in nujol : 1615 $cm.^{-1}$ (>CO).

Analysis : Found : C, 43.77 ; H, 1.85 ; I, 35.89 %

$C_{13}H_7O_4I$ requires : C, 43.94 ; H, 1.97 ; I, 35.78 %.

The dimethyl ether :

Methylation of 3,6-dihydroxy-4-iodoxanthone (0.8 g.) in acetone (50 ml.), by dimethyl sulphate (3.2 ml) in the presence of anhydrous potassium carbonate (2.0 g.) gave an alkali insoluble product which crystallised from alcohol as white needles (0.68 g.), m.p. 249-50°.

Analysis : Found C : C, 47.00 ; H, 2.55 ; I, 32.82 %

$C_{15}H_{11}O_4I$ requires : C, 47.12 ; H, 2.88 ; I, 33.24 %.

The diacetoxy ester :

3,6-Dihydroxy-4-iodoxanthone (0.5 g.) in pyridine (5 ml.) on acetylation with acetic anhydride (1 ml.) and working up as described earlier gave the diacetoxy ester which crystallised from alcohol in white needles (0.45 g.), m.p. 201-03°.

Analysis : Found : C, 46.22 ; H, 2.21 ; I, 29.35 %

$C_{17}H_{11}O_6I$ requires : C, 46.57 ; H, 2.51 ; I, 28.93 %.

Attempted synthesis of 3,6-dihydroxy-4-bromoxanthone :

3,6-Dihydroxy-4-chloroxanthone :

2-Bromoresorcinol (5.0 g.) and β-resorcylic acid (5.0 g.) were condensed in the presence of anhydrous powdered zinc chloride (20.0 g.) and phosphorus oxychloride (25 ml.) by heating for 3 hr. in a water bath at 60-65°. The oily mass was poured over crushed ice when a gummy mass separated which was washed with hydrochloric acid and purified through extraction with alkali and finally crystallised from aqueous alcohol. This gave the benzophenone as yellow needles (1.2 g.), m.p. 108-13°. This showed the presence of chlorine instead of bromine. This benzophenone was dissolved in aqueous alcohol (40 %; 25 ml.). This was heated in a sealed tube at 200° for 2 hr. The chloroxanthone obtained crystallised from aqueous alcohol as pink needles (0.8 g.), m.p. 375°.

Analysis : Found : C, 61.08 ; H, 3.04 ; Cl, 12.98 %

$C_{13}H_7O_4Cl$ requires : C, 59.90 ; H, 2.64 ; Cl, 13.50 %.

The dimethyl ether :

The above xanthone (0.5 g.) on methylation as before gave the dimethoxyxanthone, which crystallised from alcohol in white needles (0.47 g.), m.p. 182-83°.

Analysis : Found : C, 59.85 ; H, 3.75 %

$C_{15}H_{11}O_4Cl$ requires : C, 60.20 ; H, 3.70 %.

Attempted Rosenmund-von Braun reaction on 3,6-dimethoxy-4-chloroxanthone :

3,6-Dimethoxy-4-chloroxanthone (0.4 g.) was mixed

with cuprous cyanide (0.2 g.) and heated at 250-70° in an oil bath for half an hour, when slight sublimation occurred and a white product was collected on the upper side of the test tube. The sublimed product and the product obtained after extraction from the reaction with dimethyl formamide and working up as usual, were the same as the original chloroxanthone as was seen by their m.p. and mixed m.p. comparison.

No reaction occurred even when dimethyl formamide was used as a solvent and the reaction mixture refluxed for 4 hr.

3,6-Dimethoxy-4-cyanoxanthone :

3,6-Dimethoxy-4-iodoxanthone (0.7 g.) and cuprous cyanide (0.3 g.) were taken in dimethyl formamide (10 ml.) and refluxed for 4 hr. The upper solution became clear. This was filtered hot, diluted and the separated solid collected and treated with ammonia to remove the cyanide impurities. Finally the product was crystallised from acetic acid. M.p. 293°. Yield 0.5 g. IR in hexachlorobutadiene : 2230 $cm.^{-1}$ (-CN) ; 1660 $cm.^{-1}$ (>CO).

Analysis : Found : C, 66.79 ; H, 3.98 ; N, 4.98 %

$C_{15}H_{11}O_4N$ requires : C, 66.91 ; H, 4.09 ; N, 5.20 %.

Attempted hydrolysis of 3,6-dimethoxy-4-cyanoxanthone :

3,6-Dimethoxy-4-cyanoxanthone (0.6 g.) was dissolved in alcohol (20 ml.), was refluxed with alcoholic potassium hydroxide (5 % ; 15 ml.) for 2 hr. The alcohol was removed and water added. The solution on filtration

was acidified when it gave a solid which did not give any pure product on repeated crystallisations. IR spectrum of this in nujol showed the characteristic peaks at 3460 $cm.^{-1}$ for hydroxyl group and at 2240 $cm.^{-1}$ for the cyano group.

This compound (0.3 g.) on methylation with dimethyl sulphate (0.6 ml.) and potassium carbonate (1.0 g.) in acetone gave the original 3,6-dimethoxy-4-cyanoxanthone.

Attempted alkali-fusion of 3,6-dimethoxy-4-cyanoxanthone :

No benzophenone resulted when 3,6-dimethoxy-4-cyanoxanthone (0.8 g.) was fused with potassium hydroxide (2.0 g.) at 200° in an oil bath, only partial demethylation took place but no pure compound could be isolated.

Alkali-fusion of 3,6-dimethoxy-4-cyanoxanthone carried out in the above proportion but at 300-10° also did not give any pure product.

3,6-Dihydroxy-4,5-diiodoxanthone :

To 3,6-dihydroxyxanthone (1.14 g.) dissolved in alcohol (75 ml.), iodine (1.02 g.) in alcohol (30 ml.) was added. The solution was stirred and iodic acid (0.35 g.)in minimum quantity of water was added and the solution was stirred for 2 hr. more. The separated product on repeated crystallisations from alcohol gave light yellow needles (1.2 g.), m.p. 266-68° (decomp.). IR in nujol : 1640 $cm.^{-1}$ (>CO).

Analysis : Found : C, 32.18 ; H, 1.44 ; I, 52.95 %

$C_{13}H_6O_4I_2$ requires : C, 32.50 ; H, 1.25 ; I, 52.94 %.

The same product was obtained when 3,6-dihydroxy-xanthone (1.14 g.) was dissolved in ammonia (20 % ; 150 ml.) and iodine (1.27 g.) and potassium iodide (2.6 g.) in water was added slowly with constant stirring and then acidified. Yield. 0.9 g.

The same product was obtained in better yield (1.8 g.) with two mole proportions of iodine (2.54 g.).

The dimethyl ether :

A mixture of 3,6-dihydroxy-4,5-diiodoxanthone (0.5 g.), dimethyl sulphate (2 ml.) and anhydrous potassium carbonate (1.0 g.) was refluxed for 2 hr. The dimethyl ether obtained crystallised from acetic acid. M.p. 301°. Yield 0.4 g.

Analysis : Found : C, 35.78 ; H, 2.38 ; I, 50.27 %

$C_{15}H_{10}O_4I_2$ requires : C, 35.40 ; H, 1.97 ; I, 49.99 %.

The diacetoxy ester :

3,6-Dihydroxy-4,5-diiodoxanthone (0.5 g.) on acetylation by acetic anhydride (1 ml.) in pyridine (5 ml.) gave the diacetoxyxanthone which crystallisedfrom alcohol as white needles (0.4 g.), m.p. 235-36°.

Analysis : Found : C, 36.44 ; H, 2.17 ; I, 45.40 %.

$C_{17}H_{10}O_6I_2$ requires : C, 36.16 ; H, 1.77 ; I, 45.03 %.

3,6-Dimethoxy-4,5-dicyanoxanthone :

A mixture of 3,6-dimethoxy-4,5-diiodoxanthone (0.5 g.) in dimethyl formamide (15 ml.) and cuprous cyanide (0.4 g.) was refluxed for 4 hr. The solution was then filtered hot, and the residue washed with a little hot dimethyl formamide

(5 ml.). The filtrate on dilution gave a yellow solid which was washed repeatedly with ammonia and crystallised from nitrobenzene in yellow buds (0.17 g.), m.p. 373°.

Analysis : Found : C, 66.19 ; H, 3.24 ; N, 9.33 %

$C_{17}H_{10}O_4N_2$ requires : C, 66.67 ; H, 3.27 ; N, 9.15 %.

Attempted demethylation of 3,6-dimethoxy-4,5-dicyanoxanthone :

3,6-Dimethoxy-4,5-dicyanoxanthone (0.6 g.) and anhydrous aluminium chloride (2.4 g.) were mixed together and heated in an oil bath for first half an hour at 120° and then next 2 hr. at 150-60°. The reaction mixture was decomposed by adding ice-cold hydrochloric acid . The product obtained was taken in alkali and the alkaline filtrate acidified when a brownish product separated which on crystallisation from aqueous alcohol separated as brown powder (0.2 g.), m.p. 254-59°. This showed a brown colouration with alcoholic ferric chloride.

Analysis : Found : N, 5.16 %

$C_{15}H_6O_4N_2$ requires : N,10.07 %.

Attempted conversion of 3,6-dimethoxy-4,5-dicyanoxanthone to 2,2'-dihydroxy-3,3'-dicyano-4,4'-dimethoxybenzophenone :

3,6-Dimethoxy-4,5-dicyanoxanthone (0.8 g.) was fused with potassium hydroxide (2.0 g.) at 250° for half an hour, and after cooling, treating with water. This gave very little alkali soluble product, which on acidification separated. This on crystallisation from aqueous alcohol gave an impure yellow powder (0.08 g.), melting range 259-80°.

The methylation of this compound with dimethyl sulphate in acetone in the presence of anhydrous potassium carbonate gave the original dimethoxydicyanoxanthone.

Attempted hydrolysis of 3,6-dimethoxy-4,5-dicyanoxanthone :

3,6-Dimethoxy-4,5-dicyanoxanthone (0.4 g.) in alcoholic potassium hydroxide (8 % ; 50 ml.) was refluxed on a steam bath for 14 hr. After removing alcohol the reaction mixture was treated with water and filtered. The filtrate on acidification gave a product which crystallised from alcohol as brown powder (0.12 g.), melting range 260-70°. IR of this in hexachlorobutadiene showed band at 3400 $cm.^{-1}$ for the hydroxyl group and at 2240 $cm.^{-1}$ for the cyano group.

Attempted cleavage of 3,6-dimethoxy-4,5-dicyanoxanthone by sodamide to 2,2'-dicyano-3,3'-dimethoxydiphenyl ether :

3,6-Dimethoxy-4,5-dicyanoxanthone (0.5 g.) in sodium dried xylene (80 ml.) and powdered sodamide (1.0 g.) were refluxed for 6 hr., cooled and treated with ice-cold water. The xylene layer was taken and most of it was removed under vacuum. The yellow crystals separated were again crystallised from xylene as white needles (0.1 g.), m.p. 315°. This was found to be insoluble in alkali. IR in nujol : 2220 $cm.^{-1}$ (-CN) ; 1655 $cm.^{-1}$ (>CO).

Analysis : Found : C, 44.74 ; H, 2.47 ; N, 3.22 %

$C_{16}H_{12}O_3N_2$ requires : C, 68.56 ; H, 4.32 ; N, 10.00 %.

3,6-Dihydroxy-2,4,5-triiodoxanthone :

3,6-Dihydroxyxanthone (1.14 g.) in alcohol (75 ml.) heated with iodine (1.5 g.) in alcohol (50 ml.) followed by

iodic acid in minimum quantity of water and the reaction mixture stirred at 60° for 2 hr. The separated product crystallised from acetic acid in pink needles (1.9 g.), m.p. 264-65°. This xanthone could not be obtained by ammonia and iodine method. IR in nujol : 1630 $cm.^{-1}$ (>CO).

Analysis : Found : C, 25.26 ; H, 1.00 ; I, 62.44 %

$C_{13}H_5O_4I_3$ requires : C, 25.58 ; H, 0.83 ; I, 62.87 %.

The dimethyl ether :

The dimethyl ether of 3,6-dihydroxy-2,4,5-triiodoxanthone (0.5 g.) was prepared as usual and crystallised from acetic acid in white needles (0.48 g.),m.p. 268-69°.

Analysis : Found : C, 28.21 ; H, 1.55; I, 59.89 %

$C_{15}H_9O_4I_3$ requires : C, 28.39 ; H, 1.42; I, 60.09 %.

The diacetoxy ester :

3,6-Dihydroxy-2,4,5-triiodoxanthone (0.5 g.) on acetylation as usual gave 3,6-diacetoxy-2,4,5-triiodoxanthne, which crystallised from acetic acid in white needles (0.5 g.), m.p. 235-36°.

Analysis : Found : C, 29.50 ; H, 1.55 ; I, 54.91 %

$C_{17}H_9O_6I_3$ requires : C, 29.56 ; H, 1.30 ; I, 55.22 %.

Rosenmund-von Braun reaction with 3,6-dimethoxy-2,4,5-triiodoxanthone :

3,6-Dimethoxy-2,4,5-triiodoxanthone (0.8 g.) was mixed with cuprous cyanide (0.4 g.) and refluxed in dimethyl formamide (20 ml.) for 4 hr. This on filtering hot and diluting with water gave a product which was further treated

with ammonia. The yellow product obtained was crystallised from nitrobenzene in yellow buds (0.15 g.), m.p. 371-73° was found to be identical with 3,6-dimethoxy-4,5-dicyanoxanthone.

3,6-Dihydroxy-2,4,5,7-tetraiodoxanthone :

To a mixture of 3,6-dihydroxyxanthone (1.14 g.) and iodine (2.04 g.) in alcohol, iodic acid (0.71 g.) in water was added and the solution stirred and kept at 70° for 2 hr. The separated product crystallised from excess of acetic acid in yellow needles (2.1 g.), m.p. 285-86°.
IR in nujol : 1650 $cm.^{-1}$ (>CO).
Analysis : Found : C, 21.04 ; H, 0.61 ; I, 68.98 %
$C_{13}H_4O_4I_4$ requires : C, 21.31 ; H, 0.55 ; I, 69.40 %.

The same product was obtained with ammonia and iodine as follows :

3,6-Dihydroxyxanthone (1.14 g.) was dissolved in ammonia (60 ml.) diluted with water (200 ml.) and iodine (5.08 g.) in potassium iodide (10.00 g.) in water (30 ml.) added slowly with constant stirring. The solution was stirred for half an hour and then acidified with cold dilute sulphuric acid when a grayish product was obtained, which was treated with a little sodium sulphite and filtered. Crystallisation of this from acetic acid gave a product in yellow needles (2.5 g.), m.p. 285-86°.

The dimethyl ether :

The dimethyl ether was prepared as usual and crystallised from acetic acid in white needles, m.p. 266-67°.

Analysis : Found : C, 23.55 ; H, 1.33 ; I, 66.48 %

$C_{15}H_8O_4I_4$ requires : C, 23.69 ; H, 1.24 ; I, 66.85 %.

The diacetoxy ester :

Prepared as before and crystallised from acetic acid gave m.p. 271°.

Analysis : Found : C, 25.33 ; H, 1.36 ; I, 61.86 %

$C_{17}H_8O_6I_4$ requires : C, 25.00 ; H, 0.99 ; I, 62.26 %.

Rosenmund-von Braun reaction on 3,6-dimethoxy-2,4,5,7-tetraiodoxanthone :

3,6-Dimethoxy-2,4,5,7-tetraiodoxanthone (1.0 g.) was dissolved in dimethyl formamide (20 ml) and cuprous cyanide (0.6 g.) added. The solution was refluxed on a sand bath for 4 hr. and then filtered hot. On dilution a solid separated. This was filtered and treated with ammonia till it no longer gave blue colouration. It was crystallised from nitrobenzene as yellow buds (0.18 g.), m.p. 371-73°. This was found to be identical with 3,6-dimethoxy-4,5-dicyanoxanthone.

Iodination of 3-hydroxy-6-methoxyxanthone : Preparation of 3-hydroxy-6-methoxyxanthone :

3,6-Dihydroxyxanthone (7.0 g.) was dissolved in sodium hydroxide solution (2.5 g.) in 20 ml. of water. The solution was stirred and dimethyl sulphate (3.5 ml.) was added very slowly during half an hour. The solution is stirred for half an hour more and then refluxed for 15 min. The separated 3,6-dimethoxyxanthone was filtered off and the filtrate acidified . The separated product was filtered, washed with

water and taken in alcohol (400 ml.) by refluxing the solution and then filtered. Half of the alcohol from the filtrate was distilled off and the solution cooled slowly, when needles of 3-hydroxy-6-methoxyxanthone separated (2.3 g.) m.p. 304-05°.

Analysis : Found : C, 69.00 ; H, 3.85 %
$C_{14}H_{10}O_4$ requires : C, 69.42 ; H, 4.16 %.

This xanthone was also prepared by cyclising 2,2',4-trihydroxy-4'-methoxybenzophenone obtained as follows :

4-Methoxy salicylic acid (5.0 g.) and resorcinol (5.0 g.) were condensed in the presence of zinc chloride (20.0 g.) and phosphorus oxychloride (28 ml.) at 60-65° for 3 hr. This gave an oily product, which on pouring over crushed ice gave a gummy mass. This was left overnight. Next day it was washed with dilute hydrochloric acid, water, then treated with dilute solution of sodium bicarbonate and finally crystallised from water (1 litre). Further, crystallisation of this from aqueous alcohol gave yellow needles (2.3 g.), m.p. 101-02°, after drying at 70°. This showed brown colouration with alcoholic ferric chloride. This was analysed after drying at 70° in vacuum.

Analysis : Found : C, 64.15 ; H, 4.81 %
$C_{14}H_{12}O_5$ requires : C, 64.61 ; H, 4.65 %.

The tetramethyl ether :

The above benzophenone on methylation as usual with

dimethyl sulphate gave a 2,2',4,4'-tetramethoxybenzophenone, identical with that obtained from 2,2',4,4'-tetrahydroxybenzophenone after methylation reported by Grover and Shah[34].

The triacetoxy ester :

Acetylation of the above trihydroxybenzophenone resulted in a triacetoxy derivative, which crystallised from alcohol in white needles. M.p. 133°.

Analysis : Found : C, 61.81 ; H, 4.34 %

$C_{20}H_{18}O_8$ requires : C, 62.17 ; H, 4.70 %.

2,2',4-Trihydroxy-4'-methoxybenzophenone was cyclised to 3-hydroxy-6-methoxyxanthone as follows :

The benzophenone (1.0 g.) was dissolved in aqueous alcohol (30 % ; 20 ml.) and heated in sealed tube at 200-20° for 2 hr. The xanthone separated in light pink buds. This was further crystallised from alcohol in needles (0.7 g.), m.p. 305°.

The acetoxy ester :

Acetylation of above xanthone by acetic anhydride-pyridine method gave a monoacetyl derivative, which crystallised from alcohol in white needles. M.p. 178°.

Analysis : Found : C, 67.20 ; H, 3.79 %

$C_{16}H_{12}O_5$ requires : C, 67.60 ; H, 4.25 %.

3-Hydroxy-4-iodo-6-methoxyxanthone :

To a mixture of 3-hydroxy-6-methoxyxanthone (0.5 g.) and iodine (0.51 g.)in warm alcohol was added iodic acid (0.18 g.) dissolved in water with stirring and the solution was stirred

further for 2 hr. The separated product was crystallised from acetic acid in white needles (0.52 g.), m.p. 255-58°.

Analysis : Found : C, 45.39 ; H, 2.45 ; I, 34.97 %.

$C_{14}H_9O_4I$ requires : C, 45.65 ; H, 2.45 ; I, 34.51 %.

The same monoiodoxanthone was obtained when 3-hydroxy-6-methoxyxanthone (0.5 g.) was dissolved in ammonia (20 % ; 150 ml.) and a solution of iodine (1.27 g.) and potassium iodide (2.6 g.) in water (30 ml.) was added.

The dimethyl ether :

A mixture of 3-hydroxy-4-iodo-6-methoxyxanthone (0.5 g.) and dimethyl sulphate (1 ml.) in acetone (30 ml.) was refluxed for 1 hr. in the presence of anhydrous potassium carbonate. The product obtained crystallised from alcohol in white needles (0.5 g.), m.p. 249-50°. It was identical with 3,6-dimethoxy-4-iodoxanthone.

The acetoxy ester :

The monoiodoxanthone (0.5 g.) on acetylation with acetic anhydride and pyridine as usual gave the monoacetyl derivative, which crystallised from alcohol in white needles (0.48 g.), m.p. 225°.

Analysis : Found : C, 47.32 ; H, 2.74 ; I, 31.09 %

$C_{16}H_{11}O_5I$ requires : C, 46.82 ; H, 2.68 ; I, 30.97 %.

3-Hydroxy-2,4-diiodo-6-methoxyxanthone :

To a mixture of 3-hydroxy-6-methoxyxanthone (0.48 g.) dissolved in warm alcohol and iodine (1.5 g.) in alcohol (45 ml.), iodic acid (0.53 g.) dissolved in water was added

with stirring. The stirring was continued for further 2 hr. The separated solid crystallised from acetic acid. M.p. 248-51°. Yield 0.7 g.

Analysis : Found : C, 34.22 ; H, 1.40 ; I, 51.84 %
$C_{14}H_8O_4I_2$ requires : C, 34.00 ; H, 1.61 ; I, 51.40 %.

The methyl ether :

The methyl ether was prepared as usual and crystallised from acetic acid, m.p. 256°.

Analysis : Found : C, 35.90; H, 2.08; I, 49.86 %
$C_{15}H_{10}O_4I_2$ requires : C, 35.43; H, 1.96; I, 50.00 %.

The acetoxy ester :

On acetylation of 3-hydroxy-2,4-diiodo-6-methoxy-xanthone by acetic anhydride in pyridine, the monoacetyl derivative was obtained, which crystallised from benzene in light pink needles, M.p. 240-41°.

Analysis : Found : C, 36.20 ; H, 1.89 ; I, 47.78 %
$C_{16}H_{10}O_5I_2$ requires : C, 35.82 ; H, 1.86 ; I, 47.38 %.

Rosenmund-von Braun reaction on 3,6-dimethoxy-2,4-diiodo-xanthone :

3,6-Dimethoxy-2,4-diiodoxanthone (0.8 g.) was dissolved in dimethyl formamide (15 ml.) and cuprous cyanide (0.3 g.) added. The mixture was refluxed for 4 hr., filtered hot and the filtrate diluted with water. The separated solid was washed with ammonia and crystallised from acetic acid in needles (0.3 g.), m.p. 253°.

Analysis : Found : C, 67.13 ; H, 3.75 ; N, 9.30 %
$C_{17}H_{10}O_4N_2$ requires : C, 66.67 ; H, 3.27 ; N, 9.15 %.

SYNTHESIS OF BIXANTHONYLS

Synthesis of 2,2'-dihydroxy-1,1'-bixanthonyl :

Ullmann reaction on 2-methoxy-1-iodoxanthone : 2,2'-Dimethoxy--1,1'-bixanthonyl :

2-Methoxy-1-iodoxanthone (1.0 g.) was mixed with activated copper bronze (1.0 g.) and heated in an oil bath at about 250-60° for 20 min. The mass melted and solidified again. This was extracted in hot dimethyl formamide (10 ml.) and filtered. The filtrate on cooling gave yellow needles, which were recrystallised from acetic acid. M.p. 331-32°. Yield 0.18 g.

Analysis : Found : C, 74.49 ; H, 3.82 %

$C_{28}H_{18}O_6$ requires : C, 74.66 ; H, 4.00 %.

The same bixanthonyl can be obtained by refluxing the iodoxanthone in dimethyl formamide with activated copper bronze for 4 hr.

Demethylation :

2,2'-Dimethoxy-1,1'-bixanthonyl (0.5 g.) in benzene (50 ml.) when refluxed in the presence of anhydrous aluminium chloride (1.0 g.) for 3 hr. gave an alkali soluble product which crystallised from acetic acid in shining yellow needles (0.3 g.), m.p. 342-43°.

Analysis : Found : C, 73.89 ; H, 3.31 %

$C_{26}H_{14}O_6$ requires : C, 73.93 ; H, 3.34 %.

Synthesis of 3,3'-dihydroxy-4,4'-bixanthonyl :

Ullmann reaction on 3-methoxy-4-iodoxanthone : 3,3'-Dimethoxy-4,4'-bixanthonyl :

3-Methoxy-4-iodoxanthone (1.0 g.) and copper bronze (1.0 g.) were heated in an oil bath at 250° for 20 min. and extracted with dimethyl formamide (10 ml.). The extract on dilution with water gave a white solid which crystallised from aqueous acetic acid in white needles (0.21 g.), m.p. 284-85°.

Analysis : Found : C, 74.24 ; H, 4.26 %

$C_{28}H_{18}O_6$ requires : C, 74.66 ; H, 4.00 %.

Demethylation :

A mixture of 3,3'-dimethoxy-4,4'-bixanthonyl (0.5 g.) and anhydrous aluminium chloride (1.0 g.) in benzene (50 ml.) was refluxed for 4 hr. The alkali soluble product obtained after working up, crystallised from acetic acid in yellow buds (0.24 g.), m.p. 375-77°.

Analysis : Found : C, 73.56 ; H, 3.56 %

$C_{26}H_{14}O_6$ requires : C, 73.93 ; H, 3.34 %.

Synthesis of 3,3',6,6'-tetramethoxy-4,4'-bixanthonyl :

3,6-Dimethoxy-4-iodoxanthone (1.0 g.) was baked with copper bronze (1.0 g.) at 260-80° for 20 min. and the mass extracted in dimethyl formamide (10 ml.). The solid obtained on dilution with water was purified by TLC using silica gel with chloroform as a solvent. The upper band which showed a dark blue fluorescence in UV light was the deiodinated 3,6-dimethoxyxanthone (m.p.180°), the middle band which showed light blue fluorescence was the bixanthonyl (m.p. 305-6°) and the last band was of the original 3,6-dimethoxy-4-iodoxanthone. The middle band was taken in chloroform and run again similarly

on TLC and then taken up in chloroform. After removing chloroform the product crystallised from acetic acid, in white needles (0.08g.), m.p. 305-6°.

Analysis : Found : C, 70.83 ; H, 4.43 %

$C_{30}H_{22}O_8$ requires : C, 70.58 ; H, 4.34 %.

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