SUMMARY

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Xanthones form a class of oxygen heterocycles and are compounds of interest as they occur in nature and possess pharmacological activity. Though many xanthones have been isolated and synthesised, no systematic study of substitution in xanthones has been attempted so far. As a part of the systematic study on substitution in different oxygen heterocycles such as flavones, isoflavones and coumarins going on in this laboratory, the present work was undertaken. It deals mainly with iodination, nitration and diazocoupling reactions on various hydroxyxanthones and the building up of 4'-pyrone and furan rings on hydroxyxanthones.

Chapter I contains a brief review of the methods of synthesis of xanthones and some important substitution reactions carried out on xanthones.

Chapter II deals with the iodination of 2-hydroxy-, 3-hydroxy-, 3-hydroxy-6-methoxy- and 3,6-dihydroxyxanthone. The iodination was carried out with iodic acid and iodine as well as with ammonia and iodine. Iodination of 2-hydroxy-xanthone gave only monoiodoxanthone. On the basis of the NMR data it was assigned 2-hydroxy-1-iodoxanthone structure. 3-Hydroxyxanthone gave 3-hydroxy-4-iodoxanthone, the structure of which was establishment on the basis of the NMR spectrum and an independent synthesis of 3-methoxy-4-iodoxanthone. Excess of iodine and iodic acid gave 3-hydroxy-2,4-diiodo-xanthone, the structure of which was also established.

from the NMR data. 3,6-Dihydroxyxanthone could be iodinated to get various iodo derivatives : 3,6-dihydroxy-4-iodo-, 3,6-dihydroxy-4,5-diiodo-, 3,6-dihydroxy-2,4,5-triiodo- and 3,6-dihydroxy-2,4,5,7-tetraiodoxanthone with iodine and iodic acid in different molecular proportions. The structures were established on the basis of the NMR spectra. 3-Hydroxy--6-methoxyxanthone gave 3-hydroxy-4-iodo-6-methoxyxanthone and 3-hydroxy-2,4-diiodo-6-methoxyxanthone with iodine and iodic acid in one and three molecular proportions respectively. Completely methylated xanthones could not be iodinated by iodine and iodic acid.

These iodoxanthones were subjected to Rosenmund-von Braun reaction. The mono and the diiodoxanthones gave the corresponding mono and dicyanoxanthones. 3,6-Dimethoxy-2,4,5-triiodoxanthone and 3,6-dimethoxy-2,4,5,7-tetraiodo-xanthone, however, gave the 3,6-dimethoxy-4,5-dicyanoxanthone which was also obtained from 3,6-dimethoxy-4,5-diiodoxanthone. The cyanoxanthones, however, could not be hydrolysed to the corresponding carboxylic acids either by refluxing with mineral acids or with alkali.

The monoiodoxanthones were subjected to Ullmann reaction and 2,2'-dihydroxy-1,1'-bixanthonyl, 3,3'-dihydroxy-4,4'-bixanthonyl and 3,3',6,6'-tetramethoxy-4,4'-bixanthonyl were obtained.

Nitration and diazocoupling of the hydroxyxanthones are discussed in Chapter III. Nitration of xanthones has been studied with sulphuric acid - fuming nitric acid mixture and

with fuming nitric acid in acetic acid. The coupling reaction is carried out with benzenediazonium chloride. Nitration of 2-hydroxyxanthone with fuming nitric acid in acetic acid gave 2-hydroxy-1-nitro- and 2-hydroxy-1,3-dinitroxanthone. The structures have been established on the basis of NMR spectra. Both were reduced to the corresponding aminoxanthones. using sodium dithionite. 2-Methoxy-1-aminoxanthone was converted into 2-methoxy-1-iodoxanthone through diazotisation and Sandmeyer reaction. The diazocoupling of 2-hydroxyxanthone gave 2-hydroxy-1-phenylazoxanthone. This was also reduced to 2-hydroxy-1-aminoxanthone by sodium dithionite. Attempts to convert 1-amino-2-hydroxyxanthone into 1,2-dihydroxyxanthone failed. 2-Methoxyxanthone could not be nitrated by acetic acid and fuming nitric acid, but it could be nitrated by fuming nitric and sulphuric acid mixture and gave a mixture of mono-, di- and trinitroxanthones. The alcohol soluble portion of this contained the mono- and the dinitroxanthone, and the alcohol insoluble one was the trinitro derivative. It has been tentatively assigned 1,3,7-trinitro-2-methoxy-xanthone structure.

Nitration of 3-hydroxyxanthone with fuming nitric acid in acetic acid gave 3-hydroxy-4-nitroxanthone which was also synthesised by an unambiguous method as described later. The filtrate contained three products as seen by TLC. These were found to be a mononitroxanthone, 3-hydroxyxanthone and the third probably a trinitroxanthone. On separating these on silica gel column the mononitroxanthone, melting at 238°

and different from 3-hydroxy-4-nitroxanthone was obtained to which 3-hydroxy-2-nitroxanthone structure has been tentatively assigned. The next fraction gave 3-hydroxyxanthone, while the last component which was in traces remained stronly adsorbed. 3-Hydroxy-4-nitroxanthone was synthesised starting with salicylic acid and 2-nitroresorcinol, the intermediate nitrobenzophenone being cyclised under pressure. 3-Hydroxy--4-nitroxanthone was reduced with sodium dithionite to 3-hydroxy-4-aminoxanthone. 3-Methoxy-4-aminoxanthone was also converted into 3-methoxy-4-iodoxanthone. Conversion of 3-hydroxy-4-aminoxanthone to 3,4-dihydroxyxanthone failed instead a cyclic azoxy compound was obtained. Coupling of 3-hydroxyxanthone with benzenediazonium chloride gave 3-hydroxy-4-phenylazoxanthone which could be reduced to 3-hydroxy-4-aminoxanthone. Similarly, the other mononitro-xanthone, 3-hydroxy-2-nitroxanthone was reduced to the amino-xanthone. Nitration of 3-hydroxyxanthone with nitric acid-sulphuric acid mixture gave a mixture of nitro compounds, of which some portion was soluble in methanol which showed on TLC the presence of two mononitroxanthones discussed earlier, the original 3-hydroxyxanthone and 3-hydroxy-2,4,7-trinitroxanthone. The alcohol insoluble product was purely the 3-hydroxy-2,4,7-trinitroxanthone, the structure of which was arrived at on the basis of the NMR spectrum.

Nitration of 3-hydroxy-6-methoxyxanthone with fuming nitric acid in acetic acid gave two mononitroxanthones

which were separated by column chromatography on silica gel. The one, which was in major quantity was found to be 3-hydroxy-4-nitro-6-methoxyxanthone, as seen from the NMR spectrum. The other one was assigned tentatively 3-hydroxy--2-nitro-6-methoxyxanthone structure.

Nitration of 3,6-dihydroxyxanthone with fuming nitric acid in acetic acid gave 3,6-dihydroxy-4-nitroxanthone. Methyl ether of this after reduction, diazotisation and treatment with potassium iodide gave 3,6-dimethoxy-4-iodoxanthone. With sulphuric acid and nitric acid mixture 3,6-dihydroxyxanthone gave 3,6-dihydroxy-2,4,5,7-tetranitroxanthone.

Coupling of 3,6-dihydroxyxanthone with benzenediazonium chloride gave 3,6-dihydroxy-4,5-di(phenylazo)-xanthone which could be reduced to 3,6-dihydroxy-4,5-diaminoxanthone. The structure of this was arrived at from the NMR data and the conversion of 3,6-dimethoxy-4,5-di(phenylazo)xanthone into 3,6-dimethoxy-4,5-diiodoxanthone, through reduction, diazotisation and Sandmeyer reaction with potassium iodide.

Methoxyxanthones could not be nitrated with fuming nitric acid in acetic acid in the proportion used for the hydroxyxanthones.

The last Chapter deals with the building up of 4'-pyrone and furan rings on xanthones.

Fries migration of 3,6-diacetoxyxanthone gave a mixture of 3,6-dihydroxy-4-acetylxanthone and 3,6-dihydroxy-2,5-diacetylxanthone. The structure of the mono-

acetylxanthone was established on the basis of the NMR spectrum of its methyl ether. 3,6-Dihydroxy-2,5-diacetylxanthone was benzoylated and the dibenzoyloxy derivative when subjected to Baker-Venkataraman transformation gave 2',2"-diphenyl-4',4"-dipyrono(6',5' : 3,2) and (6',5' : 6,5)xanthone.

When 3-benzoyloxy-4-acetylxanthone was subjected to Baker-Venkataraman transformation, debenzoylation occurred and 3-hydroxy-4-acetylxanthone was obtained back.

Pechmann condensation of ethyl acetoacetate with 2-hydroxy-, 3-hydroxy- and 3,6-dihydroxyxanthone failed. But attempt to prepare 4'-hydroxy-2'-pyrono derivative was successful with 3,6-dihydroxy-4-acetylxanthone which gave 4',6-dihydroxy-2'-pyrono(6',5' : 3,4)xanthone.

Cyanoethylation of 2-hydroxyxanthone and 3-hydroxyxanthone proceeded well but that of 3-hydroxy-6-methoxy and 3,6-dihydroxyxanthone failed. 2-β-Cyanoethoxyxanthone and 3-β-cyanoethoxyxanthone were hydrolysed by alcoholic hydrochloric acid to the corresponding 2- and 3-β-carboxyethoxyxanthone. Though the usual cyclising agents failed, acetic anhydride and sulphuric acid mixture worked well and gave the corresponding 4'-pyrano(6',5' : 2,1)xanthone and 4'-pyrano(6',5' : 3,4)xanthone. The structures of these cyclised products were arrived at from the NMR spectra. 4'-Pyrano(6',5' : 2,1)xanthone was dehydrogenated by palladised charcoal to 4'-pyrono(6',5' : 2,1)xanthone.

3,6-Diallyloxy- and 3-allyloxy-6-methoxyxanthone on Claisen rearrangement gave 3,6-dihydroxy-4,5-diallyl-xanthone and 3-hydroxy-4-allyl-6-methoxyxanthone respectively, the structures of both were proved by NMR spectra. The allyl derivatives on acetylation, bromination and further dehydro-bromination with alcoholic potassium hydroxide gave 2',2"-di-methyl difurano(5',4' : 3,4) and (5",4" : 6,5)xanthone and 2'-methyl-6-methoxyfurano(5',4' : 3,4)xanthone respectively.

Oxidation of 3,6-dimethoxy-4,5-diallylxanthone with potassium permanganate in acetone gave 3,6-dimethoxy-xanthone-4,5-dicarboxylic acid, while that of 3,6-dimethoxy-2,5-diacetylxanthone with alkaline potassium permanganate gave 3,6-dimethoxyxanthone-2,5-dicarboxylic acid.