CHAPTER-1

GENERAL INTRODUCTION

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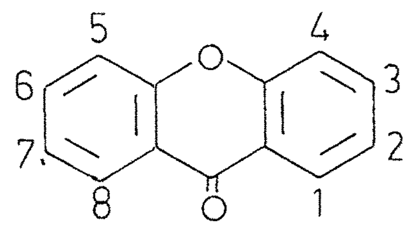
Since ancient time man has been using a variety of plants or their extracts for the curative effects and to get relief from routine ailments. The therapeutic value of these extracts has led man to systematically investigate the constituents of plants and their parts for obtaining medicinally active compounds. The chemistry of these substances which has its roots in the empirical knowledge of ancient medicines and finds its continuity in folk medicines even today makes a valuable contribution to the discovery of new drugs.

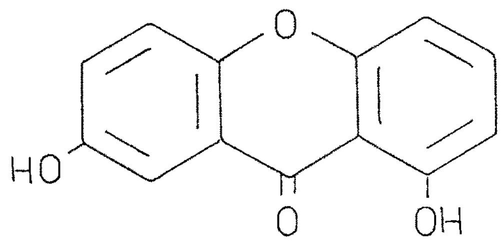
From the extracts of certain part of some plants the active constituents were isolated and their structures established by chemical and spectral studies. The structures were then confirmed by unequivocal syntheses. Recently, many such structures have been used as models in the search for better drugs. Highly sophisticated instrumentation techniques have been contributed significantly towards isolation, purification and structure elucidation. A number of compounds have been isolated, with varying structural patterns identified and synthesised. Heterocyclics (xanthone, isoflavone, quinoline, carbazole, coumarin, etc.) occupy a predominant position due to their wide occurrence in nature and their use in chemotherapy. They have attained considerable importance because of their therapeutic value and varied structural and chemical properties.

The term xanthone, from the Greek, meaning yellow, designates the chemical compound dibenzo-γ-pyrone (1).



Many xanthones have been isolated from plants and other sources. In plants they occur either in combination with glucose or xylose or both or in an uncombined state. A few representative members occuring in nature are given below.

Euxanthone[1] (2) (Chart 1) is a yellow pigment present in the heartwood of plantonia insignis Mart. Swertinin[2] (3) (Chart 1) and Decussatin[2] (4) (Chart 1) are found in Swertia decussata, the former being located in the stem and the latter in the Flowers. Ravenelin[3] (5) (Chart 1) is a fungal metabolite, while Lichexanthone[4] (6) (Chart 1) is a yellow pigment found in the lichen Parmelia formosana. Mangiferin[5] (7) (Chart 2) is a pigment present in the bark of the tree, Mangifera indica. Mangostin[6] (8) (Chart 2) is a major pigment latex of the mangosteen tree, Garcinia magostana L. Sterigmatocystin[7] (9) (Chart 2) is a metabolite of Aspergillus versicolour (Vuillemin) Tiraboschi, while Maculatoxanthone[8]



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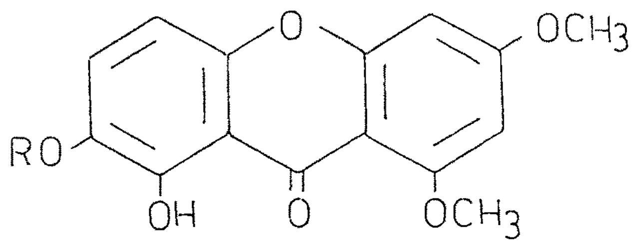
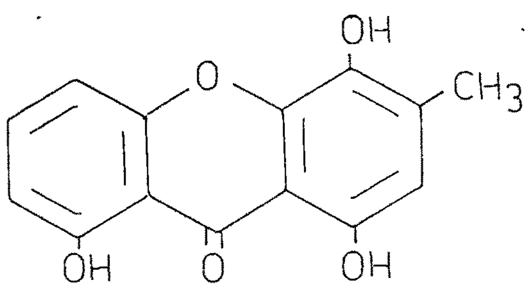


3 R=H
4 R=CH_3



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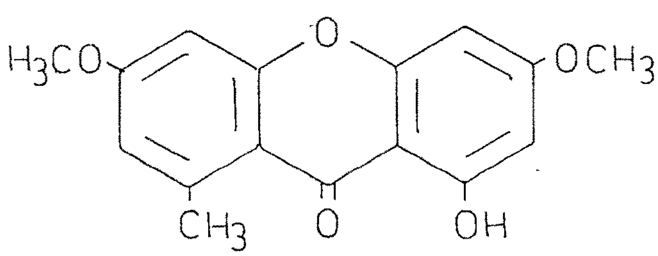

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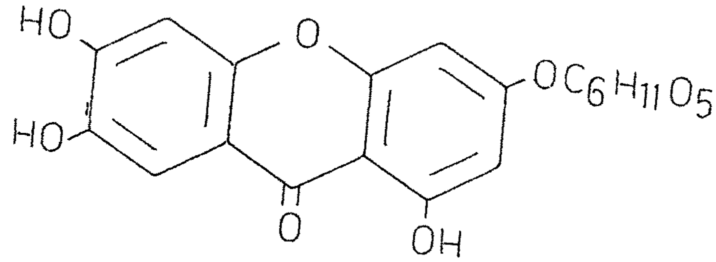
CHART-1



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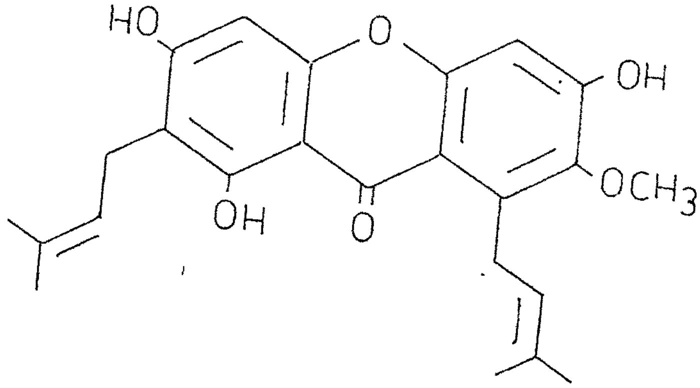

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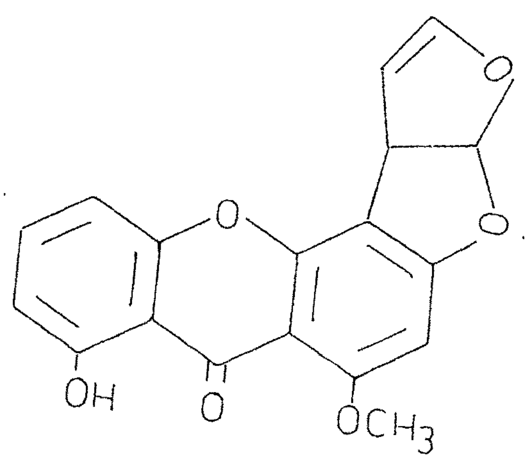

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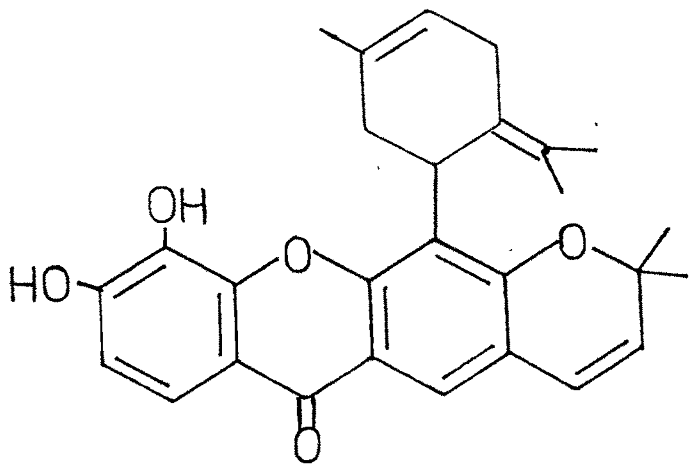
CHART-2

(10) (Chart 3) is a xanthone with a monoterpene side chain isolated from the roots of Hypericum Maculatum. Five metabolites were isolated from mycelial mats of A.Multicolor sappa[9] (i) 5,6-dimethoxy sterigmatocystin (ii) 5,6-dimethoxy-dihydro sterigmatocystin (iii) Sterigmatocystin (iv) averutin and (v) versicolorin C. A New xanthone[10] (11) (Chart 3) have been isolated from Hypericum Ericoides xanthone[11] (12) (Chart 3) was isolated from the culture broth of Cyathus intermedius.

The reviews[12-18,19,20] are the excellent sources of information on naturally occurring xanthone derivatives. Recently many workers have isolated xanthones from plants like Brazilian Guttifereae[21], Guttifereae[22], Gentiancea[23], Mammea amerikana[24], etc. and have used spectral data for arriving at the structures. TaJixanthone (13) (Chart 4) and shamixanthone (14) (Chart 4) were isolated as fungal metabol ites of Aspergillus veriecolor[25] and their structures were established[26] by ^{1}H and ^{13}C NMR spectral studies. Trapezifolixanthone (15) (Chart 4) a new diisoprenylated xanthone was isolated from Calophylum trapezifolium Thw.[27] and its synthesis has been reported by Anand and Jain.[28] Three laxanthones, 1,3-dihydroxy-6,7-dimethoxyxanthone (16) (Chart 5) 1-hydroxy-3,6-diacetoxy-7-methoxyxanthone (17)[29] (Chart 5) and 1-hydroxy-3,7-dimethoxy-6-acetoxyxanthone (18)[30] (Chart 5) were isolated from Lawasonia intermis. A review on



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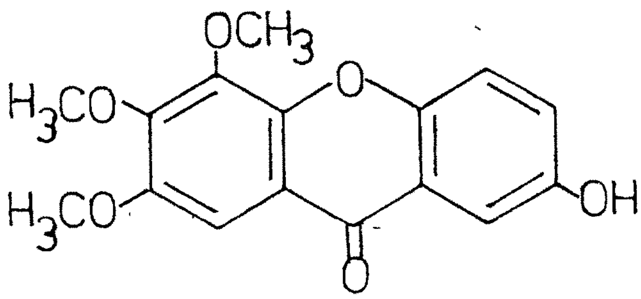

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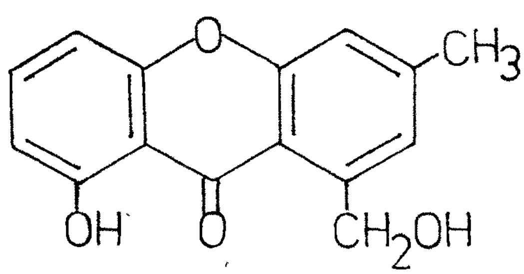

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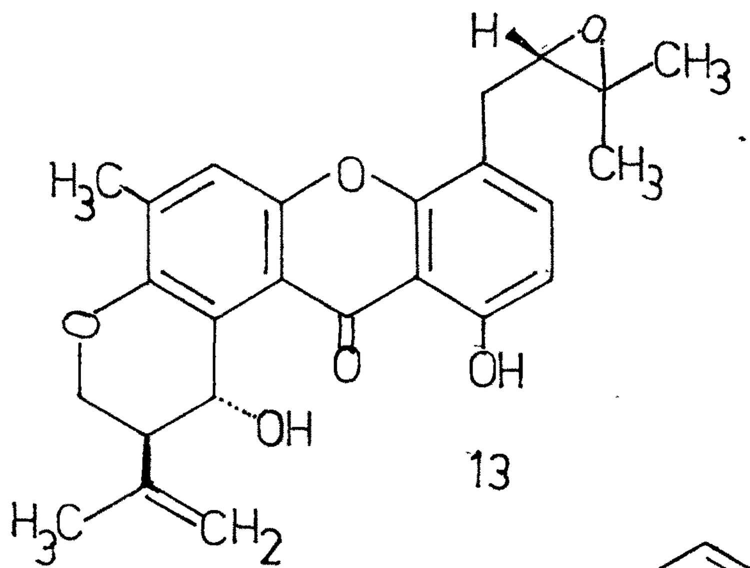
CHART – 3



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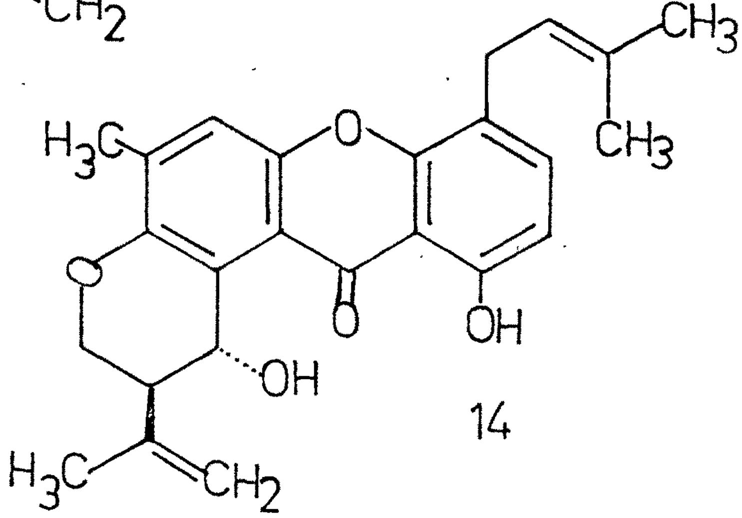

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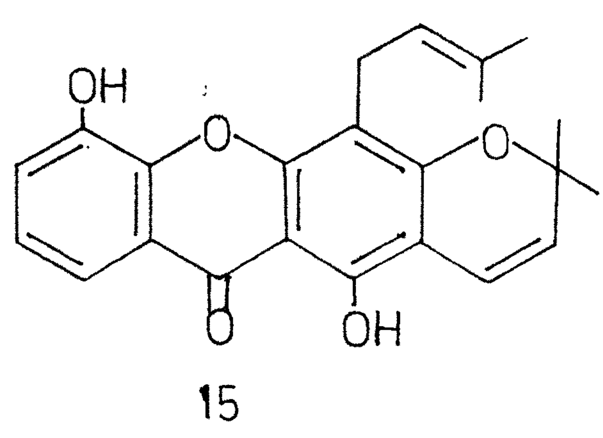

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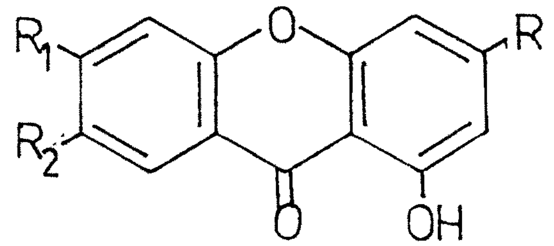
CHART- 4

naturally occuring xanthone glucosides with their chemotaxonomic significance is reported by Hosteffmann and Wagner.[31]

Xanthones have diverse pharmacological properties (antisychotic, antiallergic, tuberculostatic, bronchodilator etc.).[32-36] They are used as insecticides[37,38] and in the control of codling moth,[39] mites,[39,40,41] chicken-louse[42], acarid[43] and cabbage insect.[44] Xanthones have been tried in termite control,[45,46] and have been found to act as a termite deterrant in wood.[47]

Bromoxanthones have been found to act as urinary antiseptics,[48] while some of the aminoxanthones possess antibacterial activity.[49] Antibiotic activity was shown by some nitro- and amino-[50,51] as well as hydroxyxanthones.[52] Xanthones such as (19) (Chart 5) and its methyl ether are active antitubercular agents[53] and Miracil-A (20) (Chart 5) is active against bilharziasis (Schistosomiasis).

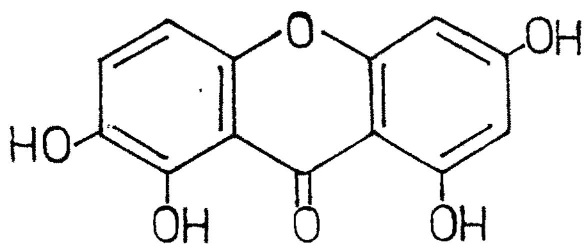
Xanthones with antiinflammatory,[54-59] antisecretory[54] and antiulcerogenic[54] properties have also been reported. Substituted xanthones suited for the treatment of the extrinsic asthma, hay fever, nettle rash, eczema and allergic dermatitis, are also reported.[60] 2-substituted xanthones such as (21) (Chart 6) showed β-adrenergic blocking potency.[61-62] Xanthones containing a tetrazole ring such as (22) (Chart 6)



16 R=OH R_1= R_2=OCH_3

17 R= R_1=$OCOCH_3$ R_2= OCH_3

18 R= R_2=OCH_3 R_1= $OCOCH_3$



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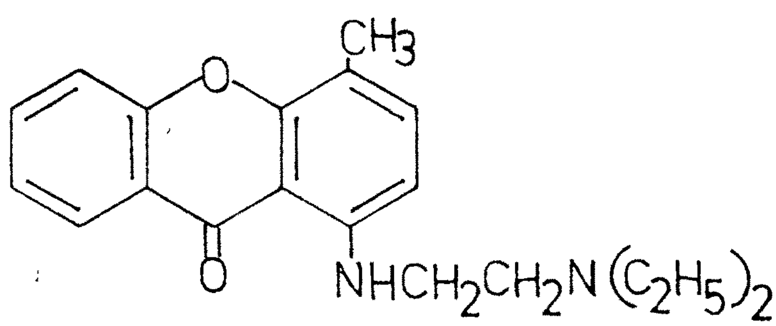

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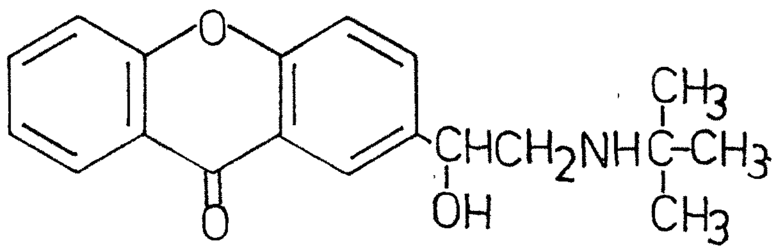
CHART - 5



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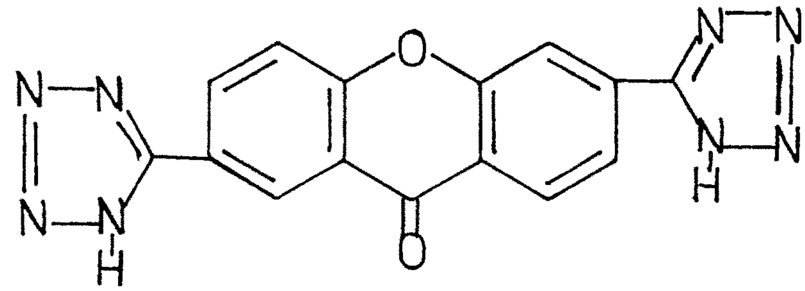

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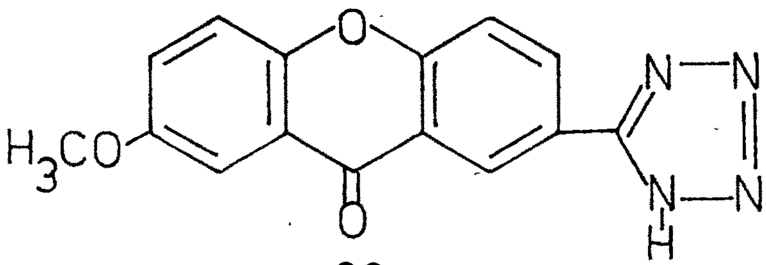

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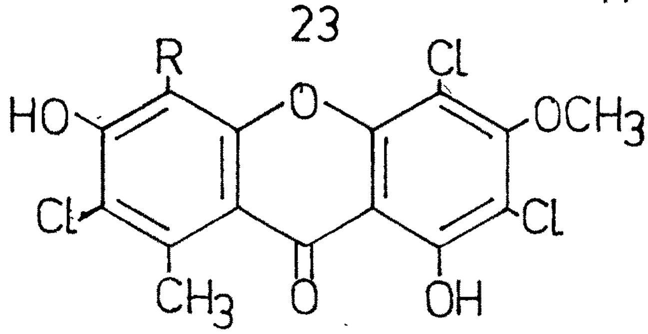

24 R=Cl

25 R=H

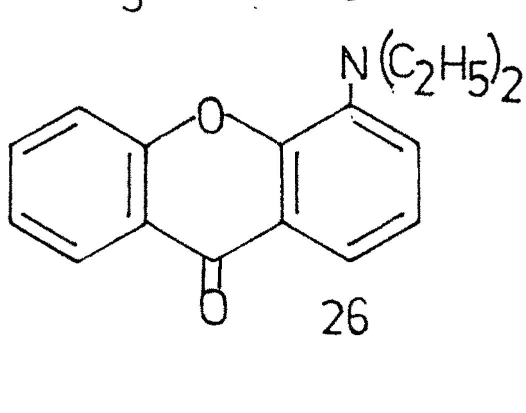

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CHART-6

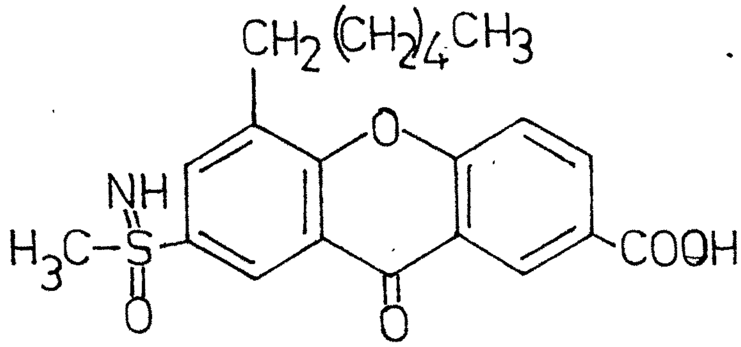
and (23) (Chart 6) are useful as antiallergics especially in the treatment of asthma.[63,64]

Monopotassium salts of xanthones such as (24) (Chart 6) and (25) (Chart 6) are found to be plant growth regulators.[65] Xanthone carboxylic acids and esters have been used as anti-histamines.[66-69] Da Re et al.[70-73] have synthesised a large number of mannich bases from xanthones. They reported[73] that 3-methoxy-4-diethylaminoxanthone (26) (Chart 6) exhibits the most powerful CNS stimulating activity, with favourable therapeutic index. Goldberg and Walker[74] have reported some N-substituted xanthones possessing antimalarial activity. Finnegan et al.[75] have reported that out of eighteen xanthones from Mammea amerikana, 1,6-dihydroxy-and 1,3-dihydroxyxanthone were the most potent inhibitors of sarcoma - 180 in vitro.

Anti-allergic and anti-asthamatic activity of xanthone-2--carboxylic acid derivatives were determined.[76] Inhibition of hypersensitivity reactions by novel xanthone (27) (Chart 7) is described.[77] Xanthone (28) (Chart 7) containing sulphur and phosphorus, kill mosquitoes at 10 ppm concentration.[78]

The present work deals with the synthesis of hydroxy-xanthones, synthesis of bromo-, furano-and pyrano xanthones.

Chapter II deals with the synthesis of some naturally occuring hydroxyxanthones, synthetic hydroxyxanthones and miscellaneous xanthone derivatives using the novel one step method for the synthesis of xanthones.



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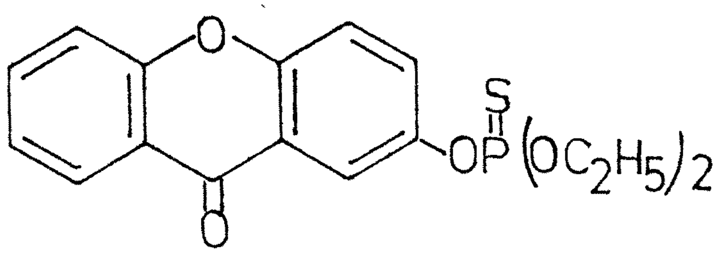

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CHART – 7

Chapter III describes the bromination studies of 1-hydroxy-, 2-hydroxy-, 3-hydroxy-, 7-bromo-, 3-hydroxy-, 1-hydroxy-3-methyl-, 3-hydroxy-4-methylxanthone and synthesis of 7-bromo-1-hydroxy and 7-bromo-3-hydroxyxanthone.

Chapter IV incorporates the synthesis of some bromo furanoxanthones, 5'-methyl furano, difurano, 5'-phenylfurano, 5'-methyl-4'-phenyl furano-, 5'-isopropyl furanoxanthones, starting from different hydroxy and bromohydroxyxanthones.

Chapter V deals with the synthesis of some pyrano xanthones by Claisen migration of propynyloxyxanthones and studies on Claisen migration of some prenyloxy xanthones.

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