CHAPTER-2

SYNTHESES OF XANTHONES

THEORETICAL

SYNTHESES OF XANTHONES

Xanthones are widely distributed in nature. Hence, many methods are available and they have been exhaustively reviewed[1] in the "Total Synthesis of Natural Products". However, some of these syntheses are briefly outlined below:

Pyrolysis of benzoic acid derivatives

Xanthone can be obtained by pyrolysis of either 2-hydroxybenzoic acid or its arylester or alkali salts of 2-halobenzoic acids.

2-Hydroxybenzoic acid and 2-hydroxynapthoic acid are converted into xanthone and benzoxanthone by distillation of the acid either alone[2] or in the presence of tungsten oxide or vanadium pentoxide and the distillation of the aryl ester[4] or the acetates.[5] Preparation of simple xanthone from salol by its distillation is the best example of this method (Fig.1).

Many dibenzoxanthones have been prepared by Kamel and Shoeb[6] and Parija et al.[7] In the preparation of hydroxyxanthones by this method dixanthone (1) (Fig.1) is often produced as a by product. Moreover, side reactions like decarboxylation and auto condensation are also possible.

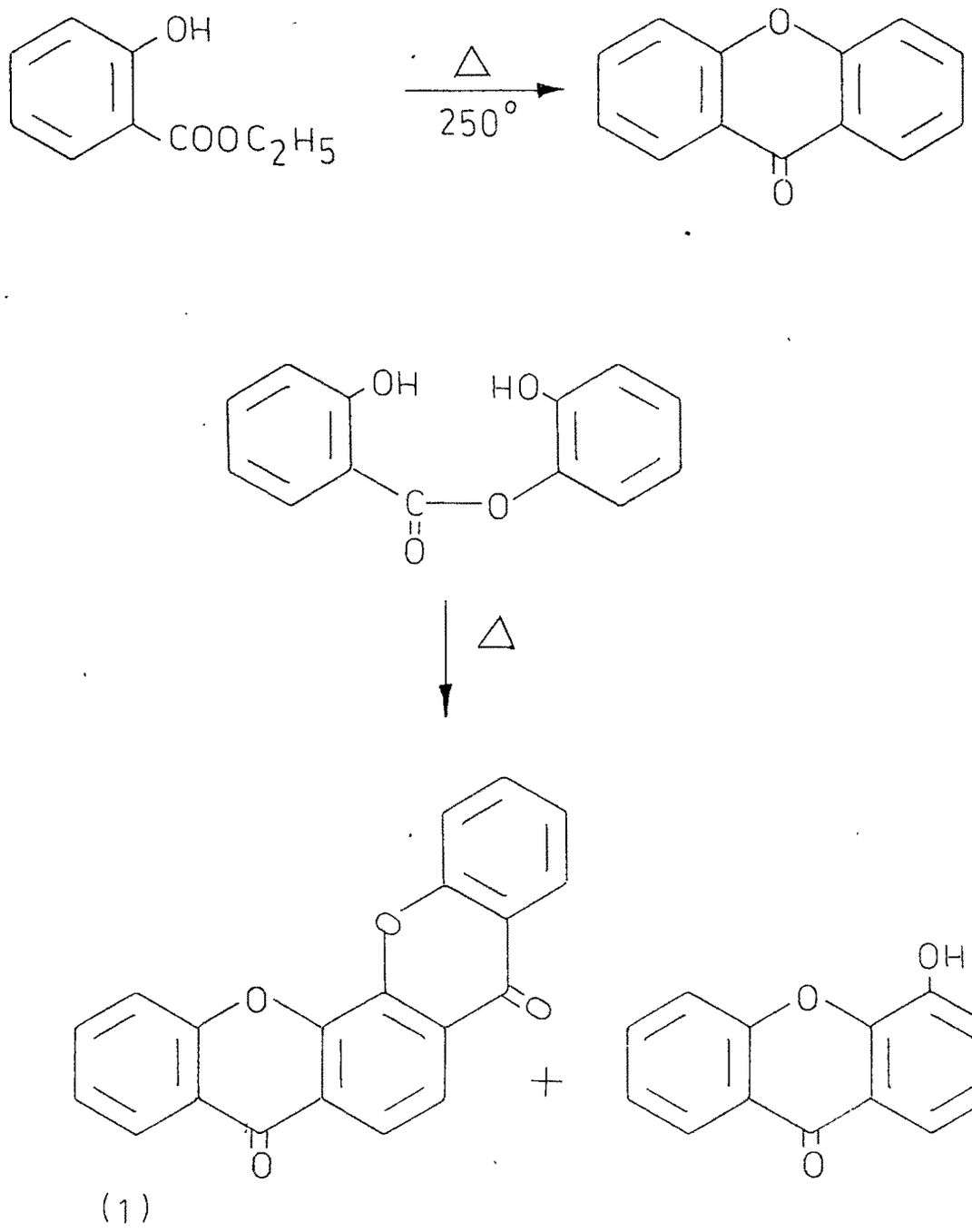


FIG - 1

Kochi[8] has reported that the alkali salts of 2-halobenzoic acids decompose smoothly at 325-80° in vacuum to produce xanthone in 50 to 70% yield. The synthesis of octafluoroxanthone[9] and other haloxanthone is also reported.[10]

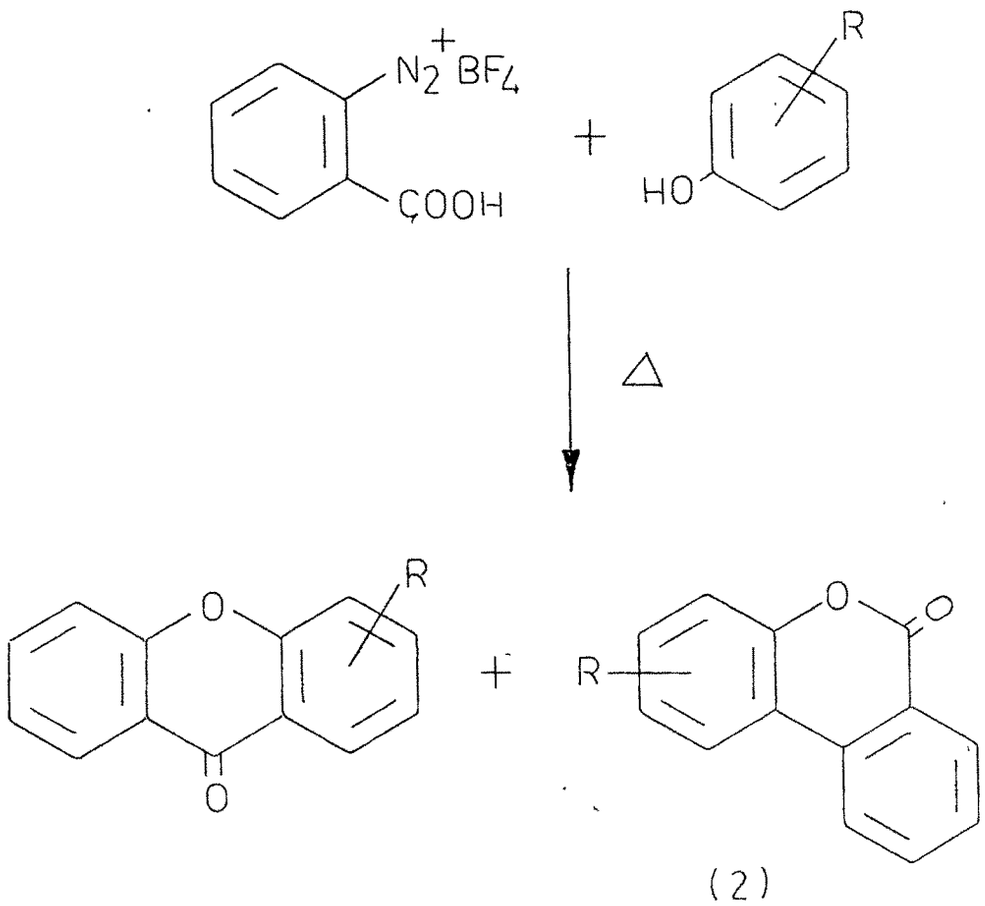
Sellers and suschitzky[11] have developed a novel pyrolysis method for the preparation of xanthones. They have carried out pyrolysis of 2-carboxyphenyldiazonium tetrafluoroborate in phenols and aryl diazonium tetra fluoroborate in substituted salicylic acid. In some cases xanthones are accompanied by 3,4-benzocoumarin (2). The thermolysis in phenols can be illustrated as shown in (Fig.2).

From diphenyl ether derivatives

Xanthones can be obtained from two types of diphenyl ethers, (A) from diphenyl ether 2-carboxylic acids and (B) from diphenyl ethers in which 2,2'-position are not occupied (Asahina - Tanase method).

(A) From diphenyl ether-2-carboxylic acids

In this method a diphenyl ether-2-carboxylic acid is first prepared by reaction between a phenol and 2-chlorobenzoic acid, and this is then cyclised to a xanthone. Diphenyl ether-2-carboxylic acid can be directly prepared



(2)

FIG-2

either by Ullmann[12] reaction or by treating 2-diazonium chloride benzoic acid with phenol.[13] The method has very wide applications and has been used for preparing unsymmetrical xanthones.

Koelsch and Lucht[14] carried out the condensation between 2-chlorobenzoic acid and 3-nitrophenol in presence of copper bronze and cuprous iodide in amyl alcohol. The use of other solvents like nitrobenzene, hexylalcohol and anisole has also been reported.[15] The synthesis of 2-hydroxy xanthone from 4-methoxyphenol and 2-chlorobenzoic acid was achieved in a better yield by Davies and Collegues.[16] The use of potassium carbonate along with copper bronze and cuprous iodide was reported.[17]

Mathner[18] also synthesised 3'-methoxydiphenyl ether-2-carboxylic acid from sodium-2-chlorobenzoate and 3-methoxy phenol, using copper powder and sodium methoxide. This method has been further used by many workers.[19-26]

Cyclisation of the diphenyl ether 2-carboxylic acid to xanthone can be carried out in excellent yields by heating or with acidic reagents such as sulphuric acid,[27] acetyl chloride,[28] a mixture of these,[29] thionyl chloride, phosphorus pentachloride,[30] oxalic acid,[31] oxyalyl chloride,[32] phosphorus pentoxide,[33] phosphorus oxychloride,[34,35] stanic chloride[36] and phosphorus pentachloride-aluminium chloride

in benzene.[18] Cyclisation of the acid chloride with aluminium chloride[37] has also been carried out. The synthesis of euxanthone[38](3) (Fig.3) may be taken as an example of this method.

(B) Asahina - Tanase method

Asahina and Tanase have cyclised substituted diphenylethers to xanthones by oxalyl chloride in the presence of aluminium chloride.[39,40] 2-phenoxybenzoyl chloride must be the intermediate in the formation of xanthone by this method, since oxalyl chloride is decomposed by aluminium chloride into phosgene and carbon monoxide.[41] The reaction may be illustrated by the example of 1-methoxyxanthone (4) as shown in (Fig.4).

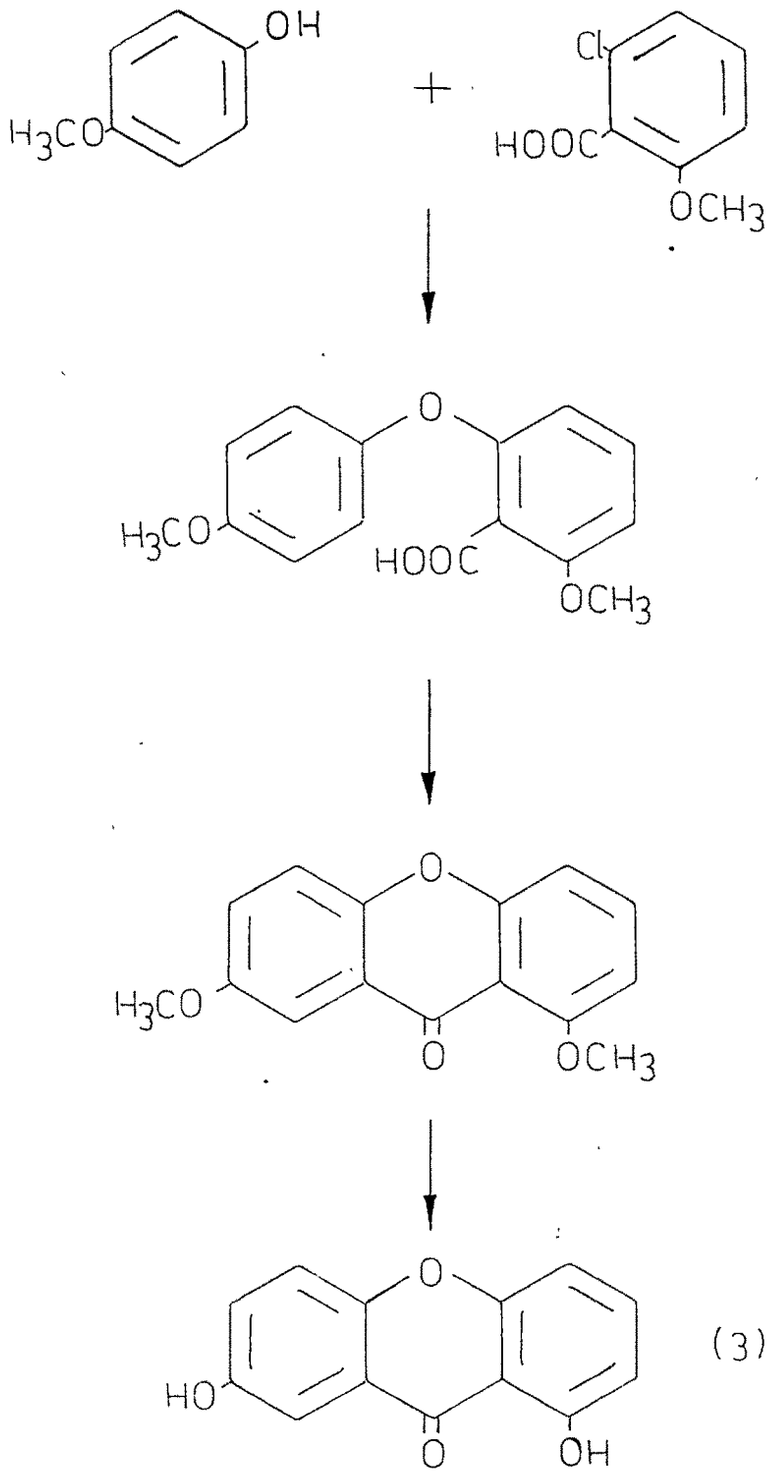
The method has been used for the preparation of 3-methoxy-, 3-methyl-, 2,3-dimethoxy-, 3,6-dimethyl- and 2,6-dimethoxyxanthone. Recently, Granoth et al.[42] have prepared 6-bromo-2-chloro and 6-bromo-2-fluoroxanthone by this method.

From benzophenone derivatives

A suitable benzophenone derivative obtained by any one of the following methods can be cyclised further to get the desired xanthone.

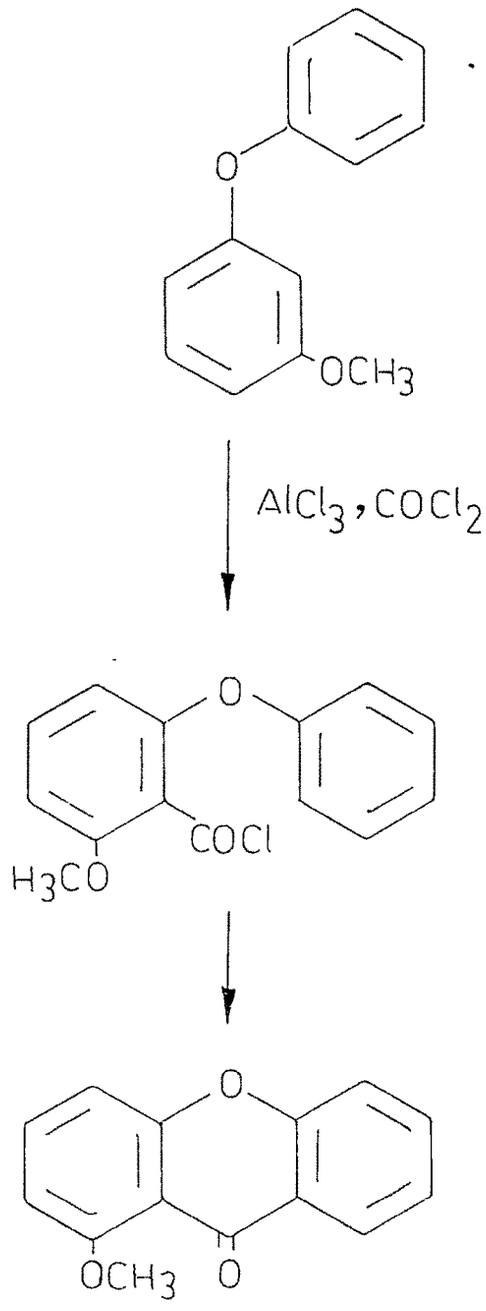
(A) Michael - Kostanecki method

In this method equimolecular proportions of a polyhydroxy



(3)

FIG-3



(4)

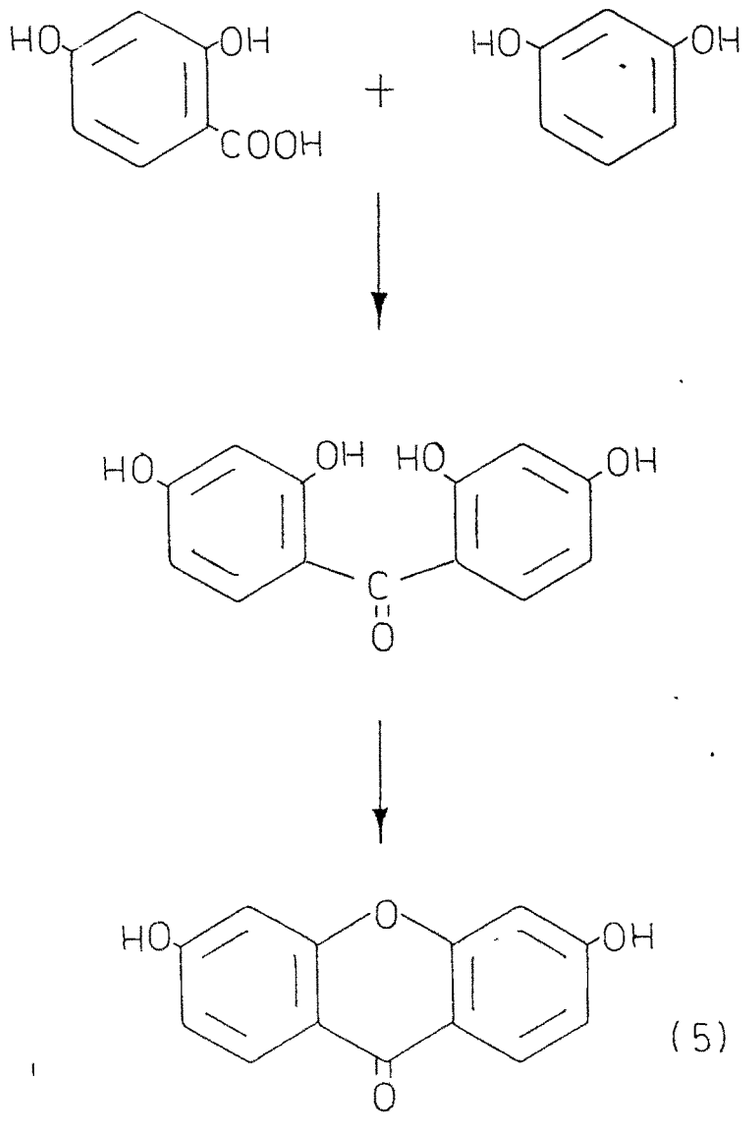
FIG-4

phenol and 2-hydroxybenzoic acid are heated with dehydrating agents such as acetic anhydride[43] or zinc chloride,[44-46] PPA[47] to get 2,2'-dihydroxybenzophenone. A modification of this method by Grover, Shah and Shah,[48,49] consists in the use of a mixture of phosphorus oxychloride and zinc chloride as condensing agent.

In this method a mixture of o-hydroxybenzoic acid, a phenol, anhydrous zinc chloride and an excess of phosphorus oxychloride was heated at 70-80^{o} to obtain benzophenone or xanthone derivative. If hydroxybenzophenone was formed as an intermediate, it was dehydrated to the hydroxyxanthone by heating at 200-220^{o} with water in a sealed tube,[50] dilute acids,[51] con. H_2SO_4,[52] or acetic anhydride in pyridine.[53] The hydroxyxanthones were obtained directly when the acidic component is a 2,6-dihydroxybenzoic acid or phloroglucinol carboxylic acid or when phenol is phloroglucinol or orcinol i.e. when the intermediate hydroxybenzophenone carries another hydroxy group at the 6- or 6'-position, as the alternative site for the cyclization is available. The method also worked well when one or both the components are methylated.

The synthesis of 3,6-dihydroxyxanthone (5) may be taken as an example to illustrate this method, (Fig.5).

Kulkarni et al,[54] have condensed different acids like o-vanillic, o-veratric, o-cresotic, m-cresotic with reactive



(5)

FIG-5

phenols such as phloroglucinol, orcinol, pyrogallol, resorcinol to obtain corresponding xanthone derivatives. At present this method has received greatest popularity amongst many research workers.[55-63] Scheinmann and coworkers[58] have recommended the use of aluminium chloride alongwith zinc chloride and phosphorus oxychloride, when the mixture of the two condensing agents failed to give desired product.

(B) Robinson-Nishikawa method

This method,[51,64] a variant of Hoesch synthesis, proceeds through a ketimino compound (6). 2,2'-Dihydroxy benzophenone obtained by alkaline hydrolysis of the ketimino compound can be cyclised to xanthone by one of those reagents discussed earlier. Thus salicylonitrile and phloroglucinol can be condensed to get 1,3-dihydroxyxanthone (7) (Fig.6).

(C) Oxidative coupling method

Lewis[53] has reported that 2,3,4-trihydroxybenzophenone (8) can be cyclised to 2,6-dihydroxyxanthone (9) (Fig.7) in high yield by oxidative coupling with potassium ferricyanide. Thus 2-hydroxybenzophenones can be cyclised to xanthones by this method.

Lewis et al,[65] have also suggested the use of DDQ for oxidative coupling and have explained the coupling on the

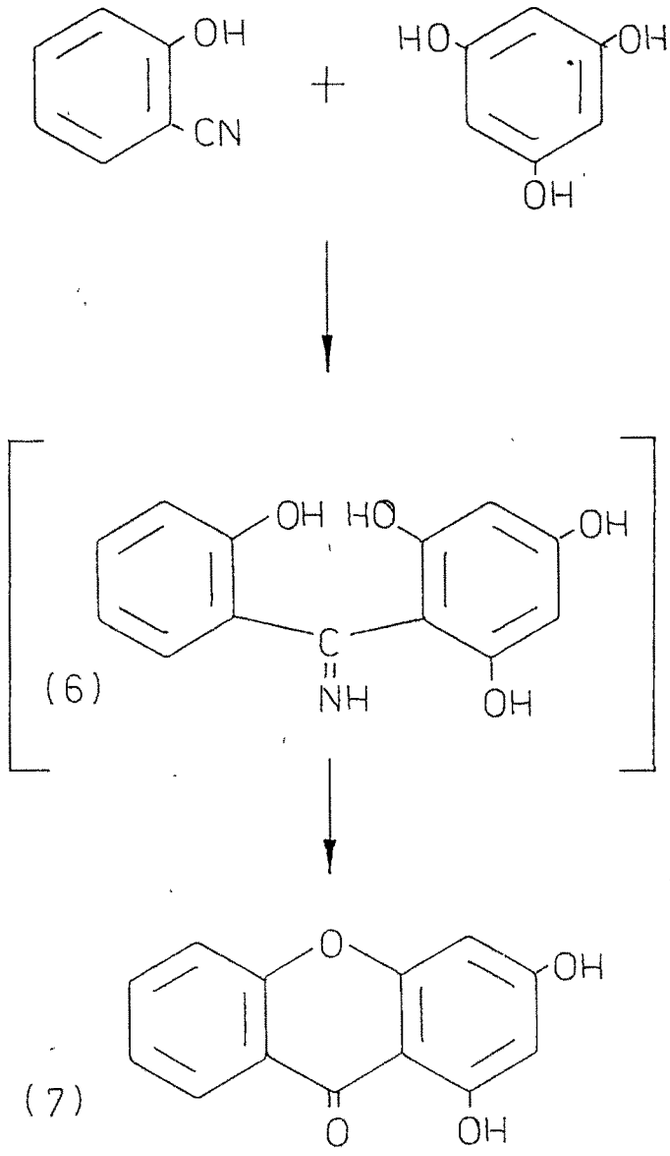


FIG - 6

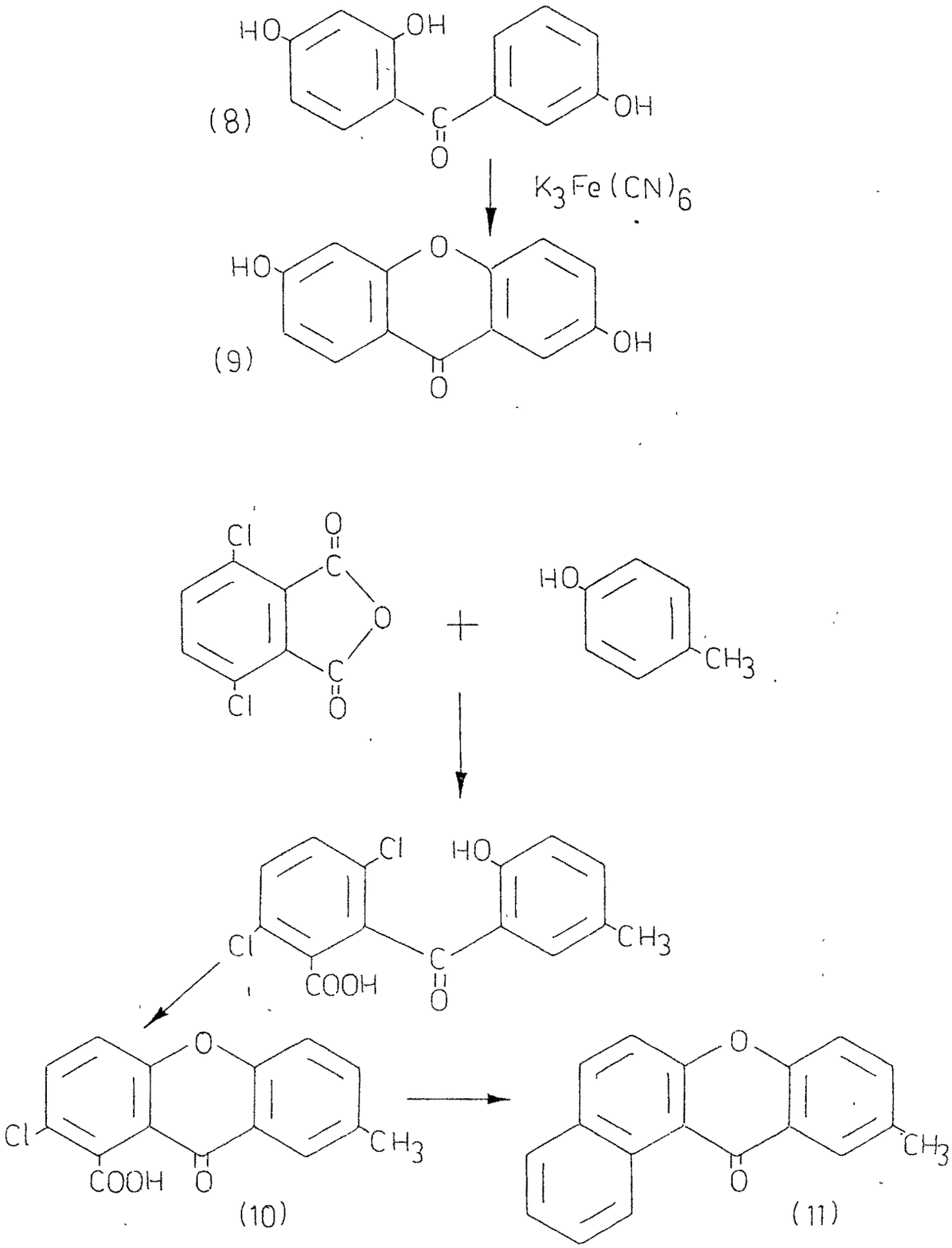

HO
OH
OH
(8)
$K_3Fe(CN)_6$
HO
OH
(9)
Cl
Cl
HO
CH_3
Cl
HO
CH_3
COOH
Cl
COOH
CH_3
(10)
CH_3
(11)

FIG-7

basis of formation of phenoxonium ion as an intermediate. They[66] extended this method to cyclise 3'-amino-2-hydroxy-benzophenone by potassium ferricyanide and potassium dichromate and studied the reaction over a pH range of 0-14. Locksley and Murray[67] have suggested the use of DDQ, manganese (III) tris (acetonylacetonate), and manganese dioxide for oxidative coupling.

(D) From 2-halo-2'-hydroxy (or methoxy) benzophenone

Ullmann and Schmidt[68] have prepared 2-methyl-5,6,7-trichloroxanthone-8-carboxylic acid from 2,3,4,5-tetra-chloro-6-carboxy-2-hydroxy-5-methylbenzophenone by cyclising the latter with 33% sodium hydroxide solution. Anna Marie and Ullmann[69] have prepared 2-methyl-7-chloroxanthone-8-carboxylic acid (10) and further 2-methyldixanthone (11) (Fig.7) from the latter by the same method.

Royer et al[70] have reported the synthesis of many xanthones such as 2-hydroxy-, 2-methyl-, 2-methyl-6-nitro, and 3-hydroxy-6-chloroxanthone from the corresponding 2-halo (chloro or bromo)-2'-methoxy benzophenones. The cyclisation was induced by pyridine-hydrochloride.

(E) By Friedel - Crafts method

Gentisin (12) (Fig.8) has been synthesised[71] by Friedel-Crafts method. In this method a suitable 2-methoxy

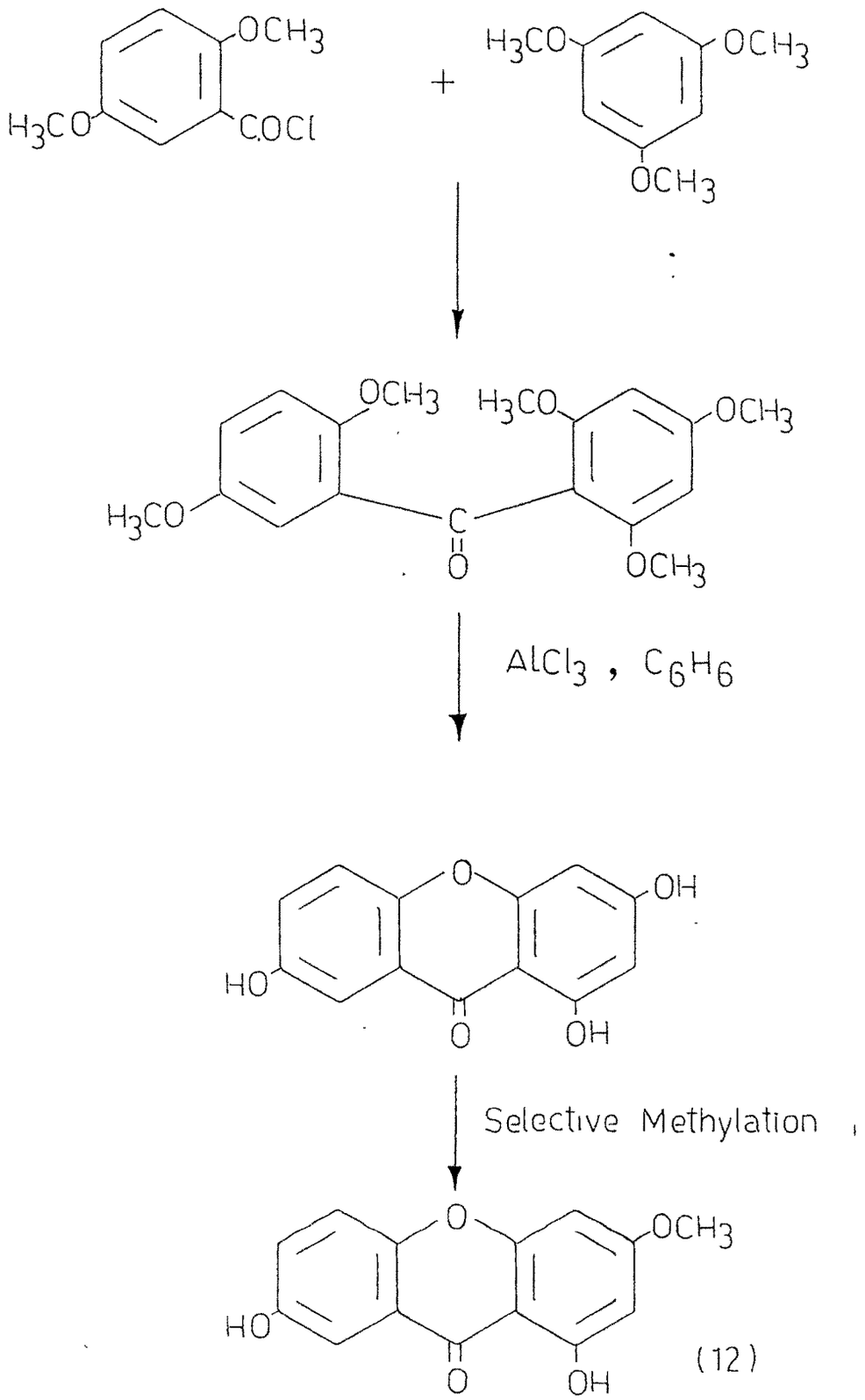

OCH3
H3CO
COCl
+
H3CO
OCH3
OCH3
OCH3
H3CO
OCH3
H3CO
C
O
OCH3
AlCl3 , C6H6
O
OH
HO
O
OH
Selective Methylation
O
OCH3
HO
O
OH
(12)

FIG-8

benzoyl chloride is condensed with fully methylated phenol in the presence of aluminium chloride. The benzophenone is demethylated and simultaneously cyclised by aluminium chloride in benzene.

Stout et al[72,73] have prepared polyoxygenated xanthones by this method. The intermediate 2-hydroxy-2'-methoxybenzophenone obtained was cyclised by the action of tetramethylammonium hydroxide in pyridine by the elimination of methanol. Recently, Scheinmann and Quillinan[74] have prepared many oxygenated xanthones by Friedel-Crafts method. For cyclising the intermediate 2-hydroxy-2'-methoxy benzophenone, they have used different alkaline agents such as, aqueous sodium hydroxide in methanol, piperidine, aqueous potassium carbonate in methanol or tetramethyl ammonium hydroxide in aqueous pyridine. They have also discussed some effective reagents such as boron trichloride, pyridine and DDQ in methanol for the preparation of xanthones with hydroxy and methoxy functions. 2-Hydroxy-2'-methoxy benzophenones can be cyclised by other alkaline reagents such as 2% alcoholic potassium hydroxide[75] and 1N potassium hydroxide in a nitrogen atmosphere.[76]

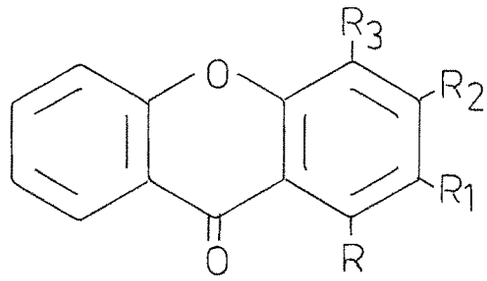
Finnegan and Merkel[77] have prepared 2,5-dihydroxy and 4,5-dihydroxyxanthones, for which the benzophenones were obtained by photo Fries migration.

PRESENT WORK

From the above review it is revealed that a number of methods have been developed for the synthesis of xanthones. They usually consist of more than one step reactions which requires good condensing agents like zinc chloride, aluminium chloride, boron trichloride, zinc chloride and phosphorus oxychloride mixture or PPA. The condensing agent must be completely free from water and its purity becomes an important factor in the synthesis because an impure condensing agent leads to the failure of the reaction or to poor yields. Such difficulties are not observed in the present one step method. It is a simple and convenient method which is adopted for the general syntheses of xanthones.

The present one step synthesis of xanthone is an extention of the novel one step method developed by Patolia and Trivedi.[79,80] They carried out the condensation of different phenols with Ethyl Salicylate in refluxing diphenyl ether to get xanthone derivatives in good yields. The details of the work is given in Table No.1. This method is a modification of the method,[81] which was adopted for the syntheses of chromones and flavones by the thermal condensation of phenols with β-ketonic ester in boiling diphenyl ether.

Table No.1



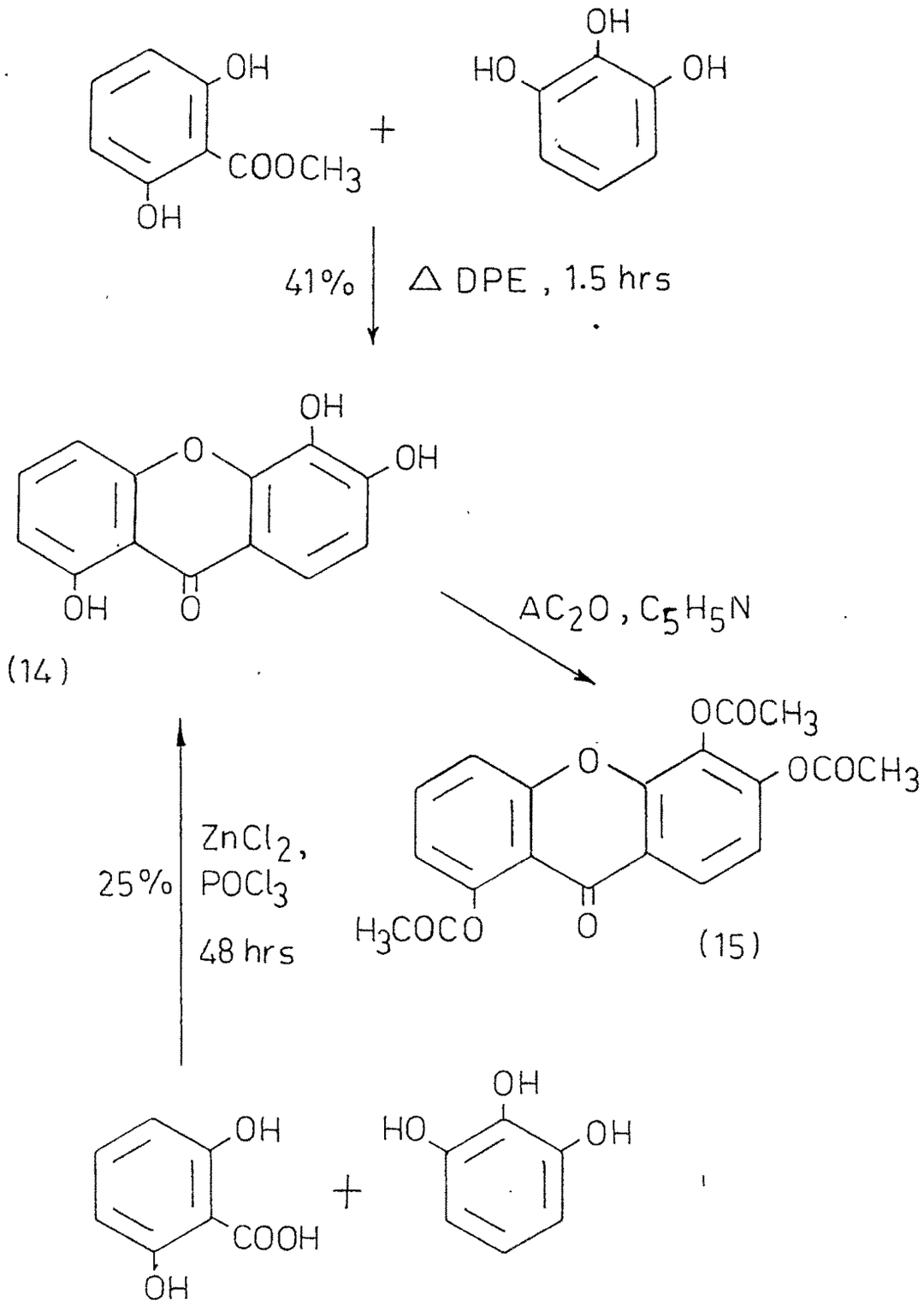
13

	R	R_1	R_2	R_3	Yield %	Reaction period. hr.
a	OH	H	H	H	8	20
b	H	H	OH	H	31	20
c	OH	H	OH	H	57	1
d	H	H	OH	OH	48	57
e	OH	H	CH_3	H	8	8-11
f	CH_3	H	OH	H	53	8-11
g	H	H	OH	CH_3	37	16-18
h	H	H	H	OH	12	20

In the present investigation, with a view to check the feasibility of one step synthesis of xanthones[79,80] with differently substituted phenyl salicylates and its applicability for the synthesis of naturally occuring xanthones, Condensation of differently substituted phenyl salicylates viz. methyl-2,6-dihydroxybenzoate, methyl-2,4-dihydroxybenzoate, methyl 2,4,6-trihydroxybenzoate etc., were carried out with various phenols in refluxing diphenyl ether to get corresponding xanthone in a good yield. The detailed studies have been done for the condensation of ethyl salicylate with hydroquinone, which may throw light on the reaction mechanism,

Condensation of pyrogallol with methyl 2,6-dihydroxybenzoate Mesuaxanthone B (1,5,6-trihydroxyxanthone) (14)

Pyrogallol on thermal condensation with methyl-2,6-dihydroxybenzoate for 1.5 hr in refluxing diphenyl ether afforded mesuaxanthone B in a good yield (41%) (lit[49]; 25%) m.p. 287° (lit.,[49] 285°). The structure of which was confirmed by i.r. mass and NMR spectrum of its acetoxy derivative (15) m.p. 210° (lit[49]; 210°). Mass m/e 370, 328, 319, 299. IR (KBr) νmax 1775, 1760 (-COO-), 1655 (C=O, γ-pyronyl) NMR ($CDCl_3$) (Fig.9) showed two doublets of J=9Hz at δ 8.15 and δ 7.2 which is attributed to protons H-8 and H-7 respectively, 7.6, d, td, J=9,9,2Hz, 1H, H-6, 7.37 double doublet for one proton J=9,2Hz, H-5,, 7.01, dd, J=9,1.5Hz,, 1H, H-2 further more it shows three singlets around δ 2.5 indicating that it is a triacetoxy derivative.



Mesuaxanthone B

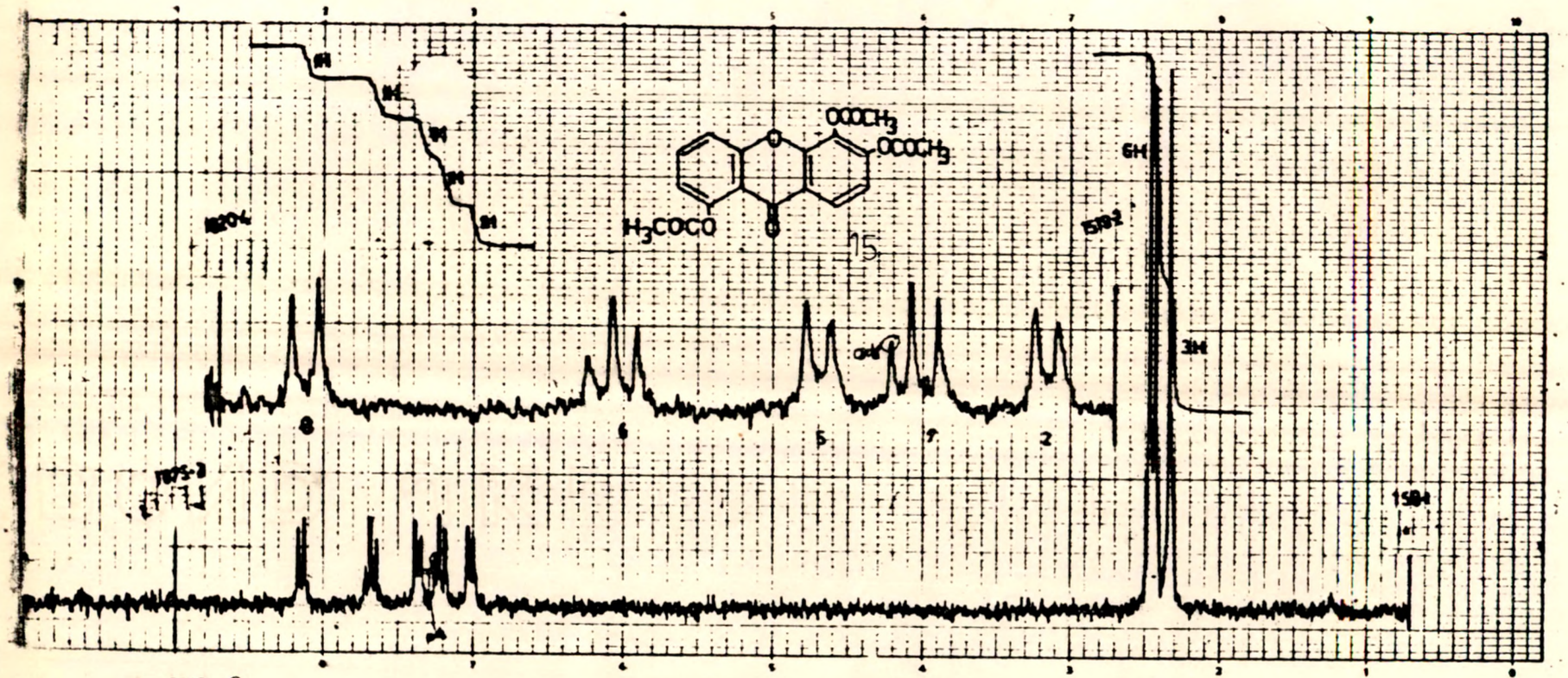


FIG 9

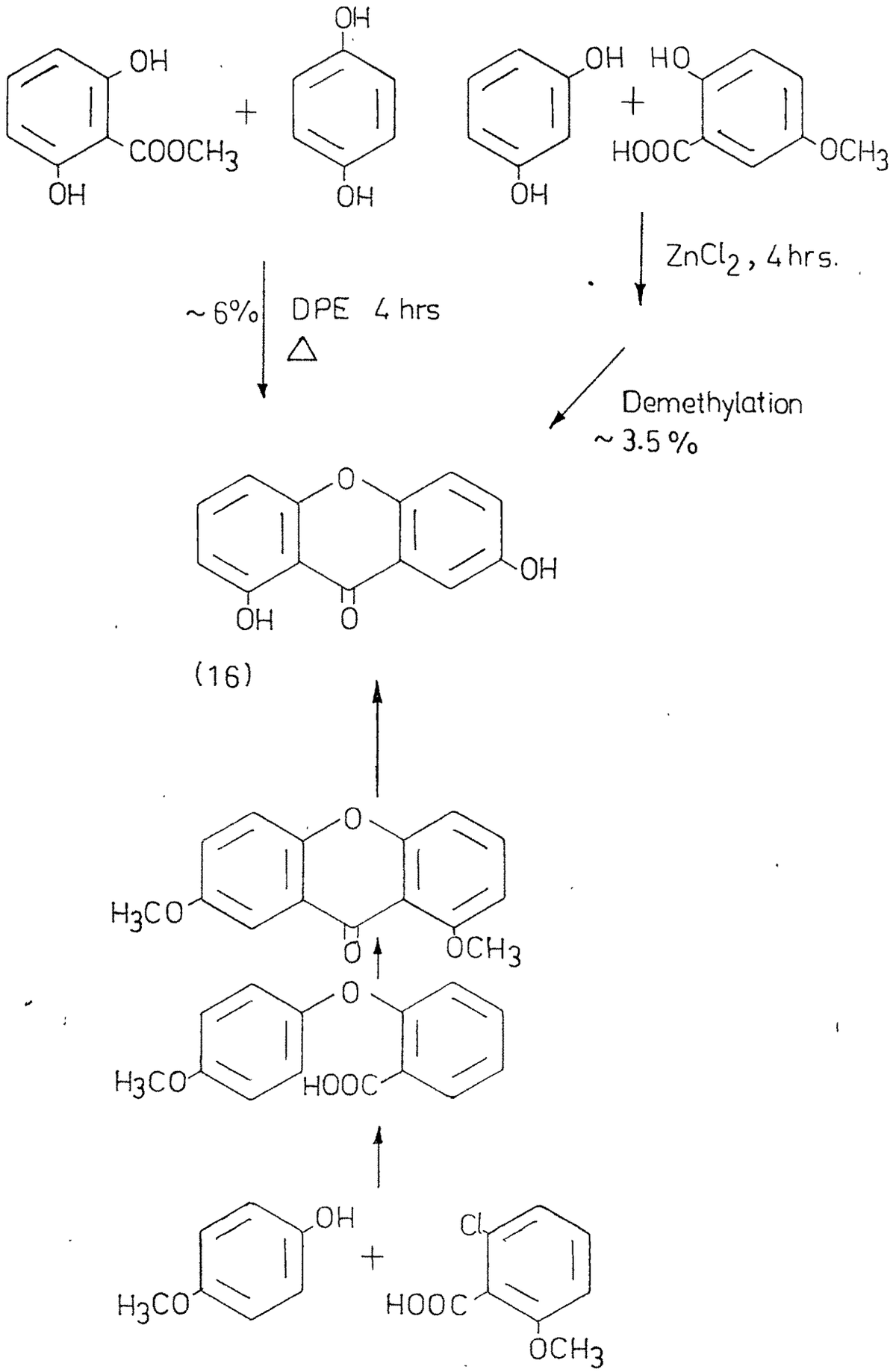
Condensation of hydroquinone with methyl 2,6-dihydroxy benzoate : Euxanthone (1,7-dihydroxyxanthone) (16)

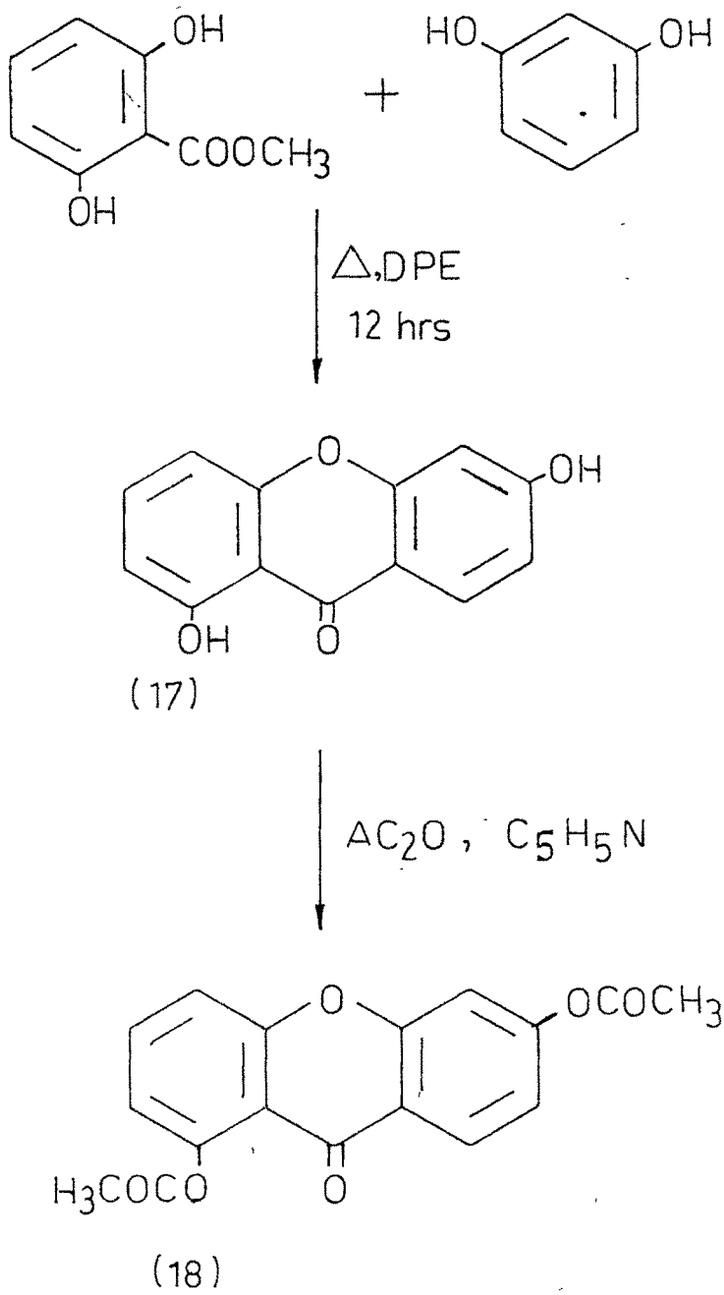
A mixture of hydroquinone and methyl 2,6-dihydroxybenzoate was refluxed with diphenyl ether for 8 hr. The product, obtained after steam distillation, was chromatographed over silica gel and eluted with benzene to give a yellow solid which further crystallised from benzene to yield Euxanthone in a comparatively good yield (6%) m.p. 230-32° (lit.,[38] 236-39°). The mass and NMR spectrum confirmed the structure. Mass : m/e 228, 212, 200. IR (KBr) νmax 3100-3330 (br-OH), 1630 (C=O, γ-pyronyl) NMR (See Experimental).

Condensation of resorcinol with methyl 2,6-dihydroxy benzoate : 3,8-Dihydroxyxanthone (17)

A mixture of resorcinol and methyl 2,6-dihydroxybenzoate was refluxed in diphenyl ether for 12 hr. The steam distillation of reaction mixture gave the product, which was characterized as 3,8-dihydroxyxanthone (17). m.p. 240° (lit.,[48] 246°).

It was acetylated with acetic anhydride and pyridine to give sodium hydroxide insoluble diacetate (18) m.p. 140°. NMR ($CDCl_3$) spectrum of which showed two singlets at δ 2.31 and 2.49 for 6H, two $OCOCH_3$; 7.0, double


OH
OH
COOCH3
OH
+
OH
OH
+
OH
HO
HOOC
OCH3
OH
ZnCl2, 4 hrs.
~ 6%
DPE 4 hrs
△
Demethylation
~ 3.5 %
O
OH
OH
O
(16)
O
H3CO
O
OCH3
O
H3CO
HOOC
OH
H3CO
+
Cl
HOOC
OCH3


OH
COOCH3
OH
+
HO
OH
△,DPE
12 hrs
O
OH
OH
O
AC2O , C5H5N
O
OCOCH3
H3COCO
O

(17)

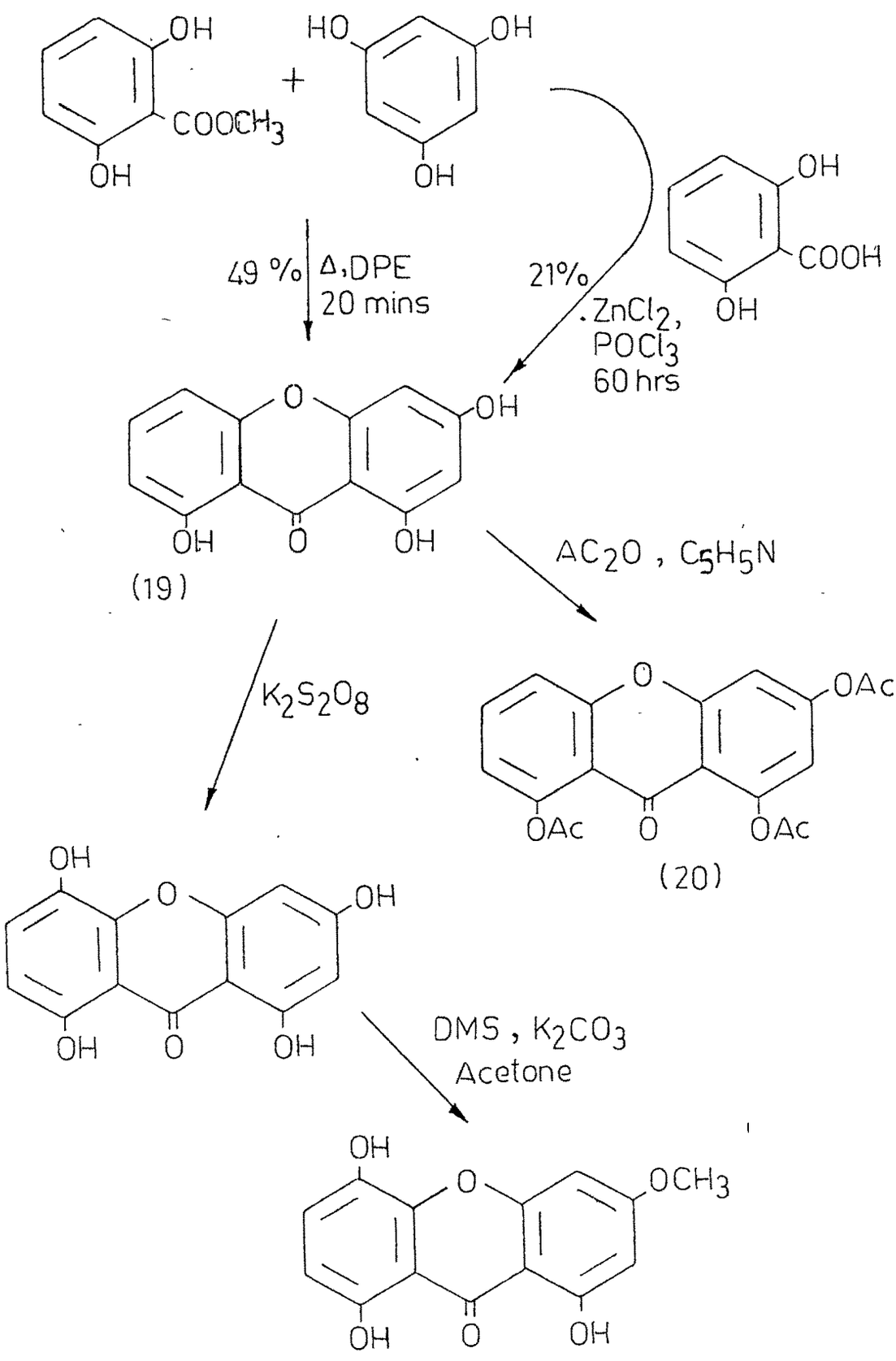
(18)

doublet for 2H, J=9,2.5Hz, H-2 and H-7, only one singlet in the down field aromatic region at δ 7.25 which could be attributed to the proton at position 4 ; 7.35, double doublet, 1H, J=9,2Hz for proton H-5, 7.65, t, 1H, J=9Hz proton at 6 position and δ 8.25 doublet for one proton J=9Hz, H-1. This confirms the assigned structure (18).

Condensation of phloroglucinol with methyl 2,6-dihydroxy benzoate : 1,3,8-Trihydroxyxanthone (19)

A starting material for the naturally occuring xanthone (Belladifolin) was obtained in a good yield, by the condensation of phloroglucinol with methyl 2,6-dihydroxy benzoate in boiling diphenyl ether for 20 min. The reaction mixture after steam distillation furnished the product, which was washed with sodium bicarbonate solution and then with water to give the titled compound (19) yield (49%), m.p. 258° (lit.,[49] 258-9°).

The product on acetylation with acetic anhydride and pyridine gave a triacetoxy derivative (20) m.p. 185°. This does not give any colour with ethanolic ferric chloride, and was insoluble in sodium hydroxide, suggesting that it is a fully acetylated compound. NMR ($CDCl_3$) (Fig.10) of which showed two singlets, one at δ 2.35 for the three protons and another at 2.45 for the six protons confirming that it is



Belladifolin

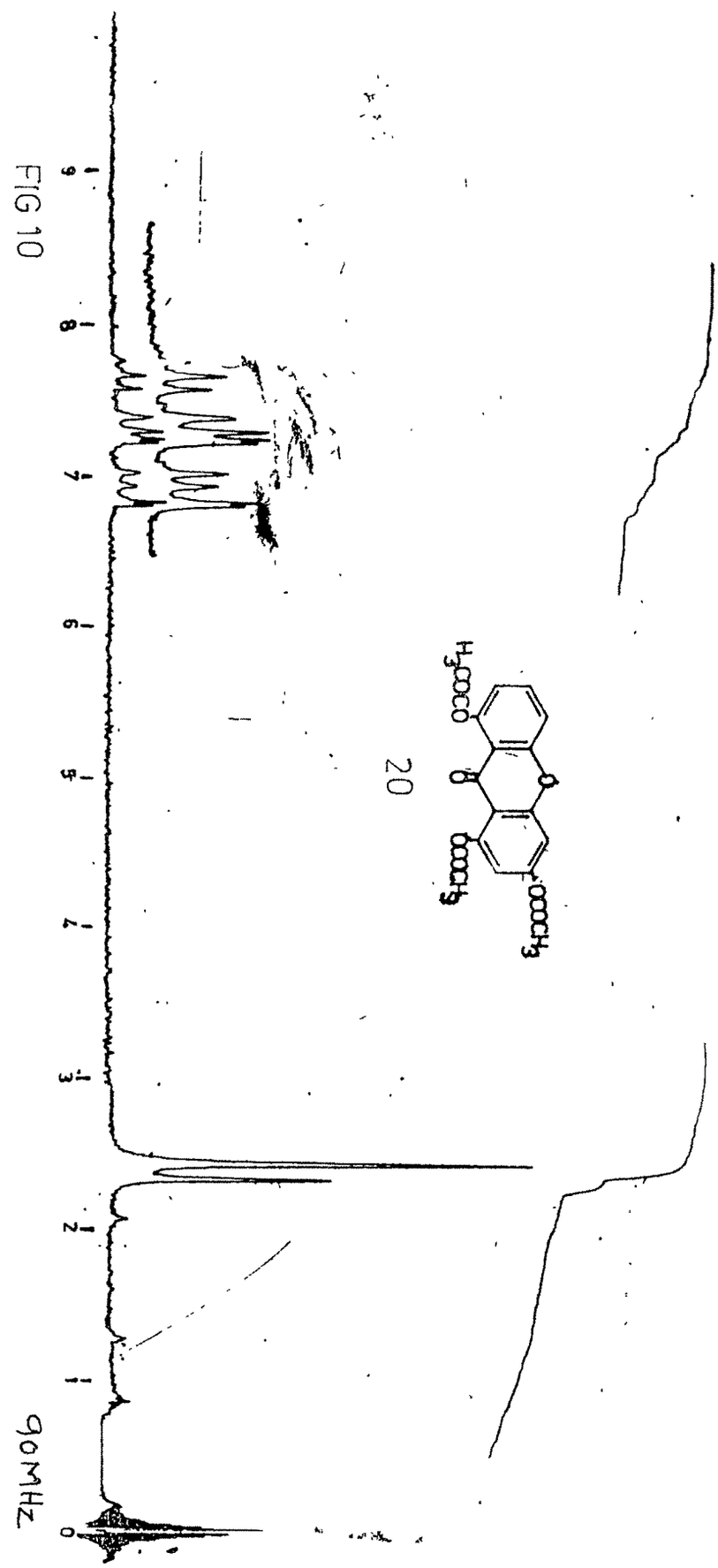
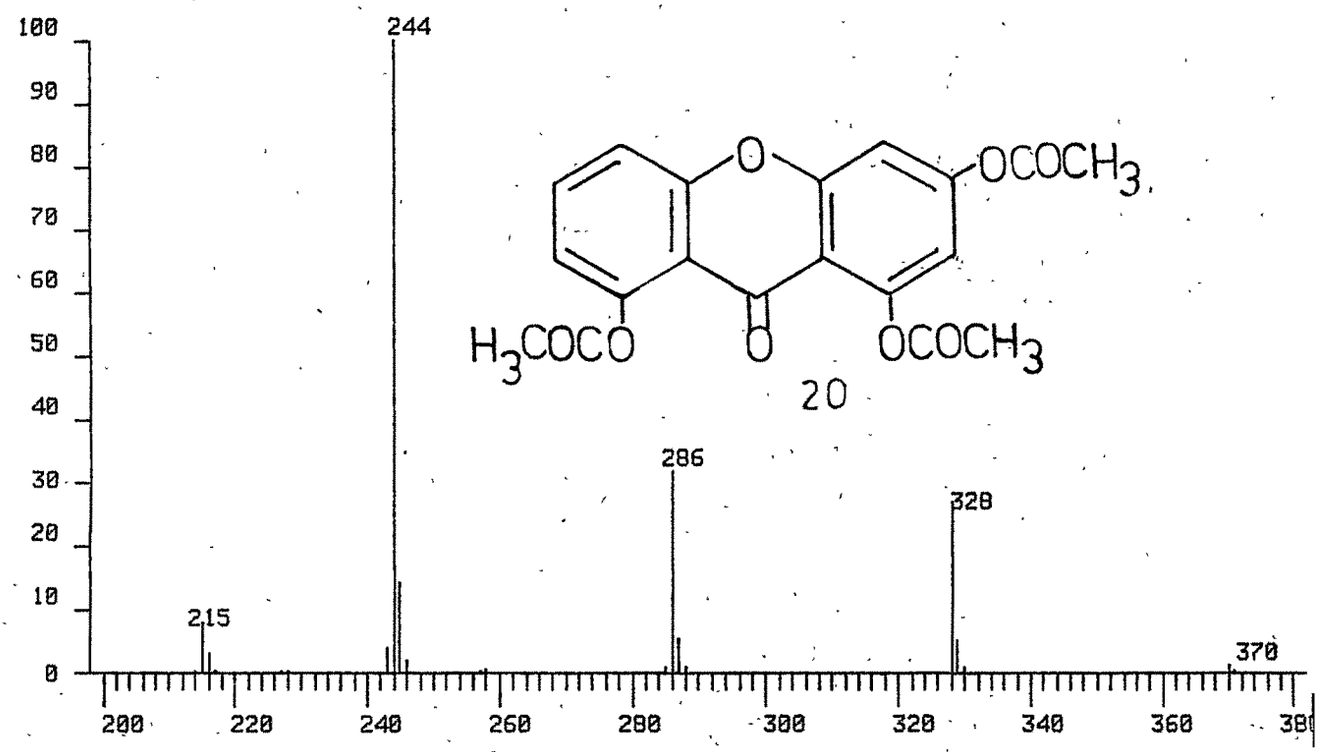


FIG 10


100
90
80
70
60
50
40
30
20
10
0
244
286
328
215
370
200
220
240
260
280
300
320
340
360
O
OCOCH3
H3COCO
O
OCOCH3

20

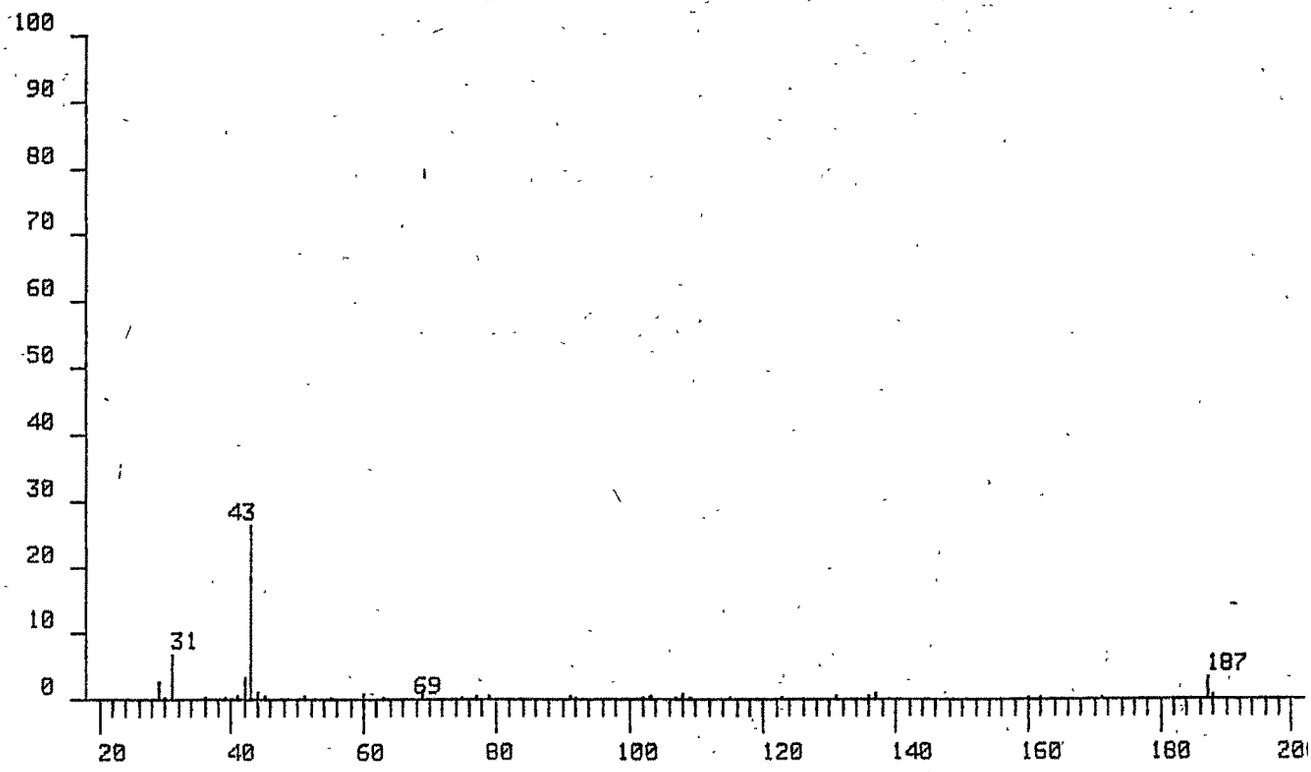

100
90
80
70
60
50
40
30
20
10
0
43
31
69
187
20
40
60
80
100
120
140
160
180

FIG 11

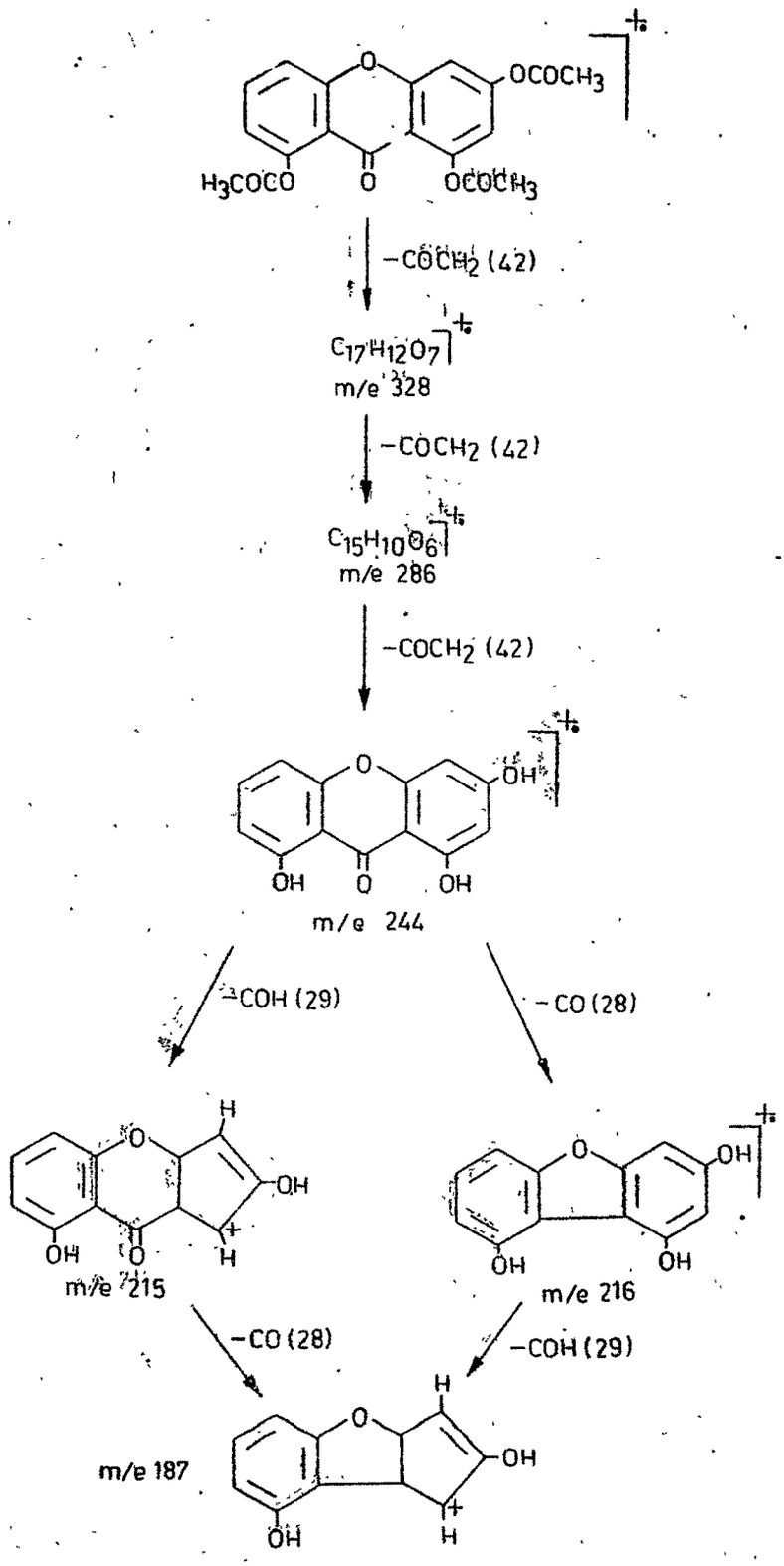
a triacetoxy derivative. In the aromatic region it showed two doublets of J value 2Hz at 7.25 and 6.82 for the protons H-5 and H-2 respectively, one triplet was observed at δ7.78 which is attributed to the proton H-6, two double doublets of J=9, 1.5Hz was appeared at δ 7.35 and 7.0 for the protons H-5 and H-7, confirms the assigned structure. further more its mass spectrum shows molecular ion peak at 370 from which three successive loss of ($-COCH_2$) 42 unit was observed and then followed the usual fragmentation of xanthone (see Scheme 1) giving full support to the assigned structure.

Condensation of catechol with methyl 2,6-dihydroxybenzoate: 1,5-Dihydroxyxanthone (21)

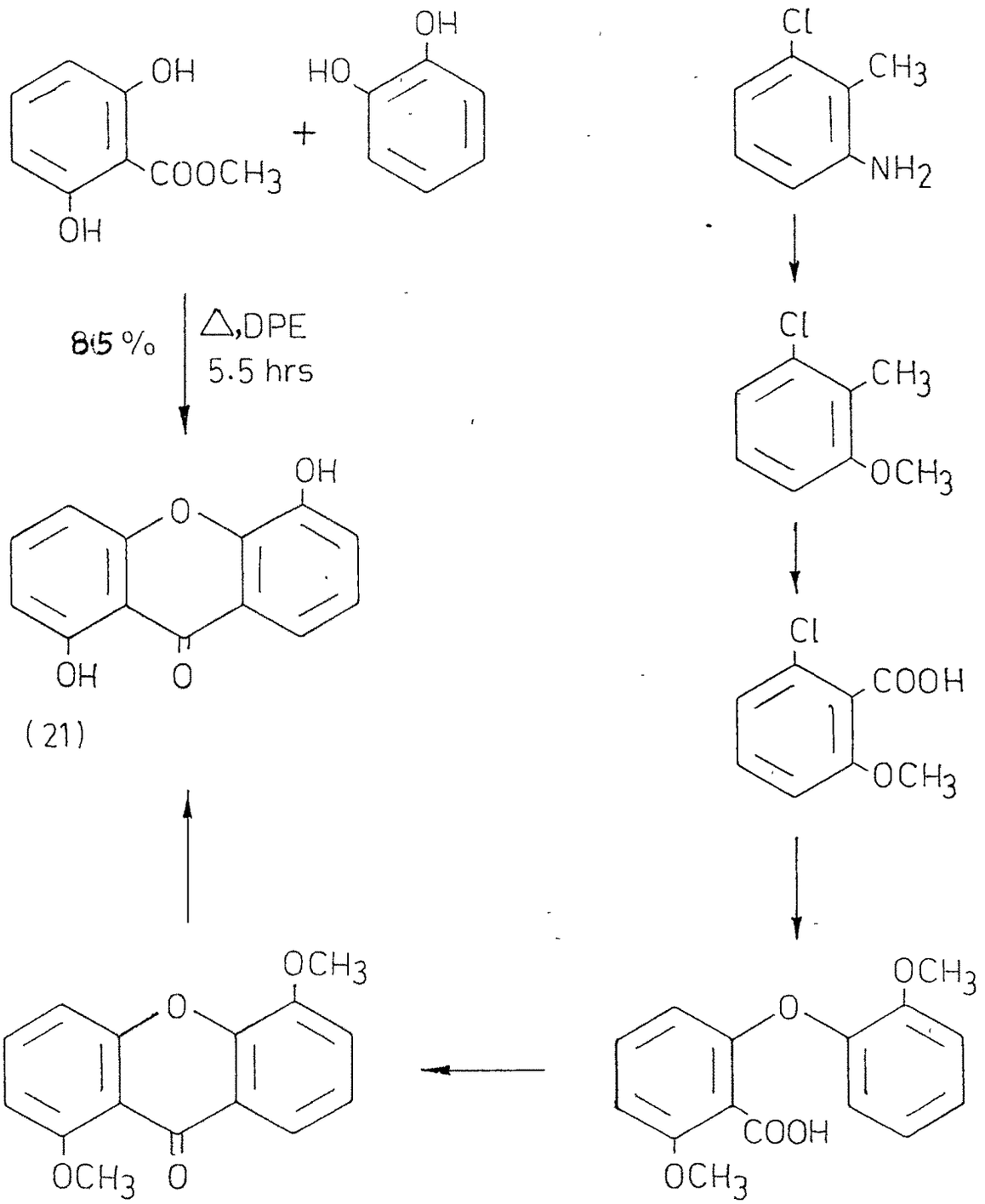
An equimolar mixture of catechol and methyl 2,6-dihydroxy benzoate was refluxed in diphenyl ether for 5 to 6 hr. The reaction mixture was steam distilled and the separated product was purified by column chromatography to furnish a naturally occuring xanthone, 1,5-dihydroxyxanthone, yield (8.5%) m.p. 266° (lit.,[82] 260°) structure was confirmed by its NMR spectral studies. NMR (CD_3SOCD_3) : δ 7.95, d, 1H, J=9Hz, H-1; 7.55, d, 1H, J=9Hz, H-7; 6.6-7.2, m, 4H, H-2, H-3, H-5 and H-6; 12.90, S, 1H, OH; 11.95, S, 1H, OH.

Condensation of β-naphthol with methyl 2,6-dihydroxybenzoate: 8-Hydroxy-1,2-benzoxanthone (22)

β-Naphthol was condensed with methyl-2,6-dihydroxy-



SCHEME – 1


OH
HO
OH
COOCH3
OH
+
Cl
CH3
NH2
85 %
△,DPE
5.5 hrs
Cl
CH3
OCH3
OH
O
OH
O
(21)
Cl
COOH
OCH3
OCH3
O
COOH
OCH3
OCH3
O
OCH3

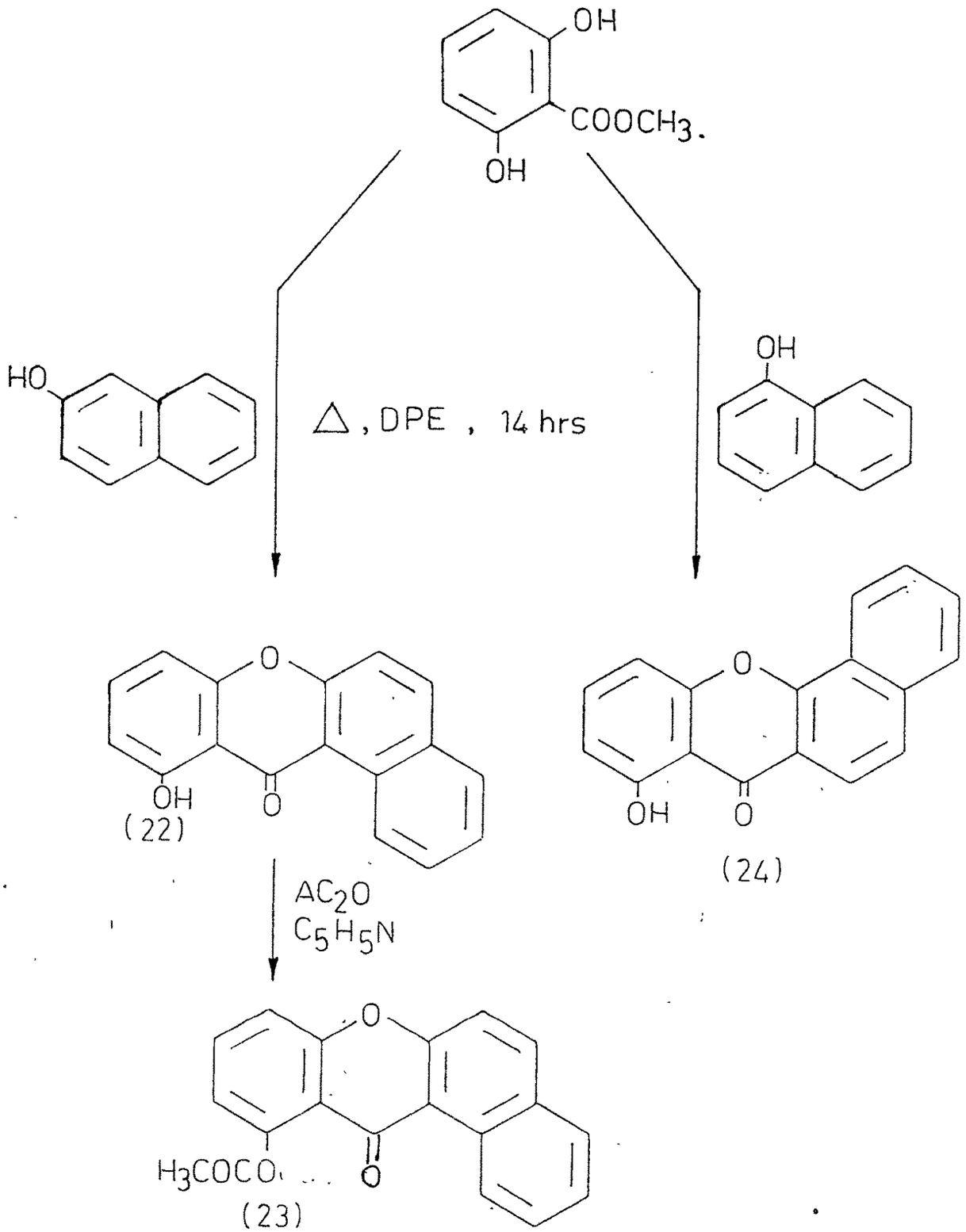
benzoate in boiling diphenyl ether for 14 hr. The removal of solvent by steam distillation yielded a product which was characterized as 8-hydroxy-1,2-benzoxanthone (22), yield 30%, m.p. 220°, on the basis of its elemental analysis, IR, NMR and Mass spectrum of its acetoxy derivative (23). NMR ($CDCl_3$) showed only one singlet in the upfield region at δ2.6 indicating that it is a mono acetate and hence precluded the possibility of benzophenone or an ester type compound. Mass : m/e 304 (M^+) 262 (M^+- 42) 234 (M^+- 42-28) NMR ($CDCl_3$) :δ8.02, d, 1H, J=9Hz, H-1'; 7.0-7.9, m, 8H, aromatic protons, 2.6, S, 3H, $OCOCH_3$.

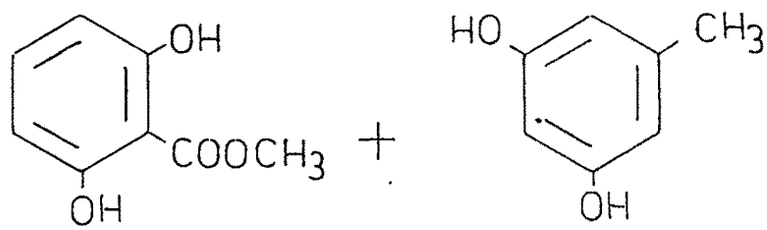
Condensation ofα-naphthol with methyl 2,6-dihydroxybenzoate: 8-Hydroxy-3,4-benzoxanthone (24)

A mixture ofα-naphthol and methyl 2,6-dihydroxybenzoate was refluxed in diphenyl ether for 14 hr. The product obtained after steam distillation of reaction mixture, was washed with sodium bicarbonate solution, crystallised and characterized as 8-hydroxy-3,4-benzoxanthone (24) m.p. 185° on the basis of its elemental analysis.

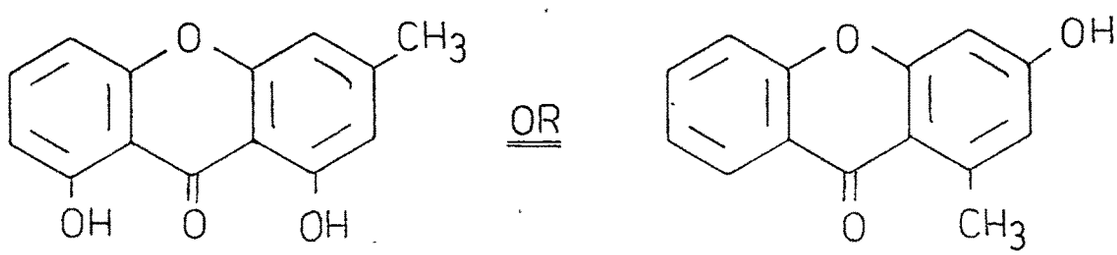
Condensation of orcinol with methyl 2,6-dihydroxybenzoate: 1,6-Dihydroxy-8-methylxanthone (25)

A mixture of orcinol and methyl 2,6-dihydroxybenzoate was refluxed in diphenyl ether for 9 hr. The product obtained, after steam distillation, was characterized as


OH
COOCH3.
OH
HO
△, DPE , 14 hrs
OH
O
OH
O
(22)
O
OH
O
(24)
AC2O
C5H5N
O
H3COCO
O
(23)

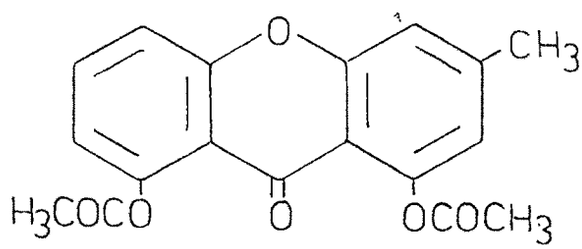


△, DPE, 9 hrs



(25) (25a)

AC_2O , C_5H_5N



(26)

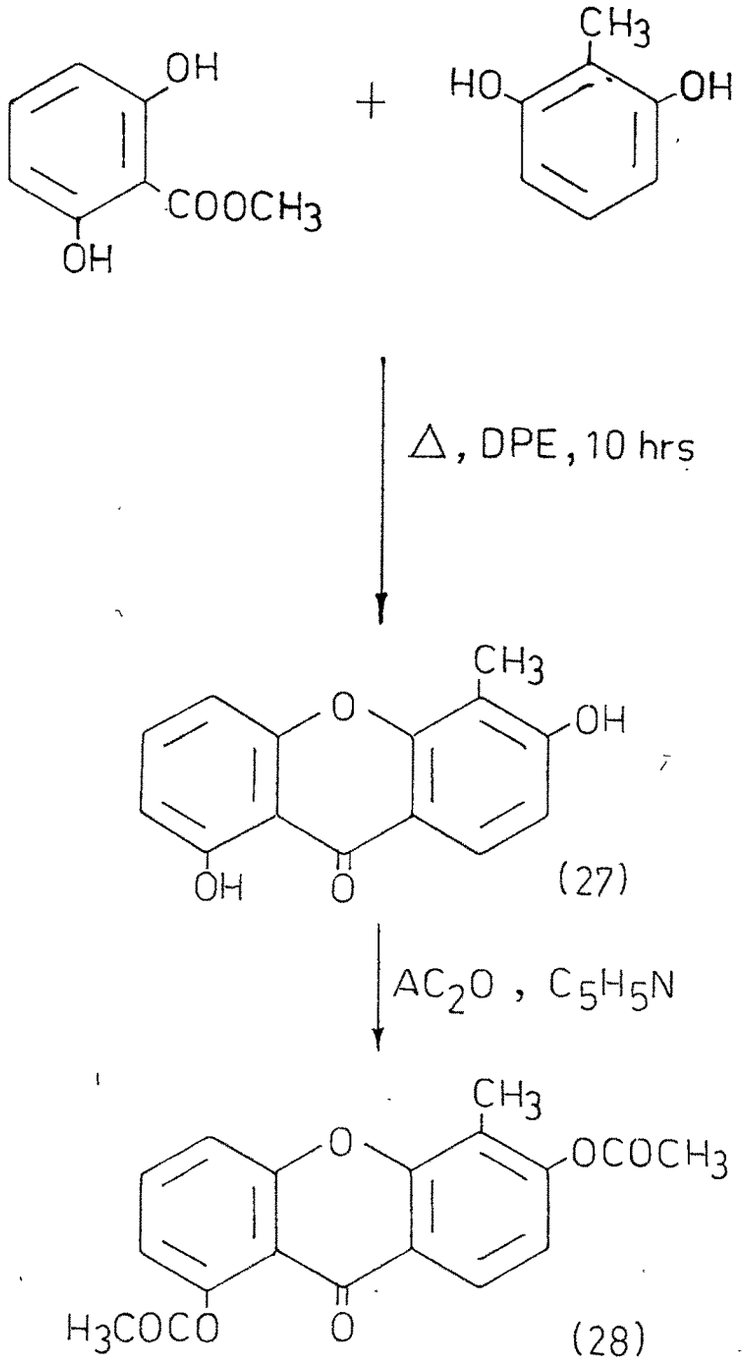
1,6-dihydroxy-8-methylxanthone (25) m.p. 225° on the basis of its elemental analysis. The possibility of structure (25a) is easily ruled out on the basis of lit[49] m.p. 198-199°.

The product (25) on acetylation with acetic anhydride and pyridine gave sodium hydroxide insoluble diacetoxy derivative (26) m.p. 142°, structure of which was confirmed by its NMR spectrum. NMR ($CDCl_3$) : δ 7.65, singlet, 1H, H-4; 7.0, s, 1H, H-2; 7.18 to 7.3, multiplet, 3H, the aromatic protons at H-5, H-6 and H-7; 2.35, singlet, 3H, $-OCOCH_3$; 2.46, singlet, 3H, $OCOCH_3$; 2.5, singlet, 3H, $ArCH_3$. This confirms the assigned structure (26).

Condensation of 2-methylresorcinol with methyl 2,6-dihydroxy benzoate : 3,8-Dihydroxy-4-methylxanthone (27)

An equimolar quantities of 2-methylresorcinol and methyl 2,6-dihydroxybenzoate was refluxed in diphenyl ether for 10 hr. The product obtained after steam distillation, crystallisation and sublimation, was characterized as 3,8-dihydroxy-4-methylxanthone (27) m.p. 243° on the basis of its elemental analysis.

The product (27) on acetylation with acetic anhydride and pyridine yielded diacetoxy derivative (28) m.p. 193° structure of which was confirmed by its NMR spectral data. NMR ($CDCl_3$) (Fig.12) displays two singlets one at δ 2.3 and


OH
COOCH3
OH
+
CH3
HO
OH
Δ, DPE, 10 hrs
CH3
O
OH
OH
O
(27)
AC2O , C5H5N
CH3
O
OCOCH3
H3COCO
O
(28)

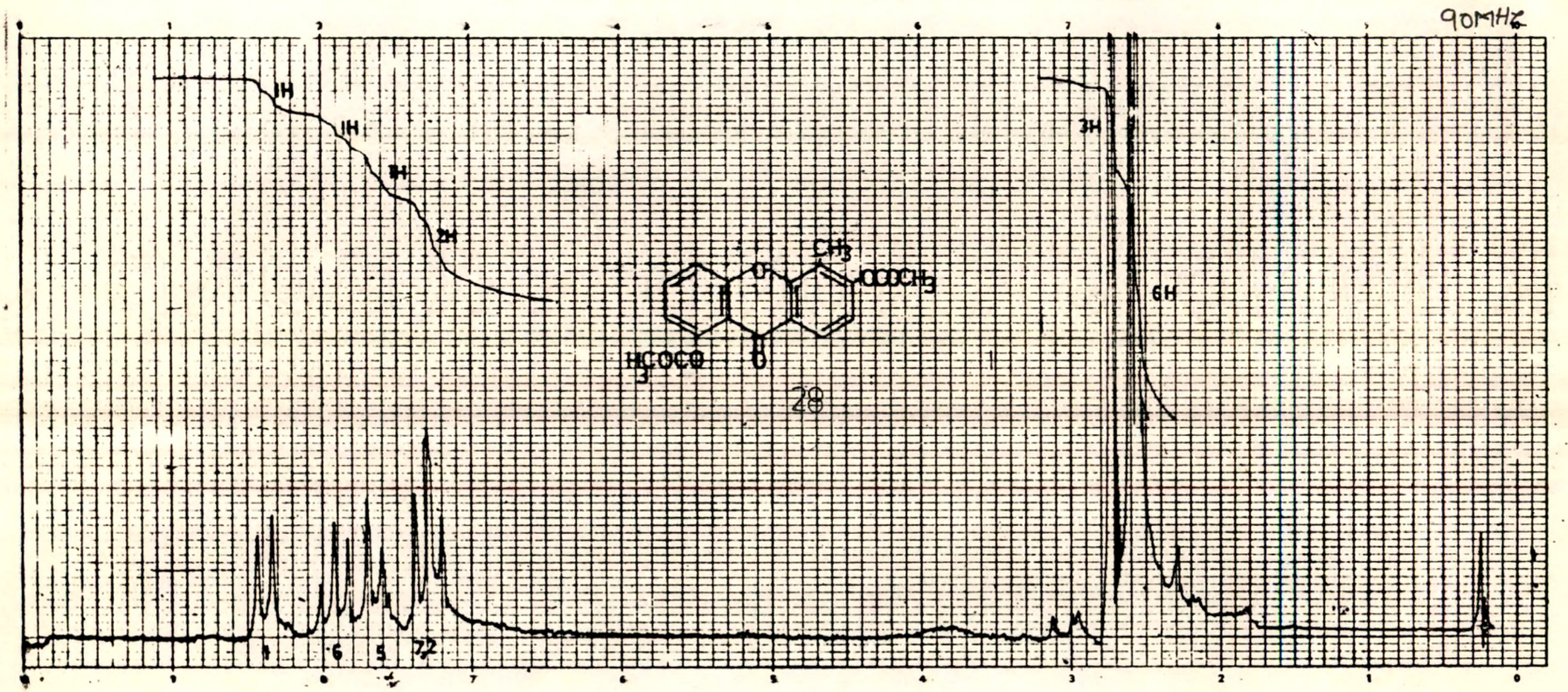


FIG 12

another at δ 2.5, the former one integrate for the six protons of the two $OCOCH_3$ group latter one corresponds to the three protons of the aromatic methyl groups, peaks of the aromatic region are interpreted as under :

8.13, d, 1H, J=9Hz, H-1; 7.6, t, 1H, J=9Hz, H-6; 7.4, dd, 1H, J=9,2Hz, H-5; 7.1, d, 1H, J=9Hz, H-2; 7.0, dd, 1H, J=9,1.5Hz, H-7.

Condensation of Phloroglucinol with methyl 2,4-dihydroxy benzoate : 1,3,6-Trihydroxyxanthone (30)

As the title compound is a good starting material for the synthesis of some of the newly isolated naturally occuring xanthones. It was synthesised by the condensation of an equimolar quantities of phloroglucinol and methyl 2,4-dihydroxybenzoate in refluxing diphenyl ether for 30 min. The usual work up of the reaction mixture gave the product, which was characterized as 1,3,6-trihydroxyxanthone (30) yield 33% m.p. 316° (lit.,[48] 323) on the basis of elemental analysis and the spectral studies of its acetoxy derivative.

The product (30) on acetylation gave (31) m.p. 170° (lit.,[48] 172°). As the elemental analysis fits with triacetate the possibility for the benzophenone or an ester type compound (29) can be ruled out easily. Further more NMR ($CDCl_3$) (Fig.13) of (31) showed two singlets one integrated for the three protons at δ 2.45 and other singlet at δ 2.3 for

31

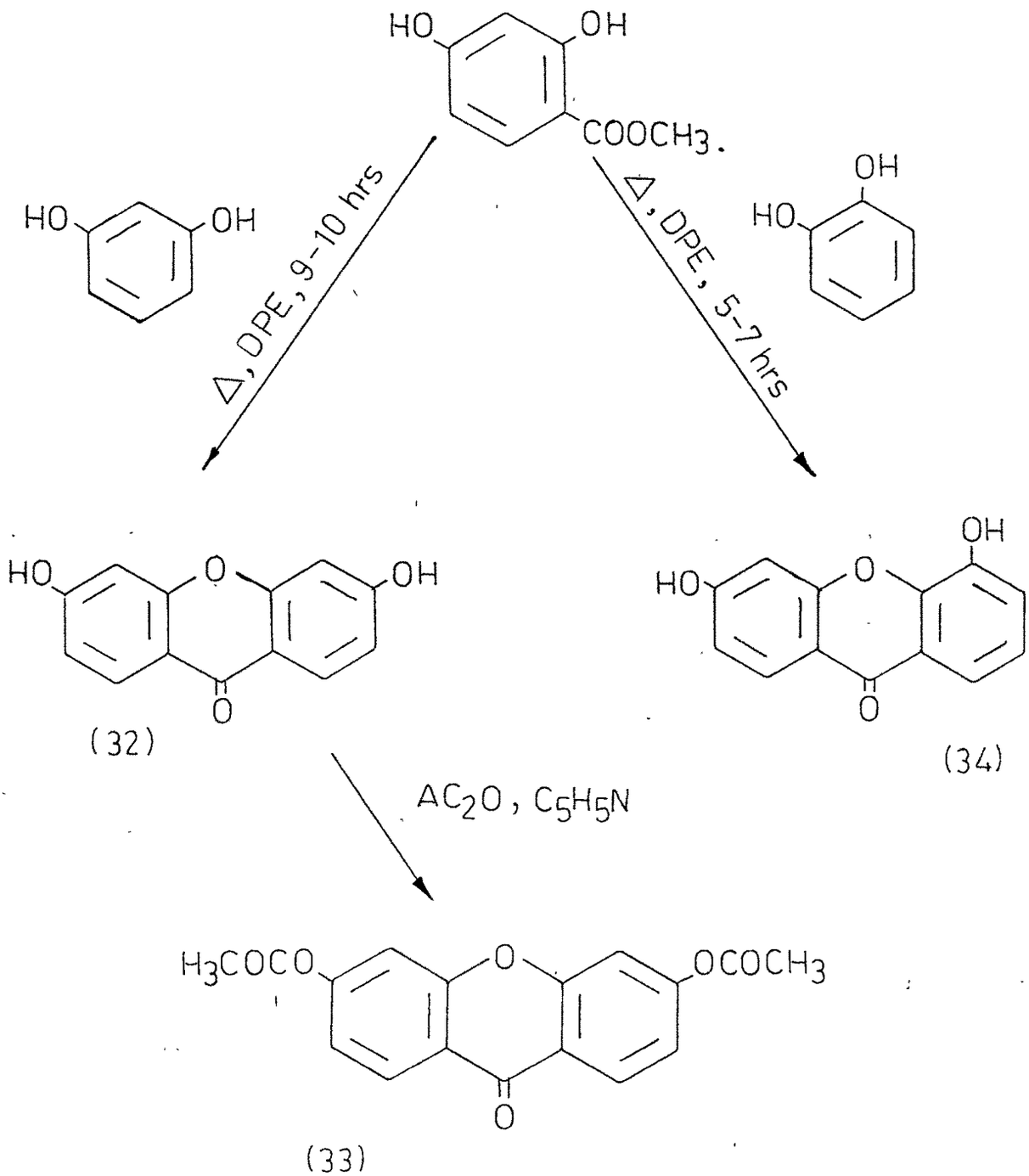
FIG 13

the six protons of two $OCOCH_3$ groups. Thus it is a triacetoxy derivative. In the aromatic region there is only one double doublet (doublet splitted in to doublet) at δ 7.15 and looking to its coupling constant (J=9,2Hz, ortho and meta coupling), the assignment were made for the proton at position 7, the highly down field doublet at δ 8.15 is due to H-8, 7.3, overlap doublet for the two protons of same value J=1.5Hz, H-4 and H-5, 6.88, doublet, J=2Hz for the proton at position 2. The assigned structure (31) was further supported by mass spectral data. Molecular ion peak observed at 328, fragmentation of which followed by the successive loss of the ($COCH_2$) 42 mass units. Further fragmentation shows usual fragmentation pattern of xanthone.

Condensation of resorcinol with methyl 2,4-dihydroxybenzoate: 3,6-Dihydroxyxanthone (32)

A mixture of resorcinol and methyl 2,4-dihydroxybenzoate was refluxed in diphenyl ether for 9 to 10 hr. The reaction mixture was worked up in usual manner to give 3,6-dihydroxy xanthone (32) yield (10%) m.p. $> 300^{\circ}$ (lit.,[48] $> 300^{\circ}$). The structure was assigned on the basis of elemental analysis of itself and other derivatives.

The product on acetylation with acetic anhydride and pyridine gave diacetoxy derivative (33) m.p. 145-50° (lit.,[48] 155°).


HO
OH
COOCH3.
HO
OH
Δ, DPE, 9-10 hrs
Δ, DPE, 5-7 hrs
OH
HO
HO
O
OH
O
(32)
OH
HO
O
O
(34)
AC2O, C5H5N
H3COCO
O
OCOCH3
O
(33)

Condensation of catechol with methyl 2,4-dihydroxybenzoate: 4,6-Dihydroxyxanthone (34)

An equimolar quantities of catechol and methyl 2,4-dihydroxybenzoate was refluxed in diphenyl ether for 5 to 7 hr. The paste obtained after steam distillation was chromatographed over silica gel and eluted with chloroform methanol mixture to give 4,6-dihydroxyxanthone (34) m.p. 210° (lit.,[53] 217-20°) structural assignments were made on the basis of its elemental analysis.

Condensation of pyrogallol with methyl 2,4-dihydroxy benzoate : 3,4,6-Trihydroxyxanthone (35)

A mixture of pyrogallol and methyl 2,4-dihydroxy-benzoate was condensed in refluxing diphenyl ether for 4 hr. The usual work up and chromatographic purification gave 3,4,6-trihydroxyxanthone (35) m.p. > 330° (lit.,[40] > 285° lit.,[49] 340°). The elemental analysis ruled out the possibility of benzophenone or an ester type compound.

The product (35) on acetylation with acetic anhydride and pyridine gave triacetoxy derivatives (36) which showed no colour reaction with ethanolic ferric chloride solution. Mass spectra of (36) showed molecular ion peak at 328 (M^+) which are in agreement with the structural formula of the compound. Three successive loss of 42 units indicated the presence of three acetoxy groups and xanthone nucleus.

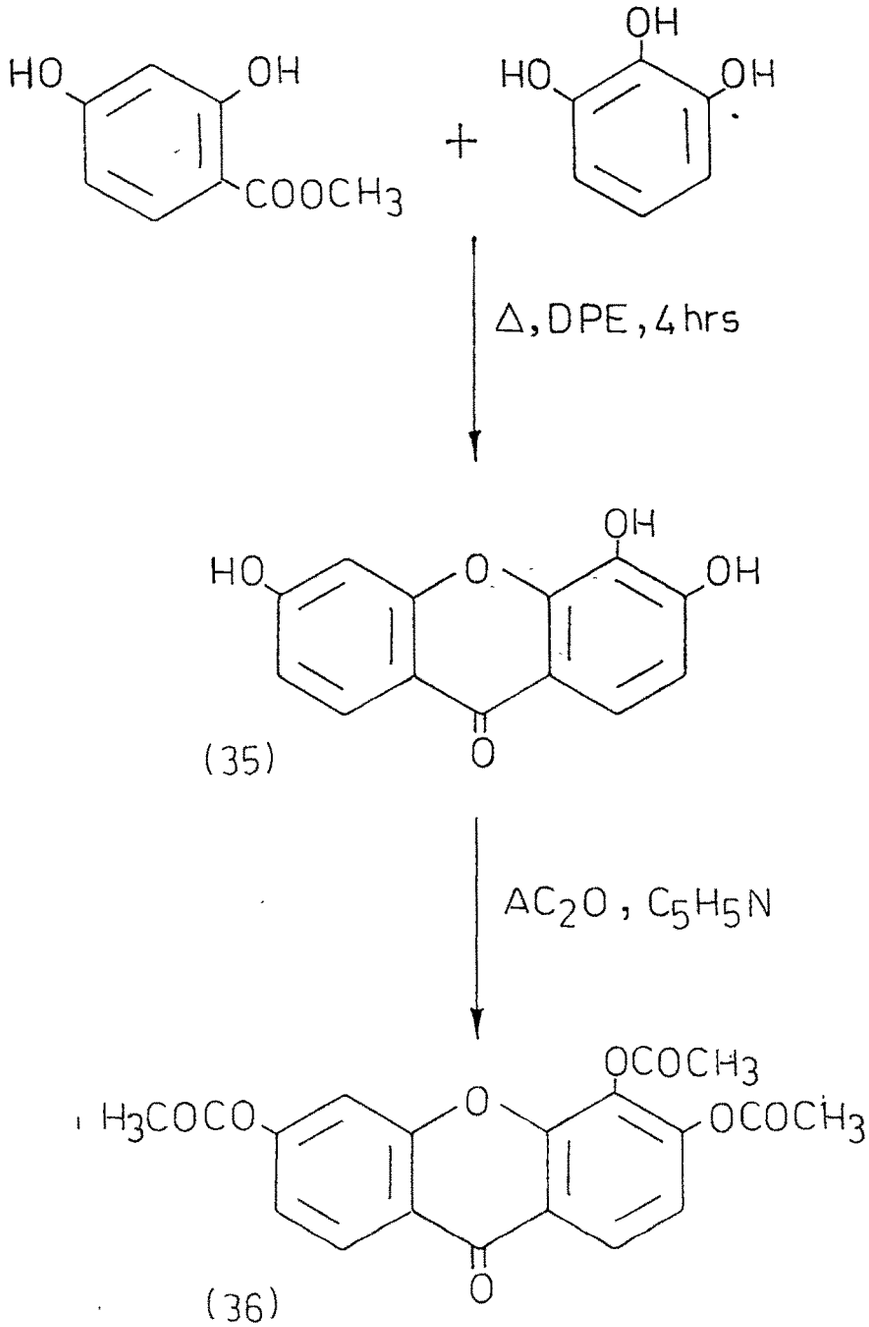

HO
OH
COOCH3
+
HO
OH
OH
Δ, DPE, 4 hrs
HO
O
OH
OH
O
(35)
AC2O , C5H5N
H3COCO
O
OCOCH3
OCOCH3
O
(36)

FIG 14

NMR ($CDCl_3$) (Fig.14) showed overlapping doublet of the protons H-8 and H-1 in the down field aromatic region at δ 8.25; 7.32, doublet, J=1.5Hz, for proton at position 5; multiplet centered at δ 7.18 for the two protons H-2 and H-7; δ 2.48, 2.42 and 2.35 singlets for the three $OCOCH_3$ groups. Thus on the basis of mass and NMR data structure (36) was confirmed.

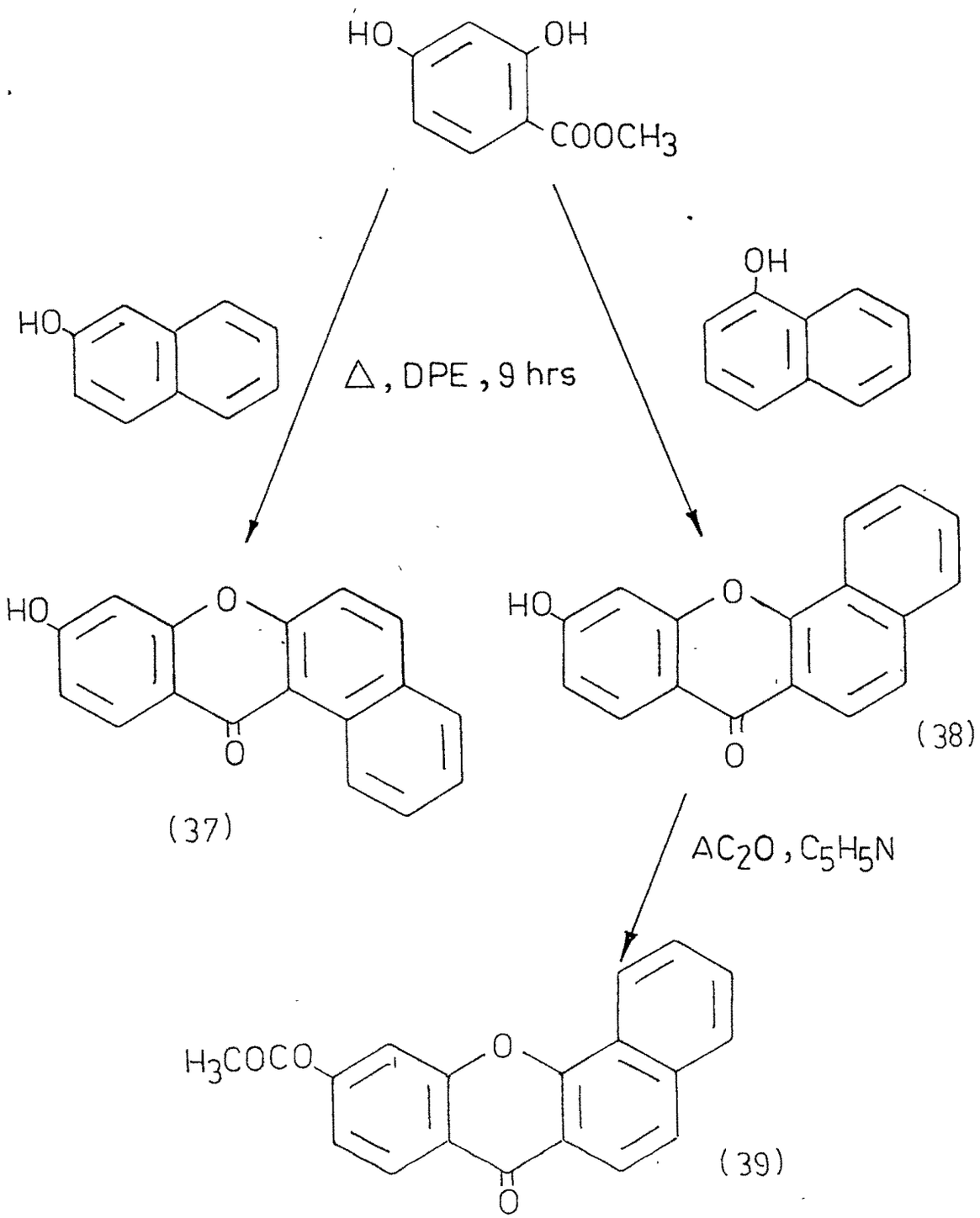
Condensation of β-naphthol with methyl 2,4-dihydroxy benzoate : 6-Hydroxy-1,2-benzoxanthone (37)

A mixture of β-naphthol and methyl 2,4-dihydroxy benzoate was refluxed for 9 hr. The product obtained after usual work up, was passed through a silica gel column and eluted with benzene to yield 6-hydroxy-1,2-benzoxanthone (37) m.p. 230-5°.

Condensation of α-naphthol with methyl 2,4-dihydroxy benzoate : 6-Hydroxy-3,4-benzoxanthone (38)

A mixture of α-naphthol and methyl 2,4-dihydroxy benzoate was refluxed in diphenyl ether for 9 hr. The product obtained after steam distillation, was characterized as 6-hydroxy-3,4-benzoxanthone (38) m.p. 285°.

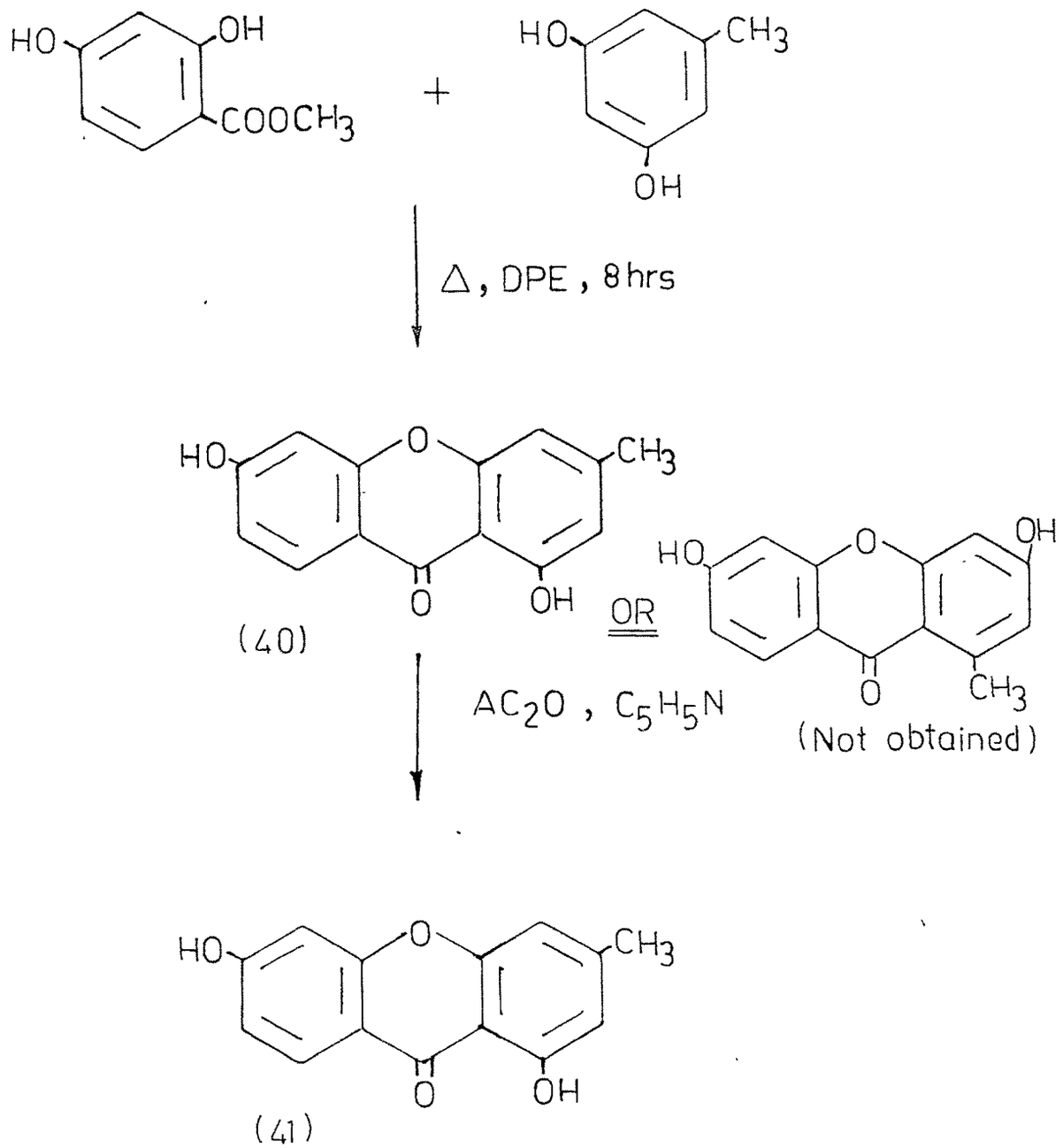
The product on acetylation yielded monoacetate (39). m.p. 190° NMR ($CDCl_3$) of which showed only one singlet in the up field region at δ 2.3 indicating that it is a monoacetate, it gave no colour reaction with ferric chloride


HO
OH
COOCH3
HO
OH
Δ, DPE, 9 hrs
HO
O
O
(37)
HO
O
O
(38)
AC2O, C5H5N
H3COCO
O
O
(39)

solution so the product obtained is a xanthone derivative. In the aromatic region it exhibits complex sets of peaks between 7.2 to 8.4 for the aromatic protons.

Condensation of orcinol with methyl 2,4-dihydroxybenzoate: 1,6-Dihydroxy-3-methylxanthone (40)

A condensation of orcinol and methyl-2,4-dihydroxy benzoate was effectively brought out in refluxing diphenyl ether for 8 hr. The product obtained after usual work up, was chromatographed using benzene as an eluant and structure was assigned as 1,6-dihydroxy-3-methylxanthone (40) m.p. 315°. (lit.,[48] 326°) on the basis of spectral evidences of its diacetoxy derivative (41) m.p. 165° (lit.,[48] 161). It gave a green colour with ethanolic $FeCl_3$ solution, indicates that it contains one chelated hydroxyl group and that must be from orcinol nucleus and hence the possibility for 3-hydroxy-1-methylxanthone derivative was ruled out easily. NMR spectrum ($CDCl_3$) of compound (41) showed δ 2.35, s, 3H, $OCOCH_3$; 2.45, s, 3H, $OCOCH_3$ and singlet at δ 2.5 for the CH_3 group attached to xanthone nucleus. Only two clear doublets were observed in the aromatic region, one in the down field region at δ 8.25, J=9Hz, due to the proton at position 8. Second one appears at δ 6.82 J=1Hz metacoupling due to the proton at position 2 and 7.18 to 7.3 multiplet of the three protons due to overlapped peaks of H-4, H-5 and H-7.


HO
OH
COOCH3
+
HO
CH3
OH
Δ, DPE, 8 hrs
HO
O
CH3
O
OH
(40)
OR
HO
O
OH
O
CH3
(Not obtained)
AC2O, C5H5N
HO
O
CH3
O
OH
(41)

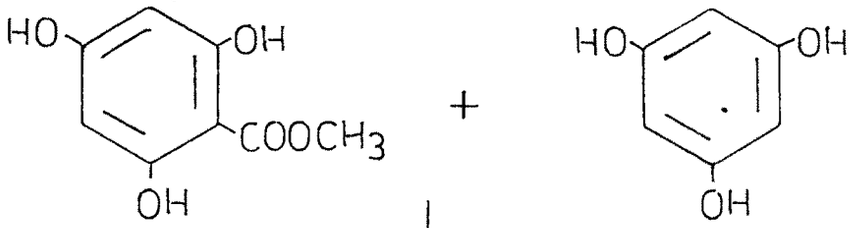
Mass m/e 326 (M^+) 284 (M^+ -42) 242 (M^+ -2x$COCH_2$) 228 (M^+ -2$COCH_2$-CH_2) further fragmentation followed the pattern of dihydroxyxanthone. Thus the spectral data confirms the assigned structure (41).

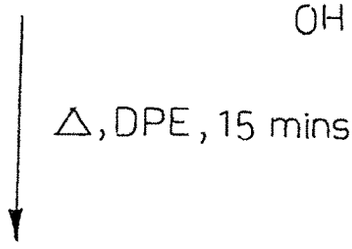
Condensation of phloroglucinol with methyl-2,4,6-trihydroxy benzoate : 1,3,6,8-Tetrahydroxyxanthone (42)

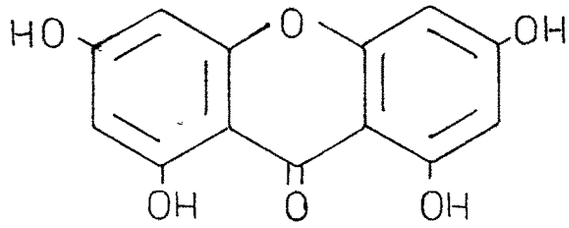
A mixture of equimolecular quantities of phloroglucinol and methyl-2,4,6-trihydroxybenzoate was refluxed in diphenyl ether for 15 min. The product obtained after steam distillation, was chromatographed over neutral alumina and eluted with alcohol to give 1,3,6,8-tetrahydroxyxanthone (42) m.p. 310° (lit.,[49] 332). The structure was established on the basis of its elemental analysis and NMR of its acetoxy derivative (43). NMR ($CDCl_3$) showed two singlets in the upfield aliphatic region at δ 2.35 and 2.45 six protons for the two -$OCOCH_3$ groups, moreover there are two doublets of J value 2Hz at δ 6.79 and 7.20 for the four proton which is attributed to H-2, H-7 and H-4, H-5 respectively.

Condensation of 2-methylresorcinol with methyl 2,4,6-trihydroxybenzoate : 3,6,8-Trihydroxy-4-methylxanthone (44)

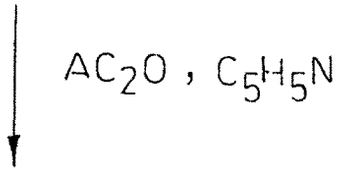
A mixture of 2-methylresorcinol and methyl 2,4,6-trihydroxybenzoate was refluxed for 4 hr. The product obtained after steam distillation was characterised as 3,6,8-trihydroxyxanthone (44) on the basis of NMR studies

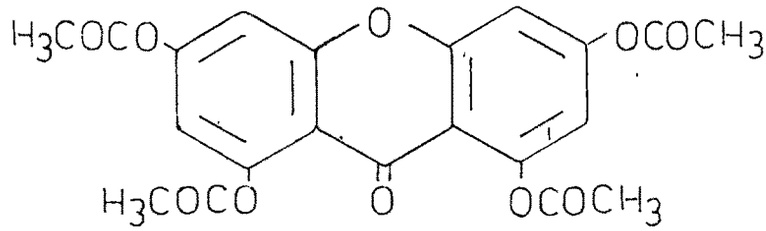

HO
OH
COOCH3
OH
+
HO
OH
OH


△, DPE, 15 mins

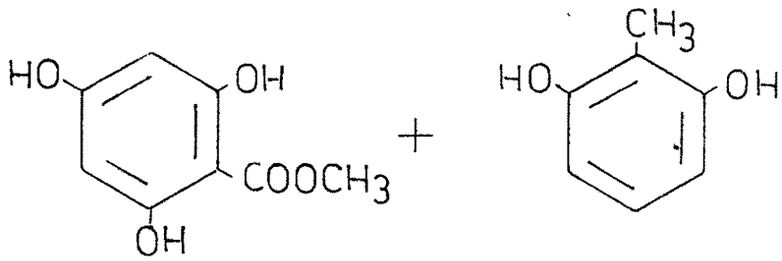

HO
O
OH
OH
O
OH

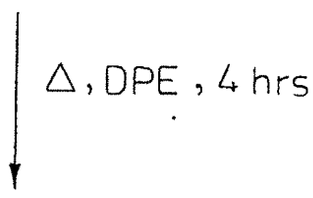
(42)

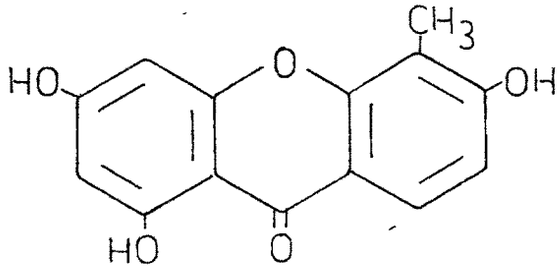

AC2O , C5H5N


H3COCO
O
OCOCH3
H3COCO
O
OCOCH3

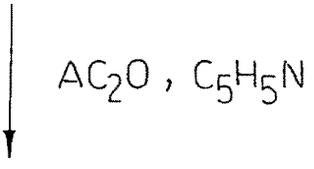
(43)

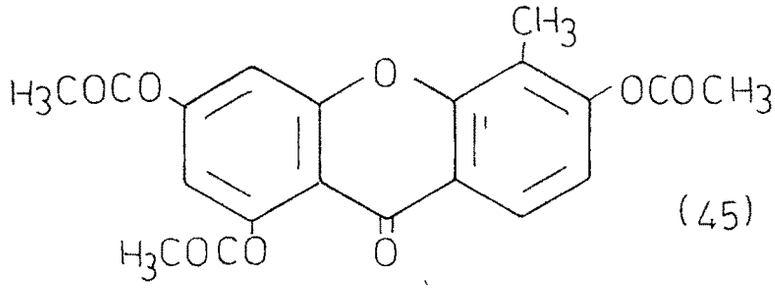

HO
OH
COOCH3
OH
+
CH3
HO
OH


Δ, DPE, 4 hrs


CH3
HO
O
OH
HO
O

(44)


AC2O, C5H5N


CH3
H3COCO
O
OCOCH3
H3COCO
O

(45)

of its acetoxy derivatives. Acetylation in usual manner gave triacetate (45), which was characterised on the basis of its NMR spectral studies. NMR ($CDCl_3$) showed δ 2.35, singlet for the nine protons of the three acetoxy groups. One singlet for the methyl group attached to the aromatic ring at δ 2.48. In the aromatic region only four groups of peaks were observed, which were classified as follow, two doublets one at δ 6.8 another at δ 7.26 of small J value 2Hz was observed, coupling constant suggest that it is a meta coupling, so assignment were made for the protons at position 7 and position 5 respectively. Further more two doublets of the same J value 9Hz were observed at δ 7.05 and δ 8.1, former is in the upfield aromatic region so it is due to the proton at position 2 and latter being in the down field was assigned to the periproton H-1. Thus confirms the assigned structure (45).

Condensation of hydroquinone with methyl 2,4,6-trihydroxy benzoate : 1,3,7-Trihydroxyxanthone (Gentisein) (46)

With a view to prepare a naturally occuring xanthone, gentisein, condensation of hydroquinone and methyl 2,4,6-trihydroxybenzoate was carried out in refluxing diphenyl ether for 2 hr. The product obtained was washed with benzene to give 1,3,7-trihydroxyxanthone (46) m.p. 316-20° (lit.,[48] 318°).

Condensation of α-naphthol with methyl 2,4,6-trihydroxy benzoate : 1,3-Dihydroxy-5,6-benzoxanthone (47)

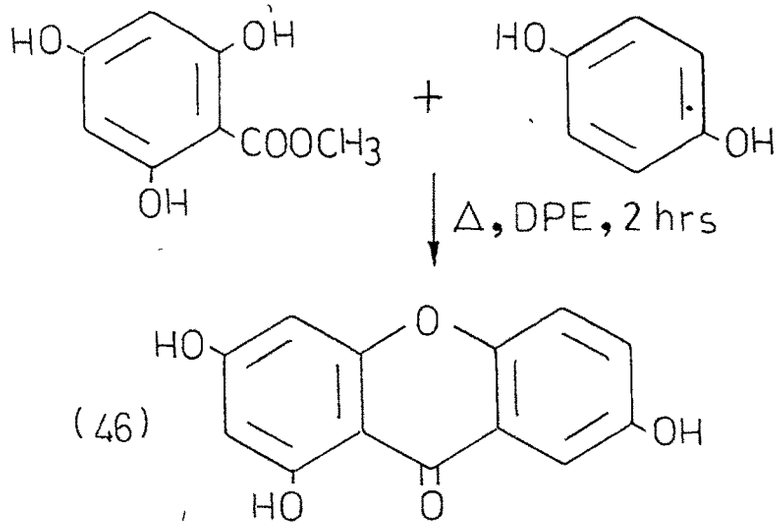
A mixture of α-naphthol and methyl 2,4,6-trihydroxy benzoate was refluxed in diphenyl ether. The product obtained after usual work up, was passed through a silica gel column gave pale yellow needles, which characterised as (46) m.p. 297°.

Condensation of β-naphthol with methyl 2,4,6-trihydroxy benzoate : 1,3-Dihydroxy-7,8-benzoxanthone (48)

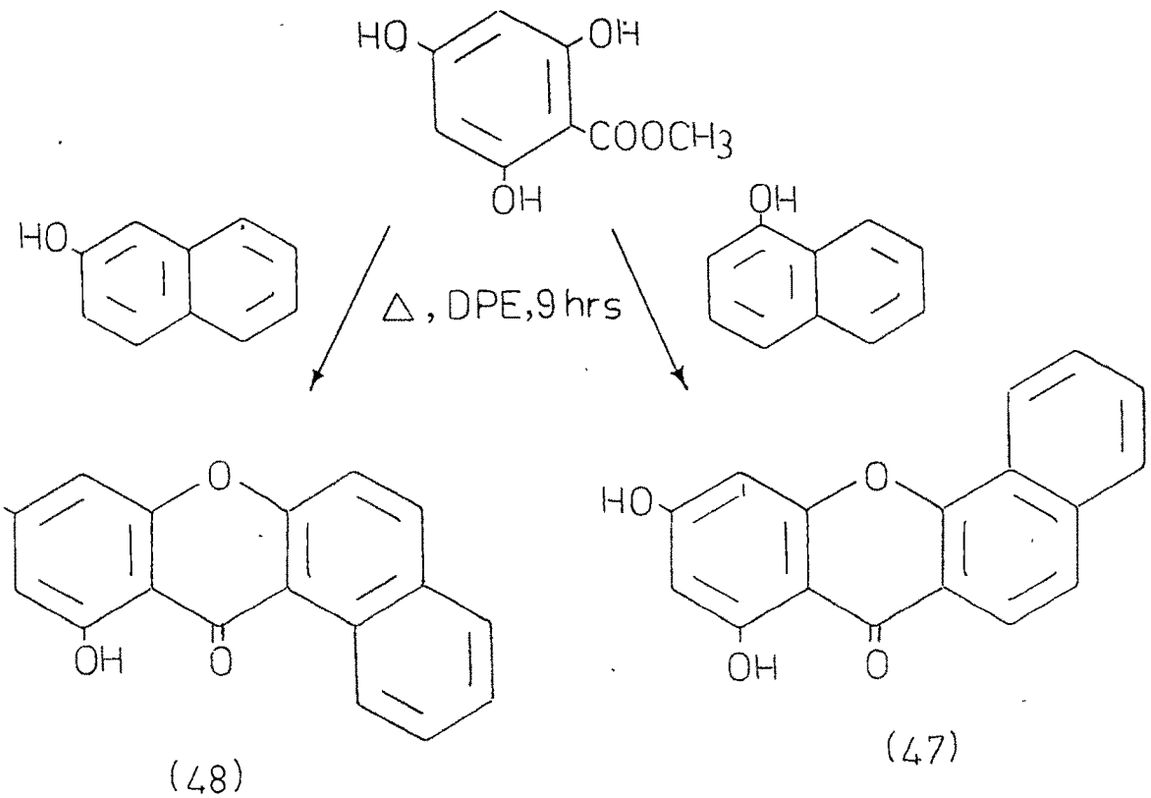
A new benzoxanthone was obtained in a good yield by the condensation of β-naphthol and methyl 2,4,6-trihydroxy benzoate in refluxing diphenyl ether. The usual working up of reaction mixture gave the product, which was chromatographed over a silica gel column and the structure was assigned as 1,3-dihydroxy-7,8-benzoxanthone (48) yield 29% m.p. 264° on the basis of its elemental analysis.

An abnormal thermal condensation ;
The condensation of hydroquinone with ethyl salicylate

With a view to obtain naturally occuring xanthone, 2-hydroxyxanthone, the thermal condensation of hydroquinone and ethyl salicylate was carried out in refluxing diphenyl ether for 40 hr. The paste obtained after the steam distillation of reaction mixture, was chromatographed over a silica gel column for the separation purpose, as it

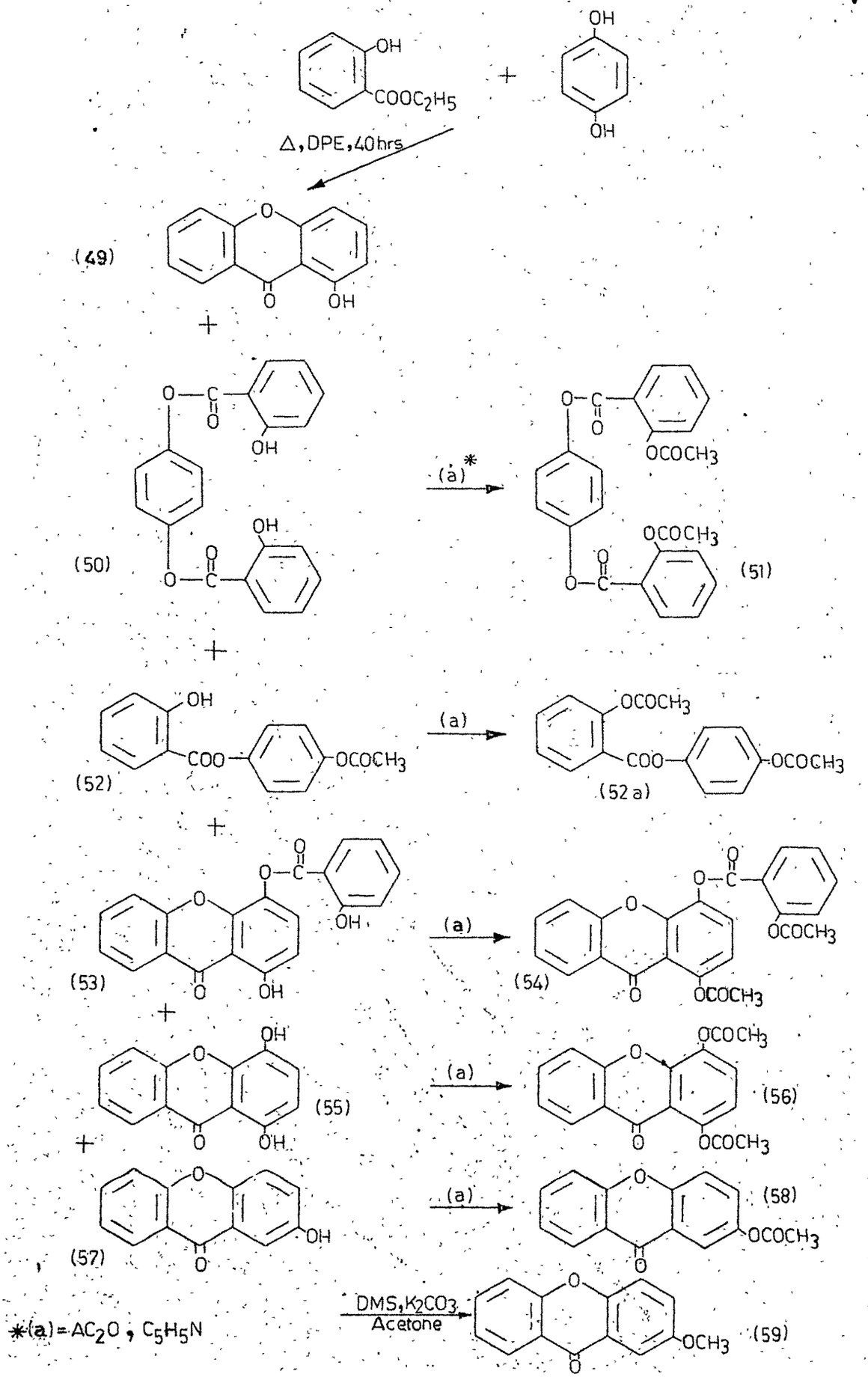

HO
OH
COOCH3
OH
+
HO
OH
Δ, DPE, 2 hrs
HO
O
OH
HO
O

(46)


HO
OH
COOCH3
OH
HO
Δ, DPE, 9 hrs
OH
HO
O
OH
O
HO
O
OH
O

(48)

(47)


OH
COOC2H5
OH
Δ, DPE, 40hrs
O
O
OH
(49)
+
O—C
O
OH
(50)
(a)*
OCOCH3
(51)
OH
COO
OCOCH3
(52)
(a)
(52a)
O
OH
(53)
(54)
(55)
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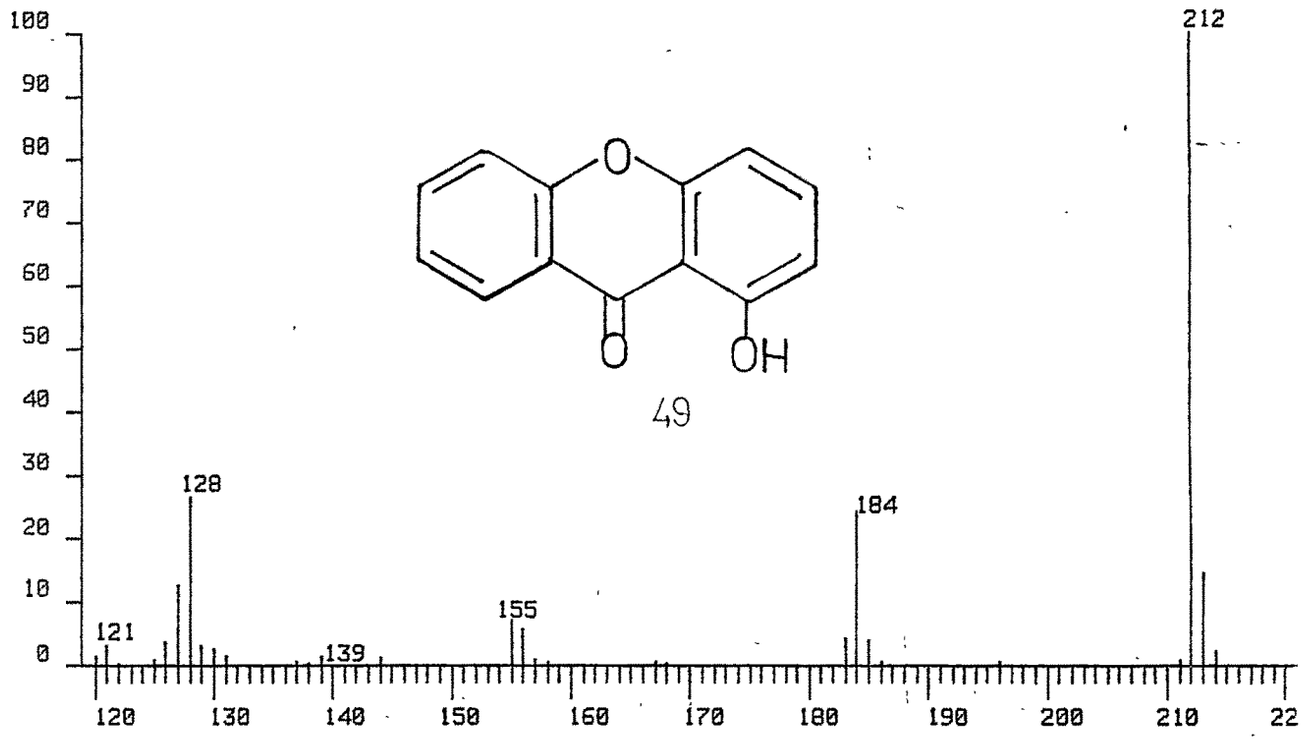
(57)
(58)
DMS, K2CO3
Acetone
OCH3
(59)
*(a) = AC2O , C5H5N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60
50
40
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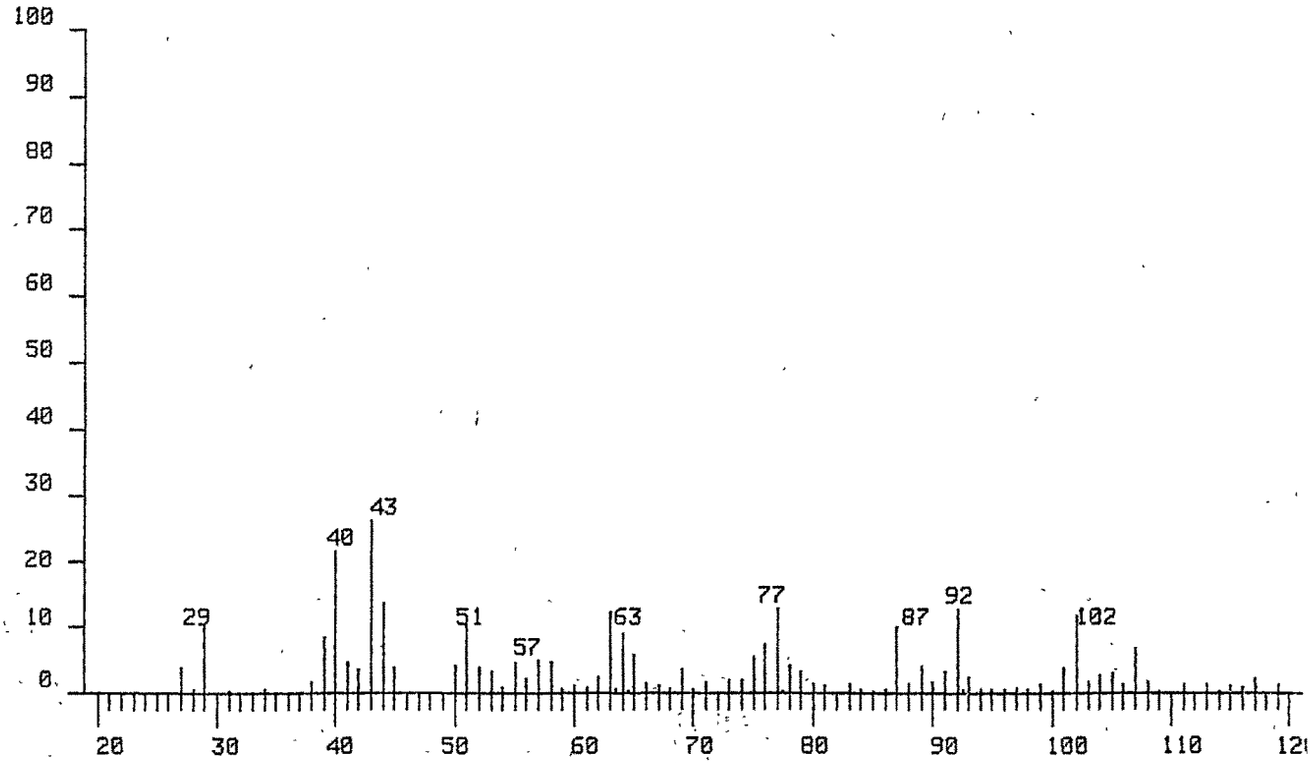
20
10
0
212
184
128
155
121
139
120
130
140
150
160
170
180
190
200
210
O
O
OH

49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43
40
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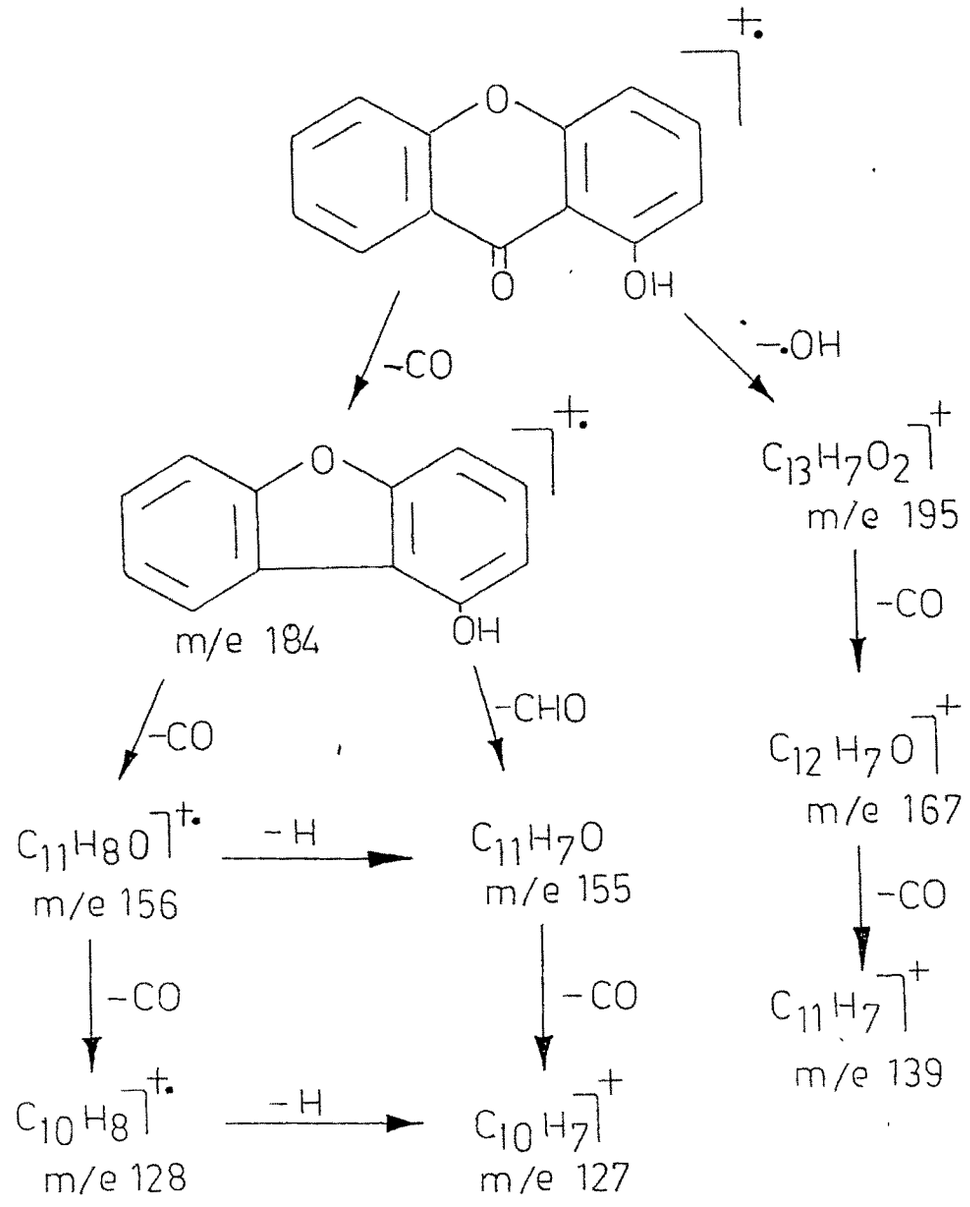
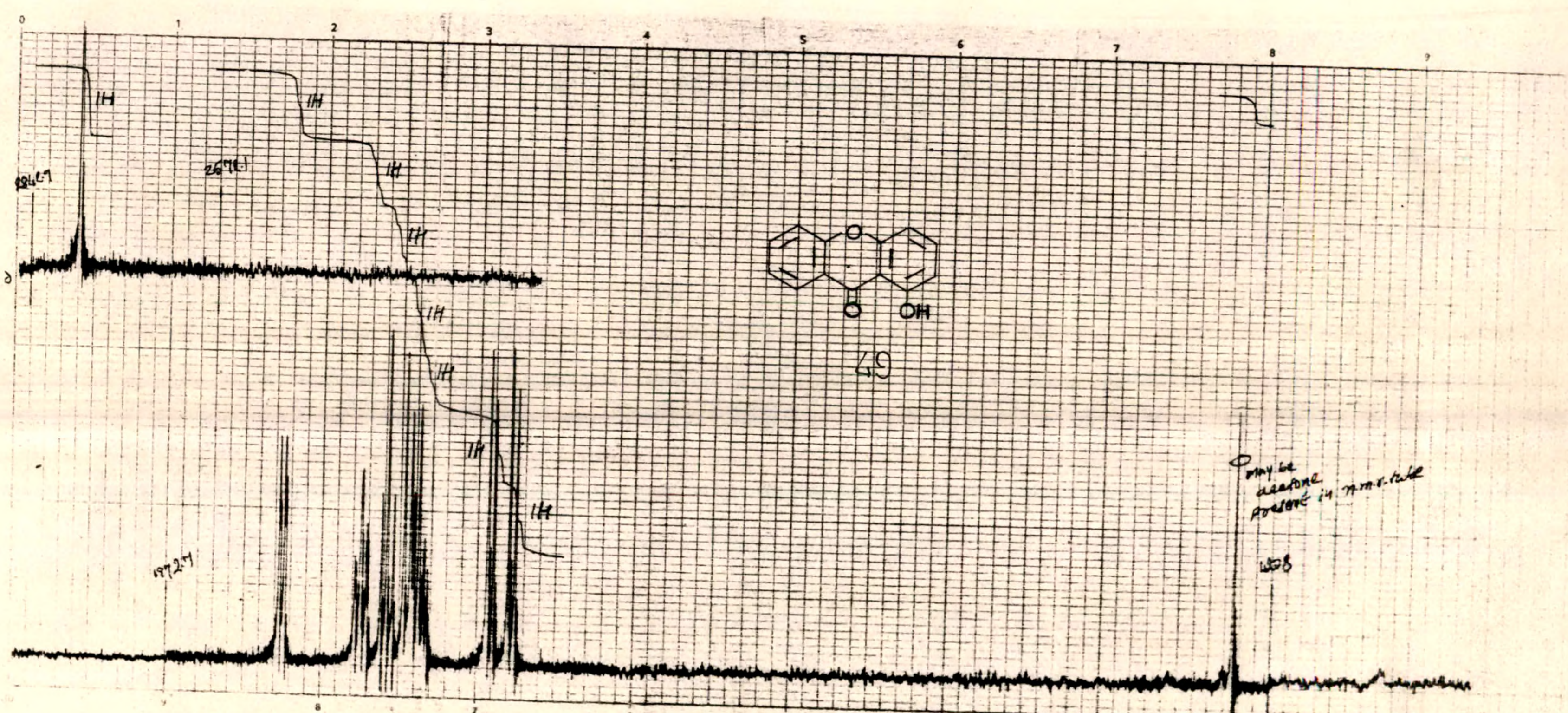
102
20
30
40
50
60
70
80
90
100
110

FIG 15


O
O
OH
-CO
-·OH
O
OH
m/e 184
-CO
-CHO
$C_{13}H_7O_2^+$
m/e 195
-CO
$C_{12}H_7O^+$
m/e 167
-CO
$C_{11}H_7^+$
m/e 139
$C_{11}H_8O^{+\cdot}$
m/e 156
-H
$C_{11}H_7O$
m/e 155
-CO
-CO
$C_{10}H_8^{+\cdot}$
m/e 128
-H
$C_{10}H_7^+$
m/e 127

SCHEME-2



49

FIG 16

220 MHz

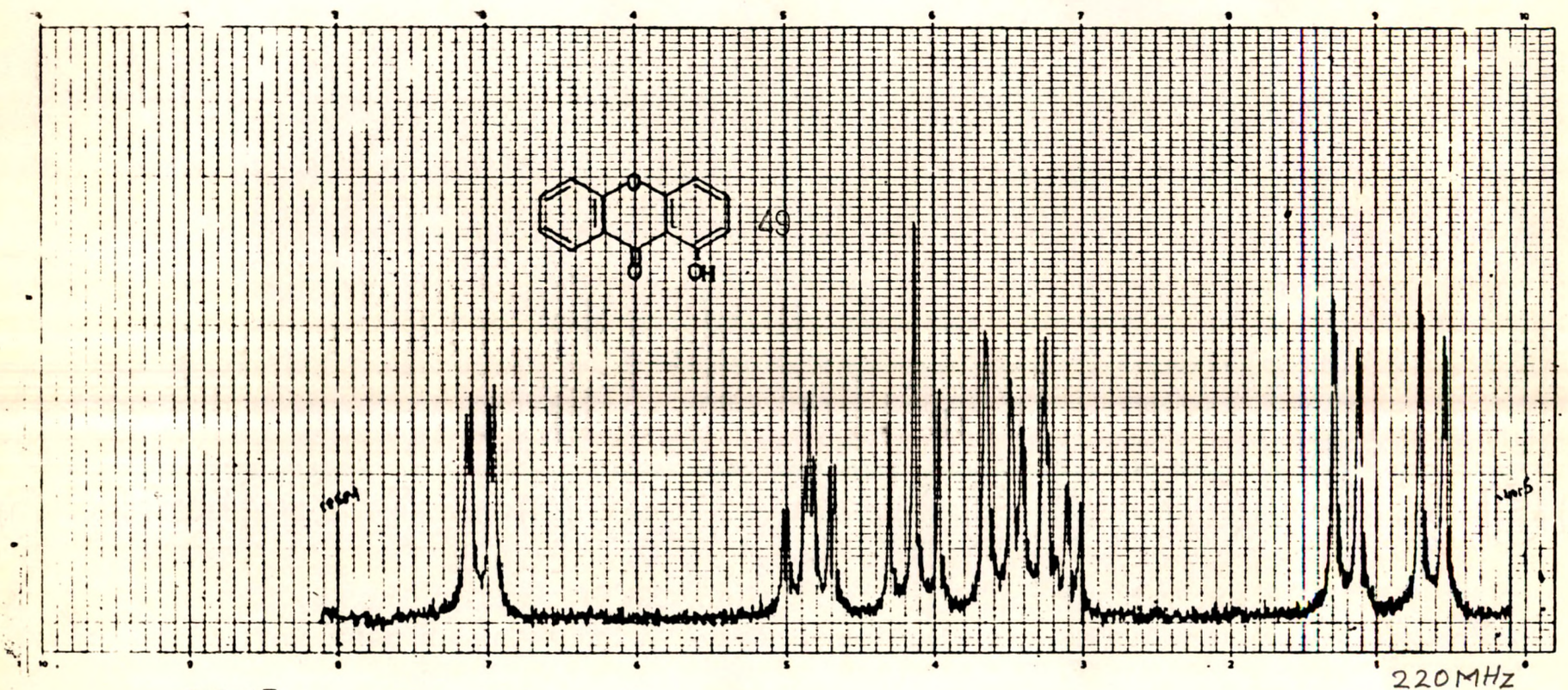


FIG 17

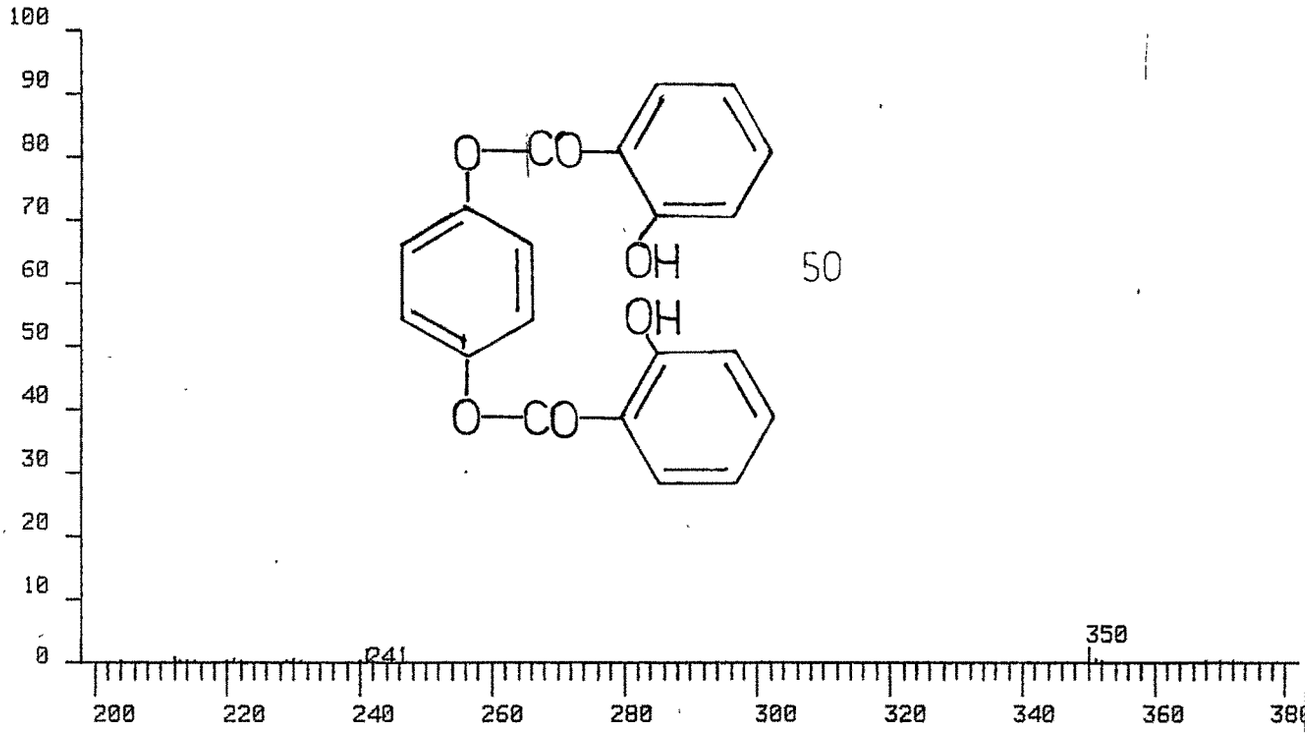
The structure (50) was fully supported by the mass and NMR spectral data of its diacetate derivative (51) mass m/e 434 (M^+) 392 (M^+ -42) 350 (M^+ - $2COCH_2$). NMR ($CDCl_3$) (Fig.19) showed double doublet in the down field aromatic region at δ 8.21 which must be due to the two equivalent protons at position H-2' and H-2", because of anisotropic effect of the vicinyl carbonyl group. δ 7.65, td., 2H, J=9,9,2Hz, H-4' and H-4" ; 7.4, td, 2H, J=9,9,2Hz, H-3' and H-3" ; 7.22, dd, J=9Hz, 4H, H-2, H-3, H-5 and H-6 ; 7.18, dd, 2H, J=9,2Hz, H-5' and H-5".

(iii) 4'-Hydroxyphenyl salicylate (52)

The third compound was eluted with petroleum ether, and characterized as 4'-hydroxyphenyl salicylate m.p. 98-101° (lit.,[80] 101°) on the basis of its elemental analysis, mix m.p. with an authentic sample, TLC comparision and by elemental analysis of the prepared diacetate m.p. 143° (lit.,[80] 143).

(iv) 1-Hydroxy-4-salicyloxyxanthone (53)

The fourth compound was identified as a salicyl derivative (53) of 1,4-dihydroxyxanthone (55) (obtained latter on) on the basis of elemental analysis and the spectral studies mass (Fig.20) m/e 348 (M^+) 228 (M^+- 120) 200 (M^+ - 120-28).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40
30
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10
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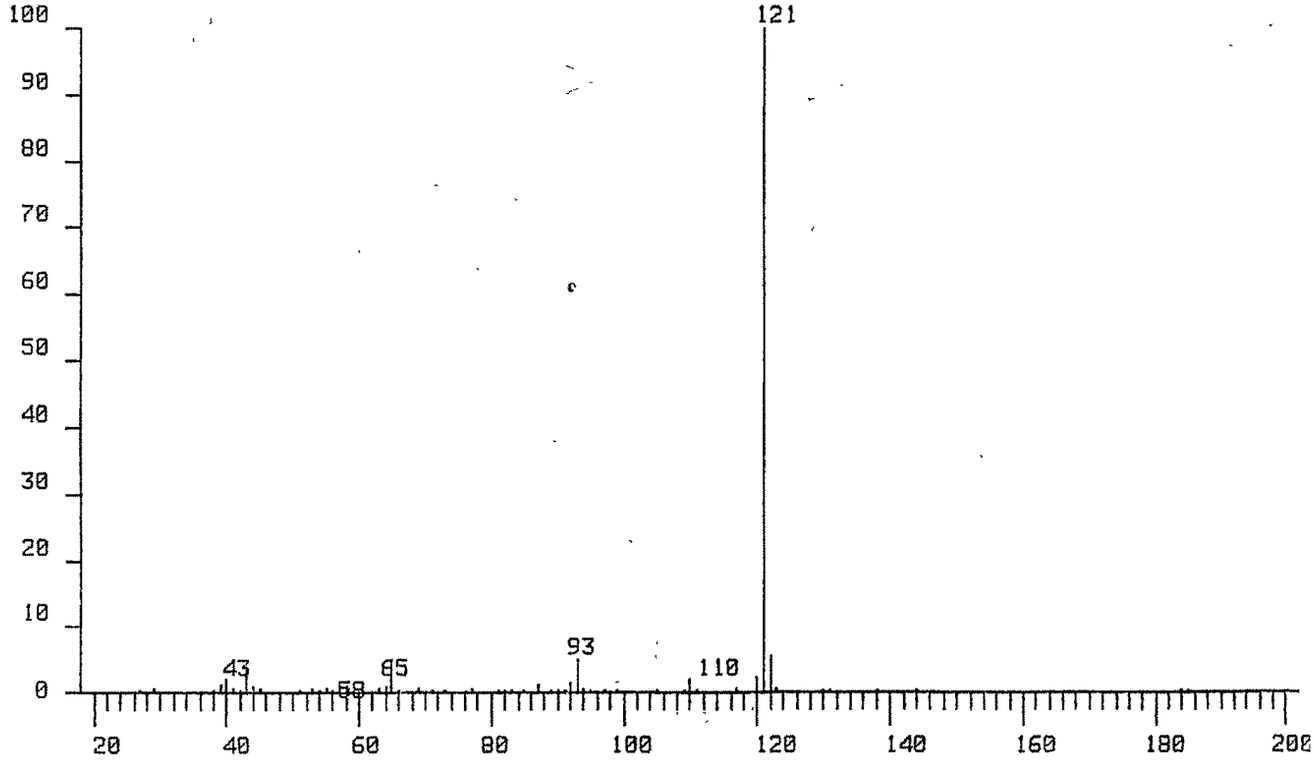
CO
OH
OH
O
CO
50
241
350
200
220
240
260
280
300
320
340
360


100
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60
50
40
30
20
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0
121
93
43
85
110
20
40
60
80
100
120
140
160
180

FIG 18

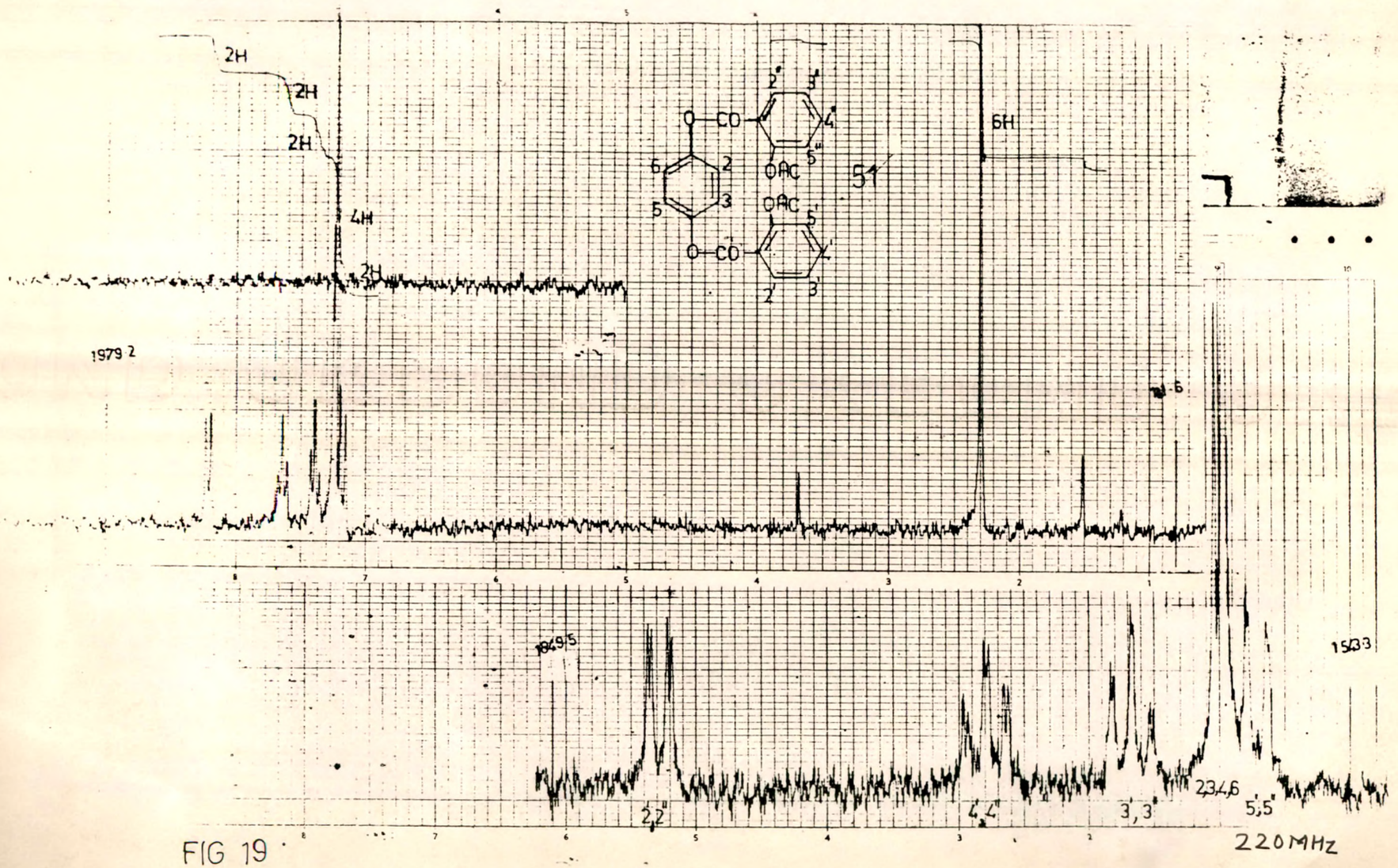


FIG 19

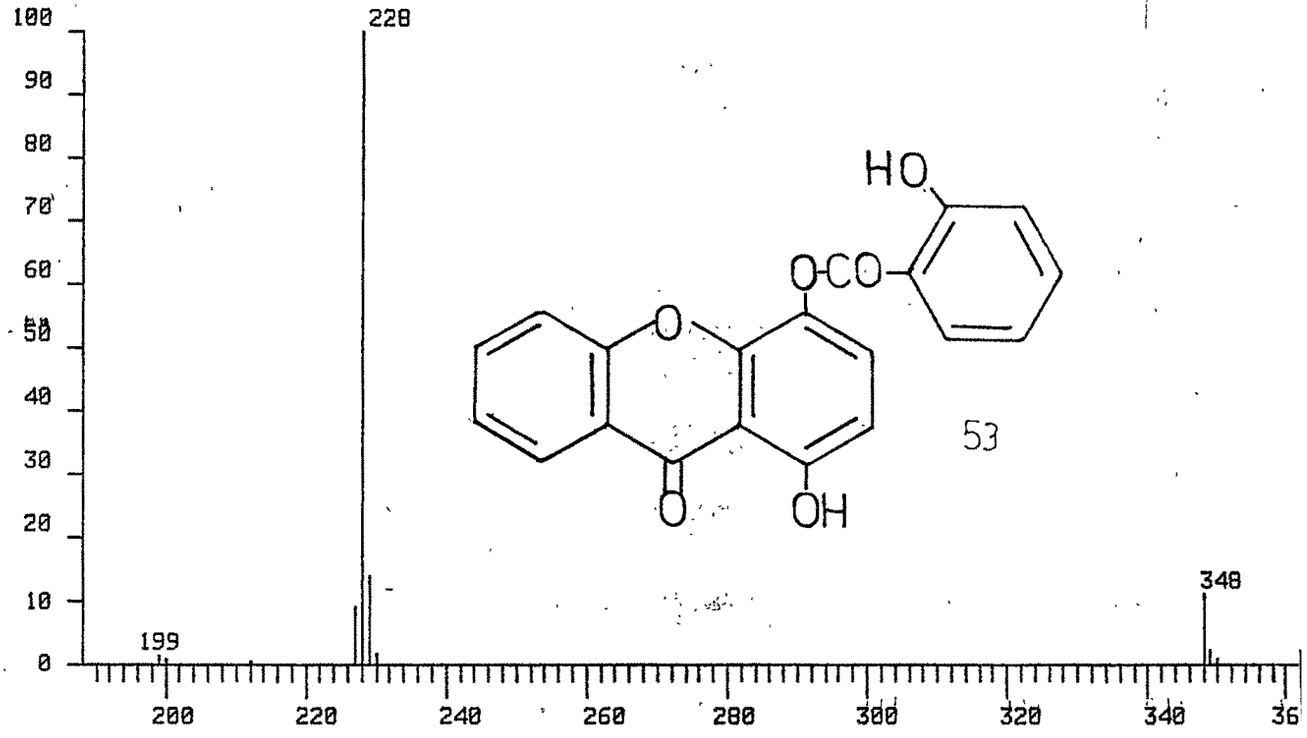
NMR spectrum (Fig.21,22) ($CDCl_3$ + CD_3SOCD_3) showed the two down field double doublets, one at δ 8.22, dd, 1H, J=9,2Hz, H-8 and another at δ 8.14, dd, 1H, J=9,2Hz, H-2' assignments for other peaks are as follows: δ 8.05, singlet, hydroxyl group at position 1 ; 7.8, td, 1H, J=9,9,2Hz, H-6, 7.65, d, 1H, J=9Hz, H-3 ; 7.58, dd, 1H, J=9,2Hz, H-5 ; 7.45, m, 2H, H-3' and H-4' ; 7.35, s, 1H, ArOH 5' position, 7.05 m, 2H, H-5' and H-7', 6.82, d, 1H, J=9Hz, H-2 .

The product (53) on acetylation with acetic anhydride and pyridine gave diacetate (54) Mass and NMR spectral studies of the compound were carried out to support the structure (58), mass m/e 432 (M^+), 390 (M^+ -$COCH_2$), 248 (M^+ -2$COCH_2$), 302 (M^+ -2$COCH_2$-CO). NMR ($CDCl_3$) spectrum (Fig.23). Assignments of peaks were made in following manner: δ 8.32, dd, 1H, J=9,2Hz, H-8, 8.23, dd, 1H, J=9,2Hz, H-2', 7.7, td, 2H, J=9,9,2Hz, H-6 and H-4', 7.57, d, 1H, J=9Hz, H-3, 7.45, td, 1H, J=9,9,2Hz, H-5 and H-3', 7.35, td, 1H, J=9,9,2Hz, H-7, 7.22, dd, 1H, J=9,9,2Hz, H-5, 7.02, d, 1H, J=9Hz, H-2, 2.48, s, 3H, -$OCOCH_3$ at position 1, 2.25, s, 3H, -$OCOCH_3$ at position 6' .

Elution with benzene gave two more products.

(v) <u>1,4-Dihydroxyxanthone (55)</u>

Fifth product obtained, was an abnormal condensation product, which was characterized as 1,4-dihydroxyxanthone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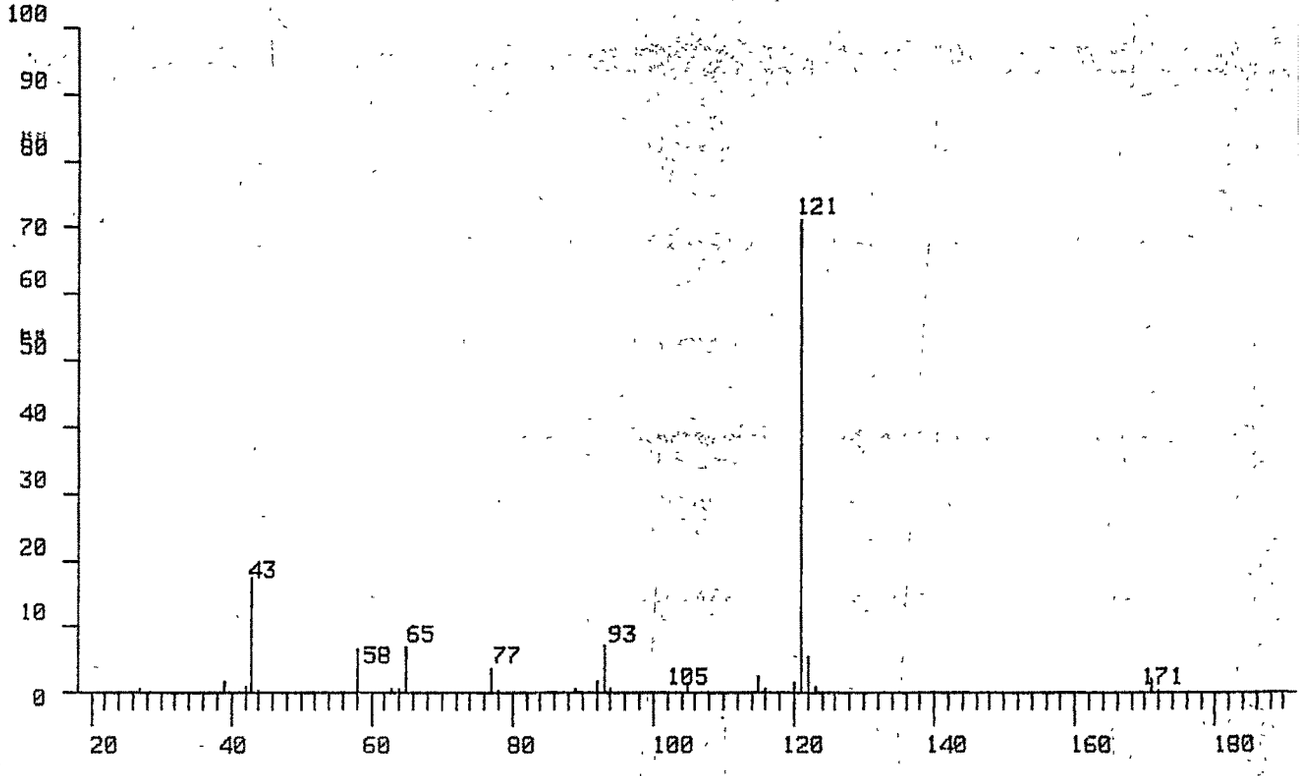
70
60
50
40
30
20
10
0
228
199
348
200
220
240
260
280
300
320
340
HO
O-CO
O
O
OH
53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80
70
60
50
40
30
20
10
0
121
43
58
65
77
93
105
171
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40
60
80
100
120
140
160
180

FIG 20

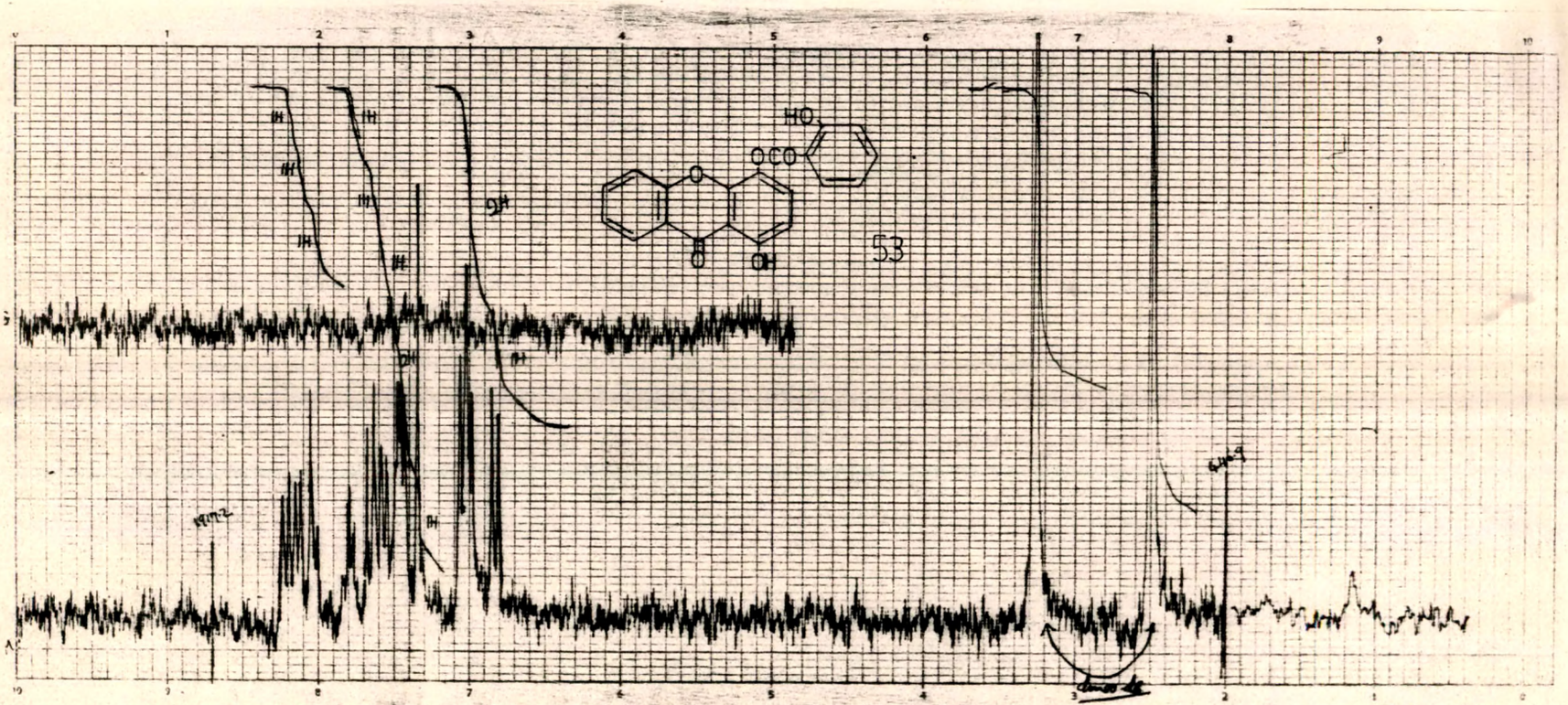


FIG 21

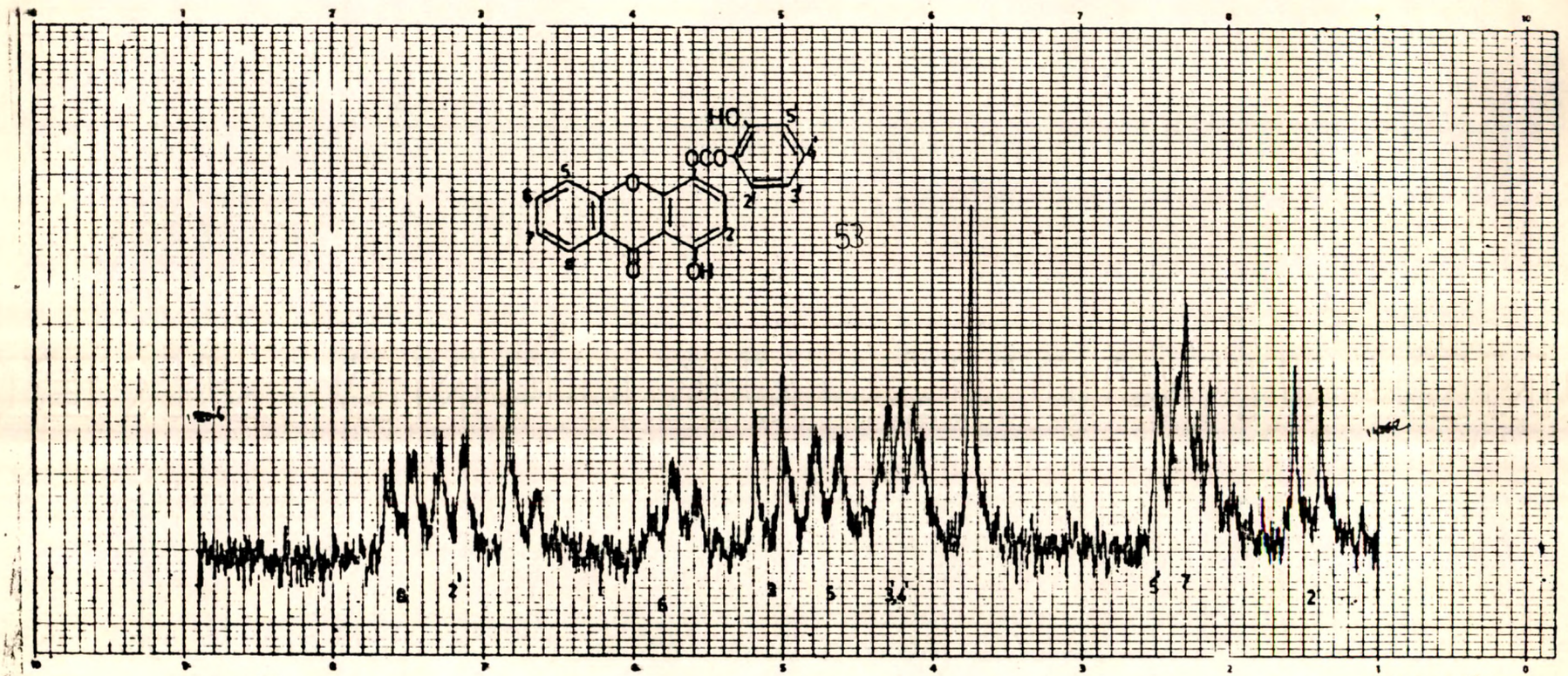


FIG 22

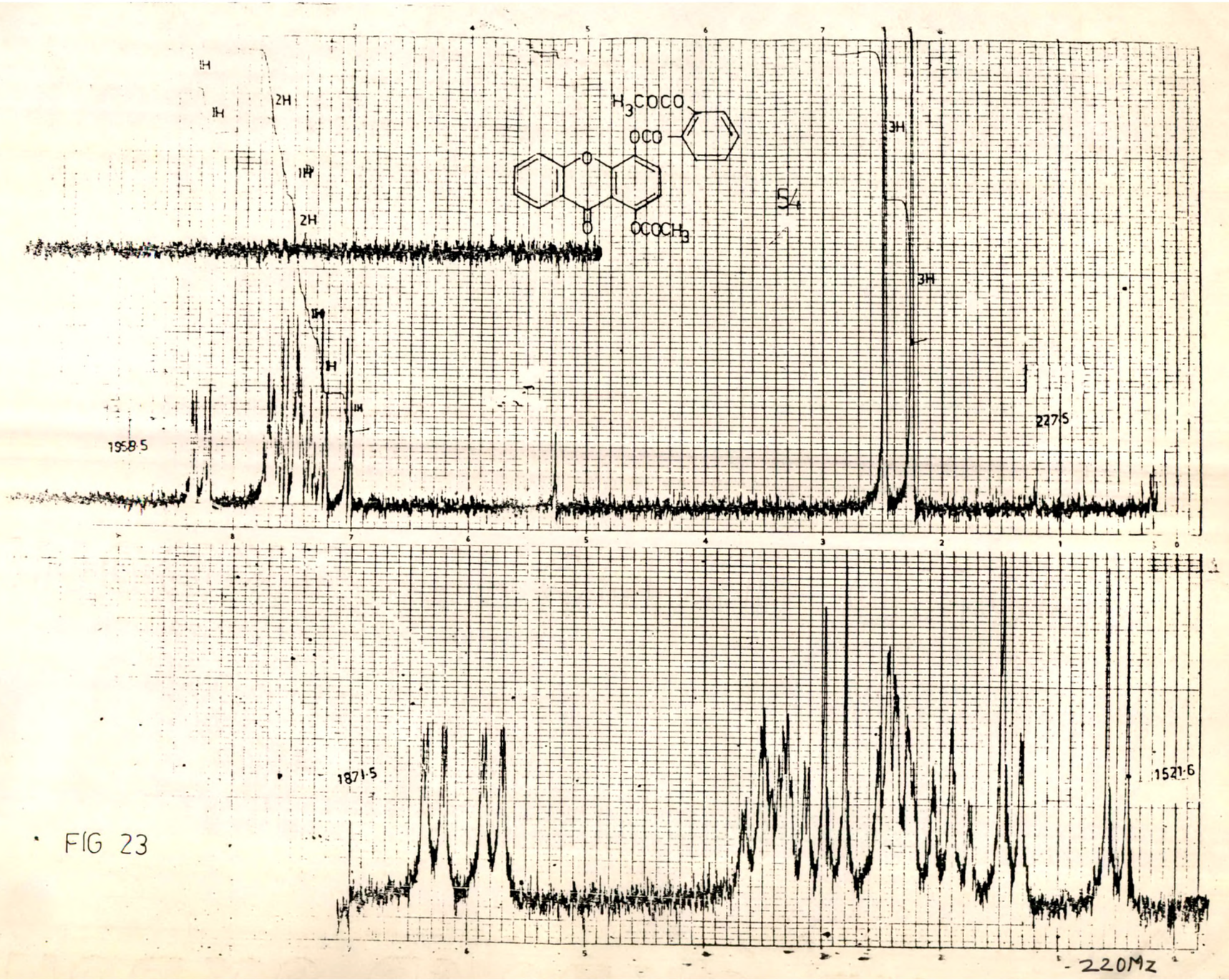
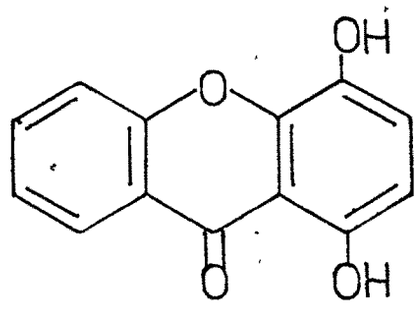


FIG 23

m.p. 235° on the basis of its elemental analysis mass and NMR spectral data.

mass (Fig.24) : m/e 228 (M^+, 100%), 212 (M^+-16) 200 (M^+-CO) suggest molecular formula $C_{13}H_8O_4$ it was in good agreement with elemental analysis. Further fragmentation is shown in Scheme (3). As its NMR ($CDCl_3$ + CD_3SOCD_3)(Fig.25,26) showed two singlets of the one proton at δ 11.82 and 9.3 suggesting that it contain two hydroxy groups, the former peak must be due to chelated hydroxy group at position 1 and latter is due to hydroxy group at position 4. The down field double doublet at δ 8.18 for one proton of J value 8,1.5Hz is attributed to only periproton H-8,, 7.77, td, 1H, J=8,8,2Hz, proton at position 6,, 7.57, dd, 1H, J=8,2Hz, H-5 ; 7.4, td, 1H, J=9,2Hz, H-7 ; 7.25, d, 1H, J_{32} = 9Hz, H-3 ; 6.58, d, 1H, J_{23} = 9Hz, H-2.

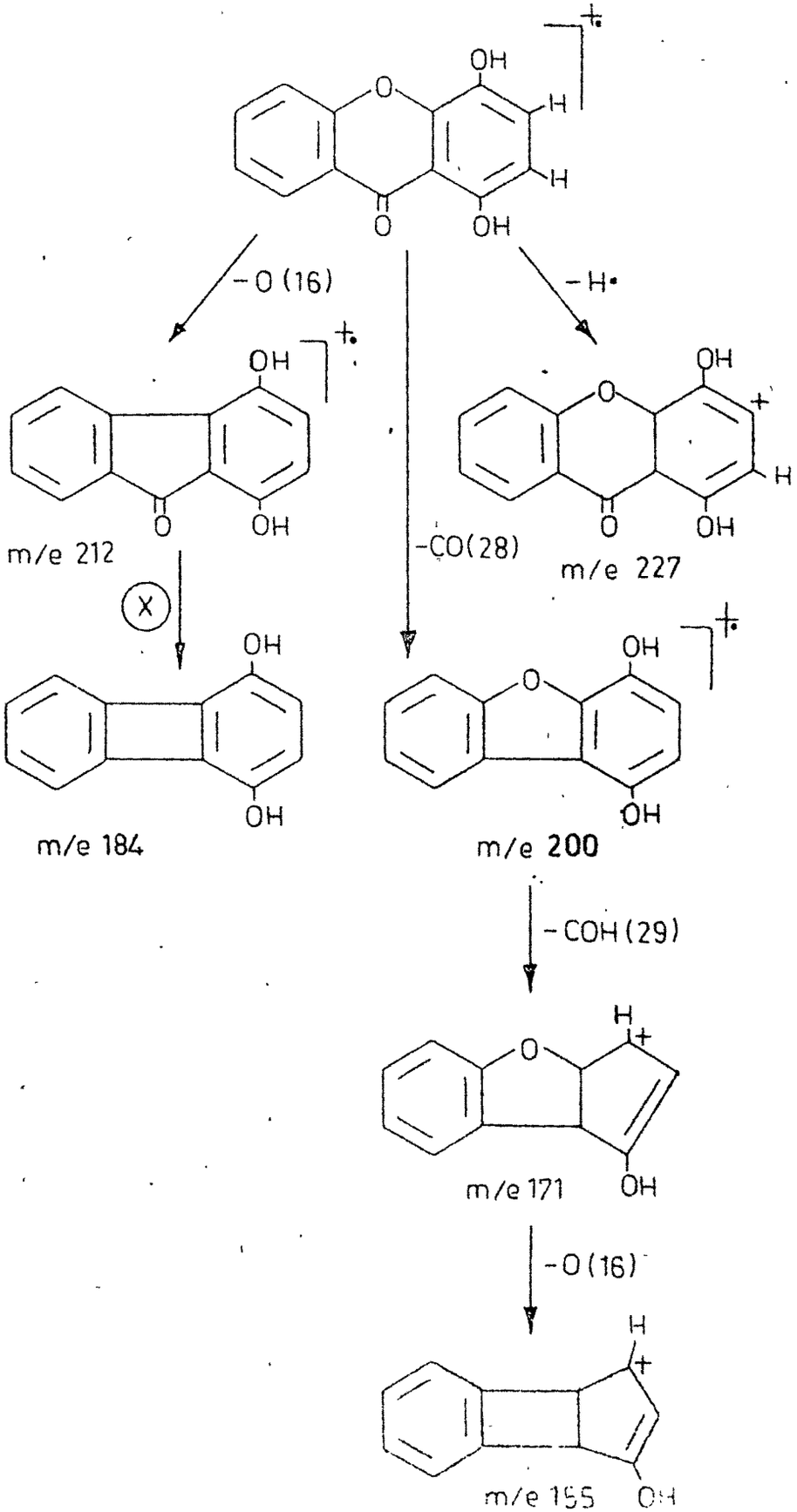
The product (55) on acetylation gave a diacetoxy derivative (56) the structure of which was confirmed by its mass and NMR spectral studies. Mass m/e 272 (M^+), as molecular ion peak is higher by 84 mass unit then the previous compound and its fragmentation followed by successive loss of two 42 units, so it is a diacetate,further more NMR ($CDCl_3$) (Fig.27) showed two singlets each integrating for 3 protons at δ 2.47 and 2.42; δ 8.22, dd, 1H, J=9,2Hz proton at position 8; 7.68, td, 1H, J=9,9,2Hz, H-6 ; 7.56, d, 1H, J=9Hz, H-3; 7.55-7.3, m, 2H, H-5 and H-7; 6.98, d, 1H, J=9Hz, H-2.


OH
O
O
OH

55

100
90
80
70
60
50
40
30
20
10
0
228
77
115
43
171
63
105
89
200
212
25
50
75
100
125
150
175
200
225

FIG 24



SCHEME - 3

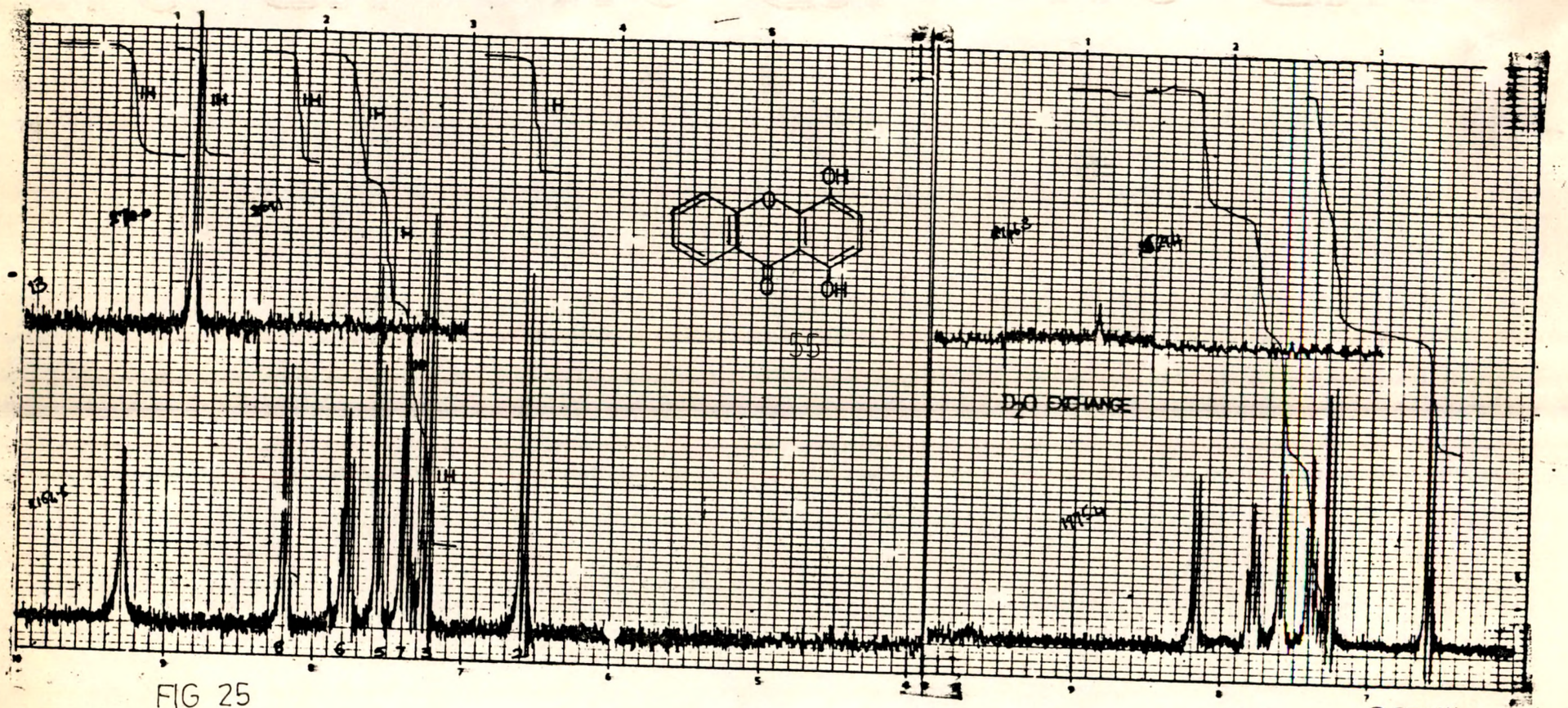


FIG 25

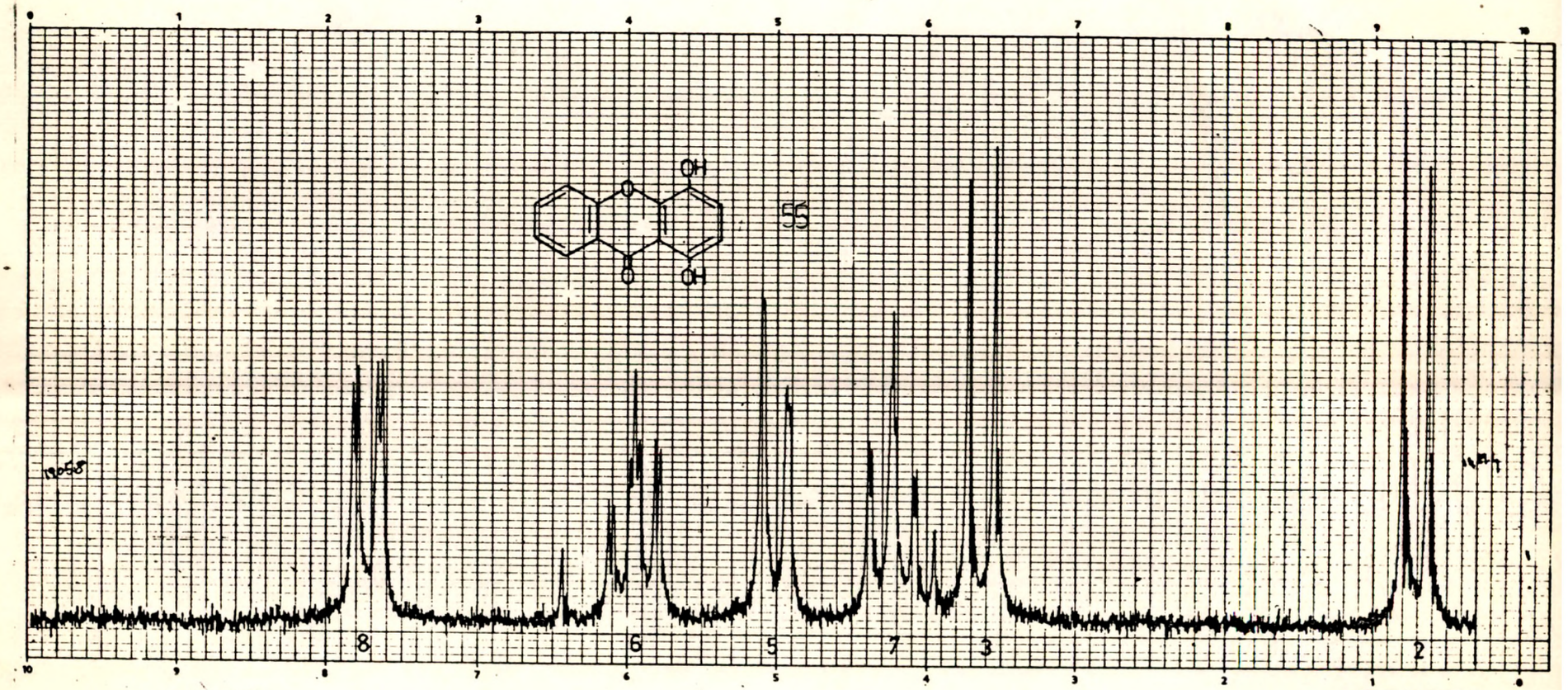
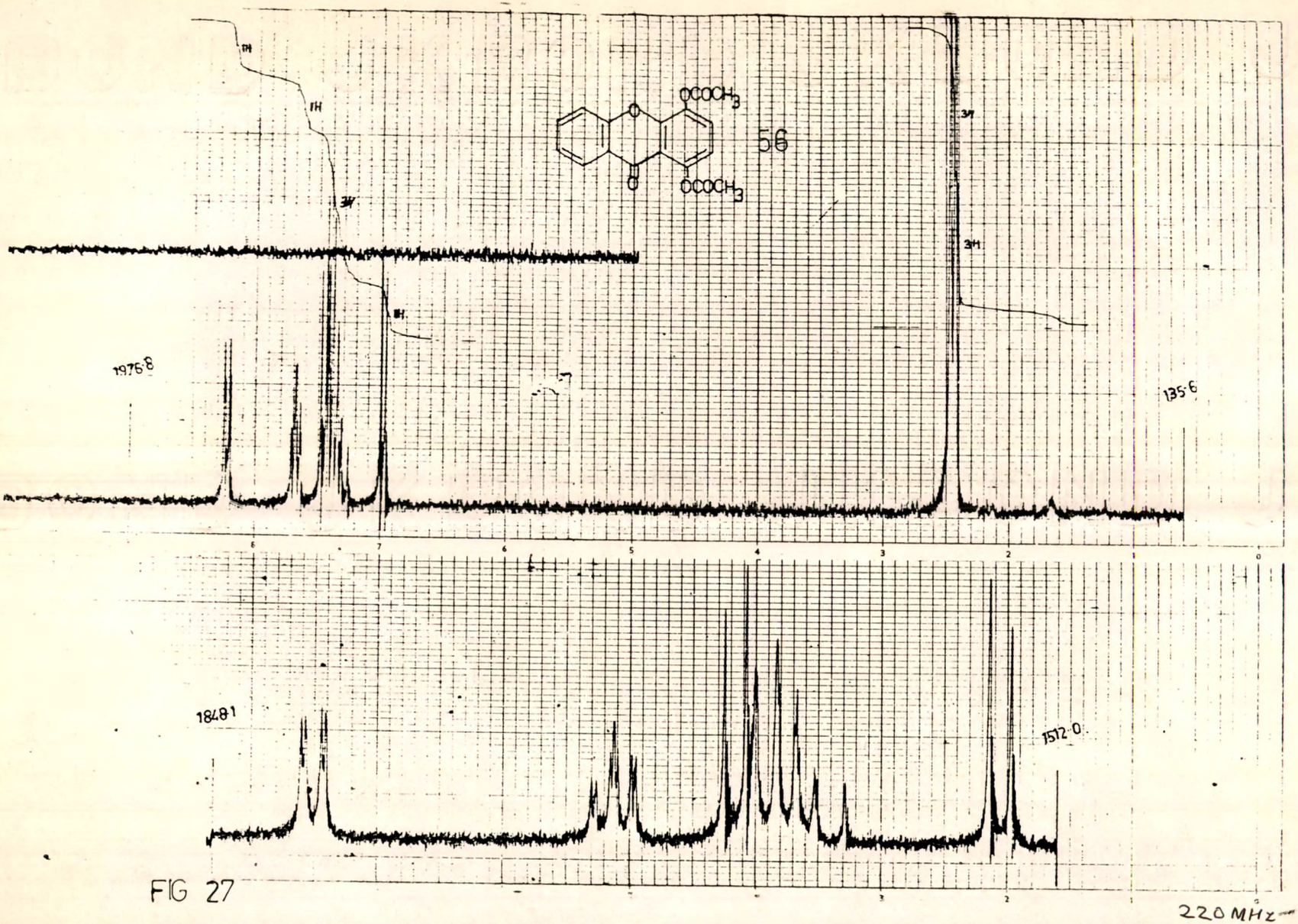


FIG 26



56

FIG 27

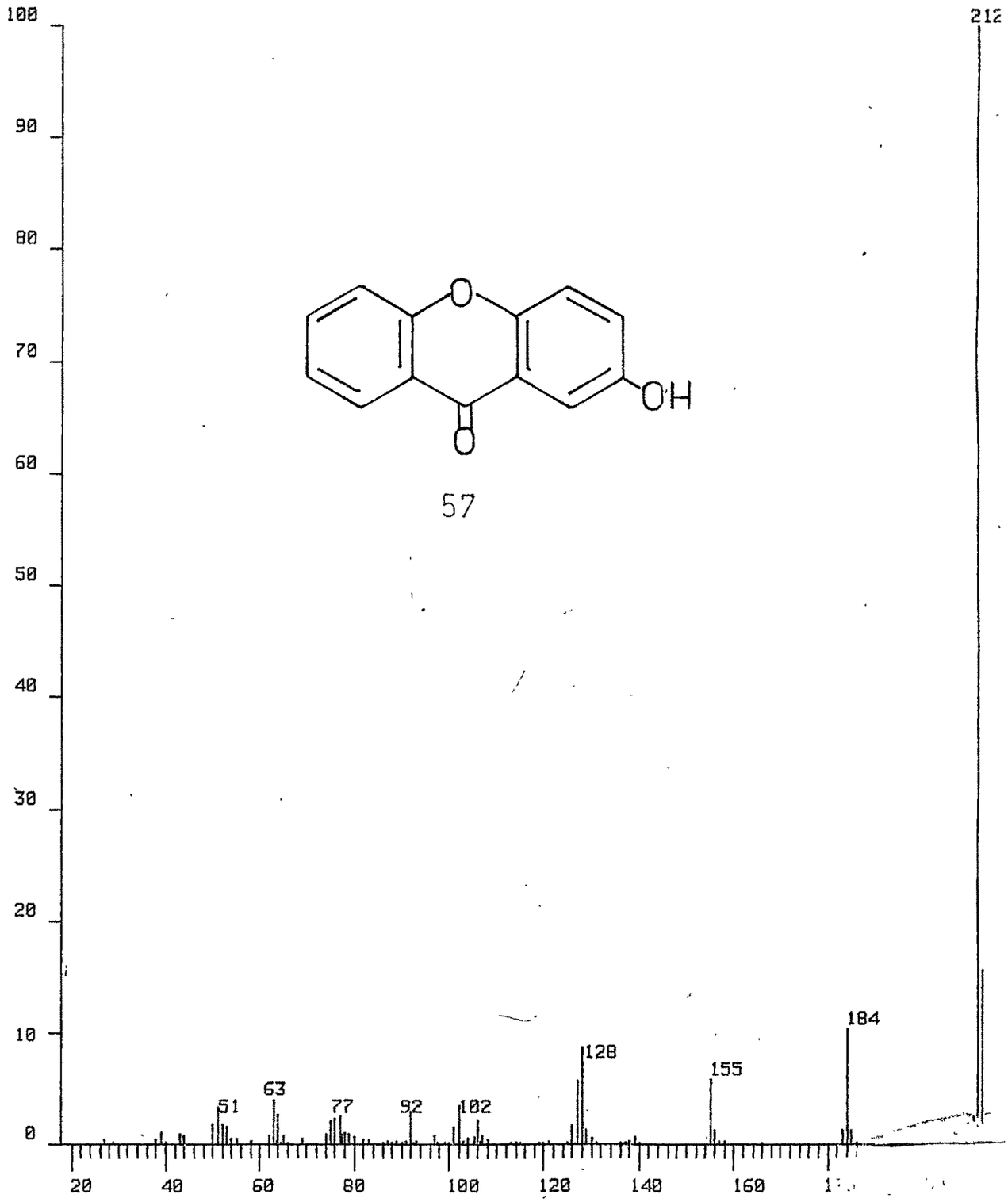
(vi) 2-Hydroxyxanthone (57)

Sixth product obtained from coloumn was the desired xanthone, 2-hydroxyxanthone (57), m.p. 244° (lit.,[16] 236-9°). Its structure was established on the basis of spectral studies. Mass (Fig.28) m/e 212 (M^+) mass fragmentation pattern is shown in Scheme (4).

The product (57) on acetylation with acetic anhydride and pyridine gave a mono acetate (58). The structure of which was confirmed by its mass and NMR spectral data. Mass m/e 254, 242, 183 NMR ($CDCl_3$) (Fig.29,30), showed double doublet in the down field aromatic region at 8.22 is assigned to the proton at position 8, δ 8.01 doublet of small coupling constant J=1.5Hz (due to metacoupling) is ment for only proton at position 1 as it can be meta coupled with proton 3 and appeared in the down field due to the carbonyl group, 7.7, td, 1H, J=9,9,2Hz, H-6, 7.5 to 7.3, m, 4H, H-3, H-4, H-5 and H-7 and 2.3, singlet for the three protons of the $OCOCH_3$ group. The methylation of (57) was carried out to obtain a naturally occuring xanthone, 2-methoxyxanthone (59) m.p. 131° (lit.,[16] m.p. 131°).

Refluxing of 4'-hydroxyphenyl salicylate in diphenyl ether (52) :

In order to know whether it is possible to get xanthone from ester derivative by the thermolysis. Refluxing of 4'-hydroxyphenyl salicylate was carried out in diphenyl ether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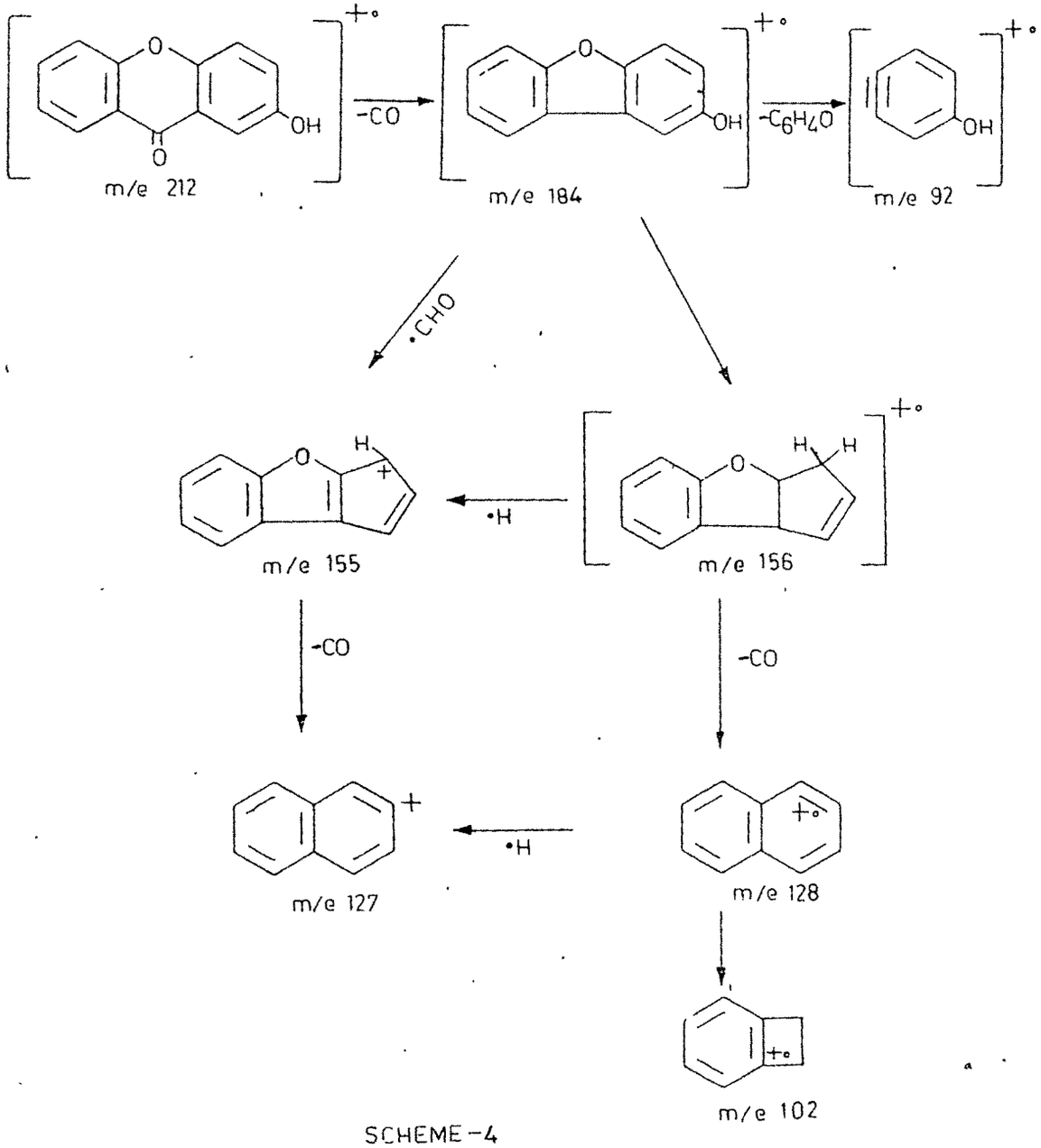
80
70
60
50
40
30
20
10
0
212
184
128
155
63
51
77
92
102
20
40
60
80
100
120
140
160
OH
O
O

57

FIG 28


m/e 212
-CO
m/e 184
-C6H4O
m/e 92
•CHO
•H
m/e 155
m/e 156
-CO
-CO
•H
m/e 127
m/e 128
m/e 102

SCHEME-4

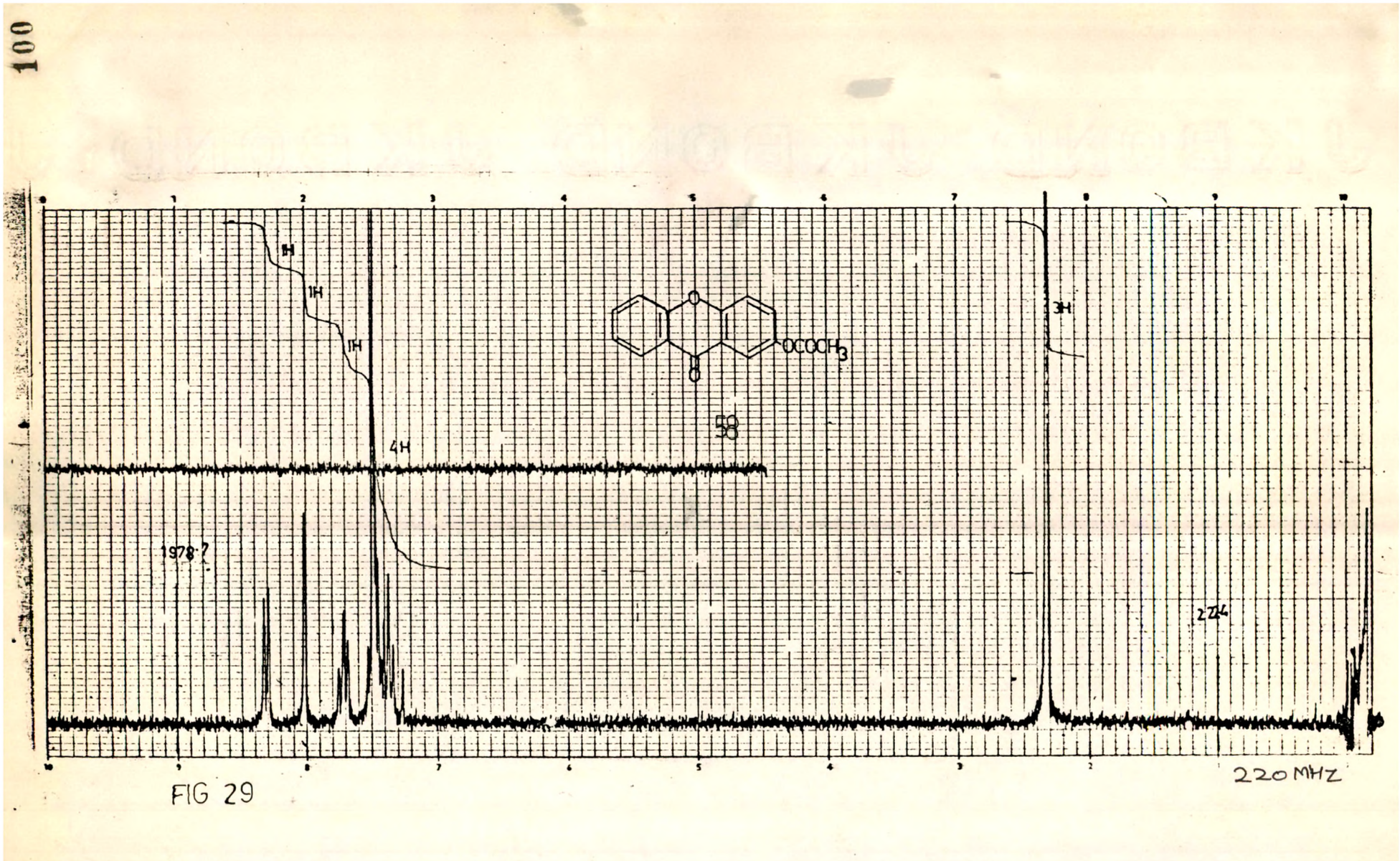


FIG 29

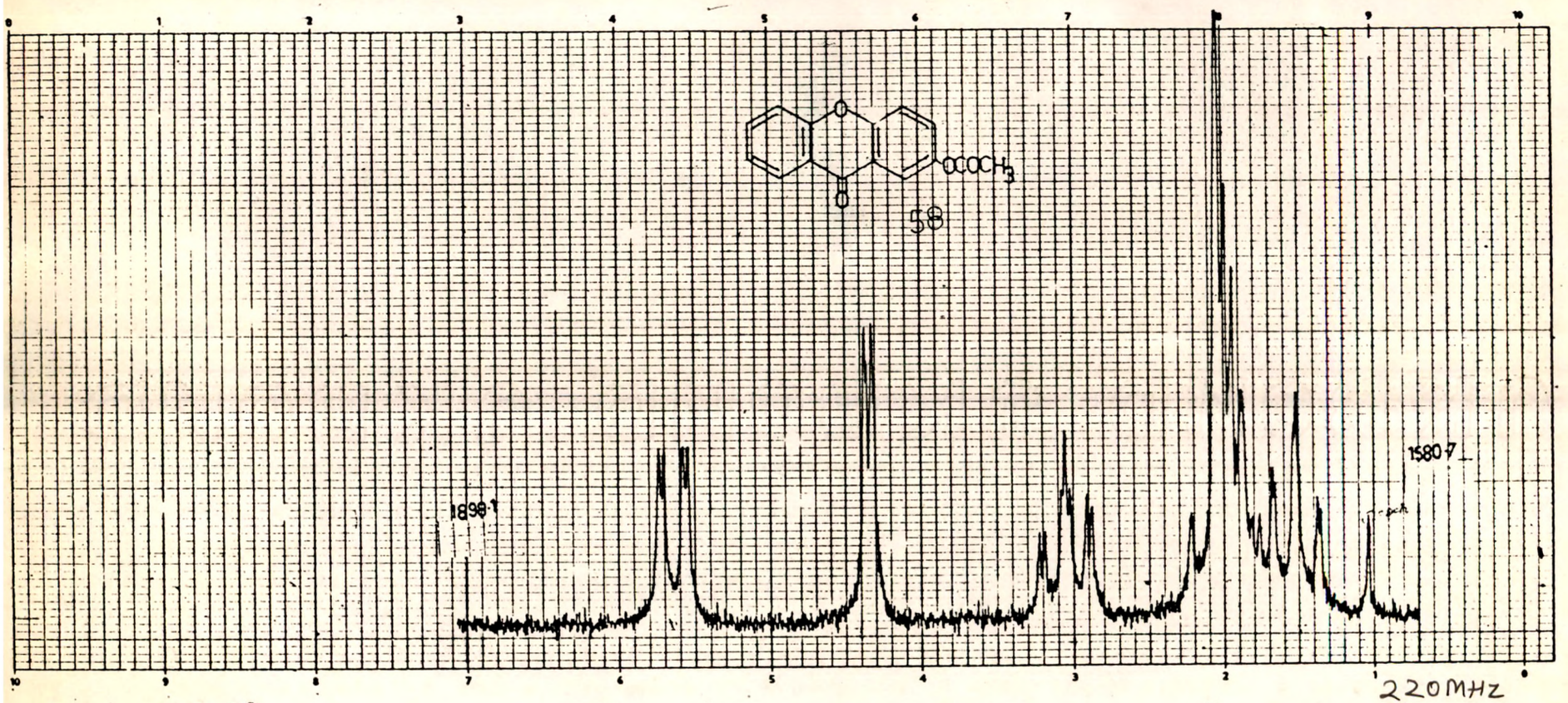


FIG 30

for 42 hr. The solvent was removed by steam distillation. The product obtained was found to be a mixture of several compounds and was subjected to silica gel column chromatography to get following compounds:

(i) 1-Hydroxyxanthone (49)

(ii) Hydroquinone disalicylate (50)

(iii) 1-Hydroxy-4-salicyloxyxanthone (54)

(iv) 1-4-Dihydroxyxanthone (55)

(v) 2-Hydroxyxanthone (57)

Condensation of hydroquinone with Salicylic acid

Thermal condensation of hydroquinone and salicylic acid in refluxing diphenyl ether for 44 hr was carried out. The reaction mixture after usual work up and column chromatography gave following compounds :

(1) 1-Hydroxyxanthone (49)

(2) Hydroquinone disalicylate (50)

(3) 4'-Hydroxyphenyl salicylate (52)

(4) 1,4-Dihydroxyxanthone (55)

(5) 2-Hydroxyxanthone (57)

In this condensation, as seen above, the yield of all the hydroxyxanthones was very poor. However, the yield of the ester (52) obtained was the highest amongst all the isolated compounds which indicates that the ester (52) was the main intermediate in the condensation reaction. The fact was further supported by the previous experiments.

In the foregoing condensation of hydroquinone with ethylsalicylate, the formation of the ester (52) and the diester (50) can be accounted on the basis of trans esterification reaction. Formation of 2-hydroxyxanthone is obvious and can be explained by the simple mechanism as shown in scheme (5). The formation of 1-hydroxyxanthone and 1,4-dihydroxyxanthone and its mono salicyloxy derivative is rather very difficult to explain. It is possible to explain the formation of 1,4-dihydroxyxanthone by taking p-benzoquinone as an intermediate in the condensation, which may be attacked by the ethylsalicylate molecule to form a structure like (B), which on ketoenol tautomarism gave (C) scheme (6) , (C) on elimination of ethanol molecule gave a ketonic structure (D), which undergoes ketoenol tautomarism to give 1,4-dihydroxyxanthone (55). As the condensation of p-benzoquinone does not give 1-hydroxy, 1,4-dihydroxy and 2-hydroxyxanthone but yielded a diester, 1,4-salicyloxy hydroquinone (50), the mechanism proposed in scheme (6) is untenable. Other explaination is to start with structure (A) [from scheme (5)] from which formation of 1,4-dihydroxyxanthone (55) can be explained in two ways.

(i) The structure (A) may undergo oxidation to form a p-quinoid intermediate (E). The p-quinone (E) [scheme (7)] can be thermally transformed into xanthone (55) by an

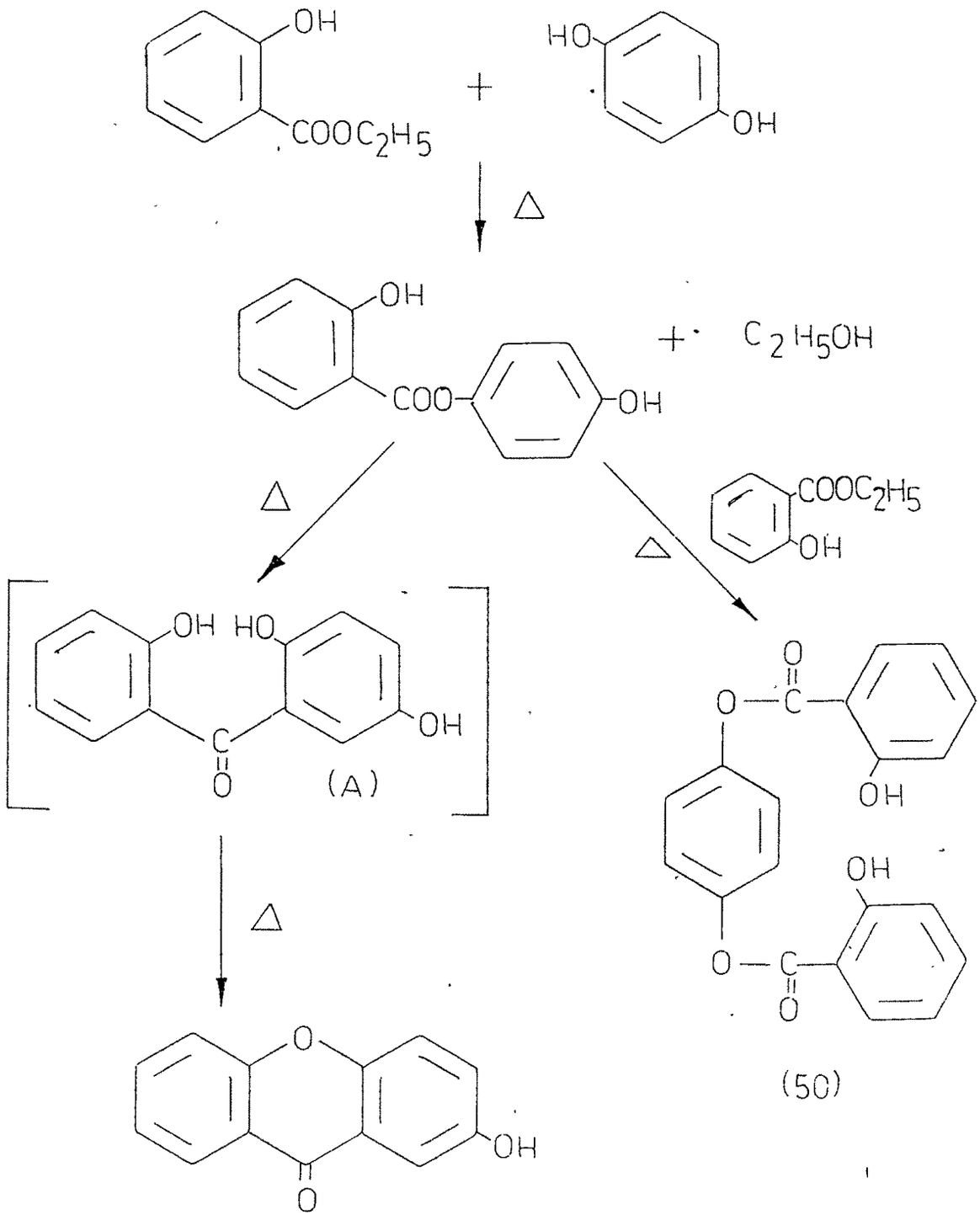
intramolecular Michael addition followed by tautomarism to give (55). This explaination is based on the observation made by Whally and coworkers[84] in the thermal conversion of 2-(2,4-dihydroxy-3-methyl benzoyl)-p-quinone (W) to 1,4,6-trihydroxy-5-methylxanthone (X).

(ii) The second way [scheme (8)] of explaination involves the formation of the diradical (F) of benzophenone (A), (F) can give, through (G) followed by ketonisation, the spiro compound (H). The spiro compound at higher temperature transformed into 1,4-dihydroxyxanthone (55).

This explaination is based on the observation made by Lewis and coworkers[85] in the conversion of 4-methoxy-2,2',5'-trihydroxy-6-methyl benzophenone (Y) into 1,4-dihydroxy-6-methoxy-8-methylxanthone (Z). One more mechanism is also proposed, which can explain the formation of all the three xanthone derivatives viz 1-hydroxyxanthone (49), 1,4-dihydroxyxanthone (55) and 2-hydroxyxanthone (57). The proposed mechanism, involves the formation of a free radical at higher temperature, is rationalised in scheme (9).

Condensation of 2-methylhydroquinone with ethyl salicylate

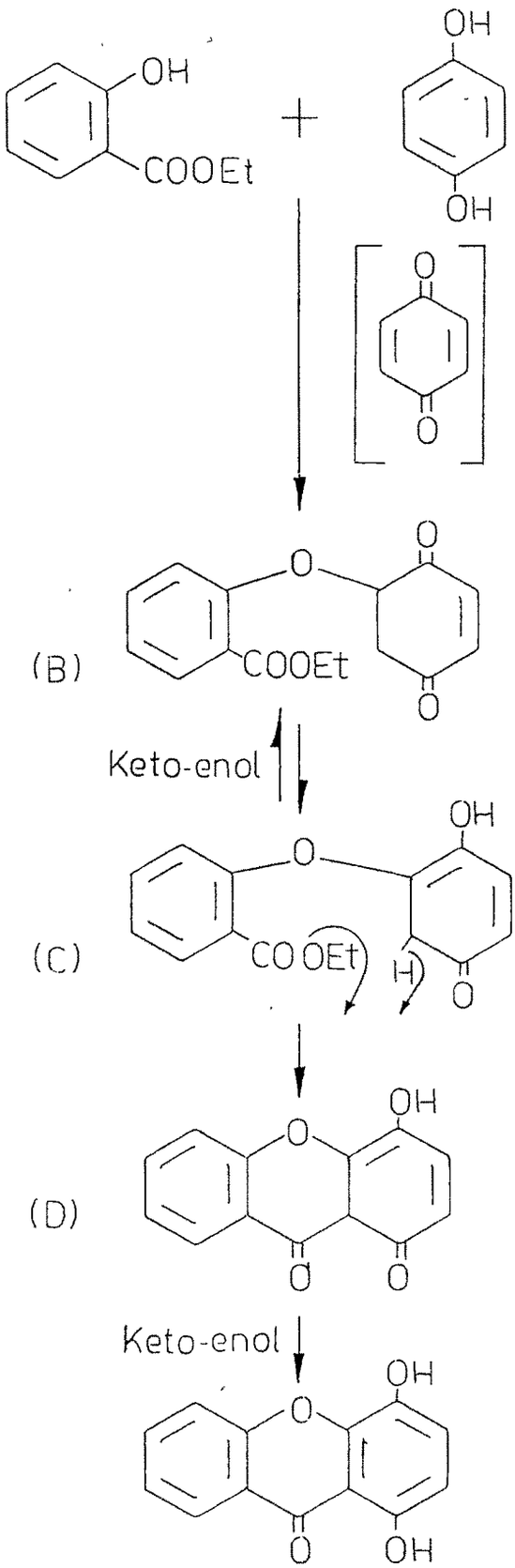
A mixture of 2-methylhydroquinone and ethyl salicylate was refluxed in diphenyl ether for 4 to 5 hr. The usual work up of the reaction mixture gave a paste, which was chromatographed over silica gel and eluted with petroleum



(50)

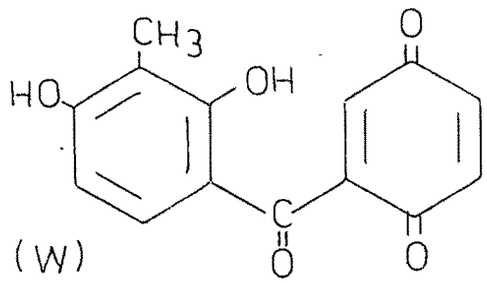
(57)

SCHEME – 5

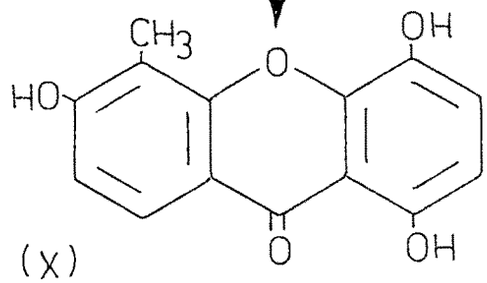

OH
COOEt
OH
OH
O
O
O
O
COOEt
(B)
Keto-enol
OH
O
CO OEt
H
O
(C)
OH
O
O
O
(D)
Keto-enol
OH
O
O
OH

(55)

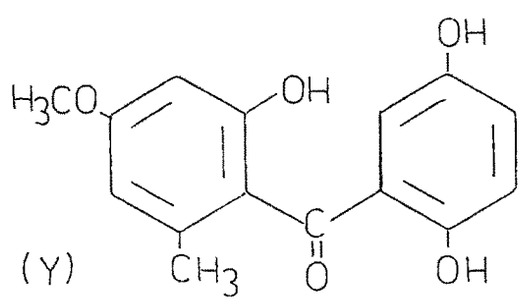
SCHEME - 6


CH3
HO
OH
O
C
O
O

(W)


CH3
HO
O
OH
O
OH

(X)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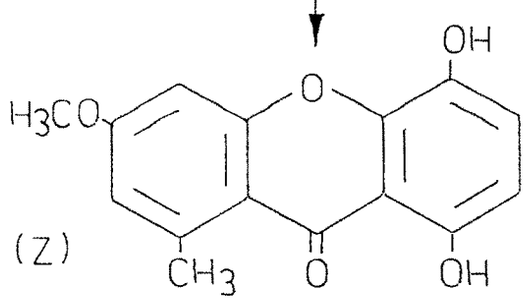
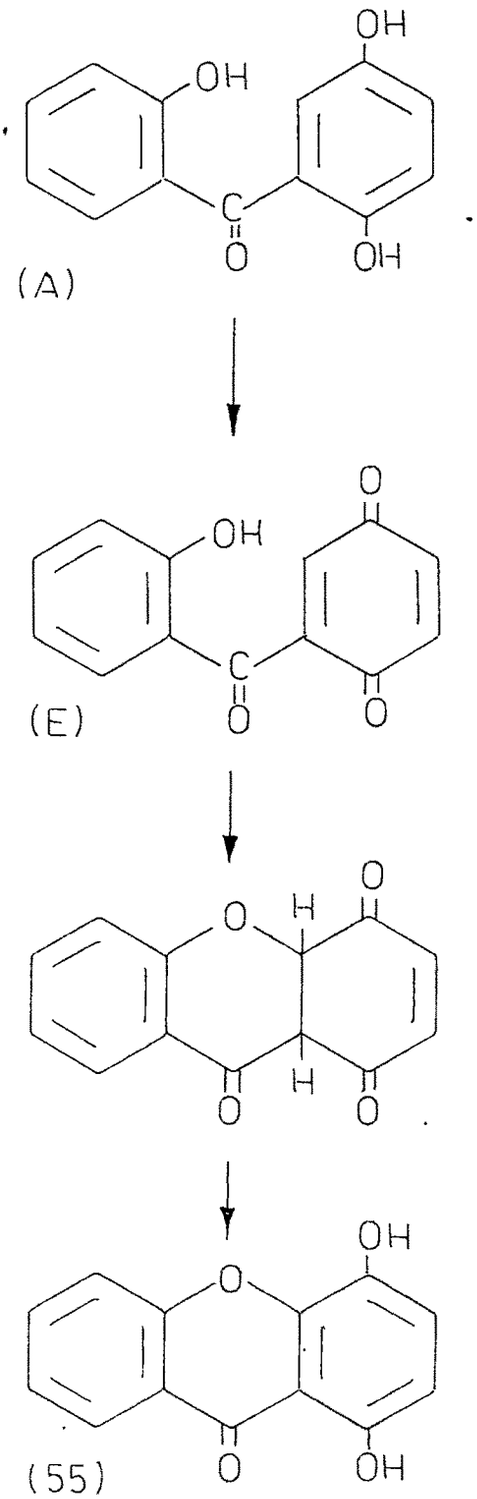
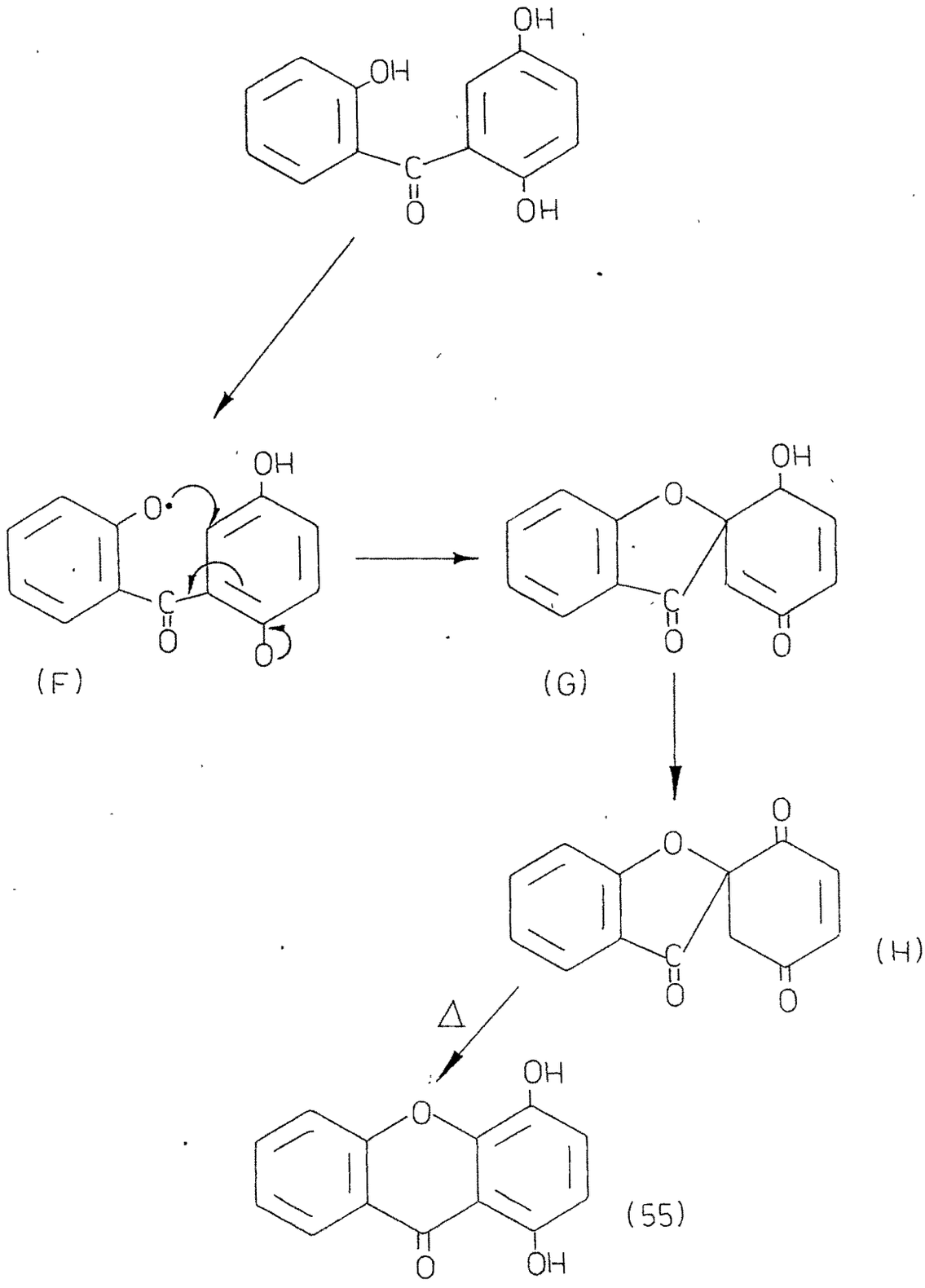
H3CO
OH
C
O
(Y)
CH3
OH

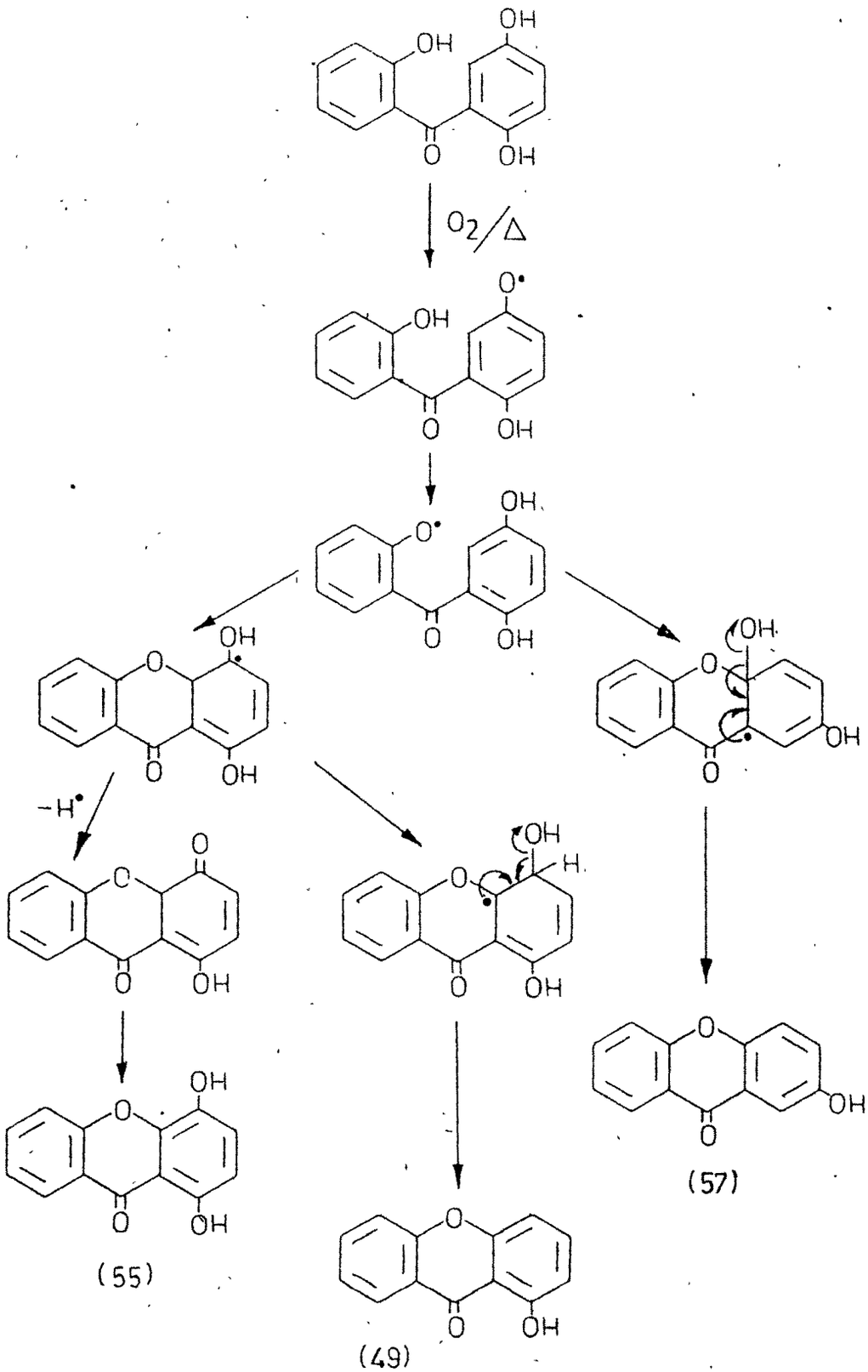

OH
H3CO
O
(Z)
CH3
O
OH



SCHEME – 7



SCHEME – 8


OH
OH
O
OH
O_2/Δ
O•
OH
O
OH
OH
O•
O
OH
OH
O
OH
OH
O
OH
$-H^{\bullet}$
O
O
OH
OH
O
H
O
OH
O
OH
OH
O
O
OH
(55)
O
O
OH
(49)
(57)

SCHEME-9

ether gave (60). m.p. 95 The further elution with petroleum ether gave a yellow oil, which solidified latter, and was purified to give a yellow crystalline compound m.p. 128-130° not identified.

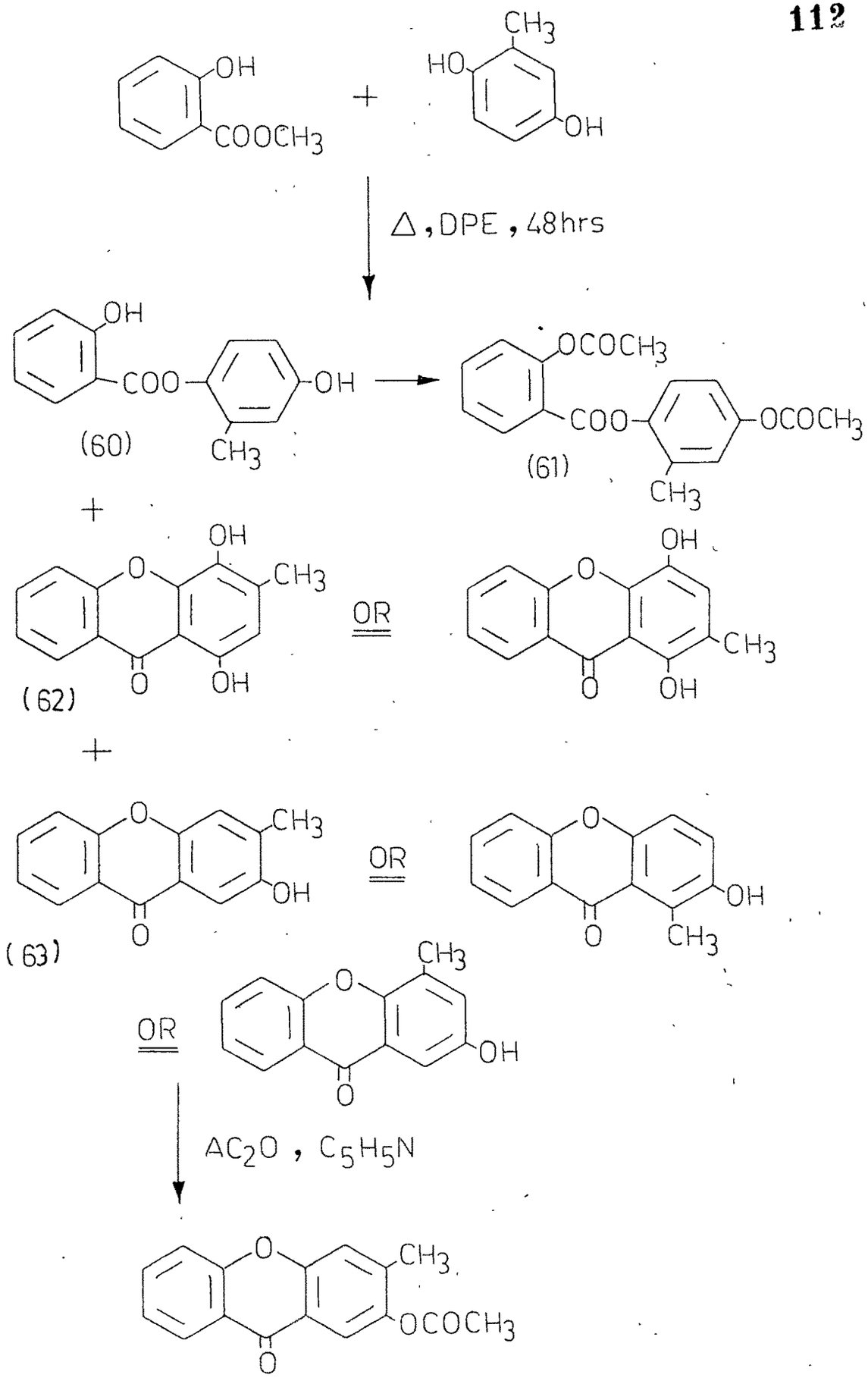
Condensation of 2-methylhydroquinone with ethyl salicylate

In order to know whether it is possible to isolate 1,4-dihydroxyxanthone type of compound with other hydroquinone derivative, the condensation of 2-methyl hydroquinone and ethyl salicylate was carried out in refluxing diphenyl ether for 48 hr. The reaction mixture was worked up in usual manner to give a pasty product, which was found to be a mixture of number of compounds by TLC examination and was column chromatographed over a silica gel column which gave six compounds out of which two compounds were not identified due to very small amount.

(i) 2'-Methyl-2,4'-dihydroxyphenyl salicylate (60)

The title ester (60) was eluted by petroleum ether and benzene mixture and characterized on the basis of its elemental analysis and spectral studies of its acetoxy derivative.

The product (60) on acetylation with acetic anhydride and pyridine gave diacetate derivative (61). NMR ($CDCl_3$) shows δ 2.2, singlet for 3H of the aromatic methyl group, 2.52, s, 6H, for the two $OCOCH_3$ groups and 7.1 - 7.7, multiplet for the remaining 7 aromatic protons.


OH
COOCH3
CH3
HO
OH
Δ, DPE, 48hrs
OH
COO
OH
CH3
(60)
OCOCH3
COO
OCOCH3
CH3
(61)
OR
(62)
OR
(63)
OR
AC2O, C5H5N
OCOCH3

(v) 1,4-Dihydroxy-3-methylxanthone (62)

Elution with higher proportion of benzene in benzene petroleum ether mixture eluted a compound, which was tentatively characterized as (62), on the basis of its elemental analysis.

(vi) 2-Hydroxy-3-methylxanthone (63)

The title compound was eluted by benzene and structure was assigned as (63) on the basis of NMR of its acetoxy derivatives in $CDCl_3$, which showed double doublet at δ 8.25 for the proton at position 8; 7.88, singlet, 1H, proton at position 1; 7.2 to 7.7, multiplet, 4H, H-5, H-6, H-7, H-4; 2.3, two singlets, 6H, protons of $-CH_3$ and $OCOCH_3$.

Condensation of 3-hydroxyxanthone with ethyl salicylate

A mixture of 3-hydroxyxanthone and ethyl salicylate was condensed in refluxing diphenyl ether for 18 hr. The reaction mixture after steam distillation gave sodium hydroxide insoluble product, which was found to be a mixture of two compounds by TLC examination and was chromatographed over silica gel column. Elution with (first 500 ml) benzene gave first compound, the ether (65). The structure of which was established on the basis of its elemental analysis and mass spectral data. Mass (Fig.31): m/e 406 (M^+).

The further elution with benzene (1.5 lit) gave second product which was characterized as dixanthone (66) on the basis of its elemental analysis and mass spectral data. Mass (Fig.32) m/e 315 (M^+).

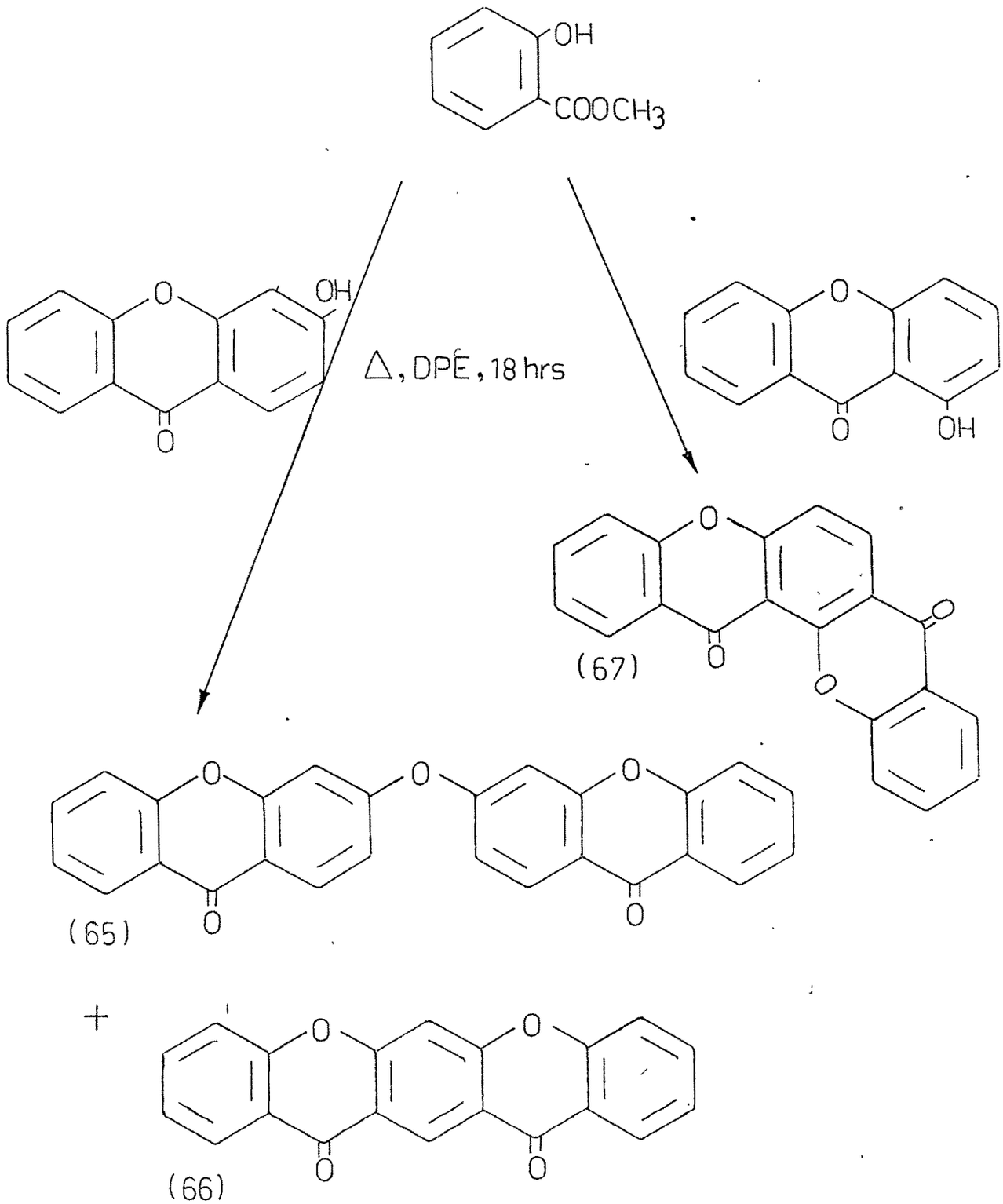
Condensation of 1-hydroxyxanthone with ethyl salicylate :

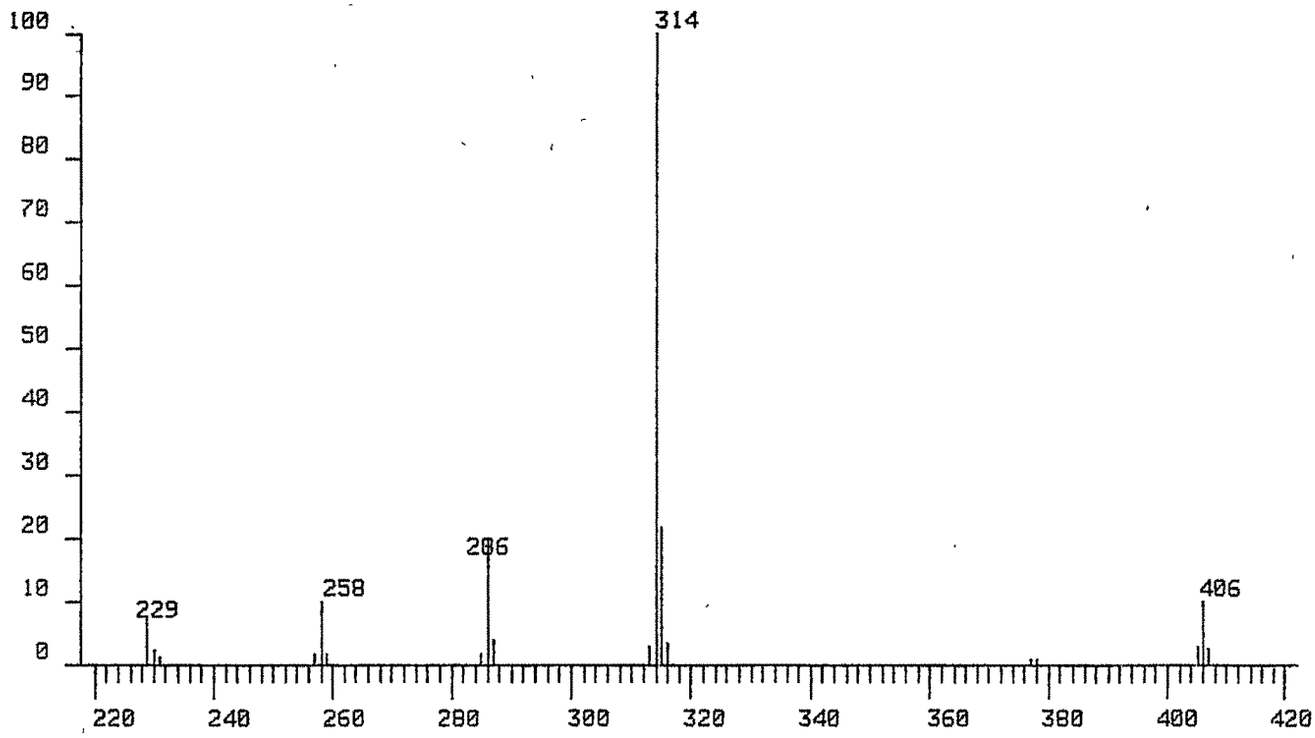
An equimolar quantities of 1-hydroxyxanthone and ethyl salicylate were condensed in refluxing diphenyl ether. The product obtained after steam distillation, showed two spots on TLC, one corresponding to 1-hydroxyxanthone and other one is of the product. It was separated by preparative TLC to give compound (67) m.p. 207° it did not develop any colour with alcoholic ferric chloride solution. The structure was established on the basis of its elemental analysis.

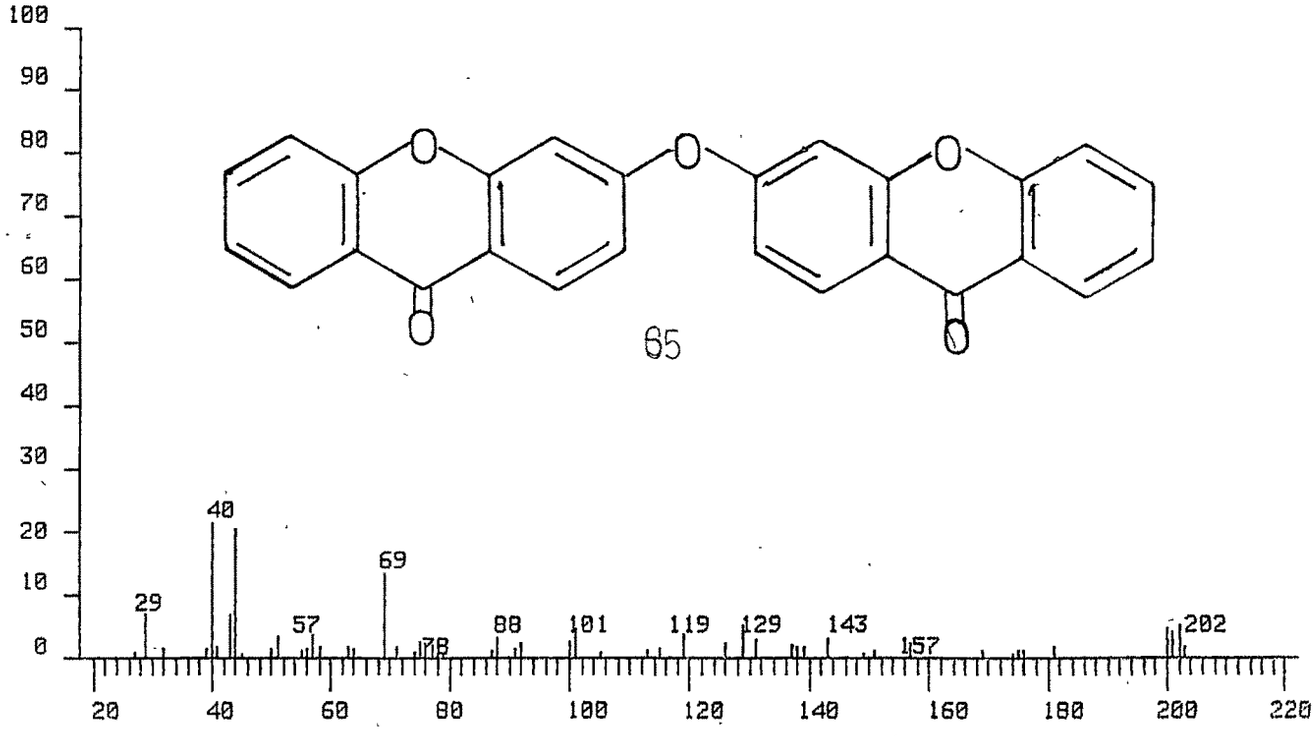
Condensation of 2,7-dihydroxy naphthalene with ethyl salicylate : 2'-Naphthyl-2,7'-dihydroxybenzoate (68)

A mixture of 2,7-dihydroxynaphthalene and ethyl salicylate was refluxed in diphenyl ether for 10 hr. to the reaction mixture petroleum ether was added. The product obtained thereby was characterised as 2'-naphthyl-2,7'-dihydroxy benzoate (68) on the basis of elemental analysis. IR (KBr) νmax 3440 (OH) 1685 (-COO).

The product on acetylation gave diacetoxy derivative (69). The structure of which was confirmed by NMR spectral studies. NMR spectrum ($CDCl_3$) showed two singlets in the

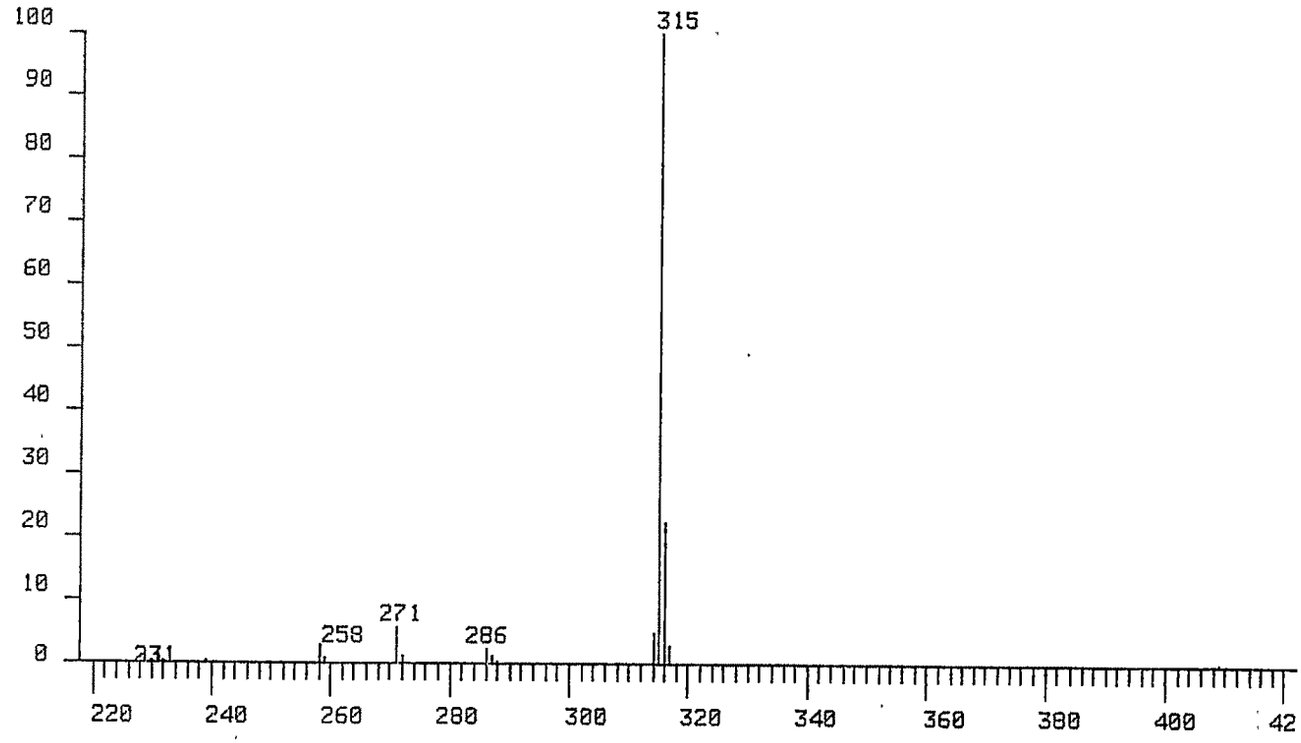

OH
COOCH3
O
OH
O
Δ, DPE, 18 hrs
O
O
OH
O
O
O
(67)
O
O
O
O
O
(65)
+
O
O
O
O
(66)

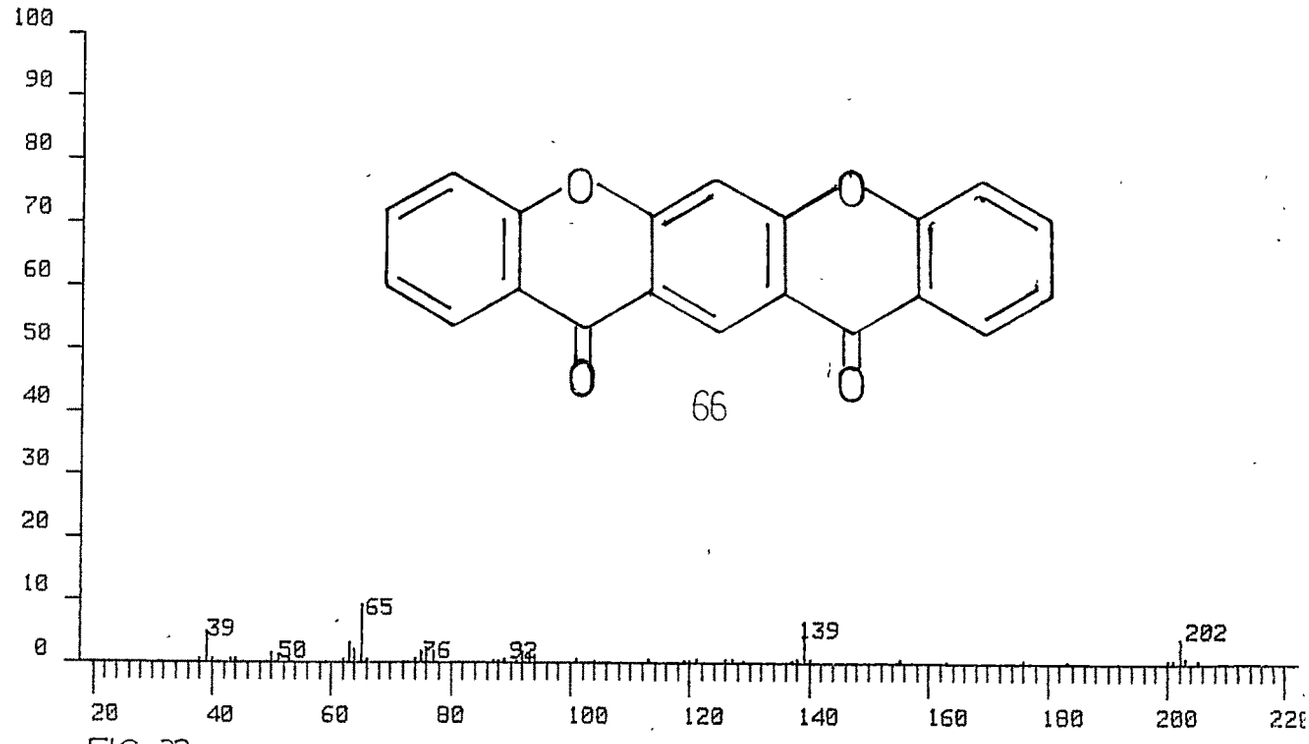

100
90
80
70
60
50
40
30
20
10
0
314
286
258
229
406
220
240
260
280
300
320
340
360
380
400
420


100
90
80
70
60
50
40
30
20
10
0
40
69
29
57
88
101
119
129
143
157
202
20
40
60
80
100
120
140
160
180
200
220

65

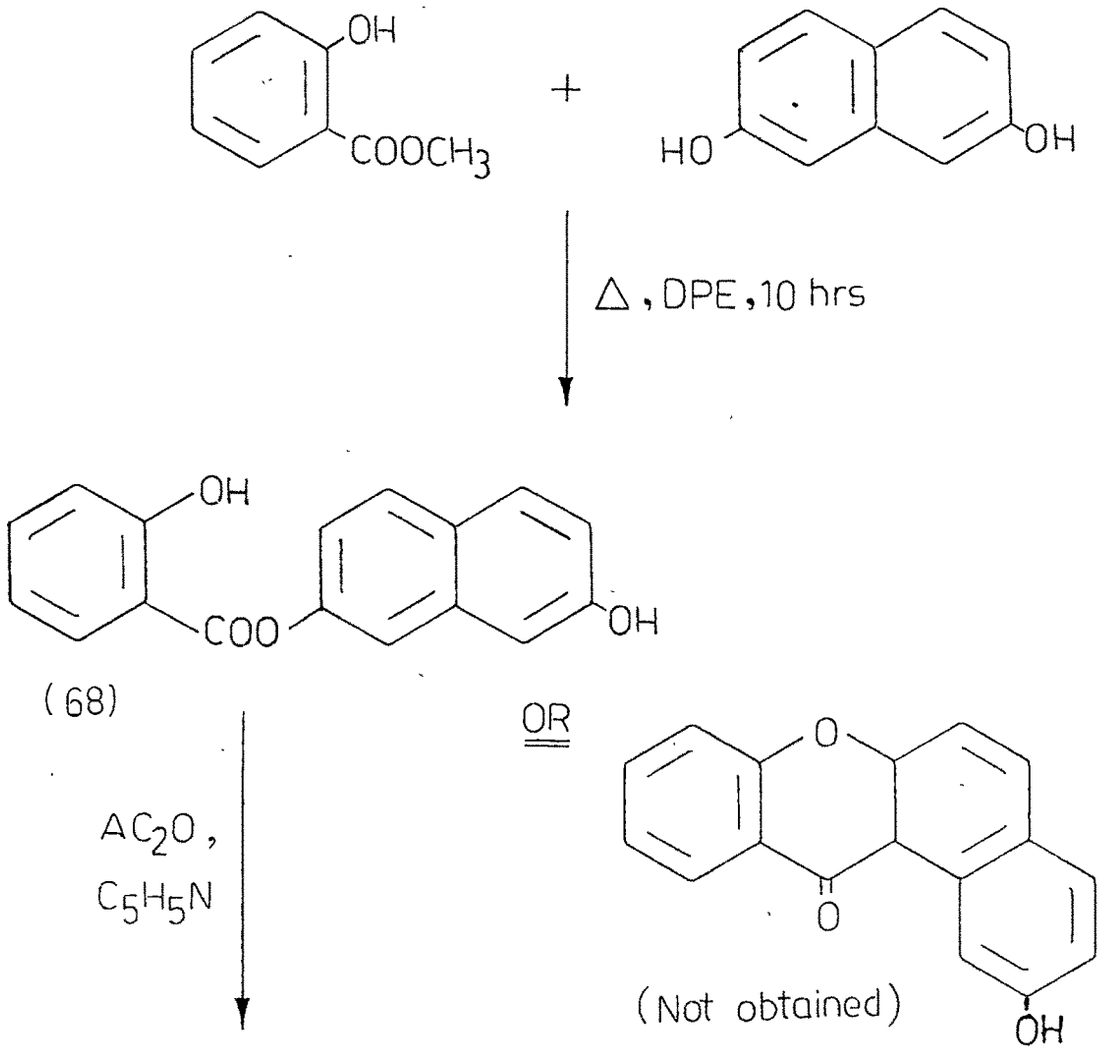
FIG 31


100
90
80
70
60
50
40
30
20
10
0
315
271
258
286
231
220
240
260
280
300
320
340
360
380
400


100
90
80
70
60
50
40
30
20
10
0
65
39
50
76
92
139
202
20
40
60
80
100
120
140
160
180
200

66

FIG 32


OH
COOCH3
+
HO
OH
Δ , DPE , 10 hrs
OH
COO
OH
(68)
OR
O
O
OH
(Not obtained)
AC2O ,
C5H5N
OCOCH3
COO
OCOCH3
(69)

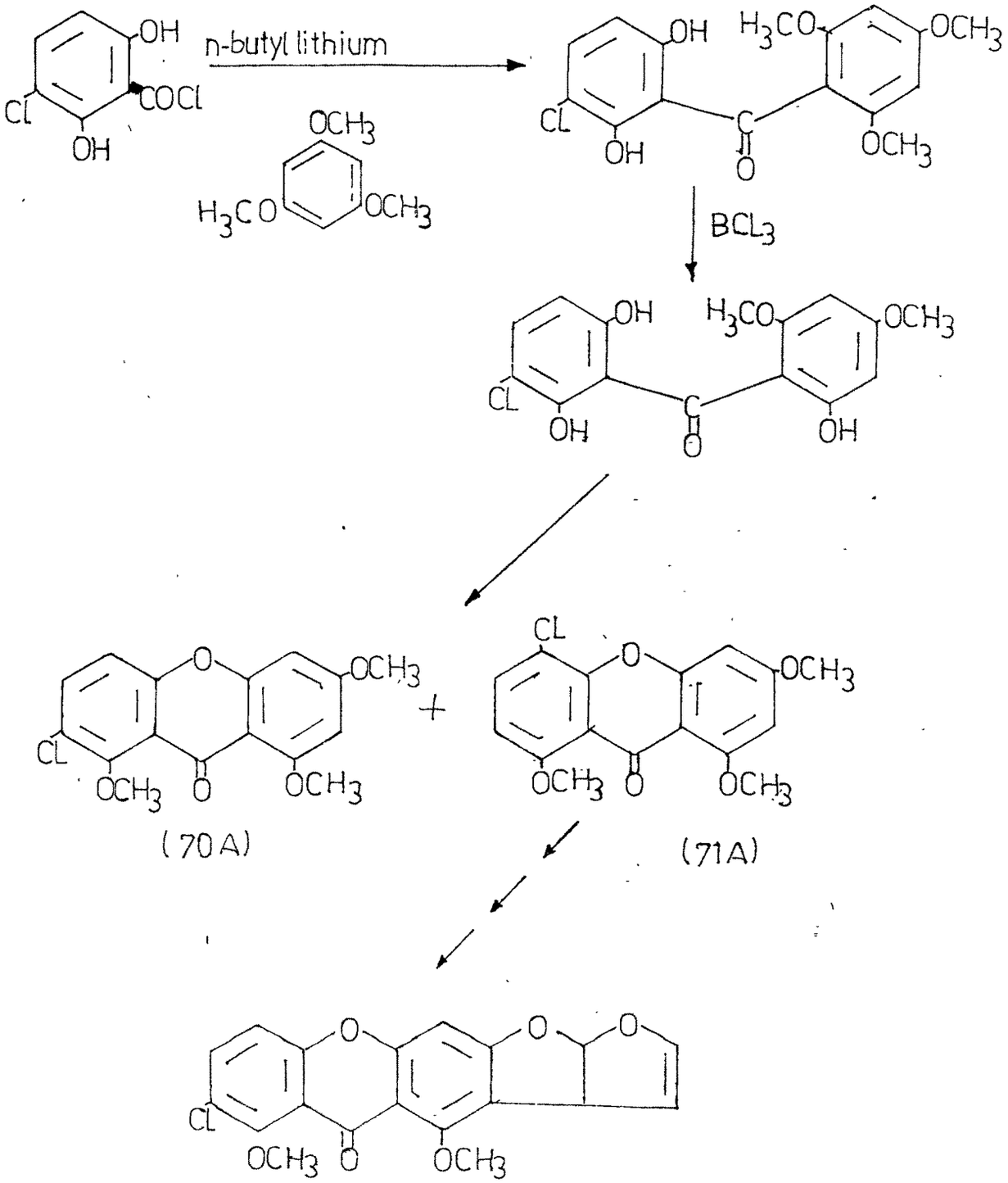
aliphatic region at 2.3 and 2.35 for the two $OCOCH_3$ groups, suggesting that it is a diacetoxy derivative. So possibility of xanthone and benzophenone structure is ruled out. Moreover it showed a set of peaks in the aromatic region corresponding to 10 aromatic protons.

Condensation of phloroglucinol with methyl-5-chloro-2,6-dihydroxybenzoate

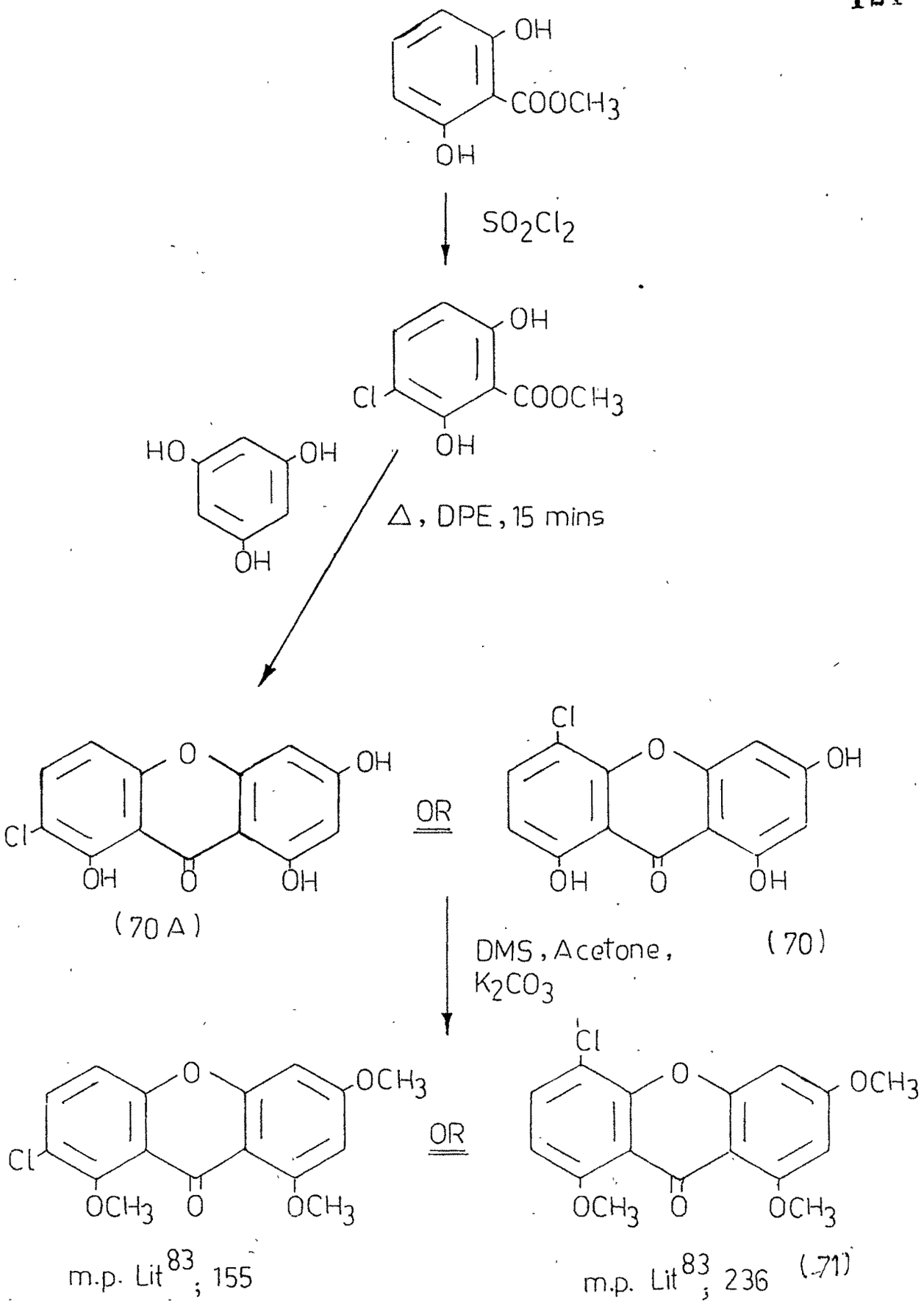
Steyn et al[83] have made attempts towards the synthesis of austocystins, starting from 3-chloro-2,6-dimethoxy benzoylchloride, which was reacted with 2,4,6-trimethoxy phenyllithium to generate benzophenone, which on selective demethylation followed by cyclisation with tetra methyl ammonium hydroxide gave two xanthones (70A) and (71A), as shown in scheme (10). The yield of former xanthone (70A) is very poor. It was therefore thought of interest to synthesise xanthone (70A). When methyl-3-chloro 2,6-dihydroxybenzoate was condensed with phloroglucinol unfortunately gave xanthone (70) but with higher yield.

1,3,8-Trihydroxy-5-chloroxanthone (70)

Methyl-3-chloro-2,6-dihydroxybenzoate was prepared by treatment of sulphuryl chloride with methyl -resorcylate in solvent ether and was condensed with phloroglucinol in refluxing diphenyl ether for 15 min. The product obtained after steam distillation of reaction mixture, was characterised as 1,3,8-trihydroxy-5-chloroxanthone (70), on the basis of its elemental analysis.


OH
n-butyl lithium
COCl
Cl
OH
OCH3
H3CO
OCH3
OH
H3CO
OCH3
Cl
C
O
OH
OCH3
BCL3
OH
H3CO
OCH3
Cl
OH
C
O
OH
O
OCH3
Cl
OCH3
O
OCH3
+
Cl
O
OCH3
OCH3
O
OCH3
(70A)
(71A)
O
O
O
Cl
OCH3
O
OCH3

SCHEME -10


OH
COOCH3
OH
SO2Cl2
OH
Cl
COOCH3
OH
HO
OH
OH
Δ, DPE, 15 mins
O
OH
Cl
OH
O
OH
(70 A)
OR
Cl
O
OH
OH
O
OH
(70)
DMS, Acetone,
K2CO3
O
OCH3
Cl
OCH3
O
OCH3
m.p. Lit83; 155
OR
Cl
O
OCH3
OCH3
O
OCH3
m.p. Lit83; 236
(71)

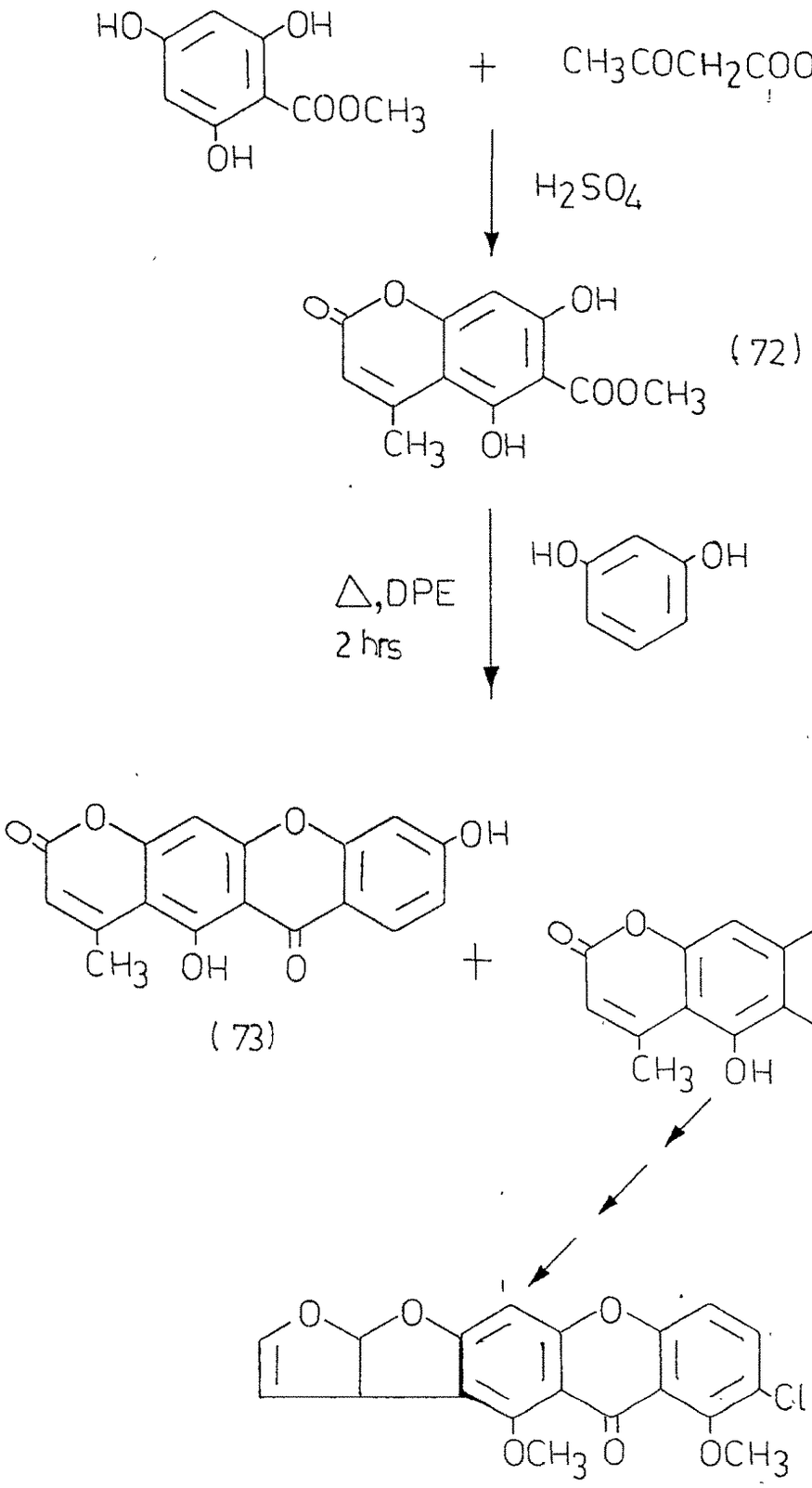
The product (70) on methylation with potassium carbonate and dimethyl sulphate gave a trimethoxy derivative (71). The structure of which was confirmed by its spectral studies. NMR (CD_3SOCD_3) showed singlet for the nine protons at δ 3.9 indicating the presence of the three methoxy groups; 7.25, doublet, J_{65}= 9Hz due to the proton at position 6; 6.90, doublet, 1H, J_{65}= 9Hz, proton at position 5; 6.55, d, 1H, J_{42} = 2Hz, H-4 and 6.45, d, 1H, J_{24} = 2Hz, H-2.

Condensation of methyl (4'-methyl-2'-pyrono (5',6':3,4) 2,6-dihydroxy benzoate (72) with resorcinol

As shown in scheme (11) this condensation is also attempted to synthesise austocystins.

(i) Synthesis of methyl (4'-methyl-2'-pyrono (5',6':3,4) 2,6-dihydroxybenzoate (72)

Using conc. sulphuric acid as a condensing agent, methyl 2,4,6-trihydroxybenzoate was condensed with ethyl acetoacetate gave (77) which was characterised on the basis of its elemental analysis and spectral studies. As NMR (CD_3SOCD_3) showed only two singlets of one proton one at δ 6.28 which can be assigned, to only remaining aromatic proton at position 8 and another at 5.85 which must be due to the proton at position 3. Furthermore the two singlets of the three protons were appeared in the aliphatic region, one which is appearing in the down field at 3.95, must be due to the $COOCH_3$ group and another at δ 2.55 is due to the CH_3 group at position 4. IR (KBr) ν max 3325 (OH), 1725 (-COO-), 1662 (-C=O -pyrone), 1620.


HO
OH
COOCH3
OH
+
CH3COCH2COOCH2CH3
H2SO4
O
OH
COOCH3
CH3
OH
(72)
△,DPE
2 hrs
HO
OH
O
O
OH
CH3
OH
O
(73)
+
O
O
OH
CH3
OH
O
OH
(74)
O
O
O
Cl
OCH3
O
OCH3

SCHEME - 11

(ii) Condensation of (72) with resorcinol

A mixture of resorcinol and compound (77) was refluxed in diphenyl ether for 2 hr. The reaction mixture after usual work up gave the product, which was found to be a mixture so it was chromatographed over a silica gel coloumn. Elution with benzene gave a yellow compound which characterised as 1,8-dihydroxy-4'-methyl-2'-pyrano (5',6'-6,7) xanthone (73). The second compound was eluted with chloroform followed by chloroform-methanol mixture to give (74). The structural assignment of 73 and 74 is tentative.

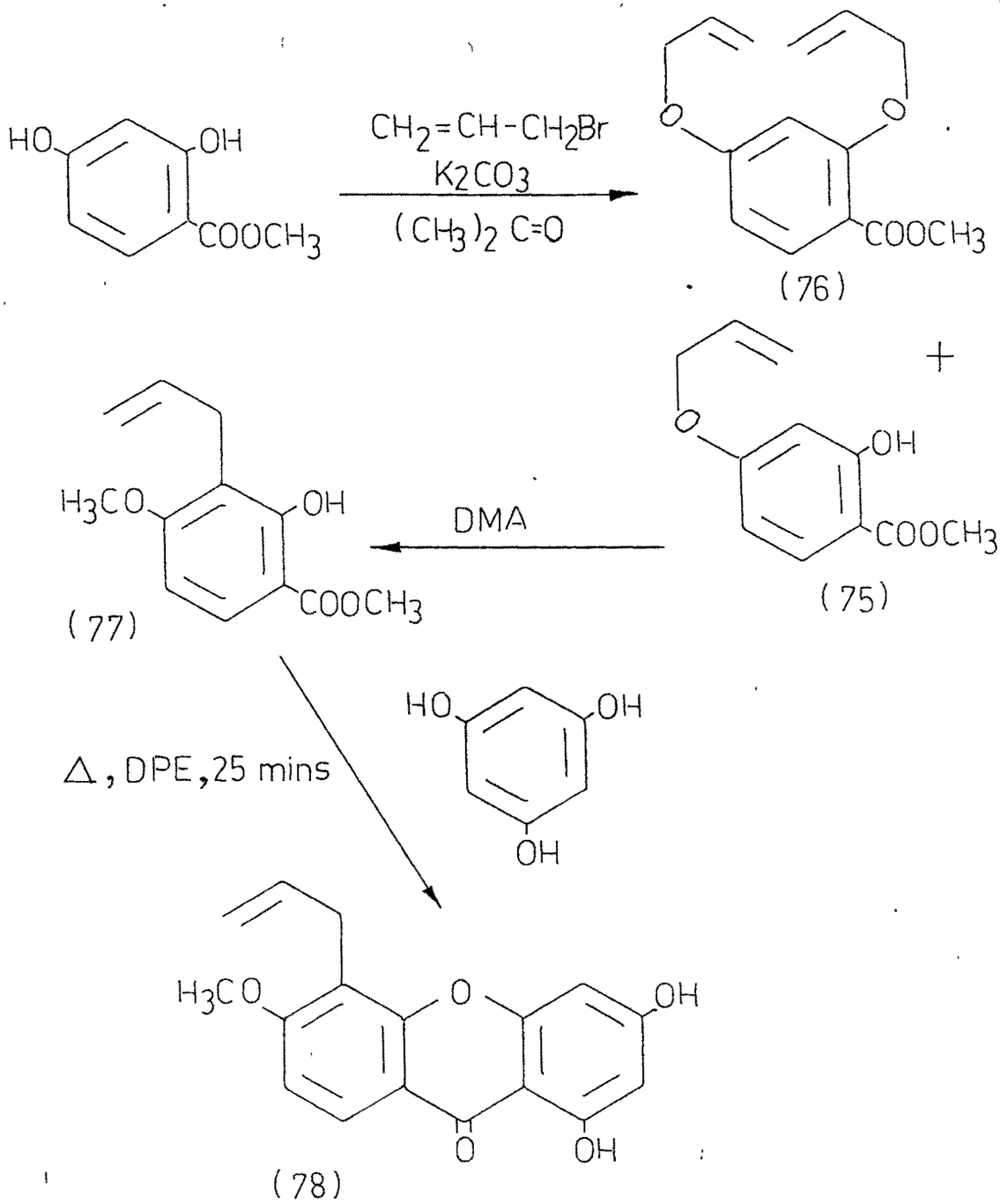
An Abnormal Claisen Migration of Methyl-4-alloyloxy-2-hydroxybenzoate (75) and synthesis of 1,3-Dihydroxy-5-allyl-6-methoxyxanthone (78)

Methyl-2,4-dihydroxybenzoate on allylation gave two oily products, (i) methyl-2,4-diallyloxybenzoate (76) NMR (CCl_4): δ 3.87, S, 3H, $COOCH_3$; 4.5, m, 4H, $2xOC\underline{H}_2CH=CH_2$; 5.16-5.6, m, 4H, $2xOCH_2CH=C\underline{H}_2$; 5.8-6.15, m, 2H, $3xO-CH_2C\underline{H}=CH_2$, 6.35-6.45, m, 2H, H-3 and H-5; 7.7, d, J=9Hz, H-6 and (ii) methyl-4-allyloxy-2-hydroxybenzoate (75) NMR (CCl_4) (Fig.33): δ 3.87, S, 3H, $COOCH_3$; 4.5, m, 2H, $OC\underline{H}_2CH=CH_2$; 5.19-5.46, m, 2H, $-OCH_2CH=C\underline{H}_2$; 5.8-6.15, m, 1H, $OCH_2C\underline{H}=CH_2$; 6.3-6.4, m, 2H, H-3 and H-5; 7.61, d, J=9Hz, H-6. The Claisen rearrangement of methyl-4-allyloxy-2-hydroxy benzoate (75) in N,N-dimethylaniline yielded a new product methyl 4-methoxy-3-allyl-2-hydroxybenzoate. Its mass spectrum showed molecular ion peak at 222 which is 14 mass unit higher than the starting compounds molecular weight. Thus suggesting that compound(77) has been incorporated

with methyl group in it. This fact is confirmed by the NMR, as the NMR ($CDCl_3$) (Fig.34) spectrum showed two singlets one at δ 3.9 and another at 3.85 suggest the presence of the two OCH_3 groups, the peaks at 3.42; d, 2H, J=8Hz, $-CH_2-CH=CH_2$; 4.95-5.15, t, J=9Hz, 2H, $CH_2CH=CH_2$; 5.89-6.15, m, 1H,$-CH_2CH=CH_2$; reveals the presence of the allyl group in the molecule, 6.45, d, 1H, J=9Hz, H-5; 7.82, d, 1H, J=9Hz, H-6;. The D_20 exchangeable peaks at δ 14.55 is a direct evidence of the presence of the one hydroxy group.

The above compound (77) was condensed with phloroglucinol in usual manner to obtain a 1,3-dihydroxy-5-allyl-6-methoxyxanthone (78) the structure of which was confirmed by NMR spectrum ($CDCl_3$) (Fig.35) which showed the peaks at δ 3.58, d, 2H, J=9Hz, $-CH_2CH=CH_2$; 5.06,m, 2H, $-CH_2CH=CH_2$; 5.9, m, 1H, $CH_2CH=CH_2$; suggest that compound (78) contain an allyl group. The two singlets in the down field at δ 10.4 and 12.9 suggest the presence of the only two hydroxy groups the former is due to -OH at position 3 and latter is due to the chelated hydroxyl group at position 1. The peaks in the aromatic region are interpreted as follows:

δ6.18, d, 1H, J=2Hz, H-2, 6.33, d, 1H, J=2Hz, H-4; 7.07, d, 1H, J=9Hz, H-7; 8.1, d, 1H, J=9Hz, H-8;. The singlet at δ4.0 is due to the OCH_3 group at position 6.


HO
OH
COOCH3
CH2=CH-CH2Br
K2CO3
(CH3)2 C=O
(76)
+
OH
COOCH3
(75)
DMA
H3CO
OH
COOCH3
(77)
Δ, DPE, 25 mins
HO
OH
OH
H3CO
O
OH
O
OH
(78)

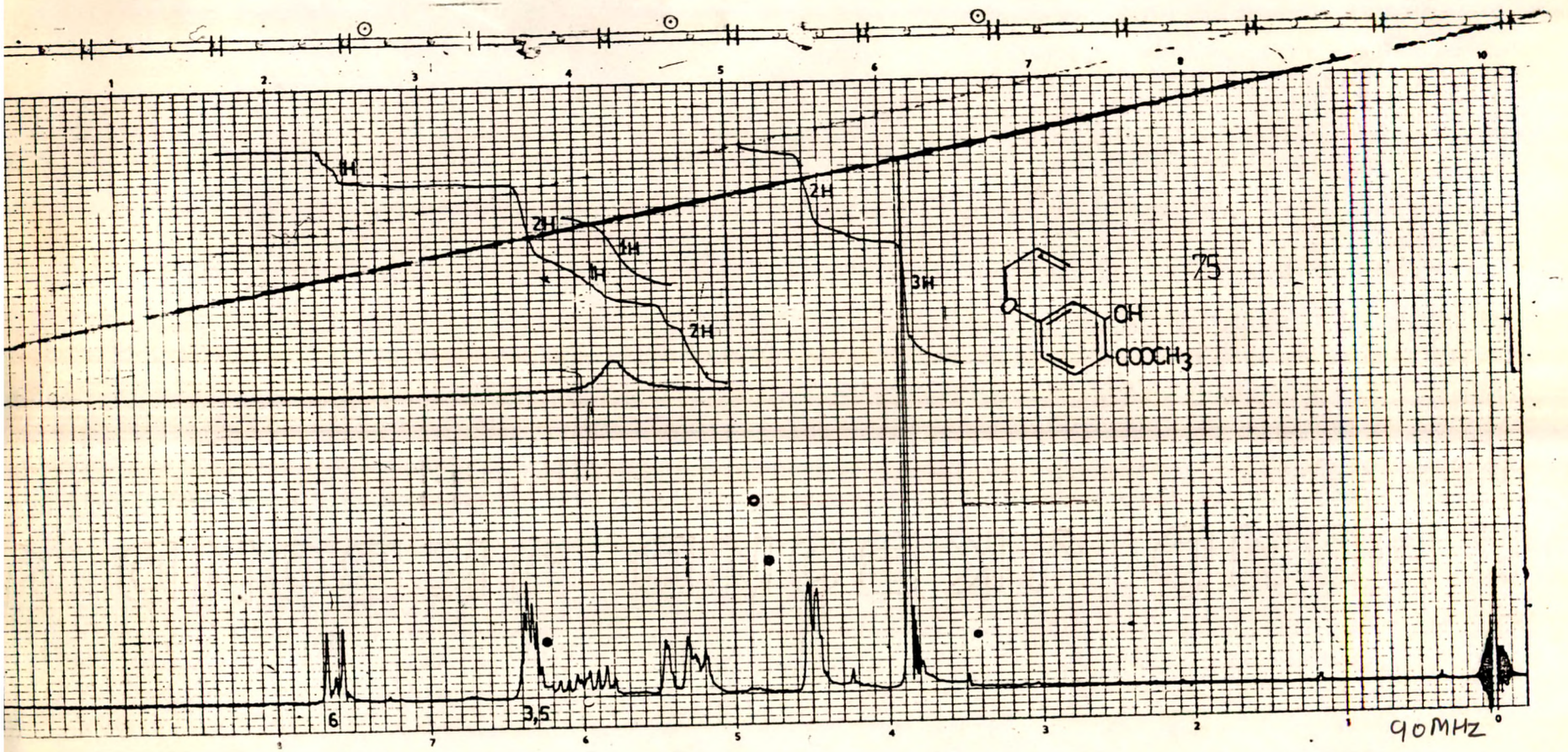


FIG 33

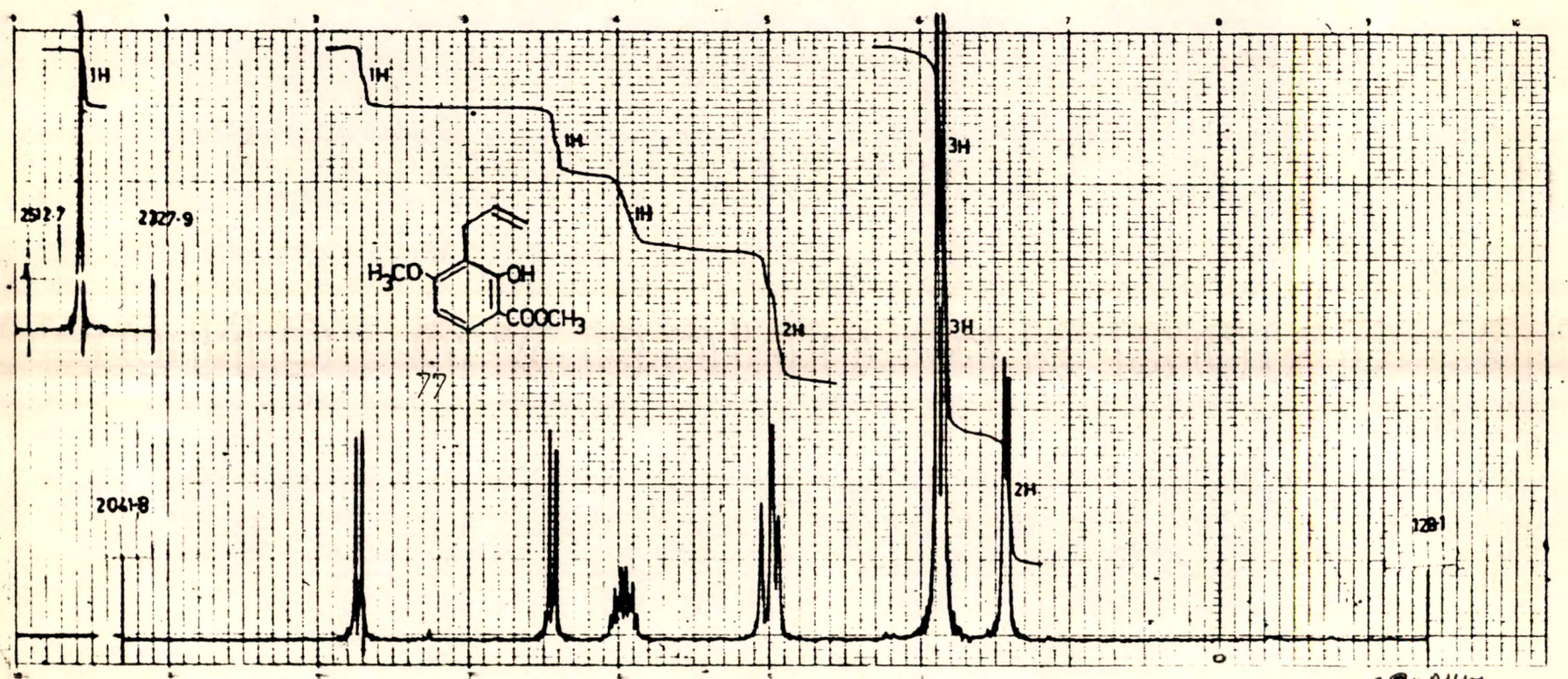

1H
1H
1H
1H
2H
3H
3H
2H
2512·7
2327·9
2041·8
1281
H_3CO
OH
$COOCH_3$
77
220MHZ

FIG 34

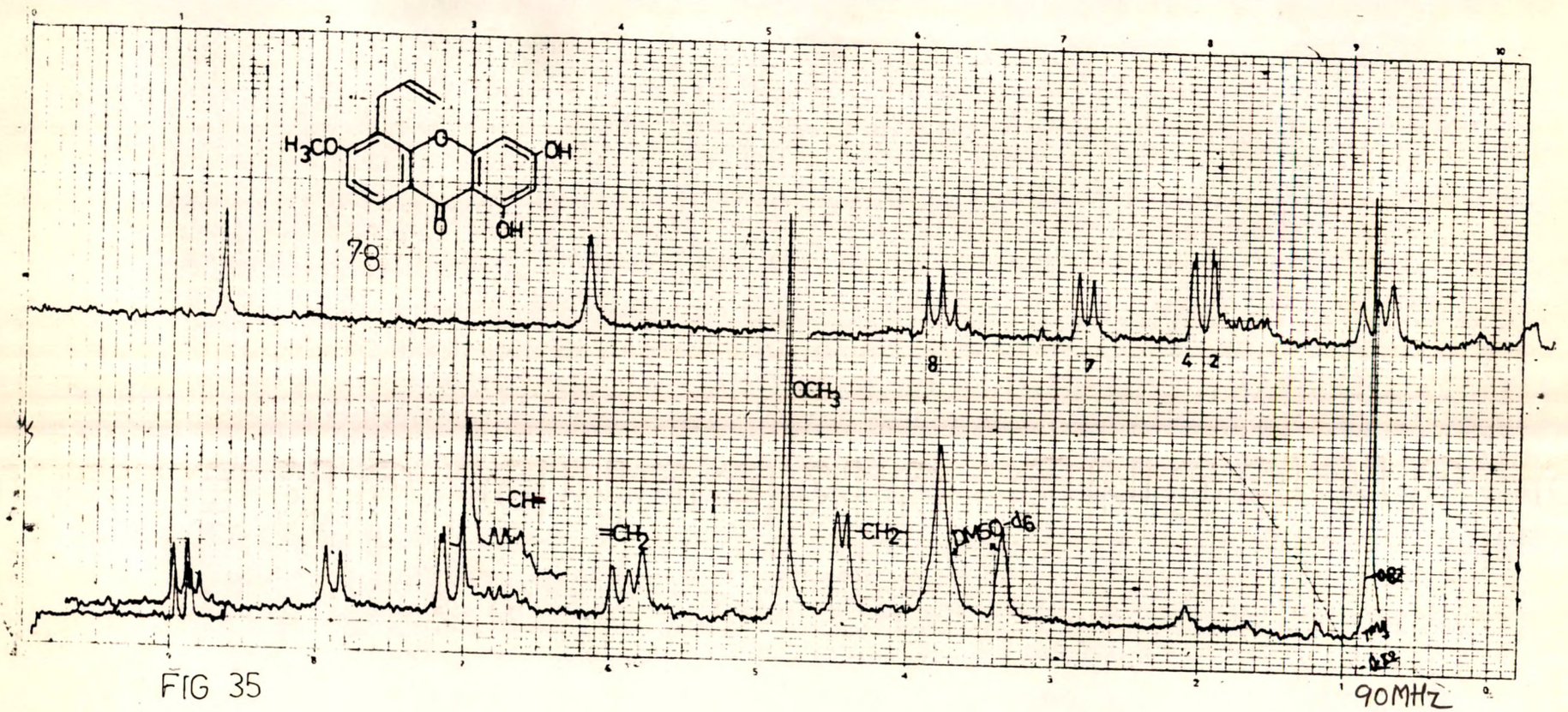


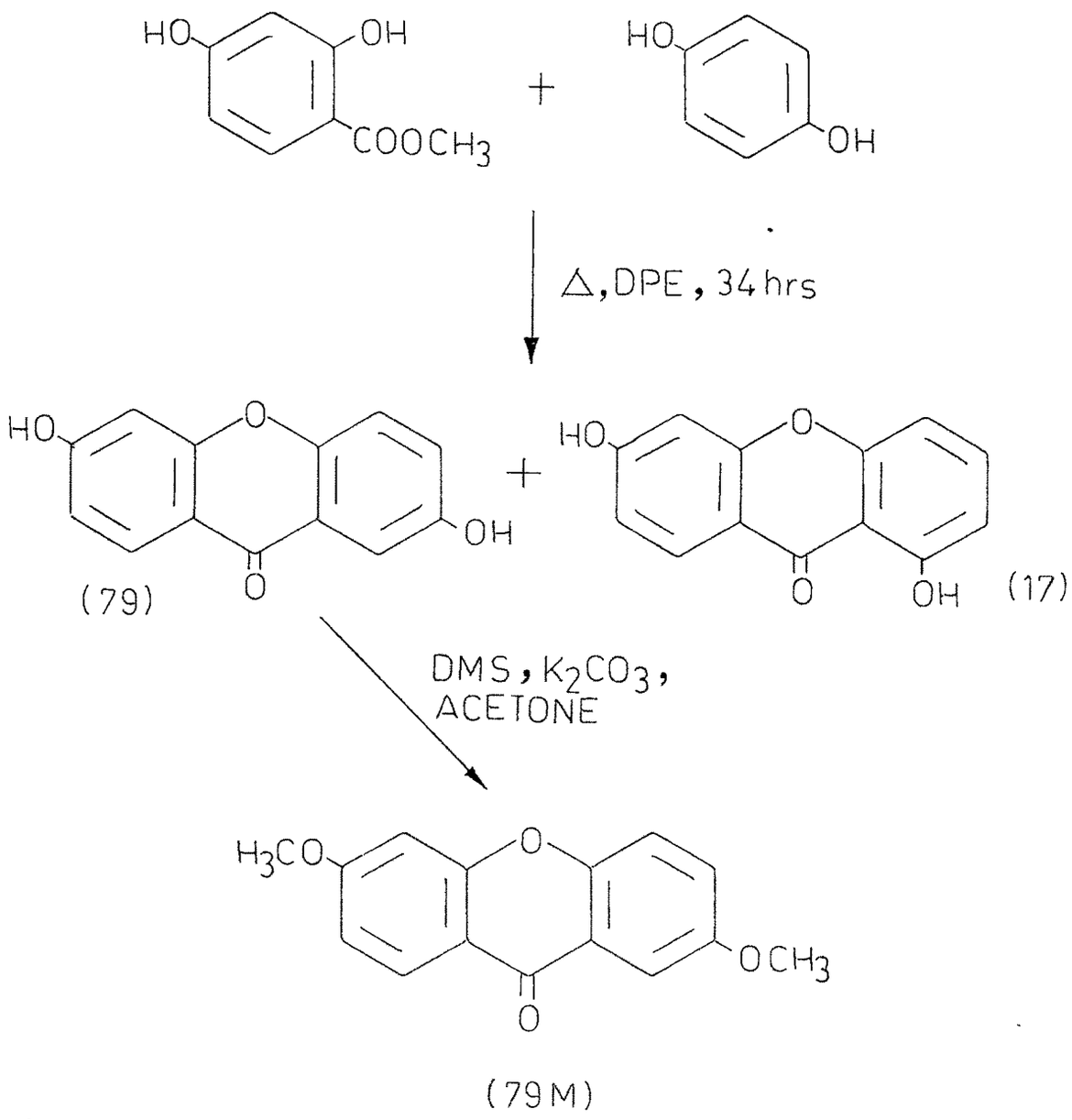
FIG 35

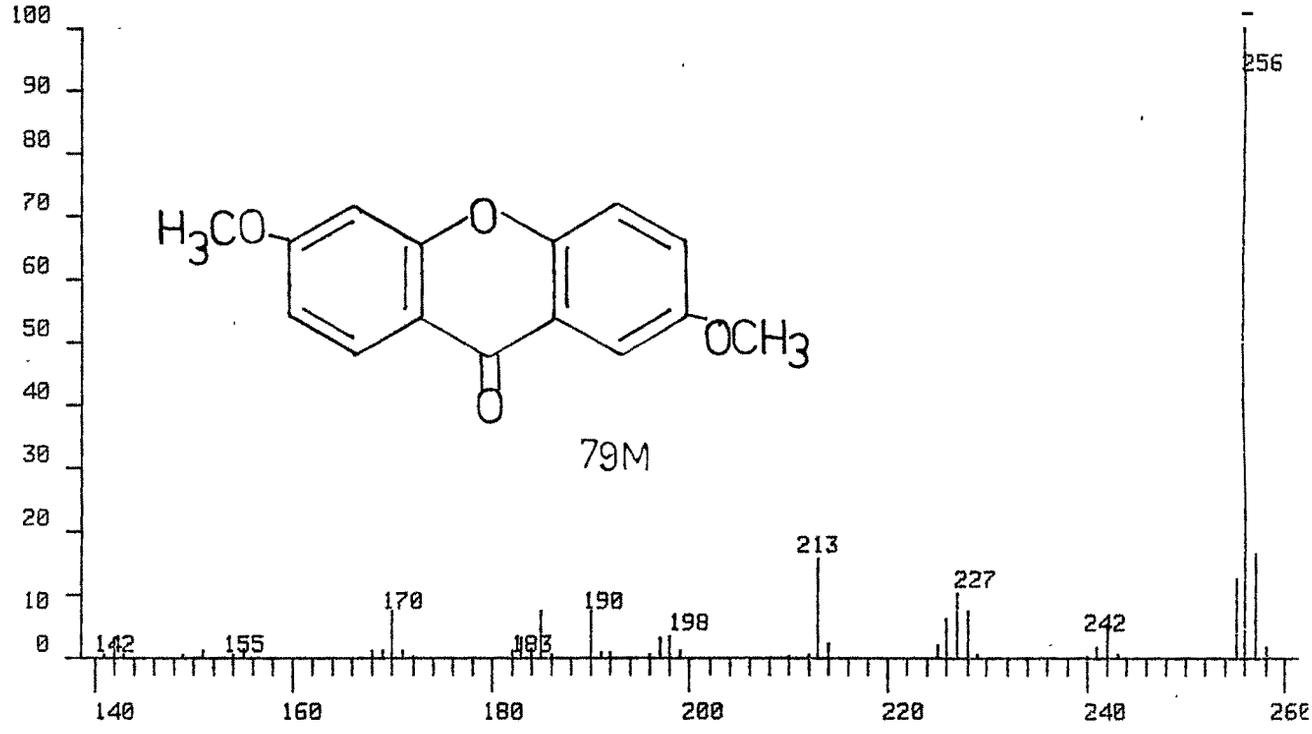
Condensation of hydroquinone with methyl-2,4-dihydroxy benzoate :

With a view to synthesise the naturally occuring xanthone, 2,6-dihydroxyxanthone, the thermal condensation of hydroquinone and methyl-2,4-dihydroxybenzoate were carried out in boiling diphenyl ether, which resulted in the formation of two xanthones, one is expected product, 2,6-dihydroxyxanthone (79) the structure of which was confirmed on the basis of lit. m.p. elemental analysis, mass and NMR spectrum of its methoxy derivative. Mass (Fig.36) m/e 256 (M^+100) 242, 227, 213, etc. The second product was characterised as 3,8-dihydroxyxanthone. Its analytical data were found to be identical (m.p., lit m.p. mass and NMR of its acetoxy derivative) with compound (17) as synthesised earlier (page 43).

Condensation of Methyl-5-bromo-2-hydroxy benzoate with Hydroquinone :

A mixture of hydroquinone and methyl-5-bromo-2-hydroxy benzoate was refluxed in diphenyl ether for 21 hr. The product obtained after steam distillation, was separated as described in experimental to give an ester and two xanthones (i) yellow saffron colour compound obtained was characterised as 2-bromo-5, 8-dihydroxyxanthone (82) on the basis of its elemental analysis and mass and NMR


HO
OH
COOCH3
+
HO
OH
Δ, DPE, 34 hrs
HO
O
OH
O
(79)
+
HO
O
O
OH
(17)
DMS, K2CO3,
ACETONE
H3CO
O
OCH3
O
(79M)


100
90
80
70
60
50
40
30
20
10
0
H3CO
O
OCH3
O
79M
256
213
227
170
190
198
242
142
155
183
140
160
180
200
220
240

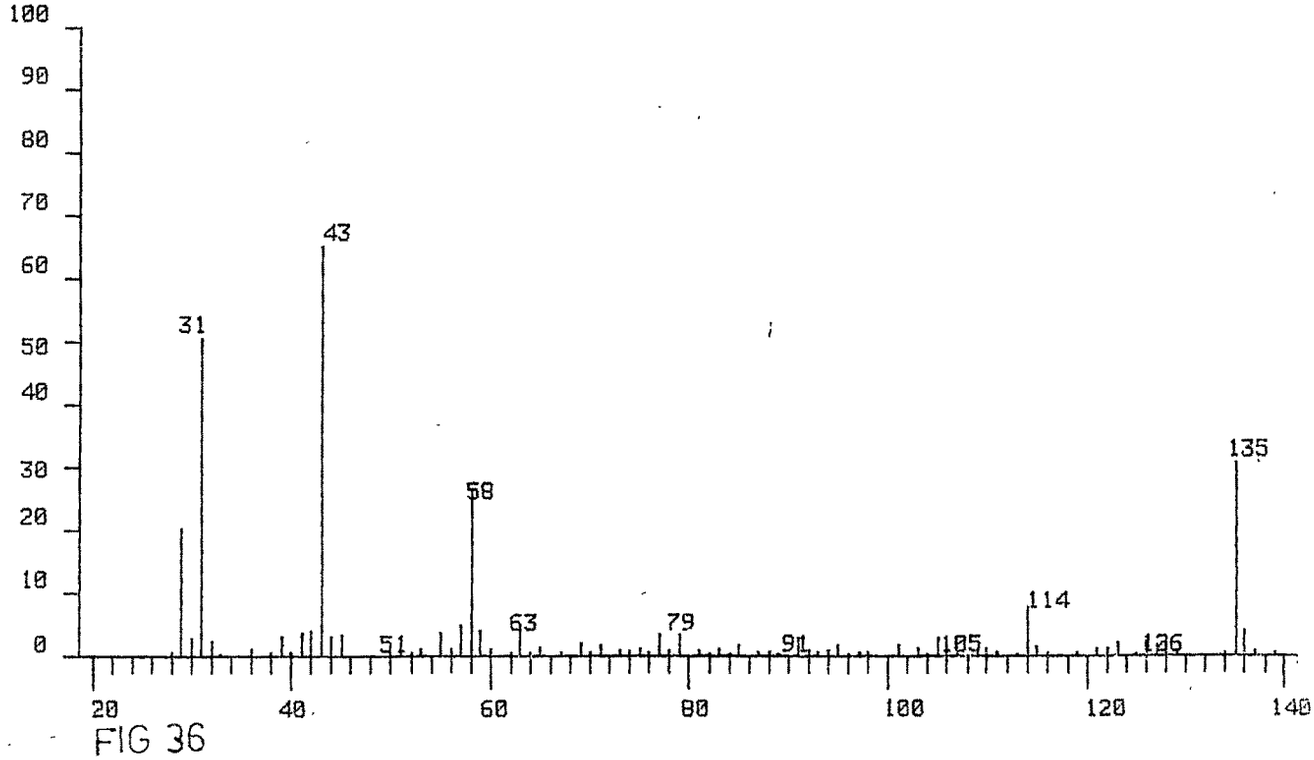
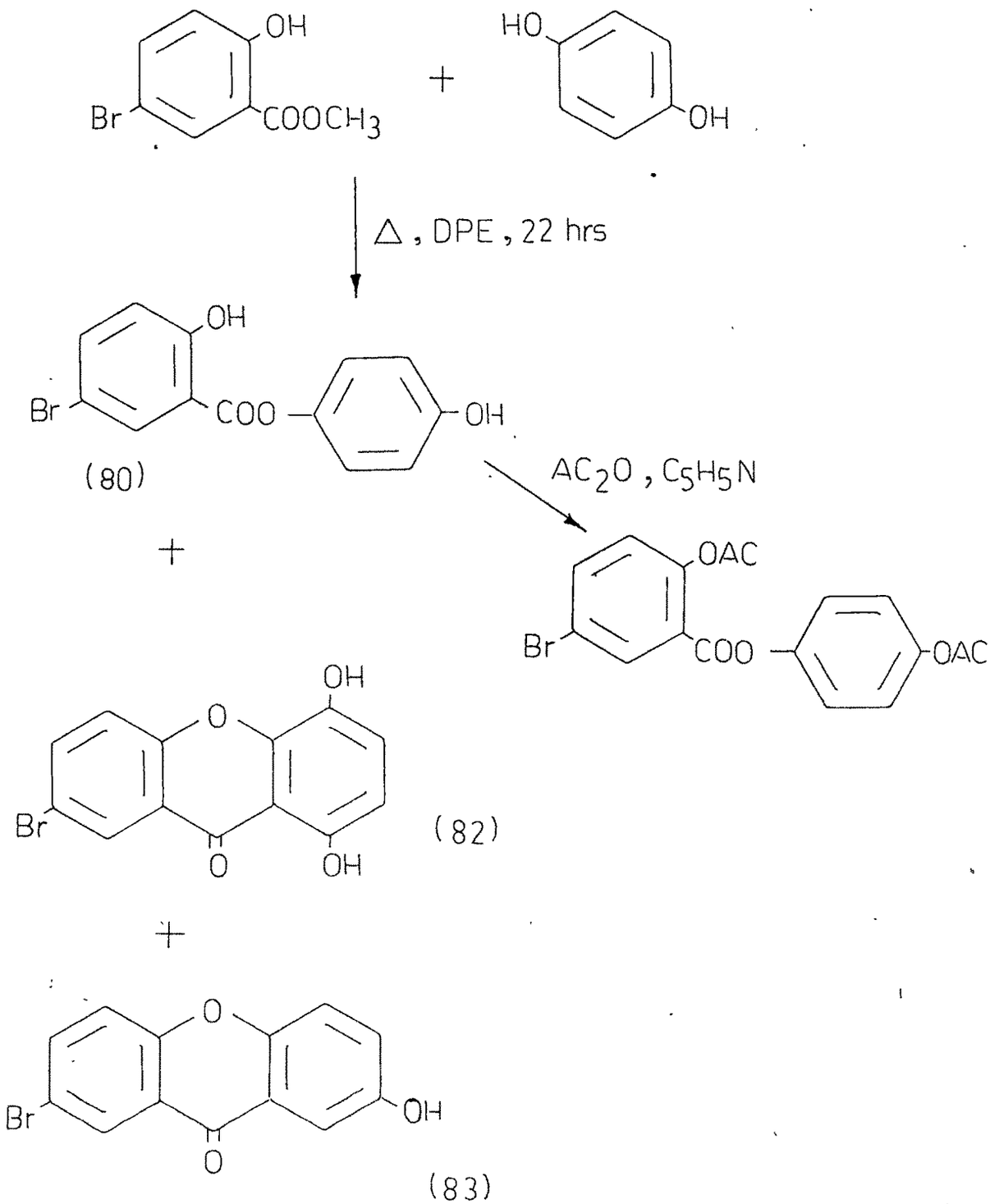

100
90
80
70
60
50
40
30
20
10
0
43
31
58
135
114
63
79
51
91
105
126
20
40
60
80
100
120
140

FIG 36

spectral data. Mass m/e 308, 306. NMR (CD_3SOCD_3) Fig.37; showed two singlets above 9 PPM one at δ9.4 for hydroxyl proton of hydroxy group at position 5; another at δ11.53 is attributed to the chelated hydroxy proton of hydroxy group at position 8; down field doublet of 2Hz at δ8.25 is assigned to peri proton at position 1; 7.92, dd, 1H, J=9Hz, 2Hz, proton at position 3; 7.58 doublet, 1H, J=9Hz, proton at position 4; 7.25, doublet, 1H, J=9Hz proton at position 6; 6.6, doublet, 1H, J=9Hz, proton at position 7. Thus confirms the assigned structure (82).

The second product obtained was characterised as 7-bromo-2-hydroxyxanthone (83). Its NMR (CD_3SOCD_3) (Fig.38) showed two singlets in the aromatic region one at δ8.1 and another at 7.4 for the proton at position 8 and 2 respectively. There are two doublets centered at δ7.67 and 7.03, each integrated for the two protons, the former one is due to the protons H-3 and H-6 and latter one is due to the proton H-4 and H-5. The appearance of peak at 10.32 indicate that it is a mono hydroxyxanthone.


OH
Br
COOCH3
HO
OH
Δ , DPE , 22 hrs
OH
Br
COO
OH
(80)
AC2O , C5H5N
OAC
Br
COO
OAC
OH
O
Br
O
OH
(82)
O
Br
OH
O
(83)

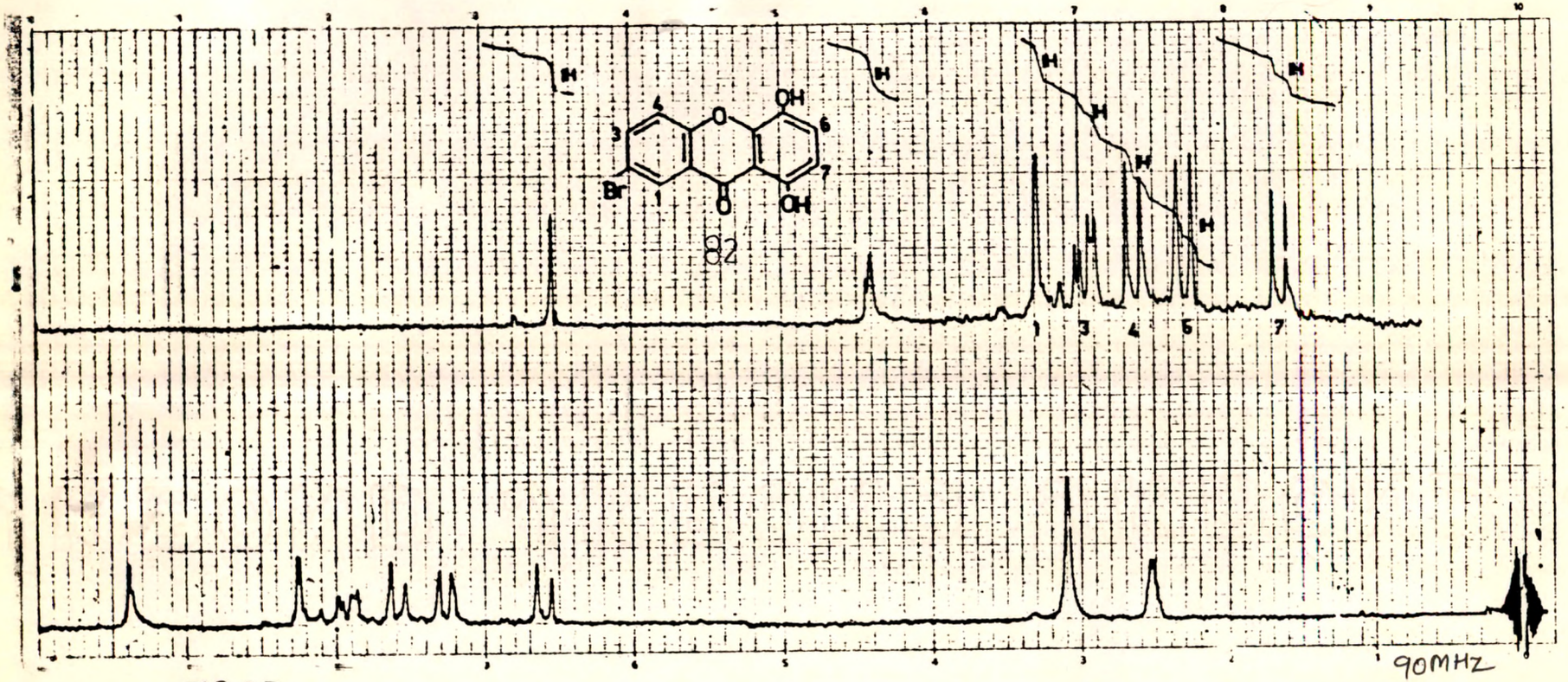


FIG 37

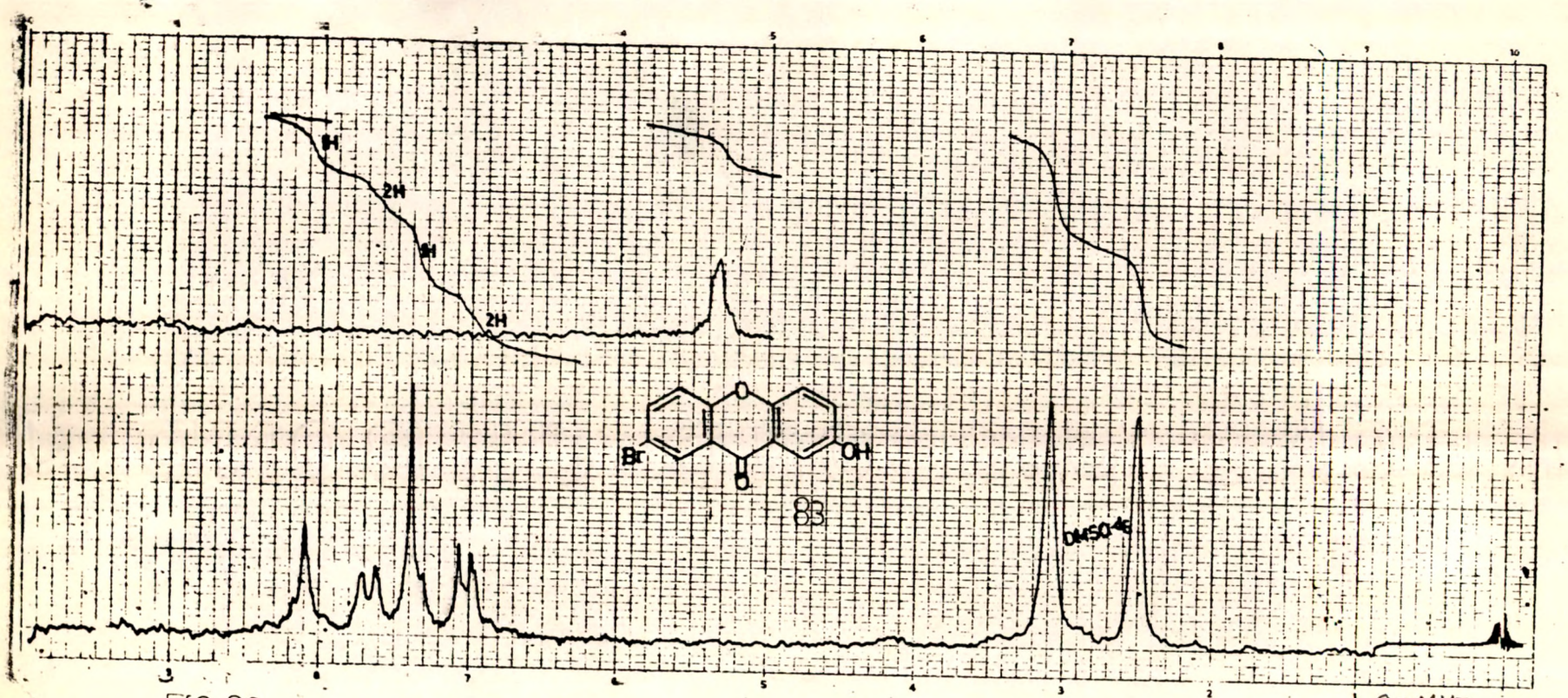


FIG 38

	Yield % in one step	Yield % literature	Reference
1,5,6-Trihydroxyxanthone (14)	41	25	49
1,7-Dihydroxyxanthone (16)	6	3.5	38
1,3,6,8-Tetrahydroxy xanthone (42)	11	20	49
1,3,8-Trihydroxyxanthone(19)	49	21	49
4,8-Dihydroxyxanthone (21)	8.5	-	82
1,3,6-Trihydroxyxanthone (30)	33	40	48
3,6-Dihydroxyxanthone (32)	10	30	48
4,6-Dihydroxyxanthone (34)	11	-	53
3,4,6-Trihydroxyxanthone (35)	20	30	49
1,6-dihydroxy-3-methyl xanthone (40)	41	41	48
1,3,7-Trihydroxyxanthone(46)	16	<16	48

The yields obtained in the thermal condensation method is higher than the methods described in the literature in most of the cases, indicating that it is a good method for the synthesis of xanthones.

EXPERIMENTAL

The reported melting points are uncorrected.

IR spectra (νmax in cm^{-1}) were recorded on a perkin-Elmer 125 spectrophotometer. NMR spectra were recorded on perkin-Elmer R 34 (220 MH_z) and perkin-Elmer R32 (90 MH_z) using TMS as an internal standard. Mass spectra were recorded on Kratos MS 30 instrument coupled to a DS 55 data system mass spectrometer and on a AEI MS12 machine.

Condensation of pyrogallol with methyl 2,6-dihydroxy benzoate : 1,5,6-Trihydroxyxanthone (14)

A mixture of pyrogallol (1.3g; 0.01 mol), methyl 2,4-dihydroxybenzoate (1.7g; 0.01 mol) and diphenyl ether (5 ml) was refluxed for 1.5 hr. The reaction mixture was subjected to steam distillation. The water soluble compound separated out on cooling, which crystallised from water or alcohol + benzene gave (14) as golden yellow leaves. m.p. 287° (Lit:[49] 285°). Yield 0.8 g.

Analysis : Found : C, 63.28; H, 3.181 %.

$C_{13}H_8O_5$ requires : C, 63.93; H, 3.278 %.

Condensation of hydroquinone with methyl 2,6-dihydroxy benzoate : 1,7-Dihydroxyxanthone (16)

A mixture of hydroquinone (1.1g; 0.01 mol), methyl 2,4-dihydroxybenzoate (1.7g; 0.01 mol) and diphenyl ether (5 ml) was refluxed for 8 hr. The removal of solvent by steam distillation gave (1.2g) of a black solid which was chromatographed on silica gel coloumn. Elution with benzene gave a yellow solid, which was further crystallised from benzene gave (16) as yellow seeds.
m.p. 230-32° (lit;[38] 236-39°). NMR (CD_3SOCD_3) δ 8.08, d, 1H, J=9Hz, H-7; 7.52, t, 1H, J=9Hz, H-6; 7.45, S, 1H, H-1; 6.85-6.95, m, 2H, H-4 and H-5; 6.72, dd, 1H, J=9,2Hz, H-3, 12.9, S, 1H, Chelated -OH Exchangeable with D_2O; 11.35, S, 1H, OH Exchangeable with D_2O.

Different phenols were similarly condensed with methyl-2,6-dihydroxybenzoate and methyl 2,4-dihydroxy benzoate to obtain the corresponding xanthone derivatives, m.ps, yields and other data are recorded in Table 2 to 4.

Condensation of phloroglucinol with methyl-2,4,6-trihydroxy benzoate : 1,3,6,8-Tetrahydroxyxanthone (42)

A mixture of phloroglucinol (1.3g; 0.01 mol), methyl 2,4,6-trihydroxybenzoate (1.8g; 0.01 mol) and diphenyl ether (5 ml) was refluxed for 15 min. The reaction mixture on steam distillation gave a product, which was washed with

Table No.2

Characterisation Data of Products in the Condensation of Various Phenolic Derivatives with Methyl 2,6-dihydroxybenzoate.

Starting Phenol	Product molecular formula	m.p. ^{o}C	Reaction period hr	Yield %	Found % C	Found % H	Reqd. % C	Reqd. % H
Resorcinol	3,8-dihydroxy xanthone (17) $C_{13}H_8O_4$	240 (246)[49]	12	10	68.83	3.725	68.42	3.508
Phloroglucinol	1,3,8-trihydroxy xanthone (19) $C_{13}H_8O_5$	258 (258)[49]	0.5	49	63.60	3.178	63.93	3.278
Catechol	4,8-dihydroxy xanthone (21) $C_{13}H_8O_4$	266 (260)[82]	5-6	8.5	68.14	3.722	68.42	3.508
β Naphthol	8-hydroxy-1,2-benzo xanthone (22) $C_{17}H_{10}O_3$	220	14	30	77.45	3.824	77.86	3.816
α Naphthol	8-hydroxy-3,4-benzo xanthone (24) $C_{17}H_{10}O_3$	185	14	19	77.61	4.061	77.86	3.816
Orcinol	1,6-dihydroxy-8-methyl xanthone (25) $C_{14}H_{10}O_3$	225	9	50	69.23	4.328	69.42	4.13
2-methyl resorcinol	3,8-dihydroxy-4-methyl xanthone (27) $C_{14}H_{10}O_3$	243	10	29	69.01	4.035	69.42	4.13

Table No.3

Characterisation Data of Products in the Condensation of Various Phenolic Derivatives with Methyl 2,4-dihydroxybenzoate.

Starting compound	Product molecular formula	m.p. °C	Reaction period hr	Yield %	Found % C	Found % H	Reqd % C	Reqd % H
Phloroglucinol	1,3,6-trihydroxy xanthone (30) $C_{13}H_8O_5$	316 (323)[48]	0.5	33	63.65	3.417	63.93	3.278
Resorcinol	3,6-dihydroxy xanthone (32) $C_{13}H_8O_4$	300 (300)[48]	9-10	10	68.55	3.806	68.42	3.508
Catechol	4,6-dihydroxy xanthone (34) $C_{13}H_8O_4$	210 (217-220)[53]	5-7	11	67.96	3.859	68.42	3.508
Pyrogallol	3,4,6-trihydroxy xanthone (35) $C_{13}H_8O_5$	330 (285)[42] (340)[49]	4	20	64.40	3.549	63.43	3.278
β Naphthol	6-hydroxy-1,2-benzo xanthone (37) $C_{17}H_{10}O_3$	230-235	9	19	77.99	4.028	77.86	3.816
∝ Naphthol	6-hydroxy-3,4-benzo xanthone (38) $C_{17}H_{10}O_3$	285	9	19	77.44	3.788	77.86	3.816
Orcinol	1,6-dihydroxy-3-methyl xanthone (40) $C_{14}H_{10}O_3$	315 (326)[48]	8	41	69.02	4.583	69.42	4.13

Table No.4

Characterisation Data of Acetoxy Derivatives of Xanthones.

Compound (molecular formula)	m.p. °C	Found % C	Found % H	Reqd. % C	Reqd. % H
15($C_{19}H_{14}O_8$)	210 (210)[49]	61.20	3.796	61.62	3.784
17($C_{17}H_{14}O_8$)	158	65.80	4.135	65.38	3.840
18($C_{17}H_{12}O_6$)	140	65.77	3.958	65.38	3.840
20($C_{19}H_{14}O_8$)	185	61.20	4.033	61.62	3.784
23($C_{19}H_{12}O_4$)	175	74.60	3.820	75.00	3.947
26($C_{18}H_{14}O_5$)	142	66.01	4.287	66.27	4.29
28($C_{18}H_{14}O_5$)	193	65.91	4.733	66.27	4.29
31($C_{19}H_{16}O_8$)	170 (172)[48]	61.17	3.895	61.62	3.784
33($C_{17}H_{12}O_6$)	145-150 (155)[48]	64.90	3.822	65.38	3.846
36($C_{19}H_{14}O_8$)	205 (210)[49]	62.03	3.878	61.62	3.784
39($C_{19}H_{12}O_4$)	190	75.41	4.321	75.00	3.947
41($C_{18}H_{14}O_6$)	165	66.28	4.514	66.27	4.29
64($C_{16}H_{12}O_4$)	188	71.94	4.393	71.64	4.47
81($C_{17}H_{13}O_6$)	159	52.00	3.709	51.77	3.299
84($C_{15}H_9O_4$)	242	53.54	2.935	54.05	2.70

sodium bicarbonate and with water. It was passed through a short coloumn of neutral alumina and eluted with alcohol gave (42) as yellow solid. m.p. 310° (lit[49]; 332) Yield 0.3 g. Analysis : Found : C, 59.67; H, 3.60 %. $C_{13}H_{18}O_6$ requires : C, 60.01 ; H, 3.10 %.

Condensation of 2-methylresorcinol with methyl 2,4,6-trihydroxybenzoate : 3,6,8-Trihydroxy-4-methylxanthone(44)

A mixture of 2-methylresorcinol (1.2 g; 0.01 mol), methyl 2,4,6-trihydroxybenzoate (1.8 g; 0.01 mol) and diphenyl ether (20 ml) was refluxed for 4 hr. The reaction mixture was subjected to steam distillation. The product obtained was washed with sodium bicarbonate solution and with water, which gave (0.8g) of solid. It crystallised from alcohol to give brown needles. m.p. 310°.
Analysis :Found : C, 64.92; H, 3.736 %.
$C_{14}H_{10}O_5$ requires : C, 65.11; H, 3.875 %.
Acetate (45) : m.p. 170°.

Condensation of hydroquinone with methyl 2,4,6-trihydroxy benzoate : 1,3,7-Trihydroxyxanthone (46)

A mixture of hydroquinone (1.1 g; 0.01 mol), methyl-2,4,6-trihydroxybenzoate (1.8 g; 0.01 mol) and diphenyl ether (15 ml) was refluxed for 2 hr. The solution was cooled and filtered. The solid obtained was washed with

benzene, dried, and crystallised from methanol water. m.p. 316-20° (lit.,[48] 318°). Yield 0.4 g.

Analysis : Found:C, 63.49; H, 3.238 %.

$C_{13}H_8O_5$ requires : C, 63.93; H, 3.278 %.

Condensation of ∝-naphthol with methyl 2,4,6-trihydroxy benzoate: 1,3-Dihydroxy-5,6-benzoxanthone (47)

A mixture of ∝-naphthol (1.5g; 0.01 mol) methyl 2,4,6-trihydroxybenzoate (1.8 g; 0.01 mol) and diphenyl ether (20 ml) was refluxed for 9 hr. The reaction mixture was subjected to steam distillation, filtered hot, washed with hot water, sodium bicarbonate solution and then again with water. The product (1.2 g) was purified by the silica gel coloumn chromatography. Elution with benzene gave pale yellow needles. m.p. 297°. Yield 0.8 g.

Analysis : Found : C, 72.99; H, 3.680 %.

$C_{17}H_{10}O_4$ requires : C, 73.38; H, 3.597 %.

Condensation of β-naphthol with methyl 2,4,6-trihydroxy benzoate : 1,3-Dihydroxy-7,8-benzoxanthone (48)

A mixture of β-naphthol (1.5 g; 0.01 mol), methyl 2,4,6-trihydroxybenzoate (1.8 g; 0.01 mol) and diphenyl ether (20 ml) was refluxed for 9 hr. The solvent was removed by steam distillation. The product obtained was washed with sodium bicarbonate and with water. The crude

product (1.1g) was coloumn chromatographed over a silica gel coloumn using benzene as an eluant. The product crystallised from benzene gave lemon yellow needles. m.p. 264°. Yield 0.8 g.

Analysis : Found : C, 72.90; H, 4.007 %.

$C_{17}H_{10}O_4$ requires : C, 73.38; H, 3.597 %.

Condensation of hydroquinone with ethyl salicylate:

A mixture of hydroquinone (20g:), ethyl salicylate (20 ml) and diphenyl ether (20 ml) was refluxed for 40 hr. The diphenyl ether was steam distilled off, there by 25 g of a pasty mass was obtained, which showed a number of spots on T.L.C. The pasty mass was dissolved in acetone and poured onto 35 to 40 g silica gel and dried. The coloumn packing were done with the help of fresh silica gel (20 g), in petroleum ether (60°-80°). Elution with (i) petroleum ether (60°-80°) 1.5 lit eluted a compound (500 mg) (1%) (M.P. 148°), which was characterised as 1-hydroxyxanthone (49)(NMR TLC and mix m.p.) found identical in all respects with an authentic specimen of 1-hydroxyxanthone,(ii) further elution with petroleum ether (60°-80°) 2 lit upto second band (dark pink) gave the second product, which crystallised from benzene gave (50) as white cubic crystals. m.p. 165°. Yield 1.1 g (~ 2 %).

Analysis : Found : C, 68.44; H, 3.883 %.

$C_{20}H_{14}O_6$: C, 68.57; H, 4.00 %.

Acetate (51) : (Acetic anhydride/pyridine) 18 hr. The product crystallised from dioxan, yielded white needles. m.p. 225°. Analysis : Found : C, 66.75; H, 3.691 %.

$C_{24}H_{18}O_8$ requires : C, 66.35; H, 4.01 %.

(iii) elution with petroleum ether (60°-80°) 5 to 7 lit gave third product. m.p. 98-101° (lit.,[80] 101). Yield 9.0 to 10.0 g. (30 %).

Analysis : Found : C, 67.59; H, 3.881 %.

$C_{13}H_{10}O_4$ requires : C, 67.82; H, 4.3 %.

Acetate : Acetic anhydride/pyridine 12 hr. The product was crystallised from acetic acid. m.p. 143° (lit.,[80] 143).

Analysis : Found : C, 65.35; H, 4.088 %.

$C_{17}H_{14}O_6$ requires : C, 64.90; H, 4.46 %.

(iv) petroleum ether (60°-80°) 1.5 lit eluted fourth product, which was crystallised from benzene petroleum ether to obtain (53) as pale yellow needles. m.p. 205°. Yield 0.3 g (~1%).

Analysis : Found : C, 70.20; H, 3.215 %.

$C_{20}H_{12}O_6$ requires : C, 68.96; H, 3.4 %.

Acetate : Acetic anhydride/pyridine 18 hr. Crystallisation from alcohol yielded (54) as white needles. m.p. 205° (mix m.p. 155° with 53).

Analysis : Found : C, 66.10; H, 3.809 %.

$C_{22}H_{14}O_7$ requires : C, 65.54; H, 4.2 %.

(v) further elution with petroleum ether did not yield any compound.

(vi) elution with benzene (3.5 to 4.5 lit) gave fifth product, which was crystallised from alcohol or benzene gave (55) as orange coloured shining needles. m.p. 235°. Yield 2.9 g (~ 9%).

Analysis : Found : C, 68.47; H, 3.587 %.

$C_{18}H_8O_4$ requires : C, 68.42; H, 3.508 %.

1,4-Diacetoxyxanthone (55a)

Acetate : Acetic anhydride / pyridine 15 hr. The product crystallised from aqueous acetic acid gave (55a) as white needles m.p. 195°.

Analysis : Found : C, 66.55; H, 3.773 %.

$C_{17}H_{12}O_6$ requires : C, 66.66; H, 3.703 %.

2-Hydroxyxanthone (57)

(vii) further elution with benzene (6 lit) gave sixth product, which crystallised from aqueous alcohol to give (57) as white needles. m.p. 244° (lit.,[16] 239°). Yield 2.0 g (~6%).

Analysis : Found : C, 73.30; H, 3.902 %.

$C_{13}H_8O_3$ requires : C, 73.58; H, 3.8 %.

2-Acetoxyxanthone (58)

Acetate : Acetic anhydride/pyridine (16 hr). The product, crystallised from aqueous alcohol yielded white needles. m.p. 162° (lit., 160°).

Analysis : Found : C, 71.27; H, 3.784 %.

$C_{15}H_{10}O_4$ requires : C, 70.87; H, 3.94 %.

2-Methoxyxanthone (59)

Compound (57) (0.2g) was dissolved in acetone (50 ml) to this was added dimethyl sulphate (1 ml) and potassium carbonate (2 g). The reaction mixture was refluxed for 3 hr; and worked up in usual manner to give a product which crystallised from aqueous alcohol to give (59) m.p. 131° (lit.,[16] 131) mix m.p. 131° does not shows any depression with the prepared sample. Violet colour, filtrate of the compound was collected and extracted with ethyl acetate. Ethyl acetate layer was washed with dil. sodium hydroxide solution, till no yellow colour developed in the alkaline extract. Ethyl acetate layer was then dried through sodium sulphate. On distallation an oil was obtained, which solidified after keeping it in vacuum. Further purification was done by preparative TLC, using $CHCl_3$: MeOH (20:2) solvent system m.p. 100° dec. Yield (0.2 %). Mass : m/e 406.

Refluxing of 4'-hydroxy phenyl salicylate in diphenyl ether

4'-Hydroxy phenylsalicylate (5g) and diphenyl ether (10 ml) was refluxed for 42 hr. The reaction mixture on steam distillation yielded a product, which showed a number of spots on T.L.C. in $CHCl_3$ solvent. Separation was achieved by coloumn chromatography on silica gel coloumn.

Elution with ;

(i) petroleum ether (1st band) gave an oil.

(ii) petroleum ether (2nd band) gave 50 mg of 1-hydroxy xanthone (49).

(iii) petroleum ether (3rd band) benzene + petroleum ether (50:50) yielded 90 mg of a white solid (50).

(iv) further elution with (50:50) petroleum ether benzene gave 50 mg of (54).

(v) elution of blue band with benzene (100 ml) gave a solid which showed three spots on tlc. which was discarded due to very small quantity of this solid.

(vi) further elution with benzene(1.5 lit)gave 100 mg of 1,4-dihydroxyxanthone (55).

(vii) further elution with benzene(1 lit)gave a green oil which showed a spot corresponding to 2-hydroxy xanthone (57).

(viii) elution with $CHCl_3$ and $CHCl_3$+MeOH gave a dirty blackish green stiky mass.

Condensation of hydroquinone with salicylic acid

A mixture of salicylic acid (10 g) hydroquinone (10 g) and diphenyl ether (15 ml) was refluxed for 44 hr. (The pH of the reaction mixture after 30 min was found to be 2.5). The reaction mixture was worked up as before and coloumn chromatographed over silica gel, furnished following compounds;

(i) 1-hydroxyxanthone (49) 150-200 mg.

(ii) hydroquinone disalicylate (50) 160 mg.

(iii) 4'-hydroxy phenyl salicyclate (52) 2-6 g.

(iv) 1,4-dihydroxyxanthone (55) 0.7 g.

(v) 2-hydroxyxanthone (57) 80 mg.

2'-Methyl-4'-hydroxy-phenyl salicylate (60)

A mixture of 2-methylhydroquinone (1.3 g; 0.01 mol), ethyl salicylate (1.5 ml) and diphenyl ether (5 ml) was refluxed for 4 to 5 hr. The reaction mixture on steam distillation gave a paste which was first washed with sodium bicarbonate solution and than with water. It was chromatographed over silica gel coloumn and eluted with petroleum ether(1.5 lit)to give (60) as white needles (major product). m.p. 95°. Yield 0.800 mg.

Analysis : Found : C, 69.25; H, 4.638 %.

$C_{14}H_{12}O_4$ requires : C, 68.85; H, 4.918 %.

2'-Methyl-4'-acetoxy phenyl salicylate (61) m.p. 195°.

Analysis : Found : C, 65.82; H, 4.782 %.

$C_{18}H_{16}O_6$ requires : C, 65.85; H, 4.878 %.

Further elution with petroleum ether gave a yellow oil which solidify after standing for a day. It crystallised from benzene petroleum ether gave yellow needles. m.p. 128-30°. Yield 80 mg.

Analysis : Found : C, 68.42; H, 4.464 %.

$C_{14}H_{12}O_4$ requires : 68.85; H, 4.918 %.

Condensation of 2-methyl hydroquinone with ethyl salicylate

A mixture of 2-methyl hydroquinone (20 g), ethyl salicylate (20 ml) and diphenyl ether (20 ml) was refluxed for 48 hr. The reaction mixture was then subjected to steam distillation. The pasty mass obtained was first washed with sodium bicarbonate solution, then with water, impragnent on silica gel and coloumn chromatographed over silica gel coloumn. Elution with;

(i) petroleum ether 0.5 lit gave an oil (DPE).

(ii) (1 lit) gave an oil containing a few crystals which showed two spots on tlc. It was separated by the preparative tlc. Two compounds obtained, could not be identified due to small amount of compounds.

(iii) petroleum ether(4 lit)gave an ester (60) m.p. 95°C.

(iv) petroleum ether(5 lit) benzene + petroleum ether (10:90)(1 lit) benzene+petroleum ether (20-80) (1lit) gave an oily product which showed a number of spots on tlc. After carrying out the preparative tlc of the above product, gave a major product which was crystallised from aqueous alcohol gave white needles. m.p. 102°. Yield 0.1g not identified.

Analysis : Found : C, 68.13; H, 5.448 %.

(v) benzene + petroleum ether (30:70)(2 lit) benzene + petroleum ether (90:10)(2 lit) gave a yellow solid which was crystallised from alcohol benzene mixture to give (62) as saffron colour needles. m.p. 242°. Yield 300 mg.

Analysis : Found : C, 68.99; H, 4.188 %.

$C_{14}H_{10}O_4$ requires : C, 69.42; H, 4.132 %.

(vi) benzene(1 lit)gave an oil which could not be identified.

(vii) benzene (4 lit) gave a greenish solid, it was crystallised from aqueous alcohol to give (63) as pale greenish needles. m.p. 250°. Yield 1.5 g.

Analysis : Found : C, 73.92; H, 4.582 %.

$C_{14}H_{10}O_3$ requires : C, 74.33; H, 4.424 %.

Condensation of 3-hydroxyxanthone with ethyl salicylate

A mixture of 3-hydroxyxanthone (2.0 g; 0.01 mol), ethyl salicylate (3.6 ml; 0.024 mol) and diphenyl ether (5 ml) was refluxed for 20 hrs. The reaction mixture was subjected to steam distillation. The solid obtained was washed with dil.sodium hydroxide solution and with water. The product (0.6 g) thus obtained showed two spots on TLC. It was chromatographed over a silica gel coloumn and eluted with (i) benzene 0.5 lit gave (65). It crystallised from benzene to yield pale yellow needles. m.p. 153°. Yield 0.15 g.

Analysis : Found : C, 76.30; H, 3.555 %.

$C_{20}H_{14}O_5$ requires : C, 76.84; H, 3.448 %.

Further elution with (i) benzene 1.5 lit furnished the second product which was crystallised from benzene to give (66) as white needles. m.p. 238-40°. Yield 0.2 g.

Analysis : Found : 76.03; H, 3.636 %.

$C_{20}H_{10}O_4$ requires : 76.43; H, 3.18 %.

Condensation of 1-hydroxyxanthone with ethyl salicylate

A mixture of 1-hydroxyxanthone (2.12 g; 0.01 mol), ethyl salicylate (1.5 ml; 0.01 mol) and diphenyl ether (5 ml) was refluxed for 18 hr. The reaction mixture was subjected to steam distillation. The solid obtained showed

two spots on TLC in $CHCl_3$. One of them was corresponded to 1-hydroxyxanthone. The product was separated by preparative TLC using the same solvent system. It was then crystallised from alcohol to give (67) as mustard colour seeds. The product shows negative test with $FeCl_3$. m.p. 207°. Yield 50 mg.

Analysis : Found : C, 76.40; H, 3.806 %.

$C_{20}H_{10}O_4$ requires : C, 76.84; H, 3.448 %.

Condensation of 2,7-dihydroxynaphthalene with ethyl salicylate: 2'-Naphthyl-2,7'-dihydroxybenzoate (68)

A mixture of 2,7-dihydroxynaphthalene (1.6 g, 0.01 mol), ethyl salicylate (1.5 ml, 0.01 mol) and diphenyl ether (5 ml) was refluxed for 10 hr. To the reaction mixture was added petroleum ether (50 ml) and decanted off, yellow crystals separated out, which were washed with petroleum ether and dried under bulb oven (at 60°) (10 hr.) It crystallised from petroleum ether to give yellow needles. m.p. 140-43°. Yield 200 mg.

Analysis : Found : C, 72.85; H, 4.232 %.

$C_{17}H_{12}O_4$ requires : C, 72.85; H, 4.285 %.

2'-Naphthyl-2,7'-diacetoxybenzoate (69) m.p.158-163°.

Analysis : Found : C, 68.81; H, 4.720 %.

$C_{21}H_{16}O_6$ requires : C, 69.23; H, 4.395 %.

Methyl-5-chloro-2,6-dihydroxybenzoate

A mixture of methyl-2,6-dihydroxybenzoate (4.2 g), freshly distilled suphuryl chloride (2.0 ml) was refluxed with solvent ether (100 ml) for 4.5 hr. The reaction mixture was cooled, washed with water for several times. The etherel layer on evaporation gave a product which crystallised from alcohol or aqueous alcohol to give white needles. m.p. 98-100°. Yield 3-8 g.

Analysis : Found : C, 47.08; H, 3.138 %.

$C_8H_7O_4Cl$ requires : C, 47.40; H, 3.456 %.

Condensation of phloroquinol with methyl 5-chloro-2,6-dihydroxybenzoate: 1,3,8-trihydroxy-5-chloroxanthone (70)

A mixture of phlorogucinol (1.3 g, 0.01 mol), methyl-5-chloro-2,6-dihydroxybenzoate (2.14 g; 0.01 mol) and diphenyl ether (5 ml) was refluxed for 15 min. The reaction mixture was subjected to steam distillation. The product crystallised from aqueous alcohol gave pale yellow needles. m.p. 245-50°. Yield 0.9 g.

Analysis : Found : C, 55.58; H, 2.918 %.

$C_{13}H_7O_5$ requires : C, 56.01; H, 2.513 %.

1,3,8-Trimethoxy-5-chloroxanthone (71)

A mixture of compound (0.2 g), potassium carbonate (5 g), dimethyl sulphate (1 ml) was refluxed in acetone (100 ml) for 5 hrs. The reaction mixture was worked up as usual.

The product crystallised from aqueous alcohol gave white needles. m.p. 215° (lit.,[83] 235°). Yield 0.1 g.
Analysis : Found : C, 59.54; H, 4.087 %.
$C_{16}H_{13}O_6Cl$ requires : C, 59.90; H, 4.056 %.

Methyl-(4'-methyl-2'-pyrono (5',6' : 3,4)) 2,6-dihydroxy benzoate (72)

Add con.sulphuric acid drop by drop (20 ml; 80 %) to a well stirred ice cooled mixture of methyl 2,4,6-trihydroxybenzoate (3.6 g; 0.02 mol) and ethyl aceto acetate (2.6 ml; 0.02 mol). The reaction mixture was stirred for 2 hr and allowed to stand for overnight. It was added to ice and cold water mixture, the solid separated was filtered, washed with sodium bicarbonate solution and with water. The product crystallised from acetone or mixture of alcohol benzene or acetic acid gave white tiny needles. m.p. 230-2°. Yield : 3.350 g.
Analysis : Found : C, 57.19; H, 4.219 %.
$C_{12}H_{10}O_6$ requires : C, 57.60; H, 4.60 %.

Condensation of resorcinol with (72); 1,8-dihydroxy-4'-methyl-2'-pyrano (5',6'- 6',7') xanthone (73)
3,8-Dihydroxy-4'-methyl-2'-pyrano (5',6'- 6,7) xanthone(74)

A mixture of resorcinol (1.1 g; 0.01 mol), and methyl (4'-methyl-2'-pyrono (6',5' : 3,4) 2,6-dihydroxybenzoate (2.18 g; 0.01 mol) and diphenyl ether (6 ml) was refluxed

for 2 hr. The reaction mixture was subjected to steam distillation. The crude product thus obtained was coloumn chromatographed over a silica gel coloumn and eluted with (i) benzene gave a yellow compound. m.p. 315°.

Analysis : Found : C, 65.32; H, 3.206 %.

$C_{17}H_{10}O_6$ requires : C, 65.80; H, 4.150 %.

(ii) further elution with chloroform and chloroform + methanol gave a brown product (74) which crystallised from alcohol. m.p. 290°.

Analysis : Found : C, 65.87; H, 3.698 %.

$C_{17}H_{10}O_6$ requires : C, 65.80; H, 3.225 %.

Methyl-4-allyloxy-2-hydroxybenzoate and Methyl 2,4-diallyloxy benzoate

A mixture of methyl 2,4-dihydroxybenzoate (5.1 g; 0.03 mol), potassium carbonate (5.0 g) and allylbromide (4.0 ml, 0.03 mol) was refluxed in acetone for 10 hr. After distilling off acetone, water was added and the solution was extracted with ether. Ethereal layer was washed with sodium hydroxide solution, which on acidification gave an oil which was characterized as methyl-4-allyloxy-2-hydroxybenzoate (75) (2g).

Ethereal layer on evaporation gave an oil (3 g) which was characterized as methyl 2,4-diallyloxy benzoate (76) by its NMR spectrum.

Claisen rearrangement of Methyl 4-allyloxy-2-hydroxy benzoate (75)

Methyl 3-allyl-4-methoxy-2-hydroxybenzoate (77)

Methyl 4-allyloxy-2-hydroxybenzoate (2 g) was refluxed in N,N-dimethylaniline (10 ml) for 8 hr. The reaction mixture was poured into cold dil.hydrochloric acid, extracted with solvent ether, ethereal layer was treated with sodium hydroxide solution, which on acidification gave an oil.

Ether layer on evaporating gave an oil which solidified after two days. This solid was purified by silica gel coloumn chromatography using petroleum ether benzene (50:50) as an eluent. The solid crystallised from petroleum ether gave white rectangular transparent crystals. m.p. 58° yield.

Analysis : Found : C, 64.94; H, 6.011 %.

$C_{12}H_{14}O_4$ requires : C, 64.86; H, 6.3 %.

Condensation of phloroglucinol with (77)

A mixture of phloroglucinol (0.96 g; 0.00075 mol), compound (77) (0.15 g; 0.00075 mol) and diphenyl ether (3 ml) was refluxed for 25 min. The steam distillation of the reaction mixture gave a product which was washed with sodium bicarbonate solution. The yellow solid thus

obtained was heated with hydrochloric acid (1:1) on a water bath for 10 min. The product crystallised from aqueous alcohol yielded cream colour needles (78). m.p. 217-220°. Yield 100 mg.

Condensation of hydroquinone with methyl-2,4-dihydroxy benzoate: 2,6-Dihydroxyxanthone (79)

A mixture of hydroquinone (10 g; 0.01 mol), methyl 2,4-dihydroxybenzoate (10 g; 0.06 mol) and diphenyl ether (15 ml) was refluxed for 34 hr. The reaction mixture was subjected to steam distillation. The water was decanted off, which on cooling gave a pale brown solid (1.3 g). Crystallization from water or alcohol yielded (79), as pale brownish needles. m.p. 310°. Yield 1.1 g.(lit.[53] 315)
Analysis : Found : C, 68.00; H, 3.825 %.
$C_{13}H_8O_4$ requires : C, 68.42; H, 3.53 %.

The separated black paste was chromatographed over a silica gel coloumn and eluted with (1) petroleum ether gave no compound, (2) benzene 1.5 lit. gave a red oil (DPE), (3) chloroform 1.5 lit gave a yellow solid which was further crystallised from chloroform to yield 3.8-dihydroxy xanthone (17) as pale yellow needles. m.p. 246-50°. Yield 500 mg.
Analysis : Found : C, 68.28; H, 3.721 %.
Requires : C, 68.42; H, 3.53 %.

(4) Further elution with chloroform methanol gave the same compound (2.4 g).

2,6-Dimethoxyxanthone

A mixture of compound (0.5 g), dimethyl sulphate (2 ml) and potassium carbonate (2 g) was refluxed with acetone for 4 hr. The reaction mixture was poured into water, the separated product was filtered, washed with sodium hydroxide solution and crystallised from alcohol to give (79M) as yellowish needles. m.p. 174°. Yield 0.28g.
Analysis : Found : C, 69.90; H, 5.01 %.
$C_{15}H_{12}O_4$ requires : C, 70.30; H, 4.72 %.

Condensation of hydroquinone with methyl 2-hydroxy-5-bromobenzoate

A mixture of hydroquinone (6g), methyl 2-hydroxy-5-bromobenzoate (6.5 g) and diphenyl ether (20 ml) was refluxed for 22 hr. The reaction mixture was then subjected to steam distillation gave a pasty mass, which was dissolved in acetone and filtered off. The solid thus obtained was crystallised from benzene to obtain (83) as white needles. m.p. 228°. Yield 0.80 g.
Analysis :Found : C, 53.31; H, 2.819 % .
$C_{13}H_7O_3Br$ requires : C, 53.79; H, 2.413 %.
Filtrate was concentrated, poured onto silica gel and chromatographed.

Elution with (1) petroleum ether gave a yellow oil (2) benzene gave a yellow orange solid which was crystallised from benzene as golden yellow shining pellets (82). m.p. 275-8°. Yield 1.0 g.

Analysis : Found : C, 51.09; H, 2.696 %.

$C_{13}H_7O_4Br$ requires : C, 50.64; H, 2.272 %.

Further elution with (3) benzene + chloroform gave a white solid, which was crystallised from chloroform gave (80) as white needles. m.p. 134°-36° Yield 1.0 g.

Analysis : Found : C, 50.09; H, 3.289 %.

$C_{13}H_{13}O_6Br$ requires : C, 50.32; H, 2.903 %.

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