CHAPTER-5

SYNTHESES OF PYRANOXANTHONES

THEORETICAL

SYNTHESES OF PYRANOXANTHONE

During the past few years, quite a number of natural products containing C_5 unit in hydroxy acetophenones, flavanoids, xanthones, coumarins, quinones and also some alkaloids have been discovered. The C_5 unit may be linked to an oxygen atom or a carbon atom of the aromatic nucleus or both. Commonly the unit is a ٢-٢-dimethyl allyl (prenyl) group, although it may be present in its various oxidized and reduced forms.

Recently many xanthones with prenyl substitutents have been isolated[1-9]. Among naturally occuring isoprenylxanthone the C_5 unit is generally present as either isoprenyl or as condensed 2,2'-dimethylpyran[10,11]. The C_5 unit can also be present as 1,1-dimethylallyl, which is formed by Claisen rearrangement of the isoprenyloxyxanthone. Such isoprene units have been introduced into hydroxyxanthone in variety of ways[12-19].

Prenylation of 1-hydroxy-3,7-dimethoxyxanthone[20] with isoprenyl bromide gave a mixture containing 2-prenyl-, 4-prenyl- and 2,4-diprenyl-, 1-hydroxy-3,7-dimethoxy xanthones. Pure prenyloxyether in N,N-dimethylaniline gave 2-prenyl- and 4-prenyl derivatives.

1,3-dihydroxy-2-prenylxanthone and 1,3-dihydroxy-2,4-diprenylxanthone.

Claisen rearrangement of 1-hydroxy-3-prenyloxy-xanthone, its 7-methoxy and 6-methoxy derivatives at 200-210°C in vacuum[25] yielded a mixture of the corresponding dealkenylated xanthones, angularly condensed 4', 4', 5'-trimethyl dihydrofurano derivatives and their linear isomers. However, 1-hydroxy-5-methoxy-3-prenyloxyxanthone afforded, besides the dealkenylated xanthone, only the linearly condensed 4', 4', 5'-trimethyl dihydrofuranoxanthone and its 4-prenylated derivatives.

Burling et al[26] have reported the prenyl migration of 1-prenyloxy-3,5,6-trimethoxyxanthone in N,N-dimethyl-aniline. They obtained 4-prenyl-1-hydroxy-3,5,6-trimethoxy-xanthone, the furanoxanthone, the normal 2-prenyl migration product and dealkenylated xanthone. In another experiment 2,4-diprenyl-3,5,6-trimethoxyxanthone was also obtained.

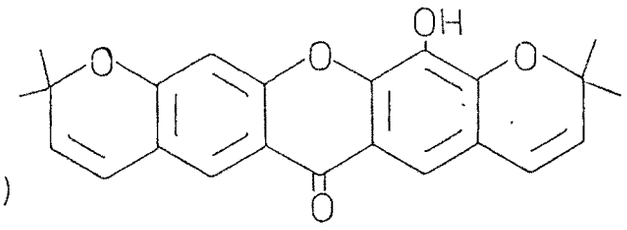
Pyrano Jacareubin, (1) has been isolated from Garcinia Devisivenia stem bark by Grichton[27]. Nilima Banerji et al.[28] have isolated three new xanthones, garcinones A, B and C from fruit hulls of G.mojostana. They have also isolated xanthones[29] (5) and (6) from the same plant. In 1981 Balasubramanium et al.[30] have isolated an unusual xanthone (7) from the heartwood of calophylium tomentosum.

Dyer et al.[21] have shown by isotopic labelling technique that the p-Claisen rearrangement proceeds largely by the intramolecular pathways.

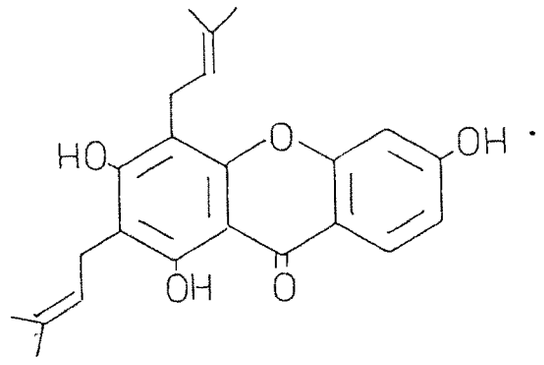
Anand and Jain[22] reported that 1-hydroxy-7-methoxy-3-prenyloxyxanthone at 200°C gave 1,3-dihydroxy-7-methoxy xanthone, the angular 4', 4', 5'-trimethyl dihydrofurano-xanthone and its linear isomer. 1-Hydroxy-3-prenyloxy-xanthone rearranged similarly, whereas 1-hydroxy-5-methoxy-3-prenyloxyxanthone gave 1,3-dihydroxy-5-methoxy-xanthone, the linear 4', 4', 5'-trimethyl dihydrofurano-xanthone and a xanthone with prenyl and dihydrofurano units.

Anand and Jain[18] also reported that 1,3-7-trihydroxy-xanthone with prenyl bromide, gave C-prenylated, and o-prenylated xanthones of which 2-prenyl-1,3,7-trihydroxy xanthone was cyclised further when dihydro osajaxanthone and dihydroisoosajaxanthone were obtained. Reaction of 1,3,7-trihydroxyxanthone with prenyl bromide in presence of methanolic sodium methoxide[23] yielded four compounds which have been identified on the basis of spectral data as 1,3,7-trihydroxy-2-prenylxanthone, its 7-prenyl ether, 1,3,7-trihydroxy-2,4-diprenylxanthone and its 7-prenyl ether. Reaction of 1,3-dihydroxyxanthone, with 2-hydroxy-2-methyl-3-butene in presence of borontrifluoride etherate[24] gave a mixture of 1,3-dihydroxy-4-prenylxanthone,

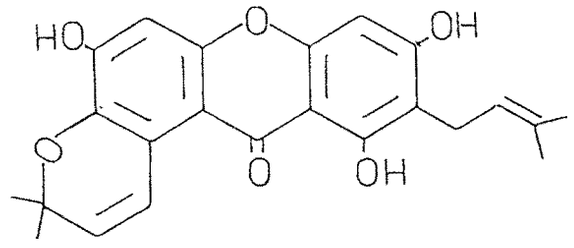
(1)



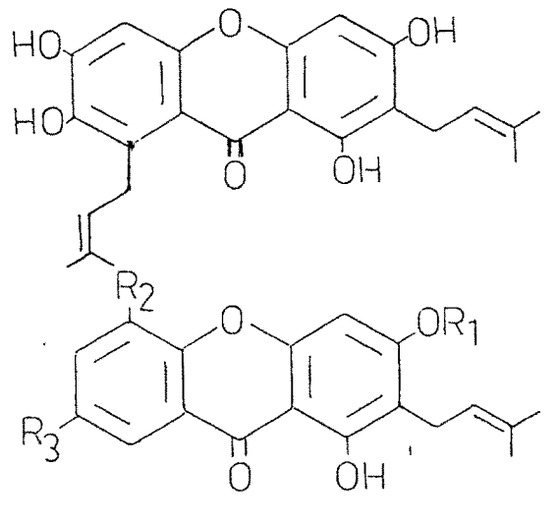
(2)



(3)



(4)



(5) $R_1=CH_3$, $R_2=OH$, $R_3=H$

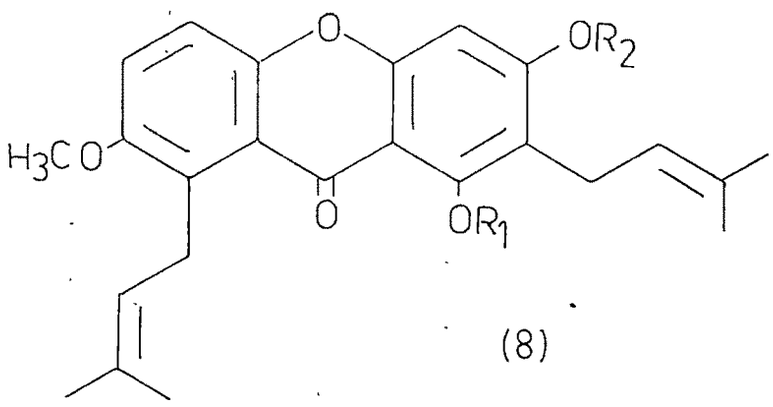
(6) $R_1=CH_3$, $R_2=H$, $R_3=OH$

(7) $R_1=H$, $R_2=OH$, $R_3=H$

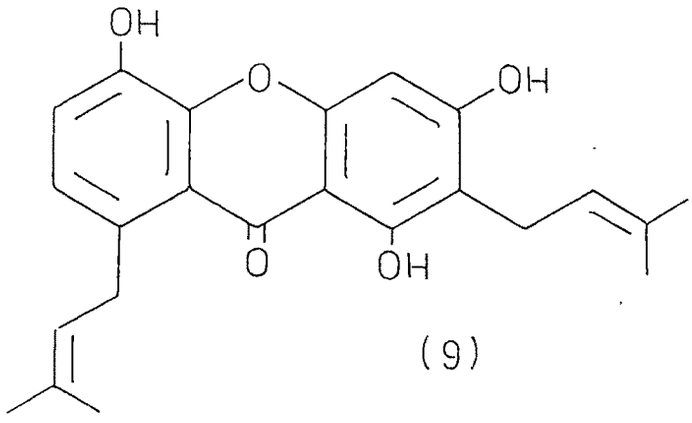
Same workers have also isolated a new xanthone, Calocalaba xanthone (8) from Calopyllum calaba[31]. In 1982 a novel xanthone (9) has been isolated from the stem bark of Garcinia quardti Faria by Waterman et al.[32].

Number of methods have been reported in the literature and reviewed[33] for the synthesis of prenylated and pyrano compounds. Jurd et al.[34] have reported isoprenylation of polyphenols in aqueous acid solutions. In the field of xanthones, toxyloxanthone[35] (10) has been synthesised, by the application of Claisen migration of the product obtained by the reaction between hydroxy xanthone and 3-chloro-3-methylbut-1-yne.

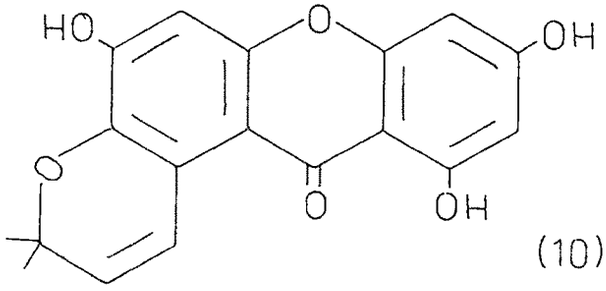
Claisen rearrangement of substituted 1-hydroxy-3-prenyloxyxanthones had been studied by Jain et al.[22,25]. No attempt had been made to study the Claisen rearrangement of simpler prenyloxyxanthones. The present chapter deals with studies of Claisen rearrangement of 3-prenyloxy-, 3-prenyloxy-4-iodo-, 3-prenyloxy-4-bromo-, 2-prenyloxy-, 3-prenyloxy-4-methylxanthone and the syntheses of some pyranoxanthones.



(8)



(9)



(10)

Toxyloxanthone

The second product was isoluble in alkali which was identified as the cyclised product 4',4',5'-trimethyl-4', 5'-dihydrofurano (2',3' : 3,4) xanthone (14). The structure of which was assigned on the basis of its IR, NMR and mass spectra.

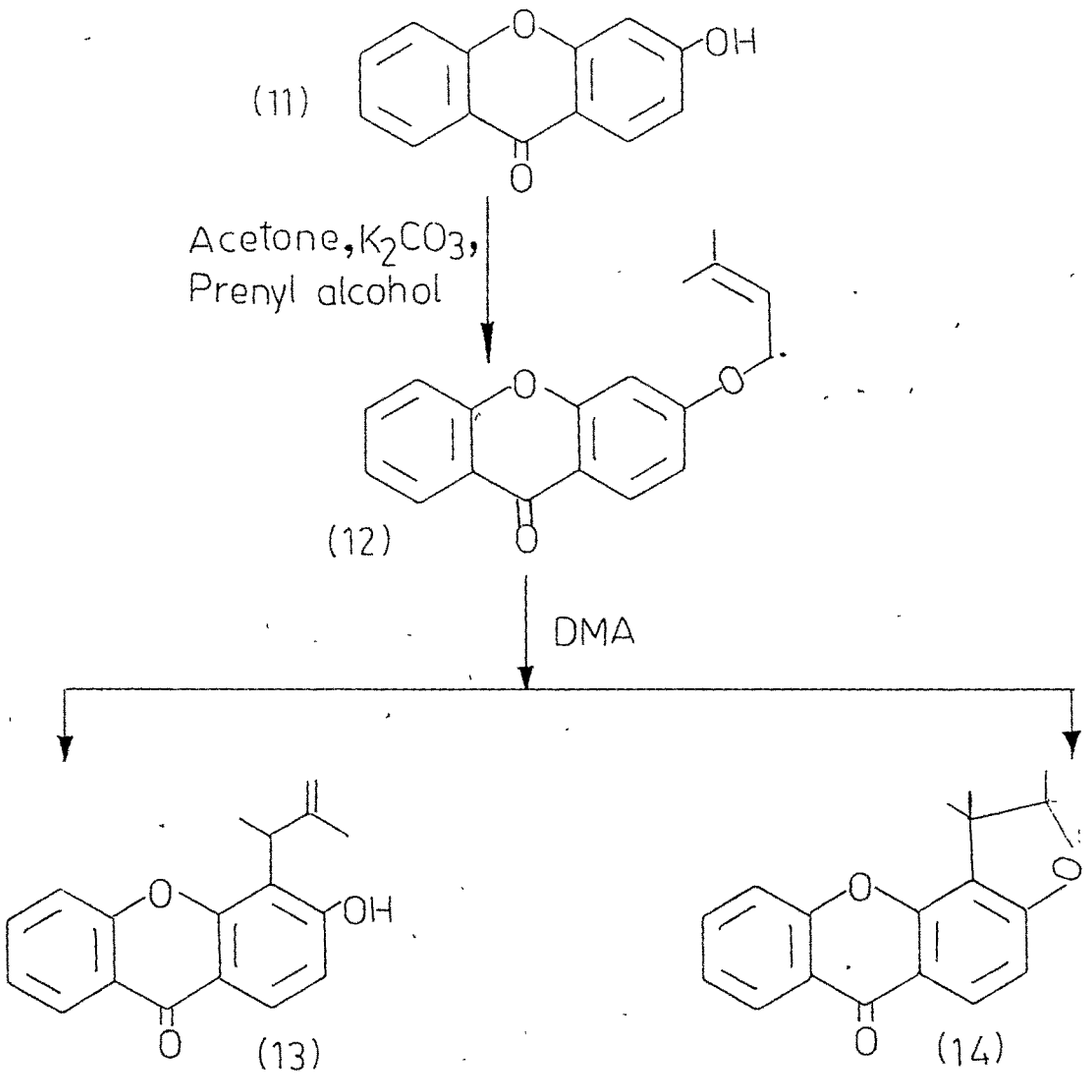
NMR ($CDCl_3$) (Fig.3) spectrum shows a characteristic quartet centered at δ 4.56 of one hydrogen flanked by the methyl group and the oxygen atom. In the upfiled region there are two singlets for the two methyl groups at δ 1.6 and 1.3, one doublet at δ 1.40., There are two doublets of J=9Hz one in the upfield aromatic region at δ 6.78 for the proton at position 2 and another in the downfield aromatic region at δ 8.16 which is assigned to the proton at position 1, indicating that it is an angular furanoxanthone. Above data and other signals at 8.3, dd, 1H, J=9,2Hz, H-8; 7.63, td, 1H, J=9,9,2Hz, H-6; 7.41, doublet, 1H, J=9Hz, H-5; confirms the assigned structure (4).

Claisen migration of 3-prenyloxyxanthone (12) in boiling N,N-dimethylaniline and butyric anhydride mixture gave butyroxy derivatives which on hydrolysis furnished 4-(1,2-dimethylpropenyl)-3-hydroxyxanthone (13), dihydro furanoxanthone (14) and 3-hydroxyxanthone (11). With a view to trap the intermediate for the abnormal Claisen

PRESENT WORK

Claisen rearrangement of 3-prenyloxyxanthone (12)

3-Hydroxyxanthone (11) on prenylation with prenyl bromide and anhydrous potassium carbonate in dry acetone yielded 3-prenyloxyxanthone (12), which on refluxing with N,N-dimethylaniline gave two products. The first product, which was soluble in sodium hydroxide, was identified as 4-(1,2-dimethyl propenyl)-3-hydroxyxanthone (13) on the basis of its IR, mass and NMR spectral studies. IR (KBr) ν max 3300 - 3000 (br-OH), 1630 (>C=O) mass : m/e 280 (M^+ 100), 265 (M^+-CH_3), 250 (M^+-2CH_3), 212 ($M^+-C_5H_8$). NMR spectrum (Fig.1,2) in $CDCl_3$ showed a characteristic quartet centered at δ 4.38 of one proton -C<u>H</u>-CH_3 and two singlets at δ 5.28 and 5.32 for $=CH_2$ group in the saturated methyl region. There is one singlet of the methyl group at δ 1.60 and one doublet of the methyl group at δ 1.55. In the down field aromatic region doublet of J=9Hz at δ 8.15 is observed which could be assigned to the proton at position 1, other doublet of 9Hz appears at δ 6.85 due to the proton at position 2 indicating that migration has taken place at position 4., 7.0, singlet, 1H, ArOH; 7.36, td, 1H, J=8,8,2Hz, H-7; 7.48, doublet, 1H, J=9Hz, H-5; 7.7, td, 1H, J=8,8,2Hz, H-6.



(12) $\xrightarrow[4\text{ hrs.}]{\text{DMA + BA}} \xrightarrow{\text{NaOH}}$ (13) + (14) + (11)

$\xrightarrow[4\text{ hrs}]{\text{BA}} \xrightarrow{\text{NaOH}}$ (13) + (11)

$\xrightarrow[AC_2O\text{ , 20 hrs}]{CH_3COONa}$ 3-acetoxyxanthone + (12)

$\xrightarrow[3\text{ hrs}]{\text{Decalin}}$ —

$\xrightarrow[\text{Vacuum, 4hrs}]{\text{Decalin, 6 hrs}}$ (11)

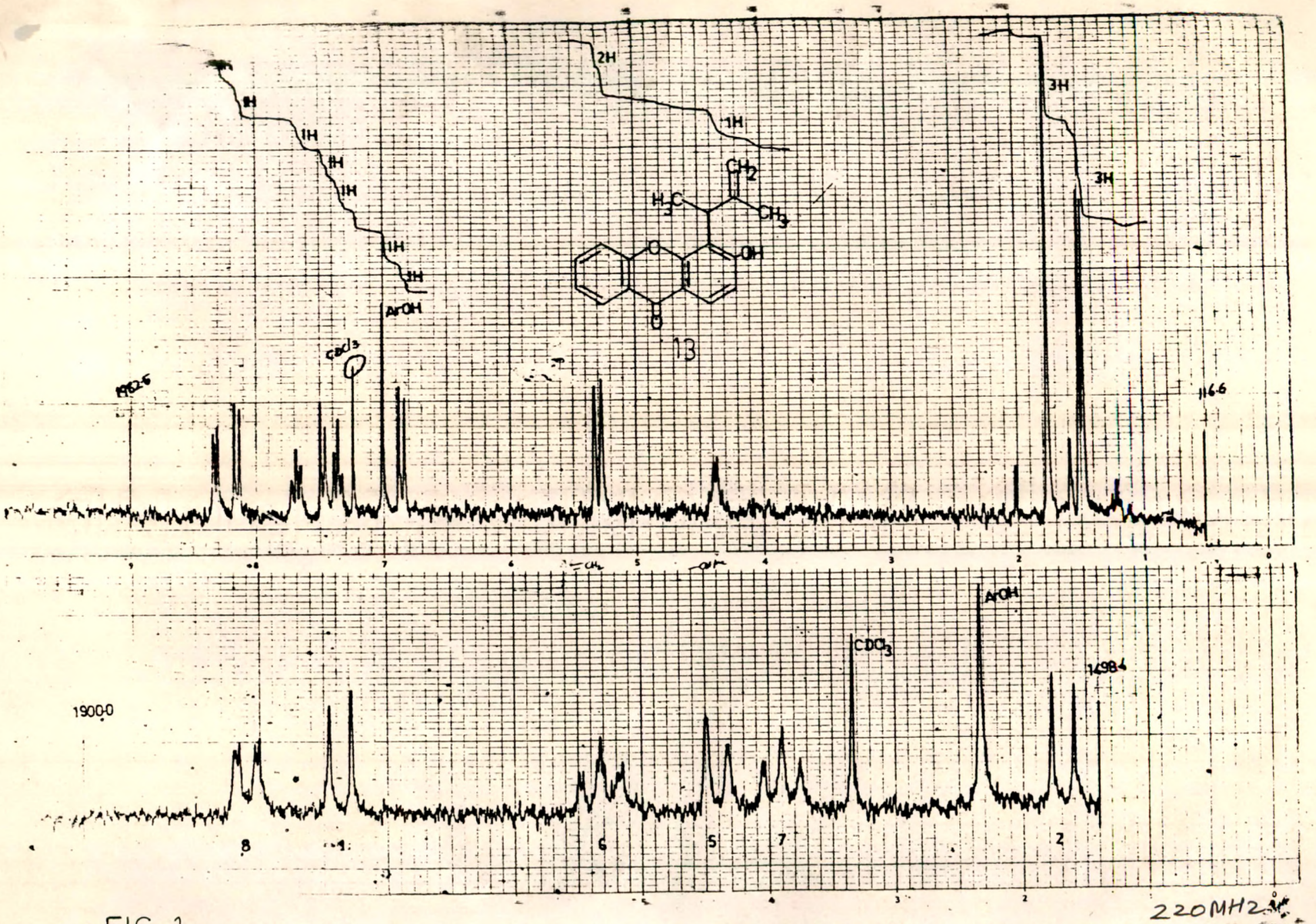

1H
1H
1H
1H
1H
1H
ArOH
CDCl3
1162.6
2H
1H
3H
3H
1166
1900.0
CDCl3
ArOH
1698.4
8
6
5
7
2
220MHz

FIG 1

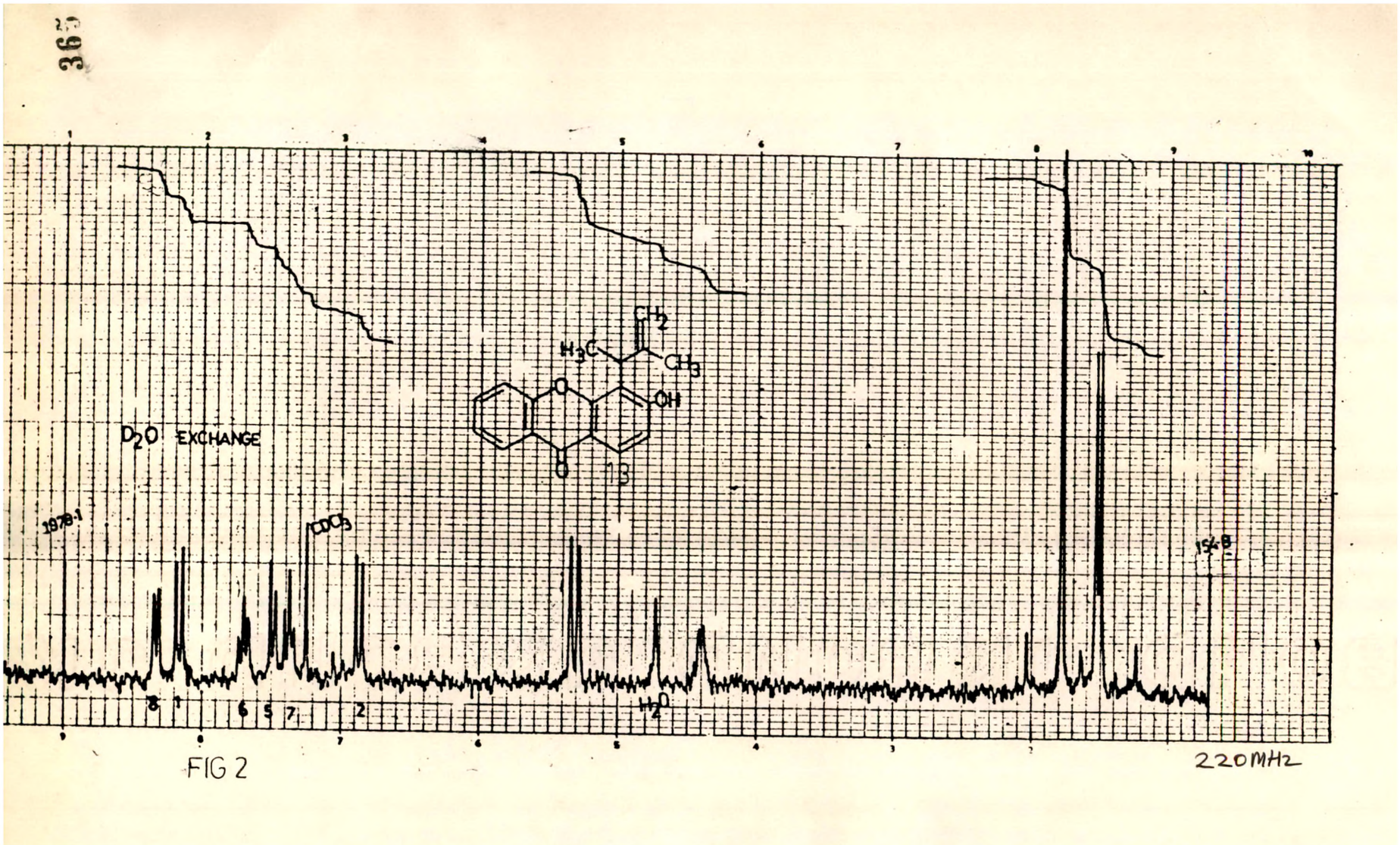


FIG 2

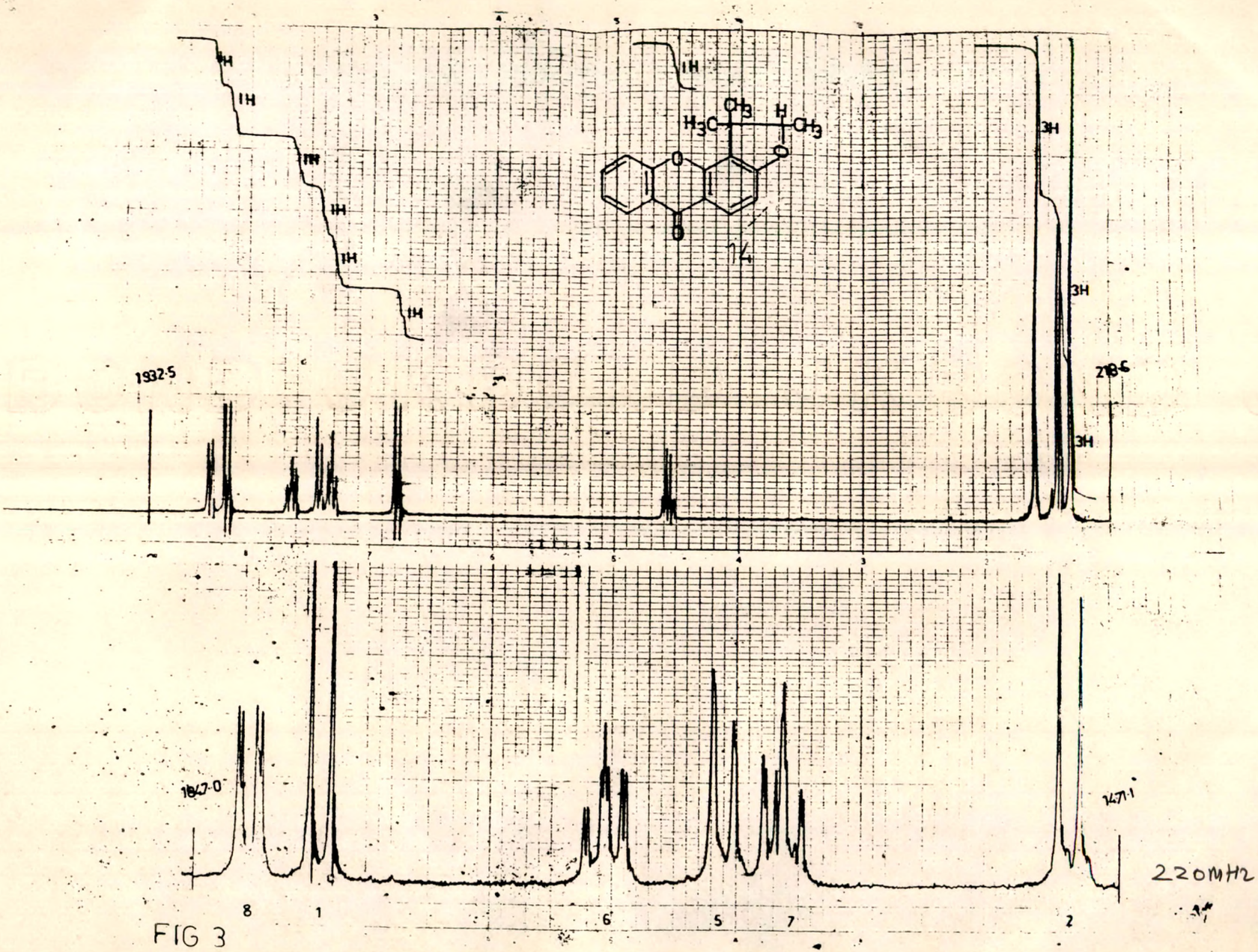
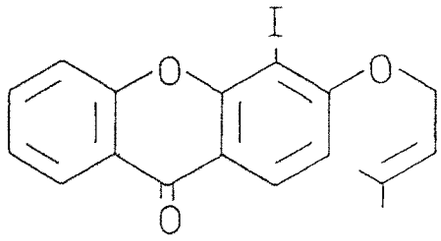

1H
1H
1H
1H
1H
1H
1932·5
1847·0
1H
3H
3H
3H
218·6
1471·1
220MHz
8
1
6
5
7
2

FIG 3

migration product or to get usual migration product, rearrangement was carried out in butyric anhydride only, but after hydrolysis of crude product, it gave the compound (13) and 3-hydroxyxanthone (11). On refluxing with freshly fused sodium acetate and acetic anhydride for 20 hr. Compound (12) gave 3-acetoxy-xanthone and the unrearranged starting compound 3-prenyloxyxanthone (12). In decalin (3 hr. refluxed) no migration was observed. When (12) was refluxed in decalin for 6 hr. or heated under vacuum for 4 hr. 3-hydroxyxanthone (11) was obtained.

Claisen rearrangement of 3-prenyloxy-4-iodoxanthone (15) and 3-prenyloxy-4-bromoxanthone (16)

3-Prenyloxy-4-iodoxanthone (15) on attempted Claisen rearrangement **in** (i) N,N-dimethylaniline heated under reflux for 25 min in a nitrogen atmosphere (ii) decalin 15 min refluxed and (iii) heating at 180° under vacuum for 2 hr. yielded 3-hydroxyxanthone (11). Compound (15) on refluxing with sodium acetate acetic anhydride for 15 hr. gave 3-acetoxy-4-iodoxanthone, while refluxing in dimethyl formamide for 4 hr. yielded deprenylated product 3-hydroxy-4-iodoxanthone.



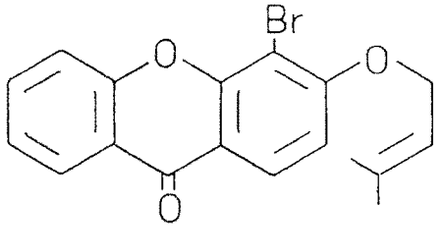
(15)

DMA , N_2 , 25 mins
Decalin , 15 mins
Vacuum at 180', 2 hrs

→ (11)

AC_2O / CH_3COONa → 3-acetoxy -4-iodoxanthone

DMF → 3-hydroxy -4-iodoxanthone



(16)

DMA , N_2 / 1 hr → 3-hydroxy xanthone (11)

Decalin → 3-hydroxy -4-bromoxanthone

Vacuum → (,,) + (11)

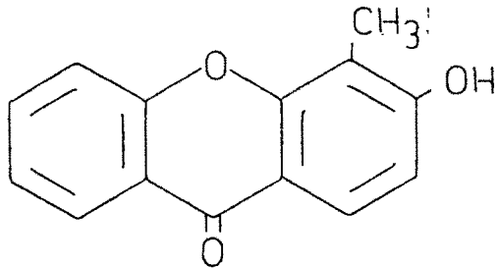
3-Prenyloxy-4-bromoxanthone (16) on refluxing in N,N-dimethylaniline under nitrogen atmosphere, within 1 hr., underwent deprenylation and debromination to give 3-hydroxyxanthone. However in decalin compound (16) gave 3-hydroxy-4-bromoxanthone and in vacuum it gave 3-hydroxyxanthone and 3-hydroxy-4-bromoxanthone.

Claisen migration of 3-prenyloxy-4-methylxanthone (18)

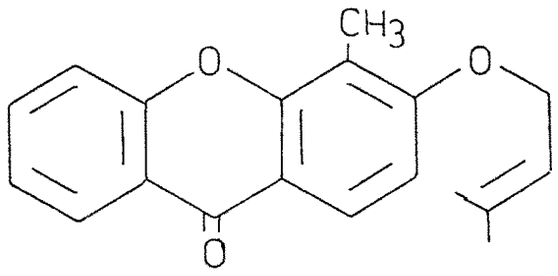
3-Hydroxy-4-methylxanthone (17) on prenylation with prenyl bromide, in presence of potassium carbonate yielded 3-prenyloxy-4-methylxanthone (18) which on refluxing with N,N-dimethylaniline gave only one product, which was characterized as 2-(1,2-dimethyl propenyl)-3-hydroxy-4-methylxanthone (19) on the basis of its NMR spectrum ($CDCl_3$) which showed a quartet of one proton at δ 3.65 for $\underline{CH}-CH_3$, doublet at δ 1.58, for CH_3 group and two singlets at δ 5.15 and 5.25 for $=CH_2$ group. Other signals were observed at δ 7.8 to 7.38, multiplet, 3H, H-5, H-6, and H-7; 8.08, singlet, 1H, proton at position 1; 8.35, dd, 1H, J=9,2Hz proton at position 8.

5',5',4',4-Tetramethyl-4',5'-dihydrofurano (3',2' : 2,3) xanthone (20)

The compound (19) on treatment with sulphuric acid yielded 5',5',4',4-tetramethyl-4',5'-dihydrofurano(3',2' : 2,3) xanthone (20) as NMR spectrum ($CDCl_3$) showed a

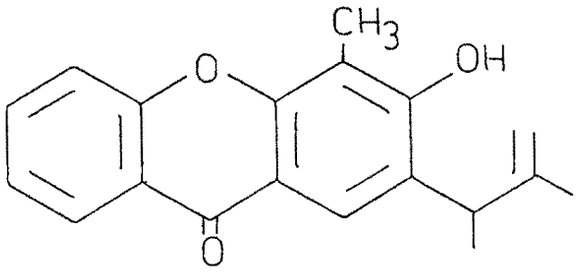


(17)



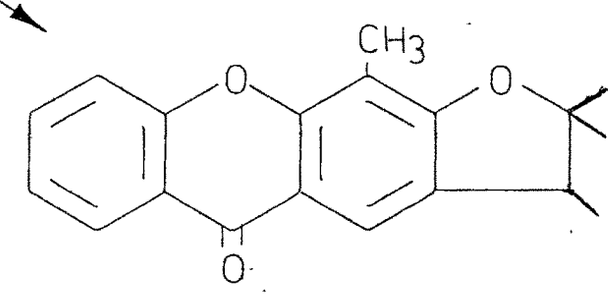
(18)

DMA



(19)

Conc.
H_2SO_4

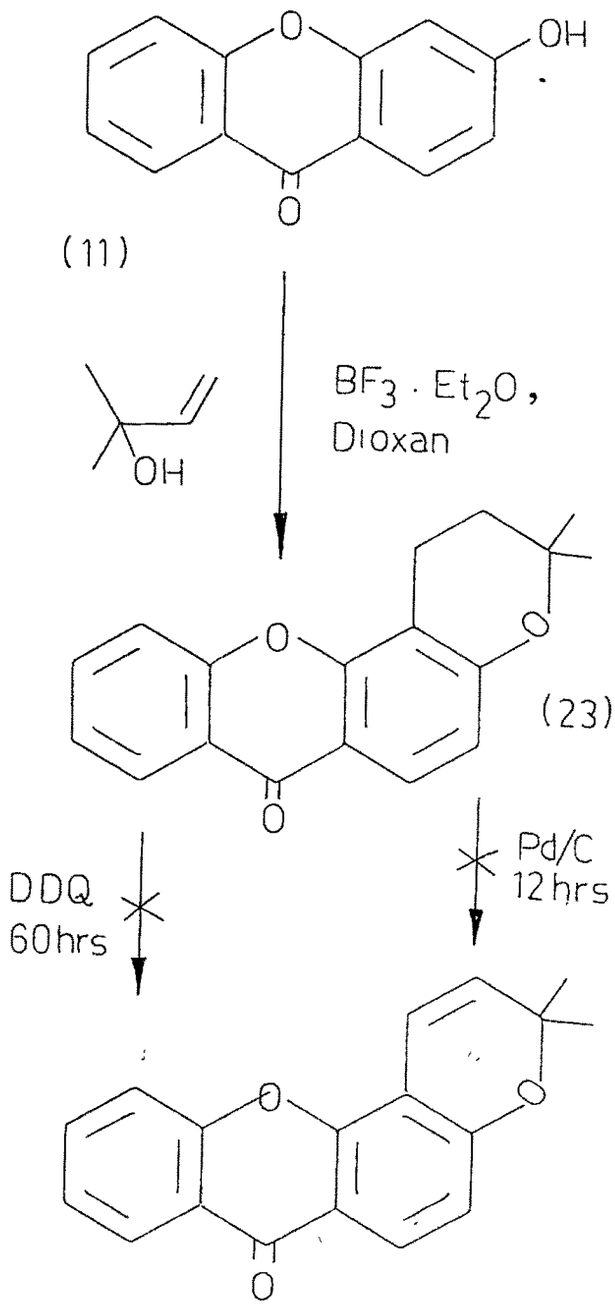


(20)

quartet centered at δ 3.3 for one proton C<u>H</u>-CH_3, doublet at δ 1.4, J=8Hz integrating for the three protons of the CH_3 group at position -4', three singlets at 2.35, 1.6 and 1.38 for the aromatic CH_3 group at position-4 and two CH_3 groups in the furan ring at position-5 respectively. In the down field aromatic region only one singlet at δ 7.85 is observed which could be assigned to the proton at position 1; 8.25, dd, 1H, J=9,1.5Hz, H-8; 7.7 to 7.3, m, 3H, H-5, H-6 and H-7 confirms the structure (20).

<u>6',6'-Dimethyl-4',5'-dihydropyrano (2',3' : 3,4)xanthone(23)</u>

3-Hydroxyxanthone (11) on treatment with prenyl alcohol and borontrifluoride etherate in dioxan yielded compound (23), the structure of which was confirmed by its NMR ($CDCl_3$) spectrum which showed a singlet integrating for the six protons of the two methyl groups at position 6' in the pyram ring. Moreover it showed two triplets the upfield signal at δ 1.45 for 2H,J=8Hz was assigned to CH_2 group at position 5' and the other one at δ 3.0 was assigned to CH_2 group at position 4', thus confirming the dihydropyran ring. Signals at 6.75, doublet, 1H, J=9Hz, proton at position 2; 7.3 to 7.75, multiplet, 3H, H-5, H-6 and H-7; 8.15, doublet, 1H, J=9Hz, periproton at position 1 and 8.28, dd, 1H, J=9,2Hz, periproton at position 8, suggest that it is an angular pyranoxanthone and confirms the assigned structure (23).


OH
O
O
(11)
OH
$BF_3 \cdot Et_2O$,
Dioxan
O
O
O
(23)
DDQ
60hrs
Pd/C
12hrs
O
O
O

The compound failed to dehydrogenate with palladised charcoal or DDQ to give pyranoxanthone.

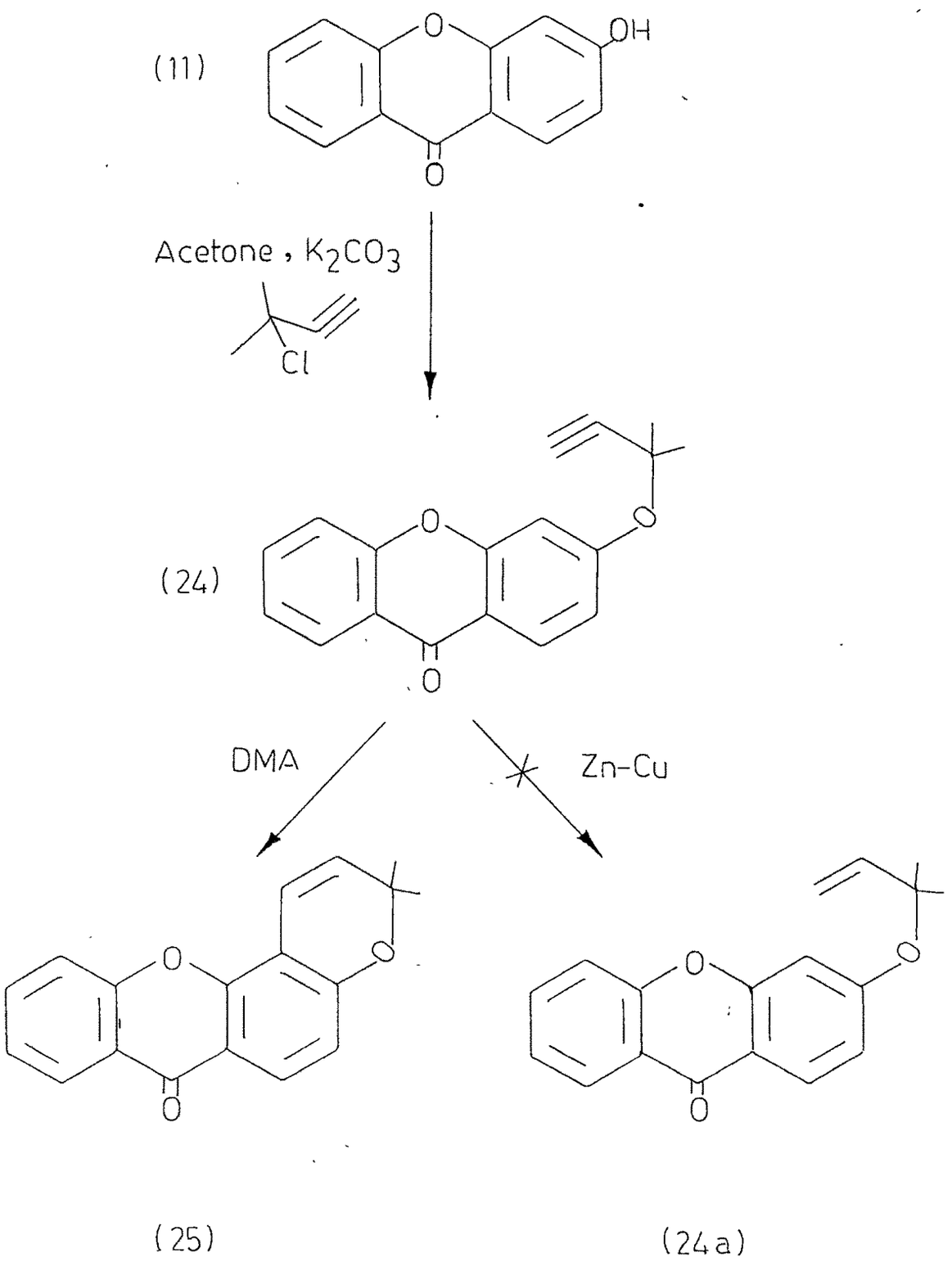
6',6'-Dimethylpyrano (2',3' : 3,4)xanthone (25)

3-Hydroxyxanthone (11) on reaction with 3-chloro-3-methyl-but-1-yne, potassium carbonate and potassium iodide in boiling acetone yielded 3-(1,1-dimethylprop-2-ynyl) ether (24). The compound (24) on Claisen rearrangement in boiling N,N-dimethylaniline gave 6',6'-dimethylpyrano (2',3' : 3,4) xanthone (25). Mass m/e 278 (M^+) 263 (M^+-CH_3), 248 (M^+-2CH_3), NMR spectrum (Fig.4) in $CDCl_3$ showed δ 8.2, dd, 1H, J=9,2Hz, H-8; 8.1, doublet, 1H, J=9Hz peri proton at position 1., 7.65, td, 1H, J=9,9,2Hz, H-6; 7.43, dd, 1H, J=9,2Hz, H-5; 7.32, td, 1H, J=9,9,2Hz, H-7; 6.92, doublet, 1H, J=9Hz, H-4'; 6.78, doublet, 1H, J=9Hz, H-2; 5.70, doublet, J=9Hz, H-5'; 1.48, singlet, 6H, two CH_3 group.

Attempts to reduce (24) with Zn-Cu couple failed.

Synthesis of 6',6'-dimethyl-1,3-dihydroxy-4',5'-dihydro pyrano (2',3'-6,7)xanthone (27)

Methyl-β-resorcylate on prenylation with prenyl alcohol, borontrifluoride etherate in dioxan gave methyl 6',6'-dimethyl-4',5'-dihydropyrano (2',3': 4,5)-1-hydroxybenzoate (26) structure of which was confirmed by its NMR spectrum (Fig.5) (CCl_4) which showed two



(25)

(24a)

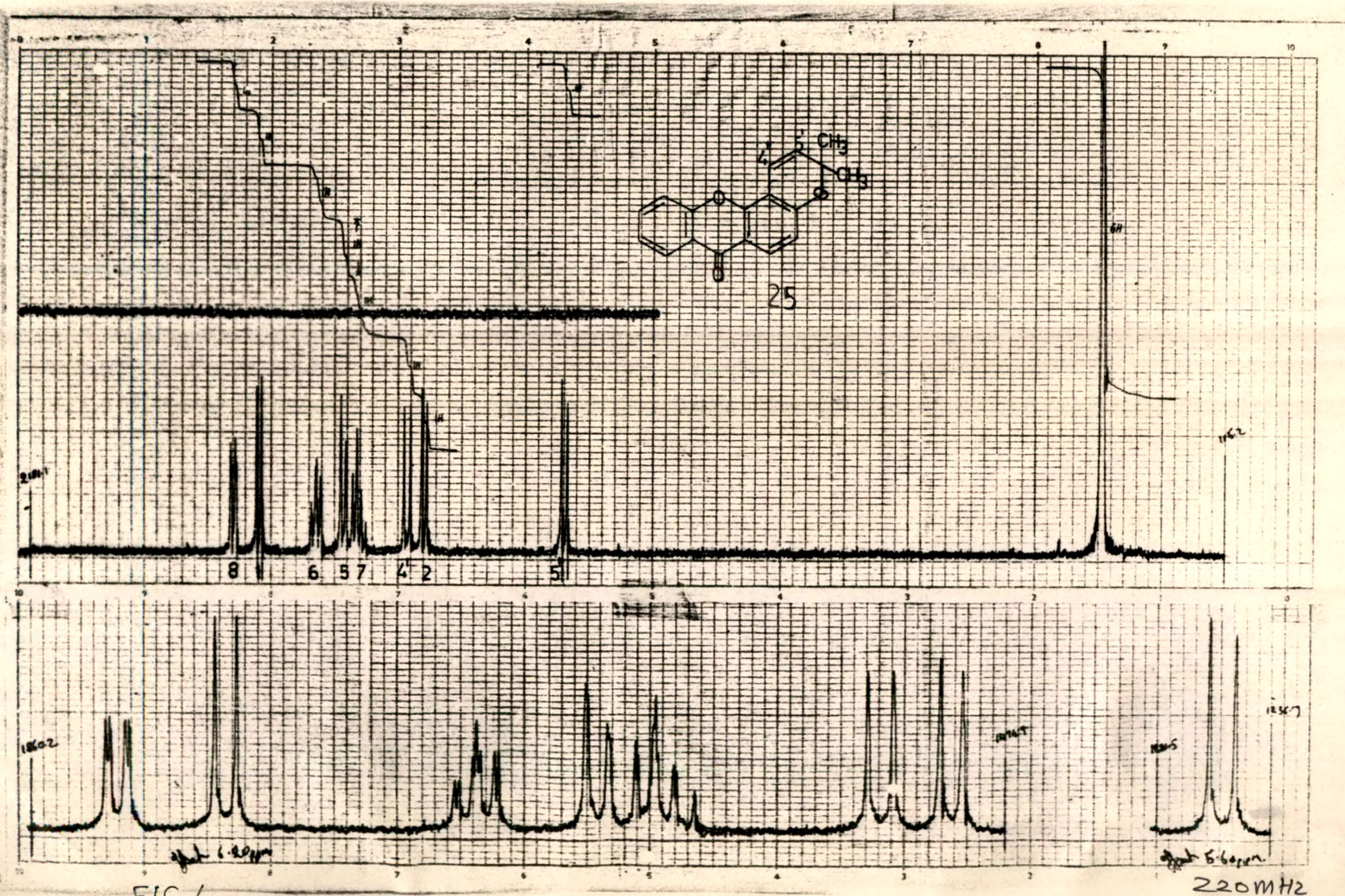
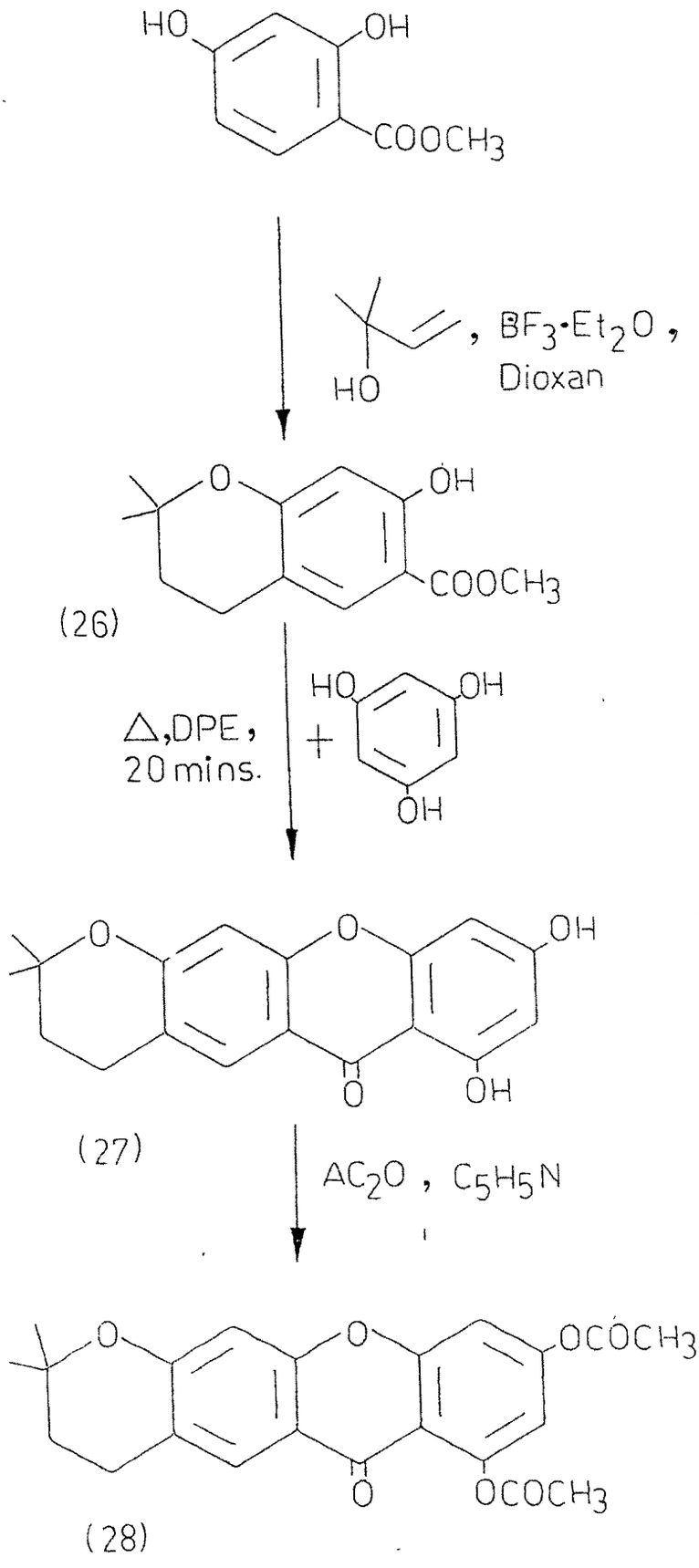


FIG 4

characteristic triplets each corresponding to two protons, at δ 2.8 and 1.8 for $-CH_2-CH_2$ linkage which ruled out the possibility for the prenyl group. Moreover in the aromatic region there were only two singlets at δ 7.05 and at δ 6.35 for the protons H-3 and H-6 meaning that it is a linear dihydropyrano compound. 3.9, singlet 3H for $COOCH_3$ and 1.3, singlet, 6H, for the two CH_3 groups thus confirmed the assigned structure (26). The compound (26) on thermal condensation with phloroglucinol in boiling diphenyl ether yielded the compound (27) the structure of which was established on the basis of its acetoxy derivative (28).
NMR ($CDCl_3$) (Fig.6) spectrum of the compound (28) showed two singlets of three protons each at δ 2.45 and 2.32 for two acetoxy groups; 1.48, singlet integrating for the six protons of the two CH_3 groups in pyran ring at position 6', two triplets at δ 1.88 and 2.89 for the two CH_2 group at position 5' and 4' respectively, 6.72, doublet, 1H, J=2Hz, H-2; 7.4, singlet, 1H, H-5; 7.3, doublet, 1H, J=2Hz, H-4; 7.93, singlet, 1H, H-8.

<u>1,3,8-Trihydroxy-6,6'-dimethyl-4',5'-dihydropyrano (2', 3': 5,6)xanthone (30)</u>

Methyl-2,4,6-trihydroxybenzoate was condensed with 2-methylbut-3-ene-2-ol, borontrifluoride etherate


HO
OH
COOCH3
HO
, BF3·Et2O ,
Dioxan
O
OH
COOCH3
(26)
△,DPE,
20 mins.
HO
OH
+
OH
O
O
OH
O
OH
(27)
AC2O , C5H5N
O
O
OCOCH3
O
OCOCH3
(28)

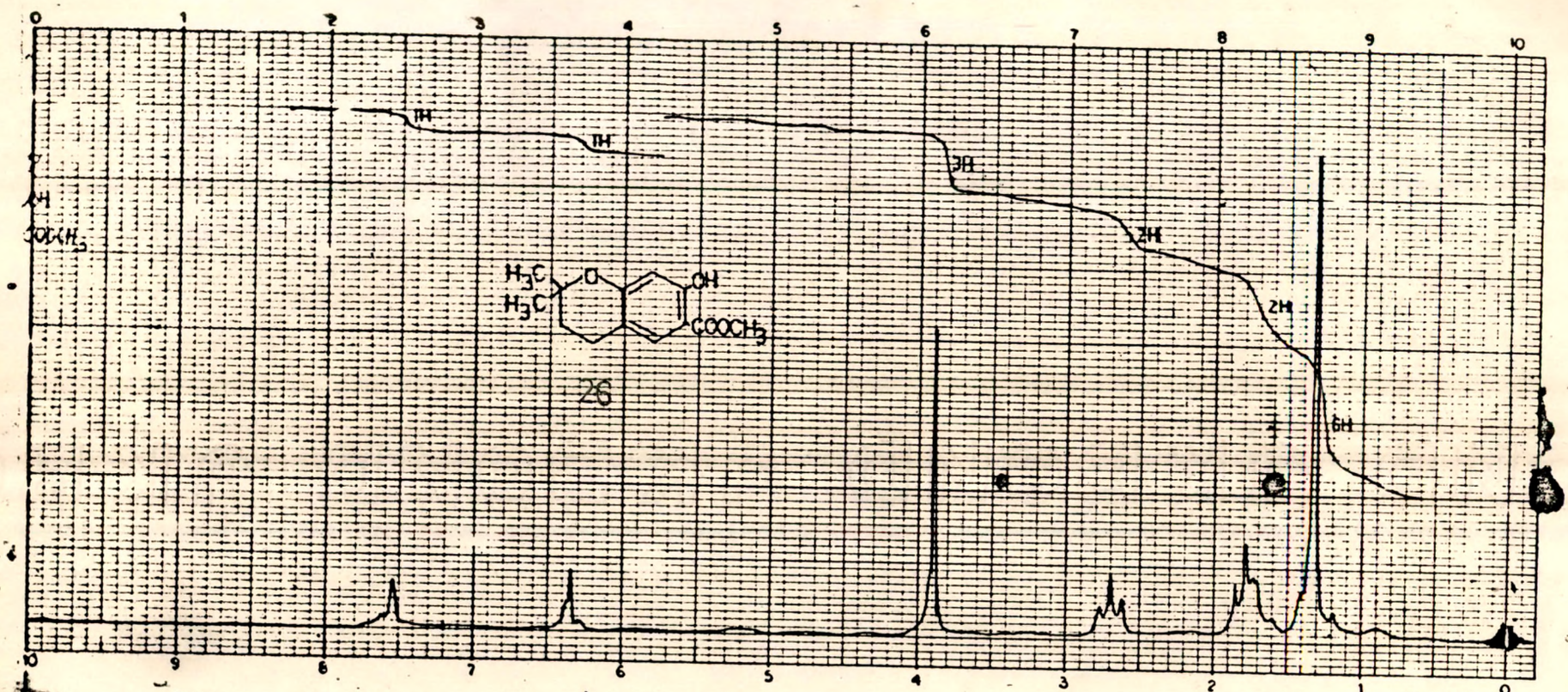


FIG 5

379

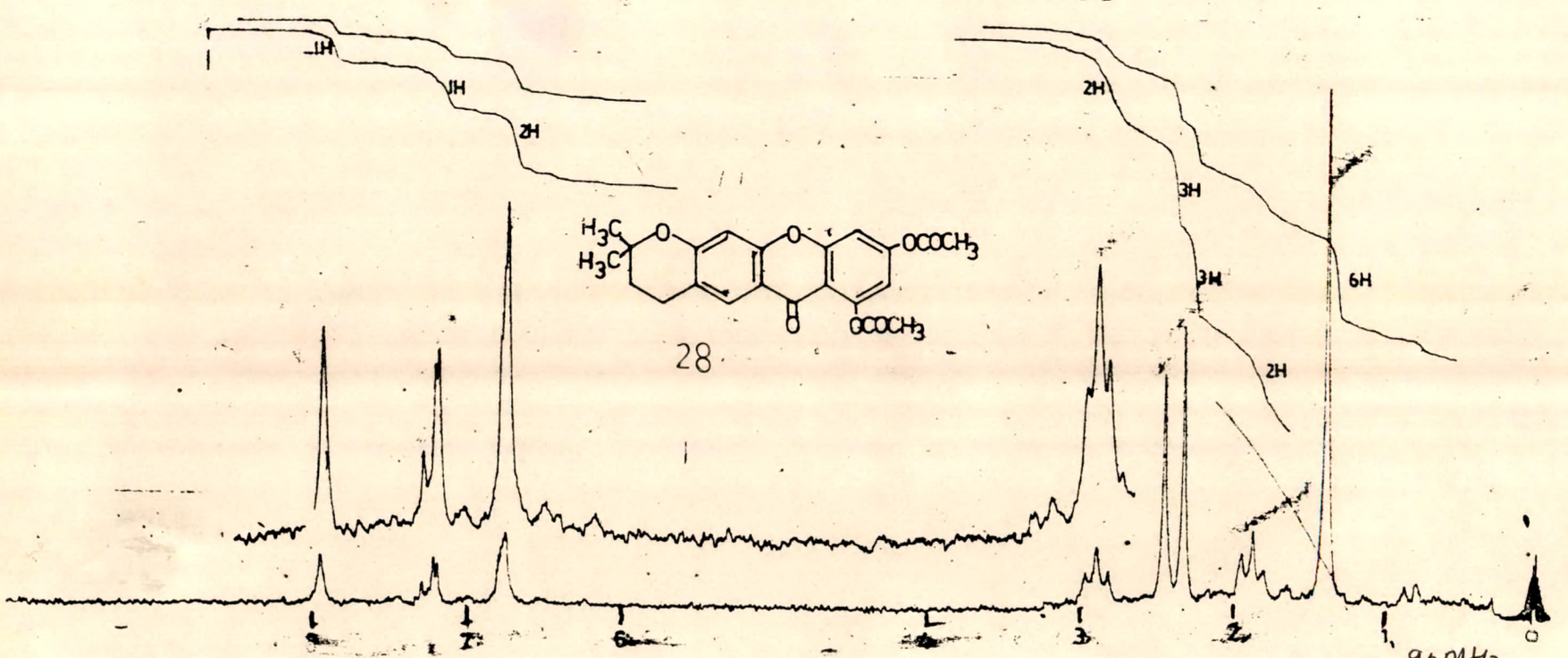
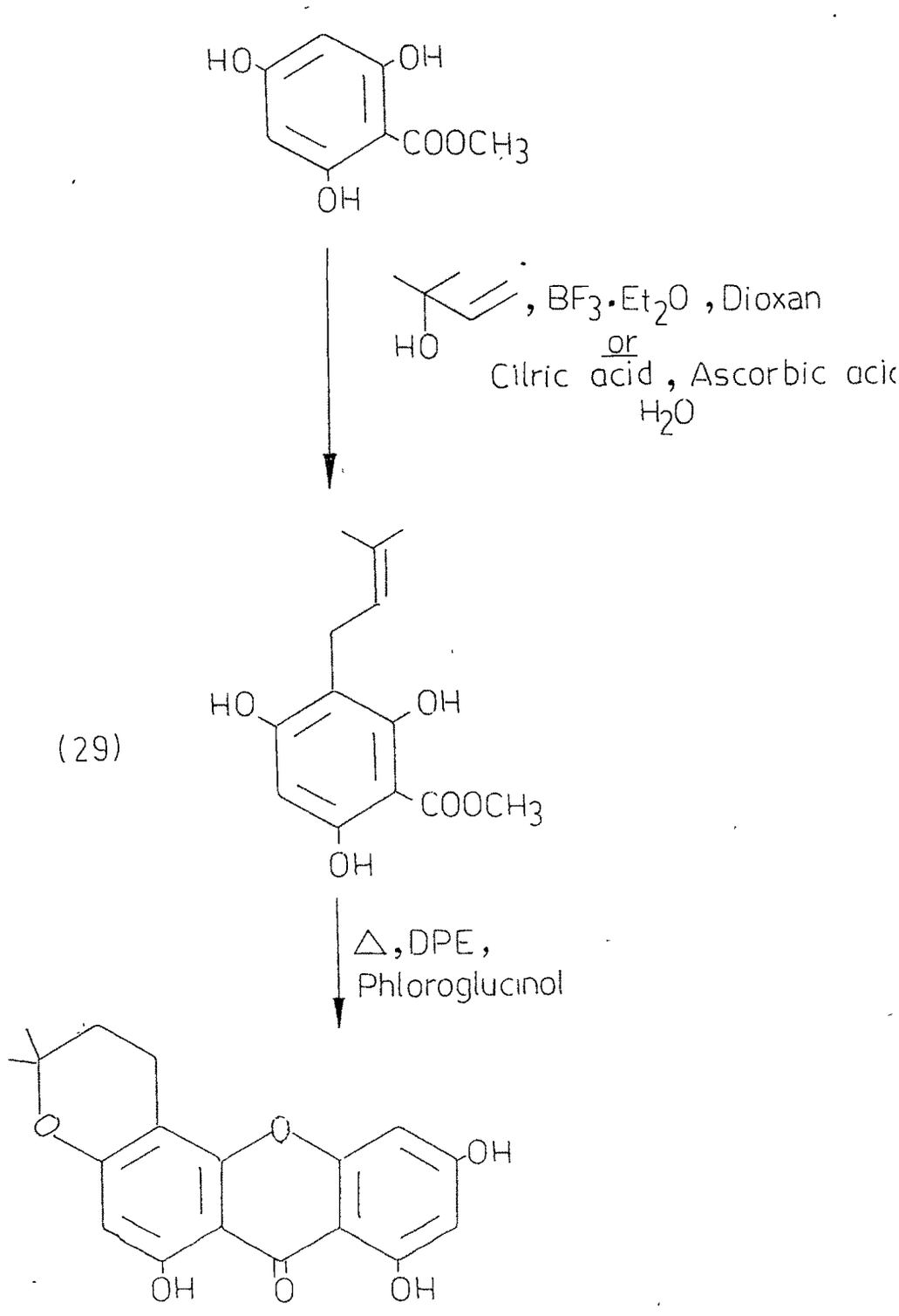


FIG 6

in dioxan or with the same alcohol in citric acid gave methyl-3-prenyl-2,4,6-trihydroxybenzoate (29) structure of which was confirmed by its NMR spectrum. NMR (CCl_4) (Fig.7) showed only one singlet in the aromatic region at δ 5.9 integrating for one proton at position H-5; 5.22, t, 1H, J=9Hz, $CH_2\underline{C}H=C(CH_3)_2$; 4.1, s, 3H, $-COOCH_3$; 3.32, doublet, 2H, J=9Hz, $-\underline{C}H_2CH=C(CH_3)_2$ and 1.85, 1.80 two singlet, 6H, $=C(CH_3)_2$. The compound (29) on thermal condensation with phloroglucinol in boiling diphenyl ether gave 1,3,8-trihydroxy-6',6'-dimethyl-4',5'-dihydropyrano (2',3': 5,6) xanthone (30) the cyclised product. NMR ($CDCl_3$) spectrum of which showed two characteristic triplets of CH_2-CH_2 group at δ 1.78 and 2.69 upfield. triplet is due to CH_2 group at position 5' and other one is due to CH_2 group at position 4'. There is also a singlet at 1.4 for the six protons due to two CH_3 in pyran ring; 6.05 to 6.18, multiplet of the three protons H-2, H-4 and H-7; 11.68, singlet, 1H, 3-OH, 11.92, singlet, 1H, 8-OH; 12.25, singlet, 1-OH.


HO
OH
COOCH3
OH
HO
, BF3·Et2O , Dioxan
or
Cilric acid , Ascorbic acic
H2O
HO
OH
COOCH3
OH
△, DPE,
Phloroglucinol
O
O
OH
OH
O
OH

(29)

(30)

382

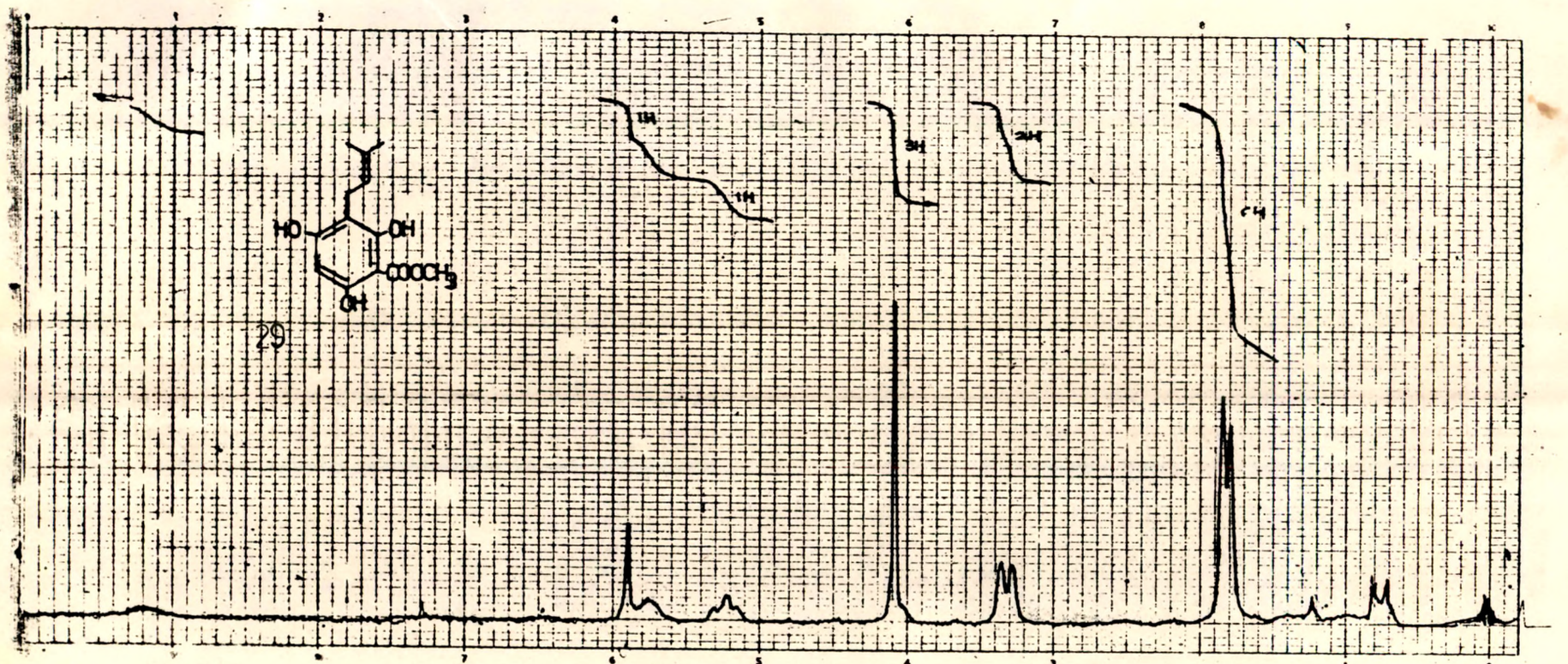


FIG 7

EXPERIMENTAL

For General Remarks, see Experimental, Chapter 2

3-Prenyloxyxanthone (12)

A mixture of 3-hydroxyxanthone (5 g) prenyl bromide (5 ml) and anhydrous potassium carbonate (25 g) was refluxed in dry acetone (150 ml) on a water bath for 15 hr. The reaction mixture was poured into water. The solid was filtered and washed with dil.sodium hydroxide to isolate the crude product (6.0g), which was crystallised from petroleum ether to obtain (12) as white needles m.p. 115° (4.2 g).

Analysis : Found : C, 77.54; H, 5.723 %.

$C_{18}H_{15}O_3$ requires : C, 77.14; H, 5.714 %.

Claisen migration of 3-prenyloxyxanthone (12)

3-Prenyloxyxanthone (12) (2.0 g) was refluxed with N,N-dimethylaniline (10 ml) for 4 hr. After cooling the reaction mixture was poured into cold dil.hydrochloric acid and extracted with ether. Ethereal layer was extracted with dil.sodium hydroxide solution, which on acidification with HCl gave a solid which crystallised from ethyl acetate to give (13) as white needles m.p. 194° (0.5 g).

Analysis : Found : C, 76.71; H, 5.373 %.

$C_{18}H_{15}O_3$ requires : C, 77.14; H, 5.714 %.

Ether solution on evaporation gave a solid which crystallised from ethyl acetate to give 4',4',5'-trimethyl-4',5'-dihydrofurano (2',3': 3,4)xanthone (14) as white needles m.p. 158-60° (1.2 g).

Analysis : Found : C, 76.95; H, 5.838 %.

$C_{18}H_{15}O_3$: requires : C, 77.14; H, 5.714 %.

mass m/e 280 (M^+,100), 265 (M^+-CH_3), 250 (M^+-2CH_3)

IR (KBr)νmax 1665 (C=O), 1105 (Furan).

(ii) DMA + Butyric anhydride

3-Prenyloxyxanthone (1.0 g) was refluxed with N,N-dimethylaniline (15 ml) and butyric anhydride (10 ml) for 9 hr. After cooling, conc. hydrochloric acid (5 ml) was added, extracted with ether and the ethereal layer was washed with sodium bicarbonate. The ether layer on evaporation gave an oil, which was refluxed with 2% sodium hydroxide solution for 6 hr. On cooling an oil separated out, which was extracted with ether, the ether layer on evaporation gave an oil which solidified afterwards. The solid on purification gave compound (14). The alkaline solution on acidification with dil.hydrochloric acid gave another solid, which showed two spots on TLC and which on separation gave compounds (13) and (11).

(iii) Butyric anhydride

The compound (12) (1.0 g) was refluxed with butyric anhydride (10 ml) for 8 hr. The reaction mixture was worked up as above to give NaOH soluble brown solid, which showed two spots on TLC. Separation by silica gel coloumn chromatography gave compounds (13) and (11).

(iv) Sodium acetate acetic anhydride

A mixture of 3-prenyloxy xanthone (12) (1.0 g), acetic anhydride (5 ml) and fused sodium acetate (2 g) was refluxed for 20 hr. The reaction mixture was poured onto crushed ice and to this was added sodium hydroxide solution till alkaline, extracted with ether, which on evaporation gave a solid, which showed two spots on TLC. After chromatographic separation the two compounds were identified as 3-prenyloxyxanthone (2) and 3-acetoxyxanthone.

3-Prenyloxy-4-iodoxanthone (15)

A mixture of 3-hydroxy-4-iodoxanthone (2.0 g), prenyl bromide (2 ml), and anhydrous potassium carbonate (4 g) in acetone was refluxed for 12 hr. The reaction mixture was worked up as before. The product crystallized from ethyl acetate in pale yellow needles m.p. 168-9^{o} (1.5 g).

Analysis : Found : C, 53.60; H, 3.856 %.

$C_{18}H_{15}O_3I$ requires : C, 53.21; H, 3.695 %.

NMR ($CDCl_3$) :δ8.25, overlap dd, 2H, J=9,2Hz, H-1 and H-8; 7.3 to 7.72, m, 3H, H-5, H-6 and H-7; 6.85, d, J=9Hz, H-2; 5.5, t, 1H, $CH_2\underline{C}\underline{H}=C(CH_3)_2$; 4.75, d, 2H, J=9Hz, $C\underline{H}_2CH=C(CH_3)_2$; 1.82, s, $6H, =C(CH_3)_2$.

3-Prenyloxy-4-bromoxanthone (16)

3-Hydroxy-4-bromoxanthone (2.5 g), prenyl chloride (4 ml), anhydrous potassium carbonate (6 g), potassium iodide (2 g) and dry acetone (100 ml) were refluxed together for 15 hr. The reaction mixture was worked up as usual. The product (2.0 g) crystallised from a mixture of benzene and petroleum ether as yellow needles m.p. 144°.

Analysis : Found : C, 60.61; H, 4.30 %.

$C_{18}H_{15}O_3Br$ requires : C, 60.167; H, 4.178 %.

3-Prenyloxy-4-methylxanthone (18)

A mixture of 3-hydroxy-4-methylxanthone (1.0 g), prenyl chloride (1 ml), anhydrous potassium carbonate (4.0 g) and potassium iodide (0.5 g) in acetone was refluxed for 12 hr. The reaction mixture was worked up as before. Crystallisation from benzene petroleum ether furnished (18) as buff coloured seeds m.p. 126° (0.7 g).

Analysis : Found : C, 77.11; H, 6.545 %.

$C_{19}H_{18}O_3$ requires : C, 77.55; H, 6.122 %.

Claisen migration of 3-prenyloxy-4-methylxanthone (18)

The compound (18) (0.4 g) was refluxed in dimethyl aniline (5 ml) for 2 hr. The reaction mixture on usual work up gave an alkali soluble product (0.1 g), which was crystallised from alcohol to obtain (19) as yellow needles m.p. 174° (0.2 g).

Analysis : Found : C, 77.36; H, 6.359 %.

$C_{19}H_{18}O_3$ requires : C, 77.55; H, 6.122 %.

5',5',4',4-tetramethyl-4',5'-dihydro furano (3',2'-2,3) xanthone (20)

Above product (19) (60 mg) was heated with con. sulphuric acid for 15 min. on a water bath. The reaction mixture was then poured onto crushed ice, separated solid was filtered off, washed with dil.sodium hydroxide and crystallised from chloroform whereby compound (20) was obtained as white needles m.p. 132° (30 mg).

Analysis : Found : C, 77.25; H, 6.131 %.

$C_{19}H_{18}O_3$ requires : C, 77.55; H, 6.122 %

2-Prenyloxyxanthone (21)

A mixture of 2-hydroxyxanthone (1.0 g), prenyl bromide (1 ml), potassium carbonate (5 g) and dry acetone (100 ml) was refluxed for 8 hr. The reaction

mixture was worked up in the usual manner. The product thus obtained was crystallised from petroleum ether to obtain (21) as brownish needles. m.p. 85° (0.8 g).

Analysis : Found : C, 77.23; H, 5.568 %.

$C_{18}H_{15}O_3$ requires : C, 77.14; H, 5.714 %.

Attempted Claisen migration of 2-prenyloxyxanthone (21)

(i) DMA: 2-Prenyloxyxanthone (0.2 g) was refluxed in N,N-dimethylaniline for 2 hr. The reaction mixture on usual work up gave 2-hydroxyxanthone m.p. 235°.

(ii) Decalin : 2-Prenyloxyxanthone (0.2 g) was refluxed in decalin (5 ml) for 4 hr. The reaction mixture on usual work up gave 2-hydroxyxanthone.

1-Prenyloxyxanthone (22)

1-Hydroxyxanthone (2 g), prenyl bromide (2 ml) and anhydrous potassium carbonate (2 g) in dry acetone were refluxed for 40 hr. (5 days) during which time daily addition of potassium carbonate (0.5 g) and prenyl bromide (0.5 ml) were made. The cooled mixture was poured into water, acidified with hydrochloric acid and filtered. The solid thus obtained showed two spots on TLC, one corresponding to 1-hydroxyxanthone and the other due to the product, which was separated by preparative TLC m.p. 102° (0.05 g).

NMR ($CDCl_3$) : δ1.85, 2 x S 6H $=C(CH_3)_2$, 4.6, m, 2H, $CH_2CH=C(CH_3)_2$, 5.5, m, 1H, $CH_2CH=C(CH_3)_2$, 6.9, dd, 1H, H-4; 7.35, m, 3H, H-7, H-5 and H-3, 7.65, td, 1H, J=9,9,2Hz, H-6, 8.2, d, 1H, J=9Hz, H-2; 8.3, dd, 1H, J=9,2Hz, H-8.

6',6'-Dimethyl-4',5'-dihydropyrano (2',3' : 3,4) xanthone (23)

A mixture of 3-hydroxyxanthone (11) (2.0 g), 2-methylbut-3-ene-2-ol (2 ml), borontrifluoride etherate (2.0 ml) and dioxan (100 ml) was heated on a water bath for 12 hr. The reaction mixture was poured into water and extracted with solvent ether, ether layer was washed with dil.sodium hydroxide solution to remove unreacted 3-hydroxyxanthone. Ether layer on evaporation gave an oil, which was subjected to silica gel coloumn chromatography. Elution with petroleum ether gave an oil which was not identified. Further elution with petroleum ether-benzene (50:50) gave a white crystalline solid m.p. 155-7° (0.8 g).

Analysis : Found : C, 76.88; H, 5.892 %.

$C_{18}H_{16}O_3$ requires : C, 77.14; H, 5.714 %.

Elution with benzene gave an oil (not identified) and then with alcohol gave a brown solid which was also not identified.

Attempted dehydrogenation of (23)

Above compound (23) (0.5 g), DDQ (0.5 g) and sodium dry benzene (30 ml) was refluxed on a water bath for 60 hr. The reaction mixture was filtered when hot. The solution thus obtained was passed through silica gel coloumn, which did not give any dehydrogenated product but gave (23) back.

The compound (23) (0.1 g), palladised charcoal (10%, 0.1 g) and diphenyl ether (10 ml) were refluxed for 12 hr. The reaction mixture was worked up as usual. The product obtained had same m.p. as that of (23), the starting material.

3-(1,1-Dimethylprop-2-ynyloxy)xanthone (24)

3-Hydroxyxanthone (1.0 g) was dissolved in dry acetone and the solution was heated under reflux. To the solution was added potassium carbonate (3.0 g) and 3-chloro-3-methylbut-1-yne (2.5 ml) and potassium iodide (2.0 g). The reaction mixture was boiled for 12 hr., poured into water, extracted with ether, and ether layer was washed with dil.sodium hydroxide solution. The ether layer on evaporation gave the product which crystallized from benzene to give (24) as brown shining needles m.p. 140° (0.8 g). IR (KBr) ν_{max} 3220, 2110 (-C≡CH), 1645 (C=O)

Analysis : Found : C, 78.03; H, 5.008%.

$C_{18}H_{14}O_3$ requires : C, 77.69; H, 5.035%.

6',6'-Dimethylpyrano (2',3' : 3,4)xanthone (25)

The above compound (24) (1.0 g) was refluxed with N,N-dimethylaniline (10 ml) for 7 hr. The reaction mixture after cooling was poured onto crushed ice containing hydrochloric acid. The separated yellow solid was filtered, washed with dil.sodium hydroxide solution and crystallised from benzene to obtain (25) as golden yellow shining needles m.p. 140° (0.7 g) mix m.p. 115-20° with (24). IR (KBr) ν max 1645 (C=O γ pyronyl) 1625 (C=C).

Analysis : Found : C, 77.64; H, 4.985 %.

$C_{18}H_{14}O_3$ requires : C, 77.69; H, 5.035 %.

Prenylation of methyl β-resorcylate

To a solution of methyl-2,4-dihydroxybenzoate (3 g.) in dioxan (35 ml) borontrifluoride etherate was added drop by drop (2 ml). Then 2-methyl-but-3-ene-2ol (2 ml) in dioxan (10 ml) was added to this solution. The reaction mixture was heated on a water bath for 8 hr. It was diluted with water, the separated oil was extracted with solvent ether, ethereal layer was washed with dil.sodium hydroxide solution and then with water, ethereal layer on evaporation yielded an oil. The oil thus obtained, on vacuum distillation gave 1.8 ml (2 g) of (26).

Condensation of Phloroglucinol with methyl [2',2'-dimethyl 3',4'-dihydropyrano (6',5': 3,4)] 2-hydroxy benzoate (26):

6',6'-dimethyl-1,3-dihydroxy-4',5'-dihydropyrano (2',3': 6,7)xanthone (27)

A mixture of phloroglucinol (1.3 g; 0.01 mol), compound (26) (2.4 g; 0.01 mol) was refluxed in diphenyl ether (5 ml) for 15-20 min. The reaction mixture was subjected to steam distillation. The residual paste was washed with sodium bicarbonate solution and with water. It was chromatographed over silica gel coloumn. Elution with benzene (100 ml) gave a yellow oil. Further elution with benzene (3 lit) gave a white solid, which crystallised from benzene to give (27) as white needles m.p. 245° Yield 0.8 g.

Analysis : Found : C, 68.81; H, 4.729 %.

$C_{18}H_{16}O_5$ requires : C, 69.23; H, 5.128 %.

Elution with alcohol + benzene (10:90) gave 0.8 g of an amorphous chocolate coloured product which was not identified.

6',6'-Dimethyl-1,3-diacetoxy-4',5'-dihydropyrano (2',3' : 6,7) xanthone (28) m.p. 197°

Analysis : Found : C, 66.99; H, 4.910 %.

$C_{22}H_{20}O_7$ requires : C, 66.60; H, 5.050 %.

Condensation of 2-methylbut-3-ene-2-ol with methyl 2,4,6-trihydroxybenzoate:

Methyl 3-prenyl-2,4,6-trihydroxybenzoate (29)

A mixture of methyl 2,4,6-trihydroxybenzoate (5 g), 2-methylbut-3-ene-2-ol (2.6 ml) and boron trifluoride etherate (4 ml) were stirred in dioxan for 3 hr. at room temperature and allowed to stand over night. The reaction mixture was diluted with water and the separated oil was extracted with solvent ether. The ether layer was washed with water, dried and evaporated to obtain an oil. The oily product thus obtained was titurated with petroleum ether-benzene (50:50) to obtain a white solid residue (starting material). Evaporating of solvent gave an oil which was chromatographed over silica gel. Elution with (i) petroleum ether 5 lit gave an oil, which was not identified (ii) petroleum ether-benzene (50:50) gave a solid which crystallised from chloroform petroleum ether to give (29) as white needles m.p. 80-85° Yield (3.0 g).

Analysis : Found : C, 61.38; H, 6.339 %.

$C_{13}H_{16}O_5$ requires : C, 61.90; H, 6.34 %.

Same product was obtained in poor yield by citric acid and ascorbic acid method of Jurd[8].

Condensation of phloroglucinol with methyl 3-prenyl-2,4,6-trihydroxybenzoate (29)

A mixture of phloroglucinol (0.250 g) and the product (29) (0.5 g) was refluxed in diphenylether (1 ml) for 20 min. The steam distillation of the reaction mixture gave a crude solid, (0.5 g) which was purified by preparative TLC from alcohol to obtain (30) as brown needles m.p. 235°. Yield (0.1 g).
Analysis : Found : C, 66.15; H, 5.315 %.
$C_{18}H_{16}O_6$ requires : C, 65.85; H, 4.87 %.

References

(1) M.L. Wolform, E.E. Dickey, P.Mcwain, A.Thompson, J.H. Looker, O.M. Win drath and F. Komitsky Jr., J. Org. Chem., 29, 689 (1964).

(2) B.Jackson, H.D.Locksley and F.Scheinmann., Tetrahedron., 24, 3059 (1968).

(3) O.R.Gottlieb, M.Traveira Magalhaes, M.Ottoni de Silva Pereira, A.A.Lins Mesquita, D. de Barros Correa and G.G. de Oliveria., Tetrahedron., 24, 1601 (1968).

(4) B.Jackson, H.D. Locksley and F.Scheinmann., J.Chem. Soc. C., 2500 (1967).

(5) T.R.Govindachari, P.S.Kalyanaraman, N.Muthukumaraswamy and B.R.Pai., Tetrahedron., 27, 3919 (1971).

(6) I.Carpenter, H.D.Locksley and F.Scheinmann., J.Chem. Soc. C., 486 (1969).

(7) H.D.Locksley, I.Moore and F.Scheinmann., J.Chem. Soc. C., 2265 (1966).

(8) T.R.Govindachari, P.S.Kalyanaraman, N.Muthukumara swamy and B.R.Pai., Indian J. Chem., 9, 505 (1971).

(9) A.Jefferson, A.J.Quilliman, F.Scheinmann and K.Y.Sim., Aust. J. Chem., 23, 2541 (1970).

(10) P.G.Waterman and E.G.Crichton., Phytochemistry., 19, 2723 (1980).

(11) I.Carpenter, H.D.Locksley and F.Scheinmann., Phytochemistry., 8, 2013 (1969).

(12) A.Jefferson and F.Scheinmann., J.Chem. Soc. C., 175 (1966).

(13) M.L.Wolfrom, K.W.Koss and H.B.Bhat., J.Org.Chem., 32, 1058 (1967).

(14) A.C.Jain, V.K.Khanna and T.R.Seshadri., Tetrahedron., 25, 2587 (1969).

(15) J.R.Lewis and J.B.Reary., J.Chem. Soc. C., 1662 (1970).

(16) H.D.Locksley, A.J.Quillinan and F.Scheinmann., J.Chem. Soc. C., 3804 (1971).

(17) S.A.Gabrial and O.R.Gottlieb., Phytochemistry., 11, 3035 (1972).

(18) S.M.Anand and A.C.Jain., Curr. Sci., 41, 883 (1972).

(19) S.M.Anand and A.C.Jain., Indian J.Chem., 11, 504 (1973).

(20) H.D.Locksley, I.Moore and F.Scheinmann., J.Chem. Soc. C., 2265 (1965).

(21) A.Dyer, A.Jefferson and F.Scheinmann., J.Org. Chem., 33, 1259 (1968).

(22) S.M.Anand and A.C.Jain., J.Chem.Soc., Chem., Commun., 18, 1026 (1972).

(23) S.M.Anand and A.C.Jain., Indian J.Chem., 11, 1233 (1973).

(24) S.M.Anand and A.C.Jain., Indian J.Chem., 11, 1237 (1973).

(25) S.M.Anand and A.C.Jain., J.Chem. Soc. Perkin I., 329 (1974).

(26) E.D.Burling, A.Jefferson and F.Scheinmann., Tetrahedron., 21, 2653 (1965).

(27) P.G.Waterman and G.Crichton; Phytochemistry., 19, 2723 (1980).

(28) A.K.Sen, K.K.Sarkar, P.C.Majumder and N.Banarji., Indian J.Chem., 19(B), 1008 (1980).

(29) A.K.Sen, K.K.Sarkar, P.C.Majumder and N.Banerji; Phytochemistry., 20, 18 (1981).

(30) S.Karunanayake,S.Sotheeswaran, M.U.S. Sultanbawa and S.Balasubramanium; Phytochemistry; 20, 1304 (1981).

(31) Vijaya Kumar, S.Sotheeswaran, S.Sivaganana sundram and S.Balasubramaniam; Phytochemistry; 21, 807 (1982).

(32) P.G.Waterman, and R.A.Hussain; Phytochemistry; 21, 2099 (1982).

(33) Pyarelal Khanna and T.R.Seshadri., J.Scient, Ind., Res (India); 33, 295 (1974).

(34) R.J.Molyneux and L.Jurd; Tetrahedron; 26, 4743 (1970).

(35) P.J.Cotterill and F.Scheinmann., J.Chem. Soc. Perkin I., 2354 (1980).