CHAPTER II

CHLOROMETHYLATION OF SOME ALKYL COUMARINS

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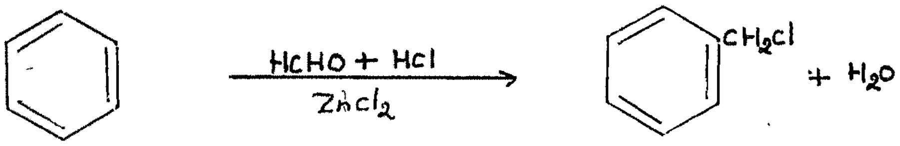
THEORETICAL

Chloromethylation consists in the replacement of a hydrogen atom by a chloromethyl group in a single operation. It is carried out by the condensation of formaldehyde with aromatic compounds in the presence of hydrogen chloride using zinc chloride as a catalyst.



Chloromethylation is of much value in synthetic work as the chloromethyl group is reactive and the chlorine atom can be replaced by other functional groups. Alcohols result when such compounds are hydrolysed by heating with water. Alcohols can also be prepared indirectly through the saponification of acetic acid esters obtained from interaction of chloromethylated compounds with acetic acid in the presence of fused sodium acetate. Chloromethyl group can be converted into the cyanomethyl group which in turn would give on saponification acetic acid derivatives. On reduction, it can be converted to the methyl group. Aldehydes are obtained by the interaction of the halomethyl compounds with hexamine (Sommelet reaction).

$$R\ CH_2Cl + (CH_2)_6N_4 \longrightarrow R\ CH_2(CH_2)_6N_4Cl \xrightarrow{+H_2O}$$
$$R\ CHO + HCl + (CH_2)_6N_4$$

On condensation with secondary amines such as diethylamine or dimethylamine the chloromethyl derivatives give various dialkyl aminomethyl derivatives which are substances of medicinal importance.

The earlier work on chloromethylation of aromatic compounds has been reviewed by Fuson and McKeever[1]. Some of the more recent work has been reviewed by Olah and Tolgyesi[2]. These authors have reviewed in detail the mechanism advanced by different workers and the role of the solvent, catalyst and temperature in this reaction.

Aromatic hydrocarbons such as, benzene, naphthalene, anthracene, phenanthrene, biphenyl and many of their derivatives have been chloromethylated. The introduction of an alkyl group in the benzene nucleus enhances the activity of the hydrocarbon.

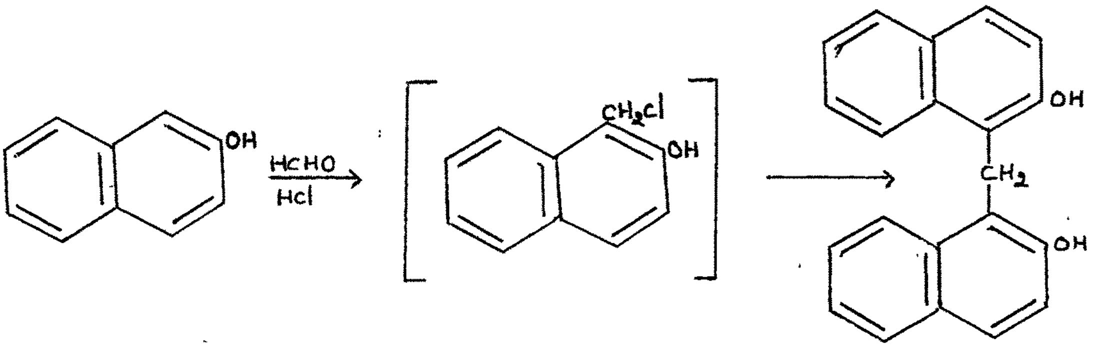
Chloromethyl group preferentially enters the para position with respect to an alkyl group, but a small amount of the ortho isomer is also formed. A second chloromethyl group usually can be introduced and sometimes excellent yields of the di-chloromethyl derivatives are obtained.

Halogen and nitro group in the aromatic ring retard the rate of reaction. The presence of alkyl group in the nucleus, however, counteracts the influence of these substituents. Ketones are generally unreactive. Fuson and McKeever[3] found that benzophenone could not be chloromethylated. Stephen et al.[3] failed to chloromethylate anthraquinone. Here also the presence of alkyl group in the nucleus counteracts this influence. Thus, Fuson and McKeever[3] successfully chloromethylated acetomesitylene and 2,4-dimethylacetophenone.

Hydroxyl groups in the nucleus greatly increases the rate of reaction the condensation proceeding vigorously yielding polymeric products. A suitable device for getting around the difficulty with phenols is to convert them to esters. The activating influence of hydroxyl group may be sufficiently attenuated by a deactivating group such as nitro, carboxyl or acetyl. Stoermer and Behn[4] successfully chloromethylated o-nitrophenol.

Phenol ethers react smoothly. Phenol ethers and phenolic compounds containing an aldehyde group also react in a satisfactory manner. Aromatic amines react vigorously but the complex condensation products are invariably the result of the reaction and usually it is not possible to isolate the simple chloromethyl derivatives from these compounds.

The most important side reaction is that leading to the formation of the corresponding diaryl methane derivatives. Highly reactive compounds tend to yield this type of product and it is impossible to isolate the intermediate chloromethyl derivatives. Castiglioni[5] chloromethylated β-naphthol and obtained the corresponding diaryl methane derivative.(I).



I

This reaction has been applied to many oxygen heterocycles. The application of this versatile reaction to the coumarin derivatives may be mentioned here as the present work deals with the study of the reaction on some alkyl coumarins. It was Sethna and coworkers[6,7] who observed that simple coumarin could notbe chloromethylated with paraformaldehyde using aqueous solutions. In glacial acetic acid using zinc chloride as catalyst it gave the 3-chloromethyl derivative. 4-Methylcoumarin on a similar chloromethylation gave 3-chloromethyl-4-methylcoumarin. 7-Methoxy-4-methylcoumarin on chloromethylation with one mole of paraformaldehyde gave the 6-chloromethyl derivative. The 3,6-dichloromethyl, 3,8-dichloromethyl and 3,6,8-trichloromethyl derivatives have been obtained using larger quantities of paraformaldehyde and their structures proved by reduction to the corresponding known methyl derivatives. Further, they chloromethylated 7-hydroxy-4-methylcoumarin-6-carboxylic acid and its methyl ether and obtained the 3,8-dichloromethyl derivative. Methyl-5-hydroxy-4-methylcoumarin-6-carboxylate, on chloromethylation gave the 8-chloromethyl derivative. These chloromethyl derivatives were reduced to the corresponding methyl derivatives.

A few studies in the chloromethylation of alkyl coumarins are made. Jainamma[8] studied the chloromethylation of 4,6-dimethyl- and 4,7-dimethylcoumarin and obtained the corresponding 3-chloromethyl derivatives which were reduced to the known 3,4,6-trimethylcoumarin and 3,4,7-trimethylcoumarin.

These 3-chloromethylcoumarins on condensation with morpholine and dimethylamine gave the 3-morpholinomethyl- and the 3-dimethylaminomethylcoumarins. On Sommelet reaction the chloromethyl derivatives did not give the desired 3-formyl derivatives, 4,6-dimethyl-3-chloromethyl and 4,7-dimethyl-3-chloromethylcoumarins on condensation with alcoholic potassium cyanide gave the corresponding 3-cyanomethyl derivatives which on hydrolysis with 70 % sulphuric acid gave 4,6-dimethylcoumarin-3-acetic acid. Their attempts to condense the ethyl ester of this acid with salicylaldehyde in the presence of piperidine, to synthesise 4,6-dimethyl-3,3'-bicoumarinyl met with failure.

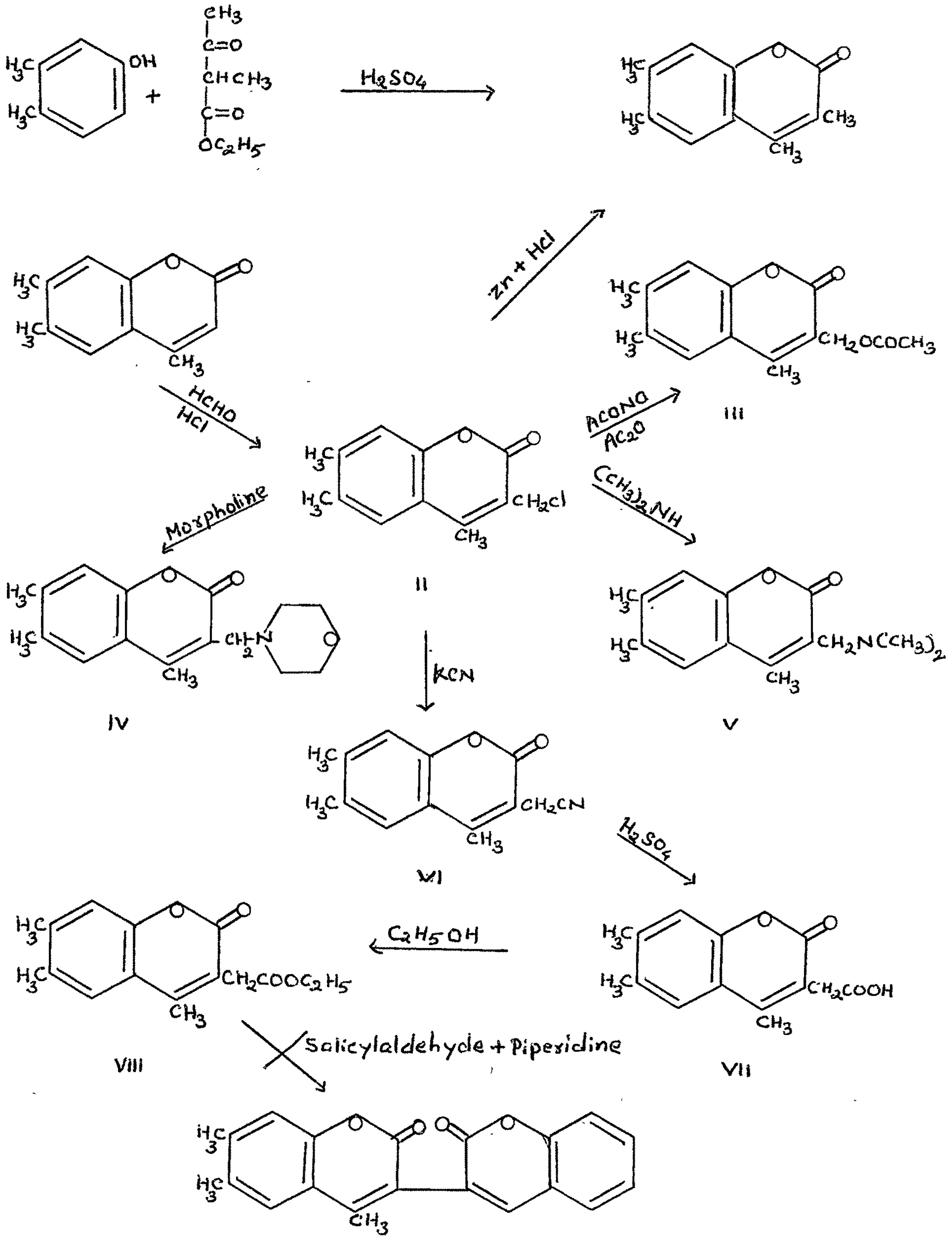
It has been observed that the chloromethylation of coumarins proceeds smoothly when there is a 4-methyl group in the pyrone ring system. Jainamma[8] attempted the chloromethylation of 6-methyl- and 7-methylcoumarin under different experimental conditions using zinc chloride as a catalyst, but they failed to isolate any pure chloromethyl derivative. So it was thought of interest to compare the chloromethylation of some alkyl coumarins with and without the methyl group in the pyrone ring. The starting coumarins used for this purpose were prepared by condensing 3,4-xylenol, 3,5-xylenol, orcinol and α-naphthol with acetoacetic ester in the presence of sulphuric acid to give 4,6,7-trimethylcoumarin, 4,5,7-trimethylcoumarin, 4,7-dimethyl-5-hydroxy~~-7-methyl~~coumarin and 4-methyl naphtha-(1,2 : 6',5')-α-pyrone respectively. The coumarins without a methyl group in the pyrone ring were prepared by condensing the above substituted phenols with malic acid in the presence of sulphuric acid to give 6,7-dimethylcoumarin, 5,7-dimethylcoumarin and 7-hydroxy-5-methylcoumarin respectively. In the course of the work it was observed that in the case of all 4-substituted coumarins the chloromethylation took place quite smoothly, to give monochloromethyl derivatives which on reduction with zinc and hydrochloric acid were converted into the coumarins of known orientation containing a methyl group at 3-position showing that the chloromethyl group enters the 3-position. Products obtained were pure and yields were good, while in the case of coumarins without a 4-methyl group in the pyrone ring either the reaction did not take place at all under the usual conditions or the products obtained were unworkable. In the case of hydroxycoumarins a vigorous reaction occurred to give a polymarised product.

The methyl ethers, however, give the desired chloromethyl derivatives. The chloromethyl derivatives have been used for the synthesis of other derivatives as described later.

Chloromethylation of 4,6,7-trimethylcoumarin and 6,7-dimethylcoumarin

4,6,7-Trimethylcoumarin on chloromethylation with one mole of paraformaldehyde in acetic acid at room temperature gave a mixture of a monochloromethyl derivative and the original coumarin. However, at 70° in the presence of fused zinc chloride it gave the monochloromethyl derivative in 75 % yield. This monochloromethyl derivative on reduction with zinc and hydrochloric acid gave a product which was found to be identical on direct comparison with the known 3,4,6,7-tetramethylcoumarin prepared by the Pechmann condensation of 3,4-xylenol with ethyl-α-methyl acetoacetate according to Clayton[9]. 4,6,7-Trimethyl-3-chloromethylcoumarin structure (II) has, therefore, been assigned to the chloromethyl product.

On heating with acetic anhydride in the presence fused sodium acetate, the above chloromethyl derivative gave 4,6,7-trimethyl-3-acetoxymethylcoumarin (III). When heated with hexamine in chloroform or in acetic acid, the product obtained was not the 3-formyl derivative. It did not give a 2,4-dinitrophenylhydrazone nor did the analysis correspond to that for 4,6,7-trimethyl~~coumarin~~-3-formylcoumarin. 4,6,7-Trimethyl-3-chloromethylcoumarin on condensation with morpholine and dimethylamine gave 4,6,7-trimethyl-3-morpholinomethyl-


H₂SO₄
Zn + HCl
HCHO
HCl
AcONa
Ac₂O
III
Morpholine
(CH₃)₂NH
II
IV
V
KCN
VI
H₂SO₄
C₂H₅OH
VIII
VII
Salicylaldehyde + Piperidine
CH₂Cl
CH₂OCOCH₃
CH₂N(CH₃)₂
CH₂CN
CH₂COOH
CH₂COOC₂H₅
OC₂H₅

-coumarin (IV) and 4,6,7-trimethyl-3-dimethylaminomethylcoumarin (V) respectively.

On heating with alcoholic potassium cyanide, the chloromethylcoumarin afforded 4,6,7-trimethyl-3-cyanomethylcoumarin (VI) which was then hydrolysed with 70 % sulphuric acid to 4,6,7-trimethylcoumarin-3-acetic acid (VII). This acid was converted into ethyl-4,6,7-trimethylcoumarin-3-acetate (VIII) by treating with ethyl alcohol in the presence of conc. sulphuric acid. Attempt was then made to synthesise 4,6,7-trimethyl-3,3'-bicoumarinyl from this ester by condensing it with salicylaldehyde in the presence of piperidine, but it did not succeed and the original ester was obtained back.

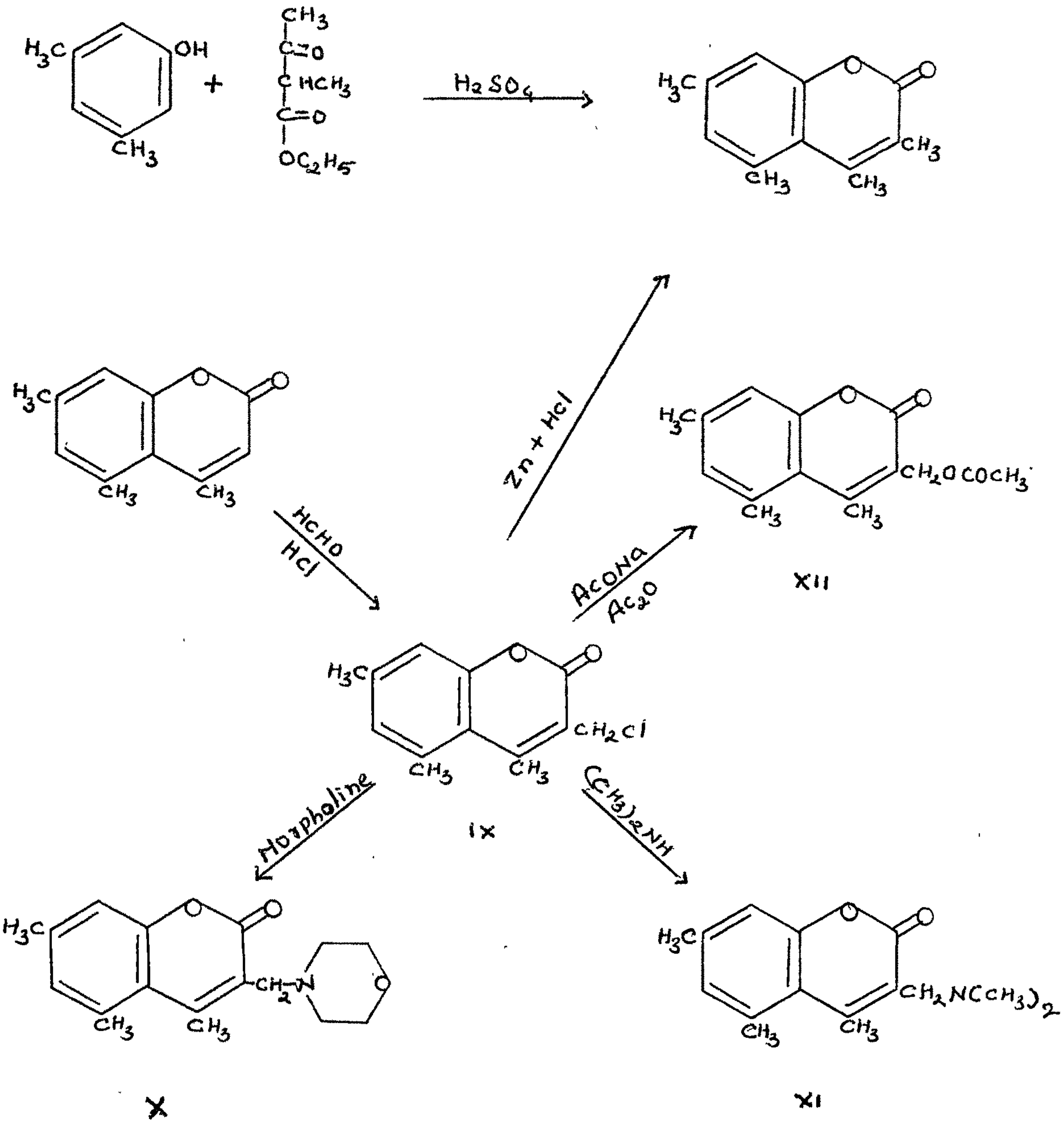
The chloromethylation of 6,7-dimethylcoumarin was attempted under different conditions. At room temperature, with one mole of paraformaldehyde, in the presence of zinc chloride as a catalyst, the original coumarin was obtained back. At higher temperature, however, an unworkable product was obtained which could not be crystallised from any of the solvents. The chloromethylation was also attempted in different solvents like chloroform, dioxan, acetone without using catalyst.

Chloromethylation of 4,5,7-trimethylcoumarin and 5,7-dimethylcoumarin

4,5,7-Trimethylcoumarin on chloromethylation in acetic acid with one mole of paraformaldehyde at 70°, in the presence of fused zinc chloride gave a monochloromethyl derivative which on reduction with zinc and hydrochloric acid afforded a product which was found on direct comparison to be identical with 3,4,5,7-tetramethylcoumarin prepared by the Pechmann condensation of 3,5-xylenol with ethyl-α-methyl-acetoacetate according to Clayton[9]. So the 3-chloromethyl structure (IX) was assigned to the chloromethyl derivative.

An unworkable product was obtained on heating the chloromethyl derivative with hexamine in acetic acid or chloroform.

4,5,7-Trimethyl-3-chloromethylcoumarin, on reaction with morpholine and dimethylamine in dry benzene gave 4,5,7-trimethyl-3-morpholinomethyl (X) and 4,5,7-trimethyl-3-dimethylaminomethylcoumarins (XI) respectively. On heating with sodium acetate and acetic anhydride it gave 4,5,7-trimethyl-3-acetoxymethylcoumarin (XII). Attempts to prepare 4,5,7-trimethyl-3-cyanomethylcoumarin by treating the 3-chloromethyl derivative with alcoholic potassium cyanide did not succeed. It gave a water soluble product which was recovered from the reaction mixture by ether extraction in a pasty form. This product could not be obtained in pure solid form even after repeated column chromatography on alumina or by crystallisation. Attempts were then made to hydrolyse this pasty product directly with hydrochloric acid and acetic acid into the corresponding 3-acetic acid, but no pure product could be obtained. The reaction was also tried in acetone, dimethyl formamide and dioxane.



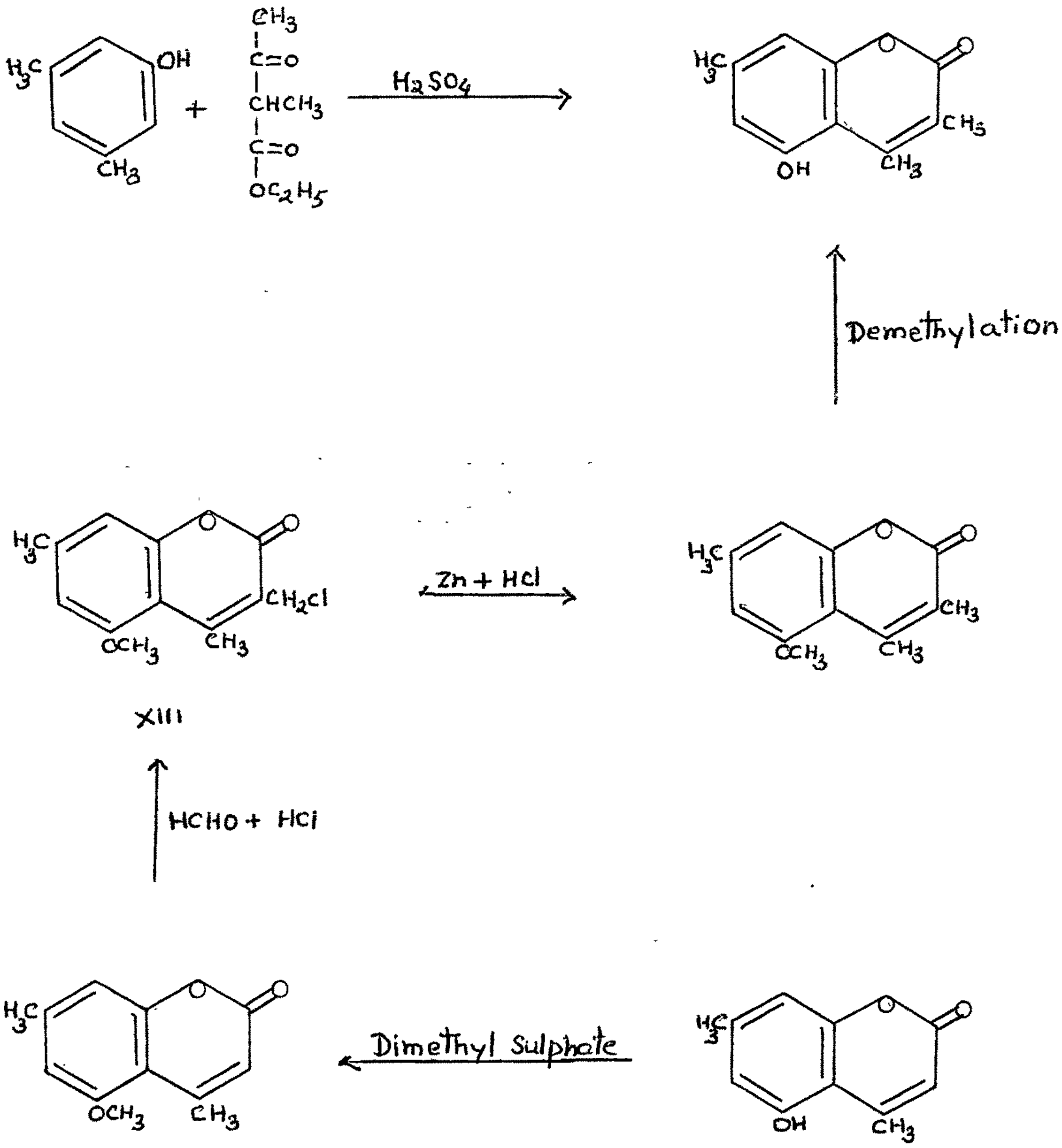
5,7-Dimethylcoumarin on chloromethylation with paraformaldehyde (1 mole) at 70° gave a mixture of original coumarin derivative and a polymeric unworkable .

product. On repeated extraction of this polymeric product with dry benzene and on removal of the solvent a product was obtained of which the carbon, hydrogen and chlorine analysis agreed with a dichloromethyl derivative. As the product was obtained in a very poor yield, further reactions could not be carried out to prove its structure. On heating with sodium acetate and acetic anhydride it gave a diacetoxymethyl derivative.

Chloromethylation of 5-hydroxy-4,7-dimethylcoumarin and 5-methyl-7-hydroxycoumarin

The chloromethylation of 5-hydroxy-4,7-dimethylcoumarin did not succeed under the normal conditions. Even at 0° a vigorous reaction took place to give a polymeric product even without the use of any catalyst.So its methyl ether was prepared by heating it with dimethyl sulphate in presence of potassium carbonate. The chloromethylation of this methyl ether in acetic acid gave a polymeric product. The reaction was then carried out in dioxane at a low temperature. After keeping the reaction mixture overnight, and the removal of the solvent a product was obtained which on purification and analysis was found to be a monochloromethyl derivative.

The above monochloromethyl derivative on reduction with zinc and hydrochloric acid and on demethylation was found on direct comparison to be identical with the known 3,4,7-trimethyl-5-hydroxycoumarin prepared by the Pechmann condensation of orcinol with ethyl-α-methylacetoacetate in



the presence of sulphuric acid[10]. So the 3-chloromethyl structure (XIII) was assigned to the monochloromethyl derivative.

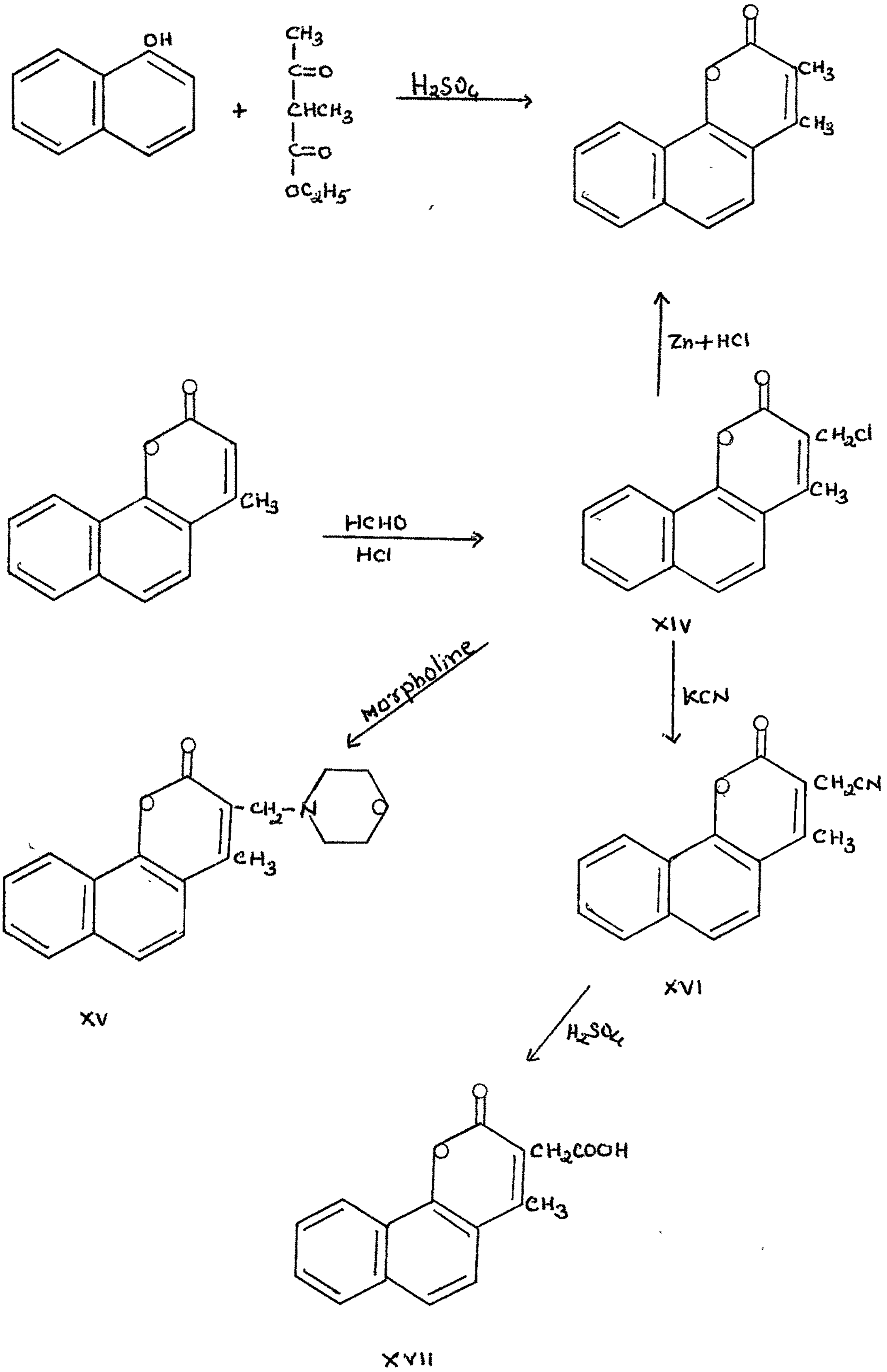
Attempts to chloromethylate 5-methyl-7-hydroxycoumarin or its methyl ester under different experimental conditions did not succeed.

Chloromethylation of 4'-methyl naphtha(1,2 : 6',5')-α-pyrone

4'-Methyl naphtha(1,2 : 6',5')-α-pyrone on chloromethylation with one mole of paraformaldehyde in glacial acetic acid with zinc chloride as a catalyst at room temperature gave a monochloromethyl derivative which melted at 214°. Lele and Sethna[6] reported the m.p. 205°. This monochloromethyl derivative on reduction with zinc and hydrochloric acid gave a product which was identical with 3',4'-dimethyl naphtha(1,2 :6',5')-α-pyrone ~~to be~~ obtained by the Pechmann condensation of α-naphthol with ethyl-α-methyl acetoacetate[11]. The 3'-chloromethyl-4'methyl naphtha (1,2 : 6',5')-α-pyrone structure (XIV) is therefore assigned to the monochloromethyl derivative.

3'-Chloromethyl-4'-methyl naphtha(1,2 : 6',5')-α-pyrone on condensation with morpholine in dry benzene gave 3'-morpholinomethyl-4'-methyl naphtha(1,2 : 6', 5')-α-pyrone (XV).

3'-Chloromethyl-4'-methyl naphtha(1,2 : 6',5')-α-pyrone on heating with alcoholic potassium cyanide gave 3'-cyanomethyl-4'-methyl naphtha(1,2 : 6',5')-α-pyrone (XVI). This on hydrolysis with conc. sulphuric acid (70 %) gave 4'-methyl naphtha(1,2 : 6',5')-α-pyrone-3'-acetic acid (XVII). On heating with hexamine and acetic acid 3'-chloromethyl-4'-methyl naphtha(1,2 :6',5')-α-pyrone gave a product which


OH
+
CH3
C=O
CHCH3
C=O
OC2H5
H2SO4
CH3
CH3
Zn+HCl
CH3
HCHO
HCl
CH2Cl
CH3
XIV
Morpholine
KCN
CH2-N
CH3
XV
CH2CN
CH3
XVI
H2SO4
CH2COOH
CH3
XVII

melted at 175°. Its analysis did not aggee with that of 3'-formyl-4'-methyl naphtha(1,2 : 6',5')-α-pyrone, it also did not give a 2,4-dinitrophenylhydrazone derivative.

EXPERIMENTAL

Chloromethylation of 4,6,7-trimethylcoumarin : 4,6,7-Trimethyl-3-chloromethylcoumarin (II) :

Paraformaldehyde (0.6 g.) was taken in acetic acid (10 ml.) and saturated with hydrogen chloride gas . 4,6,7-Trimethylcoumarin (1.0 g.) was then added and this was followed by fused zinc chloride (0.1 g.). Hydrogen chloride gas was passed through the solution maintained at 70° for 4 hr. The reaction mixture was then kept overnight and the solid which separated crystallised from benzene-petroleum ether in white shining needles (0.6 g.), m.p. 164°.

Analysis : Found : C, 65.85 ; H, 5.38 ; Cl, 14.84 %

$C_{13}H_{13}O_2Cl$ requires : C, 65.95 ; H, 5.50 ; Cl, 15.01 %.

3,4,6,7-Tetramethylcoumarin :

4,6,7-Trimethyl-3-chloromethylcoumarin (0.5 g.) was dissolved in sufficient quantity of acetic acid and zinc dust (2.0 g.) was added. This was followed by conc. hydrochloric acid (5 ml.) portion-wise. The reaction mixture after heating for 1 hr. on a steam bath was filtered. The filtrate on dilution provided 3,4,6,7-tetramethylcoumarin. It was crystallised from alcohol. M.p. 142°. Mixed m.p. with 3,4,6,7-tetramethylcoumarin obtained by Pechmann reaction between 3,4-xylenol and ethyl-α-methyl-acetoacetic ester was not depressed. (Lit.[9] m.p. 135°).

4,6,7-Trimethyl-3-acetoxymethylcoumarin (III) :

The chloromethyl derivative (0.5 g.) was refluxed with acetic anhydride (5 ml.) and fused sodium acetate (2.0 g.) for 1 1/2 hr. The reaction mixture was poured in water and the product obtained crystallised from aqueous alcohol in white needles (0.3 g.), m.p. 153°.

Analysis : Found : C, 69.02 ; H, 6.07 %

$C_{15}H_{16}O_4$ requires : C, 69.23 ; H, 6.15 %.

Attempted preparation of 4,6,7-trimethyl-3-formylcoumarin :

A mixture of 4,6,7-trimethyl-3-chloromethylcoumarin (0.5 g.) and hexamine (2.0 g.) in glacial acetic acid (25 ml.) was heated directly on a wire gauze for 30 min. The product separating on pouring the reaction mixture in cold water crystallised from dilute acetic acid in pale yellow needles. M.p. 275°. It did not give a 2,4-dinitrophenylhydrazone.

4,6,7-Trimethyl-3-morpholinomethylcoumarin (IV) :

4,6,7-Trimethyl-3-chloromethylcoumarin (0.5 g.) was dissolved in minimum amount of dry benzene and morpholine (1 ml.) was added. The reaction mixture was refluxed on a steam bath for 2 hr. Benzene was removed and the product crystallised from petroleum ether, Yield 0.25 g. M.p.172°.

Analysis : Found : C, 71.24 ; H, 7.15 ; N, 4.56 %

$C_{17}H_{21}O_3N$ requires : C, 71.08 ; H, 7.32 ; N, 4.88 %.

4,6,7-Trimethyl-3-dimethylaminomethylcoumarin (V) :

4,6,7-Trimethyl-3-chloromethylcoumarin (0.5 g.) was dissolved in minimum amount of dry benzene and dimethylamine (2 ml.) was added and the reaction mixture refluxed on a steam bath for 2 hr. Benzene was then removed and the product crystallised from benzene-petroleum ether in white needles (0.3 g.), m.p. 148°.

Analysis : Found : C, 73.79 ; H, 7.79 ; N, 5.35 %

$C_{15}H_{19}O_2N$ requires : C, 73.47 ; H, 7.76 ; N, 5.71 %.

4,6,7-Trimethyl-3-cyanomethylcoumarin (VI) :

A solution of 4,6,7-trimethyl-3-chloromethylcoumarin (1.0 g.) in alcohol was mixed with an aqueous solution of potassium cyanide (1.0 g.) and the reaction mixture refluxed on a steam bath for 3 hr. The product separating on dilution of the reaction mixture with water crystallised from dilute alcohol in white needles (0.6 g.), m.p. 187°.

Analysis : Found : C, 74.23 ; H, 5.85 ; N, 6.20 %

$C_{14}H_{13}O_2N$ requires: C, 74.01 ; H, 5.72 ; N, 6.16 %.

4,6,7-Trimethylcoumarin-3-acetic acid (VII) :

The above cyanomethylcoumarin (1.0 g.) was dissolved in sulphuric acid (70 % ; 25 ml.) and heated on a water bath for 2 hr. This was then diluted. The separated product was taken in sodium bicarbonate solution. On acidification of the bicarbonate extract the acid obtained was crystallised from aqueous alcohol in white tiny needles (0.8 g.), m.p. 199°.

Analysis : Found : C, 67.87 ; H, 5.36 %

$C_{14}H_{14}O_4$ requires : C, 68.29 ; H, 5.69 %.

Ethyl-4,6,7-trimethylcoumarin-3-acetate (VIII) :

The above acid (1.0 g.) was dissolved in ethyl alcohol (50 ml.) and conc. sulphuric acid (4 ml.) was added. The mixture was heated on a steam bath for 6 hr. The product separating on dilution of the reaction mixture with water was washed with sodium bicarbonate solution and crystallised from aqueous alcohol in wooly needles (0.8 g.), m.p. 150°.

Analysis : Found : C, 70.13 ; H, 6.46 %

$C_{16}H_{18}O_4$ requires : C, 70.06 ; H, 6.56 %.

Attempted synthesis of 4,6,7-trimethyl-3,3'-bicoumarinyl :

A solution of ethyl-4,6-dimethylcoumarin-3-acetate (0.8 g.) was mixed with salicylaldehyde (0.3 g.) and four drops of piperidine. The reaction mixture was heated on a steam bath for 8 hr. The solid obtained on pouring the reaction mixture in water was heated on a steam bath for 8 hr. The solid obtained on pouring the reaction mixture in cold hydrochloric acid was washed with dilute sodium hydroxide solution and crystallised from aqueous alcohol in white needles. M.p. 150°. Mixed m.p. with the original ester was not depressed.

Chloromethylation of 4,5,7-trimethylcoumarin : 4,5,7-Trimethyl-3-chloromethylcoumarin (IX) :

4,5,7-Trimethylcoumarin (1.0 g.) dissolved in glacial acetic acid was mixed with paraformaldehyde (0.6 g.) dissolved in acetic acid (10 ml.) in which dry hydrogen chloride gas was passed. Zinc chloride (0.1 g.) was then added and hydrogen chloride gas was passed for 4 hr. at 70°. On keeping the reaction mixture overnight at room temperature a solid separated. It crystallised from benzene-petroleum ether and gave m.p. 181°. Yield 1.5 g.

Analysis : Found : C, 65.75 ; H, 5.21 ; Cl, 14.82 %

$C_{13}H_{13}O_2Cl$ requires : C, 65.93 ; H, 5.50 ; Cl, 15.01 %.

3,4,5,7-Tetramethylcoumarin :

The above chloromethyl derivative (0.5 g.) was dissolved in acetic acid and zinc dust (2.0 g.) was added. This was followed by conc. hydrochloric acid (5 ml.) added in small lots while the reaction mixture was heated on a steam bath for 1 hr. The product which separated on dilution of the reaction mixture with water crystallised from alcohol in white needles, m.p. 159°. The mixed m.p. of this product with 3,4,5,7-~~tri~~tetramethylcoumarin, prepared from 3,5-xylenol and ethyl-α-methyl acetoacetate, by Pechmann reaction was not depressed. (Lit.[9] m.p. 154°).

4,5,7-Trimethyl-3-morpholinomethylcoumarin :

4,5,7-Trimethyl-3-chloromethylcoumarin (0.5 g.) was dissolved in dry benzene and morpholine (1 ml.) was added. This was heated on a steam bath for 3 hr. After removal of benzene, the solid which separated was crystallised from benzene in plates. M.p. 165°.

Analysis : Found . : C, 70.92 ; H, 7.08 ; N, 4.39 %

$C_{17}H_{21}O_3N$ requires : C, 71.08 ; H, 7.32 ; N, 4.88 %.

4,5,7-Trimethylcoumarin-3-dimethylaminomethylcoumarin :

A solution of 4,5,7-trimethyl-3-chloromethylcoumarin (0.5 g.) in dry benzene was mixed with dimethylamine

(2 ml.) and heated on a steam bath for 3 hr. The solid separating on removal of benzene crystallised from benzene-petroleum ether. M.p. 135°.

Analysis : Found : C, 73.30 ; H, 7.64 ; N, 5.38 %

$C_{15}H_{19}O_2N$ requires : C, 73.47 ; H, 7.76 ; N, 5.71 %.

4,5,7-Trimethyl-3-acetoxymethylcoumarin (XII) :

4,5,7-Trimethyl-3-chloromethylcoumarin (1.0 g.) was heated with acetic anhydride (20 ml.) and sodium acetate (2.5 g.) for 2 hr. The reaction mixture was poured into ice cold water. The product obtained was crystallised from aqueous alcohol into fine needles. M.p. 129°.

Analysis : Found : C, 69.07 ; H, 6.04 %

$C_{15}H_{16}O_4$ requires : C, 69.23 ; H, 6.15 %.

Attempted chloromethylation of 5,7-dimethylcoumarin :

5,7-Dimethylcoumarin (1 mole) was dissolved in glacial acetic acid and mixed with paraformaldehyde (1 mole) dissolved in glacial acetic acid (10 ml.) through which hydrogen chloride gas was passed. In the presence of zinc chloride (0.1 g.) as a catalyst the reaction did not proceed at room temperature. When the reaction mixture was heated to 70° for 1 hr. a polymeric product separated after cooling the reaction mixture. The reaction was then carried out at 70° without using zinc chloride. A product separated which was repeatedly extracted with benzene. After the removal of benzene, the residue was found to contain a little original coumarin and a chloromethyl derivative. The analysis agreed with a dichloromethyl derivative. As the product obtained was in very poor yield it was not possible to reduce it to the tetramethylcoumarin of known orientation. It was crystallised from benzene-petroleum ether in white plates. M.p. 193°.

Analysis : Found : C, 57.17 ; H, 4.06 ; Cl, 25.67 %

$C_{13}H_{12}O_2Cl_2$ requires : C, 57.55 ; H, 4.29 ; Cl, 26.20 %.

The above dichloromethyl derivative (0.3 g.) on heating with acetic anhydride (5 ml.) and sodium acetate (1.0 g.) gave a diacetoxymethyl derivative which was crystallised from aqueous alcohol. M.p. 160°.

Analysis : Found : C, 64.21 ; H, 5.56 %

$C_{17}H_{18}O_6$ requires : C, 64.15 ; H, 5.66 %.

Chloromethylation of 5-methoxy-4,7-dimethylcoumarin :

5-Methoxy-4,7-dimethyl-3-chloromethylcoumarin (XIII) :

5-Methoxy-4,7-dimethylcoumarin (1.0 g.) was dissolved in minimum quantity of dioxane. Paraformaldehyde (1.0 g.) was dissolved in dioxane and dry hydrogen chloride gas was passed. The two solutions were mixed and zinc chloride (1.0 g.) was added. The reaction mixture was kept on a steam bath and hydrogen chloride gas was passed for 3 hr. After the removal of dioxane a product was obtained which crystallised from benzene. M.p. 165°.

Analysis : Found : C, 61.52 ; H, 4.74 ; Cl, 14.22 %

$C_{13}H_{12}O_3Cl$ requires : C, 62.02 ; H, 4.76 ; Cl, 14.76 %.

5-Hydroxy-3,4,7-trimethylcoumarin :

The above 5-methoxy-4,7-dimethyl-3-chloromethyl-

-coumarin (0.5 g.) was dissolved in acetic acid and zinc dust (2.0 g.) was added. This was followed by conc. hydrochloric acid (5 ml.) protion-wise. The reaction mixture was then heated on a steam bath for 2 hr. The product which separated on dilution of the reaction mixture with water crystallised from alcohol. M.p. 193-95°. This product (0.5 g.) was dissolved in dry benzene (20 ml.) and anhydrous aluminium chloride (2.0 g.) was added. The reaction mixture was refluxed on a water bath for 2 hr. It was then decomposed with hydrochloric acid in ice cold water. The product separated was extracted with ether. To this dilute sodium hydroxide was added and the sodium hydroxide layer was separated and acidified with hydrochloric acid. The solid separated was washed with water and crystallised from aqueous alcohol into fine needles, m.p. 252°. The mixed m.p. of this product with that of 5-hydroxy-3,4,7-trimethyl-coumarin obtained by the Pechmann reaction between orcinol and 2-methyl acetoacetic ester was not depressed. Chakrawarti[10] reported the m.p. 250°.

Chloromethylation of 4'-methyl naphtha(1,2 : 6',5')-α-pyrone : 3'-Chloromethyl-4'-methyl naphtha(1,2 : 6',5')-α-pyrone (XIV) :

4'-Methyl naphtha(1,2 : 6',5')-α-pyrone (1.0 g.) was dissolved in glacial acetic acid(30 ml.). To this paraformaldehyde (1.0 g.) dissolved in glacial acetic acid and fused zinc chloride (0.1 g.) was added. The reaction mixture was heated on a steam bath for 3 hr. and left overnight. The separated product was crystallised from benzene

(0.6 g.), m.p. 214°. Lele, Sethna and Savant[6] reported m.p. 205° and yield 33 %. This chloromethyl derivative on reduction with zinc and hydrochloric acid gave the known[10] 3',4'-dimethyl naphtha(1,2 : 6',5')-α-pyrone, m.p. 199°.

3'-Morpholinomethyl-4'-methyl naphtha(1,2 : 6',5')-α-pyrone (XV) :

3'-Chloromethyl-4'-methyl naphtha(1,2 : 6',5')-α-pyrone (0.5 g.) was dissolved in dry benzene and morpholine (1 ml.) was added. This was heated on a steam bath for 3 hr. After the removal of benzene the solid which separated was crystallised from benzene. M.p. 197°. Yield 0.3 g.

Analysis : Found : C, 73.64 ; H, 5.77 ; N, 4.80 %
$C_{19}H_{19}O_3N$ requires : C, 73.80 ; H, 6.14 ; N, 5.20 %.

3'-Cyanomethyl-4'-methyl naphtha(1,2 : 6',5')-α-pyrone (XVI) :

3'-Chloromethyl-4'-methyl naphtha(1,2 : 6',5')-α-pyrone (1.0 g.) was dissolved in alcohol and mixed with a solution of potassium cyanide (2.0 g.) in water. The reaction mixture was refluxed on a steam bath for 3 hr. The product which separated on pouring the reaction mixture in water crystallised from dilute acetic acid into needles, m.p. 213°. Yield 0.6 g.

Analysis : Found : C, 77.00 ; H, 4.19 ; N, 5.20 %
$C_{16}H_{11}O_2N$ requires : C, 77.11 ; H, 4.42 ; N, 5.62 %.

4'-Methyl naphtha(1,2 : 6',5')-α-pyrone-3'-acetic acid (XVII) :

The above 3'-cyanomethyl-4'-methyl naphtha(1,2 : 6',5')-α-pyrone (0.5 g.) was dissolved in 70 % sulphuric acid and heated on a steam bath for 2 hr. The reaction mixture was then poured in water. The solid which separated was dissolved in sodium bicarbonate solution. The solid separating on acidification of the bicarbonate extract was crystallised from dilute acetic acid. in white needles (0.25 g.), m.p. 253° (effer.)

Analysis : Found : C, 71.85 ; H, 4.25 %

$C_{16}H_{12}O_4$ requires : C, 71.77 ; H, 4.48 %.

Attempted preparation of 4'-methyl-3'-formyl naphtha(1,2 : 6',5') -α-pyrone :

A mixture of 3'-chloromethyl-4'-methyl naphtha-(1,2 : 6',5')-α-pyrone (1.0 g.) and hexamine (3.0 g.) in acetic acid (20 ml.) was refluxed gently on a wire gauze for 30 min. Hydrochloric acid (10 ml. ; 1 : 1) was then added and heating continued for further 15 min. The product which separated on pouring the reaction mixture in ice cold water was crystallised from dilute acetic acid into pale yellow needles. M.p. 175°. It did not give a 2,4-dinitrophenyl hydrazone.

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