APPENDIX I

CYANOETHYLATION OF SOME XYLENOLS

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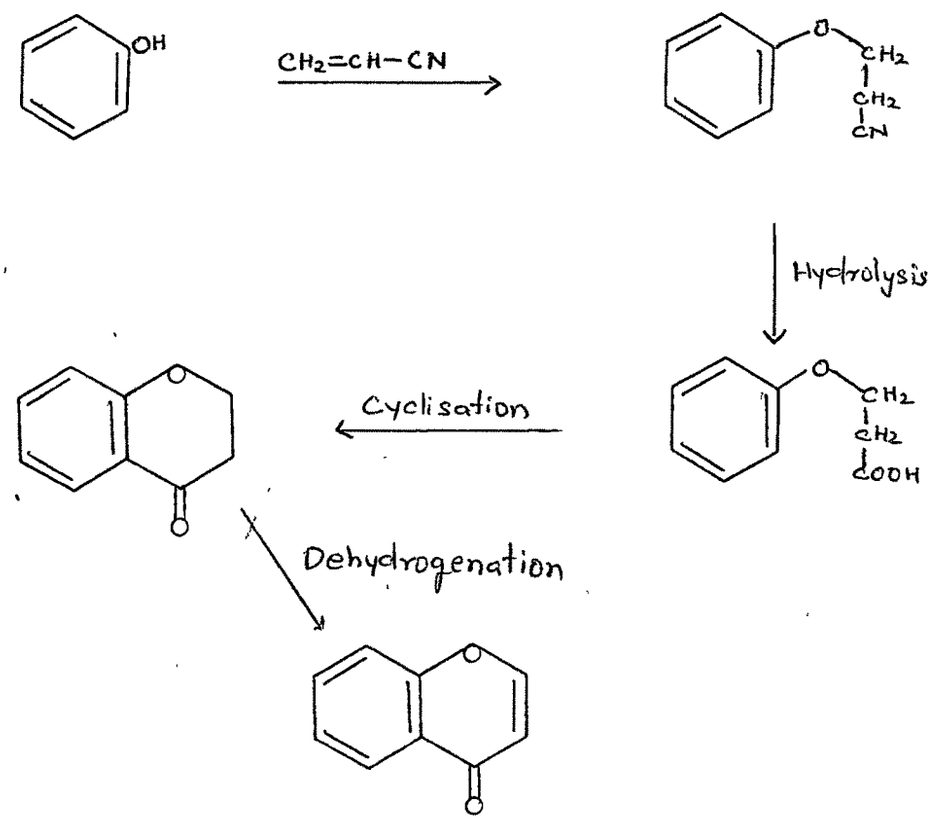
CYANOETHYLATION OF SOME XYLENOLS : ATTEMPTED SYNTHESIS OF 6,7-DIMETHYLCHROMONE AND 5,7-DIMETHYLCHROMONE

Chromones form yet another group of important heterocycles which are widely distributed in nature and a large number of them have been synthesised by one or the other of the methods available for their synthesis. In the present work attempts have been made to synthesise 5,7-dimethyl- and 6,7-dimethylchromone from the appropriate xylenols as these chromones have not been synthesised so far.

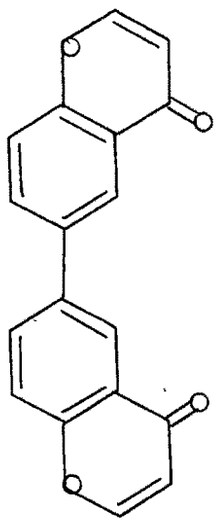
Auwers and Döll[1] prepared 2,5,7-trimethylchromanone from m-xylylmethyl ether by condensing with acrylyl chloride in the presence of aluminium chloride. They also prepared 2,2,5,7-tetramethylchromanone from m-xylylmethyl ether by condensing it with β-β-dimethylacrylyl chloride in the presence aluminium chloride. Adamas and Mecorney[2] reported the formation of 2,5,7-trimethyl-6-chlorochromone by the Pechmann condensation of 4-chloro-3,5-xylenol with ethyl acetoacetate in the presence of sulphuric acid.

Cyanoethylation of phenols provides a convenient method for the synthesis of chromone derivatives, unsubstituted in the heterocyclic ring. The intermediate β-phenoxypropionitrile can be hydrolysed to the corresponding acid and the acid cyclised to a chromanone using cyclising agents such as

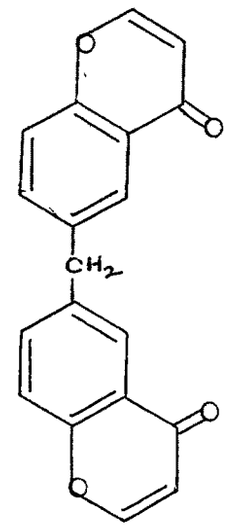
anhydrous hydrofluoric acid[3] or conc. sulphuric acid. Alternately the corresponding propionitrile can be cyclised using Friedel-Crafts catalyst such as anhydrous aluminium chloride[4]. Heininger[5] cyclised β-aryloxy propionitriles to chromanones through the intermediate formation of chromonimines. Bechman and Levine[6] cyclised various β-aryloxy propionitriles to chromanones using either sulphuric acid or phosphoric acid. These chromanonescan be dehydrogenated to chromanes by using palladium and charcoal or selenium dioxide. The sequence of reactions is given below :



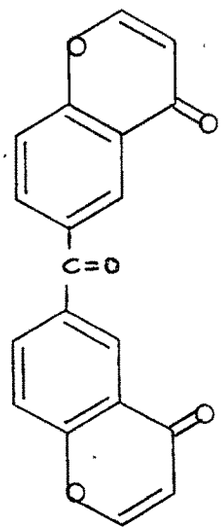
Merchant et al.[7,8,9] have built up a γ-pyrone ring on various hydroxycoumarins, through cyanoethylation. Prajapati and Sethna[10] synthesised a number of bichromonyls from diphenyl derivatives through cyanoethylation. Thus they synthesised 8,8'-bichromonyl and 6,6'-bichromonyl (I), 8,8'-bichromonylmethane and 6,6'-bichromonylmethane (II), 6,6'-bichromonyl ketone (III) and 6,6'-bichromonyl sulfone (IV) from



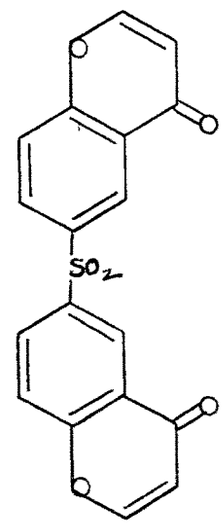
I



II



III



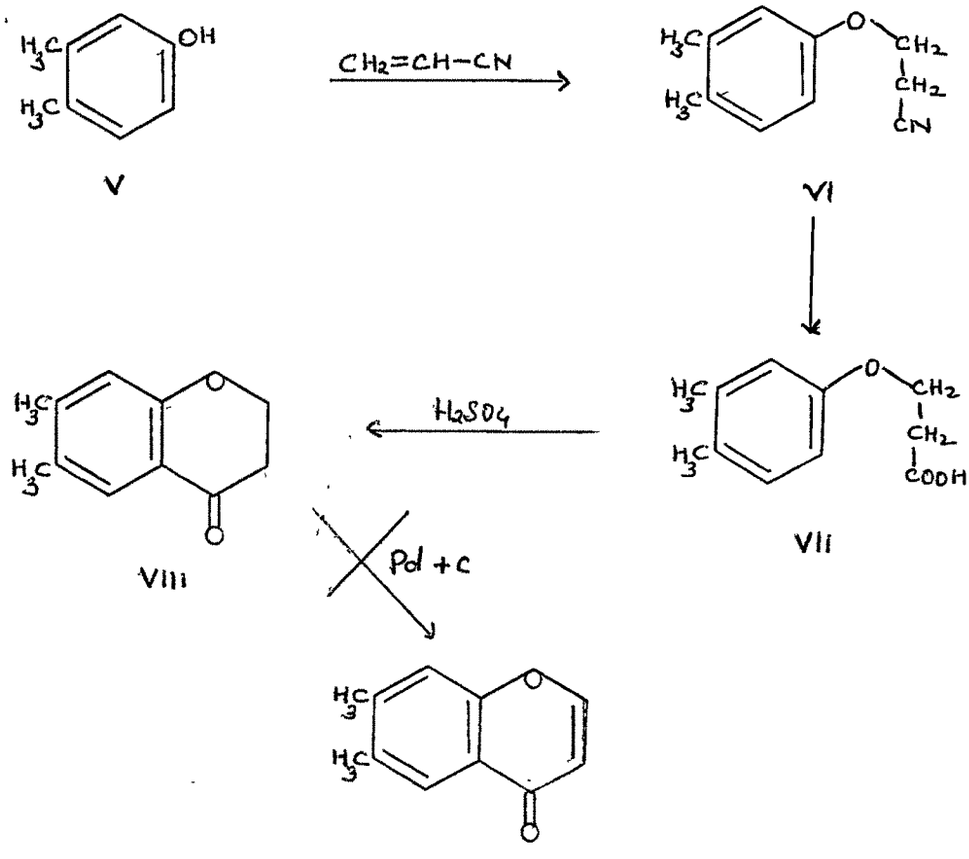
IV

2,2'-dihydroxy- and 4,4'-dihydroxydiphenyl,2,2'-dihydroxy- and 4,4'-dihydroxydiphenylmethane, 4,4'-dihydroxybenzophenone and 4,4'-dihydroxydiphenyl sulfone respectively. Various condensing agents used by them were sodium hydroxide, sodium methoxide, cuprous chloride, cupric oxide and triton B. They reported the best yield when cupric oxide was used.

The present work deals with the attempted synthesis of (1) 6,7-dimethylchromone and (2) 5,7-dimethylchromone.

Attempted synthesis of 6,7-dimethylchromone

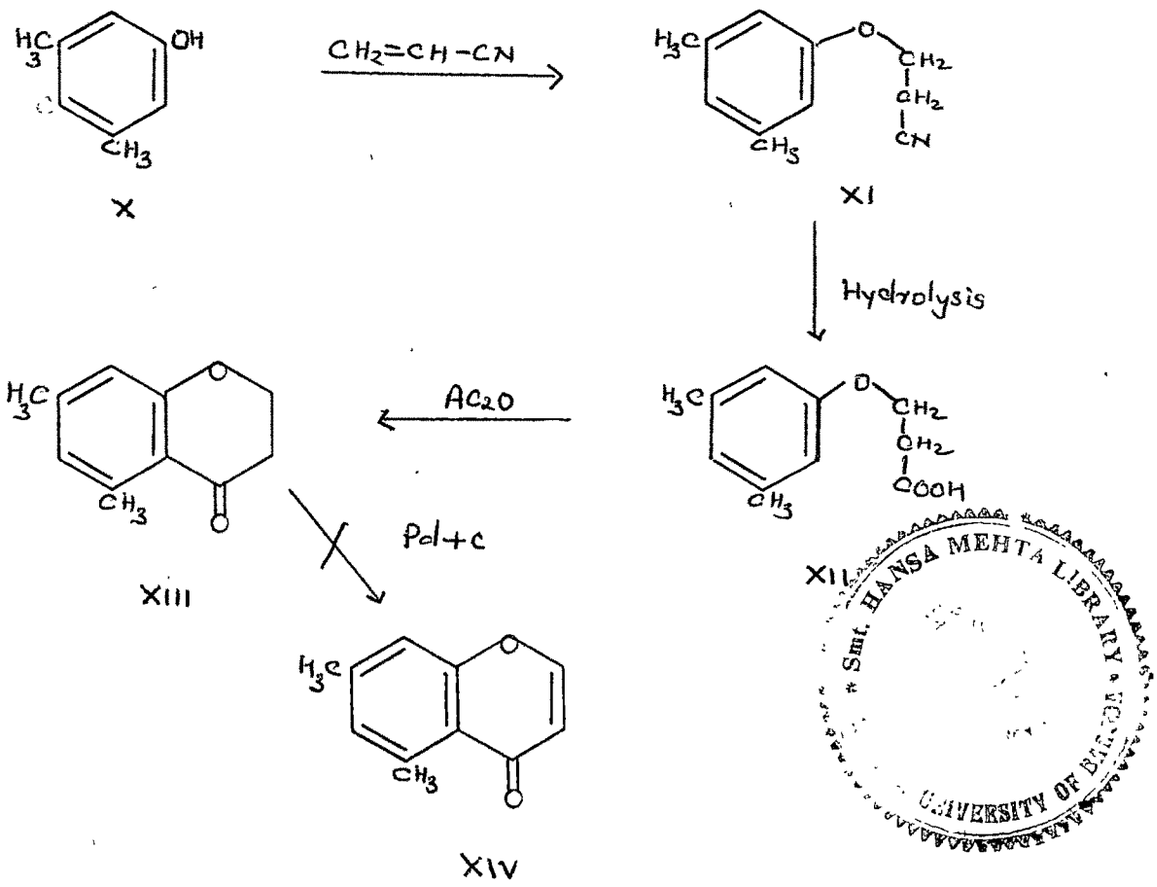
3,4-Xylenol (V) was condensed with acrylonitrile in the presence of cupric oxide and the β-(3,4-dimethylphenoxy)-



-propionitrile (VI) obtained was hydrolysed by heating with hydrochloric acid and acetic acid to the β-(3,4-dimethyl-phenoxy)propionic acid (VII). Attempts ~~were made~~ to cyclise this acid by heating with polyphosphoric acid did not succeed. It was cyclised by keeping it with conc. sulphuric acid for 10 minutes to give 6,7-dimethylchromanone (VIII) in a very poor yield. Its dehydrogenation with palladium and charcoal to 6,7-dimethylchromone (IX), however, did not succeed.

Attempted synthesis of 5,7-dimethylchromone

3,5-Xylenol (X) was condensed with acrylonitrile in the presence of cupric oxide and the β-(3,5-dimethyl-phenoxy)propionitrile (XI) obtained was hydrolysed by heating with hydrochloric acid and acetic acid to ~~the~~ β-(3,5-dimethyl-phenoxy)propionic acid (XII). Attempts were made to cyclise this acid to 5,7-dimethylchromanone (XIII) by keeping it with acetic anhydride when a syrupy product was obtained which was insoluble in sodium bicarbonate and sodium hydroxide solutions. Attempts were made to purify it by crystallisation and by chromatography but it could not be obtained in a pure solid form. However, IR spectrum of this syrupy product showed absorption at 1685 cm^{-1} characteristic of γ-pyrone carbonyl group. Attempts were made to dehydrogenate this syrupy product directly to 5,7-dimethylchromone (XIV) but it met with failure and an uncrystallisable product was obtained back.



X

XI

XII

XIII

XIV

EXPERIMENTAL

β-(3,4-Dimethylphenoxy)propionitrile (VI) :

3,4-Xylenol (1.0 g.) was refluxed with acrylonitrile (5 ml.) and cupric oxide (0.1 g.) for 28 hr. on a wire gauze. The reaction mixture was then filtered and poured in dilute sodium hydroxide. The solid separated was washed with water and crystallised from petroleum ether. M.p. 69°. Yield 0.7 g. IR in nujol : 2260 $cm.^{-1}$ (-CN).

Analysis : Found : C, 75.35 ; H, 7.44 ; N, 8.13 %

$C_{11}H_{13}ON$ requires : C, 75.44 ; H, 7.43 ; N, 8.00 %.

β-(3,4-Dimethylphenoxy)propionic acid (VII) :

The above nitrile derivative (1.0 g.) was refluxed with acetic acid (10 ml.) and hydrochloric acid (20 ml.) for 5 hr. on a wire gauze. The solid separating on cooling and diluting the reaction mixture with water was purified by the treatment of sodium bicarbonate solution which on acidification gave the acid which crystallised from dilute alcohol in fine white needles. IR in nujol : 1700 $cm.^{-1}$ (-COOH).

Analysis : Found : C, 67.70 ; H, 7.06 %

$C_{11}H_{14}O_3$ requires : C, 68.05 ; H, 7.22 %.

6,7-Dimethylchromanone (VIII) :

The above acid (0.5 g.) was kept with conc. sulphuric acid for 15 min. and the mixture was ~~decomposed in~~ added to ice cold water. The solid which separated was washed with sodium bicarbonate and water and crystallised from alcohol. M.p. 221°. IR in nujol : 1680 $cm.^{-1}$ (γ-pyrone).

Analysis : Found : C, 75.43 ; H, 6.20 %
$C_{11}H_{10}O_2$ requires : C, 75.88 ; H, 5.75 %.

Attempted dehydrogenation of 6,7-dimethylchromanone (IX) :

The above chromanone (0.5 g.) in diphenyl ether (2 ml.) was refluxed with palladised charcoal (2.0 g.) for 10 hr. It was filtered hot and the solid separated by cooling the reaction mixture was crystallised from alcohol. M.p. 221°. Mixed m.p. with 6,7-dimethylchromanone was not depressed.

β-(3,5-Dimethylphenoxy)propionitrile (X) :

3,5-Xylenol (1.0 g.) was dissolved in acrylonitrile (10 ml.) and the mixture was heated with cupric oxide (0.1 g.) for 25 hr. on a wire gauze. It was then filtered and poured in dilute sodium hydroxide. The solid separated was washed with sodium hydroxide solution and water and crystallised from petroleum ether. M.p. 93°. Yield 0.8 g. IR in nujol : 2250 $cm.^{-1}$ (-CN).

Analysis : Found : C, 75.82 ; H, 7.76 ; N, 7.63 %
$C_{11}H_{13}ON$ requires : C, 75.44 ; H, 7.43 ; N, 8.00 %.

β-(3,5-Dimethylphenoxy)propionic acid (XI) :

The above cyano derivative (1.0 g.) was dissolved in minimum quantity of acetic acid and hydrochloric acid (20 ml.) was added. The mixture was refluxed on a wire gauze for 5 hr. The solid separating, on cooling and diluting the reaction mixture, was purified by sodium bicarbonate as usual.

It was crystallised from petroleum ether M.p. 93°. The mixed m.p. with cyano derivative was depressed by 20°. IR in nujol : 1720 $cm.^{-1}$ (-COOH).

Analysis : Found : C, 67.57 ; H, 6.92 %

$C_{11}H_{14}O_3$ requires : C, 68.05 ; H, 7.21 %.

Attempted cyclisation of the above acid :

The above acid (0.5 g.) was kept with acetic anhydride (10 ml.) overnight. The reaction mixture was poured into water when a pasty product separated which was insoluble in sodium bicarbonate. Attempts were made to purify it by crystallisation or chromatography but syrupy product was obtained in each case. Attempts were then made to dehydrogenate it with palladised charcoal with a hope to obtain 5,7-dimethyl-chromone in a pure form, but it did not work and the same syrupy product was obtained. IR in nujol : 1685 $cm.^{-1}$ (γ-pyrone).

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