CHAPTER - II

PYRANOINDOLE DERIVATIVES

INTRODUCTION
Pyrones are six membered heterocyclic rings with one oxygen atom and a carbonyl group in the ring. They occupy important class of oxygen heterocycles with two isomeric forms, \( \alpha \)-pyrone and \( \gamma \)-pyrone. Each of this pyrone has got alternative canonical form consisting of pyrylium betaine. For the pyrylium betaine in which oxygen substituent is located at C-3, a carbonyl form cannot be written.

\[
\begin{align*}
&\text{103} \\
\text{104} \\
\text{105}
\end{align*}
\]

\( \alpha \)-pyrone (2H-pyrone) \quad \gamma \)-pyrone (4H-pyrone)

In the pyrone chemistry there is an intriguing question whether the heterocyclic ring is aliphatic or aromatic. The potential for aromaticity is brought out in the betaine structures 104 and 105. Both pyrones show some reactions characteristics of alkenes and others characteristics of arenes. In case of \( \alpha \)-pyrone however the balance does lie heavily in favour of reactions of the former type (alkene). \( \alpha \)-Pyrone is best thought of as an enol lactone rather than as pyrylium betaine, \( \alpha \)-pyrones have exhibited important biological properties. A number of steroidal \( \alpha \)-pyrones have achieved considerable importance on account of their powerful action on cardiac muscle such as scillaren 106 produced by \textit{Scilla maritima} and bufatolin 107 is one of the active ingredients of the poisonous secretion found in skin of certain toads.\textsuperscript{172-173}
Naturally occurring α-pyrone such as kawain 108, yangonin 109, methysticin 110 and β-erythroidin 111 are known to exhibit muscle relaxant properties\textsuperscript{174}.

Sliskovic \textit{et. al}\textsuperscript{175} have described 4-hydroxypyran-2-ones 112 and 113 as inhibitors of cholesterol biosynthesis.
Weber and associates\textsuperscript{176} have reported the \(\alpha\)-pyrones possessing phenolic moiety as potent scavengers of active oxygen species. The compound \textbf{114} is useful for the treatment of oxidative tissue injury in human disease.

![Chemical structure of compound 114](image)

Pereda and coworkers\textsuperscript{177} have isolated 5,6-dihydro-\(\alpha\)-pyrone, a spicegerolide \textbf{115} from \textit{Hyptis specegera} as cytotoxic.

![Chemical structure of compound 115](image)

Wrigley and coworkers\textsuperscript{178} have isolated (6S)-4,6-dimethylodeca-2E, 4E-dienoyleseters \textbf{116} and \textbf{117} from \textit{Phomopsis} sp with cytokine production inhibitory activity.

49
Antonio et. al\textsuperscript{179} have reported the antifungal activity of \(\alpha\)-pyrones 118 commonly called as fusapyrones from \textit{Fusarium semitectum}.

Cohen and Jiang\textsuperscript{180} have synthesised \(\alpha\)-pyrones of the type 119 which are useful for treating cancer and infections especially of bacterial infection.
R₁, R₂ = H, cell penetrating moiety, lipophilic solubiliser
R₃ = solubilising moiety sugar.

Christian and Jaconnet¹⁸¹ have reported the antifungal activity of 6-substituted-5,6-dihydro-α-pyrone 120 from *Ravensera anisata*.

Ansary and Mikhail¹⁸² have reported the preparation of linear and angular furobenzo-α-pyrones 121 and 122 and screened them for their photosensitizing and also for their antimicrobial activities against *Bacillus subtilis*.

R₁, R₂ = H, Me

R₁, R₂ = H, Me, OMe
Hussein and coworkers\textsuperscript{183} have synthesised $\alpha$-pyrones of the type 123 and 124 and reported their antimicrobial activity.

\begin{center}
\includegraphics[width=0.4\textwidth]{123.png}

123
\end{center}

\begin{center}
\includegraphics[width=0.4\textwidth]{124.png}

124
\end{center}

$X = \text{CONHN} = \text{CHAr, CONH NH-CS- NHR.}$

$\text{Ar} = \text{Ph, 4-O}_2\text{N-C}_6\text{H}_4, 4\text{-Cl-C}_6\text{H}_4, \text{etc.,}$

$\text{R} = \text{Pr, Cyclohexyl, Ph, Bz; } R_1 = \text{Pr, Et, Ph, Bz}$

Jenkins and associates\textsuperscript{184} isolated solanopyrone 125 from marine fungus possessing antialgal property and also reported the phytotoxic associations between marine fungi and algae.

\begin{center}
\includegraphics[width=0.3\textwidth]{125.png}

125
\end{center}

Elgamal and coworkers\textsuperscript{185} have synthesised furocoumarins 126, 127, 128 and reported their antimicrobial activity.
Trkovnik and Ivezic\textsuperscript{186} have prepared polyhydroxycoumarins \textbf{129} and reported their antiviral activity.

Kesten and associates\textsuperscript{187} have prepared 4-substituted coumarin derivatives \textbf{130} as potent and selective human dopamine D\textsubscript{4} antagonists.

\[ \text{The compound is active against HIV-I.} \]

\[ \text{Kesten and associates}^{187} \text{ have prepared 4-substituted coumarin derivatives} \textbf{130} \text{ as potent and selective human dopamine D}_{4} \text{ antagonists.} \]
Anderson et al. have prepared arylcoumarins 131 which modulate gene expression through the estrogen receptor.

\[
R^2(CH_2)_nO
\]

\[
R^3O
\]

n = 0-4; p = 0-2; \( R^1 = \) (substituted) aryl, aralkyl, heterocyclyl, heterocyclylalkyl;

\[
R^2 = \text{substituted heterocyclyl, } NH_2, \text{alkyl, aryl, heterocyclyl}; \ R^3 = H.
\]

Ovaska et al. have prepared 3-arylcoumarins 132 which are used for the treatment of stunned myocardium, subsequent to ischemia reperfusion.

\[
131
\]

\[
132
\]
Bombardelli and Vanlenti\textsuperscript{190} have prepared 8-(arylpropenoyl)-coumarins 133 and 134 as antiproliferative agents.

\begin{化学式}
\begin{align*}
\text{R} & = \text{OH, OR}^{10}, \text{OCOR}^{11}; \text{R}^{10} = \text{(un)substituted alkyl, alkenyl or alkynyl;} \\
\text{R}^{11} & = \text{alkyl, alkenyl, alkynyl or Ph; R}^1 = \text{H or (un)substituted alkyl.}
\end{align*}
\end{化学式}

Compound 133 is useful for treating menopausal disorders and osteoporosis while 134 is useful to treat breast cancer.

Shah \textit{et al.}\textsuperscript{191} have prepared sulfonamide derivatives of coumarin 135 and 136 and reported their antibacterial activity.

\begin{化学式}
\begin{align*}
\text{R} & = \text{Me, MeO, AcNH, Cl, Br; R}^1 = \text{H, Br.}
\end{align*}
\end{化学式}
The derivatives 136 showed good antibacterial activity against *E. coli*, *S. aureus*, *S. typhosa* and *S. albus*.

Kuriyama and coworkers\(^{192}\) have prepared 3-tetrazolylcoumarins 137 and reported their anaphylaxis activity.

Flavin and associates\(^{193}\) have synthesised coumarin derivatives of the type 138 and 139 and reported their antiviral activity.
Sharma and Pritmani\textsuperscript{194} have prepared 3-aza-4-methyl-7-hydroxycoumarins 140 and reported their antimicrobial activity.

\begin{center}
\begin{tikzpicture}
\node[species] {140};
\end{tikzpicture}
\end{center}

$R, R^1, R^2, R^3 = \text{H, Me, MeO, OH, NO}_2, \text{Br, Cl}$.

Santana and coworkers\textsuperscript{195} have prepared 4-methylcoumarin derivatives of the type 141 and reported their photobiological activity.

\begin{center}
\begin{tikzpicture}
\node[species] {141};
\end{tikzpicture}
\end{center}

$R = \text{H, (CH}_2\text{)}_2\text{NMe}_2$

El-Hady and Nagawa\textsuperscript{196} have synthesised dihydro derivative of the type 142.

\begin{center}
\begin{tikzpicture}
\node[species] {142};
\end{tikzpicture}
\end{center}

Vicario et al\textsuperscript{197} reported the asymmetric total synthesis of (-)-callystatin 143.

\textsuperscript{57}
γ-Pyrones:

The carbonyl group in γ-pyrone is devoid of normal ketonic properties such as hydrazone or oxime formation. This system does not react normally with phenyl hydrazine but cleavage of the heterocyclic ring occurs\textsuperscript{198}. The lack of reaction at the carbon of the carbonyl group is compensated by exceptional reactivity at oxygen atom of this group. Lewis acids as well as protic acids form oxonium salts, boron trifluoride, for instance, forms derivative of type 144.

\[
\begin{align*}
\text{O} & \quad \text{BF}_3 \\
\end{align*}
\]

The carbonyl stretching frequency in the IR spectrum of γ-pyrones\textsuperscript{199} occurs near 1650 cm\textsuperscript{-1} and is comparable to stretching frequency (1650 cm\textsuperscript{-1}) of cross conjugated cyclohexadienones. Hence, the possibility of single bond character in the carbonyl group of γ-pyrone arising from the aromatic betaine form was ruled out. The \textsuperscript{1}H NMR spectra\textsuperscript{200} gives the evidence for an aromatic ring current. The signals for C-2 and C-3 protons in γ-pyrone were found to appear at 8.0 δ and 6.5 δ respectively.
γ-Pyrones of biological importance:

Only simple γ-pyrones have been reported as natural products. Maltol 145 is one of them which has been isolated from pine needles and larch bark 201. It is of special interest, particularly to brewers, as one of the flavouring agents produced when barley is roasted in the production of malt.

Another important natural γ-pyrone is kojic acid 146 which is produced when various moulds mainly Asperigillus species are grown on glucose or xylose 202. It is known as an acid because the hydroxy function in position −3 is usually acidic (pKa = 7.9). The monoesters of kojic acid 147 have been found 203 useful as toilet powder component.

Kojic acid derivatives 148 were prepared 204 and found to be proteinase inhibitors for prevention or treatment of elastase mediated diseases such as antiinflammatory connective tissue diseases.

R, R₁ = C₁₀⁻₂₀ alkoxy or alkoxymethyl, COOH (CH₂)ₙOCOR₂
[R₂ = C₁⁻₆ alkyl and n = 0, 1 C₆⁻₁₅ aralkyl, benzyloxy, 2-pyranloyxy 2-pyranloyxymethyl]
Khellin 149, a furochromone is an important constituent of Ammi Visnaga extracts. It has been shown to possess a direct relaxing action on visceral smooth muscle and used frequently in the treatment of coronary deficiency diseases.205

A few synthetic 5,8-dimethoxychromones, which may be regarded as defurokhellin derivatives, have shown greater reactivity than khellin itself in animal testing. Koo207 synthesised many 2-substituted-5,8-dimethoxy chromones but only 5,8-dimethoxy-2-(3-pyridyl)chromone 150 was found to be the most active CNS depressant.

Rucheton and Jeanteur208 studied the inhibition of DNA-polymerase from murine sarcoma leukemia virus by the hydrochloride of amikhellin 151. The extent of inhibition varied with the nature of the primer template used.
Flavones and isoflavones are considered to be the key members of the flavonoid family of natural products in the light of their important biological functions. Pfister and coworkers tested sodium salts of flavone-6-carboxylic acid 152 in male rats as postcoitally or orally as inhibitors of histamine induced gastric secretion.

![Chemical Structure 152](image)

\[R = \text{Cl, F, CH}_3, \text{alkoxy} ; \ R_1 = \text{H, OH, OCH}_3, \text{OCH} \left(\text{CH}_3\right)_2 ; n = 1 \text{ or } 3\]

Flavone of the type 153 have been tested as inhibitors of arachidonate 5-lipoxygenase. Modification of R in 153 with a C6-C10 alkyl group markedly increased the inhibitory activity.

![Chemical Structure 153](image)

Meyer and associates synthesised a series of 3-methoxy-flavones and established their structure activity relationship with antiviral activities and cytotoxicities. The most interesting compound was 4,7-dihydroxy-3-methoxy-5,6-dimethylflavone 154 possessing in vitro TI_{99} (Therapeutic index) value of > 1000 and > 200 against poliovirus type 1 and rhinovirus type 155 respectively.
Synthesis and cardiovascular activity of b-ring substituted 7-hydroxyflavones 155 have been reported by He and coworkers\textsuperscript{212}. These compounds exhibited marked inhibition of myocardial contractility.

![Chemical Structure of 155](image)

Flavones are also known to exhibit central nervous depressant, hypotensive and hyperthermic\textsuperscript{213}, antiplatelet\textsuperscript{214} and antimicrobial activities\textsuperscript{215, 216}.

Eckstein \textit{et al}\textsuperscript{217} synthesised xanthone-2-carboxylic acids of the type 156 and tested for their antiinflammatory and analgesic properties. In the carrageenic paw oedema test, compound (R = 5-Cl) displayed an activity approximately one their of that of ketoprofen.

![Chemical Structure of 156](image)

R = H, Cl, Br, NO\textsubscript{2}, alkoxy
Cairns et al. reported the synthesis and antiallergic activity of a large number of linear and angular benzopyran dicarboxylic acids. Antiallergic activity of these compounds was determined by using the homologous passive anaphylaxis (PCA) reaction in the rat. The linear benzodipyrones 157 were found to be more active.

\[
\text{R} = \text{H, CH}_3, \text{OCH}_3 \\
\text{R}_1 = \text{H, CH}_3, \text{C}_2\text{H}_5(\text{CH}_2)_2\text{CH}_3, \text{CH}_2\text{OC}_2\text{H}_5, \text{NO}_2
\]

Benzodipyrone derivatives are also known to exhibit fish toxicity and antifeedant activity.

Pyran[2,3-c]quinoline-2-carboxylate 158, an antiallergic drug was tested for its cardiovascular activity in dogs, rats and guinea pigs. This compound was also used to study terogenicity in rabbits.

Cairns and associates synthesised antiallergic pyranoquinoline dicarboxylic acid 159 with potential for the topical treatment of asthma.
A new class of benzopyranobenzodiazepin-1,3-ones 160 have been synthesised by Devi et al.\textsuperscript{222} and evaluated their hypnotic, analgesic and antiinflammatory\textsuperscript{222a} and antipsychotic activity\textsuperscript{222b}.

\[
\text{NHCH}_3 \quad \text{O} \\
\text{HOOC-} \quad \text{N} \\
\text{CH}_2\text{CH}_2\text{CH}_3 \quad \text{COOH}
\]

159

\[
\begin{array}{c}
\text{R} \quad \text{R}_1 \\
\text{R}_2 = \text{CH}_3, \text{C}_2\text{H}_5, \text{CH}_2\text{C}_6\text{H}_5
\end{array}
\]

160

R = H, CH\textsubscript{3}, Cl; R\textsubscript{1} = H, CH\textsubscript{3}
R\textsubscript{2} = CH\textsubscript{3}, C\textsubscript{2}H\textsubscript{5}, CH\textsubscript{2}C\textsubscript{6}H\textsubscript{5}

Recently, Jean-Pierre and Jean-Francois\textsuperscript{223} prepared compounds of the type 161 which gave > 50% inhibition of 5-HT induced arterial pressure increase in rats at 40 mg / kg orally.

\[
\text{OMe} \quad \text{O} \\
\text{F}
\]

161

A series of pyrano[2,3-c]pyrazol-4-one 162 was synthesised and evaluated for bovine brain adenosine A\textsubscript{1} and A\textsubscript{2A} receptor binding affinity\textsuperscript{224}. 
Few pyranoindol-4-one 163 reported by Brown et al.225,226 are found to be useful in preventing allergy225 and asthma225b,c,d.

R = R1 = H, OH, C1-6 alkyl, alkoxy, halo, CF3
R1R2 = OCH2O
R2 = H, C1-6 - alkyl, C6H5, CH2C6H5
R3 = CONH2, CN, Tetrazolyl, COOH, COOR4, R4 = C1-6 - alkyl

Goerlitzer and Dehne227 synthesised many derivatives of pyrano[3,2-b]indol-4-ones 164 which are of considerable interest because of their potential antiallergic activities.

R = CHO, CH2OH, COOH, tetrazolyl
The synthesis of pyranoindolones 165 and pyranobisindolones 166 has been reported by Eiden and Hirschmueller\textsuperscript{228}.

\[ R = \text{CH}_3, \text{COOC}_2\text{H}_5 ; R'_1 = \text{OC}_2\text{H}_5 \]

\[ RR'_1 = \text{NCH}_3\text{CONCH}_3 \]

Bargiotti \textit{et al.}\textsuperscript{229} reported substituted benzopyranones 167 and 168 as telomerase inhibitors and also their preparation, pharmaceutical composition and use in treatment of cancer.

\[ R, R', R'' = \text{H, halo, cyano, OH, alkoxy, acyloxy, aryloxy, etc.} \]

\[ R^3, R^4 = \text{H, halo, cyano, OH, alkoxy etc} \]

\[ R^6, R^7, R^8, R^9, R^{10} = \text{H, alkyl, aryl.} \]

Bose and associates\textsuperscript{230} reported the synthesis of the compound of the type 169.
Lee et al. synthesized prenylicoflavone 170a and licoflavone 170b as inhibitors of bone resorption pits formation.

170a \( R = \text{Prenyl} \); 170b \( R = \text{H} \)
Present Work: Part A

Synthesis of 2H-pyrano[6,5-f]indol-2-one derivatives
In the light of wide varieties of biological properties exhibited by 2H-pyran-2-ones and coumarins, we were very much encouraged to undertake the synthesis of 2H-pyranindoles where in 2H-pyran-2-one is linearly fused to the benzene nucleus of the biodynamic indole nucleus.

In the present investigation, the starting materials viz, 1-substituted-3-acetyl-5-hydroxy-2-methylindoles were prepared by reacting p-benzoquinone with acetylacetone imine by adopting the Nenitzescu reaction conditions. These 5-hydroxyindoles were subjected to regioselective Friedel-Crafts acetylation with acetyl chloride and anhydrous aluminium chloride in freshly distilled nitrobenzene to obtain the desired 3,6-diacetyl-5-hydroxyindole derivatives which were further reacted with ethyl cyanoacetate in presence of piperidine by heating at 180°C in an oilbath with a desire to get linearly fused 6-substituted-3-cyano-8-acetyl-4,7-dimethyl-2H-pyrano[6,5-f]indol-2-ones but only starting materials 3,6-diacetyl-5-hydroxyindoles were recovered.

Meanwhile, we noticed that Brown and Mihm have reported that 2-methylpyridine is a stronger base than pyridine presumably due to electron donating inductive effect of methyl group. Hence, we thought on similar lines and used 2-methylpiperidine in the above reaction instead of piperidine which produced readily the desired novel linearly fused 6-substituted-3-cyano-8-acetyl-4,7-dimethyl-2H-pyrano[6,5-f]indol-2-ones. [Scheme – 1].
Scheme – 1

CH$_3$COCI, AICI$_3$, nitrobenzene
90°-100°

\[
\begin{array}{c}
\text{Compd. R} \\
\text{a} \quad \text{-C}_6\text{H}_4\text{CH}_3\text{P} \\
\text{b} \quad \text{-C}_6\text{H}_5
\end{array}
\]
IR spectrum of compound 174a (Fig-1) displayed a stretching band at 3229 cm\(^{-1}\) due to the H-bonded C\(_5\)-OH while C\(_6\) - and C\(_3\)-acetyl carbonyls showed strong stretching bands at 1642 cm\(^{-1}\) and 1615 cm\(^{-1}\) respectively. \(^1\)H NMR spectrum of 174a (Fig. 2) exhibited singlets at 2.53 \(\delta\), 2.59 \(\delta\), and 2.70 \(\delta\) due to C\(_3\)-acetyl methyl, C\(_6\)-acetyl methyl, p-tolyl methyl and C\(_2\)-methyl protons respectively. Two doublets at 7.22 \(\delta\) and 7.44 \(\delta\) accounted for p-tolyl protons. Singlet 7.32 \(\delta\) belong to C\(_7\)-proton while another singlet at 7.50 \(\delta\) assigned to C\(_4\)-proton. The C\(_3\)-OH appeared as singlet at 12.08 \(\delta\) which vanished on D\(_2\)O exchange.

The IR spectrum of compound 174b (Fig-3) displayed a stretching band at 2919 cm\(^{-1}\) due to intramolecular H-bonded C\(_5\)-OH group while C\(_6\) - and C\(_3\)-acetyl carbonyls showed strong stretching bands at 1641 cm\(^{-1}\) and 1628 cm\(^{-1}\) respectively. \(^1\)H NMR spectrum of 174b (Fig-4) exhibited singlets at 2.53 and 2.63 \(\delta\) due to C\(_3\)-acetyl methyl and C\(_6\)-acetyl methyl protons and the C\(_2\)-methyl protons displayed singlet at 2.71 \(\delta\). The C\(_7\)-proton resonated as singlet at 7.33 \(\delta\) while another singlet at 7.63 \(\delta\) was assigned to C\(_4\)-proton. Five aromatic protons of 1-phenyl group displayed multiplet ranging from 7.36 to 7.66 \(\delta\). The C\(_3\)-OH proton showed singlet at 12.08 \(\delta\) which disappeared on D\(_2\)O exchange.

IR spectrum of compound 175a (Fig-5) exhibited a strong stretching band at 2224 cm\(^{-1}\) due to cyano group, while lactone carbonyl and C\(_8\)-acetyl carbonyls showed strong bands at 1716 and 1640 cm\(^{-1}\) respectively. \(^1\)H NMR spectrum of 175a (Fig-6) showed singlet at 2.55 \(\delta\) due to C\(_8\)-acetyl methyl and another singlet observed at 2.64 \(\delta\) was assigned to C\(_6\)-phenyl methyl protons. The C\(_7\)-methyl protons resonated at 2.66 \(\delta\) as singlet while singlet at 2.72 \(\delta\) was assigned to C\(_4\)-methyl protons. Multiplet ranging from 7.23 to 8.032 \(\delta\) was accounted for six aromatic protons.
Scheme – 2

\[ \text{m/z (\%)} \]
\[ 91(3) \]
\[ F_3 \]

\[ \text{m/z (\%)} \]
\[ 370(54) \]
\[ CH_3 + \text{c=о} \]

\[ \text{m/z (\%)} \]
\[ 306(12) \]
\[ F_2 \]

\[ \text{m/z (\%)} \]
\[ 355(100) \]
\[ F_1 \]
The mass spectrum 175a (Fig-7) displayed molecular ion peak M+ at m/z (%) 370 (54). The M+1 peak was observed at 371 (14). Fragment F$_1$ gave a base peak at m/z (%) 355 (100) after the loss of CH$_3$ from the molecular ion and the loss of C$_4$H$_2$N from the molecular ion displayed a peak at m/z (%) 306 (12). The peak at m/z (%) at 91 was obtained by the loss of C$_{16}$H$_{11}$N$_2$O$_3$ from the molecular ion [Scheme-2].

IR spectrum of compound 175b (Fig.-8) exhibited a stretching band at 2221 cm$^{-1}$ due to cyano group. Strong stretching bands at 1715 and 1641 cm$^{-1}$ were to lactone carbonyl and C$_8$-acetyl carbonyl respectively. $^1$H NMR spectrum of 175b (Fig.-9) showed a singlet at 2.65 $\delta$ due to C$_4$-methyl and C$_8$-acetyl methyl protons and singlet observed at 2.73 $\delta$ was related to C$_7$-methyl protons. Seven aromatic protons displayed multiplet ranging from 6.92 to 8.04 $\delta$. 
Present Work : Part B

Synthesis of 4H-pyrano[2,3-f]indol-4-one derivatives
There are some reports in literature on the 4H-pyranoindol-4-ones, where in γ-pyrone ring is fused to 2,3-position of the indole and to the benzenoid part of the indole moiety. It is interesting to note that the biological activities of 1,3-dibenzolylmethanes are attributed to the presence of C=O pharmacophore. Moreover, the α, β-unsaturated ketonic group is believed to be responsible for the antibacterial activity (Gram-positive and Gram-negative) of clavacin 176 and penicillic acid 177.

Styrylchromones have been described to possess interesting biological activities. In the light of all the above reports, it was desired to undertake the synthesis of 4H-pyrano[2,3-f]indole-4-one which contains α, β-unsaturated ketonic function.

The chromones are synthesised by various methods and in the present work, we have adopted the method involving Baker-Venkatraman transformation. The method consists three stages.

a) Esterification:

It has been found that esterification of o-hydroxyacetophenones with aromatic acids can be effected in pyridine in presence of POCl₃. Wadodkar and Marathe studied the mechanism of this esterification. Esterification is an acid catalysed process and involves an addition elimination mechanism, which is not possible here, when pyridine, a basic medium is used. The in situ formation of acid chloride in the reaction mixture and its subsequent use for esterification is ruled out since acid chloride cannot be formed using...
POCl₃. The mechanism was best explained by the formation of triaryl phosphate from the phenolic ketone with POCl₃ and its subsequent utilisation for the reaction with the organic acid to produce ester. The stepwise reaction is as shown in the following equations (i) and (ii). The HCl and H₃PO₄, formed in the reaction are taken up by the pyridine.

\[
3 \text{ArOH} + \text{POCl}_3 + 3\text{C}_5\text{H}_5\text{N} \rightarrow (\text{ArO})_3\text{PO} + 3\text{C}_5\text{H}_5\text{N-HCl} \quad \ldots \ldots \text{(i)}
\]

\[
(\text{ArO})_3\text{PO} + 3\text{Ar'}\text{COOH} \rightarrow \text{ArOCOAr'} + \text{H}_3\text{PO}_4 \quad \ldots \ldots \text{(ii)}
\]

The condition used in this esterification limits the temperature to about 60°C.

b) Baker – Venkataraman Transformation

Baker-Venkataraman transformation²⁴⁴,²⁴⁵ is the conversion of o-acetyl / aroyloxyacetoarones 178 into diketones 182. Baker in his original work²⁴⁴ used aroyloxyacetophenones as the starting material for the rearrangement to o-hydroxydibenzoylmethane with anhydrous potassium carbonate in benzene or toluene. Venkataraman²⁴⁵,²⁴⁶ used sodamide in dry ether. Since then, various solvents have been tried²⁴⁷,²⁴⁸ to effect the rearrangement.

Doyle et. al²⁴⁹ studied the mechanism of Baker-Venkataraman transformation and showed that transformation of o-hydroxyacetoarones 178 into o-hydroxydiaroyl methanes 182 is a base catalysed intramolecular Claisen condensation involving transition compound 179.
Gowan and Wheeler\textsuperscript{250} suspected the possibility of intermolecular reaction, involving the dissociation of 178 into anion 180 and the aroyl cation 181 and they later condense to form diketone 182. To clarify this, they carried out cross over experiments with a mixture of o-(p-nitrobenzoyloxy) acetonaphone and 2,4-dibenzoyloxyacetophenone in pyridine solution using powdered potassium hydroxide. In their experiment, cross products were not isolated, thus indicating the intramolecular nature of transformation. Thus, it was concluded that Baker-Venkataraman transformation involves internal base catalysed Claisen condensation between ester and a ketone.

The method leading to the synthesis of pyranoindoles utilised 3,6-diacetyl-5-hydroxyindole 174b as starting material which was obtained by the Friedel-Craft's acetylation of 5-hydroxyindole 173b. The 5-hydroxy-6-acetyldindole derivative 174b was condensed with aromatic acids using POCl\textsubscript{3} producing the corresponding esters 183a-e which were subjected to Baker-Venkataraman transformation reaction to yield 1,3-diketones 184a-e. The acid catalysed cyclisation of these 1,3-diketones 184a-e produced the desired 4H-pyrano[2,3-f]indol-4-ones 185a-e and 186a-e [Scheme – 3].
Scheme - 3

\[
\begin{align*}
174b & \xrightarrow{R-COOH} 183a-e \\
& \xrightarrow{POCl_3, \text{Pyridine \ stirr, } 50-60^\circ} \\
& \xrightarrow{\text{AcOH + HCl}} 185a-e \\
& \xrightarrow{\Delta} 186a-e \\
& \xrightarrow{\text{Ac}_2O, \text{ACoNa}} \\
\end{align*}
\]

<table>
<thead>
<tr>
<th>R</th>
<th>Compound</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>C_6H_4-Cl(o)</td>
</tr>
<tr>
<td>b</td>
<td>C_6H_4-OCH_3(p)</td>
</tr>
<tr>
<td>c</td>
<td>C_6H_4-NHCOCH_3(p)</td>
</tr>
<tr>
<td>d</td>
<td>C_6H_4-(NO_2)_2(3,5)</td>
</tr>
<tr>
<td>e</td>
<td>C_6H_4-NO_3(m)</td>
</tr>
</tbody>
</table>
IR spectrum of (Fig-10) 5-o-chlorobenzoxyloxy-3,6-diacetyl-1-phenyl-2-methylindole 183a displayed absorption bands at 1752 cm\(^{-1}\), 1678 cm\(^{-1}\) and 1634 cm\(^{-1}\) due to C5-ester, C6-acetyl and C3-acetyl carbonyls respectively. The IR band of C5-OH was found to be absent. The \(^1\)H NMR spectrum of this compound 183a (Fig. 11) exhibited singlets at 2.48 \(\delta\), 2.62 \(\delta\) and 2.69 \(\delta\) representing C3-acetyl, C6-acetyl and C2-methyl protons respectively. The multiplet ranging from 7.30 to 8.29 \(\delta\) was accounted for eleven aromatic protons.

IR spectrum of 5-p-methoxybenzoxyloxy-3,6-diacetyl-1-phenyl-2-methylindole 183b (Fig-12) displayed stretching bands at 1789 cm\(^{-1}\), 1653 cm\(^{-1}\) and 1628 cm\(^{-1}\) due to the C5-ester, C6-acetyl and C3-acetyl carbonyls respectively. The stretching band of C5-OH was found to be absent. The \(^1\)H NMR spectrum of the same compound 183b (Fig. 13) exhibited singlets at 2.49 \(\delta\), 2.62 \(\delta\), 2.70 \(\delta\) representing C3-acetyl, C6-acetyl and C2-methyl protons respectively. The methoxy protons were observed as singlet at 3.92 \(\delta\) while the multiplet ranging from 7.05 to 8.23 \(\delta\) accounted for ten aromatic protons.

The 5-benzoyloxyindole derivatives 183a-e were subjected to Baker-Venkataraman transformation with dry pyridine and powdered potassium hydroxide to obtain the desired 6-benzoylacetyl-5-hydroxyindoles 184a-e in quantitative yields.

The IR spectrum of 3-acetyl-6-o-chlorobenzoxylacetyl-5-hydroxy-1-phenyl-2-methylindole 184a (Fig-14) showed strong carbonyl bands at 1640 cm\(^{-1}\) and 1600 cm\(^{-1}\) due to C6-benzoxylacetyl and C3-acetyl groups. The broad stretching band at 3419 cm\(^{-1}\) was due to C5-OH and enolic OH. \(^1\)H NMR spectrum of this sample 184a (Fig-15) displayed singlet at 2.61 \(\delta\) due to C3-acetyl methyl protons and singlet at 2.72 \(\delta\) was accounted for C2-methyl protons. The olefinic proton was observed as singlet at 6.59 \(\delta\) and the multiplet ranging from 7.27 to 7.61 \(\delta\) was accounted for eleven aromatic protons.
Singlets at 11.86 δ and 15.17 δ were due to the C5-OH and enolic OH which vanished on D2O exchange.

The IR spectrum of 3-acetyl-6-p-methoxybenzoylacetyl-5-hydroxy-1-phenyl-2-methylindole 184b (Fig-16) exhibited strong carbonyl bands at 1640 cm⁻¹ and 1623 cm⁻¹ due to C6-benzoylacetyl and C3-acetyl groups respectively. The broad band due to C5-OH and enolic OH was observed at 3431 cm⁻¹. ¹H NMR spectrum of this sample 184b (Fig-17) showed singlets at 2.59 δ and 2.71 δ due to C3-acetyl and C2-methyl protons. The methoxy protons were observed as singlet at 3.88 δ and singlet at 6.48 δ was due to olefinic proton. The multiplet ranging from 6.96 to 7.80 δ were accounted for eleven aromatic protons. Singlets at 11.96 δ and 15.84 δ were assigned to C5-OH and enolic OH which disappeared on D2O exchange.

These 6-benzoylacetyl indole derivatives 184a-e were further subjected to cyclodehydration with glacial acetic acid containing few drops of concentrated hydrochloric acid to afford the desired 2-aryl-6-phenyl-7-methyl-8-acetyl-4H-pyrano[2,3-f]indole-4-ones 185a-e. When 6-benzoylacetyl-5-hydroxyindoles 184a-e were heated with acetic anhydride and freshly fused sodium acetate gave the required 8-acetyl-3-benzoyl-2,7-dimethyl-4H-pyrano[2,3-f]indol-4-ones 186a-e in good yields [Scheme-3].

IR spectrum of 2-o-chlorophenyl-6-phenyl-7-methyl-8-acetyl-4H-pyrano[2,3-f]indol-4-one 185a (Fig-18) exhibited stretching bands at 1638 cm⁻¹ and 1623 cm⁻¹ due to the γ-pyrone ring and C8-acetyl carbonyl functions respectively. ¹H NMR spectrum of this sample 185b (Fig-19) showed singlets at 2.67 δ and 2.76 δ corresponding to the C8-acetyl and C7-methyl protons respectively. The C3-proton appeared as singlet at 6.72 δ and another singlet at 8.31 δ was assigned to C5-proton which appeared down field due to the deshielding effect of the carbonyl of γ-pyrone. Singlet at 7.91 δ was due to C9-proton while multiplet ranging from 7.28 to 7.72 δ was accounted for nine aromatic protons.
The mass spectrum of 185a (Fig-20) exhibited molecular ion peaks $M^+$ at m/z (%) 427/429 (60/20) due to the isotopic effect of chlorine. The cleavage of methyl from the molecular ion produced fragment $F_1$ at m/z (%) 412 (90). The peak at m/z (%) 385 was due to fragment $F_2$ resulted after the loss of $C_2H_2O$ from molecular ion and fragment $F_3$ was obtained by losing $C_8H_4Cl$ from the molecular ion which appeared at m/z (%) 292 (6) [Scheme – 4].
Scheme – 4

\[ \text{Reactions and intermediate products} \]

\[ \text{Product F}_1, \text{M}^+, \text{427/429 (60/20)} \]

\[ \text{Product F}_3, \text{292 (6)} \]

\[ \text{Product F}_4, \text{385 (6)} \]
IR spectrum of 2-p-anisyl-6-phenyl-7-methyl-8-acetyl-4H-pyrano[2,3-f]indol-4-one 185b (Fig-21) exhibited stretching bands at 1648 cm\(^{-1}\) and 1621 cm\(^{-1}\) due to the carbonyls of the \(\gamma\)-pyrone ring and C\(_8\)-acetyl functions respectively. \(^1\)H NMR spectrum of the sample 185b (Fig-22) showed singlets at 2.66 \(\delta\) and 2.78 \(\delta\) corresponding to the C\(_8\)-acetyl and C\(_7\)-methyl protons respectively. Singlet at 3.92 \(\delta\) was due to the methoxy protons and C\(_3\)-proton appeared as singlet at 6.74 \(\delta\). Another singlet at 8.34 \(\delta\) was accounted for C\(_5\)-proton while multiplet ranging from 7.05 to 7.99 \(\delta\) was accounted for ten aromatic protons.

The IR spectrum of 3-o-chlorobenzoyl-2,7-dimethyl-6-phenyl-8-acetyl-4H-pyrano[2,3-f]indol-4-one 186a (Fig-23) displayed carbonyl stretching bands at 1748, 1673 and 1634 cm\(^{-1}\) due to C\(_3\)-benzoyl, \(\gamma\)-pyrone and C\(_8\)-acetyl respectively. \(^1\)H NMR spectrum of this sample 186a (Fig-24) exhibited singlets at 2.65 \(\delta\), 2.67 \(\delta\) and 2.76 \(\delta\) due to protons of C\(_2\)-methyl, C\(_8\)-acetyl and C\(_7\)-methyl groups respectively. Singlet at 8.28 \(\delta\) was assigned to C\(_5\)-proton while singlet at 7.90 \(\delta\) was due to C\(_9\)-proton. Multiplet ranging from 7.28 to 7.77 \(\delta\) was accounted for nine aromatic protons.

The actual mass of the compound 186a is 469.92. The mass spectrum (Fig. 25) of 186a exhibited molecular ion peaks m\(^+\) at m/z (%) 470/472 (10/3) due to the isotopic effect of chlorine. The loss of Cl and HCl from the molecular ion gave peaks at m/z (%) 435 (30) and 434 (100) respectively. [Scheme – 5]
Scheme – 5

\[ \text{M}^+ \quad 470/472 \quad (10/3) \]

\[ \text{F}_1 \quad m/z (\%) \quad 435 (30) \]

\[ \text{F}_2 \quad m/z (\%) \quad 434 (100) \]
Fig. 1: IR Spectrum

Fig. 2: $^1$H NMR Spectrum

CDCl$_3$

On D$_2$O exchange
Fig. 3: IR Spectrum

Fig. 4: $^1$H NMR Spectrum

CDCl$_3$
Fig. 8: IR Spectrum

Fig. 9: $^1$H NMR Spectrum
CDCl$_3$
Fig. 10: IR Spectrum

Fig. 11: $^1$H NMR Spectrum
CDCl$_3$
Fig. 14: IR Spectrum

Fig. 15: $^1$H NMR Spectrum

On D$_2$O exchange
Fig. 16: IR Spectrum

Fig. 17: $^1$H NMR Spectrum
CDCl$_3$

On D$_2$O exchange
Fig. 21: IR Spectrum

Fig. 22: $^1$H NMR Spectrum
CDCl$_3$
Fig. 23: IR Spectrum

Fig. 24: $^1$H NMR Spectrum
CDCl$_3$
Fig. 25: Mass Spectrum
EI
Experimental
p-Benzoinone : 171

Hydroquinone (100 g) in water (1:1) was heated to 50°C on a water bath till a clear solution was obtained. The solution was cooled to 20°C and sulphuric acid (50 mL, 5N) was added slowly in small portions. Potassium bromate (56 g) was carefully added in small lots to the mixture while heating the flask to 60°C on a water bath. The formation of greenish black precipitate of quinhydrone was the indication of beginning of the reaction. Heating was stopped as the temperature rose to 75°C and the reaction was considered to be complete as soon as the black colour of reaction mixture changed to bright yellow colour of p-benzoquinone. The reaction mixture was heated to 80°C till p-benzoquinone dissolved and then cooled to 0°C. The separated solid (p-benzoquinone) was filtered, washed with cold water, air dried and recrystallised from benzene as bright orange yellowish needles, m.p. 116-17°C, yield : 80 g, 75%.

1-Substituted-3-acetyl-5-hydroxyindoles : 173a-b

Acetylacetone imine 172 prepared by the reaction of acetylacetone (100g, 0.5mol) with appropriate primary amine (0.5mol) in chloroform (100mL) was added with shaking to p-benzoquinone (0.55mol) dissolved in chloroform (500mL). The reaction mixture was heated at reflux for 2 hours. The solvent and resultant water were removed under reduced pressure. The residue was treated with ethanol and left overnight. The separated solid was filtered, washed with ethanol and recrystallised from dioxane.
1-p-Tolyl-3,6-diacetyl-5-hydroxy-2-methylindoles : 174a

To a suspension of 5-hydroxyindole derivative 173a (8.37 g, 0.03 mol) in freshly distilled nitrobenzene (100 mL) and acetyl chloride (4.25 mL, 0.06 mol) was added anhydrous aluminium chloride (9.89 g, 0.075 mol) in portions rapidly as it dissolved. The reaction mixture was heated for 3 hours on a steam bath and left overnight. It was poured into ice water (500 mL) containing concentrated hydrochloric acid (75 mL) and then subjected to steam distillation to remove nitrobenzene. The solid mass that separated on cooling to room temperature was filtered and recrystallised from dioxane to obtain the title compound as yellow flowery crystals m.p. 221-222°C, yield: 60.6%.

1-Phenyl-3,6-diacetyl-5-hydroxy-2-methylindole : 174b

This was prepared from 5-hydroxyindole 173b as per the procedure given for 173a and solid was recrystallised as green needles from dioxane m.p. 197-198°C, yield: 59.6%.
6-p-Tolyl-3-cyano-8-acetyl-4,7-dimethyl-2H-pyrano[6,5-f]indol-2-one : 175a

A mixture of 1-p-tolyl-3,6-diacetyl-5-hydroxy-2-methylindole \(174a\) (0.64g, 0.002mol) ethyl cyanoacetate (0.22g, 0.002mol) and 2-methylpiperidine (0.5 mL) in a 100 mL R. B. flask fitted with water condenser was heated in an oil bath at 180°C. The heating was continued for 5 hours, cooled to room temperature and the solid mass was triturated with benzene-petroleum ether (40-60). The separated solid was filtered and recrystallised from ethanol as yellow granules, m.p. <300°C, yield : 80%.

Anal. Calcd for \(C_{23}H_{18}N_2O_3\) : C, 74.56; H, 4.90; N, 7.5. Found C, 74.50; H, 4.96; N, 7.29.

6-Phenyl-3-cyano-8-acetyl-4,7-dimethyl-2H-pyrano[6,5-f]indol-2-one : 175b

This compound \(175b\) was also prepared as per the procedure given for compound \(175a\) and it was recrystallised from ethanol as pale green flakes, m.p. 270°C, yield : 74%.

Anal. Calcd. for \(C_{22}H_{16}N_2O_3\) : C, 74.13; H, 4.52; N, 7.86. Found : C, 74.18; H, 4.58; N, 7.82.

1-Phenyl-5-benzoyloxy-3,6-diacetyl-2-methylindoles : 183a-e

To a stirred solution of 3,6-diacetyl-5-hydroxyindole derivative \(174b\) (0.005mol) and substituted benzoic acid (0.0055mol) in dry pyridine (20 mL), was added phosphorous oxychloride (0.3 mL) with constant stirring and external cooling. The reaction mixture was stirred further for 2 hours at 50-60°C and then poured onto crushed ice (50 g). It was then neutralised with dilute hydrochloric acid to remove pyridine and the separated solid was filtered, successfully washed with water, aqueous sodium carbonate solution (10%) and water. The dried sample was recrystallised from suitable solvents (Table –1).
1-Phenyl-3-acetyl-6-benzoylacetyl-5-hydroxy-2-methylindoles : 184a-e

A mixture of 6-acetyl-5-benzoyloxyindole derivatives 183a-e (0.003 mol), powdered potassium hydroxide (0.5 g, 0.009 mol) and dry pyridine (20 mL) was stirred for 2 hours at room temperature. The reaction mixture was then poured on to crushed ice (50 g) and neutralised with dilute hydrochloric acid. The separated solid was filtered, washed with sodium bicarbonate solution (10%), water and recrystallised from suitable solvents (Table -2).

2-Aryl-6-phenyl-7-methyl-8-acetyl-4H-pyrano[2,3-f]indol-4-ones : 185a-e

To 6-benzoylacetyl-5-hydroxyindole derivatives (184a-e) (0.001 mol) in glacial acetic acid (10 mL) was added a drop of concentrated hydrochloric acid and the mixture was heated at reflux for 1 hour. After attaining room temperature, the reaction mixture was poured into ice cold water (20 mL). The separated solid was filtered, washed with water, dried and recrystallised from appropriate solvents (Table-3).

6-Phenyl-8-acetyl-3-aroyl-2,7-dimethyl-4H-pyrano[2,3-f]indol-4-ones : 186a-e

A mixture of 6-benzoylacetyl-5-hydroxyindoles 184a-e (0.001 mol), freshly fused sodium acetate (2.5 g) and acetic anhydride (10 mL) was heated at 150-160 C in an oil bath for 2 hour. It was then cooled and poured onto crushed ice (25 g). The separated solid was filtered, washed with water and recrystallised from suitable solvents (Table-4).
<table>
<thead>
<tr>
<th>Compd.</th>
<th>Substituent</th>
<th>m.p. (°C)</th>
<th>Yield %</th>
<th>Nature (Solvent)</th>
<th>Molecular formula</th>
<th>Elemental analysis found (Calcd.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>183a</td>
<td>C₆H₄-Cl(o)</td>
<td>232-233</td>
<td>64</td>
<td>Yellow granules</td>
<td>C₂₆H₂₀NO₄Cl</td>
<td>C: 70.09 (70.03)  H: 4.47 (4.51)  N: 3.10 (3.14)</td>
</tr>
<tr>
<td>183b</td>
<td>C₆H₄-OCH₃ (p)</td>
<td>221-222</td>
<td>62</td>
<td>Yellow granules</td>
<td>C₂₇H₂₃NO₅</td>
<td>C: 73.49 (73.45)  H: 5.29 (5.25)  N: 3.10 (3.17)</td>
</tr>
<tr>
<td>183c</td>
<td>C₆H₄-NHCOCH₃ (p)</td>
<td>226-227</td>
<td>58</td>
<td>Yellow granules</td>
<td>C₂₈H₂₄N₂O₅</td>
<td>C: 71.72 (71.78)  H: 5.10 (5.15)  N: 5.91 (5.97)</td>
</tr>
<tr>
<td>183e</td>
<td>C₆H₄-NO₂ (m)</td>
<td>234-235</td>
<td>62</td>
<td>Yellow granules</td>
<td>C₂₆H₂₆N₂O₆</td>
<td>C: 68.48 (68.41)  H: 4.49 (4.40)  N: 6.10 (6.13)</td>
</tr>
</tbody>
</table>

Table-1
<table>
<thead>
<tr>
<th>Compd.</th>
<th>Substituent</th>
<th>m.p. (°C)</th>
<th>Yield %</th>
<th>Nature (Solvent)</th>
<th>Molecular formula</th>
<th>Elemental analysis found (Calcd.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>184a</td>
<td>C₆H₄-Cl(ο)</td>
<td>210-211</td>
<td>60</td>
<td>Brown granules</td>
<td>C₂₆H₂₀NO₄Cl</td>
<td>70.08 (70.03) 4.45 (4.51) 3.19 (3.14)</td>
</tr>
<tr>
<td>184b</td>
<td>C₆H₄-OCH₃ (p)</td>
<td>208-209</td>
<td>58</td>
<td>Pale Yellow</td>
<td>C₂₇H₂₅NO₅</td>
<td>73.40 (73.45) 5.21 (5.25) 3.12 (3.17)</td>
</tr>
<tr>
<td>184c</td>
<td>C₆H₄-NHCOCH₃ (p)</td>
<td>238-239</td>
<td>62</td>
<td>Yellow granules</td>
<td>C₂₈H₂₄N₂O₅</td>
<td>71.72 (71.78) 5.10 (5.15) 5.91 (5.97)</td>
</tr>
<tr>
<td>184d</td>
<td>C₆H₂-(NO₂)₂ (3,5)</td>
<td>226-227</td>
<td>52</td>
<td>Yellow granules</td>
<td>C₂₆H₁₉N₃O₈</td>
<td>62.20 (62.27) 3.74 (3.80) 8.30 (8.37)</td>
</tr>
<tr>
<td>184e</td>
<td>C₆H₄-NO₂ (m)</td>
<td>249-250</td>
<td>58</td>
<td>Yellow granules</td>
<td>C₂₆H₂₀N₂O₆</td>
<td>68.48 (68.41) 4.34 (4.40) 6.18 (6.13)</td>
</tr>
</tbody>
</table>

Table-2
Table-3

<table>
<thead>
<tr>
<th>Compd.</th>
<th>Substituent</th>
<th>m.p. (°C)</th>
<th>Yield %</th>
<th>Nature (Solvent)</th>
<th>Molecular formula</th>
<th>Elemental analysis found (Calcd.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>185a</td>
<td>C₆H₄-Cl(o)</td>
<td>264-265</td>
<td>48</td>
<td>Dark brown granules (Ethanol)</td>
<td>C₂₆H₁₈NO₃Cl</td>
<td>C 72.92 (72.98)  H 4.28 (4.23)  N 3.20 (3.27)</td>
</tr>
<tr>
<td>185b</td>
<td>C₆H₄-OCH₃ (p)</td>
<td>248-249</td>
<td>46</td>
<td>Dark brown granules (Ethanol)</td>
<td>C₂₇H₂₁NO₄</td>
<td>C 76.52 (76.58)  H 4.94 (4.99)  N 3.36 (3.30)</td>
</tr>
<tr>
<td>185c</td>
<td>C₆H₄-NHCOCH₃ (p)</td>
<td>262-263</td>
<td>50</td>
<td>Yellow granules (Dioxan)</td>
<td>C₂₈H₂₂N₂O₄</td>
<td>C 74.60 (74.65)  H 4.98 (4.92)  N 6.26 (6.21)</td>
</tr>
<tr>
<td>185d</td>
<td>C₆H₃-(NO₂)₂ (3,5)</td>
<td>248-249</td>
<td>44</td>
<td>Yellow granules (Ethanol)</td>
<td>C₂₆H₁₇N₂O₇</td>
<td>C 64.52 (64.59)  H 3.59 (3.54)  N 8.66 (8.60)</td>
</tr>
<tr>
<td>185e</td>
<td>C₆H₄-NO₂ (m)</td>
<td>276-277</td>
<td>40</td>
<td>Yellow granules (Ethanol)</td>
<td>C₂₆H₁₉N₂O₅</td>
<td>C 71.26 (71.22)  H 4.10 (4.13)  N 6.32 (6.38)</td>
</tr>
<tr>
<td>Compd.</td>
<td>Substituent</td>
<td>m.p. (°C)</td>
<td>Yield %</td>
<td>Nature (Solvent)</td>
<td>Molecular formula</td>
<td>Elemental analysis found (Calcd.)</td>
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<td>--------</td>
<td>-------------</td>
<td>-----------</td>
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</tr>
<tr>
<td>186a</td>
<td>C₆H₄-Cl(o)</td>
<td>240-242</td>
<td>56</td>
<td>Brown granules</td>
<td>C₂₉H₂₀NO₄Cl</td>
<td>C 71.62 (71.68)  H 4.22 (4.28) N 2.30 (2.98)</td>
</tr>
<tr>
<td>186b</td>
<td>C₆H₄- OCH₃ (p)</td>
<td>279-280</td>
<td>50</td>
<td>Brown granules</td>
<td>C₂₉H₂₃NO₅</td>
<td>C 74.88 (74.82)  H 4.91 (4.97) N 3.08 (3.00)</td>
</tr>
<tr>
<td>186c</td>
<td>C₆H₄- NHCOCH₃ (p)</td>
<td>211-212</td>
<td>52</td>
<td>Yellow granules</td>
<td>C₃₀H₂₄N₂O₅</td>
<td>C 73.10 (73.15)  H 4.84 (4.91) N 5.62 (5.68)</td>
</tr>
<tr>
<td>186d</td>
<td>C₆H₃-(NO₂)₂ (3,5)</td>
<td>282-283</td>
<td>50</td>
<td>Yellow granules</td>
<td>C₂₈H₁₉N₃O₄</td>
<td>C 64.06 (64.00)  H 3.68 (3.64) N 7.92 (7.99)</td>
</tr>
<tr>
<td>186e</td>
<td>C₆H₄-NO₂ (m)</td>
<td>264-265</td>
<td>54</td>
<td>Yellow granules</td>
<td>C₂₈H₂₀N₂O₄</td>
<td>C 69.94 (69.99)  H 4.14 (4.19) N 5.88 (5.80)</td>
</tr>
</tbody>
</table>