Synthesis and Characterization of 2H-Pyrrole-2-Ones and 2-Pyrrolidinones based on 3-(isoindol-1,3-dione methyl)-6-hydroxy benzoic acid hydrazide (IHBH)

Overview

The present chapter deals with the heterocyclization of Schiff bases of 3-(isoindol-1,3-dione methyl)-6-hydroxy benzoic acid hydrazide (IHBH) (3a-3h) mentioned in Chapter-2 into (2H)-Pyrrole-2-ones and 2-pyrrolidinone derivatives. In this context, the present chapter is divided into two parts.

Part-A covers with the brief review, synthesis, and characterization of (2H)-Pyrrole-2-ones of IHBH, and

Part-B deals the brief review, synthesis and characterization of 2-pyrrolidinone derivatives of IHBH.
Synthesis and Characterization of 2H-pyrrole-2-ones based on 3-(isoindol-1,3-dione methyl)-6-hydroxy benzoic acid hydrazide

This Part is further divided into two sections. The brief review on (2H)-pyrrole-2-one is summarized in Section-I and the experimental work is described in Section-II.
Brief review on the 2H-pyrrole-2-ones

5.1 PYRROLES

Pyrrole (1) is unsaturated, five-membered nitrogen containing ring. The existence of pyrrole in coal-tar, bone oil, and in general, in products obtained by the dry distillation of proteins was first summarized by Runge [1] in 1834, when he noticed that a substance was present in the ammonia liberated which would impart a red colour to a wood splint moistened with mineral acid. It is also known as azole, imidole, and divinyl enimine.

\[
\begin{array}{c}
\text{N} \\
\text{H} \\
\end{array}
\]

(1)

5.1.1 Physical Properties of Pyrroles

- It is a liquid.
- It possess agreeable empyreumatic odour resembling that of chloroform.
- It is colourless when freshly distilled, darkens unless every trace of oxygen is removed.
- Its density is 0.9690 g/ml at 20°C and 1 atm. pressure, and boiling point is 129.8°C.
- It is best distilled in vacuum.
- Flash point in closed cup is 390°C.
- It is freely soluble in alcohol, ether, and benzene.
- It is sparingly soluble in water and is insoluble in aqueous alkalies.
- It is soluble in dilute acids with decomposition.
Solutions in dilute hydrochloric acid yield pyrrole red, an amorphous, orange coloured substance. Polymerization also takes place under the influence of acids and glycols.

### 5.1.2 Synthesis of Pyrroles

Pyrrole is prepared by distilling succinimide (2) with zinc or sodium metal [2].

\[
\begin{align*}
\text{O} & \quad \text{Zn or Na} \\
\text{N} & \quad \text{distillation} \\
\text{O} & \quad \text{N} \\
& \quad \text{(2)}
\end{align*}
\]

Pyrrole is prepared from reaction of succinaldehyde (3) and ammonia in the presence of acetic acid [3].

\[
\begin{align*}
\text{H} & \quad \text{CH}_3\text{COOH} \\
\text{O} & \quad \text{N} \\
\text{H} & \quad \text{(3)}
\end{align*}
\]

It seems reasonable to suppose that the pyrrole formed by pyrolysis of proteins stems mainly from glutamic acid residues. Thus, it is known that glutamic acid (4) is converted to pyrrolidone-2-carboxylic acid (5) on heating [4]. Pyrolysis of the calcium salt of this acid leads to Pyrrole [5].

\[
\begin{align*}
\text{O} & \quad \text{Ca(OH)}_2 \\
\text{H} & \quad \text{(4)}
\end{align*}
\]
It has been shown that the addition of chalk or barium hydroxide to bone or albumin increases the yield of pyrrole [6], which is found in the non-basic oil fraction.

Pyrrole obtained from bone tar was first purified and analyzed by Anderson [7] in 1857.

The presentation from ammonium mucate (6) [8] or ammonium saccharate [9] superseded the source of Pyrrole. The stoichiometry of this reaction may be made clear by the assumption of a hypothetical dienolic intermediate (VII). The amide of Pyrrole-2-carboxylic acid (VIII) has been isolated as a by-product in this reaction [10]. This method is still preferred for the preparation of Pyrrole in the laboratory [11], although its isolation from manufactured gas may be feasible [12].

\[
\text{NH}_4^+ \cdot \text{OOC(CHOH)}_4\text{COO} \cdot \text{NH}_4^+ \rightarrow \text{NH}_4^+ \cdot \text{OOC-} \overset{\text{OH}}{\text{COO-}} \cdot \text{NH}_4^+ \\
(6)
\]

A promising method for investigation of Pyrrole is that of Reppe et al [13], who prepare Pyrrole from acetylene, formaldehyde, and ammonia. The intermediate 2-butyne-1,4-diol (9) reacts as succinidialdehyde.

\[
\text{HC}≡\text{CH} + \text{CH}_2\text{O} \rightarrow \text{HOH}_2\text{CC≡CCH}_2\text{OH} + \text{NH}_3 \rightarrow \text{NH} \\
(9)
\]
5.2 2H-PYRROLE-2-ONES

The 2-carbonyl derivative of Pyrrole is known as 2H-pyrrole-2-one. It is also known as 2-hydroxypyrrole. 2-hydroxypyrroles are thought to exist in oxo forms such as (10) or (11); structure (12) illustrates a third possible oxo form [14].

Chemical evidence for transformation in the hydroxypyrrole has been reviewed by Fischer and Orth [15]. Since 2-hydroxypyrrole itself is unstable and rapidly resinifies, studies have been confined to some of its more stable derivatives.

5.2.1 Spectral Properties

The ultraviolet spectrum of a compound (13) \((R = \text{COOEt})\) is different from that of (14) and (13) \((R = \text{COOEt})\) does not give a positive test with ferric chloride [16,17], which led to its formulation as shown.

On the basis of their infrared (and ultraviolet) spectra, compounds (15) \((R = \text{H})\) [18], and (16) [19] must exist in oxo forms since they exhibit \(\text{C=O}\) absorption bands: (15) \((R = \text{H})\) at \((1695 \text{ cm}^{-1})\) and (16) \((R = \text{Ac})\) two bands at \((1904 \text{ and } 1681 \text{cm}^{-1})\). Proton resonance spectra confirm structure (15) \((R = \text{H})\) [19a].

The \(\Delta^4\) - structure was assigned to (16) because it added water reversibly, and this is considered to be a characteristic reaction of \(\Delta^4\) - pyrrolones [20], whereas the \(\Delta^3\) - structure was assigned to (15) \((R = \text{H})\) because the ultraviolet spectrum appeared to be of the crotonic acid type [18].
Ultraviolet spectra suggested, and NMR spectra proved that (17) \((R = H, \text{OH})\) should be assigned the \(\Delta^3\)-structure shown.

### 5.2.2 Bioactive 2\(H\)-pyrrole-2-ones

Moore [21] prepared the \(\alpha,\beta\)-unsaturated-\(\gamma\)-lactams (19) from TiCl₄ mediated transformation of vinylogous iron formyl complexes (20) with anilines in CH₂Cl₂.

\[
Q = \begin{array}{c}
\text{CHO} \\
\text{Ph}
\end{array}
\quad \text{and} \quad Q' = \begin{array}{c}
\text{CHO} \\
\text{Ph}
\end{array}
\]

Where, \(R^1=\text{Ph}; R^2=\text{H}; R^1R^2=Q, Q', (\text{CH}_2)_4; R^3=\text{Ph}, \text{etc.}\)
Amidation of 2,4-dichloro-6-methyl phenyl acetic acid with H₂N(Me)(i-Pr)CN via the acid chloride using SOCl₂, followed by alcoholysis of the nitrile using H₂SO₄ and MeOH quench and cyclization of the resultant ester with KOBu-tert in THF, gave title compound (21), and was useful as pesticides and herbicides [22].

Moriyashu et al [23] synthesized 3-pyrrolin-2-one derivatives as herbicides.

Emerson David W and co-workers [24] have prepared 4-substituted-1,5-dihydro-3-hydroxy-2-oxo-1,5-diphenyl-2H-pyrrole by ring opening reactions of 6-oxo-substituted spiro-pyrrolidinediones.

Emerson and co-workers [24] have prepared 4-substituted-1,5-dihydro-3-hydroxy-2-oxo-1,5-diphenyl-2H-pyrrole by ring opening reactions of 6-oxo-substituted spiro-pyrrolidinediones.
Kazuki et al. [25] prepared 2,3-diaryl-2-pyrrolin-5-ones (24) by the reaction of furan or thiophenecarbothioamide, ArCS_{2}NH_{2} with 2-furanacrylic acid.

\[
\text{X}R\text{X'}\text{N}\text{H}\text{O}X
\]

Where, Ar= 2-furyl, 2-thienyl; (24\text{\text{\text{\text{\text{a}}}}}), X=O; Ar'= 2-furyl, 2-thienyl.

\alpha-(2-thienylidene)-\gamma\text{-}aryl-\Delta^{\beta\gamma} butenoids (25) react with ammonia in ethanol to give the corresponding 5-oxo-2-pyrrolines (26). The butenolides (25) and 5-oxo-2-pyrrolines (24) inhibit the growth of yeast and gram negative strains [26].

Where, R=H, Cl, Me, OMe, etc.

Kummer Rudolf et al. [27] prepared 3,4-dihydro-2-pyridones (27) and 2-pyrrolinones (28) as drug and herbicide intermediates.

Where, R^{1}\text{-}R^{5}= H, alkyl, cycloalkyl, aryl, etc.
Toja Emilio and co-workers [28] have prepared and formulate 1-arylsulphonyl-1,5-dihydro-2H-pyrrole-2-ones (29) and tested as memory enhancing drug.

\[
\text{SO}_2R \\
R'O - N - CO \\
(29)
\]

Where, \( R = \) (substituted) aryl, aromatic heterocyclic; \( R' = \) H, alkyl, acyl, etc.

Nobuhiro et al. [29] have prepared 3-pyrrolin-2-ones (30) as anticancer agents.

\[
\text{N} \\
R - O - R' \quad \text{O} \\
(30)
\]

Where, \( R = \) (un)substituted \( C_{2-25} \) alkyl, alkenyl;
\( R' = \) (un)substituted alkyl, aryl, acyl, etc.

Margaret et al. [30] have prepared 3-ethyl-5-hydroxy-4,5-dimethyl-delta-3-pyrrolin-2-ones and they examined the mauve factor of porphyria and its effects on behavior of rats and mice.

Gein and co-workers [31] prepared the 4-substituted-1-mehtyl-5-aryl and 1,5-diaryltetrahydropyrrole-2,3-diones (31) and tested them for their antiviral action.

\[
\text{N} - \text{R'} \\
\text{HO} \\
R - \text{N} - \text{Ar} \\
(31)
\]

Antony et al. [32] tested 2H-pyrrole-2-ones (32) for inhibition of mouse skin tumor promotion by tenuazonic acid.
Synthesis and *in vivo* cytotoxicity of diastereoisomerically modified dolastatin 15 analogs (33) was carried out by Roux, Florence and co-workers [33].
Section-B

Synthesis and Characterization of 2H-Pyrrole-2-Ones Derivatives of 3-(isoindol-1,3-dione methyl)-6-hydroxy benzoic acid hydrazide (IHBH)

5.3 EXPERIMENTAL

Various Schiff bases (3a-3h) on heterocyclization reactions with maleic anhydride gave the desired products 2H-pyrrole-2-ones (8a-8h). Their structures have been characterized on the basis of their analytical and spectral data. The research work is scanned in Scheme-5.1 and the experimental procedures for the synthesis of the series of compounds have been adopted according to the reported method [34].

5.3.1 Materials

The Schiff bases (3a-3h), which are utilized for the synthesis of said compounds, have already been described in Chapter-2. Other chemicals used were of LR grade.

5.3.2 Synthesis of 1-[3-(isoindol-1,3-dione methyl)-6-hydroxy- benzoyl amino]-2-oxo-5-aryl-3,5-dihydro-1H-pyrrole-4-carboxylic acid (8a-h)

Maleic anhydride (0.1 mol) and an imine (3a-3h) (0.1 mol) are refluxed in chloroform (30mL) for about 5 h with TLC monitoring. Then the mixture was allowed to stand for 2 days and then solid was filtered. The product thus formed was recrystallized from ethanol to afford pure 1-[3-(isoindol-1,3-dione methyl)-6-hydroxy- benzoyl amino]-2-oxo-5-aryl-3,5-dihydro-1H-pyrrole-4-carboxylic acid in (8a-8h) good yield. The analytical and spectral data of the prepared compounds (8a-8h) are described.
Ar = a - phenyl
    b - 4 - hydroxy phenyl
    c - 2 - hydroxy phenyl
    d - 4 -methoxy phenyl
    e - 4 - hydroxy-3-methoxy phenyl
    f - 4 - chlorophenyl
    g - 2 - nitro phenyl
    h - 5 -bromo-2-hydroxy-phenyl

Scheme 5.1
Compound-8a

1-[3-(Isoindol-1,3-dione methyl)-6-hydroxy- benzoyl amino]-2-oxo-5-phenyl-3,5-
dihydro-1H-pyrrole-4-carboxylic acid

<table>
<thead>
<tr>
<th>Molecular Formula: C_{27}H_{19}N_{3}O_{7}</th>
<th>Elemental Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Weight: 497 g/mol</td>
<td>% C    % H    % N</td>
</tr>
<tr>
<td>Melting Point: 175-76°C (uncorrected)</td>
<td>Calculated 65.19 3.82 8.45</td>
</tr>
<tr>
<td>Yield: 67%</td>
<td>Found    65.0 3.7 8.4</td>
</tr>
</tbody>
</table>

Infrared spectral features (KBr, cm\(^{-1}\))

- 3054, 1532 Aromatic C-H
- 1667 C=O of COOH
- 1717 C=O of pyrrole-2-one

Other bands same as parent Schiff bases

\(^1\)H NMR spectral features (DMSO-d\(_6\), ppm)

- 6.15-8.13 (Multiplet, Aromatic H + NH of CONH)
- 4.7 (H, s, C\(_5\)H)
- 5.15 (H, s, C\(_3\)H)
- 12.92 (H, s, COOH)
- 2.65 (2H of CH\(_2\))
- 3.9 (H, s, OH)

\(^{13}\)C NMR spectral features (DMSO-d\(_6\), ppm)

- 102-133 Aromatic C
- 145-166 C of COOH/CO
- 55 CH
- 35 CH\(_2\)
Compound-8b

\[
\begin{align*}
\text{Molecular Formula: } & \quad C_{27}H_{19}N_3O_8 \\
\text{Molecular Weight: } & \quad 513 \text{ g/mol} \\
\text{Melting Point: } & \quad 180-82 \degree \text{C (uncorrected)} \\
\text{Yield: } & \quad 67\% \\
\text{Infrared spectral features (KBr, } & \quad 3054, 1532 \text{ Aromatic C-H} \\
& \quad 1667 \text{ C=O of COOH} \\
& \quad 1717 \text{ C=O of pyrrole-2-one} \\
& \quad \text{Other bands same as parent Schiff bases} \\
\text{NMR spectral features (DMSO-} & \quad 6.15-8.13 \text{ (Multiplet, Aromatic H + NH of CONH)} \\
\text{d6, ppm)} & \quad 4.7 \text{ (H, s, C_5H)} \\
& \quad 5.15 \text{ (H, s, C_3H)} \\
& \quad 12.92 \text{ (H, s, COOH)} \\
& \quad 2.65 \text{ (2H of CH\textsubscript{2})} \\
& \quad 3.9 \text{ (H, s, OH)} \\
\text{NMR spectral features (DMSO-} & \quad 102-133 \text{ Aromatic C} \\
\text{d6, ppm)} & \quad 145-166 \text{ C of COOH/CO} \\
& \quad 55 \text{ CH} \\
& \quad 35 \text{ CH_2}
\end{align*}
\]

1-[3-(Isoindol-1,3-dione methyl)-6-hydroxy- benzoyl amino]-2-oxo-5-(4-hydroxy phenyl)-3,5-dihydro-1H-pyrrole-4-carboxylic acid
**Compound-8c**

![Chemical Structure](image)

1-[3-(Isoindol-1,3-dione methyl)-6-hydroxy- benzoyl amino]-2-oxo-5-
(2-hydroxy phenyl)-3,5-dihydro-1H-pyrrole-4-carboxylic acid

---

**Molecular Formula:** C$_{27}$H$_{19}$N$_3$O$_8$

**Molecular Weight:** 513 g/mol

**Melting Point:** 178-80°C (uncorrected)

**Yield:** 73%

**Elemental Analysis**

<table>
<thead>
<tr>
<th></th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated</td>
<td>63.15</td>
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</tr>
<tr>
<td>Found</td>
<td>63.1</td>
<td>3.6</td>
<td>8.1</td>
</tr>
</tbody>
</table>

**Infrared spectral features (KBr, cm$^{-1}$)**

- 3054, 1532 Aromatic C-H
- 1667 C=O of COOH
- 1717 C=O of pyrrole-2-one

Other bands same as parent Schiff bases

**$^1$H NMR spectral features (DMSO-d$_6$, ppm)**

- 6.15-8.13 (Multiplet, Aromatic H + NH of CONH)
- 4.7 (H, s, C$_3$H)
- 5.15 (H, s, C$_3$H)
- 12.92 (H, s, COOH)
- 2.65 (2H of CH$_2$)
- 3.9 (H, s, OH)

**$^{13}$C NMR spectral features (DMSO-d$_6$, ppm)**

- 102-133 Aromatic C
- 145-166 C of COOH/CO
- 55 CH
- 35 CH$_2$
1-[3-(Isoindol-1,3-dione methyl)-6-hydroxy- benzoyl amino]-2-oxo-5-(4-methoxy phenyl)-3,5-dihydro-1H-pyrrole-4-carboxylic acid

**Compound-8d**

![Chemical Structure](image)

Molecular Formula: C_{28}H_{21}N_{3}O_{8}
Molecular Weight: 527 g/mol
Melting Point: 188-89°C (uncorrected)
Yield: 72%

**Infrared spectral features (KBr, cm⁻¹)**
- 3054, 1532: Aromatic C-H
- 1667: C=O of COOH
- 1717: C=O of pyrrole-2-one

Other bands same as parent Schiff bases

**Elemental Analysis**

<table>
<thead>
<tr>
<th></th>
<th>Calculated</th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td></td>
<td>63.6</td>
<td>3.8</td>
<td>7.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>63.75</td>
<td>3.98</td>
<td>7.96</td>
</tr>
</tbody>
</table>

**¹H NMR spectral features (DMSO-d₆, ppm)**
- 6.15-8.13: (Multiplet, Aromatic H + NH of CONH)
- 4.7: (H, s, C₃H)
- 5.15: (H, s, C₃H)
- 12.92: (H, s, COOH)
- 2.65: (2H of CH₂)
- 3.78: (3H of OCH₃)
- 3.9: (H, s, OH)

**¹³C NMR spectral features (DMSO-d₆, ppm)**
- 102-133: Aromatic C
- 145-166: C of COOH/CO
- 55: CH
- 35: CH₂
- 60: OCH₃
Compound-8e

1-[3-(Isoindol-1,3-dione methyl)-6-hydroxy- benzoyl amino]-2-oxo-5-
(4-hydroxy-3-methoxy phenyl)-3,5-dihydro-1H-pyrrole-4-carboxylic acid

Molecular Formula: C_{28}H_{21}N_{3}O_{9}
Molecular Weight: 543 g/mol
Melting Point: 182-84°C (uncorrected)
Yield: 75%

Elemental Analysis
% C  % H  % N
Calculated 61.87 3.86 7.73
Found 61.7 3.7 7.7

Infrared spectral features (KBr, cm\(^{-1}\))
3054, 1532  Aromatic C-H
1667        C=O of COOH
1717        C=O of pyrrole-2-one
Other bands same as parent Schiff bases
6.15-8.13  (Multiplet, Aromatic H + NH of CONH)
4.7        (H, s, C\(_5\)H)
5.15        (H, s, C\(_3\)H)
12.92        (H, s, COOH)
2.65        (2H of CH\(_2\))
3.78        (3H of OCH\(_3\))
3.9        (H, s, OH)

\(^{13}\)C NMR spectral features (DMSO-d\(_6\), ppm)
102-133 Aromatic C
145-166 C of COOH/CO
55       CH
35       CH\(_2\)
60       OCH\(_3\)
Compound-8f

1-[3-(Isoindol-1,3-dione methyl)-6-hydroxy- benzoyl amino]-2-oxo-5-
(4-chloro phenyl)-3,5-dihydro-1H-pyrrole-4-carboxylic acid

Molecular Formula: C$_{27}$H$_{18}$N$_{3}$O$_{7}$Cl
Molecular Weight: 531.5 g/mol
Melting Point: 178-80°C (uncorrected)
Yield: 64%

**Elemental Analysis**

<table>
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<tr>
<th></th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated</td>
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<tr>
<td>Found</td>
<td>60.8</td>
<td>3.3</td>
<td>7.8</td>
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</table>

**Infrared spectral features (KBr, cm$^{-1}$)**

<table>
<thead>
<tr>
<th>Wavenumber</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>3054, 1532</td>
<td>Aromatic C-H</td>
</tr>
<tr>
<td>1667</td>
<td>C=O of COOH</td>
</tr>
<tr>
<td>1717</td>
<td>C=O of pyrrole-2-one</td>
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Other bands same as parent Schiff bases

**$^1$H NMR spectral features (DMSO-d$_6$, ppm)**

<table>
<thead>
<tr>
<th>ppm</th>
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<tbody>
<tr>
<td>6.15-8.13</td>
<td>(Multiplet, Aromatic H + NH of CONH)</td>
</tr>
<tr>
<td>4.7</td>
<td>(H, s, C$_5$H)</td>
</tr>
<tr>
<td>5.15</td>
<td>(H, s, C$_3$H)</td>
</tr>
<tr>
<td>12.92</td>
<td>(H, s, COOH)</td>
</tr>
<tr>
<td>2.65</td>
<td>(2H of CH$_2$)</td>
</tr>
<tr>
<td>3.9</td>
<td>(H, s, OH)</td>
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</table>

**$^{13}$C NMR spectral features (DMSO-d$_6$, ppm)**

<table>
<thead>
<tr>
<th>ppm</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>102-133</td>
<td>Aromatic C</td>
</tr>
<tr>
<td>145-166</td>
<td>C of COOH/CO</td>
</tr>
<tr>
<td>55</td>
<td>CH</td>
</tr>
<tr>
<td>35</td>
<td>CH$_2$</td>
</tr>
</tbody>
</table>
Compounds-8g

1-[3-(Isoindol-1,3-dione methyl)-6-hydroxy- benzoyl amino]-2-oxo-5-(2-nitro phenyl)-3,5-dihydro-1H-pyrrole-4-carboxylic acid

**Molecular Formula:** C$_{27}$H$_{18}$N$_{4}$O$_{9}$

**Molecular Weight:** 542 g/mol

**Melting Point:** 207-08°C (uncorrected)

**Yield:** 66%

**Elemental Analysis**

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<th>% H</th>
<th>% N</th>
</tr>
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<tr>
<td><strong>Calculated</strong></td>
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<td>3.32</td>
<td>7.74</td>
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<tr>
<td><strong>Found</strong></td>
<td>59.7</td>
<td>3.3</td>
<td>7.7</td>
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**Infrared spectral features (KBr, cm$^{-1}$)**

<table>
<thead>
<tr>
<th>Wavenumber</th>
<th>Description</th>
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<tbody>
<tr>
<td>3054, 1532</td>
<td>Aromatic C-H</td>
</tr>
<tr>
<td>1667</td>
<td>C=O of COOH</td>
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<tr>
<td>1717</td>
<td>C=O of pyrrole-2-one</td>
</tr>
<tr>
<td>Other bands same as parent Schiff bases</td>
<td></td>
</tr>
</tbody>
</table>

**1H NMR spectral features (DMSO-d$_6$, ppm)**

<table>
<thead>
<tr>
<th>ppm</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.15-8.13</td>
<td>Multiplet, Aromatic H + NH of CONH</td>
</tr>
<tr>
<td>4.7</td>
<td>(H, s, C$_5$H)</td>
</tr>
<tr>
<td>5.15</td>
<td>(H, s, C$_3$H)</td>
</tr>
<tr>
<td>12.92</td>
<td>(H, s, COOH)</td>
</tr>
<tr>
<td>2.65</td>
<td>(2H of CH$_2$)</td>
</tr>
<tr>
<td>3.9</td>
<td>(H, s, OH)</td>
</tr>
</tbody>
</table>

**13C NMR spectral features (DMSO-d$_6$, ppm)**

<table>
<thead>
<tr>
<th>ppm</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>102-133</td>
<td>Aromatic C</td>
</tr>
<tr>
<td>145-166</td>
<td>C of COOH/CO</td>
</tr>
<tr>
<td>55</td>
<td>CH</td>
</tr>
<tr>
<td>35</td>
<td>CH$_2$</td>
</tr>
</tbody>
</table>
Compound-8h

1-[3-(Isoindol-1,3-dione methyl)-6-hydroxy- benzoyl amino]-2-oxo-5-
(5-bromo-2-hydroxy phenyl)-3,5-dihydro-1H-pyrrole-4-carboxylic acid

<table>
<thead>
<tr>
<th>Molecular Formula: C_{27}H_{18}N_{3}O_{8}Br</th>
<th>Elemental Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Weight: 592 g/mol</td>
<td>% C  % H  % N</td>
</tr>
<tr>
<td>Melting Point: 192-194°C (uncorrected)</td>
<td>Calculated</td>
</tr>
<tr>
<td>Yield: 60%</td>
<td>Found</td>
</tr>
</tbody>
</table>

Infrared spectral features (KBr, cm⁻¹)

| 3054, 1532 | Aromatic C-H |
| 1667       | C=O of COOH  |
| 1717       | C=O of pyrrole-2-one |

Other bands same as parent Schiff bases

1H NMR spectral features (DMSO-d₆, ppm)

| 6.15-8.13 (Multiplet, Aromatic H + NH of CONH) |
| 4.7 (H, s, C₃H)                               |
| 5.15 (H, s, C₃H)                             |
| 12.92 (H, s, COOH)                           |
| 2.65 (2H of CH₂)                             |
| 3.9 (H, s, OH)                               |

13C NMR spectral features (DMSO-d₆, ppm)

| 102-133 | Aromatic C |
| 145-166 | C of COOH/CO |
| 55      | CH         |
| 35      | CH₂        |
Fig. 5.1 IR Spectrum of Compound 8a

Fig. 5.2 IR Spectrum of Compound 8d
Fig. 5.3 IR Spectrum of Compound 8e
Fig. 5.4 $^1$H NMR Spectrum of Compound 8a
Fig. 5.5 $^1$H NMR Spectrum of Compound 8d
Fig. 5.6 $^1$H NMR Spectrum of Compound 8e
Fig. 5.7 $^{13}$C NMR Spectrum of Compound 8a
Fig. 5.8 $^{13}$C NMR Spectrum of Compound 8b
Fig. 5.9 $^{13}$C NMR Spectrum of Compound 8e
Fig. 5.10 Mass spectrum of Compound 8a
5.4 RESULTS AND DISCUSSION

Structures of Schiff bases (3a-3h) have been already confirmed in the Chapter-2 of the thesis. As we know that the Schiff bases are the crucial material for the preparation of heterocyclic compounds like 2H-pyrrole-2-ones, 2-pyrrolidinones, etc. These Schiff bases (3a-3h) on cyclocondensation reaction with maleic anhydride afford the biologically active 2 H-pyrrole-2-one derivatives (8a-8h).

Their structures were confirmed by analytical and spectral data. The C, H, and N contents of the prepared compounds were consistent with their predicted structures as shown in Scheme-5.1. The infrared spectra show the band in the region 1680-1710 cm\(^{-1}\) for carbonyl (\(\text{\textgreater C=O}\)) group, which is the characteristic band for the cyclic 2 H-pyrrole-2-one ring.

The proton magnetic resonance spectra of the prepared compounds (8a-8h) show singlet at 5.15 ppm for CH proton at position-5 in the 2H-pyrrole-2-one ring. All other signals are at their respective positions in the PMR spectrum.

The Mass spectrum of compound-8a (Fig. 5.10) predicts that the molecular mass of compound-8a agreed with the peak obtained at 498 m/z.

The analytical and spectral data for all the compounds (8a-8h) are shown. The IR, PMR and \(^{13}\)C NMR spectra are scanned in Fig. 5.1-5.9 for selective compounds.
Synthesis and Characterization of 2-pyrrolidinones based on 3-(isoindol-1,3-dione methyl)-6-hydroxy benzoic acid hydrazide (IHBH)

This Part-B is divided into two sections.

The brief review on 2-pyrrolidinones is summarized in Section-I and the experimental part is described in Section-II.

The present part deals with the heterocyclization of Schiff bases of 3-(isoindol-1,3-dione methyl)-6-hydroxy benzoic acid hydrazide (IHBH) mentioned in Chapter-2 into 2-pyrrolidinones derivatives. In this context, the brief notes on 2-pyrrolidinones are summarized in Section-I. The experimental parts for the series of compounds are described in section-II.
Brief review on 2-pyrrolidinones

Section-I deals with the introductions of Pyrrolidines and 2-pyrrolidinones.

5.5 PYRROLIDINE(S)

It is a saturated, five membered nitrogen containing ring. It is also known as tetrahydro Pyrrole. It is found in tobacco and carrot leaves. Its probable biosynthesis is from amithine and putrescine.

\[
\begin{array}{c}
\text{N} \\
\text{H}
\end{array}
\]

(34)

5.5.1 Physical properties of Pyrrolidines

- Pyrrolidine is almost colourless liquid with unpleasant ammonia like odour.
- It readily form salts which serve identification.
- It is a strong base and miscible with water.
- It is soluble in alcohol, ether, chloroform.
- Its b.p. is 88.5-89°C and density is 0.8520 g/ml at 22.5°C.

The Pyrrolidine differ strongly from Pyrrole in their basic properties. The contrasting basic properties of the pyrrolines and pyrrolidines on the one hand, and the Pyrrole on the other hand, lead further support to concept that the resonance of Pyrrole suppresses its basic properties and accentuates its acidic character.
5.5.2 Synthetic methods for pyrrolidines

Pyrrolidine can be prepared by the reduction of Pyrrole by means of phosphorous and hydrogen iodide [35] or by catalytic hydrogenation [36].

\[
\begin{array}{c}
\text{Pyrrole} \\
\text{HI / P} \\
\text{Pyrroline} \\
\text{Pyrollidine} \\
\end{array}
\]

It is also prepared by electrolytic reaction of substituted succinimide [37].

\[
\begin{array}{c}
\text{succinimide} \\
\text{catalytic reduction} \\
\text{pyrrolidine} \\
\end{array}
\]

A very convenient method for obtaining certain pyrrolidines involves reaction of the commercially available 1,4-dibromobutane or 1,4-dibromopentane with ammonia or a primary amine [38].

\[
\begin{array}{c}
\text{BrCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Br} + \text{NH}_3 / \text{R-NH}_2 \\
\text{Pyrollidine} \\
\text{Where, R= H, alkyl, aryl, etc.} \\
\end{array}
\]

5.6 2-PYRROLIDINONES

The 2-carbonyl derivative of Pyrrolidine is known as 2-pyrrolidinone. It is also known as 2-pyrrolidone, 2-oxopyrrolidine, pyrrolidone, 2-ketopyrrolidine.
5.6.1 Physical Properties of 2-Pyrrolidinones

- It is liquid above 25°C.
- Its b.p. is 245°C and flash point in open cup is 129°C (265°F).
- In the presence of the stoichiometric amount of water a crystalline monohydrate, m.p. 30°C, can be formed.
- It is non-corrosive.
- It has good chemical stability.
- It is miscible with water, ethanol, ether, chloroform, benzene, ethylacetate, CS₂, etc.

5.6.2 Use of 2-Pyrrolidinones

It is an intermediate in the manufacturing of polyvinylpyrrolidinone and polypyrrolidone (a polymer, formed in the presence of alkaline catalysts). It is also used as high boiling solvent in petroleum processing, acrylonitrile manufacturing.

It is an industrial solvent for polymers, chlordane, DDT, sorbitol, glycerol, iodine, sugars. It is used in speciality printers ink. It is used as plasticizer and coalescing agent for acrylicstyrene emulsion type floor polishes.

5.6.3 Synthetic methods for 2-Pyrrolidinones

It is prepared from glutamic acid [39].

It is prepared on a large scale from butyrolacetone by Reppe process [40].
5.6.4 Biologically Active 2-Pyrrolidinone Derivatives

Waldemar and Aimin [41] studied the high facial selectivity through chelation of magnesium ions in the DMD epoxidation of unsaturated imides with chiral pyrrolidinone auxiliaries (36).

\[
\begin{align*}
R' & \quad O \\
& \quad R'' \\
& \quad (36)
\end{align*}
\]

Where, R’=H, R’’=Ph; R’=PH₃C, R”=Me, Ph.

Estimation of the lipophilicity of antiarrhythmic and antihypertensive active-1-substituted pyrrolidin-2-one and Pyrrolidine derivatives was carried out by Katarzyna and Barbara [42].

Cristiana et al [43] carried out the stereo selective reductive amination of chiral trans-3-acetyl-4-alkyl pyrrolidin-2-ones.

\[
\begin{align*}
(37a) & \quad (37b) & \quad (37c) & \quad (37d)
\end{align*}
\]

Where, R= CH₂=Ch, EtO₂CCH₂ (37 a & b)  
R= CH₂=CH, EtO₂CCH₂; X= Ac (37 c & d)  
R= CH₂=CH; X= Boc (37c)
Huang Pei-Qiang and co-workers [44] prepared (S)-vasicol and (S)-3-hydroxy-2-pyrrolidinone (38).

![Chemical Structure](image)

Where, R= H, NH₂.

Thamotharan et al [45] prepared 1-[2-(4-nitrophenoxy)acetyl]pyrrolidin-2-one as an antiamnestic agent.

Guindon and Bancheqroun [46] studied the influence of N-substituted lactams (39) on acyclic free radical based hydrogen transfer.

![Chemical Structure](image)

Where, R= H, Et, CHMe₂, etc.

Preparation of 3-acylamino-3-methyl pyrrolidin-2-ones and analogs (40) as metabotropic glutamate receptor antagonists was carried out by Clark, Barry Peter and co-workers [47].
Where, \( n = 0-2 \); \( X = O, S, NH, N-OH \); \( R', R'' = H, CN, COOR, alkyl; \)
\( R''' = alkyl, alkenyl, CH_2OH, etc.; Z = unsub. Indanyl, indenyl, etc. \)

The 1,3-dipolar cycloaddition reaction of N-benzyl-C-heteroaryl nitrones gave preferentially trans substituted 3,5-disubstituted isoazolidines (endo approach) which can be further converted into the corresponding 5-heteroaryl-3-pyrrolidinones. A theoretical study of the cycloaddition reaction by using both semiempirical (AMI, PM3) and ab initio (HF/3-21G, HF/6-31G*//3-21G) methods has also been carried out by Merino, Pedro and co-workers [48].

Becker Michael et al [49] have been carried out synthesis, SAR and in vivo activity of novel thienopyridine sulphonamide pyrrolidones as factor Xa inhibitors.

Jacobson [50] have prepared pyrrolidinone hydroxamic acid derivatives (41,42) for their use in the treatment of diseases related to connective tissue degradation.

Donal et al [51] have studied the transdermal and dermal enhancing activity of pyrrolidinones in hairless mouse skin.
Saturnino et al [52] have prepared a new class of pyrrolidin-2-ones and were tested for the anticonvulsant activity on pentylenetetrazole treated mice.

Hajime and co-workers [53] have synthesized pyrrolidinone derivatives with antipsychotic and cerebral antiischemic activity.

Where, $R' = C_{1-12}$ alkyl, hydrogenated $C_{9-15}$ condensed polycyclic hydrocarbon, unsub. Ph; $R'' = H, C_{1-12}$ alkyl; $n = 1-3$; $A =$ certain (un)sub. Cyclic amino (Pyrrolidine, piperidine, etc.) upto 10-membered ring.; $R = CH_2OH$.

Cushman and Mudaj [34] carried out the mechanistic interpretation of the electronic and steric effects that determine the stereochemical outcome of the reaction of Schiff bases with homophthalic anhydride and 3-phenylsuccinic anhydride.

Where, $R =$ alkyl, aryl, etc. (45), $R = H, Cl, Me$, etc.; $R' = Me, H$, etc. (46).
Synthesis and characterization of 2-Pyrrolidinone derivatives

5.7 EXPERIMENTAL

Various Schiff bases (3a-3h) on heterocyclization reactions with succinic anhydride gave the desired products, that is, 2-pyrrolidinones (9a-9h). Their structures have been characterized on the basis of their analytical and spectral data. The research work is presented in Scheme-5.2 and the experimental procedures for the synthesis of the series of compounds have been adopted according to the reported method [34].

5.7.1 Materials

The Schiff bases (3a-3h), which utilized for the synthesis of said compounds, have already been described in Chapter-2. Other chemicals used were of LR grade.

5.7.2 Synthesis of 1-[3-(isoindol-1,3-dione methyl)-6-hydroxy- benzoyl amino]-2-oxo-5-aryl-pyrrolidinone-4-carboxylic acid (9a-9h)

Succinic anhydride (0.1mol) and an imine compound (3a-3h) (0.1mol) were heated under reflux in chloroform (30 ml) for about 5 h with TLC monitoring. After the mixture was allowed to stand for 2 days, the solid was filtered. The product thus formed was recrystallized from ethanol to give pure 1-[3-(isoindol-1,3-dione methyl)-6-hydroxy- benzoyl amino]-2-oxo-5-aryl-3,5-dihydro-1H-pyrrolidinone-4-carboxylic acid (9a-9h) in good yield.

The analytical and spectral data of the compounds (9a-9h) are described as follow.
Schiff base formation with succinic anhydride:

\[
\text{CHAr} \quad \text{(3a-h)} \quad \text{schiff base}
\]

\[
\text{CONHN} \equiv \text{CHAr}
\]

\[
\text{Succinic anhydride}
\]

\[
\text{CONHN} \equiv \text{Ar}
\]

\[
\text{COOH}
\]

\[
\text{(9a-h)}
\]

Ar = a - phenyl
b - 4 - hydroxy phenyl
c - 2 - hydroxy phenyl
d - 4 - methoxy phenyl
e - 4 - hydroxy-3-methoxy phenyl
f - 4 - chlorophenyl
g - 2 - nitro phenyl
h - 5 -bromo-2-hydroxy-phenyl

Scheme-5.2
Compound-9a

1-[3-(Isoindol-1,3-dione methyl)-6-hydroxy- benzoyl amino]-2-oxo-5-phenyl-3,5-dihydro-1H-pyrrolidinone-4-carboxylic acid

Molecular Formula: C_{27}H_{21}N_{3}O_{7}
Molecular Weight: 499 g/mol
Melting Point: 183-85°C (uncorrected)
Yield: 72%

Elemental Analysis

<table>
<thead>
<tr>
<th></th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated</td>
<td>64.92</td>
<td>4.20</td>
<td>8.41</td>
</tr>
<tr>
<td>Found</td>
<td>64.85</td>
<td>4.15</td>
<td>8.35</td>
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</table>

Infrared spectral features (KBr, cm\(^{-1}\))

<table>
<thead>
<tr>
<th>Wave Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>3055, 1508</td>
<td>Aromatic C-H</td>
</tr>
<tr>
<td>1670</td>
<td>C=O of COOH</td>
</tr>
<tr>
<td>1717</td>
<td>C=O of Pyrrolidinone</td>
</tr>
</tbody>
</table>

PMR spectral features (DMSO-d\(_6\), ppm)

<table>
<thead>
<tr>
<th>Wave Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.3-8.1</td>
<td>(Multiplet, Aromatic + NH of CONH)</td>
</tr>
<tr>
<td>5.15</td>
<td>(H, d, C(_5))</td>
</tr>
<tr>
<td>4.7</td>
<td>(H, m, C(_4))</td>
</tr>
<tr>
<td>3.4 - 3.8</td>
<td>(2H, d, C(_3))</td>
</tr>
<tr>
<td>12.9</td>
<td>(H, s, COOH)</td>
</tr>
<tr>
<td>2.63</td>
<td>(2H of CH(_2))</td>
</tr>
<tr>
<td>4.60</td>
<td>(H of OH)</td>
</tr>
</tbody>
</table>

CMR spectral features (DMSO-d\(_6\), ppm)

<table>
<thead>
<tr>
<th>Wave Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>102-131</td>
<td>Aromatic C</td>
</tr>
<tr>
<td>165/166</td>
<td>C of COOH/ CONH</td>
</tr>
<tr>
<td>55</td>
<td>CH</td>
</tr>
<tr>
<td>33</td>
<td>CH(_2)</td>
</tr>
<tr>
<td>90</td>
<td>CH(_2)CO</td>
</tr>
</tbody>
</table>
Compound-9b

1-[3-(Isoindol-1,3-dione methyl)-6-hydroxy-benzoyl amino]-2-oxo-5-(4-hydroxy phenyl)-3,5-dihydro-1H-pyrrolidinone-4-carboxylic acid

Molecular Formula: C_{27}H_{21}N_{3}O_{8}
Molecular Weight: 515 g/mol
Melting Point: 192-93°C (uncorrected)
Yield: 65%

Elemental Analysis

<table>
<thead>
<tr>
<th></th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated</td>
<td>62.91</td>
<td>4.07</td>
<td>8.15</td>
</tr>
<tr>
<td>Found</td>
<td>62.85</td>
<td>4.05</td>
<td>8.15</td>
</tr>
</tbody>
</table>

Infrared spectral features (KBr, cm\(^{-1}\))

- 3055, 1508: Aromatic C-H
- 1670: C=O of COOH
- 1717: C=O of Pyrrolidinone

Other bands same as parent Schiff base

PMR spectral features (DMSO-\(d_6\), ppm)

- 6.3-8.1: (Multiplet, Aromatic H + NH of CONH)
- 5.15: (H, d, C\(_3\))
- 4.7: (H, m, C\(_4\))
- 3.4 - 3.8: (2H, d, C\(_3\))
- 12.9: (H, s, COOH)
- 2.63: (2H of CH\(_2\))
- 4.60: (H of OH)

CMR spectral features (DMSO-\(d_6\), ppm)

- 102-131: Aromatic C
- 165/166: C of COOH/CONH
- 55: CH
- 33: CH\(_2\)
- 90: CH\(_2\)CO
Compound-9c

1-[3-(Isoindol-1,3-dione methyl)-6-hydroxy- benzoyl amino]-2-oxo-5-
(2-hydroxy phenyl)-3,5-dihydro-1H-pyrrolidinone-4-carboxylic acid

Molecular Formula: C_{27}H_{21}N_{3}O_{8}  
Molecular Weight: 515 g/mol  
Melting Point: 192-93°C (uncorrected)  
Yield: 65%

<table>
<thead>
<tr>
<th>Infrared Spectral Features cm^{-1}</th>
<th>PMR spectral features (DMSO-d_{6}, ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3050, 1600 Aromatic C-H</td>
<td>6.1-8.1 ( Multiplet, Aromatic H +</td>
</tr>
<tr>
<td>1670 C=O of COOH</td>
<td>NH of CONH)</td>
</tr>
<tr>
<td>1717 C=O of Pyrrolidinone</td>
<td>3.9 (H, s, OH)</td>
</tr>
<tr>
<td></td>
<td>12.92 (H, s, COOH)</td>
</tr>
<tr>
<td>Other bands same as parent Schiff base</td>
<td>5.15 (H, d, C_{3})</td>
</tr>
<tr>
<td></td>
<td>4.7 (H, m, C_{4})</td>
</tr>
<tr>
<td></td>
<td>3.4 - 3.8 (2H, d, C_{3})</td>
</tr>
<tr>
<td></td>
<td>2.60 (2H of CH_{2})</td>
</tr>
<tr>
<td></td>
<td>4.60 (H of OH)</td>
</tr>
</tbody>
</table>

CMR spectral features (DMSO-d_{6}, ppm)

102-128 Aromatic C  
165/166 C of COOH/CONH  
55 CH  
33 CH_{2}  
91 CH_{2}CO
Compound-9d

1-[2-Methyl-perimidin-1,N-acetyl hydrazide]-2-oxo-5-(4-methoxy phenyl)-pyrrolidine-4-carboxylic acid

Molecular Formula: C_{28}H_{23}N_{3}O_{8}
Molecular Weight: 529 g/mol
Melting Point: 182-83°C (uncorrected)
Yield: 65%

<table>
<thead>
<tr>
<th>Elemental Analysis</th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated</td>
<td>63.51</td>
<td>4.34</td>
<td>7.93</td>
</tr>
<tr>
<td>Found</td>
<td>63.45</td>
<td>4.30</td>
<td>7.85</td>
</tr>
</tbody>
</table>

Infrared spectral features (KBr, cm⁻¹)

- 3050, 1500 Aromatic C-H
- 1670 C=O of COOH
- 1717 C=O of pyrrolidinone

Other bands same as parent Schiff base

PMR spectral Features (DMSO-d₆, ppm)

- 6.3-8.1 (Multiplet, Aromatic H + NH of CONH)
- 3.9 (H, s, -OH)
- 12.92 (H, s, COOH)
- 5.15 (H, d, C₃)
- 4.7 (H, m, C₄)
- 3.4 - 3.8 (2H, d, C₃)
- 2.65 (2H of CH₂)
- 3.83 (3H, s, OCH₃)

CMR spectral features (DMSO-d₆, ppm)

- 102-129 Aromatic C
- 165/166 C of COOH/CONH
- 55 CH
- 33 CH₂
- 90 CH₂CO
Compound-9e

1-[3-(Isoindol-1,3-dione methyl)-6-hydroxy- benzoyl amino]-2-oxo-5-
(4-hydroxy-3-methoxy phenyl)-3,5-dihydro-1H-pyrrolidinone-4-carboxylic acid

Molecular Formula: C$_{28}$H$_{23}$N$_{3}$O$_{9}$
Molecular Weight: 545 g/mol
Melting Point: 196-97°C (uncorrected)
Yield: 83 %

Elemental Analysis

<table>
<thead>
<tr>
<th></th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated</td>
<td>61.65</td>
<td>4.22</td>
<td>7.70</td>
</tr>
<tr>
<td>Found</td>
<td>61.50</td>
<td>4.20</td>
<td>7.60</td>
</tr>
</tbody>
</table>

Infrared spectral features (KBr, cm$^{-1}$)

- 3055, 1508 Aromatic C-H
- 1670 C=O of COOH
- 1717 C=O of pyrrolidinone

Other bands same as parent Schiff base

PMR spectral features (DMSO-d$_6$, ppm)

- 6.1-8.1 (Multiplet, Aromatic H + NH of CONH)
- 12.92 (H, s, COOH)
- 5.15 (H, d, C$_5$)
- 4.7 (H, m, C$_4$)
- 3.4 - 3.8 (2H, d, C$_3$)
- 2.65 (2H of CH$_2$)
- 3.83 (3H, s, OCH$_3$)
- 3.9 (H, s, OH)

CMR spectral Features (DMSO-d$_6$, ppm)

- 102-130 Aromatic C
- 165/166 C of COOH/CO
- 55 CH
- 33 CH$_2$
**Compound-9f**

![Chemical Structure](image)

1-[3-(Isoindol-1,3-dione methyl)-6-hydroxy- benzoyl amino]-2-oxo-5-(4-chloro phenyl)-3,5-dihydro-1H-pyrrolidinone-4-carboxylic acid

---

**Molecular Formula:** C$_{27}$H$_{20}$N$_3$O$_7$Cl

**Molecular Weight:** 533.5 g/mol

**Melting Point:** 208-10°C (uncorrected)

**Yield:** 78%

**Infrared spectral features (KBr, cm$^{-1}$)**

- 3050, 1500 Aromatic C-H
- 1670 C=O of COOH
- 1717 C=O of Pyrrolidinone

*Other bands same as parent Schiff base*

**Elemental Analysis**

<table>
<thead>
<tr>
<th></th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Calculated</strong></td>
<td>60.73</td>
<td>3.74</td>
<td>7.87</td>
</tr>
<tr>
<td><strong>Found</strong></td>
<td>60.65</td>
<td>3.70</td>
<td>7.75</td>
</tr>
</tbody>
</table>

**PMR spectral features (DMSO-d$_6$, ppm)**

- 6.3-7.9 (Multiplet, Aromatic H + NH of CONH)
- 2.63 (2H, s, CH$_2$)
- 12.92 (H, s, COOH)
- 5.15 (H, d, C$_5$)
- 4.7 (H, m, C$_4$)
- 3.4 - 3.8 (2H, d, C$_3$)
- 3.9 (H, s, -OH)

**CMR spectral Features (DMSO-d$_6$, ppm)**

- 102-131 Benzene
- 165/166 C of COOH/CONH
- 55 CH
- 33 CH$_2$
- 90 CH$_2$CO
Compound-9g

1-[2-Methyl-perimidine-1,N-acetyl hydrazide]-2-oxo-5-(2-nitro phenyl)-pyrrolidine-4-carboxylic acid

Molecular Formula: C_{27}H_{20}N_{4}O_{9}
Molecular Weight: 544 g/mol
Melting Point: 195-96°C (uncorrected)
Yield: 75%

Infrared spectral features (KBr, cm\(^{-1}\))
- 3050, 1500 Aromatic C-H
- 1670 C=O of COOH
- 1717 C=O of pyrrolidinone

Other bands same as parent Schiff base

Elemental Analysis

<table>
<thead>
<tr>
<th></th>
<th>% C</th>
<th>% H</th>
<th>% N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated</td>
<td>59.55</td>
<td>3.67</td>
<td>10.29</td>
</tr>
<tr>
<td>Found</td>
<td>59.50</td>
<td>3.65</td>
<td>10.25</td>
</tr>
</tbody>
</table>

PMR spectral features (DMSO-d\(_6\), ppm)
- 6.3-7.9 (Multiplet, Aromatic H + NH of CONH)
- 3.9 (H, s, OH)
- 12.92 (H, s, COOH)
- 5.15 (H, d, C\(_5\))
- 4.7 (H, m, C\(_4\))
- 3.4 - 3.8 (2H, d, C\(_3\))
- 2.62 (2H of CH\(_2\))

CMR spectral Features (DMSO-d\(_6\), ppm)
- 102-132 Aromatic
- 165/166 C of COOH/CONH
- 55 CH
- 33 CH\(_2\)
- 93 CH\(_2\)CO
**Compound-9h**

![Chemical Structure](image)

1-[3-(Isoindol-1,3-dione methyl)-6-hydroxy-benzoyl amino]-2-oxo-5-(2-hydroxy-5-bromo phenyl)-3,5-dihydro-1H-pyrrolidinone-4-carboxylic acid

<table>
<thead>
<tr>
<th>Molecular Formula: C_{27}H_{20}N_{3}O_{8}Br</th>
<th>Elemental Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Weight: 595 g/mol</td>
<td>% C    % H    % N</td>
</tr>
<tr>
<td>Melting Point: 205-07°C (uncorrected)</td>
<td>Calculated 54.45 3.36 7.05</td>
</tr>
<tr>
<td>Yield: 78%</td>
<td>Found 54.40 3.35 7.00</td>
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</tbody>
</table>

**Infrared spectral features (KBr, cm^{-1})**

- 3050, 1500 Aromatic C-H
- 1670 C=O of COOH
- 1717 C=O of pyrrolidinone

Other bands same as parent Schiff base

**PMR spectral features (DMSO-d$_6$, ppm)**

- 5.9-7.9 (Multiplet, Aromatic H + NH of CONH)
- 12.92 (H, s, COOH)
- 4.7-5.15 (H, d, C$_5$)
- 4.7 (H, m, C$_4$)
- 3.4 - 3.8 (2H, d, C$_3$)
- 2.64 (2H of CH$_2$)

**CMR spectral features (DMSO-d$_6$, ppm)**

- 102-133 Aromatic C
- 165/166 C of COOH/CONH
- 55 CH
- 33 CH$_2$
- 90 CH$_2$CO
Fig. 5.11 IR spectrum of compound 9a

Fig. 5.12 IR spectrum of compound 9d
Fig. 5.13 IR spectrum of compound 9e
Fig. 5.14 $^1$H NMR Spectrum of Compound 9a
Fig. 5.15 $^1$H NMR Spectrum of Compound 9d
Fig. 5.16 $^1$H NMR Spectrum of Compound 9e
Fig. 5.17 $^{13}$C NMR Spectrum of Compound 9a
Fig. 5.18 $^{13}$C NMR Spectrum of Compound 9d
Fig. 5.19 $^{13}$C NMR Spectrum of Compound 9e
Fig. 5.20 Mass spectrum of Compound 9a
5.8 RESULTS AND DISCUSSION

Azomethines (3a-3h) on cyclocondensation reaction with succinic anhydride yields 2-pyrrolidinone (9a-9h). Their structures were confirmed by analytical and spectral data. The C, H and N contents of the prepared compounds were consistent with their predicted structures as shown in Scheme-5.2. The infrared spectra show the band in the region 1680-1700 cm\(^{-1}\) for carbonyl group of 2-pyrrolidinone ring.

The NMR spectra show a doublet at 5.1 ppm for CH proton at position-5 in the 2-pyrrolidinone ring and multiplet at 4.7 ppm for CH protons at position-4 of the 2-pyrrolidinone ring. All other signals are at their respective positions for the respective protons in the NMR spectra.

The Mass spectrum of compound-9a (Fig. 5.20) indicates that the molecular mass of compound-9a agreed with the peak obtained at 500 m/z.

The analytical and spectral data of the compounds (9a-9h) are shown. The IR, PMR and \(^{13}\)C NMR spectra are scanned in Fig. 5.11-5.19 for the selective compounds.
References:

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