PART - I


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Chapter 1
INTRODUCTION

Synthesis of 3-aryl-[1]-benzofurano [3, 2-c]-1-substituted pyrazoles:

Since many drugs and dyes contain the pyrazole nucleus, this class has been widely studied and continues to attract even to-day much attraction of scientists.

An unsaturated five membered ring containing adjacent nitrogen atoms was termed as pyrazole by Knorr\(^1\) in 1883. The dihydropyrazole is known as pyrazoline (B). Pyrazole can also be regarded as an isoxazole nucleus (C) in which \(-O-\) has been replaced by \(-NH\) grouping. The numbering of pyrazole is as shown in (A).

Since five decades, pyrazole has attracted scientists because of their ready accessibility, diverse chemical reactivity, broad spectrum of biological activity and variety of industrial applications. They are known for their versatile physiological activity\(^2\text{-}^6\). It was established

that a system incorporating these moieties may result in the formation of some interesting bioactive compounds. Pyrazoles have played an important role in the medicinal chemistry.

Pyrazoles are frequently synthesized from hydrazines and α,β-unsaturated carbonyl compounds substituted at α or β-position with readily replaceable groups. Among the replaceable groups bromine has been widely studied as the α-substituent and the intermediate hydrazone is isolated sometimes if it is of low solubility.

\[
\begin{align*}
R_1 - C - C = CH - R_2 + R_3.NH.NH_2 \\
\text{O}   \quad \downarrow \quad \text{X} \\
\text{R}_1 - \quad \quad \quad \quad \quad \text{R}_2 - \text{N} - \text{N} - \text{R}_3
\end{align*}
\]

(1a)

The formation of substituted pyrazoles from 1,3-dicarbonyl compounds and substituted hydrazines has been reported by Jacobs and also by Finar and Simond. It has been reported that the formation of isomeric pyrazoles depends on steric hindrance, electromeric effect.

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of groups and also on the pH of the reaction medium\textsuperscript{12-16}.

The most common method for the synthesis of pyrazoles is the action of hydrazine or substituted hydrazine on 1,3-dicarbonyl compounds. Monohydrazone is the intermediate in this reaction, which has been occasionally isolated\textsuperscript{17-23}.

Monohydrazone (2a) have been converted to corresponding pyrazoles (2b) by thermal action or by treating it with acid\textsuperscript{1,20,23-26}.

\begin{equation}
\begin{array}{c}
\text{R-C-CH}_2\text{-C-R} \\
\text{(2)}
\end{array}
\xrightarrow{\text{NH}_2\text{NH}_2} \\
\begin{array}{c}
\text{N-NH}_2 \\
\text{R-C-CH}_2\text{-C-R} \\
\text{(2a)}
\end{array}
\end{equation}

\begin{equation}
\begin{array}{c}
\text{Acid} \\
\text{Heat}
\end{array}
\rightarrow \\
\begin{array}{c}
\text{N} \\
\text{H} \\
\text{R} \\
\text{N} \\
\text{R} \\
\text{H}
\end{array}
\end{equation}

\textsuperscript{12} Knorr, L., \textit{Ber. dt. Chem. Ges.}, 20(1887), 1104.
\textsuperscript{14} Brady, O. L., \textit{J. Am. Soc.}, (1931), 756.
\textsuperscript{17} Von Auwers, K. and Schmidt, W., \textit{Ber. dt. Chem. Ges.}, 58(1925), 528.
\textsuperscript{18} Von Auwers, K. and Ottens, B., \textit{Ber. dt. Chem. Ges.}, 58(1925), 2072.
\textsuperscript{20} Von Auwers, K. and Mauss, H., \textit{Leibig's Ann.}, 452(1927), 182.
\textsuperscript{22} Borsche, W. and Hahn, H., \textit{Leibig's Ann.}, 537(1939), 219.
\textsuperscript{25} Barot, C., \textit{J. Indian Chem. Soc.}, 8(1931), 801.
\textsuperscript{26} Von Auwers, K. and Mauss, H., \textit{Ber. dt. Chem. Ges.}, 59(1931), 2394.
Benzoyl acetone (3) with phenyl hydrazine gives only 1,5-diphenyl methyl pyrazole (3a) but with methyl hydrazine it gives a mixture of 1,3-dimethyl-5-phenyl pyrazole (3b) and 1,5-dimethyl-3-phenyl pyrazole (3c)\textsuperscript{27,28}.

When hydrazine or substituted hydrazine reacts with chalcone dibromides (4) give substituted pyrazoles (4a) of unquivocal structure\textsuperscript{29-30}.

\textsuperscript{27} Durmm, P. J., Proc. Roy. Irish Acad., 4013(1931), 106.
β-substituted, α, β-unsaturated carbonyl compounds (5) which may be regarded as the enol form of dicarbonyl compounds are reported to give substituted pyrazoles (5a) on reaction with hydrazine or substituted hydrazine.

An interesting synthesis of pyrazoles (6a) was reported from 2-anisoyl-5-methyl-coumaran-3-ones (6) on treatment with phenyl-hydrazine hydrochloride in ethanol or pyridine medium.

Benzofurano pyrazoles are generally synthesized from coumaran-3-ones. Coumaran-3-one and benzofuran are structurally related compounds. Benzofuran is known as coumarone (7). The 2,3-dihydrobenzofuran is known as coumaran (8) and 3-keto-2,2-dihydro-benzofuran is known as coumaranone or coumaran-3-one (9).

![Chemical structures](image)

Several methods are available for the synthesis of coumaran-3-ones. Condensation of an coumaranone and aromatic aldehyde gives 2-benzylidene coumaran-3-one\(^\text{34}\) (10).

![Chemical structure](image)

The direct synthesis of 2-acetyl-coumaran-3-one (11a) by refluxing methyl salicylate and chloroacetone in anhydrous acetone using K\(_2\)CO\(_3\) as base have been reported by Geissman et al.\(^\text{35}\).

\[\begin{align*}
\text{(11)} & \quad + \quad \text{(12)} \\
\rightarrow & \quad \text{(12a)}
\end{align*}\]

\(^{34}\) Bate, E. C., Smith and Geissman, T. A., Nature, 167 (1951), 688.

Synthesis of 2-aryloxy-coumaran-3-ones have also been reported by base catalyzed Baker-Venkatraman transformation of ω-halo-aryloxy-acetophenones\textsuperscript{36-38}.

Doifode\textsuperscript{39} reported that α-bromodibenzoyl methane (12) on treatment with alcoholic alkali formed 2-benzoyl-coumaran-3-one (12a).

\[ \text{C-CH-C} \]
\[ \begin{array}{c}
\text{II} \\
\text{0 Br 0} \\
\text{OH} \\
\text{O}
\end{array} \rightarrow \]
\[ \text{(12)} \]
\[ \begin{array}{c}
\text{C-CH-C} \\
\text{II} \\
\text{0 Br 0} \\
\text{OH} \\
\text{O}
\end{array} \]
\[ \text{(12a)} \]

Wadodkar and Marathey\textsuperscript{40} have reported the synthesis of 2-aryloxy-coumaran-3-ones by subjecting O-aryloxy-ω-bromo acetophenones to base catalyzed Baker-Venkataraman transformation using pulverized KOH in dioxane.

Joshi\textsuperscript{41} reported that coumaran-3-ones (13) on condensation with phenylhydrazine hydrochloride in pyridine medium give benzo-furano [3, 2-c] pyrazoles (13a).

\begin{itemize}
\item \textsuperscript{38} Krohnke, F. and Arhenhotz, G. W., J. Prakt. Chem., 11(1960), 239.
\item \textsuperscript{39} Doifode, K. B., ‘Chemistry of β-diketones’, Ph.D. Thesis, Nagpur University (1965).
\item \textsuperscript{40} Wadodkar, P. N. and Marathey, M. G., Indian J. Chem., 10(1972), 145-48.
\end{itemize}
Ahluwalia et al.\textsuperscript{42}, have reported the synthesis of pyrazolo [3, 4-c] pyrazoles (14b).

Synthesis of substituted thieno [3',2'; 3, 4] cyclopenteno [2, 1-c] pyrazoles (15a) have been reported by Sharda et al.\textsuperscript{43}.

The treatment of hydrazine with ethyl acetoacetate, ethyl-cynoacetate and acetyl acetone afforded 4-pyrazolyl-benzofurano [3, 2-d] pyrimidines (16).

Wang Jin-Jun et al.\textsuperscript{45}, have reported the synthesis of 3,4-dihydro isobenzopyran [3, 4-c] pyrazoles (17a,b,c) by Claisen condensation reaction of 3, 4-dihydro isobenzopyran.

Giuseppe et al.\textsuperscript{46}, reported the synthesis of [2]-benzopyran [4,3-c] pyrazoles.

Devinder et al.\textsuperscript{47}, synthesized isomeric pyranopyrazoles (18a, b, c, d).

Synthesis of [1] benzopyrano [4,3-c] pyrazoles (19b) by using Vilsmeier reagent have been reported\(^{48}\).

Mulwad et al.\(^{49}\), synthesized some 4-hydroxy-3-[3',5'-substituted pyrazole] benzopyran-2-ones (20b).
Nagar et al.\textsuperscript{50}, have been reported the synthesis of 2-amino-3-cyano-4,5-dimethyl-7-N-phenyl-4-(p-aroylaminophenyl)-pyranopyrazoles (21a).

Chapter 2

ORIGIN OF THE PROBLEM

Various methods for the synthesis of pyrazoles have been reviewed in the introduction part of the thesis.

Thus the most convenient route for the synthesis of pyrazoles involved the action of hydrazine or phenyl hydrazine on 2-arylcoumaran-3-ones.

The synthesis of coumaran-3-ones involved the base catalyzed Baker-Venkataraman transformation of 2-aryloxy-ω-iodoacetophenones by pulverized KOH in dioxane during which cyclization and elimination of hydrogenchloride takes place simultaneously.

From the literature survey, it is found that the synthesis of 3-aryl-[1] benzofurano [3, 2-c]-1-substituted pyrazoles from 2-arylcoumaran-3-ones and nucleophiles like isonicotinic acid hydrazide/semicarbazide hydrochloride/thiosemicarbazide in pyridine has not been yet reported. Therefore it was thought of interest to synthesize 3-aryl-[1] benzofurano [3, 2-c]-1-substituted pyrazoles.
PROBLEM

The work presented in this part of thesis deals with the synthesis of new 3-aryl-[1]-benzofuran-3, 2-c]-1-isonicotinoyl/1-carboxyamido/1-thiocarboxamido-pyrazoles (5a-f, 6a-f, 7a-f) from 2-aroyl-coumaran-3-ones (4a-f) on condensation with nucleophiles like isonicotinic acid hydrazide/semicarbazide hydrochloride/thiosemicarbazide in pyridine medium.

The structures of these compounds were confirmed by elemental analysis, chemical properties and IR and ¹H NMR spectral analysis. The purity of the compounds was checked by TLC on silica gel-G plates. The plausible mechanism is also suggested.
**SCHEME**

1. Benzoyl chloride + Anisic acid → (2a-f)

2. ICl / ACOH → (3a-f)

3. KOH/Dioxane → (4a-f)

4. BVT → (5a-f)

5. H₂NNHOC → Pyridine reflux

6. H₂NCONH₂ → Pyridine reflux

7. H₂NCSNH₂ → Pyridine reflux

8. (5a-f) → (6a-f) → (7a-f)
Chapter 3

SUMMARY OF THE WORK

STARTING MATERIALS

2-Hydroxy-5-chloro acetophenone (1), 2-aryloxy-5-chloro acetophenones (2a-f), 2-aryloxy-5-chloro-ω-iodo acetophenones (3a-f) and 2-arylcoumaran-3-ones (4a-f) were prepared by the procedures as described in chapter 4 of Part I of this thesis.

3-Aryl-[1] Benzofurano [3, 2-c] 1-isonicotinoyl/1-carboxamido/1-thiocarboxamido pyrazoles (5a-f/6a-f/7a-f):

Pyrazoles (5a-f/6a-f/7a-f) were prepared by refluxing 2-arylcoumaran-3-ones (4a-f) with isonicotinic acid hydrazide/semi-carbazide hydrochloride/thiosemicarbazide in pyridine medium for about 4 hours. Thus the following pyrazoles were synthesized.

1. (5a) 3-Phenyl-[1]-5-chloro-benzofurano [3, 2-c]-1-isonicotinoyl pyrazole, m.p. 176°C.
2. (5b) 3-Phenyl-[1]-5-chloro-7-bromo-benzofurano [3,2-c]-1-isonicotinoyl pyrazole, m.p. 210°C.
3. (5c) 3-Phenyl-[1]-5-chloro-7-nitro-benzofurano [3,2-c]-1-isonicotinoyl pyrazole, m.p. 208°C.
4. (5d) 3-(4-Methoxy phenyl-[1]-5-chloro-benzofurano [3,2-c]-1-isonicotinoyl pyrazole, m.p. 174°C.
5. (5e) 3-(4-Methoxy phenyl-[1]-5-chloro-7-bromo-benzofurano [3,2-c]-1-isonicotinoyl pyrazole, m.p. 178°C.
6. (5f) 3-(4-Methoxy phenyl)-[1]-5-chloro-7-nitro-benzofurano [3,2-c]-1-isonicotinoyl pyrazole, m.p. 182°C.

10. (6a) 3-Phenyl-[1]-5-chloro benzofurano [3,2-c]-1-carboxamido pyrazole, m.p. 210°C.

11. (6b) 3-Phenyl-[1]-5-chloro-7-bromo-benzofurano [3,2-c]-1-carboxamido pyrazole, m.p. 198°C.

12. (6c) 3-Phenyl-[1]-5-chloro-7-nitro-benzofurano [3,2-c]-1-carboxamido pyrazole, m.p. 240°C.

13. (6d) 3-(4-Methoxy phenyl)-[1]-5-chloro benzofurano [3,2-c]-1-carboxamido pyrazole, m.p. 204°C.

14. (6e) 3-(4-Methoxy phenyl)-[1]-5-chloro-7-bromo- benzofurano [3,2-c]-1-carboxamido pyrazole, m.p. 203°C.

15. (6f) 3-(4-Methoxy phenyl)-[1]-5-chloro-7-nitro-benzofurano [3,2-c]-1-carboxamido pyrazole, m.p. 172°C.

10. (7a) 3-Phenyl-[1]-5-chloro benzofurano [3,2-c]-1-thiocarboxamido pyrazole, m.p. 180°C.

11. (7b) 3-Phenyl-[1]-5-chloro-7-bromo-benzofurano [3,2-c]-1-thiocarboxamido pyrazole, m.p. 220°C.

12. (7c) 3-Phenyl-[1]-5-chloro-7-nitro-benzofurano [3,2-c]-1-thiocarboxamido pyrazole, m.p. 270°C.

13. (7d) 3-(4-Methoxy phenyl)-[1]-5-chloro benzofurano [3,2-c]-1-thiocarboxamido pyrazole, m.p. 168°C.
Part-I Chapters Summary of the work

14. (7e) 3-(4-Methoxy phenyl)-[1]-5-chloro-7-bromo-benzo-furano [3,2-c]-1-thiocarboxamido pyrazole, m.p. 194°C.

15. (7f) 3-(4-Methoxy phenyl)-[1]-5-chloro-7-nitro-benzo-furano [3,2-c]-1-thiocarboxamido pyrazole, m.p. 198°C.

The synthesized compounds have been characterized by chemical properties, elemental analysis and IR, ^1H NMR spectral analysis. Purity of these heterocycles was checked by TLC on silica gel-G plates.
Chapter 4
EXPERIMENTAL AND DISCUSSION OF THE RESULTS

According to literature pyrazoles are synthesized by various methods. This part is devoted to the synthesis of new pyrazoles from 2-aroyl-coumaran-3-ones in pyridine medium.

Coumaran-3-ones have been synthesized from base catalyzed Baker-Venkataraman transformation of 2-aroyloxy-ω-iodo-acetophenones. The synthesis of new 2-aroyloxy-ω-iodo-acetophenones is achieved by using iodinemonochloride in acetic acid as iodinating agent.

The 2-aroyloxy-ω-iodo-acetophenones have been subjected to Baker-Venkataraman transformation by using pulverized KOH in dioxane medium, to obtain 2-aroyl-coumaran-3-ones. 2-Aroyl-coumaran-3-ones showed keto-enol tautomerism and developed deep violet colouration with ethanolic neutral FeCl₃ solution, indicating β-diketone type structure.

Present work deals with the stepwise synthesis of 3-aryl-[1]benzofurano [3, 2-c]-1-isonicotinoyl/1-carboxamido/1-thiocarboxamido pyrazoles (5a-f, 6a-f, 7a-f) from 2-aroyl-coumaran-3-ones (4a-f) on refluxing with isonicotinic acid hydrazide/semicarbazide hydrochloride/thiosemicarbazide in pyridine medium.

Characterization of synthesized compounds was carried out on the basis of chemical properties, elemental analysis and spectral
analysis (IR and NMR). IR spectra were recorded on Perkin Elmer spectrophotometer. The NMR spectra were recorded on Brucker AC-300 FTNMR (300 MHz), using (CDCl$_3$ + DMSO) as an internal standard.

Melting points were recorded on open capillary silicon oil-bath and are uncorrected. The purity of the synthesized compounds was checked by TLC on silicon gel-G plates. Chemicals and reagents used for the synthesis were of analytical grade.
EXPERIMENT NO. 1

Acetylation of p-chlorophenol:

Acetylation was carried out by the treatment of p-chlorophenol (50 ml) with acetic anhydride (60 ml) and fused anhydrous sodium acetate (5 gm). The mixture was refluxed for about 1.5 hours. The reaction mixture was cooled and poured into cold water. Acetate layer was separated and washed with water several times. It was finally purified by distillation. The distillate was collected at about 232°C, b.p. 232°C, yield 55 ml.

EXPERIMENT NO. 2

Preparation of 2-hydroxy-5-chloro acetophenone:

p-chlorophenyl acetate (55 ml) and anhydrous aluminium chloride (120 gm) were heated at 120°C for 1.5 hours in an oil bath. The reaction mixture was cooled and decomposed with ice cold water containing a little HCl to get the crude ketone. It was purified by dissolving in acetic acid and poured the solution dropwise into cold water with stirring to get 2-hydroxy-5-chloro acetophenone as a pale greenish-white solid, m.p. 53°C, yield 50 gm.
EXPERIMENT NO. 3

Preparation of 2-hydroxy-3-bromo-5-chloro acetophenone:

2-Hydroxy-5-chloroacetophenone (0.01 mol, 1.70 gm.) and sodium acetate (1.7 g) were dissolved in glacial acetic acid (10 ml) and then to this bromine in acetic acid reagent (20 ml) (25% w/v) was added dropwise with constant stirring. The temperature of the reaction mixture was maintained below 10°C. The reaction mixture was allowed to stand for about 30 minutes. It was poured into ice cold water with stirring. The pale yellow solid product separated was filtered and crystallized from ethanol, m.p. 80°C, yield 1.5 gm.

![Reaction Scheme]

EXPERIMENT NO. 4

Preparation of 2-hydroxy-3-nitro-5-chloro acetophenone:

2-Hydroxy-5-chloro acetophenone (0.01 mol, 1.70 gm.) was dissolved in glacial acetic acid (10 ml) in a 500 ml beaker. To this mixture concentrated sulphuric acid (3ml) was added. Nitrating mixture (11 ml HNO₃ + 7ml H₂SO₄, 3:2 V/v) was added dropwise over a period of 30 minutes to reaction mixture with constant stirring and keeping temperature below 10°C. The reaction mixture was allowed to stand for 1 hour. Poured the reaction mixture on crushed ice. The crude product obtained was filtered, washed with water and crystallized from ethanol, m.p. 110°C, yield 1.5 gm.
EXPERIMENT NO. 5

Preparation of 2-benzoyloxyacetophenones (2a–c):

To the mixture of 2-hydroxy acetophenones (0.04 mol) and benzoyl chloride (0.05 mol), NaOH (10%, 30 ml) solution was added. The reaction mixture was shaken for about half an hour. The product thus separated was filtered, washed with water followed by sodium bicarbonate (10%) solution and then again with water. The solid product was crystallized from ethanol to obtain the corresponding 2-benzoyloxy acetophenones (2a–c). Thus the following esters were prepared:

2-Benzoyloxy-5-chloro acetophenone (2a), m.p. 68°C, yield 80%

2-Benzoyloxy-3-bromo-5-chloro acetophenone (2b), m.p. 100°C, yield 75%
2-Benzoyloxy-3-nitro-5-chloro acetophenone (2c), m.p. 80°C, yield 70%

![Chemical Structure of 2c]

EXPERIMENT NO. 6
Preparation of 2-(4-methoxy benzoyloxy)-5-chloro acetophenones (2d-f):

2-Hydroxy acetophenones (0.04 mol, 6.8 gm) and anisic acid (0.05 mol, 7.6 gm) were placed in dry pyridine (30 ml) in 250 ml beaker. To this reaction mixture POCI₃ (3 ml) was added dropwise with constant stirring and with external cooling. After complete addition, the reaction mixture was allowed to stand for about 2 hours and then treated with ice-cold water containing a little HCl to neutralize pyridine. The solid obtained was filtered and washed with water and then with sodium bicarbonate (10%) to remove any organic acid and again with dil. NaOH (1%) to remove unreacted phenolic ketone. The product was filtered and crystallized from ethanol-acetic acid mixture to obtain the corresponding 2-(4-methoxy benzoyloxy)-5-chloro acetophenones (2d-f). Thus the following esters were prepared:

2-(4-Methoxy benzoyloxy)-5-chloro acetophenone (2d), m.p. 80°C, yield 75%
2-(4-Methoxy benzoyloxy)-3-bromo-5-chloro acetophenone (2e), m.p. 80°C, yield 70%

2-(4-Methoxy benzoyloxy)-3-nitro-5-chloro acetophenone (2f), m.p. 78°C, yield 70%

Synthesis of 2-aroyloxy-ω-iodo-acetophenones:

The substitution of bromine at ω-position of aromatic ketones cannot be obtained by usual bromination methods. Kosower⁵¹, Doifode⁵² and Wadodkar⁴⁸ used copper (II) bromide in dioxane medium to obtain ω-bromo-2-aroyloxy acetophenone.

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Kosower\textsuperscript{51} studied the mechanism of halogenation by copper (II) halides, and showed that cupric bromide may be the effective reagent for $\omega$-bromination.

Joshi\textsuperscript{53} reported the $\omega$-iodination of 2-aryloxy-5-methyl-acetophenone.

Therefore an attempt has been made to study the action of iodinemonochloride in acetic acid on 2-aryloxy acetophenones.

EXPERIMENT NO. 7

Preparation of 2-aryloxy-$\omega$-ido acetophenones (3a-f):

To a suspension of 2-aryloxy acetophenones (2a-f) (0.01 mol) in acetic acid (15 ml) was added a solution of iodinemonochloride in acetic acid (10 ml, 16.25% wt/vol) and the reaction mixture was refluxed for about 1 hour. On cooling the mixture was diluted with water, the solid obtained was filtered and crystallized from ethanol to obtain the yellow crystals of the corresponding 2-aryloxy-$\omega$-iodo acetophenones (3a-f).

Thus the following 2-aryloxy-$\omega$-ido acetophenones (3a-f) were prepared by this method.

<table>
<thead>
<tr>
<th>S.N.</th>
<th>2-Aroyloxy-ω-iodo-acetophenones</th>
<th>m.p.</th>
<th>yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td><img src="image1" alt="Structure" /></td>
<td>60°C</td>
<td>60%</td>
</tr>
<tr>
<td>3b</td>
<td><img src="image2" alt="Structure" /></td>
<td>90°C</td>
<td>65%</td>
</tr>
<tr>
<td>3c</td>
<td><img src="image3" alt="Structure" /></td>
<td>70°C</td>
<td>65%</td>
</tr>
<tr>
<td>3d</td>
<td><img src="image4" alt="Structure" /></td>
<td>150°C</td>
<td>70%</td>
</tr>
</tbody>
</table>

2-Benzoyloxy-5-chloro-ω-iodo-acetophenone

2-Benzoyloxy-3-bromo-5-chloro-ω-iodo-acetophenone

2-Benzoyloxy-3-nitro-5-chloro-ω-iodo-acetophenone

2-(4-Methoxy benzoyloxy)-5-chloro-ω-iodo-acetophenone
Part-I

Chapter 4

Experimental and Discussion

S.N. 2-Aroyloxy-ω-iodo-acetophenones

<table>
<thead>
<tr>
<th>S.N.</th>
<th>2-(4-Methoxy benzoyloxy)-3-bromo-5-chloro-ω-iodo-acetophenone</th>
<th>m.p.</th>
<th>yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>3e</td>
<td><img src="image1" alt="Structure" /></td>
<td>90°C</td>
<td>60%</td>
</tr>
<tr>
<td>3f</td>
<td><img src="image2" alt="Structure" /></td>
<td>140°C</td>
<td>65%</td>
</tr>
</tbody>
</table>

2-(4-Methoxy benzoyloxy)-3-nitro-5-chloro-ω-iodo-acetophenone

MECHANISM OF ω-IODINATION

Wadodkar\(^5\) reported the ω-bromo-2-aroyloxy acetophenones when brominated by dioxane-dibromide complex in DMF as HBr scavenger and suggested an addition elimination mechanism. The addition of bromine takes place across the double bond in the enol form of 2-aroyloxyacetophenone followed by elimination of HBr. On similar lines the formation of 2-aroyloxy-ω-iodo acetophenone may be formulated as below:

1] First step is enolisation

2] Second step is the addition of ICl across the double bond in the enolic form.

\[
\begin{align*}
\text{R-O-C-CH}_2\text{OH} & \rightarrow \text{R-O-C-CH}_2\text{I} \\
\text{Cl} & \text{Cl}
\end{align*}
\]

3] Third step is the elimination of HCl and subsequent formation of \(\omega\)-iodo compound.

\[
\begin{align*}
\text{R-O-C-CH}_2\text{OH} & \rightarrow \text{R-O-C-CH}_2\text{I} \\
\text{Cl} & \text{Cl}
\end{align*}
\]

**BAKER-VENKATARAMAN TRANSFORMATION OF 2-AROYLOXY-\(\omega\)-IODO ACETOPHENONES**

**Synthesis of 2-arylcoumaran-3-ones:**

Auwers\(^{55}\) reported that simply refluxing 2-aryloxy-\(\omega\)-iodoacetophenone in benzene with dry potassium carbonate, 2-acylcoumaran-3-ones were formed. The reaction probably proceed by way of intermediate diketone, which looses hydrogen chloride to give 2-acetyl-coumaran-3-ones.

\(^{55}\) Von Auwers, K., Ber., 43 (1910), 2196.
The observation of Auwers has been supported by Philbin et al.\textsuperscript{56}. They observed that 2-acetyl-5-methyl-coumaran-3-one is formed at room temperature in dioxane from 2-acetoxy-\(\omega\)-chloroacetophenone in presence of one of the Claisen condensation bases—sodium hydride, potassium hydroxide, sodium methoxide, sodium phenate, sodium peroxide, etc. The yield depends on the strength of base.

Jones et al.\textsuperscript{57}, pointed out that Auwer’s synthesis is analogous to Baker-Venkataraman transformation. The intermediate \(\alpha\)-halo diketones could seldom be isolated. The presence of chlorine on reactive methylene group facilitates the ring closure so much so that it occurs during the rearrangement itself\textsuperscript{58}.

EXPERIMENT NO. 8

Preparation of 2-aroyl-coumaran-3-ones (4a-f):

The mixture of 2-aroyloxy-ω-iodo acetophenones (3a-f) (0.005 mol) in dioxane (20 ml) was treated with pulverized KOH (0.015 mol) and was refluxed for about 30 minutes on water bath. The reaction mixture was worked up after an hour with 50% HCl to neutralize KOH. The product obtained was filtered and recrystallized from ethanol to obtain yellow crystals of the corresponding 2-aroyl-coumaran-3-ones (4a-f).

Thus the following coumaran-3-ones (4a-f) were prepared.

<table>
<thead>
<tr>
<th>S.N.</th>
<th>2-Aroyl-coumaran-3-ones</th>
<th>m.p.</th>
<th>yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>2-Benzoyl-5-chloro-coumaran-3-one</td>
<td>130°C</td>
<td>65%</td>
</tr>
<tr>
<td>4b</td>
<td>2-Benzoyl-5-chloro-7-bromo-coumaran-3-one</td>
<td>150°C</td>
<td>65%</td>
</tr>
</tbody>
</table>
S.N.  | 2-Aroyl-coumaran-3-ones | m.p. | yield |
4c   | 150°C | 60% |
| 2-Benzoyl-5-chloro-7-nitro-coumaran-3-one |
4d   | 140°C | 75% |
| 2-(4-Methoxy benzoyl)-5-chloro-coumaran-3-one |
4e   | 130°C | 65% |
| 2-(4-Methoxy benzoyl)-5-chloro-7-bromo-coumaran-3-one |
4f   | 160°C | 65% |
| 2-(4-Methoxy benzoyl)-5-chloro-7-nitro-coumaran-3-one |

Properties and constitution of the compounds (4a-f):

1) They gave deep violet colouration with ethanolic ferric chloride solution indicating the presence of free phenolic or enolic group
2) All are yellow crystalline compounds.
3) The spectral data of the compound (4d) is as follows;
a) The IR spectrum of compound (4d) (Spectrum No. 1) showed the following absorption bands:

<table>
<thead>
<tr>
<th>Frequency (cm⁻¹)</th>
<th>Intensity</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>2842.4</td>
<td>S</td>
<td>C-H stretch</td>
</tr>
<tr>
<td>1685.4</td>
<td>S</td>
<td>-OH stretch</td>
</tr>
<tr>
<td>1427.9</td>
<td>S</td>
<td>C=C stretch</td>
</tr>
<tr>
<td>1262.5</td>
<td>S</td>
<td>-C-O-C stretch</td>
</tr>
<tr>
<td>770</td>
<td>S</td>
<td>C-Cl stretch</td>
</tr>
</tbody>
</table>

b) The NMR spectrum of compound (4d) was recorded in CDCl₃+DMSO. The observed chemical shift can be correlated as follows (Spectrum No. 2):

<table>
<thead>
<tr>
<th>Chemical shift in (δ)ppm</th>
<th>Multiplicity</th>
<th>No. of Protons</th>
<th>Types of Proton</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.85</td>
<td>S</td>
<td>3H</td>
<td>-OCH₃</td>
</tr>
<tr>
<td>6.8</td>
<td>S</td>
<td>1H</td>
<td>H of furano ring</td>
</tr>
<tr>
<td>7-8.5</td>
<td>m</td>
<td>7H</td>
<td>Ar-H</td>
</tr>
</tbody>
</table>
05/05/04 14:25 R.C./SAIF.P.U.CHD.
X: 4 scans, 4.0cm⁻¹, flat, smooth, abex
spl.code:J-1

Spectrum No. 1
SYNTHESIS OF 3-ARYL-[1]-BENZOFURANO [3, 2-c]-1-SUBSTITUTED PYRAZOLES:

As reported earlier the most straightforward protocol for the synthesis of pyrazole is the action of hydrazine or substituted hydrazine on 1,3-dicarbonyl compounds. The 1,3-dicarbonyl compounds are characterized by keto-enol tautomerism.

However, literature survey reveals that no attempt has been made to study the action of isonicotinic acid hydrazide/semicarbazide hydrochloride/thiosemicarbazide on 2-aroyl-coumaran-3-ones. Thus it was thought of interest to synthesize 3-aryl-[1]-benzo-furano [3, 2-c]-1-substituted pyrazoles by the action of nucleophiles like isonicotinic acid hydrazide/semicarbazide hydrochloride/thiosemicarbazide on 2-aroyl-coumaran-3-ones in pyridine medium.

The present work deals with the synthesis of 3-aryl-[1]-benzo-furano [3, 2-c]-1-substituted pyrazoles on treatment of 2-aroyl-coumaran-3-ones with isonicotinic acid hydrazide/semicarbazide hydrochloride/thiosemicarbazide in pyridine medium.

The structures of the synthesized compounds have been elucidated by elemental analysis, chemical analysis, IR and $^1$H NMR spectral analysis. The purity of the compounds was checked by TLC on silica gel-G plate.
Action of isonicotinic acid hydrazide/semicarbazide hydrochloride/thiosemicarbazide on 2-arylcoumaran-3-ones: Synthesis of Pyrazoles (5a-f/6a-f/7a-f):

**General Procedure:**

A mixture of 2-arylcoumaran-3-ones (4a-f) (0.005 mol) and isonicotinic acid hydrazide/semicarbazide hydrochloride/thiosemicarbazide (0.01 mol) in pyridine (20 ml) was refluxed for about 4 hours. On cooling, the reaction mixture was diluted with water and subsequently acidified by HCl (1:1) to get sticky mass. This was triturated with ethanol and the solid obtained was filtered and crystallized from ethanol to obtain the pyrazoles (5a-f/6a-f/7a-f).

EXPERIMENT NO. 9

Synthesis of 3-phenyl-[1]-5-chloro benzofurano [3, 2-c]-1-isonicotinoyl pyrazole (5a):

The mixture of coumaran-3-one (4a) (0.005 mol, 1.36 gm) and isonicotinic acid hydrazide (0.01 mol, 1.37 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (5a), m.p. 176°C, yield 60%.

Properties and constitution of the compound (5a):

1) Compound (5a) did not show ferric chloride colouration indicating the absence of phenolic -OH group.
2) It developed yellow colouration with conc. $\text{H}_2\text{SO}_4$.

3) TLC:  
Solvent (CCl$_4$) height : 6.7 cm  
Solute height : 3.8 cm  
Rf-value : 0.63

3) Elemental Analysis:

\[
\text{N\%} \quad \text{Found} \quad 11.08, \quad \text{Calculated} \quad 11.26
\]

From analytical data, the molecular formula of the compound (5a) was found to be C$_{21}$H$_{12}$ClN$_3$O$_2$.

From chemical properties and analytical results, the compound (5a) was assigned the structure as, 3-phenyl-[1]-5-chloro benzofuran-3,2-c]-1-isonicotinoyl pyrazole.

EXPERIMENT NO. 10

Synthesis of 3-phenyl-[1]-5-chloro-7-bromo-benzofuran-3,2-c]-1-isonicotinoyl pyrazole (5b):

The mixture of coumaran-3-one (4b) (0.005 mol, 1.76 gm) and isonicotinic acid hydrazide (0.01 mol, 1.37 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (5b), m.p. 210°C, yield 75%.
Properties and constitution of the compound (5b):

1) The compound (5b) showed properties similar to those of compound (5a).

2) TLC: Solvent (CCl₄) height : 6.5 cm
   Solute height : 4.2 cm
   Rf-value : 0.64

3) Elemental Analysis:
   N% Found 8.94, Calculated 9.31

From analytical data, the molecular formula of the compound (5b) was found to be C_{21}H_{11}ClBrN₃O₂.

From chemical properties and analytical results, the compound (5b) was assigned the structure as, 3-phenyl-[1]-5-chloro-7-bromo-benzofurano [3, 2-c]-1-isonicotinoyl pyrazole.
EXPERIMENT NO. 11

Synthesis of 3-phenyl-[1]-5-chloro-7-nitro-benzofurano [3, 2-c]-1-isonicotinoyl pyrazole (5c):

The mixture of coumaran-3-one (4c) (0.005 mol, 1.58 gm) and isonicotinic acid hydrazide (0.01 mol, 1.37 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (5c), m.p. 208°C, yield 65%.

Properties and constitution of the compound (5c):

1) The compounds (5c) showed properties similar to those of compound (5a).

2) TLC:

<table>
<thead>
<tr>
<th>Solvent (CCl₄) height</th>
<th>6.5 cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solute height</td>
<td>4.5 cm</td>
</tr>
<tr>
<td>Rf-value</td>
<td>0.69</td>
</tr>
</tbody>
</table>

3) Elemental Analysis:

N% Found 13.14, Calculated 13.39

From analytical data, the molecular formula of the compound (5c) was found to be C₂₁H₁₁Cl₄N₄O₄.

From chemical properties and analytical results, the compound (5c) was assigned the structure as, 3-phenyl-[1]-5-chloro-7-nitro-benzofurano [3, 2-c]-1-isonicotinoyl pyrazole.
EXPERIMENT NO. 12

Synthesis of 3-(4-methoxy phenyl)-[1]-5-chloro benzofurano [3, 2-c]-1-isonicotinoyl pyrazole (5d):

The mixture of coumaran-3-one (4d) (0.005 mol, 1.51 gm) and isonicotinic acid hydrazide (0.01 mol, 1.37 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (5d), m.p. 174°C, yield 70%.

Properties and constitution of the compound (5d):

1) The compounds (5d) showed properties similar to those of compound (5a).

2) TLC:
   - Solvent (CCl₄) height : 6.5 cm
   - Solute height : 4.4 cm
   - Rf-value : 0.67

3) Elemental Analysis:
   - N% Found 9.89, Calculated 10.42
From analytical data, the molecular formula of the compound (5d) was found to be C\textsubscript{22}H\textsubscript{14}ClN\textsubscript{3}O\textsubscript{3}.

4) The spectral data of the compound (5d) is as follows;
   a) The IR spectrum of compound (5d) (Spectrum No. 3) showed the following absorption bands:

<table>
<thead>
<tr>
<th>Frequency (cm\textsuperscript{-1})</th>
<th>Intensity</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>2843.7</td>
<td>(b)</td>
<td>(C-H) stretching</td>
</tr>
<tr>
<td>2361.8</td>
<td>(S)</td>
<td>(N-H) stretching</td>
</tr>
<tr>
<td>1685.6</td>
<td>(S)</td>
<td>(C=O) stretching</td>
</tr>
<tr>
<td>1603.1</td>
<td>(S)</td>
<td>(C=N) stretching</td>
</tr>
<tr>
<td>1427.3</td>
<td>(S)</td>
<td>(C=C) stretching</td>
</tr>
<tr>
<td>1261.3</td>
<td>(S)</td>
<td>(C-N) stretching</td>
</tr>
<tr>
<td>771.2</td>
<td>(S)</td>
<td>(C-Cl) stretching</td>
</tr>
</tbody>
</table>

   b) The NMR spectrum of compound (5d) was recorded in (CDCl\textsubscript{3}+DMSO) The observed chemical shift can be correlated as follows (Spectrum No. 4):

<table>
<thead>
<tr>
<th>Chemical shift</th>
<th>Multiplicity</th>
<th>No. of Proton</th>
<th>Types of Proton</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.8</td>
<td>S</td>
<td>3H</td>
<td>-OCH\textsubscript{3}</td>
</tr>
<tr>
<td>6.9-8.02</td>
<td>m</td>
<td>17H</td>
<td>Ar-H</td>
</tr>
</tbody>
</table>

From chemical properties, analytical data and spectral analysis, the compound (5d) was assigned the structure as, 3-(4-methoxy phenyl)-[1]-5-chloro benzofurano [3, 2-c]-1-isonicotinoyl pyrazole.
Spectrum No. 3

05/05/04 14:29 R.C./SAIF.P.U.CHD.
Z: 4 scans, 4.0cm⁻¹, flat, smooth, abex
spl.code:J-2
EXPERIMENT NO. 13

Synthesis of 3-(4-methoxy phenyl)-[1]-5-chloro-7-bromo-benzofurano [3, 2-c]-1-isonicotinoyl pyrazole (5e):

The mixture of coumaran-3-one (4e) (0.005 mol, 1.90 gm) and isonicotinic acid hydrazide (0.01 mol, 1.37 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (5e), m.p. 178°C, yield 60%.

Properties and constitution of the compound (5e):
1) The compound (5e) showed properties similar to those of compound (5a).
2) TLC: Solvent (CCl₄) height : 6.4 cm
   Solute height : 5.0 cm
   Rf-value : 0.78
3) Elemental Analysis:
   N% Found 8.42, Calculated 8.73
From analytical data, the molecular formula of the compound (5e) was found to be C_{22}H_{13}ClBrN_{3}O_{3}.

From chemical properties and analytical results, the compound (5e) was assigned the structure as, 3-(4-methoxy phenyl)-[1]-5-chloro-7-bromo-benzofurano [3, 2-c]-1-isonicotinoyl pyrazole.

![Structure of 5e]

EXPERIMENT NO. 14

Synthesis of 3-(4-methoxy phenyl)-[1]-5-chloro-7-nitro-benzofurano [3, 2-c]-1-isonicotinoyl pyrazole (5f):

The mixture of coumaran-3-one (4f) (0.005 mol, 1.74 gm) and isonicotinic acid hydrazide (0.01 mol, 1.37 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (5f), m.p. 182°C, yield 65%.

![Chemical structure of 4f and 5f]

Properties and constitution of the compound (5f):

1) The compounds (5f) showed properties similar to those of compound (5a).
2) TLC: Solvent (CCl\textsubscript{4}) height : 6.5 cm

Solute height : 4.5 cm

Rf-value : 0.69

3) Elemental Analysis:

\[ \text{N\% Found 11.83, Calculated 12.05} \]

From analytical data, the molecular formula of the compound (5f) was found to be \( \text{C}_{22}\text{H}_{13}\text{ClN}_{5}\text{O}_{5} \).

From chemical properties and analytical results, the compound (5f) was assigned the structure as, \( 3-(4\text{-methoxy phenyl})-[1]-5\text{-chloro-7-nitro-benzofurano [3, 2-c]-1-isonicotinoyl pyrazole.} \)

![Structure of (5f)](image)

**EXPERIMENT NO. 15**

**Synthesis of 3-phenyl-[1]-5-chloro benzofurano [3, 2-c]-1-carboxamido pyrazole (6a):**

The mixture of coumaran-3-one (4a) (0.005 mol, 1.36 gm) and semicarbazide hydrochloride (0.01 mol, 1.11 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (6a), m.p. 210\textdegree C, yield 75%. 

![Reaction Scheme](image)
Properties and constitution of the compound (6a):

1) The compounds (6a) showed properties similar to those of compound (5a).

2) TLC:
   Solvent (CCl₄) height : 6.5 cm
   Solute height : 3.8 cm
   Rf-value : 0.58

3) Elemental Analysis:
   N% Found 12.97, Calculated 13.50

From analytical data, the molecular formula of the compound (6a) was found to be C₁₆H₁₀ClN₃O₂.

From chemical properties and analytical results, the compound (6a) was assigned the structure as, 3-phenyl-[1]-5-chloro benzofurano [3, 2-c]-1-carboxamido pyrazole.

![Structure of (6a)](image)

EXPERIMENT NO. 16

Synthesis of 3-phenyl-[1]-5-chloro-7-bromo-benzofurano [3, 2-c]-1-carboxamido pyrazole (6b):

The mixture of coumaran-3-one (4b) (0.005 mol, 1.76 gm) and semicarbazide hydrochloride (0.01 mol, 1.11 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (6b), m.p. 198°C, yield 60%.
Properties and constitution of the compound (6b):

1) The compounds (6b) showed properties similar to those of compound (5a).

2) TLC:
   - Solvent (CCl₄) height: 6.0 cm
   - Solute height: 3.8 cm
   - Rf-value: 0.63

3) Elemental Analysis:
   - N% Found: 10.58, Calculated: 10.79

From analytical data, the molecular formula of the compound (6b) was found to be C₁₆H₉ClBrN₃O₂.

From chemical properties and analytical results, the compound (6b) was assigned the structure as, 3-phenyl-[1]-5-chloro-7-bromo-benzofurano [3, 2-c]-1-carboxamido pyrazole.
EXPERIMENT NO. 17

Synthesis of 3-phenyl-[1]-5-chloro-7-nitro-benzofurano [3, 2-c]-1-carboxamido pyrazole (6c):

The mixture of coumaran-3-one (4c) (0.005 mol, 1.58 gm) and semicarbazide hydrochloride (0.01 mol, 1.11 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (6c), m.p. 240°C, yield 70%.

Properties and constitution of the compound (6c):

1) The compounds (6c) showed properties similar to those of compound (5a).

2) TLC:  
   Solvent (CCl₄) height : 6.5 cm  
   Solute height : 4.4 cm  
   Rf-value : 0.67

3) Elemental Analysis:
   N%  Found  15.65,  Calculated  15.73

From analytical data, the molecular formula of the compound (6c) was found to be C₁₆H₉ClN₄O₄.

From chemical properties and analytical results, the compound (6c) was assigned the structure as, 3-phenyl-[1]-5-chloro-7-nitro-benzofurano [3, 2-c]-1-carboxamido pyrazole.
EXPERIMENT NO. 18

Synthesis of 3-(4-methoxy phenyl)-1-[1]-5-chloro benzofurano [3, 2-c]-1-carboxamido pyrazole (6d):

The mixture of coumaran-3-one (4d) (0.005 mol, 1.51 gm) and semicarbazide hydrochloride (0.01 mol, 1.11 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (6d), m.p. 204°C, yield 65%.

Properties and constitution of the compound (6d):

1) The compounds (6d) showed properties similar to those of compound (5a).

2) TLC:   Solvent (CCl₄) height : 6.0 cm
         Solute height    : 3.6 cm
         Rf-value        : 0.60

3) Elemental Analysis:
   N% Found  12.24, Calculated  12.31
From analytical data, the molecular formula of the compound \((6d)\) was found to be \(C_{17}H_{12}ClN_3O_3\).

4) The spectral data of the compound \((6d)\) is as follows;

a) The IR spectrum of compound \((6d)\) (Spectrum No. 5) showed the following absorption bands:

<table>
<thead>
<tr>
<th>Frequency (cm(^{-1}))</th>
<th>Intensity</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>2843.2</td>
<td>(b)</td>
<td>(C-H) stretching</td>
</tr>
<tr>
<td>2360.0</td>
<td>(b)</td>
<td>(N-H) stretching</td>
</tr>
<tr>
<td>1686.0</td>
<td>(S)</td>
<td>(C=O) stretching</td>
</tr>
<tr>
<td>1603.5</td>
<td>(S)</td>
<td>(C=N) stretching</td>
</tr>
<tr>
<td>1427.5</td>
<td>(S)</td>
<td>(C=C) stretching</td>
</tr>
<tr>
<td>1261.5</td>
<td>(S)</td>
<td>(C-N) stretching</td>
</tr>
<tr>
<td>771.0</td>
<td>(S)</td>
<td>(C-Cl) stretching</td>
</tr>
</tbody>
</table>

b) The NMR spectrum of compound \((6d)\) was recorded in \((CDCl_3 + DMSO)\). The observed chemical shift can be correlated as follows (Spectrum No. 6):

<table>
<thead>
<tr>
<th>Chemical shift in ((\delta))ppm</th>
<th>Multiplicity</th>
<th>No. of Proton</th>
<th>Types of Proton</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.95</td>
<td>S</td>
<td>3H</td>
<td>-OCH(_3)</td>
</tr>
<tr>
<td>6.8-8.5</td>
<td>m</td>
<td>7H</td>
<td>Ar-H</td>
</tr>
<tr>
<td>7.3</td>
<td>S</td>
<td>2H</td>
<td>NH(_2)</td>
</tr>
</tbody>
</table>

From chemical properties, analytical data and spectral analysis, the compound \((6d)\) was assigned the structure as, \(3-(4\text{-methoxy phenyl})-\{1\}-5\text{-chloro benzofurano [3, 2-c]-1-carboxamido pyrazole}.\)
EXPERIMENT NO. 19

Synthesis of 3-(4-methoxy phenyl)-[1]-5-chloro-7-bromo-benzofurano [3, 2-c]-1-carboxamidopyrazole (6e):

The mixture of coumaran-3-one (4e) (0.005 mol, 1.90 gm) and semicarbazide hydrochloride (0.01 mol, 1.11 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (6e), m.p. 203°C, yield 60%.

Properties and constitution of the compound (6e):

1) The compounds (6e) showed properties similar to those of compound (5a).

2) TLC: Solvent (CCl₄) height : 6.3 cm
   Solute height : 4.8 cm
   Rf-value : 0.72

3) Elemental Analysis:

   N%   Found 9.93, Calculated 10.02

From analytical data, the molecular formula of the compound (6e) was found to be C₁₇H₁₁ClBrN₃O₃.
From chemical properties and analytical results, the compound (6e) was assigned the structure as, 3-(4-methoxy phenyl)-[1]-5-chloro-7-bromo-benzofurano [3, 2-c]-1-carboxamido pyrazole.

EXPERIMENT NO. 20

Synthesis of 3-(4-methoxy phenyl)-[1]-5-chloro-7-nitro-benzofurano [3, 2-c]-1-carboxamido pyrazole (6f):

The mixture of coumaran-3-one (4f) (0.005 mol, 1.73 gm) and semicarbazide hydrochloride (0.01 mol, 1.11 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (6f), m.p. 172°C, yield 60%.

Properties and constitution of the compound (6f):

1) The compounds (6f) showed properties similar to those of compound (5a).

2) TLC: Solvent (CCl₄) height : 6.0 cm
   Solute height : 3.7 cm
   Rf-value : 0.61
3) Elemental Analysis:

N% Found 14.41, Calculated 14.50

From analytical data, the molecular formula of the compound (6f) was found to be $C_{17}H_{11}ClN_4O_5$.

From chemical properties and analytical results, the compound (6f) was assigned the structure as, 3-(4-methoxy phenyl)-[1]-5-chloro-7-nitro-benzofurano [3, 2-c]-1-carboxamido pyrazole.

EXPERIMENT NO. 21

Synthesis of 3-phenyl-[1]-5-chloro benzofurano [3, 2-c]-1-thiocarboxamido pyrazole (7a):

The mixture of coumaran-3-one (4a) (0.005 mol, 1.36 gm) and thiosemicarbazide (0.01 mol, 0.91 gm) in pyridine (20 ml) was refluxed for about 4 hours and worked up as given in general procedure to obtain the compound (7a), m.p. 180°C, yield 75%.
Properties and constitution of the compound (7a):

1) The compounds (7a) showed properties similar to those of compound (5a).

2) TLC: Solvent (CCl₄) height : 6.5 cm
   Solute height : 4.2 cm
   Rf-value : 0.64

3) Elemental Analysis:
   \[ \text{N\%} \quad \text{Found} \quad 12.70, \quad \text{Calculated} \quad 12.84 \]

From analytical data, the molecular formula of the compound (7a) was found to be \( \text{C}_{16}\text{H}_{10}\text{ClSNO} \).

From chemical properties and analytical results, the compound (7a) was assigned the structure as, 3-phenyl-[1]-5-chloro-benzofurano [3, 2-c]-1-thiocarboxamido pyrazole.

\[
\begin{array}{c}
\text{Cl} \\
\text{N} \\
\text{N} \\
\text{S} = \text{C} - \text{NH}_2 \\
\end{array}
\]

(7a)

EXPERIMENT NO. 22

Synthesis of 3-phenyl-[1]-5-chloro-7-bromo-benzofurano [3, 2-c]-1-thiocarboxamido pyrazole (7b):

The mixture of coumaran-3-one (4b) (0.005 mol, 1.76 gm) and thiosemicarbazide (0.01 mol, 0.91 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (7b), m.p. 220°C, yield 70%.
Properties and constitution of the compound (7b):

1) The compounds (7b) showed properties similar to those of compound (5a).

2) TLC:  
   Solvent (CCl₄) height : 6.0 cm  
   Solute height : 3.5 cm  
   Rf-value : 0.58

3) Elemental Analysis:  
   N%  Found 10.24, Calculated 10.37

From analytical data, the molecular formula of the compound (7b) was found to be C₁₆H₉ClBrSN₃O.

From chemical properties and analytical results, the compound (7b) was assigned the structure as, 3-phenyl-[1]-5-chloro-7-bromo-benzofurano [3, 2-c]-1-thiocarboxamido pyrazole.
EXPERIMENT NO. 23

Synthesis of 3-phenyl-[1]-5-chloro-7-nitro-benzofurano [3, 2-c]-1-thiocarboxamido pyrazole (7c):

The mixture of coumaran-3-one (4c) (0.005 mol, 1.58 gm) and thiosemicarbazide (0.01 mol, 0.91 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (7c), m.p. above 270°C, yield 65%.

Properties and constitution of the compound (7c):

1) The compounds (7c) showed properties similar to those of compound (5a).

2) TLC: Solvent (CCl₄) height : 6.0 cm

Solute height : 3.2 cm

Rf-value : 0.53

3) Elemental Analysis:

N% Found 14.92, Calculated 15.05

From analytical data, the molecular formula of the compound (7c) was found to be C₁₆H₁₂ClSN₄O₃.

From chemical properties and analytical results, the compound (7c) was assigned the structure as, 3-phenyl-[1]-5-chloro-7-nitro-benzofurano [3, 2-c]-1-thiocarboxamido pyrazole.
EXPERIMENT NO. 24

Synthesis of 3-(4-methoxy phenyl)-[1]-5-chloro benzofurano [3, 2-c]-1-thiocarboxamido pyrazole (7d):

The mixture of coumaran-3-one (4d) (0.005 mol, 1.51 gm) and thiosemicarbazide (0.01 mol, 0.91 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (7d), m.p. 168°C, yield 70%.

Properties and constitution of the compound (7d):
1) The compounds (7d) showed properties similar to those of compound (5a).
2) TLC: Solvent (CCl₄) height : 6.0 cm
   Solute height : 3.9 cm
   Rf-value : 0.65
3) Elemental Analysis:
   N% Found 11.61, Calculated 11.76

From analytical data, the molecular formula of the compound (7d) was found to be C₁₇H₁₂ClSN₃O₂.
4) The spectral data of the compound (7d) is as follows;

   a) The IR spectrum of compound (7d) (Spectrum No. 7) showed the following absorption bands:

<table>
<thead>
<tr>
<th>Frequency ( \text{cm}\text{^{-1}} )</th>
<th>Intensity</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>2841.9</td>
<td>(b)</td>
<td>(C-H) stretching</td>
</tr>
<tr>
<td>1683.4</td>
<td>(S)</td>
<td>(C=O) stretching</td>
</tr>
<tr>
<td>1602.1</td>
<td>(S)</td>
<td>(C=N) stretching</td>
</tr>
<tr>
<td>1427.5</td>
<td>(S)</td>
<td>(C=C) stretching</td>
</tr>
<tr>
<td>1261.8</td>
<td>(S)</td>
<td>(C-N) stretching</td>
</tr>
<tr>
<td>768.5</td>
<td>(S)</td>
<td>(C-Cl) stretching</td>
</tr>
</tbody>
</table>

   b) The NMR spectrum of compound (7d) was recorded in CDCl\textsubscript{3}. The observed chemical shift can be correlated as follows (Spectrum No. 8):

<table>
<thead>
<tr>
<th>Chemical shift in (&amp;)ppm</th>
<th>Multiplicity</th>
<th>No. of Proton</th>
<th>Types of Proton</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.0</td>
<td>S</td>
<td>3H</td>
<td>-OCH\textsubscript{3}</td>
</tr>
<tr>
<td>6.9-8</td>
<td>m</td>
<td>7H</td>
<td>Ar-H</td>
</tr>
<tr>
<td>8.5</td>
<td>S</td>
<td>2H</td>
<td>NH\textsubscript{2}</td>
</tr>
</tbody>
</table>

From chemical properties, analytical data and spectral analysis, the compound (7d) was assigned the structure as, 3-(4-methoxy phenyl)-[1]-5-chloro benzofurano [3, 2-c]-1-thiocarboxamido pyrazole.
05/05/04 14:41 R.C./SAIF.P.U.CHD.
X: 4 scans, 4.0cm⁻¹, flat, smooth, abex
spl.code:J-4

Spectrum No. 7
EXPERIMENT NO. 25

Synthesis of 3-[(4-methoxy phenyl)-[1]-5-chloro-7-bromo-benzofurano [3, 2-c]-1-thiocarboxamido pyrazole (7e):

The mixture of coumaran-3-one (4e) (0.005 mol, 1.90 gm) and thiosemicarbazide (0.01 mol, 0.91 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (7e), m.p. 194°C, yield 60%.

Properties and constitution of the compound (7e):

1) The compounds (7e) showed properties similar to those of compound (5a).

2) TLC:
   Solvent (CCl₄) height : 6.6 cm
   Solute height : 4.6 cm
   Rf-value : 0.69

3) Elemental Analysis:
   N% Found 9.50, Calculated 9.65

From analytical data, the molecular formula of the compound (7e) was found to be C₁₇H₁₁ClBrSN₃O₂.

From chemical properties and analytical results, the compound (7e) was assigned the structure as, 3-[(4-methoxy phenyl)-[1]-5-chloro-7-bromo-benzofurano [3, 2-c]-1-thiocarboxamido pyrazole.
EXPERIMENT NO. 26

Synthesis of 3-(4-methoxy phenyl)-[1]-5-chloro-7-nitrobenzofurano [3, 2-c]-1-thiocarboxamido pyrazole (7f):

The mixture of coumaran-3-one (4f) (0.005 mol, 1.73 gm) and thiosemicarbazide (0.01 mol, 0.91 gm) in pyridine (20 ml) was refluxed for about 4 hours and then processed as given in general procedure to obtain the compound (7f), m.p. 198°C, yield 75%.

Properties and constitution of the compound (7f):
1) The compounds (7f) showed properties similar to those of compound (5a).

2) TLC:
   Solvent (CCl₄) height  :  6.5 cm
   Solute height        :  4.3 cm
   Rf-value             :  0.66

3) Elemental Analysis:
   N% Found 13.82, Calculated 13.93

From analytical data, the molecular formula of the compound (7f) was found to be C₁₇H₁₁ClSN₄O₄.
From chemical properties and analytical results, the compound (7f) was assigned the structure as, 3-(4-methoxy phenyl)-[1]-5-chloro-7-nitro-benzofurano [3, 2-c]-1-thio-carboxamido pyrazole.
Plausible Mechanism