CHAPTER II

Synthesis of novel mercury heterocycles
2.1 INTRODUCTION

The work in this chapter deals with the reaction of 4-bromomethylcoumarins and 4-bromomethyl 1-aza coumarins with o-mercurated phenols leading to the formation of o-mercurated 4-aryloxymethylcoumarins. Reactivity of the o-mercurated 4-aryloxymethyl coumarins has been studied during the present investigation. In view of this an attempt has been made to present the earlier work on mercuration of coumarins, their importance and few applications of organomercurials in organic synthesis have been cited from the recent literature.

2.1.1 MERCURATION OF COUMARINS

Mercuration of coumarins was of interest in view of the olefinic character of the C3-C4 double bond and a probable electrophilic substitution in the benzene ring. One of the earliest reports on the mercuration of coumarins was by Sen and Chakravarthi\(^1\) who were successful in introducing mercury into the coumarin nucleus. Boiling the dilute solution of coumarin 1 in alkali with yellow mercuric oxide and acidification with HCl, monochloro 2 and dichloromercurycoumarins 3 were obtained.

\[
\text{\textbf{1) HgO}} \quad \text{\textbf{2) HCl}}
\]

Naik and Patel\(^2\) have studied the effect of substituents on the mercuration of coumarins. Coumarin dissolved in 5 % NaOH, the excess of alkali neutralized with acetic acid and a solution of mercuric acetamide added gives 6, 8-bis hydroxymercury derivative 4, treatment with dil. HCl resulted in the dichloromercury compound 3.

\[
\text{\textbf{dil.HCl}}
\]
7-Hydroxy-4-methyl coumarin on reaction with mercuric acetamide in acetic acid, resulted in 6, 8-bis hydroxyl mercury derivative 6 which on treatment with CS$_2$ yielded the thio mercury compound 7.

Sheshadri and Rao$^3$ have investigated the reaction of mercury salts on coumarins. They found that mercuric acetate in methanol reacted with the double bond of the coumarins and further mercurates the benzene ring. If the 6$^{th}$ and 8$^{th}$ positions are free, the reaction leads to 3, 6, 8-triacetoxymercuro-4-methoxy melilotic anhydride 8.

Panigrahi and Raut$^4$ reported the synthesis of mercurated coumarinyl amino thiazoles 10 from 2-arylamino 4-3' coumarinyl thiazoles 9 which proved to be potent fungicides.
2.1.2. RECENT APPLICATIONS OF ORGANOMERCURIALS IN HETEROCYCLES

Mercury organometallics are used in halodemercuration or palladium-promoted coupling reactions. 2-alkylated indole has been mercurated to give the compound 12 using mercury (II) acetate and coupled to dichloroquinone under palladium catalysis to give the corresponding indole 13 which is further used in the synthesis of insulin mimetic demethylasterriquinones.

(±) Pterocarpin and other chromanocoumarans 15 were synthesized in one step by the reaction of 2-H-chromenes with o-chloromercury phenols in presence of lithium chloropalladite.

3-Chloromercuriated benzofurans 17 have been obtained by mercury (II) acetate-promoted cyclizations of alkynes. Compound 17 is demercurated with NaBH₄ to the corresponding benzofuran which is a useful intermediate in the synthesis of different neolignans.
Mercury derived non aromatic heterocycles arise as intermediates in carbon-carbon double bond addition processes. In the synthesis of 3-deoxy-D-lyxo-2-heptulosonic acid derivatives, or in the preparation of fused cyclic polyethers where the pyran 18 is treated with mercury (II) trifluoroacetate to give a R-mercurial acetal intermediate 19 which has been converted to the dihydropyran 20 by treatment with ethyl vinyl ether.\(^6\)
2.1.3. INTRAMOLECULAR REACTIONS OF 4-ARYLOXY AND 4-THIOARYLOXYMETHYL COUMARINS:

4-Aryloxymethylcoumarins with carbonyl functions at the ortho position in heteroaryl moiety have been converted to the corresponding benzofuranyl coumarins\(^9\) by an intramolecular carbanion addition across carbonyl followed by dehydration.

\[
\begin{align*}
\text{R}^1 &= 6\text{-CH}_3, 7\text{-CH}_3, 6\text{-OCH}_3, 5, 6 \text{ benzo, 7, 8-benzo} \\
\text{R}^2 &= \text{H, 5-Cl, 5-CH}_3, \text{ R}^3 = \text{H, CH}_3, \text{-OCH}_3
\end{align*}
\]

3-Amino benzofuranyl coumarins were the intermediates in the synthesis of polycyclic coumarins\(^10\) which were again obtained by the intramolecular reaction of the nitriles at the ortho position.

\[
\begin{align*}
\text{R} &= 6\text{-CH}_3, 7\text{-CH}_3, 6\text{-OCH}_3, 6\text{-Cl, 6-Br} \\
\text{R}' &= \text{H, CH}_3, \text{CH}_2\text{CH}_3
\end{align*}
\]

Shastri\(^{11}\) et al. have reported the synthesis of (1, 4) benzothiazine linked coumarins 25 by the following sequence in which the key step is the C-C bond formation.
Oxygenated triheterocycles 27 have been obtained from the reaction of \( o\)-hydroxy phenyl furyl ketones 26 and 4-bromomethyl coumarins in a single step via the intermediacy of the 4-aryloxymethyl coumarins.\textsuperscript{12}

The above cited literature indicates the importance of mercurated coumarins and intramolecular cyclization of 4-substituted coumarins involving C4-\( \text{CH}_2 \) and various groups located in the stereo electronically favored \textit{ortho} position in the aryloxy or thio aryloxy moiety.

\textbf{In light of the above observations and paucity of literature on} heterocyclic systems containing mercury it was thought to be of immense interest to study the reactivity of 4-aryloxymethylcoumarins and 1-aza 4-bromomethyl coumarins possessing halo/acetoxymercury substituents at the \textit{ortho} position.
2.2. PRESENT WORK AND DISCUSSION

The proposed work in this chapter is shown in (schemes 1, 2 and 3). The required starting compounds 4-bromomethyl coumarins\(^\text{13}\) (1) were synthesized from various phenols and 4-bromoethylacetoacetate under Pechmann cyclization conditions (0-5 °C) using conc. sulphuric acid as the cyclizing agent. 4-Bromo ethylacetoacetate\(^\text{14}\) in turn was prepared by the bromination of ethylacetoacetate using liquid bromine in dry ether at 0 °C. The resulting 4-bromomethyl coumarins (1) were crystalline solids and were crystallized from warm acetic acid (scheme 1).

4-bromo methyl coumarins (1) have been reacted with o-chloromercury phenol\(^\text{15}\) (2a) leading to the formation of 4-o-chloromercury-4-aryloxymethylcoumarins (3). Reaction of the organomercurial (3) with anhydrous AlCl\(_3\) in chloroform lead to the formation of o-chloro-4-aryloxymethyl coumarins (4). Apparently the expected intramolecular carbon-mercury bond formation did not occur under the Friedel-Crafts conditions employed and it lead to demercuration with simultaneous chlorination of the aryloxy moiety.
Scheme- 1: Synthesis of organomercurial intermediates (3) and cyclized compounds (6)

Formation of compound (4a, R= 6-CH₃) has been confirmed by the reaction of 6-methyl 4-bromomethyl coumarin with o-chlorophenol. The identity of the two samples was confirmed by IR and mixed melting points.

Another attempt to bring about ring closure at C-3 in coumarin was carried out using pyridine acetic anhydride which resulted only in anion exchange reaction leading to the formation of acetoxymercurated 4-aryloxymethyl coumarins (5) (scheme 1).

Carbon-mercury bond formation was finally achieved by using neutral alumina (activated) in presence of anhydrous potassium carbonate in refluxing conditions.
xylene, under N₂ atmosphere. This was a modified condition based on the use of basic alumina in carbon mercury bond formation in p-benzoquinones.¹⁷ All these cyclized compounds were then separated by filtration, solvent evaporation and subjected to routine purification methods.

In order to ascertain the effect of different leaving groups as this intramolecular mercuration, mercurated p-cresol was used in this sequence. Compound (2b) was obtained by mercuration of p-cresol using mercuric acetate in acetic acid using the reported methods.¹⁸ The two step sequence lead to the cyclized products (8a-8b) with the intermediacy of the ethers (7a-7b) (scheme 2).

**Scheme- 2: Synthesis of acetoxy-mercurated 4-aryloxymethyl coumarins (7) and cyclized compounds (8a-8b)**

This sequence was applied to 1-aza 4-bromomethyl coumarins¹⁹ (9) which were obtained by the two step sequence by the bromination of acetoacetonilides in chloroform. The intermediate α-bromoacetoacetanilide subsequently cyclizes in presence of H₂SO₄ at 60-70 °C. (scheme 3).

The reaction sequence involving nucleophilic allylic substitution followed by intramolecular mercuration lead to the cyclized products (11) via
the intermediacy of the ethers (10). These compounds exhibited the lactam carbonyl at 1673 cm\(^{-1}\) and the cyclized product again exhibited lower carbonyl frequency at 1650 cm\(^{-1}\). In the \(^1\)H-NMR the upfield shift of the methylene protons was observed in these two compounds also. The spectral features of all the intermediates and the cyclized products are in conformity with their structure and has been confirmed by the spectroscopic methods.

Scheme- 3: Synthesis of \(\text{o-chloromercury 4-aryloxymethyl carbostyrils (10)}\) and cyclized compounds (11a-11b)

Formation of the \(\text{o-chloromercurated 4-aryloxymethyl coumarins (3)}\) (scheme 1) was confirmed by the spectral data. In the IR spectrum the lactone carbonyl in (3e, R= 6-OCH\(_3\)) was observed at 1710 cm\(^{-1}\) (spectrum No. 1) and the \(^1\)H NMR showed a singlet at 5.45 ppm due to the C4 methylene protons.
attached to the aryloxy moiety. The other signals in the spectrum at 3.85, 6.65 and 7.46-7.02 are due to OCH₃, C3-H and aromatic protons (spectrum No. 2). The ¹³C NMR spectrum exhibited C4-CH₂ at 67.02 and methoxy carbon at 48.02 (spectrum No. 3). ESI mass spectrum showed m/z peak at 517 (M+H), 519 (M+2+H) (scheme 1).

The mercurated heterocycles (6) indicated the absence of C3 proton in the ¹H NMR spectrum. A marked decrease in the IR carbonyl stretching was observed in (6). It was observed that a clear difference of 25 cm⁻¹ (spectrum No. 4). This was consistent with all the other compounds. A comparison of the lactone and lactam carbonyls in the uncyclized 4-(o-mercuriated) aryloxymethyl compounds and mercury heterocycles is presented in table No.1. Compounds (3) and (6) is presented. (Table No. 1).
Table No- 1: Carbonyl frequency of intermediate ethers (3, 7, 10) and corresponding cyclized compounds (6, 8, 11)

<table>
<thead>
<tr>
<th>Compd.</th>
<th>R</th>
<th>R'</th>
<th>X</th>
<th>Y</th>
<th>$\nu_{\text{CO}}$ (cm$^{-1}$)</th>
<th>Compd.</th>
<th>$\nu_{\text{CO}}$ (cm$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>6-CH$_3$</td>
<td>H</td>
<td>O</td>
<td>-Cl</td>
<td>1722</td>
<td>6a</td>
<td>1685</td>
</tr>
<tr>
<td>3b</td>
<td>7-CH$_3$</td>
<td>H</td>
<td>O</td>
<td>-Cl</td>
<td>1728</td>
<td>6b</td>
<td>1686</td>
</tr>
<tr>
<td>3c</td>
<td>5,7-CH$_3$</td>
<td>H</td>
<td>O</td>
<td>-Cl</td>
<td>1714</td>
<td>6c</td>
<td>1690</td>
</tr>
<tr>
<td>3d</td>
<td>7,8-CH$_3$</td>
<td>H</td>
<td>O</td>
<td>-Cl</td>
<td>1704</td>
<td>6d</td>
<td>1687</td>
</tr>
<tr>
<td>3e</td>
<td>6-OCH$_3$</td>
<td>H</td>
<td>O</td>
<td>-Cl</td>
<td>1709</td>
<td>6e</td>
<td>1663</td>
</tr>
<tr>
<td>3f</td>
<td>6-Cl</td>
<td>H</td>
<td>O</td>
<td>-Cl</td>
<td>1716</td>
<td>6f</td>
<td>1685</td>
</tr>
<tr>
<td>3g</td>
<td>5,6-Benzo</td>
<td>H</td>
<td>O</td>
<td>-Cl</td>
<td>1722</td>
<td>6g</td>
<td>1672</td>
</tr>
<tr>
<td>3h</td>
<td>7,8-Benzo</td>
<td>H</td>
<td>O</td>
<td>-Cl</td>
<td>1722</td>
<td>6h</td>
<td>1673</td>
</tr>
<tr>
<td>7a</td>
<td>6-CH$_3$</td>
<td>CH$_3$</td>
<td>O</td>
<td>-OOCOCH$_3$</td>
<td>1723</td>
<td>8a</td>
<td>1662</td>
</tr>
<tr>
<td>7b</td>
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<td>CH$_3$</td>
<td>O</td>
<td>-OOCOCH$_3$</td>
<td>1729</td>
<td>8b</td>
<td>1682</td>
</tr>
<tr>
<td>10a</td>
<td>H</td>
<td>H</td>
<td>NH</td>
<td>-Cl</td>
<td>1673</td>
<td>11a</td>
<td>1650</td>
</tr>
<tr>
<td>10b</td>
<td>6-Cl</td>
<td>H</td>
<td>NH</td>
<td>-Cl</td>
<td>1682</td>
<td>11b</td>
<td>1652</td>
</tr>
</tbody>
</table>

The C4 methylene protons in 6e (R= 6-OCH$_3$) (scheme 1) indicated an upfield shift and were found to resonate as a singlet in the range 3.4 ppm and in few cases were found to be merged in the DMSO signal at 3.3 (spectrum No. 50).
However upon addition of TFA exhibited a downfield shift due to the protonation of the oxygen which is depicted as follows (spectrum No. 6).

In the $^{13}$C NMR spectrum, the methylene carbon appeared at 67.02 in the ether (3e, spectrum No.3) whereas in the cyclized product the methylene carbon showed a slight upfield shift and appeared at 57 ppm (spectrum No. 7).

FAB mass spectrum showed $m/z$ peak at 481, which confirms the formation of compound (spectrum No. 8).

In conclusion it can be seen that this intramolecular mercuration has resulted in new heterocyclic system containing a hetero atom and mercury carbon bonds. The detailed procedures of the synthetic steps involved are presented in the experimental section.
Table No.- 2: A comparison of the C4 methylene (C4-\(\text{CH}_2\)) proton and carbon chemical shifts (\(\delta\) ppm) in ethers (3, 7, 10) and corresponding cyclized compounds (6, 8, 11).

\[
\begin{array}{ccccccccc}
\text{Compd.} & \text{X} & \text{Y} & \text{R} & \text{R'} & \text{chemical shifts of C4-CH}_2 & \text{Compd.} & \text{chemical shifts of C4-CH}_2 \\
& & & & & ^1\text{H} & ^13\text{C} & ^1\text{H} & ^13\text{C} \\
3a & O & -\text{Cl} & 6-\text{CH}_3 & H & 5.27 & 67.03 & 6a & 4.08 & 57.07 \\
3b & O & -\text{Cl} & 7-\text{CH}_3 & H & 5.32 & 65.07 & 6b & 4.08 & 57.10 \\
3c & O & -\text{Cl} & 5,7-\text{CH}_3 & H & 5.55 & 67.03 & 6c & 4.03 & 57.22 \\
3d & O & -\text{Cl} & 7,8-\text{CH}_3 & H & 5.41 & 67.23 & 6d & 4.09 & 57.09 \\
3e & O & -\text{Cl} & 6-\text{OCH}_3 & H & 5.45 & 67.02 & 6e & 4.08 & 57.02 \\
3f & O & -\text{Cl} & 6-\text{Cl} & H & 5.44 & 65.76 & 6f & 4.09 & 57.02 \\
3g & O & -\text{Cl} & 5,6-\text{Benzo} & H & 5.83 & 67.08 & 6g & 4.12 & 57.06 \\
3h & O & -\text{Cl} & 7,8-\text{Benzo} & H & 5.53 & 67.10 & 6h & 4.10 & 57.10 \\
7a & O & -\text{OCOCH}_3 & 6-\text{CH}_3 & \text{CH}_3 & 5.86 & 67.22 & 8a & 4.08 & 57.12 \\
7b & O & -\text{OCOCH}_3 & 6-\text{OCH}_3 & \text{CH}_3 & 5.30 & 67.28 & 8b & 4.08 & 57.13 \\
10a & \text{NH} & -\text{Cl} & H & H & 5.43 & 66.76 & 11a & 4.08 & 57.36 \\
10b & \text{NH} & -\text{Cl} & 6-\text{Cl} & H & 5.72 & 64.12 & 11b & 4.07 & 57.36 \\
\end{array}
\]
Spectrum No. 1: IR (KBr) spectrum of compound 3e
Spectrum No. 2: $^1$H NMR (DMSO) of compound 3e
Spectrum No. 3: $^{13}$C NMR (DMSO) of compound $3e$
Spectrum No. 4: IR (KBr) spectrum of compound 6c
Spectrum No. 5: $^1$H NMR (DMSO) of compound 6e
Spectrum No. 6: 'H NMR (DMSO/TFA) of compound 6e
Spectrum No. 7: $^{13}$C NMR (DMSO/TFA) of compound 6e
Spectrum No. 8: FAB mass spectrum of compound 6e
2.3. EXPERIMENTAL

Part A

This part describes the preparation of some of the starting materials employed in the present work and general procedures adapted for synthesis of new compounds. The phenols used for the preparation of 4-bromomethyl coumarins were commercial samples and were used after purification.

2.3.1 Preparation of 4-bromoethyl acetoacetate

Liquid bromine (20.5 mL, 0.38 mol) was added with stirring during the course of one hour to an ice cold solution of ethylacetoacetate in 60 mL, of dry ether. Reaction mixture was allowed to stand at room temperature for about 24 hours. It was decomposed with crushed ice, separated ether layer was washed with water and dried over anhydrous calcium chloride. Solvent was removed under reduced pressure and pale yellow coloured 4-bromo ethylacetoacetate which is lachrymatory in nature was stored in dark colored bottles.

2.3.2 Preparation of 4-bromomethyl coumarins

General Procedure

30 mL of conc. sulphuric acid was added with stirring to a mixture of equimolar quantity of substituted phenols and 4-bromoethyl acetoacetate (0.1 mol), maintaining the temperature between 0-5 °C. The reaction mixture was allowed to stand in ice chest overnight and the deep red colored solution was poured into the stream of crushed ice. Solid separated was filtered and washed with water and then with cold ethanol so as to get colorless compound. All the substituted 4-bromomethyl coumarins were crystallized from acetic acid.

2.3.3 Synthesis of o- chloromercury phenol

Two liters of water is heated to boiling in a 3 liter flask, meanwhile 50 g of phenol in a 250 cc beaker provided with a small glass mechanical stirrer, is heated to 170 °C on an electric heater. The heat is turned off and 100 g (0.31 mol) of powdered mercuric acetate is added gradually (5-10 min.) to the stirred
phenol. After all the mercuric acetate has been dissolved in the phenol, the mercuration mixture is poured slowly into the hot water in a clean flask and the burner having previously been removed. Beaker rinsed out with some of hot water. Mixture boiled for 5 min. and then filtered through the filter paper in a large Buchner funnel which has been previously been heated by blowing steam through it. The pink residue consists of small amount of dimercurated phenol and some polymerization products.

The filtrate is again brought to boiling in a clean flask and treated with a solution of 20 g (0.34 mol) of NaCl in 200 mL of boiling water. The precipitate formed is p-chloromercuryphenol together with some colored impurities. The mixture is heated to boiling and filtered through a large preheated Buchner funnel. The filtrate on cooling deposits white feathery crystals of o-chloromercury phenol. Mixture allowed to stand at least 12 hrs and then filtered. The crystals are dried and recrystallized from hot water. Average Yield: 44%

2.3.4 Synthesis of o-acetoxymercurated p-cresol\(^18\) (2b).

An equimolar mixture of p-cresol and mercuric acetate (0.01 mol) was refluxed in acetic acid 50 mL for 18 hrs. After the completion of reaction as monitored on TLC, acetic acid was removed by distillation and the reaction mixture cooled to room temperature and triturated with acetone, obtained crude solid was washed with alcohol and crystallized from warm acetic acid.

2.3.5 Synthesis of chlorophenoxymethyl coumarins\(^16\) (4).

A mixture of substituted 4-bromomethylcoumarins (0.001 mol) and (0.33 g, 0.0025 mol) of anhydrous AlCl\(_3\) is refluxed in dry chloroform for about 12-14 h. After completion of the reaction as monitored on TLC (5 mL chloroform), chloroform concentrated under \textit{vacuo} and the crude solid obtained is washed with 1:1 HCl, then with water and finally with dilute alcohol. The obtained solid is crystallized from acetic acid.
2.3.6 Preparation of the 4-(2-Chloromercury-phenoxymethyl)-6-chromene-2-ones (3, 7, 10) (General Procedure)

To a dry 100 mL flask, equipped with a stir bar was added substituted 4-bromo methyl coumarins/l-aza coumarins (0.005 mol), o-chloro mercury phenol/o-acetoxymercurated p-cresol (0.005 mol), anhydrous K$_2$CO$_3$ (1.72 g, 0.0125 mol) and dry butanone (50 mL). The solution was refluxed for 20-24 h. After this time, butanone was concentrated and the reaction mixture was poured onto crushed ice. The crude solid obtained was filtered, washed with dil. HCl, water and finally with alcohol and crystallized from warm acetic acid.

2.3.7 Synthesis of substituted 13H-5, 12-dioxa-7-mercura-[4, 5]cyclohepta [1, 2-a] naphthalene 6-ones (6, 8, 11) (General procedure).

Preparation of Activated Al$_2$O$_3$/K$_2$CO$_3$

A mixture of neutral Al$_2$O$_3$ (1 g, 0.01 mol) and anhydrous K$_2$CO$_3$ (2.76 g, 0.02 mol) is ground thoroughly in a glass mortar and heated on the Bunsen flame for 4 h followed by the direct usage into the reaction vessel without allowing the mixture to attain room temperature.

To a dry 100 mL flask equipped with a stir bar was added substituted o-chloromercury phenoxy methylcoumarins/o-chloromercury phenoxy 1-aza coumarins (13 mmol), activated Al$_2$O$_3$;K$_2$CO$_3$ (1.41 g,) and dry xylene (25 mL). The solution was refluxed for 24-28 h. After this time the reaction was cooled to room temperature, the crude solid which separates out was filtered and washed with minimum amount of xylene. Xylene was further concentrated to get crude product. Compound was recrystallized from dry xylene (Table 1).
PART B

Part B of the experimental section details the results of the newly synthesized compounds.

Materials and Methods

Reactions were performed in oven-dried glassware under nitrogen atmosphere containing a Teflon coated stir bar and dry septum. Butanone was dried over calcium chloride and dry distilled before use. Xylene was dried over Na pressed wire and dry distilled before use. Mercuric acetate was purchased from Fishers Scientific Ltd. TLC analyses were performed on commercial Kieselgel 60 F254 silica gel plates. IR Spectra were recorded on a Bruker EQUINOX 55 FTIR. NMR spectra were obtained on Bruker Spectrometer using DMSO as solvent, with proton and carbon resonances at 300, 400 and 75 MHz, respectively. Mass spectral data (ESI) were recorded on HCT Ultra ETD II. Bruker Daltonics, Germany and FAB mass data were recorded on a JEOL SX 102/DA-6000 Mass Spectrometer.

PHYSICAL AND SPECTRAL DATA

2.3.6.1. 4-(2-Chloromercury-phenoxy methyl)-6-methyl-chromene-2-one (3a).

Yield: 2.20 g (86 %). mp 238-240 °C. FT-IR (KBr, cm⁻¹) 1722. ¹H NMR (300 MHz, DMSO) δ: 7.45-7.09 (m, 7H), 6.67 (s, 1H, C₃-H of coum.), 5.27 (s, 2H, CH₂O), 2.39 (s, 3H, CH₃). ¹³C NMR (75 MHz, DMSO) δ: 152.66, 151.64, 132.62, 131.89, 131.09, 130.69, 125.06, 123.22, 122.10, 121.62, 121.32, 117.32, 113.82, 112.26, 109.19, 67.03, 23.00. MS (ESI+) m/z = 501(M+H), 503 (M+2+H). Anal. calc. for C₁₇H₁₃ClHgO₃: C, 40.73; H, 2.61. Found: C, 40.64; H, 2.53.
2.3.6.2. 4-(2-Chloromercury-phenoxymethyl)-7-methyl-chromene-2-one (3b).

Yield: 2.20 g (86 %). mp 250-252 °C. FT-IR (KBr, cm⁻¹) 1728. \(^1\)H NMR (300 MHz, DMSO) δ: 7.50-7.02 (m, 7H), 6.62 (s, 1H, C3-H of coum.), 5.32 (s, 2H, CH₂O), 2.46 (s, 3H, CH₃). \(^1\)C NMR (75 MHz, DMSO) δ: 152.45, 151.38, 132.82, 131.55, 130.89, 130.60, 125.08, 123.85, 122.98, 122.26, 121.64, 117.65, 113.82, 112.79, 110.00, 65.07, 22.53. MS (ESI+) \(m/z = 501\) (M+H), 503 (M+2+H). Anal. calcd. for C₁₇H₁₃ClHgO₃: C, 40.73; H, 2.61. Found: C, 40.72; H, 2.65.

2.3.6.3. 4-(2-Chloromercury-phenoxymethyl)-5, 7-methyl-chromene-2-one (3c).

Yield: 2.00 g (78 %). mp 260-262 °C. FT-IR (KBr, cm⁻¹) 1714. \(^1\)H NMR (300 MHz, DMSO) δ: 7.51-7.02 (m, 6H), 6.56 (s, 1H, C3-H of coum.), 5.55 (s, 2H, CH₂O), 2.70 (s, 3H, CH₃), 2.50 (s, 3H, CH₃). \(^1\)C NMR (75 MHz, DMSO) δ: 152.76, 151.24, 132.52, 131.89, 131.09, 130.22, 125.86, 123.82, 122.60, 121.66, 121.22, 117.32, 113.88, 112.32, 109.86, 67.03, 23.52, 23.02. MS (ESI+) \(m/z = 515.3\) (M+H), 517 (M+2+H). Anal. calcd. for C₁₄H₁₅ClHgO₃ C, 41.95; H, 2.93. Found: C, 41.98; H, 2.99.

2.3.6.4. 4-(2-Chloromercury-phenoxymethyl)-7, 8-methyl-chromene-2-one (3d).

Yield: 2.05 g (80 %). mp 264-266 °C. FT-IR (KBr, cm⁻¹) 1704. \(^1\)H NMR (300 MHz, DMSO) δ: 7.85-7.00 (m, 6H), 6.55 (s, 1H, C3-H of coum.), 5.41(s, 2H, CH₂O), 2.37 (s, 3H, CH₃), 2.29 (s, 3H, CH₃). \(^1\)C NMR (75 MHz, DMSO) δ: 152.76,
2.3.6.5. 4-(2-Chloromercury-phenoxymethyl)-6-methoxy-chromene-2-one (3e).

Yield: 2.12 g (82 %). mp 216-218 °C. FT-IR (KBr, cm\(^{-1}\)) 1710. \(^1\)H NMR (400 MHz, DMSO) \(\delta\): 7.48 (s, 1H, C5-H of coumar.), 7.46-7.02 (m, 6H), 6.65 (s, 1H, C3-H of coumar.), 5.45 (s, 2H, \(\text{CH}_2\text{O}\)), 3.85 (s, 3H, OCH\(_3\)). \(^{13}\)C NMR (75 MHz, DMSO) \(\delta\): 153.22, 152.06, 138.22, 132.92, 132.62, 132.09, 125.02, 123.44, 122.82, 121.00, 120.90, 119.22, 115.68, 114.92, 110.00, 67.02, 48.02. MS (ESI+) \(m/z = 517\) (M+H), 519 (M+2+H). Anal. calcd. for C\(_{17}\)H\(_{13}\)O\(_4\)HgCl: C, 39.47; H, 2.53. Found: C, 39.49; H, 2.60.

2.3.6.6. 4-(2-Chloromercury-phenoxymethyl)-6-chloro-chromene-2-one (3f).

Yield: 1.97 g (79 %). mp 260-264 °C. FT-IR (KBr, cm\(^{-1}\)) 1716. \(^1\)H NMR (300 MHz, DMSO) \(\delta\): 7.99 (s, 1H, C5-H of coumar.), 7.31-7.03 (m, 6H), 6.68 (s, 1H, C3-H of coumar.), 5.44 (s, 2H, \(\text{CH}_2\text{O}\)). \(^{13}\)C NMR (75 MHz, DMSO) \(\delta\): 152.49, 151.31, 137.86, 132.54, 130.03, 129.44, 125.05, 122.75, 121.42, 119.27, 119.07, 117.61, 113.80, 112.89, 109.99, 65.76. MS (ESI+) \(m/z = 521\) (M+H), 522.7 (M+2+H). Anal. calcd. for C\(_{16}\)H\(_{10}\)Cl\(_2\)HgO\(_3\): C, 36.83; H, 1.93. Found: C, 36.85; H, 1.99.
2.3.6.7. 4-(2-Chloromercury-phenoxydimethyl)-5, 6 benzo-chromene-2-one (3g).

Yield: 2.01 g (75 %). mp 238-240 °C. FT- IR (KBr, cm⁻¹) 1722. ¹H NMR (300 MHz, DMSO) δ: 8.35-7.04 (m, 10H), 6.88 (s, 1H, C3-H of coum.), 5.83 (s, 2H, CH₂O). ¹³C NMR (75 MHz, DMSO) δ: 153.44, 152.16, 138.12, 132.62, 132.32, 132.09, 125.22, 125.16, 123.44, 123.26, 122.96, 122.82, 121.00, 120.90, 120.62, 119.22, 115.68, 114.92, 110.00, 67.08. MS (ESI+) m/z = 537 (M+H), 539.3 (M+2+H). Anal. calcd. for C₂₀H₁₃ClHgO₃: C, 44.70; H, 2.44. Found: C, 44.66; H, 2.43.

2.3.6.8. 4-(2-Chloromercury-phenoxydimethyl)-7, 8 benzo-chromene-2-one (3h).

Yield: 1.92 g (72 %). mp 238-240 °C. FT- IR (KBr, cm⁻¹) 1722. ¹H NMR (300 MHz, DMSO) δ: 8.40-7.02 (m, 10H), 6.73 (s, 1H, C3-H of coum.), 5.53 (s, 2H, CH₂O). ¹³C NMR (75 MHz, DMSO) δ: 153.44, 152.12, 138.10, 132.64, 132.62, 132.39, 123.34, 122.96, 122.68, 121.22, 120.90, 120.58, 119.22, 115.88, 114.92, 114.12, 109.00, 67.10. MS (ESI+) m/z = 537 (M+H), 539.3 (M+2+H). Anal. calcd. for C₂₀H₁₃ClHgO₃: C, 44.70; H, 2.44. Found: C, 44.62; H, 2.50.

2.3.6.9. 4-(2-Acetoxymercury, 4-methyl-phenoxymethyl)-6-methyl-chromene-2-one (7a).

Yield: 0.87 g (69 %). mp 216-218 °C. FT- IR (KBr, cm⁻¹) 1749, 1723. ¹H NMR (300 MHz, DMSO) δ: 7.48-7.10 (m, 6H), 6.52 (s, 1H, C3-H of coum.), 5.86 (s, 2H, CH₂O), 2.42 (s, 3H,
2.3.6.10.4-(2-Acetoxymercury,4-methyl-phenoxymethyl)-6-methoxy- 
chromene-2-one (7b).

Yield: 2.24 g (81 %). mp 236-238 °C. FT-IR (KBr; cm⁻¹) 1748, 1729. ¹H NMR (300 MHz, DMSO) δ: 7.36-6.92 (m, 6H), 6.49 (s, 1H, C3-H of coum.), 5.30 (s, 2H, CH₂O), 3.85 (s, 1H, OCH₃ of coum.), 2.43 (s, 1H, CH₃), 2.30 (s, 1H, CH₃). ¹³C NMR (75 MHz, DMSO) δ: 169.22, 160.22, 160.02, 157.32, 157.12, 156.22, 155.88, 149.14, 147.04, 126.34, 124.58, 121.47, 118.09, 117.22, 112.10, 108.37, 67.22, 23.82, 23.12, 23.02. MS (ESI⁺) m/z = 539 (M+H). Anal. calcd. for C₂₀H₁₈HgO₅: C, 44.57; H, 3.37. Found: C, 44.56; H, 3.39.

2.3.6.11.4-(2-Chloromercury-phenoxymethyl)-azachromene-2-one (10a).

Yield: 1.94 g (80 %). mp 230-232 °C. FT-IR (KBr; cm⁻¹) 1673. ¹H NMR (300 MHz, DMSO) δ: 11.74 (s, 1H, NH), 7.84-7.00 (m, 8H), 6.67 (s, 1H, C3-H of coum.), 5.43 (s, 2H, CH₂O). ¹³C NMR (75 MHz, DMSO) δ: 169.48, 160.49, 160.22, 157.00, 155.86, 148.54, 147.03, 123.44, 119.05, 118.75, 115.42, 113.07, 112.61, 107.80, 106.89, 66.76. MS (ESI⁺) m/z = 486.2 (M+H), 488 (M+2+H). Anal. calcd. for C₁₅H₁₂ClHgNO₂: C, 39.52; H, 2.49; N, 2.88. Found: C, 39.52; H, 2.50; N, 2.86.
2.3.6.12. 4-(2-Chloromercury-phenoxymethyl)-6-chloro-azachromene-2-one (10b).

Yield: 1.87 g (72 %). mp 272-274 °C. FT-IR (KBr, cm\(^{-1}\)) 1682. \(^1\)H NMR (300 MHz, DMSO) \(\delta\): 11.78 (s, 1H, NH), 7.89-7.06 (m, 7H), 6.68 (s, 1H, C3-H of coum.), 5.72 (s, 2H, CH2O). \(^13\)C NMR (75 MHz, DMSO) \(\delta\): 170.12, 160.82, 160.00, 157.48, 150.62, 147.22, 134.24, 133.26, 129.26, 121.47, 118.88, 118.34, 117.62, 112.22, 108.12, 64.12. MS (ESI+) \(m/z\) = 520 (M+H), 521.7(M+2+H). Anal. calcd. for C\(_{16}\)H\(_{11}\)Cl\(_2\)HgNO\(_2\): C, 36.90; H, 2.13, N, 2.69. Found: C, 36.92; H, 2.11 N, 2.62.

2.3.7.1. 2-Methyl-13H-5, 12-dioxa-7-mercura-benzo[4,5]cyclohepta[1,2-a]naphthalene 6-one (6a).

Yield: 0.51 g (80 %). FT-IR (KBr, cm\(^{-1}\)) 1685. \(^1\)H NMR (300 MHz, DMSO) \(\delta\): 7.61 (s, 1H, C5-H), 6.71-7.41 (m, 6H), 4.08 (s, 2H, CH2O), 2.48 (s, 3H, CH\(_3\)). \(^13\)C NMR (75 MHz, DMSO) \(\delta\): 153.24, 152.62, 138.02, 132.22, 130.62, 130.02, 124.62, 123.10, 121.82, 119.62, 119.09, 117.22, 114.27, 113.06, 110.01, 57.07, 23.00. MS (ESI+) \(m/z\) = 465.2 (M+H). Anal. calcd. for C\(_{17}\)H\(_{12}\)HgO\(_3\): C, 43.92; H, 2.60. Found: C, 43.90; H, 2.60.

2.3.7.2. 3-Methyl-13H-5, 12-dioxa-7-mercura-benzo[4,5]cyclohepta[1,2-a]naphthalene 6-one (6b).

Yield 0.47 g (73 %). FT-IR (KBr) 1686. \(^1\)H NMR (300 MHz, DMSO) \(\delta\): 7.68 (s, 1H, C5-H), 6.65-7.38 (m, 6H), 4.08 (s, 2H, CH2O), 2.42 (s, 3H, CH\(_3\)). \(^13\)C NMR (75 MHz, DMSO) \(\delta\): 153.28, 152.66, 138.22, 132.22, 130.62, 130.02, 124.88, 123.62, 121.96, 119.62, 119.09, 117.32, 114.27, 113.26, 110.10, 57.10, 23.08. MS (ESI+) \(m/z\) = 465 (M+H). Anal. calcd. for C\(_{17}\)H\(_{12}\)HgO\(_3\): C, 43.92; H, 2.60. Found: C, 43.88; H, 2.65.
2.3.7.3. 1, 3-Dimethyl-13H-5,12-dioxa-7-mercura-benzo [4, 5] cyclohepta [1, 2-a] naphthalene 6-one (6c).
Yield: 0.49 g (77 %). FT-IR (KBr, cm\(^{-1}\)) 1690. 
\(^1\)H NMR (300 MHz, DMSO) \(\delta\): 8.00-6.64 (m, 6H), 4.03 (s, 2H, CH\(_2\)O), 2.52 (s, 3H, CH\(_3\)), 2.32 (s, 3H, CH\(_3\)). \(^{13}\)C NMR (75 MHz, DMSO) \(\delta\): 153.22, 152.44, 138.02, 132.40, 130.72, 130.23, 124.66, 123.09, 121.88, 119.84, 119.66, 117.32, 114.33, 113.12, 109.92, 57.22, 23.00, 22.95. MS (ESI+) \(m/z = 479\) (M+H). Anal. calcd. for C\(_{18}\)H\(_{14}\)HgO\(_3\): C, 45.14; H, 2.95. Found: 45.10; H, 2.93.

2.3.7.4. 3, 4-Dimethyl-13H-5, 12-dioxa-7-mercura-benzo [4, 5] cyclohepta [1, 2-a] naphthalene 6-one (6d).
Yield: 0.50 g (79 %). FT-IR (KBr, cm\(^{-1}\)) 1687. 
\(^1\)H NMR (300 MHz, DMSO) \(\delta\): 8.20-6.72 (m, 6H), 4.09 (s, 2H, CH\(_2\)O), 2.48 (s, 3H, CH\(_3\)), 2.30 (s, 3H, CH\(_3\)). \(^{13}\)C NMR (75 MHz, DMSO) \(\delta\): 153.27, 152.64, 138.22, 132.46, 130.62, 130.32, 124.72, 123.29, 121.78, 119.92, 119.57, 117.82, 114.82, 113.19, 109.97, 57.09, 23.00, 22.96. MS (ESI+) \(m/z = 479\) (M+H). Anal. calcd. for C\(_{18}\)H\(_{14}\)HgO\(_3\): C, 45.14; H, 2.95. Found: 45.18; H, 2.93.

2.3.7.5. 2-Methoxy-13H-5, 12-dioxa-7-mercura-benzo [4, 5] cyclohepta [1, 2-a] naphthalene 6-one (6e).
Yield: 0.51 g (76 %). FT-IR (KBr, cm\(^{-1}\)) 1663. 
\(^1\)H NMR (400 MHz, DMSO) \(\delta\): 7.93 (s, 1H, C5-H), 7.69-6.96 (m, 6H), 4.08 (s, 2H, CH\(_2\)O), 3.81 (s, 3H, OCH\(_3\)). \(^{13}\)C NMR (75 MHz, DMSO) \(\delta\): 152.63, 151.76, 137.22, 130.23, 129.22, 124.09, 123.65, 122.32, 119.06,
119.02, 117.27, 113.44, 112.07, 112.05, 109.14, 57.02, 48.03. MS (FAB+) m/z = 481 (M+H). Anal. calcd. for C_{17}H_{12}HgO_4: C, 42.46; H, 2.52. Found: C, 42.48; H, 2.50.

2.3.7.6. 2-Chloro-13H-5, 12-dioxo-7-mercura-benzo [4, 5] cyclohepta [1, 2-a] naphthalene 6-one (6f).

Yield: 0.41 g (62 %). FT-IR (KBr, cm\(^{-1}\)) 1685. \(^1\)H NMR (300 MHz, DMSO) \(\delta\): 7.93-7.02 (m, 7H), 4.09 (s, 2H, CH\(_2\)O). \(^13\)C NMR (75 MHz, DMSO) \(\delta\): 152.66, 151.42, 148.21, 130.62, 123.62, 123.12, 121.00, 119.99, 119.82, 117.06, 113.98, 113.00, 112.89, 109.82, 57.02. MS (ESI+) m/z = 485.2 (M+H), 487 (M+2+H).

Anal. calcd. for C_{16}H_{9}ClHgO_3: C, 39.60; H, 1.87. Found: C, 39.64; H, 1.81.

2.3.7.7. 1, 2-Benz-13H-5, 12-dioxo-7-mercura-benzo [4, 5] cyclohepta [1, 2-a] naphthalene 6-one (6g).

Yield: 0.50 g (72 %). FT-IR (KBr, cm\(^{-1}\)) 1672. \(^1\)H NMR (300 MHz, DMSO) \(\delta\): 8.20-7.22 (m, 10H), 4.12 (s, 2H, CH\(_2\)O). \(^13\)C NMR (75 MHz, DMSO) \(\delta\): 153.48, 152.58, 138.20, 132.68, 130.68, 130.72, 124.66, 123.62, 121.82, 121.65, 120.98, 120.22, 119.72, 119.12, 117.42, 114.32, 113.82, 113.10, 110.10, 57.06. MS (ESI+) m/z = 501.2 (M+H).

Anal. calcd. for C_{20}H_{12}HgO_3: C, 47.96; H, 2.41. Found: C, 47.95; H, 2.46.

2.3.7.8. 3, 4- Benzo-13H-5, 12-dioxo-7-mercura-benzo [4, 5] cyclohepta [1, 2-a] naphthalene 6-one (6h).

Yield: 0.51 g (71 %). FT-IR (KBr, cm\(^{-1}\)) 1673. \(^1\)H NMR (300 MHz, DMSO) \(\delta\): 8.40-7.10 (m, 10H), 4.10 (s, 2H, CH\(_2\)O). \(^13\)C NMR (75 MHz, DMSO) \(\delta\): 153.42, 152.62, 138.08, 132.22, 130.24, 130.02, 124.82, 123.44, 121.82, 121.66, 120.58, 120.22, 119.22, 118.12, 117.19, 114.54, 113.66, 113.22, 110.66, 57.10. MS
2.3.7.9. 2, 9-Dimethyl-13H-5, 12-dioxa-7-mercura-benzo [4, 5] cyclohepta [1, 2-a] naphthalene-6-one (8a).

Yield: 0.44 g (71%). FT-IR (KBr, cm\(^{-1}\)) 1662. 

\(^1\)H NMR (300 MHz, DMSO) \(\delta\): 8.28-7.28 (m, 6H), 4.08 (s, 2H, CH\(_2\)O), 2.36 (s, 3H, CH\(_3\)), 2.30 (s, 3H, CH\(_3\)). \(^{13}\)C NMR (75 MHz, DMSO) \(\delta\): 152.72, 151.33, 138.17, 130.88, 130.09, 123.82, 123.12, 121.12, 119.92, 119.82, 117.06, 113.98, 113.00, 112.89, 109.82, 57.12, 23.22, 23.02. MS (ESI+) \(m/z = 479.2\) (M+H). Anal. calcd. for C\(_{18}\)H\(_{14}\)HgO\(_3\): C, 45.14; H, 2.95. Found: C, 45.21; H, 2.94.

2.3.7.10. 2-Methoxy-9-methyl-13H-5, 12-dioxa-7-mercura-benzo [4, 5] cyclohepta [1, 2-a] naphthalene-6-one (8b).

Yield: 0.44 g (72%). FT-IR (KBr, cm\(^{-1}\)) 1682. 

\(^1\)H NMR (300 MHz, DMSO) \(\delta\): 8.40-7.35 (m, 6H), 4.08 (s, 2H, CH\(_2\)O), 3.85 (s, 1H, OCH\(_3\) of coum.), 2.36 (s, 1H, CH\(_3\)). \(^{13}\)C NMR (75 MHz, DMSO) \(\delta\): 153.72, 152.55, 138.17, 132.46, 130.77, 130.32, 124.65, 123.09, 121.78, 119.92, 119.57, 117.22, 114.66, 113.20, 109.88, 57.13, 48.00, 23.00. MS (ESI+) \(m/z = 495\) (M+H). Anal. calcd. for C\(_{18}\)H\(_{14}\)HgO\(_4\): C, 43.68; H, 2.85. Found: C, 43.62; H, 2.87.

2.3.7.11. 5H, 13 H-12-Oxa-5-aza-7-mercura-benzo [4, 5] cyclohepta [1, 2-a] naphthalene-6-one (11a).

Yield: 0.48 g (76%). FT-IR (KBr, cm\(^{-1}\)) 1650. 

\(^1\)H NMR (300 MHz, DMSO) \(\delta\): 11.79 (s, 1H, NH), 7.88-7.06 (m, 8H), 4.08 (s, 2H, CH\(_2\)O). \(^{13}\)C NMR (75 MHz, DMSO) \(\delta\): 152.32, 151.16, 137.26, 131.12, 130.42, 127.45, 126.82, 125.36, 119.23, 118.95, 117.45, 112.86, 112.26, 111.26, 110.26, 57.36. MS (ESI+) \(m/z = 450.2\) (M+H). Anal. calcd. for C\(_{16}\)H\(_{11}\)HgNO\(_2\): C, 42.72; H, 2.46; N, 3.11. Found: C, 42.73; H, 2.42; N, 3.15.
2.3.7.12. 2-Chloro-5H, 13 H-12-Oxa-5-aza-7-mercura-benzo [4, 5] cyclohepta [1, 2-a] naphthalene-6-one (11b).

Yield: 0.39 g (60 %). FT-IR (KBr, cm\(^{-1}\)) 1652. \(^1\)H NMR (300 MHz, DMSO) \(\delta\): 11.82 (s, 1H, NH), 7.86-7.04 (m, 7H), 4.07 (s, 2H, CH\(_2\)O). \(^{13}\)C NMR (75 MHz, DMSO) \(\delta\): 153.74, 152.22, 149.22, 130.86, 130.22, 125.22, 125.02, 122.86, 120.24, 119.32, 117.26, 116.62, 115.24, 111.14, 109.00, 57.24. MS (ESI\(^+\) \(m/z = 484.3\) (M+H), 486 (M+2+H). Anal. calcd. for C\(_{16}\)H\(_{10}\)ClHgNO\(_2\): C, 39.68; H, 2.08; N, 2.89. Found: C, 39.64; H, 2.10; N, 2.83.
2.4. REFERENCES