CHAPTER 1

Synthesis of novel linear Pyrrolochromenes by bromine assisted intramolecular ring closure reaction

In this chapter, we have reported rapid and efficient method for the synthesis of Pyrrolochromenes (74a-h, 85a-g and 87) starting from maleic anhydride and primary aromatic amines.

This chapter is divided into two sections.

Section A: Preparation of N-aryl maleimide and substituted salicylaldehydes.

Section B: Bromine assisted intramolecular cyclization to pyrrolochromenes.

1.1. Introduction

Heterocyclic compounds containing chromene (benzopyran) represent a privileged structure motif, that was found in biologically active natural products [1-3] and also auspicious in medicinal, agrochemicals, cosmetics, pigment industries and synthetic compounds. Enormous biological active natural product containing chromene as structural units has been isolated [4]. Beside this it is valuable as organic building blocks, bioactive molecules, pharmaceuticals and organic materials. The construction of such types of ring structures was achieved from o-hydroxybenzaldehyde (Salicylaldehyde) as a starting material, which has wide applicability for the construction of oxygen containing heterocyclic systems. This method predominates the linear ring growth and generally permits the direct and regiospecific introduction of substituents in the newly formed
heterocyclic ring. Among numerous possibilities for ortho joined functionalities containing carbon and oxygen are of particular interest, because of easy accessibility of simple derivatives provides them with exceptional versatility in hetero annulation reaction. From literature it was noted that salicylaldehyde, the first and best known member of this class of compounds has been utilized for the synthesis of various oxygen containing heterocycles (e.g. chromenes) [5-26]. They have been used as valuable leads to design and synthesis of new pharmacophores for medicinal chemistry and drug development owing to their valuable biological activities [27]. Substituted chromenes are endowed with broad spectrum of pharmacological properties such as anti-HIV [28], anticancer [29] antibacterial [30], anti-fungal [31], antileishmanial [32], insecticidal [33], temicides [34], antitrypanosomal [35], Endothelein A receptor antagonist [36, 37], COX-2 inhibitor [12, 13], antihypertensive [38, 39], Pottasium channel openers and activators [40-42]. In addition, chromene containing drug such as Acolbifene 1 is useful for the breast cancer treatment [43], Catechin 2 and epigallocatechin gallate 3 (EGCG) show both an antiallergic effects and anticancer action [44–46], benzo[f]chromenes (naphthopyrans) 4 are of special interest as photochromic compounds [47] which have a wide variety of applications such as ophthalmic glasses, electronic display systems, optical switches and temporary or permanent memories. Robalzoton 5 was useful for potential treatment of depression and anxiety [48].
Figure 1: Applications of benzopyran containing scaffold in active drug and material chemistry.

Literature pertaining to the synthesis of pyrrolo chromeno fused skeletons revealed only limited reports [26]. These literature reports and our continuous interest in this area prompted us to report the novel route towards the synthesis of pyrrollochromenes derivatives, which may have potential biological activities.

** Literature method for the synthesis of 2H- chromene**

Wang et al. [12, 13] synthesizes the novel benzopyran class which showed activity against cyclooxygenase-2 inhibitors. Compound 8 was obtained from reaction between substituted salicylaldehydes 6 and unsaturated ester 7 in presence of base in DMF or DMSO, which on hydrolysis afford acid derivative of chromenes 9 which is highly potent against cyclooxygenase-2 inhibitors.
Areias et al. [49] reported novel synthesis of chromene which act as an adenosine $A_{2A}$ receptor. The Knoevenagel condensation of salicylaldehydes $10$ with cyanoacetamides $11$ carried out at room temperature, using aqueous sodium bicarbonate or sodium carbonate. This green route allowed the isolation of the 2-imino-2H-chromenes $12a-f$ in 38-100% yield. Compound $12a-f$ upon heating at $90^\circ C$ in an aqueous HCl, afforded the 2-oxo-2H-chromenes compound $13a-f$ in 25-100% yield.

\[
\begin{align*}
&\text{R}_1 \quad \text{OCH}_3 \quad \text{H} \quad \text{OCH}_3 \quad \text{H} \quad \text{OH} \quad \text{H} \quad \\
&\text{R}_2 \quad \text{H} \quad \text{Cl} \quad \text{Br} \quad \text{Br} \quad \text{Br} \quad \text{H}
\end{align*}
\]

Jana et al. [50] reported the synthesis of 2-H chromenes via intramolecular Alkyne – Carbonyl metathesis reaction. Alkynyl ether of salicylaldehyde derivative $14$ on reflux with FeCl$_3$ in acetonitrile undergoes intramolecular alkyne-aldehyde metathesis to gives $15$.

Konoike et al. [17] reported synthesis of 4-methoxycromene-3-carboxylic acid (23) intermediate as endothelin antagonist. Compound $16$ on reaction with isopropyl bromide
in $K_2CO_3$ afforded compound 17, which on further reaction with aldehyde 18 in 2N NaOH gave chromene 19 through chalcone intermediate, which on Vilsmeier Haack Formylation afforded the compound 20. Formyl group in 20 is oxidized using NaClO$_2$ and Na$_2$SO$_3$H in toluene at reflux condition to afforded compound 24. Compound 20 on reaction with NaOMe in MeOH at reflux temperature afforded acid 21 which is further converted to respected ester 22 in $K_2CO_3$ at room temperature. Compound 22 on reaction with Grignard regent afforded compound 23, which shows endothelin receptor activity.

Yin et al. [18] reported an efficient synthesis of (R) and (S)-8-ethoxy-2-(4-fluorophenyl)-3-nitro-2H-chromene. Compound 28 was obtained by domino oxa Michel-Henry reaction. Reacting compound 26 with $\beta$-nitrostyrene 27, as a chiral chromene as a racemic mixture. Tert-butyldimethylsilylloxy group of compound 28 was deprotected in acidic condition to respected phenol. Compound 29 was resolved by using chemical
derivation method, which on reaction with chiral α-methoxy phenyl acetic acid gives resolved compound 30. Resolved compounds 32 and 33 were obtained from compound by 31 by protecting phenolic –OH in ethyl iodide in K₂CO₃.

Varma et al. [11] reported 2-amino substituted isoflav-3-enes by microwave irradiation. Compound 36 obtained by enamine approach of aldehyde 34 with cyclic secondary amines 35 in household microwave oven, 36 on reaction with various salicylaldehyde derivatives 37 in NH₄OAc in microwave irradiation afforded tetrahydrachromene 38, which on dehydration gives 2-amino substituted isoflav-3-enes derivatives 39 in 73-85% yield.
Youn et al. [19] reported the synthesis of benzofuran and benzopyran via Pd-catalysed oxidative ring closing. One pot synthetic procedure for cyclization of compound 40 in, benzoquinone, Na₂CO₃ in dioxane at room temperature in the presence of Pd(CH₃CN)₂Cl₂ catalyst afforded the chromene compound 41 in 77% yield. Reaction involves olefin activation, nucleophilic attack and β-hydride elimination.

Lui et al. [51, 52] reported the synthesis of 2-substituted 2H-chromenes using potassium Vinyltrifluororoborates. Compound 42 on reacting with Vinyltrifluororoborates 43 in 20 mol % benzyl amine at 80°C temperature afforded the compound 2-substituted 2H-chromenes 44 in 51% yield and predicted to potentially interact with transforming growth factor-β receptors, was screened for bioactivity in living zebrafish embryos.
Wang et al. [53] reported the synthesis of 2-substituted chromenes by catalytic Petasis reaction. Compound 47 was obtained by catalytic Petasis reaction between salicylaldehyde 42, boronic acid 45 and dibenzylamine (5 mol %) in dioxane for 12 h at 90°C in 92 % yield. While mixture of product 46 and 47 was obtained when morpholine used as a base in Petasis reaction. Compound 46 is converted to cyclise compound 47 by using 2, 6-lutidine as a base at 90°C temperature for 30 min.

Kumari et al. [54] reported the preparation of 5H-chromeno[3,4-c]pyridine 51. The established strategy related to domino Knoevenagel/Diels–Alder reaction, involved reaction of O-propargyl salicylaldehyde 48 and malononitrile or ethyl cyanoacetate or cyanoacetamide 49. The Knoevenagel condensation between the CHO function of 48 and active CH₂ of compound 49, afforded compound 50, followed by a [4+2] cycloaddition afforded desired product 51.
When the model reaction of \( O\)-propargyl salicylaldehyde 54 and malononitrile was examined using CuI (30 mol %) as a catalyst in acetonitrile under reflux without the aid of base, a yellow crystalline product 56 was obtained in 63% yield. Further yield was increased to 90 % by adding \((\text{NH}_4)_2\text{HPO}_4\) (10 mol %) The catalytic activity of other copper salts such as CuBr, CuCl, CuSO\(_4\) and Cu(OAc)\(_2\) were also examined, which led to an edge for Cu(I) over Cu(II) salts to achieve the product 56.

Perumal et al. [55] reported that aryl propargyl ethers 57 were cyclized in the presence of catalytic amount of Pd(OAc)\(_2\) in conjunction with stoichiometric amount of CuBr\(_2\) and LiBr to the corresponding 3-bromo-2H-chromene derivatives 58 in good yield. The protocol was further extended to synthesize 3-bromo-benzofused 2H-chromene derivatives.
Kaye et al. [56] reported that reactions of 2-hydroxybenzaldehydes 59 with various activated alkenes 60 under Baylis–Hillman conditions have been shown to proceed with regeoselective cyclisation to afford the corresponding 3-substituted chromene derivatives 61 in 53% and 62 in 29% yield respectively.

Wang et al. [57] reported the series of functionalized tetrahydro chromenes 65 by using a novel FeCl₃-catalyzed benzylation–cyclization tandem reaction.

Brase et al. [58] reported that 3-formyl-2 H-chromenes 68, which were readily accessible through an oxa-Michael reaction of salicylaldehydes 66 and unsaturated aldehydes 67, undergo a smooth decarbonylation reaction upon treatment with rhodium catalysts.
Wojciechowski et al. [26] reported a formation of chromenopyrrole 2, 3 dione 73 by thermal excursion of sulphur dioxide from the benzsaltone 70. Heating of benzsaltone with 1, 2 dichlorobenzene at 180°C generates an quinonemethides 71 as a dine intermediates which on reaction with maleimide dienophile 72 undergoes Diels-Alder [4+2] reaction and afforded the chromenopyrrole 2,3 dione 73 in 37-64% yield.

1.2 Present Work

In the present chapter, we describe novel route for the synthesis of pyrrolo [2,3-b] chromenes. One pot synthetic procedure is also reported for the synthesis of (E)-3-(2-hydroxybenzylidene)-1-phenylpyrrolidine-2, 5-dione by Wittig Reaction, starting from maleimide, TPP and aromatic aldehydes, without isolation of triphenylphosphinearenylidenesuccinamide intermediates. The retro synthetic pathway which we planned for the synthesis of these heterocycles is illustrated bellow.
Reterosynthesis of 2-phenylchromeno [2,3-b]pyrrole derivatives.

Scheme-1

1.3 Results and Discussion

1.3.1 Section: A, Synthesis of N-aryl maleimides and substituted salicylaldehydes

1.3.1.1. Synthesis of N-aryl maleimide derivatives

We have synthesized N-aryl maleimide using recently reported procedure in our laboratory [59].

Scheme-2

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<td>g</td>
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Aromatic amines reacted with maleic anhydride gives in situ generated maleanilic acid, which undergoes dehydrative cyclization yielded N-aryl maleimide derivatives 77a-h in 67-80% yields.

The IR spectrum of the compound 77a showed characteristic absorption bands at 1712 cm\(^{-1}\) corresponded to imide carbonyl group. The \(^{1}\)H NMR spectra (CDCl\(_3\)) of this solid showed singlet at \(\delta\ 6.84\) for two protons of vinyl carbon and multiplet at \(\delta\ 7.27\) for five protons of aromatic phenyl ring. The \(^{13}\)C NMR (CDCl\(_3\)) of 77a showed peaks at \(\delta\ 122.3\) corresponded to the two carbons of imide ring carbon. The signal at \(\delta\ 172.2\) represented imide carbonyl carbon, while all other four aromatic carbons appeared at their respective chemical shift positions in between \(\delta\ 125.5\) and 149.2. The mass spectrum of these solid

![Figure No.2: \(^{1}\)H NMR Spectra of N-aryl maleimide, 77a](image)
showed characteristic M+ peaks at 173 \text{ m/z}. Further, the elemental analysis was in agreement with molecular formula C_{10}H_7NO_2.

1.3.1.2. Synthesis of substituted-2-hydroxybenzaldehydes, 81a-g [60]

![Scheme-3](image)

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<td>I</td>
<td>Cl</td>
<td>CH_3</td>
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Substituted phenols 80a-g was reacted with paraformaldehyde in presence of anhydrous MgCl_2 and triethylamine resulted in the formation of substituted salicylaldehydes 81a-g.

1.3.1.3. Synthesis of 2-hydroxynaphthalene-1-carbaldehyde, 83 [61]

![Scheme-4](image)

Compound 83 was obtained by Remer Tiemann reaction, refluxing β-Naphthol 82 with chloroform and aq.NaOH for 1 h gives the ortho formilated product 83 in 78% yield.
1.3.2 Section: B, Bromine assisted intramolecular cyclization to pyrrolochromenes.

General approach for the synthesis of pyrrolo chromenes is outlined in, Scheme-5

![Diagram of pyrrolochromene synthesis](image)

Scheme-5

1.3.2.1. Synthesis of Triphenylphosphinesuccinamide, 76a-h

![Diagram of succinamide synthesis](image)

Scheme-6

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<td>f</td>
<td>4-ClC₆H₄</td>
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<tr>
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<td>d</td>
<td>4-FC₆H₄</td>
<td>h</td>
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The N-aryl maleimides 77a-h on reaction with triphenylphosphine in ethanol afforded triphenylphosphine adducts 76a-h in high yield. We have an advantage to use green solvent ethanol over benzene, acetic acid and THF.
The obtained solid was characterized by IR, $^1$H NMR, $^{13}$C NMR, Mass Spectroscopy and elemental analysis. For instance, the IR spectra of this solid showed bands at 3085, 1712, 1615 1379 cm$^{-1}$ corresponding to -CH$_2$, C=O imide and P=C stretching respectively. The $^1$H NMR spectra (CDCl$_3$) of this solid showed singlet at $\delta$ 3.76 for two protons of methylene group and multiplet at $\delta$ 7.21-7.73 for 20 aromatic protons. In $^{13}$C NMR spectrum (CDCl$_3$) of this solid the signal at $\delta$ 46.4 corresponded to methylene carbon while all other seventeen aromatic carbons appeared at their respective chemical shift positions in between $\delta$ 116.7 and 147.5, while two carbonyl carbon observe at $\delta$ 163.3 and $\delta$ 172.4 respectively Further, the mass spectra of this solid showed the characteristic M$^+$ peaks at 435 m/z. The elemental analysis was in agreement with the molecular formula C$_{28}$H$_{22}$NO$_2$P. On the basis of above spectral and analytical data structure 76a was assigned to this solid i.e., Triphenylphosphinesuccinamide, 76a.
1.3.2.2. Synthesis of (E)-3-(2-hydroxybenzylidene)-1-phenylpyrrolidine-2, 5-dione, 75a-h, 84a-g & 86[62-66]

Scheme-7

The obtained phosphorous ylide 76a-h, was further reacted with aromatic aldehydes having ortho hydroxy functionality for further hetero cyclization. Reaction of the phosphorous ylide 76a-h with salicylaldehyde, substituted salicylaldehyde derivatives and Naphthaldehyde in benzene or ethanol afforded the compound 75a-h, 84a-g and 86 in high yield respectively. All the above compounds 75a-h, 84a-g and 86 were also synthesized in one pot synthesis from maleimide without isolation of triphenylphosphine adducts 76a-h.
One pot synthesis of (E)-3-(2-hydroxybenzylidene)-1-phenylpyrrolidine-2, 5-dione, 75a-h, 84a-g, 86

\[
\text{Scheme-8}
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<td>4-CH_3OC_6H_4</td>
<td>g</td>
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<td>d</td>
<td>4-FC_6H_4</td>
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</table>

N-aryl maleimides 77a-h on reaction with triphenylphosphine and suitably o-hydroxybenzaldehydes/2-hydroxy-1-naphthaldehyde provided the corresponding 75a-h, 103a-g, 104 in high yields via an in situ generation of Wittig adduct as the reacting
species. All the synthesized compounds were characterized by spectral and analytical methods.

For instance, the IR spectrum of this solid showed bands at 3319, 3210, 1753, 1701 cm\(^{-1}\) for –OH, methylene, C=O and C=O conjugated with hydroxy respectively.

![Figure No.4: \(^1\)H NMR Spectra of (E)-3-(2-hydroxybenzylidene)-1-phenylpyrrolidine-2,5-dione, 75a](image)

The obtained compound was characterized by spectral and analytical methods.
In $^1$H NMR spectrum (DMSO-$d_6$) of this solid the protons at $\delta$ 3.85 gives singlet for CH$_2$, while the proton at $\delta$ 6.97-7.63 gives multiplet for nine proton, the proton at vinylic position appeared at $\delta$ 7.91 and the phenolic proton observed at $\delta$ 10.25 as a broad singlet which is D$_2$O exchangeable. The $^{13}$C NMR spectrum (DMSO-$d_6$) of this solid showed signal at $\delta$ 173.5 and 170.1 corresponded to carbonyl carbon of imide ring carbonyl, while all other eleven aromatic carbons appeared at their respective chemical shift positions in between $\delta$ 115.8 and 157.1 while aliphatic CH$_2$ is observed at $\delta$ 33.9. The mass spectrum of this solid showed the characteristic M$^+$ 279 m/z. Further, the elemental analysis was in agreement with the molecular formula C$_{17}$H$_{13}$NO$_3$. On the basis of above

Figure No.5: $^{13}$C NMR Spectra of (E)-3-(2-hydroxybenzylidene)-1-phenylpyrrolidine-2,5-dione, 75a
spectral and analytical data structure 75a was assigned to this solid i.e., (E)-3-(2-hydroxybenzyldene)-1-phenylpyrrolidine-2,5-dione.

1.3.2.3. Synthesis of linear tricyclic 5,7-dibromo-2-phenylchromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione, 74a-h

We first time report such type of synthetic strategy for the synthesis of linear tricyclic phenyl chromenopyrrole by bromine assisted intramolecular cyclisation.

Plausible reaction mechanism for the synthesis of pyrrol chromene:

<table>
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Scheme-9

Scheme-10
The reaction of o-hydroxybenzylidinesuccinimides 75a-h on treatment with excess of molecular bromine (4.5 equiv.) in DMF at 60 °C directly furnished the corresponding pyrrolochromenes 74a-h in 72-92% yield, plausibly via the intermediates 88 and 89 (Scheme 10). As anticipated, initially the aromatic ring under goes double electrophilic substitution to form the corresponding dibromo intermediates. Then bromine reacts with the carbon–carbon double bond to form the bromonium bridged intermediates 88. The released bromide ion abstracts the corresponding trans proton from active methylene unit for steric reasons and forms the requisite maleimide intermediates 89. The o-hydroxy group instantaneously attacks in a S\textsubscript{N}2′ fashion on the proximal carbon–carbon double bond with the displacement of an allylic bromide atom leading to the intramolecular cyclization to form the pyrrolochromenes 74a-h. The reaction does not go to completion on of use of molar equivalent bromine. This reaction was generalized by employing mono and disubstituted o-hydroxy benzaldehydes as depicted in scheme-11, 84a-g on reaction with bromine also furnished the corresponding pyrrolechromenes 85a-g following the similar route again in good yields (79-91%). The quantity of bromine used to obtain 85a-h from 84a-g is given in experimental procedure. The analytical and spectral data obtained for products 74a-h, 85a-g and 86 was in complete agreement with the assigned structures.
1.3.2.4. Synthesis of substituted pyrrol[b]chromene derivatives, 85a-g

Substituted pyrrol[b]chromene derivatives 85a-g was obtained by reacting 84a-g with bromine in DMF at 60°C. Compound 84c required 3.6 equivalents of bromine, 84a-b and 84f-g required 2.4 equivalents of bromine and 84d-e required 1.2 equivalent of bromine respectively.

1.3.2.5. Synthesis of benzo[f]chromene, 87

Compound 87 was obtained by reacting compound 86 with Br₂ in DMF at 60°C for 1h, this reaction required 2.4 equivalents of bromine, 1.2 equivalents for bromination of phenol and next equivalents for the cyclization.

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Scheme-11

Scheme-12
Figure No. 6: $^1$H NMR Spectra of 5, 7-dibromo-2-phenylchromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione, 74a

Figure No. 7: $^{13}$C NMR Spectra of 5,7-dibromo-2-phenylchromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione, 74a
The obtained solid was characterized by spectral and analytical methods. For instance, the IR spectrum of showed absorption at 3060 for aliphatic -CH-, 1780 and 1718 for cyclic imides respectively, 1688 aromatic C=C bond and 743 for Br absorption. $^1$H NMR spectrum (DMSO-$d_6$) of this solid showed doublet at $\delta$ 5.86 ($J = 2.4$ Hz) for one protons of pyran ring at C$_2$ position. The multiplet are observe for aromatic five proton at $\delta$ 7.56–7.39, the doublet observed at $\delta$ 7.60 ($J = 2.4$ Hz) and $\delta$ 7.80 ($J = 2.4$ Hz) respectively shows meta coupling with each other the high value of one aromatic proton at $\delta$ 7.80 is due to proton flanked between two bromine, also one doublet is observe for one proton at 7.91 ($J = 2.4$ Hz) shows ‘W’ coupling with C$_2$ proton. In $^{13}$C NMR spectrum (DMSO-$d_6$) of this solid the two carbonyl carbon appeared at 168.8 and 163.6, while carbon near to oxygen goes downfield and it appeared at 150.2, remaining eleven aromatic carbons appeared at their respective chemical shift positions in between 136.6 and 111.1, while aliphatic C$_2$ near to oxygen appeared at 71.6. Further, the mass spectrum of this solid showed the characteristic M$^+$, M+2 and M+4 peaks at 432, 434 and 436 $m/z$ respectively due to presence of two chlorine atom. The elemental analysis was in agreement with the molecular formula C$_{17}$H$_9$Br$_2$NO$_3$. On the basis of above spectral and analytical data structure 74a was assigned to this compound i.e., 5, 7-Dibromo-2-phenylchromeno [2, 3-c]pyrrole-1,3(2H,3aH)-dione. Analogously, the derivatives 74b-h were synthesized and structures were confirmed by spectral and analytical data.

1.4 Conclusion

In summary, we have demonstrated a new practical two-step synthetic protocol for the synthesis of desired pyrrolochromenes. Our present diversity oriented approach to pyrrolochromenes is general in nature and will be useful to design their focused mini-
libraries for SAR studies. Our present results also provide an important clue that the bromine present in sea water also might be effecting such type of intramolecular cyclizations in the formation of natural products of marine origin.

1.5 Experimental Section

Preparation of N-aryl maleimides, 77a-h

![Chemical Structure](attachment:structure.png)

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General Procedure

To a stirred solution of Anilines 78a (10 gm, 107.5 mmoles) in Acetic Acid (20 ml) was added maleic anhydride 79 (10.54 gm, 107.5 mmoles), Solid obtained was stirred for 20 min for completion of reaction. To the same reaction mixture was added dropwise Conc.H₂SO₄ (7 ml) at 60°C and resultant solution was stirred for 2 hr for completion of reaction (TLC Checked). Cool the reaction mixture and was poured on crushed ice and solid separated was filtered, washed with diluted aq.NaHCO₃ solution and dried to furnish yellow solid 77a. Recrystallized from Ethanol, Yield -87%.

1-phenyl-1H-pyrrole-2, 5-dione, 77a

Yellow solid; Yield: 18.04 g (97%); M.p.90-92°C; Rf = 0.42 (ethyl acetate:hexane, 3:7); IR: ν = 3095, 1772, 1704, 1591, 1502, 1390, 1143, 694. ¹H NMR (300 MHz, CDCl₃):
7.27-7.21 (m, 5H, Ar-H), 6.89(s, 2H, =CH-). MS (70 eV): \( m/z = 173(M+H) \). Anal. Calcd. For C\(_{10}\)H\(_7\)NO\(_2\): Calcd.: C, 69.36; H, 4.07; N, 8.09%. Found: C, 69.55; H, 3.86; N, 8.25%.

1-p-tolyl-1H-pyrrole-2, 5-dione, 77b

Yellow solid; Yield: 3.70 g (97%); M.p.149-151\(^\circ\)C; \( R_f = 0.42 \) (ethyl acetate:hexane, 3:7); IR: \( \tilde{\nu} = 3093, 1712, 1406, 1134, 833 \). \(^1\)H NMR (400 MHz, CDCl\(_3\)): 7.26 (d, \( J=8.8 \) Hz, 2H, Ar-H), 7.20 (d, \( J=8.8 \) Hz, 2H, Ar-H), 6.83 (s, 2H, =CH-), 2.38 (s, 3H, -CH\(_3\)). MS (70 eV): \( m/z = 188(M+H) \). Anal. Calcd. For C\(_{11}\)H\(_9\)NO\(_2\): Calcd.: C, 70.58; H, 4.85; N, 7.48%.

1-(4-methoxyphenyl)-1H-pyrrole-2, 5-dione, 77c

Yellow solid; Yield: 4.01 g (97%); M.p.156-158\(^\circ\)C; \( R_f = 0.42 \) (ethyl acetate:hexane, 3:7); IR: \( \tilde{\nu} = 3053, 1701, 1620, 1508, 1246, 829 \). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): 7.21 (d, \( J=9.2 \) Hz, 2H, Ar-H), 7.13 (s, 2H, =CH-), 7.00 (d, \( J=9.2 \) Hz, 2H, Ar-H), 3.77 (s, 3H, -CH\(_3\)). MS (70 eV): \( m/z = 204(M+H) \). Anal. Calcd. For C\(_{11}\)H\(_9\)NO\(_3\): Calcd.: C, 65.02; H, 4.46; N, 6.89%. Found: C, 64.83; H, 4.65; N, 6.73%.

1-(4-fluorophenyl)-1H-pyrrole-2, 5-dione, 77d

Yellow solid; Yield: 3.64 g (95%); M.p.162-164\(^\circ\)C; \( R_f = 0.42 \) (ethyl acetate:hexane, 3:7); IR: \( \tilde{\nu} = 1704, 1620, 1509, 1146, 929 \). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)): 8.17 (d, \( J=9.3 \) Hz, 2H), 7.73 (2H, d, \( J = 9.3 \) Hz), 6.97 (s, 2H). MS (70 eV): \( m/z = 191(M+H) \). Anal. Calcd. For C\(_{10}\)H\(_6\)FNO\(_2\): Calcd.: C, 62.83; H, 3.16; N, 7.33%. Found: C, 62.72; H, 2.96; N, 7.63%.

1-(3-chlorophenyl)-1H-pyrrole-2, 5-dione, 77e

Yellow solid; Yield: 4.05 g (96%); M.p.89-91\(^\circ\)C; \( R_f = 0.42 \) (ethyl acetate:hexane, 3:7); IR: \( \tilde{\nu} = 1718, 1645, 1545, 1143, 625 \). \(^1\)H NMR (300 MHz, CDCl\(_3\)):
7.43-7.27 (m, 4H, Ar-H), 6.87 (s, 2H). MS (70 eV): \( m/z = 207(M+H), 209(M+2) \). Anal. Calcd. For \( \text{C}_{10}\text{H}_6\text{ClNO}_2 \): Calcd.: C, 57.85; H, 2.91; N, 6.75%. Found: C, 58.03; H, 2.78; N, 6.62%.

1-(4-chlorophenyl)-1H-pyrrole-2, 5-dione, 77f

Yellow solid; Yield: 4.01 g (95%); M.p.116-118°C [Literature M.p.115.3°C]; \( R_f = 0.42 \) (ethyl acetate:hexane, 3:7); IR: \( \nu = 3082, 1716, 1498, 1394, 1145, 831 \). \(^1\)H NMR (400 MHz, DMSO-\( d_6 \)): 7.44 (d, \( J = 8.7 \) Hz, 2H, Ar-H), 7.31 (d, \( J = 8.7 \) Hz, 2H, Ar-H), 6.86 (s, 2H, =CH-). MS (70 eV): \( m/z = 206(M-H), 208(M+2) \). Anal. Calcd. For \( \text{C}_{10}\text{H}_6\text{ClNO}_2 \): Calcd.: C, 57.85; H, 2.91; Cl, N, 6.75%. Found: C, 57.64; H, 3.13; N, 6.53%.

1-(4-bromophenyl)-1H-pyrrole-2, 5-dione, 77g

Yellow solid; Yield: 4.79 g (94%); M.p.125-127°C [Literature M.p.126°C]; \( R_f = 0.40 \) (ethyl acetate:hexane, 3:7); IR: \( \nu = 1715, 1615, 1455, 1147, 725 \). \(^1\)H NMR (400 MHz, DMSO-\( d_6 \)): 7.67 (d, \( J = 8.4 \) Hz, 2H, Ar-H), 7.30 (d, \( J = 8.4 \) Hz, 2H, Ar-H), 7.17 (s, 2H, =CH-). MS (70 eV): \( m/z = 251(M+H), 253(M+2) \). Anal. Calcd. for \( \text{C}_{10}\text{H}_6\text{BrNO}_2 \): Calcd.: C, 47.65; H, 2.40; N, 5.56%. Found: C, 47.97; H, 2.29; N, 5.75%.

1-benzyl-1H-pyrrole-2, 5-dione, 77h

Yellow solid; Yield: 3.61 g (95%); M.p.68-70°C [Literature M.p. 69.5-70.5°C]; \( R_f = 0.42 \) (ethyl acetate: hexane, 3:7); IR: \( \nu = 2947, 1758, 1730, 1697, 1187, 879 \). \(^1\)H NMR (300 MHz, CDCl\( _3 \)): 7.25-7.34 (m, 5H, Ar-H), 6.68 (s, 2H, =CH-), 4.66 (s, 2H, -CH\( _2 \)). MS (70 eV): \( m/z = 187(M+H) \). Anal. Calcd. For \( \text{C}_{11}\text{H}_9\text{NO}_2 \): Calcd.: C, 70.58; H, 4.85; N, 7.48%; Found: C, 70.41; H, 5.03; N, 7.69%.
General procedure

A dry 500 mL, three necked round bottomed flask equipped with a stirring bar, reflux condenser and rubber septa is purged with argon gas. Anhydrous magnesium dichloride (9.52 g, 100 mmol) and solid paraformaldehyde (4.5 g, 150 mmol) are added, while a positive pressure of argon gas is maintained. Dry tetrahydrofuran (250 mL) is added by syringe. Triethylamine (10.2 g, 100 mmol) is added dropwise by syringe and the mixture is stirred for 10 min. 4-chlorophenol 91b (mL, 50 mmol) is added dropwise by syringe, resulting in a light, opaque pink mixture. This mixture is immersed in an oil bath at about 75°C (bath temperature) and soon turns a bright orange-yellow color. Heating at gentle reflux is maintained for 4 hr. The reaction mixture is cooled to a room temperature and 100 mL of ether is added. The resulting organic phase is transferred to a 1-L separatory funnel and washed successively with 1N HCl (3x100 mL) and water (3x100 mL), dried over anhydrous magnesium sulfate (MgSO₄) and filtered. The solvent was removed by rotary evaporation leaving white oil that solidifies on further vacum
drying at 1-22 mmHg. The resulting white solid (8.0 g), consisting mainly pure 5-chloro-2-hydroxybenzaldehyde 92b is sufficiently pure.

**Synthesis of Triphenylphosphinelidinesuccinimides, 76a-h**

![Chemical structure of 76a-h](image)

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</table>

**General procedure**

To a solution of compound 77 (1.31 gm, 7.01 mmoles) in Ethanol (10 ml), was added portion wise TPP (0.935 gm, 7.01 mmoles) and the reaction mixture was stirred for 1 hr for completion of reaction (Checked by TLC), white solid separated was filtered washed with cold ethanol and dried. Recrystallized from Acetone-DMF (Yield-94%)

**N-Phenyl Triphenylphosphinelidinesuccinimides, 76a**

White solid; Yield: 3.09g (94%); M.p. 177°C [Literature [68] M.p. 175.5-178.5 °C]; IR: $\tilde{\nu}$ = 3085, 1712, 1645, 1490, 1379, 1161, 757. $^1$H NMR (300 MHz, CDCl$_3$): 7.68-7.19 (m, 20 H, Ar-H), 3.68 (s, 2H, -CH$_2$). MS (70 eV): $m/z$ = 436(M+H). Anal. Calcd. For C$_{28}$H$_{22}$NO$_2$P: Calcd.: C, 77.23; H, 5.09; N, 3.22%. Found: C, 77.04; H, 5.30; N, 3.39%.

**N-(p-tolyl) Triphenylphosphinelidinesuccinimides, 76b**

White solid; Yield: 4.70 g (98%); M.p. 183°C; IR: $\tilde{\nu}$ = 3051, 1710, 1643, 1514, 1435, 1386, 1305, 1165, 690, 540. $^1$H NMR (300 MHz, CDCl$_3$): 7.67-7.49 (m, 15 H, Ar-H), 7.31 (d, $J$= 6 Hz, 2H, Ar-H), 7.19 (d, $J$= 6 Hz, 2H, Ar-H), 3.14 (d, $J$= 0.6 Hz, 2H, -CH$_2$),
2.31 (s, 3H, -CH₃). MS (70 eV): \( m/z = 449 \text{(M+H)} \). Anal. Calcd. for C₂₉H₂₄NO₂P: Calcd.: C, 77.49; H, 5.38; N, 3.12\%. Found: C, 77.71; H, 5.59; N, 2.91\%.

**N-(p-MeO-Phenyl) Triphenylphosphinidelinesuccinimides, 76c**

White solid; Yield: 4.48 g (98\%); M.p. 180° C ; IR: \( \nu = 3051, 1708, 1510, 1433, 1379, 1165, 694 \). \(^1\)H NMR (300 MHz, \( d_6\)-DMSO): 7.70 - 7.60 (m, 15 H, Ar-H), 7.18 (d, \( J = 6.3 \) Hz, 2H, Ar-H), 6.94 (d, \( J = 6.6 \) Hz, 2H, Ar-H), 3.74 (s, 3H, -OCH₃), 3.04 (s, 2H, -CH₂). MS (70 eV): \( m/z = 465 \text{(M+H)} \). Anal. Calcd. for C₂₉H₂₄NO₃P: Calcd.: C, 74.83; H, 5.20; N, 3.01\%. Found: C, 74.64; H, 5.43; N, 3.22\%.

**N-(m-Cl-Phenyl) Triphenylphosphinidelinesuccinimides, 76d**

White solid; Yield: 4.35 g (96\%); M.p. 187° C ; IR: \( \nu = 3055, 1715, 1645, 1155, 695 \). \(^1\)H NMR (300 MHz, \( d_6\)-DMSO) \( \delta = 3051, 1708, 1510, 1433, 1379, 1165, 694 \). \(^1\)H NMR (300 MHz, \( d_6\)-DMSO) \( \delta = 7.76 - 7.62 \) (m, 15 H, Ar-H), 7.46 - 7.32 (m, 4H, Ar-H), 3.12 (s, 2H, -CH₂). MS (70 eV): \( m/z = 470 \text{(M+H)} \). Anal. Calcd. for C₂₈H₂₁ClNO₂P: Calcd.: C, 71.57; H, 4.50; N, 2.98\%. Found: C, 71.79; H, 4.32; N, 3.17\%.

**N-(p-Cl-Phenyl) Triphenylphosphinidelinesuccinimides, 76e**

White solid; Yield: 4.48g (99\%); M.p. 176° C ; IR: \( \nu = 3051, 1714, 1640, 1369, 1155, 690 \). \(^1\)H NMR (300 MHz, \( d_6\)-DMSO): 7.72-7.61 (m, 15 H, Ar-H), 7.46-7.32 (m, 4H, Ar-H), 3.12 (s, 2H, -CH₂). MS (70 eV): \( m/z = 470 \text{(M+H)} \). Anal. Calcd. for C₂₈H₂₁ClNO₂P: Calcd.: C, 71.57; H, 4.50; N, 2.98\%. Found: C, 71.76; H, 4.73; N, 2.77\%.

**N-(p-Br-Phenyl) Triphenylphosphinidelinesuccinimides, 76f**

White solid; Yield: 4.02 g (98\%); M.p. 184° C ; IR: \( \nu = 3021, 1718, 1665, 1321, 597 \). \(^1\)H NMR (300 MHz, \( d_6\)-DMSO) \( \delta = 7.72-7.58 \) (m, 15H, Ar-H), 7.34 (d, \( J = 6.3 \) Hz, 2H, Ar-H), 6.34 (d, \( J = 6.3 \) Hz, 2H, Ar-H), 3.07 (s, 2H, -CH₂). MS (70 eV): \( m/z = 469.1 \text{(M+H)} \). Anal. Calcd. for C₂₈H₂₁ClNO₂P: Calcd.: C, 71.57; H, 4.50; N, 2.98\%. Found: C, 71.76; H, 4.73; N, 2.77\%.
514(M+H). Anal. Calcd. For C_{28}H_{21}BrNO_2P: Calcd.: C, 65.38; H, 4.12; N, 2.72%.
Found: C, 65.19; H, 4.30; N, 2.94%.

**N-(benzyl) Triphenylphosphinelidinesuccinimides, 76g**
White solid; Yield: 4.61 g (96%); M.p. 169°C; IR: \( \bar{\nu} = 3055, 3021, 1717, 1655, 1317, 1130, 695; ^1H\) NMR (300 MHz, \( d_6\)-DMSO): 7.76-7.62 (m, 20H, Ar-H), 4.34 (s, 2H, -CH_2), 3.13 (s, 2H, -CH_2). MS (70 eV): \( m/z = 448\) (M+H). Anal. Calcd. For C_{29}H_{24}NO_2P:
Calcd.: C, 77.49; H, 5.38; N, 3.12%. Found: C, 77.70; H, 5.57; N, 2.90%.

**Synthesis of (E)-3-(2-Hydroxybenzylidene)-1-phenylpyrrolidine-2, 5-diones, 75a-h**

```
Ph_3P

\begin{align*}
\text{76a-h} & \quad \text{EtOH, 1h} \\
\text{90} & \\
\rightarrow & \\
\text{75a-h} \\
\end{align*}
```

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To a suspension of compound 76a (3 gm, 11.49 mmoles) in EtOH (30 ml) added dropwise solution of Salicylaldehyde 90 (0.84 ml, 11.49 mmoles) in EtOH (5ml) and reaction mixture was stirred for 1 h (TLC Checked), after completion of reaction separated white solid was filtered and washed with cold Ethanol (30x2), dried and recrystallized in Ethanol-DMF (10:1), Yield-93%.
One pot procedure for the synthesis of \((E)\)-3-(2-Hydroxybenzylidene)-1-phenylpyrrolidine-2, 5-diones, 75a-h

\[
\begin{align*}
\text{N–Ar} & \quad \text{TPP, EtOH} \quad \text{rt} \\
77a-h & \rightarrow 76a-h \rightarrow 75a-h \\
\end{align*}
\]

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General procedure for the synthesis of compound 75a-h, 84a-g and 86:

To a solution of compound N-aryl maleimides 77a-h (11.56 mmol) in ethanol (15 mL) was added portion wise triphenylphosphine (11.56 mmol) and stirred at rt for 30 min. To this reaction mixture was added dropwise solution of \(o\)-hydroxybenzaldehydes (12.00mmol) in ethanol (5 mL) and further stirred for 1 h. The separated solid product 75a-h was filtered, washed with cold ethanol, dried and recrystallized from EtOH/DMF (9:1).

\((E)\)-3-(2-Hydroxybenzylidene)-1-phenylpyrrolidine-2, 5-dione, 75a

White solid; yield: 2.99 g (95%); M.p. 250–252 °C; \(R_f=\) 0.46(Hexane: Ethyl acetate, 9:1);

IR (KBr): 3319, 1753, 1701 cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-\(d_6\)): \(\delta = 3.85\) (s, 2H), 7.05–6.97 (m, 2H), 7.63–7.14 (m, 7H), 7.91(s, 1H), 10.25 (br s, 1H); \(^1\)C NMR (75 MHz, DMSO-\(d_6\)): \(\delta =33.9, 115.8, 119.4, 120.9, 123.3, 127.1, 127.4, 128.1, 128.7, 129.1, 131.4,
132.6, 157.1, 170.1, 173.5 ppm; MS (EI): m/z 279[M–1]+; Analysis Calculated for C_{17}H_{13}NO_3: Calcd: C, 73.11; H, 4.69; N, 5.02%; Found: C, 72.93; H, 4.90; N, 5.04%.

*(E)-3-(2-Hydroxybenzylidene)-1-p-tolylpyrrolidine-2, 5-dione, 75b*

White solid; yield: 3.15 g (93%); M.p. 282–284 °C; Rf= 0.51(Hexane: Ethyl acetate, 9:1); IR (KBr):3321, 3070, 1757, 1697 cm\(^{-1}\); \(^1\)H NMR (400 MHz,DMSO-\(d_6\)):\(\delta = 2.34\) (s, 3H), 3.76 (d, \(J = 2\) Hz, 2H), 6.89 (t, \(J = 7.6\) Hz, 1H), 6.93 (d, \(J = 8\) Hz, 1H), 7.20 (d, \(J = 8.2\) Hz, 2H), 7.24 (d, \(J = 8\) Hz, 1H), 7.29 (d, \(J = 8.2\) Hz, 2H), 7.52 (d, \(J = 7.6\) Hz, 1H), 7.87 (d, \(J = 2\) Hz, 1H), 10.21 (s, 1H); \(^13\)C NMR (100 MHz, DMSO-\(d_6\)): \(\delta = 20.6, 33.9, 115.8, 119.3, 120.9, 123.3, 126.8, 127.3, 129.1, 129.9, 131.4, 137.6, 157.0, 170.1, 173.5 ppm; MS (EI): m/z 293[M–1]+; Analysis Calculated for C_{18}H_{15}NO_3: Calcd: C, 73.71; H, 5.15; N, 4.78%; Found: C, 73.49; H, 4.95; N, 4.57%.

*(E)-3-(2-Hydroxybenzylidene)-1-(4-methoxyphenyl) pyrrolidine-2, 5-dione, 75c*

White solid; yield: 3.10 g (87%); M.p. 272–273 °C; Rf= 0.60(Hexane: Ethyl acetate, 9:1); IR (KBr):3242, 1768, 1676 cm\(^{-1}\); \(^1\)H NMR (400 MHz,DMSO-\(d_6\)):\(\delta = 3.75\) (s, 2H), 3.78 (s, 3H), 6.89 (t, \(J = 7.6\) Hz, 1H), 6.93 (d, \(J = 8.4\) Hz, 1H), 7.03 (d, \(J = 8.8\) Hz, 2H), 7.27–7.23 (m, 3H), 7.52 (d, \(J = 7.6\) Hz, 1H), 7.86 (s, 1H), 10.21 (s, 1H); MS (EI): m/z 308[M–1]+; Analysis Calculated for C_{18}H_{15}NO_4: Calcd:C, 69.89; H, 4.89; N, 4.53%; Found: C, 69.66; H, 4.90; N, 4.42%.

*(E)-3-(2-Hydroxybenzylidene)-1-(4-flurophenyl) pyrrolidine-2, 5-dione, 75d*

White solid; yield: 2.83 g (91%); M.p. 253-254°C; Rf=0.56 (Hexane: Ethyl acetate, 9:1); IR (KBr): 3421, 1761, 1678, 575 cm\(^{-1}\); \(^1\)H NMR (400 MHz, DMSO-\(d_6\)):\(\delta = 3.78\) (s, 2H), 6.98–7.10 (m, 2H), 7.32 (t, \(J = 7.2\) Hz, 1H), 7.40 (d, \(J = 8.8\) Hz, 2H), 7.56 (d, \(J = 7.6\) Hz,
1H), 7.76 (d, J = 8.8 Hz, 2H), 7.89 (s, 1H), 10.26 (br s, 1H); MS (EI): m/z 297[M+1]+; Analysis Calculated for C\textsubscript{17}H\textsubscript{12}FNO\textsubscript{3}: Calcd: C, 68.68; H, 4.07; N, 4.71%; Found: C, 68.50; H, 3.89; N, 4.89%.

\textit{(E)-3-(2-Hydroxybenzylidene)-1-(3-chlorophenyl) pyrrolidine-2, 5-dione, 75e}

White solid; yield: 3.22 g (89%); M.p. 247–249 °C; Rf = 0.50 (Hexane: Ethyl acetate, 9:1); IR (KBr): 3361, 1757, 1701, 765 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (300 MHz, DMSO-\textsubscript{d}6): \delta = 3.79 (s, 2H), 6.99–6.86 (m, 2H), 7.40–7.70 (m, 2H), 7.59–7.48 (m, 4H), 7.94 (s, 1H), 10.39 (br s, 1H); MS (EI): m/z 313[M–1]+; Analysis Calculated for C\textsubscript{17}H\textsubscript{12}ClNO\textsubscript{3}: Calcd: C, 65.08; H, 3.86; N, 4.46%; Found: C, 65.31; H, 3.99; N, 4.25%.

\textit{(E)-3-(2-Hydroxybenzylidene)-1-(4-chlorophenyl) pyrrolidine-2, 5-dione, 75f}

White solid; yield: 3.43 g (95%); M.p. 280–281 °C; Rf = 0.48 (Hexane: Ethyl acetate, 9:1); IR (KBr): 3421, 1761, 1678, 575 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (400 MHz, DMSO-\textsubscript{d}6): \delta = 3.77 (s, 2H), 6.95–6.87 (m, 2H), 7.26 (t, J = 7.2 Hz, 1H), 7.39 (d, J = 8.8 Hz, 2H), 7.53 (d, J = 7.6 Hz, 1H), 7.57 (d, J = 8.8 Hz, 2H), 7.89 (s, 1H), 10.24 (br s, 1H); MS (EI): m/z 313[M–1]+; Analysis Calculated for C\textsubscript{17}H\textsubscript{12}ClNO\textsubscript{3}: Calcd: C, 65.08; H, 3.86; N, 4.46%; Found: C, 65.23; H, 3.70; N, 4.51%.

\textit{(E)-3-(2-Hydroxybenzylidene)-1-(4-bromophenyl) pyrrolidine-2, 5-dione, 75g}

White solid; yield: 3.20 g (92%); M.p. 261–263 °C; Rf = 0.56 (Hexane: Ethyl acetate, 9:1); IR (KBr): 3421, 1761, 1678, 575 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (400 MHz, DMSO-\textsubscript{d}6): \delta = 3.79 (s, 2H), 6.98–7.07 (m, 2H), 7.29 (t, J = 7.2 Hz, 1H), 7.41 (d, J = 8.8 Hz, 2H), 7.56 (d, J = 7.6 Hz, 1H), 7.59 (d, J = 8.8 Hz, 2H), 7.87 (s, 1H), 10.26 (br s, 1H); MS (EI): m/z 357[M–1]+; Analysis Calculated for C\textsubscript{17}H\textsubscript{12}BrNO\textsubscript{3}: Calcd: C, 56.00; H, 3.07; N, 3.91%; Found: C, 56.12; H, 3.10; N, 3.99%.
1]^1, 360[M+2]; Analysis Calculated for C_{17}H_{12}BrNO_3: Calcd: C, 57.00; H, 3.38; N, 3.91 
% ; Found: C, 57.18; H, 3.57; N, 3.72 %.

\((E)-3-(2-Hydroxybenzylidene)-1-benzylpyrrolidine-2, 5-dione, 75h\)

White solid; yield: 3.04 g (90%); M.p. 261–263 °C; \(R_f= 0.47\)(Hexane: Ethyl acetate, 9:1); IR (KBr): 3364, 3105, 1768, 1712 cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-\(d_6\)): \(\delta = 3.73\) (s, 2H), 4.68 (s, 2H), 6.88 (t, \(J= 7.5\) Hz, 1H), 6.94 (d, \(J= 8.1\) Hz, 1H), 7.36–7.23 (m, 6H), 7.50 (d, \(J= 7.5\) Hz, 1H), 7.84 (s, 1H), 10.26 (br s, 1H); \(^{13}\)C NMR (75 MHz, DMSO-\(d_6\)): \(\delta = 33.6, 41.3, 115.8, 119.3, 120.9, 123.2, 127.2, 127.3, 127.4, 128.4, 129.1, 131.4, 136.3, 157.0, 170.6, 174.2\) ppm; MS (EI): \(m/z\) 293[M–1]^1; Analysis Calculated for C_{18}H_{15}NO_3: Calcd:C, 73.71; H, 5.15; N, 4.78%; Found: C, 73.92; H, 5.00; N, 4.98%.

One pot procedure for the synthesis of \((E)-3-(2-Hydroxybenzylidene)-1-phenylpyrrolidine-2, 5-dione derivatives, 84a-g\)

\[
\begin{array}{c}
81a-g \\
84a-g
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\]

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To a solution of compound 77a (2.0g, 11.5 mmol) in ethanol (15 mL) was added portion wise triphenylphosphine (3.03g, 11.5 mmol) and the reaction mixture was stirred at room temperature for 30 min, to the same mixture was added dropwise solution of o-
substituted salicylaldehydes 81 (1.8 g, 12.00 mmol) in ethanol (5 mL) and further stirred for 1 h. The separated solid product was filtered, washed with cold ethanol, dried and recrystallized from EtOH/DMF (9:1).

*(E)-3-(2-Hydroxy-5-methylbenzylidene)-1-phenylpyrrolidine-2, 5-dione, 843a*

White solid; yield: 3.08 g (91%); M.p. 245–246 °C; *Rf* = 0.61 (Hexane: Ethyl acetate, 9:1); IR (KBr): 3157, 2989, 1778, 1684 cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆): δ = 2.49 (s, 3H), 4.02 (s, 2H), 7.13 (s, 1H), 7.31 (s, 1H), 7.74–7.62 (m, 6H), 8.17 (s, 1H), 10.28 (br s, 1H); ¹³C NMR (75 MHz, DMSO-d₆): δ = 20.1, 33.9, 115.7, 120.6, 122.8, 127.0, 127.6, 128.0, 128.0, 128.7, 129.1, 132.1, 132.6, 155.0, 170.1, 173.5 ppm; MS (EI): *m/z* 293[M–1]⁺; Analysis Calculated for C₁₈H₁₅NO₃: Calcd: C, 73.71; H, 5.15; N, 4.78%; Found: C, 73.51; H, 4.97; N, 5.01%.

*(E)-3-(5-Chloro-2-hydroxybenzylidene)-1-phenylpyrrolidine-2, 5-dione, 843b*

White solid; yield: 3.37 g (93%); M.p. 250–252 °C; *Rf* = 0.43 (Hexane: Ethyl acetate, 9:1); IR (KBr): 3155, 1770, 1724, 1706, 1384, 1197, 696 cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆): δ = 3.86 (s, 2H), 6.99 (d, *J*=8.7Hz, 1H), 7.54–7.30 (m, 7H), 7.80 (s, 1H), 10.59 (br s, 1H); ¹³C NMR (75 MHz, DMSO-d₆): δ =34.1, 117.4, 122.5, 123.0, 125.0, 126.0, 127.0, 128.0, 128.1, 128.7, 130.9, 132.4, 155.8, 169.7, 173.3 ppm; MS (EI): *m/z* 313 [M–1]⁺; Analysis Calculated for C₁₇H₁₂ClNO₃: Calcd:C, 65.08; H, 3.86; N, 4.46%; Found: C, 65.26; H, 3.58; N, 4.29%.

*(E)-3-(4-bromo-2-hydroxybenzylidene)-1-phenylpyrrolidine-2, 5-dione, 84c*

White solid; yield: 3.68 g (89%); M.p. 231-232°C; *Rf* = 0.52 (Hexane: Ethyl acetate, 9:1); IR (KBr): 3473, 1787, 1724, 1706, 1384, 1197, 696 cm⁻¹; ¹H NMR (200 MHz, DMSO-
δ = 3.64 (d, J=2 Hz, 2H), 6.81 (d, J=8 Hz, 1H), 7.41-7.29 (m, 6H), 7.42 (s, 1H), 7.97 (s, 1H), 9.93 (s, 1H); MS (EI): m/z 357 [M–1]^+, 359 [M+2]; Analysis Calculated for C_{17}H_{12}BrNO_3: Calcd: C, 57.00; H, 3.38; N, 3.91%; Found: C, 56.87; H, 3.51; N, 4.07%.

(E)-3-(3, 5-dichloro-2-hydroxybenzylidene)-1-phenylpyrrolidine-2, 5-dione, 84d

White solid; yield: 3.57 g (89%); M.p. 265-266 °C; Rf= 0.56(Hexane: Ethyl acetate, 9:1); IR (KBr): 3555, 1768, 1710, 1643, 1170, 865 cm⁻¹; ¹H NMR (200 MHz, DMSO-d_6): δ = 3.84 (d, J=2 Hz, 2H), 7.55-7.34 (m, 5H), 7.78 (s, 2H), 8.10 (d, J=2 Hz, 1H), 10.20 (bs, 1H); MS (EI): m/z 347 [M–1]^+; Analysis Calculated for C_{17}H_{11}Cl_2NO_3: Calcd: C, 58.64; H, 3.18; N, 4.02%; Found: C, 58.81; H, 3.32; N, 3.89%.

(E)-3-(2-hydroxy-3, 5-diiodobenzylidene)-1-phenylpyrrolidine-2, 5-dione, 84e

White solid; yield: 5.58 g (91%); M.p. 239-240 °C; Rf= 0.58(Hexane: Ethyl acetate, 9:1); IR (KBr): 3142, 1770, 1687, 11643, 1193, 692 cm⁻¹; ¹H NMR (200 MHz, DMSO-d_6): δ = 3.71 (s, 2H), 7.65-7.51 (m, 5H), 7.94 (s, 1H), 8.15 (d, J=2 Hz, 1H), 8.36 (d, J=2 Hz, 1H), 10.43 (br s, 1H); MS (EI): m/z 532 [M+1]^+; Analysis Calculated for C_{17}H_{11}I_2NO_3: Calcd: C, 38.45; H, 2.09; N, 2.64%; Found: C, 38.57; H, 1.88; N, 2.82%.

(E)-3-(2-hydroxy-3-methylbenzylidene)-1-phenylpyrrolidine-2, 5-dione, 84f

White solid; yield: 3.11 g (92%); M.p. 213-214 °C; Rf= 0.43(Hexane: Ethyl acetate, 9:1); IR (KBr): 3342, 2989, 1770, 1708, 1145 cm⁻¹; ¹H NMR (200 MHz, DMSO-d_6): δ = 2.38 (s, 3H), 3.69 (s, 2H), 7.49-7.21 (m, 5H), 7.39 (s, 1H), 7.41 (s, 1H), 7.63 (s, 1H), 8.86 (s, 1H), 10.25 (s, 1H); MS (EI): m/z 293 [M–1]^+; Analysis Calculated for C_{18}H_{15}NO_3: Calcd: C, 73.71; H, 5.15; N, 4.78%; Found: C, 73.89; H, 4.98; N, 4.92%.
(E)-3-(3-chloro-2-hydroxybenzylidene)-1-phenylpyrrolidine-2,5-dione, 84g

White solid; yield: 3.29 g (91%); M.p. 217–218 °C; Rf=0.54 (Hexane: Ethyl acetate, 9:1); IR (KBr): 3554, 2950, 1774, 1705, 1699, 1133, 525 cm⁻¹; ¹H NMR (300 MHz, DMSO- d₆): δ =3.89 (d, J=2 Hz, 2H), 7.56-7.36 (m, 7H), 7.65 (d, J=2 Hz, 1H), 7.82 (s, 1H), 10.44 (bs, 1H); MS (EI): m/z 313 [M‒1]+; Analysis Calculated for C₁₇H₁₂ClNO₃: Calcd: C, 65.08; H, 3.86; N, 4.46%; Found: C, 65.23; H, 3.69; N, 4.28%.

One pot procedure for the synthesis of (E)-3-(2-Hydroxynaphthalidene)-1-phenylpyrrolidine-2, 5-dione, 86

![Chemical structure](image)

General procedure:

To a solution of compound 77 (11.00 mmol) in ethanol (15 mL) was added portion wise triphenylphosphine (11.00 mmol) and the reaction mixture was stirred at room temperature for 30 min, to the same mixture was added dropwise solution of o-naphthaldehyde 83 (12.00 mmol) in ethanol (5 mL) and further stirred for 1 h. The separated solid product was filtered, washed with cold ethanol, dried and recrystallized from EtOH/DMF (9:1).

(E)-3-((2-Hydroxynaphthalen-1-yl) methylene)-1-phenylpyrrolidine-2, 5-dione, 86

White solid; yield: 3.38 g (95%); M.p. 275–277 °C; Rf=0.54 (Hexane: Ethyl acetate, 9:1); IR (KBr): 3336, 3056, 1768, 1691 cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆): δ = 3.41 (s, 2H), 7.55–7.34 (m, 8H), 7.88–7.77 (m, 3H), 7.98 (s, 1H), 10.50 (br s, 1H); ¹³C NMR
(75 MHz, DMSO-$d_6$): $\delta = 34.2, 112.9, 118.3, 123.1, 123.3, 127.0, 127.1, 127.7, 128.1, 128.4, 128.5, 128.7, 131.0, 131.9, 132.6, 153.3, 169.2, 173.3$ ppm; MS (EI): $m/z$ 329[M–1]$^+; Analysis Calculated for C$_{21}$H$_{15}$NO$_3$: Calcd: C, 76.58; H, 4.59; N, 4.25%; Found: C, 76.80; H, 4.82; N, 4.14%.

**Synthesis of 5, 7-Dibromo-2-phenylchromeno [2, 3-b] pyrrole-1, 3(2H, 3aH)-dione derivatives, 74a-h**

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</table>

**General procedure:**

To a stirred suspension of compound 75a-h (5.00 mmol) in DMF (10mL) was added dropwise a solution of bromine (22.50 mmol) in DMF (5mL) at rt. The reaction mixture was heated at 60 °C for 1 h and allowed to cool to rt. It was poured on crushed ice and separated out product was filtered, washed with aq.NaHSO$_4$ (3x30 mL) gives off-white solid, dried and recrystallized from EtOH/DMF.

**5, 7-Dibromo-2-phenylchromeno [2, 3-b] pyrrole-1, 3(2H, 3aH)-dione, 74a**

Off-white solid; yield: 1.89 g (87%); M.p. 239–241 °C; $R_f= 0.42$(Hexane: Ethyl acetate, 9:1); IR (KBr): 1780, 1718, 1668, 743 cm$^{-1}$; $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta = 5.86$ (d,
\( J = 2.4 \text{Hz, 1H}, 7.56–7.39 \text{ (m, 5H), 7.60 (d, } J = 2.4 \text{ Hz, 1H), 7.80 (d, } J = 2.4 \text{ Hz, 1H)} \)

\( 13 \text{C NMR (75 MHz, DMSO-}\text{d}_6): \delta = 71.6, 111.1, 114.3, 123.4, 124.8, 125.7, 127.0, 128.7, 128.9, 131.4, 131.6, 136.6, 150.2, 163.6, 168.8 \text{ ppm; MS (EI): } m/z 432 \text{[M–1]}^+; \text{Analysis Calculated for C}_{17}H_9Br_2NO_3: Calcd: C, 46.93; H, 2.09; N, 3.22%; Found: C, 46.63; H, 2.19; N, 3.03\%.

### 5, 7-Dibromo-2-p-tolylchromeno [2,3-b] pyrrole-1,3(2H, 3aH)-dione, 74b

Off-white solid; yield: 1.97 g (92%); M.p. 260–261°C; \( R_f = (\text{Hexane: Ethyl acetate, 9:1}); \)

IR (KBr): 3070, 1778, 1718, 792, 495 cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-\text{d}_6): \( \delta = 2.39 \text{ (s, 3H), 5.82 (s, 1H), 7.26 (d, } J = 6 \text{ Hz, 2H), 7.30 (d, } J = 6 \text{ Hz, 2H), 7.56 (s, 1H), 7.84 (s, 1H), 7.89 (s, 1H)} \)

\( 13 \text{C NMR (75 MHz, DMSO-}\text{d}_6): \delta = 20.6, 71.5, 111.0, 114.2, 123.4, 124.8, 125.6, 126.7, 128.7, 129.3, 131.6, 136.6, 138.2, 150.2, 163.7, 168.8 \text{ ppm; MS (EI): } m/z 447 \text{[M–1]}^+; \text{Analysis Calculated for C}_{18}H_{11}Br_2NO_3: Calcd: C, 48.14; H, 2.47; N, 3.12%; Found: C, 47.98; H, 2.49; N, 3.17\%.

### 5,7-Dibromo-2-(4-methoxyphenyl)chromeno[2,3-b]pyrrole-1,3(2H, 3aH)-dione, 74c

Off-white solid; yield: 1.58 g (75%); M.p. 282–284 °C. \( R_f = (\text{Hexane: Ethyl acetate, 9:1}); \)

IR (KBr): 3055, 1774, 1720, 798, 676 cm\(^{-1}\); \(^1\)H NMR (400 MHz, DMSO-\text{d}_6): \( \delta = 3.79 \text{ (s, 3H), 5.80 (d, } J = 2.4 \text{ Hz, 1H), 7.05 (d, } J = 9.2 \text{ Hz, 2H), 7.29 (d, } J = 9.2 \text{ Hz, 2H), 7.56 (d, } J = 2.4 \text{ Hz, 1H), 7.78 (d, } J = 2.4 \text{ Hz, 1H), 7.89 (d, } J = 2.4 \text{ Hz, 1H)} \)

\( 13 \text{C NMR (100 MHz, DMSO-}\text{d}_6): \delta = 55.7, 71.9, 111.5, 114.5, 114.7, 123.9, 124.2, 125.2, 125.9, 128.6, 132.0, 137.0, 151.5, 159.5, 164.5, 169.4 \text{ ppm; MS (EI): } m/z 461 \text{[M–1]}^+; \text{Analysis Calculated for C}_{18}H_{11}Br_2NO_4: Calcd: C, 46.48; H, 2.38; N, 3.01%; Found: C, 46.27; H, 2.47; N, 2.79\%.
5, 7-Dibromo-2-(4-fluorophenyl) chromeno [2,3-b]pyrrole-1,3(2H,3aH)-dione, 74d

Off-white solid; yield: 1.43 g (94%); M.p. 254–255 °C. Rf = 0.42 (Hexane: Ethyl acetate, 9:1); IR (KBr): 1781, 1724, 798, 676 cm\(^{-1}\); \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta = 5.86\) (d, \(J = 2\) Hz, 1H), 7.54 (d, \(J = 8.8\) Hz, 2H), 7.86 (d, \(J = 8.8\) Hz, 3H), 7.91 (d, \(J = 2\) Hz, 1H), 7.94 (d, \(J = 2\) Hz, 1H); \(^13\)C NMR (75 MHz, DMSO-\(d_6\)): \(\delta = 71.8, 111.6, 114.5, 123.7, 124.9, 126.4, 128.9, 129.6, 130.6, 135.4, 136.3, 146.6, 152.2, 163.7, 168.8 ppm; MS (EI): \(m/z\) 453\([M+1]^+\); Analysis Calculated for C\(_{17}\)H\(_8\)Br\(_2\)FNO\(_3\): Calcd: C, 45.07; H, 1.78; N, 3.09\%; Found: C, 45.25; H, 1.91; N, 2.92\%.

5, 7-Dibromo-2-(3-chlorophenyl) chromeno [2,3-b]pyrrole-1,3(2H,3aH)-dione, 74e

Off-white solid; yield: 1.86 g (89%); M.p. 259–261 °C. Rf = (Hexane: Ethyl acetate, 9:1); IR (KBr): 1782, 1724, 779, 680 cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-\(d_6\)): \(\delta = 5.80\) (d, \(J = 2.4\) Hz, 1H), 7.50–7.25 (m, 4H), 7.75 (d, \(J = 2.4\) Hz, 1H), 7.78 (d, \(J = 2.4\) Hz, 1H), 7.80 (d, \(J = 2.4\) Hz, 1H); \(^13\)C NMR (75 MHz, DMSO-\(d_6\)): \(\delta = 71.4, 115.1, 119.1, 122.3, 125.6, 169.3, 126.3, 127.3, 127.9, 128.1, 128.7, 130.2, 132.2, 134.1, 135.3, 148.1, 163.5 ppm; MS (EI): \(m/z\) 466\([M–1]^+\); Analysis Calculated for C\(_{17}\)H\(_8\)Br\(_2\)ClNO\(_3\): Calcd: C, 43.49; H, 1.72; N, 2.98\%; Found: C, 43.28; H, 1.69; N, 3.01\%.

5, 7-Dibromo-2-(4-chlorophenyl) chromeno [2, 3-b]pyrrole-1, 3(2H, 3aH)-dione, 74f

Off-white solid; yield: 1.90 g (91%); M.p. 284–285 °C. Rf = (Hexane: Ethyl acetate, 9:1); IR (KBr): 1780, 1722,796, 671 cm\(^{-1}\); \(^1\)H NMR (400 MHz, DMSO-\(d_6\)): \(\delta = 5.84\) (d, \(J = 2\) Hz, 1H), 7.46 (d, \(J = 8.8\) Hz, 2H), 7.62 (d, \(J = 8.8\) Hz, 3H), 7.80 (d, \(J = 2\) Hz, 1H), 7.91 (d, \(J = 2\) Hz, 1H); \(^13\)C NMR (75 MHz, DMSO-\(d_6\)): \(\delta = 71.6, 111.1, 114.3, 123.3, 124.8, 125.9, 128.8, 129.0, 130.3, 131.6, 133.2, 136.7, 152.2, 163.4, 168.6 ppm; MS (EI): \(m/z\)
468[M+1]^+; Analysis Calculated for C_{17}H_{8}Br_2ClNO_3: Calcd: C, 43.49; H, 1.72; N, 2.98%; Found: C, 43.67; H, 1.79; N, 3.15%.

5, 7-Dibromo-2-(4-bromophenyl) chromeno [2,3-b]pyrrole-1,3(2H,3aH)-dione, 74g
Off-white solid; yield: 1.87 g (87%); M.p. 277–279 ºC. Rf= 0.40(Hexane: Ethyl acetate, 9:1); IR (KBr): 1778, 1728, 795, 673 cm⁻¹; ¹H NMR (400 MHz, DMSO-ᵈ): δ = 5.86 (d, J= 2 Hz, 1H), 7.48 (d, J= 8.8 Hz, 2H), 7.64 (d, J= 8.8 Hz, 3H), 7.81 (d, J= 2 Hz, 1H), 7.94 (d, J= 2 Hz, 1H); MS (EI): m/z 513[M+1]^+; Analysis Calculated for C_{17}H_{8}Br_2NO_3:
Calcd: C, 39.73; H, 1.57; N, 2.73%; Found: C, 39.91; H, 1.75; N, 2.55%.

2-Benzyl-5, 7-dibromochromeno [2, 3-c] pyrrole-1, 3(2H, 3aH)-dione, 74h
Off-white solid; yield: 1.54 g (72 %); M.p. 220–222 ºC. Rf= 0.45(Hexane: Ethyl acetate, 9:1); IR (KBr): 3058, 1774, 1716, 800 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ = 4.79 (s, 2H), 5.34 (d, J=2.4 Hz, 1H), 7.45–7.25 (m, 7H), 7.68 (d, J=2.4 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃): δ = 42.5, 71.4, 112.3, 115.4, 122.6, 126.6, 128.2, 128.8, 129.0, 131.2, 135.9, 137.9, 150.5, 163.9, 168.7, ppm; MS (EI): m/z 448[M‒1]^+; Analysis Calculated for C_{18}H_{11}Br_2NO_3: Calcd: C, 48.14; H, 2.47; N, 3.12%; Found: C, 47.92; H, 2.33; N, 3.00%.

Synthesis of substituted-2-phenylchromeno [2, 3-b] pyrrole-1, 3(2H, 3aH)-dione, 85a-g

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To a stirred suspension of compound 84a-g (5.00 mmol) in DMF (10mL) was added dropwise a solution of bromine (12.00 mmol) in DMF (5mL) at rt. The reaction mixture was heated at 60 °C for 1 h and allowed to cool to rt. It was poured on crushed ice and separated out product was filtered, washed with aq.NaHSO₄ (3x30 mL) gives off-white solid, dried and recrystallized from EtOH/DMF.

**7-bromo-5-methyl-2-phenylchromeno [2, 3-b] pyrrole-1, 3(2H, 3aH)-dione, 85a**

Off-white solid; yield: 1.59 g (90%); M.p. 237-238°C; \( R_f = 0.46 \) (Hexane: Ethyl acetate, 9:1); IR (KBr): 1796, 1728, 694 cm⁻¹; \(^1\)H NMR (200 MHz, DMSO-\(d_6\)): \( \delta = 7.82 \) (s, 1H), 7.67 (s, 1H), 7.62 (s, 1H), 7.49-7.19 (m, 5H), 5.86 (s, 1H), 2.39 (s, 3H); MS (EI): \( m/z \) 369 [M–1]⁺; Analysis Calculated for C₁₈H₁₂BrNO₃: Calcd: C, 58.40; H, 3.27; N, 3.78%; Found: C, 58.57; H, 3.43; N, 3.57%.

**7-bromo-5-chloro-2-phenylchromeno [2, 3-b]pyrrole-1,3(2H,3aH)-dione, 85b**

Off-white solid; yield: 1.49 g (86%); M.p. 243-244 °C. \( R_f = 0.43 \) (Hexane: Ethyl acetate, 9:1); IR (KBr): 1774, 1715, 1701, 1145, 725, 525cm⁻¹; \(^1\)H NMR (300 MHz, DMSO-\(d_6\)): \( \delta = 5.87 \) (s, 1H), 7.64–7.49 (m, 6H), 7.85 (s, 1H), 7.93 (s, 1H); MS (EI): \( m/z \) 389 [M-1]⁺; Analysis Calculated for C₁₇H₁₉BrClNO₃: Calcd: C, 52.27; H, 2.32; N, 3.59%; Found: C, 52.43; H, 2.52; N, 3.38%.

**5, 6, 7-tribromo-2-phenylchromeno [2, 3-b] pyrrole-1, 3(2H, 3aH)-dione, 85c**

Off-white solid; yield: 1.82 g (91%); M.p. 256-257 °C. \( R_f = 0.52 \) (Hexane: Ethyl acetate, 9:1); IR (KBr): 1774, 1726, 1712, 1130, 696 cm⁻¹; \(^1\)H NMR (200 MHz, DMSO-\(d_6\)): \( \delta = 5.73 \) (s, 1H), 7.56-7.48 (m, 5H), 7.87 (s, 1H), 8.03 (s, 1H); MS (EI): \( m/z \) 510 [M–1]⁺;
Analysis Calculated for C₁₇H₇Br₃NO₃: Calcd: C, 39.73; H, 1.57; N, 2.73%; Found: C, 39.89; H, 1.75; N, 2.51%.

5, 7-diiodo-2-phenylchromeno [2,3-b]pyrrole-1, 3(2H,3aH)-dione, 85d

Off-white solid; yield: 1.24 g (89%); M.p. 273-274°C. Rf= 0.53 (Hexane: Ethyl acetate, 9:1); IR (KBr): 1767, 1710, 1658, 1155, 725 cm⁻¹. ¹H NMR (200 MHz, DMSO-d₆): δ = 5.87 (s, 1H), 7.64 -7.49 (m, 5H), 8.18 (s, 1H), 8.26 (s, 1H), 8.69 (s, 1H); MS (EI): m/z 528 [M–1]⁺; Analysis Calculated for C₁₇H₇I₂NO₃: Calcd: C, 38.59; H, 1.71; N, 2.65%; Found: C, 38.77; H, 1.89; N, 2.47%.

5, 7-dichloro-2-phenylchromeno [2, 3-b]pyrrole-1, 3(2H,3aH)-dione, 85e

Off-white solid; Yield: 1.21 g (86%); M.p. 289-290 °C; Rf= 0.43 (Hexane: Ethyl acetate, 9:1); IR (KBr): 1768, 1729, 1701, 1154, 525 cm⁻¹; ¹H NMR (200 MHz, DMSO-d₆): δ = 8.15 (d, J=2 Hz, 1H), 7.93 (s, 1H), 7.85 (s, J=2 Hz, 1H), 7.55-7.50 (m, 5H), 5.74 (d, J=2 Hz, 1H); MS (EI): m/z 345 [M–1]⁺; Analysis Calculated for C₁₇H₉Cl₂NO₃: Calcd: C, 58.98; H, 2.62; N, 4.05%; Found: C, 59.12; H, 2.79; N, 3.89%.

5-Bromo-7-methyl-2-phenylchromeno [2, 3-b] pyrrole-1, 3(2H, 3aH)-dione, 85f

Off-white solid; yield: 1.63 g (92%); M.p. 237-238°C; Rf= 0.46 (Hexane: Ethyl acetate, 9:1); IR (KBr): 1793, 1729, 698 cm⁻¹; ¹H NMR (200 MHz, DMSO-d₆): δ = 7.83 (s, 1H), 7.65 (s, 1H), 7.60 (s, 1H), 7.51-7.17 (m, 5H), 5.88 (s, 1H), 2.38 (s, 3H); MS (EI): m/z 370 [M]⁺; Analysis Calculated for C₁₈H₁₂BrNO₃: Calcd: C, 58.40; H, 3.27; N, 3.78%; Found: C, 58.22; H, 3.45; N, 3.59%.
5-Bromo-7-chloro-2-phenylchromeno [2, 3-b] pyrrole-1, 3(2H, 3aH)-dione, 85g

Off-white solid; yield: 1.56 g (90%); M.p. 289–291 °C. Rf = 0.47 (Hexane: Ethyl acetate, 9:1); IR (KBr): 1766, 1710, 730, 511 cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆): δ = 5.88 (s, 1H), 7.66–7.28 (m, 6H), 7.84 (s, 1H), 7.95 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ = 72.3, 115.1, 118.3, 121.1, 121.3, 125.1, 127.9, 128.1, 133.5, 133.8, 138.1, 140.5, 152.8, 160.1, 168.2 ppm; MS (EI): m/z 390[M+1]; Analysis Calculated for C₁₇H₉BrClNO₃: Calcd: C, 52.27; H, 2.32; N, 3.59%; Found: C, 52.01; H, 2.14; N, 3.38%.

Synthesis of 5-Bromobenzo[f] 2-phenylchromeno [2, 3-c] pyrrole-1, 3(2H, 3aH)-dione, 87

General procedure:

To the solution of compound 86 (1.5 g, 8.72 mmol) in DMF (5mL) was added dropwise by using pressure equalizing funnel a solution of Br₂ (1.08 mL, 20.9 mmol) in DMF (2mL) for 10 min then resultant solution was heated at 60°C for 1 h afforded compound 87 (Checked by TLC), cool these reaction mixture to room temperature and poured it on to crushed ice (50 g) yellowish solid separated was filtered and washed with aq.NaHSO₄ solution (2x25 mL) gives off-white solid, dried and recrystallized from EtOH/DMF.
5-Bromobenzo[f] 2-phenylchromeno [2, 3-c] pyrrole-1, 3(2H, 3aH)-dione, 87

Off-white solid; Yield: 1.87 g (95%); M.p. 297–299 °C; Rf= (Hexane: Ethyl acetate, 9:1); IR (KBr): 1795, 1728, 694 cm⁻¹; \(^1\)H NMR (400 MHz, CDCl₃): δ = 5.87 (d, J=2.4Hz, 1H), 7.32 (d, J = 9Hz, 1H), 7.42–7.38 (m, 2H), 7.48–7.42 (m, 1H), 7.56–7.50 (m, 2H), 7.62 (dd, J= 9, 2.1 Hz, 1H), 7.44 (d, J= 9Hz, 1H), 7.88 (d, J= 9 Hz, 1H), 7.91 (t, J= 2.3 Hz, 1H), 8.15 (d, J= 2.4 Hz, 1H); \(^13\)C NMR (75 MHz, CDCl₃): δ = 71.6, 111.8, 116.1, 121.3, 123.6, 124.3, 126.1, 128.1, 129.9, 130.0, 131.2, 131.9, 132.1, 134.6, 136.2, 140.1, 150.4, 163.2, 168.4 ppm; MS (EI): m/z 406[M+1]+; Analysis Calculated for C₂₁H₁₂BrNO₃: Calcd: C, 62.09; H, 2.98; N, 3.45%; Found: C, 61.78; H, 3.09; N, 3.39%.
References:


