GOLD(III) CHLORIDE AS A GREEN CATALYST

Gold (Au) has accompanied mankind from the very early days, no name of a chemist is associated with the discovery of the element gold. It is probably the only chemical element that literally very adult has heard about. A highly positive normal potential is responsible for a low reactivity and allows gold to occur in nature in elemental form, for example, as nuggets. As is generally known, the endeavor to produce gold synthetically plays a significant role in the development of chemistry over a long time.\(^1\) The stoichiometric chemistry of gold has intensively and continuously been investigated. The close relationship between gold and chemical applications got lost during the development of catalysis reactions. Catalysis by gold has rapidly become a hot topic in chemistry, with a new discovery being made almost every week. Gold is equally effective as a heterogeneous or a homogeneous catalyst. In the field of homogeneous catalysis only a few gold catalyzed processes are known to date, which however, are characterized by the need for extremely small amounts of gold salts. In view of the high catalytic activity of gold salts, therefore, the higher price for gold salts is relativized in comparison to that for the corresponding palladium and ruthenium compounds. A gold rush is occurring as exemplified by the number of reports\(^2\), highlights\(^3-5\) and reviews\(^2,6-9\) on the Au-catalyzed organic reactions. Au-catalyzed reactions have been often carried out efficiently using gold salts \(i.e.\) Au(I) and Au(III). Between them, Au(III) is the most important catalyst in organic synthesis. The reason for its general acceptance is, it has a very high standard electrode potential of Au (+1.4 V) \textit{vs} NHE (Normal Hydrogen Electrode), mild Lewis acid catalyst, ease of handling and solubility in water as well as ethanol. The enormous growth in the use of this reagent is evidenced by the publication of a large number of papers and several reviews concerning Au(III) mediated reactions.\(^{10,11}\)
What makes gold so unique among the transition series elements? The answer lies in ability of gold to display stable oxidation states +1 and +3. The most stable oxidation state of Au is +3 state. Gold in its ground state has an electronic configuration of \([\text{Xe}]4f^{14}5d^{10}6s^1\), where Xe represents the xenon configuration. The electronic configuration of Au\(^{+1}\) is \([\text{Xe}]4f^{14}5d^{10}\) and Au\(^{+3}\) is \([\text{Xe}]4f^{14}5d^8\) which exhibits respectively tetrahedral and square planar geometry. In aqueous solution, in the absence of stabilizing ligands, Au(I) spontaneously disproportionate to Au(III) and Au(0) \((\text{Equation 1})\). The most important compound of gold in which it exhibit stable (+3) oxidation state is gold(III) chloride, traditionally called auric chloride while gold(I) chloride called aurous chloride and it exhibits as a dimeric structure with the molecular formula \(\text{Au}_2\text{Cl}_6\) as shown in Figure 1.

\[
3\text{Au}^{+1} \rightleftharpoons \text{Au}^{+1} + \text{Au}^0
\]

\text{Equation 1}

![Figure 1](image)

In dimeric structure each gold centre is square planar and chlorine atoms form the bridges. The bonding in \(\text{AuCl}_3\) is considered as covalent. The large reduction potential value of gold (+1.4 V) \(\text{vs} \ \text{NHE}\) endowed in Au\(^{+3}\) makes Au(III) reagents superior oxidizing agents as compared to other transition metal ions.

The major virtue of gold(III) chloride in homogeneous catalyst is its unique ability to activate C-C multiple bonds as soft carbophilic Lewis acid, allowing for the
formation of new C-C, C-O, C-N and C-S bonds by nucleophilic attack at these activated substrates in several organic transformation reactions.

**Application in Organic Synthesis**

In 1906, Bone and Wheeler\textsuperscript{12} published the probably first example of gold catalyzed organic reaction. They studied the uptake of hydrogen by the gold in the presence of O\textsubscript{2} at 600 °C.\textsuperscript{13} In 1950, Couper and Eley demonstrated that gold surface could convert *para*-hydrogen to *ortho*-hydrogen.\textsuperscript{14}

Erkelens *et al.* reported that gold films at 469-615 K had catalyzed the hydrogenation product cyclohexane (2) and the dehydrogenation product benzene (3) from cyclohexene (1). *(Scheme 1).*\textsuperscript{15}

![Scheme 1](image)

The hydrogenation of 1-pentene (4) to pentane (5) was catalyzed by 0.01 wt\% gold on SiO\textsubscript{2} support at 373 K *(Scheme 2).*\textsuperscript{16}

![Scheme 2](image)

The intramolecular addition of amine to carbon-carbon triple bonds in 5-alkylamines (6), were heated under reflux in acetonitrile in the presence of a catalytic amount of sodium tetrachloroaurate(III) dehydrate, the reaction proceeded with high
selectivity to give 2,3,4,5-tetrahydropyridines (8) followed by the intermediate (7) in good yield. (Scheme 3).\(^{17}\)

\[
\begin{array}{c}
\text{R}^1 = \text{C}_6\text{H}_{13}, \text{R}^2 = \text{H}; \text{R}^1 = \text{Et}, \text{R}^2 = \text{H}; \text{R}^1 = \text{C}_5\text{H}_{11}, \text{R}^2 = \text{Me}; \text{R}^1 = \text{H}, \text{R}^2 = \text{C}_6\text{H}_{13} \\
\text{R}^1 = \text{Ph}, \text{R}^2 = \text{H}; \text{R}^1 = \text{H}, \text{R}^2 = \text{C}_{11}\text{H}_{23}; \text{R}^1 = (\text{CH}_2)_{2}\text{CH} = \text{CH}_2, \text{R}^2 = \text{H}
\end{array}
\]

\text{Scheme 3}

The cross-coupling reaction of allenyl ketones (9) with \(\alpha,\beta\)-unsaturated ketones (10) were carried out using 1 mol\% of \text{AuCl}_3 in acetonitrile to give the corresponding substituted furan derivatives (11) in good yield (Scheme 4).\(^{18}\)

\[
\begin{array}{c}
\text{R} = \text{CH}_2-4-\text{MeOC}_6\text{H}_4, \text{R}^1 = \text{Me}, \text{R}^2 = \text{H}; \text{R} = \text{CH}_2-4-\text{MeOC}_6\text{H}_4, \text{R}^1 = \text{Et}, \text{R}^2 = \text{Me} \\
\text{R} = 3-\text{MeOC}_6\text{H}_4, \text{R}^1 = \text{Me}, \text{R}^2 = \text{H}; \text{R}^1 = \text{H}, \text{R}^2 = \text{H}, \text{R} = 
\end{array}
\]

\text{Scheme 4}

The electrophilic cyclization of functionalized \(\alpha\)-hydroxyallenes (12) were smoothly converted into the corresponding 2,5-dihydrofurans (13) by using 5-10 mol\% of gold(III) chloride as catalyst at room temperature (Scheme 5).\(^{19}\)
Chapter V

The Aza-Michael reaction of enones (14) with carbamates (15) was catalyzed by AuCl₃ to give the corresponding Michael adduct (16) in DCM at room temperature (Scheme 6).

The gold(III) chloride-catalyzed cycloisomerization of various α-aminoallenes (17) gave the corresponding 3-pyrrolines (18) in good to high chemical yields (Scheme 7).

\[
\begin{align*}
(12) & \quad \text{R}^1 = H, \text{t-Bu}, \text{H}_2\text{C}=\text{CH(CH}_2)_2; \quad \text{R}^2 = H, \text{Me}, \text{Bu}, \text{n-Hex} \\
(13) & \quad \text{R}^3 = H, \text{Me}; \quad \text{R}^4 = \text{CH}_2\text{OMe}, \text{CO}_2\text{Et}, \text{CO}_2\text{Me}, \text{CH}_2\text{OH}, \text{CH}_2\text{OTBS}
\end{align*}
\]

Scheme 5

\[
\begin{align*}
\text{R}^1 = \text{Alkyl, Aryl}; \quad \text{R}^2 = \text{R}^3 = \text{R}^4 = \text{R}^5 = H, \text{Alkyl}; \quad \text{R}^6 = \text{Alkyl, Bn}
\end{align*}
\]

Scheme 6

\[
\begin{align*}
\text{R} = \text{Me}, \text{R}^1 = \text{Bn}; \quad \text{R} = \text{n-Hexyl}, \text{R}^1 = \text{TBS}; \quad \text{R} = \text{Ph}, \text{R}^1 = \text{TBS}
\end{align*}
\]

Scheme 7
AuCl₃ efficiently catalyzed the cyclization of tert-butyllallenoates (19) into 2,4-disubstituted butenolides (20) under mild reaction condition (Scheme 8).²²

\[
\begin{align*}
R^1 & = \text{Ph, PhCH}_2, \text{CH}_3(\text{CH}_2)_8, \\
R^2 & = \text{H, CH}_3, \text{Ph, PhCH}_2
\end{align*}
\]

Scheme 8

Gold(III) catalyzed Meyer-Schuster rearrangement of propargyl alcohols (21) was reported for the synthesis of isomeric α,β-unsaturated carbonyl compounds (22) in dichloromethane and ethanol at room temperature (Scheme 9).²³

\[
\begin{align*}
R^1 & = \text{Ph, Et, } t\text{-Bu, 4-}t\text{-Bu-cyclohexyl, Adamantyl} \\
R^2 & = \text{H, Me, Et, Ph; } R^3 = \text{Ph, OEt}
\end{align*}
\]

Scheme 9

Gold(III) chloride/silver triflate was found to be a highly efficient catalyst in the ring-opening of aziridines (23) with electron-rich arenes (24) and the desired β-arylamines (25) were afforded in good to excellent yields under mild reaction conditions (Scheme 10).²⁴
A highly efficient approach to \((Z)\)-conjugated enynes \((27)\) was developed by utilizing an Au(III)-catalyzed ring opening reaction of 1-cyclopropyl-2-yn-1-ols \((26)\) with nucleophiles under mild conditions \((\text{Scheme 11})\).\(^{25}\)

Diastereoselective alkylation reaction of resorcin dimethyl ether \((28)\) with chiral acetates \((29)\) was catalyzed by gold(III) chloride in nitromethane to give the corresponding \emph{syn} and \emph{anti} products \((30 \& 31)\) at room temperature \((\text{Scheme 12})\).\(^{26}\)
**Scheme 12**

A one-pot three-component reaction of activated quinoline (32) with dialkylacetylenedicarboxylate (33) and alkynes (34) was reported for the synthesis of a series of alkynyl-substituted 1,2-dihydroquinolines (35) using gold(III) chloride at room temperature (Scheme 13).²⁷

**Scheme 13**

An unprecedented gold(III) chloride catalyzed the intermolecular dimerization of 2-ethynylanilines (36) to a wide range of highly substituted quinolines (37) (Scheme 14).²⁸

**Scheme 14**

\[ R = \text{H, 4-Me, 4-F, 4-NO}_2, \text{4-Cl, 4-CN, 4-MeO, 3,4-Me}_2, \text{2-Cl-4-Br, 2,4-Me}_2, \text{2-Cl-4-Me, 2,4-Br}_2, \text{2-MeO-4-NO}_2, \text{2-MeO-4-COOMe} \]
A general gold-catalyzed oxidative homo and hetero-coupling of arenes (38) using [PhI(OAc)$_2$] (39) as the oxidant, was reported for the synthesis of biaryl derivatives (40) in acetic acid at 55 °C (Scheme 15).$^{29}$

![Scheme 15]

Na[AuCl$_4$]/Cs$_2$CO$_3$ was found to be a simple bench top, recyclable and selective catalyst system for the aerobic oxidation of various types of alcohols (41) into their corresponding aldehydes and ketones (42) at room temperature without the need for any further polymeric and/or oxidic support (Scheme 16).$^{30}$

![Scheme 16]

Gold(I) and gold(III) salts were found to be highly effective for the catalysis of intramolecular cyclic ether (45) formation from 1,5-diols (44). Initially diols (44) were prepared in each case from the reduction of ketoacids or ester (43) (Scheme 17).$^{31}$
Verniest et al. has reported that the synthesis of oxazoles (48 & 49) or β-carbolinones (50) from indole substituted N-propargylamides (46 & 47) was catalyzed by gold(III) chloride in dichloromethane or toluene at room temperature under heating conditions (Scheme 18).32

Scheme 17

Scheme 18
β-alkynyl β-ketoesters (51) were used for the synthesis of trisubstituted furans (52) using gold(III) chloride catalyst in methanol at 65 °C (Scheme 19).33

\[
\begin{align*}
5 \text{ mol\% AuCl}_3 & \quad \text{MeOH, 65 °C} \\
\text{R}^1 & = \text{CH}_3, \text{CH}_3\text{CH}_2, \text{Ph, 4-O}_2\text{NC}_6\text{H}_4; \text{R}^2 = \text{Me, Et; R}^3 = \text{H, Ph, 4-ClC}_6\text{H}_4, 4-\text{MeOC}_6\text{H}_4
\end{align*}
\]
SPIROCHROMENES

The indole ring system is among the most important heterocyclic systems present as structural framework in a large number of bioactive natural products and pharmaceuticals. Spirocyclic compounds are generally known as “Spirocyclane” which was first introduced by Baeyer in 1900. The complexity of these ring structures are represented by the quaternary carbon center and two fused rings. One of the most important spirocycles is spirooxindole alkaloids, are present in many biologically active natural products that are isolated from the plant of Apocynaceae and Rubiaceae families. In particular, spirooxindoles annulated with heterocycles in 3-position have been reported an attractive synthetic targets because of their prevalence in numerous natural products, pharmacological and biological activities such as antimicrobial, antitumor, antibiotic, and inhibitor of human NK-1 receptor.

Gelesmine (53) was reported to be the major component of the alkaloids in Gelsemium sempervirens, and its structure was elucidated by X-ray analysis and NMR in 1959.

![Gelesmine structure](image)

Two novel diketopiperazine alkaloids, spirotryprostatins A (54) and B (55) were isolated as new inhibitors of the mammalian cell cycle from the secondary metabolites of Aspergillus fumigatus through a separation procedure guided by cell cycle inhibitory activity.
Horsfiline (56), alstonisine (57) and elacomine (58) possess a wide range of structural complexity which have potential as an antineoplastic agent.\(^{46}\)

A series of small molecules derived from MK-0677 (59), a potent synthetic growth hormone secretagogue (GHS), mimicking the N-terminal Gly-Ser-O-(n-octanoyl)-L-Ser-Phe segment of ghrelin were synthesized and tested in binding and in a functional assay measuring intracellular calcium elevation in HEK-293 cells expressing hGHS R\(_{1a}\).\(^{47}\)
Pteropodine (60) and isopteropodine (61) were found to be heteroyohimbine-type oxindoles alkaloid which positively modulate the function of muscarinic M₁ and 5-HT₂ receptors expressed in *xenopus* oocytes.⁴⁸

![Chemical structures of Pteropodine (60) and Isopteropodine (61)](image)

The synthesis and antimicrobial and antifungal activity of 1-N-methyl-spiro[2.3']oxindole-spiro[3.2'']1''-cyclohexanone-4-aryl-pyrrolidines (66) were found by the reaction of 2-arylidene-cyclohexanones (65) in methanol or 1,4-dioxane with isatin (62) and sarcosine (63) via the formation of an intermediate (64) (Scheme 20).⁴⁹

![Scheme 20](image)
2'-(indol-3-yl)-2-oxospiro(indoline-3,4'-pyran) derivatives (70) were synthesized by the reaction of isatin derivatives (67), malononitrile/ethylcyanoacetate (68) and 3-cyanoacetyl indole (69) in the presence of triethylamine/methanol at room temperature which were evaluated for anti-microbial activity (Scheme 21).50

![Scheme 21](image)

Scheme 21

A solution phase synthesis of spiro[pyrrolidine-2,3'-oxindoles] (75) was prepared via a three component 1,3-dipolar cycloaddition reaction through the formation of an intermediate azomethine ylide (73), generated by the decarboxylative condensation of isatin (71) with an α-amino acids (72) was trapped by a trans-chalcone (74) Scheme 22.51

![Scheme 22](image)

Scheme 22
A convenient synthesis of enantiomerically pure spiro oxindoles (79) was done by the reaction of 1-phenyl isatin (76) with proline (77) and (78) in aqueous dioxane at 80-90 °C (Scheme 23).52

\[ \text{(76)} + \text{(77)} + \text{(78)} \rightarrow \text{(79)} \]

Scheme 23

The synthesis of chroman-4'-one-spiro-[3',2]-(1-aryl)-7-oxaindolizidione-spiro[3,3'']-oxindoles (82) was accomplished by regioselective 1,3-dipolar cycloaddition reaction of E-3-arylidene-4-chromanones (80) with isatin (62) and morpholine (81) via deprotonation route. (Scheme 24).53

\[ \text{(80)} + 2 \text{(62)} + \text{(81)} \rightarrow \text{(82)} \]

R = H, Me, MeO, Cl, NO₂

Scheme 24
A facile synthesis of dispiro[oxindolecyclohexanone]pyrroloisoquinoline derivatives (85) was accomplished by regioselective 1,3-dipolar cycloaddition reaction of \((E)-2\)-arylidene-1-cyclohexanones (83) with isatin (62) and 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (84) in boiling aqueous methanol (Scheme 25).\(^{54}\)

![Scheme 25]

A microwave assisted three-component, regioselective one-pot condensation method was developed for the synthesis of a series of novel spiro[indole-thiazolidinones] (89) as potent antifungal agents using isatins (86) with heterocyclic amines (87) and thioacids (88) under microwave irradiation at atmospheric pressure in open vessel (Scheme 26).\(^{55}\)

![Scheme 26]
A new InCl$_3$-catalyzed facile and efficient method for the one-pot three-component synthesis of new spirooxindoles derivatives (92) was described by the reaction of isatins (67) with malononitrile/ethylenecyanoacetate (90) and 1-naphthol/2-naphthol (91) under conventional and solvent-free microwave irradiation (Scheme 27).$^{56}$

![Scheme 27](image)

A simple and efficient method for the synthesis of spirooxindoles derivatives (94) by one-pot reaction of isatins (71), activated methylene reagents (90) and activated carbonyl compounds (93) in water under microwave-irradiation was reported in short reaction time with high yields and easy work-up procedure (Scheme 28).$^{57}$

![Scheme 28](image)
Spirooxindoles derivatives (96 & 98) were synthesized by the reaction of isatins (71) with activated methylene reagents (90) and 4-hydroxy coumarin (95) or barbituric acid (97) using supramolecular catalysis involving recyclable β-cyclodextrin in water (Scheme 29).58

![Scheme 29](image)

R = R1 = H, X = CN; R = 4-Br, R1 = H, X = CN; R = H, R1 = CH3, X = COOCH3
R = H, R1 = CH3, X = CN; R = R1 = H, X = COOCH3

Spirooxindole derivatives (101) were reported by way of a palladium-catalyzed decarboxylative cyclization of γ-methylidene-δ-valerolactones (99) with isatins (67) using a newly prepared phosphoramidite ligand (100) at 40 °C (Scheme 30).59

![Scheme 30](image)

R = CH3; R1 = Ph, R2 = Me; R1 = Ph, R2 = t-Bu; R1 = 4-MeOC6H4, R2 = t-Bu
R1 = 3-MeC6H4, R2 = t-Bu; R1 = 2-MeC6H4, R2 = t-Bu; R1 = Naphthyl, R2 = t-Bu
R1 = 3-Thienyl, R2 = t-Bu; R1 = CH2Ph, R2 = Ph
The synthesis of spiro[indoline-3,4-pyrazolo[3,4-b]pyridine]-2,6'(1'H)-diones (104) by the reaction of 4-hydroxycumarin (95), isatins (102) and 1H-pyrazol-5-amines (103) in water under ultrasonic irradiation was reported (Scheme 31).60

\[
\begin{align*}
&\text{R} = \text{H, Me, NO}_2, \text{Br, Me}; R^1 = \text{H, Me, Et, CH}_2\text{Ph}; R^2 = \text{H, NO}_2
\end{align*}
\]

Scheme 31

The efficient assembly of hydroindane derivatives incorporating a spirooxindole motif (108) was realized via a three-component domino reaction of (E)-4-(1-methyl-2-oxoindolin-3-ylidene)-3-oxobutanoates (105) and two molecules of \(\alpha,\beta\)-unsaturated aldehydes (106) under quadruple iminium-enamineiminium-enamine catalysis (107) and benzoic acid (BA) in dichloroethane (DCE) at room temperature to 35 °C (Scheme 32).61

\[
\begin{align*}
&\text{R} = \text{t-Bu; R}^1 = \text{Me, MeO; R}^2 = \text{R}^3 = \text{Me, Ph, } p-\text{MeOC}_6\text{H}_4, p-\text{FC}_6\text{H}_4, p-\text{FC}_6\text{H}_4, o-\text{BrC}_6\text{H}_4, m-\text{ClC}_6\text{H}_4, 2-\text{Thienyl, 1-Propenyl}
\end{align*}
\]

Scheme 32
A regio- and stereoselective cyclization between isatins (67) and 5-methoxyoxazoles (109) was developed using catalytic titanium(IV) chloride (10-20 mol %) to afford either 2-oxazoline or 3-oxazoline spirocycles (110 & 111) in excellent yields (Scheme 33).62

\[
\begin{align*}
\text{H}_3\text{COOC}_{\text{H}_4}\text{O} & + \\
\text{TiCl}_4 (10-20 \text{ mol\%}) & \to \\
\text{CH}_2\text{Cl}_2, \text{rt} & \\
\text{or} & \\
\text{R} & = \text{CH}_3; \text{R}^1 = \text{H, CH}_3, \text{Pr} \\
\text{Ar} & = \text{H, 4-BrC}_{\text{H}_4}\text{H}_4, 2-\text{CH}_3\text{OC}_{\text{H}_4}\text{H}_4, 4-\text{CH}_3\text{OC}_{\text{H}_4}\text{H}_4, 3,4,5-\text{Trimethoxyphenyl (TMP)}
\end{align*}
\]

Scheme 33

Ultrasound-promoted synthesis of spirooxindolo dicyano pyrrolidines (113) and pyrroliizidines (115) were synthesized from the reaction of various arylidenemalononitrile Knoevenagel adducts (112) with \(\alpha\)-amino acid [proline (77) or \(N\)-phenyl glycine (114)] and isatin (62) through regioselective azomethine ylide cycloaddition reaction (Scheme 34).63

\[
\begin{align*}
\text{R} & = \text{H, 4-Me, 4-Cl, 3-Br, 4-Br, 4-F, 3,4-MeO}
\end{align*}
\]
A facile and rapid synthesis of dispiroacenaphthenone derivatives (118) via TiO$_2$-SiO$_2$ mediated one-pot three-component 1,3-dipolar cycloaddition reaction of tetrahydroisoquinoline-3-carboxylic acid (83) with acenaphthenequinone (116) and 2-arylidene-1,3-in-danediones (117) was reported in moderate to good yields (Scheme 35).$^{64}$

An efficient microwave-assisted zirconium oxychloride (ZrOCl$_2$.8H$_2$O) mediated synthesis of novel pyrrolizidinonindole derivatives (120 & 121) was reported through [3+2] cycloaddition reaction of azomethine ylides derived from acenaphthenequinone (116) and L-proline (77) with (E)-2-oxindolino-3-ylidene acetophenones (119) as dipolarophiles in good yields (Scheme 36).$^{65}$
Ultrasound-promoted synthesis of novel spiroacenaphthen dicyano pyrrolidines (122) and pyrrolizidines (123) were carried out from the reaction of various aryldienemalononitrile Knoevenagel adducts (112) with α-amino acid [proline (77) or N-phenyl glycine (114)] and acenaphthenequinone (116) through regioselective azomethine ylide cycloaddition reaction (Scheme 37).63
Scheme 37
OBJECT OF THE PRESENT WORK

Multicomponent reaction (MCR), an important sub-class of tandem reactions\textsuperscript{66}, is one-pot processes that reacts at least three easily accessible components to form a single product, which incorporates essentially all of the atoms of the starting materials.\textsuperscript{67} MCRs are highly flexible, convergent and atom efficient processes of high exploratory power.\textsuperscript{68,69} The growing interest for novel multi-component procedure is closely related to the synthesis of combinatorial small-molecule heterocyclic libraries which is becoming an important and promising area of organic synthesis.\textsuperscript{70,71} Thus, the success of combinatorial chemistry in the drug discovery process is considerably dependent on further advances in heterocyclic multicomponent reaction methodology and according to current synthetic requirements, environmentally benign multicomponent procedures are particularly welcome.

Compounds containing an indole moiety exhibit antibacterial and antifungal activities.\textsuperscript{72} Furthermore, it has been reported that the use of the indole 3-carbon in the formation of spiroindoline derivatives highly enhances biological activity.\textsuperscript{73} The heterocyclic spirooxindole ring system is a widely distributed structural framework of many pharmaceuticals and natural products\textsuperscript{74}, including cytostatic alkaloids such as spirottryprostatins A and B\textsuperscript{75}, isolated from the fermentation broth of \textit{Aspergillus fumigates} in which spirottryprostatins B has been shown to inhibit completely the G2/M progression of mammalian tsFT210 cells at concentrations over 12.5μg/mL. While the horsfiline and elacomine are more straightforward derivatives of the natural occurring oxindole alkaloids with cell cycle inhibition activity.\textsuperscript{46} Among them oxygen-containing heterocycles fused with spirooxindole ring system, functionally substituted 4\textit{H}-chromenes have received considerable attention due to a wide-range of
biological properties like anticoagulant, diuretic, anticancer and antianaphylactic activities.\textsuperscript{76}

There are several methods have been reported for the synthesis of spirooxindoles with fused chromenes in which conventional synthesis involves the one-pot three-component reaction of isatin with cyclic 1,3-diketones and malononitrile or 2-aminobenzothiazole.\textsuperscript{77} Shanthi \textit{et al.} have reported a three-component reaction for the synthesis of spirooxindole derivatives catalyzed by InCl\textsubscript{3} with 70-90\% yield\textsuperscript{56} This reaction was also carried out in the presence of \textit{p}-TSA within 1 h under reflux condition.\textsuperscript{78} Other more effective procedure for the synthesis of spirooxindoles employed quaternary cationics\textsuperscript{79} and electrochemical methods.\textsuperscript{80} Thus, each of the known procedures for the synthesis of spiro[(4\textit{H}-chromene)-4,3\textsuperscript{'}-oxindole] has its merits, however, further studies are still necessary for the essence of a new facile, efficient, environmental and economical multicomponent methodology for the synthesis of these heterocyclic compounds.

In recent years, gold catalyzed reactions have focused not only on the development of new processes, but also on improving the sustainability of existing transformations such as cycloaddition, isomerisation, hydroamination or nucleophilic cyclization of allenes.\textsuperscript{81,82} In transition metal catalysis, cationic gold(I) and gold(III) salts are soft carbophilic Lewis acids, have shown extraordinary capability of activating C-C double and triple bond for an inter or intra molecular nucleophilic attack to form a new C-C and C-X bond formation reactions.\textsuperscript{83,84} On the other hand, the versatility of homogeneous mixture of PEG and gold(III) chloride (HAuCl\textsubscript{4}.3H\textsubscript{2}O) encouraged us to couple them together to evaluate their utility as a novel and highly efficient catalytic system for the synthesis of spirooxindole derivatives.
Due to increasing awareness of environmental problems for the synthetic chemists in chemical research and industry, efforts have been made to develop an environmentally benign chemical synthesis both in academia and chemical research. In such situation, the search for alternative reaction media to replace the volatile organic solvents (VOCs) with various aqueous solutions has been attracted much attention in organic synthesis and industrial research. Meanwhile, water used as green solvent has been well documented for organic reactions, but the practical utilization is limited due to the hydrophobic nature of organic compounds and the sensitivity of catalysts towards moisture. Infact, recently PEG has attracted great interest as novel solvent for catalytic processes since it is relatively inexpensive, completely non halogenated, readily available and biodegradable (PEG is approved for use in beverages). Many organic reactions have been carried out using PEGs as recyclable solvent, such as multicomponent reactions, Heck reaction, Suzuki cross coupling reaction and the Wacker reaction.

Thus, in continuation to our ongoing endeavor and aimed to develop an environmentally benign synthetic method for pharmacologically important skeletons. Herein, we wish to report an efficient and green protocol for one-pot three-component reaction of of isatins with active methylene compounds and cyclic 1,3-diketones to afford a series of spirooxindole derivatives in polyethylene glycol (PEG) as green solvent media catalyzed by gold(III) chloride (HAuCl₄•3H₂O) at 70 °C.
RESULTS AND DISCUSSION

Initially, the synthesis of spirooxindole (127a) via one-pot three-component reaction was carried out using 1 equiv. each of isatin (124a), malononitrile (125a) and dimedone (126a) as a model substrate (Scheme 38). The reaction mixture was stirred at 70 °C in PEG (5 mL). During the reaction, it was observed that the yield of product was 91% in the presence of 3 mol% of HAuCl₄.3H₂O after 30 min (Table 1, Entry 8). In contrast to this, the yield of product was very low in the absence of catalyst even after longer reaction time (Table 1, Entry 1).

The effect of catalyst loading for this transformation was also studied. Interestingly, when increasing the amount of gold(III) chloride could improve the product yields significantly. Inspired by the result, we have increased the amount of catalyst from 3 mol% to 5 mol%, increased the product yields from 91% to 95%, respectively (Table 1, Entries 8-10). It shows that using 5 mol% of gold(III) chloride in PEG is sufficient to push this reaction forward. More amount of catalyst did not improve the product yields.

To evaluate the catalytic activity of catalyst, the same reaction was carried out in the presence of various Lewis acid catalysts such as ZnCl₂, BiCl₃, InCl₃, FeCl₃.3H₂O, SnCl₂.2H₂O, p-TSA and HAuCl₄.3H₂O, among them HAuCl₄.3H₂O was found to be the best choice for this multicomponent condensation reaction (MCRs) (Table 1, Entry 9). On the basis of above observations, we chose gold(III) chloride (HAuCl₄.3H₂O) as a potential catalyst for the synthesis of spirooxindole derivatives under similar conditions.

A screening of solvents was also carried out under similar reaction conditions. There are many solvents such as C₂H₅OH, CH₃CN, H₂O, DMSO, DMF and PEGs
were used and it turned out that PEG 400 was found to be a better suited solvent for this reaction with excellent yield of product and less reaction time (Table 2, Entry 8). In addition, when the reaction was performed under solvent-free conditions to give only trace amount of product (Table 2, Entry 6). This results show that the catalytic performance is strongly affected by the type of solvent but a direct correlation between solvent properties and their efficiency could not be established in any case. The results are as summarized in Table 2.

The effect of temperature was also studied. The reaction was carried out at different temperature, increasing from room temperature to 80 °C. We observed that the yield of product was improved and the reaction time was shortened as the temperature was increased from room temperature to 70 °C. The product yields plateaued when temperature was further increased up to 80 °C (Table 2, Entry 10). Consequently, 70 °C was found to be the most suitable reaction temperature for an optimum yield of desired product (Table 2, Entry 8).

In order to prove that the use of polyethylene glycol as green solvent is also practical, it must be conveniently recycled with minimum loss and decomposition. The reaction mixture was cooled in dry ice-bath to precipitate the PEG 400 and extracted with ether (PEG being insoluble in ether) and the retained PEG phase may be reused. The recycled PEG does not change in its reactivity but approximately 5% weight loss of PEG was observed from cycle to cycle (Table 3). Therefore, we also examined the recyclability of the catalyst after the extraction of product with an organic solvent (diethyl ether) was accompanied by considering leaching of the catalyst, so the recyclability of the gold(III) chloride is not possible.

After optimization of reaction conditions, to delineate this approach, especially in regard to library construction, this methodology was evaluated by using different
isatins, active methylene compounds and cyclic 1,3-diketones for the synthesis of a series of tetrahydrospiro[chromene-4,3'-indoline] derivatives (127a-n) and (128a-d) (Scheme 39, Table 4). Several types of substituted isatins including either electron withdrawing or electron donating groups, active methylene compounds (125a-b) and cyclic 1,3-diketones (126a-c) or 4-hydroxycoumarin (126d) were used in this reaction. It was observed that all these cyclic 1,3-diketones or 4-hydroxycoumarin were suitable for this reaction which gives a satisfactory yield of desired products.

Encouraged by these remarkable results, further to extend this green protocol and in order to explore the scope of the HAuCl₄·3H₂O catalyst, we also examined one-pot three-component reaction using acenaphthoquinone (129), instead of isatins under similar conditions. We first used the optimized reaction conditions of Table 1, Entry 9 and Table 2, Entry 8 to convert the model reactant 129, 125a and 126a into the corresponding product spiro acenaphthyleneone 130a. After applying the same reaction conditions, we prepared a variety of spiro acenaphthyleneone derivatives (130a-f) with excellent yields (Scheme 40, Table 5).

Mechanistically, the synthesis of spiro derivatives was described in Scheme 41. Typically, in the first step isatin (124a) condenses with malononitrile (125a) to produce the isatylidene malononitrile derivative (131) in the presence of gold(III) chloride (HAuCl₄·3H₂O) in PEG 400. This step could be regarded as a fast Knoevenagel condensation. Further, in the second step electron deficient Knoevenagel adduct (131) was attacked via Michael addition of dimedone (126a) to give the intermediate (132) which involves the cycloaddition of hydroxyl group (from enolic form of 1,3-diketone) to the cyano moiety to form the desired product 127a (Scheme 41).
Scheme 38: Model reaction.

\[
\begin{align*}
\text{(124a)} & \quad \text{(125a)} & \quad \text{(126a)} & \quad \text{(127a)} \\
\text{HAuCl}_4\cdot3\text{H}_2\text{O} & \quad (5 \text{ mol}%) & \quad \text{PEG 400, 70 }^\circ\text{C}
\end{align*}
\]

Scheme 39: HAuCl₄·3H₂O catalyzed one-pot three-component reaction of isatins, active methylene compounds and cyclic 1,3-diketones or 4-hydroxycoumarin.
Scheme 40: HAuCl₄·3H₂O catalyzed one-pot three-component reaction of acenaphthoquinone, active methylene compounds and cyclic 1,3 diketones or 4-hydroxycoumarin.
Scheme 41: Tentative mechanism for the synthesis of spirooxindole (127a).
EXPERIMENTAL

In a 50 mL round bottom flask, a mixture of isatins (or acenaphthoquinone) (1 mmol), active methylene compounds (1 mmol) and HAuCl₄·3H₂O (5 mol%) in polyethylene glycol (PEG 400) (5 mL) were placed over a magnetic stirrer and the contents were stirred. To this stirred mixture, cyclic 1,3-diketones/4-hydroxycoumarin (1 mmol) was added. The reaction mixture was heated at 70 °C for 30 min. The progress of the reaction mixture was monitored by TLC using hexane:ethyl acetate (2:1) as an eluent. After completion of the reaction, the reaction mixture was allowed to cool in dry ice-bath to precipitate the PEG 400 and extracted with ether (PEG being insoluble in ether). The combined ether layer was filtered in order to recover the PEG. The filtrate was mixed with water and dried over anhydrous sodium sulphate (Na₂SO₄) and concentrated under reduced pressure. The crude product was washed with cold ethanol (3 x 10 mL) and dried. Further, the product was purified through silica-gel column chromatography using 20% ethylacetate and 80% hexane as an eluent to yield the desired products. The recovered PEG 400 could be reused for further reactions. The structures of all the products were established on the basis of their spectral analysis (IR, ¹H NMR, ¹³C NMR and mass spectral data). The melting points of the known synthesized products are identical with those reported previously.⁷⁷,⁷⁹,⁸⁰,⁹⁴
Table 1: Optimization of reaction conditions.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Amount (mol%)</th>
<th>Time (min)</th>
<th>Yield (%) \textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>-</td>
<td>600</td>
<td>24</td>
</tr>
<tr>
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<td>BiCl\textsubscript{3}</td>
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<td>360</td>
<td>38</td>
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<td>InCl\textsubscript{3}</td>
<td>5</td>
<td>120</td>
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<td>5</td>
<td>FeCl\textsubscript{3}.6H\textsubscript{2}O</td>
<td>5</td>
<td>450</td>
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<tr>
<td>6</td>
<td>SnCl\textsubscript{2}.2H\textsubscript{2}O</td>
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<td>270</td>
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<td>7</td>
<td>p-TSA</td>
<td>5</td>
<td>300</td>
<td>50</td>
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<tr>
<td>8</td>
<td>HAuCl\textsubscript{4}.3H\textsubscript{2}O</td>
<td>3</td>
<td>30</td>
<td>91</td>
</tr>
<tr>
<td>9</td>
<td>HAuCl\textsubscript{4}.3H\textsubscript{2}O</td>
<td>5</td>
<td>30</td>
<td>95</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Reaction conditions: isatin (1 mmol), malononitrile (1 mmol), dimedone (1 mmol); solvent PEG 400 (5 mL); temperature 70 °C.
\textsuperscript{b}Isolated yields.

Table 2: Screening of solvent and temperature.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>Time (min)</th>
<th>Yield (%) \textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C\textsubscript{2}H\textsubscript{5}OH</td>
<td>Reflux</td>
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<td>CH\textsubscript{3}CN</td>
<td>Reflux</td>
<td>240</td>
<td>&lt;35</td>
</tr>
<tr>
<td>3</td>
<td>H\textsubscript{2}O</td>
<td>Reflux</td>
<td>240</td>
<td>&lt;35</td>
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<td>4</td>
<td>DMSO</td>
<td>Reflux</td>
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<td>Trace</td>
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<td>5</td>
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<td>50</td>
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<td>12</td>
<td>PEG 400</td>
<td>40</td>
<td>120</td>
<td>70</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Reaction conditions: isatin (1 mmol), malononitrile (1 mmol), dimedone (1 mmol); catalyst gold(III) chloride (5 mol\%); different solvent (5 mL); at different temperatures.
\textsuperscript{b}Isolated yields.
### Table 3: Recyclability of PEG 400.\textsuperscript{a}

<table>
<thead>
<tr>
<th>No. of cycles\textsuperscript{a}</th>
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<th>Run 1</th>
<th>Run 2</th>
<th>Run 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield (%)\textsuperscript{b}</td>
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<td>94</td>
<td>92</td>
<td>90</td>
</tr>
<tr>
<td>Time/min</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Reaction conditions: isatin (1 mmol), malononitrile (1 mmol), dimeredone (1 mmol); catalyst gold(III) chloride (5 mol%); solvent PEG 400 (5 mL); temperature 70 °C.

\textsuperscript{b}Isolated yields.

### Table 4: Synthesis of spirooxindole derivatives (127a-n & 128a-d).\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>R\textsuperscript{1}</th>
<th>Active methylene compounds</th>
<th>Cyclic 1,3-diketones/4-hydroxycoumarin</th>
<th>Product</th>
<th>Yield (%)\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>H</td>
<td>125a</td>
<td>126a</td>
<td>127a</td>
<td>95</td>
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<td>H</td>
<td>H</td>
<td>125a</td>
<td>126b</td>
<td>127b</td>
<td>92</td>
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<tr>
<td>3</td>
<td>H</td>
<td>H</td>
<td>125a</td>
<td>126c</td>
<td>127c</td>
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<td>CH\textsubscript{3}</td>
<td>125a</td>
<td>126a</td>
<td>127d</td>
<td>91</td>
</tr>
<tr>
<td>5</td>
<td>H</td>
<td>CH\textsubscript{3}</td>
<td>125a</td>
<td>126b</td>
<td>127e</td>
<td>93</td>
</tr>
<tr>
<td>6</td>
<td>H</td>
<td>CH\textsubscript{3}</td>
<td>125a</td>
<td>126c</td>
<td>127f</td>
<td>88</td>
</tr>
<tr>
<td>7</td>
<td>H</td>
<td>Ac</td>
<td>125a</td>
<td>126a</td>
<td>127g</td>
<td>89</td>
</tr>
<tr>
<td>8</td>
<td>H</td>
<td>Ac</td>
<td>125a</td>
<td>126b</td>
<td>127h</td>
<td>86</td>
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<tr>
<td>9</td>
<td>H</td>
<td>Ac</td>
<td>125a</td>
<td>126c</td>
<td>127i</td>
<td>82</td>
</tr>
<tr>
<td>10</td>
<td>5-Cl</td>
<td>H</td>
<td>125a</td>
<td>126a</td>
<td>127j</td>
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</tr>
<tr>
<td>11</td>
<td>5-Cl</td>
<td>H</td>
<td>125a</td>
<td>126b</td>
<td>127k</td>
<td>83</td>
</tr>
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<td>12</td>
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<td>125a</td>
<td>126c</td>
<td>127l</td>
<td>90</td>
</tr>
<tr>
<td>13</td>
<td>H</td>
<td>H</td>
<td>125b</td>
<td>126a</td>
<td>127m</td>
<td>86</td>
</tr>
<tr>
<td>14</td>
<td>H</td>
<td>H</td>
<td>125b</td>
<td>126b</td>
<td>127n</td>
<td>82</td>
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<tr>
<td>15</td>
<td>H</td>
<td>H</td>
<td>125a</td>
<td>126d</td>
<td>128a</td>
<td>92</td>
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<tr>
<td>16</td>
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<td>H</td>
<td>125b</td>
<td>126d</td>
<td>128b</td>
<td>82</td>
</tr>
<tr>
<td>17</td>
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<td>CH\textsubscript{3}</td>
<td>125a</td>
<td>126d</td>
<td>128c</td>
<td>90</td>
</tr>
<tr>
<td>18</td>
<td>5-Cl</td>
<td>H</td>
<td>125a</td>
<td>126d</td>
<td>128d</td>
<td>91</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Reaction conditions: isatins (1 mmol), active methylene compounds (1 mmol), cyclic 1,3-diketones or 4-hydroxycoumarin (1 mmol); catalyst gold(III) chloride (5 mol%); solvent PEG 400 (5 mL); temperature 70 °C.

\textsuperscript{b}Isolated yields.
Table 5: Synthesis of products (130a-f) from acenaphthoquinone, cyclic 1,3-diketones and active methylene compounds.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Active methylene compounds</th>
<th>Cyclic 1,3-diketones/4-hydroxycoumarin</th>
<th>Product</th>
<th>Yield (%)\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>125a</td>
<td>126a</td>
<td>130a</td>
<td>91</td>
</tr>
<tr>
<td>2</td>
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<td>3</td>
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<td>126c</td>
<td>130c</td>
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<td>126a</td>
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<td>126b</td>
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</tr>
<tr>
<td>6</td>
<td>125a</td>
<td>126d</td>
<td>130f</td>
<td>90</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Reaction conditions: acenaphthoquinone (1 mmol), active methylene compounds (1 mmol), cyclic 1,3-diketones or 4-hydroxycoumarin (1 mmol); catalyst gold(III) chloride (5 mol%); solvent PEG 400 (5 mL); temperature 70 °C.

\textsuperscript{b}Isolated yields.
Spectroscopic data of synthesized Spirochromenes (127a-n, 128a-d and 130a-f)

2-Amino-7,7-dimethyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile (127a): White solid; mp: 288-289 °C; IR (KBr/cm⁻¹): νmax = 3377, 3314, 3142, 2960, 2192, 1720, 1659, 1605, 1472, 1348, 1227, 1055, 924; ¹H NMR (DMSO-d6, 400 MHz): δ = 10.32 (s, 1H, NH), 7.14 (br s, 2H, NH₂), 7.06 (t, J = 7.8 Hz, 1H, ArH), 6.89 (d, J = 7.3 Hz, 1H, ArH), 6.81 (t, J = 7.7 Hz, 1H, ArH), 6.70 (d, J = 7.8 Hz, 1H, ArH), 2.49 (d, J = 3.7 Hz, 2H, CH₂), 2.12 (d, J = 16.1 Hz, 1H, CH), 2.04 (d, J = 16.1 Hz, 1H, CH), 0.95 (s, 3H, CH₃), 0.92 (s, 3H, CH₃); ¹³C NMR (DMSO-d6, 100 MHz): δ = 194.91, 178.05, 164.16, 158.78, 142.06, 134.42, 128.19, 123.02, 121.70, 117.34, 110.79, 109.26, 57.52, 50.01, 46.83, 31.95, 27.61, 27.04; m/z 335.3566 (M+1, C₁₉H₁₇N₃O₃ requires 335.1270).

2-Amino-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile (127b): White solid; mp: > 300 °C; IR (KBr/cm⁻¹): νmax = 3462, 3291, 3169, 2933, 2194, 1714, 1666,1612, 1468, 1392, 1214, 1064, 1012, 931; ¹H NMR (DMSO-d6, 400 MHz): δ = 10.37 (s, 1H, NH), 7.17 (br s, 2H, NH₂), 7.08 (t, J = 8.6 Hz, 1H, ArH), 6.94 (d, J = 7.8 Hz, 1H, ArH), 6.83 (t, J = 7.3 Hz, 1H, ArH), 6.74 (d, J = 7.3 Hz, 1H, ArH), 2.43-2.60 (m, 2H, CH₂), 2.18-2.24 (m, 2H, CH₂), 1.85-1.90 (m, 2H, CH₂); ¹³C NMR (DMSO-d6, 100 MHz): δ = 194.74, 178.34, 166.38, 158.60, 141.92, 134.41, 128.17, 123.99, 121.67, 117.45, 111.61, 109.18, 57.68, 47.84, 36.28, 26.82, 19.31; m/z 307.3034 (M+1, C₁₇H₁₃N₃O₃ requires 307.0957).

2-Amino-2',5-dioxo-6,7-dihydro-5H-spiro[cyclopenta[b]pyran-4,3'-indoline]-3-carbonitrile (127c): White solid; mp: > 300 °C; IR (KBr/cm⁻¹): νmax = 3352, 3240, 3165, 2917, 2223, 1713, 1649, 1592, 1469, 1337, 1214, 1013, 907, 749, 620; ¹H NMR (DMSO-d6, 400 MHz): δ = 10.54 (s, 1H, NH), 7.47 (br s, 2H, NH₂), 7.18 (t, J = 7.6 Hz,
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2-Amino-1',7,7-trimethyl-2'5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile (127d): White solid; mp: 254-255 °C; IR (KBr): $\nu_{\max} = 3459, 3234, 3139, 2933, 2193, 1708, 1667, 1605, 1496, 1391, 1256, 1142, 1063, 912$ cm$^{-1}$; $^1$H NMR (DMSO-$d_6$, 400 MHz): $\delta = 7.21-7.24$ (m, 3H, NH$_2$, ArH), 7.05 (d, $J = 7.8$ Hz, 1H, ArH), 6.96-7.00 (m, 2H, ArH), 3.35 (s, 3H, CH$_3$), 2.49-2.56 (m, 2H, CH$_2$), 2.04-2.16 (m, 2H, CH$_2$), 1.01 (s, 3H, CH$_3$), 0.97 (s, 3H, CH$_3$); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): $\delta = 195.06, 176.69, 164.26, 158.93, 143.53, 133.56, 128.54, 122.88, 122.27, 117.24, 110.67, 108.31, 57.53, 50.43, 46.82, 32.09, 27.08, 27.09, 25.97; $m/z$ 349.3832 (M+1, C$_{20}$H$_{19}$N$_3$O$_3$ requires 349.1426).

2-Amino-1'-methyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile (127e): White solid; mp: 248-249 °C; IR (KBr/cm$^{-1}$): $\nu_{\max} = 3565, 3466, 3355, 3145, 2962, 2195, 1702, 1676, 1331, 1216, 1196, 1075, 1013, 757$; $^1$H NMR (DMSO-$d_6$, 400 MHz): $\delta = 7.19-7.24$ (m, 3H, NH$_2$, ArH), 7.06 (d, $J = 7.6$ Hz, 1H, ArH), 6.94-6.98 (m, 2H, ArH), 3.20 (s, 3H, CH$_3$), 2.63-2.66 (m, 2H, CH$_2$), 2.18-2.22 (m, 2H, CH$_2$), 1.89-1.92 (m, 2H, CH$_2$); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): $\delta = 194.98, 176.55, 166.15, 158.64, 143.60, 133.82, 128.57, 123.11, 122.49, 117.34, 111.99, 108.08, 56.82, 47.52, 37.32, 27.07, 26.23, 19.84; $m/z$ 321.3300 (M+1, C$_{18}$H$_{16}$N$_3$O$_3$ requires 321.1113).

2-Amino-1'-methyl-2',5-dioxo-6,7-dihydro-5$H$-spiro[cyclopenta[b]pyran-4,3'-indoline]-3-carbonitrile (127f): White solid; mp: 279-280 °C; IR (KBr/cm$^{-1}$): $\nu_{\max} = 3566, 3456, 3345, 3140, 2960, 2195, 1706, 1675, 1498, 1350, 1216, 1190, 1078, 1016,
756; $^1$H NMR (DMSO-$_d_6$, 400 MHz): $\delta = 7.29-7.45$ (m, 3H, NH$_2$, ArH), 7.10 (d, $J = 7.1$ Hz, 1H, ArH), 7.01-7.03 (m, 2H, ArH), 3.18 (s, 3H, CH$_3$), 2.85 (t, $J = 4.0$ Hz, 2H, CH$_2$), 2.28-2.32 (m, 2H, CH$_2$); $^{13}$C NMR (DMSO-$_d_6$, 100 MHz): $\delta = 199.72$, 177.56, 176.15, 160.82, 142.62, 132.24, 128.23, 124.12, 122.54, 117.30, 115.26, 108.10, 56.38, 47.51,
36.30, 27.23, 26.36; $m/z$ 307.3034 (M+1, C$_{17}$H$_{14}$N$_3$O$_3$ requires 307.0957).

1'-Acetyl-2-amino-7,7-dimethyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile (127g): White Solid; mp: 230-232 °C; IR (KBr/cm$^{-1}$): $\nu_{\text{max}} = 3462, 3194, 2933, 2193, 1757, 1726, 1663, 1354, 1256, 1099$ cm$^{-1}$; $^1$H NMR (DMSO-$_d_6$, 400 MHz): $\delta = 8.07$ (d, $J = 8.1$ Hz, 1H, ArH), 7.52 (br s, 2H, NH$_2$), 7.27-7.36 (m, 1H, ArH), 7.18-7.22 (m, 2H, ArH), 2.66 (s, 3H, CH$_3$CO), 2.55 (s, 2H, CH$_2$), 2.48-2.49 (m, 2H, CH$_2$), 1.03 (s, 3H, CH$_3$), 0.99 (s, 3H, CH$_3$); $^{13}$C NMR (DMSO-$_d_6$, 100 MHz): $\delta = 195.41$, 177.84, 170.24, 164.93, 158.74, 139.17, 132.71, 128.67, 125.50, 123.30, 116.93, 115.30, 110.75, 56.96, 49.47, 47.39, 39.91, 32.12, 27.53, 27.02, 25.95; $m/z$ 377.3933 (M+1, C$_{21}$H$_{19}$N$_3$O$_4$ requires 377.1376).

1'-Acetyl-2-amino-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile (127h): White Solid; mp: 253-255 °C; IR (KBr/cm$^{-1}$): $\nu_{\text{max}} = 3462, 3194, 2933, 2193, 1757, 1726, 1663, 1354, 1256, 1099$ cm$^{-1}$; $^1$H NMR (DMSO-$_d_6$, 400 MHz): $\delta = 8.01$ (d, $J = 8.0$ Hz, 1H, ArH), 7.44 (br s, 2H, NH$_2$), 7.23-7.26 (m, 1H, ArH), 7.03-7.16 (m, 2H, ArH), 2.54-2.64 (m, 2H, CH$_2$), 2.49 (s, 3H, CH$_3$CO), 2.13-2.21 (m, 2H, CH$_2$); $^{13}$C NMR (DMSO-$_d_6$, 100 MHz): $\delta = 195.44$, 178.08, 170.25, 166.66, 158.52, 139.12, 133.02, 128.64, 125.51, 123.48, 117.06, 115.03, 111.74, 56.98, 47.44, 43.51, 26.60, 25.95, 19.70; $m/z$ 349.1063 (M+1, C$_{21}$H$_{15}$N$_3$O$_4$ requires 349.0880).

1'-Acetyl-2-amino-2',5-dioxo-6,7-dihydro-5$^H$-spiro[cyclopenta[b]pyran-4,3'-indoline]-3-carbonitrile (127i): White Solid; mp: 282-284 °C; IR (KBr/cm$^{-1}$): $\nu_{\text{max}} = 3463, 3324, 2919, 2198, 1752, 1721, 1665, 1324, 1253, 1168, 1071, 910, 757$; $^1$H NMR
(DMSO-d$_6$, 400 MHz): $\delta = 8.02$ (d, $J = 8.1$ Hz, 1H, ArH), 7.70 (br s, 2H, NH$_2$), 7.27-7.31 (m, 1H, ArH), 7.13-7.20 (m, 2H, ArH), 2.77 (t, $J = 4.7$ Hz, 2H, CH$_2$), 2.49 (s, 3H, CH$_3$CO), 2.31 (t, $J = 5.0$ Hz, 2H, CH$_2$); $^{13}$C NMR (DMSO-d$_6$, 100 MHz): $\delta = 200.13$, 177.98, 170.32, 163.15, 160.50, 139.44, 130.51, 129.39, 125.85, 124.53, 117.33, 115.57, 112.96, 56.03, 47.44, 34.62, 26.12, 25.18; m/z 335.3135 (M+1, C$_{18}$H$_{13}$N$_3$O$_4$ requires 335.0906).

2-Amino-5'-chloro-2',5-dioxo-7,7-dimethyl-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile (127j): White solid; mp: 288-290 °C; IR (KBr/cm$^{-1}$): $\nu$ max = 3445, 3285, 3146, 2932, 2194, 1725, 1663, 1605, 1479, 1392, 1256, 1164, 1063, 905; $^1$H NMR (DMSO-d$_6$, 400 MHz): $\delta = 10.39$ (s, 1H, NH), 7.24 (br s, 2H, NH$_2$), 7.12 (d, $J = 8.0$ Hz, 1H, ArH), 7.02 (s, 1H, ArH), 6.71 (d, $J = 8.8$ Hz, 1H, ArH), 2.41-2.53 (m, 2H, CH$_2$), 2.03-2.11 (m, 2H, CH$_2$), 0.94 (s, 3H, CH$_3$), 0.90 (s, 3H, CH$_3$); $^{13}$C NMR (DMSO-d$_6$, 100 MHz): $\delta = 195.01$, 177.77, 164.51, 158.86, 141.02, 136.43, 128.15, 125.72, 123.18, 117.14, 110.70, 110.12, 56.33, 50.48, 46.80, 32.00, 27.52, 27.23; m/z 369.8016 (M+1, C$_{19}$H$_{16}$ClN$_3$O$_3$ requires 369.0880).

2-Amino-5'-chloro-2',5-dioxo-7,7-dimethyl-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile (127k): White solid; mp: 293–295 °C; IR (KBr/cm$^{-1}$): $\nu$ max = 3468, 3287, 3142, 2932, 2116, 1722, 1668,1608, 1497, 1391, 1256, 1162, 1063, 908; $^1$H NMR (DMSO-d$_6$, 400 MHz): $\delta = 10.49$ (s, 1H, NH), 7.26 (br s, 2H, NH$_2$), 7.15 (d, $J = 7.9$ Hz, 1H, ArH), 7.10 (s, 1H, ArH), 6.74 (d, $J = 8.0$ Hz, 1H, ArH), 2.45-2.60 (m, 2H, CH$_2$), 2.00-2.20 (m, 2H, CH$_2$), 1.85-1.91 (m, 2H, CH$_2$); $^{13}$C NMR (DMSO-d$_6$, 100 MHz): $\delta = 195.24$, 177.97, 166.66, 158.78, 140.96, 136.53, 128.02, 125.58, 123.42, 117.17, 111.29, 110.48, 56.79, 47.06, 32.01, 26.86, 19.56; m/z 341.7485 (M+1, C$_{19}$H$_{17}$ClN$_3$O$_3$ requires 341.0567).
2-Amino-5'-chloro-2',5-dioxo-6,7-dihydro-5H-spirocyclopenta[b]pyran-4,3'-indoline]-3-carbonitrile (127l): White solid; mp: > 300 °C; IR (KBr/cm⁻¹): ν_max = 3465, 3282, 3135, 2915, 2191, 1720, 1671, 1466, 1213, 1158, 1098, 1010, 912, 753; ¹H NMR (DMSO-d₆, 400 MHz): δ = 10.70 (s, 1H, NH), 7.57 (br s, 2H, NH₂), 7.20, 7.24 (m, 2H, ArH), 6.84 (d, J = 7.8 Hz, 1H, ArH), 2.78-2.80 (m, 2H, CH₂), 2.36-2.49 (m, 2H, CH₂); ¹³C NMR (DMSO-d₆, 100 MHz): δ = 199.95, 178.00, 176.57, 160.73, 141.73, 136.94, 134.09, 128.81, 124.52, 117.43, 114.22, 110.98, 55.88, 46.79, 33.20, 25.01; m/z 327.7219 (M+1, C₁₆H₁₀ClN₃O₃ requires 327.0413).

Ethyl-2-Amino-7,7-dimethyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carboxylate (127m): White solid; mp: 256-257 °C, IR (KBr/cm⁻¹): ν_max = 3429, 2997, 2128, 1686, 1620, 1473, 1222, 1027, 952, 762; ¹H NMR (DMSO-d₆, 400 MHz): δ = 10.24 (s, 1H, NH), 7.72 (br s, 2H, NH₂), 6.71-7.08 (m, 4H, ArH), 3.64 (q, J = 5.1 Hz, 2H, CH₂), 2.51 (d, J = 3.5 Hz, 2H, CH₂), 2.13 (d, J = 15.2 Hz, 1H, CH), 2.06 (d, J = 15.2 Hz, 1H, CH), 1.03 (s, 3H, CH₃), 0.94 (s, 3H, CH₃), 0.82 (t, J = 6.6 Hz, 3H, CH₃); ¹³C NMR (DMSO-d₆, 100 MHz): δ = 195.18, 179.80, 168.23, 162.81, 159.65, 143.32, 134.12, 127.41, 123.01, 121.62, 114.36, 109.12, 78.58, 59.61, 52.32, 46.85, 34.09, 27.39, 27.11, 13.65; m/z 382.4098 (M+1, C₂₁H₂₂N₂O₅ requires 382.1529).

Ethyl-2-Amino-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carboxylate (127n): White solid; mp: 262-263 °C; IR (KBr/cm⁻¹): ν_max = 3465, 3289, 2932, 1656, 1642, 1532, 1469, 1212, 1065, 1015, 934, 740; ¹H NMR (DMSO-d₆, 400 MHz): δ = 10.37 (s, 1H, NH), 7.69 (br s, 2H, NH₂), 7.02-7.43 (m, 4H, ArH), 3.66 (q, J = 5.8 Hz, 2H, CH₂), 1.95-2.83 (m, 6H, CH₂), 0.76 (t, J = 6.9 Hz, 3H, CH₃); ¹³C NMR (DMSO-d₆, 100 MHz): δ = 195.40, 178.43, 169.65, 165.12, 159.56, 141.93, 134.42, 127.18, 123.94, 121.65, 115.84, 108.46, 77.95, 59.17, 47.36, 38.22, 27.62, 19.30, 13.51; m/z 354.3566 (M+1, C₁₉H₁₈N₂O₅ requires 354.1216).
2'-Amino-2,5'-dioxo-5'H-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-3'-carbonitrile (128a): White solid; mp: 284-286 °C; IR (KBr/cm⁻¹): ν max = 3467, 3294, 3197, 2932, 2275, 1727, 1660, 1602, 1543, 1496, 1391, 1256, 1172, 1099, 970; ¹H NMR (DMSO-d₆, 400 MHz): δ = 10.68 (s, 1H, NH), 7.94 (d, J = 7.8 Hz, 1H, ArH), 7.75 (t, J = 7.3 Hz, 1H, ArH), 7.66 (br s, 2H, NH₂), 7.40 (t, J = 7.8 Hz, 1H, ArH), 7.34 (d, J = 8.7 Hz, 1H, ArH), 7.20 (t, J = 7.8 Hz, 2H, ArH), 6.92 (t, J = 7.8 Hz, 1H, ArH), 6.85 (d, J = 7.4 Hz, 1H, ArH); ¹³C NMR (DMSO-d₆, 100 MHz): δ = 177.26, 159.66, 158.49, 155.24, 152.13, 142.19, 133.69, 132.91, 129.92, 125.05, 124.13, 123.09, 122.71, 117.11, 117.05, 112.57, 109.78, 101.51, 56.91, 47.63; m/z 357.3190 (M+1, C₂₀H₁₁N₃O₄ requires 357.0750).

Ethyl-2'-Amino-2,5'-dioxo-5'H-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-3'-carboxylate (128b): White Solid; mp: 252-253 °C; IR (KBr/cm⁻¹): ν max = 3455, 3282, 3015, 2920, 1725, 1658, 1563, 1473, 1434, 1315, 1274, 1184, 1027, 949, 754; ¹H NMR (DMSO-d₆, 400 MHz): δ = 10.40 (s, 1H, NH), 9.90 (br s, 2H, NH₂), 7.41-7.50 (m, 2H, ArH), 7.34 (t, J = 8.1 Hz, 1H, ArH), 7.26 (d, J = 8.0 Hz, 1H, ArH), 7.01-7.10 (m, 2H, ArH), 6.77-6.83 (m, 2H, ArH), 3.69-3.75 (m, 2H, CH₂O), 0.81 (t, J = 6.9 Hz, 3H, CH₃); ¹³C NMR (DMSO-d₆, 100 MHz): δ = 177.28, 159.68, 158.53, 155.29, 152.17, 142.16, 133.68, 132.986, 129.95, 125.08, 124.16, 123.15, 122.75, 117.18, 117.10, 112.58, 109.72, 101.49, 62.34, 56.95, 47.64, 14.45; m/z 404.3722 (M+1, C₂₂H₁₆N₂O₆ requires 404.1008).

2'-Amino-1-methyl-2,5'-dioxo-5'H-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-3'-carbonitrile (128c): White solid; mp: 283-285 °C; IR (KBr/cm⁻¹): ν max = 3456, 3291, 3168, 2915, 2227, 1719,1664, 1607, 1465, 1373, 1223, 1127, 1099, 949; ¹H NMR (DMSO-d₆, 400 MHz): δ = 7.91 (d, J = 7.8 Hz, 1H, ArH), 7.64 (t, J = 8.5 Hz, 1H, ArH), 7.57 (br s, 2H, NH₂), 7.53 (t, J = 7.8 Hz, 1H, ArH), 7.33 (d, J = 8.0 Hz, 1H, ArH), 7.31 (t,
$J = 7.8$ Hz, 1H, ArH), 7.29 (d, $J = 6.6$ Hz, 1H, ArH), 7.05 (d, $J = 7.8$ Hz, 1H, ArH), 7.0 (t, $J = 6.6$ Hz, 1H, ArH), 3.14 (s, 3H, CH$_3$); $^{13}$C NMR (DMSO-d$_6$, 100 MHz): $\delta = 171.75$, 162.38, 158.62, 155.69, 149.78, 147.31, 137.63, 132.28, 128.56, 125.54, 124.25, 123.45, 118.05, 117.96, 112.95, 111.58, 110.53, 57.12, 47.62, 26.11; $m/z$ 371.3456 (M+1, C$_{21}$H$_{13}$N$_3$O$_4$ requires 371.0906).

2'-Amino-5-chloro-2,5'-dioxo-5'H-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-3'-carbonitrile (128d): White solid; mp: $>300$ °C; IR (KBr/cm$^{-1}$): $\nu_{\text{max}} = 3459, 3322, 3210, 2932, 2196, 1713, 1667, 1605, 1440, 1391, 1256, 1171, 1098, 971$; $^1$H NMR (DMSO-d$_6$, 400 MHz): $\delta = 10.80$ (s, 1H, NH), 7.93 (d, $J = 7.6$ Hz, 1H, ArH), 7.72-7.77 (m, 3H, ArH, NH$_2$), 7.53 (t, $J = 7.3$ Hz, 1H, ArH), 7.47 (d, $J = 8.1$ Hz, 1H, ArH), 7.41 (s, 1H, ArH), 7.26 (d, $J = 8.1$ Hz, 1H, ArH), 6.84 (d, $J = 7.3$ Hz, 1H, ArH); $^{13}$C NMR (DMSO-d$_6$, 100 MHz): $\delta = 176.91$, 159.02, 158.39, 155.43, 152.30, 141.01, 134.92, 133.71, 128.74, 126.10, 124.97, 124.50, 122.65, 116.88, 116.64, 112.71, 110.79, 100.69, 56.36, 47.85; $m/z$ 391.7641 (M+1, C$_{20}$H$_{10}$ClN$_3$O$_4$ requires 391.0360).

2'-Amino-7',7'-dimethyl-2,5'-dioxo-5',6',7',8'-tetrahydro-2H-spiro[acenaphthylene-1,4'-chromene]-3'-carbonitrile (130a): Light yellow solid; mp: 261-263 °C; IR (KBr/cm$^{-1}$): $\nu_{\text{max}} = 3468, 3186, 2932, 2192, 1718, 1663, 1497, 1256, 1098$; $^1$H NMR (DMSO-d$_6$, 400 MHz): $\delta = 8.41-8.44$ (m, 1H. ArH), 8.24 (d, $J = 7.4$ Hz, 1H, ArH), 8.17 (d, $J = 7.6$ Hz, 1H, ArH), 7.91-8.01 (m, 3H, ArH), 7.31 (br s, 2H, NH$_2$), 2.47-2.49 (m, 2H, CH$_2$), 2.11 (d, $J = 16.1$ Hz, 1H, CH), 2.06 (d, $J = 16.0$ Hz, 1H, CH), 1.02 (s, 3H, CH$_3$), 1.42 (s, 3H, CH$_3$); $^{13}$C NMR (DMSO-d$_6$, 100 MHz): $\delta = 203.61$, 195.34, 164.62, 158.65, 143.20, 140.48, 132.17, 131.52, 130.14, 129.84, 128.93, 124.51, 121.40, 119.84, 117.45, 112.05, 57.92, 51.04, 49.73, 32.09, 27.52, 27.20; $m/z$ 370.4006 (M+1, C$_{23}$H$_{18}$N$_2$O$_3$ requires 370.1317).
2'-Amino-2,5'-dioxo-5',6',7',8'-tetrahydro-2H-spiro[acenaphthylene-1,4'-
chromene]-3'-carbonitrile (130b): Orange solid; mp: 244-246 °C; IR (KBr/cm-1):  ν\text{max} = 3490, 3072, 2933, 2116, 1720, 1672, 1498, 1389, 1256, 1064; \textsuperscript{1}H NMR (DMSO-d\textsubscript{6}, 400 MHz): δ = 8.40-8.44 (t, J = 8.0 Hz, 1H, ArH), 8.25 (d, J = 7.3 Hz, 1H, ArH), 8.18 (d, J = 7.3 Hz, 1H, ArH), 7.93-8.01 (m, 3H, ArH), 7.29 (br s, 2H, NH\textsubscript{2}), 2.48-2.49 (m, 2H, CH\textsubscript{2}) 2.13-2.18 (m, 2H, CH\textsubscript{2}), 1.89-1.95 (m, 2H, CH\textsubscript{2}); \textsuperscript{13}C NMR (DMSO-d\textsubscript{6}, 100 MHz): δ = 203.72, 198.34, 168.30, 156.06, 143.39, 140.79, 132.20, 130.13, 129.43, 128.54, 123.66, 123.15, 122.86, 117.35, 113.19, 57.25, 51.30, 36.81, 27.14, 21.32; m/z 342.3475 (M+1, C\textsubscript{21}H\textsubscript{14}N\textsubscript{2}O\textsubscript{3} requires 342.1004).

2'-Amino-2,5'-dioxo-6',7'-dihydro-2H,5'H-spiro[acenaphthylene-1,4'-
cyclopenta[\textit{b}]/pyran]-3'-carbonitrile (130c): Orange solid; mp: > 300 °C; IR (KBr/cm\textsuperscript{-1}):  ν\text{max} = 3440, 3072, 2933, 2117, 1722, 1613, 1495, 1385, 1223, 1026, 983, 780; \textsuperscript{1}H NMR (DMSO-d\textsubscript{6}, 400 MHz): δ = 8.43 (t, J = 8.8 Hz, 1H, ArH), 8.34 (d, J = 7.4 Hz, 1H, ArH), 7.92-8.01 (m, 3H, ArH), 7.57 (br s, 2H, NH\textsubscript{2}), 2.86-2.87 (m, 2H, CH\textsubscript{2}), 2.47-2.49 (m, 2H, CH\textsubscript{2}); \textsuperscript{13}C NMR (DMSO-d\textsubscript{6}, 100 MHz): δ = 203.09, 200.16, 177.84, 155.98, 141.31, 140.73, 132.33, 129.40, 129.09, 128.74, 125.08, 123.27, 122.05, 121.08, 117.70, 111.72, 56.99, 50.92, 33.10, 25.06; m/z 328.3209 (M+1, C\textsubscript{20}H\textsubscript{12}N\textsubscript{2}O\textsubscript{3} requires 328.0848).

Ethyl-2'-Amino-7',7'-dimethyl-2,5'-dioxo-5',6',7',8'-tetrahydro-2H-
spiro[acenaphthylene-1,4'-chromene]-3'-carboxylate (130d): White solid; mp: 263-264 °C; IR (KBr/cm\textsuperscript{-1}):  ν\text{max} = 3421, 3185, 2939, 2182, 1717, 1602, 1487, 1277, 1014; \textsuperscript{1}H NMR (DMSO-d\textsubscript{6}, 400 MHz): δ = 7.52-8.41 (m, 6H. ArH), 7.90 (s, 2H, NH\textsubscript{2}), 4.48 (q, J = 6.1 Hz, 2H, CH\textsubscript{2}), 2.48-2.49 (m, 2H, CH\textsubscript{2}), 1.35-1.38 (m, 2H, CH\textsubscript{2}), 1.09 (s, 3H, CH\textsubscript{3}), 1.07 (s, 3H, CH\textsubscript{3}), 0.45 (t, J = 6.8 Hz, 3H, CH\textsubscript{3}); \textsuperscript{13}C NMR (DMSO-d\textsubscript{6}, 100 MHz): δ = 196.42, 195.25, 167.60, 164.98, 159.73, 145.26, 134.18,
Ethyl-2'-Amino-2,5'-dioxo-5',6',7',8'-tetrahydro-2H-spiro[acenaphthylene-1,4'-chromene]-3'-carboxylate (130e): Yellow solid; mp: 224–226 °C; IR (KBr/cm$^{-1}$): $\nu_{\text{max}} = 3486, 3280, 2986, 1717, 1675, 1586, 1362, 1276, 1013, 755$; $^1$H NMR (DMSO-d$_6$, 400 MHz): $\delta = 7.86-8.59$ (m, 6H, ArH), 7.32 (s, 2H, NH$_2$), 4.48 (q, $J = 7.3$ Hz, 2H, CH$_2$), 2.30-2.31 (m, 2H, CH$_2$), 1.35-1.37 (m, 2H, CH$_2$), 0.34 (t, $J = 6.8$ Hz, 3H, CH$_3$); $^{13}$C NMR (DMSO-d$_6$, 100 MHz): $\delta = 196.88, 195.41, 168.16, 165.43, 144.10, 132.30, 129.22, 128.62, 128.32, 128.16, 127.98, 124.34, 121.23, 116.11, 78.79, 62.41, 59.32, 39.70, 33.14, 27.84, 13.82; m/z 389.1263 (M+1, C$_{23}$H$_{19}$NO$_5$ requires 389.4007).

2'-Amino-2,5'-dioxo-2H,5'H-spiro[acenaphthylene-1,4'-pyran[3,2-c]chromene]-3'-carbonitrile (130f): Brown solid; mp: 255-256 °C; IR (KBr/cm$^{-1}$): $\nu_{\text{max}} = 3414, 3062, 2129, 1725, 1659, 1486, 1379, 1230, 1026$; $^1$H NMR (DMSO-d$_6$, 400 MHz): $\delta = 8.32-8.39$ (m, 2H, ArH), 8.13 (d, $J = 7.3$ Hz, 1H, ArH), 7.82-8.00 (m, 3H, ArH), 7.77 (br s, 2H, NH$_2$), 7.42-7.66 (m, 4H); $^{13}$C NMR (DMSO-d$_6$, 100 MHz): $\delta = 195.35, 176.87, 158.49, 156.11, 152.24, 142.11, 133.84, 132.34, 131.38, 129.97, 129.36, 128.87, 128.56, 127.85, 127.11, 126.43, 125.28, 123.75, 121.21, 117.26, 100.25, 57.75, 55.36; m/z 392.7026 (M+1, C$_{24}$H$_{12}$N$_2$O$_4$ requires 392.0797).
REFERENCES


