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Synthesis of fused pyrroles containing 4-hydroxycoumarins by regioselective metal-free multicomponent reactions†

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The reaction of arylglyoxals, 4-hydroxycoumarin, and aromatic amines such as 7-amino-2-methylchromone, 6/7-aminoflavone, 7-amino-4-methylcoumarin, 1-amino-9-fluorenone, 1-aminoanthraquinone and aniline derivatives in acetic acid medium under microwave conditions provides the corresponding regioselective fused pyrroles having hydroxycoumarin and aryl substituents. Alternatively, we have developed another method using *in situ* arylglyoxals from acetophenone derivatives by I_2/DMSO promoted C–H oxidation followed by one-pot three component cyclization reactions to provide similar fused pyrroles. Using both the methods a series of novel pyrroles fused with pharmacologically important chromone, flavone, coumarin, fluorenone, and anthraquinone moieties were synthesized under metal-free reaction conditions in good to very good yields within a short reaction time. The structures of the synthesized fused pyrroles have been unambiguously confirmed by spectroscopic techniques, mass analysis and single crystal XRD.

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Introduction

Fused pyrroles and their derivatives are prevalent in many natural products, agrochemicals, and pharmaceuticals as well as in synthetic molecules with promising optical and electronic properties.[1] Considering their wide range of applications the design and development of fused pyrroles has remained one of the popular and demanding areas in medicinal and organic chemistry.[2] Similarly, chromones, flavones and coumarins are very useful natural products with numerous bioactivities.[3] As per the molecular hybridization concept hybrid molecules obtained from two or more pharmacophoric moieties with different bioactivities can offer novel drug candidates with better efficacy.[4] Pyrroles fused with chromones, flavones and coumarins are hybrid molecules with promising bioactivities. These types of hybrid molecules are useful as antitumor,[5] anticancer[6] and fluorescent neuroimaging agents.[7] They also exhibit redox switching properties.[8] A few representative pyrroles fused with flavones and coumarin derivatives along with their applications are shown in Fig. 1.

From the literature, we realized that the number of available methods for the easy access of chromone/flavone as well as coumarin fused pyrroles is still very limited.[9] Recently, Zhang *et al.* have reported a photo-induced intramolecular annulation method for the synthesis of chromone fused heteroaromatics.[10] Suresh *et al.* have reported a two component copper catalyzed coupling reaction for the synthesis of chromone fused pyrazoles.[11] Multicomponent reactions are considered as one of the simple, straightforward and green approaches for the synthesis of diverse heterocycles in a step, atom, and pot economical way.[12] Similarly, microwave heating in organic synthesis offers many advantages such as a short reaction time and few byproducts.[13] Thus the use of microwave heating in multicomponent reactions is considered to be effective for efficient and rapid synthesis of diverse heterocycles.[14]

Considering the efficiency as well as green chemistry aspects of microwave assisted multicomponent reactions, recently we have developed a multicomponent reaction for the synthesis of pyrimidine fused pyrroles.[15] In continuation of our work on the design and development of multicomponent reactions to access novel heterocycles we turned our attention to developing a novel multicomponent reaction for the efficient synthesis of diverse fused pyrroles from the combination of arylglyoxal/acetophenone derivatives, 4-hydroxy coumarins and various amines under metal-free reaction conditions as shown in Scheme 1.

Molecular iodine is a versatile non-metallic catalyst for a wide range of organic transformations.[16] Due to its benign

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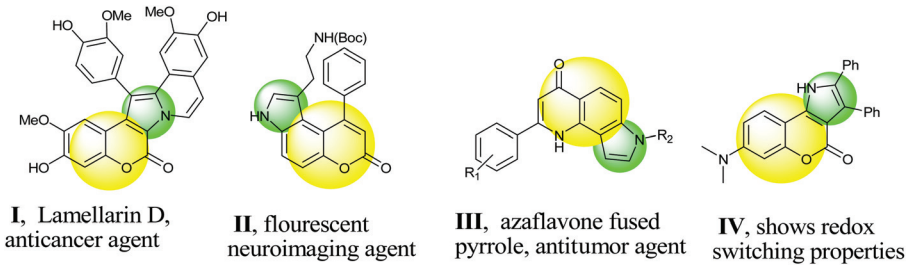
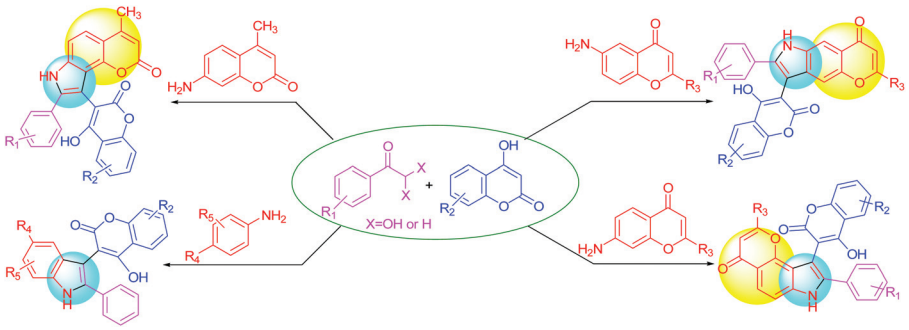
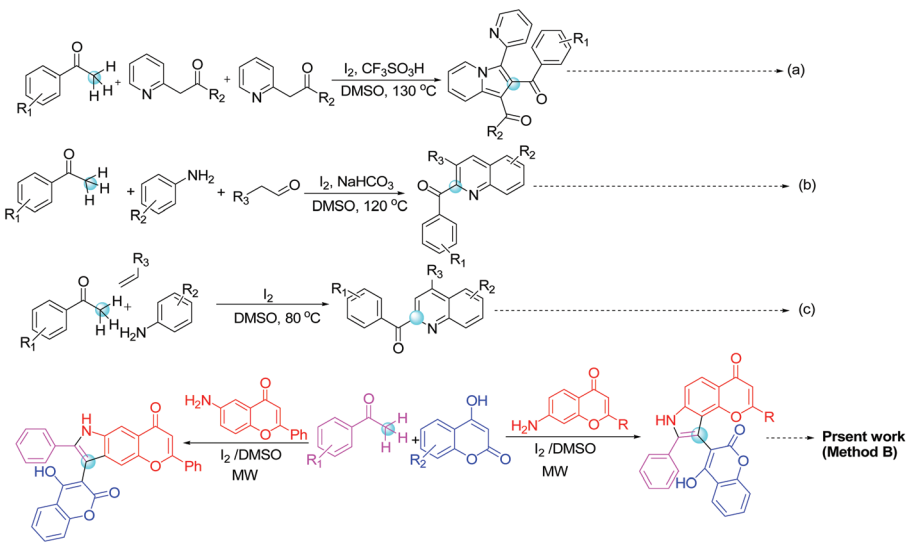


Fig. 1 Representative examples of useful flavone and coumarin fused pyrroles.



Scheme 1 Proposed multicomponent reactions for the synthesis of fused pyrroles containing 4-hydroxycoumarins.

and versatile properties, substantial attention has been paid towards the exploration of iodine in organic synthesis. Very recently, Wu *et al.* have reported an I_2 catalyzed three component reaction for the synthesis of 3-(pyridin-2-yl)indolizine skeletons from the reaction of acetophenone and 2-(pyridin-2-yl)acetate derivatives using a [3 + 1 + 1] annulation process (Scheme 2a).[17] The same group also reported the iodine catalyzed synthesis of a quinoline derivative using [4 + 2] cycloaddition of methyl ketones, arylamines and aryl/alkyl acetaldehydes as shown in Scheme 2b.[18] Quinoline derivatives have also been synthesized by Wu *et al.* using a three component reaction of aromatic methyl ketones, aryl amines and styrenes following a [3 + 2 + 1] cycloaddition process (Scheme 2c).[19] Interestingly, in all these methods the reaction goes *via* the formation of *in situ* arylglyoxals and only the aldehyde functionality of the arylglyoxal derivatives is involved in the cycloaddition process (Scheme 2). In this paper, we demonstrate for the first time a three component synthesis of



Scheme 2 Comparison of the present work (method B) with the literature reported three component reactions by I_2/DMSO mediated C(sp^3)–H oxidation of acetophenone derivatives.

novel fused pyrroles by oxidative cyclization of acetophenone derivatives *via* [3 + 2] cycloaddition involving both the keto and aldehyde functionalities of arylglyoxals as shown in Scheme 2 (method B).

Results and discussion

Initially we began our study by investigating the reaction of phenylglyoxal monohydrate (**1a**), 4-hydroxycoumarin (**2a**), and 7-amino-2-methylchromone (**3a**). This combination under solvent and catalyst-free conditions did not provide any three component product even after 24 hours of stirring at room temperature. Next, we tried the reaction in water as the solvent without adding any catalyst and in this case also, we did not observe any three component product (Table 1, entry 2). Interestingly, when this model reaction was performed under microwave heating conditions for 30 minutes in ethanol as a reaction medium, only a trace amount of a three component product **4a** was obtained.

Compound **4a** was characterized by ^{1}H and ^{13}C NMR spectroscopy as well as by HRMS. After obtaining this encouraging result, we wanted to optimize the reaction conditions by using either acidic or basic catalysts such as molecular iodine, PTSA, acetic acid and Et_3N. Under acidic conditions we observed better yields (Table 1, entries 4, 5 and 7) and in the presence of a base such as Et_3N the reaction did not provide any detectable three component product. From the result of entry 7 we realized that an excess amount of acetic acid may enhance the yield of **4a**. Thus, next we tried this model reaction in acetic acid as the reaction medium cum promoter under microwave heating at 80 °C for 30 minutes and we ended with 55% yield.

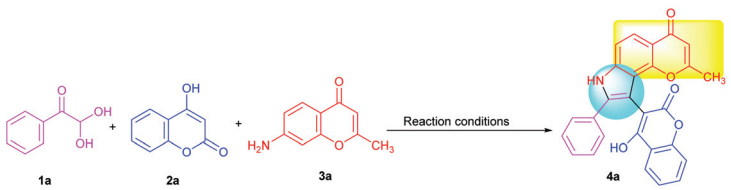
Finally, the optimum yield (88%) was observed in acetic acid as the reaction medium under microwave heating at 130 °C for 30 minutes (Table 1, entry 10). It is noteworthy to mention that in this three component reaction out of the four possible regioisomers as shown in Scheme 3, only one regioisomer **4a** was obtained. In this reaction, aminochromone acts as a 1,3-*C*,*N*-binucleophile using its NH_2 group and the *ortho* positions. Both the *ortho* positions with respect to the NH_2 group, *i.e.* the positions 6 and 8 of aminochromone **3a** are electron-rich due to the presence of the NH_2 group. However position 8 is expected to be more nucleophilic, considering the extra electron donating effect of the adjacent oxygen of the pyrone ring. The analysis of the electron density distribution in a molecular system can be estimated by either Mulliken population analysis (MPA),[20] or natural population analysis (NPA).[21] To establish our assumption that position 8 has more electron density than the 6 position of **3a**, MPA and NPA were calculated using density functional theory (DFT) and the obtained results are shown in Fig. 2 and 3, respectively.

From both these methods it is evident that the electron density at position 8 is more than the position 6 of **3a**.

Generally, for aromatic electrophilic substitution of *meta* disubstituted benzenes having both the electron donating groups, van der Waals repulsions between both the substituents with the incoming electrophiles direct substitution *ortho* to most electron-donating groups and *para* to other groups instead of the position in between the two substituents. Interestingly, our observed product has formed by using position 8 as the *C*-nucleophilic site for cyclization. The structure of the three component product **4a** was unambiguously confirmed by recording single crystal XRD patterns as shown in Fig. 4.

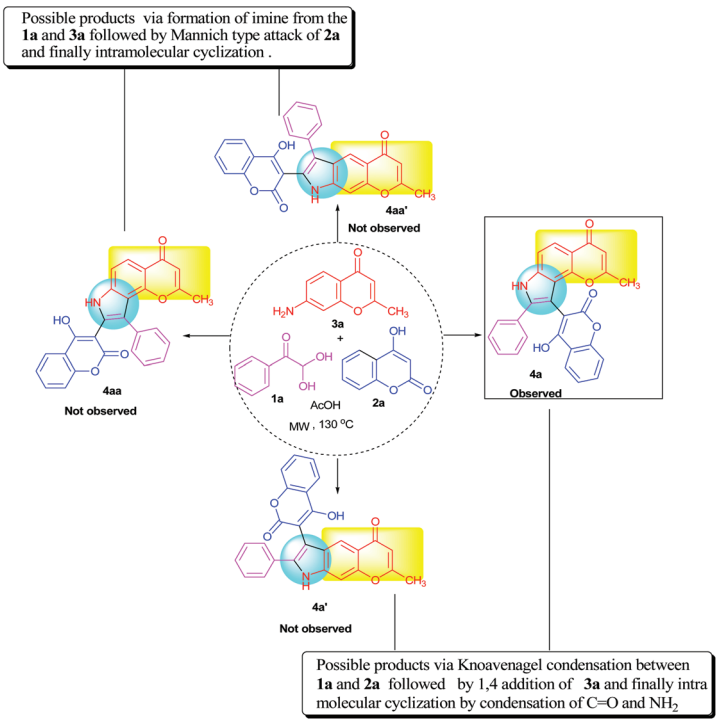
After having these optimized conditions in hand, next we investigated the substrate scope and general applicability of this three component reaction by varying all the starting materials independently. Using the optimized reaction conditions, arylglyoxals tethered with both electron donating and withdrawing groups provided the corresponding chromone

Table 1 Optimization of reaction conditions[a]



Entry	Solvent	Reaction conditions	Catalyst	% Yield
1.	No	r.t.	No	Nil
2.	H_2O	r.t.	No	Nil
3.	EtOH	80 °C (MW)	No	Trace amount
4.	EtOH	80 °C (MW)	I_2 (10%)	15
5.	EtOH	80 °C (MW)	PTSA (10%)	20
6.	EtOH	80 °C (MW)	Et_3N (10%)	Nill
7.	EtOH	80 °C (MW)	AcOH (10%)	30
8.	AcOH	80 °C (MW)	No	55
9.	AcOH	100 °C (MW)	No	65
10.	AcOH	130 °C (MW)	No	88

[a] Reaction conditions: 1.0 mmol **1a**, 1.0 mmol **2a** and 1.0 mmol **3a**.



Scheme 3 Regioselectivity and structures of possible four regioisomers of fused pyrroles from the three component reaction of **1a**, **2a** and **3a**.

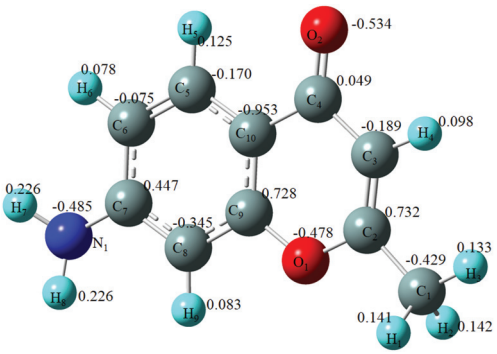


Fig. 2 Atomic charges from Mulliken population analysis of **3a**.

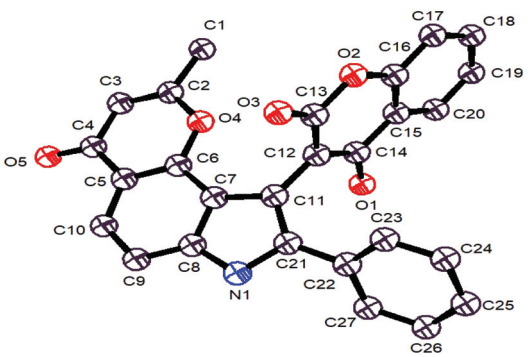


Fig. 4 XRD structure of chromone fused pyrrole (**4a**) (CCDC 1579680). Hydrogens have been omitted for clarity of the structure.

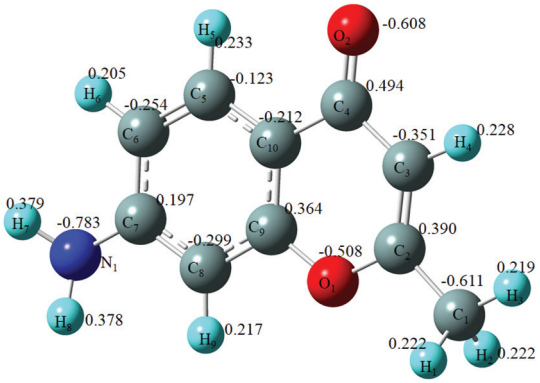
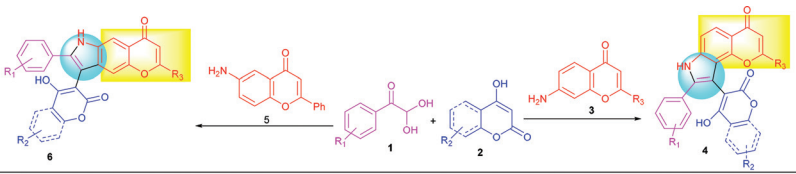
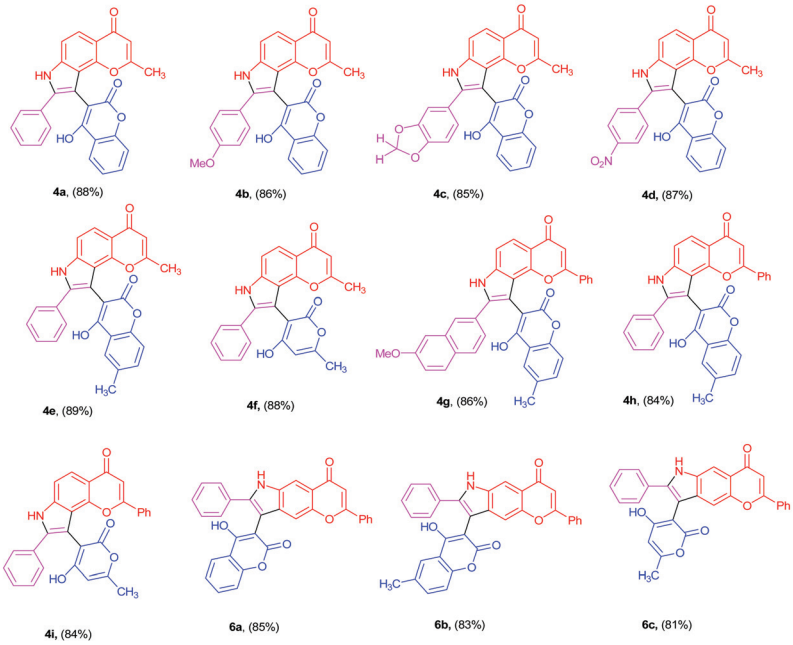


Fig. 3 The natural charges at the different atomic sites of **3a**.

fused pyrroles in good to very good yields (Table 2, **4b–4d**). 4-Hydroxy-6-methyl-2-pyrone and 4-hydroxy-6-methylcoumarin were also found to be suitable for this three component reaction and allowed access to the corresponding fused pyrroles **4e–4f** in good yields. Similar to 7-amino-2-methylchromone, its corresponding flavone derivative, 7-aminoflavone, also underwent a three component reaction with 4-hydroxycoumarin and arylglyoxal derivatives to provide the corresponding flavone fused pyrroles (**4g–4i**) in good yields. Likewise, we further varied the amine derivative by using 6-aminoflavones (**5**) in this three component reaction and the corresponding fused pyrrroles (**6a–6c**) were observed in good to very good yields. All the products were fully characterized by IR, ^{1}H, ^{13}C NMR and HRMS.

Table 2 Substrate scope for the three component synthesis of chromone and flavone fused pyrroles[a]



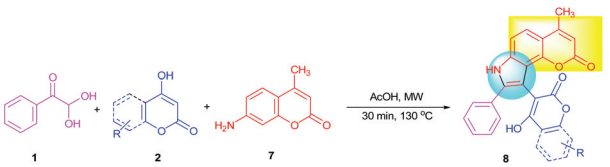


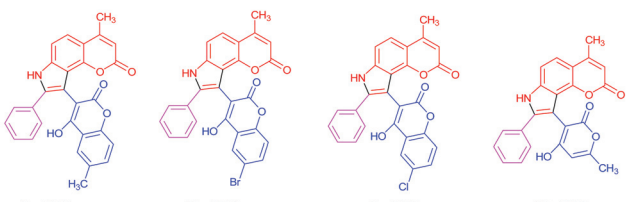
[a] Reaction conditions: Aryl/naphthyl glyoxal monohydrate (1.0 mmol), 4-hydroxycoumarin/derivatives/hydroxylpyrone (1.0 mmol), amino chromones/flavones (1.0 mmol) in 2 ml acetic acid, MW heating for 30 min at 130 °C.

Encouraged by the good results for chromone and flavone fused pyrroles, next we wanted to synthesize some coumarin fused pyrroles by using 7-amino-4-methylcoumarin as the amine substrate in our multicomponent reaction under similar reaction conditions. Interestingly, in this case also we observed the corresponding regioselective coumarin fused pyrroles (**8a–8d**) in good yields and the results are summarized in Table 3.

To further study the generality and scope of this methodology next, we wanted to explore the synthesis of indoles by using some aniline derivatives. Interestingly, when we tried the reaction of 4-methylaniline and phenylglyoxal monohydrate with 4-hydroxycoumarin under similar reaction conditions the corresponding substituted indole derivative **10a** was obtained in 65% yield (Table 4), although a similar reaction with aniline provided a mixture of products and could not be purified. Similar to 4-methylaniline other aniline derivatives having electron donating groups such as 4-methoxy, 3,4-dimethoxy, and 3,4-ethylenedioxy were found to be suitable for this multicomponent reaction and the corresponding substituted indole derivatives (**10b**, **10c** and **10d**) were obtained in good yields and the results are summarized in Table 4. It is noteworthy to mention that 3,4-dimethoxyaniline and

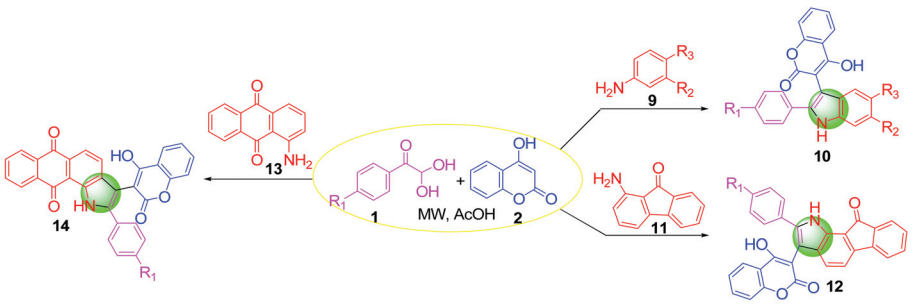
Table 3 Substrate scope for the three component synthesis of coumarin fused pyrroles[a]

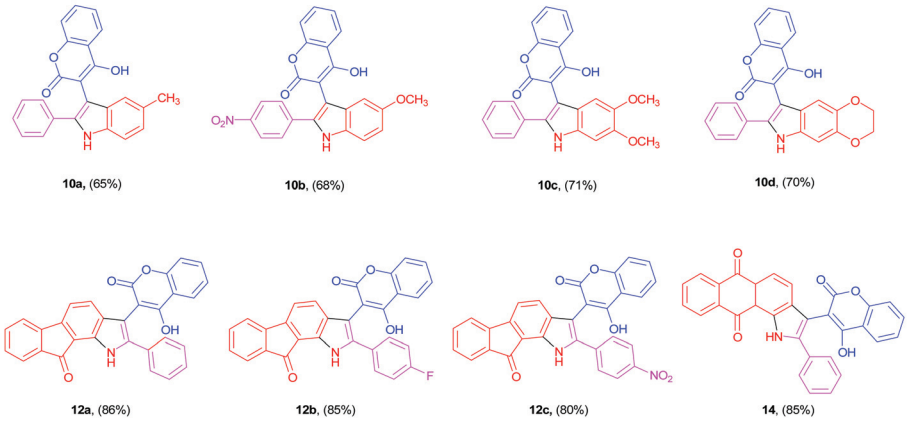




[a] Reaction conditions: Phenylglyoxal monohydrate (**1**) (1.0 mmol), 4-hydroxycoumarin/4-hydroxy-6-methyl-2-pyrone (**2**) (1.0 mmol), 7-amino-4-methylcoumarin (**7**) (1.0 mmol) in 2 ml acetic acid, MW heating for 30 min at 130 °C.

Table 4 Substrate scope for the synthesis of indole and polycyclic fused pyrrole derivatives[a]





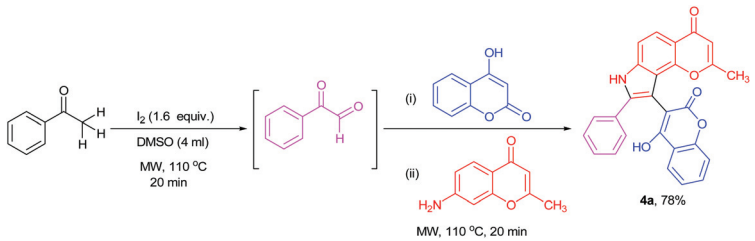
[a] Reaction conditions: Arylglyoxal monohydrate (**1**) (1.0 mmol), 4-hydroxycoumarin (**2**) (1.0 mmol), arylamine (**9**)/1-amino-9-fluorenone(**11**)/1-aminoanthraquinone (**14**) (1.0 mmol) in 2 ml acetic acid, MW heating for 30 min at 130 °C.

3,4-ethylenedioxyaniline provided the indole derivatives using the other position (position 6) of the aromatic ring instead of position 2 (in between the two substituents). This difference in regioselectivity of these two substrates may be due to more van der Waals repulsion between both the substituents with the electrophile. However, in the case of 7-amino-2-methylchromone this steric hindrance will be minimum considering the rigid ring fused with the aniline moiety. Aniline derivatives having electron withdrawing groups such as NO_2 and CN were found not to be suitable for this three component reaction.

We also extended this methodology to other polycyclic aromatic amines such as 1-amino-9-fluorenone and the corresponding fused pyrroles **12a–12c** were obtained in good yields. Likewise, 1-aminoanthraquinone provided the corresponding fused pyrrole **14** in good yield using similar reaction conditions.

After synthesizing all these diverse fused pyrroles using arylglyoxal as one of the starting materials, next we wanted to develop an alternative multicomponent methodology by generating *in situ* arylglyoxals from acetophenone or its derivatives. From the literature we realized that acetophenone and its derivatives have been used in many reactions for generating *in situ* arylglyoxals by using I_2/DMSO chemistry.[17–19] Thus we also wanted to explore the metal-free oxidation chemistry of I_2/DMSO for the access of diverse fused pyrroles *via* C(sp^3)–H oxidation of acetophenone derivatives. To prove our assumption we took acetophenone as the model substrate. Initially, the screening was started by adding I_2 (1.0 mmol) in the solution of acetophenone (1.0 mmol) in 3 ml DMSO under microwave heating at 100 °C for 20 minutes. 4-Hydroxycoumarin was added to that reaction vial and stirred for 5 min. Finally, to this mixture the amine derivative 7-amino-2-methylchromone (1.0 equiv.) was added and the resultant mixture was then kept under microwave heating and stirring for another 20 minutes at 100 °C under sealed conditions.

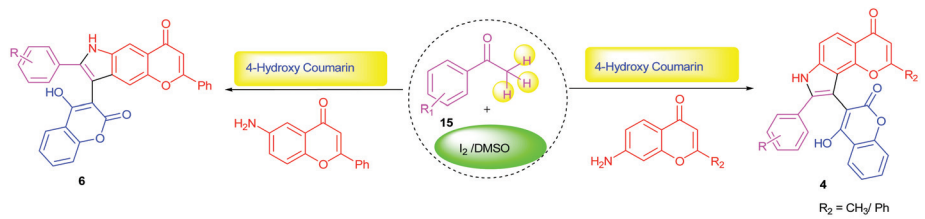
Interestingly, we obtained the desired three component product **4a** in 31% yield. With this positive result in hand, next we tried to optimize the yield obtained by varying the amount of I_2 and DMSO and the reaction temperature. The best result was obtained by taking acetophenone (1.0 mmol) with 1.6 equiv. of molecular iodine (I_2) in 4 ml DMSO under microwave heating at 110 °C for 20 minutes followed by sequential addition of 4-hydroxycoumarin (1.0 equiv.) and 7-amino-2-methylchromone (1.0 equiv.) and again microwave heating of the mixture at the same temperature for 20 minutes (Scheme 4). After having these optimum conditions in hand, next we explored the substrate scope of this methodology. Acetophenone tethered with both electron withdrawing groups such as 4-NO_2 and electron donating 4-Me, 4-OMe groups underwent this three component reaction smoothly to provide

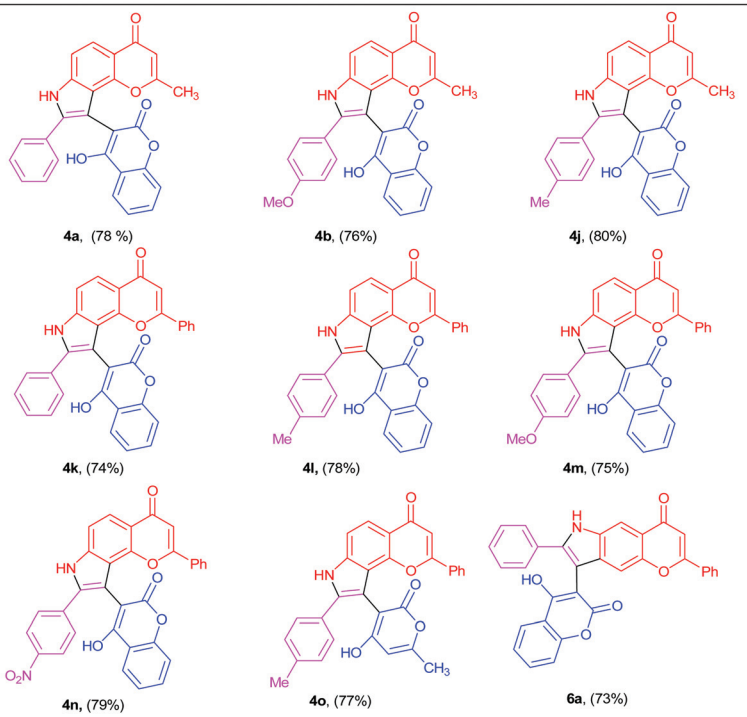


Scheme 4 Optimized reaction conditions for the I_2/DMSO catalyzed oxidative three component cyclization *via in situ* arylglyoxals.

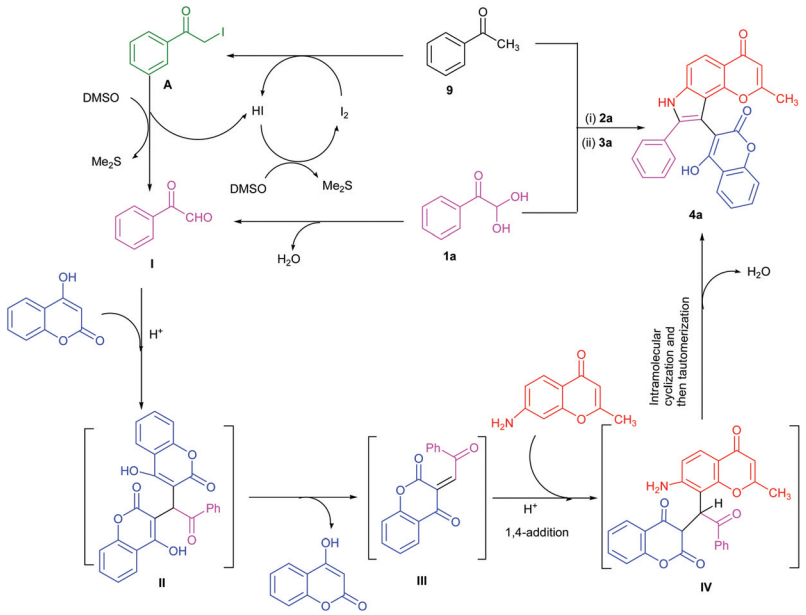
the corresponding fused pyrroles in good yields and the results are summarized in Table 5. 4-Hydroxy-6-methyl-2-pyranone also provided the corresponding fused pyrrole **4o** in good yield (77%) under the optimized reaction conditions by replacing 4-hydroxycoumarin with 6-methyl-4-hydroxy-2-pyranone. We also have checked the variability of amine derivatives by employing 6-aminoflavone and 7-aminoflavone in place of 7-amino-2-methylchromone. In these cases also, good yields of the corresponding fused pyrroles were observed. Unfortunately, using this oxidative cyclization method when we tried to synthesise indole derivatives employing aryl amines such as aniline/4-methylaniline or 4-methoxyaniline we ended up with mixtures of inseparable compounds. Similarly, we failed to utilize heterocyclic methyl ketones such as 2-acetyl

Table 5 Substrate scope for I_2/DMSO mediated three component synthesis of regioselective fused pyrroles *via* C(sp^3)–H oxidation of acetophenone derivatives[a]





[a] Acetophenone or its derivatives (1.0 mmol), iodine (1.6 mmol) in DMSO (4 ml), MW heating for 20 min at 110 °C then add 4-hydroxycoumarin (1.0 mmol) followed by amino chromones/flavones (1.0 mmol) and MW heating for another 20 min at 110 °C.



Scheme 5 Proposed reaction pathway for the formation of fused pyrrole **4a** by methods A and B.

pyridine, 2-acetylthiophene and 2-acetylfuran in place of acetophenone derivatives under similar reaction conditions. In these cases, we ended up with mixtures of inseparable compounds. Thus we believe that this *in situ* method is not suitable for heterocyclic methyl ketones.

Mechanistically, we believe that the reaction goes *via* intermediates **II** and **III** in both the methods. Then 1,4 addition of 7-amino-2-methylchromone to intermediate **III** gives trisubstituted methane **IV** which undergoes intramolecular cyclization followed by tautomerization to provide our desired fused pyrrole **4a**. In method B, acetophenone undergoes C–H oxidation to provide *in situ* arylglyoxal (**I**) *via* intermediate **A** as shown in Scheme 5.

Conclusion

In conclusion we have developed two novel methodologies for the synthesis of a wide spectrum of chromone, flavone, coumarin, fluorenone and anathraquinone fused pyrroles as well as substituted indoles containing 4-hydroxycoumarin as the substitutent using one-pot sequential three component reactions. All the reactions provide good to very good yields within short times. The salient features of both the methods are: short reaction time, metal-free reaction conditions, regioselective products, no need for column chromatography, and a wide substrate scope. All the products are novel and have pharmacologically important skeletons. Considering the hybrid structure of all the products having more than one bioactive heterocycles such as pyrrole, hydroxycoumarin, and chromone/flavone or coumarin moieties, these products are expected to have interesting bioactivities and useful properties for application in medicinal chemistry.

Experimental section

General

All starting materials were purchased from either Sigma Aldrich or Alfa Aesar and used without further purification. Microwave irradiation was carried out with Initiator 2.5 Microwave Synthesizers from Biotage, Uppsala, Sweden. NMR spectra were recorded on a Bruker 400 or 500 MHz for ^{1}H NMR and 100 or 125 MHz for ^{13}C NMR in DMSO-d_6, chemical shift values are reported in δ values ppm downfield from tetramethylsilane. Infrared spectra were recorded on a Shimadzu FTIR spectrometer. Single Crystal XRD was recorded using a BRUKER AXS (D8 Quest System) X-ray diffractometer. HRMS data were recorded using a BRUKER Impact HD mass spectrometer (ESI with positive mode). Melting points were recorded using SRS EZ-Melt automated melting point apparatus by capillary methods and uncorrected.

Computational details

To estimate the relative electron density in different atoms of **3a**, Mulliken population analysis and natural population analysis were calculated using theoretical calculations. The calculations were carried out using GAUSSIAN 09 Revision A.02 program suite.[22] The geometry of the molecule was optimized under vacuum using the B3LYP/6-31+G(d,p) level.[23]

General procedure for the synthesis of fused pyrroles using arylglyoxals (method A)

A mixture of phenylglyoxal monohydrate or its derivative (1.0 mmol) and 4-hydroxy coumarin/derivative (1.0 mmol) in acetic acid (2 mL) was stirred at room temperature for 15 minutes in a microwave reaction vial. To this mixture the amine derivative (1.0 mmol) (7-amino-2-methylchromone or

6/7-aminoflavone or 7-amino-4-methylcoumarin) or aniline derivative or 1-aminofluorinone/1-aminoanthraquinone was added and the resultant mixture was sealed. The sealed vial was then kept under microwave heating at 130 °C for 30 minutes under stirring conditions. After completion of the reaction, the reaction mixture was cooled to room temperature and the solid product was separated by just filtration, washed with cold water and finally purified by recrystallization from the mixture of methanol and DMSO (9 : 1). All the products in Tables 2–4 were prepared using this procedure.

General procedure for the synthesis of fused pyrroles using *in situ* arylglyoxals from acetophenone or its derivatives (method B)

To a solution of acetophenone/its derivatives (1.0 mmol) in DMSO (4 mL) in a microwave reaction vial, I_2 (1.6 mmol) was added, and the resultant mixture was sealed and kept under microwave heating at 110 °C for 20 minutes. After completion of the first step, (as monitored by TLC) 4-hydroxycoumarin and 7-amino-2-methylchromone were added sequentially in the reaction vial and sealed again. Then the sealed vial was irradiated by MW for another 20 minutes at 110 °C. After completion of the reaction, the reaction vial was cooled to room temperature and poured to a solution of 10 mL (10% aqueous) $Na_2S_2O_3$ solution. The desired products came out as precepitates and the precipitates were filtered and washed with water three times. Finally crude products were transferred to a round bottom flask having 20 mL MeOH and were stirred under reflux conditions for 10 minutes. The pure products were obtained just by filtration under hot conditions.

9-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-2-methyl-8-phenyl-7*H*-pyrano[2,3-*e*]indol-4-one (4a). White solid (383 mg, 88%); mp 395–397 °C; I.R. (A.T.R.) 3229, 2820, 1709, 1667, 1642, 1608, 1566, 1537, 1494, 1471, 1392, 1376, 1217, 1196, 1077, 1031, 936 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 12.36 (s, 1H, OH), 11.27 (s, 1H, NH), 7.94 (dd, J = 8.0, 4.0 Hz, 1H, ArH), 7.76–7.66 (m, 4H, ArH), 7.54–7.39 (m, 5H, ArH), 7.34 (t, J = 8.0 Hz, 1H, ArH), 6.13 (s, 1H, =CH), 1.92 (s, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ = 177.2, 164.6, 162.5, 162.4, 153.1, 151.8, 139.9, 138.2, 132.8, 132.3, 129.3, 128.5, 127.2, 124.5, 124.1, 117.9, 117.6, 116.7, 116.6, 116.2, 110.7, 110.3, 102.8, 100.3, 19.6 ppm. HRMS (m/z) (ESI-TOF) calcd for $C_{27}H_{17}NO_5$ [M + H^+], 436.1179, found 436.1243.

9-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-8-(4-methoxy-phenyl)-2-methyl-7*H*-pyrano[2,3-*e*]indol-4-one (4b). White solid (401 mg, 86%); mp 387–389 °C; I.R. (A.T.R.) 3231, 2916, 1677, 1645, 1610, 1565, 1547, 1506, 1470, 1392, 1374, 1251, 1179, 1126, 1078, 1033, 965 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 12.26 (s, 1H, OH), 11.22 (s, 1H, NH), 7.95 (d, J = 8.0 Hz, 1H, ArH), 7.73–7.67 (m, 2H, ArH), 7.61 (d, J = 8.0 Hz. 2H, ArH), 7.52–7.49 (m, 2H, ArH), 7.41 (t, J = 8.0 Hz, 1H, ArH), 7.02 (d, J = 8.0 Hz, 2H, ArH), 6.31 (s, 1H, =CH), 3.76 (s, 3H, OCH_3), 1.92 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ = 177.3, 164.6, 162.6, 162.4, 159.6, 153.1, 151.7, 139.8, 138.4, 132.8, 128.6, 124.8, 124.5, 124.1, 117.7, 117.5, 116.6, 116.2, 114.7, 110.5, 110.2, 101.7, 100.4, 55.6, 19.6 ppm; HRMS (m/z) (ESI-TOF) calcd for $C_{28}H_{19}NO_6$ [M + H^+], 466.1285, found 466.1353.

8-Benzo[1,3]dioxol-5-yl-9-(4-hydroxy-2-oxo-2*H*-chromen-3-yl)-2-methyl-7*H*-pyrano[2,3-*e*]indol-4-one (4c). White solid (408 mg, 85%); mp 376–378 °C; I.R. (A.T.R.) 3544, 3238, 1681, 1642, 1605, 1569, 1500, 1470, 1374, 1244, 1214, 1103, 1039, 964 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ = 12.21 (s, 1H, OH), 11.21 (s, 1H, NH), 7.95 (d, J = 5.0 Hz, 1H, ArH), 7.73–7.68 (m, 2H, ArH), 7.49 (d, 2H, J = 10.0 Hz, ArH), 7.41 (t, J = 5.0 Hz, 1H, ArH), 7.16 (s, 1H, ArH), 7.15 (d, J = 10.0 Hz, 1H, ArH), 7.00 (d, J = 10.0 Hz, 1H, ArH), 6.11 (s, 1H, ArH), 6.05 (s, 2H, –OCH_2O–), 1.90 (s, 3H, CH_3) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ = 177.2, 164.5, 162.5, 162.5, 153.1, 151.7, 148.0, 147.7, 139.7, 138.2, 132.8, 126.2, 124.5, 124.1, 121.4, 117.8, 117.6, 116.7, 116.6, 116.2, 110.5, 110.3, 109.2, 107.5, 102.1, 101.8, 100.3, 19.6 ppm; HRMS (m/z) (ESI-TOF) calcd for $C_{28}H_{17}NO_7$ [M + H^+], 480.1078 found 480.1134.

9-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-2-methyl-8-(4-nitro-phenyl)-7*H*-pyrano[2,3-*e*]indol-4-one (4d). Yellow solid (418 mg, 87%); mp 403–405 °C; I.R. (A.T.R.) 3352, 1693, 1642, 1599, 1563, 1521, 1470, 1392, 1340, 1253, 1195, 1109, 1075, 957 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ = 12.62 (s, 1H, OH), 11.43 (s, 1H, NH), 8.32 (d, J = 10.0 Hz, 2H, ArH), 7.97 (d, J = 10.0 Hz, 1H, ArH), 7.94 (d, J = 10.0 Hz, 2H, ArH), 7.81 (d, J = 10.0 Hz, 1H, ArH), 7.71 (t, J = 10.0 Hz, 1H, ArH), 7.56 (d, J = 5.0 Hz, 1H, ArH), 7.50 (d, J = 5.0 Hz, 1H, ArH), 7.42 (t, J = 10.0 Hz, 1H, ArH), 6.15 (s, 1H, ArH), 1.91 (s, 3H, CH_3) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ = 177.1, 164.7, 162.9, 162.3, 153.3, 152.1, 146.9, 140.4, 138.8, 135.8, 132.9, 127.9, 124.6, 124.5, 124.2, 119.2, 117.6, 116.8, 116.7, 116.5, 110.9, 110.5, 105.9, 99.7, 19.5 ppm. HRMS (ESI-TOF) calcd for $C_{27}H_{16}N_2O_7$ [M + H^+], 481.1030, found 480.1093.

9-(4-Hydroxy-6-methyl-2-oxo-2*H*-chromen-3-yl)-2-methyl-8-phenyl-7*H*-pyrano[2,3-*e*]indol-4-one (4e). White solid (400 mg, 89%); mp 397–399 °C; I.R. (A.T.R.) 3319, 1666, 1642, 1611, 1566, 1536, 1497, 1473, 1437, 1389, 1193, 1160, 1127, 1078, 865 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ = 12.33 (s, 1H, OH), 11.14 (s, 1H, NH), 7.75–7.73 (m, 2H, ArH), 7.65 (d, J = 10.0 Hz, 2H, ArH), 7.51 (t, J = 10.0 Hz, 2H, ArH), 7.43 (t, J = 10.0 Hz, 2H, ArH), 7.38 (d, J = 10.0 Hz, 1H, ArH), 7.34 (t, J = 10.0 Hz, 1H, ArH), 6.13 (s, 1H, =CH), 2.51 (s, 3H, CH_3), 1.93 (s, 3H, CH_3) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ = 177.2, 164.6, 162.7, 162.4, 151.9, 151.3, 139.9, 138.2, 133.8, 133.6, 132.3, 129.2, 128.5, 127.2, 123.7, 117.9, 116.5, 116.2, 110.7, 110.3, 102.9, 100.2, 20.9, 19.6 ppm. HRMS (m/z) (ESI-TOF) calcd for [M + H^+], $C_{28}H_{19}NO_5$ 450.1336, found 450.1385.

9-(4-Hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2-methyl-8-phenyl-7*H*-pyrano[2,3-*e*]indol-4-one (4f). White solid (352 mg, 88%); mp 362–364 °C; I.R. (A.T.R.) 3233, 1703, 1673, 1640, 1562, 1535, 1447, 1393, 1360, 1276, 1213, 1195, 1156, 1035, 990 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ = 12.19 (s, 1H, OH), 11.14 (s, 1H, NH), 7.72 (d, J = 10.0 Hz, 1H, ArH), t7.66 (d, J = 5.0 Hz, 2H, ArH), 7.49–7.44 (m, 3H, ArH), 7.35 (t, J = 5.0 Hz, 1H, ArH), 6.17 (s, 2H, =CH), 2.29 (s, 3H, CH_3), 2.19 (s, 3H, CH_3) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ = 177.3, 167.5, 164.8, 164.5, 162.1, 151.9, 139.7, 137.0, 132.7, 129.2, 128.3,

127.1, 117.8, 117.4, 116.2, 110.6, 110.3, 104.1, 100.5, 97.0, 19.9, 19.8 ppm; HRMS (*m*/*z*) (ESI-TOF) calcd for $C_{24}H_{17}NO_5$ [M + H^+], 400.1179 found 400.1224.

9-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-8-(6-methoxy-naphthalen-2-yl)-2-methyl-7*H*-pyrano[2,3-*e*]indol-4-one (4g). White solid (444 mg, 86%); mp 365–367 °C; I.R. (A.T.R.) 3230, 1643, 1601, 1562, 1532, 1465, 1384, 1207, 1162, 1126 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ = 12.44 (s, 1H, OH), 11.29 (s, 1H, NH), 8.15 (s, 1H, ArH), 7.96 (d, *J* = 5.0 Hz, 1H, ArH), 7.83 (t, *J* = 10.0 Hz, 2H, ArH), 7.78 (d, *J* = 10.0 Hz, 1H, ArH), 7.73 (d, *J* = 10.0 Hz, 1H, ArH), 7.69 (t, *J* = 10.0 Hz, 1H, ArH), 7.56 (d, *J* = 10.0 Hz, 1H, ArH), 7.51(d, *J* = 10.0 Hz, 1H, ArH), 7.40 (t, *J* = 10.0 Hz, 1H, ArH), 7.30 (d, *J* = 5.0 Hz, 1H, ArH), 7.19 (dd, *J* = 10.0, 5.0 Hz, 1H, ArH), 6.15 (s, 1H, =CH), 3.87 (s, 3H, OCH_3), 1.94 (s, 3H, CH_3) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ = 177.3, 172.5, 164.6, 162.6, 162.5, 158.2, 153.2, 151.8, 140.0, 138.5, 134.2, 132.8, 130.1, 128.7, 127.7, 127.6, 126.1, 125.6, 124.5, 124.1, 119.8, 117.7, 116.7, 116.6, 116.3, 110.6, 110.3, 106.4, 102.9, 100.5, 55.7, 19.6 ppm; HRMS (*m*/*z*) (ESI-TOF) calcd for [M + H^+], $C_{32}H_{21}NO_6$ 516.1442, found 516.1503.

9-(4-Hydroxy-6-methyl-2-oxo-2*H*-chromen-3-yl)-2,8-diphenyl-7*H*-pyrano[2,3-*e*]indol-4-one (4h). Pale white solid (430 mg, 84%); mp 383–385 °C; I.R. (A.T.R.) 3422, 2947, 1694, 1634, 1601, 1580, 1565, 1465, 1450, 1381, 1234, 1192, 1150, 1078, 1008, 951 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ = 12.43 (s,1H, OH), 11.39 (s, 1H, NH), 7.83 (d, *J* = 10.0 Hz, 1H, ArH), 7.73 (s, 1H, ArH), 7.64–7.59 (m, 4H, ArH), 7.55 (d, *J* = 10.0 Hz, 2H, ArH), 7.48–7.44 (m, 3H, ArH), 7.36 (t, *J* = 10.0 Hz, 2H, ArH), 6.98 (s, 1H, =CH), 6.91 (t, *J* = 10.0 Hz, 2H, ArH), 2.43 (s, 3H, CH_3) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ = 177.4, 162.8, 161.5, 151.7, 151.4, 140.3, 138.5, 134.1, 133.9, 132.2, 131.7, 131.6, 129.3, 128.9, 128.6, 127.5, 125.9, 123.9, 118.1, 117.9, 116.8, 116.7, 116.4, 111.2, 107.6, 100.5, 20.9 ppm. HRMS (*m*/*z*) (ESI-TOF) calcd for [M + H^+], $C_{33}H_{21}NO_5$ 512.1492, found 512.1550.

9-(4-Hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2,8-diphenyl-7*H*-pyrano[2,3-*e*]indol-4-one (4i). Pale white solid (388 mg, 84%), mp 394–396 °C; I.R. (A.T.R.) 3143, 1672, 1634, 1601, 1565, 1535, 1450, 1408, 1375, 1216, 1159, 1135, 990 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ = 12.30 (s, 1H, OH), 11.22 (s, 1H, NH), 7.81 (d, *J* = 10.0 Hz, 1H, ArH), 7.76 (d, *J* = 5.0 Hz, 2H, ArH), 7.63–7.58 (m, 3H, ArH), 7.55 (d, *J* = 10.0 Hz, 1H, ArH), 7.52–7.46 (m, 4H, ArH), 7.37 (t, *J* = 5.0 Hz, 1H, ArH), 6.99 (s, 1H, =CH), 6.23 (s, 1H, =CH), 2.36 (s, 3H, CH_3) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ = 177.4, 167.7, 164.6, 162.3, 161.7, 151.8, 140.1, 137.4, 132.5, 132.1, 131.9, 129.4, 129.2, 128.4, 127.4, 126.2, 117.8, 116.8, 111.1, 107.7, 103.8, 100.9, 97.3, 20.1 ppm; HRMS (*m*/*z*) (ESI-TOF) calcd for [M + H^+], $C_{29}H_{19}NO_5$ 462.1336, found 462.1376.

3-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-2,6-diphenyl-1*H*-pyrano[2,3-*f*]indol-8-one (6a). White solid (423 mg, 85%), mp 299–301 °C; I.R. (A.T.R.) 3464, 3239, 1691, 1631, 1495, 1450, 1372, 1249, 1225, 1201, 1132, 1102, 1090, 951 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ = 12.28 (s, 1H, OH), 10.24 (s, 1H, NH), 8.05 (m, 2H, ArH), 7.94 (d, *J* = 5.0 Hz, 1H, ArH), 7.77 (d, *J* = 5.0 Hz, 1H, ArH), 7.63–7.57 (m, 7H, ArH), 7.43–7.39 (m, 3H, ArH), 7.32 (t, *J* = 10.0 Hz, 2H, ArH), 6.84 (s, 1H, =CH); ^{13}C NMR (125 MHz, DMSO-d_6) δ = 178.1, 163.6, 160.2, 158.6, 153.6, 152.9, 140.8, 134.4, 132.9, 131.8, 131.7, 131.6, 129.6, 128.9, 128.5, 128.1, 126.4, 124.1, 123.9, 123.8, 118.9, 117.7, 117.2, 116.5, 112.6, 108.2, 105.6, 104.8 ppm. HRMS (*m*/*z*) (ESI-TOF) calcd for [M + H^+], $C_{32}H_{19}NO_5$ 498.1336 found 498.1372.

3-(4-Hydroxy-7-methyl-2-oxo-2*H*-chromen-3-yl)-2,6-diphenyl-1*H*-pyrano[2,3-*f*]indol-8-one (6b). White solid (425 mg, 83%); mp 268–270 °C; I.R. (A.T.R.) 3471, 3241, 1690, 1628, 1589, 1499, 1482, 1454, 1434, 1327, 1367, 1327, 1252, 1159, 1153, 1111, 1083, 1068, 1018, 954 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ = 12.25 (s, 1H, OH), 10.16 (s, 1H, NH), 8.06–8.04 (m, 2H, ArH), 7.93 (d, *J* = 10.0 Hz, 1H, ArH), 7.59–7.55 (m, 7H, ArH), 7.40 (t, *J* = 10.0 Hz, 3H, ArH), 7.32 (t, *J* = 10.0 Hz, 2H, ArH), 6.82 (s, 1H, =CH), 2.37 (s, 3H, CH_3) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ = 177.6, 163.3, 159.7, 158.2, 153.1, 150.6, 140.2, 133.9, 132.6, 132.4, 131.8, 131.3, 131.2, 129.1, 128.4, 127.9, 127.6, 125.9, 123.6, 123.1, 118.4, 117.2, 116.4, 115.7, 112.1, 107.7, 105.2, 104.3, 20.4 ppm. HRMS (*m*/*z*) (ESI-TOF) calcd for [M + H^+], $C_{33}H_{21}NO_5$ 512.1492 found 512.1552.

3-(4-Hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2,6-diphenyl-1*H*-pyrano[2,3-*f*]indol-8-one (6c). Brown solid (374 mg, 81%), mp 283–285 °C; I.R. (A.T.R.) 3648, 3061, 2833, 1676, 1631, 1592, 1488, 1451, 1400, 1358, 1302, 1260, 1207, 1162, 1024, 993 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 12.10 (s, 1H, NH), 10.18 (s, 1H, NH), 8.08–8.06 (m, 2H, ArH), 7.87 (d, *J* = 8.0 Hz, 1H, ArH), 7.59–7.58 (m, 5H, ArH), 7.52 (d, *J* = 8.0 Hz, 1H, ArH), 7.43 (t, *J* = 8.0 Hz, 2H, ArH), 7.34 (t, *J* = 8.0 Hz, 1H, ArH), 6.88 (s, 1H, =CH), 5.96 (s, 1H, =CH), 2.24 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ = 177.9, 165.5, 164.2, 159.9, 159.8, 153.6, 139.8, 134.1, 133.4, 131.9, 131.7, 129.6, 128.9, 128.2, 127.9, 126.4, 123.9, 118.7, 117.9, 112.3, 108.3, 106.9, 101.6, 100.7, 19.9 ppm. HRMS (*m*/*z*) (ESI-TOF) calcd for [M + H^+], $C_{29}H_{19}NO_5$ 462.1336 found 462.1382.

9-(4-Hydroxy-7-methyl-2-oxo-2*H*-chromen-3-yl)-4-methyl-8-phenyl-7*H*-pyrano[2,3-*e*]indol-2-one (8a). Yellow solid (378 mg, 84%); mp 394–396 °C; I.R. (A.T.R.) 3335, 3069, 1674, 1605, 1572, 1500, 1483, 1433, 1389, 1367, 1300, 1242, cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ = 11.99 (s, 1H, OH), 11.11 (s, 1H, NH), 7.72 (s, 1H, ArH), 7.65–7.63 (m, 3H, ArH), 7.50 (d, *J* = 10.0 Hz, 1H, ArH), 7.43–7.40 (m, 3H, ArH), 7.36 (d, *J* = 10.0 Hz, 1H, ArH), 7.32 (t, *J* = 10.0 Hz, 1H, ArH), 6.22 (s, 1H, =CH), 2.42 (s, 3H, CH_3), 2.41 (s, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ = 162.9, 162.4, 161.1, 154.8, 151.4, 150.2, 139.4, 138.8, 133.7, 133.6, 132.6, 129.2, 128.4, 127.5, 127.2, 123.8, 116.6, 116.4, 115.8, 113.9, 111.4, 103.7, 98.8, 97.9, 20.9, 19.1 ppm. HRMS (*m*/*z*) (ESI-TOF) calcd for $C_{28}H_{19}NO_5$ [M + H^+], 450.1336, found 450.1358.

9-(7-Bromo-4-hydroxy-2-oxo-2*H*-chromen-3-yl)-4-methyl-8-phenyl-7*H*-pyrano[2,3-*e*]indol-2-one (8b). Yellow solid (443 mg, 86%), mp 385–387 °C; I.R. (A.T.R.) 3349, 3056, 1668, 1619, 1574, 1430, 1300, 1201, 1151, 1046, 979 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ = 12.00 (s, 1H, OH), 11.48 (s, 1H, NH), 8.02 (s, 1H, ArH), 7.83 (dd, *J* = 10.0, 5.0 Hz, 1H, ArH), 7.69 (s, 1H, ArH), 7.63 (d, *J* = 10.0 Hz, 2H, ArH), 7.46–7.39 (m, 4H, ArH), 7.32(t, *J* = 10.0 Hz, 1H, ArH), 6.21 (s, 1H, =CH), 2.42 (s,

3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ = 161.8, 161.7, 161.0, 154.8, 152.3, 150.2, 139.5, 138.8, 135.1, 132.5, 129.2, 128.5, 127.3, 127.2, 126.3, 119.2, 118.8, 116.2, 115.9, 114.0, 111.4, 103.3, 99.9, 97.9, 19.2 ppm. HRMS (ESI-TOF) calcd for [M + H^+], $C_{27}H_{16}BrNO_5$ 514.0285, found 514.0300.

9-(7-Chloro-4-hydroxy-2-oxo-2*H*-chromen-3-yl)-4-methyl-8-phenyl-pyrano[2,3-*e*]indol-2(7*H*)-one (8c). Yellow solid (390 mg, 83%); mp 342–344 °C; I.R. (A.T.R.) 3349, 3072, 1677, 1574, 1500, 1433, 1367, 1256, 1170, 1 120 1046 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ = 12.01 (s, 1H, OH), 11.50 (s, 1H, NH), 7.90 (s, 1H, ArH), 7.73 (dd, *J* = 10.0, 5.0 Hz, 1H, ArH), 7.69 (s, 1H, ArH), 7.63 (d, *J* = 10.0 Hz, 2H, ArH), 7.52 (d, *J* = 10.0 Hz, 1H, ArH), 7.43 (t, *J* = 10.0 Hz, 2H, ArH), 7.40 (s, 1H, ArH), 7.33 (t, *J* = 5.0 Hz, 1H, ArH), 6.22 (s, 1H, =CH), 2.43 (s, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ = 161.9, 161.8, 161.0, 154.8, 151.9, 150.2, 139.4, 138.7, 132.5, 132.4, 129.2, 128.5, 127.3, 127.2, 123.4, 118.9, 118.4, 115.9, 113.9, 111.4, 103.3, 99.9, 97.9, 19.2 ppm. HRMS (*m*/*z*) (ESI-TOF) calcd for $C_{27}H_{16}ClNO_5$ [M + H^+], 470.0790, found 470.0811.

9-(4-Hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-4-methyl-8-phenyl-7*H*-pyrano[2,3-*e*]ind ol-2-one (8d). Yellow solid (348 mg, 87%), mp 340–342 °C; I.R. (A.T.R.) 3310, 3080, 1680, 1627, 1572, 433, 1342, 1300, 1256, 1203, 1142, 1054, 993 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ = 11.83 (s, 1H, OH), 11.14 (s, 1H, NH), 7.61 (d, *J* = 10.0 Hz, 2H, ArH), 7.51 (s, 1H, ArH), 7.43 (t, *J* = 10.0 Hz, 2H, ArH), 7.34–7.31 (m, 2H, ArH), 6.22 (s, 1H, =CH), 6.14 (s, 1H, =CH), 2.44 (s, 3H, CH_3), 2.28 (s, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ = 167.8, 164.1, 162.3, 161.1, 154.6, 150.0, 138.5, 138.3, 133.0, 129.1, 128.2, 127.0, 115.9, 113.7, 111.4, 104.6, 100.7, 97.8, 95.4, 19.9, 19.1 ppm. HRMS (*m*/*z*) (ESI-TOF) calcd for $C_{24}H_{17}NO_5$[M + H^+], 400.1179, found 400.1200.

4-Hydroxy-3-(5-methyl-2-phenyl-1*H*-indol-3-yl)-chromen-2-one (10a). Brown solid, m.p. 189–191 °C. (120 mg = 65%), I.R. (A.T.R.) = 3637, 3339, 1663, 1 606 1492, 1263, 1102, 1062, 690 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 11.50 (s, 1H, NH), 11.02 (s, 1H, OH), 7.92 (d, *J* = 8.0 Hz, 1H, ArH), 7.68 (t, *J* = 8.0 Hz, 1H, ArH), 7.61 (d, *J* = 8.0 Hz, 2H, ArH), 7.45 (d, *J* = 1.2 Hz, 1H, ArH), 7.38–7.35 (m, 4H, ArH), 7.27 (t, *J* = 8.0 Hz, 1H, ArH), 6.99 (d, *J* = 8.0 Hz, 2H, ArH), 2.34 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 162.4, 162.3, 153.2, 137.2, 135.2, 135.1, 133.4, 132.6, 129.9, 129.1, 128.1, 127.8, 127.0, 124.4, 124.1, 123.7, 118.9, 116.7, 116.6, 102.1, 99.9, 21.6 ppm. HRMS (*m*/*z*) (ESI-TOF) calcd for $C_{24}H_{17}NO_3$ [M + H^+] 368.1281, found 368.1345.

4-Hydroxy-3-[5-methoxy-2-(4-nitro-phenyl)-1*H*-indol-3-yl]-chromen-2-one (10b). Yellow solid, m.p. 285–287 °C. (146 mg = 68%), I.R. (A.T.R.) = 3626, 3312, 1680, 1613, 1504, 1328, 1264, 1199, 1157, 1025, 967 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 11.80 (s, 1H, NH), 11.21 (s, 1H, OH), 8.26 (d, *J* = 8.0 Hz, 2H, ArH), 7.94 (d, *J* = 8.0 Hz, 1H, ArH), 7.83 (d, *J* = 8.0 Hz, 2H, ArH), 7.70 (s, 1H, ArH), 7.48–7.41(m, 3H, ArH), 6.88 (d, *J* = 8.0 Hz, 1H, ArH), 6.74 (s, 1H, ArH), 3.70 (s, 3H, OCH_3), ^{13}C NMR (100 MHz, DMSO-d_6) δ = 162.6, 162.1, 154.4, 153.3, 146.3, 135.1, 132.8, 132.6, 129.9, 127.5, 124.5, 124.4, 124.2, 116.8, 114.2, 113.0, 105.7, 101.1, 99.3, 55.8 ppm. HRMS (*m*/*z*) (ESI-TOF) calcd for $C_{24}H_{16}N_2O_6$ [M + H^+] 429.1081, found 429.1127.

3-(5,6-Dimethoxy-2-phenyl-1*H*-indol-3-yl)-4-hydroxy-chromen-2-one (10c). Grey solid, m.p. 300–302 °C. (147 mg = 71%), I.R. (A.T.R.) 3410, 3318, 1684, 1616, 1484, 1339, 1197, 1 188 837 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 11.34 (s, 1H, NH), 10.95 (s, 1H, OH), 7.88 (d, J = 8.0 Hz, 1H, ArH), 7.67 (t, *J* = 8.0 Hz, 1H, ArH), 7.53 (d, *J* = 8.0 Hz, 2H, ArH), 7.44 (d, *J* = 8.0 Hz, 1H, ArH), 7.39–7.34 (m, 3H, ArH,), 7.25 (t, *J* = 8.0 Hz, 1H, ArH), 6.97 (s, 1H, ArH), 6.69 (s, 1H, ArH), 3.81 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 161.8, 152.7, 147.0, 144.8, 134.9, 133.2, 132.1, 130.8, 128.5, 126.8, 126.1, 123.9, 123.7, 122.2, 116.3, 116.2, 102.0, 101.4, 99.6, 95.1, 56.0, 55.9 ppm. HRMS (*m*/*z*) (ESI-TOF) calcd for $C_{25}H_{19}NO_5$ [M + H^+] 414.1336, found 414.1395.

4-Hydroxy-3-(2-phenyl-6,7-dihydro-1*H*-5,8-dioxa-1-aza-cyclopenta[*b*]naphthalen-3-yl)-chromen-2-one (10d). Yellow solid, m.p. 300–302 °C. (144 mg = 70%), I.R. (A.T.R.) 3318, 3062, 1679, 1613, 1502, 1471, 1342, 1302, 1177, 1036, 1023, 960 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 11.24 (s, 1H, NH), 11.96 (s, 1H, OH), 7.88 (d, *J* = 4.0 Hz, 1H, ArH), 7.66 (t, *J* = 8.0 Hz, 1H, ArH), 7.54 (d, *J* = 8.0 Hz, 2H, ArH), 7.43 (d, *J* = 8.0 Hz, 1H, ArH), 7.39–7.33 (m, 3H, ArH), 7.22 (t, J = 4.0 Hz, 1H, ArH), 6.88 (s, 1H, ArH), 6.58 (s, 1H, ArH), 4.21 (d, *J* = 1.2 Hz, 4H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 161.7, 152.6, 140.7, 138.6, 136.2, 133.0, 131.5, 128.5, 127.0, 126.2, 123.9, 123.7, 123.6, 123.5, 116.3, 116.2, 105.1, 101.4, 99.4, 98.1, 64.2, 63.9 ppm. HRMS (*m*/*z*) (ESI-TOF) calcd for $C_{25}H_{17}NO_5$ [M + H^+] 412.1179, found 412.1232.

3-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-2-phenyl-1*H*-1-aza-cyclopenta[*a*]fluoren-10-one (12a). Brown solid (196 mg = 86%), m.p. 322–324 °C, I.R. (A.T.R.) 3380, 1698, 1679, 1604, 1568, 1488, 1430, 1259, 1255, 1214, 1158, 1109, 1004, 951 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 11.97 (s, 1H, NH), 11.24 (s, 1H, OH), 7.90 (d, *J* = 5.0 Hz, 1H, ArH), 7.67–7.63 (m, 4H, ArH), 7.52–7.44 (m, 4H, ArH), 7.40–7.37 (m, 4H, ArH), 7.32–7.26 (m, 2H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 193.2, 162.9, 162.3, 153.2, 145.7, 141.7, 140.3, 135.1, 134.1, 133.8, 132.8, 132.6, 132.1, 128.7, 128.6, 128.5, 128.4, 126.8, 124.5, 124.1, 123.7, 120.7, 116.7, 116.6, 116.4, 113.3, 104.6, 98.6 ppm; HRMS (*m*/*z*) (ESI-TOF) calcd for $C_{30}H_{17}NO_4$[M + H^+] 456.1275, found 456.1275.

2-(4-Fluoro-phenyl)-3-(4-hydroxy-2-oxo-2*H*-chromen-3-yl)-1*H*-1-aza cyclopenta[*a*] fluoren-10-one (12b). Brown solid, m.p. 352–354 °C. (201 mg = 85%), I.R. (A.T.R.) = 3374, 3029, 1701, 1607, 1551, 1491, 1424, 1289, 1235, 1170, 1112, 1001, cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 12.05 (s, 1H, NH), 7.91 (s, 1H, ArH), 7.68 (s, 4H, ArH), 7.54–7.39 (m, 6H, ArH), 7.25 (s, 3H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 193.2, 163.4, 163.3, 162.3, 161.4, 153.3, 145.7, 140.7, 140.4, 135.1, 130.6, 130.5, 128.8, 126.9, 124.4, 124.2, 123.7, 120.7, 116.7, 116.3, 115.7, 115.5, 113.2, 104.8, 98.2 ppm. HRMS (*m*/*z*) (ESI-TOF) calcd for $C_{30}H_{16}FNO_4$ [M + H^+] 474.1136 found 474.1563.

3-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-2-(4-nitro-phenyl)-1*H*-1-aza cyclopenta[*a*] fluoren-10-one (12c). Red solid (200 mg = 80%), m.p. 388–390 °C. I.R. (A.T.R.) = 3412, 3175, 1676, 1629,

1607, 1507, 1408, 1 385 1333, 1289, 1217, 1152, 1109, 1015, 1008, 956 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 12.29 (s, 1H, NH), 11.39 (s, 1H, OH), 8.25 (d, J = 5.0 Hz, 2H, ArH), 7.91 (t, J = 5.0 Hz, 3H, ArH), 7.71–7.68 (m, 2H, ArH), 7.56 (d, J = 5.0 Hz, 1H, ArH), 7.52 (t, J = 10.0 Hz, 2H, ArH), 7.46 (d, J = 10.0 Hz, 2H, ArH), 7.39 (t, J = 5.0 Hz, 1H, ArH), 7.29 (t, J = 5.0 Hz, 1H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 193.1, 163.2, 162.1, 153.3, 147.0, 145.5, 141.5, 139.1, 138.6, 135.2, 134.0, 133.4, 132.9, 129.3, 129.4, 127.7, 124.5, 124.2, 123.9, 123.8, 120.9, 116.8, 116.6, 116.5, 113.7, 107.4, 98.0 ppm. HRMS (m/z) (ESI-TOF) calcd for $C_{30}H_{16}N_2O_6$ [M + H^+] 501.1081, found 501.1138.

3-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-2-phenyl-5a,11a-dihydro-1*H*-naphtho[2,3-*g*]indole-6,11-dione (14). White solid (206 mg = 85%), 295–297 °C. I.R. 3455, 3302, 1698, 1659, 1612, 1574, 1496, 1488, 1457, 1330, 1291, 1228, 1205, 1109, 1005, 959 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 11.82 (s, 1H, NH), 8.26 (dd, J = 1.2, 8.0 Hz, 2H, ArH), 7.95 (d, J = 8.0 Hz, 3H, ArH), 7.81 (d, J = 8.0 Hz, 1H, ArH), 7.71 (d, J = 8.0 Hz, 4H, ArH), 7.62 (d, J = 8.0 Hz, 1H, ArH), 7.46 (t, J = 8.0 Hz, 3H, ArH), 7.35–7.28 (m, 3H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 184.4, 182.7, 162.8, 161.8, 152.8, 144.1, 135.8, 134.4, 134.3, 133.4, 133.3, 132.6, 128.6, 127.8, 126.8, 126.2, 125.6, 124.6, 124.1, 123.8, 118.3, 117.2, 116.3, 116.1, 115.9, 115.7, 104.6, 97.5 ppm. HRMS (m/z) (ESI-TOF) calcd for $C_{31}H_{19}NO_5$ [M + H^+] 484.1179, found 484.1221.

9-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-2-methyl-8-*p*-tolylpyrano[2,3-*e*]indol-4(7*H*)-one (4j). White solid (359 mg, 80%), mp 390–392 °C; I.R. (A.T.R.) 3629, 3463, 3238, 2921, 1679, 1642, 1608, 1575, 1544, 1502, 1476, 1412, 1392, 1378, 1229, 1204, 1122, 1074, 1027, 968 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ = 12.28 (s, 1H, OH), 11.17 (s, 1H, NH), 7.94 (d, J = 4.0 Hz, 1H, ArH), 7.72 (t, J = 8.0 Hz, 2H, ArH), 7.56–7.48 (m, 4H, ArH), 7.40 (t, J = 8.0 Hz, 1H, ArH), 7.25 (d, J = 4.0 Hz, 2H, ArH), 6.12 (s, 1H, =CH), 2.31 (s, 3H, CH_3), 1.92 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 177.3, 164.6, 162.6, 153.1, 151.8, 139.8, 138.4, 138.0, 132.7, 129.8, 129.6, 127.2, 124.8, 124.5, 124.1, 119.7, 117.7, 117.6, 116.7, 116.2, 110.6, 110.3, 100.4, 88.9, 21.3, 19.6 ppm. HRMS (m/z) (ESI-TOF) calcd for $C_{28}H_{19}NO_5$ [M + H^+], 450.1336, found 450.1398.

9-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-2,8-diphenyl-7*H*-pyrano[2,3-*e*]indol-4-one (4k). White solid (368 mg, 74%), mp 394–396 °C; I.R. (A.T.R.) 3016, 2206, 1688, 1634, 1601, 1582, 1563, 1471, 1406, 1386, 1221, 1193, 1158, 1131, 1079, 954 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 12.48 (s, 1H, OH), 11.54 (s, 1H, NH), 7.94 (d, J = 8.0 Hz, 1H, ArH), 7.84–7.78 (m, 2H, ArH), 7.64–7.57 (m, 4H, ArH), 7.53 (d, J = 8.0 Hz, 2H, ArH), 7.45 (t, J = 8.0 Hz, 3H, ArH), 7.37–7.32 (m, 2H, ArH), 6.99 (s, 1H, =CH), 6.87 (t, J = 8.0 Hz, 2H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 177.5, 162.9, 162.7, 161.5, 153.2, 151.7, 140.4, 138.6, 133.16, 132.1, 131.7, 129.3, 128.9, 127.5, 125.8, 124.86, 124.39, 118.1, 117.9, 116.9, 116.8, 116.7, 111.3, 107.6, 102.7, 100.5 ppm. HRMS (m/z) (ESI-TOF) calcd for $C_{32}H_{19}NO_5$ [M + H^+], 498.1336, found 498.1395.

9-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-2-phenyl-8-*p*-tolyl-7*H*-pyrano[2,3-*e*]indol-4-one (4l). Pale yellow solid (399 mg, 78%), mp 390–392 °C; I.R. (A.T.R.) 3014, 2768, 1671, 1634, 1608, 1579, 1504, 1493, 1383, 1222, 1191, 1154, 1131, 1103, 1079, 954 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 12.41 (s, 1H, OH), 11.49 (s, 1H, NH), 7.95 (d, J = 8.0 Hz, 1H, ArH), 7.81 (t, J = 8.0 Hz, 2H, ArH), 7.59–7.52 (m, 6H, ArH), 7.46 (t, J = 8.0 Hz, 1H, ArH), 7.34 (t, J = 8.0 Hz, 1H. ArH), 7.26 (d, J = 8.0 Hz, 2H, ArH), 6.99 (s, 1H, =CH), 6.87 (t, J = 8.0 Hz, 2H, ArH), 2.30 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 177.5, 162.7, 161.4, 153.2, 151.6, 140.3, 138.7, 138.2, 133.1, 131.7, 131.6, 129.9, 129.3, 128.9, 127.4, 125.8, 124.8, 124.4, 118.1, 117.8, 116.9, 116.8, 111.1, 107.6, 102.1, 101.1, 21.3 ppm. HRMS (m/z) (ESI-TOF) calcd for $C_{33}H_{21}NO_5$ [M + H^+], 512.1492, found 511.1462.

9-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-8-(4-methoxy-phenyl)-2-phenyl-7*H*-pyrano[2,3-*e*]indol-4-one (4m). White solid (396 mg, 75%), mp 328–330 °C; I.R. (A.T.R.) 3034, 2881, 1669, 1607, 1565, 1504, 1494, 1475, 1380, 1246, 1222, 1178, 1152, 1129, 1078, 1030, 986 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 12.37 (s, 1H, OH), 11.48 (s, 1H, NH), 7.96 (d, J = 4.0 Hz, 1H, ArH), 7.80 (t, J = 8.0 Hz, 2H, ArH), 7.60–7.53 (m, 6H, ArH), 7.47 (t, J = 8.0 Hz, 1H, ArH), 7.34 (t, J = 8.0 Hz, 1H, ArH), 7.04 (d, J = 8.0 Hz, 2H, ArH), 6.99 (s, 1H, =CH), 6.87 (t, J = 8.0 Hz, 2H, ArH), 3.76 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 177.5, 162.8, 162.7, 161.4, 159.7, 153.2, 151.5, 140.3, 138.7, 133.1, 131.7, 131.6, 128.9, 128.8, 125.8, 124.8, 124.5, 124.4, 118.2, 117.6, 116.9, 116.8, 114.8, 111.1, 107.5, 101.5, 100.7, 55.6 ppm; HRMS (m/z) (ESI-TOF) calcd for $C_{33}H_{21}NO_6$ [M + H^+], 528.1442, found 528.1505.

9-(4-Hydroxy-2-oxo-2*H*-chromen-3-yl)-8-(4-nitro-phenyl)-2-phenyl-7*H*-pyrano[2,3-*e*]indol-4-one (4n). Grey solid (429 mg, 79%), mp 392–394 °C; I.R. (A.T.R.) 3362, 3207, 1676, 1594, 1563, 1513, 1496, 1473, 1412, 1386, 1339, 1190, 1159, 1128, 1105, 1077, 964 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 12.76 (s, 1H, OH), 11.69 (s, 1H, NH), 8.34 (d, J = 8.0 Hz, 2H, ArH), 7.95 (d, J = 8.0 Hz, 1H, ArH), 7.90–7.87 (m, 3H, ArH), 7.82 (t, J = 8.0 Hz, 1H, ArH), 7.65–7.59 (m, 2H, ArH), 7.53 (d, J = 8.0 Hz, 2H, ArH), 7.46 (t, J = 8.0 Hz, 1H, ArH), 7.34 (t, J = 8.0 Hz, 1H, ArH), 7.01 (s, 1H, =CH), 6.88 (t, J = 8.0 Hz, 2H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 177.3, 162.6, 161.6, 153.3, 151.9, 147.0, 140.9, 138.5, 136.1, 133.3, 131.7, 131.6, 129.6, 128.9, 128.3, 126.7, 125.8, 124.8, 124.7, 124.5, 119.2, 118.1, 117.1, 116.8, 111.5, 107.9, 105.5, 99.8 ppm. HRMS (m/z) (ESI-TOF) calcd for [M + H^+], $C_{32}H_{18}N_2O_7$ 543.1187, found 543.1277.

9-(4-Hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-8-phenyl-2-*p*-tolyl-7*H*-pyrano[2,3-*e*]indol-4-one (4o). Brown solid (366 mg, 77%), mp 380–382 °C; I.R. (A.T.R.) 3057, 1633, 1604, 1499, 1378, 1216, 1191, 1151, 1133, 1019, 995 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 12.26 (s, 1H, OH), 11.38 (s, 1H, NH), 7.80–7.74 (m, 3H, ArH), 7.59 (t, J = 8.0 Hz, 2H, ArH), 7.55–7.49 (m, 4H, ArH), 7.27 (d, J = 8.0 Hz, 2H, ArH), 6.99 (s, 1H, ArH), 6.22 (s, 1H, =CH), 2.55 (s, 3H, CH_3), 2.33 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 177.6, 167.9, 164.8, 162.2, 161.7, 151.7, 140.1, 137.9, 137.6, 132.1, 131.9, 129.8, 129.7, 129.4, 127.3, 126.2, 117.8, 117.6, 116.7, 111.1, 107.6, 103.5, 101.0, 97.3, 21.2, 20.0 ppm. HRMS (m/z) (ESI-TOF) calcd for $C_{30}H_{21}NO_5$ [M + H^+], 476.1492, found 476.1551.

Conflicts of interest

The authors declare no competing financial interest.

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