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A versatile route to 2-alkyl-/aryl-amino-3-formyl- and hetero-annelated-chromones, through a facile nucleophilic substitution at C2 in 2-(*N*-methylanilino)-3-formylchromones

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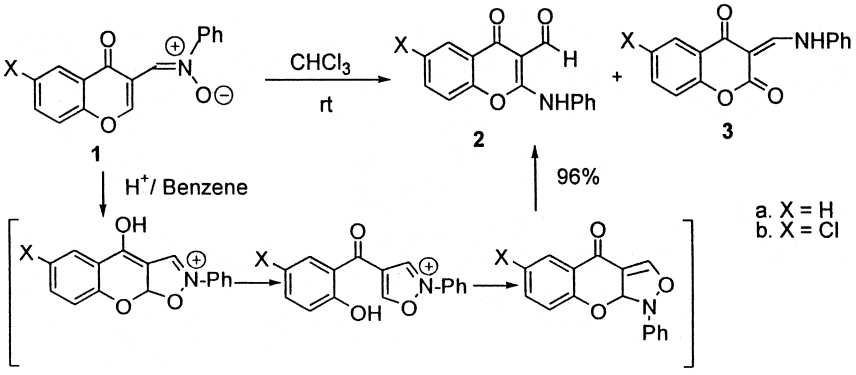
Abstract—The *N*-methylanilino group in 2-(*N*-methylanilino)-3-formylchromones, obtained in high yield by rearrangement of C(4-oxo-4*H*[1]-benzopyran-3-yl)-*N*-phenylnitrones to 2-anilino-3-formyl-chromones followed by *N*-methylation, undergoes facile nucleophilic substitution by a variety of nitrogen nucleophiles, thereby paving the way for synthesis of a variety of novel 2-substituted-3-formylchromone derivatives as well as hetero-annelated chromones. © 2002 Published by Elsevier Science Ltd.

1. Introduction

Besides forming the basic nucleus of an entire class of natural products, i.e. flavones,[1] the chromone moiety is also part of a large number of molecules of medicinal significance.[2] Consequently, considerable attention is being devoted to isolation from natural resources, chemistry and synthesis of chromone derivatives, and evaluation of their biological activity with stress on their potential medicinal applications.[2–4] Some of the biological activities recently ascribed to chromone derivatives include cytotoxic (anticancer),[4a–c] P-glycoprotein binding (to overcome multi-drug resistance, anticancer),[4d] neuroprotective,[4e] HIV-inhibitory,[4f] antimicrobial,[4g,h] cyclin-dependent kinase inhibitory (anticancer),[4i] antifungal[4j] and antioxidant activity.[4k] 3-Formylchromone has emerged as a valuable synthon for incorporation of the chromone moiety[5] and attempts are being made to develop its solid supported synthetic equivalents.[5g] However, it has been observed that nucleophilic attack at C2 in 3-formylchromone or its derivatives, results in either pyrone ring opening or loss of the C2–C3– π bond, thereby, limiting its synthetic applications.[2,3,5] This facile pyrone ring opening has also attracted the attention of theoreticians.[6] We had earlier observed[7] that C-(4-oxo-4*H*[1]-benzopyran-3-yl)-*N*-phenylnitrones (**1**, R=H, Me, Cl) undergo intramolecular rearrangement to yield **2**-anilino-**3**-formylchromones (**2**, 70–90%) and 3-phenyliminomethyl-enechromone-2,4-diones (**3**, 10–25%, Scheme 1).

We report herein that *N*-methylation of **2** yields 2-(*N*-methylanilino)-3-formylchromone (**4**) in high yield (>95%) and the 2-*N*-methylanilino group in the latter undergoes facile



Scheme 1.

Keywords: chromones; substitution; addition elimination; diazepines; heterocycles.

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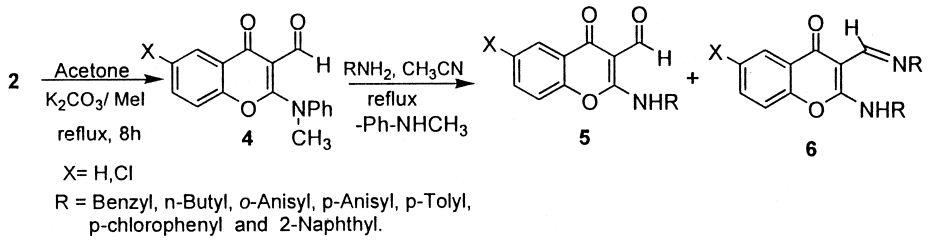
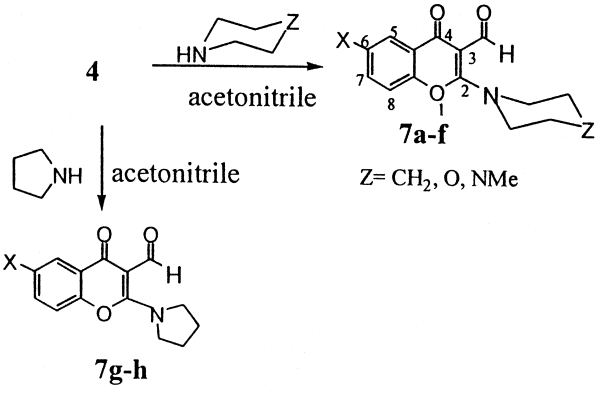


Scheme 2.

Table 1. Reaction times, yields (%) and melting points of the products (**5a**–**n**) for reactions of 2-(*N*-methylanilino)-3-formyl-chromones (**4a**,**b**) with various primary amines in aqueous-acetonitrile

Entry	X	R	Reaction time (h)	Product (% yield)	Melting point (°C)
1	Cl	Benzyl	1	**5a** (90)	156–157
2	Cl	*n*-Butyl	1	**5b** (89)	91–92
3	Cl	*p*-Anisyl	3	**5c** (94)	175–176
4	Cl	*p*-Tolyl	4	**5d** (91)	149–150
5	Cl	2-Naphthyl	4	**5e** (86)	191–192
6	Cl	*o*-Anisyl	7	**5f** (92)	219–220
7	Cl	*p*-Chloro	5	**5g** (84)	217–218
8	H	Benzyl	1	**5h** (91)	152–153
9	H	*n*-Butyl	1	**5i** (88)	89–90
10	H	*p*-Anisyl	3	**5j** (94)	173–174
11	H	*p*-Tolyl	4	**5k** (88)	142–143
12	H	2-Naphthyl	4	**5l** (84)	186–187
13	H	*o*-Anisyl	7	**5m** (91)	205–206
14	H	*p*-Chloro	5	**5n** (82)	211–212

substitution by various nitrogen nucleophiles, paving the way for the preparation of a large number of novel 2-substituted-3-formylchromones and heteroannelated-chromones. To further enhance the synthetic potential of this approach, taking cognizance of a literature report on the acid promoted cyclization of 3-formylchromone-oxime,[31] the yield of **2** has been improved to 96% by refluxing the nitrone **1** in dry benzene in the presence of a catalytic amount of acetic acid (Scheme 1); the product obtained can be directly methylated (without any separation from **3**) to **4**, which is crystallized out.



Scheme 3.

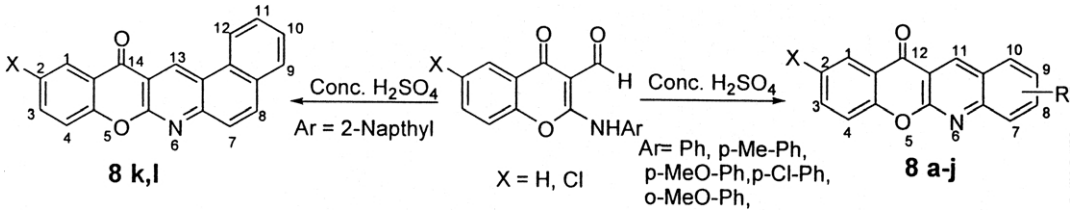
2. Results and discussion

Initially, the reactions of **4b** (X=Cl) were carried out with 1 molar equiv. of primary aromatic/aliphatic amines (benzylamine, *n*-butylamine and *p*-ansidine) in dry acetonitrile, which afforded, the 2-substituted product (**5a**–**c**) in 23–29% yield, along with 2-arylamino-3-(*N*-arylimino-methyl)chromones (**6a**–**c**, 30–36%); the rest of **4** was recovered unreacted. On the other hand, when the reaction was carried out with 2 molar equiv. of the above amines the yields of (**6a**–**c**) were more than 90%. However, when the reactions were carried out in refluxing aqueous-acetonitrile (CH_3CN–H_2O 65:35), **5** were obtained as the only product; the latter reaction has been extended to *o*-ansidine, *p*-toluidine, *p*-chloroaniline and β-naphthylamine (Scheme 2, Table 1).

The reaction has been extended to some cyclic-amines like pyrrolidine, piperidine, morpholine and *N*-methylpiperazine,

Table 2. Reaction times, yields (%) and melting points of the products (**7a**–**h**) for reactions of **4a**,**b** with cyclic-amines in dry-acetonitrile

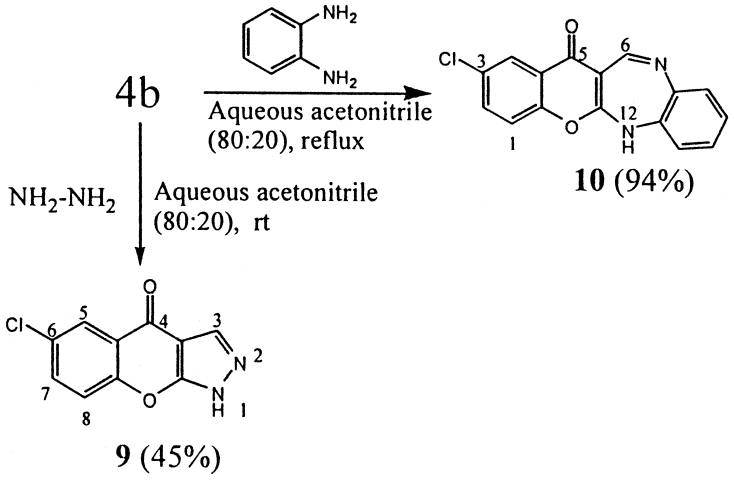
Entry	X	Amine reacted	Reaction time (min)	Product (% yield)	Melting point (°C)
1	Cl	Piperidine	30	**7a** (90)	157–158
2	Cl	Morpholine	30	**7b** (92)	177–178
3	Cl	*N*-Methylpiperazine	30	**7c** (92)	155–156
4	H	Piperidine	30	**7d** (91)	160–161
5	H	Morpholine	30	**7e** (94)	180–181
6	H	*N*-Methylpiperazine	30	**7f** (91)	152–153
7	Cl	Pyrrolidine	45	**7g** (91)	188–189
8	H	Pyrrolidine	45	**7h** (90)	190–191



Scheme 4.

Table 3. Reaction times, yields (%) and melting points of products (**8a**–**l**) from cyclization of 2-*N*-arylamino-3-formylchromones

Entry	X	Ar	Reaction time (h)	Product (% yield)	Melting point (°C)
1	Cl	Phenyl	6	**8a** (96)	211–212
2	Cl	*p*-Tolyl	6	**8b** (94)	218–219
3	Cl	*p*-Anisyl	5	**8c** (95)	221–223
4	Cl	*o*-Anisyl	5	**8d** (96)	251–252
5	Cl	*p*-Cl-Phenyl	6	**8e** (91)	221–222
6	H	Phenyl	5	**8f** (94)	217–218
7	H	*p*-Tolyl	5	**8g** (96)	209–210
8	H	*p*-Anisyl	5	**8h** (95)	245–246
9	H	*o*-Anisyl	5	**8i** (98)	243–244
10	H	*p*-Cl-Phenyl	6	**8j** (90)	214–215
11	Cl	2-Naphthyl	5	**8k** (97)	252–253
12	H	2-Naphthyl	5	**8l** (94)	241–243



Scheme 5.

which react with **4** under anhydrous conditions, in acetonitrile, to afford 2-substituted-3-formyl chromones (**7a**–**h**) in high yields (Scheme 3, Table 2). The assigned structures of the products are based on detailed spectroscopic analysis and microanalytical data.

Hetero-annulated chromones have been particularly targeted due to their medicinal significance.[2,8] Therefore, to demonstrate the usefulness of present approach, compounds **5c**–**g** and **5j**–**n** have been cyclized to chromanoquinolines (**8a**–**l**, Scheme 4, Table 3);[†] valuable pharmacological activities have been attributed to such compounds.[8]

The products (**8a**–**l**) have been characterized by rigorous spectroscopic analysis. The H-11 resonance in the ^{1}H NMR spectra of **8a**–**j** appeared as a singlet (1H) at $\sim\delta$ 9.1 and the corresponding resonance of H-13 in **8k**,**l** was located at $\sim\delta$ 10.0. The orientation of cyclization in **5e**,**l** leading to **8k**,**l** is based on the presence of a 1H doublet in the ^{1}H NMR spectra of the latter at δ 8.8, which is attributed to H-12 and also there is present only one singlet in the ^{1}H NMR of **8k** (H-13), whereas three singlets are anticipated for the alternative linear structure. It may be mentioned here that these compounds fluoresce even in the solid state and display strong fluorescence bands in the region 420–570 nm (CH_3CN solvent, excited at 350 and 390 nm).

Investigations have also been extended to reactions of **4a** with diamines i.e. *o*-phenylenediamine and hydrazine to afford chromone annelated heterocyclic systems (**9**,**10**, Scheme 5); best yields of products (**9**,**10**) are obtained in aqueous-acetonitrile (80:20) and use of anhydrous solvent

[†] The presently described method of cyclization employing sulfuric acid is a marked improvement over the $AlCl_3$ effected cyclization of **5** (Ar=Ph) reported by us earlier.[7a]

led only to a highly insoluble product which could not be investigated further.

The structures of various products have been again established by rigorous spectroscopic analysis (UV, IR, ^{1}H and ^{13}C NMR, Mass) and microanalytical data, and comparison of the spectroscopic data with related systems.[3n,4f,9]

Mechanistically, the substitution reaction at C2 can be best described as a conjugate-addition–elimination; the high nucleofugality of *N*-methylanilino group completely prevents any chromone ring opening The reaction not only provides an easy access to a large number of novel 2-substituted-chromone derivatives, but also has a lot of other interesting applications. For instance, the reaction can be utilized to introduce other moieties at C2 to obtain biologically active molecules. The reaction can also be utilized to obtain chromano-diaza-heterocycles (like **9** and **10**) as well as macrocycles bearing intact chromone moieties on the periphery, i.e. by reacting **4** with α,ω-diamino compounds, combining nucleophilic substitution at C2 with condensation with the C3-formyl group; recently chromone based macrocycles have found some interesting applications.[10]

3. Experimental

3.1. General

NMR spectra ware recorded on Bruker 200, 300 and 400 MHz FT NMR spectrometers, using TMS as internal standard and $CDCl_3$/DMSO-d_6 as solvents. Chemical shifts are reported in ppm as down field displacements from tetramethylsilane used as internal standard. Mass spectra were recorded on Shimadzu GCMS-QP-2000A spectrometer. The microanalytical data were collected on a Perkin–Elmer 240C elemental analyzer. IR spectra were recorded on a Shimadzu DR 2001 IR spectrophotometer in $CHCl_3$ solution or as pellets with KBr and are reported in wave numbers (cm^{-1}). All melting points are uncorrected and measured in open glass-capillaries. Column chromatography was conducted using silica gel 60–120 mesh (Acme, India). Solvents, starting materials and reagents were purchased from commercial suppliers and used after purification (crystallization/distillation). 3-Formylchromones were purchased from Aldrich and used as such.

3.1.1. Conversion of nitrone 1 to 2-anilino-3-formylchromone (2). Nitrone (**1a**,**b**, 5.0 g, 18.8 and 16.72 mmol, respectively) were taken in dry benzene (100 mL) and a few drops of acetic acid added to it. The contents were refluxed for 6 h. The solvent was evaporated under vacuum and the resulting compounds were directly crystallized in methanol to afford products (**2a**,**b**) as yellow crystalline solids.

2a: yield: 4.8 g (96%): mp 156–157°C; Lit.[7a] mp 156–158°C; **2b**: yield: 4.85 g (97%): mp 159–160°C; Lit.[7c] mp 158–159°C.

3.1.2. 2-(*N*-Methylanilino)-3-formylchromone (4a). 2-Anilino-3-formylchromone (**2a**, 3.0 g, 11.3 mmol) was dissolved in dry acetone (160 mL) and anhydrous (fused) potassium carbonate (1.5 g), and dried methyl iodide (5 mL, excess) were added. The contents were refluxed with stirring and the reaction was monitored by TLC. After completion of reaction (8 h) the K_2CO_3 was filtered-off, and residue was washed with a little acetone and the solvent from filtrate was evaporated under vacuum. The resulting solid was suspended in 10 mL of acetonitrile, filtered and washed with acetonitrile (2 mL) to obtain **4a** (3.1 g, ~98%). The obtained product is utilized as such for further reactions and an analytical sample was obtained by re-crystallization from acetonitrile. Faint yellow solid, mp 168–169°C; (Found: C, 72.88; H, 4.86; N, 4.93. $C_{17}H_{13}NO_3$ requires C, 73.11; H, 4.69; N, 5.02%); λ_{max} (MeOH): 325, 286, 248 nm; ν_{max} (KBr): 1670, 1631, 1621, 1518 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 3.56 (s, 3H, N–CH_3), 7.10–7.60 (m, 8H, arom.-Hs), 8.18 (br d, 1H, J=7.8 Hz, C5–H), 10.09 (s, 1H, CHO); δ_C (50 MHz, $CDCl_3$): 42.97 (N–CH_3), 102.63 (C3), 116.71 (C8), 123.14 (C4a), 124.98 (CH), 125.41 (CH), 126.07 (CH), 127.43 (CH), 129.55 (CH), 133.69 (C7), 143.99 (quat. Arom.), 153.34 (C8a), 163.70 (C2), 178.65 (C4), 186.7 (CHO); *m*/*z* (%): 279 (M^+, 21), 278 (100), 250 (29), 91 (78).

3.1.3. 6-Chloro-2-(*N*-methylanilino)-3-formylchromone (4b). It was obtained by reacting 2-anilino-6-chloro-3-formylchromone (**2b**, 3.0 g, 10.0 mmol) with methyliodide (5 mL, excess) in presence of anhyd. K_2CO_3 (1.5 g) in refluxing dry acetone (175 mL) according to method described above, as a cream colored solid (CH_3CN, 3.1 g, 99%), mp 174–176°C; (Found C, 65.32; H, 3.97; N, 4.27. $C_{17}H_{12}NClO_3$ requires C, 65.08; H, 3.86; N, 4.46%); λ_{max} (MeOH): 328, 292, 260 nm; ν_{max} (KBr): 1675, 1634, 1531, 1446 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 3.54 (s, 3H, N–Me), 7.03 (d, 1H, J=8.64 Hz, C8–H), 7.51–7.25 (m, 6H, arom.-Hs), 8.13 (d, 1H, J=2.4 Hz, C5–H), 10.09 (s, 1H, –CH═O); δ_C ($CDCl_3$, 50 MHz): 43.27 (N–Me), 102.33 (C3), 118.21 (C8), 125.04 (CH), 125.59 (CH), 126.5 (CH), 127.61 (CH), 129.05 (CH), 131.24 (C6), 133.46 (C7), 143.55 (quat. arom.), 151.5 (C8a), 163.35 (C2), 177.09 (C4), 186.28 (*C*H═O); *m*/*z* (%) 315 (M^++2, 22), 313 (M^+, 61), 284 (63), 91 (100).

3.2. General procedure for reactions of 4b with primary-amines in dry acetonitrile leading to 5a–c and 6a–c

6-Chloro-2-(*N*-methylanilino)-3-formylchromone (**4b**, 313 mg, 1.0 mmol) was dissolved in dry acetonitrile (60 mL) and a solution of amine (1.0 mmol) in acetonitrile (3 mL) was added to it. The contents were refluxed under an anhydrous setup and progress of the reaction was monitored by TLC. After completion of reaction (1–4 h, TLC), the solvent was distilled off and the products were separated by column chromatography over silica gel column packed in hexane, eluted with 6% EtOAc/hexane.

3.2.1. Reaction of 4b with benzylamine in dry acetonitrile. Reaction of **4b** (313 mg, 1 mmol) with benzylamine (107 mg, 1 mmol) afforded *2-benzylamino-6-chloro-3-formylchromone* (**5a**, 91 mg, 29%) as white crystalline solid (hexane–$CHCl_3$, 4:1); (Found: C, 64.91; H, 3.97; N, 4.37. $C_{17}O_3H_{12}NCl$ requires C, 65.08; H, 3.86; N, 4.46%); λ_{max} (MeOH): 325, 273, 247 nm; ν_{max} ($CHCl_3$): 3175, 2925,

1671, 1640.9, 1576.8, 1495, 1465 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 4.75 (d, 2H, *J*=6.2 Hz, benzylic-Hs), 7.22 (d, 1H, *J*=8.8 Hz, C8–H), 7.30–7.42 (m, 5H, arom.-Hs), 7.53 (dd, 1H, *J*=8.8, 2.6 Hz, C7–H), 8.15 (d, 1H, *J*=2.6 Hz, C5–H), 10.20 (s, 1H, HC═O), 10.96 (bs, 1H, N–H); δ_C (50 MHz, $CDCl_3$): 44.93 (benzylic-C), 99.21 (C3), 118.01 (C8), 124.05 (C4a), 125.91 (CH), 126.38 (C5), 127.28 (CH), 129.08 (CH), 131.67 (C6), 133.40 (C7), 135.44 (quat.arom.), 151.41 (C8a), 164.08 (C2), 174.1 (C4), 189.25 (CH═O); *m/z* (%) 315 (M^++2, 18), 314 (M^{+1}, 9), 313 (M^+, 50), 284 (58), 91 (100). *2-Benzylamino-6-chloro-3-(N-benzyliminomethyl)chromone* (**6a**, 121 mg, 30%) as cream colored solid (hexane–$CHCl_3$, 4:1); mp 118–119°C; (Found: C, 71.72; H, 4.93; N, 6.83. $C_{24}H_{19}ClN_2O_2$ requires C, 71.55; H, 4.75; N, 6.95%); λ_{max} (MeOH): 386, 349, 328, 278, 247 nm; ν_{max} ($CHCl_3$): 3225, 1669.8, 1623.8, 1576.8, 1465.7 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 4.66 (br d, 4H, benzylic-Hs,), 7.09–7.28 (m, 11H, arom.-Hs), 7.41 (dd, 1H, *J*=8.9, 2.3 Hz, C7–H), 8.07 (d, 1H, *J*=2.3 Hz, C5–H), 8.73 (s, 1H, imino-H), 10.97 (broad, 1H, N–H); δ_C (75 MHz, $CDCl_3$): 47.00 (benzlylic-C), 59.19 (benzylic-C), 96.01 (C3), 117.82 (C8), 123.16 (C4a), 125.91 (CH), 126.29 (CH), 127.19 (CH), 127.33 (CH), 128.35 (CH), 129.58 (CH), 129.97 (CH), 132.87 (C6), 133.43 (C7), 137.88 (quat.arom.), 138.63 (quat.arom.), 152.29 (C8a), 157.19 (CH═N), 158.42 (C2), 174.38 (C4); *m/z* (%) 402 (M^+, 32), 311 (12), 284 (14), 91 (100).

3.2.2. Reaction of 4b with *n*-butylamine in dry acetonitrile. Reaction of (**4b**, 313 mg, 1 mmol) with *n*-butylamine (73 mg, 1 mmol) afforded *2-(n-butylamino)-6-chloro-3-formylchromone* (**5b**, 75 mg, 27%) as an off-white solid (hexane–$CHCl_3$, 4:1); (Found: C, 59.97; H, 5.19; N, 4.90. $C_{14}H_{14}NO_3Cl$ requires C, 60.11; H, 5.04; N, 5.01%); λ_{max} (MeOH): 322.5, 292.5, 247 nm; ν_{max} ($CHCl_3$): 3190, 2917, 1676.8, 1632.4, 1581.1, 1495.6 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 1.00 (t, 3H, *J*=7.7 Hz, CH_3), 1.41–1.54 (m, 2H, CH_2), 1.67–1.77 (m, 2H, CH_2), 3.59 (dt, 2H, *J*=6.9, 6.1 Hz, N–CH_2), 7.26 (d, 1H, *J*=8.7 Hz, C8–H), 7.55 (dd, 1H, *J*=8.7, 2.6 Hz, C7–H), 8.77 (d, 1H, *J*=2.6 Hz, C5–H), 10.20 (s, 1H, HC═O), 10.63 (broad, 1H, N–H); δ_C (75 MHz, $CDCl_3$): 13.57 (CH_3), 19.95 (CH_2), 31.28 (CH_2), 40.62 (N–CH_2), 99.11 (C3), 118.16 (C8), 124.1 (C4a), 125.77 (C5), 131.5 (C7), 133.41 (C7), 151.55 (C8a), 164.12 (C2), 174.24 (C4), 189.03 (HC═O); *m/z* (%) 280 (M^++1, 19), 279 (M^+85), 250 (100), 91 (60). *2-(n-Butylamino)-6-chloro-3-(N-n-butyliminomethyl)chromone* (**6b**, 107 mg, 32%) as pale-yellow solid (hexane–$CHCl_3$, 4:1); mp 84–85°C; (Found C, 64.41; H, 7.03; N, 8.32. $C_{18}H_{23}N_2O_2Cl$ requires C, 64.57; H, 6.92; N, 8.37%); λ_{max} (MeOH): 330, 278.5, 269.5, 247 nm; ν_{max} ($CHCl_3$): 3161, 1666.6, 1628.1, 1572.8, 1461.4 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 1.00 (overlapping ts, 6H, 2×CH_3), 1.37–1.52 (m, 4H, 2×CH_2), 1.58–1.79 (m, 4H, 2×CH_2), 3.50–3.60 (m, 4H), 7.14 (dd, 1H, *J*=8.8 Hz, C–8H), 7.45 (dd, 1H, *J*=8.8, 2.5 Hz, C7–H), 8.11 (d, 1H, *J*=2.5 Hz, C5–H), 8.65 (bs, 1H, CH═N), 11.98 (broad, 1H, N–H); δ_C (75 MHz, $CDCl_3$): 13.69 (2×CH_3), 20.08 (CH_2), 20.33 (CH_2), 32.31 (CH_2), 33.09 (CH_2), 42.30 (NH–CH_2), 55.27 (═NCH_2), 95.54 (C3), 117.77 (C8), 123.26 (C4a), 125.64 (C5), 129.62 (C6), 132.54 (C7), 152.27 (C8a), 156.41 (C2), 158.62 (C═N), 174.15 (C4); *m/z* (%): 336 (M^++2, 14), 334 (M^+, 40), 319 (26), 317 (77), 291 (71), 58 (100).

3.2.3. Reaction of 4b with *p*-anisidine. Reaction of (**4b**, 313 mg, 1 mmol) with *p*-anisidine (123 mg, 1 mmol) afforded *2-(p-anisylamino)-6-chloro-3-formylchromone* (**5c**, 69 mg, 21%) as a pale-yellow solid (hexane–$CHCl_3$, 3:1); (Found: C, 61.95; H, 3.79; N, 4.14. $C_{17}H_{12}NO_4Cl$ requires C, 61.92; H, 3.67; N, 4.25%); λ_{max}(MeOH): 323, 288.5, 247 nm; ν_{max} (KBr): 3210, 2925, 1670, 1625, 1612, 1502, 1451 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 3.70 (s, 3H, OCH_3), 6.98 (d, 2H, *J*=6.7 Hz, arom.-Hs), 7.22 (d, 1H, *J*=6.8 Hz, C8–H), 7.36 (d, 2H, *J*=6.7 Hz, arom.Hs), 7.55 (dd, 1H, *J*=8.8, 2.5 Hz, C7–H), 8.20 (d, 1H, *J*=2.5 Hz, C–5H), 10.29 (s, 1H, HC═O), 12.31 (broad, 1H, N–H); δ_C (50 MHz, $CDCl_3$): 55.66 (OCH_3), 99.43 (C3), 114.85 (CH), 116.49 (C8), 122.17 (C4a), 125.03 (C5), 126.00 (CH), 131.96 (C6), 133.62 (C7), 135.14 (quat. arom.), 151.9 (C8a), 158.60 (quat. arom.), 162.7 (C2), 174.6 (C4), 189.67 (HC═O); *m/z* (%): 330 (52, M^++1), 329 (M^+, 100), 328 (98), 300 (96), 284 (20). *2-(p-Anisylamino)-6-chloro-3-(N-p-anisyliminomethyl)-chromone* (**6c**, 156 mg, 36%) as light-yellow solid (hexane–$CHCl_3$, 4:1); mp 185–186°C; (Found: C, 66.41; H, 4.53; N, 6.31. $C_{24}H_{19}N_2O_4Cl$ requires C, 66.29; H, 4.40; N, 6.44%); λ_{max} (MeOH): 370, 317.5, 285.5 nm; ν_{max} (KBr): 3300, 3040, 1660, 1622, 1580, 1511, 1449 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 3.70 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 6.78 (broad d, 4H, *J*=8.7 Hz, arom.-Hs), 6.96 (d, 1H, *J*=8.7 Hz, C8–H), 7.09–7.16 (m, 4H), 7.32 (dd, 1H, *J*=8.8, 2.4 Hz, C7–H), 7.95 (d, 1H, *J*=2.4 Hz, C5–H), 8.82 (broad s, 1H, HC═N), 13.92 (broad, 1H, N–H); δ_C (50 MHz, $CDCl_3$): 55.35 (OCH_3), 55.29 (OCH_3), 97.58 (C3), 114.13 (CH), 114.82 (CH), 117.97 (C8), 120.17 (CH), 122.62 (C4a), 124.39 (CH), 125.91 (C5), 129.80 (C6), 133.19 (C7), 134.79 (quat. arom.), 135.32 (quat. arom.), 149.57 (CH═N), 152.46 (C8a), 154.42 (quat. arom.), 156.72 (quat. arom.), 158.07 (C2), 173.97 (C4); *m/z* (%) 435 (M^++2, 40), 434 (M^++1, 52), 433 (M^+, 61), 171 (60), 58 (100).

3.3. General procedure for reaction of 2-(*N*-methylanilino)-3-formylchromones (4a,b) with primary amines in aqueous-acetonitrile

2-(*N*-Methylanilino)-3-formylchromones (**4a**,**b**, 1.0 mmol) were dissolved in refluxing aqueous-acetonitrile (60 mL) and a solution of an amine (1.0 mmol) in acetonitrile (3 mL) was added to it. The contents were refluxed and the progress of reaction was monitored by TLC. After completion of reaction (1–4 h, TLC), the solvent was distilled off and the traces were removed under vacuum and the compounds were purified by column chromatography over silica gel using 6% ethyl acetate/hexane as eluent.

3.3.1. 2-Benzylamino-6-chloro-3-formylchromone (5a). Reaction of **4a** (313 mg, 1 mmol) with benzylamine (107 mg, 1 mmol) afforded the title compound (**5a**, 282 mg).

3.3.2. 2-(*n*-Butylamino)-6-chloro-3-formylchromone (5b). Reaction of **4a** (313 mg, 1 mmol) with *n*-butylamine (73 mg, 1 mmol) afforded the title compound (**5b**, 248 mg).

3.3.3. 2-(*p*-Anisylamino)-6-chloro-3-formylchromone (5c). Reaction of **4a** (313 mg, 1 mmol) with *p*-ansidine (123 mg, 1 mmol) afforded the title compound (**5c**, 309 mg).

3.3.4. 6-Chloro-2-(*p*-tolylamino)-3-formylchromone (5d). Reaction of **4a** (313 mg, 1 mmol) with *p*-toluidine (107 mg, 1 mmol) afforded the title compound (**5d**, 285 mg) as yellowish solid (hexane–$CHCl_3$ 3:1); (Found: C, 64.92; H, 3.99; N, 4.33. $C_{17}H_{12}NO_3Cl$ requires C, 65.08; H, 3.86; N, 4.46%); λ_{max} (MeOH): 324, 292, 252 nm; ν_{max} (KBr): 3230, 1665, 1632, 1618, 1582 cm^{-1}; δ_H ($CDCl_3$ 300 MHz): 2.41 (s, 3H, CH_3), 7.21–7.58 (m, 6H, arom.-Hs), 8.20 (d, 1H, *J*=2.6 Hz, C5–H), 10.28 (s, 1H, CHO), 12.37 (bs, 1H, NH); *m/z* (%) 313 (M^+, 2), 302 (6), 169 (85), 112 (27), 111 (48), 91 (100).

3.3.5. 6-Chloro-2-(β-naphthylamino)-3-formylchromone (5e). Reaction of **4a** (313 mg, 1 mmol) with β-naphthylamine (143 mg, 1 mmol) afforded the title compound (**5e**, 301 mg) as yellow solid (hexane–$CHCl_3$ 3:1); (Found: C, 68.59; H, 3.53; N, 3.84. $C_{20}H_{12}NO_3Cl$ requires C, 68.68; H, 3.46; N, 4.00%); λ_{max} (MeOH): 323, 282, 245 nm; ν_{max} (KBr): 3210, 2925, 1673, 1632, 1587, 1465, 1308 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 7.26–7.30 (m, 2H, arom.-Hs), 7.46–7.60 (m, 4H, arom.-Hs), 7.85–7.95 (m, 3H, arom.-Hs), 8.21 (d, 1H, *J*=2.5 Hz, C5–H), 10.33 (s, 1H, CHO), 12.62 (bs, 1H, NH); *m/z* (%) 350 (M^++2, 4), 349 (M^+, 18), 348 (7), 331 (45), 171 (22), 58 (100).

3.3.6. 6-Chloro-2-(*o*-anisylamino)-3-formylchromone (5f). Reaction of **4b** (313 mg, 1 mmol) with *p*-chloroaniline (123 mg, 1 mmol) afforded the title compound (**5f**, 303 mg) as a faint-yellow solid (hexane–$CHCl_3$, 3:1); (Found: C, 61.95; H, 3.79; N, 4.44. $C_{17}H_{12}NO_4Cl$ requires C, 61.92; H, 3.67; N, 4.25%); λ_{max}($CHCl_3$): 301, 287, 248 nm; ν_{max} (KBr): 3260, 3048, 1676, 1648, 1578, 1463 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 3.93 (s, 3H, OCH_3), 6.99–6.91 (m, 2H, C3′ and C8–Hs), 7.12–7.26 (m, 2H, C4′, C5′–Hs), 7.49 (dd, 1H, *J*=8.8, 2.5 Hz, C7–H), 7.70 (dd, 1H, *J*=7.2, 1.4 Hz, C6′–H), 8.14 (d, 1H, *J*=2.5 Hz, C5–H), 10.23 (s, 1H, HC═O), 12.56 (broad, 1H, N–H); *m/z* (%) 329 (M^+, 12), 328 (24), 169 (100).

3.3.7. 6-Chloro-2-(*p*-chloroanilino)-3-formylchromone (5g). Reaction of **4b** (313 mg, 1 mmol) with *p*-chloroaniline (117 mg, 1 mmol) afforded the title compound (**5g**, 280 mg) as a yellow crystalline solid (hexane–$CHCl_3$ 3:1); (Found: C, 57.57; H, 2.84; N, 4.17. $C_{16}H_9NO_3Cl_2$ requires C, 57.51; H, 2.71; N, 4.19%); λ_{max}($CHCl_3$): 218.5, 291.5, 246 nm; ν_{max} (KBr): 3230, 3100, 1681, 1627, 1583, 1452 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 6.95 (d, 1H, *J*=8.8 Hz, C8–H), 7.16–7.35 (m, 2H, arom.-Hs), 7.49–7.57 (m, 2H, arom.-Hs), 7.65 (dd, 1H, *J*=8.8, 2.5 Hz, C7–H), 8.17 (d, 1H, *J*=2.5 Hz, C5–H), 10.26 (s, 1H, CH═O), 12.28 (bs, 1H, NH); *m/z* (%) 335 (M^++2, 3), 333 (M^+, 9), 169 (100), 112 (29), 11 (46), 94 (21), 89 (29), 84 (32), 83 (48).

3.3.8. 2-Benzylamino-3-formylchromone (5h). Reaction of **4b** (279 mg, 1 mmol) with benzylamine (107 mg, 1 mmol) afforded the title compound (**5h**, 254 mg) as a white crystalline solid (hexane–$CHCl_3$ 3:1); (Found: C, 72.93; H, 4.73; N, 4.92. $C_{17}H_{13}NO_3$ requires C, 73.11; H, 4.69; N, 5.02%); λ_{max} (MeOH): 318, 270, 228 nm; ν_{max} (KBr): 3276, 2930, 1670, 1636, 1586, 1499 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 4.69 (d, 2H, *J*=6.0 Hz, benzylic Hs), 7.19–7.35 (m, 7H, arom.-Hs), 7.53 (distorted t, 1H, *J*=7.0 Hz, C7–H), 8.13 (dd, 1H, *J*=8.4, 1.6 Hz, C5–H), 10.15 (s, 1H, CHO), 10.88 (bs, 1H, NH); *m/z* (%) 280 (M^++1, 11), 279 (M^+, 52), 251 (24), 250 (100).

3.3.9. 2-*n*-Butylamino-3-formylchromone (5i). Reaction of **4a** (279 mg, 1 mmol) with *n*-butylamine (73 mg, 1 mmol) afforded the title compound (**5i**, 216 mg) as cream colored solid (hexane–$CHCl_3$ 3:1); (Found: C, 68.69; H, 6.02; N, 5.87. $C_{14}H_{15}NO_3$ requires C, 68.56; H, 6.16; N, 5.71%); λ_{max} (MeOH): 320, 268, 247 nm; ν_{max} (KBr): 3225, 2944, 1672, 1635, 1608, 1575, 1455 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 1.00 (t, 3H, *J*=7.4 Hz, CH_3), 1.42–1.54 (m, 2H, CH_2), 1.67–1.77 (m, 2H, CH_2), 3.57–3.63 (m, 2H, N–CH_2), 7.29 (d, 1H, *J*=7.9 Hz, C8–H), 7.38 (distorted triplet, 1H, *J*=7.8 Hz, C6–H), 7.61 (split triplet, 1H, *J*=7.6, 2.3 Hz, C7–H), 8.21 (dd, 1H, *J*=7.9, 2.3 Hz, C5–H), 10.23 (s, 1H, CHO), 10.60 (bs, 1H, N–H); *m/z* (%) 246 (16, M^++1), 245 (M^+, 95), 217 (69), 216 (32), 188 (28), 121 (100).

3.3.10. 2-(*p*-Anisylamino)-3-formylchromone (5j). Reaction of **4a** (279 mg, 1 mmol) with *p*-ansidine (123 mg, 1 mmol) afforded the title compound (**5j**, 277 mg) as yellow solid (hexane–$CHCl_3$ 3:1); (Found: C, 68.93; H, 4.57; N, 4.87. $C_{17}H_{13}NO_4$ requires C, 69.15; H, 4.44; N, 4.74%); λ_{max} (MeOH): 324, 291, 248 nm; ν_{max} (KBr): 3330. 3150, 2940, 1668, 1635, 1575, 1455 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 3.84 (s, 3H, OCH_3), 6.98 (d, 2H, *J*=6.8, arom.-Hs), 7.00–7.30 (m, 2H, arom.-Hs), 7.36–7.43 (m, 2H, C6 and C8–Hs), 7.58–7.64 (m, 1H, C7–H), 8.24 (dd, 1H, *J*=8.1, 2.5 Hz, C5–H), 10.35 (s, 1H, CHO), 12.66 (bs, 1H, NH); *m/z* (%) 295 (M^+, 16), 294 (24), 279 (60), 266 (26), 167 (31), 149 (90), 58 (100).

3.3.11. 2-(*p*-Tolylamino)-3-formylchromone (5k). Reaction of **4a** (279 mg, 1 mmol) with *p*-toluidine (107 mg, 1 mmol) afforded the title compound (**5k**, 246 mg) as yellow solid (hexane–$CHCl_3$ 3:1); (Found: C, 73.19; H, 4.74; N, 4.91. $C_{17}H_{13}NO_3$ requires C, 73.11; H, 4.69; N, 5.02%); λ_{max} (MeOH): 371, 321, 285 nm; ν_{max} (KBr): 3350, 3140, 2940, 1670, 1620, 1462 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 2.41 (s, 3H, CH_3), 7.17–7.48 (m, 6H, arom.-Hs), 7.59 (split triplet, 1H, *J*=7.9, 1.3 Hz, C7–H), 8.23 (br d, 1H, *J*=7.7 Hz, C5–H), 10.29 (s, 1H, CHO), 12.38 (bs, 1H, NH); *m/z*: 279 (M^+, 20), 278 (33), 171 (25), 149 (20), 58 (100).

3.3.12. 2-(β-Naphthylamino)-3-formylchromone (5l). Reaction of **4a** (279 mg, 1 mmol) with β-naphthylamine (143 mg, 1 mmol) afforded the title compound (**5l**, 264 mg) as a yellow solid (hexane–$CHCl_3$ 3:1); (Found: C, 76.06; H, 4.23; N, 4.35. $C_{20}H_{13}NO_3$ requires C, 76.18; H, 4.16; N, 4.44%); λ_{max} (MeOH): 332, 318, 287, 250 nm; ν_{max} (KBr): 3290, 3210, 2940, 1672, 1638, 1608, 1577, 1472; δ_H (200 MHz, $CDCl_3$): 7.25–7.95 (m, 10H, arom.-Hs), 8.08 (d, 1H, *J*=8.0 Hz, C5–H), 10.35 (s, 1H, CHO), 12.61 (bs, 1H, NH); *m/z* (%) 315 (M^+, 3.7), 269 (4.5), 240 (20), 117 (38), 58 (100).

3.3.13. 2-(*o*-Anisylamino)-3-formylchromone (5m). Reaction of **4a** (279 mg, 1 mmol) with *o*-ansidine (123 mg, 1 mmol) afforded the title compound (**5m**, 268 mg) as a yellow solid (hexane–$CHCl_3$ 3:1); (Found: C, 69.16; H, 4.47; N, 4.69. $C_{17}H_{13}NO_4$ requires C, 69.15; H, 4.44; N, 4.74%); λ_{max} ($CHCl_3$): 318, 288, 248 nm; ν_{max}

(KBr): 3330, 3050, 1660, 1636, 1582, 1480; δ_H (200 MHz, $CDCl_3$): 3.93 (s, 3H, OCH_3), 6.91–6.99 (m, 2H, C3′, C8–Hs), 7.11–7.19 (m, 1H, C6–H), 7.25–7.36 (m, 2H, C4′ and C5′–Hs), 7.51–7.55 (m, 1H, C7–H), 7.76 (dd, 1H, J=7.9, 1.4 Hz, C6′–H), 8.18 (dd, 1H, J=7.8, 1.7 Hz, C5–H), 10.24 (s, 1H, HC=O), 12.56 (broad, 1H, N–H); m/z (%) 295 (M^+, 32), 294 (69), 284 (20), 169 (100).

3.3.14. 2-(*p*-Chloroanilino)-3-formylchromone (5n). Reaction of **4a** (279 mg, 1 mmol) with *p*-chloroaniline (127 mg, 1 mmol) afforded the title compound (**5n**, 246 mg) as a yellow solid (hexane–$CHCl_3$ 3:1); (Found: C, 64.18; H, 3.47; N, 4.83. $C_{16}H_{10}NO_3Cl$ requires C, 64.12; H, 3.36; N, 4.67%); λ_{max} ($CHCl_3$): 389.5, 281.5, 248.5 nm; ν_{max} (KBr): 3440, 3082, 1677, 1612, 1461, 1321 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 7.23–7.74 (m, 7H, arom.-Hs), 8.25 (dd, 1H, J=7.8, 2.4 Hz, C5–H), 10.30 (s, 1H, CH=O), 12.44 (bs, 1H, NH); m/z (%) 300 (M^++1, 1), 299 (M^+, 3), 169 (100), 112 (29), 111 (43), 94 (22).

3.4. General procedure for reactions of 2-(*N*-methylanilino)-3-formylchromones (4a,b) with *sec*-cyclic-amines leading to 2-*sec*-cyclic-amino-3-formylchromones (7a–h)

2-(*N*-Methylanilino)-3-formylchromones (**4a**,**b**, 1.0 mmol) were dissolved in dry acetonitrile (50 mL) and to the stirred solution, at 80–90°C bath temperature, was added, dropwise, the solution of an amine (1–1.2 mmol) in dry acetonitrile (5 mL). After completion of reaction (30–45 min, TLC), the solvent was distilled off so as to concentrate the reaction mixture to ~1/7 of its original volume and the concentrate was ice-cooled in a refrigerator for 2 h, when the crystalline products separated out, which were filtered, and re-crystallized from acetonitrile.

3.4.1. 6-Chloro-2-piperidino-3-formylchromone (7a). Obtained by reacting **4b** (313 mg, 1 mmol) with piperidine (92 mg, 1.08 mmol) as cream-colored solid (**7a**, 262 mg); (Found: C, 61.63; H, 4.96; N, 4.71. $C_{15}H_{14}NO_3Cl$ requires C, 61.76; H, 4.84; N, 4.80%); λ_{max} (MeOH): 367, 324, 284.4, 227 nm; ν_{max} (KBr): 1670, 1620, 1542, 1443, 1416 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 1.79 (broad m, 6H, 3×CH_2), 3.64 (broad m, 4H), 7.22 (d, 1H, J=8.8 Hz, C8–H), 7.54 (dd, 1H, J=8.8, 2.4 Hz, C7–H), 8.13 (d, 1H, J=2.4 Hz, C5–H), 10.11 (s, 1H, HC=O); δ_C (75 MHz, $CDCl_3$): 23.65 (CH_2), 26.07 (CH_2), 50.86 (CH_2), 101.49 (C3), 118.15 (C8), 125.53 (C4a), 126.61 (C5), 130.92 (C6), 133.53 (C7), 151.35 (C8a), 162.36 (C2), 177.65 (C4), 186.28 (CHO); m/z (%) 293 (M^++2, 11) 292 (30), 291 (M^+, 30), 167 (25), 149 (79), 71 (58), 70 (47), 58 (100).

3.4.2. 6-Chloro-2-morpholino-3-formylchromone (7b). Obtained by reacting **4b** (313 mg, 1 mmol) with morpholine (94 mg, 1.08 mmol) as light-yellow solid (**7b**, 271 mg); (Found: C; 57.45; H, 4.21; N, 4.89. $C_{14}H_{12}NO_4Cl$ requires C, 57.28; H, 4.12; N, 4.77%); λ_{max} (MeOH): 365.2, 327, 285.6, 230.8 nm; ν_{max} (KBr): 1672, 1639, 1619, 1542, 1434 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 3.69 (dist.t, 4H, J=5.1 Hz), 3.91 (dist. t, 4H, J=5.1 Hz), 7.22 (d, 1H, J=8.8 Hz, C8–H), 7.55 (dd, 1H, J=8.8, 2.5 Hz, C7–H), 8.26 (d, 1H, J=2.5 Hz, C5–H), 10.11 (s, 1H, HC=O); δ_C (75 MHz, $CDCl_3$): 49.93 (CH_2), 66.6 (CH_2), 101.69 (C3), 116.16 (C8), 120.17 (C4a), 124.04 (C5), 131.44 (C6), 133.64 (C7), 151.39 (C8a), 162.64 (C2), 177.53 (C4), 186.59 (HC=O); m/z (%) 295 (M^++2, 9), 294 (M^++1, 5), 293 (M^+, 24), 169 (100), 112 (26).

3.4.3. 6-Chloro-2-[4]*N*-methylpiprazino-3-formylchromone (7c). Reaction of **4b** (313 mg, 1 mmol) with *N*-methylpiperazine (110 mg, 1.1 mmol) afforded **7c** as yellow solid (282 mg); (Found: C, 58.82; H, 5.01; N, 9.36. $C_{15}H_{15}N_2O_3Cl$ requires C, 58.73; H, 4.93; N, 9.13%); λ_{max} (MeOH): 365, 320, 284.5, 228 nm; ν_{max} (KBr): 1673, 1631, 1615, 1544 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 2.37 (s, 3H, *N*–Me), 2.63 (dist.t, 4H, J=5.7 Hz, 2×CH_2), 3.72 (dist.t, 4H, J~5.7 Hz, 2×CH_2), 7.25 (d, 1H, J=8.8 Hz, C8–H), 7.55 (dd, 1H, J=8.8, 2.5 Hz, C7–H), 8.10 (d, 1H, J=2.5 Hz, C5–H), 10.11 (s, 1H, HC=O); δ_C (75 MHz, $CDCl_3$): 45.85 (NCH_3), 49.57 (CH_2), 54.78 (CH_2), 101.68 (C3), 118.17 (C8), 124.07 (C4a), 125.81 (C5), 131.33 (C6), 133.79 (C7), 151.43 (C8a), 162.51 (C2), 177.72 (C4), 186.53 (CHO); m/z (%) 307 (M^+, 4), 283 (15), 169 (94), 112 (26), 111 (46), 71 (100).

3.4.4. 2-Piperidino-3-formylchromone (7d). **4a** (279 mg, 1 mmol) was reacted with piperidine (92 mg, 1.08 mmol) to obtain the title compound (**7d**) as creamy solid (234 mg); (Found: C, 69.84; H, 5.76; N, 5.67. $C_{15}H_{15}NO_3$ requires C, 70.02; H, 5.88; N, 5.44%); λ_{max} (MeOH): 322, 281, 232 nm; ν_{max} (KBr): 1672, 1638, 1590, 1572, 1515, 1465 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 1.80 (broad multiplet, 6H, 3×CH_2), 3.65 (bm, 4H, 2×CH_2), 7.15 (d, 1H, J=8.3 Hz, C8–H), 7.25–7.63 (m, 2H, C6–H and C7–H), 8.20 (dd, 1H, J=7.7, 1.4 Hz, C5–H), 10.12 (s, 1H, CHO); m/z (%) 257 (M^+, 8), 255 (18), 241 (32), 214 (72), 169 (76), 11934), 94 (20), 83 (35), 70 (100).

3.4.5. 2-Morpholino-3-formylchromone (7e). Reacting **4a** (279 mg, 1 mmol) with morpholine (94 mg, 1.08 mmol) afforded **7e** as creamy solid. (243 mg); (Found: C, 64.71; H, 5.22; N, 5.22. $C_{14}H_{13}NO_4$ requires C, 64.86; H, 5.05; N, 5.40%); λ_{max} (MeOH): 318, 280, 234 nm; ν_{max} (KBr): 1671, 1640, 1615, 1590, 1560, 1462 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 3.71 (dist.t, 4H, J=5.3 Hz, 2×CH_2), 3.92 (dist.t, 4H, J=5.3 Hz, 2×–CH_2), 7.27 (d, 1H, J=7.5 Hz, C8–H), 7.39 (dis t, 1H, J=8.0 Hz, C6–H), 7.63 (dis t, 1H, J=7.5 Hz, C7–H), 8.19 (dd, 1H, J=8.0, 1.1 Hz, C5–H), 10.15 (s, 1H, CHO); m/z (%) 260 (17, M^++1), 259 (M^+, 54), 243 (10), 242 (10), 201 (10), 174 (36), 171 (37), 83 (22), 71 (53), 58 (100).

3.4.6. 2-[4]*N*-Methylpiperazino-3-formylchromone (7f). Reacting **4a** (279 mg, 1 mmol) and *N*-methylpiperizine (110 mg, 1.1 mmol) afforded **7f** as creamish-yellow solid. (248 mg); (Found: C, 66.03; H, 5.82; N, 10.51. $C_{15}H_{16}N_2O_3$ requires C, 66.16; H, 5.92; N, 10.29%); λ_{max} (MeOH): 357, 322, 280, 225 nm; ν_{max} (KBr): 1674, 1634, 1612, 1545, 1470, 1430 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 2.36 (bs, 3H, N–CH_3), 2.63 (bm, 4H, 2×–CH_2), 3.72 (bm, 4H, 2×–CH_2), 7.27–7.36 (m, 2H, arom.-Hs), 7.59–7.64 (m, 1H, C7–H), 8.12 (br d, 1H, J=7.8 Hz, C5–H), 10.13 (s, 1H, CHO); m/z (%) 272 (M^+,10), 270 (17), 269 (45), 267 (10), 169 (95), 111 (48), 97 (22), 94 (39), 83 (43), 71 (100).

3.4.7. 6-Chloro-2-pyrrolidino-3-formylchromone (7g). Obtained by reacting **4b** (313 mg, 1 mmol) with pyrrolidine

(85 mg, 1.19 mmol) as pale-yellow solid (**7g**, 252 mg); (Found: C, 60.39; H, 4.49; N, 4.93. $C_{14}H_{12}NO_3Cl$ requires C, 60.55; H, 4.36; N, 5.04%); λ_{max} (MeOH): 317, 278, 227 nm; ν_{max} (KBr): 1674, 1638, 1624, 1545, 1440 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 2.06 (broad, 4H, 2×CH_2), 3.67 (broad, 4H, 2×CH_2), 7.19 (d, 1H, *J*=8.7 Hz, C8–H), 7.49 (dd, 1H, *J*=8.7, 2.6 Hz, C7–H), 8.18 (bs, 1H, C5–H), 10.19 (s, 1H, CH═O); δ_C (75 MHz, $CDCl_3$): 25.16 (CH_2), 51.27 (N–CH_2), 101.5 (C3), 118.04 (C8), 120.12 (C4a), 125.59 (C5), 129.59 (C6), 133.37 (C7), 151.48 (C8a), 161.19 (C2), 176.88 (C4), 187.02 (HC═O); *m/z* (%) 279 (M^++2, 12), 278 (M^++1, 14), 277 (M^+, 21), 249 (65), 241 (41), 221 (100).

3.4.8. 2-Pyrolidino-3-formylchromone (7h). The title compound (**7h**) was obtained by reacting **4a** (279 mg, 1 mmol) with pyrrolidine (85 mg, 1.19 mmol) as cream colored solid. (219 mg); (Found: C, 69.39; H, 5.24; N, 5.61. $C_{14}H_{13}NO_3$ requires C, 69.11; H, 5.39; N, 5.76%); λ_{max} (MeOH): 318, 277, 229 nm; ν_{max} (KBr): 1672, 1636, 1610, 1580, 1534 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 2.05 (broad, 4H, 2×–CH_2), 3.69 (broad, 4H, 2×–CH_2), 7.26 (d, 1H, *J*=8.2 Hz, C8–H), 7.35 (distorted triplet, 1H, *J*=7.3 Hz, C6–H), 7.59 (split triplet, 1H, *J*=7.7, 1.6 Hz, C7–H), 8.18 (dd, 1H, *J*=7.9, 1.6 Hz, C5–H), 10.25 (s, 1H, CHO); *m/z* (%) 244 (M^++1, 2), 243 (M^+, 12), 215 (12), 187 (13), 171 (28), 160 (14), 83 (34), 58 (100).

3.5. General method of preparation of quinilino[2,3-*b*]-chromones (8a–l)

2-Arylamino-3-formylchromones (**2a**,**b**, **5c**–**g** and **5j**–**n**, 1.0 mmol) were stirred with concentrated sulfuric acid (1 mL) to make a paste, which was allowed to stand at room temperature for 5–6 h. It was treated with ice-cold water (100 mL), stirred and extracted with chloroform (2×100 mL). The chloroform extract was washed thoroughly with water and dried over anhyd. sodium-sulfate, filtered and the solvent was distilled off. The obtained solid products (>95% pure, ^1H NMR) were re-crystallized from chloroform–pet. ether (4:1).

3.5.1. Quinolino[2,3-*b*]chroman-12-one (8a). The title compound was obtained by treating **2a** (265 mg, 1 mmol) with sulfuric acid (1 mL) as white solid. (237 mg); mp 211–212°C, Lit.[7a] mp 210–211°C.

3.5.2. 9-Methyl-quinolino[2,3-*b*]chroman-12-one (8b). The title compound (**8b**) was obtained by treating **5k** (279 mg, 1 mmol) with sulfuric acid as light green solid, (251 mg); (Found: C, 78.06; H, 4.37; N, 5.51. $C_{17}H_{11}NO_2$ requires C, 78.15; H, 4.24; N, 5.36%); λ_{max} (CH_3CN): 377.5, 321.5, 308, 256.5, 29.5 nm; ν_{max}: 1670, 1602, 1497, 1461, 1435, 1382 cm^{-1}; δ_H (400 MHz, $CDCl_3$): 2.54 (s, 3H, –CH_3), 7.39 (ddd, 1H, *J*=7.5, 7.4, 0.7 Hz), 7.59 (d, 1H, *J*=8.3, arom.-H), 7.68 (dd, 1H, *J*=8.7, 1.8, arom.-H), 7.75–7.79 (m, 2H, arom.-Hs), 7.95 (d, 1H, *J*= 8.7 Hz, arom.-H), 8.30 (dd, 1H, *J*=7.9, 1.6 Hz, C5–H), 9.12 (s, 1H, C11–H); δ_C (100 MHz, $CDCl_3$): 21.46 (CH_3); 116.33 (C11a), 118.39 (C4), 120.95 (C12a), 124.22 (CH), 126.23 (C10a), 126.92 (CH), 127.76 (CH) 128.01 (CH), 135.92 (CH), 135.96 (C9), 136.36 (C3), 138.96 (C11), 147.94 (C6a), 156.18 (C4a), 157.04 (C5a), 178.11 (C═O); *m/z* (%) 261 (M^+, 11), 169 (100), 111 (46), 84 (37), 83 (47).

3.5.3. 9-Methoxy-quinolino[2,3-*b*]chroman-12-one (8c). The title compound (**8c**) was obtained by treating **5j** (295 mg, 1 mmol) with sulfuric acid, as creamy green solid (265 mg); (Found: C, 73.87; H, 4.07; N, 4.94. $C_{17}H_{11}NO_3$ requires C, 73.64; H, 4.00; N, 5.05%); λ_{max} (CH_3CN): 404, 317.5, 306, 259, 212 nm; ν_{max} (KBr): 1659, 1601, 1560, 1497, 1462 cm^{-1}; δ_H (400 MHz, $CDCl_3$): 3.95 (s, 3H, OMe), 7.26 (dist. t, 1H, *J*=2.7 Hz, C10–H), 7.40 (dt, 1H, J=7.5, 7.1, 1.0 Hz, arom.-H), 7.54 (dd, 1H, *J*=9.3, 2.8 Hz), 7.60 (dd, 1H, *J*=8.4, 0.6 Hz, 1H), 7.78 (ddd, 1H, *J*=7.8, 7.7, 1.7 Hz), 7.97 (d, 1H *J*=9.3 Hz, C7–H), 8.32 (dd, 1H, *J*=7.9, 1.7 Hz), 9.12 (s, 1H, C11–H); δ_C (100 MHz, $CDCl_3$): 55.72 (OCH_3); 105.76 (C10), 116.42 (C11a), 118.44 (CH), 121.00 (C12a), 124.19 (CH), 126.93 (CH), 127.17 (CH), 129.47 (CH), 135.92 (CH), 137.84 (CH), 145.66 (C6a), 156.24 (C4a), 156.26 (C9), 157.64 (C5a), 178.17 (C═O); *m/z* (%) 277 (M^+, 12), 169 (95), 112 (31), 11 (44), 94 (23), 89 (32), 84 (32), 83 (46), 71 (98), 70 (79), 69 (100).

3.5.4. 7-Methoxy-quinolino[2,3-*b*]chroman-12-one (8d). The title compound (**8d**) was obtained by treating **5m** (295 mg, 1 mmol) with sulfuric acid, as light green solid (271 mg); (Found: C, 73.81; H, 4.25; N, 5.32. $C_{17}H_{11}NO_3$ requires C, 73.64; H, 4.00; N, 5.05%); λ_{max} (CH_3CN): 375, 320, 269, 227 nm; ν_{max} (KBr): 1663, 1605, 1519, 1498, 1396 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 4.05 (s, 3H, OCH3), 7.58–7.10 (m, 5H, arom.-Hs), 7.70–7.60 (m, 1H, arom.-H), 8.25 (bd, 1H, *J*=8.0 Hz, C1–H), 9.16 (s, 1H, C11–H); *m/z* (%) 277 (M^+, 9), 169 (100), 154 (50), 153 (55), 112 (34), 111 (46), 98 (31), 97 (39), 96 (40), 84 (48), 83 (65), 71 (48), 70 (84), 69 (75).

3.5.5. 9-Chloro-quinolino[2,3-*b*]chroman-12-one (8e). The title compound (**8e**) was obtained by treating **5n** (299 mg, 1 mmol) with sulfuric acid, as yellow crystalline solid (253 mg); (Found: C, 68.06; H, 2.99; N, 5.04. $C_{16}H_8NO_2Cl$ requires C, 68.22; H, 2.86; N, 4.97%); λ_{max} (CH_3CN): 376.5, 317.5, 290.5, 248 nm; ν_{max}(KBr): 1658, 1605, 1578, 1493, 1472, 1448, 1410, 1300 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 7.43–7.25 (m, 4H, arom.-Hs), 7.68 (d, 2H, *J*=8.8 Hz, arom.Hs), 8.25 (dd, 1H, *J*=7.8, 1.3 Hz, C1–H), 9.05 (s, 1H, C11–H); *m/z* (%) 281 (M^+, 22), 169 (100), 112 (61), 111 (90), 94 (64), 84 (64), 83 (92), 71 (99), 69 (91).

3.5.6. 2-Chloro-quinolino[2,3-*b*]chroman-12-one (8f). It was obtained by treating **5d** (299 mg, 1 mmol) with sulfuric acid, as colorless crystals (**8f**, 264 mg); (Found: C, 68.48; H, 2.96; N, 5.07. $C_{16}H_8NO_2Cl$ requires C, 68.32; H, 2.84; N, 4.98%); ν_{max} (KBr): 1668, 1628, 1601, 1575, 1495, 1470 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 7.40 (d, 1H, *J*= 6.9 Hz, arom.-Hs), 7.49–7.75 (m, 2H, arom.-Hs), 7.92 (m, 1H, arom.-Hs), 8.09 (dd, 1H, *J*=7.0, 2.5 Hz, C3–H), 8.28 (d, 1H, *J*=2.5 Hz, C1–H), 9.28 (s, 1H, C11–H); δ_C (50 MHz, $CDCl_3$): 116.82 (C11a), 118.52 (C4), 121.97 (C12a), 125.60 (CH), 126.61 (C10a), 127.17 (CH), 128.34 (CH), 129.04 (C2), 129.96 (CH), 133.69 (CH), 135.99 (C3), 140.24 (C11), 149.25 (C6a), 155.11 (C4a), 162.95 (C5a), 176.29 (C12); *m/z* (%) 283 (M^++2, 65), 281 (M^+, 100).

3.5.7. 2-Chloro-9-methyl-quinolino[2,3-*b*]chroman-12-one (8g). The title compound (**8g**) was obtained by treating **5d** (313 mg, 1 mmol) with sulfuric acid as light green solid (277 mg); (Found: C, 69.23; H, 3.53; N, 4.90. $C_{17}H_{10}NO_2Cl$ requires C, 69.05; H, 3.41; N, 4.74%); λ_{max} (CH_3CN): 385, 372, 317, 250, 207 nm; ν_{max} (KBr): 1655, 1600, 1508, 1470 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 2.61 (s, 3H, CH_3), 7.57 (d, 1H, *J*=8.8 Hz), 7.72 (bd, 2H, *J*=8.8 Hz), 7.83 (s, 1H, C10–H), 7.99 (d, 1H, *J*=8.6 Hz, C3–H), 8.27 (d, 1H, *J*=2.5 Hz, C5–H), 9.16 (s, 1H, C11–H); *m/z* (%) 297 (M^++2, 0.2), 296 (M^++1, 0.3), 295 (M^+, 3), 169 (100), 112 (29), 111 (41), 94 (22), 89 (31), 84 (35), 83 (46), 69 (48).

3.5.8. 2-Chloro-9-methoxy-quinolino[2,3-*b*]chroman-12-one (8h). The title compound (**8h**) was obtained by treating **5c** (329 mg, 1 mmol) with sulfuric acid as light green solid. (295 mg); (Found: C, 65.69; H, 3.37; N, 4.43. $C_{17}H_{10}NO_3Cl$ requires C, 65.50; H, 3.23; N, 4.49%); λ_{max} (CH_3CN): 400.5, 315, 307, 255, 211 nm; ν_{max} (KBr): 1658 (sharp), 1602, 1560, 1509, 1470 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 3.91 (s, 3H, OCH3), 7.16–7.22 (m, 1H, arom.-Hs), 7.53–7.48 (m, 2H, arom.-Hs), 7.66–7.62 (m, 1H, arom.-Hs), 7.92 (d, 1H, *J*=8.5 Hz, C3–H), 8.22 (bs, 1H, C1–H), 9.08 (s, 1H, C11–H); *m/z* (%) 311 (M^+, (2)), 169 (98), 112 (31), 111 (45), 94 (22), 89 (29), 70 (69), 69 (48), 59 (100).

3.5.9. 2-Chloro-7-methoxy-quinolino[2,3-*b*]chroman-12-one (8i). The title compound (**8i**) was obtained by treating **5f** (329 mg, 1 mmol) with sulfuric acid as light green solid (299 mg); (Found: C, 65.66; H, 3.37; N, 4.56. $C_{17}H_{10}NO_3Cl$ requires C, 65.50; H, 3.23; N, 4.49%); λ_{max} (CH_3CN): 392.5, 347.5, 317.5, 272, 235 nm; ν_{max} (KBr): 1661, 1605, 1558, 1519, 1498, 1477 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 4.07 (s, 3H, OCH_3), 7.12–7.19 (m, 1H, arom.-H), 7.42–7.68 (m, 4H, arom.-Hs), 8.22 (d, 1H, 2.8 Hz, C1–H), 9.17 (s, 1H, C11–H); *m/z* (%) 312 (M^++1, 19), 311 (M^+, 48), 169 (100), 112 (31), 111 (47), 89 (29), 84 (32), 83 (47), 69 (44).

3.5.10. 2,9-Dichloro-quinolino[2,3-*b*]chroman-12-one (8j). The title compound (**8j**) was obtained by treating **5g** (333 mg, 1 mmol) with sulfuric acid, as light green solid. (286 mg); (Found: C, 60.93; H, 2.41; N, 4.28. $C_{16}H_7NO_2Cl_2$ requires C, 60.79; H, 2.23; N, 4.43%); λ_{max} (CH_3CN): 370.5, 313, 304, 252, 207.5 nm; ν_{max} (KBr): 1645, 1604, 1588, 1551, 1451, 1404, 1297 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 7.36–7.21 (m, 2H, arom.-Hs), 7.52–7.41 (m, 3H, arom.-Hs), 8.25 (d, 1H, *J*=2.6 Hz, C1–H), 9.11 (s, 1H, C11–H); *m/z* (%) 316 (M+$^+$1, 1), 315 (M^+, 2), 169 (92), 112 (29), 11 (45), 94 (22), 89 (29), 84 (36), 58 (100).

3.5.11. Benzo(*f*)quinolino[2,3-*b*]chroman-14-one (8k). The title compound (**8k**) was obtained by treating **5l** (314 mg, 1 mmol) with sulfuric acid, as golden yellow solid. (279 mg); (Found: C, 80.93; H, 3.62; N, 4.94. $C_{20}H_{11}NO_2$ requires C, 80.80; H, 3.73; N, 4.71%); λ_{max} (CH_3CN): 384, 364.5, 346, 286, 278, 247.5, 219.5 nm; ν_{max} (KBr): 1664, 1645, 1610, 1445, 1404, 1310 cm^{-1}; δ_H (400 MHz, $CDCl_3$): 7.46 (ddd, 1H, *J*=8.0, 7.4, 1.1 Hz, C2–H), 7.67 (dd, 1H, *J*=8.4, 1.1 Hz, C4–H), 7.71 (ddd, 1H, *J*=8.4, 7.4, 1.5 Hz, C3–H), 7.80–7.84 (m, 2H, C10–H, C11–H), 7.98 and 7.96 (overlapping doublets, 2H, *J*=8.2, 9.2 Hz, C9–H, C8–H), 8.16 (d, 1H, *J*=9.2 Hz, C7–H), 8.40 (dd, 1H, *J*=8.0, 1.5 Hz, C1–H), 8.80 (br d, 1H, *J*=8.2 Hz, C12–H), 10.00 (s, 1H, C13–H); δ_C (100 MHz, $CDCl_3$): 115.37 (C13a), 118.53 (C4), 121.37 (C14a), 123.14 (CH), 123.83 (C12a′), 124.52 (CH), 126.77 (CH), 126.98 (CH), 127.86 (CH), 128.47 (CH), 129.15 (CH), 130.07 and 131.16 (C8a and C12a), 133.60 (CH), 135.67 (CH), 135.88 (CH), 150.93 (C6a), 156.11 (C4a), 158.25 (C5a), 178.08 (C14); *m/z* (%) 298 (M^++1, 1), 297 (M^+, 5), 169 (100), 112 (30), 111 (41), 97 (29), 94 (28), 85 (25), 84 (35), 83 (48).

3.5.12. 2-Chlorobenzo(*f*)quinolino[2,3-*b*]chroman-14-one (8l). The title compound (**8l**) was obtained by treating **5e** (348 mg, 1 mmol) with sulfuric acid as golden yellow solid. (323 mg); (Found: C, 72.56; H, 3.24; N, 4.34. $C_{20}H_{10}NO_2Cl$ requires C, 72.41; H, 3.04; N, 4.22%); λ_{max} (CH_3CN): 386.5, 367, 348.5, 290, 247 nm; ν_{max} (KBr): 1656, 1604, 1480, 1465, 1410, 1381 cm^{-1}; δ_H (200 MHz, $CDCl_3$): 7.64–7.82 (m, 4H, arom.-Hs), 7.82–7.96 (m, 2H, arom.-Hs), 8.16 (d, 1H, *J*=9.2 Hz, arom.-H, C7–H), 8.34 (d, 1H, *J*=1.5 Hz, C1–H), 8.78 (d, 1H, *J*=8.0 Hz, C12–H), 9.96 (s, 1H, C13–H); *m/z* (%) 333 (M+$^+$2, 7), 332 (M+$^+$1, 4), 331 (M^+, 10), 169 (100), 112 (28), 111 (46), 94 (22), 89 (31), 84 (33), 83 (46).

3.5.13. 6-Chloro-1*H*-[1]-benzopyrano[2,3-*c*]pyrazole-4-one (9). 6-Chloro-2-*N*-methylanilino-3-formyl-chromone (**4b**, 313 mg, 1 mmol) was dissolved in hot aqueous acetonitrile (80:20, 60 mL) and the hydrazine hydrate (50 mg, 1 mmol) was added to the above solution, and the contents stirred overnight at room temperature. A yellow solid (110 mg), practically insoluble in any solvent, separated out, which was filtered off. The filtrate was concentrated under vacuum to ~1/5 of its original volume and kept at room temperature, when the title compound (**9**) separated out as a white crystalline solid in a day, and was re-crystallized from acetone (99 mg, 45%); mp 241–242°C; (Found: C, 54.26; H, 2.39; N, 12.93. $C_{10}H_5N_2O_2Cl$ requires C, 54.44; H, 2.28; N, 12.70%); λ_{max} (MeOH): 322, 265, 223 nm; ν_{max} (KBr): 3274, 1649, 1636, 1586, 1465 cm^{-1}; δ_H (300 MHz, DMSO-d_6): 7.49 (d, 1H, *J*=8.9 Hz, C8–H), 7.64 (dd, 1H, *J*=8.9, 2.73 Hz, C7–H), 8.20 (d, 1H, *J*=2.7 Hz, C5–H), 8.24 (s, 1H, C3–H), 13.57 (b, 1H, N–H); δ_C(75 MHz, DMSO-d_6): 105.30 (C3), 119.35 (C8), 123.01 (C4a), 125.59 (C5), 127.95 (C1′), 128.33 (C6), 133.70 (C7), 153.80 (C8a), 161 (C2), 173 (C4); *m/z* (%) 222 (M^++2, 18), 221 (M^++1, 9), 220 (M^+, 45), 171 (10), 167 (29), 149 (72), 112 (15), 83 (77), 71 (58), 58 (100).

3.5.14. 3-Chloro-12*H*-[1]-benzopyrano[2,3-*e*]-1,5-benzodiazepine (10). Chromone (**4b**, 313 mg, 1 mmol) was dissolved in refluxing aqueous acetonitrile (80:20) and the solution of *o*-phenylenediamine (108 mg, 1 mmol) in acetonitrile (4 mL) was added to the above refluxing solution. The contents were refluxed for 6 h and cooled. A yellow crystalline solid which separated out was filtered and washed with little cold acetonitrile and re-crystallized from hexane–$CHCl_3$ (3:1), to obtain the title compound (**10**, 278 mg, 94%); mp 273–274°C; (Found: C, 64.89; H, 2.95; N, 9.32. $C_{16}H_9N_2O_2Cl$ requires C, 64.77; H, 3.06; N, 9.44%); λ_{max} (MeOH): 406, 340, 302, 247 nm; ν_{max} (KBr): 3315, 2960, 1663, 1641, 1602, 1581, 1564, 1499 cm^{-1}; δ_H

(200 MHz, $CDCl_3$): 7.24–7.31 (m, 2H, arom.-Hs), 7.54–7.59 (m, 2H, arom.-Hs), 7.66–7.74 (m, 2H, arom.-Hs), 8.31 (d, 1H, J=2.47 Hz, C4–H), 9.32 (s, 1H, C6–H), 11.67 (bs, 1H, NH); m/z (%) 298 (M^++2, 4.1), 297 (M^++1, 3.2), 296 (M^+, 10), 283 (4), 183 (16), 171 (22), 149 (15), 112 (20), 71 (48), 58 (100).

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