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REACTION OF 3-IODOCHROMONE WITH NUCLEOPHILES 3. FORMATION OF 2-AMINOMETHYLENE-3(2*H*)-BENZOFURANONES BY THE REACTION WITH SECONDARY AMINES

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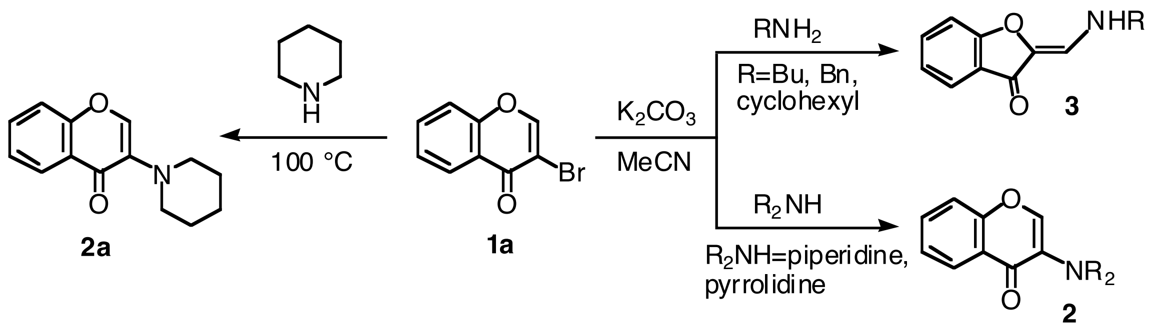
Abstract – 3-Iodochromone (**4a**) easily reacted with secondary amines in the presence of potassium carbonate to give 2-aminomethylene-3(2*H*)-benzofuranones in good yields. Under similar conditions without potassium carbonate, **4a** was reacted with piperidine to give the enamino ketone (**5**) as the major product.

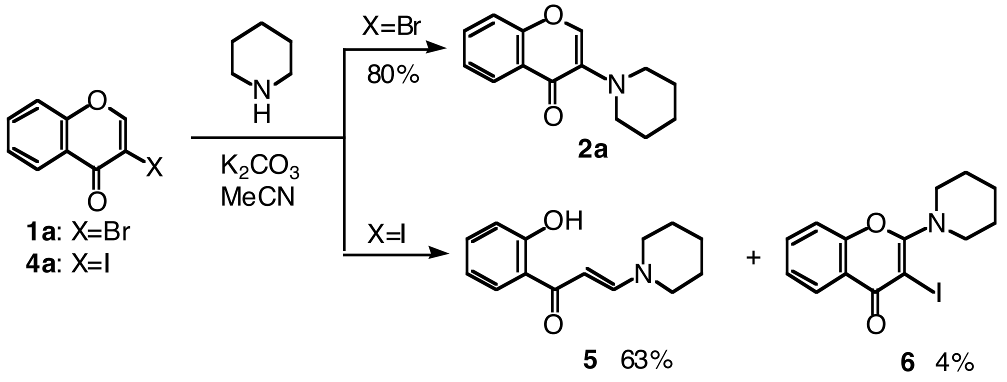
4*H*-Benzopyran-4-ones (chromones) and 3(2*H*)-benzofuranones are important classes of oxygenated heterocyclic compounds that have attracted the attention of organic chemists and biochemists because of their biological activities and occurrence in natural products.[1] Furthermore, chromones having an electron-withdrawing group at the 3-position are highly functional molecules, capable of reacting as Michael acceptors,[2] heterodienes,[3] and dienophiles.[4] During the course of our investigations to develop new reactions of chromones with several reagents, we found that the 3-halochromones, especially 3-iodochromone, act as a good Michael acceptor in conjugate addition reactions.[5] In our previous paper,[5a] we reported the Michael-type reaction of 3-iodochromone with azoles such as imidazole, pyrrole, pyrazole, triazole, and indazole in the presence of potassium carbonate in DMF to produce the 2-(1-azolyl)chromones in high yields. Interestingly, the treatment with indole as a nucleophile afforded 2-(1-indolyl)chromone and the contraction product, 2-(1-indolylmethylene)-3(2*H*)-benzofuranone. The formation of the benzofuranone derivatives was found to be affected by the electron density on the nitrogen atom in the indole ring. Thus, the nitrogen atom in the indole is more electron rich than the other azoles.[6] We postulated in previous reports that the treatment of 3-iodochromone with electron rich-amines under similar reaction conditions will produce the 2-aminomethylene-3(2*H*)-benzofuranones as the major product.

This postulation is supported by a few reports.[7] While Winter and Hamilton reported that the reaction of 3-bromochromone (**1a**) with piperidine at 100 °C gave the 3-piperidinochromone (**2a**) as the major product,[7a] Gammill and co-workers reported that the reaction of **1a** with primary and secondary amines under the K_2CO_3-mediated reaction conditions (2 eq. amine/1.5 eq. K_2CO_3/MeCN/rt) (reaction condition A) gave two products (**2** and **3**) (Scheme 1).[7c] Primary amines gave the ring-contraction products (**3**) as the major product and the secondary amines such as piperidine and pyrrolidine gave the 3-aminochromones (**2**) as the sole product.



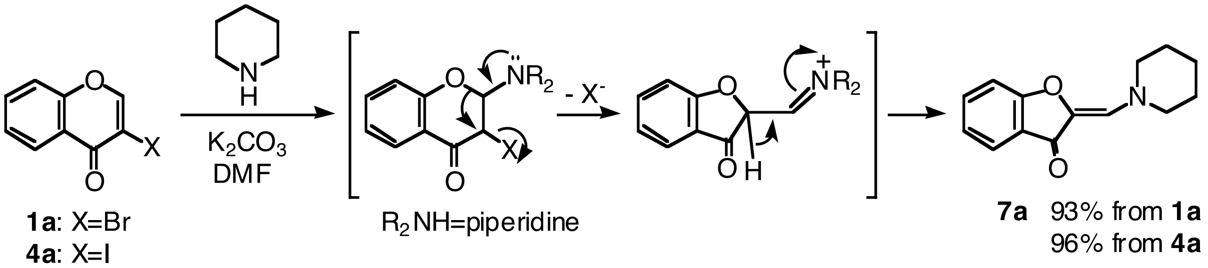
Scheme 1

When we repeated the Gammill's reaction[7c] with 3-bromochromone (**1a**), the 3-piperidinochromone (**2a**) was obtained as the major product. However, when the reaction was carried out with 3-iodochromone (**4a**),[8] the enamino ketone (**5**)[9] and 3-iodo-2-piperidinochromone (**6**) were obtained in 63 and 4% yields, respectively, and no 3-piperidinochromone (**2a**) was detected (Scheme 2).



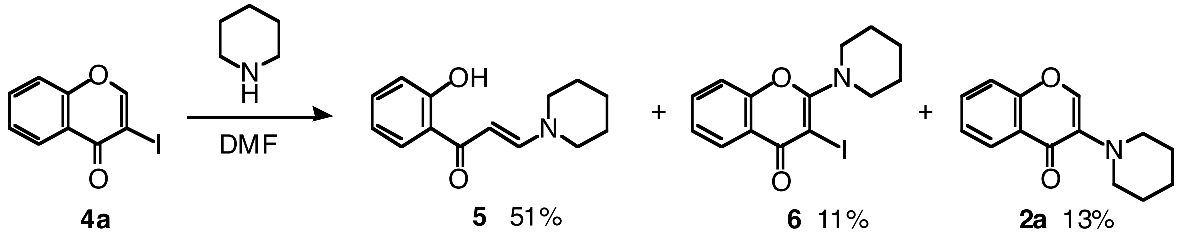
Scheme 2

When DMF was employed as the solvent (reaction condition B), the ring-contraction product, 3-piperidinomethylene-3(2*H*)-benzofuranone (**7a**), was obtained in high yield (Scheme 3). The possible reaction pathway is shown in Scheme 3.[5a,7c]



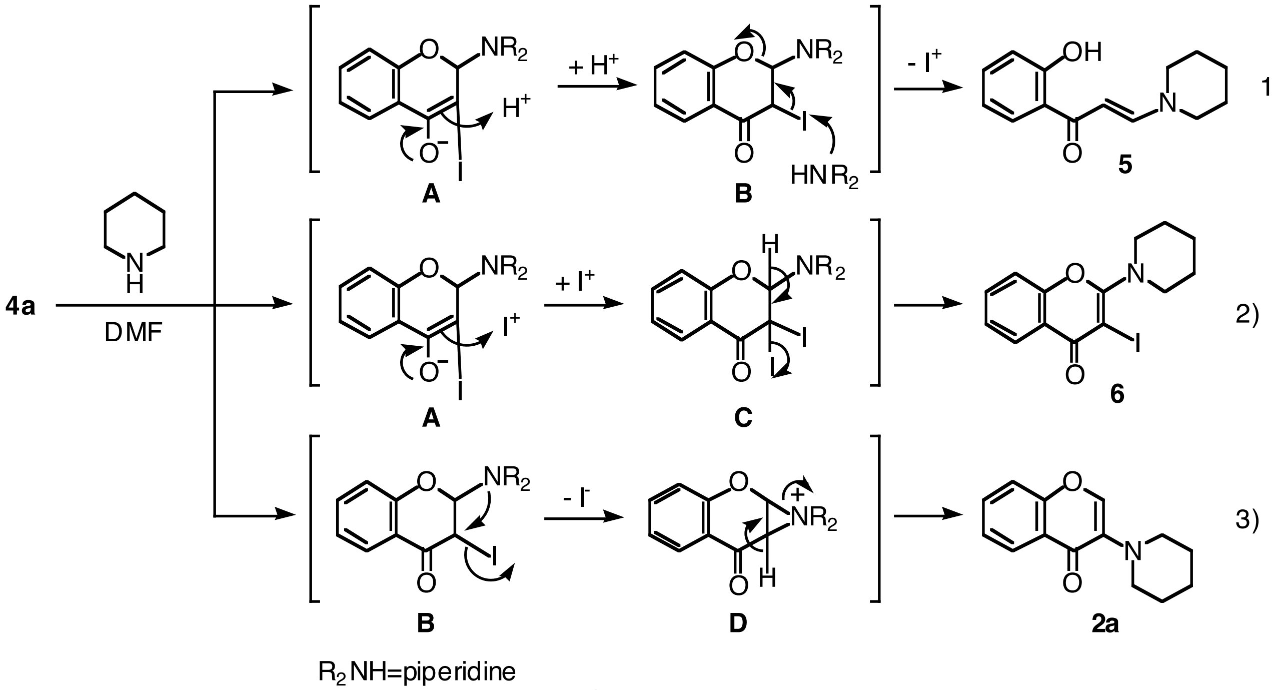
Scheme 3

However, in the reaction without potassium carbonate, **4a** did not give the benzofuranone (**7a**), but the enamino ketone (**5**), 3-iodo-2-piperidinochromone (**6**), and 3-piperidinochromone (**2a**) were obtained (Scheme 4).



Scheme 4

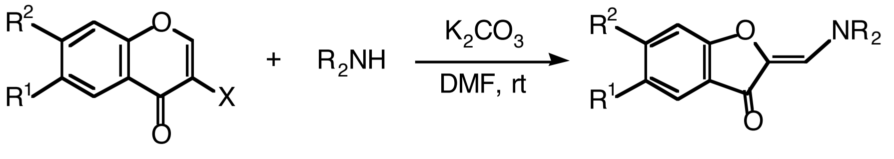
The formation of the compound (**5**) possibly involves the attack of the amine at the iodine atom of the α-iodo ketone moiety in the formed intermediate (**B**) followed by cleavage of the carbon-oxygen bond of the benzopyran ring (eq. 1, Scheme 5).[9] The plausible reaction mechanisms for the formation of the products (**5**, **6**, and **2a**) in the absence of potassium carbonate are shown in Scheme 5. In this reaction, we expected that the addition of iodine to the reaction mixture would promote the formation of the intermediate (**C**) and the yield of **6** would be increased. As expected, the addition of iodine changed the yield for 3-iodo-2-piperidinochromone (**6**) from 11% to 24% and that for the enamino ketone (**5**) from 51% to 16%. This fact supports the reaction mechanism (eq. 2).



Scheme 5

The obtained ring-contraction product (**7a**) was found to have the molecular formula, $C_{14}H_{15}NO_2$, based on the elemental analytical data and the MS spectra [*m/z* 229 (M^+)]. The ^{1}H-NMR spectrum showed a singlet at 7.05 ppm for the new olefinic proton and four aromatic proton signals of the benzofuran ring at 7.14, 7.21, 7.49, and 7.80 ppm along with the aliphatic proton signals of the piperidine ring.

Further examples for the formation of benzofuranones from 3-halochromones with several secondary amines are summarized in Table 1. Both 3-iodochromone (**4a**) and 3-bromochromone (**1a**) effectively reacted with piperidine to give **7a** in high yields (Entries 1 and 2). 3-Chlorochromone (**8a**) also gave **7a** in 72% yield but required a long reaction (Entry 3). 3-Iodochromone having a methoxy group also gave the corresponding benzofuranones (**7b**, **7c**) in high yields (Entries 4 and 5). Furthermore, the benzofuranones were obtained in more than 80% yield irrespective of the ring size of the secondary amines (Entries 6-8). Other secondary amines such as the morpholine, thiomorpholine, and piperazine derivatives also gave the corresponding benzofuranones (**12-16**) in high yield (Entries 9-17).

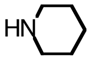
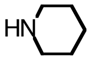
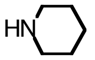
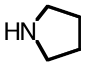
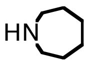
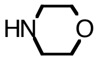
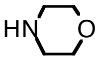
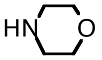
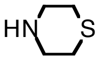
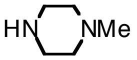
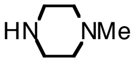
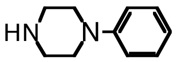
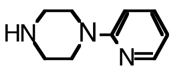


4: X=I, **1**: X=Br, **8**: X=Cl

a: R^1=R^2=H, **b**: R^1=OMe, R^2=H, **c**: R^1=H, R^2=OMe

7, 9-16

Table 1. Reactions of 3-iodochromones with the secondary amines (reaction condition B)

Entry	Chromone	Amine	Time/h	Product	Yield/%
1	**4a**		0.5	**7a**	96
2	**1a**		4	**7a**	93
3	**8a**		20	**7a**	72
4	**4b**		1	**7b**	91
5	**4c**		2	**7c**	84
6	**4a**		2	**9a**	88
7	**4a**		1	**10a**	95
8	**4a**	$HNEt_2$	1	**11a**	89
9	**4a**		1	**12a**	88
10	**4b**		2	**12b**	91
11	**4c**		3.5	**12c**	93
12	**4a**		1	**13a**	88
13	**4a**		1	**14a**	90
14	**4b**		2	**14b**	87
15	**4c**		2.5	**14c**	88
16	**4a**		2	**15a**	93
17	**4a**		1	**16a**	91

In summary, we have demonstrated that the reaction of the 3-halochromones with secondary amines in the presence of K_2CO_3 using DMF as the solvent (reaction condition B) gave the corresponding 2-aminomethylene-3(2*H*)-benzofuranones in good yields. In this study, we extended our synthetic methodology for the oxygenated heterocyclic compounds. This ring-contraction reaction may be used as the entry for the syntheses of some benzofuran systems.

EXPERIMENTAL

All melting points were determined using a Yanagimoto micro-hot stage apparatus and are uncorrected. IR spectra were recorded using a JASCO FT/IR-5300 spectrophotometer and NMR spectra were measured using a JEOL JNM-A500 with tetramethylsilane as an internal standard. MS spectra were recorded using a JEOL JMS-700 spectrometer. Column chromatography was done on a BW-820 MH (Fuji silysia).

General Procedure for the Reaction of 3-Iodochromone with Secondary Amines. To a mixture of 3-iodochromone (**4a**) (272 mg, 1 mmol) and K_2CO_3 (1.4 g, 10 mmol) in DMF (10 mL) was added a solution of a secondary amine (1.5 mmol) in DMF (2 mL) at rt. After being stirred for 1-2 h, the reaction mixture was diluted with ice-water and extracted with $CHCl_3$ (20 mL x 3). The organic layer was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/AcOEt = 1 : 1 with gradual increase of ethyl acetate) to afford the 2-aminomethylene-3(2*H*)-benzofuranone. The yields are given in Table 1.

2-Piperidinomethylene-3(2*H*)-benzofuranone (7a): yellow prism (from Et_2O-hexane), mp 120-121 °C; IR (KBr) 1680, 1620, 1580, 1454 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.72 (6H, m, CH_2), 3.70 (4H, m, CH_2), 7.05 (1H, s, =CH), 7.14 (1H, ddd, *J* = 7.7, 7.3, 0.9 Hz, H-5), 7.21 (1H, dd, *J* = 8.2, 0.9 Hz, H-7), 7.49 (1H, ddd, *J* = 8.2, 7.3, 1.5 Hz, H-6), 7.80 (1H, dd, *J* = 7.7, 1.5 Hz, H-4); ^{13}C-NMR ($CDCl_3$) δ 23.76, 26.22, 49.37, 55.36, 112.13, 121.83, 123.25, 124.08, 129.04, 129.80, 132.98, 161.37, 180.10; MS *m/z* 229 (M^+). *Anal.* Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.23; H, 6.47; N, 6.03.

5-Methoxy-2-piperidinomethylene-3(2*H*)-benzofuranone (7b): orange prism (from AcOEt-hexane), mp 154-155 °C; IR (KBr) 1674, 1574, 1487, 1451 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.70 (6H, m, CH_2), 3.70 (4H, m, CH_2), 3.83 (3H, s, OMe), 7.04 (1H, s, =CH), 7.10 (1H, dd, *J* = 8.8, 2.4 Hz, H-6), 7.12 (1H, dd, *J* = 8.8, 0.9 Hz, H-7), 7.23 (1H, dd, *J* = 2.4, 0.9 Hz, H-4); ^{13}C-NMR ($CDCl_3$) δ 23.72, 26.20, 48.81, 55.23, 55.77, 103.75, 112.88, 122.71, 124.11, 129.83, 129.90, 155.04, 156.43, 180.09; MS *m/z* 259 (M^+). *Anal.* Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.38; H, 6.44; N, 5.32.

6-Methoxy-2-piperidinomethylene-3(2*H*)-benzofuranone (7c): pale yellow needles (from AcOEt-hexane), mp 118-119 °C; IR (KBr) 1671, 1647, 1620, 1566, 1494, 1466 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.70 (4H, m, CH_2), 1.88 (2H, m, CH_2), 3.67 (4H, m, CH_2), 3.86 (3H, s, OMe), 6.67 (1H, d, *J* = 2.1 Hz, H-7), 6.72 (1H, dd, *J* = 8.5, 2.1 Hz, H-5), 6.93 (1H, s, =CH), 7.68 (1H, d, *J* = 8.5 Hz, H-4); ^{13}C-NMR ($CDCl_3$) δ 23.72, 26.09, 52.14, 55.49, 95.69, 110.88, 117.12, 123.98, 128.42, 129.39, 163.43, 164.51, 179.45; MS *m/z* 259 (M^+). *Anal.* Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.28; H, 6.48; N, 5.27.

2-Pyrrolidinomethylene-3(2*H*)-benzofuranone (9a): yellow needles (from AcOEt-hexane), mp 140-141 °C; IR (KBr) 1678, 1620, 1574, 1478, 1456, 1431 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 2.02 (4H, m, CH_2), 3.65 (2H, m, CH_2), 3.85 (2H, m, CH_2), 7.14 (1H, ddd, *J* = 7.7, 7.3, 0.6 Hz, H-5), 7.19 (1H, dd, *J* = 8.5, 0.6 Hz, H-7), 7.34 (1H, s, =CH), 7.48 (1H, ddd, *J* = 8.5, 7.3, 1.5 Hz, H-6), 7.81 (1H, dd, *J* = 7.7, 1.5 Hz, H-4); ^{13}C-NMR ($CDCl_3$) δ 24.91, 25.92, 49.20, 53.50, 112.15, 121.63, 123.35, 124.36, 127.86, 130.65, 132.82, 161.88, 179.43; MS *m/z* 215 (M^+). *Anal.* Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.43; H, 6.01; N, 6.45.

2-Hexamethyleneiminomethylene-3(2*H*)-benzofuranone (10a): pale yellow prism (from AcOEt-hexane), mp 121-122 °C; IR (KBr) 1680, 1618, 1578, 1472, 1445 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.61 (4H, m, CH_2), 1.82 (2H, m, CH_2), 1.90 (2H, m, CH_2), 3.52 (2H, t, *J* = 6.1 Hz, CH_2), 3.88 (2H, t, *J* = 6.1 Hz, CH_2), 7.12 (1H, s, =CH), 7.14 (1H, ddd, *J* = 7.9, 7.3, 0.6 Hz, H-5), 7.20 (1H, dt, *J* = 8.5, 0.6 Hz, H-7), 7.48 (1H, ddd, *J* = 8.5, 7.3, 1.5 Hz, H-6), 7.81 (1H, ddd, *J* = 7.9, 1.5, 0.6 Hz, H-4); ^{13}C-NMR ($CDCl_3$) δ 25.99, 27.09, 27.83, 29.46, 50.29, 57.45, 112.10, 121.67, 123.23, 124.10, 129.51, 130.89, 132.82, 161.63, 179.71; MS *m/z* 243 (M^+). *Anal.* Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 73.94; H, 6.99; N, 5.67.

2-Diethylaminomethylene-3(2*H*)-benzofuranone (11a): pale yellow oil; IR ($CHCl_3$) 1680, 1620, 1578, 1468, 1443 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.32 (6H, t, *J* = 7.2 Hz, Me), 3.55 (4H, m, CH_2), 7.11 (1H, s, =CH), 7.14 (1H, ddd, *J* = 7.7, 7.3, 0.6 Hz, H-5), 7.21 (1H, dt, *J* = 8.2, 0.6 Hz, H-7), 7.49 (1H, ddd, *J* = 8.5, 7.3, 1.5 Hz, H-6), 7.81 (1H, ddd, *J* = 7.7, 1.5, 0.6 Hz, H-4); ^{13}C-NMR ($CDCl_3$) δ 14.16, 44.64, 50.85, 112.01, 121.57, 123.06, 123.95, 129.29, 129.58, 132.76, 161.49, 179.52; High-resolution MS *m/z* Calcd for $C_{13}H_{15}NO_2$ (M^+): 217.1103, Found: 217.1110.

2-Morpholinomethylene-3(2*H*)-benzofuranone (12a): pale yellow needles (from AcOEt-hexane), mp 142-143 °C; IR (KBr) 1690, 1630, 1597, 1451 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.76 (4H, m, CH_2), 3.82 (4H, m, CH_2), 6.98 (1H, s, =CH), 7.16 (1H, ddd, *J* = 7.6, 7.3, 0.6 Hz, H-5), 7.20 (1H, dt, *J* = 8.5, 0.6 Hz, H-7), 7.52 (1H, ddd, *J* = 8.5, 7.3, 1.5 Hz, H-6), 7.80 (1H, ddd, *J* = 7.6, 1.5, 0.6 Hz, H-4); ^{13}C-NMR ($CDCl_3$) δ 50.79, 66.63, 112.16, 122.09, 123.39, 123.64, 128.54, 129.50, 133.57, 161.86, 180.73; MS *m/z* 231 (M^+). *Anal.* Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.40; H, 5.53; N, 5.98.

5-Methoxy-2-morpholinomethylene-3(2*H*)-benzofuranone (12b): pale yellow needles (from AcOEt-hexane), mp 148-149 °C; IR (KBr) 1680, 1591, 1491, 1458 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.75 (4H, m, CH_2), 3.82 (4H, m, CH_2), 3.83 (3H, s, OMe), 6.97 (1H, s, =CH), 7.10 (1H, d, *J* = 8.8 Hz, H-7), 7.13 (1H, dd, *J* = 8.8, 2.4 Hz, H-6), 7.22 (1H, d, *J* = 2.4 Hz, H-4); ^{13}C-NMR ($CDCl_3$) δ 50.73, 55.72, 66.59, 103.84, 112.90, 123.23, 123.68, 128.57, 130.27, 155.15, 156.91, 180.73; MS *m/z* 261 (M^+). *Anal.* Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.52; H, 5.96; N, 5.11.

6-Methoxy-2-morpholinomethylene-3(2*H*)-benzofuranone (12c): pale yellow prism (from AcOEt-hexane), mp 177-178 °C; IR (KBr) 1680, 1620, 1593, 1493, 1437 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.70 (4H, m, CH_2), 3.81 (4H, m, CH_2), 3.87 (3H, s, OMe), 6.65 (1H, d, *J* = 2.1 Hz, H-7), 6.73 (1H, dd, *J* = 8.5, 2.1 Hz, H-5), 6.84 (1H, s, =CH), 7.68 (1H, d, *J* = 8.5 Hz, H-4); ^{13}C-NMR ($CDCl_3$) δ 50.60, 55.56, 66.54, 95.75, 111.05, 116.68, 124.17, 127.12, 129.98, 164.00, 164.92, 179.95; MS *m/z* 261 (M^+). *Anal.* Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.63; H, 5.86; N, 5.08.

2-Thiomorpholinomethylene-3(2*H*)-benzofuranone (13a): pale yellow needles (from AcOEt-hexane), mp 185-186 °C; IR (KBr) 1690, 1624, 1593, 1453 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 2.48 (4H, t, *J* = 5.2 Hz, CH_2), 4.00 (4H, m, CH_2), 6.95 (1H, s, =CH), 7.16 (1H, ddd, *J* = 7.9, 7.3, 0.6 Hz, H-5), 7.21 (1H, dd, *J* = 8.5, 0.6 Hz, H-7), 7.52 (1H, ddd, *J* = 8.5, 7.3, 1.2 Hz, H-6), 7.79 (1H, dd, *J* = 7.9, 1.2 Hz, H-4); ^{13}C-NMR ($CDCl_3$) δ 27.72, 53.30, 112.22, 122.16, 123.47, 123.68, 128.42, 129.46, 133.63, 161.95, 180.88; MS *m/z* 247 (M^+). *Anal.* Calcd for $C_{13}H_{13}NO_2S$: C, 63.14; H, 5.30; N, 5.66. Found: C, 62.95; H, 5.17; N, 5.64.

2-[(4-Methylpiperazino)methylene]-3(2*H*)-benzofuranone (14a): pale yellow needles (from AcOEt-hexane), mp 138-140 °C; IR (KBr) 1686, 1626, 1595, 1456 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 2.35 (3H, s, Me), 2.55 (4H, t, *J* = 5.2 Hz, CH_2), 3.77 (4H, m, CH_2), 7.00 (1H, s, =CH), 7.15 (1H, ddd, *J* = 7.6, 7.0, 0.6 Hz, H-5), 7.20 (1H, dt, *J* = 8.5, 0.6 Hz, H-7), 7.50 (1H, ddd, *J* = 8.5, 7.0, 1.5 Hz, H-6), 7.79 (1H, ddd, *J* = 7.6, 1.5, 0.6 Hz, H-4); ^{13}C-NMR ($CDCl_3$) δ 45.95, 50.56, 54.74, 112.14, 121.97, 123.34, 123.83, 128.95, 129.36, 133.33, 161.68, 180.51; MS *m/z* 244 (M^+). *Anal.* Calcd for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.69; H, 6.48; N, 11.41.

5-Methoxy-2-[(4-methylpiperazino)methylene]-3(2*H*)-benzofuranone (14b): pale yellow needles (from AcOEt-hexane), mp 146-147 °C; IR (KBr) 1682, 1618, 1593, 1487, 1451 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 2.35 (3H, s, Me), 2.54 (4H, t, *J* = 5.2 Hz, CH_2), 3.77 (4H, m, CH_2), 3.83 (3H, s, OMe), 6.99 (1H, s, =CH), 7.12 (2H, m, H-6 and 7), 7.22 (1H, m, H-4); ^{13}C-NMR ($CDCl_3$) δ 45.88, 50.65, 54.68, 55.71, 103.79, 112.87, 123.00, 123.85, 129.00, 130.12, 155.08, 156.71, 180.47; MS *m/z* 274 (M^+). *Anal.* Calcd for $C_{15}H_{18}N_2O_3$: C, 65.68; H, 6.61; N, 10.21. Found: C, 65.56; H, 6.49; N**,** 10.15**.**

6-Methoxy-2-[(4-methylpiperazino)methylene]-3(2*H*)-benzofuranone (14c): pale yellow needles (from AcOEt-hexane), mp 151-152 °C; IR (KBr) 1688, 1626, 1584, 1497, 1462, 1441 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 2.35 (3H, s, Me), 2.52 (4H, t, *J* = 5.2 Hz, CH_2), 3.72 (4H, m, CH_2), 3.87 (3H, s, OMe), 6.66 (1H, d, *J* = 2.1 Hz, H-7), 6.73 (1H, dd, *J* = 8.5, 2.1 Hz, H-5), 6.87 (1H, s, =CH), 7.68 (1H, d, *J* = 8.5 Hz, H-4); ^{13}C-NMR ($CDCl_3$) δ 45.92, 50.49, 54.66, 55.56, 95.73, 110.98, 116.87, 124.11, 127.54, 129.80, 163.79, 164.76, 179.79; MS m/z 274 (M^+). *Anal.* Calcd for $C_{15}H_{18}N_2O_3$: C, 65.68; H, 6.61; N, 10.21. Found: C, 65.53; H, 6.42; N, 10.12.

2-[(4-Phenylpiperazino)methylene]-3(2*H*)-benzofuranone (15a): yellow needles (from AcOEt-hexane), mp 163-164 °C; IR (KBr) 1686, 1628, 1595, 1501, 1451 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 3.32 (4H, t, *J* = 5.2 Hz, CH_2), 3.90 (4H, m, CH_2), 6.92-6.98 (3H, m, Ph), 7.06 (1H, s, =CH), 7.16 (1H, ddd, *J* = 7.7, 7.3, 0.6 Hz, H-5), 7.22 (1H, dt, *J* = 8.5, 0.6 Hz, H-7), 7.31 (2H, dd, *J* = 8.5, 7.3 Hz, Ph), 7.52 (1H, ddd, *J* = 8.5, 7.3, 1.5 Hz, H-6), 7.80 (1H, ddd, *J* = 7.7, 1.5, 0.6 Hz, H-4); ^{13}C-NMR ($CDCl_3$) δ 49.66, 50.43, 112.16, 116.75, 120.77, 122.04, 123.35, 123.74, 128.53, 129.20, 129.49, 133.45, 150.55, 161.77, 180.60; MS *m/z* 306 (M^+). *Anal.* Calcd for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.14. Found: C, 74.37; H, 5.93; N, 9.04.

2-{[4-(2-Pyridyl)piperazino]methylene}-3(2*H*)-benzofuranone (16a): yellow needles (from AcOEt-hexane), mp 165-167 °C; IR (KBr) 1688, 1634, 1591, 1487, 1439 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 3.72 (4H, m, CH_2), 3.86 (4H, m, CH_2), 6.68-6.74 (2H, m, Py), 7.07 (1H, s, =CH), 7.16 (1H, ddd, *J* = 7.7, 7.0, 0.6 Hz, H-5), 7.23 (1H, dd, *J* = 8.5, 0.6 Hz, H-7), 7.52 (1H, ddd, *J* = 8.5, 7.0, 1.0 Hz, H-6), 7.54 (1H, m, Py), 7.80 (1H, dd, *J* = 7.7, 1.0 Hz, H-4), 8.23 (1H, m, Py); ^{13}C-NMR ($CDCl_3$) δ 45.35, 50.27, 107.22, 112.16, 114.12, 122.02, 123.33, 123.71, 128.55, 129.52, 133.45, 137.65, 147.93, 158.65, 161.77, 180.58; MS *m/z* 307 (M^+). *Anal.* Calcd for $C_{18}H_{17}N_3O_2$: C, 70.34; H, 5.58; N, 13.67. Found: C, 70.30; H, 5.39; N, 13.61.

Reaction of 3-iodochromone (4a) with piperidine in the absence of potassium carbonate. To a solution of 3-iodochromone (**4a**) (272 mg, 1 mmol) in DMF (10 mL) was added a solution of piperidine (170 mg, 2 mmol) in DMF (2 mL) at 0 °C. After being stirred for 1 h at rt, the reaction mixture was diluted with ice-water and extracted with ether (20 mL x 3). The combined organic layers were dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/AcOEt = 8 : 1) to afford the enamino ketone (**5**, 118 mg, 51%), 3-iodo-2-piperidinochromone (**6**, 39 mg, 11%), and 3-piperidinochromone (**2a**, 30 mg, 13%).

The reaction of **4a** (272 mg, 1 mmol) with piperidine (170 mg, 2 mmol) under similar conditions in the presence of iodine (254 mg, 1 mmol) also gave **5** (37 mg, 16%), **6** (85 mg, 24%), and **2a** (32 mg, 14%).

1-[2-(2-Hydroxybenzoyl)ethenyl]piperidine (5): pale yellow needles (from AcOEt-hexane), mp 125-

126 °C (lit.,[9] 128 °C); IR (KBr) 3432, 1622, 1537, 1487 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.70 (6H, m, CH_2), 3.42 (4H, m, CH_2), 5.88 (1H, d, *J* = 12.2 Hz, CH=CH), 6.81 (1H, ddd, *J* = 7.9, 7.0, 1.2 Hz, H-5'), 6.93 (1H, dd, *J* = 8.2, 1.2 Hz, H-3'), 7.34 (1H, ddd, *J* = 8.2, 7.0, 1.5 Hz, H-4'), 7.67 (1H, dd, *J* = 7.9, 1.5 Hz, H-6'), 7.87 (1H, d, *J* = 12.2 Hz, CH=CH), 14.00 (1H, s, OH); MS m/z 231 (M^+).

3-Iodo-2-piperidino-4*H*-1-benzopyran-4-one (6): colorless prism (from Et_2O-hexane), mp 146-147 °C; IR (KBr) 1615, 1591, 1547, 1460, 1447 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.65-1.80 (6H, m, CH_2), 3.62 (4H, t, *J* = 5.5 Hz, CH_2), 7.33 (1H, dd, *J* = 8.2, 0.9 Hz, H-8), 7.35 (1H, ddd, *J* = 7.9, 7.3, 0.9 Hz, H-6), 7.59 (1H, ddd, *J* = 8.2, 7.3, 1.5 Hz, H-7), 8.19 (1H, dd, *J* = 7.9, 1.5 Hz, H-5); ^{13}C-NMR ($CDCl_3$) δ 24.07, 25.69, 50.39, 67.26, 116.24, 120.10, 125.08, 126.59, 132.82, 153.43, 163.26, 175.13; High-resolution MS *m/z* Calcd for $C_{14}H_{14}NO_2I$ (M^+): 355.0069, Found: 355.0065.

3-Piperidino-4*H*-1-benzopyran-4-one (2a): colorless needles (from AcOEt-hexane), mp 131-132 °C (lit.,[7d] 130-132 °C); ^{1}H-NMR ($CDCl_3$) δ 1.58 (2H, quint, *J* = 5.5 Hz, CH_2), 1.77 (4H, quint, *J* = 5.5 Hz, CH_2), 2.99 (4H, t, *J* = 5.5 Hz, CH_2), 7.34 (1H, ddd, *J* = 8.2, 7.3, 0.9 Hz, H-6), 7.40 (1H, dd, *J* = 8.5, 0.9 Hz, H-8), 7.55 (1H, s, H-2), 7.61 (1H, ddd, *J* = 8.5, 7.3, 1.5 Hz, H-7), 8.26 (1H, dd, *J* = 8.2, 1.5 Hz, H-5).

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